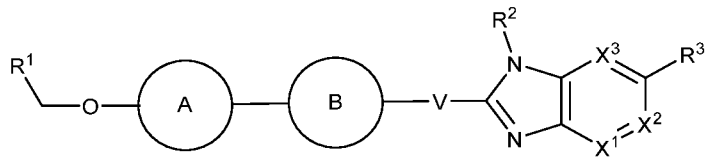
WHAT IS CLAIMED IS:

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



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is

i) 5-membered heteroaryl, optionally substituted with one to four R^4;

ii) 5-membered heteroaryl fused to a heteroaryl or aryl to form a heteroaryl ring system, wherein the heteroaryl ring system is optionally substituted with one to four R^4;

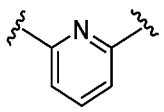
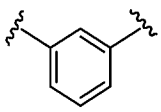
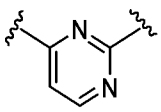
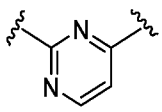
iii) 5-membered heteroaryl substituted with two R^4 groups attached to adjacent ring atoms and optionally substituted with one or two additional R^4, wherein the two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6;

iv) 6-membered heteroaryl or phenyl substituted with C_2-alkynyl, wherein the 6-membered heteroaryl or phenyl is optionally substituted with one to three R^4, wherein the C_2-alkynyl is substituted with $-C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl, wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5;

v) 6-membered heteroaryl or phenyl substituted with $-C(O)NR^aR^b$, wherein the heteroaryl or phenyl is optionally substituted with one to four R^4; or

vi) 6-membered heteroaryl or phenyl, wherein the 6-membered heteroaryl or phenyl is substituted with heteroaryl, C_{3-10} cycloalkyl, or heterocycle and optionally substituted with one to three R^4, wherein the heteroaryl, C_{3-10} cycloalkyl, or heterocycle is each substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl, wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6;

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

ring A is , , , or , each optionally substituted with one to three Z^{1a} groups, each independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, -OH, or -CN;

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

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

R^2 is H, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or heterocyclyl, wherein the alkyl, alkynyl, cycloalkyl, or heterocyclyl is each optionally substituted with one to four Z^1, wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkoxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -OH, -CN, C_{1-6} alkyl-CN, -O-C_{3-6} cycloalkyl, heterocyclyl, C_{3-10} cycloalkyl, or heteroaryl optionally substituted with 1 to 4 groups each independently C_{1-6} alkyl, C_{1-6} alkoxy, halogen, -CN, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

R^3 is -C(O)OR^{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-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^{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})$_2$, -OCH_2P(O)(OR^{9c})$_2$, C(O)OCH_2P(O)(OR^{9c})$_2$, -P(O)(R^{9c})(OR^{9d}), -OP(O)(R^{9c})(OR^{9d}), -CH_2P(O)(R^{9c})(OR^{9d}), -OCH_2P(O)(R^{9c})(OR^{9d}), -C(O)OCH_2P(O)(R^{9c})(OR^{9d}), -P(O)(N(R^{9c})$_2$)$_2$, -OP(O)(N(R^{9c})$_2$)$_2$, -CH_2P(O)(N(R^{9c})$_2$)$_2$, -OCH_2P(O)(N(R^{9c})$_2$)$_2$, -C(O)OCH_2P(O)(N(R^{9c})$_2$)$_2$, -P(O)(N(R^{9c})$_2$)(OR^{9d}), -OP(O)(N(R^{9c})$_2$)(OR^{9d}), -CH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -OCH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -C(O)OCH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -P(O)(R^{9c})(N(R^{9d})$_2$), -OP(O)(R^{9c})(N(R^{9d})$_2$), -CH_2P(O)(R^{9c})(N(R^{9d})$_2$), -OCH_2P(O)(R^{9c})(N(R^{9d})$_2$), -C(O)OCH_2P(O)(R^{9c})(N(R^{9d})$_2$), or C_{1-6} alkyl-heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens;

each R^4 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, -OR^{10a}, -C(O)R^{10a}, -C(O)O-R^{10a}, -C(O)-

$N(R^{10a})(R^{10b})$, $-N(R^{10a})(R^{10b})$, $-N(R^{10a})_2(R^{10b})^+$, $-N(R^{10a})C(O)-R^{10b}$, $-N(R^{10a})C(O)OR^{10b}$, $-N(R^{10a})C(O)N(R^{10b})(R^{10c})$, $-N(R^{10a})S(O)_2(R^{10b})$, $-NR^{10a}S(O)_2N(R^{10b})(R^{10c})$, $-NR^{10a}S(O)_2O(R^{10b})$, $-OC(O)R^{10a}$, $-OC(O)OR^{10a}$, $-OC(O)-N(R^{10a})(R^{10b})$, $-S-R^{10a}$, $-S(O)R^{10a}$, $-S(O)(NH)R^{10a}$, $-S(O)_2R^{10a}$, $-S(O)_2N(R^{10a})(R^{10b})$, $-S(O)(NR^{10a})R^{10b}$, or $-Si(R^{10a})_3$;

wherein each alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one to four R^5;

each R^5 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, C_{3-15} cycloalkyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-N_3$, -CN, -O- R^{10a}, $-C(O)-R^{10a}$, $-C(O)OR^{10a}$, $-C(O)N(R^{10a})(R^{10b})$, $-N(R^{10a})(R^{10b})$, $-N(R^{10a})C(O)R^{10b}$, $-N(R^{10a})C(O)OR^{10b}$, $-N(R^{10a})C(O)N(R^{10b})(R^{10c})$, $-N(R^{10a})S(O)_2(R^{10b})$, $-NR^{10a}S(O)_2N(R^{10b})(R^{10c})$, $-NR^{10a}S(O)_2O(R^{10b})$, $-OC(O)R^{10a}$, $-OC(O)OR^{10a}$, $-OC(O)-N(R^{10a})(R^{10b})$, $-S-R^{10a}$, $-S(O)R^{10a}$, $-S(O)(NH)R^{10a}$, $-S(O)_2R^{10a}$, $-S(O)_2N(R^{10a})(R^{10b})$, $-S(O)(NR^{10a})R^{10b}$, or $-Si(R^{10a})_3$,

wherein each alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one to four R^6;

each R^6 and 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, $-NO_2$, $-NH_2$, $-N_3$, -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 each alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1 to 3 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)$_2$,

wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens;

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, 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^{6c1}, or -$N(R^{6c2})(R^{6c3})$,

wherein the alkyl, cycloalkyl, or heterocyclyl is each optionally substituted with one to four R^{6b1}; or

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

R^{6a} or R^{6c} 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};

each 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;

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

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 R^{9c}, R^{9d}, R^{10a}, R^{10b}, and R^{10c} 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 R^6;

R^a and R^b are 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 R^6;

optionally R^a and R^b are combined with the atom to which they are attached to form a 5- or 6-membered heterocyclyl, which is optionally substituted with one to four R^6;

each R^{2a}, R^{2b}, 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 R^6;

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, -$P(O)(OR^{9c})_2$, -$CH2P(O)(OR^{9c})_2$, -$OCH_2P(O)(OR^{9c})_2$, -$C(O)OCH_2P(O)(OR^{9c})_2$, -$P(O)(R^{9c})(OR^{9d})$, -$OP(O)(R^{9c})(OR^{9d})$, -$CH_2P(O)(R^{9c})(OR^{9d})$, -$C(O)OCH_2P(O)(R^{9c})(OR^{9d})$, -$P(O)(N(R^{9c})_2)_2$, -$CH_2P(O)(N(R^{9c})_2)_2$, -$C(O)OCH_2P(O)(N(R^{9c})_2)_2$, -$P(O)(N(R^{9c})_2)(OR^{9d})$, -$CH_2P(O)(N(R^{9c})_2)(OR^{9d})$, -$C(O)OCH_2P(O)(N(R^{9c})_2)(OR^{9d})$, -$P(O)(R^{9c})(N(R^{9d})_2)$, -$CH_2P(O)(R^{9c})(N(R^{9d})_2)$, or -$C(O)OCH_2P(O)(R^{9c})(N(R^{9d})_2)$;

wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four R^6; 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 three to twelve ring members and has one to four heteroatoms, each independently N, O, or S; and

wherein each heteroaryl has five to twelve ring members and one to four heteroatoms, each independently N, O, or S.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is

i) 5-membered heteroaryl, optionally substituted with one to four R^4;

ii) 5-membered heteroaryl fused to a heteroaryl or aryl to form a heteroaryl ring system, wherein the heteroaryl ring system is optionally substituted with one to four R^4; or

iii) 5-membered heteroaryl substituted with two R^4 groups attached to adjacent ring atoms and optionally substituted with one or two additional R^4,

wherein the 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 R^6.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein

R^1 is

pyrrolyl, pyrazolyl, thienyl, indolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, furyl, oxadiazolyl, thiadiazolyl, benzothiazolyl, benzoxazolyl, indazolyl, benzofuranyl, benzimidazolyl, pyrrolo[2,3-*b*]pyridinyl, triazolyl, tetrazolyl, thiazolo[5,4-*b*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrazinyl, or $1\lambda^2$-thieno[3,2-*d*]pyrazolyl, optionally substituted with one to four R^4; or

5-membered heteroaryl substituted with two to four R^4,

wherein two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-6} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein

R^1 is

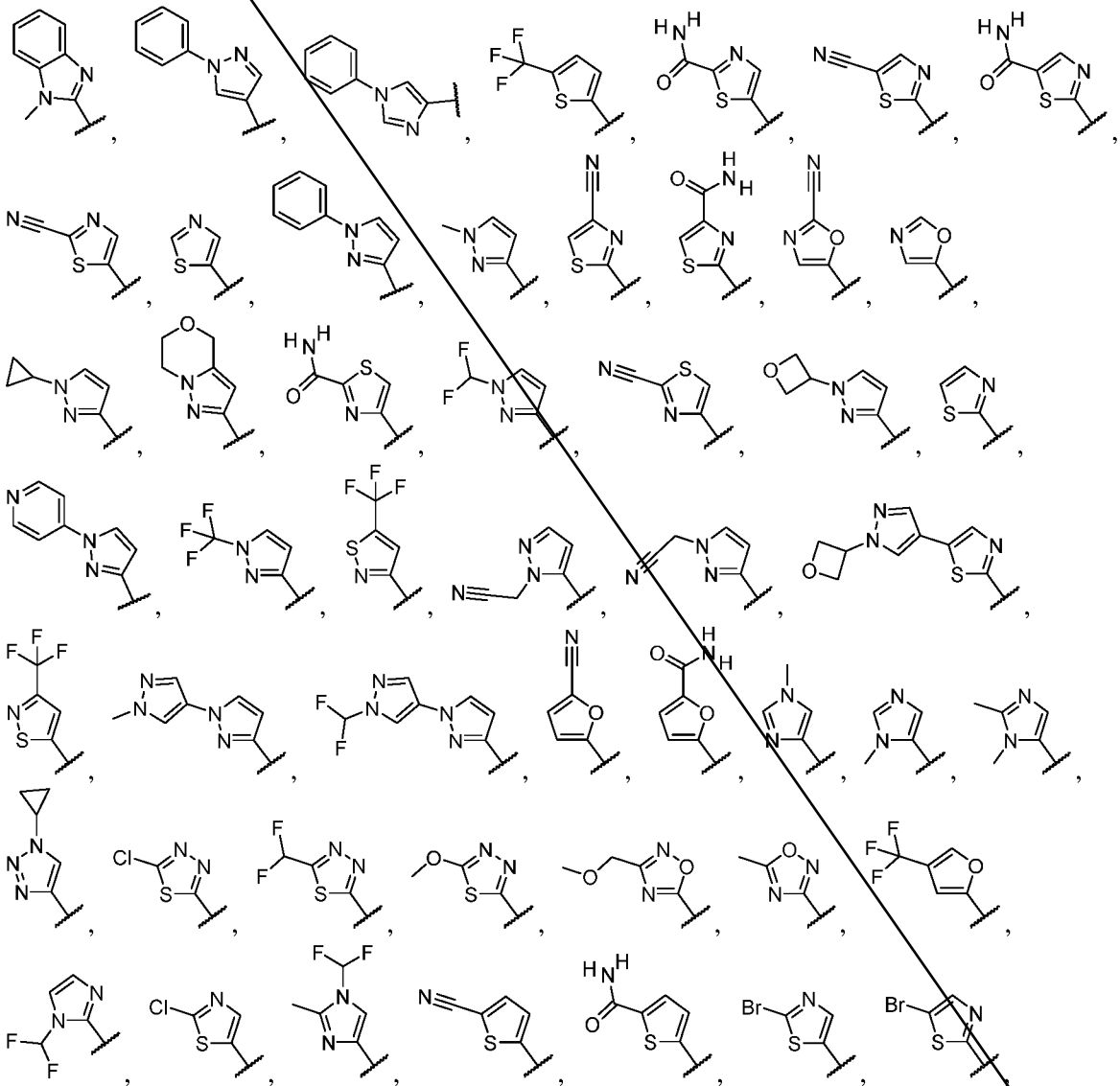
pyrazolyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, furyl, oxadiazolyl, thiadiazolyl, benzimidazolyl, triazolyl, thiazolo[5,4-*b*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrazinyl, or $1\lambda^2$-thieno[3,2-*d*]pyrazolyl, optionally substituted with one to four R^4; or

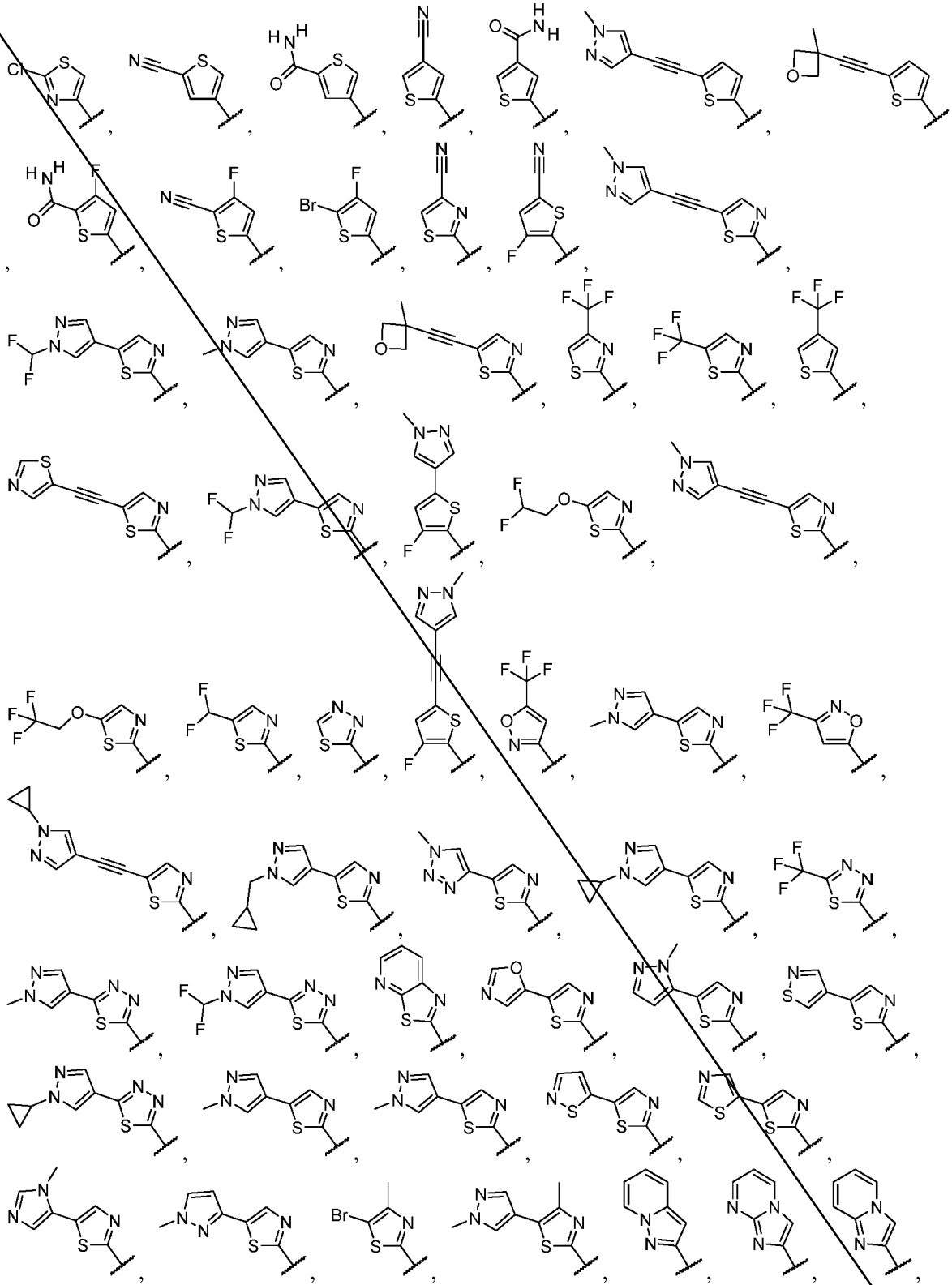
pyrazolyl substituted with two to four R^4,

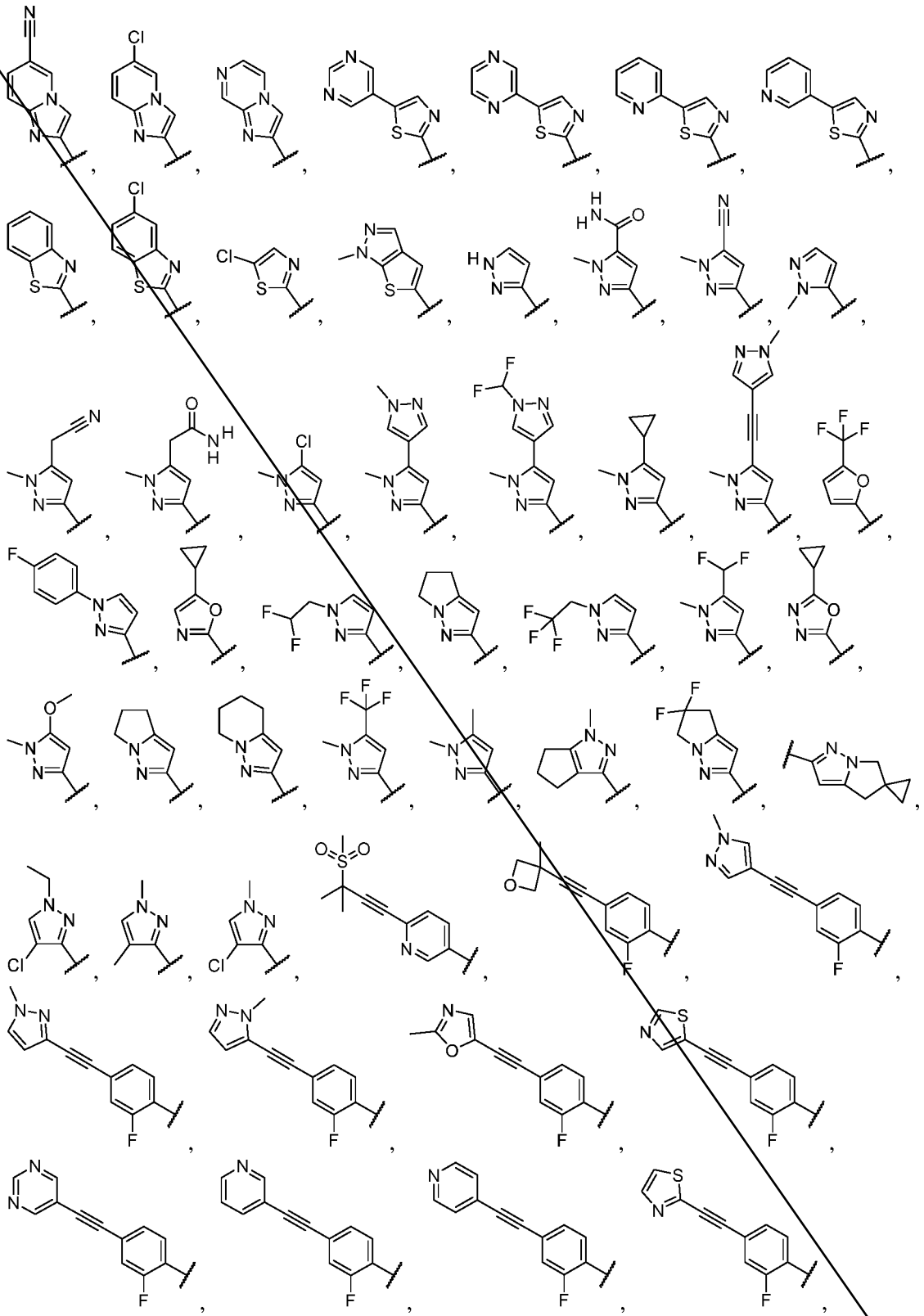
wherein two R^4 groups attached to adjacent pyrazolyl atoms are combined with the atoms to which they are attached to form a C_{5-6} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6.

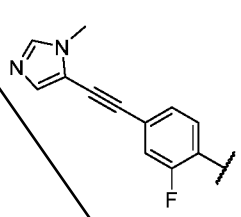
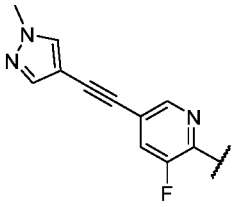
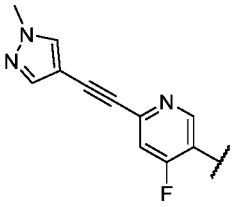
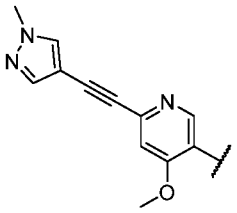
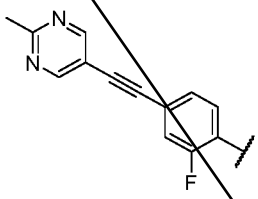
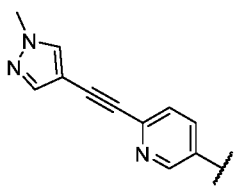
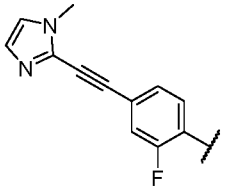
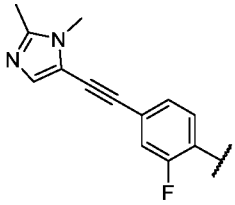
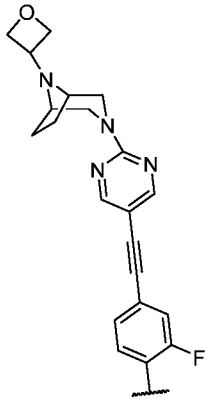
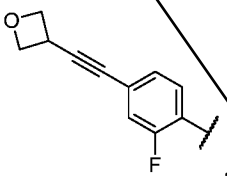
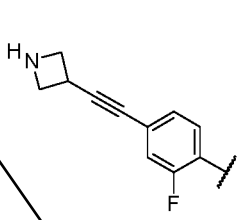
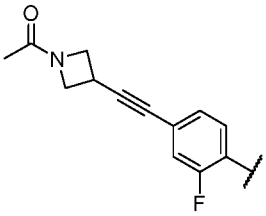
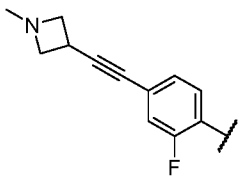
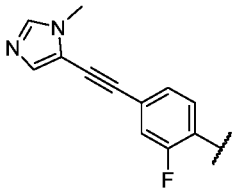
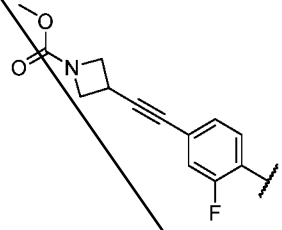
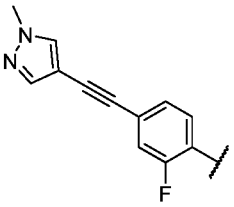
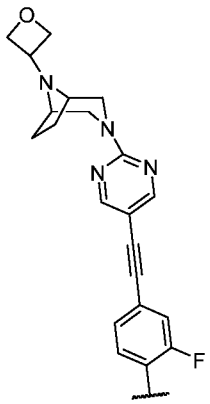
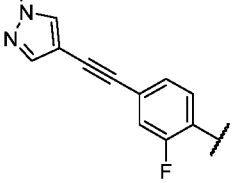
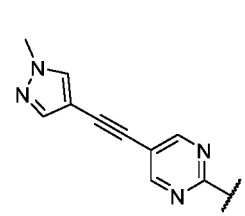
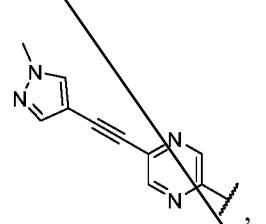
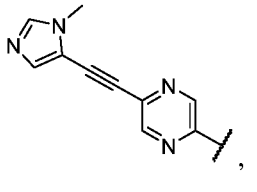
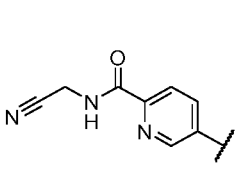
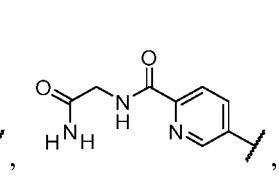
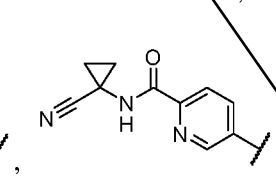
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein

R^1 is







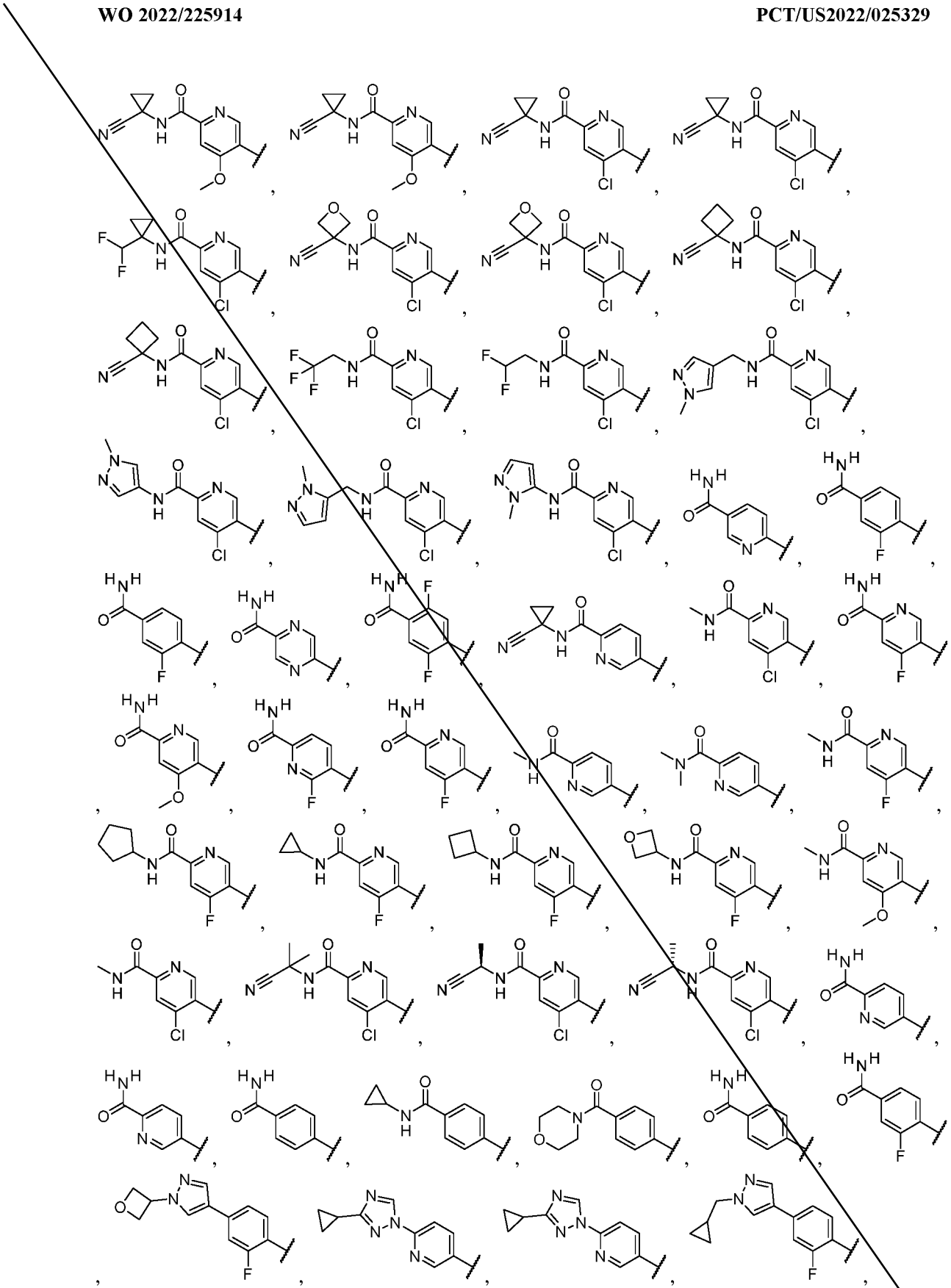

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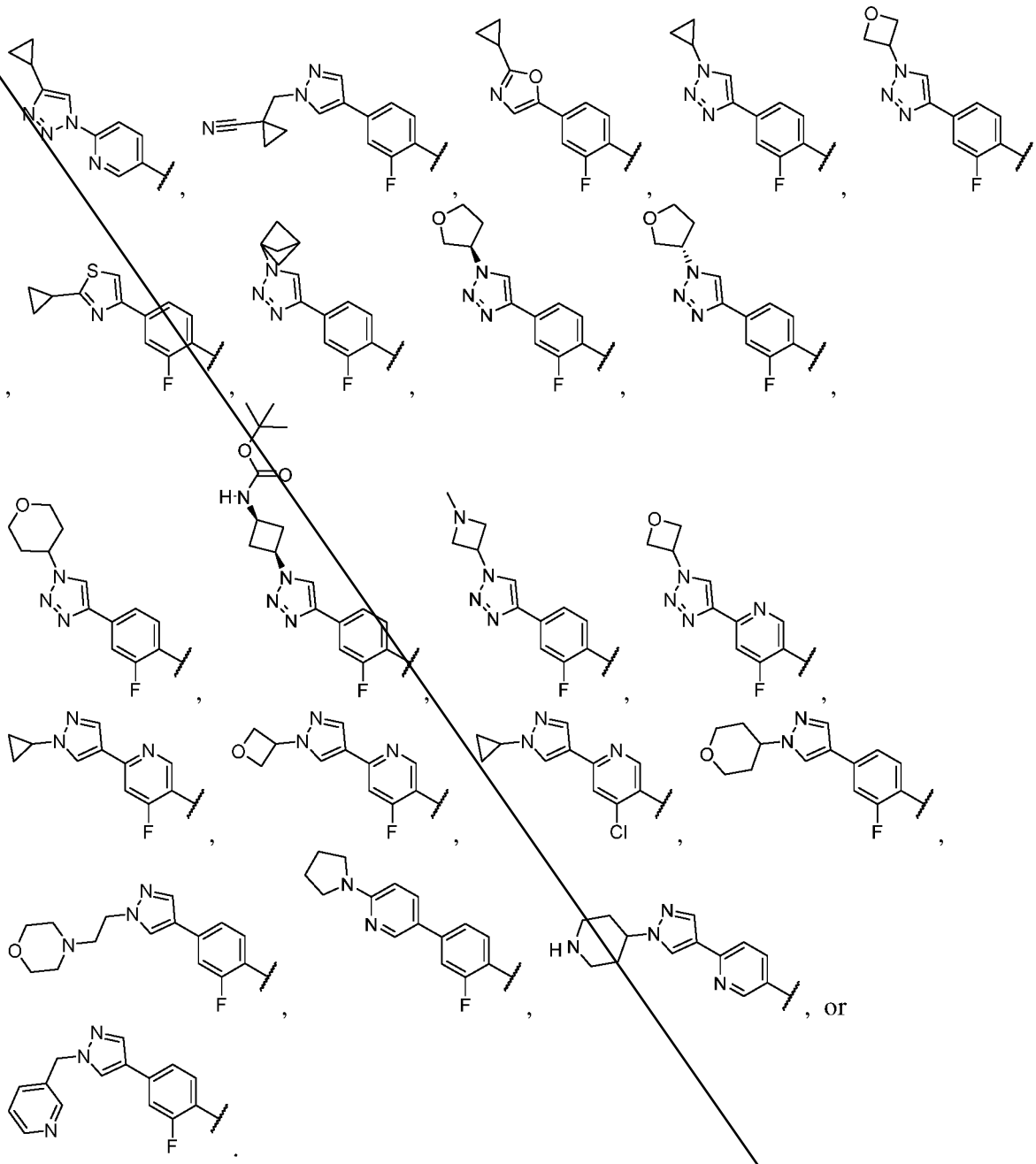
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6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is 6-membered heteroaryl or phenyl substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one, or phenyl, substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

8. The compound of claim 6 or 7, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, or phenyl, substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

9. The compound of any one of claims 6-8, or a pharmaceutically acceptable salt thereof, wherein

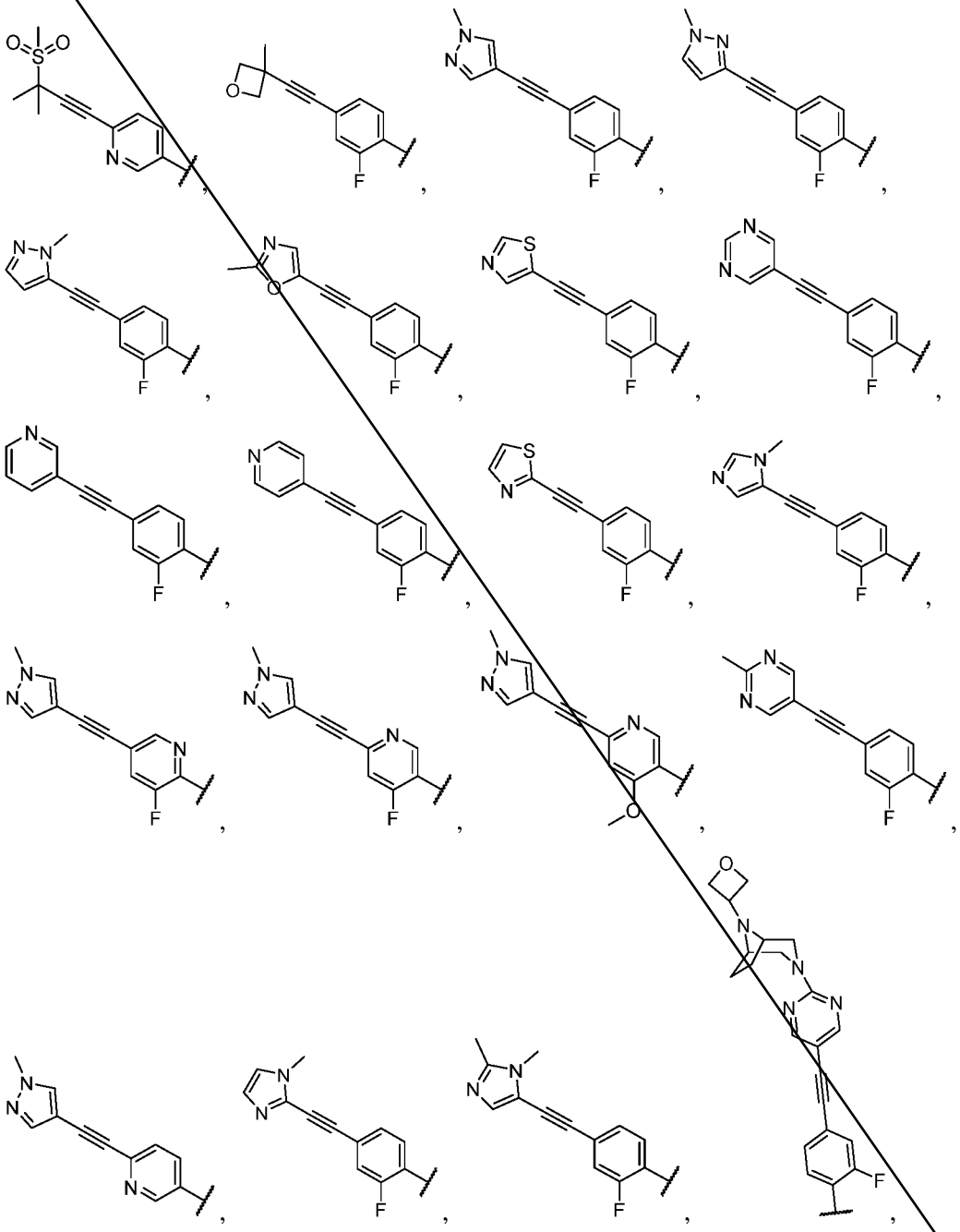
R^1 is pyridyl, pyrazinyl, pyrimidinyl, or phenyl, substituted with C_2-alkynyl and optionally substituted with one R^4,

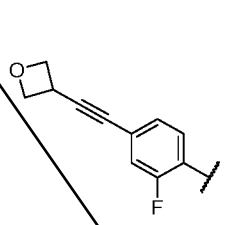
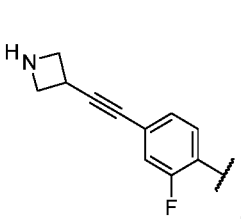
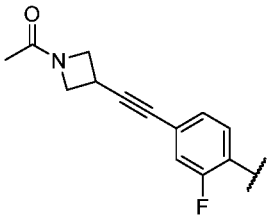
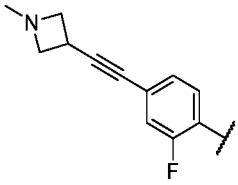
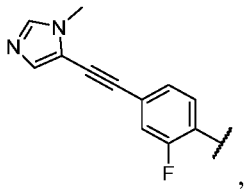
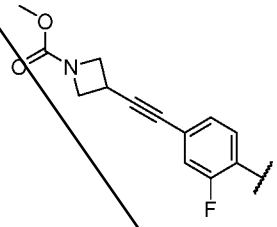
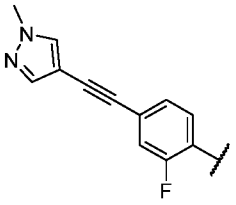
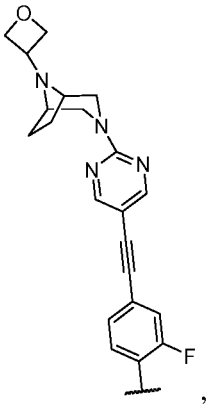
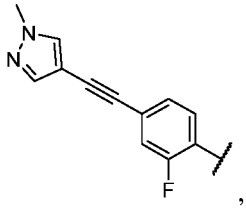
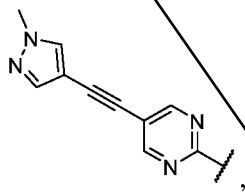
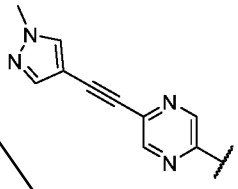
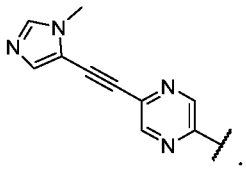
wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

10. The compound of any one of claims 1 and 6-9, or a pharmaceutically acceptable salt thereof, wherein

R^1 is




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11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is 6-membered heteroaryl or phenyl substituted with $–C(O)NR^aR^b$,

wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein R^1 is

pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one; or

phenyl substituted with $–C(O)NR^aR^b$, wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

13. The compound of claim 11 or 12, or a pharmaceutically acceptable salt thereof, wherein R^1 is

pyridyl, pyrazinyl, or phenyl substituted with –C(O)NR^{a}R^b,

wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

14. The compound of any one of claims 11-13, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, or phenyl substituted with –C(O)NR^{a}R^b,

wherein the pyridyl, pyrazinyl, or phenyl is optionally substituted with one R^4.

15. The compound of any one of claims 11-14, or a pharmaceutically acceptable salt thereof, wherein

R^a and R^b are independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} 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 R^6; or

optionally R^a and R^b are combined with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocyclyl, wherein the heterocyclyl is optionally substituted with one to four R^6.

16. The compound of any one of claims 11-15, or a pharmaceutically acceptable salt thereof, wherein

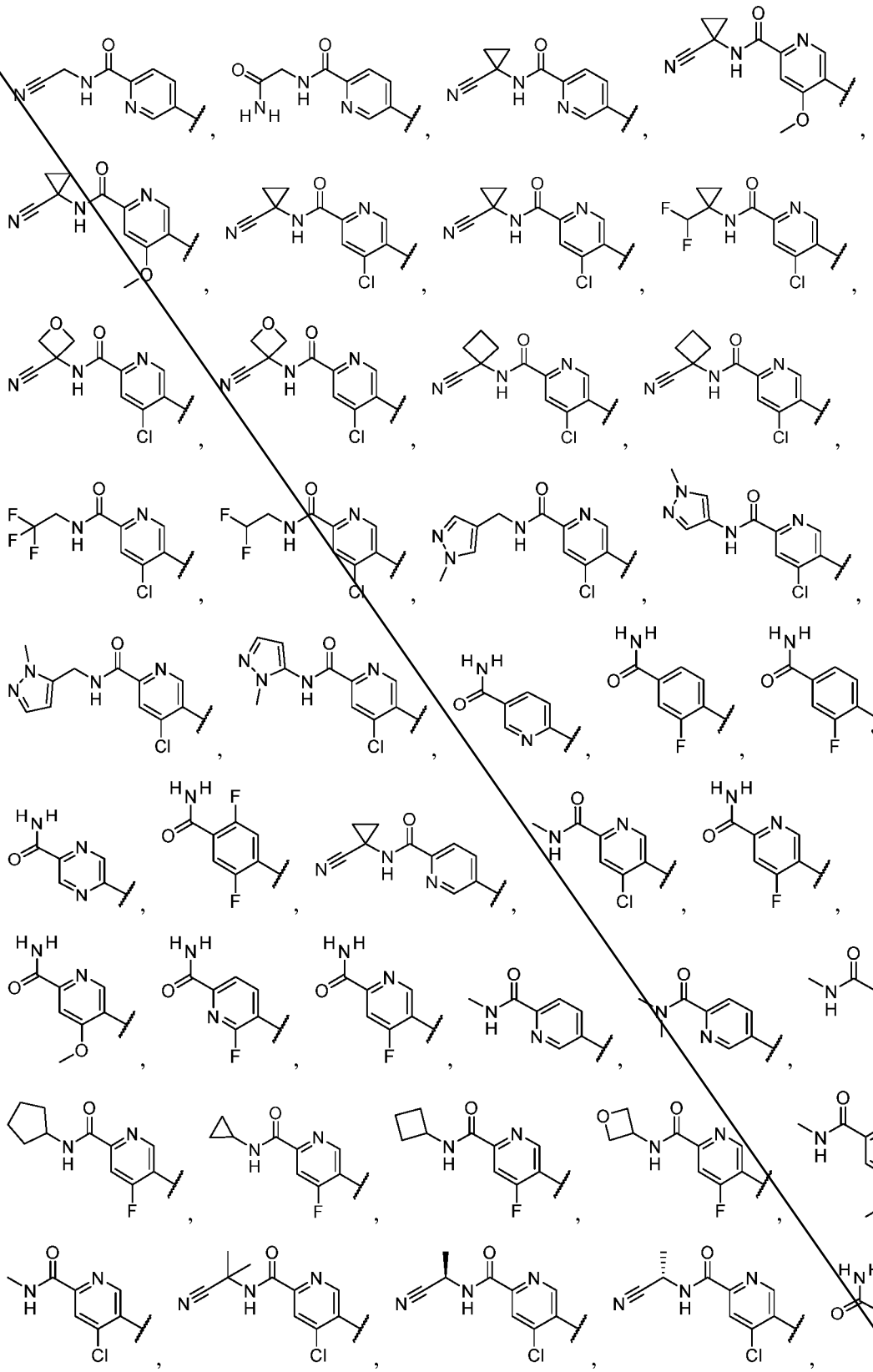
R^a and R^b are independently H, C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocyclyl, or heteroaryl wherein the alkyl, cycloalkyl, heterocyclyl, or heteroaryl is each optionally substituted with one to four R^6; or

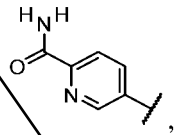
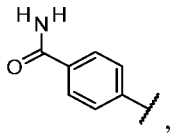
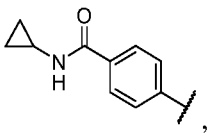
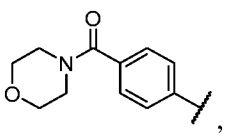
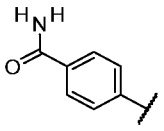
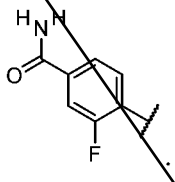
optionally R^a and R^b are combined with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocyclyl,

wherein the heterocyclyl is optionally substituted with one to four R^6.

17. The compound of any one of claims 1 and 11-16, or a pharmaceutically acceptable salt thereof, wherein

R^1 is:



, , , , , or .

18. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is 6-membered heteroaryl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

19. The compound of claim 18 or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one, or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

20. The compound of claim 18 or 19, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

21. The compound of any one of claims 18-20, or a pharmaceutically acceptable salt thereof, wherein

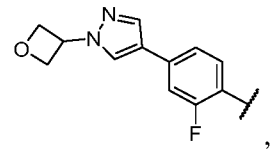
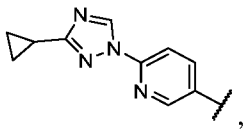
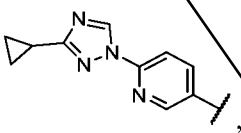
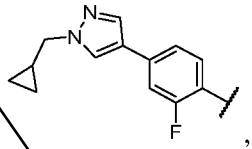
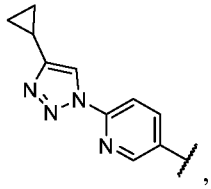
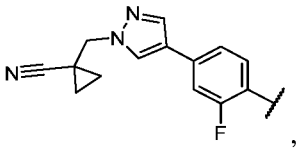
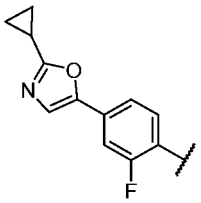
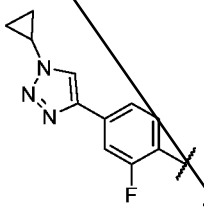
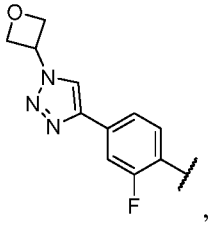
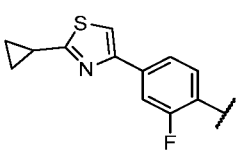
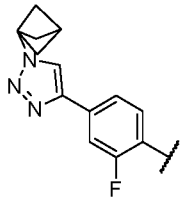
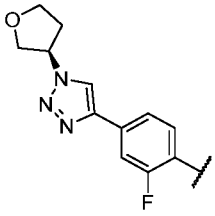
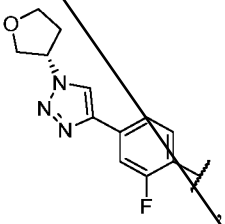
R^1 is pyridyl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

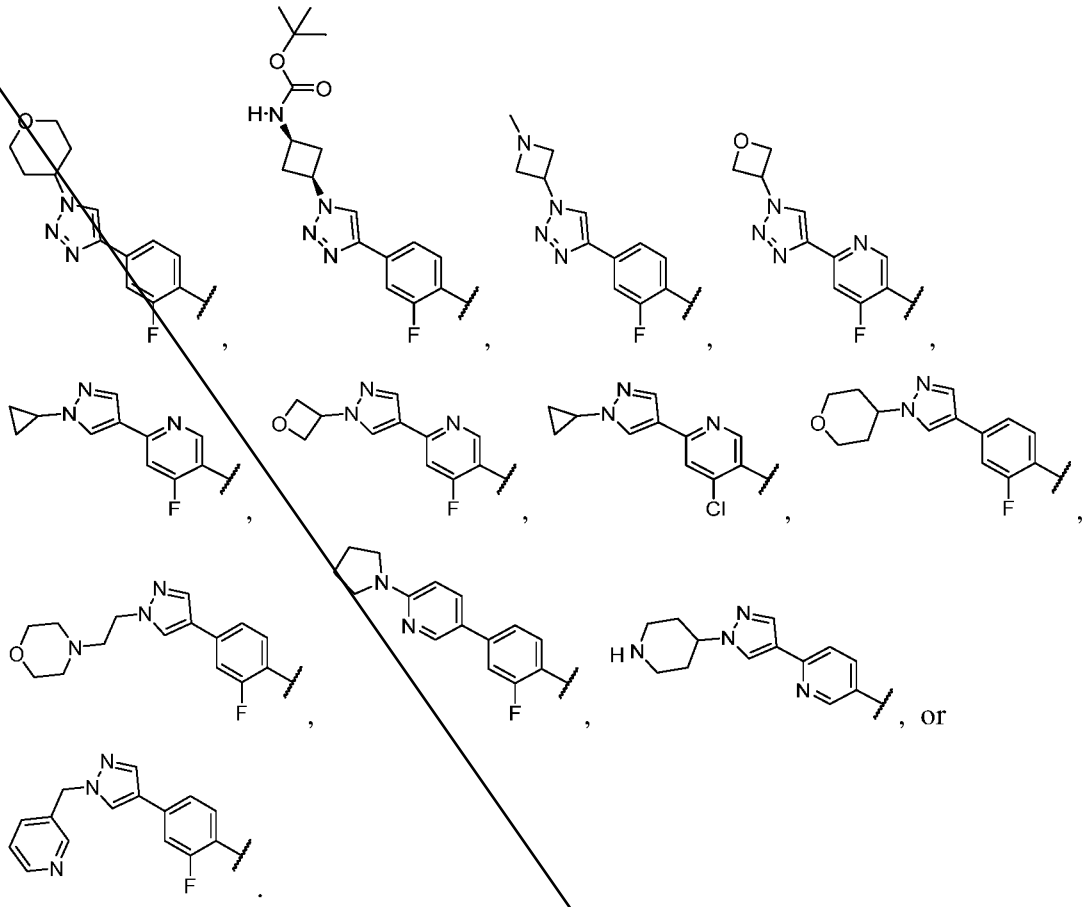
wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

22. The compound of any one of claims 1 and 18-21, or a pharmaceutically acceptable salt thereof, wherein

R^1 is:


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,

,

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,

,

,

,

,

,



23. The compound of claim any one of claims 1-22, or a pharmaceutically acceptable salt thereof, wherein

ring B is C_{6-10} aryl, optionally substituted with one to four R^4.

24. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is independently C_{1-9} alkyl or halogen.

25. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is independently methyl or F.

26. The compound of any one of claims 1-25, or a pharmaceutically acceptable salt thereof, wherein

ring B is substituted with two R^4.

27. The compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is F.

28. The compound of claim any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein

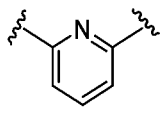
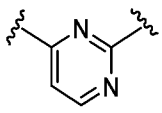
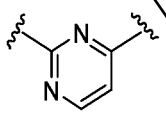
V is $–C(R^{6b})(R^{6c})–$.

29. The compound of claim any one of claims 1-28, or a pharmaceutically acceptable salt thereof, wherein

V is $–CH_2–$.

30. The compound of claim any one of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein

ring A is


, 
, or 
, each optionally substituted with one halogen.

31. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, wherein

two of X^1, X^2, and X^3 is –CH= and one is –C(F)=.

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

R^2 is C_{1-6} alkyl or heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four Z^1,

wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkoxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -OH, -CN, C_{1-6} alkyl-CN, -O-C_{3-6} cycloalkyl, heterocyclyl, or heteroaryl optionally substituted with 1 to 4

groups each independently C_{1-6} alkyl, C_{1-6} alkoxy, halogen, -CN, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy.

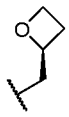
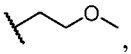
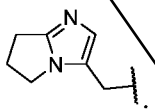
33. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl or heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four Z^1,

wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, or heterocyclyl.

34. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt thereof, wherein

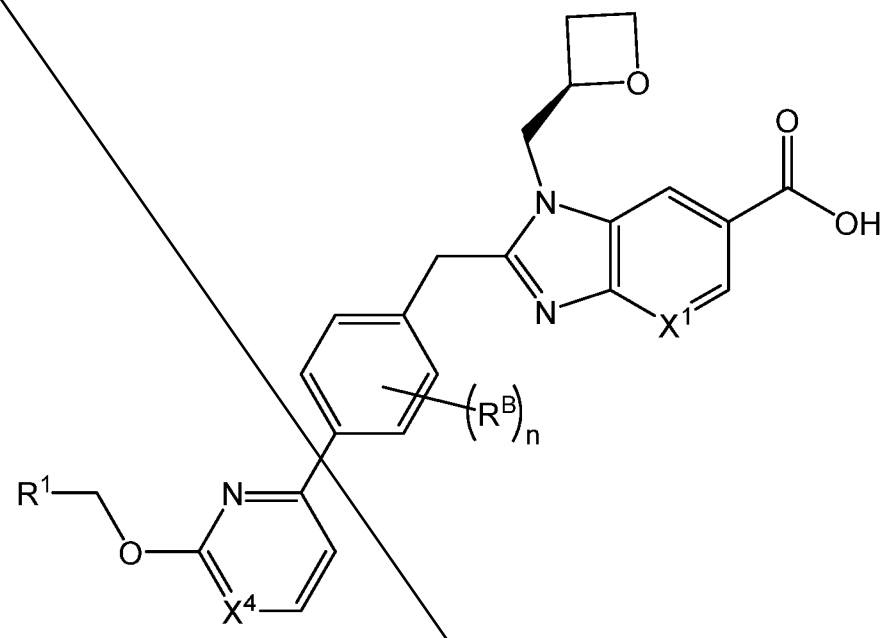
R^2 is


, 
, or 
.

35. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, wherein

R^3 is –C(O)OH.

36. A compound of Formula (II)



(II)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is thiazolyl optionally substituted with R^4;

X^1 is –C(H)= or –C(R^8)=;

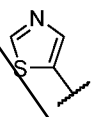
X^4 is -CH=, –C(R^8)= or N;

each R^B is independently C_{1-9} alkyl, C_{1-8} haloalkyl, or halogen;

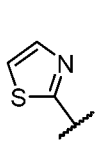
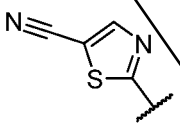
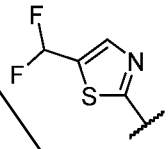
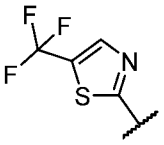
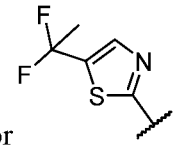
each R^8 is independently halogen; and

n is 0, 1, 2, or 3.

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

R^1 is  or , which is each substituted with $C_{1\text{-}8}$ haloalkyl.

38. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^1 is

, , , , or .

39. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^8 is F or Cl.

40. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, having the structure of a compound in Table 2.

41. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

42. The pharmaceutical composition of claim 41 further comprising one or more additional therapeutic agents.

43. The pharmaceutical composition of claim 41 for use in treating a glucagon-like peptide 1 receptor (GLP-1R) mediated disease or condition.

44. 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 1-40, or a pharmaceutically acceptable salt thereof.

45. The method of claim 44, wherein the disease or condition comprises a liver disease.

46. The method of claim 45, 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).

47. The method of claim 46, wherein the disease or condition comprises non-alcoholic fatty liver disease (NAFLD).

48. The method of claim 46, wherein the disease or condition comprises non-alcoholic steatohepatitis (NASH).

49. The method of claim 44, wherein the disease or condition comprises a metabolic disease.

50. The method of claim 44, 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.

51. The method of any one of claims 44 to 50, wherein the compound or pharmaceutically acceptable salt thereof is administered in combination with an additional therapeutic agent.

52. The pharmaceutical composition of claim 42 or the method of claim 51, 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 farnesoid 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.

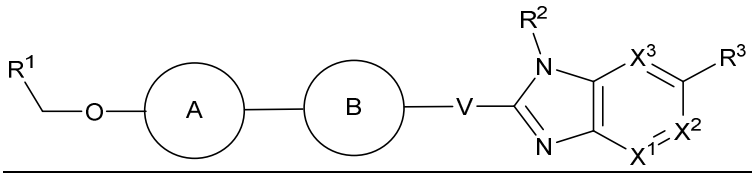
53. A method for manufacturing a medicament for treating a GLP-1R mediated disease or condition in a human in need thereof, characterized in that a compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, is used.

54. Use of the compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a GLP-1R mediated disease or condition.

55. The compound of any one of claims 1-40 or a pharmaceutically acceptable salt thereof, for use in treating a GLP-1R mediated disease or condition in a human in need thereof.

WHAT IS CLAIMED IS:

1~~.~~ A compound of Formula (**I**):



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is

i) 5-membered heteroaryl, optionally substituted with one to four R^4;

ii) 5-membered heteroaryl fused to a heteroaryl or aryl to form a heteroaryl ring system, wherein the heteroaryl ring system is optionally substituted with one to four R^4;

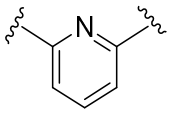
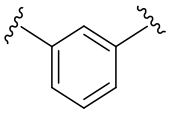
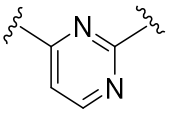
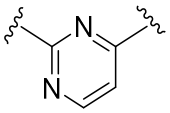
iii) 5-membered heteroaryl substituted with two R^4 groups attached to adjacent ring atoms and optionally substituted with one or two additional R^4, wherein the two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a $C_{5\text{-}10}$ cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6;

iv) 6-membered heteroaryl or phenyl substituted with C_2-alkynyl, wherein the 6-membered heteroaryl or phenyl is optionally substituted with one to three R^4, wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl, wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5;

v) 6-membered heteroaryl or phenyl substituted with $–C(O)NR^aR^b$, wherein the heteroaryl or phenyl is optionally substituted with one to four R^4; or

vi) 6-membered heteroaryl or phenyl, wherein the 6-membered heteroaryl or phenyl is substituted with heteroaryl, $C_{3\text{-}10}$ cycloalkyl, or heterocycle and optionally substituted with one to three R^4, wherein the heteroaryl, $C_{3\text{-}10}$ cycloalkyl, or heterocycle is each substituted with $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, $C_{1\text{-}6}$ alkyl-$C_{3\text{-}10}$ cycloalkyl, $C_{1\text{-}6}$ alkyl-heterocyclyl, or $C_{1\text{-}6}$ alkyl-heteroaryl, wherein the $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, $C_{1\text{-}6}$ alkyl-$C_{3\text{-}10}$ cycloalkyl, $C_{1\text{-}6}$ alkyl-heterocyclyl, or $C_{1\text{-}6}$ alkyl-heteroaryl is optionally substituted with one to four R^6;

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

ring A is , , , or , each optionally substituted with one to three Z^{1a} groups, each independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, -OH, or -CN;

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

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

R^2 is H, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or heterocyclyl, wherein the alkyl, alkynyl, cycloalkyl, or heterocyclyl is each optionally substituted with one to four Z^1, wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkoxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -OH, -CN, C_{1-6} alkyl-CN, -O-C_{3-6} cycloalkyl, heterocyclyl, C_{3-10} cycloalkyl, or heteroaryl optionally substituted with 1 to 4 groups each independently C_{1-6} alkyl, C_{1-6} alkoxy, halogen, -CN, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

R^3 is -C(O)OR^{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-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^{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})$_2$, -OCH_2P(O)(OR^{9c})$_2$, C(O)OCH_2P(O)(OR^{9c})$_2$, -P(O)(R^{9c})(OR^{9d}), -OP(O)(R^{9c})(OR^{9d}), -CH_2P(O)(R^{9c})(OR^{9d}), -OCH_2P(O)(R^{9c})(OR^{9d}), -C(O)OCH_2P(O)(R^{9c})(OR^{9d}), -P(O)(N(R^{9c})$_2$)$_2$, -OP(O)(N(R^{9c})$_2$)$_2$, -CH_2P(O)(N(R^{9c})$_2$)$_2$, -OCH_2P(O)(N(R^{9c})$_2$)$_2$, -C(O)OCH_2P(O)(N(R^{9c})$_2$)$_2$, -P(O)(N(R^{9c})$_2$)(OR^{9d}), -OP(O)(N(R^{9c})$_2$)(OR^{9d}), -CH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -OCH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -C(O)OCH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -P(O)(R^{9c})(N(R^{9d})$_2$), -OP(O)(R^{9c})(N(R^{9d})$_2$), -CH_2P(O)(R^{9c})(N(R^{9d})$_2$), -OCH_2P(O)(R^{9c})(N(R^{9d})$_2$), -C(O)OCH_2P(O)(R^{9c})(N(R^{9d})$_2$), or C_{1-6} alkyl-heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens;

each R^4 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, -OR^{10a}, -C(O)R^{10a}, -C(O)O-R^{10a}, -C(O)-

$N(R^{10a})(R^{10b})$, $-N(R^{10a})(R^{10b})$, $-N(R^{10a})_2(R^{10b})^+$, $-N(R^{10a})C(O)-R^{10b}$, $-N(R^{10a})C(O)OR^{10b}$, $-N(R^{10a})C(O)N(R^{10b})(R^{10c})$, $-N(R^{10a})S(O)_2(R^{10b})$, $-NR^{10a}S(O)_2N(R^{10b})(R^{10c})$, $-NR^{10a}S(O)_2O(R^{10b})$, $-OC(O)R^{10a}$, $-OC(O)OR^{10a}$, $-OC(O)-N(R^{10a})(R^{10b})$, $-S-R^{10a}$, $-S(O)R^{10a}$, $-S(O)(NH)R^{10a}$, $-S(O)_2R^{10a}$, $-S(O)_2N(R^{10a})(R^{10b})$, $-S(O)(NR^{10a})R^{10b}$, or $-Si(R^{10a})_3$;

wherein each alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one to four R^5;

each R^5 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, C_{3-15} cycloalkyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, $-N_3$, -CN, -O- R^{10a}, $-C(O)-R^{10a}$, $-C(O)OR^{10a}$, $-C(O)N(R^{10a})(R^{10b})$, $-N(R^{10a})(R^{10b})$, $-N(R^{10a})C(O)R^{10b}$, $-N(R^{10a})C(O)OR^{10b}$, $-N(R^{10a})C(O)N(R^{10b})(R^{10c})$, $-N(R^{10a})S(O)_2(R^{10b})$, $-NR^{10a}S(O)_2N(R^{10b})(R^{10c})$, $-NR^{10a}S(O)_2O(R^{10b})$, $-OC(O)R^{10a}$, $-OC(O)OR^{10a}$, $-OC(O)-N(R^{10a})(R^{10b})$, $-S-R^{10a}$, $-S(O)R^{10a}$, $-S(O)(NH)R^{10a}$, $-S(O)_2R^{10a}$, $-S(O)_2N(R^{10a})(R^{10b})$, $-S(O)(NR^{10a})R^{10b}$, or $-Si(R^{10a})_3$, wherein each alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one to four R^6;

each R^6 and 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, $-NO_2$, $-NH_2$, $-N_3$, -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 each alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1 to 3 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)$_2$,

wherein the alkyl or heterocyclyl is each optionally substituted with one to four halogens;

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, 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^{6c1}, or -$N(R^{6c2})(R^{6c3})$,

wherein the alkyl, cycloalkyl, or heterocyclyl is each optionally substituted with one to four R^{6b1}; or

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

R^{6a} or R^{6c} 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};

each 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;

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

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 R^{9c}, R^{9d}, R^{10a}, R^{10b}, and R^{10c} 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 R^6;

R^a and R^b are 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 R^6;

optionally R^a and R^b are combined with the atom to which they are attached to form a 5- or 6-membered heterocyclyl, which is optionally substituted with one to four R^6;

each R^{2a}, R^{2b}, 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 R^6;

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, -$P(O)(OR^{9c})_2$, -CH2$P(O)(OR^{9c})_2$, -$OCH_2P(O)(OR^{9c})_2$, -$C(O)OCH_2P(O)(OR^{9c})_2$, -$P(O)(R^{9c})(OR^{9d})$, -$OP(O)(R^{9c})(OR^{9d})$, -$CH_2P(O)(R^{9c})(OR^{9d})$, -$C(O)OCH_2P(O)(R^{9c})(OR^{9d})$, -$P(O)(N(R^{9c})_2)_2$, -$CH_2P(O)(N(R^{9c})_2)_2$, -$C(O)OCH_2P(O)(N(R^{9c})_2)_2$, -$P(O)(N(R^{9c})_2)(OR^{9d})$, -$CH_2P(O)(N(R^{9c})_2)(OR^{9d})$, -$C(O)OCH_2P(O)(N(R^{9c})_2)(OR^{9d})$, -$P(O)(R^{9c})(N(R^{9d})_2)$, -$CH_2P(O)(R^{9c})(N(R^{9d})_2)$, or -$C(O)OCH_2P(O)(R^{9c})(N(R^{9d})_2)$;

wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is each optionally substituted with one to four R^6; 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 three to twelve ring members and has one to four heteroatoms, each independently N, O, or S; and

wherein each heteroaryl has five to twelve ring members and one to four heteroatoms, each independently N, O, or S.

22. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is

i) 5-membered heteroaryl, optionally substituted with one to four R^4;

ii) 5-membered heteroaryl fused to a heteroaryl or aryl to form a heteroaryl ring system, wherein the heteroaryl ring system is optionally substituted with one to four R^4; or

iii) 5-membered heteroaryl substituted with two R^4 groups attached to adjacent ring atoms and optionally substituted with one or two additional R^4,

wherein the two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a $C_{5\text{-}10}$ cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6.

33. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein

R^1 is

pyrrolyl, pyrazolyl, thienyl, indolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, furyl, oxadiazolyl, thiadiazolyl, benzothiazolyl, benzoxazolyl, indazolyl, benzofuranyl, benzimidazolyl, pyrrolo[2,3-*b*]pyridinyl, triazolyl, tetrazolyl, thiazolo[5,4-*b*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrazinyl, or $1\lambda^2$-thieno[3,2-*d*]pyrazolyl, optionally substituted with one to four R^4; or

5-membered heteroaryl substituted with two to four R^4,

wherein two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a $C_{5\text{-}6}$ cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6.

44. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein

R^1 is

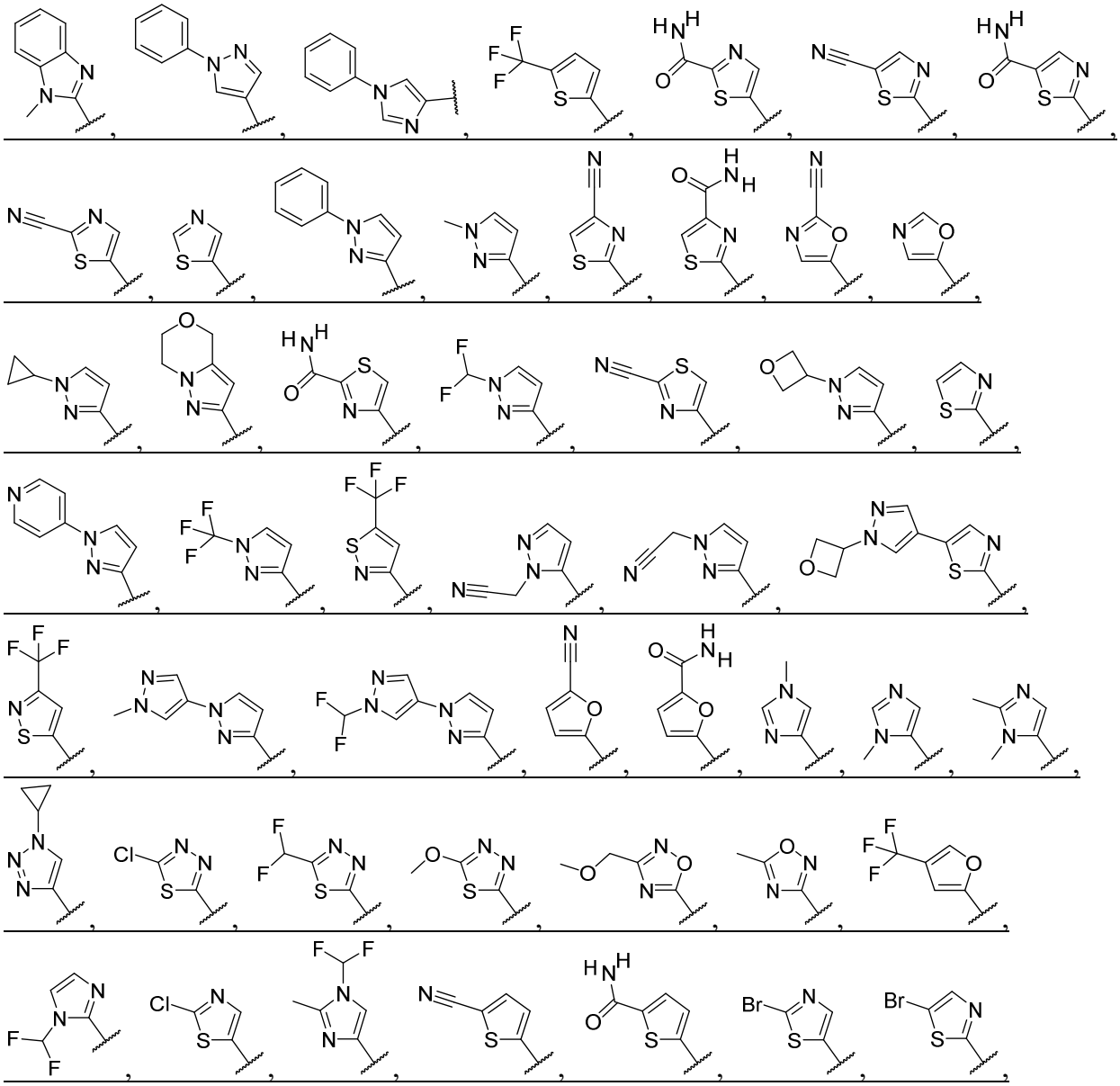
pyrazolyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, furyl, oxadiazolyl, thiadiazolyl, benzimidazolyl, triazolyl, thiazolo[5,4-*b*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrazinyl, or $1\lambda^2$-thieno[3,2-*d*]pyrazolyl, optionally substituted with one to four R^4; or

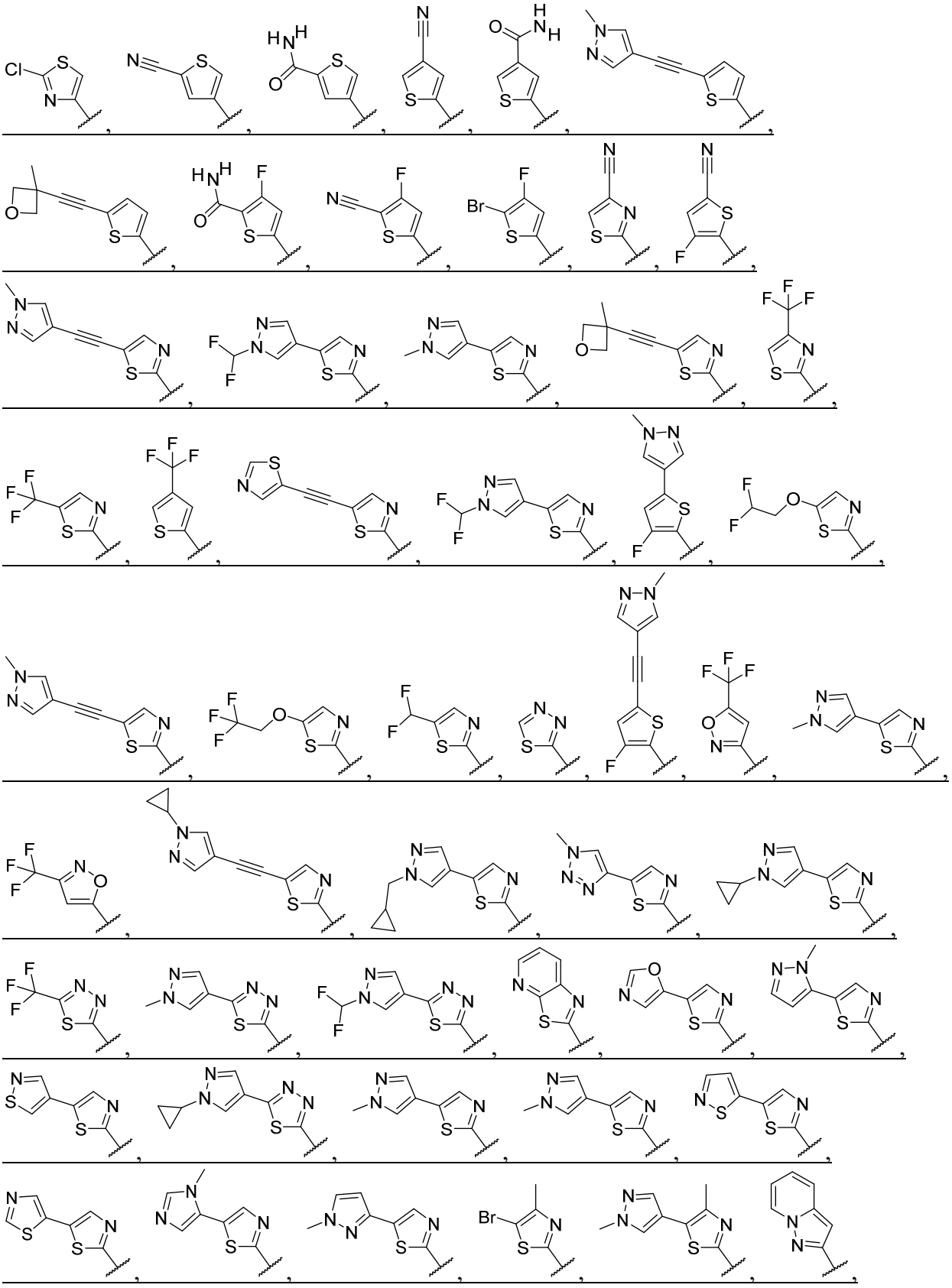
pyrazolyl substituted with two to four R^4,

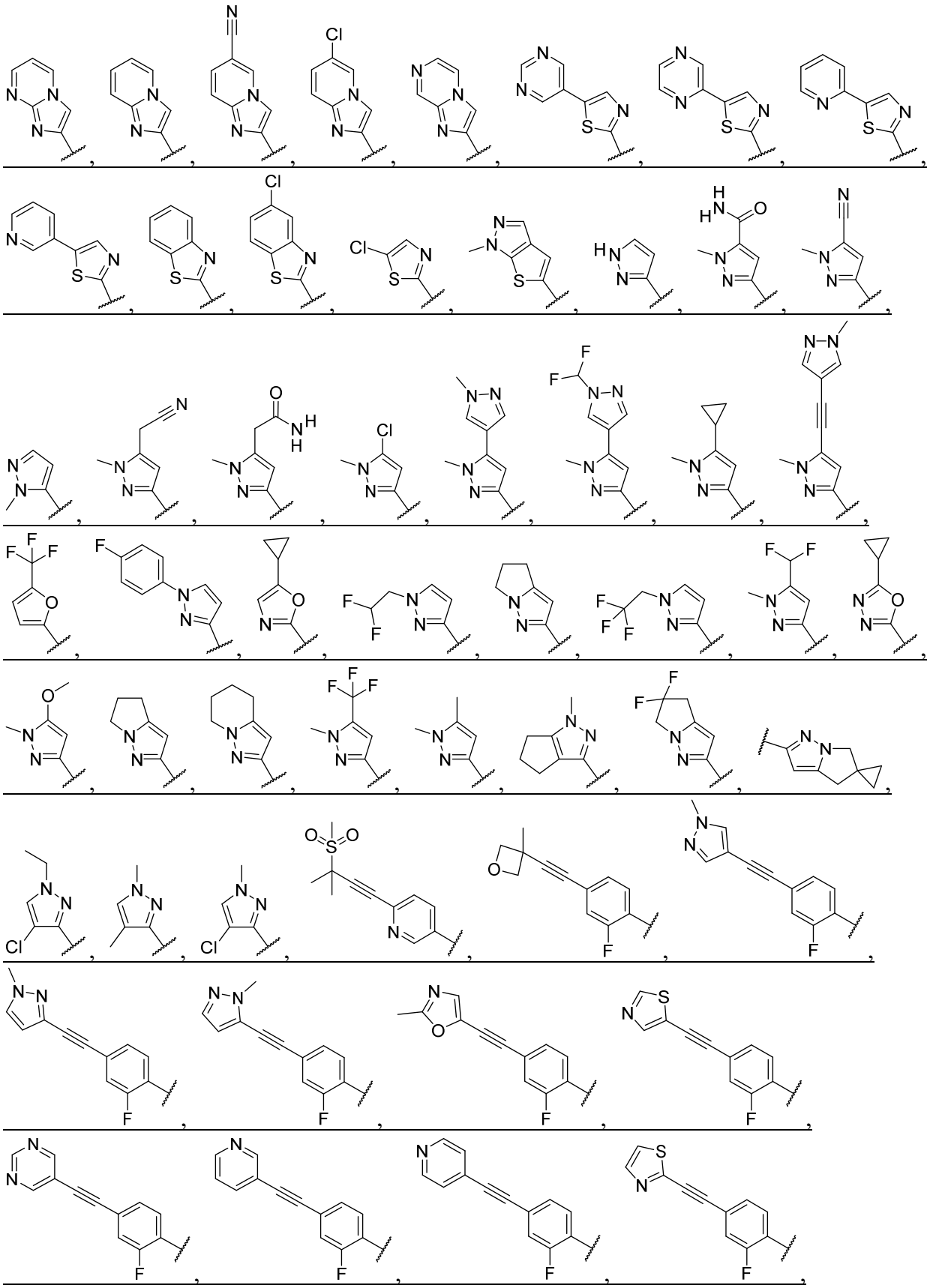
wherein two R^4 groups attached to adjacent pyrazolyl atoms are combined with the atoms to which they are attached to form a C_{5-6} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^6.

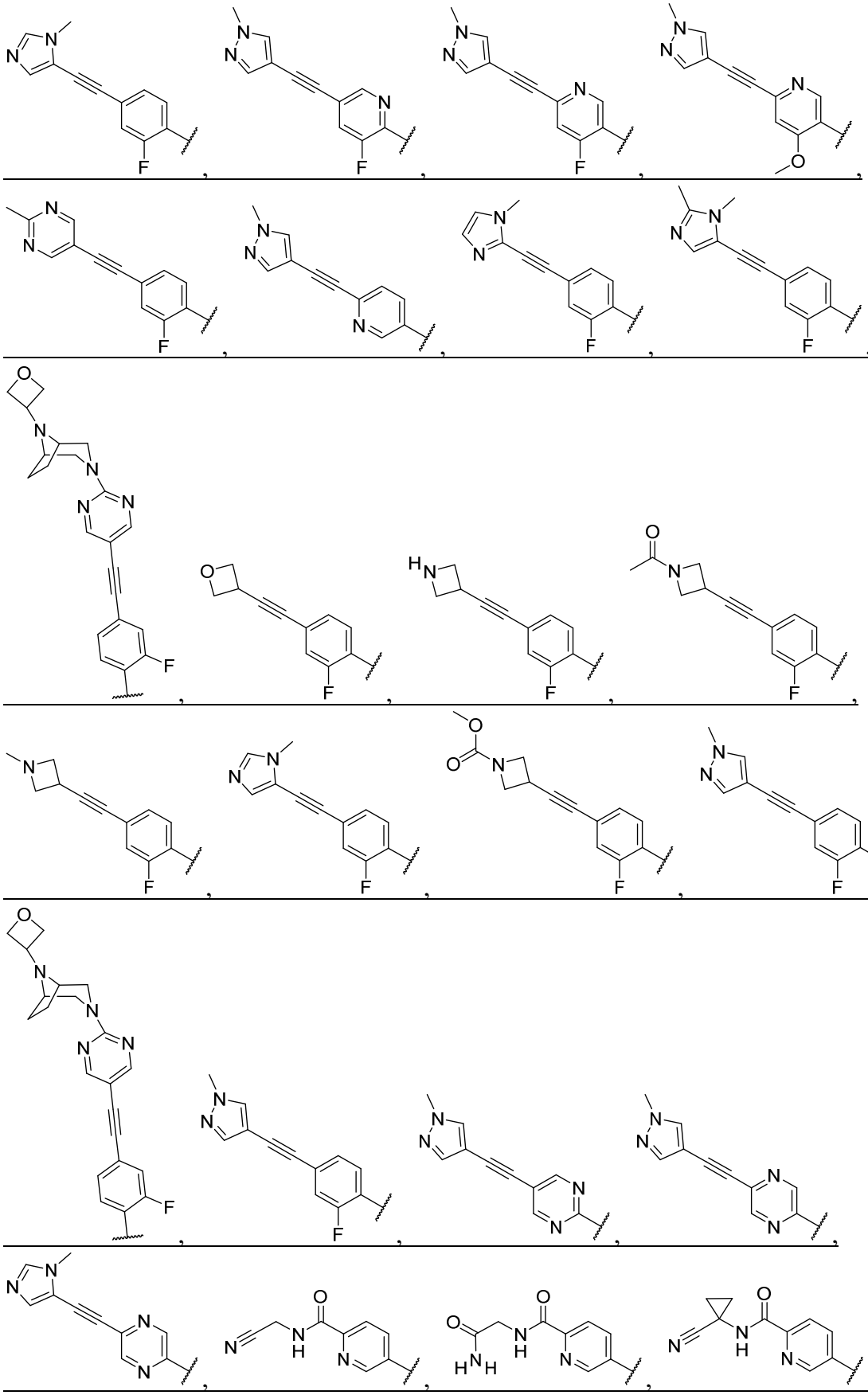
55. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein

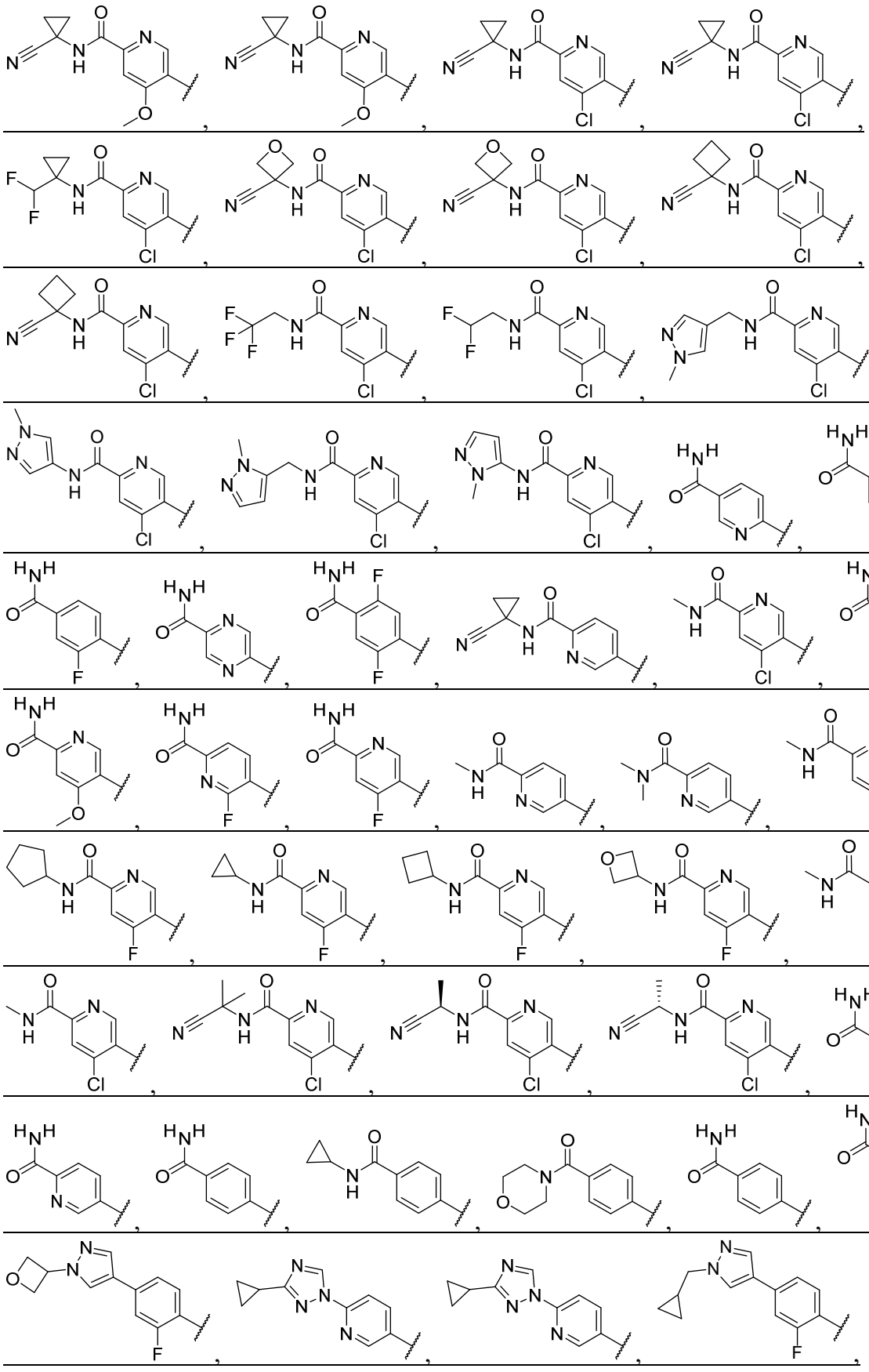
R^1 is

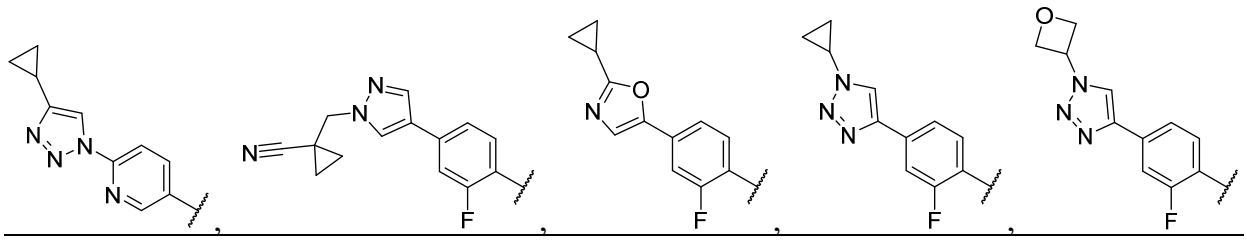
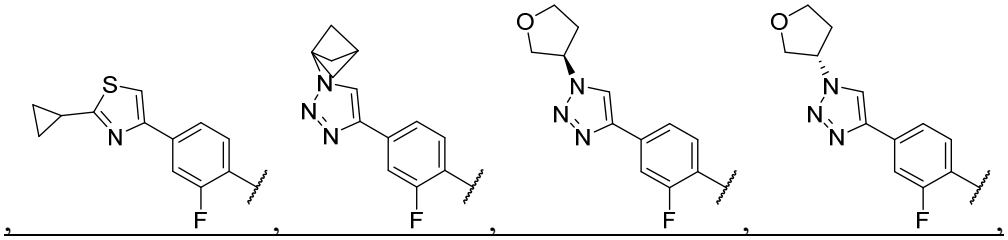
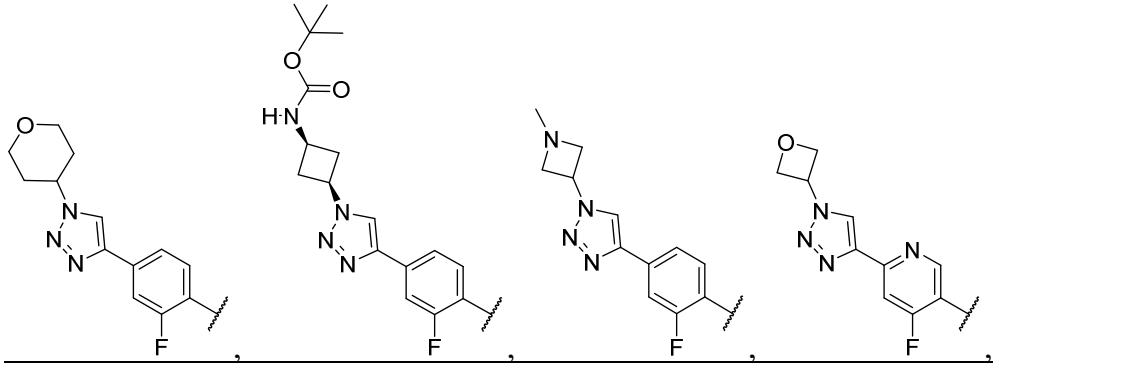
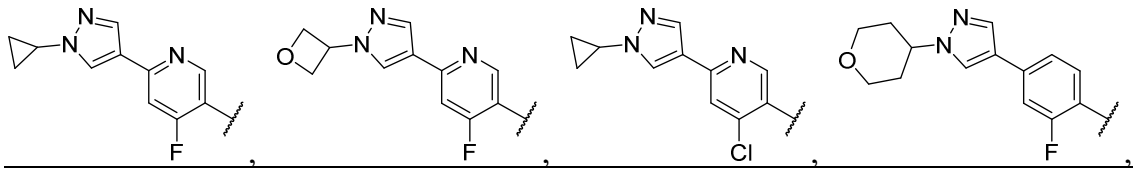
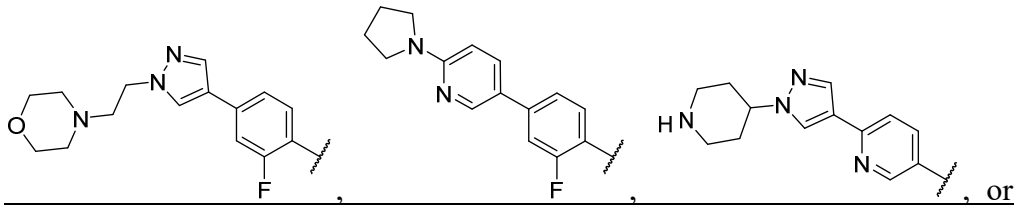










66. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is 6-membered heteroaryl or phenyl substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

77. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one, or phenyl, substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

88. The compound of claim 6 or 7, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, or phenyl, substituted with C_2-alkynyl and optionally substituted with one to three R^4,

wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

99. The compound of any one of claims 6-8, or a pharmaceutically acceptable salt thereof, wherein

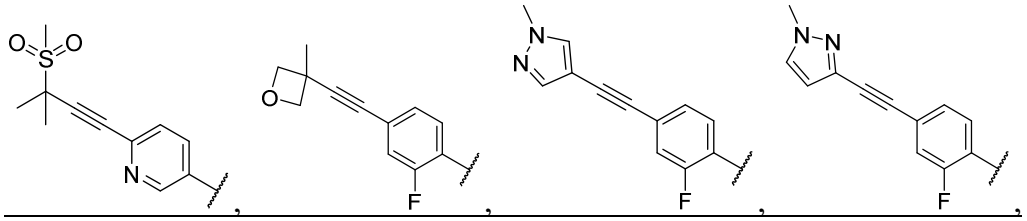
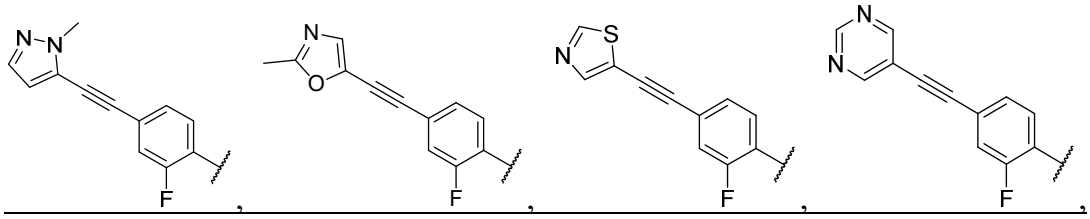
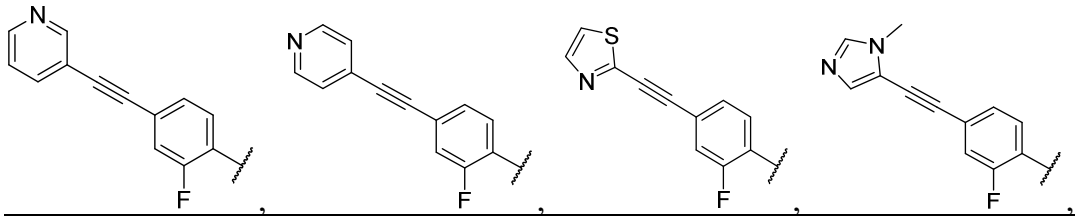
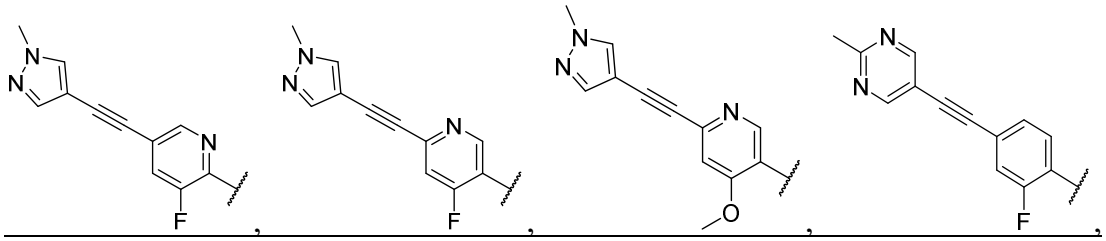
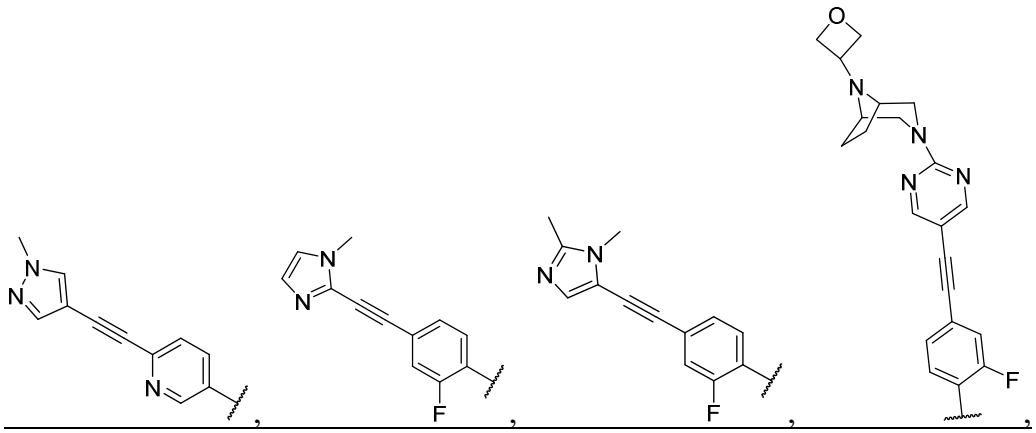
R^1 is pyridyl, pyrazinyl, pyrimidinyl, or phenyl, substituted with C_2-alkynyl and optionally substituted with one R^4,

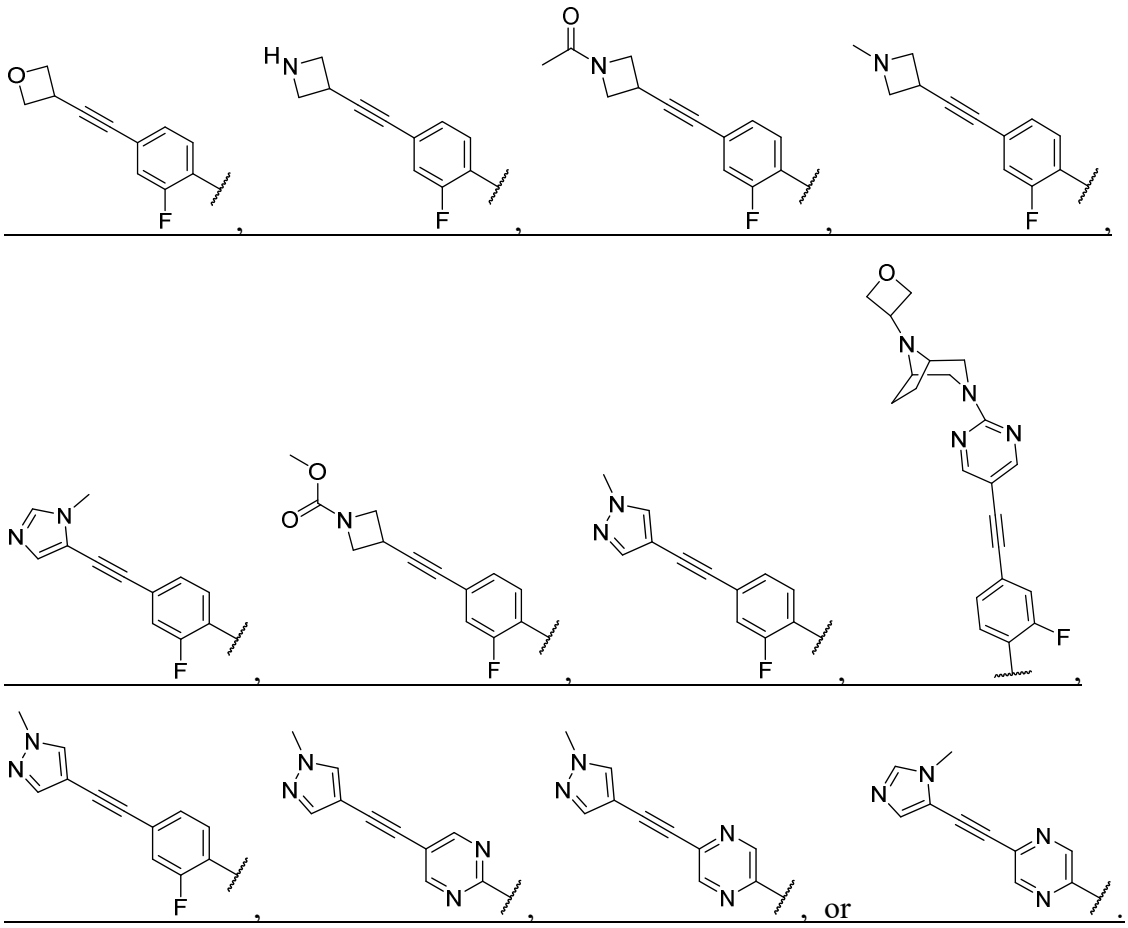
wherein the C_2-alkynyl is substituted with $–C(CH_3)_2SO_2CH_3$, aryl, heteroaryl, or heterocyclyl,

wherein the aryl, heteroaryl or heterocyclyl is optionally substituted with one to four R^5.

10~~10~~. The compound of any one of claims 1 and 6-9, or a pharmaceutically acceptable salt thereof, wherein

R^1 is



11~~11~~. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is 6-membered heteroaryl or phenyl substituted with $–C(O)NR^aR^b$,

wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

12~~12~~. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein R^1 is

pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one; or

phenyl substituted with $–C(O)NR^aR^b$, wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

13~~13~~. The compound of claim 11 or 12, or a pharmaceutically acceptable salt thereof, wherein R^1 is

pyridyl, pyrazinyl, or phenyl substituted with –C(O)NR^{a}R^b,

wherein the heteroaryl or phenyl is optionally substituted with one to four R^4.

1414. The compound of any one of claims 11-13, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, or phenyl substituted with –C(O)NR^{a}R^b,

wherein the pyridyl, pyrazinyl, or phenyl is optionally substituted with one R^4.

1515. The compound of any one of claims 11-14, or a pharmaceutically acceptable salt thereof, wherein

R^a and R^b are independently H, C$_{1-6}$ alkyl, C$_{2-6}$ alkenyl, C$_{2-6}$ alkynyl, C$_{3-6}$ 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 R^6; or

optionally R^a and R^b are combined with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocyclyl, wherein the heterocyclyl is optionally substituted with one to four R^6.

1616. The compound of any one of claims 11-15, or a pharmaceutically acceptable salt thereof, wherein

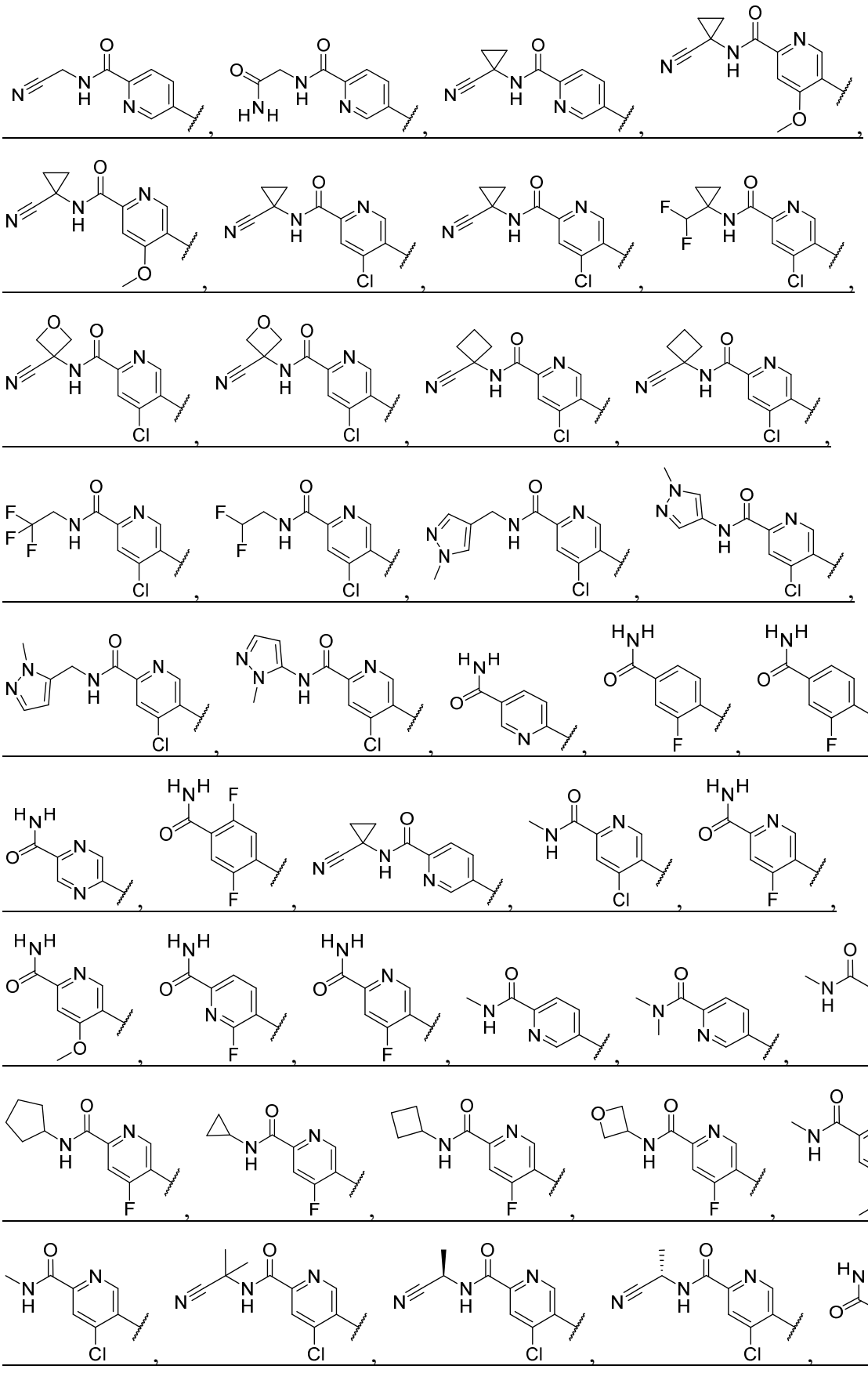
R^a and R^b are independently H, C$_{1-4}$ alkyl, C$_{3-6}$ cycloalkyl, heterocyclyl, or heteroaryl wherein the alkyl, cycloalkyl, heterocyclyl, or heteroaryl is each optionally substituted with one to four R^6; or

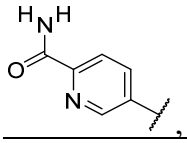
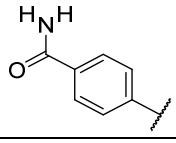
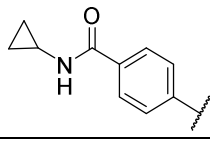
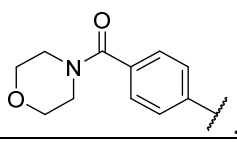
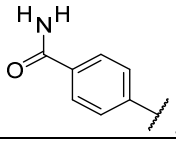
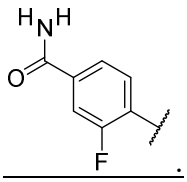
optionally R^a and R^b are combined with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocyclyl,

wherein the heterocyclyl is optionally substituted with one to four R^6.

1717. The compound of any one of claims 1 and 11-16, or a pharmaceutically acceptable salt thereof, wherein

R^1 is:




, 
, 
, 
, 
, or 
.

18~~18~~. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is 6-membered heteroaryl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

19~~19~~. The compound of claim 18 or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, quinoxalyl, quinazolyl, thianaphthenyl, quinazolinyl-4(3H)-one, or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

20~~20~~. The compound of claim 18 or 19, or a pharmaceutically acceptable salt thereof, wherein

R^1 is pyridyl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

21~~21~~. The compound of any one of claims 18-20, or a pharmaceutically acceptable salt thereof, wherein

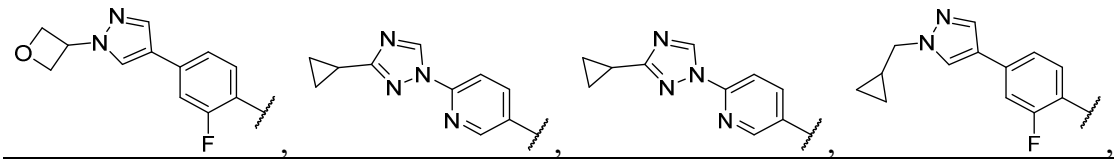
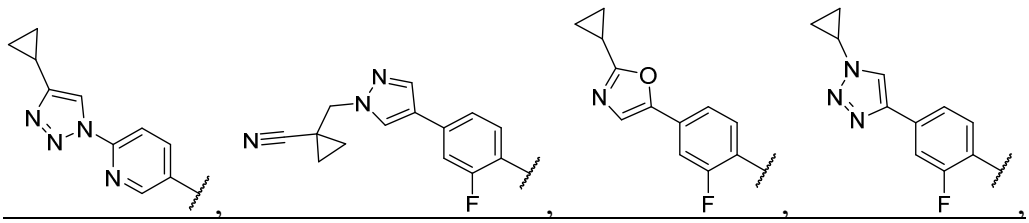
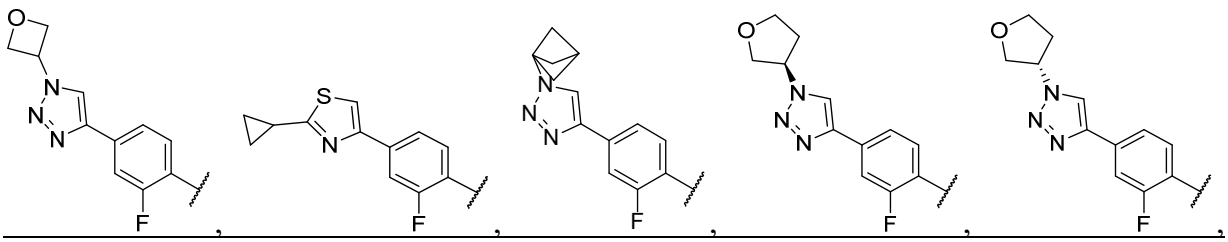
R^1 is pyridyl or phenyl, each substituted with heteroaryl and optionally substituted with one to three R^4,

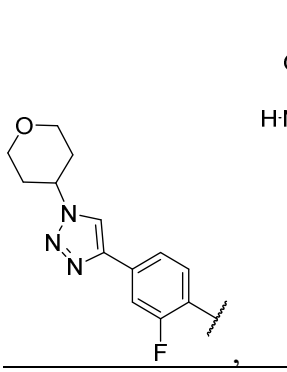
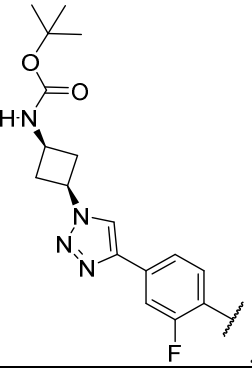
wherein the heteroaryl is substituted with C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl,

wherein the C_{3-10} cycloalkyl, heterocyclyl, C_{1-6} alkyl-C_{3-10} cycloalkyl, C_{1-6} alkyl-heterocyclyl, or C_{1-6} alkyl-heteroaryl is optionally substituted with one to four R^6.

22~~22~~. The compound of any one of claims 1 and 18-21, or a pharmaceutically acceptable salt thereof, wherein

R^1 is:

ring B is substituted with two R^4.

27~~27~~. The compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein

each R^4 is F.

28~~28~~. The compound of claim any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein

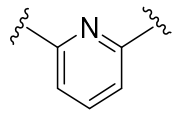
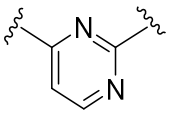
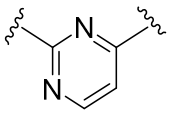
V is $–C(R^{6b})(R^{6c})–$.

29~~29~~. The compound of claim any one of claims 1-28, or a pharmaceutically acceptable salt thereof, wherein

V is $–CH_2–$.

30~~30~~. The compound of claim any one of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein

ring A is


, 
, or 
, each optionally substituted with one halogen.

31~~31~~. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, wherein

two of X^1, X^2, and X^3 is –CH= and one is –C(F)=.

32~~32~~. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl or heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four Z^1,

wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkoxyalkyl, halogen, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, -OH, -CN, C_{1-6} alkyl-CN, -O-C_{3-6} cycloalkyl, heterocyclyl, or heteroaryl optionally substituted with 1 to 4

groups each independently C_{1-6} alkyl, C_{1-6} alkoxy, halogen, -CN, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy.

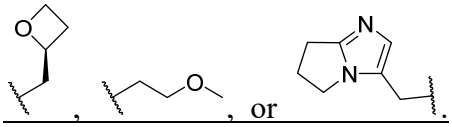
3333. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt thereof, wherein

R^2 is C_{1-6} alkyl or heterocyclyl, wherein the alkyl or heterocyclyl is each optionally substituted with one to four Z^1,

wherein each Z^1 is independently C_{1-6} alkyl, C_{1-6} alkoxy, or heterocyclyl.

3434. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt thereof, wherein

R^2 is

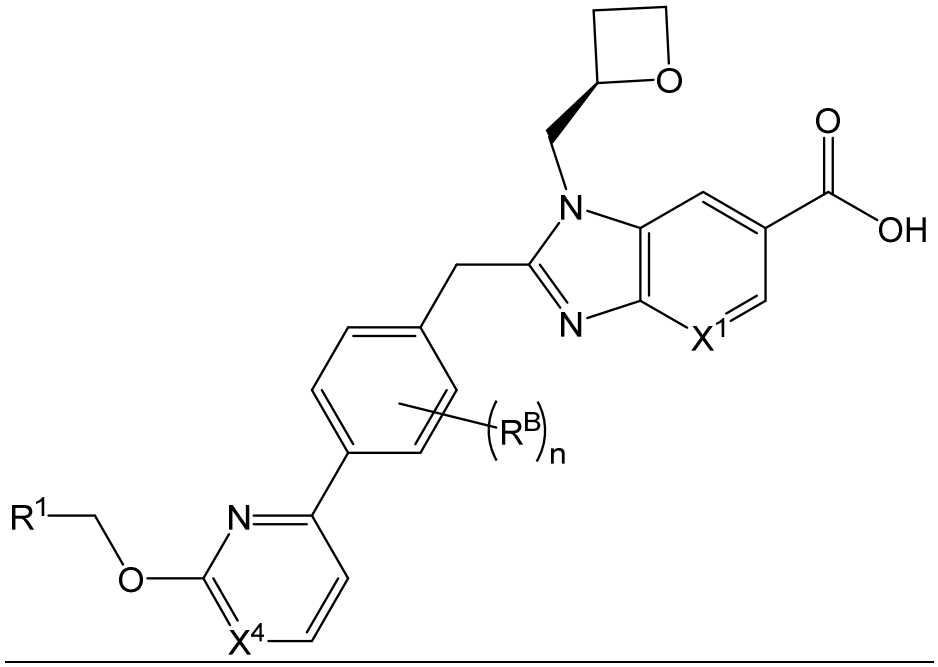


, , or .

3535. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, wherein

R^3 is –C(O)OH.

36. A compound of Formula (II)



(II)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is thiazolyl optionally substituted with R^4;

X^1 is –C(H)= or –C(R^8)=;

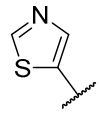
X^4 is -CH=, –C(R^8)= or N;

each R^B is independently C_{1-9} alkyl, C_{1-8} haloalkyl, or halogen;

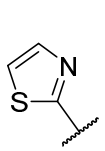
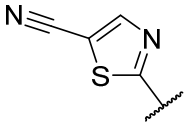
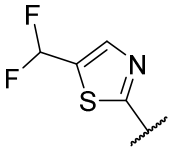
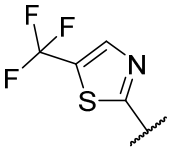
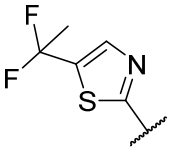
each R^8 is independently halogen; and

n is 0, 1, 2, or 3.

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

R^1 is  or , which is each substituted with $C_{1\text{-}8}$ haloalkyl.

38. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^1 is

, , , , or .

39. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^8 is F or Cl.

40. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, having the structure of a compound in Table 2.

41. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

42. The pharmaceutical composition of claim 41 further comprising one or more additional therapeutic agents.

43. Use of the compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a GLP-1R mediated disease or condition.

44. The use of claim 43, wherein the disease or condition comprises a liver disease.

45. The use of claim 44, 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).

46. The use of claim 45, wherein the disease or condition comprises non-alcoholic fatty liver disease (NAFLD).

47. The use of claim 45, wherein the disease or condition comprises non-alcoholic steatohepatitis (NASH).

48. The use of claim 43, wherein the disease or condition comprises a metabolic disease.

49. The use of claim 43, 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.

50. The use of any one of claims 43 to 49, wherein the compound or pharmaceutically acceptable salt thereof is administered in combination with an additional therapeutic agent.

51. The pharmaceutical composition of claim 42 or the use of claim 50, 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 farnesoid 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.