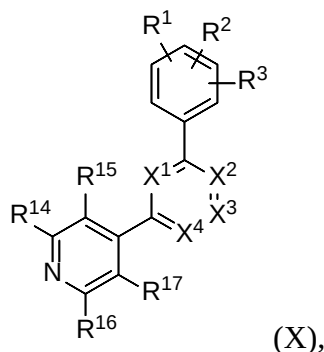


Claims:

Claim 1. A compound of Formula (X):



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

R¹ is -C(O)OR⁹, -C(O)NR⁸R⁹, -S(O)₂NR⁸R⁹, -NR¹⁰C(O)NR⁸R⁹, -NR¹⁰C(O)R⁹, -NR¹⁰S(O)₂R⁹, -OR²⁶, -SR⁹, -S(O)R⁹, -S(O)₂R⁹, -NR⁸R⁹, -NR¹⁰C(O)OR⁹, -C(O)R²⁶, -NR¹⁰S(O)₂NR⁸R⁹, -C(O)NR¹⁰S(O)₂R⁹, or -C(O)NR¹⁰NR⁸R⁹;

wherein each of R⁸, R⁹, and R¹⁰ is independently selected from the group consisting of hydrogen, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, (C₆₋₁₀)aryl, (C₆₋₁₀)aryl(C₁₋₁₀)alkyl, heteroaryl, and heteroaryl-alkyl,

R²⁶ is (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, (C₆₋₁₀)aryl, (C₆₋₁₀)aryl(C₁₋₁₀)alkyl, heteroaryl, or heteroaryl-alkyl,

each (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, (C₆₋₁₀)aryl, (C₆₋₁₀)aryl(C₁₋₁₀)alkyl, heteroaryl, and heteroaryl-alkyl of R⁸, R⁹, R¹⁰, and R²⁶ is independently unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, (C₁₋₁₀)alkyl, (C₁₋₁₀)haloalkyl, cyano, oxo, -OR¹⁹, -C(O)NR¹⁹R¹⁹, -NR¹⁹C(O)R¹⁹, -NR¹⁹C(O)NR¹⁹R¹⁹, -NR¹⁹R¹⁹, -S(O)₂NR¹⁹R¹⁹, -NR¹⁹S(O)₂R¹⁹, -S(O)_{n4}R²⁰, -C(O)OR¹⁹, -C(O)R²⁰, and -(OR³⁸)_{n15}OR¹⁹,

each R¹⁹ is independently hydrogen, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, or heterocycloalkyl; or two R¹⁹, together

with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R²⁰ is independently (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, or heterocycloalkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo,

each R³⁸ is independently (C₁₋₁₀)alkylene or (C₁₋₁₀)haloalkylene,

each n₁₅ is independently an integer from 1 to 5, and

n₄ is 0, 1, or 2;

or R⁸ and R⁹, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, (C₁₋₁₀)alkyl, (C₂₋₁₀)alkenyl, (C₂₋₁₀)alkynyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, (C₆₋₁₀)aryl, (C₆₋₁₀)aryl(C₁₋₁₀)alkyl, heteroaryl, heteroaryl-alkyl, -OR²³, -C(O)NR²³R²³, -NR²³C(O)R²³, -NR²³C(O)OR²³, -NR²³C(O)NR²³R²³, -NR²³R²³, -S(O)₂NR²³R²³, -NR²³S(O)₂R²⁴, -S(O)_{n₆}R²⁴, -C(O)OR²³, -C(O)R²⁴, and -(OR³⁹)_{n₁₆}OR²³,

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkyl-alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, aryl, aryl-alkyl, heteroaryl, and heteroaryl-alkyl is independently unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, oxo, alkyl, haloalkyl, -OR³¹, -C(O)NR³¹R³¹, -NR³¹C(O)R³¹, -NR³¹C(O)OR³¹, -NR³¹C(O)NR³¹R³¹, -NR³¹S(O)₂R³¹, and -S(O)_{n₉}R³¹, wherein each R³¹ is independently hydrogen, alkyl, or haloalkyl, and each n₉ is independently 0, 1, or 2,

each R²³ is independently hydrogen, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, or heterocycloalkyl; or two R²³, together

with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R^{24} is independently (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo,

each R^{39} is independently (C_{1-10}) alkylene or (C_{1-10}) haloalkylene,

each n_{16} is independently an integer from 1 to 5, and

n_6 is 0, 1, or 2;

R^2 and R^3 are independently selected from the group consisting of hydrogen, halo, cyano, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, $-OR^{25}$, $-C(O)NR^{25}R^{25}$, $-NR^{25}C(O)R^{25}$, $-NR^{25}C(O)NR^{25}R^{25}$, $-NR^{25}R^{25}$, $-S(O)_2NR^{25}R^{25}$, $-NR^{25}S(O)_2R^{25}$, $-S(O)_{n_7}R^{30}$, $-NR^{25}C(O)OR^{25}R^{25}$, $-C(O)OR^{25}$, and $-C(O)R^{30}$,

wherein each (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, and (C_{3-10}) cycloalkyl (C_{1-10}) alkyl is independently unsubstituted or substituted with one or more halo,

each R^{25} is independently hydrogen (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl; or two R^{25} , together with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R^{30} is independently (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo, and

n_7 is 0, 1, or 2;

X^1 , X^2 , X^3 and X^4 are independently CR^4 or N, wherein X^2 , X^3 and X^4 may not all be N;

when at least one of X^1 , X^2 , X^3 and X^4 is N, each R^4 is independently selected from the group consisting of hydrogen, halo, cyano, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, heterocycloalkyl connected by an annular carbon atom, heterocycloalkyl-alkyl, $-OR^{27}$, $-C(O)NR^{27}R^{27}$, $-S(O)_2NR^{27}R^{27}$, $-S(O)_{n8}R^{28}$, $-C(O)OR^{27}$, and $-C(O)R^{28}$,

wherein each (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, heterocycloalkyl, and heterocycloalkyl-alkyl is independently unsubstituted or substituted with one or more halo,

each R^{27} is independently hydrogen or (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl; or two R^{27} , together with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R^{28} is independently (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo,

$n8$ is 0, 1 or 2; or

when each of X^1 , X^2 , X^3 and X^4 is CR^4 , each R^4 is independently selected from the group consisting of hydrogen, halo, cyano, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, $-OR^{27}$, $-C(O)NR^{27}R^{27}$, $-NR^{27}C(O)R^{27}$, $-NR^{27}R^{27}$, $-NR^{27}S(O)_2R^{27}$, $-S(O)_2NR^{27}R^{27}$, $-S(O)_{n8}R^{28}$, $-C(O)OR^{27}$, and $-C(O)R^{28}$,

wherein each (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, heterocycloalkyl, and heterocycloalkyl-alkyl is independently unsubstituted or substituted with one or more halo,

each R^{27} is independently hydrogen, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, or heterocycloalkyl; or two R^{27} , together

with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R²⁸ is independently (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, or heterocycloalkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo, and

n₈ is 0, 1, or 2; or

two R⁴ on adjacent annular carbon atoms together with the carbon atoms to which they are attached may form a carbocyclyl or heterocyclyl,

wherein the carbocyclyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, cyano, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, -OR²⁷, -C(O)NR²⁷R²⁷, -NR²⁷C(O)R²⁷, -NR²⁷R²⁷, -S(O)₂NR²⁷R²⁷, -NR²⁷S(O)₂R²⁷, -S(O)_{n8}R²⁸, and -C(O)R²⁸,

or the heterocyclyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, cyano, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl connected by an annular carbon atom, heterocycloalkyl-alkyl, -OR²⁷, -C(O)NR²⁷R²⁷, -S(O)₂NR²⁷R²⁷, -S(O)_{n8}R²⁸, and -C(O)R²⁸,

each R²⁷ is independently hydrogen, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl; or two R²⁷, together with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each of the foregoing alkyl, cycloalkyl, or heterocycloalkyl moieties is independently unsubstituted or substituted with one or more halo,

each R²⁸ is independently (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, wherein each of the foregoing is independently unsubstituted or substituted with one or more halo, and

n₈ is 0, 1, or 2;

R¹⁵ and R¹⁷ are independently hydrogen, halo, alkyl, or -OR²⁹, wherein each R²⁹ is independently hydrogen, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, or (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, and each alkyl or cycloalkyl in R¹⁵ or R¹⁷, if present, is independently unsubstituted or substituted with one or more halo;

R¹⁴ is (C₁₋₁₀)alkyl, (C₁₋₁₀)alkenyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkenyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl connected through an annular carbon atom, heterocycloalkenyl connected through an annular carbon atom, heterocycloalkyl-alkyl, -OR⁵, -C(O)NR⁵R⁵, -R⁵C(O)NR⁵R⁵, -S(O)₂NR⁵R⁵, -S(O)_{n1}R⁶, or -C(O)R⁶;

R¹⁶ is hydrogen, fluoro, (C₁₋₁₀)alkyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl connected through an annular carbon atom, heterocycloalkyl-alkyl, -OR⁵, -C(O)NR⁵R⁵, -R⁵C(O)NR⁵R⁵, -S(O)₂NR⁵R⁵, -S(O)_{n1}R⁶, or -C(O)R⁶;

wherein the (C₁₋₁₀)alkyl, (C₁₋₁₀)alkenyl, (C₃₋₁₀)cycloalkyl, (C₃₋₁₀)cycloalkenyl, (C₃₋₁₀)cycloalkyl(C₁₋₁₀)alkyl, heterocycloalkyl, heterocycloalkenyl, or heterocycloalkyl-alkyl of R¹⁴ or R¹⁶ is independently unsubstituted or substituted with one or more substituents independently selected from the group consisting of (C₁₋₁₀)alkyl, cycloalkyl, heterocycloalkyl, halo, cyano, oxo, -OR⁷, -C(O)OR⁷, -C(O)NR⁷R⁷, -NR⁷C(O)R⁷, -NR⁷C(O)NR⁷R⁷, -NR⁷R⁷, -S(O)₂NR⁷R⁷, -NR⁷S(O)₂R⁷, -S(O)_{n2}R¹³, and -C(O)R¹³;

wherein each alkyl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with one or more substituents selected from the group consisting of halo, cycloalkyl, halocycloalkyl, heterocycloalkyl, haloheterocycloalkyl, and -(OR³³)_{n10}OR³², wherein each n₁₀ is independently an integer from 0 to 5, each R³² is independently hydrogen, (C₁₋₁₀)alkyl or (C₁₋₁₀)haloalkyl, and each R³³ is independently (C₁₋₁₀)alkylene or (C₁₋₁₀)haloalkylene;

each R⁵ is independently hydrogen, (C₁₋₁₀)alkyl, or (C₃₋₁₀)cycloalkyl; or two R⁵, together with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each alkyl, cycloalkyl, or heterocycloalkyl is independently unsubstituted or substituted with one or more substituents selected from the group consisting of halo, cyano, oxo, alkyl, haloalkyl, -C(O)OR³⁴, -C(O)NR³⁴R³⁴, -NR³⁴C(O)R³⁴, -NR³⁴C(O)NR³⁴R³⁴, -NR³⁴R³⁴,

$-\text{S}(\text{O})_2\text{NR}^{34}\text{R}^{34}$, $-\text{NR}^{34}\text{S}(\text{O})_2\text{R}^{34}$, $-\text{S}(\text{O})_{n11}\text{R}^{34}$, $-\text{C}(\text{O})\text{R}^{34}$, and $-(\text{OR}^{35})_{n12}\text{OR}^{34}$, wherein each R^{34} is independently hydrogen, (C_{1-10}) alkyl, or (C_{1-10}) haloalkyl; each $n11$ is independently 0, 1, or 2; each $n12$ is independently an integer from 0 to 5; and each R^{35} is independently (C_{1-10}) alkylene or (C_{1-10}) haloalkylene;

each R^6 is independently (C_{1-10}) alkyl or (C_{3-10}) cycloalkyl, wherein each alkyl or cycloalkyl is independently unsubstituted or substituted with one or more halo;

each $n1$ is independently 0, 1, or 2;

each R^7 is independently hydrogen, unsubstituted (C_{1-10}) alkyl, or (C_{1-10}) alkyl substituted with one or more halo;

each $n2$ is independently 0, 1, or 2,

and each R^{13} is independently unsubstituted (C_{1-10}) alkyl or (C_{1-10}) alkyl substituted with one or more halo;

or R^{14} and R^{15} , together with the atoms to which they are attached, form a carbocyclyl or heterocyclyl,

wherein the carbocyclyl or heterocyclyl is unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, cyano, oxo, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, (C_{3-10}) cycloalkyl (C_{1-10}) alkyl, $-\text{OR}^{18}$, $-\text{C}(\text{O})\text{NR}^{18}\text{R}^{18}$, $-\text{NR}^{18}\text{C}(\text{O})\text{R}^{18}$, $-\text{NR}^{18}\text{C}(\text{O})\text{NR}^{18}\text{R}^{18}$, $-\text{NR}^{18}\text{R}^{18}$, $-\text{S}(\text{O})_2\text{NR}^{18}\text{R}^{18}$, $-\text{NR}^{18}\text{S}(\text{O})_2\text{R}^{18}$, $-\text{S}(\text{O})_{n3}\text{R}^{21}$, $-\text{C}(\text{O})\text{OR}^{18}$, and $-\text{C}(\text{O})\text{R}^{21}$,

wherein each (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, and (C_{3-10}) cycloalkyl (C_{1-10}) alkyl is independently unsubstituted or substituted with one or more substituents independently selected from the group consisting of halo, alkyl, haloalkyl, cyano, oxo, $-\text{C}(\text{O})\text{OR}^{36}$, $-\text{C}(\text{O})\text{NR}^{36}\text{R}^{36}$, $-\text{NR}^{36}\text{C}(\text{O})\text{R}^{36}$, $-\text{NR}^{36}\text{C}(\text{O})\text{NR}^{36}\text{R}^{36}$, $-\text{NR}^{36}\text{R}^{36}$, $-\text{S}(\text{O})_2\text{NR}^{36}\text{R}^{36}$, $-\text{NR}^{36}\text{S}(\text{O})_2\text{R}^{36}$, $-\text{S}(\text{O})_{n13}\text{R}^{36}$, $-\text{C}(\text{O})\text{R}^{36}$, and $-(\text{OR}^{37})_{n14}\text{OR}^{36}$, wherein each R^{36} is independently hydrogen, (C_{1-10}) alkyl, or (C_{1-10}) haloalkyl; each $n13$ is independently 0, 1, or 2; each $n14$ is independently an integer from 0 to 5; and each R^{37} is independently (C_{1-10}) alkylene or (C_{1-10}) haloalkylene;

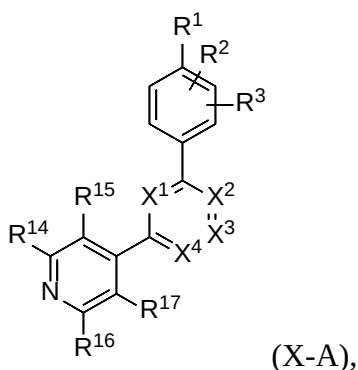
wherein each R¹⁸ is independently hydrogen, (C₁₋₁₀)alkyl, or (C₃₋₁₀)cycloalkyl; or two R¹⁸, together with the nitrogen atom to which they are attached, form a heterocycloalkyl; wherein each alkyl, cycloalkyl, or heterocycloalkyl is independently unsubstituted or substituted with one or more halo;

each R²¹ is independently (C₁₋₁₀)alkyl or (C₃₋₁₀)cycloalkyl, wherein each alkyl or cycloalkyl is independently unsubstituted or substituted with one or more halo;

and

each n₃ is independently 0, 1, or 2.

Claim 2. The compound of claim 1, wherein the compound is of Formula (X-A):



or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R¹, R², R³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, X¹, X², X³, and X⁴ are as defined for Formula (X).

Claim 3. The compound of any one of claims 1 or 2, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R¹ is -C(O)NR⁸R⁹, -S(O)₂NR⁸R⁹, -NR¹⁰C(O)OR⁹, -NR¹⁰S(O)₂R⁹, or -NR¹⁰S(O)₂NR⁸R⁹.

Claim 4. The compound of any one of claims 1 to 3 [[7]], or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R¹ is -C(O)NR⁸R⁹, -NR¹⁰C(O)OR⁹, or -NR¹⁰S(O)₂R⁹.

Claim 5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R⁸ is hydrogen.

Claim 6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^9 is hydrogen, (C_{1-10}) alkyl, (C_{3-10}) cycloalkyl, or heterocycloalkyl-alkyl.

Claim 7. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^1 is $-C(O)NR^8R^9$, and the R^8 and R^9 together with the nitrogen to which they are attached form an unsubstituted or substituted heterocycloalkyl.

Claim 8. The compound of claim 7, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein the heterocycloalkyl is substituted and the substituents are independently selected from the group consisting of halo, oxo, (C_{1-10}) alkyl, $-OR^{23}$, $-C(O)OR^{23}$, and $-NR^{23}C(O)OR^{23}$, wherein each (C_{1-10}) alkyl is unsubstituted or substituted with $-OR^{31}$.

Claim 9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^2 is halo or alkyl.

Claim 10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein X^1 , X^2 , and X^4 are CR^4 , and X^3 is N.

Claim 11. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein each of X^1 , X^2 , X^3 and X^4 is CR^4 .

Claim 12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^{14} is (C_{1-10}) alkyl unsubstituted or substituted with one to three substituents selected from the group consisting of (C_{1-10}) alkyl, halo, $-C(O)OR^7$, oxo, and $-OR^5$.

Claim 13. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^{14} is unsubstituted (C_{3-10}) cycloalkyl or (C_{3-10}) halocycloalkyl.

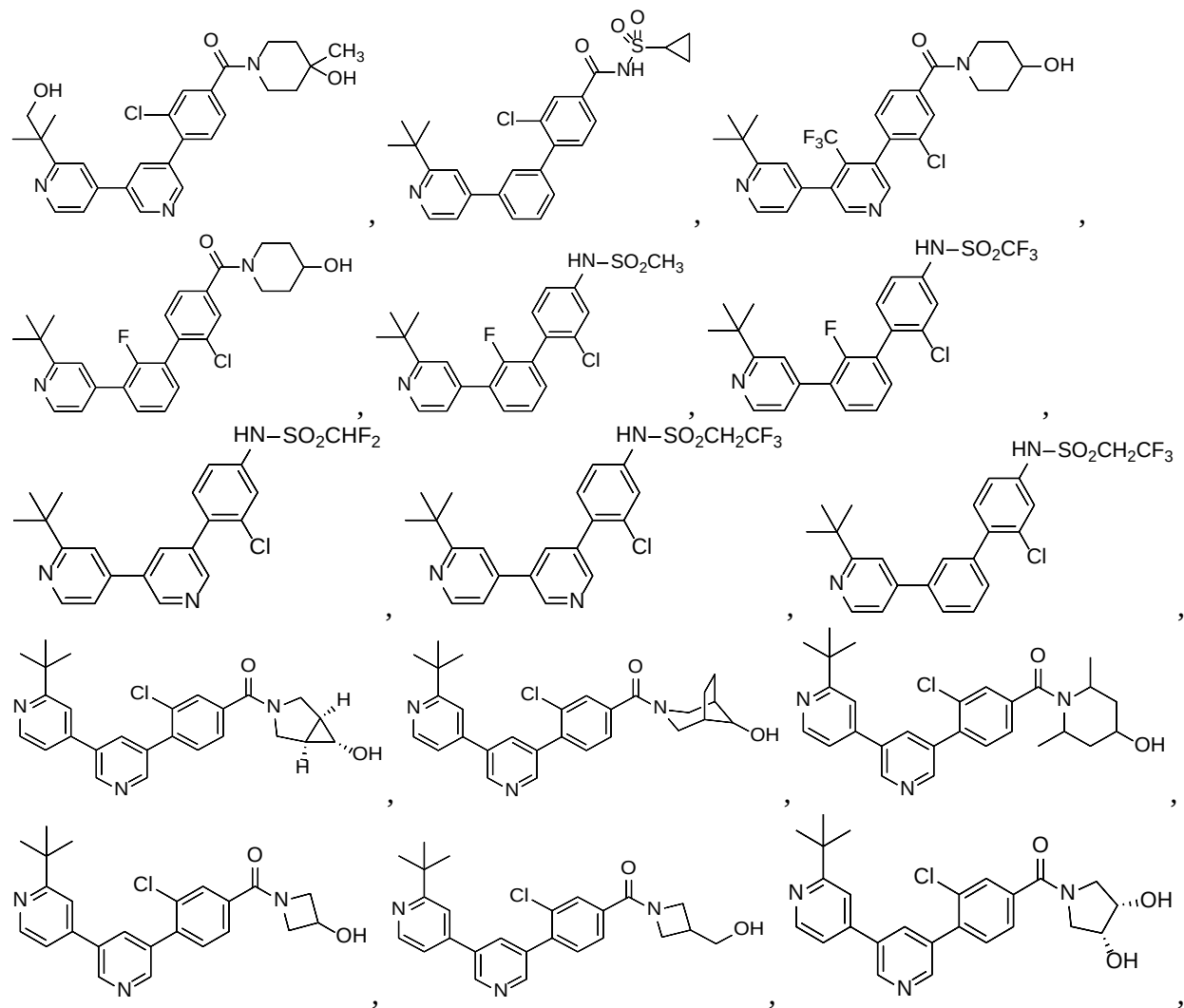
Claim 14. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R^{14} is $-OR^5$.

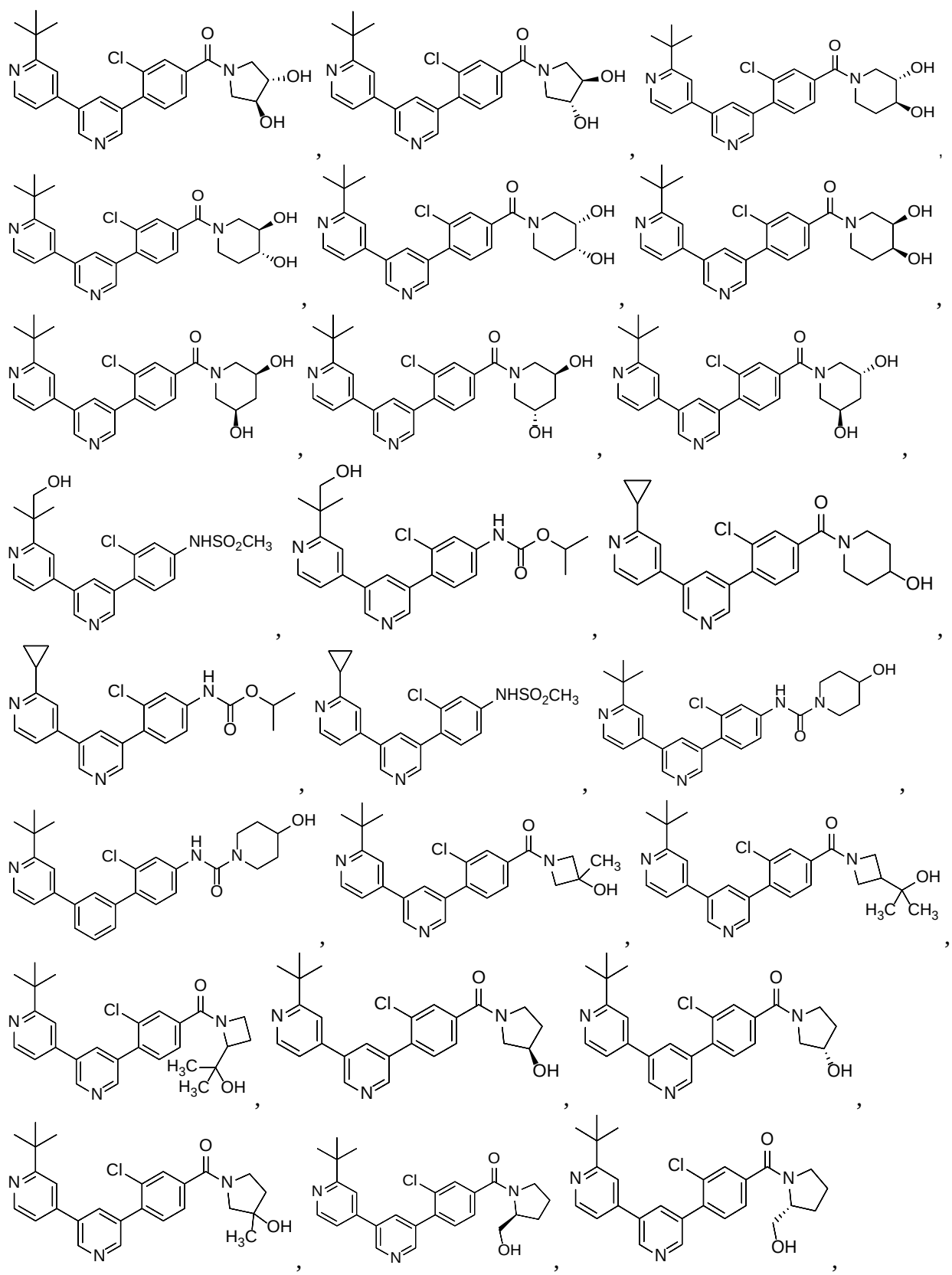
Claim 15. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R¹⁵, R¹⁶, and R¹⁷ are hydrogen.

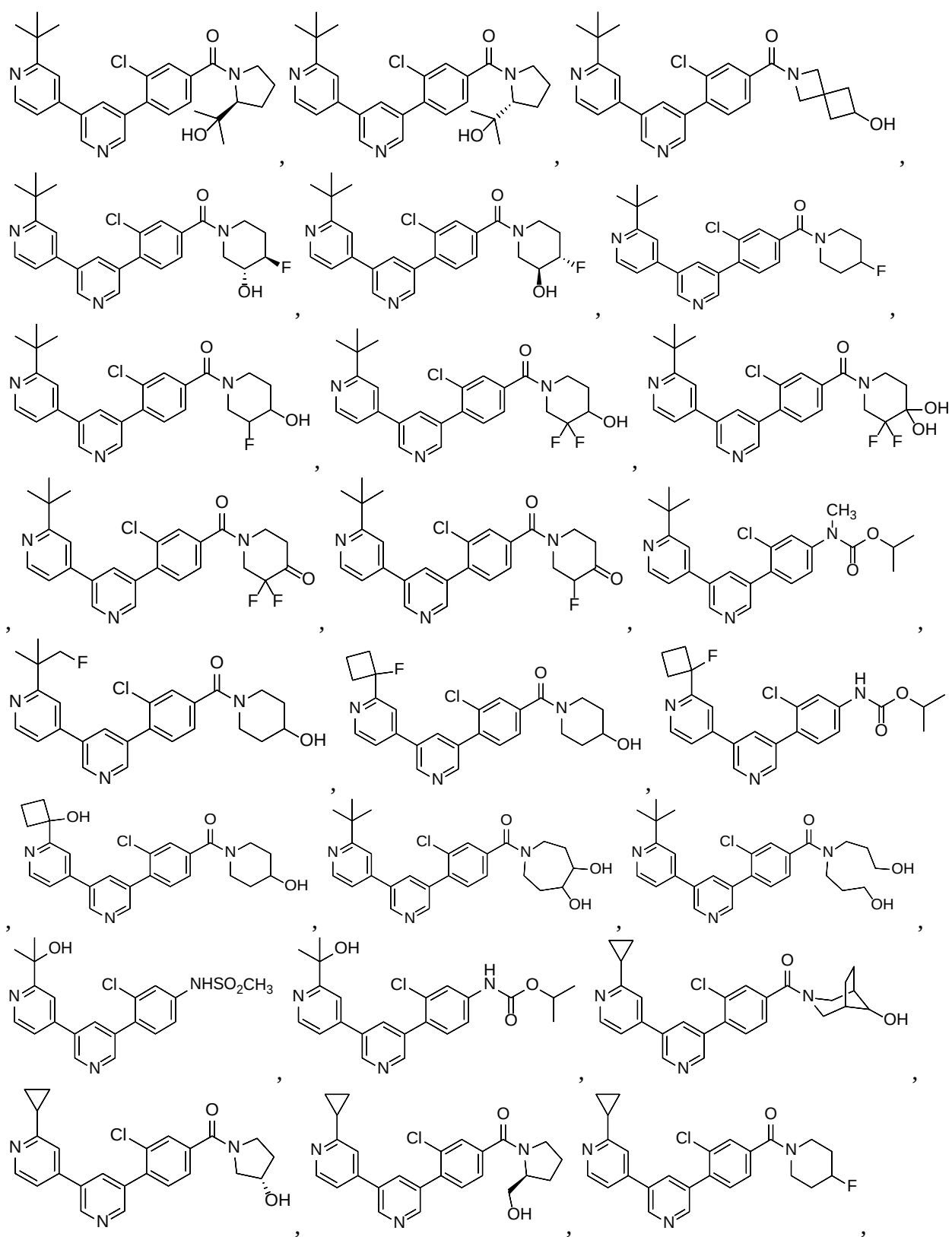
Claim 16. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R¹⁴ and R¹⁵, together with the atoms to which they are attached, form a heterocycl.

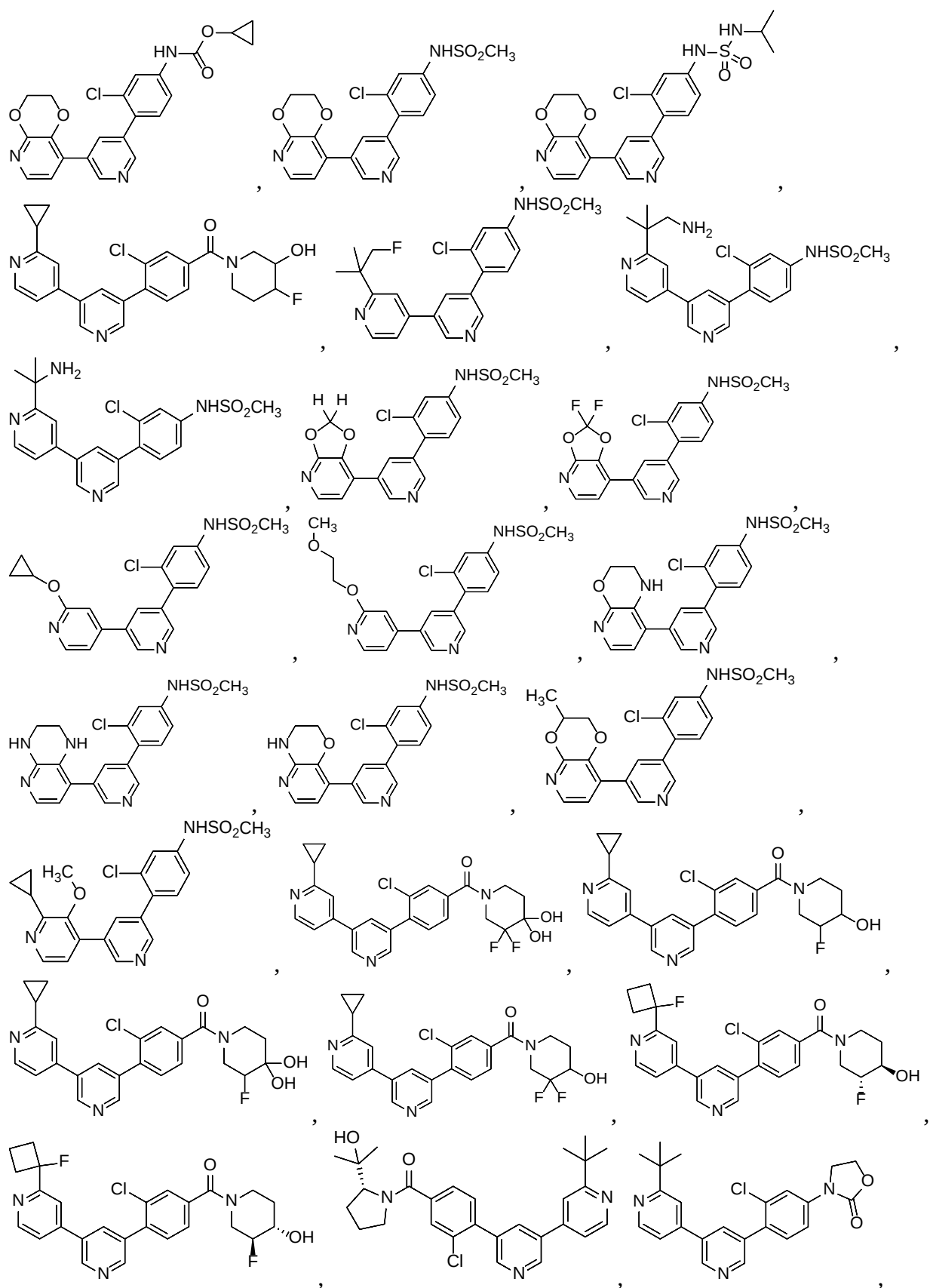
Claim 17. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, wherein R³ is hydrogen, halo, or alkyl.

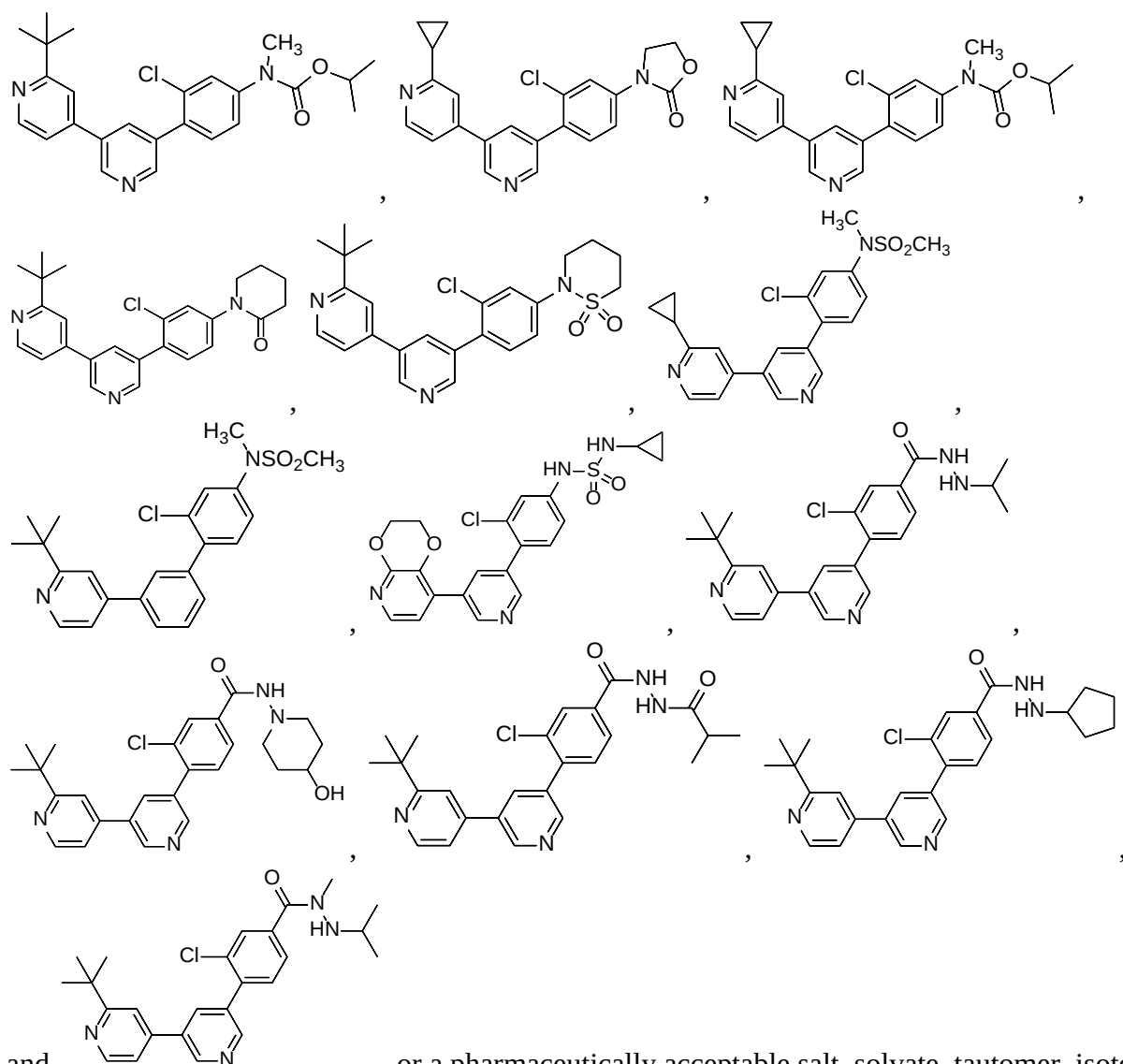
Claim 18. The compound of claim 1, selected from the group consisting of:

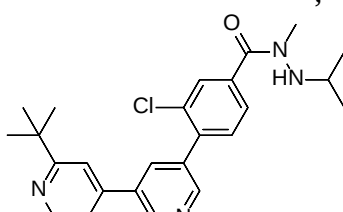




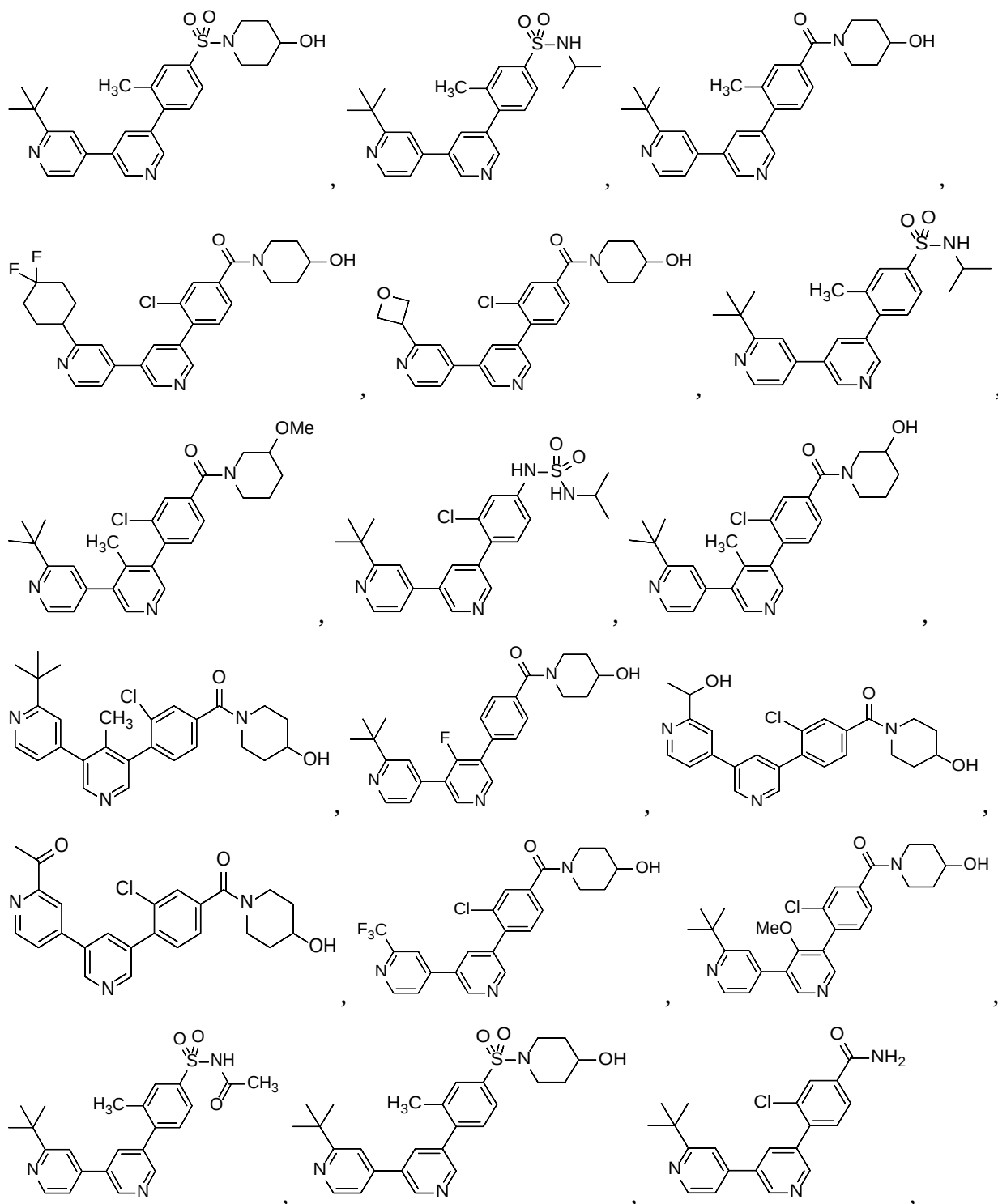


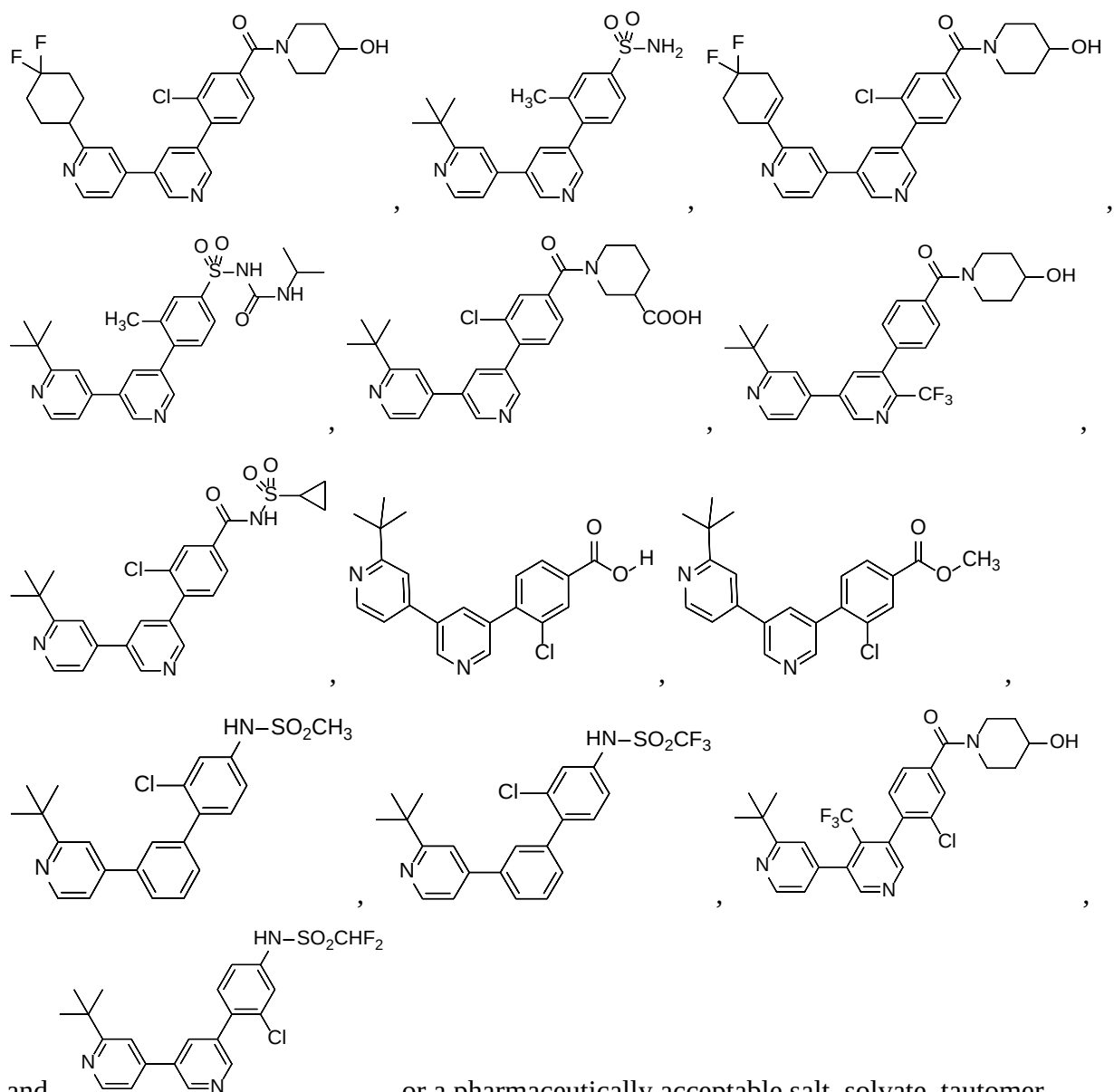




and , or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer of any of the foregoing.

Claim 19. The compound of claim 1, selected from the group consisting of:

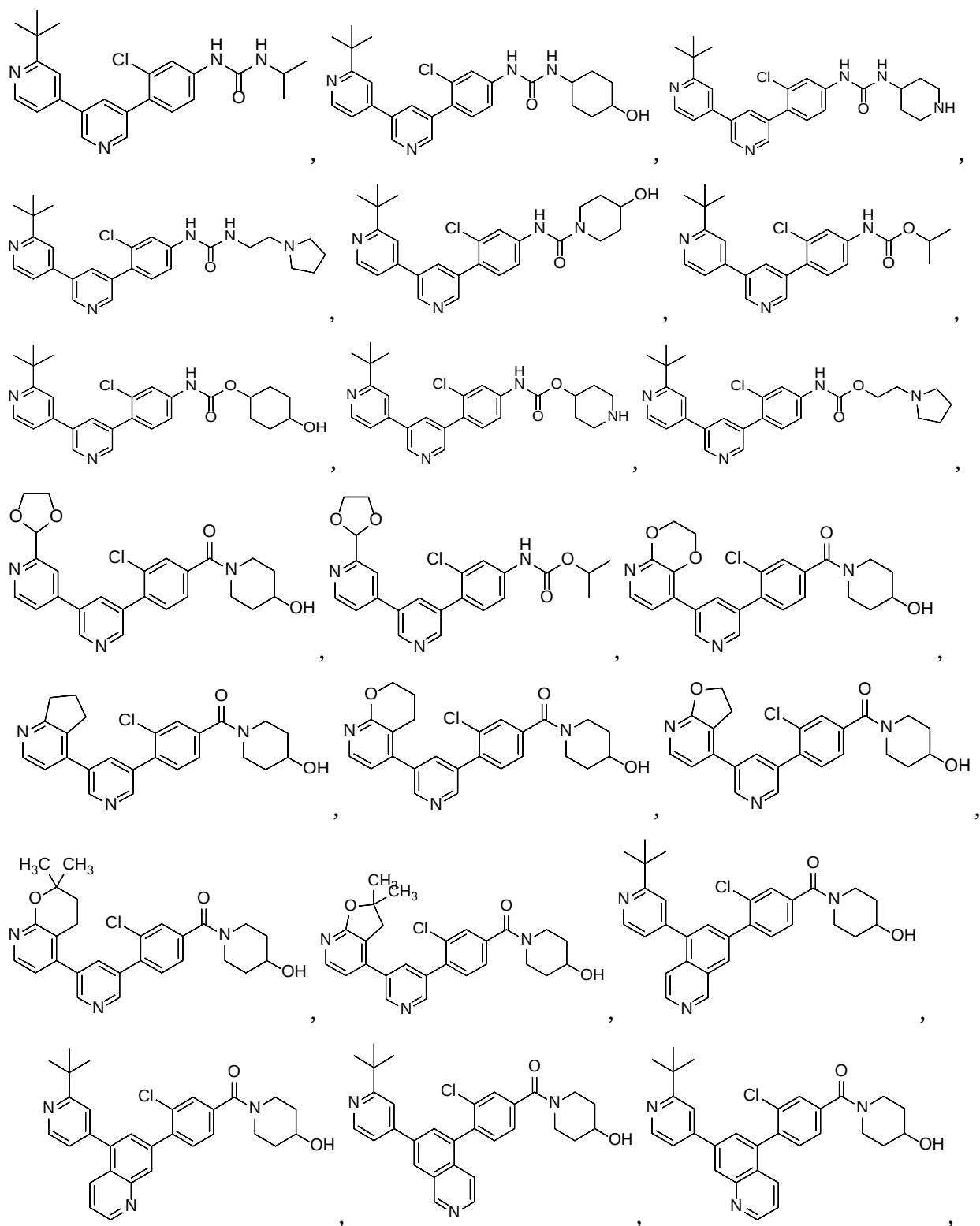


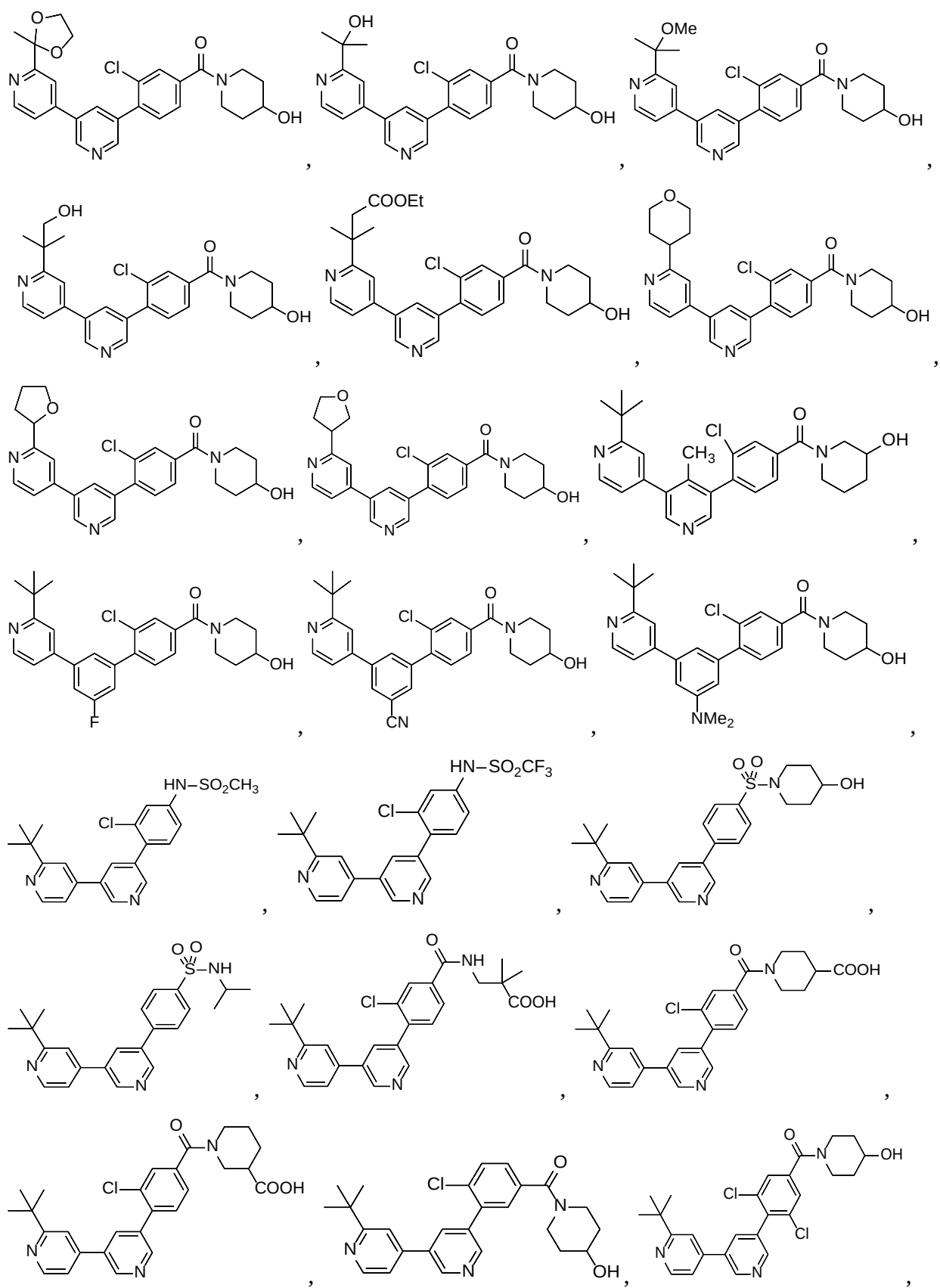


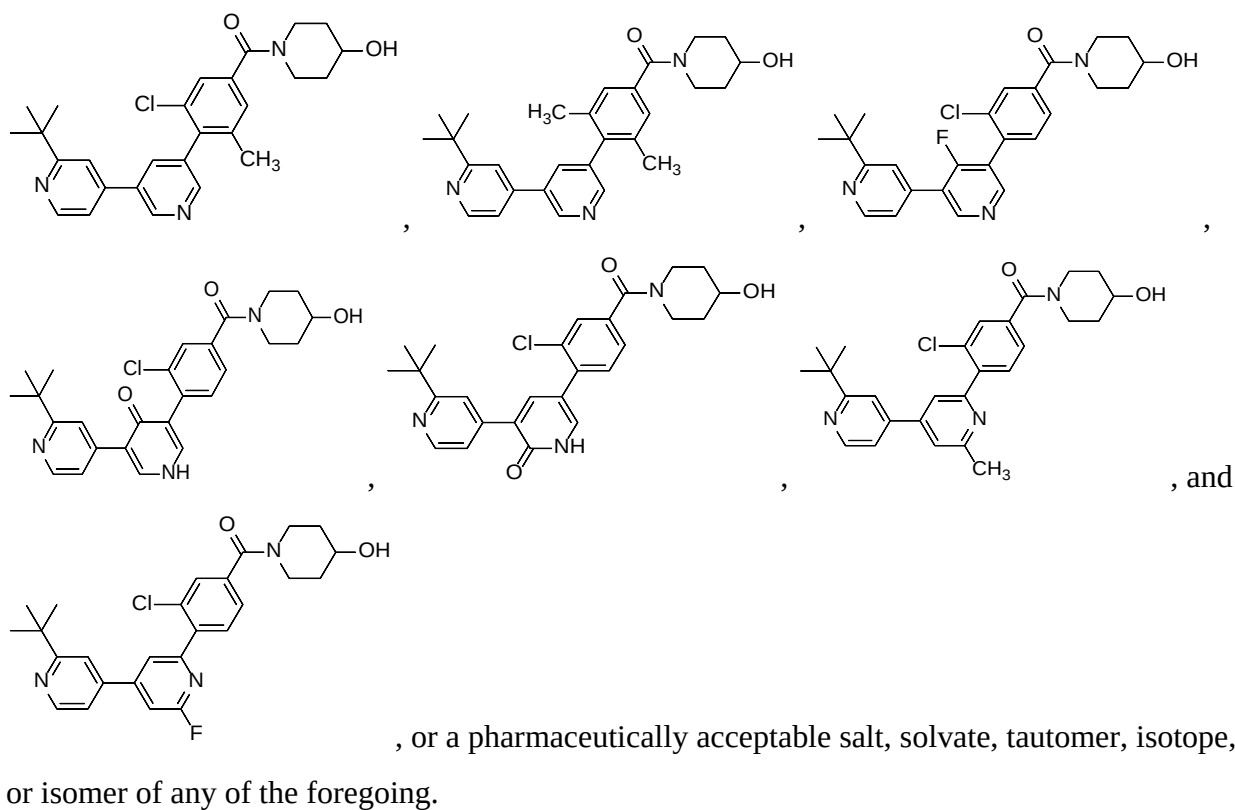
and , or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer of any of the foregoing.

Chemical structures of 12 compounds (1-12) are shown, all featuring a 4-chlorobenzoyl group linked to a 4-(4-(tert-butyl)pyridin-2-yl)pyridine moiety via a carbonyl group. The structures vary in the substitution pattern of the pyridine rings and the presence of a hydroxyl group on the piperidine ring.

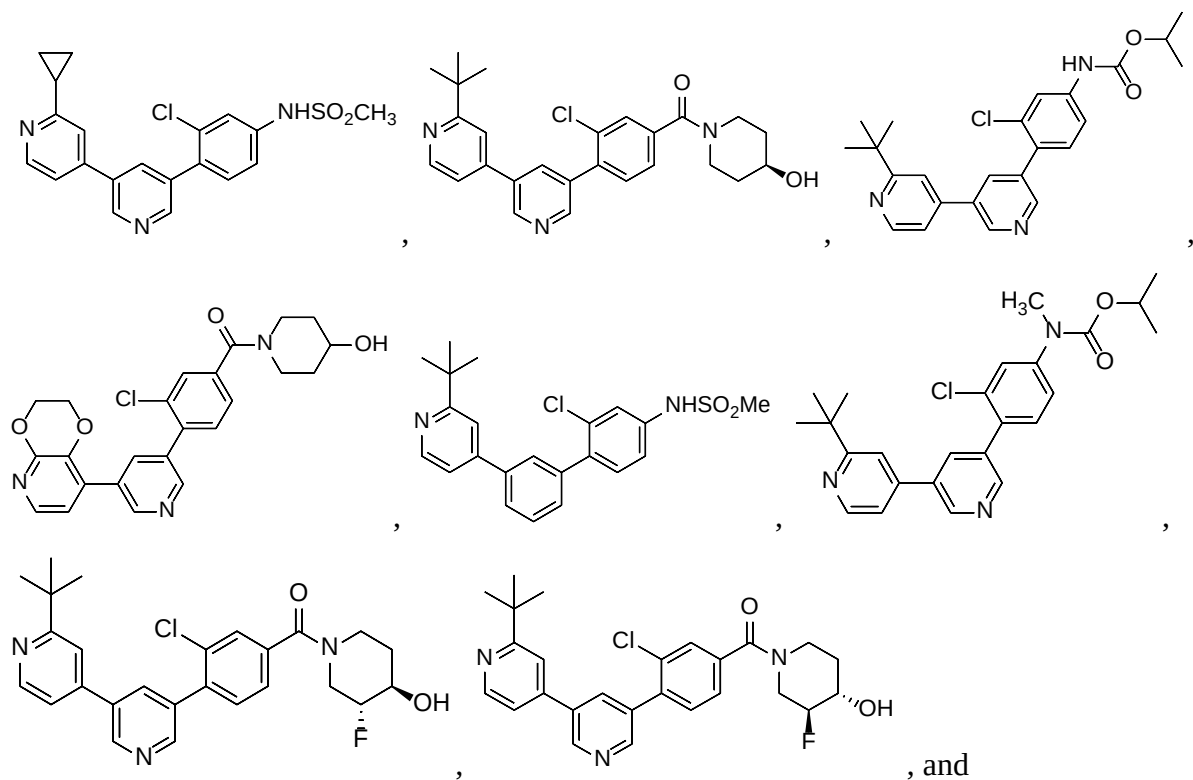
1. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
2. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
3. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
4. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
5. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
6. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
7. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
8. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
9. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
10. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
11. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).
12. 4-(4-(tert-butyl)pyridin-2-yl)pyridine-2-carboxamide, N-(4-hydroxypiperidin-1-yl).

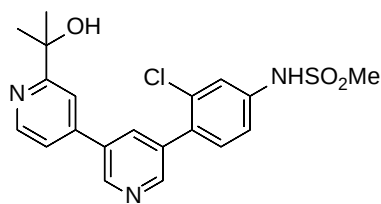






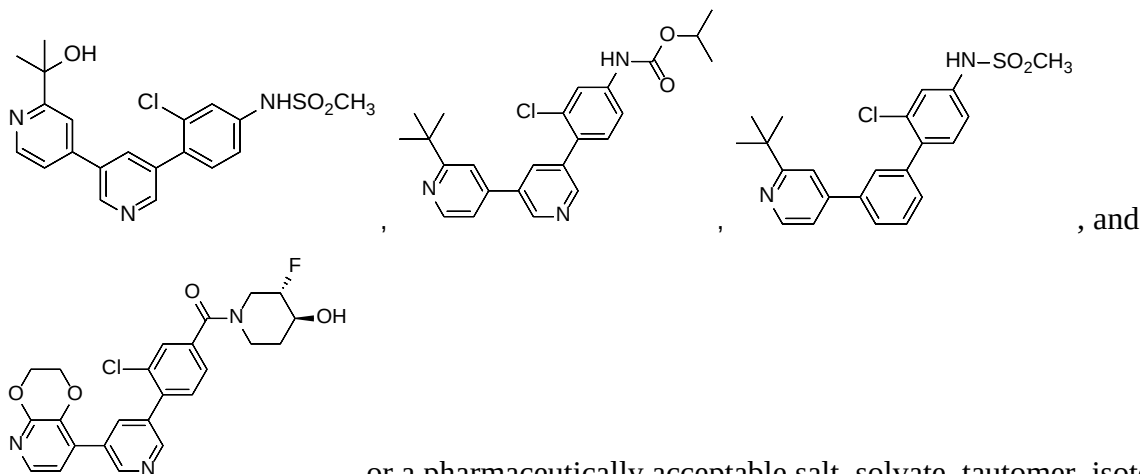
Claim 21. The compound of claim 1, selected from the group consisting of:





, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer of any of the foregoing.

Claim 22. The compound of claim 1, selected from the group consisting of:



, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer of any of the foregoing.

Claim 23. A pharmaceutical composition, comprising the compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, and a pharmaceutically acceptable excipient.

Claim 24. A compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, or the pharmaceutical composition of claim 23, for use in therapy.

Claim 25. A compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, or the pharmaceutical composition of claim 23, for use in treating a disorder in a subject in need thereof, wherein the disorder is Metabolic Syndrome, type 2 diabetes, obesity, liver disease, insulin resistance, adiposopathy, or dyslipidemia, endotoxic shock, systemic inflammation, atherosclerosis, non-alcoholic

steatohepatitis (NASH), or a hyperproliferative disorder mediated by a sterol regulatory element-binding protein (SREBP).

Claim 26. Use of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, or the pharmaceutical composition of claim 23 in the manufacture of a medicament for inhibiting a sterol regulatory element-binding protein (SREBP), wherein the medicament is formulated to contact the SREBP or to contact an SREBP cleavage activating-protein (SCAP).

Claim 27. Use of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, or the pharmaceutical composition of claim 23 in the manufacture of a medicament for inhibiting the proteolytic activation of a sterol regulatory element-binding protein (SREBP), wherein the medicament is formulated to contact an SREBP cleavage activating-protein (SCAP).

Claim 28. Use of an effective amount of a compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt, solvate, tautomer, isotope, or isomer thereof, or the pharmaceutical composition of claim 23 in the manufacture of a medicament for the treatment of a disorder in a subject in need thereof, wherein the disorder is Metabolic Syndrome, type 2 diabetes, obesity, liver disease, insulin resistance, adiposopathy, or dyslipidemia, endotoxic shock, systemic inflammation, atherosclerosis, non-alcoholic steatohepatitis (NASH), or a hyperproliferative disorder mediated by a sterol regulatory element-binding protein (SREBP), and wherein the medicament is to be administered to the subject in need thereof.