

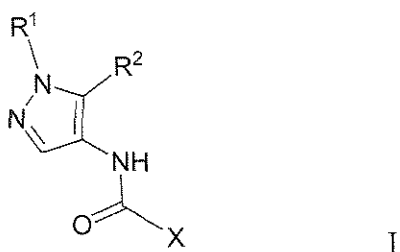
carcinoma (Li et al. (2006) Cancer Research 66 (13):6741-7; Fujii et al. (2005) Int J Cancer 114 (2):209-18.

Beyond oncology therapeutic and diagnostic applications, Pim kinases could play an important role in normal immune system function and Pim inhibition could be therapeutic for a number of different immunologic pathologies including tumorigenesis (Nawijn et al (2011) Nature Rev. 11:23-34), inflammation, autoimmune conditions, allergy, and immune suppression for organ transplantation (Aho et al. (2005) Immunology 116 (1):82-8).

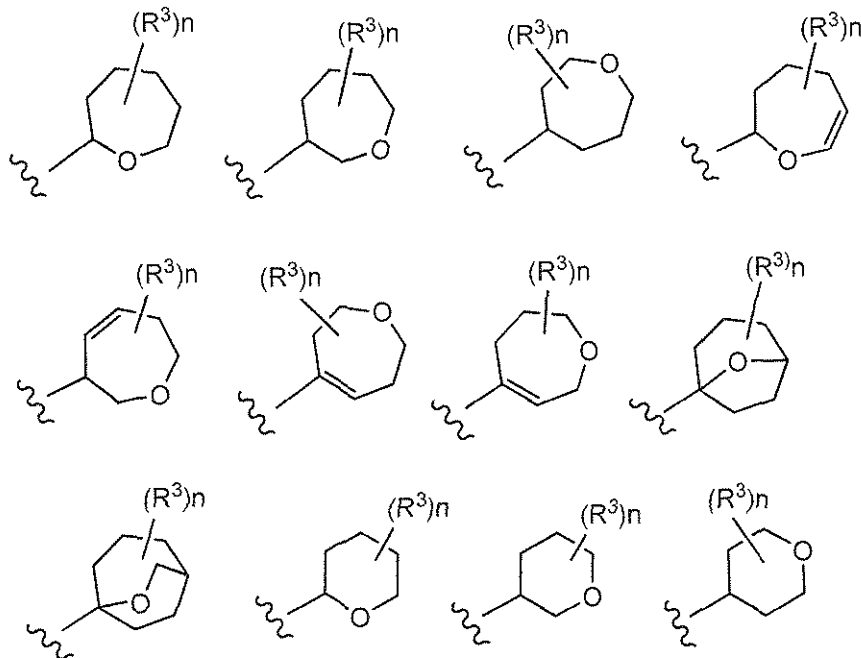
SUMMARY OF THE INVENTION

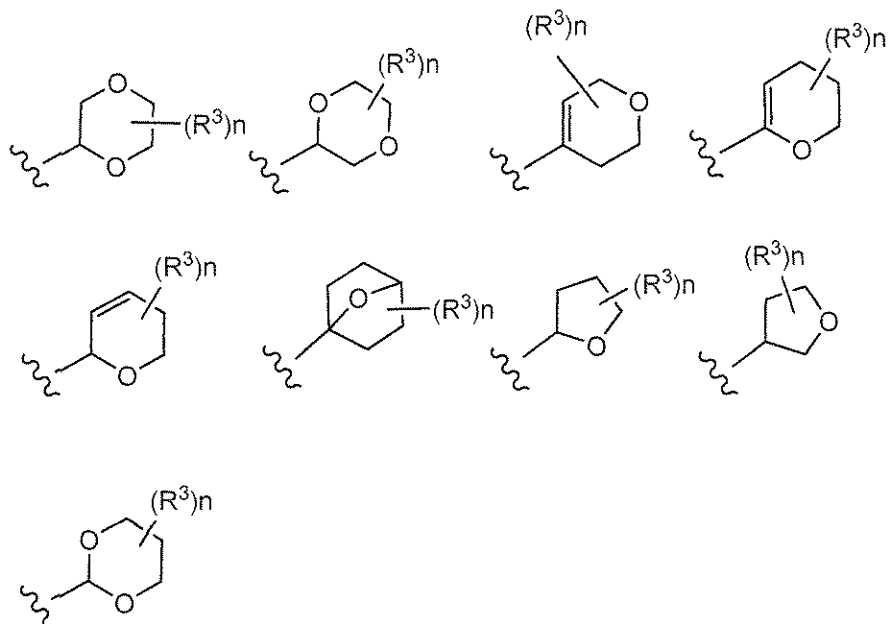
The invention relates to cyclic ether pyrazol-4-yl-heterocycl-yl-carboxamide compounds for treating disorders mediated by Pim kinase (Pim-1, Pim-2, and/or Pim-3) inhibitors Formula I compounds.

Formula I compounds have the structure:



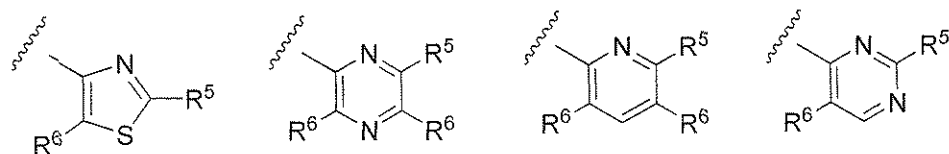
where R^2 is selected from the structures:





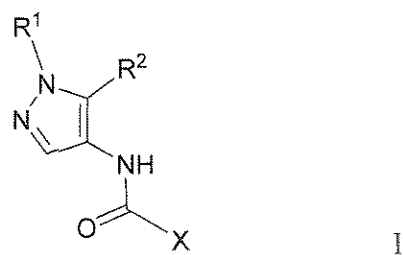
where the wavy line indicates the site of attachment and the dashed line indicates an optional double bond;

X is selected from the structures:



and stereoisomers, geometric isomers, tautomers, and pharmaceutically acceptable salts thereof. The various substituents, including R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and X are as defined herein.

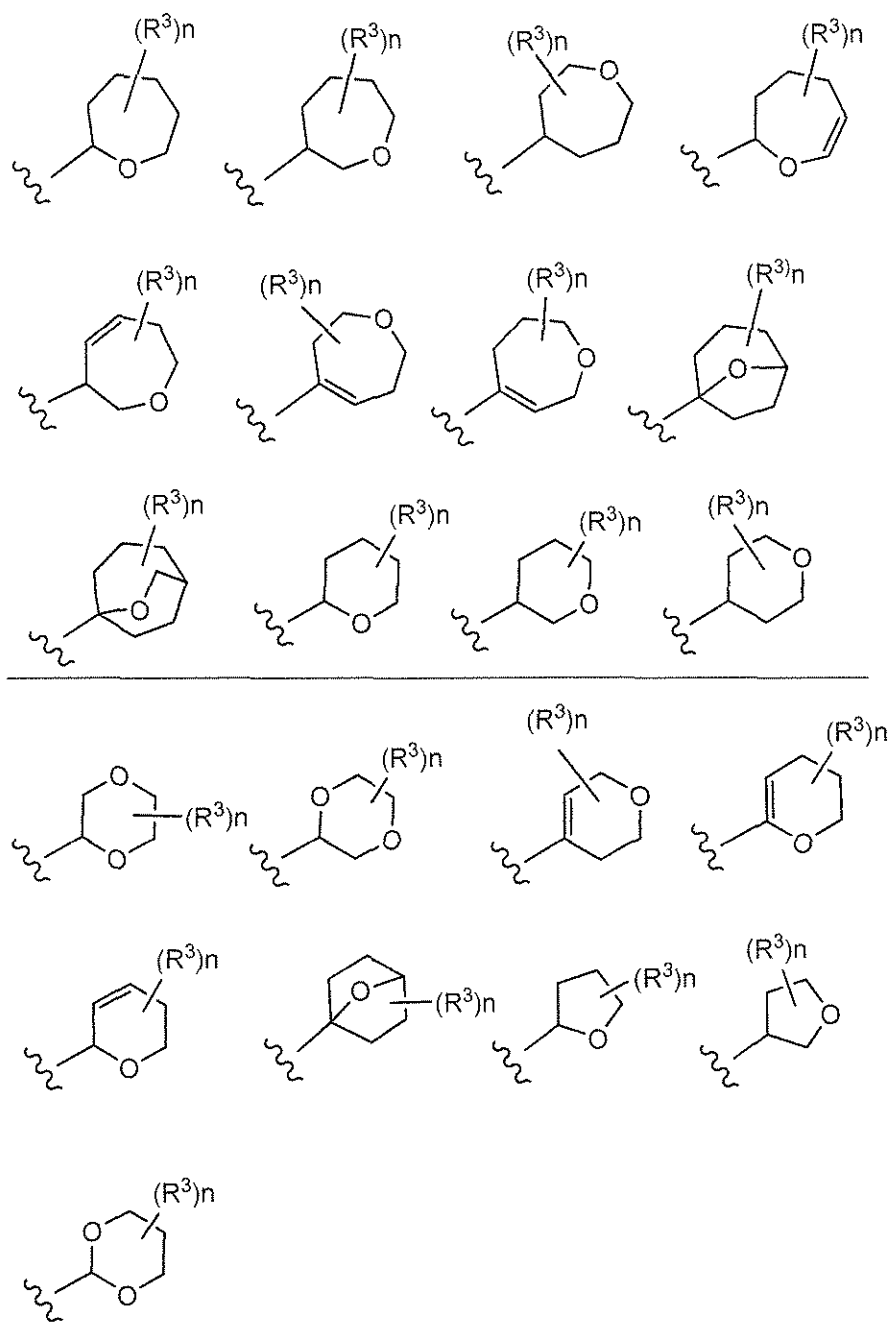
One aspect of the disclosure is a compound selected from Formula I:



and stereoisomers, geometric isomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

R^1 is selected from H, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_6 - C_{20} aryl, C_3 - C_{12} carbocyclyl, C_2 - C_{20} heterocyclyl, C_1 - C_{20} heteroaryl, and $-(C_1$ - C_{12} alkylene)-(C_2 - C_{20} heterocyclyl);

R^2 is selected from the structures:



where the wavy line indicates the site of attachment:

- 5 R^3 is independently selected from F, Cl, Br, I, $-CH_3$, $-CH_2CH_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, $-CH_2CH(CH_3)_2$, $-CH=CH_2$, $-CH=C(CH_3)_2$, $=CH_2$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2OH$, $-CH_2OCH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2CH_2NH_2$, $-CH_2CHCH_2NH_2$, $-CH_2CH(CH_3)NH_2$, $-CH_2OH$, $-CH_2CH_2OH$, $-C(CH_3)_2OH$, $-CH(OH)CH(CH_3)_2$, $-C(CH_3)_2CH_2OH$, $-CH_2CH_2SO_2CH_3$, $-CN$, $-CO_2H$, $-COCH_3$, $-COCH_2NH_2$, $-CO_2CH_3$, $-CO_2C(CH_3)_3$, $-COCH(OH)CH_3$, $-CONH_2$, $-CONHCH_3$, $-CON(CH_3)_2$, $-C(CH_3)_2CONH_2$, $-NO_2$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-NHCH_2CHF_2$, $-NHCH_2CF_3$, $-NHCH_2CH_2OH$, $-NHCOCH_3$, $-N(CH_3)COCH_3$, $-NHC(O)OCH_2CH_3$, $-NHC(O)OCH_2CH_3$, $-NHC(O)OC_6H_5$, $-NHS(O)_2CH_3$, $-N(CH_3)C(CH_3)_2CONH_2$, $-N(CH_3)CH_2CH_2S(O)_2CH_3$, $=O$, $-OH$, $-OCH_3$, $-OCHF_2$, $-OCH_2F$, $-OCH_2CH_3$, $-OCH(CH_3)_2$, $-$
- 10

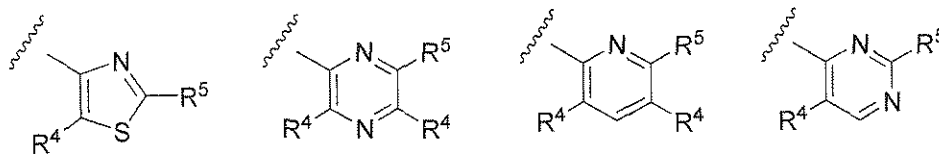
OCH₂CH(CH₃)₂, -OC(CH₃)₃, -S(O)₂N(CH₃)₂, -SCH₃, -CH₂OCH₃, -S(O)₂CH₃, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, azetidiny, azepanyl, oxetanyl, oxetan-3-ylmethylamino, (3-methyloxetan-3-yl)methylamino, pyrrolidinyl, piperazinyl, piperidinyl, (piperidin-4-yl)ethyl, pyranyl, (piperidin-4-ylmethyl), morpholinomethyl, and morpholino;

5 or where two geminal R³ groups form a spiro ring selected from a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl, azetidiny, azepanyl, oxetanyl, pyrrolidinyl, piperazinyl, or piperidinyl ring, where the spiro ring is optionally substituted with one or more groups independently selected from -F, -OH, =O, -CH₃, -NH₂, -CH₂F, -CH₂OH, -CH₂OCH₃, -CH₂NH₂, and -CF₃;

10 or where two vicinal R³ groups form a five-membered or six-membered heterocyclyl fused ring, where the heterocyclyl fused ring is optionally substituted with one or more groups independently selected from -F, -OH, =O, -CH₃, -NH₂, -CH₂F, -CH₂OH, -CH₂OCH₃, -CH₂NH₂, and -CF₃;

n is 0, 1, 2, 3, 4, 5, or 6;

15 X is selected from the structures:



where the wavy line indicates the site of attachment;

R⁴ is independently H, F, -CH₃, or -NH₂; and

R⁵ is selected from H, Cl, Br, C₁-C₁₂ alkyl, -O-(C₁-C₁₂ alkyl), -(C₁-C₁₂ alkylene)-(C₃-C₁₂ carbocyclyl), -(C₁-C₁₂ alkylene)-(C₂-C₂₀ heterocyclyl), -(C₂-C₈ alkenylene)-(C₃-C₁₂ carbocyclyl), -(C₂-C₈ alkenylene)-(C₂-C₂₀ heterocyclyl), C₆-C₂₀ aryl, -(C₆-C₂₀ arylene)-(C₂-C₂₀ heterocyclyl), -(C₆-C₂₀ arylene)-(C₆-C₂₀ arylene), -(C₆-C₂₀ arylene)-(C₁-C₁₂ alkylene)-(C₂-C₂₀ heterocyclyl), -(C₆-C₂₀ arylene)-O-(C₂-C₂₀ heterocyclyl), -(C₆-C₂₀ arylene)-O-(C₁-C₁₂ alkyl), C₃-C₁₂ carbocyclyl, C₂-C₂₀ heterocyclyl, C₁-C₂₀ heteroaryl, -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl), and -(C₁-C₂₀ heteroaryl)-(C₁-C₁₂ alkyl); where alkyl, alkenyl, alkynyl, alkylene, carbocyclyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one or more groups independently selected from F, Cl, Br, I, -CH₃, -CH₂CH₃, -CH(CH₃)₂, -CH₂CH(CH₃)₂, -CH₂NH₂, -CH₂CH₂NH₂, -CH₂CHCH₂NH₂, -CH₂CH(CH₃)NH₂, -CH₂OH, -CH₂CH₂OH, -CH(CH₂OH)₂, -C(CH₂OH)₃, -CH(CH₃)OH, -C(CH₃)₂OH, -CH(OH)CH(CH₃)₂, -C(CH₃)₂CH₂OH, -CH₂CH₂SO₂CH₃, -CN, -CF₃, -CHF₂, -CH₂F, -CO₂H, -COCH₃, -COCH(CH₃)₂, -CO₂CH₃, -CO₂C(CH₃)₃, -COCH(OH)CH₃, -CONH₂, -CONHCH₃, -CON(CH₃)₂, -C(CH₃)₂CONH₂, -NO₂, -NH₂, -NHCH₃, -N(CH₃)₂, -NHCOCH₃, -N(CH₃)COCH₃, -NHS(O)₂CH₃, -N(CH₃)C(CH₃)₂CONH₂, -N(CH₃)CH₂CH₂S(O)₂CH₃, =O, -OH, -OCH₃, -OCF₃, -OCH(CH₃)₂, -S(O)₂N(CH₃)₂, -SCH₃, -

CH₂OCH₃, -S(O)₂CH₃, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, azetidiny,
azepanyl, oxetanyl, phenyl, pyrrolidiny, piperaziny, piperidiny, (piperidin-4-yl)ethyl, pyranyl,
(piperidin-4-ylmethyl), morpholinomethyl, and morpholino.

~~One~~ Another aspect of the ~~invention~~ disclosure is a pharmaceutical composition

5 comprised of a Formula I compound and a pharmaceutically acceptable carrier, glidant, diluent, or excipient. The pharmaceutical composition may further comprise a chemotherapeutic agent.

The disclosure ~~invention~~ includes a method of treating a disease or disorder which method comprises administering a therapeutically effective amount of a Formula I compound to a patient with a disease or disorder selected from cancer, immune disorders, cardiovascular
10 disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Pim kinase. The method includes further administering an additional therapeutic agent selected from a chemotherapeutic agent, an anti-inflammatory agent, an immunomodulatory agent, a neurotropic factor, an agent for treating cardiovascular disease, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent
15 for treating diabetes, and an agent for treating immunodeficiency disorders.

The disclosure ~~invention~~ includes use of a Formula I compound in the manufacture of a medicament for the treatment of cancer, immune disorders, cardiovascular disease, viral infection,

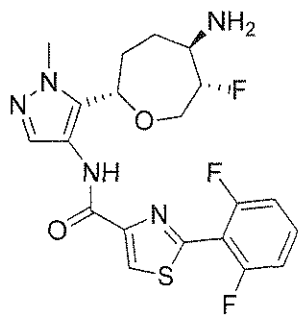
inflammation, metabolism/endocrine function disorders and neurological disorders, wherein the medicament mediates Pim kinase.

The ~~disclosure invention~~ includes a kit for treating a condition mediated by Pim kinase, comprising: a) a first pharmaceutical composition comprising a Formula I compound; and b) instructions for use.

The ~~disclosure invention~~ includes a Formula I compound for use as a medicament, and for use in treating a disease or disorder selected from cancer, immune disorders, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Pim kinase.

The ~~disclosure invention~~ includes methods of making a Formula I compound.

Another aspect of the disclosure is a pharmaceutical composition comprised of a compound having the structure:



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier,

glidant, diluent, or excipient.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Reference will now be made in detail to certain embodiments of the invention, examples of which are illustrated in the accompanying structures and formulas. While the invention will be described in conjunction with the enumerated embodiments, it will be understood that they are not intended to limit the invention to those embodiments. On the contrary, the invention is intended to cover all alternatives, modifications, and equivalents which may be included within the scope of the present invention as defined by the claims. One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. The present invention is in no way limited to the methods and materials described. In the event that one or more of the incorporated literature, patents, and similar materials differs from or contradicts this application, including but not limited to defined terms, term usage, described techniques, or the like, this application controls. Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. The nomenclature used in this Application is based on IUPAC
5 systematic nomenclature, unless indicated otherwise.

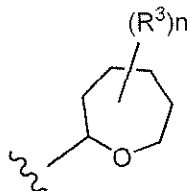
DEFINITIONS

When indicating the number of substituents, the term “one or more” refers to the range from one substituent to the highest possible number of substitution, i.e. replacement of one hydrogen up to replacement of all hydrogens by substituents. The term “substituent” denotes an
10 atom or a group of atoms replacing a hydrogen atom on the parent molecule. The term

heterocyclyl).

6. The compound of claim 5 wherein R^1 is oxetan-3-ylmethyl.

7. The compound of claim 5 wherein R has the structure:



8. The compound of claim 1 wherein R^3 is independently selected from F, Cl, -OH, -CH₃, -CH₂CH₃, -CF₃, -NH₂, -NHCH₃, -N(CH₃)₂, -NHCH₂CHF₂, -NHCH₂CF₃, -CH₂NHCH₃, and -OCH₃; and n is 1, 2, or 3.

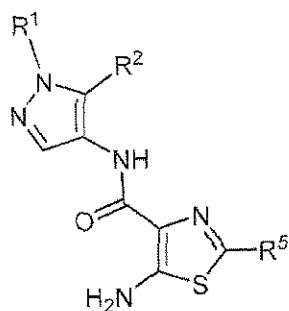
9. The compound of claim 1 wherein R^4 is -NH₂.

10. The compound of claim 1 wherein R^4 is H.

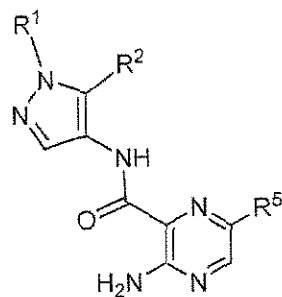
11. The compound of claim 1 wherein R^5 is C₆-C₂₀ aryl.

12. The compound of claim 11 wherein R^5 is phenyl substituted with one or more F.

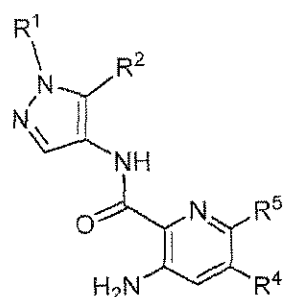
13. The compound of claim 1 having the structure of Formula Ia-Id:



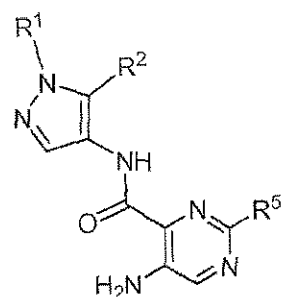
Ia



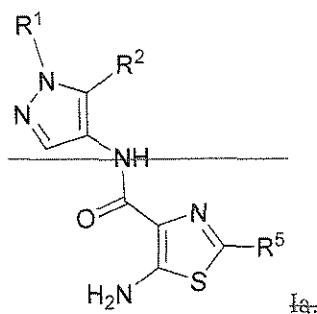
Ib



Ic

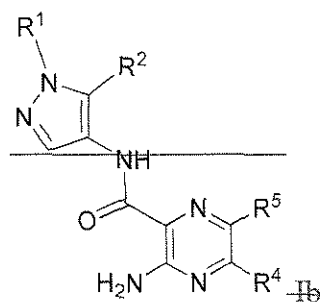


Id

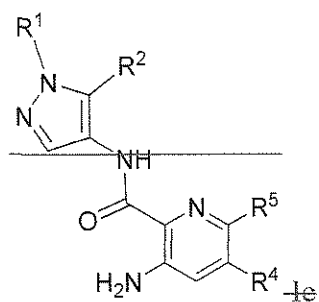


Ie

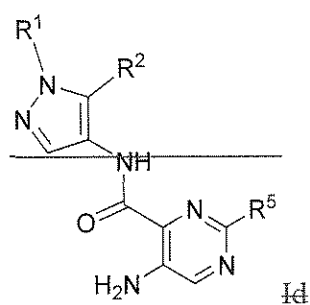
~~14. The compound of claim 1 having the structure of Formula Ib:~~



~~15. The compound of claim 1 having the structure of Formula Ic:~~



16. The compound of claim 1 having the structure of Formula Id:

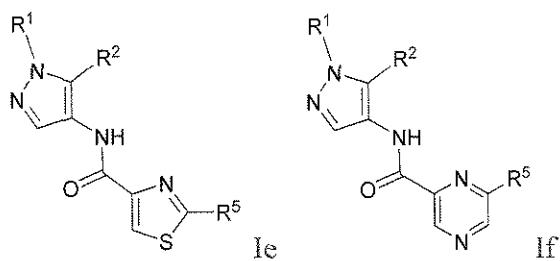
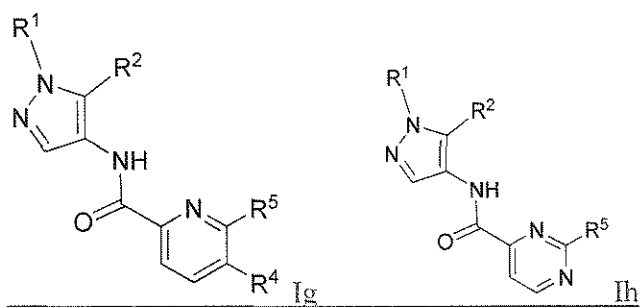


17. The compound of claim 1 selected from Table 1a:

18. The compound of claim 1 selected from Table 1b:

19. The compound of claim 1 selected from Table 1c:

14. The compound of claim 1 selected from Formula Ie-Ih:



15. The compound of claim 1 selected from the group consisting of:

5-amino-2-(2,6-difluorophenyl)-N-[5-(3,6-dihydro-2H-pyran-4-yl)-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-[5-(3,4-dihydro-2H-pyran-6-yl)-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-[5-(2-methoxytetrahydropyran-2-yl)-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-(1-methyl-5-tetrahydropyran-2-yl-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-2-(3-fluoro-2-pyridyl)-N-[5-(2-methoxytetrahydropyran-2-yl)-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-(5-((1S,4S,5S)-4-hydroxy-8-oxabicyclo[3.2.1]octan-1-yl)-1-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-[5-(2-amino-8-oxabicyclo[3.2.1]octan-5-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-(5-((2R,7R)-5-hydroxy-7-methyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-[5-(2-hydroxy-8-oxabicyclo[3.2.1]octan-5-yl)-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-amino-2-(2,6-difluorophenyl)-N-(5-((5R,6S)-5,6-dihydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-(5-((2R,7R)-5-amino-7-ethyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2R,7R)-5-amino-7-methyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-[5-(6-amino-4,4-difluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((1S,4S,5S)-4-amino-8-oxabicyclo[3.2.1]octan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((1S,4R,5S)-4-amino-8-oxabicyclo[3.2.1]octan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((1R,4S,5R)-4-amino-8-oxabicyclo[3.2.1]octan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((1R,4R,5R)-4-amino-8-oxabicyclo[3.2.1]octan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-

difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2R,5R,7R)-5-amino-7-methyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2R,5S,7R)-5-amino-7-methyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-(6-amino-4,4-difluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((5S,6S)-6-amino-5-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-(5-amino-6-fluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2R,7R)-5-amino-7-ethyloxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((5R,6S)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((4R,5R)-4-amino-5-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((5S,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((4S,5S)-4-amino-5-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((5S,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-(6-amino-4,4-difluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-2-(2,6-difluorophenyl)-N-[5-(5-hydroxyoxepan-2-yl)-1-methyl-pyrazol-4-yl]thiazole-4-
carboxamide
5-amino-N-[5-(5-amino-4-fluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2S,4R,5R)-5-amino-4-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2R,4S,5S)-5-amino-4-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((2R,4S,5S)-5-amino-4-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-

difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-[1-(aminomethyl)-7-oxabicyclo[2.2.1]heptan-4-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
fluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-(5-amino-4-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-(5-((4R,5R)-4-amino-5-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-(4-amino-5-hydroxy-3,5-dimethyl-tetrahydropyran-2-yl)-1-methyl-pyrazol-4-yl]-2-
(2,6-difluorophenyl)thiazole-4-carboxamide
5-amino-N-[5-(6-aminooxepan-3-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-
carboxamide
5-amino-N-[5-(6-aminooxepan-3-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-
carboxamide
5-Amino-N-[5-[6-amino-5-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-2-(2,6-difluorophenyl)-N-(5-((2S,4R)-4-hydroxytetrahydro-2H-pyran-2-yl)-1-methyl-1H-
pyrazol-4-yl)thiazole-4-carboxamide
5-amino-N-[5-(6-aminooxepan-3-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-
carboxamide
5-Amino-N-[5-[5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-amino-2-(2,6-difluorophenyl)-N-(5-((2R,4S)-4-hydroxytetrahydro-2H-pyran-2-yl)-1-methyl-1H-
pyrazol-4-yl)thiazole-4-carboxamide
5-Amino-N-[5-[5-(2S,5R)-5-amino-4-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-Amino-N-[5-[5-(2R,5S)-5-amino-4-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-Amino-N-[5-[5-(5-amino-6,6-difluoro-oxepan-2-yl)-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-Amino-N-[5-[5-(2R,5S,6S)-6-amino-5-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide
5-Amino-N-[5-[5-(2S,5R,6R)-5-amino-6-methoxy-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide; and
5-Amino-N-[5-[5-(aminomethyl)tetrahydrofuran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-
difluorophenyl)thiazole-4-carboxamide,
or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1 selected from the group consisting of:

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-3-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethoxy)phenyl)thiazole-4-carboxamide

Amino-N-[5-[4-aminotetrahydropyran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[4-aminotetrahydropyran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[4-aminotetrahydropyran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[2-amino-8-oxabicyclo[3.2.1]octan-5-yl]-1-methyl-pyrazol-4-yl]-2-(3-fluoro-4-pyridyl)thiazole-4-carboxamide

5-Amino-2-(2,6-difluorophenyl)-N-[5-[(2R,5R)-5-ethyl-5-(hydroxymethyl)-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-Amino-2-(2,6-difluorophenyl)-N-[5-[(2S,5S)-5-ethyl-5-(hydroxymethyl)-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-Amino-2-(2,6-difluorophenyl)-N-[5-[5-(hydroxymethyl)-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-Amino-2-(2,6-difluorophenyl)-N-[5-[5-(hydroxymethyl)-5-methyl-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

5-Amino-N-[5-[5-(aminomethyl)-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R)-5-amino-6,6-difluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2R,5S)-5-amino-6,6-difluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[4-amino-5-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2R,5R)-5-(aminomethyl)tetrahydrofuran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5S)-5-(aminomethyl)tetrahydrofuran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[5-(aminomethyl)-5-ethyl-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R,6S)-5-amino-6-(trideuteriomethoxy)oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-

(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[5-(aminomethyl)-5-methyl-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2R,5S,6R)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[5-(aminomethyl)-5-methyl-1,3-dioxan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[5-amino-4,4-difluoro-5,6-dimethyl-tetrahydropyran-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2R,5S,6R)-5-amino-6-(trideuteriomethoxy)oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R,6R)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,3-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R,6R)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(3-fluoro-4-pyridyl)thiazole-4-carboxamide

5-Amino-N-[5-[(2S,5R,6R)-5-amino-6-methoxy-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2-fluorophenyl)thiazole-4-carboxamide

5-Amino-N-(5-((2R,5S,6R)-5-amino-4,4-difluoro-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-(5-((2S,5R,6S)-5-amino-4,4-difluoro-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-Amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-methoxyphenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-methoxyethoxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-hydroxyethoxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-Amino-6-hydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-methoxyethoxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-

methoxyethoxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(3-hydroxyoxetan-3-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(3-fluorooxetan-3-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(4-hydroxytetrahydro-2H-pyran-4-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-((tetrahydro-2H-pyran-4-yl)oxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-hydroxycyclobutyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(methoxymethyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-hydroxypropan-2-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-methoxyphenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(3-methoxyoxetan-3-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(3-methoxyoxetan-3-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-hydroxycyclopropyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-propionylphenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(4-fluorotetrahydro-2H-pyran-4-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-hydroxyethyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-hydroxyphenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-Amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-hydroxyethoxy)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-

hydroxyethyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-methoxyethyl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1,2,3-trihydroxypropan-2-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(4-(cyclopropyl(methoxy)methyl)-2,6-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(4-(1,3-dihydroxypropan-2-yl)-2,6-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(3-hydroxytetrahydrofuran-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(tetrahydrofuran-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(((R)-tetrahydrofuran-3-yl)oxy)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(((S)-tetrahydrofuran-3-yl)oxy)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,3-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(3-hydroxyoxetan-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(1-hydroxycyclopropyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-5-fluoro-6-(2-fluoro-4-methoxyphenyl)picolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2-chloro-3-fluorophenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-(2-hydroxy-2-

methylpropyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-3-methoxyphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-methylpyridin-2-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-methoxypyridin-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-oxo-1,2-dihydropyridin-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3,5-dimethylisoxazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-cyclopropyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,5-trifluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-fluoropyridin-2-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-5-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-fluoropyridin-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-fluoropyridin-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1,3-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1,5-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3,5-dimethylisoxazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-fluoropyridin-3-

yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3,5-difluoropyridin-4-yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-chloro-2-fluorophenyl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3'-chloro-2,2'-difluoro-[1,1'-biphenyl]-3-yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-3-fluorophenyl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2'-chloro-3',6'-difluoro-[1,1'-biphenyl]-2-yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1,3-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1,5-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-isopropyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1,5-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-((5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-4-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,5-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,5-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-((5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-

5-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-methoxyphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethoxy)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-fluoro-2-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-3-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-methylphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(cyclopent-1-en-1-yl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-cyclopentylthiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-methylphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-5-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-(cyclopropyl(hydroxy)methyl)-2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-(cyclopropyl(methoxy)methyl)-2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluoro-6-methoxyphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-6-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6R)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-chloro-2-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-methyl-5-

(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1-methyl-5-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-6-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-ethoxy-2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-fluoro-1,3-dimethyl-1H-pyrazol-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-4-methoxyphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-methoxyphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(2-hydroxypropan-2-yl)phenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-(1-hydroxycyclobutyl)phenyl)-5-fluoropicolinamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-chloro-2-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-5-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-4-methoxyphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(1-hydroxyethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(1-hydroxycyclobutyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-methoxyphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(2-hydroxypropan-2-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(difluoromethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-bromo-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-fluoropyridin-4-

yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,5-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-chloro-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-3-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-((R)-1-hydroxyethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-((S)-1-hydroxyethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-ethyl-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-chloro-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-3-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-cyclopropyl-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethyl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-chloro-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(6-(trifluoromethyl)pyridin-2-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-methylphenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-4-methylphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-

fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-phenylthiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,4-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(pyridin-2-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-phenylthiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-6-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-6-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-methylphenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-6-(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3,6-trifluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(cyclopent-1-en-1-yl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-cyclopentylthiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-(difluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-fluoro-2-

(trifluoromethyl)phenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-chloro-3-fluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-chloro-2-fluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(3-methoxyoxetan-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-(3-fluorooxetan-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2R,4R,5S,6R)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,4S,5R,6S)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2R,4R,5S,6R)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide

N-(5-((2S,4S,5R,6S)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide

5-amino-N-(5-((2R,4R,5S,6R)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

5-amino-N-(5-((2S,4S,5R,6S)-4-amino-5-hydroxy-5,6-dimethyltetrahydro-2H-pyran-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide; and

N-(5-((2S,5R,6S)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-methylpyridin-2-yl)thiazole-4-carboxamide,

or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1 selected from the group consisting of:

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-chloro-5-fluoropyridin-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6R)-5-amino-6-hydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2R,5S,6S)-5-amino-6-hydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-hydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-((2R,5S,6R)-5-amino-6-hydroxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-(dimethylcarbamoyl)-2,6-difluorophenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-methylphenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-5-methoxyphenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-methoxyphenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-cyclopropyl-2,6-difluorophenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(4-chloro-2-fluorophenyl)-5-fluoropicolinamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluoro-3-methylsulfonyl-phenyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2-fluoro-3-methyl-phenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-3-methoxyphenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(3-cyclopropyl-2,6-difluorophenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,4,6-trifluorophenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluoro-4-((S)-1-hydroxyethyl)phenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,3-difluoro-4-((R)-1-hydroxyethyl)phenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-isobutrylphenyl)thiazole-4-carboxamide

N-((2S,5R,6S)-5-amino-6-methoxyoxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-3-methoxyphenyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2-fluoro-6-methyl-phenyl)-5-methyl-thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2,6-difluorophenyl)-5-methyl-thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-((S)-tetrahydrofuran-2-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4,5-dimethyl-1H-pyrazol-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(6,6-dimethyl-4,5,6,7-tetrahydro-1H-indazol-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4,5,6,7-tetrahydro-1H-indazol-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(4-chloro-2,6-difluorophenyl)-5-fluoropicolinamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-[3-(dimethylcarbamoyl)-2,6-difluoro-phenyl]thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-[3-(difluoromethyl)-2,6-difluoro-phenyl]thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-[3-(difluoromethyl)-2-fluoro-6-methoxy-phenyl]thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1H-pyrazol-3-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluoro-4-((R)-tetrahydrofuran-2-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1H-indazol-3-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-[2-fluoro-6-(hydroxymethyl)phenyl]thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(3-pyridyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(2-isopropoxy-3-pyridyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-[6-(dimethylamino)-3-pyridyl]thiazole-4-carboxamide

2-(6-acetamido-3-pyridyl)-N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5-fluoro-1-methyl-2-oxo-1,2-dihydropyridin-4-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1H-pyrazol-1-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4,5,6,7-tetrahydro-1H-indazol-1-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4,5,6,7-tetrahydro-2H-indazol-2-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(5,7-difluoro-2,3-dihydrobenzofuran-6-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-6-(2,6-difluoro-4-methylphenyl)-5-fluoropicolinamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2-fluoro-4-(3-methyloxetan-3-yl)phenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(4-(1,1-difluoroethyl)-2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1H-indazol-1-yl)thiazole-4-carboxamide

N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2H-indazol-2-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-6-(2,6-difluorophenyl)-5-fluoro-pyridine-2-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(3-methyl-2-pyridyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1,5-naphthyridin-3-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(5-fluoro-1H-indol-4-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(3-benzyloxyphenyl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1-methylindazol-4-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1-methylindazol-7-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1H-indazol-6-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1H-indazol-7-yl)thiazole-4-carboxamide

N-[5-[(2S,5R,6S)-5-amino-6-fluoro-oxepan-2-yl]-1-methyl-pyrazol-4-yl]-2-(1H-indazol-4-yl)thiazole-4-carboxamide

N-(5-((3S,4R,5R)-5-amino-4-methoxy-3-methylazepan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((3R,4S,5S)-5-amino-4-methoxy-3-methylazepan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

N-(5-((3R,4R,5R)-5-amino-4-methoxy-3-methylazepan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide; and

N-(5-((3S,4S,5S)-5-amino-4-methoxy-3-methylazepan-1-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide

or a pharmaceutically acceptable salt thereof.

2018. A pharmaceutical composition comprised of a compound of any one of claims 1 to 19 and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

2119. The pharmaceutical composition according to claim 2018, further comprising a chemotherapeutic agent.

2220. The pharmaceutical composition of claim 2018 for use in treating a disease or disorder selected from cancer, immune disorders, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Pim kinase.

~~23. A method of treating a disease or disorder which method comprises administering a therapeutically effective amount of a pharmaceutical composition of claim 20 to a patient with a disease or disorder selected from cancer, immune disorders, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Pim kinase.~~

24. The method of claim 23 wherein the disease or disorder is cancer selected from multiple myeloma, breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, non-small cell lung carcinoma (NSCLC), small cell carcinoma, lung

adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, pancreatic, myeloid disorders, lymphoma, hairy cells, buccal cavity, naso-pharyngeal, pharynx, lip, tongue, mouth, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system, Hodgkin's, leukemia, bronchus, thyroid, liver and intrahepatic bile duct, hepatocellular, gastric, glioma/glioblastoma, endometrial, melanoma, kidney and renal pelvis, urinary bladder, uterine corpus, uterine cervix, acute myelogenous leukemia, chronic myelogenous leukemia, lymphocytic leukemia, myeloid leukemia, oral cavity and pharynx, non-Hodgkin lymphoma, melanoma, and villous colon adenoma.

25. The method of claim 24 further comprising administering an additional therapeutic agent selected from a chemotherapeutic agent, an anti-inflammatory agent, an immunomodulatory agent, a neurotropic factor, an agent for treating cardiovascular disease, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, and an agent for treating immunodeficiency disorders.

26. Use of a compound of any one of claims 1 to 19 in the manufacture of a medicament for the treatment of cancer, immune disorders, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, wherein the medicament mediates Pim kinase.

27. A kit for treating a condition mediated by Pim kinase, comprising:

- a) a pharmaceutical composition of claim 20; and
- b) instructions for use.

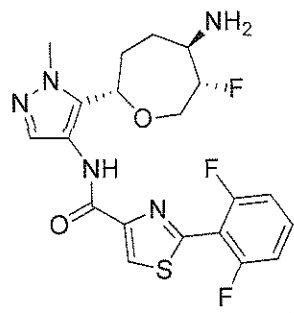
28. Compound according to any one of claims 1 to 19 for use in the treatment of cancer, immune disorders, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Pim kinase.

29. Compound according to claims 1 to 19 for the use in the treatment of cancer selected from multiple myeloma, breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, non-small cell lung carcinoma (NSCLC), small cell carcinoma, lung adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, pancreatic, myeloid disorders, lymphoma, hairy cells, buccal cavity, naso-pharyngeal, pharynx, lip, tongue,

mouth, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system, Hodgkin's, leukemia, bronchus, thyroid, liver and intrahepatic bile duct, hepatocellular, gastric, glioma/glioblastoma, endometrial, melanoma, kidney and renal pelvis, urinary bladder, uterine corpus, uterine cervix, acute myelogenous leukemia, chronic myelogenous leukemia, lymphocytic leukemia, myeloid leukemia, oral cavity and pharynx, non-Hodgkin lymphoma, melanoma, and villous colon adenoma.

21. The compound of claim 16, wherein said compound is N-(5-((2S,5R,6S)-5-amino-6-fluorooxepan-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(2,6-difluorophenyl)thiazole-4-carboxamide, or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprised of a compound having the structure:



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

23. The pharmaceutical composition of claim 22, further comprising a chemotherapeutic agent.