

SOMATOSTATIN MODULATORS AND USES THEREOF

CROSS-REFERENCE

[0001] This application claims benefit of U.S. Provisional Patent Application No. 62/362,493, filed on July 14, 2016; and U.S. Provisional Patent Application No. 62/411,338, filed on October 21, 2016; each of which is incorporated herein by reference in its entirety.

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with the support of the United States government under SBIR Grant No. 1R44NS092231-01 by the National Institutes of Health.

FIELD OF THE INVENTION

[0003] Described herein are compounds that are somatostatin modulators, methods of making such compounds, pharmaceutical compositions and medicaments comprising such compounds, and methods of using such compounds in the treatment of conditions, diseases, or disorders that would benefit from modulating somatostatin activity.

BACKGROUND OF THE INVENTION

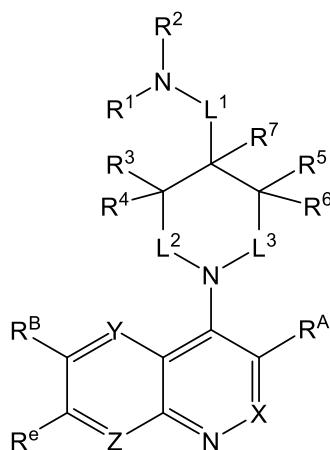
[0004] Somatostatin is a peptide hormone that regulates the endocrine system and affects neurotransmission and cell proliferation via interaction with G-protein-coupled somatostatin receptors and inhibition of the release of numerous secondary hormones. Six subtype somatostatin receptor proteins have been identified (SSTR1, SSTR2a, SSTR2b, SSTR3, SSTR4, SSTR5) and are encoded by five different somatostatin receptor genes. Modulation of a particular subtype somatostatin receptor, or combination thereof, is attractive for the treatment of conditions, diseases, or disorders that would benefit from modulating somatostatin activity.

SUMMARY

[0005] Compounds described herein are somatostatin modulator compounds. In some examples, compounds described herein modulate one or more of the subtype somatostatin receptor proteins. In some examples, compounds described herein modulate two or more of the subtype somatostatin receptor proteins. Somatostatin peptide analogs, such as octreotide and pasireotide, formulated as depot injections, are routinely used to normalize hormone levels for the treatment of GH secreting adenomas, pancreatic neuroendocrine tumors, and carcinoid tumors. Unfortunately, these analogs are only effective in about half of acromegalic patients with GH adenomas, and patients with carcinoid tumors frequently become resistant to therapy due to internalization and desensitization of the SST2A receptor. In addition, these peptide drugs are extremely expensive and require frequent doctor's office visits for painful injections that can lead

to injection site reactions. Compounds described herein are molecules that are structurally different from peptide analogs. The compounds described herein are somatostatin modulators that are potent inhibitors of hormone secretion.

[0005a] In one aspect, the present disclosure refers to a compound that has the structure of Formula (A), or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof:



Formula (A)

wherein:

R^A is an unsubstituted or substituted ring A that is an unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, unsubstituted or substituted bicyclic carbocycle, or unsubstituted or substituted bicyclic heterocycle, wherein if ring A is substituted then ring A is substituted with m R^a and n R^b ;

each R^a and R^b is independently hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, or -C(=NOR¹⁵)R¹⁵;

m is 1 or 2; n is 0, 1 or 2;

or if one R^a and one R^b are on adjacent atoms of ring A then the adjacent R^a and R^b groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

R^B is an unsubstituted or substituted ring B that is an unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, unsubstituted or substituted bicyclic carbocycle, or unsubstituted or substituted bicyclic heterocycle, wherein if the ring B is substituted then the ring B is substituted with p R^c and q R^d ;

each R^c and R^d is independently hydrogen, halogen, unsubstituted or substituted

C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -C(=O)R¹⁵, -OC(=O)R¹⁵, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -OC(=O)N(R¹⁵)₂, -NR¹⁵C(=O)N(R¹⁵)₂, -NR¹⁵C(=O)OR¹⁴, -NR¹⁵C(=O)NR¹⁵OR¹⁴, -C(=O)NR¹⁵OR¹⁵, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, -C(=NOR¹⁵)R¹⁵, -N(R¹⁵)SO₂R¹⁴, -C(=O)NR¹⁵S(=O)₂R¹⁴, -S(=O)₂NR¹⁵C(=O)R¹⁴, -C(=NR¹⁵)N(R¹⁵)₂, -NR¹⁵C(=NR¹⁵)N(R¹⁵)₂, -NR¹⁵C(=CR¹⁴R¹⁵)N(R¹⁵)₂, -C(=O)NR¹⁵C(=NR¹⁵)N(R¹⁵)₂, or -C(=O)NR¹⁵C(=CR¹⁴R¹⁵)N(R¹⁵)₂;

p is 1 or 2; q is 0, 1 or 2;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

X is CR^f or N;

Y is CR^f or N;

Z is CR^f or N;

R^e is hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, or -SO₂N(R¹⁵)₂;

each R^f is independently hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, or -SO₂N(R¹⁵)₂;

R^1 and R^2 are independently hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_3 - C_6 cycloalkyl, or substituted or unsubstituted C_2 - C_6 heterocycloalkyl;

or R¹ and R² are taken together with the nitrogen atom to which they are attached to form ring C that is an unsubstituted or substituted *N*-containing C₂-C₈heterocycloalkyl;

R³ and R⁵ are each independently selected from the group consisting of hydrogen, halogen, -OH, -OR¹⁴, -SR¹⁴, -S(=O)R¹⁴, -S(=O)₂R¹⁴, -N(R¹⁵)₂, -CN, -C(=O)OR¹⁵, -C(=O)N(R¹⁵)₂, unsubstituted or substituted C₁-C₆ alkyl, unsubstituted or substituted C₁-C₆ heteroalkyl, and unsubstituted or substituted C₁-C₆fluoroalkyl;

or R³ and R⁵ are taken together to form a bond or C₁-C₂alkylene;

or R² and R⁵ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4-7 membered saturated *N*-containing heterocyclic ring;

R⁴ and R⁶ are each independently selected from the group consisting of hydrogen, unsubstituted or substituted C₁-C₆ alkyl, and unsubstituted or substituted C₁-C₆fluoroalkyl;

R⁷ is hydrogen, unsubstituted or substituted C₁-C₆alkyl, or unsubstituted or substituted C₁-C₆fluoroalkyl;

or R² and R⁷ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted *N*-containing C₂-C₈heterocycloalkyl;

L¹ is absent or -CR⁸R⁹-;

L² is -CR¹⁰R¹¹- or absent;

L³ is -(CR¹²R¹³)_t- or absent;

t is 1 or 2;

each R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ is independently selected from the group consisting of hydrogen, unsubstituted or substituted C₁-C₆alkyl, and unsubstituted or substituted C₁-C₆fluoroalkyl;

or R⁵ and R⁸ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;

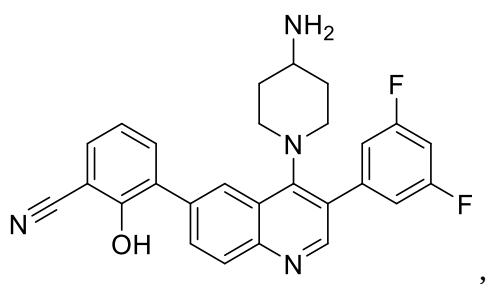
or R⁵ and R¹³ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;

or R⁷ and R⁸ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;

each R¹⁴ is independently selected from unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-

C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; and each R¹⁵ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or two R¹⁵ on the same N atom are taken together with the N atom to which they are attached to form an unsubstituted or substituted N-containing heterocycle; wherein each substituted alkyl, substituted fluoroalkyl, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of halogen, C₁-C₆alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -OR¹⁶, -CO₂R¹⁶, -C(=O)N(R¹⁶)₂, -N(R¹⁶)₂, -NR¹⁶C(=O)R¹⁷, -SR¹⁶, -S(=O)R¹⁷, -SO₂R¹⁷, and -SO₂N(R¹⁶)₂; each R¹⁶ is independently selected from hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl; or two R¹⁶ groups are taken together with the N atom to which they are attached to form a N-containing heterocycle; and each R¹⁷ is independently selected from C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl.

[0005b] In one aspect, the present disclosure refers to a compound that has the following structure:



or a pharmaceutically acceptable salt thereof.

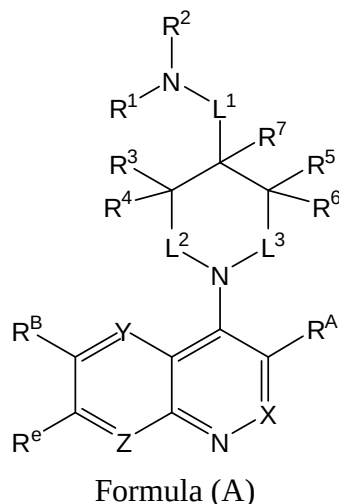
[0005c] In another aspect, the present disclosure refers to the compound as described herein, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, for use in therapy.

[0005d] In another aspect, the present disclosure refers to use of a compound as described herein, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, in the manufacture of a medicament for treating acromegaly, neuroendocrine tumor, or combinations thereof, in a mammal in need thereof.

[0005e] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, and at least one pharmaceutically acceptable excipient.

[0005f] In yet another aspect, the present disclosure refers to use of a compound as described herein, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, in the manufacture of a medicament for treating a disease or condition in a mammal that would benefit from the modulation of the somatostatin receptor subtype 2 (SSTR2) activity, wherein the disease or condition is acromegaly, neuroendocrine tumor, pain or combinations thereof, in a mammal in need thereof.

[0006] In one example, described herein is a compound of Formula (A), or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate, diastereomeric mixture, enantiomer or prodrug thereof:



wherein:

R^A is hydrogen, halogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₂-C₆alkenyl, unsubstituted or substituted C₂-C₆alkynyl, unsubstituted or substituted C₁-C₆heteroalkyl, or a unsubstituted or substituted ring A that is an unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted bicyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, or unsubstituted or substituted bicyclic heterocycle, wherein if the ring A is substituted then the ring A is substituted with m R^a and n R^b;

each R^a and R^b is independently hydrogen, halogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆fluoroalkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂ or -C(=NOR¹⁵)R¹⁵;

m is 1 or 2; n is 0, 1 or 2;

or if one R^a and one R^b are on adjacent atoms of ring A then the adjacent R^a and R^b groups are taken together with the intervening atoms to which they are attached to

or R⁵ and R¹³ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic or unsubstituted or substituted monocyclic heterocyclic ring;

or R⁷ and R⁸ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic or unsubstituted or substituted monocyclic heterocyclic ring;

each R¹⁴ is independently selected from unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

each R¹⁵ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

or two R¹⁵ on the same N atom are taken together with the N atom to which they are attached to form an unsubstituted or substituted N-containing heterocycle;

wherein each substituted alkyl, substituted fluoroalkyl, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of halogen, C₁-C₆alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -OR¹⁶, -CO₂R¹⁶, -C(=O)N(R¹⁶)₂, -N(R¹⁶)₂, -NR¹⁶C(=O)R¹⁷, -SR¹⁶, -S(=O)R¹⁷, -SO₂R¹⁷, or -SO₂N(R¹⁶)₂;

each R¹⁶ is independently selected from hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl; or two R¹⁶ groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

each R¹⁷ is independently selected from C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl.

[0007] In one example, the compound of Formula (A) has the structure of Formula (I), or a pharmaceutically acceptable salt, pharmaceutically acceptable solvate, diastereomeric mixture, enantiomer or prodrug thereof:

wherein each substituted alkyl, substituted fluoroalkyl, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of halogen, C₁-C₆alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -OR¹⁶, -CO₂R¹⁶, -C(=O)N(R¹⁶)₂, -N(R¹⁶)₂, -NR¹⁶C(=O)R¹⁷, -SR¹⁶, -S(=O)R¹⁷, -SO₂R¹⁷, or -SO₂N(R¹⁶)₂; each R¹⁶ is independently selected from hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl; or two R¹⁶ groups are taken together with the N atom to which they are attached to form a N-containing heterocycle; each R¹⁷ is independently selected from C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl and 6-membered heteroaryl.

[0008] Also described herein is a pharmaceutical composition comprising a compound described herein, or a pharmaceutically acceptable salt, or solvate thereof, and at least one pharmaceutically acceptable excipient. In some examples, the pharmaceutical composition is formulated for administration to a mammal by intravenous administration, subcutaneous administration, oral administration, inhalation, nasal administration, dermal administration, or ophthalmic administration. In some examples, the pharmaceutical composition is formulated for administration to a mammal by oral administration. In some examples, the pharmaceutical composition is in the form of a tablet, a pill, a capsule, a liquid, a suspension, a gel, a dispersion, a solution, an emulsion, an ointment, or a lotion. In some examples, the pharmaceutical composition is in the form of a tablet, a pill, or a capsule.

[0009] Also described herein is a method of treating a disease or condition in a mammal that would benefit from the modulation of somatostatin receptor activity comprising administering a small molecule non-peptidyl compound, or pharmaceutically acceptable salt, or solvate thereof, to the mammal in need thereof. In some examples, the small molecule non-peptidyl compound is orally administered. In some examples, the small molecule non-peptidyl compound is a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof. . In some examples, the small molecule non-peptidyl compound is a SSTR2 modulator as described herein, or a pharmaceutically acceptable salt or solvate thereof. In some examples, the disease or condition is acromegaly, a neuroendocrine tumor, an ophthalmic disease or condition, neuropathy, nephropathy, a respiratory disease or condition, cancer, pain, a neurodegenerative disease or condition, an inflammatory disease or condition, a psychiatric disease or condition, or combinations thereof.

[0010] In any of the aforementioned examples are further examples in which the effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is: (a) systemically administered to the mammal; and/or (b) administered orally to the mammal; and/or (c) intravenously administered to the mammal; and/or (d) administered by inhalation; and/or (e) administered by nasal administration; or and/or (f) administered by injection to the mammal; and/or (g) administered topically to the mammal; and/or (h) administered by ophthalmic administration; and/or (i) administered rectally to the mammal; and/or (j) administered non-systemically or locally to the mammal.

[0011] In any of the aforementioned examples are further examples comprising single administrations of the effective amount of the compound, including further examples in which the compound is administered once a day to the mammal or the compound is administered to the mammal multiple times over the span of one day. In some examples, the compound is administered on a continuous dosing schedule. In some examples, the compound is administered on a continuous daily dosing schedule.

[0012] In any of the examples disclosed herein, the mammal is a human.

[0013] In some examples, compounds provided herein are orally administered to a human.

[0014] Articles of manufacture, which include packaging material, a compound of Formula (I), or a pharmaceutically acceptable salt thereof, within the packaging material, and a label that indicates that the compound or composition, or pharmaceutically acceptable salt, tautomers, pharmaceutically acceptable N-oxide, pharmaceutically active metabolite, pharmaceutically acceptable prodrug, or pharmaceutically acceptable solvate thereof, is used for modulating one or more subtype somatostatin receptor proteins, or for the treatment, prevention or amelioration of one or more symptoms of a disease or condition that would benefit from modulating one or more subtype somatostatin receptor proteins, are provided.

[0015] Other objects, features and advantages of the compounds, methods and compositions described herein will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific examples, are given by way of illustration only, since various changes and modifications within the spirit and scope of the instant disclosure will become apparent to those skilled in the art from this detailed description.

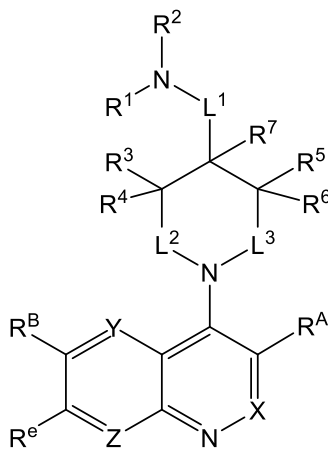
DETAILED DESCRIPTION OF THE INVENTION

[0016] Somatostatin (SST), also known as somatotropin release inhibiting factor (SRIF) was initially isolated as a 14-amino acid peptide from ovine hypothalamii (Brazeau *et al.*, *Science*

CLAIMS

WHAT IS CLAIMED IS:

1. A compound that has the structure of Formula (A), or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof:



Formula (A)

wherein:

R^A is an unsubstituted or substituted ring A that is an unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, unsubstituted or substituted bicyclic carbocycle, or unsubstituted or substituted bicyclic heterocycle, wherein if ring A is substituted then ring A is substituted with m R^a and n R^b ;

each R^a and R^b is independently hydrogen, halogen, unsubstituted or substituted C_1 -

C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, or -C(=NOR¹⁵)R¹⁵;

m is 1 or 2; n is 0, 1 or 2;

or if one R^a and one R^b are on adjacent atoms of ring A then the adjacent R^a and R^b groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

R^B is an unsubstituted or substituted ring B that is an unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, unsubstituted or substituted bicyclic carbocycle, or unsubstituted or substituted bicyclic heterocycle, wherein if the ring B is substituted then the ring B is substituted with p R^c and q R^d ; each R^c and R^d is independently hydrogen, halogen, unsubstituted or substituted C_1 -

C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -C(=O)R¹⁵, -OC(=O)R¹⁵, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -OC(=O)N(R¹⁵)₂, -NR¹⁵C(=O)N(R¹⁵)₂, -NR¹⁵C(=O)OR¹⁴, -NR¹⁵C(=O)NR¹⁵OR¹⁴, -C(=O)NR¹⁵OR¹⁵, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, -C(=NOR¹⁵)R¹⁵, -N(R¹⁵)SO₂R¹⁴, -C(=O)NR¹⁵S(=O)₂R¹⁴, -S(=O)₂NR¹⁵C(=O)R¹⁴, -C(=NR¹⁵)N(R¹⁵)₂, -NR¹⁵C(=NR¹⁵)N(R¹⁵)₂, -NR¹⁵C(=CR¹⁴R¹⁵)N(R¹⁵)₂, -C(=O)NR¹⁵C(=NR¹⁵)N(R¹⁵)₂, or -C(=O)NR¹⁵C(=CR¹⁴R¹⁵)N(R¹⁵)₂;

p is 1 or 2; q is 0, 1 or 2;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

X is CR^f or N;

Y is CR^f or N;

Z is CR^f or N;

R^e is hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, or -SO₂N(R¹⁵)₂;

each R^f is independently hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, or -SO₂N(R¹⁵)₂;

R^1 and R^2 are independently hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_3 - C_6 cycloalkyl, or substituted or unsubstituted C_2 - C_6 heterocycloalkyl;

or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form ring C that is an unsubstituted or substituted *N*-containing C_2 - C_8 heterocycloalkyl;

R^3 and R^5 are each independently selected from the group consisting of hydrogen, halogen, -OH, -OR¹⁴, -SR¹⁴, -S(=O)R¹⁴, -S(=O)₂R¹⁴, -N(R¹⁵)₂, -CN, -C(=O)OR¹⁵, -C(=O)N(R¹⁵)₂, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, and unsubstituted or substituted C_1 - C_6 fluoroalkyl;

or R^3 and R^5 are taken together to form a bond or C_1 - C_2 alkylene;

or R^2 and R^5 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4-7 membered saturated *N*-containing heterocyclic ring;

R^4 and R^6 are each independently selected from the group consisting of hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, and unsubstituted or substituted C_1 - C_6 fluoroalkyl;

R^7 is hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, or unsubstituted or substituted C_1 - C_6 fluoroalkyl;

or R^2 and R^7 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted *N*-containing C_2 - C_8 heterocycloalkyl;

L^1 is absent or -CR⁸R⁹-;

L^2 is -CR¹⁰R¹¹- or absent;

L^3 is -(CR¹²R¹³)_t- or absent;

t is 1 or 2;

each R^8 , R^9 , R^{10} , R^{11} , R^{12} , and R^{13} is independently selected from the group consisting of hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, and unsubstituted or substituted C_1 - C_6 fluoroalkyl;

or R^5 and R^8 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;

- or R⁵ and R¹³ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;
- or R⁷ and R⁸ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic carbocyclic, or unsubstituted or substituted monocyclic heterocyclic ring;
- each R¹⁴ is independently selected from unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; and
- each R¹⁵ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;
- or two R¹⁵ on the same N atom are taken together with the N atom to which they are attached to form an unsubstituted or substituted N-containing heterocycle;
- wherein each substituted alkyl, substituted fluoroalkyl, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R⁵ groups independently selected from the group consisting of halogen, C₁-C₆alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -OR¹⁶, -CO₂R¹⁶, -C(=O)N(R¹⁶)₂, -N(R¹⁶)₂, -NR¹⁶C(=O)R¹⁷, -SR¹⁶, -S(=O)R¹⁷, -SO₂R¹⁷, and -SO₂N(R¹⁶)₂;
- each R¹⁶ is independently selected from hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl; or two R¹⁶ groups are taken together with the N atom to which they are attached to form a N-containing heterocycle; and
- each R¹⁷ is independently selected from C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl.
2. The compound of claim 1, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

R¹ and R² are independently hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₁-C₆fluoroalkyl, unsubstituted or substituted C₃-C₆cycloalkyl, or substituted or unsubstituted C₂-C₆heterocycloalkyl;

or R¹ and R² are taken together with the nitrogen atom to which they are attached to form an unsubstituted or substituted *N*-containing C₂-C₈heterocycloalkyl;

R⁴ and R⁶ are each independently selected from the group consisting of hydrogen and -CH₃;

R⁷ is hydrogen, -CH₃, or -CH₂CH₃;

or R² and R⁷ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted *N*-containing C₂-C₈heterocycloalkyl; and

each R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ is independently selected from the group consisting of hydrogen and -CH₃.

3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

L¹ is absent, -CH₂-, -CHCH₃-, or -CH(CH₂CH₃)-

L² is -CH₂- or absent;

L³ is -CH₂-, -CH₂CH₂-, or absent; and

X is CR^f; Y is CR^f; and Z is CR^f;

or X is N; Y is CR^f; and Z is CR^f;

or X is CR^f; Y is N; and Z is CR^f;

or X is CR^f; Y is CR^f; and Z is N;

or X is N; Y is N; and Z is CR^f;

or X is CR^f; Y is N; and Z is N;

or X is N; Y is N; and Z is N.

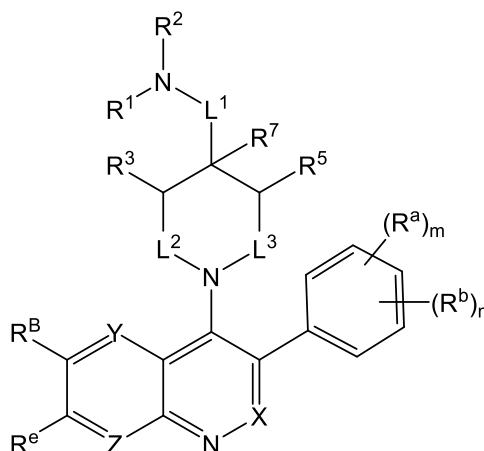
4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

R^e is hydrogen, halogen, C₁-C₄alkyl, C₁-C₄fluoroalkyl, -CN, -OH, or -OR¹⁴; and

each R^f is independently hydrogen, halogen, C₁-C₄alkyl, C₁-C₄fluoroalkyl, -CN, -OH, or -OR¹⁴.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
- R^A is an unsubstituted or substituted ring A that is an unsubstituted or substituted phenyl, an unsubstituted or substituted monocyclic 5- or 6-membered heteroaryl containing 1-4 N atoms and 0 or 1 O or S atom, or an unsubstituted or substituted monocyclic 5- or 6-membered heteroaryl containing 0-4 N atoms and 1 O or S atoms; and
- R^B is an unsubstituted or substituted ring B that is an unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic 5- or 6-membered heteroaryl containing 1-4 N atoms and 0 or 1 O or S atom, or unsubstituted or substituted monocyclic heteroaryl containing 0-4 N atoms and 1 O or S atoms.
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
- R^A is an unsubstituted or substituted ring A that is an unsubstituted or substituted phenyl, unsubstituted or substituted furanyl, unsubstituted or substituted pyrrolyl, unsubstituted or substituted oxazolyl, unsubstituted or substituted thiazolyl, unsubstituted or substituted imidazolyl, unsubstituted or substituted pyrazolyl, unsubstituted or substituted triazolyl, unsubstituted or substituted tetrazolyl, unsubstituted or substituted isoxazolyl, unsubstituted or substituted isothiazolyl, unsubstituted or substituted oxadiazolyl, unsubstituted or substituted thiadiazolyl, unsubstituted or substituted pyridinyl, unsubstituted or substituted pyrimidinyl, unsubstituted or substituted pyrazinyl, unsubstituted or substituted pyridazinyl, or unsubstituted or substituted triazinyl; and
- R^B is an unsubstituted or substituted ring B that is an unsubstituted or substituted phenyl, unsubstituted or substituted furanyl, unsubstituted or substituted pyrrolyl, unsubstituted or substituted oxazolyl, unsubstituted or substituted thiazolyl, unsubstituted or substituted imidazolyl, unsubstituted or substituted pyrazolyl, unsubstituted or substituted triazolyl, unsubstituted or substituted tetrazolyl, unsubstituted or substituted isoxazolyl, unsubstituted or substituted isothiazolyl, unsubstituted or substituted oxadiazolyl, unsubstituted or substituted thiadiazolyl, unsubstituted or substituted pyridinyl, unsubstituted or substituted pyrimidinyl, unsubstituted or substituted pyrazinyl, unsubstituted or substituted pyridazinyl, or unsubstituted or substituted triazinyl.

7. The compound of any one of claims 1 to 6, wherein the compound has the following structure, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof:



wherein:

each R^a and R^b is independently hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, or -C(=NOR¹⁵)R¹⁵;

m is 1 or 2; n is 0, 1 or 2;

or if one R^a and one R^b are on adjacent atoms of ring A then the adjacent R^a and R^b groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

R^B is an unsubstituted or substituted ring B that is an unsubstituted or substituted phenyl, or an unsubstituted or substituted pyridinyl, wherein if the ring B is substituted then the ring B is substituted with p R^c and q R^d ;

each R^c and R^d is independently hydrogen, halogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, -OR¹⁴, -

$C(=O)R^{15}$, $-OC(=O)R^{15}$, $-CO_2R^{15}$, $-CH_2CO_2R^{15}$, $-C(=O)N(R^{15})_2$, $-OC(=O)N(R^{15})_2$, $-NR^{15}C(=O)N(R^{15})_2$, $-NR^{15}C(=O)OR^{14}$, $-NR^{15}C(=O)NR^{15}OR^{14}$, $-C(=O)NR^{15}OR^{15}$, $-CH_2C(=O)N(R^{15})_2$, $-N(R^{15})_2$, $-CH_2N(R^{15})_2$, $-CH(CF_3)N(R^{15})_2$, $-NR^{15}C(=O)R^{14}$, $-CH_2NR^{15}C(=O)R^{14}$, $-SR^{14}$, $-S(=O)R^{14}$, $-SO_2R^{14}$, $-SO_2N(R^{15})_2$, $-C(=NOR^{15})R^{15}$, $-N(R^{15})SO_2R^{14}$, $-C(=O)NR^{15}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}C(=O)R^{14}$, $-C(=NR^{15})N(R^{15})_2$, $-NR^{15}C(=NR^{15})N(R^{15})_2$, $-NR^{15}C(=CR^{14}R^{15})N(R^{15})_2$, $-C(=O)NR^{15}C(=NR^{15})N(R^{15})_2$, or $-C(=O)NR^{15}C(=CR^{14}R^{15})N(R^{15})_2$;

p is 1 or 2; q is 0, 1 or 2;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle;

X is CR^f or N;

Y is CR^f or N;

Z is CR^f or N;

R^e is hydrogen, halogen, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, $-CN$, $-OH$, or $-OR^{14}$;

each R^f is independently hydrogen, halogen, C_1 - C_4 alkyl, C_1 - C_4 fluoroalkyl, $-CN$, $-OH$, or $-OR^{14}$;

R^1 and R^2 are independently hydrogen, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, unsubstituted or substituted C_1 - C_6 fluoroalkyl, unsubstituted or substituted C_3 - C_6 cycloalkyl, or substituted or unsubstituted C_2 - C_6 heterocycloalkyl;

or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form ring C that is an unsubstituted or substituted N -containing C_2 - C_8 heterocycloalkyl;

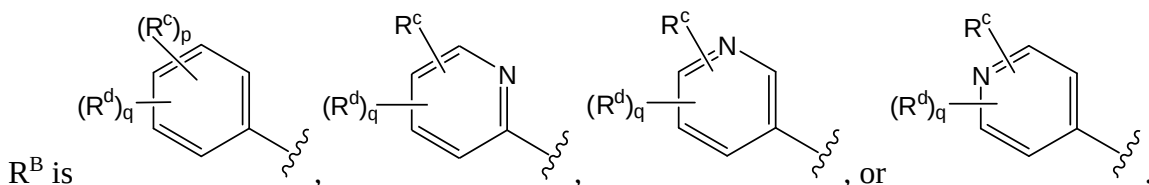
R^3 and R^5 are each independently selected from the group consisting of hydrogen, halogen, $-OH$, $-OR^{14}$, $-SR^{14}$, $-S(=O)R^{14}$, $-S(=O)_2R^{14}$, $-N(R^{15})_2$, $-CN$, $-C(=O)OR^{15}$, $-C(=O)N(R^{15})_2$, unsubstituted or substituted C_1 - C_6 alkyl, unsubstituted or substituted C_1 - C_6 heteroalkyl, and unsubstituted or substituted C_1 - C_6 fluoroalkyl;

or R^3 and R^5 are taken together to form a bond or C_1 - C_2 alkylene;

or R² and R⁵ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4-7 membered saturated N-containing heterocyclic ring;
 R⁷ is hydrogen, or unsubstituted or substituted C₁-C₄alkyl;
 or R² and R⁷ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted N-containing C₂-C₈heterocycloalkyl;
 L¹ is absent or -CHR⁸-;
 L² is -CH₂- or absent;
 L³ is -CH₂-, -CH₂CH₂-, or absent;
 R⁸ is hydrogen or C₁-C₄alkyl;
 each R¹⁴ is independently selected from unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; and
 each R¹⁵ is independently selected from hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆heteroalkyl, unsubstituted or substituted C₃-C₁₀cycloalkyl, substituted or unsubstituted C₂-C₁₀heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;
 or two R¹⁵ on the same N atom are taken together with the N atom to which they are attached to form an unsubstituted or substituted N-containing heterocycle;
 wherein each substituted alkyl, substituted fluoroalkyl, substituted heteroalkyl, substituted carbocycle, and substituted heterocycle is substituted with one or more R^s groups independently selected from the group consisting of halogen, C₁-C₆alkyl, monocyclic carbocycle, monocyclic heterocycle, -CN, -OR¹⁶, -CO₂R¹⁶, -C(=O)N(R¹⁶)₂, -N(R¹⁶)₂, -NR¹⁶C(=O)R¹⁷, -SR¹⁶, -S(=O)R¹⁷, -SO₂R¹⁷, and -SO₂N(R¹⁶)₂;
 each R¹⁶ is independently selected from hydrogen, C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl; or two R¹⁶ groups are taken together with the N atom to which they are attached to form a N-containing heterocycle;

each R¹⁷ is independently selected from C₁-C₆alkyl, C₁-C₆heteroalkyl, C₃-C₆cycloalkyl, C₂-C₆heterocycloalkyl, phenyl, benzyl, 5-membered heteroaryl, and 6-membered heteroaryl.

8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:



9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

each R^a is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted C₁-C₄heteroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, or -C=N(R¹⁴)OR¹⁵; and each R^b is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted C₁-C₄heteroalkyl, -CN, -OH, -O-(unsubstituted or substituted C₁-C₄alkyl), or -O-(unsubstituted or substituted C₁-C₄fluoroalkyl).

10. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

each R^a is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted C₁-C₄heteroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, or -CH₂NR¹⁵C(=O)R¹⁴;

each R^b is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted C₁-C₄heteroalkyl, -CN, -OH, -O-(unsubstituted or substituted C₁-C₄alkyl), or -O-(unsubstituted or substituted C₁-C₄fluoroalkyl);

each R^c is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted C₁-C₄heteroalkyl, -CN, -OH, -OR¹⁴, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -NR¹⁵C(=O)NR¹⁵OR¹⁴, -C(=O)NR¹⁵OR¹⁵, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SR¹⁴, -S(=O)R¹⁴, -SO₂R¹⁴, -SO₂N(R¹⁵)₂, -C=N(R¹⁵)OR¹⁵, or N(R¹⁵)SO₂R¹⁴; and

R^d is independently hydrogen, halogen, unsubstituted or substituted C₁-C₄alkyl, unsubstituted or substituted C₁-C₄fluoroalkyl, unsubstituted or substituted monocyclic 4-7-membered heterocycle, -CN, -OH, -O-(unsubstituted or substituted C₁-C₄alkyl), -O-(unsubstituted or substituted C₁-C₄heteroalkyl), -O-(unsubstituted or substituted C₁-C₄fluoroalkyl), -C(=O)R¹⁵, -OC(=O)R¹⁵, -CO₂R¹⁵, -CH₂CO₂R¹⁵, -C(=O)N(R¹⁵)₂, -OC(=O)N(R¹⁵)₂, -NR¹⁵C(=O)N(R¹⁵)₂, -NR¹⁵C(=O)OR¹⁴, -NR¹⁵C(=O)NR¹⁵OR¹⁴, -C(=O)NR¹⁵OR¹⁵, -CH₂C(=O)N(R¹⁵)₂, -N(R¹⁵)₂, -CH₂N(R¹⁵)₂, -CH(CF₃)N(R¹⁵)₂, -NR¹⁵C(=O)R¹⁴, -CH₂NR¹⁵C(=O)R¹⁴, -SO₂N(R¹⁵)₂, -C(=NOR¹⁵)R¹⁵, -N(R¹⁵)SO₂R¹⁴, -C(=O)NR¹⁵S(=O)₂R¹⁴, -S(=O)₂NR¹⁵C(=O)R¹⁴, or -C(=NR¹⁵)N(R¹⁵)₂;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic carbocycle, or an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle.

11. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

each R^a is independently hydrogen, F, Cl, Br, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -C(CH₃)₃, -CH₂OH, -CH₂CN, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, -OCH₂CH₃, -OCF₃, -CH₂CH₂OH, -CO₂H, -CO₂CH₃, -CO₂CH₂CH₃, -CH₂CO₂H, -CH₂CO₂CH₃, -CH₂CO₂CH₂CH₃, -C(=O)NH₂, -C(=O)NHCH₃, -C(=O)N(CH₃)₂, -CH₂C(=O)NH₂, -CH₂C(=O)NHCH₃, -CH₂C(=O)N(CH₃)₂, -NH₂, -NHCH₃, -N(CH₃)₂, -CH₂NH₂, -CH₂NHCH₃, or -CH₂N(CH₃)₂;

each R^b is independently hydrogen, F, Cl, Br, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -C(CH₃)₃, -CH₂OH, -CH₂CN, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, -OCH₂CH₃, or -OCF₃;

each R^c is independently hydrogen, F, Cl, Br, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -C(CH₃)₃, -CH₂OH, -CH₂CN, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, -OCH₂CH₃, -OCF₃, -CO₂H, -CO₂CH₃, -CO₂CH₂CH₃, -CH₂CO₂H, -CH₂CO₂CH₃, -CH₂CO₂CH₂CH₃, -C(=O)NH₂, -C(=O)NHCH₃, -C(=O)NHOCH₃, -C(=O)N(CH₃)₂, -SO₂N(CH₃)₂, -C(=NOCH₃)H, -CH₂C(=O)NH₂, -CH₂C(=O)NHCH₃, -CH₂C(=O)N(CH₃)₂, -NH₂, -NHCH₃, -N(CH₃)₂, -NHCO₂CH₃, -NHCO₂CH₂CH₃, -CH₂NH₂, -CH₂NHCH₃, -CH₂N(CH₃)₂, -CH(CF₃)NH₂, azetidiny, or pyrrolidinyl; and

each R^d is independently hydrogen, F, Cl, Br, -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -C(CH₃)₃, -CH₂OH, -CH₂CN, -CH₂F, -CHF₂, -CF₃, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, -CN, -OH, -OCH₃, -OCH₂CH₃, -OCF₃, -OCH₂OCH₃, -OCH₂OCH₂CH₃, -OCH₂CH₂OH, -C(=O)NHOCH₃, -C(=NOH)H, -C(=NOCH₃)H, -CH₂C(=O)NH₂, -NH₂, -NHCO₂CH₃, -NHCO₂CH₂CH₃, -NH(C=O)NHCH₃, -NH(C=O)NHOCH₃, or -CH(CF₃)NH₂;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5- or 6-membered monocyclic heterocycle.

12. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

each R^a is independently hydrogen, F, Cl, Br, -CH₃, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, -OCF₃, -CH₂OH, or -CH₂CH₂OH;

each R^b is independently hydrogen, F, Cl, Br, -CH₃, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, or -OCF₃;

each R^c is independently hydrogen, F, Cl, Br, -CH₃, -CH₂F, -CHF₂, -CF₃, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, -CN, -OH, -OCH₃, -OCF₃, -NH₂, -C(=O)NH₂, -C(=NOH)H, -C(=NOCH₃)H, -SO₂CH₃, -SO₂N(CH₃)₂, azetidiny, or pyrrolidinyl; and

each R^d is independently hydrogen, F, Cl, Br, -CH₃, -CH₂F, -CHF₂, -CF₃, -CN, -OH, -OCH₃, -OCF₃, -OCH₂OCH₃, -CH₂OH, -OCH₂CH₂OH, -C(=O)NH₂, -C(=O)NHOCH₃, -NH₂, -NHCO₂CH₃, -NH(C=O)NHOCH₃, or -CH₂(C=O)NH₂;

or if one R^c and one R^d are on adjacent atoms of ring B then the adjacent R^c and R^d groups are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 5-membered monocyclic heterocycle.

13. The compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

X is CR^f; Y is CR^f; and Z is CR^f;

or X is N; Y is CR^f; and Z is CR^f;

or X is CR^f; Y is N; and Z is CR^f;

or X is CR^f; Y is CR^f; and Z is N;

or X is N; Y is N; and Z is CR^f;

or X is CR^f; Y is N; and Z is N;

or X is N; Y is N; and Z is N;

L¹ is absent, -CH₂-, -CH(CH₃)-, or -CH(CH₂CH₃)-; and

L² is -CH₂-, and L³ is -CH₂-;

or L² is absent, and L³ is -CH₂CH₂-;

or L² is absent, or L³ is absent.

or L² is absent, or L³ is -CH₂-.

14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:

R¹ hydrogen;

R² is hydrogen, unsubstituted or substituted C₁-C₆alkyl, unsubstituted or substituted C₁-C₆fluoroalkyl, unsubstituted or substituted C₃-C₆cycloalkyl, or substituted or unsubstituted C₂-C₆heterocycloalkyl;

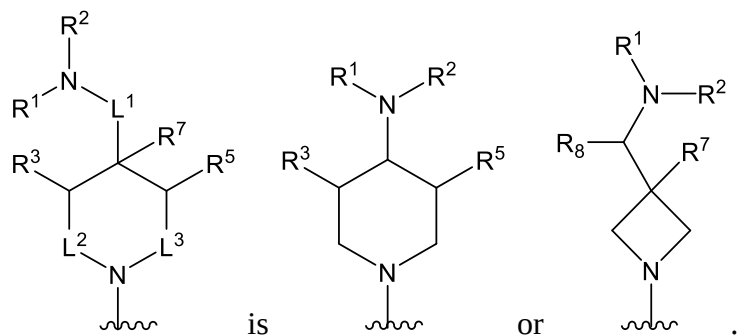
or R¹ and R² are taken together with the nitrogen atom to which they are attached to form ring C that is an unsubstituted or substituted N-containing C₂-C₆heterocycloalkyl;

R³ is hydrogen;

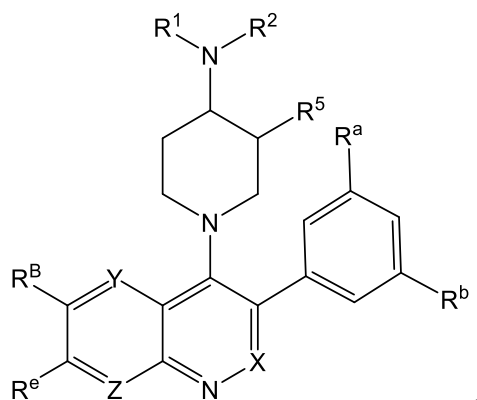
- R^5 are each independently selected from the group consisting of hydrogen, halogen, -OH, -OR¹⁴, -S(=O)₂R¹⁴, -N(R¹⁵)₂, -CN, -C(=O)OR¹⁵, -C(=O)N(R¹⁵)₂, unsubstituted or substituted C₁-C₆ alkyl, and unsubstituted or substituted C₁-C₆ fluoroalkyl;
- or R^3 and R^5 are taken together to form a bond, $\text{--CH}_2\text{--}$, or $\text{--CH}_2\text{CH}_2\text{--}$;
- or R^2 and R^5 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4- to 7-membered saturated *N*-containing heterocyclic ring; and
- R^7 is hydrogen or C₁-C₄alkyl;
- or R^2 and R^7 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted 4- to 7-membered *N*-containing C₂-C₈ heterocycloalkyl.
15. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
- R^1 hydrogen;
- R^2 is hydrogen, -CH₃, -CH₂CH₃, -CH₂CH₂OH, -CH₂CH₂OCH₃, -CH₂CH₂F, -CH₂CH₂NH₂, -CH₂CH₂NHCH₃, -CH₂CH₂N(CH₃)₂, -CH₂CH₂CH₃, -CH(CH₃)₂, cyclopropyl, -CH₂CH₂CH₂F, -CH₂CH₂CH₂OH, -CH₂CH₂CH₂OCH₃, -CH₂CH₂CH₂CH₃, -CH₂CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -C(CH₃)₃, cyclobutyl, cyclopentyl, cyclohexyl, oxetanyl, tetrahydrofuranyl, or tetrahydropyranyl;
- or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form ring C that is an unsubstituted or substituted azetidiny, unsubstituted or substituted pyrrolidinyl, unsubstituted or substituted piperidinyl, unsubstituted or substituted morpholinyl, unsubstituted or substituted thiomorpholinyl, unsubstituted or substituted piperazinyl, or unsubstituted or substituted azepanyl;
- R^3 is hydrogen;
- R^5 is hydrogen, F, Cl, Br, -OH, -OCH₃, -NH₂, -NHCH₃, -N(CH₃)₂, -OCH₂CH₃, -OCF₃, -CH₃, -CH₂CH₃, -CH₂F, -CHF₂, -CF₃, -CN, -C(=O)OCH₃, -C(=O)NH₂, -C(=O)NHCH₃, or -C(=O)N(CH₃)₂;
- or R^2 and R^5 are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic 4- to 7-membered heterocyclic ring selected from unsubstituted or substituted azetidiny, unsubstituted or substituted pyrrolidinyl,

unsubstituted or substituted piperidinyl, unsubstituted or substituted morpholinyl, unsubstituted or substituted thiomorpholinyl, unsubstituted or substituted piperazinyl, or unsubstituted or substituted azepanyl; and
 R^7 is hydrogen, $-CH_3$, or $-CH_2CH_3$;
 or R^2 and R^7 are taken together with the nitrogen atom to which they are attached to form an unsubstituted or substituted monocyclic 4- to 7-membered heterocyclic ring selected from unsubstituted or substituted azetidiny, unsubstituted or substituted pyrrolidinyl, unsubstituted or substituted piperidinyl, unsubstituted or substituted morpholinyl, unsubstituted or substituted thiomorpholinyl, unsubstituted or substituted piperazinyl, or unsubstituted or substituted azepanyl.

16. The compound of any one of claims 1 to 15, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:



17. The compound of any one of claims 1 to 16, wherein the compound has the following structure, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof:



18. The compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
 R^1 is hydrogen; and
 R^2 is hydrogen, methyl, ethyl, 2-fluoroethyl, 2-hydroxyethyl, 2-methoxyethyl, n-propyl, i-propyl, cyclopropyl, 3-fluoropropyl, 3-methoxypropyl, n-butyl, i-butyl, sec-butyl, cyclobutyl, or tert-butyl, or oxetanyl.
19. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
 R^1 is hydrogen; and
 R^2 is hydrogen.
20. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
each R^a is independently hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-CH_2OH$, or $-CH_2CH_2OH$;
each R^b is independently hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CN$, $-OH$, $-OCH_3$, or $-OCF_3$;
each R^c is independently hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-NH_2$, $-C(=O)NH_2$, $-C(=NOH)H$, $-C(=NOCH_3)H$, $-SO_2CH_3$, $-SO_2N(CH_3)_2$, azetidiny, or pyrrolidinyl;
each R^d is independently hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-OCH_2OCH_3$, $-CH_2OH$, $-OCH_2CH_2OH$, $-C(=O)NH_2$, $-C(=O)NHOCH_3$, $-NH_2$, $-NHCO_2CH_3$, $-NH(C=O)NHOCH_3$, or $-CH_2(C=O)NH_2$;
 R^e is hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CN$, $-OH$, $-OCH_3$, or $-OCF_3$;
each R^f is hydrogen;
 R^1 hydrogen;
 R^2 is hydrogen; and
 R^5 is hydrogen, F, Cl, Br, $-OH$, $-OCH_3$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-OCH_2CH_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CN$, $-C(=O)OCH_3$, $-C(=O)NH_2$, $-C(=O)NHCH_3$, or $-C(=O)N(CH_3)_2$;

- or R² and R⁵ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted monocyclic 6-membered heterocyclic ring selected from unsubstituted or substituted piperidinyl, unsubstituted or substituted morpholinyl, unsubstituted or substituted thiomorpholinyl, or unsubstituted or substituted piperazinyl.
21. The compound of any one of claims 1 to 20, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, wherein:
- each R^a is independently hydrogen, F, Cl, -CH₃, -CF₃, -CN, -OH, -OCH₃, -OCF₃, -CH₂OH, or -CH₂CH₂OH
- each R^b is independently hydrogen, F, Cl, -CH₃, -CF₃, -CN, -OH, -OCH₃, or -OCF₃;
- each R^c is independently hydrogen, F, Cl, -CH₃, -CF₃, -CN, -OH, -OCH₃, or -OCF₃;
- each R^c is independently hydrogen, F, Cl, -CH₃, -CF₃, -CN, -OH, -OCH₃, -NH₂, -C(=O)NH₂, -C(=NOH)H, or -C(=NOCH₃)H;
- each R^d is independently hydrogen, F, Cl, -CH₃, -CF₃, -CN, -OH, -OCH₃, -OCF₃, or -NH₂;
- X is CR^f; Y is CR^f; and Z is CR^f;
- or X is N; Y is CR^f; and Z is CR^f;
- or X is CR^f; Y is N; and Z is CR^f;
- or X is CR^f; Y is CR^f; and Z is N;
- R^e is hydrogen, F, or Cl;
- each R^f is hydrogen;
- R¹ hydrogen;
- R² is hydrogen;
- R⁵ is hydrogen;
- or R² and R⁵ are taken together with the intervening atoms to which they are attached to form an unsubstituted or substituted morpholinyl.
22. The compound of claim 1, wherein the compound is:
- 1-1:** 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3,5-dimethylphenyl)cinnolin-6-yl]-5-fluorobenzamide;
- 1-2:** 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3,5-dimethylphenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-4: 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-5-fluorobenzamide;

1-5: 3-{4-[trans-4-amino-3-fluoropiperidin-1-yl]-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-6: 3-{4-[cis-4-amino-3-fluoropiperidin-1-yl]-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-7: 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-8: 5-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-9: 4-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-10: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-11: 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3,5-dichlorophenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-12: 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-13: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-5-fluorobenzamide;

1-14: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)cinnolin-6-yl]-5-fluorobenzamide;

1-15: 3-[4-(4-aminopiperidin-1-yl)-6-(3-fluoro-5-methylphenyl)cinnolin-3-yl]-5-fluorobenzamide;

1-16: 5-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-17: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-18: 3-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-19: 3-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-fluorophenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-20: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-21: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-dichlorophenyl)cinnolin-6-yl]-2-hydroxybenzonitrile;

1-22: 3-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-23: 6-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-24: 4-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-6-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-25: 3-[7-chloro-3-(3-fluoro-5-methylphenyl)-4-{4-[(2-fluoroethyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-26: 3-{4-[trans-4-amino-3-hydroxypiperidin-1-yl]-7-chloro-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-27: 3-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3,5-dichlorophenyl)cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-28: 6-[4-(4-aminopiperidin-1-yl)-3-(3,5-dichlorophenyl)cinnolin-6-yl]-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

1-29: 2-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-6-fluorophenol;

1-30: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-dichlorophenyl)cinnolin-6-yl]-5-fluorobenzamide;

1-31: 3-[3-(3,5-dichlorophenyl)-4-{4-[(oxetan-3-yl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-32: 3-[3-(3,5-dichlorophenyl)-4-{4-[(3,3,3-trifluoropropyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-33: 3-[3-(3,5-dichlorophenyl)-4-{4-[(2-fluoroethyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-34: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3,5-dichlorophenyl)cinnolin-6-yl}-5-fluorobenzamide

1-35: 3-[7-chloro-3-(3-chloro-5-methylphenyl)-4-{4-[(2-fluoroethyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-36: 3-[7-chloro-3-(3-chloro-5-methylphenyl)-4-{4-[(2-fluoroethyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-37: 3-[7-chloro-3-(3-chloro-5-methylphenyl)-4-{4-[(3,3,3-trifluoropropyl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-38: 3-[7-chloro-3-(3-chloro-5-methylphenyl)-4-{4-[(oxetan-3-yl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-39: 3-[7-chloro-3-(3-chloro-5-methylphenyl)-4-{4-[(oxetan-3-yl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-40: 3-[3-(3-chloro-5-methylphenyl)-4-{4-[(oxetan-3-yl)amino]piperidin-1-yl}cinnolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

1-41: 3-{4-[trans-4-amino-3-fluoropiperidin-1-yl]-7-chloro-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-42: 6-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]pyridine-2-carboxamide;

1-43: 6-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-5-chloropyridine-2-carboxamide;

1-44: 2-[4-(4-aminopiperidin-1-yl)-7-chloro-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]pyridine-4-carboxamide;

1-45: 2-[4-(4-aminopiperidin-1-yl)-3-(3-chloro-5-methylphenyl)cinnolin-6-yl]-6-fluoro-3-methylphenol;

1-46: 3-{4-[(3S)-3-aminopiperidin-1-yl]-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-47: 3-{4-[(3R)-3-aminopiperidin-1-yl]-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-48: 3-{4-[cis-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-49: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-5-fluorobenzamide;

1-50: 3-[3-(3-chloro-5-methylphenyl)-4-{1,7-diazaspiro[3.5]nonan-7-yl}cinnolin-6-yl]-5-fluorobenzamide;

1-51: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-dichlorophenyl)cinnolin-6-yl}-2-hydroxybenzonitrile;

1-52: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-chloro-5-methylphenyl)cinnolin-6-yl}-2-hydroxybenzonitrile;

1-53: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-2-hydroxybenzonitrile;

1-54: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)cinnolin-6-yl}-2-hydroxybenzonitrile;

1-55: 5-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)cinnolin-6-yl}-4-aminopyridine-3-carbonitrile;

1-56: 5-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-4-aminopyridine-3-carbonitrile;

1-57: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)cinnolin-6-yl}-3-aminopyridine-4-carbonitrile;

1-58: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)cinnolin-6-yl}-3-aminopyridine-4-carbonitrile;

2-1: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-2: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-3: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-4: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}benzonitrile;

2-5: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]benzonitrile;

2-6: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]phenol;

2-7: 6-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]pyridine-2-carboxamide;

2-8: 4-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

2-9: 5-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

2-10: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

2-12: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-13: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-chloro-5-methylphenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-14: 3-{4-[3-(aminomethyl)-3-methylazetidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-5-fluorobenzamide;

2-15: 3-{4-[3-(aminomethyl)-3-methylazetidin-1-yl]-3-(3-chloro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-16: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

2-17: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-18: 3-(4-{3-[(ethylamino)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluoro-2-hydroxybenzonitrile.

2-19: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-20: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-21: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-chloro-5-fluorophenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-22: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-chloro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-23: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-24: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(2-fluoroethyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-25: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(propan-2-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-26: 3-(4-{3-[(ethylamino)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluorobenzamide;

2-27: 3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(2-methoxyethyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

2-28: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(3-fluoropropyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-29: 3-(4-{3-[(cyclopropylamino)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluoro-2-hydroxybenzonitrile;

2-30: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-[3-(pyrrolidin-1-ylmethyl)azetidin-1-yl]quinolin-6-yl]-2-hydroxybenzonitrile;

2-31: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-{3-[(propylamino)methyl]azetidin-1-yl}quinolin-6-yl]-2-hydroxybenzonitrile;

2-32: 3-{4-[3-(aminomethyl)azetidin-1-yl]-3-(3-chloro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-33: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(oxetan-3-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-34: 3-(4-{3-[(cyclopentylamino)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluoro-2-hydroxybenzonitrile;

2-35: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-[3-(morpholin-4-ylmethyl)azetidin-1-yl]quinolin-6-yl]-2-hydroxybenzonitrile;

2-36: 3-[3-(3-fluoro-5-methylphenyl)-4-[3-(piperazin-1-ylmethyl)azetidin-1-yl]quinolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

2-37: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(oxan-4-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-38: 2-(4-{3-[(ethylamino)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-6-fluoro-3-methylphenol;

2-39: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(1-methoxy-2-methylpropan-2-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-40: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(2-hydroxy-2-methylpropyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-41: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(1-hydroxybutan-2-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-42: 3-[3-(3-fluoro-5-methylphenyl)-4-{3-[(propylamino)methyl]azetidin-1-yl}quinolin-6-yl]-2-hydroxybenzonitrile;

2-43: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(2-hydroxyethyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-44: 3-[4-(3-{[ethyl(2-hydroxyethyl)amino]methyl}azetidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoro-2-hydroxybenzonitrile;

2-45: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(oxolan-3-yl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-46: 3,6-difluoro-2-[3-(3-fluoro-5-methylphenyl)-4-{3-[(propylamino)methyl]azetidin-1-yl}quinolin-6-yl]phenol;

2-47: 3-(4-{3-[(3,3-difluoropyrrolidin-1-yl)methyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluoro-2-hydroxybenzonitrile;

2-48: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(3R)-3-fluoropyrrolidin-1-yl]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-49: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(3S)-3-fluoropyrrolidin-1-yl]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-50: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-[3-(piperidin-1-yl)methyl]azetidin-1-yl]quinolin-6-yl]-2-hydroxybenzonitrile;

2-51: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-{[(2-hydroxypropyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-52: 2,6-difluoro-4-[3-(3-fluoro-5-methylphenyl)-4-{3-[(propylamino)methyl]azetidin-1-yl}quinolin-6-yl]phenol;

2-53: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-[(3-hydroxypropyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-(methoxymethoxy)benzonitrile;

2-54: 5-fluoro-3-[3-(3-fluoro-5-methylphenyl)-4-(3-[(3-hydroxypropyl)amino]methyl}azetidin-1-yl)quinolin-6-yl]-2-hydroxybenzonitrile;

2-55: 4-fluoro-6-[3-(3-fluoro-5-methylphenyl)-4-{3-[(propylamino)methyl]azetidin-1-yl}quinolin-6-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

2-56: 2-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyanophenoxy}acetic acid;

2-57: 4-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyanophenoxy}butanoic acid;

2-58: 3-{4-[cis-4-amino-3-hydroxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-(methoxymethoxy)benzonitrile;

2-59: 3-{4-[(3R, 4R)-4-amino-3-fluoropiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-60: 3-{4-[cis-4-amino-3-hydroxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-61: 3-{4-[(3S,4R)-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-62: 3-{4-[(3R,4S)-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-(methoxymethoxy)benzonitrile;

2-63: 3-{4-[cis-4-amino-3-hydroxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-65: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-(2-hydroxyethoxy)benzonitrile;

2-66: 3-{4-[(3R,4S)-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-67: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-[(1,3-dihydroxypropan-2-yl)oxy]benzamide;

2-68: 3-[4-(4-aminopiperidin-1-yl)-3-[3-fluoro-5-(2-methoxyethoxy)phenyl]quinolin-6-yl]-2-hydroxybenzonitrile;

2-69: 3-[4-(4-aminopiperidin-1-yl)-3-[3-fluoro-5-(oxetan-3-yloxy)phenyl]quinolin-6-yl]-2-hydroxybenzonitrile;

2-70: 3-[4-(4-aminopiperidin-1-yl)-3-{3-fluoro-5-[(1E)-(methoxyimino)methyl]phenyl}quinolin-6-yl]-2-hydroxybenzonitrile;

2-72: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-(2-methoxyethoxy)benzonitrile;

2-73: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-(oxetan-3-yloxy)benzonitrile;

2-74: 1-[3-(3,5-difluorophenyl)-6-[5-fluoro-4-(oxetan-3-yloxy)pyridin-3-yl]quinolin-4-yl]piperidin-4-amine;

2-75: 5-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-(azetidin-1-yl)pyridine-3-carbonitrile;

2-76: 5-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-(azetidin-1-yl)pyridine-3-carboxamide;

2-77: 2-amino-3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]benzonitrile;

2-78: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-(methoxymethoxy)benzonitrile;

2-79: 3-[4-(4-aminopiperidin-1-yl)-3-{3-[(ethoxyimino)methyl]-5-fluorophenyl}quinolin-6-yl]-2-hydroxybenzonitrile;

2-80: 6-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

2-81: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-[(methoxyimino)methyl]phenol;

2-82: 3-(4-{3-[(1S)-1-aminopropyl]azetidin-1-yl}-3-(3-fluoro-5-methylphenyl)quinolin-6-yl)-5-fluoro-2-hydroxybenzonitrile;

2-83: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,6-difluorophenyl}carbamate;

2-84: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-(methoxymethoxy)benzonitrile;

2-85: 6-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridine-2-carboxamide;

2-86: N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,6-difluorophenyl}methanesulfonamide;

2-87: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-[(2-methoxyethoxy)methoxy]benzonitrile;

2-88: 2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-(azetidine-1-carbonyl)phenol;

2-89: 3-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-90: 3-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-91: 3-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-92: trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-93: propan-2-yl trans-4-amino-1-[3-(3,5-difluorophenyl)-6-(3-ethynyl-2-hydroxyphenyl)quinolin-4-yl]piperidine-3-carboxylate;

2-94: cis-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-95: 3-{4-[trans-4-amino-3-(2-hydroxyethoxy)piperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-96: 3-{4-[cis-4-amino-3-(2-hydroxyethoxy)piperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-97: 3-{4-[trans-4-amino-3-(2-methoxyethoxy)piperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-98: 3-{4-[cis-4-amino-3-(2-methoxyethoxy)piperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-99: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,5-difluoro-2-hydroxybenzonitrile;

2-100: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-101: 3-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-102: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-103: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,5-difluoro-2-hydroxybenzonitrile;

2-104: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-105: 3-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-106: 3-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-107: 3-{4-[cis-4-amino-3-hydroxypiperidin-1-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-108: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,6-difluoro-3-methylphenol;

2-109: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,6-difluoro-3-methylphenol;

2-110: 2-{4-[trans-decahydropyrido[3,4-b][1,4]oxazepin-7-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,6-difluoro-3-methylphenol;

2-111: 2-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,6-difluoro-3-methylphenol;

2-112: 2-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,6-difluoro-3-methylphenol;

2-113: cis-4-amino-1-[6-(3,5-difluoro-2-hydroxy-6-methylphenyl)-3-(3-fluoro-5-methoxyphenyl)quinolin-4-yl]piperidin-3-ol;

2-114: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-fluoro-6-[(methoxyimino)methyl]phenol;

2-115: 2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-[(methoxyimino)methyl]phenol;

2-116: 2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4-fluoro-6-[(methoxyimino)methyl]phenol;

2-117: 2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-3,4-difluoro-6-[(methoxyimino)methyl]phenol;

2-118: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4-fluoro-6-[(1E)-(methoxyimino)methyl]phenol;

2-119: trans-4-amino-1-[6-(3-cyano-5,6-difluoro-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-120: cis-4-amino-1-[6-(3-cyano-5,6-difluoro-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-121: trans-4-amino-1-[6-(3-cyano-5,6-difluoro-2-hydroxyphenyl)-3-(3-fluoro-5-methylphenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-122: cis-4-amino-1-[6-(3-cyano-5,6-difluoro-2-hydroxyphenyl)-3-(3-fluoro-5-methylphenyl)quinolin-4-yl]piperidine-3-carbonitrile;

2-123: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-3,4,6-trifluorophenyl} carbamate;

2-124: methyl N-{3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-fluoropyridin-4-yl} carbamate;

2-125: methyl N-{3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-cyanopyridin-4-yl} carbamate;

2-126: 1-[3-(3,5-difluorophenyl)-6-{3-fluoro-2-[(hydroxyimino)methyl]phenyl}quinolin-4-yl]piperidin-4-amine;

2-127: 1-(6-{3-chloro-2-[(hydroxyimino)methyl]phenyl}-3-(3,5-difluorophenyl)quinolin-4-yl)piperidin-4-amine;

2-128: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-[(hydroxyimino)methyl]benzonitrile;

2-129: 1-[3-(3,5-difluorophenyl)-6-{3-fluoro-2-[(methoxyimino)methyl]phenyl}quinolin-4-yl]piperidin-4-amine;

2-130: 1-(6-{3-chloro-2-[(methoxyimino)methyl]phenyl}-3-(3,5-difluorophenyl)quinolin-4-yl)piperidin-4-amine;

2-131: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-[(1E)-(methoxyimino)methyl]benzonitrile;

2-132: 1-{6-[3-(1-amino-2,2,2-trifluoroethyl)phenyl]-3-(3,5-difluorophenyl)quinolin-4-yl}piperidin-4-amine;

2-133: 1-{6-[2-(1-amino-2,2,2-trifluoroethyl)-3-fluorophenyl]-3-(3,5-difluorophenyl)quinolin-4-yl}piperidin-4-amine;

2-134: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-chloro-3,4-difluorophenol;

2-135: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-chloro-3,4-difluorophenol;

2-136: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-chloro-4-fluorophenol;

2-137: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-chlorophenol;

2-138: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-chlorophenol

2-139: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-methoxyurea;

2-140: 1-(2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,6-difluorophenyl)-3-methoxyurea;

2-141: 6-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-chloro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

2-142: 5-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2,3-dihydro-1,3-benzoxazol-2-one;

2-143: methyl trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carboxylate;

2-144: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-fluorophenol;

2-145: trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carboxylic acid;

2-146: trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carboxamide;

2-147: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-chloro-4-fluoro-2-hydroxybenzonitrile;

2-148: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyanophenyl} carbamate;

2-149: trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]-N-methylpiperidine-3-carboxamide;

2-150: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-3,4,6-trifluorophenol;

2-151: trans-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]-N,N-dimethylpiperidine-3-carboxamide;

2-152: 1-[3-(3,5-difluorophenyl)-6-{5-fluoro-4-[(hydroxyimino)methyl]pyridin-3-yl}quinolin-4-yl]piperidin-4-amine;

2-153: N-[(2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-fluorophenyl)methylidene]hydroxylamine;

2-154: N-[(2-{4-[(trans)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4,6-difluorophenyl)methylidene]hydroxylamine;

2-155: N-[(2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-6-fluorophenyl)methylidene]hydroxylamine;

2-156: 4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-[3-fluoro-2-(1H-imidazol-2-yl)phenyl]-3-(3-fluoro-5-methoxyphenyl)quinoline;

2-157: 4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-[3-fluoro-2-(1H-imidazol-5-yl)phenyl]-3-(3-fluoro-5-methoxyphenyl)quinoline;

2-158: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-159: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-4,5-difluoro-2-hydroxybenzonitrile;

2-160: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl}-3,4,6-trifluorophenol;

2-161: 1-[3-(3-fluoro-5-methoxyphenyl)-6-(2,3,5-trifluoro-6-hydroxyphenyl)quinolin-4-yl]piperidin-4-ol;

2-162: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-hydroxypyridin-4-yl}-3-methoxyurea;

2-163: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-6-chlorophenyl}-3-methoxyurea;

2-164: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-methoxyurea;

2-165: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-4,6-difluorophenyl}carbamate;

2-166: 1-(6-{3-fluoro-2-[(hydroxyimino)methyl]phenyl}-3-(3-fluoro-5-methoxyphenyl)quinolin-4-yl)piperidin-4-amine;

2-167: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-6-cyanophenyl}carbamate;

2-168: 1-(6-{5-fluoro-4-[(hydroxyimino)methyl]pyridin-3-yl}-3-(3-fluoro-5-methylphenyl)quinolin-4-yl)piperidin-4-amine;

2-169: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-4-amine;

2-170: methyl (trans)-4-amino-1-[6-(3-cyano-2-hydroxyphenyl)-3-(3,5-difluorophenyl)quinolin-4-yl]piperidine-3-carboxylate;

2-171: methyl N-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-4-yl}carbamate;

2-172: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-4-yl}-3-methoxyurea;

2-173: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-6-fluorophenyl}carbamate;

2-174: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-6-fluorophenyl}-3-methoxyurea;

2-175: N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methoxyphenyl)quinolin-6-yl]-6-fluorophenyl}azetidine-1-carboxamide;

2-176: 1-(6-{5-fluoro-4-[(hydroxyimino)methyl]pyridin-3-yl}-3-[3-fluoro-5-(trifluoromethyl)phenyl]quinolin-4-yl)piperidin-4-amine;

2-177: 4-amino-5-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]pyridine-3-carbonitrile;

2-178: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-2-amine;

2-179: 2-amino-3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4,5-difluorobenzonitrile;

2-180: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyano-3,4-difluorophenyl}carbamate;

2-181: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-chloropyridin-4-amine;

2-182: methyl N-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-2-yl}carbamate;

2-183: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoropyridin-2-yl}-3-methoxyurea;

2-184: methyl N-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-chloropyridin-4-yl}carbamate;

2-185: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-cyanophenyl}carbamate;

2-186: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-chloropyridin-4-yl}-3-methoxyurea;

2-187: 4-amino-5-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]pyridine-3-carbonitrile;

2-188: 1-[3-(3,5-difluorophenyl)-6-{5-[(hydroxyimino)methyl]-1-methyl-1H-pyrazol-4-yl}quinolin-4-yl]piperidin-4-amine;

2-189: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-cyanophenyl}-3-methoxyurea;

2-190: 3-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-191: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyano-3,4-difluorophenyl}-3-methoxy-3-methylurea;

2-192: 1-(6-{5-chloro-4-[(hydroxyimino)methyl]pyridin-3-yl}-3-(3,5-difluorophenyl)quinolin-4-yl)piperidin-4-amine;

2-193: 3-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-hydroxybenzonitrile;

2-194: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-5-fluoro-2-(methoxymethoxy)benzonitrile;

2-195: 1-[3-(3,5-difluorophenyl)-6-{3-[(hydroxyimino)methyl]pyridin-2-yl}quinolin-4-yl]piperidin-4-amine;

2-196: 1-[3-(3,5-difluorophenyl)-6-{2-[(hydroxyimino)methyl]pyridin-3-yl}quinolin-4-yl]piperidin-4-amine;

2-197: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}carbamate;

2-198: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-methoxy-3-methylurea;

2-199: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3,3-dimethylurea;

2-200: 1-[3-(3,5-difluorophenyl)-6-{6-[(hydroxyimino)methyl]pyridin-2-yl}quinolin-4-yl]piperidin-4-amine;

2-201: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-cyanophenyl methyl carbonate;

2-202: 1-[3-(3,5-difluorophenyl)-6-{3-fluoro-2-[(hydroxyimino)methyl]-6-methylphenyl}quinolin-4-yl]piperidin-4-amine;

2-203: 1-[3-(3,5-difluorophenyl)-6-{2-[(hydroxyimino)methyl]pyridin-4-yl}quinolin-4-yl]piperidin-4-amine;

2-204: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoro-2-(2-methoxyethoxy)benzonitrile;

2-205: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-cyano-3,4-difluorophenyl} carbamate;

2-206: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-cyano-3,4-difluorophenyl}-3-methoxy-3-methylurea;

2-207: 1-(2-{4-[cis-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,6-difluorophenyl)-3-methoxyurea;

2-208: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-cyano-3,4-difluorophenyl}-3-methylurea;

2-209: methyl N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-fluorophenyl} carbamate;

2-210: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-fluorophenyl}-3-methoxy-3-methylurea;

2-211: 1-[6-(3-amino-1-methyl-1H-pyrazol-4-yl)-3-(3-fluoro-5-methylphenyl)quinolin-4-yl]piperidin-4-amine;

2-212: 1-{4-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-1-methyl-1H-pyrazol-3-yl}-3-methoxyurea;

2-213: 4-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-2-[(methoxyimino)methyl]phenol;

2-214: methyl N-{4-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-1-methyl-1H-pyrazol-3-yl} carbamate;

2-215: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4-methylpyridin-2-yl}-3-methoxyurea;

2-216: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-(propan-2-yloxy)urea;

2-217: trans-1-(6-{3-fluoro-2-[(hydroxyimino)methyl]phenyl}-3-(3-fluoro-5-methylphenyl)quinolin-4-yl)-3-methoxypiperidin-4-amine;

2-218: methyl N-(2-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-6-cyanophenyl) carbamate;

2-219: cis-3-{4-[4-amino-3-hydroxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-220: cis-3-{4-[4-amino-3-hydroxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-5-fluoro-2-(2-methoxyethoxy)benzonitrile;

2-221: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-6-[(methoxyimino)methyl]phenol;

2-222: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4-cyanophenyl}-3-methoxyurea;

2-223: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluorophenyl}-3-methoxyurea;

2-224: cis-3-{4-[4-amino-3-hydroxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-2-(2-methoxyethoxy)benzonitrile;

2-225: cis-3-{4-[4-amino-3-hydroxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-2-(2-methoxyethoxy)benzonitrile;

2-226: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]pyridin-2-yl}-3-methoxyurea;

2-227: cis-4-amino-1-(6-{3-fluoro-2-[(hydroxyimino)methyl]phenyl}-3-(3-fluoro-5-methylphenyl)quinolin-4-yl)piperidin-3-ol;

2-228: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-ethoxyurea;

2-229: 1-[3-(3-fluoro-5-methylphenyl)-6-{3-[(2-methoxyethyl)amino]-1-methyl-1H-pyrazol-4-yl}quinolin-4-yl]piperidin-4-amine;

2-230: N-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-2-methoxyacetamide;

2-231: 3-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-2-(cyanomethoxy)benzonitrile;

2-232: cis-3-{4-[4-amino-3-hydroxypiperidin-1-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoro-2-(2-methoxyethoxy)benzonitrile;

2-233: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4,6-difluorophenyl}-3-(2,2,2-trifluoroethoxy)urea;

2-234: 3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-5-fluoro-N-(2-methoxyethyl)pyridin-2-amine;

2-235: methyl N-(2-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,6-difluorophenyl)carbamate;

2-236: 1-(2-{4-[trans-4-amino-3-methoxypiperidin-1-yl]-3-(3-fluoro-5-methylphenyl)quinolin-6-yl}-4,6-difluorophenyl)-3-methoxyurea;

2-237: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-4-cyano-6-fluorophenyl}-3-methoxyurea;

2-238: 1-{2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-cyanophenyl}-3-(2,2,2-trifluoroethoxy)urea;

2-239: 1-{3-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-methylpyridin-2-yl}-3-methoxyurea;

2-240: 1-{4-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]phenyl}-3-methoxyurea;

2-241: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-6-bromo-3,4-difluorophenol;

2-242: 5-[4-(4-aminopiperidin-1-yl)-3-(3-fluoro-5-methylphenyl)quinolin-6-yl]-6-[(2-methoxyethyl)amino]pyridine-3-carbonitrile;

2-243: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-[(1E)-(methoxyimino)methyl]phenol;

2-244: 5-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-aminopyridine-3-carbonitrile;

2-245: 4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-methyl-1H-pyrazol-3-amine;

2-246: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-amine;

2-247: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-amine;

2-248: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-ol;

2-249: 4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-methyl-1H-pyrazol-5-amine;

2-250: 2-[4-(4-aminopiperidin-1-yl)-3-(3,5-difluorophenyl)quinolin-6-yl]-4-methylpyridin-3-amine;

2-251: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-3-hydroxypyridine-4-carbonitrile;

2-252: 5-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-[(2-methoxyethyl)amino]pyridine-3-carbonitrile;

2-253: N-[(4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-methyl-1H-pyrazol-5-yl)methylidene]hydroxylamine

2-254: 5-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-hydroxypyridine-3-carbonitrile;

2-255: 4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyrimidin-5-amine;

2-256: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoropyridin-4-ol;

2-257: 4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-methyl-1H-pyrazole-3-carboxamide;

2-258: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-ol;

2-259: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoropyridin-2-ol;

2-260: N-[(4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-methyl-1H-pyrazol-3-yl)methylidene]hydroxylamine;

2-261: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-3-fluoropyridine-4-carbonitrile;

2-262: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-3-aminopyridine-4-carbonitrile;

2-263: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-3-ol;

2-264: N-[(3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-yl)methylidene]hydroxylamine;

2-265: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoropyridin-3-amine;

2-266: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-[(methoxyimino)methyl]pyridin-4-amine;

2-267: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-cyclopropylpyridin-4-amine;

2-268: 4-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-1-(oxetan-3-yl)-1H-pyrazol-5-amine;

2-269: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

2-272: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-(prop-1-yn-1-yl)pyridin-4-amine;

2-273: 1-(3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-yl)-3-methoxyurea;

2-274: 3-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-ethynylpyridin-4-amine;

2-275: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-chloropyridin-3-amine;

2-276: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-cyclopropylpyridin-3-amine;

2-278: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-(oxetan-3-yl)phenol;

2-279: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-(oxetan-2-yl)phenol;

2-280: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-(oxetan-3-yl)pyridin-3-amine;

2-281: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-(oxetan-2-yl)pyridin-3-amine;

2-283: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-3-amine;

2-284: 2-{4-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methoxypyridin-3-amine;

2-285: 2-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-[(methoxyimino)methyl]phenol;

2-286: 2-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-6-[(methoxyimino)methyl]phenol;

2-287: 2-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

2-288: 2-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

2-289: 2-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-3-aminopyridine-4-carbonitrile;

2-290: 2-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-3-aminopyridine-4-carbonitrile;

2-291: (5-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-aminopyridin-3-carbonitrile;

2-292: (5-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-aminopyridin-3-carbonitrile;

2-293: 3-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-amine;

2-294: 3-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}pyridin-2-amine;

2-295: 2-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-amine;

2-296: 2-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-amine;

2-297: 2-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-ol;

2-298: 2-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-4-methylpyridin-3-ol;

2-299: 3-{4-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

2-300: 3-{4-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-3-(3,5-difluorophenyl)quinolin-6-yl}-5-fluoro-2-hydroxybenzonitrile;

3-1: 3-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-5-fluorobenzamide;

3-2: 3-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-5-fluoro-2-hydroxybenzonitrile;

3-3: 4-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-6-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-4: 5-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-5: 6-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-6: 3-[8-(4-aminopiperidin-1-yl)-7-(3-chloro-5-methylphenyl)-1,5-naphthyridin-2-yl]-5-fluoro-2-hydroxybenzonitrile;

3-7: 3-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-2-hydroxybenzonitrile;

3-8: 2-[8-(4-aminopiperidin-1-yl)-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl]-6-fluorophenol.

3-9: 6-[8-(4-aminopiperidin-1-yl)-7-(3,5-difluorophenyl)-1,5-naphthyridin-2-yl]-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-10: 6-{8-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-7-(3,5-difluorophenyl)-1,5-naphthyridin-2-yl}-4-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-11: 4-{8-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-7-(3-fluoro-5-methylphenyl)-1,5-naphthyridin-2-yl}-6-fluoro-2,3-dihydro-1H-1,3-benzodiazol-2-one;

3-12: 4-{8-[trans-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-7-(3,5-difluorophenyl)-1,5-naphthyridin-2-yl}-1H,2H,3H-imidazo[4,5-c]pyridin-2-one;

4-1: 3-[5-(4-aminopiperidin-1-yl)-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl]-2-hydroxybenzonitrile;

4-2: 3-[5-(4-aminopiperidin-1-yl)-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl]-2-hydroxybenzonitrile;

4-3: 3-[5-(4-aminopiperidin-1-yl)-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl]-5-fluoro-2-hydroxybenzonitrile;

4-4: 3-[5-(4-aminopiperidin-1-yl)-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl]-2-hydroxybenzonitrile;

4-5: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-6: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-7: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-5-fluoro-2-hydroxybenzonitrile;

4-8: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-5-fluoro-2-hydroxybenzonitrile;

4-9: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-5-fluoro-2-hydroxybenzonitrile;

4-10: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-5-fluoro-2-hydroxybenzonitrile;

4-11: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-12: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-13: 5-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-4-aminopyridine-3-carbonitrile;

4-14: 5-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b]morpholin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-4-aminopyridine-3-carbonitrile;

4-15: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-16: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-17: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-18: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-19: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-20: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-3-aminopyridine-4-carbonitrile;

4-21: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

4-22: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

4-23: 2-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

4-24: 2-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-4-[(methoxyimino)methyl]pyridin-3-amine;

4-25: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-26: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-27: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-28: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-29: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methoxyphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-30: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methoxyphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-31: 3-{5-[(4 α R,8 α R)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-32: 3-{5-[(4 α S,8 α S)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-33: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-dichlorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-34: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-dichlorophenyl)-1,8-naphthyridin-3-yl}-2-hydroxybenzonitrile;

4-35: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-36: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-difluorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-37: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-38: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methylphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-39: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methoxyphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-40: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-fluoro-5-methoxyphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-41: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-42: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-fluorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

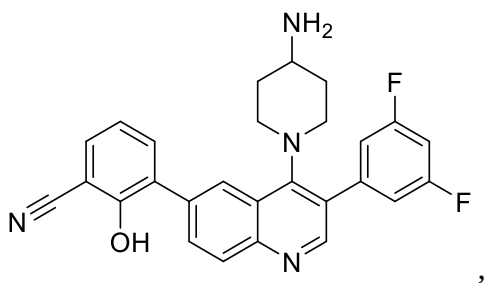
4-43: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-44: 3-{5-[(4aS,8aS)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3-chloro-5-methylphenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-45: 3-{5-[(4aR,8aR)-octahydro-1H-pyrido[3,4-b][1,4]oxazin-6-yl]-6-(3,5-dichlorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;

4-46: 3-{5-[(4a*S*,8a*S*)-octahydro-1*H*-pyrido[3,4-*b*][1,4]oxazin-6-yl]-6-(3,5-dichlorophenyl)-1,8-naphthyridin-3-yl}pyridin-2-amine;
or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof.

23. A compound that has the following structure:



- or a pharmaceutically acceptable salt thereof.
24. The compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, for use in therapy.
25. Use of a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, in the manufacture of a medicament for treating acromegaly, neuroendocrine tumor, or combinations thereof, in a mammal in need thereof.
26. A pharmaceutical composition comprising a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, and at least one pharmaceutically acceptable excipient.
27. Use of a compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt, diastereomeric mixture, or individual enantiomers thereof, in the manufacture of a medicament for treating a disease or condition in a mammal that would benefit from the modulation of the somatostatin receptor subtype 2 (SSTR2) activity, wherein the disease or condition is acromegaly, neuroendocrine tumor, pain or combinations thereof, in a mammal in need thereof.
28. The pharmaceutical composition of claim 26, wherein the pharmaceutical composition is in the form of a tablet, a pill, or a capsule.