GEM-DISUBSTITUTED PIPERIDINE MELANOCORTIN SUBTYPE-2 RECEPTOR (MC2R) ANTAGONISTS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/949,854 filed on December 18, 2019, which is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] Described herein are compounds that modulate the activity of one or more melanocortin receptors, 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 melanocortin subtype-2 receptor (MC2R) activity.

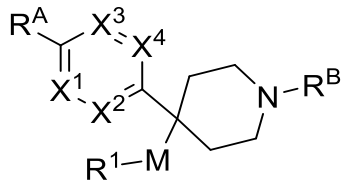
BACKGROUND OF THE INVENTION

[0003] The melanocortin receptors form a family of G protein-coupled receptor (GPCRs) (MC1R, MC2R, MC3R, MC4R, and MC5R) that are selectively activated by different melanocortin peptides adrenocorticotropic hormone (ACTH), and the melanocortin peptides α-, β-, and γ-melanocyte-stimulating hormone (α-MSH, β-MSH, and γ-MSH) that are all derived proteolytically from proopiomelanocortin hormone, or POMC. ACTH is a 39 amino acid peptide that is the primary regulator of adrenal glucocorticoid synthesis and secretion and only has affinity for MC2R . As the central actor in this hypothalamic-pituitary-adrenal (HPA) axis, ACTH is secreted by the pituitary in response to stressful stimuli and acts at the adrenal gland to stimulate the synthesis and secretion of cortisol. Modulation of MC2R is attractive for the treatment of conditions, diseases, or disorders that would benefit from modulating melanocortin receptor activity.

SUMMARY ~~OF THE INVENTION~~

[0004] Compounds described herein are melanocortin receptor modulator compounds. In some ~~embodiment~~examples, compounds described herein modulate one or more of the subtype melanocortin receptor proteins. In some ~~embodiment~~examples, compounds described herein modulate two or more of the subtype melanocortin receptor proteins. In some ~~embodiment~~examples, compounds described herein modulate MC2R.

[0004a] In an aspect of the present disclosure, there is provided a compound of Formula (I), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (I)

wherein:

R^A is unsubstituted or substituted heteroaryl or unsubstituted or substituted aryl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c;

R^a, R^b, and R^c are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl, wherein any substituted group of R^a, R^b, and R^c is substituted with one or more R^6 groups;

or one R^a and one R^b, when present on adjacent atoms of R^A, are taken together with the intervening atoms connecting R^a to R^b to form a 5- to 6-membered monocyclic carbocycle or 5- to 6-membered monocyclic heterocycle, wherein the carbocycle or heterocycle is unsubstituted or substituted with one or more R^6 groups;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, 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 C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

R^B is unsubstituted or substituted aryl or unsubstituted or substituted heteroaryl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f;

R^d, R^e, and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, $-C(=O)N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl, wherein any substituted group of R^d, R^e, and R^f is substituted with one or more R^6 groups;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, -$C(=O)R^7$, 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 C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

X^1 is CR^{11} or N;

X^2 is CR^{12} or N;

X^3 is CR^{13} or N;

X^4 is CR^{14} or N;

R^{11}, R^{12}, R^{13}, and R^{14} are each 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 C_3-C_6cycloalkyl, -CN, -OR^4, -SR^4, -CO_2R^4, -$C(=O)N(R^4)_2$, or -$N(R^4)_2$;

M is -(C=O)-, -NR^3-, -O-, -S-, -SO_2-, *-NR^3-(C=O)-, *-(C=O)-NR^3-, *-O-(C=O)NR^3-, *-NR^3-(C=O)O-, -NR^3-(C=O)NR^3-, *-$NR^3(SO_2)$-, *-SO_2NR^3-, or 5-membered heterocycle, wherein * indicates the attachment point to R^1;

R^1 is 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted -(C_1-C_6 alkyl)-(C_3-C_6 cycloalkyl), or unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, -$N(R^4)_2$, -OR^5, -CN, -CO_2R^5, -$C(=O)N(R^4)_2$, -SR^5, -$S(=O)R^7$, -$S(=O)_2R^7$, -$NR^4C(=O)R^5$, -$NR^4SO_2R^7$, -SO_2R^7, or -$SO_2N(R^4)_2$;

each R^3 is independently hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

each R^4 is independently selected from the group consisting of hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted aryl, and unsubstituted or substituted heteroaryl;

or two R^4 are taken together with the nitrogen atom to which they are attached to form an unsubstituted or substituted 3- to 6-membered monocyclic heterocycle;

each R^5 is independently selected from the group consisting of hydrogen, substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted

C_1-C_6fluoroalkyl, unsubstituted or substituted aryl, and unsubstituted or substituted heteroaryl;

each R^6 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_4alkyl, unsubstituted or substituted C_1-C_4alkoxy, unsubstituted or substituted C_1-C_4fluoroalkyl, unsubstituted or substituted C_1-C_4fluoroalkoxy, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, $-CO_2R^5$, $-CH_2CO_2R^5$, $-C(=O)N(R^4)_2$, $-C(=O)N(R^4)OR^5$, $-CH_2C(=O)N(R^4)_2$, $-N(R^4)_2$, $-CH_2N(R^4)_2$, $-C(R^5)_2N(R^4)_2$, $-NR^4C(=O)R^5$, $-CH_2NR^4C(=O)R^5$, $-NR^4C(=O)N(R^5)_2$, $-NR^4C(=O)N(R^4)_2$, $C(R^5)=N(R^4)-OR^5$, $-SR^5$, $-S(=O)R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$; and

each R^7 is independently selected from the group consisting substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl.

[0004b] In another aspect of the present disclosure, there is provided a compound that is:

1-1: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-2: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-3: N-(2-aminoethyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-4: N-[(2R)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-5: N-(3-aminopropyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-6: N-[(2S)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-7: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-8: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-9: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-10: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-11: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-12: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-13: N-(2-aminoethyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-14: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-15: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-16: N-[(2S)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-17: N-[(2R)-2-amino-3-hydroxypropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-18: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-19: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-20: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-21: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[3,3'-bipyridin]-6-yl}-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-22: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[3,3'-bipyridin]-6-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-23: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-24: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-25: 3-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[(3R)-1-methylpyrrolidin-3-yl]carbamoyl}piperidin-1-yl)-6-(trifluoromethyl)pyridine-2-carboxamide;

1-26: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-27: 3-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[(3S)-1-methylpyrrolidin-3-yl]carbamoyl}piperidin-1-yl)-6-(trifluoromethyl)pyridine-2-carboxamide;

1-28: N-[(2S)-2-amino-3-hydroxypropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-29: 1-[2-chloro-6-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-30: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-31: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-32: 1-(2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-33: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]-1-[4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-34: 1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-35: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]-1-[5-(trifluoromethyl)pyridin-2-yl]piperidine-4-carboxamide;

1-36: 1-(4-acetyl-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-37: 1-[2-cyano-4-(difluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-38: 1-[4-cyano-2-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-39: 1-[2-cyano-4-(trifluoromethoxy)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-40: 1-(2,4-dicyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-41: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S,4S)*-4-hydroxy-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-42: 1-[3-cyano-5-(trifluoromethyl)pyridin-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-43: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrazol-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-44: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2R)-3-hydroxy-2-(methylamino)propyl]piperidine-4-carboxamide;

1-45: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-46: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R,4R)*-4-hydroxy-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-47: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-3-hydroxy-2-(methylamino)propyl]piperidine-4-carboxamide;

1-48: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-51: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-(2-ethoxypyridin-3-yl)pyrazin-2-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-52: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-53: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,3-dihydro-1-benzofuran-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-54: 4-[6-(1-benzofuran-7-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-55: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(hydroxymethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-56: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-57: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-58: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-(2-ethoxypyridin-3-yl)pyrazin-2-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-59: 1-[2-cyano-4-(1,1-difluoroethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-60: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-61: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,3-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-62: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-ethyl-1H-pyrazol-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-63: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-propoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-64: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-65: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3,5-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-66: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-67: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,2-difluoro-2H-1,3-benzodioxol-4-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-68: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,5-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-69: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxy-5-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-70: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[1-(3-methylbutyl)-1H-pyrazol-5-yl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-71: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-{6-[2-(trifluoromethoxy)phenyl]pyridin-3-yl}piperidine-4-carboxamide;

1-72: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxy-3-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-73: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indazol-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-74: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-75: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)-3-fluorophenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-76: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-77: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-{6-[2-(trifluoromethyl)phenyl]pyridin-3-yl}piperidine-4-carboxamide;

1-78: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyanophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-79: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(methoxymethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-80: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-methoxythiophen-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-81: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-82: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-83: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-84: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(1,1-difluoroethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-85: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2'-(difluoromethoxy)-[2,3'-bipyridin]-5-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-86: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-87: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3,5-difluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-88: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-89: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-90: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-91: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-92: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-93: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-94: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-95: 1-(2,4-dichlorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-96: 1-(2-cyano-4-fluorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-97: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-98: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-99: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-100: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-101: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-102: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-103: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-104: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-105: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(4-methylpyrimidin-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-106: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2-(2-ethoxypyridin-3-yl)pyrimidin-5-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-107: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2-(2-ethoxypyridin-3-yl)pyrimidin-5-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-108: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-109: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-110: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-111: 1-(4-chloro-2-cyano-6-fluorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-112: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-113: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-114: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(difluoromethoxy)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-115: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-116: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylfuran-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-117: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-propylphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-118: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethyl-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-119: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-120: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylfuran-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-121: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-122: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]-4-[6-(2-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-123: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-124: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-125: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-126: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-127: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-128: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-129: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-hydroxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-130: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxy-5-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-131: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-132: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-133: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-134: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-135: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-136: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-137: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(cyanomethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-138: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(4-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-139: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-140: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-141: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-142: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-143: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]-4-[6-(1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-144: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-145: 4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-146: 4-[6-(2-acetylthiophen-3-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-147: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylthiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-148: 4-[6-(2-cyano-3-fluorophenyl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-149: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-methyl-1,2-oxazol-4-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-150: 1-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-151: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(difluoromethyl)phenyl]pyridin-3-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-152: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-153: 4-[6-(5-cyano-1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-154: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-155: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-156: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-157: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-methyl-1,2-oxazol-4-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-158: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-cyclopropyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-159: 4-[4-(2-ethoxypyridin-3-yl)phenyl]-1-[2-methoxy-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-160: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-161: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-162: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-163: 1-(4-chloro-2-cyanophenyl)-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-164: 4-[4-(2-ethoxypyridin-3-yl)phenyl]-1-[2-methyl-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-165: 1-[3-chloro-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-166: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-167: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-168: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-169: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-170: 1-(4-chloro-2-cyanophenyl)-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-171: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-172: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethyl-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-173: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-174: 4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-175: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-176: 4-{[2,2'-bipyridin]-5-yl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-177: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3'-methyl-[2,2'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-178: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3'-methoxy-[2,2'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-179: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-180: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-cyclopropyl-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-181: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2'-(difluoromethyl)-[2,3'-bipyridin]-5-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-182: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-cyclopropyl-1,3-oxazol-4-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-183: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-184: ethyl (3S)-3-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-amido}pyrrolidine-1-carboxylate;

1-185: N-[(3S)-1-acetylpyrrolidin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-186: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-187: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-188: N-[(3R)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-189: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyquinolin-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-190: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indol-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-191: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indol-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-192: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-193: 4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-194: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-195: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-196: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-197: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[3-(methylamino)propyl]piperidine-4-carboxamide;

1-198: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-199: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[3-(dimethylamino)propyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-200: 4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-201: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-202: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-203: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-204: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-205: N-(3-aminopropyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-206: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[3-(methylamino)propyl]piperidine-4-carboxamide;

1-207: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[3-(dimethylamino)propyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-208: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-ethyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-209: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3,5'-difluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-210: 4-{3,5'-difluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-211: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-212: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-213: N-{[(2S)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-214: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-215: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-216: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-217: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2S)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-218: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-219: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-220: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-221: N-{1-azabicyclo[2.2.1]heptan-4-yl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-222: N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-223: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-224: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-225: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-226: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-227: 4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-228: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-229: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-230: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-231: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2R)-pyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-232: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2R)-1-methylpyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-233: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,3S)-3-aminocyclobutyl]piperidine-4-carboxamide;

1-234: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1R,3R)-3-aminocyclobutyl]piperidine-4-carboxamide;

1-235: N-{[(2S)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-236: N-{[(2R)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-237: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4S)-4-fluoropyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-238: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-fluoropyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-239: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,3S)-3-(dimethylamino)cyclobutyl]piperidine-4-carboxamide;

1-240: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1R,3R)-3-(dimethylamino)cyclobutyl]piperidine-4-carboxamide;

1-241: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2S)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-242: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-243: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-fluoro-1-methylpyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-244: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2R)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-245: N-[2-(azetidin-1-yl)ethyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-246: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoropyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-247: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoropyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-248: N-[2-(azetidin-1-yl)ethyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-249: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-250: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-251: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,2S,4R)-7-methyl-7-azabicyclo[2.2.1]heptan-2-yl]piperidine-4-carboxamide;

1-252: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(1S,2S,4R)-7-methyl-7-azabicyclo[2.2.1]heptan-2-yl]piperidine-4-carboxamide;

1-253: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1,3-dimethylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-254: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-255: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-256: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-257: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-258: rac-N-[(1R,2S)-2-aminocyclopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-259: rac-N-[(1R,2R)-2-aminocyclopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-260: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-1-(dimethylamino)propan-2-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-261: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-262: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{3-[(dimethylamino)methyl]oxetan-3-yl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-263: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[1-(dimethylamino)cyclopropyl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-264: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4S)-4-(dimethylamino)oxolan-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-265: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{2-[ethyl(methyl)amino]ethyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-266: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{2-[cyclopropyl(methyl)amino]ethyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-267: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4R)-4-methoxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-268: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-methoxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-269: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-hydroxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-270: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4S)-4-hydroxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-271: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-272: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-273: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-274: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-275: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-276: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-277: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-278: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-279: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S)-4,4-difluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-280: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2R)-4,4-difluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-281: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-282: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-283: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-284: N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-285: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-286: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-287: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-288: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-289: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-290: 4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-291: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]piperidine-4-carboxamide;

1-292: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-293: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-294: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-295: N-[(2S)-1-(dimethylamino)propan-2-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-296: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-297: N-[(2S)-1-(dimethylamino)propan-2-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-298: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-299: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-300: N-[2-(dimethylamino)ethyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-301: 4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-302: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-303: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-304: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-305: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-306: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-307: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-308: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-309: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-310: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-311: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-312: N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-313: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-314: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-315: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-316: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-317: N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-318: 1-(2,4-dichlorophenyl)-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-319: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-320: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-321: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-322: 1-(2,4-dichlorophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-323: 1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-324: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-325: 1-(4-chloro-2-cyanophenyl)-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-326: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-327: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2S)-4-methylmorpholin-2-yl]methyl}piperidine-4-carboxamide;

1-328: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(3S)-4-methylmorpholin-3-yl]methyl}piperidine-4-carboxamide;

1-329: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(3R)-4-methylmorpholin-3-yl]methyl}piperidine-4-carboxamide;

1-330: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2R)-4-methylmorpholin-2-yl]methyl}piperidine-4-carboxamide;

1-331: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]piperidine-4-carboxamide;

1-332: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-2-(dimethylamino)propyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-333: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)propyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-334: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-335: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

2-1: 2-{4-[2-(dimethylamino)ethoxy]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-1-yl}-5-(trifluoromethyl)benzonitrile;

2-2: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl N-[2-(dimethylamino)ethyl]carbamate;

2-3: 3-amino-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}propanamide;

2-4: 3-amino-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}propanamide;

2-5: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)propanamide;

2-6: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}pyrrolidine-3-carboxamide;

2-7: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylpyrrolidine-3-carboxamidev;

2-8: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}pyrrolidine-3-carboxamide;

2-9: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-10: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(dimethylamino)propanamide;

2-11: (2S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylpyrrolidine-2-carboxamide;

2-12: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}carbamate;

2-13: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}carbamate;

2-14: 2-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-[(2-hydroxyethyl)amino]piperidin-1-yl)-5-(trifluoromethyl)benzonitrile;

2-15: 2-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[2-(methylamino)ethyl]amino}piperidin-1-yl)-5-(trifluoromethyl)benzonitrile;

2-16: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-17: (2R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylpyrrolidine-2-carboxamide;

2-18: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}carbamate;

2-19: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-20: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-21: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)pyrrolidine-1-carboxamide;

2-22: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}carbamate;

2-23: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)azetidine-1-carboxamide;

2-24: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)pyrrolidine-1-carboxamide;

2-25: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylazetidine-3-carboxamide;

2-26: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-2-(dimethylamino)acetamide;

2-27: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-28: (3S)-N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-29: (3R)-N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-30: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-3-(dimethylamino)propanamide;

2-31: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-2-(dimethylamino)acetamide;

2-32: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-33: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-34: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-2-(dimethylamino)acetamide;

2-35: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-36: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

2-37: N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-1-methylazetidine-3-carboxamide;

2-38: N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-2-(dimethylamino)acetamide;

2-39: (3S)-N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-40: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-41: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-42: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-43: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-44: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}pyrrolidine-3-carboxamide;

2-45: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-46: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide; and

2-47: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-48: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-49: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-50: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-51: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-52: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-53: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-54: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-55: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-56: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-57: 2-(dimethylamino)ethyl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-58: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[2-(dimethylamino)ethyl]urea;

2-59: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(1-methylazetidin-3-yl)urea;

2-60: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-61: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-2-(dimethylamino)acetamide;

2-62: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

2-63: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(methylamino)propanamide;

2-64: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

or a pharmaceutically acceptable salt, or solvate thereof.

[0004c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0004d] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, or solvate thereof, in the manufacture of a medicament for treating a disease or condition in a mammal that would benefit from the modulation of melanocortin subtype-2 receptor (MC2R) activity; wherein the disease or condition comprises growth of fat pads in the collarbone, back of neck, face and trunk, excessive sweating, dilation of capillaries, thinning of the skin, muscle weakness, hirsutism, depression/anxiety, hypertension, osteoporosis, insulin resistance, hyperglycemia, and heart disease.

[0004e] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, or solvate thereof, in the manufacture of a medicament for treating Cushing’s syndrome, ectopic Cushing's syndrome, congenital adrenal hyperplasia (CAH), or for reducing the secretion of adrenocorticotropic hormone (ACTH) in a mammal.

[0004f] In another aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt, or solvate thereof, for use in therapy.

[0005] In one ~~aspect~~example, described herein is a compound of Formula (I), or a pharmaceutically acceptable salt, or solvate thereof:

each R^6 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_4alkyl, unsubstituted or substituted C_1-C_4alkoxy, unsubstituted or substituted C_1-C_4fluoroalkyl, unsubstituted or substituted C_1-C_4fluoroalkoxy, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, $-CO_2R^5$, $-CH_2CO_2R^5$, $-C(=O)N(R^4)_2$, $-C(=O)N(R^4)OR^5$, $-CH_2C(=O)N(R^4)_2$, $-N(R^4)_2$, $-CH_2N(R^4)_2$, $-C(R^5)_2N(R^4)_2$, $-NR^4C(=O)R^5$, $-CH_2NR^4C(=O)R^5$, $-NR^4C(=O)N(R^5)_2$, $-NR^4C(=O)N(R^4)_2$, $C(R^5)=N(R^4)-OR^5$, $-SR^5$, $-S(=O)R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$; and

each R^7 is independently selected from the group consisting substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl.

[0006] 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 ~~embodiment~~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 ~~embodiment~~examples, the pharmaceutical composition is formulated for administration to a mammal by oral administration. In some ~~embodiment~~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 ~~embodiment~~examples, the pharmaceutical composition is in the form of a tablet, a pill, or a capsule.

[0007] In any of the aforementioned ~~aspect~~examples are further ~~embodiment~~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.

[0008] In any of the aforementioned ~~aspect~~examples are further ~~embodiment~~examples comprising single administrations of the effective amount of the compound, including further ~~embodiment~~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 ~~embodiment~~examples, the compound is administered on a continuous dosing schedule. In some ~~embodiment~~examples, the compound is administered on a continuous daily dosing schedule.

[0009] In any of the ~~embodiment~~examples disclosed herein, the mammal is a human.

[0010] In some ~~embodiment~~examples, compounds provided herein are orally administered to a human.

[0011] 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 melanocortin 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 melanocortin receptor proteins, are provided.

[0012] 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 ~~embodiment~~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

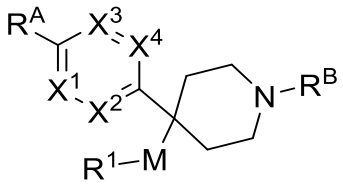
[0013] Adrenocorticotropic hormone (ACTH) is a 39 amino acid peptide synthesized by anterior pituitary corticotrophic cells by proteolytic cleavage of the proopiomelanocortin hormone (POMC). ACTH is the primary regulator of adrenal glucocorticoid (GC; cortisol in humans and most other species; corticosterone in rodents) synthesis and secretion. As the central actor in this hypothalamic-pituitary-adrenal (HPA) axis, ACTH is secreted by the pituitary in response to stressful stimuli and acts at the adrenal gland to stimulate the synthesis and secretion of cortisol. This stimulation is mediated through a highly specific G protein-coupled receptor (GPCR) which is expressed almost uniquely in the adrenal cortex. The receptor is the melanocortin 2 receptor (MC2R), and, along with ACTH, is part of the larger melanocortin system.

[0014] The melanocortin system comprises a family of five GPCRs (MC1R, MC2R, MC3R, MC4R, and MC5R); their natural agonists, the melanocortin peptides α-, β-, and γ-melanocyte-stimulating hormone (α-MSH, β-MSH, and γ-MSH) and ACTH; and endogenous melanocortin antagonists agouti and agouti-related protein (AGRP). The melanocortin receptors (MCRs) have different selectivities for endogenous agonist and antagonist peptides and are expressed in diverse tissues where they serve varied and discreet physiological functions (Gantz, I. and T.M. Fong, *Am. J. Physiol. Endocrinol. Metab.*, 284: E468–E474, 2003).

CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (I), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (I)

wherein:

R^A is unsubstituted or substituted heteroaryl or unsubstituted or substituted aryl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c;

R^a, R^b, and R^c are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl, wherein any substituted group of R^a, R^b, and R^c is substituted with one or more R^6 groups;

or one R^a and one R^b, when present on adjacent atoms of R^A, are taken together with the intervening atoms connecting R^a to R^b to form a 5- to 6-membered monocyclic carbocycle or 5- to 6-membered monocyclic heterocycle, wherein the carbocycle or heterocycle is unsubstituted or substituted with one or more R^6 groups;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, 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 C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

R^B is unsubstituted or substituted aryl or unsubstituted or substituted heteroaryl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f;

R^d, R^e, and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, $-C(=O)N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, and

unsubstituted or substituted heteroaryl, wherein any substituted group of R^d, R^e, and R^f is substituted with one or more R^6 groups;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, -C(=O)R^7, 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 C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

X^1 is CR^{11} or N;

X^2 is CR^{12} or N;

X^3 is CR^{13} or N;

X^4 is CR^{14} or N;

R^{11}, R^{12}, R^{13}, and R^{14} are each 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 C_3-C_6cycloalkyl, -CN, -OR^4, -SR^4, -CO_2R^4, -C(=O)N(R^4)$_2$, or -N(R^4)$_2$;

M is -(C=O)-, -NR^3-, -O-, -S-, -SO_2-, *-NR^3-(C=O)-, *-(C=O)-NR^3-, *-O-(C=O)NR^3-, *-NR^3-(C=O)O-, -NR^3-(C=O)NR^3-, *-NR^3(SO_2)-, *-SO_2NR^3-, or 5-membered heterocycle, wherein * indicates the attachment point to R^1;

R^1 is 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted -(C_1-C_6 alkyl)-(C_3-C_6 cycloalkyl), or unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, -N(R^4)$_2$, -OR^5, -CN, -CO_2R^5, -C(=O)N(R^4)$_2$, -SR^5, -S(=O)R^7, -S(=O)$_2R^7$, -NR^4C(=O)R^5, -$NR^4SO_2R^7$, -SO_2R^7, or -SO_2N(R^4)$_2$;

each R^3 is independently hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl;

each R^4 is independently selected from the group consisting of hydrogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted aryl, and unsubstituted or substituted heteroaryl;

or two R^4 are taken together with the nitrogen atom to which they are attached to form an unsubstituted or substituted 3- to 6-membered monocyclic heterocycle;

each R^5 is independently selected from the group consisting of hydrogen, substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted aryl, and unsubstituted or substituted heteroaryl;

each R^6 is independently hydrogen, halogen, unsubstituted or substituted C_1-C_4alkyl, unsubstituted or substituted C_1-C_4alkoxy, unsubstituted or substituted C_1-C_4fluoroalkyl, unsubstituted or substituted C_1-C_4fluoroalkoxy, unsubstituted or substituted monocyclic carbocycle, unsubstituted or substituted monocyclic heterocycle, -CN, -OH, $-CO_2R^5$, $-CH_2CO_2R^5$, $-C(=O)N(R^4)_2$, $-C(=O)N(R^4)OR^5$, $-CH_2C(=O)N(R^4)_2$, $-N(R^4)_2$, $-CH_2N(R^4)_2$, $-C(R^5)_2N(R^4)_2$, $-NR^4C(=O)R^5$, $-CH_2NR^4C(=O)R^5$, $-NR^4C(=O)N(R^5)_2$, $-NR^4C(=O)N(R^4)_2$, $C(R^5)=N(R^4)-OR^5$, $-SR^5$, $-S(=O)R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$; and

each R^7 is independently selected from the group consisting substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, unsubstituted or substituted C_1-C_6fluoroalkyl, unsubstituted or substituted phenyl, and unsubstituted or substituted heteroaryl.

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

M is $-NR^3$-, -O-, *-NR^3-(C=O)-, *-(C=O)-NR^3-, *-O-(C=O)NR^3-, *-NR^3-(C=O)O-, or -NR^3-(C=O)NR^3-, wherein * indicates the attachment point to R^1; and

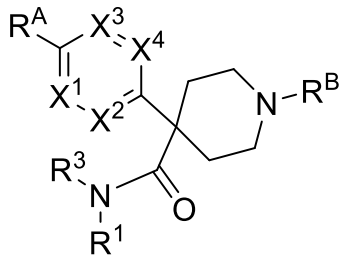
each R^3 is independently hydrogen, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, or $-CH(CH_3)_2$.

~~3. The compound of any one of claims 1-2, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

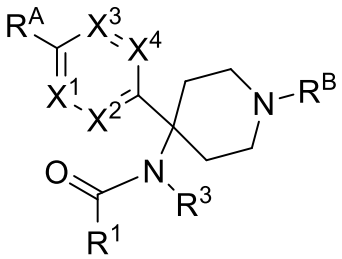
~~M is * NR^3 (C=O) or * (C=O) NR^3, wherein * indicates the attachment point to R^1; and~~

~~R^3 is hydrogen.~~

~~4.~~3. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (IIa) or Formula (IIb), or a pharmaceutically acceptable salt thereof:



Formula (IIa)



Formula (IIb).

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

R^A is unsubstituted or substituted monocyclic 6-membered heteroaryl, unsubstituted or substituted phenyl, or unsubstituted or substituted monocyclic 5-membered heteroaryl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c.

~~6. The The compound of any one of claims 1-5, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^A is unsubstituted or substituted monocyclic 6-membered heteroaryl or unsubstituted or substituted phenyl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c.~~

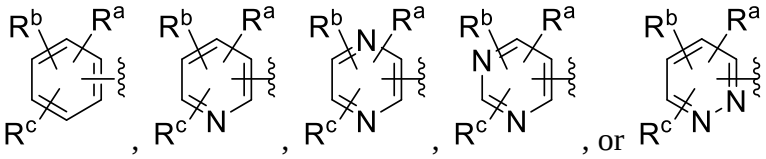
~~7.~~5. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is unsubstituted or substituted pyridinyl, unsubstituted or substituted pyrimidinyl, unsubstituted or substituted pyrazinyl, or unsubstituted or substituted pyridazinyl, or unsubstituted or substituted phenyl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c.

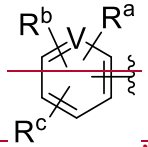
~~8. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^A is unsubstituted or substituted pyridinyl or unsubstituted or substituted phenyl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^c.~~

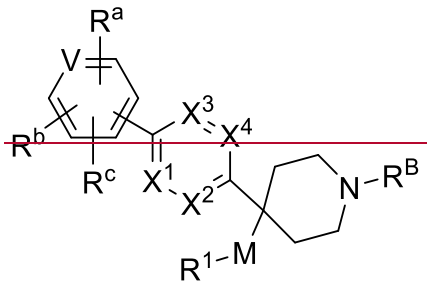
~~9.~~6. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is .

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

~~R^A is~~  ~~, where V is CH, CR^a, CR^b, or N.~~

~~11. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (IV), or a pharmaceutically acceptable salt, or solvate thereof:~~



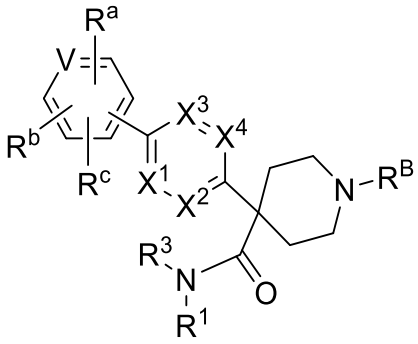
~~Formula (IV)~~

~~wherein V is CH, CR^a, CR^b, or N.~~

~~12. The compound of claim 11, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~M is * NR^3 (C=O) or * (C=O) NR^3 , wherein * indicates the attachment point to R^1; and R^3 is hydrogen.~~

~~13.~~7. The compound of claim ~~11~~1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (IVa), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IVa)

wherein V is CH, CR^a, CR^b, or N.

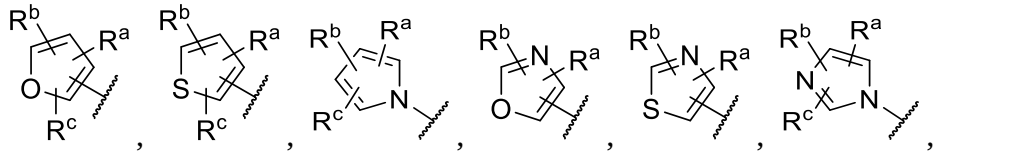
~~14. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

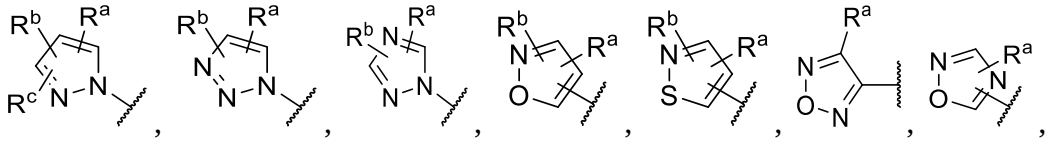
~~R^A is unsubstituted or substituted monocyclic 5-membered heteroaryl, wherein if R^A is substituted then R^A is substituted with 1, 2, or 3 groups selected from R^a, R^b, and R^c.~~

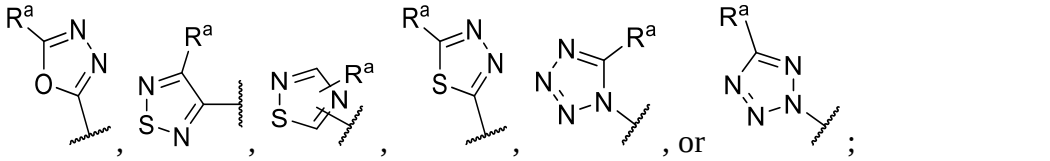
~~15. The compound of claim 14, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^A is unsubstituted or substituted furanyl, unsubstituted or substituted thienyl, or unsubstituted or substituted pyrrolyl, wherein if R^A is substituted then R^A is substituted with 1, 2, or 3 groups selected from R^a, R^b, and R^c.~~

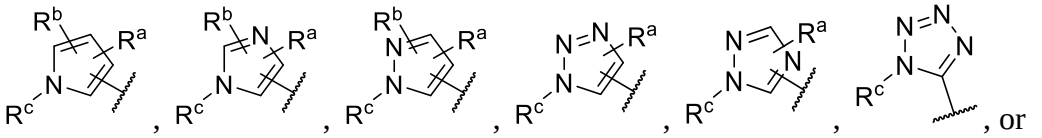
~~16.~~8. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

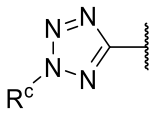
R^A is 



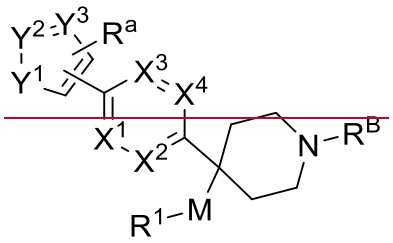


, or ;

or R^A is 

, where R^c is hydrogen, -C(=O)R^7, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl.

~~17. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (III), or a pharmaceutically acceptable salt, or solvate thereof:~~



~~Formula (III)~~

~~wherein:~~

~~Y^1 is NR^e, O, or S;~~

~~Y^2 and Y^3 are independently CH, CR^a, CR^b, or N; and~~

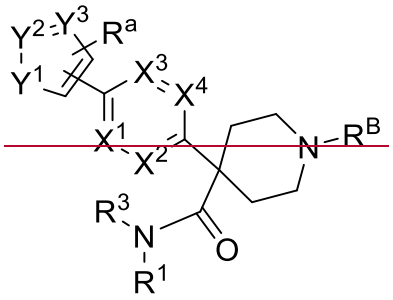
~~R^e is hydrogen, -C(=O)R^7, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl.~~

~~18. The compound of claim 17, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~M is * NR^3 (C=O) or * (C=O) NR^3, wherein * indicates the attachment point to R^1; and~~

~~R^3 is hydrogen.~~

19. The compound of claim 17, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (IIIa), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIIa)

wherein:

Y^1 is NR^e, O, or S;

Y^2 and Y^3 are independently CH, CR^a, CR^b, or N; and

R^e is hydrogen, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl.

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

R^A is unsubstituted or substituted bicyclic 9- to 10-membered heteroaryl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^e.

21. The compound of claim 20, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is unsubstituted or substituted quinolinyl, unsubstituted or substituted indolyl, unsubstituted or substituted indazolyl or unsubstituted or substituted benzofuranyl, wherein if R^A is substituted then R^A is substituted with 1, 2, 3 or 4 groups selected from R^a, R^b, and R^e.

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

R^B is an unsubstituted or substituted phenyl, unsubstituted or substituted naphthyl, unsubstituted or substituted monocyclic 6-membered heteroaryl, unsubstituted or substituted monocyclic 5-membered heteroaryl, or unsubstituted or substituted bicyclic heteroaryl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f.

23.9. The compound of any one of claims 1-218, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^B is an unsubstituted or substituted phenyl or unsubstituted or substituted monocyclic 6-membered heteroaryl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f.

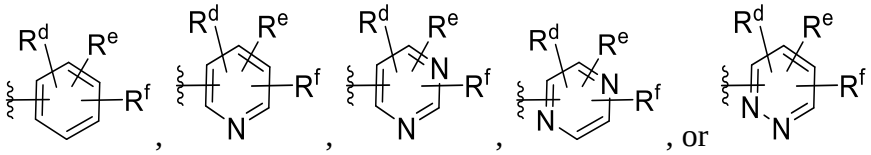
~~24. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^B is unsubstituted or substituted phenyl, unsubstituted or substituted pyridinyl, unsubstituted or substituted pyrimidinyl, unsubstituted or substituted pyrazinyl, or unsubstituted or substituted pyridazinyl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f.~~

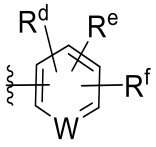
~~25. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^B is unsubstituted or substituted phenyl or unsubstituted or substituted pyridinyl, wherein if R^B is substituted then R^B is substituted with 1, 2, 3 or 4 groups selected from R^d, R^e, and R^f.~~

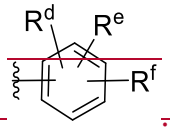
~~26.~~10. The compound of any one of claims 1-~~23~~9, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^B is .

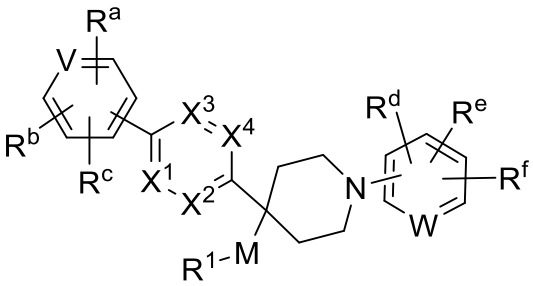
~~27.~~11. The compound of any one of claims 1-~~9~~23, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^B is , where W is CH, CR^d, CR^e, or N.

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

~~R^B is~~ ~~.~~

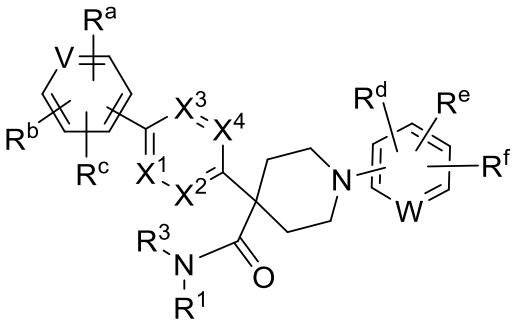
~~29.~~12. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (VI), or a pharmaceutically acceptable salt, or solvate thereof:



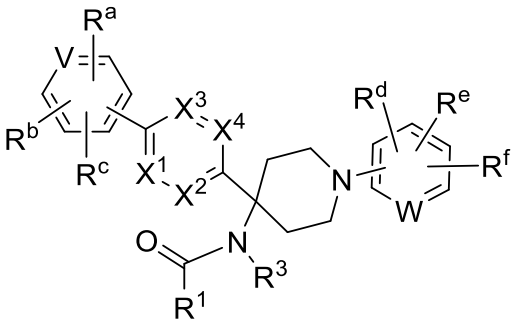
Formula (VI)

wherein V is CH, CR^a, CR^b, or N; and W is CH, CR^d, CR^e, or N.

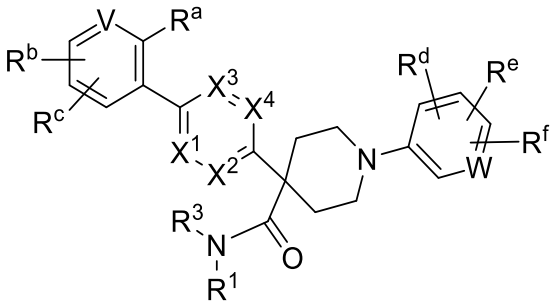
~~30.~~13. The compound of claim 12~~29~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (VIa)~~, or~~ Formula (VIc), Formula (VIb), Formula (VId), Formula (VIIb) or Formula (VIIe), or a pharmaceutically acceptable salt, or solvate thereof:



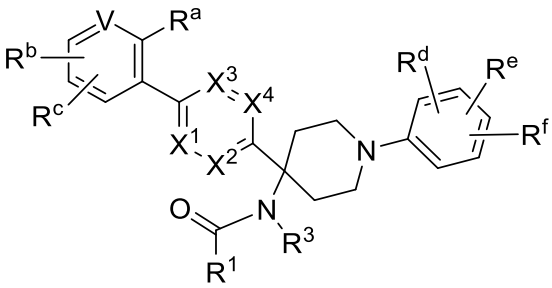
Formula (VIa)



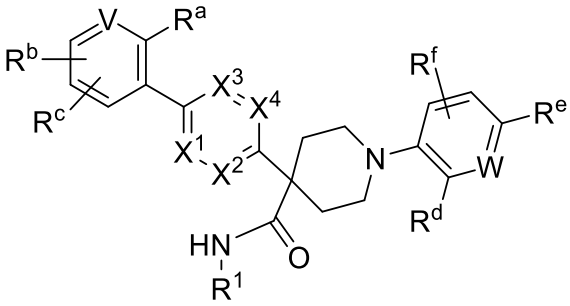
Formula (VIc~~a~~)



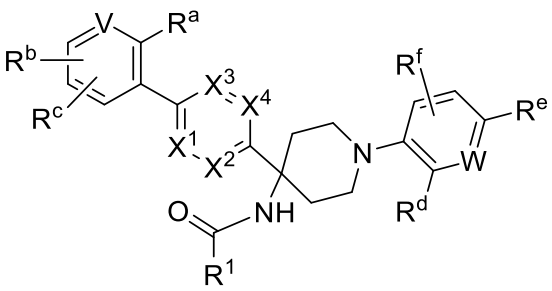
Formula (VIb)



Formula (VId)



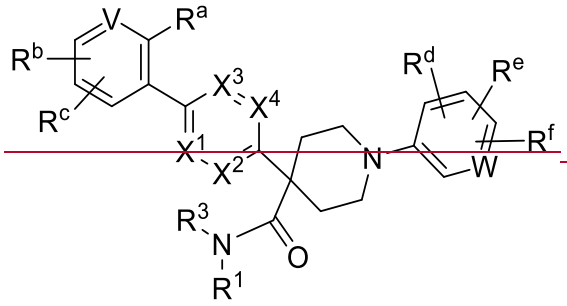
Formula (VIIb) or



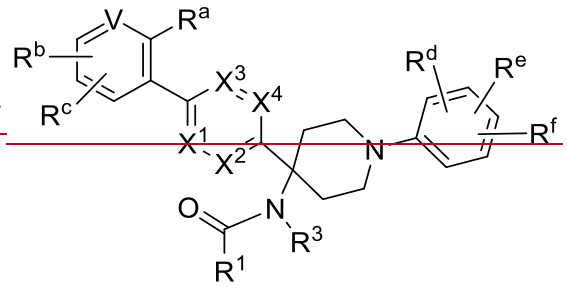
Formula (VIIe);

wherein V is CH, CR^a, CR^b, or N; and W is CH, CR^d, CR^e, or N.

31. The compound of claim 29 or claim 30, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (VIb) or Formula (VId), or a pharmaceutically acceptable salt, or solvate thereof:



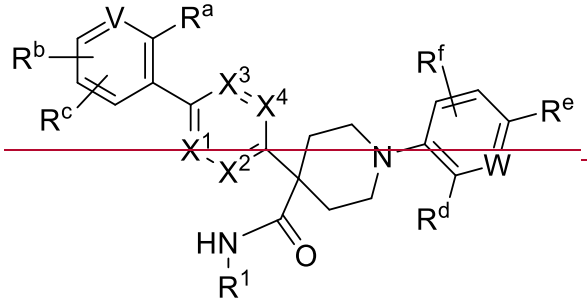
Formula (VIb)



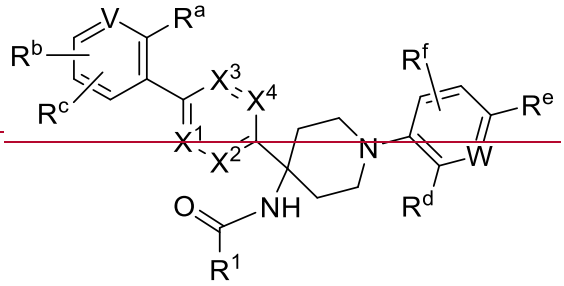
Formula (VIb)

wherein V is CH, CR^{a}, CR^{b}, or N; and W is CH, CR^{d}, CR^{e}, or N.

32. The compound of claim 29 or claim 30, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (VIIb) or Formula (VIIc), or a pharmaceutically acceptable salt, or solvate thereof:

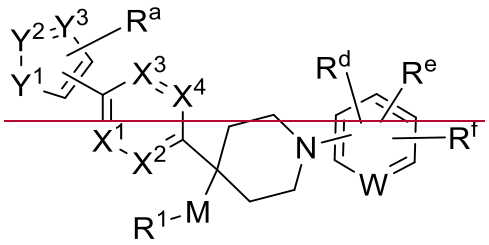


Formula (VIIb)



Formula (VIIc).

33. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (V), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (V)

wherein:

Y^{1} is NR^{c}, O, or S;

Y^{2} and Y^{3} are independently CH, CR^{a}, CR^{b}, or N;

R^{c} is hydrogen, -C(=O)R^{7}, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl; and

W is CH, CR^{d}, CR^{e}, or N.

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

~~R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-4 N atoms and 0 or 1 O or S atoms, unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms, or unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, $-N(R^4)_2$, $-OR^5$, -CN, $-CO_2R^5$, $-C(=O)N(R^4)_2$, $-SR^5$, $-S(=O)R^7$, $-S(=O)_2R^7$, $-NR^4C(=O)R^5$, $-NR^4SO_2R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$.~~

~~35.~~14. The compound of any one of claims 1-~~34~~13, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, $-N(R^4)_2$, $-OR^5$, -CN, $-CO_2R^5$, $-C(=O)N(R^4)_2$, $-SR^5$, $-S(=O)R^7$, $-S(=O)_2R^7$, $-NR^4C(=O)R^5$, $-NR^4SO_2R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-4 N atoms and 0 or 1 O or S atoms.

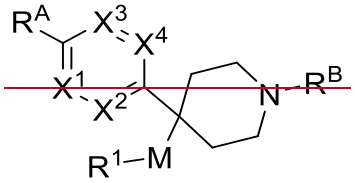
~~36.~~15. The compound of claim 14~~35~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-4 N atoms and 0 or 1 O or S atoms.

~~37. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (VIII), or a pharmaceutically acceptable salt, or solvate thereof:~~



~~Formula (VIII)~~

~~wherein:~~

~~R^A is unsubstituted or substituted phenyl, unsubstituted or substituted pyridinyl, unsubstituted or substituted furanyl, unsubstituted or substituted thienyl, unsubstituted or substituted pyrrolyl, unsubstituted or substituted pyrazolyl, unsubstituted or substituted isoxazolyl, unsubstituted or substituted quinolinyl, unsubstituted or substituted indolyl, unsubstituted or substituted indazolyl, or unsubstituted or substituted benzofuranyl, wherein if R^A is substituted then R^A is substituted with 1 or 2 groups selected from R^a, R^b, and R^c;~~

~~R^B is unsubstituted or substituted phenyl or unsubstituted or substituted pyridinyl, wherein if R^B is substituted then R^B is substituted with 1, 2, or 3 groups selected from R^d, R^e, and R^f; and~~

~~M is $-NR^3-$, $-O-$, $*-NR^3-(C=O)-$, $*-(C=O)-NR^3-$, $*-O-(C=O)NR^3-$, $*-NR^3-(C=O)O-$, or $-NR^3-(C=O)NR^3-$, wherein * indicates the attachment point to R^1.~~

~~38.~~16. The compound of any one of claims 1-15~~37~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

X^1 is CR^{11}; X^2 is CR^{12}; X^3 is CR^{13}; and X^4 is CR^{14};

or X^1 is N; X^2 is CR^{12}; X^3 is CR^{13}; and X^4 is CR^{14};

or X^1 is CR^{11}; X^2 is N; X^3 is CR^{13}; and X^4 is CR^{14};

or X^1 is N; X^2 is CR^{12}; X^3 is CR^{13}; and X^4 is N;

or X^1 is N; X^2 is N; X^3 is CR^{13}; and X^4 is CR^{14};

or X^1 is N; X^2 is CR^{12}; X^3 is N; and X^4 is CR^{14};

or X^1 is CR^{11}; X^2 is CR^{12}; X^3 is CR^{13}; and X^4 is CR^{14}.

~~39. The compound of any one of claims 1-37, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~X^1 is N; X^2 is CR^{12}; X^3 is CR^{13}; and X^4 is CR^{14}.~~

~~40.~~17. The compound of any one of claims 1-~~37~~15, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

X^1 is CH, CF, or N;

X^2 is CH, CF, or N;

X^3 is CH, CF, or N; and

X^4 is CH, CF, or N.

~~41.~~18. The compound of any one of claims 1-15~~37~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

X^1 is N;

X^2 is CH;

X^3 is CH or CF; and

X^4 is CH.

~~42.~~19. The compound of any one of claims 1-18~~41~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^a, R^b, and R^c are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^a, R^b, and R^c is substituted with one or more R^6 groups;

or one R^a and one R^b, when present on adjacent atoms of R^A, are taken together with the intervening atoms connecting R^a to R^b to form a 5- to 6-membered monocyclic carbocycle or 5- to 6-membered monocyclic heterocycle, wherein the carbocycle or heterocycle is unsubstituted or substituted with one or more R^6 groups;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl; and

R^d, R^e, and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, $-C(=O)N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d, R^e, and R^f is substituted with one or more R^6 groups;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, -C(=O)R^7, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_3-C_6 cycloalkyl, or unsubstituted or substituted C_2-C_7 heterocycloalkyl.

~~43.~~20. The compound of any one of claims 1-18~~41~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^a is selected from the group consisting of hydrogen, halogen, -OR^4, -CN, -$N(R^4)_2$, -C(=O)R^7, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, and unsubstituted or substituted C_3-C_6 cycloalkyl, wherein any substituted group of R^a is substituted with one or more R^6 groups; and

R^b and R^c are independently selected from the group consisting of hydrogen, halogen, -OR^4, -CN, -$N(R^4)_2$, -C(=O)R^7, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl, wherein any substituted group of R^b and R^c is substituted with one or more R^6 groups;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, -C(=O)R^7, or unsubstituted or substituted C_1-C_6 alkyl;~~.~~

R^d is selected from the group consisting of hydrogen, halogen, -OR^4, -CN, -$N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d is substituted with one or more R^6 groups; and

R^e and R^f are independently selected from the group consisting of hydrogen, halogen, -OR^4, -CN, -$N(R^4)_2$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, -C(=O)R^7, or unsubstituted or substituted C_1-C_6 alkyl.

~~44.~~21. The compound of any one of claims 1-18~~41~~, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^a is selected from the group consisting of hydrogen, F, Cl, Br, -CN, -OH, -OCH_3, -OCH_2CH_3, -C(O)CH_3, -C(O)CH_2CH_3, -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH(CH_3)_2$, -$CH_2CH_2CH_2CH_3$, -$CH_2CH(CH_3)_2$, -$CH(CH_3)(CH_2CH_3)$, -$C(CH_3)_3$, -$CH_2CH_2CH(CH_3)_2$, -CH_2OH, -CH_2CN, -CH_2F, -CHF_2, -CF_3, -CH_2CH_2OH, -CH_2CH_2CN, -CH_2CH_2F, -CH_2CHF_2, -CH_2CF_3, -CH_2OCH_3, -$CH_2CH_2OCH_3$, -

CH_2NH_2, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$, $-CH_2CH_2N(CH_3)_2$, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^b and R^c are independently selected from the group consisting of hydrogen, F, Cl, Br, -CN, -OH, $-OCH_3$, $-OCH_2CH_3$, $-C(O)CH_3$, $-C(O)CH_2CH_3$, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)(CH_2CH_3)$, $-C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2OH$, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_2OH$, $-CH_2CH_2CN$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$, and $-CH_2CH_2N(CH_3)_2$;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(O)CH_3$, $-C(O)CH_2CH_3$, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)(CH_2CH_3)$, $-C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2OH$, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_2OH$, $-CH_2CH_2CN$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$, and $-CH_2CH_2N(CH_3)_2$;.

~~45. The compound of any one of claims 1-41, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~one R^a and one R^b on adjacent atoms of R^A are taken together with the intervening atoms connecting R^a to R^b to form a 5- to 6-membered monocyclic cycloalkyl or 5- to 6-membered monocyclic heterocycloalkyl, wherein the cycloalkyl or heterocycloalkyl is unsubstituted or substituted with one or more R^6 groups.~~

~~46. The compound of claim 45, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~one R^a and one R^b on adjacent atoms of R^A are taken together with the intervening atoms connecting R^a to R^b to form a 5-membered monocyclic heterocycloalkyl, wherein the heterocycloalkyl is unsubstituted or substituted with one or more R^6 groups.~~

~~47. The compound of any one of claims 1-46, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^d is selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic~~

~~heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d is substituted with one or more R^6 groups; and~~

~~R^e and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl;~~

~~wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl.~~

~~48. The compound of any one of claims 1-46, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

R^d is selected from the group consisting of hydrogen, F, Cl, Br, -CN, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)(CH_2CH_3)$, $-C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2OH$, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_2OH$, $-CH_2CH_2CN$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$, $-CH_2CH_2N(CH_3)_2$, unsubstituted or substituted cyclopropyl, unsubstituted or substituted cyclobutyl, unsubstituted or substituted cyclopentyl, unsubstituted or substituted cyclohexyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d is substituted with one or more R^6 groups; and

R^e and R^f are independently selected from the group consisting of hydrogen, F, Cl, Br, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)(CH_2CH_3)$, $-C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2OH$, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CF_3$, -CN, -OH, $-OCH_3$, and $-OCH_2CH_3$;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(O)CH_3$, $-C(O)CH_2CH_3$, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)(CH_2CH_3)$, $-C(CH_3)_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2OH$, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_2OH$, $-CH_2CH_2CN$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$, and $-CH_2CH_2N(CH_3)_2$.

~~49.~~22. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is unsubstituted or substituted 6-membered or 5-membered heteroaryl containing 1 or 2 N atoms or unsubstituted or substituted phenyl, wherein if R^A is substituted then R^A is substituted with 1, or 2 groups selected from R^a, R^b, and R^c;

R^a is selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, and unsubstituted or substituted C_3-C_6 cycloalkyl, wherein any substituted group of R^a is substituted with one or more R^6 groups;

R^b and R^c are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl, wherein any substituted group of R^b and R^c is substituted with one or more R^6 groups;

wherein, if R^a, R^b, or R^c is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl;

R^B is unsubstituted or substituted phenyl or unsubstituted or substituted 5- or 6-membered heteroaryl containing 1 or 2 N atoms, wherein if R^B is substituted then R^B is substituted with 1, 2, or 3 groups selected from R^d, R^e, and R^f;

R^d is selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d is substituted with one or more R^6 groups;

R^e and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl;

X^1 is CR^{11} or N;

X^2 is CR^{12} or N;

X^3 is CR^{13} or N;

X^4 is CR^{14} or N;

R^{11}, R^{12}, R^{13}, and R^{14} are each independently hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, or C_1-C_6 heteroalkyl, -CN, $-OR^4$, or $-N(R^4)_2$;

M is *-NR^3-(C=O)- or *-(C=O)-NR^3-, wherein * indicates the attachment point to R^1;

R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, -$N(R^4)_2$, -OR^5, -CN, -CO_2R^5, -$C(=O)N(R^4)_2$, -SR^5, -$S(=O)R^7$, -$S(=O)_2R^7$, -$NR^4C(=O)R^5$, -$NR^4SO_2R^7$, -SO_2R^7, or -$SO_2N(R^4)_2$;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.

~~50.~~23. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is unsubstituted or substituted pyridinyl, unsubstituted or substituted phenyl, or unsubstituted or substituted pyrrolyl, wherein if R^A is substituted then R^A is substituted with 1, or 2 groups selected from R^a, R^b, and R^c;

R^B is unsubstituted or substituted phenyl or unsubstituted or substituted pyridinyl, wherein if R^B is substituted then R^B is substituted with 1, 2, or 3 groups selected from R^d, R^e, and R^f;

X^1 is CH or N;

X^2 is CH or N;

X^3 is CR^{13} or N;

X^4 is CH or N;

M is *-NR^3-(C=O)- or *-(C=O)-NR^3-, wherein * indicates the attachment point to R^1;

R^{11}, R^{12}, R^{13}, and R^{14} are each independently hydrogen, F, Cl, -CH_3, CF_3, -CN, -OR^4, or -$N(R^4)_2$;

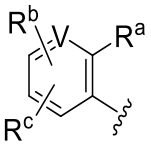
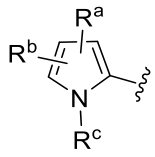
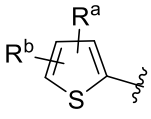
R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, C_1-C_4 alkyl, -$N(R^4)_2$, or -OR^5;

or R^1 is unsubstituted or substituted azetidinyl, unsubstituted or substituted pyrrolidinyl, or unsubstituted or substituted piperidinyl;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

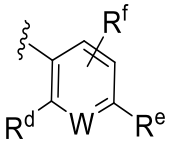
or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.

~~51.~~24. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is , or R^A is ; or R^A is ; where V is CH or N;

R^a is selected from the group consisting of hydrogen, halogen, -OR^4, -CN, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_3-C_6 cycloalkyl; and

R^b and R^c are independently selected from the group consisting of hydrogen, halogen, -OR^4, -CN, unsubstituted or substituted C_1-C_6 alkyl, and unsubstituted or substituted C_1-C_6 fluoroalkyl;

R^B is , where W is CH or N;

R^d is selected from the group consisting of hydrogen, halogen, -OR^4, -CN, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_3-C_6 cycloalkyl; and

R^e and R^f are independently selected from the group consisting of hydrogen, halogen, -OR^4, -CN, unsubstituted or substituted C_1-C_6 alkyl, and unsubstituted or substituted C_1-C_6 fluoroalkyl;

X^1 is CH, CF, or N;

X^2 is CH, CF, or N;

X^3 is CH, CF, or N;

X^4 is CH, CF, or N;

M is *-NH-(C=O)- or *-(C=O)-NH-, wherein * indicates the attachment point to R^1;

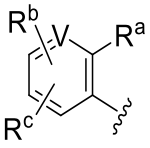
R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, -$N(R^4)_2$, -OR^5, -CN, -CO_2R^5, -$C(=O)N(R^4)_2$, -SR^5, -$S(=O)R^7$, -$S(=O)_2R^7$, -$NR^4C(=O)R^5$, -$NR^4SO_2R^7$, -SO_2R^7, or -$SO_2N(R^4)_2$;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

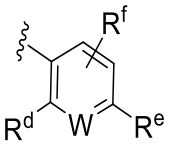
or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.

~~52.~~25. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is , where V is CH or N;

R^a is selected from the group consisting of hydrogen, F, Cl, Br, -CN, -OCH_3, -OCH_2CH_3, -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH(CH_3)_2$, -$CH_2CH_2CH_2CH_3$, -$CH_2CH(CH_3)_2$, -$CH(CH_3)(CH_2CH_3)$, -$C(CH_3)_3$, -CH_2F, -CHF_2, and -CF_3; and

R^b and R^c are independently selected from the group consisting of hydrogen, F, Cl, -CH_3, -CH_2F, -CHF_2, -CF_3, -CN, and -OCH_3;

R^B is , where W is CH or N;

R^d is selected from the group consisting of hydrogen, F, Cl, Br, -CN, -OCH_3, -OCH_2CH_3, -CH_3, -CH_2CH_3, -$CH_2CH_2CH_3$, -$CH(CH_3)_2$, -$CH_2CH_2CH_2CH_3$, -$CH_2CH(CH_3)_2$, -$CH(CH_3)(CH_2CH_3)$, -$C(CH_3)_3$, -CH_2F, -CHF_2, and -CF_3;

R^e and R^f are independently selected from the group consisting of hydrogen, F, Cl, Br, -CH_3, -CH_2F, -CHF_2, -CF_3, -CN, -OH, and -OCH_3;

X^1 is CH or N;

X^2 is CH or N;

X^3 is CH, CF, or N;

X^4 is CH or N;

M is *-NH-(C=O)- or *-(C=O)-NH-, wherein * indicates the attachment point to R^1;

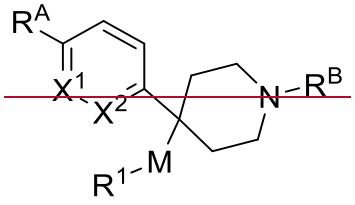
R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, -$N(R^4)_2$, -OR^5, -CN, -CO_2R^5, -$C(=O)N(R^4)_2$, -SR^5, -$S(=O)R^7$, -$S(=O)_2R^7$, -$NR^4C(=O)R^5$, -$NR^4SO_2R^7$, -SO_2R^7, or -$SO_2N(R^4)_2$;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.

~~53. The compound of claim 1, or a pharmaceutically acceptable salt, or solvate thereof, wherein the compound has the structure of Formula (IX), or a pharmaceutically acceptable salt, or solvate thereof:~~



~~Formula (IX)~~

~~wherein,~~

~~R^A is unsubstituted or substituted 6-membered or 5-membered heteroaryl containing 1 or 2 N atoms or unsubstituted or substituted phenyl, wherein if R^A is substituted then R^A is substituted with 1 or 2 groups selected from R^a, R^b, and R^e;~~

~~R^a is selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, unsubstituted or substituted C_1-C_6 heteroalkyl, and unsubstituted or substituted C_3-C_6 cycloalkyl, wherein any substituted group of R^a is substituted with one or more R^6 groups; and~~

~~R^b and R^e are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, $-C(=O)R^7$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl, wherein any substituted group of R^b and R^e is substituted with one or more R^6 groups;~~

~~wherein, if R^a, R^b, or R^e is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl;~~

~~R^B is unsubstituted or substituted phenyl or unsubstituted or substituted 5- or 6-membered heteroaryl containing 1 or 2 N atoms, wherein if R^B is substituted then R^B is substituted with 1, 2, or 3 groups selected from R^d, R^e, and R^f;~~

~~R^d is selected from the group consisting of hydrogen, halogen, $-OR^4$, -CN, $-N(R^4)_2$, 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 C_3-C_6 cycloalkyl, unsubstituted or substituted C_2-C_7 heterocycloalkyl,~~

unsubstituted or substituted phenyl, unsubstituted or substituted monocyclic heteroaryl, and unsubstituted or substituted bicyclic heteroaryl, wherein any substituted group of R^d is substituted with one or more R^6 groups; and

R^e and R^f are independently selected from the group consisting of hydrogen, halogen, $-OR^4$, $-CN$, $-N(R^4)_2$, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 fluoroalkyl, and unsubstituted or substituted C_1-C_6 heteroalkyl;

wherein, if R^d, R^e, or R^f is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl;

X^1 is CR^{11} or N;

X^2 is CR^{12} or N;

R^{11} and R^{12} are each independently hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, or C_1-C_6 heteroalkyl, $-CN$, $-OR^4$, or $-N(R^4)_2$;

M is $-NR^3-$, $-O-$, $*-NR^3-(C=O)-$, $*-(C=O)-NR^3-$, $*-O-(C=O)NR^3-$, $*-NR^3-(C=O)O-$, or $-NR^3-(C=O)NR^3-$, wherein * indicates the attachment point to R^1; and

R^1 is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted monocyclic heterocycle, $-N(R^4)_2$, $-OR^5$, $-CN$, $-CO_2R^5$, $-C(=O)N(R^4)_2$, $-SR^5$, $-S(=O)R^7$, $-S(=O)_2R^7$, $-NR^4C(=O)R^5$, $-NR^4SO_2R^7$, $-SO_2R^7$, or $-SO_2N(R^4)_2$;

or R^1 is unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycle containing 1-4 N atoms and 0 or 1 O or S atoms;

or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;

or R^1 is unsubstituted or substituted $-(C_1$-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.

54. The compound of claim 53, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^A is unsubstituted or substituted pyridinyl, unsubstituted or substituted phenyl, or unsubstituted or substituted pyrrolyl, wherein if R^A is substituted then R^A is substituted with 1 or 2 groups selected from R^a, R^b, and R^e;

wherein, if R^a, R^b, or R^e is attached to the N atom of a heteroaryl, then it is hydrogen, $-C(=O)R^7$, or unsubstituted or substituted C_1-C_6 alkyl;

~~R^B is unsubstituted or substituted phenyl or unsubstituted or substituted pyridinyl, wherein if R^B is substituted then R^B is substituted with 1, 2, or 3 groups selected from R^d, R^e, and R^f;~~

~~X^1 is CR^{11} or N;~~

~~X^2 is CR^{12} or N;~~

~~R^{11} and R^{12} are each independently hydrogen, F, Cl, $-CH_3$, CF_3, -CN, $-OR^4$, or $-N(R^4)_2$;~~

~~R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, C_1-C_4 alkyl, $-N(R^4)_2$, or $-OR^5$;~~

~~or R^1 is unsubstituted or substituted azetidinyl, unsubstituted or substituted pyrrolidinyl, or unsubstituted or substituted piperidinyl;~~

~~or R^1 is unsubstituted or substituted bridged C_2-C_7 heterocycloalkyl containing 1-2 N atoms;~~

~~or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the C_2-C_7 heterocycloalkyl is an unsubstituted or substituted monocyclic 4-, 5- or 6-membered heterocycloalkyl containing 1-2 N atoms.~~

~~55.~~26. The compound of any one of claims 1-~~54~~25, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein any substituted group of R^1 is substituted with one or more halogen, C_1-C_4 alkyl, $-N(R^4)_2$, or $-OR^5$;

or R^1 is unsubstituted or substituted azetidinyl, unsubstituted or substituted pyrrolidinyl, or unsubstituted or substituted piperidinyl;

or R^1 is unsubstituted or substituted -(C_1-C_6 alkyl)-(C_2-C_7 heterocycloalkyl), wherein the C_2-C_7 heterocycloalkyl is an unsubstituted or substituted azetidinyl, unsubstituted or substituted pyrrolidinyl, or unsubstituted or substituted piperidinyl.

~~56.~~27. The compound of any one of claims 1-~~55~~25, or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R^1 is unsubstituted or substituted azetidinyl, unsubstituted or substituted pyrrolidinyl, or unsubstituted or substituted piperidinyl;

or R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein if R^1 is unsubstituted or substituted then it is substituted with one or more halogen, C_1-C_4 alkyl, $-N(R^4)_2$, or $-OR^5$.

~~57. The compound of any one of claims 1-55, or a pharmaceutically acceptable salt, or solvate thereof, wherein:~~

~~R^1 is unsubstituted or substituted C_1-C_6 heteroalkyl containing 1 N atom, wherein if R^1 is unsubstituted or substituted then it is substituted with one or more halogen, C_1-C_4 alkyl, -$N(R^4)_2$, or -OR^5.~~

~~58.~~28. A compound that is:

1-1: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-2: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-3: N-(2-aminoethyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-4: N-[(2R)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-5: N-(3-aminopropyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-6: N-[(2S)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-7: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-8: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidine-4-carboxamide;

1-9: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-10: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-11: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-12: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-13: N-(2-aminoethyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-14: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-15: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-16: N-[(2S)-2-aminopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-17: N-[(2R)-2-amino-3-hydroxypropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-18: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-19: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-20: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-21: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[3,3'-bipyridin]-6-yl}-N-[(3R)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-22: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[3,3'-bipyridin]-6-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-23: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-24: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-25: 3-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[(3R)-1-methylpyrrolidin-3-yl]carbamoyl}piperidin-1-yl)-6-(trifluoromethyl)pyridine-2-carboxamide;

1-26: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-27: 3-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[(3S)-1-methylpyrrolidin-3-yl]carbamoyl}piperidin-1-yl)-6-(trifluoromethyl)pyridine-2-carboxamide;

1-28: N-[(2S)-2-amino-3-hydroxypropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-29: 1-[2-chloro-6-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-30: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-31: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-32: 1-(2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-33: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]-1-[4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-34: 1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-35: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]-1-[5-(trifluoromethyl)pyridin-2-yl]piperidine-4-carboxamide;

1-36: 1-(4-acetyl-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-37: 1-[2-cyano-4-(difluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-38: 1-[4-cyano-2-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-39: 1-[2-cyano-4-(trifluoromethoxy)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-40: 1-(2,4-dicyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-41: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S,4S)*-4-hydroxy-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-42: 1-[3-cyano-5-(trifluoromethyl)pyridin-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-43: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrazol-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-44: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2R)-3-hydroxy-2-(methylamino)propyl]piperidine-4-carboxamide;

1-45: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-46: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3R,4R)*-4-hydroxy-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-47: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-3-hydroxy-2-(methylamino)propyl]piperidine-4-carboxamide;

1-48: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-51: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-(2-ethoxypyridin-3-yl)pyrazin-2-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-52: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-53: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,3-dihydro-1-benzofuran-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-54: 4-[6-(1-benzofuran-7-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-55: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(hydroxymethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-56: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-57: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-58: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-(2-ethoxypyridin-3-yl)pyrazin-2-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-59: 1-[2-cyano-4-(1,1-difluoroethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-60: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-61: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,3-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-62: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-ethyl-1H-pyrazol-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-63: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-propoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-64: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-65: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3,5-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-66: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-67: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,2-difluoro-2H-1,3-benzodioxol-4-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-68: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2,5-difluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-69: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxy-5-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-70: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[1-(3-methylbutyl)-1H-pyrazol-5-yl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-71: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-{6-[2-(trifluoromethoxy)phenyl]pyridin-3-yl}piperidine-4-carboxamide;

1-72: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxy-3-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-73: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indazol-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-74: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-fluorophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-75: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)-3-fluorophenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-76: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-77: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-{6-[2-(trifluoromethyl)phenyl]pyridin-3-yl}piperidine-4-carboxamide;

1-78: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyanophenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-79: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(methoxymethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-80: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-methoxythiophen-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-81: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-82: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-83: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-84: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(1,1-difluoroethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-85: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2'-(difluoromethoxy)-[2,3'-bipyridin]-5-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-86: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-87: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3,5-difluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-88: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-89: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-90: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-91: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-92: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-93: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-94: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-95: 1-(2,4-dichlorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-96: 1-(2-cyano-4-fluorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-97: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-98: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-99: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-100: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-101: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-102: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-103: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-104: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-105: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(4-methylpyrimidin-5-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-106: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2-(2-ethoxypyridin-3-yl)pyrimidin-5-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-107: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2-(2-ethoxypyridin-3-yl)pyrimidin-5-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-108: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-109: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-110: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-111: 1-(4-chloro-2-cyano-6-fluorophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-112: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-113: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-114: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(difluoromethoxy)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-115: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-116: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylfuran-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-117: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(2-propylphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-118: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethyl-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-119: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-120: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methylfuran-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-121: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-cyclopropylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-122: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]-4-[6-(2-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-123: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-124: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-125: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-126: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-127: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-128: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-129: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-fluoro-2-hydroxyphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-130: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxy-5-methylphenyl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-131: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-132: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-133: 1-[2-cyano-6-(trifluoromethyl)pyridin-3-yl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-134: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-135: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-136: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-137: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(cyanomethyl)phenyl]pyridin-3-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-138: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]-4-[6-(4-methylthiophen-3-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-139: 1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-140: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-141: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-142: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-143: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]-4-[6-(1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-144: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-145: 4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-146: 4-[6-(2-acetylthiophen-3-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-147: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylthiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-148: 4-[6-(2-cyano-3-fluorophenyl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-149: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(3-methyl-1,2-oxazol-4-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-150: 1-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-151: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{6-[2-(difluoromethyl)phenyl]pyridin-3-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-152: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-pyrrolidin-3-yl]piperidine-4-carboxamide;

1-153: 4-[6-(5-cyano-1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-154: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{5'-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-155: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-156: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethylphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-157: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-methyl-1,2-oxazol-4-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-158: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-cyclopropyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-159: 4-[4-(2-ethoxypyridin-3-yl)phenyl]-1-[2-methoxy-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-160: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-161: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-162: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-163: 1-(4-chloro-2-cyanophenyl)-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-164: 4-[4-(2-ethoxypyridin-3-yl)phenyl]-1-[2-methyl-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-165: 1-[3-chloro-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-166: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-167: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxythiophen-3-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-168: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-169: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-170: 1-(4-chloro-2-cyanophenyl)-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-171: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-172: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethyl-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-173: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-174: 4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-175: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-176: 4-{[2,2'-bipyridin]-5-yl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-177: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3'-methyl-[2,2'-bipyridin]-5-yl}-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-178: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3'-methoxy-[2,2'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-179: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-180: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-cyclopropyl-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-181: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[2'-(difluoromethyl)-[2,3'-bipyridin]-5-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-182: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(5-cyclopropyl-1,3-oxazol-4-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-183: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-184: ethyl (3S)-3-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-amido}pyrrolidine-1-carboxylate;

1-185: N-[(3S)-1-acetylpyrrolidin-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-186: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-187: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-188: N-[(3R)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-189: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyquinolin-3-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-190: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indol-7-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-191: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-indol-2-yl)pyridin-3-yl]-N-[(3R)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-192: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-193: 4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-194: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-195: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-196: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-197: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[3-(methylamino)propyl]piperidine-4-carboxamide;

1-198: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-199: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[3-(dimethylamino)propyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-200: 4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-201: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-202: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-203: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-204: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(5-fluoro-2-methoxyphenyl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-205: N-(3-aminopropyl)-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-206: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[3-(methylamino)propyl]piperidine-4-carboxamide;

1-207: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[3-(dimethylamino)propyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-208: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-ethyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-209: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{3,5'-difluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-210: 4-{3,5'-difluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3S)-1-methylpyrrolidin-3-yl]piperidine-4-carboxamide;

1-211: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-212: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-213: N-{[(2S)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-214: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-215: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-216: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-217: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2S)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-218: N-[(3S)-1-azabicyclo[2.2.2]octan-3-yl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-219: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-(1-methylazetidin-3-yl)piperidine-4-carboxamide;

1-220: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1-methylazetidin-3-yl)methyl]piperidine-4-carboxamide;

1-221: N-{1-azabicyclo[2.2.1]heptan-4-yl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-222: N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-223: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-224: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-225: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-226: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-227: 4-[6-(2-ethoxyphenyl)pyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-228: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-229: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-230: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-231: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2R)-pyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-232: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2R)-1-methylpyrrolidin-2-yl]methyl}piperidine-4-carboxamide;

1-233: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,3S)-3-aminocyclobutyl]piperidine-4-carboxamide;

1-234: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1R,3R)-3-aminocyclobutyl]piperidine-4-carboxamide;

1-235: N-{[(2S)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-236: N-{[(2R)-azetidin-2-yl]methyl}-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-237: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4S)-4-fluoropyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-238: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-fluoropyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-239: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,3S)-3-(dimethylamino)cyclobutyl]piperidine-4-carboxamide;

1-240: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1R,3R)-3-(dimethylamino)cyclobutyl]piperidine-4-carboxamide;

1-241: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-{[(2S)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-242: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-243: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-fluoro-1-methylpyrrolidin-3-yl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-244: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2R)-1-methylazetidin-2-yl]methyl}piperidine-4-carboxamide;

1-245: N-[2-(azetidin-1-yl)ethyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-246: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoropyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-247: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoropyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-248: N-[2-(azetidin-1-yl)ethyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-249: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-250: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-251: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(1S,2S,4R)-7-methyl-7-azabicyclo[2.2.1]heptan-2-yl]piperidine-4-carboxamide;

1-252: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[(1S,2S,4R)-7-methyl-7-azabicyclo[2.2.1]heptan-2-yl]piperidine-4-carboxamide;

1-253: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S)-1,3-dimethylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-254: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-255: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-256: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-257: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-258: rac-N-[(1R,2S)-2-aminocyclopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-259: rac-N-[(1R,2R)-2-aminocyclopropyl]-1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-260: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-1-(dimethylamino)propan-2-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-261: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-262: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{3-[(dimethylamino)methyl]oxetan-3-yl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-263: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[1-(dimethylamino)cyclopropyl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-264: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4S)-4-(dimethylamino)oxolan-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-265: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{2-[ethyl(methyl)amino]ethyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-266: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{2-[cyclopropyl(methyl)amino]ethyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-267: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4R)-4-methoxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-268: rac-1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-methoxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-269: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3R,4R)-4-hydroxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-270: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(3S,4S)-4-hydroxy-1-methylpyrrolidin-3-yl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-271: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-272: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-273: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-274: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-275: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-276: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-277: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4S)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-278: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S,4R)-4-fluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-279: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2S)-4,4-difluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-280: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-{[(2R)-4,4-difluoro-1-methylpyrrolidin-2-yl]methyl}-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-281: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-282: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-283: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-284: N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-285: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-286: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidine-4-carboxamide;

1-287: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-288: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-289: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-290: 4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-291: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]piperidine-4-carboxamide;

1-292: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)-5-fluoropyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-293: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-294: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-295: N-[(2S)-1-(dimethylamino)propan-2-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-296: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-297: N-[(2S)-1-(dimethylamino)propan-2-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-298: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-299: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-300: N-[2-(dimethylamino)ethyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-301: 4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-302: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-303: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{3-fluoro-2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-304: N-[2-(dimethylamino)ethyl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-305: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-306: 1-[2-fluoro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-307: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-308: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-309: 1-[2-chloro-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-310: 1-[2-chloro-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-311: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[2-(methylamino)ethyl]piperidine-4-carboxamide;

1-312: N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-313: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-314: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-315: 4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-316: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-317: N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

1-318: 1-(2,4-dichlorophenyl)-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-319: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-320: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-321: 4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-322: 1-(2,4-dichlorophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-323: 1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-324: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidine-4-carboxamide;

1-325: 1-(4-chloro-2-cyanophenyl)-N-[(2S)-1-(dimethylamino)propan-2-yl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-326: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]-N-[(2S)-1-(methylamino)propan-2-yl]piperidine-4-carboxamide;

1-327: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2S)-4-methylmorpholin-2-yl]methyl}piperidine-4-carboxamide;

1-328: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(3S)-4-methylmorpholin-3-yl]methyl}piperidine-4-carboxamide;

1-329: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(3R)-4-methylmorpholin-3-yl]methyl}piperidine-4-carboxamide;

1-330: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]-N-{[(2R)-4-methylmorpholin-2-yl]methyl}piperidine-4-carboxamide;

1-331: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]piperidine-4-carboxamide;

1-332: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2S)-2-(dimethylamino)propyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-333: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)propyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-334: 1-[2-cyano-4-(trifluoromethyl)phenyl]-N-[(2R)-2-(dimethylamino)-3-hydroxypropyl]-4-{2'-ethoxy-3-fluoro-[2,3'-bipyridin]-5-yl}piperidine-4-carboxamide;

1-335: N-[2-(dimethylamino)ethyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]piperidine-4-carboxamide;

2-1: 2-{4-[2-(dimethylamino)ethoxy]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-1-yl}-5-(trifluoromethyl)benzonitrile;

2-2: 1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl N-[2-(dimethylamino)ethyl]carbamate;

2-3: 3-amino-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}propanamide;

2-4: 3-amino-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}propanamide;

2-5: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)propanamide;

2-6: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}pyrrolidine-3-carboxamide;

2-7: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylpyrrolidine-3-carboxamidev;

2-8: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}pyrrolidine-3-carboxamide;

2-9: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-10: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(dimethylamino)propanamide;

2-11: (2S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylpyrrolidine-2-carboxamide;

2-12: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}carbamate;

2-13: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}carbamate;

2-14: 2-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-[(2-hydroxyethyl)amino]piperidin-1-yl)-5-(trifluoromethyl)benzonitrile;

2-15: 2-(4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}-4-{[2-(methylamino)ethyl]amino}piperidin-1-yl)-5-(trifluoromethyl)benzonitrile;

2-16: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-17: (2R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[4-(2-ethoxypyridin-3-yl)phenyl]piperidin-4-yl}-1-methylpyrrolidine-2-carboxamide;

2-18: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}carbamate;

2-19: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-20: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-21: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)pyrrolidine-1-carboxamide;

2-22: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}carbamate;

2-23: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)azetidine-1-carboxamide;

2-24: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-3-(methylamino)pyrrolidine-1-carboxamide;

2-25: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylazetidine-3-carboxamide;

2-26: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-2-(dimethylamino)acetamide;

2-27: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-28: (3S)-N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-29: (3R)-N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-30: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-3-(dimethylamino)propanamide;

2-31: N-[1-(4-chloro-2-cyanophenyl)-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl]-2-(dimethylamino)acetamide;

2-32: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-33: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-34: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-2-(dimethylamino)acetamide;

2-35: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-36: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

2-37: N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-1-methylazetidine-3-carboxamide;

2-38: N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-2-(dimethylamino)acetamide;

2-39: (3S)-N-[1-(4-chloro-2-cyanophenyl)-4-{2'-ethoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl]-1-methylpyrrolidine-3-carboxamide;

2-40: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-{2'-methoxy-[2,3'-bipyridin]-5-yl}piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-41: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-42: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-43: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-44: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}pyrrolidine-3-carboxamide;

2-45: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylazetidine-3-carboxamide;

2-46: (3S)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide; and

2-47: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-48: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(1-methyl-1H-pyrrol-2-yl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-49: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-50: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-51: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-52: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-53: (3S)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-54: (3R)-1-methylpyrrolidin-3-yl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-55: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3S)-1-methylpyrrolidin-3-yl]urea;

2-56: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[(3R)-1-methylpyrrolidin-3-yl]urea;

2-57: 2-(dimethylamino)ethyl N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}carbamate;

2-58: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-[2-(dimethylamino)ethyl]urea;

2-59: 1-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(1-methylazetidin-3-yl)urea;

2-60: (3R)-N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-1-methylpyrrolidine-3-carboxamide;

2-61: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-2-(dimethylamino)acetamide;

2-62: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

2-63: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[5-fluoro-6-(2-methoxyphenyl)pyridin-3-yl]piperidin-4-yl}-3-(methylamino)propanamide;

2-64: N-{1-[2-cyano-4-(trifluoromethyl)phenyl]-4-[6-(2-ethoxypyridin-3-yl)pyridazin-3-yl]piperidin-4-yl}-3-(dimethylamino)propanamide;

or a pharmaceutically acceptable salt, or solvate thereof.

59.29. A pharmaceutical composition comprising a compound of any one of claims 1-2858, or a pharmaceutically acceptable salt, or solvate thereof, and at least one pharmaceutically acceptable excipient.

60. The pharmaceutical composition of claim 59, wherein 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.

61. The pharmaceutical composition of claim 59, wherein 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.

62.30. Use of a compound of any one of claims 1-28, or a pharmaceutically acceptable salt, or solvate thereof, in the manufacture of a medicament for A method of treating a disease or condition in a mammal that would benefit from the modulation of melanocortin subtype-2 receptor (MC2R) activity; wherein the disease or condition comprises growth of fat pads in the collarbone, back of neck, face and trunk, excessive sweating, dilation of capillaries, thinning of the skin, muscle weakness, hirsutism, depression/anxiety, hypertension, osteoporosis, insulin resistance, hyperglycemia, and heart disease comprising administering a compound of any one of claims 1-58, or a pharmaceutically acceptable salt, or solvate thereof, to the mammal in need thereof.

63. The method of claim 62, wherein the disease or condition comprises growth of fat pads in the collarbone, back of neck, face and trunk, excessive sweating, dilation of capillaries, thinning of the skin, muscle weakness, hirsutism, depression/anxiety, hypertension, osteoporosis, insulin resistance, hyperglycemia, and heart disease.

64.31. Use of a compound of any one of claims 1-28, or a pharmaceutically acceptable salt, or solvate thereof, in the manufacture of a medicament for A method of treating Cushing's syndrome, ectopic Cushing's syndrome, congenital adrenal hyperplasia (CAH), or for reducing the secretion of adrenocorticotropic hormone (ACTH) in a mammal comprising administering a compound of any one of claims 1-58, or a pharmaceutically acceptable salt, or solvate thereof, to the mammal in need thereof.

65.32. A compound of any one of claims 1-28, or a pharmaceutically acceptable salt, or solvate thereof, for use in therapymethod of treating ectopic Cushing's syndrome in a mammal comprising administering a compound of any one of claims 1-58, or a pharmaceutically acceptable salt, or solvate thereof, to the mammal in need thereof.

66. ~~A method of treating congenital adrenal hyperplasia (CAH) in a mammal comprising administering a compound of any one of claims 1-58, or a pharmaceutically acceptable salt, or solvate thereof, to the mammal in need thereof.~~

67. ~~A method of reducing the secretion of adrenocorticotropic hormone (ACTH) in a mammal comprising administering a compound of any one of claims 1-58, or a pharmaceutically acceptable salt, or solvate thereof to the mammal in need thereof.~~