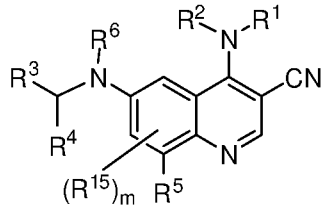
CLAIMS:

1. A compound of the following Formula I:



(I)

wherein

R^1 is hydrogen, -O-R^7, -N(R^8)(R^9), -C(O)-R^7, -S(O)$_2$-R^7, -C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, and heteroaryl may be optionally substituted with one to four Z^1;

R^2 is hydrogen, -C(O)-R^7, -C(O)O-R^7, -C(O)N(R^7)$_2$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^2;

or R^1 and R^2 together with the nitrogen to which they are attached to form a heterocyclyl or heteroaryl, wherein each heterocyclyl or heteroaryl is optionally substituted with one to four Z^2;

R^3 is heterocyclyl or heteroaryl, wherein each heterocyclyl or heteroaryl is optionally substituted with one to four Z^3;

R^4 is aryl, heterocyclyl or heteroaryl, wherein each aryl, heterocyclyl, or heteroaryl is optionally substituted with one to four Z^4;

R^5 is hydrogen, halo, -CN, -NO_2, -O-R^7, -N(R^8)(R^9), -S(O)-R^7, -S(O)$_2$$R^7$, -S(O)$_2$N($R^7$)$_2$, -C(O)$R^7$, -OC(O)-$R^7$, -C(O)O-$R^7$, -OC(O)O-$R^7$, -OC(O)N($R^{10}$)($R^{11}$), -C(O)N($R^7$)$_2$, -N($R^7$)C(O)($R^7$), C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-9} alkylthio, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-9} alkylthio, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^5;

R^6 is $-C(O)O-R^{16}-OP(O)(OR^{12})_2$ $-C(O)-R^{16}-OP(O)(OR^{12})_2$, $-R^{16}-OP(O)(OR^{12})_2$, $-C(O)O-R^{16}-OR^{17}$; $-C(O)O-R^{16}-OH$; $-C(O)O-R^{16}-OC(O)R^{17}$; $-C(O)-C(O)OR^{12}$, or $-C(O)O-R^{16}-OC(O)R^{17}NH_2$;

each R^7 is independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^7;

R^8 and R^9 at each occurrence are independently hydrogen, $-S(O)_2R^{10}$, $-C(O)-R^{10}$, $-C(O)O-R^{10}$, $-C(O)N(R^{10})(R^{11})$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl may be optionally substituted with one to four Z^8;

R^{10} and R^{11} at each occurrence are independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl,

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl optionally is substituted with one to four Z^{1b};

each Z^1, Z^2, Z^3, Z^4, Z^5, Z^6, Z^7, and Z^8 is independently hydrogen, oxo, halo, $-NO_2$, $-N_3$, -CN, thioxo, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)-R^{12}$, $-C(O)O-R^{12}$, $-C(O)-N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})C(O)-R^{12}$, $-N(R^{12})C(O)O-R^{12}$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-NR^{12}S(O)_2N(R^{13})(R^{14})$, $-NR^{12}S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-P(O)(OR^{12})_2$, $-OP(O)(OR^{12})_2$, $-CH_2P(O)(OR^{12})_2$, $-OCH_2P(O)(OR^{12})_2$, $-C(O)OCH_2P(O)(OR^{12})_2$, $-P(O)(R^{12})(OR^{12})$, $-OP(O)(R^{12})(OR^{12})$, $-CH_2P(O)(R^{12})(OR^{12})$, $-OCH_2P(O)(R^{12})(OR^{12})$, $-C(O)OCH_2P(O)(R^{12})(OR^{12})$, $-P(O)(N(R^{12})_2)_2$, $-OP(O)(N(R^{12})_2)_2$, $-CH_2P(O)(N(R^{12})_2)_2$, $-OCH_2P(O)(N(R^{12})_2)_2$, $-C(O)OCH_2P(O)(N(R^{12})_2)_2$, $-P(O)(N(R^{12})_2)(OR^{12})$, $-OP(O)(N(R^{12})_2)(OR^{12})$, $-CH_2P(O)(N(R^{12})_2)(OR^{12})$, $-OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-C(O)OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-P(O)(R^{12})(N(R^{12})_2)$, -

$OP(O)(R^{12})(N(R^{12})_2)$, $-CH_2P(O)(R^{12})(N(R^{12})_2)$, $-OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-C(O)OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

each Z^{1a} is independently oxo, halo, thioxo, $-NO_2$, -CN, $-N_3$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)R^{12}$, $-C(O)O-R^{12}$, $-C(O)N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})-C(O)R^{12}$, $-N(R^{12})C(O)O(R^{12})$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-N(R^{12})S(O)_2-N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)OR^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

each R^{12} is independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, aryl, heteroaryl or heterocyclyl,

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

R^{13} and R^{14} at each occurrence are each independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, aryl, heteroaryl or heterocyclyl;

wherein any alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl or heterocyclyl is optionally substituted with one to four Z^{1b} groups, or R^{13} and R^{14} together with the nitrogen to which they are attached form a heterocyclyl, wherein said heterocyclyl is optionally substituted with one to four Z^{1b} groups;

each R^{15} is independently halo, -CN, $-NO_2$, $-O-R^7$, $-N(R^8)(R^9)$, $-S(O)-R^7$, $-S(O)_2R^7$, $-S(O)_2N(R^7)_2$, $-C(O)R^7$, $-OC(O)-R^7$, $-C(O)O-R^7$, $-OC(O)O-R^7$, $-OC(O)N(R^{10})(R^{11})$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)(R^7)$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-9} alkylthio, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

R^{16} is $-C_{1-3}$ alkyl or cyclopropyl optionally substituted with one to four C_{1-3} alkyl or cyclopropyl;

R^{17} is C_{1-9} alkyl, cycloalkyl, or heterocyclyl optionally substituted with one to three R^{16};

and

each Z^1, Z^2, Z^4, Z^5, Z^7, and Z^8 is independently hydrogen, oxo, halo, $-NO_2$, $-N_3$, -CN, thioxo, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)-R^{12}$, $-C(O)O-R^{12}$, $-C(O)-N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})C(O)-R^{12}$, $-N(R^{12})C(O)O-R^{12}$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-NR^{12}S(O)_2N(R^{13})(R^{14})$, $-NR^{12}S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-P(O)(OR^{12})_2$, $-OP(O)(OR^{12})_2$, $-CH_2P(O)(OR^{12})_2$, $-OCH_2P(O)(OR^{12})_2$, $-C(O)OCH_2P(O)(OR^{12})_2$, $-P(O)(R^{12})(OR^{12})$, $-OP(O)(R^{12})(OR^{12})$, $-CH_2P(O)(R^{12})(OR^{12})$, $-OCH_2P(O)(R^{12})(OR^{12})$, $-C(O)OCH_2P(O)(R^{12})(OR^{12})$, $-P(O)(N(R^{12})_2)_2$, $-OP(O)(N(R^{12})_2)_2$, $-CH_2P(O)(N(R^{12})_2)_2$, $-OCH_2P(O)(N(R^{12})_2)_2$, $-C(O)OCH_2P(O)(N(R^{12})_2)_2$, $-P(O)(N(R^{12})_2)(OR^{12})$, $-OP(O)(N(R^{12})_2)(OR^{12})$, $-CH_2P(O)(N(R^{12})_2)(OR^{12})$, $-OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-C(O)OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-P(O)(R^{12})(N(R^{12})_2)$, $-OP(O)(R^{12})(N(R^{12})_2)$, $-CH_2P(O)(R^{12})(N(R^{12})_2)$, $-OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-C(O)OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

Z^9 is hydrogen, halo, –CN, or $-O-R^{12}$;

each Z^{1a} is independently oxo, halo, thioxo, $-NO_2$, -CN, $-N_3$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)R^{12}$, $-C(O)O-R^{12}$, $-C(O)N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})-C(O)R^{12}$, $-N(R^{12})C(O)O(R^{12})$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-N(R^{12})S(O)_2-N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)OR^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

each Z^{1b} is independently oxo, thioxo, hydroxy, halo, $-NO_2$, $-N_3$, -CN, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O(C_{1-9}$ alkyl), $-O(C_{2-6}$ alkenyl), $-O(C_{2-6}$ alkynyl), $-O(C_{3-15}$ cycloalkyl), $-O(C_{1-8}$ haloalkyl), -O(aryl), -O(heteroaryl), - O(heterocyclyl), $-NH_2$, $-NH(C_{1-9}$ alkyl), $-NH(C_{2-6}$ alkenyl), $-NH(C_{2-6}$ alkynyl), $-NH(C_{3-15}$ cycloalkyl), $-NH(C_{1-8}$ haloalkyl), -NH(aryl), -

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

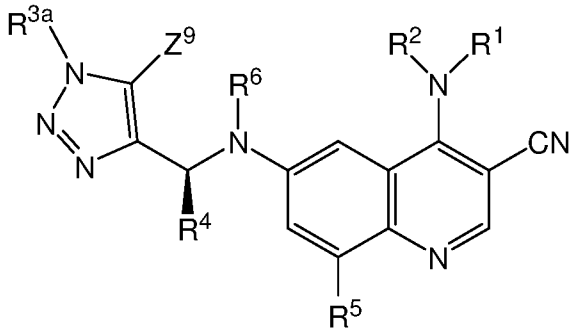
wherein any alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with one to four halo, C_{1-9} alkyl, C_{1-8} haloalkyl, -OH, -NH_2, -NH(C_{1-9} alkyl), -NH(C_{3-15} cycloalkyl), -NH(C_{1-8} haloalkyl), -NH(aryl), -NH(heteroaryl), -NH(heterocyclyl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -

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

m is 0, 1, or 2;

or a pharmaceutically acceptable salt, stereoisomer, mixture of stereoisomers, or deuterated analog thereof.

2. The compound of claim 1 having a structure according to Formula II:



(II)

wherein

R^1 is hydrogen, -O-R^7, -N(R^8)(R^9), -C(O)-R^7, -$S(O)_2$-R^7, -C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, and heteroaryl may be optionally substituted with one to four Z^1;

R^2 is hydrogen, -C(O)-R^7, -C(O)O-R^7, -C(O)N(R^7)$_2$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^2;

or R^1 and R^2 together with the nitrogen to which they are attached form a heterocyclyl or heteroaryl, wherein each heterocyclyl or heteroaryl is optionally substituted with one to four Z^2;

R^{3a} is hydrogen, oxo, halo, $-NO_2$, $-N_3$, -CN, thioxo, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)-R^{12}$, $-C(O)O-R^{12}$, $-C(O)-N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})C(O)-R^{12}$, $-N(R^{12})C(O)O-R^{12}$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-NR^{12}S(O)_2N(R^{13})(R^{14})$, $-NR^{12}S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-P(O)(OR^{12})_2$, $-OP(O)(OR^{12})_2$, $-CH_2P(O)(OR^{12})_2$, $-OCH_2P(O)(OR^{12})_2$, $-C(O)OCH_2P(O)(OR^{12})_2$, $-P(O)(R^{12})(OR^{12})$, $-OP(O)(R^{12})(OR^{12})$, $-CH_2P(O)(R^{12})(OR^{12})$, $-OCH_2P(O)(R^{12})(OR^{12})$, $-C(O)OCH_2P(O)(R^{12})(OR^{12})$, $-P(O)(N(R^{12})_2)_2$, $-OP(O)(N(R^{12})_2)_2$, $-CH_2P(O)(N(R^{12})_2)_2$, $-OCH_2P(O)(N(R^{12})_2)_2$, $-C(O)OCH_2P(O)(N(R^{12})_2)_2$, $-P(O)(N(R^{12})_2)(OR^{12})$, $-OP(O)(N(R^{12})_2)(OR^{12})$, $-CH_2P(O)(N(R^{12})_2)(OR^{12})$, $-OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-C(O)OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-P(O)(R^{12})(N(R^{12})_2)$, $-OP(O)(R^{12})(N(R^{12})_2)$, $-CH_2P(O)(R^{12})(N(R^{12})_2)$, $-OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-C(O)OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-Si(R^{12})_3$, $-S-R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

R^4 is aryl, heterocyclyl or heteroaryl, wherein each aryl, heterocyclyl, or heteroaryl is optionally substituted with one to four Z^4;

R^5 is hydrogen, halo, -CN, $-NO_2$, $-O-R^7$, $-N(R^8)(R^9)$, $-S(O)-R^7$, $-S(O)_2R^7$, $-S(O)_2N(R^7)_2$, $-C(O)R^7$, $-OC(O)-R^7$, $-C(O)O-R^7$, $-OC(O)O-R^7$, $-OC(O)N(R^{10})(R^{11})$, $-C(O)N(R^7)_2$, $-N(R^7)C(O)(R^7)$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-9} alkylthio, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-9} alkylthio, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^5;

R^6 is $-C(O)O-R^{16}-OP(O)(OR^{12})_2$;

each R^7 is independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl may be optionally substituted with one to four Z^7;

R^8 and R^9 at each occurrence are independently hydrogen, $-S(O)_2R^{10}$, $-C(O)-R^{10}$, $-C(O)O-R^{10}$, $-C(O)N(R^{10})(R^{11})$, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl;

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl may be optionally substituted with one to four Z^8;

R^{10} and R^{11} at each occurrence are independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl,

wherein each C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl optionally is substituted with one to four Z^{1b};

each R^{12} is independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, aryl, heteroaryl or heterocyclyl,

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

R^{13} and R^{14} at each occurrence are each independently hydrogen, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, aryl, heteroaryl or heterocyclyl;

wherein any alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl or heterocyclyl is optionally substituted with one to four Z^{1b} groups, or R^{13} and R^{14} together with the nitrogen to which they are attached form a heterocyclyl, wherein said heterocyclyl is optionally substituted with one to four Z^{1b} groups;

R^{16} is $-C_{1-2}$ alkyl optionally substituted with one to four C_{1-2} alkyl or cyclopropyl;

and

each Z^1, Z^2, Z^4, Z^5, Z^7, and Z^8 is independently hydrogen, oxo, halo, $-NO_2$, $-N_3$, -CN, thioxo, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, C_{1-8} haloalkyl, aryl, heteroaryl, heterocyclyl, $-O-R^{12}$, $-C(O)-R^{12}$, $-C(O)O-R^{12}$, $-C(O)-N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})C(O)-R^{12}$, $-N(R^{12})C(O)O-R^{12}$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-NR^{12}S(O)_2N(R^{13})(R^{14})$, $-NR^{12}S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)-N(R^{13})(R^{14})$, $-P(O)(OR^{12})_2$, $-OP(O)(OR^{12})_2$, $-CH_2P(O)(OR^{12})_2$, $-OCH_2P(O)(OR^{12})_2$, -

$C(O)OCH_2P(O)(OR^{12})_2$, $-P(O)(R^{12})(OR^{12})$, $-OP(O)(R^{12})(OR^{12})$, $-CH_2P(O)(R^{12})(OR^{12})$, $-OCH_2P(O)(R^{12})(OR^{12})$, $-C(O)OCH_2P(O)(R^{12})(OR^{12})$, $-P(O)(N(R^{12})_2)_2$, $-OP(O)(N(R^{12})_2)_2$, $-CH_2P(O)(N(R^{12})_2)_2$, $-OCH_2P(O)(N(R^{12})_2)_2$, $-C(O)OCH_2P(O)(N(R^{12})_2)_2$, $-P(O)(N(R^{12})_2)(OR^{12})$, $-OP(O)(N(R^{12})_2)(OR^{12})$, $-CH_2P(O)(N(R^{12})_2)(OR^{12})$, $-OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-C(O)OCH_2P(O)(N(R^{12})_2)(OR^{12})$, $-P(O)(R^{12})(N(R^{12})_2)$, $-OP(O)(R^{12})(N(R^{12})_2)$, $-CH_2P(O)(R^{12})(N(R^{12})_2)$, $-OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-C(O)OCH_2P(O)(R^{12})(N(R^{12})_2)$, $-Si(R^{12})_3$, $-S\text{-}R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

Z^9 is hydrogen, halo, –CN, or $-O\text{-}R^{12}$;

each Z^{1a} is independently oxo, halo, thioxo, $-NO_2$, -CN, $-N_3$, $C_{1\text{-}9}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{3\text{-}15}$ cycloalkyl, $C_{1\text{-}8}$ haloalkyl, aryl, heteroaryl, heterocyclyl, $-O\text{-}R^{12}$, $-C(O)R^{12}$, $-C(O)O\text{-}R^{12}$, $-C(O)N(R^{13})(R^{14})$, $-N(R^{13})(R^{14})$, $-N(R^{13})_2(R^{14})^+$, $-N(R^{12})\text{-}C(O)R^{12}$, $-N(R^{12})C(O)O(R^{12})$, $-N(R^{12})C(O)N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2(R^{12})$, $-N(R^{12})S(O)_2\text{-}N(R^{13})(R^{14})$, $-N(R^{12})S(O)_2O(R^{12})$, $-OC(O)R^{12}$, $-OC(O)OR^{12}$, $-OC(O)\text{-}N(R^{13})(R^{14})$, $-Si(R^{12})_3$, $-S\text{-}R^{12}$, $-S(O)R^{12}$, $-S(O)(NH)R^{12}$, $-S(O)_2R^{12}$ or $-S(O)_2N(R^{13})(R^{14})$;

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

each Z^{1b} is independently oxo, thioxo, hydroxy, halo, $-NO_2$, $-N_3$, -CN, $C_{1\text{-}9}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{3\text{-}15}$ cycloalkyl, $C_{1\text{-}8}$ haloalkyl, aryl, heteroaryl, heterocyclyl, $-O(C_{1\text{-}9}$ alkyl), $-O(C_{2\text{-}6}$ alkenyl), $-O(C_{2\text{-}6}$ alkynyl), $-O(C_{3\text{-}15}$ cycloalkyl), $-O(C_{1\text{-}8}$ haloalkyl), -O(aryl), -O(heteroaryl), - O(heterocyclyl), $-NH_2$, $-NH(C_{1\text{-}9}$ alkyl), $-NH(C_{2\text{-}6}$ alkenyl), $-NH(C_{2\text{-}6}$ alkynyl), $-NH(C_{3\text{-}15}$ cycloalkyl), $-NH(C_{1\text{-}8}$ haloalkyl), -NH(aryl), -NH(heteroaryl), -NH(heterocyclyl), $-N(C_{1\text{-}9}$ alkyl)$_2$, $-N(C_{2\text{-}6}$ alkenyl)$_2$, $-N(C_{2\text{-}6}$ alkynyl)$_2$, $-N(C_{3\text{-}15}$ cycloalkyl)$_2$, $-N(C_{1\text{-}8}$ haloalkyl)$_2$, -N(aryl)$_2$, -N(heteroaryl)$_2$, -N(heterocyclyl)$_2$, $-N(C_{1\text{-}9}$ alkyl)($C_{2\text{-}6}$ alkenyl), $-N(C_{1\text{-}9}$ alkyl)($C_{2\text{-}6}$ alkynyl), $-N(C_{1\text{-}9}$ alkyl)($C_{3\text{-}15}$ cycloalkyl), $-N(C_{1\text{-}9}$ alkyl)($C_{1\text{-}8}$ haloalkyl), $-N(C_{1\text{-}9}$ alkyl)(aryl), $-N(C_{1\text{-}9}$ alkyl)(heteroaryl), $-N(C_{1\text{-}9}$ alkyl)(heterocyclyl), $-C(O)(C_{1\text{-}9}$ alkyl), $-C(O)(C_{2\text{-}6}$ alkenyl), $-C(O)(C_{2\text{-}6}$ alkynyl), $-C(O)(C_{3\text{-}15}$ cycloalkyl), $-C(O)(C_{1\text{-}8}$ haloalkyl), -C(O)(aryl), -C(O)(heteroaryl), -C(O)(heterocyclyl), $-C(O)O(C_{1\text{-}9}$ alkyl), $-C(O)O(C_{2\text{-}6}$ alkenyl), $-C(O)O(C_{2\text{-}6}$ alkynyl), -

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

wherein any alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with one to four halo, C_{1-9} alkyl, C_{1-8} haloalkyl, -OH, -NH_2, -NH(C_{1-9} alkyl), -NH(C_{3-15} cycloalkyl), -NH(C_{1-8} haloalkyl), -NH(aryl), -NH(heteroaryl), -NH(heterocyclyl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(aryl), -NHC(O)(heteroaryl), -NHC(O)(heterocyclyl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(aryl), -NHC(O)O(heteroaryl), -NHC(O)O(heterocyclyl), -NHC(O)NH(C_{1-9} alkyl), -S(O)(NH)(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(aryl), -S(O)$_2$(heteroaryl), -S(O)$_2$(heterocyclyl), -S(O)$_2$NH(C_{1-9} alkyl), -S(O)$_2$N(C_{1-9} alkyl)$_2$, -O(C_{3-15}

cycloalkyl), -O(C_{1-8} haloalkyl), -O(aryl), -O(heteroaryl), -O(heterocyclyl), or -O(C_{1-9} alkyl);

or a pharmaceutically acceptable salt, stereoisomer, mixture of stereoisomers, or deuterated analog thereof.

3. The compound of any of the preceding claims, wherein R^1 is -C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, or C_{3-15} cycloalkyl, heterocyclyl, aryl, or heteroaryl each of which may be optionally substituted with one to four halo.

4. The compound of any of the preceding claims, wherein R^1 is -C_{1-9} alkyl optionally substituted with one to four halo.

5. The compound of any of the preceding claims, wherein R^2 is hydrogen.

6. The compound of any of the preceding claims, wherein R^{3a} is hydrogen, C_{1-9} alkyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, or heteroaryl;

wherein said C_{1-9} alkyl, C_{3-15} cycloalkyl, aryl, or heterocyclyl, may be optionally substituted with one to four substituents independently selected from the group consisting of cyano, halo, -O-R^{12}, -C(O)-R^{12}, -OC(O)-R^{12}, -C(O)O-R^{12}, -C(O)-N(R^{13})(R^{14}), -N(R^{13})(R^{14}), -N(R^{13})$_2$(R^{14})$^+$, -S(O)$_2$-R^{12}, -Si(R^{12})$_3$, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl; and

wherein said C_{1-9} alkyl, C_{3-15} cycloalkyl, heterocyclyl, or aryl may be optionally substituted with one to three substituents independently selected from the group consisting of halo, -O(C_{1-9} alkyl), -C(O)N(C_{1-9} alkyl)$_2$, C_{1-9} alkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

7. The compound of any of the preceding claims, wherein R^{3a} is hydrogen or C_{1-9} alkyl;

wherein said C_{1-9} alkyl may be optionally substituted with one to four substituents independently selected from the group consisting of cyano, halo, -O-R^{12}, -C(O)-R^{12}, -OC(O)-R^{12}, -C(O)O-R^{12}, -C(O)-N(R^{13})(R^{14}), -N(R^{13})(R^{14}), -N(R^{13})$_2$(R^{14})$^+$, -S(O)$_2$-R^{12}, -Si(R^{12})$_3$, C_{1-8} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl; and

wherein said C_{3-15} cycloalkyl, aryl, heterocyclyl, or heteroaryl may be optionally substituted with one to three substituents independently selected from the group consisting of halo, -O(C_{1-9} alkyl), -C(O)N(C_{1-9} alkyl)$_2$, C_{1-9} alkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

8. The compound of any of the preceding claims, wherein R^{3a} is C_{3-15} cycloalkyl, heterocyclyl, aryl, or heteroaryl;

wherein said C_{1-9} alkyl, C_{3-15} cycloalkyl, aryl, or heterocyclyl, may be optionally substituted with one to four substituents independently selected from the group consisting of cyano, halo, -O-R^{12}, -C(O)-R^{12}, -OC(O)-R^{12}, -C(O)O-R^{12}, -C(O)-N(R^{13})(R^{14}), -N(R^{13})(R^{14}), -N(R^{13})$_2$(R^{14})$^+$, -S(O)$_2$-R^{12}, -Si(R^{12})$_3$, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{3-15} cycloalkyl, aryl, heterocyclyl, and heteroaryl; and

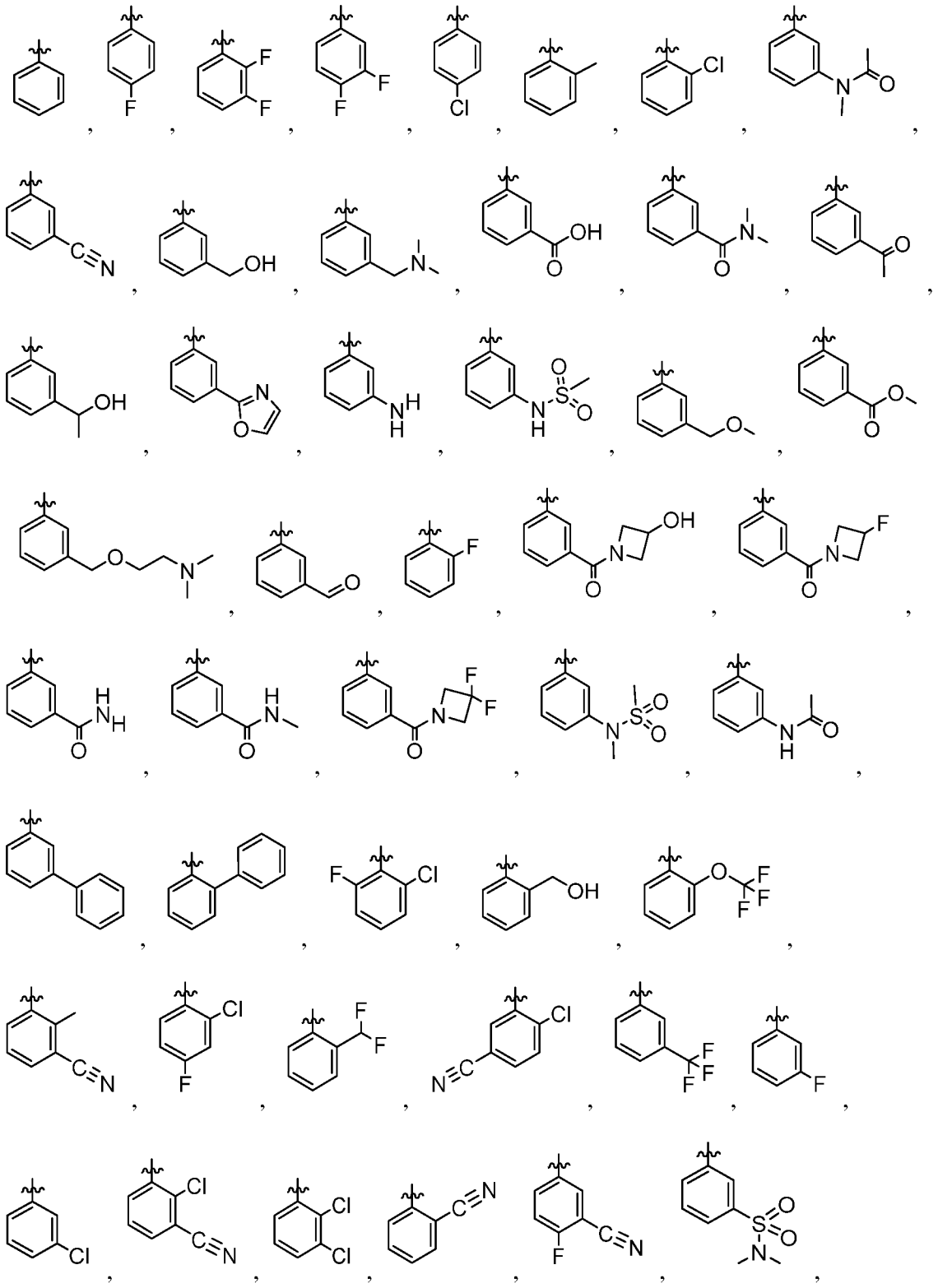
wherein said C_{1-9} alkyl, C_{3-15} cycloalkyl, heterocyclyl, or aryl may be optionally substituted with one to three substituents independently selected from the group consisting of halo, -O(C_{1-9} alkyl), -C(O)N(C_{1-9} alkyl)$_2$, C_{1-9} alkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

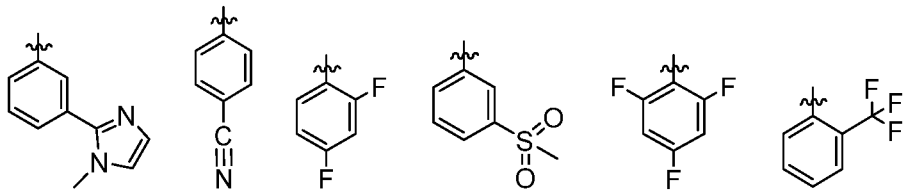
9. The compound of any of the preceding claims, wherein R^{3a} is C_{3-15} cycloalkyl optionally substituted with one to four substituents independently selected from the group consisting of cyano, halo, -O-R^{12}, -C(O)O-R^{12}, -OC(O)-R^{12}, -N(R^{13})(R^{14}), -N(R^{13})$_2$(R^{14})$^+$, C_{1-9} alkyl, C_{1-8} haloalkyl, heterocyclyl, and heteroaryl, or a pharmaceutically acceptable salt thereof.

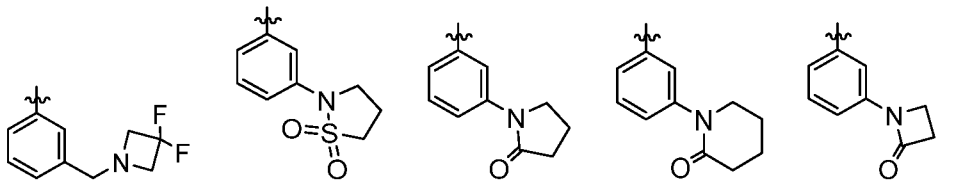
10. The compound of any of the preceding claims, wherein R^4 is aryl optionally substituted with one to three substituents independently selected from the group consisting of –CN, halo, -O-R^{12}, -C(O)-R^{12}, -C(O)O-R^{12}, -S(O)$_2$-R^{12}, -N(R^{12})C(O)-R^{12}, -N(R^{12})S(O)$_2$$R^{12}$, -C(O)N($R^{13}$)($R^{14}$), -N($R^{13}$)($R^{14}$), C_{1-9} alkyl, C_{3-15} cycloalkyl, heterocyclyl, aryl, and heteroaryl;

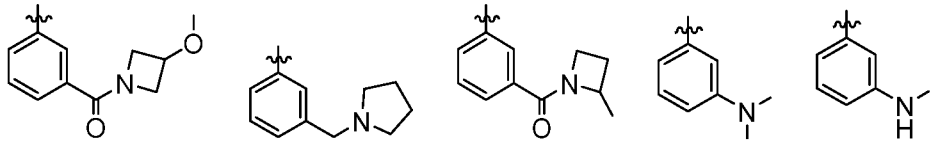
wherein said C_{1-9} alkyl, C_{3-15} cycloalkyl, or heteroaryl may be optionally substituted with one to three substituents independently selected from the group consisting of halo, -CN, -O-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, and heterocyclyl.

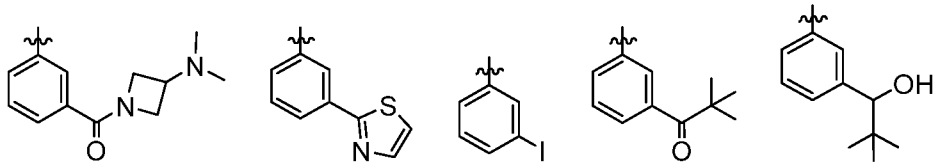
11. The compound of any of the preceding claims, wherein R^4 is

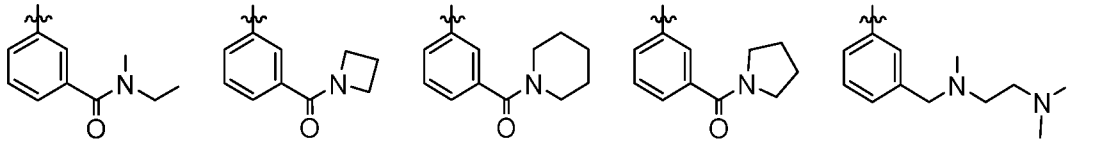


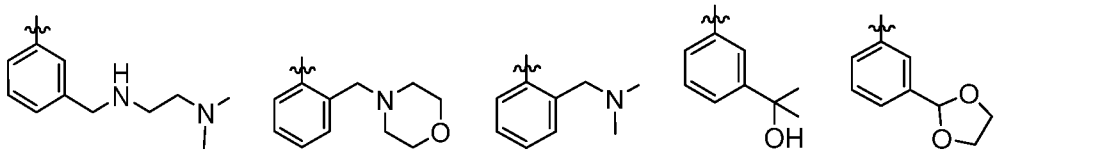


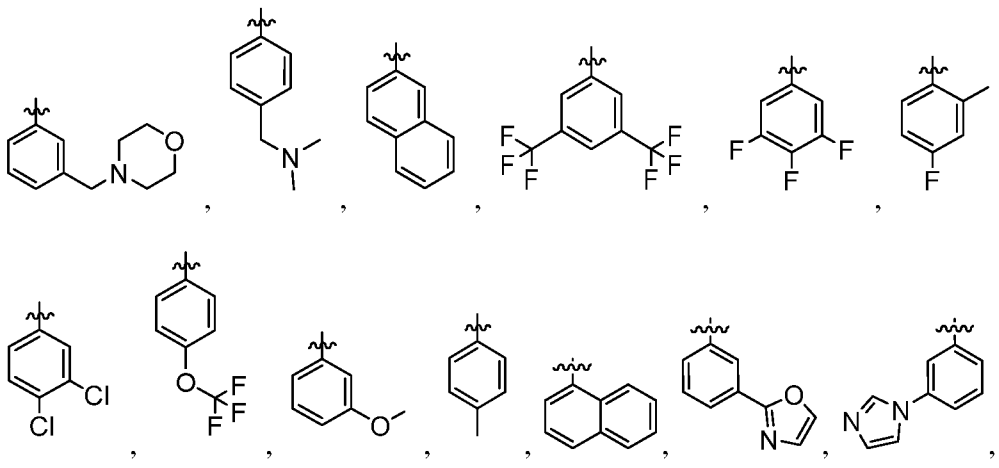


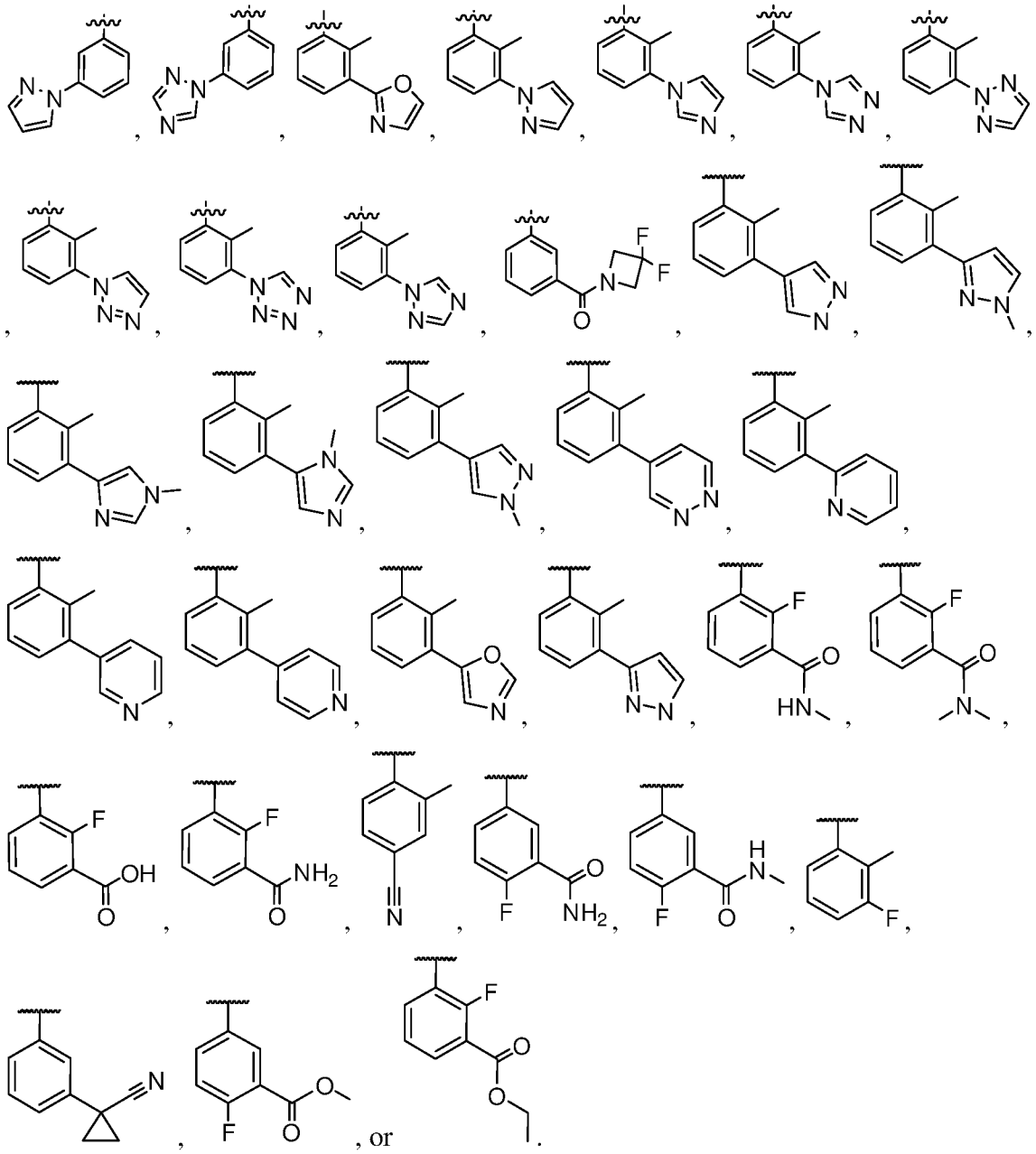












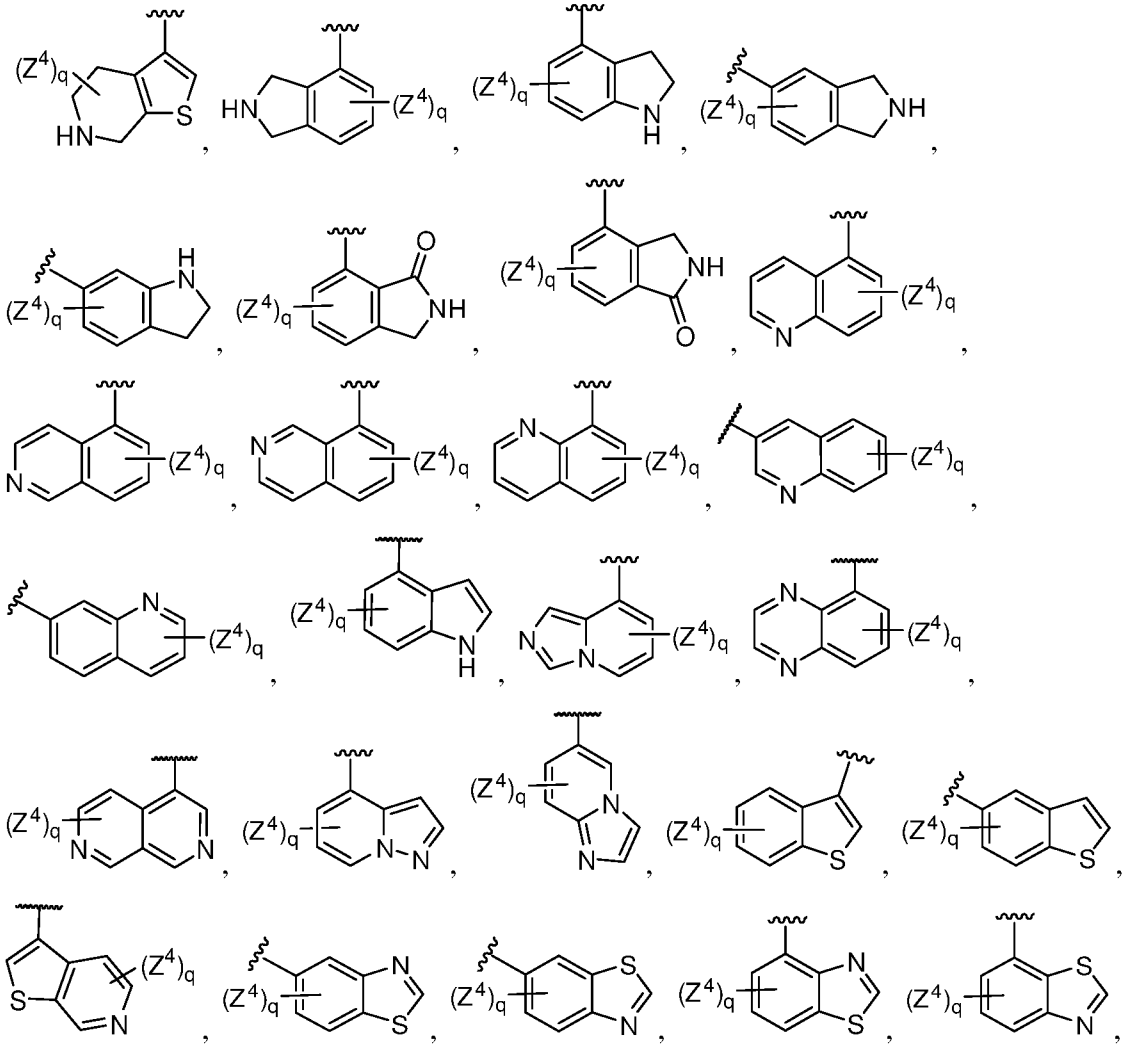
12. The compound of claim 1 or 2, wherein R^4 is heterocyclyl, or heteroaryl optionally substituted with one to three substituents independently selected from the group consisting of cyano, halo and C_{1-9} alkyl, or a pharmaceutically acceptable salt thereof.

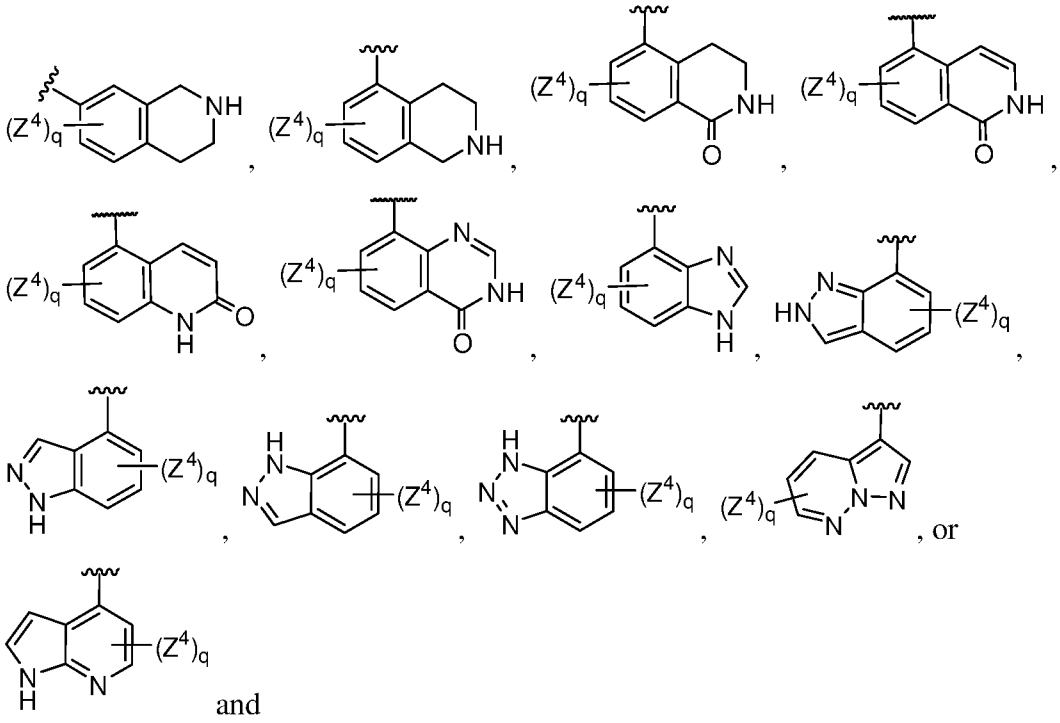
13. The compound of claim 1 or 2, wherein R^4 is heterocyclyl or heteroaryl; and said heterocyclyl or heteroaryl is optionally substituted with one to three substituents independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1 or 2, wherein R^4 is heteroaryl optionally substituted with one to three substituents independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

15. The compound of claim 1 or 2, wherein R^4 is heterocyclyl optionally substituted with one to three substituents independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl, or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1 or 2, wherein R^4 is





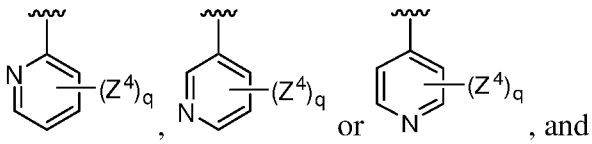
and

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

wherein Z^4 is independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl,

or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1 or 2, wherein R^4 is



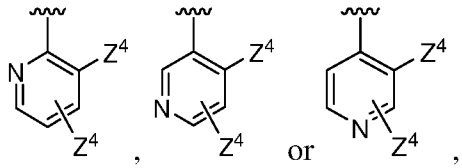
, and

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

wherein Z^4 is independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl,

or a pharmaceutically acceptable salt thereof.

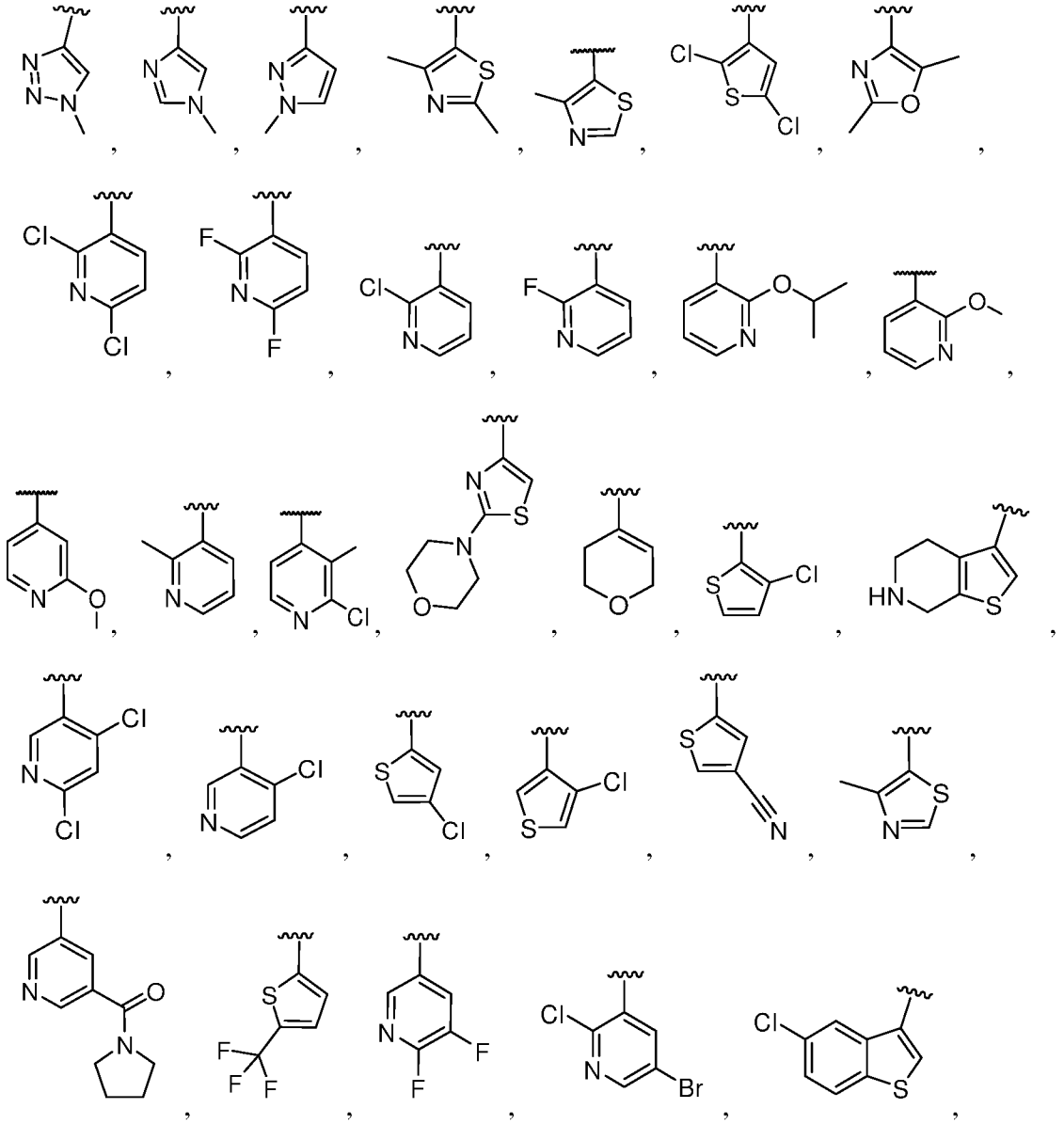
18. The compound of claim 1 or 2, wherein R^4 is

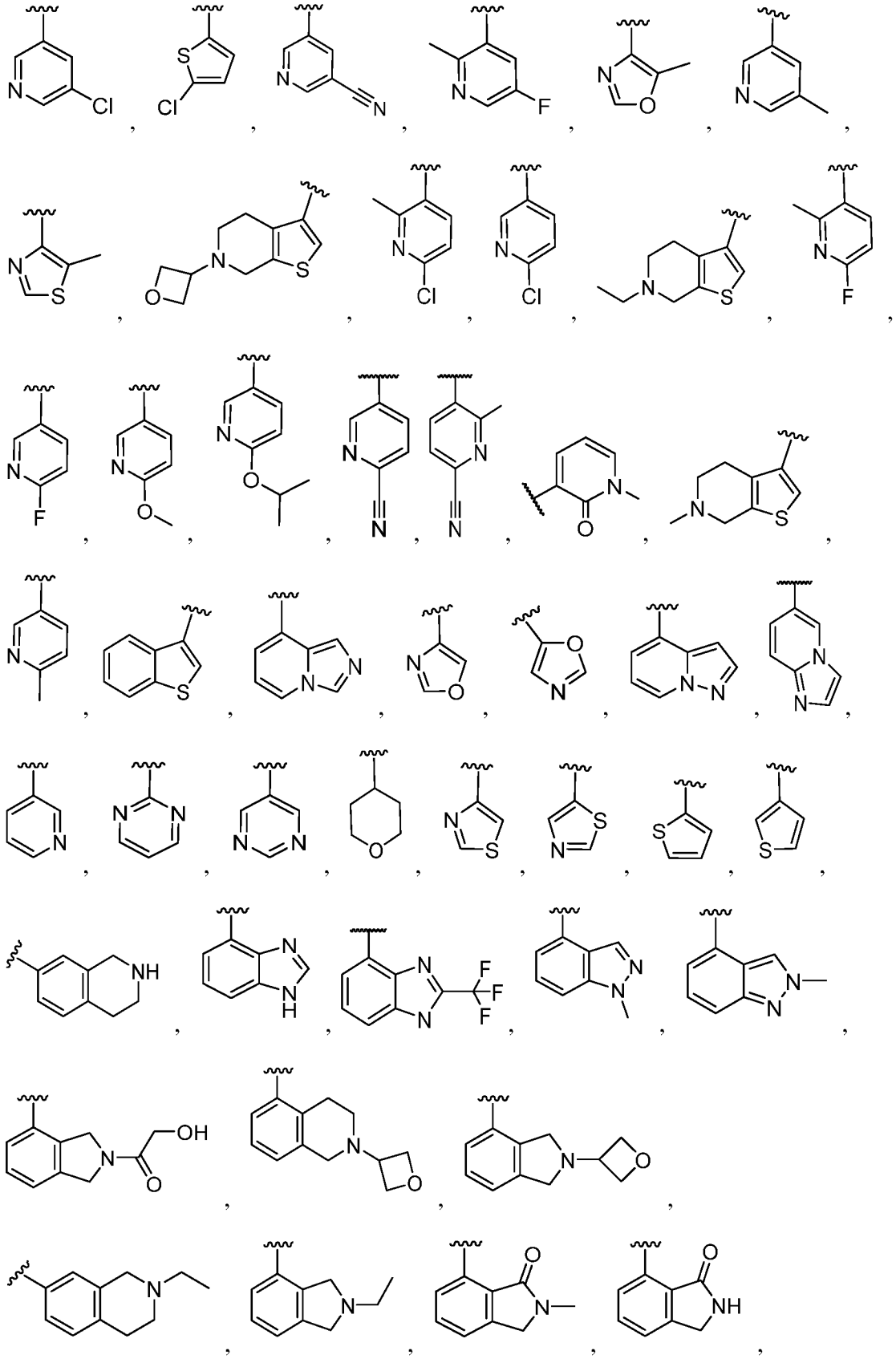


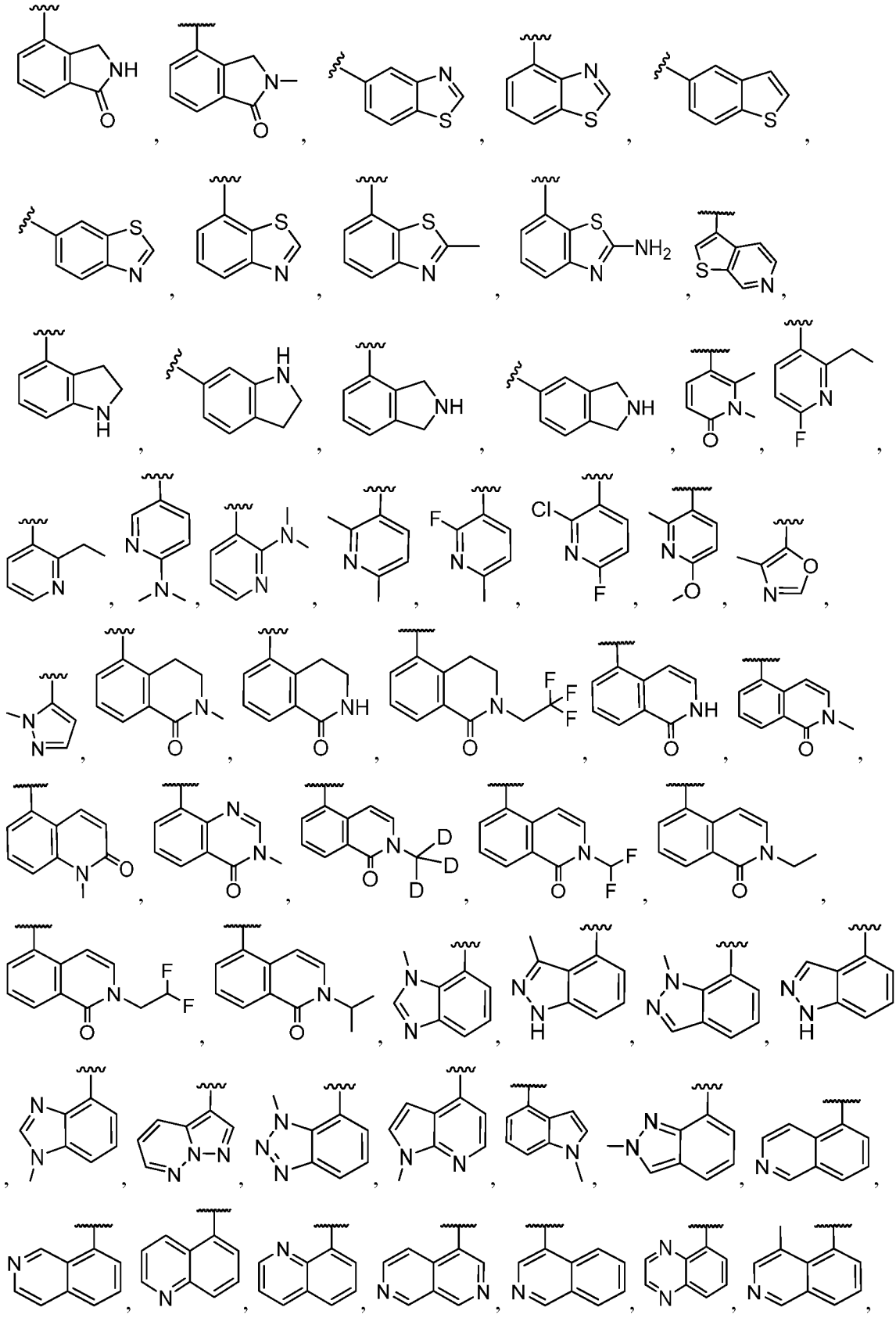
wherein Z^4 is independently selected from the group consisting of -CN, halo, -O-R^{12}, -C(O)-R^{12}, -N(R^{13})(R^{14}), C_{1-9} alkyl, C_{1-8} haloalkyl, and heterocyclyl,

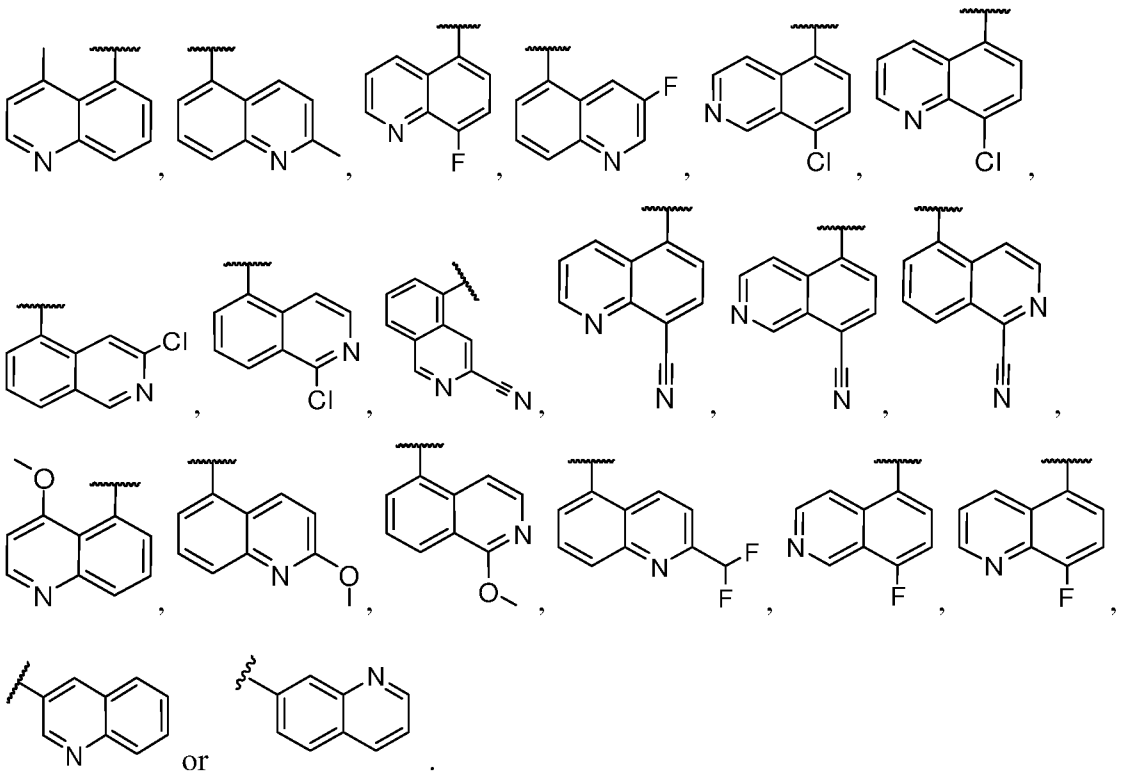
or a pharmaceutically acceptable salt thereof.

19. The compound of claim 1 or 2, wherein R^4 is









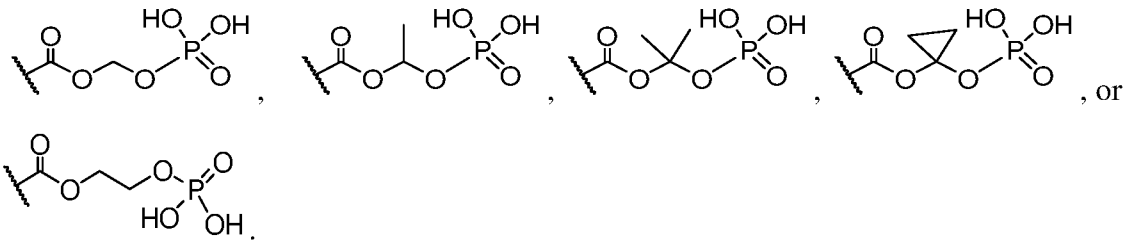
20. The compound of any preceding claim, wherein R^5 is hydrogen, cyano, or halo, or a pharmaceutically acceptable salt thereof.

21. The compound of any preceding claim, wherein R^5 is hydrogen, cyano, chloro, or bromo, or a pharmaceutically acceptable salt thereof.

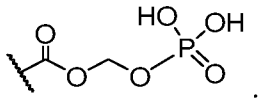
22. The compound of claim 1 or 2, wherein R^6 is $-C(O)O-R^{16}-OP(O)(OH)_2$.

23. The compound of claim 1 or 2, wherein R^{16} is C_{1-3} alkyl.

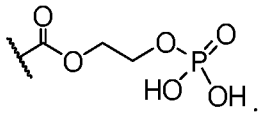
24. The compound of claim 1 or 2, wherein R^6 is



25. The compound of claim 1 or 2, wherein R^6 is

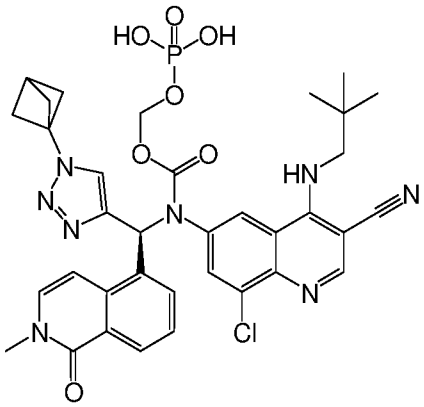


26. The compound of claim 1 or 2, wherein R^6 is



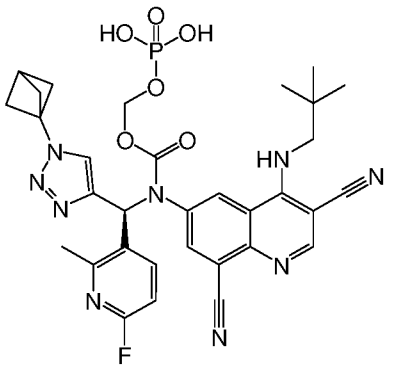
27. The compound of claim 1 or 2, wherein Z^9 is hydrogen.

28. The compound of claim 1 or 2, wherein the compound is



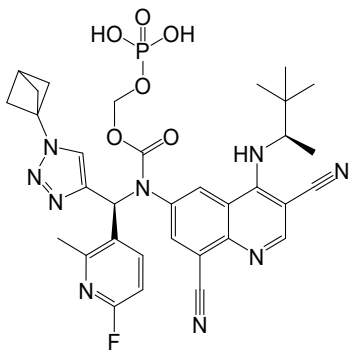
or a pharmaceutically acceptable salt thereof.

29. The compound of claim 1 or 2, wherein the compound is



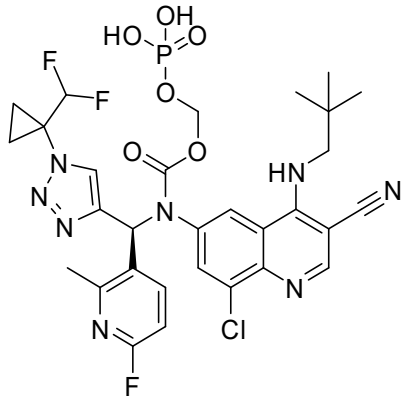
or a pharmaceutically acceptable salt thereof.

30. The compound of claim 1 or 2, wherein the compound is



or a pharmaceutically acceptable salt thereof.

31. The compound of claim 1 or 2, wherein the compound is



or a pharmaceutically acceptable salt thereof.

32. A composition comprising a compound of any of the preceding claims.

33. The use of a compound or composition according to any one of claims 1-32 in the manufacture of a medicament.

34. The use of a compound or composition according to any one of claims 1-32 in the manufacture of a medicament for the treatment of a disease or condition mediated by cancer Osaka thyroid (Cot) in a human patient.

35. The use according to claim 34 wherein said disease or condition is selected from cancer, diabetes, inflammatory disease and inflammatory bowel disease (IBD).

36. The use according to 34, wherein the disease or condition is a liver disease.

37. The use according to claim 35 wherein said disease or condition is a solid tumor selected from pancreatic cancer, bladder cancer, colorectal cancer, breast cancer, prostate cancer, renal cancer, hepatocellular cancer, lung cancer, ovarian cancer, cervical cancer, gastric cancer, esophageal cancer, head and neck cancer, melanoma, neuroendocrine cancers, CNS cancers, brain tumors (e.g., glioma, anaplastic oligodendroglioma, adult glioblastoma multiforme, and adult anaplastic astrocytoma), bone cancer, and soft tissue sarcoma.

38. The use according to claim 35 wherein said disease or condition is selected from type 1 and type 2 diabetes, gestational diabetes, prediabetes, insulin resistance, metabolic syndrome, impaired fasting glycaemia and impaired glucose tolerance.

39. The use according to claim 35 wherein said disease or condition is selected from systemic lupus erythematosus (SLE), myestenia gravis, rheumatoid arthritis (RA), acute disseminated encephalomyelitis, idiopathic thrombocytopenic purpura, multiple sclerosis (MS), inflammatory bowel disease (IBD), sepsis, psoriasis, Sjoegren's syndrome, autoimmune hemolytic anemia, asthma, or chronic obstructive pulmonary disease (COPD), ankylosing spondylitis, reactive arthritis, monoarticular arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, juvenile onset rheumatoid arthritis, juvenile rheumatoid and psoriatic arthritis.

40. The use according to claim 35 wherein said disease or condition is selected from diversion colitis, ischemic colitis, infectious colitis, chemical colitis, microscopic colitis (including collagenous colitis and lymphocytic colitis), atypical colitis, pseudomembranous colitis, fulminant colitis, autistic enterocolitis, indeterminate colitis, Behçet's disease, gastroduodenal CD, jejunoileitis, ileitis, ileocolitis, Crohn's (granulomatous) colitis, irritable bowel syndrome, mucositis, radiation induced enteritis, short bowel syndrome, celiac disease, stomach ulcers, diverticulitis, pouchitis, proctitis, and chronic diarrhea.

41. The use according to claim 35 wherein said disease or condition is systemic lupus erythematosus (SLE), lupus nephritis, lupus-related, and autoimmune disorders or a symptom of SLE.

42. The use according to claim 34 wherein said disease or condition is a chronic intrahepatic or extrahepatic cholestatic condition, liver fibrosis, a chronic or obstructive inflammatory disorder of the liver,liver cirrhosis, liver steatosis or an associated syndrome, a cholestatic or fibrotic effect that is associated with alcohol-induced cirrhosis or with a viral-

borne form of hepatitis, acute or chronic liver failure, liver ischemia after major liver resection, chemotherapy associated steatohepatitis (CASH), Primary Biliary Cirrhosis (PBC), Primary Sclerosing Cholangitis (PSC), a neoplastic diease of the gastrointestinal tract or liver, diabetic kidney disease (DKD), Non-Alcoholic Fatty Liver Disease (NAFLD), or Non-Alcoholic Steatohepatitis (NASH).