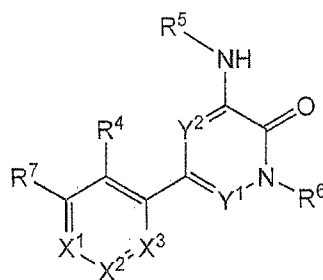


I

including stereoisomers, tautomers, or pharmaceutically acceptable salts thereof. The various substituents are defined herein below.

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



I

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

X¹ is CR¹-or-N;

X² is CR²-or-N;

X³ is CR³-or-N;

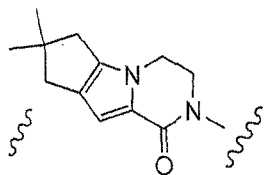
where one or two of X¹, X², and X³ are N;

R¹, R² and R³ are independently selected from H, F, Cl, NH₂, NHCH₃, N(CH₃)₂, OH, OCH₃, OCH₂CH₃, OCH₂CH₂OH, and C₁-C₃ alkyl;

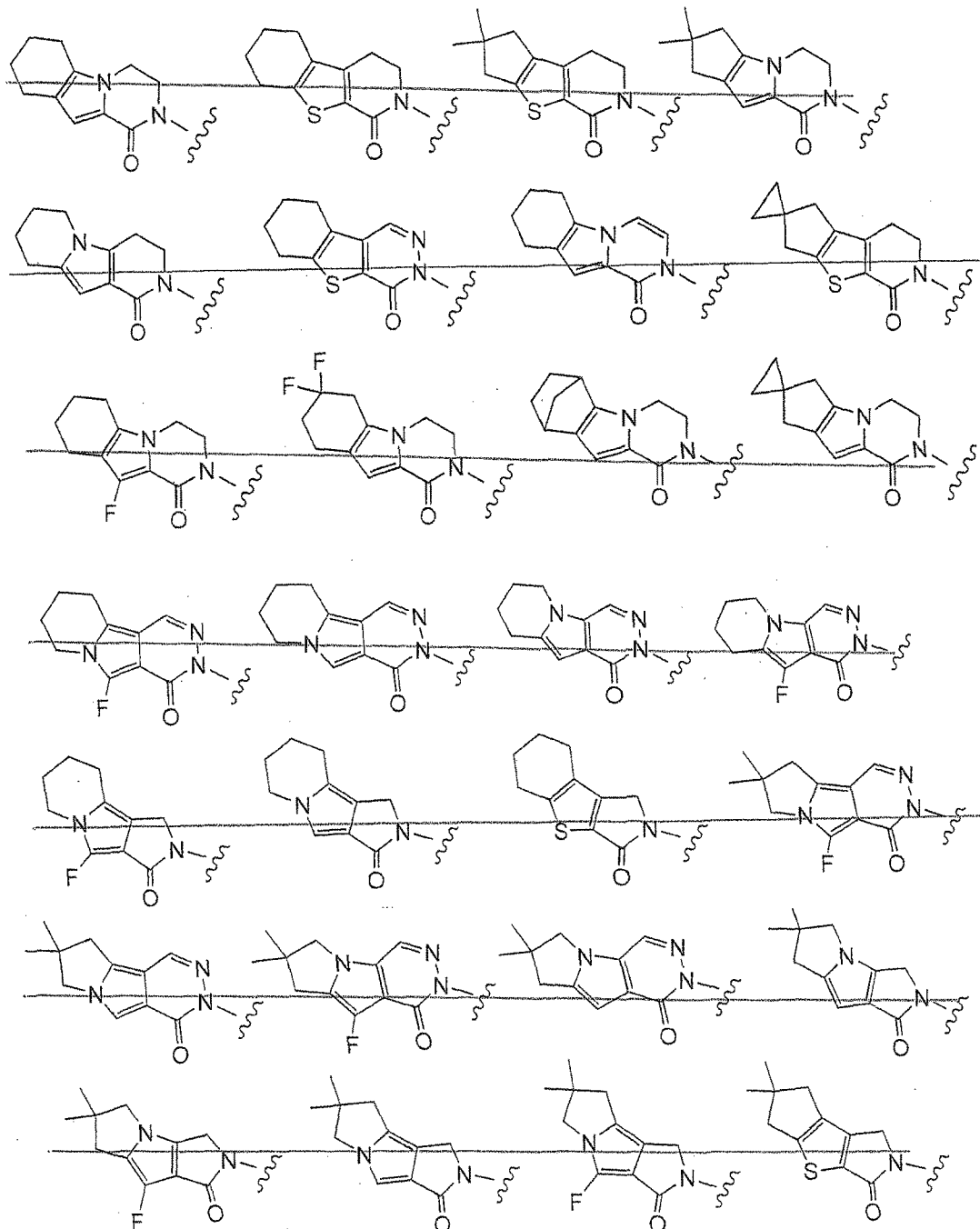
R⁴ is selected from H, F, Cl, CN, CH₂OH, CH(CH₃)OH, C(CH₃)₂OH, CH(CF₃)OH, CH₂F, CHF₂, CH₂CHF₂, CF₃, C(O)NH₂, C(O)NHCH₃, C(O)N(CH₃)₂, NH₂, NHCH₃, N(CH₃)₂, NHC(O)CH₃, OH, OCH₃, OCH₂CH₃, OCH₂CH₂OH, cyclopropyl, cyclopropylmethyl, 1-hydroxycyclopropyl, imidazolyl, pyrazolyl, 3-hydroxy-oxetan-3-yl, oxetan-3-yl, and azetidin-1-yl;

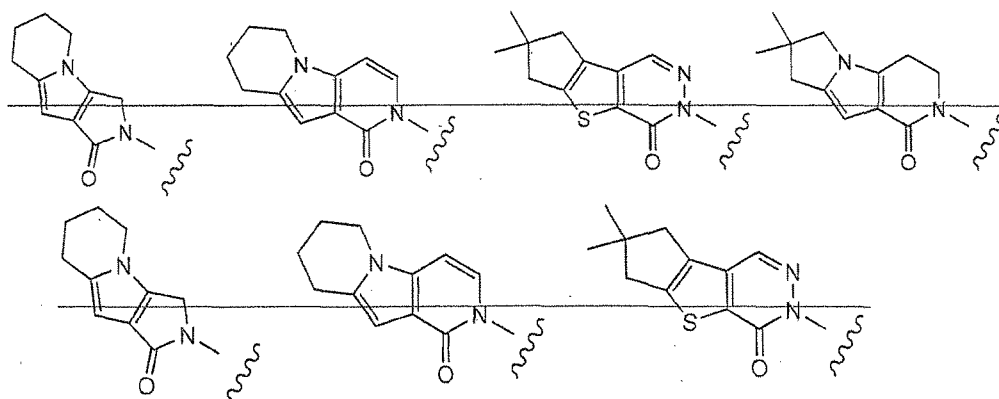
R⁵ is optionally substituted C₆-C₂₀ aryl, C₃-C₁₂ carbocyclyl, C₂-C₂₀ heterocyclyl, C₁-C₂₀ heteroaryl, -(C₆-C₂₀ aryl)-(C₂-C₂₀ heterocyclyl), -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl), -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl)-(C₂-C₂₀ heterocyclyl), -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl)-(C₁-C₆ alkyl), -(C₁-C₂₀ heteroaryl)-(C₁-C₆ alkyl), -(C₂-C₂₀ heterocyclyl)-(C₁-C₆ alkyl), -(C₂-C₂₀ heterocyclyl)-(C₃-C₁₂ carbocyclyl), -(C₁-C₂₀ heteroaryl)-(C₃-C₁₂ carbocyclyl), or -(C₁-C₂₀ heteroaryl)-C(=O)-(C₂-C₂₀ heterocyclyl);

R^6 is H, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2OH$, $-CHF_2$, $-NH_2$, or $-OH$;



R^7 is selected from the structures:





where the wavy line indicates the site of attachment; and

Y^1 and Y^2 are independently selected from CH and N, where Y^1 and Y^2 are not each

5 N;

where alkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one or more groups independently selected from F, Cl, Br, I, -CN, -CH₃, -CH₂CH₃, -CH(CH₃)₂, -CH₂CH(CH₃)₂, -CH₂OH, -CH₂OCH₃, -CH₂CH₂OH, -C(CH₃)₂OH, -CH(OH)CH(CH₃)₂, -C(CH₃)₂CH₂OH, -CH₂CH₂SO₂CH₃, -CH₂OP(O)(OH)₂, -CH₂F, -CHF₂,
 10 -CF₃, -CH₂CF₃, -CH₂CHF₂, -CH(CH₃)CN, -C(CH₃)₂CN, -CH₂CN, -CO₂H, -COCH₃, -CO₂CH₃, -CO₂C(CH₃)₃, -COCH(OH)CH₃, -CONH₂, -CONHCH₃, -CON(CH₃)₂, -C(CH₃)₂CONH₂, -NH₂, -NHCH₃, -N(CH₃)₂, -NHCOCH₃, -N(CH₃)COCH₃, -NHS(O)₂CH₃,
 15 -N(CH₃)C(CH₃)₂CONH₂, -N(CH₃)CH₂CH₂S(O)₂CH₃, -NO₂, =O, -OH, -OCH₃, -OCH₂CH₃, -OCH₂CH₂OCH₃, -OCH₂CH₂OH, -OCH₂CH₂N(CH₃)₂, -OP(O)(OH)₂, -S(O)₂N(CH₃)₂, -SCH₃, -S(O)₂CH₃, -S(O)₃H, cyclopropyl, oxetanyl, azetidiny, 1-methylazetidin-3-yl)oxy, N-methyl-N-oxetan-3-ylamino, azetidin-1-ylmethyl, and morpholino.

In another aspect, there is provided a compound selected from:

20 2-{[4-Hydroxymethyl-1'-methyl-5'-[5-(4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6'-oxo-1',6'-dihydro-[3,3']bipyridinyl-5-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{[3'-Hydroxymethyl-1-methyl-5-[5-(4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

25 2-{[3'-Hydroxymethyl-1-methyl-5-[5-((S)-2-methyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(5-methyl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-6-oxo-5-(pyrimidin-4-ylamino)-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[4-Hydroxymethyl-1'-methyl-5'-(5-methyl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6'-oxo-1',6'-dihydro-[3,3']bipyridinyl-5-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{3'-Hydroxymethyl-1-methyl-5-[5-((R)-2-methyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{5-[5-((2S,5R)-2,5-Dimethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(5-oxetan-3-yl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{5-[5-((S)-2-Ethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[5-(6,7-Dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-2-ylamino)-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[5-(2,6-Dimethyl-pyrimidin-4-ylamino)-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(2-methyl-pyrimidin-4-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(6-methyl-pyrimidin-4-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{3-Hydroxymethyl-4-[6-(imidazo[1,2-a]pyridin-7-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-pyridin-2-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one; and

2-[3'-Hydroxymethyl-1-methyl-6-oxo-5-(pyrazin-2-ylamino)-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one.

Another aspect of the disclosure is a pharmaceutical composition comprised of a Formula I compound and a pharmaceutically acceptable carrier, glidant, diluent, or excipient. The pharmaceutical composition may further comprise a second therapeutic agent.

Another aspect of the disclosure is a process for making a pharmaceutical composition which comprises combining a Formula I compound with a pharmaceutically acceptable carrier.

Another aspect of the disclosure is a pharmaceutical composition as defined above for use in the treatment of a disease or disorder selected from immune disorders, cancer, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Bruton's tyrosine kinase.

The disclosure 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 immune disorders, cancer, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Bruton's tyrosine kinase.

Another aspect of the disclosure includes a kit for treating a condition mediated by Bruton's tyrosine kinase, comprising: a) a first pharmaceutical composition comprising a Formula I compound; and b) instructions for use.

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

The disclosure includes use of a Formula I compound in the manufacture of a medicament for the treatment of immune disorders, cancer, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and where the medicament mediates Bruton's tyrosine kinase. Another aspect of the disclosure includes use of a pharmaceutical composition as defined above in the manufacture of a medicament for the treatment of immune disorders, cancer, cardiovascular disease, viral

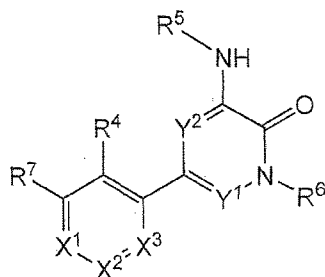
infection, inflammation, metabolism/endocrine function disorders and neurological disorders; and wherein the medicament mediates the Bruton's tyrosine kinase.

The disclosure includes methods of making a Formula I compound.

BRIEF DESCRIPTION OF THE DRAWINGS

We Claim:

1. A compound selected from Formula I:



I

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

X¹ is CR¹-or-N;

X² is CR²-or-N;

X³ is CR³-or-N;

where one or two of X¹, X², and X³ are N;

R¹, R² and R³ are independently selected from H, F, Cl, NH₂, NHCH₃, N(CH₃)₂,

OH, OCH₃, OCH₂CH₃, OCH₂CH₂OH, and C₁-C₃ alkyl;

R⁴ is selected from H, F, Cl, CN, CH₂OH, CH(CH₃)OH, C(CH₃)₂OH,

CH(CF₃)OH, CH₂F, CHF₂, CH₂CHF₂, CF₃, C(O)NH₂, C(O)NHCH₃, C(O)N(CH₃)₂,

NH₂, NHCH₃, N(CH₃)₂, NHC(O)CH₃, OH, OCH₃, OCH₂CH₃, OCH₂CH₂OH,

cyclopropyl, cyclopropylmethyl, 1-hydroxycyclopropyl, imidazolyl, pyrazolyl, 3-hydroxy-

oxetan-3-yl, oxetan-3-yl, and azetidin-1-yl;

R⁵ is optionally substituted C₆-C₂₀ aryl, C₃-C₁₂ carbocyclyl, C₂-C₂₀ heterocyclyl,

C₁-C₂₀ heteroaryl, -(C₆-C₂₀ aryl)-(C₂-C₂₀ heterocyclyl), -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀

heterocyclyl), -(C₁-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl)-(C₂-C₂₀ heterocyclyl), -(C₁-C₂₀

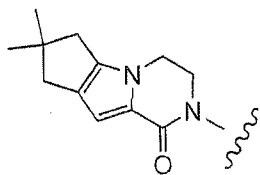
heteroaryl)-(C₂-C₂₀ heterocyclyl)-(C₁-C₆ alkyl), -(C₁-C₂₀ heteroaryl)-(C₁-C₆ alkyl), -(C₂-

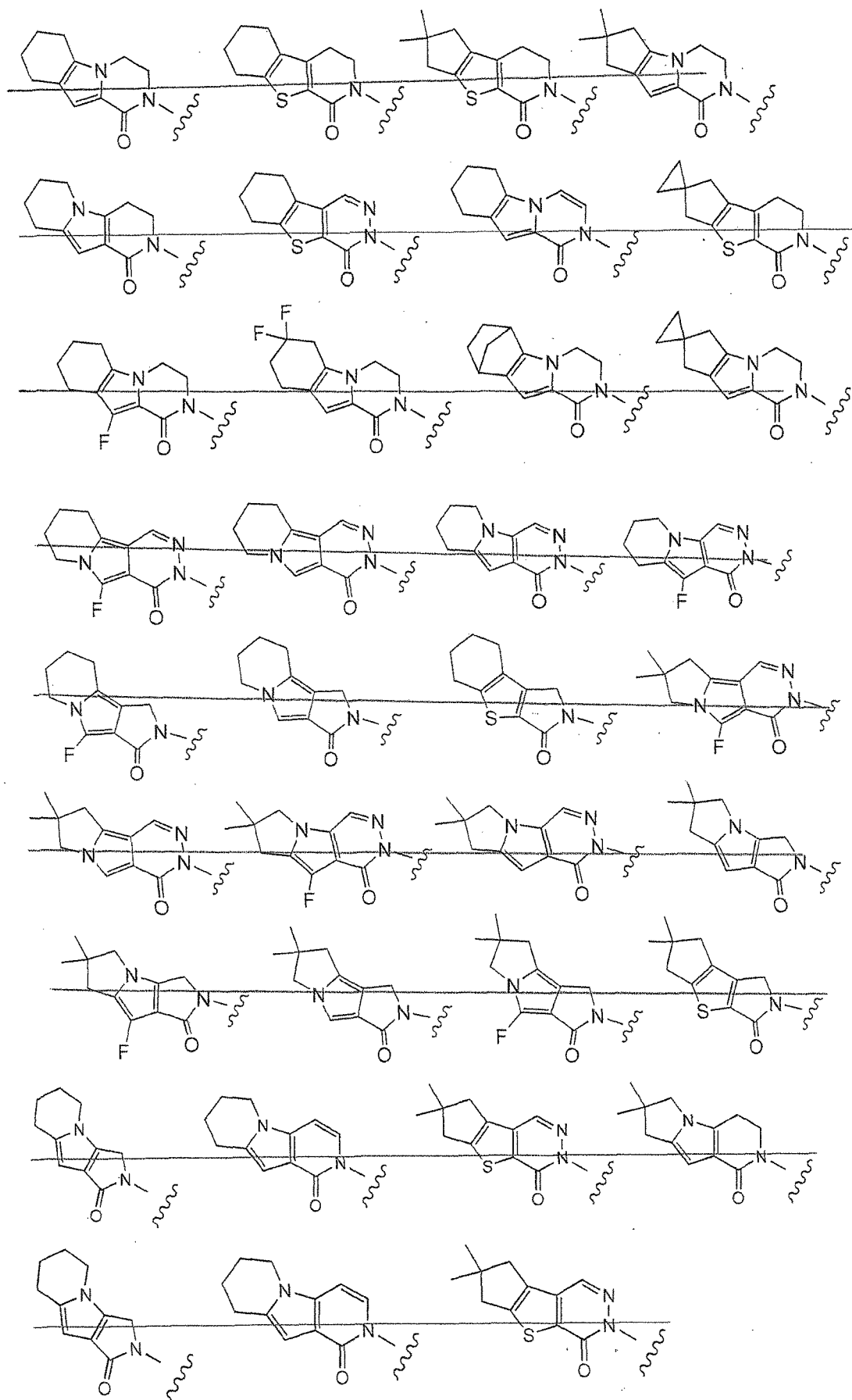
C₂₀ heterocyclyl)-(C₁-C₆ alkyl), -(C₂-C₂₀ heterocyclyl)-(C₃-C₁₂ carbocyclyl), -(C₁-C₂₀

heteroaryl)-(C₃-C₁₂ carbocyclyl), or -(C₁-C₂₀ heteroaryl)-C(=O)-(C₂-C₂₀ heterocyclyl);

R⁶ is H, -CH₃, -CH₂CH₃, -CH₂CH₂OH, -CHF₂, -NH₂, or -OH;

R⁷ is selected from the structures:





where the wavy line indicates the site of attachment; and

Y^1 and Y^2 are independently selected from CH and N, where Y^1 and Y^2 are not each N;

where alkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl are optionally substituted
5 with one or more groups independently selected from F, Cl, Br, I, -CN, -CH₃, -CH₂CH₃, -CH(CH₃)₂, -CH₂CH(CH₃)₂, -CH₂OH, -CH₂OCH₃, -CH₂CH₂OH, -C(CH₃)₂OH, -CH(OH)CH(CH₃)₂, -C(CH₃)₂CH₂OH, -CH₂CH₂SO₂CH₃, -CH₂OP(O)(OH)₂, -CH₂F, -CHF₂, -CF₃, -CH₂CF₃, -CH₂CHF₂, -CH(CH₃)CN, -C(CH₃)₂CN, -CH₂CN, -CO₂H, -COCH₃, -CO₂CH₃, -CO₂C(CH₃)₃, -COCH(OH)CH₃, -CONH₂, -CONHCH₃, -CON(CH₃)₂, -
10 C(CH₃)₂CONH₂, -NH₂, -NHCH₃, -N(CH₃)₂, -NHCOCH₃, -N(CH₃)COCH₃, -NHS(O)₂CH₃, -N(CH₃)C(CH₃)₂CONH₂, -N(CH₃)CH₂CH₂S(O)₂CH₃, -NO₂, =O, -OH, -OCH₃, -OCH₂CH₃, -OCH₂CH₂OCH₃, -OCH₂CH₂OH, -OCH₂CH₂N(CH₃)₂, -OP(O)(OH)₂, -S(O)₂N(CH₃)₂, -SCH₃, -S(O)₂CH₃, -S(O)₃H, cyclopropyl, oxetanyl, azetidiny, 1-methylazetidin-3-yl)oxy, N-methyl-N-oxetan-3-ylamino, azetidin-1-ylmethyl, and
15 morpholino.

2. — The compound of claim 1 wherein X^1 is N.

3. — The compound of claim 1 wherein X^2 is N.

4. — The compound of claim 1 wherein X^3 is N.

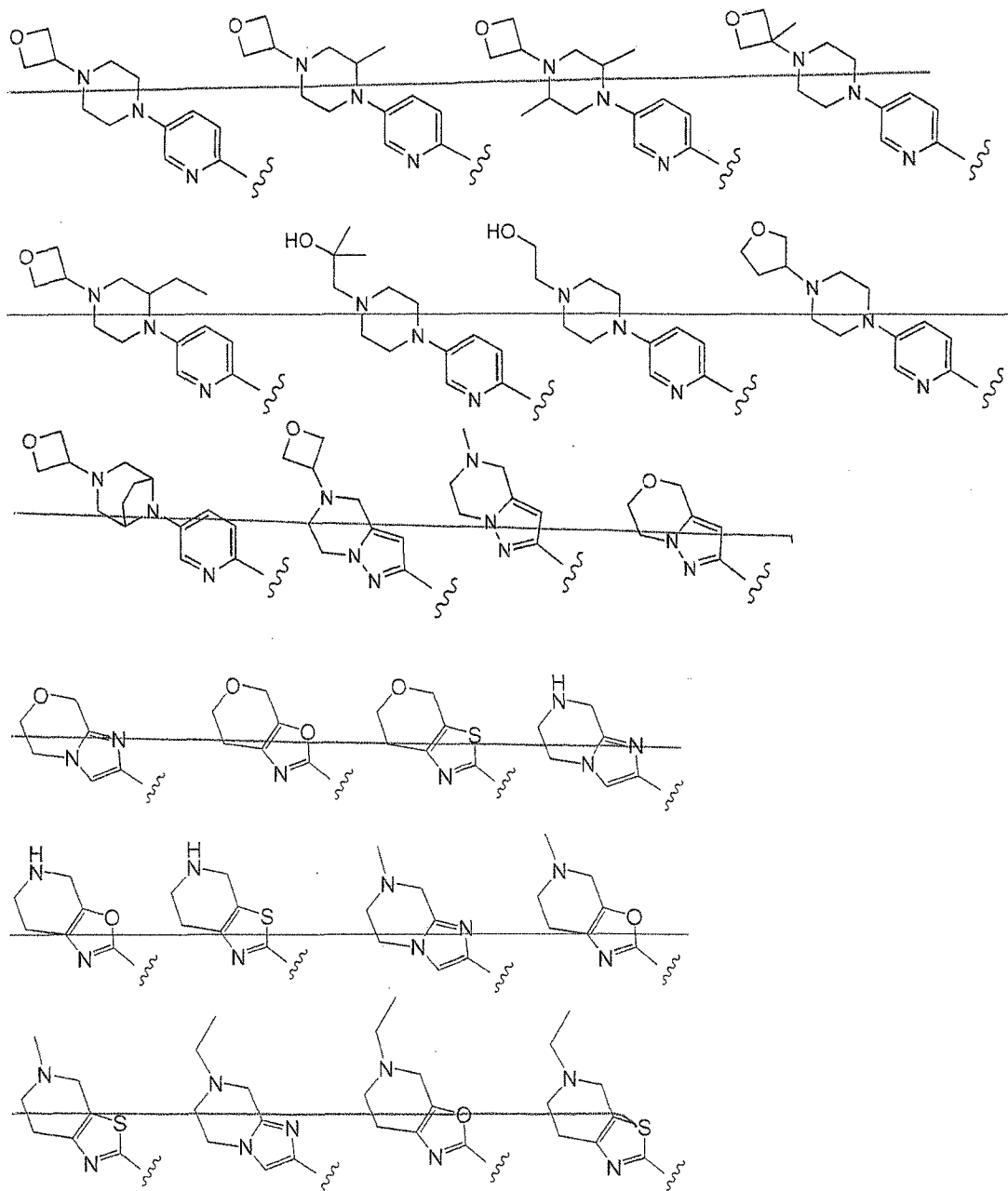
5. — The compound of claim 1 wherein X^1 and X^3 are N, X^1 and X^2 are N, or X^2
20 and X^3 are N.

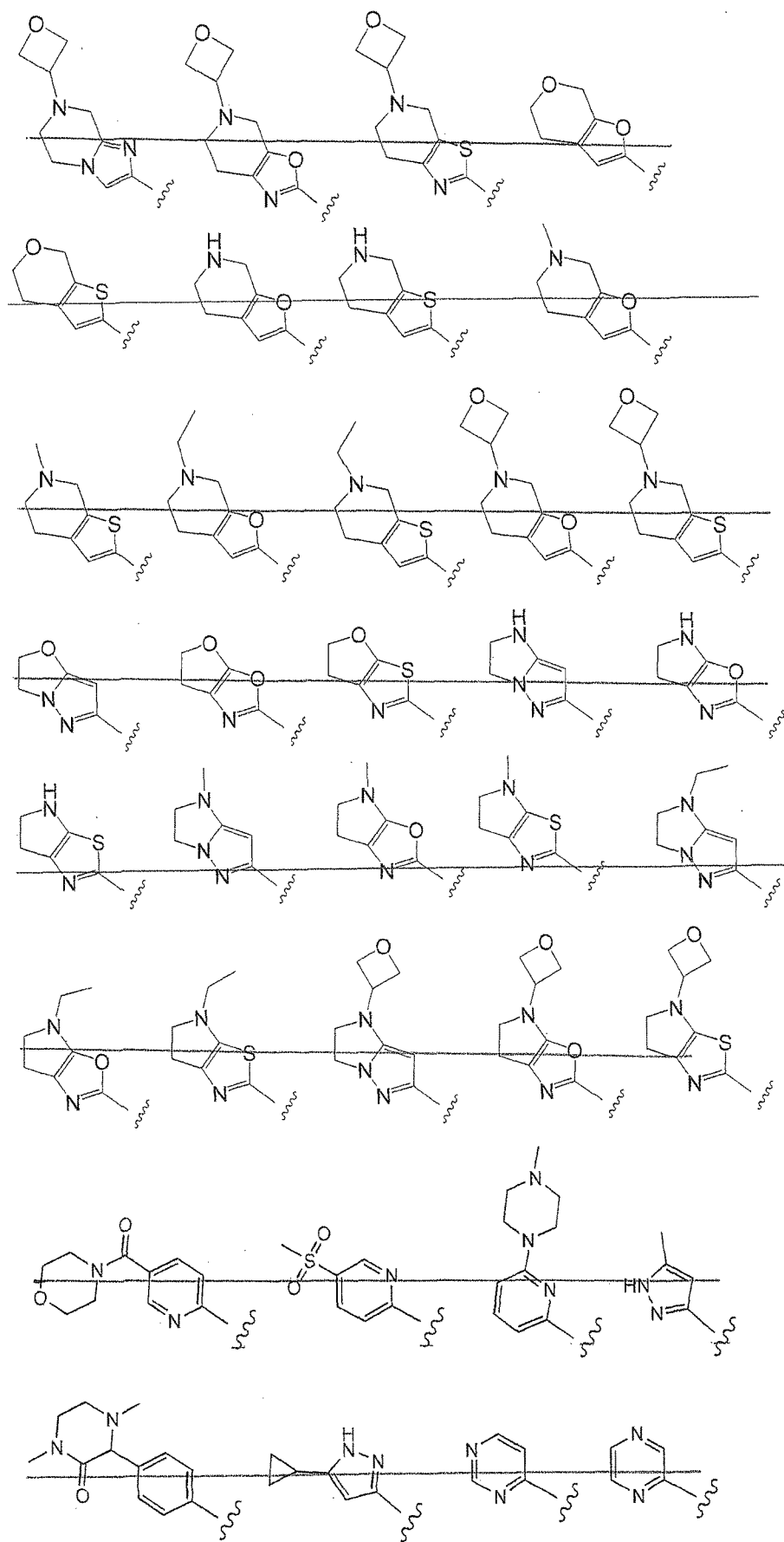
6. — The compound of claim 1 wherein R^5 is optionally substituted C₄-C₂₀
heteroaryl selected from pyrazolyl, pyridinyl, pyrimidinyl, 5-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-2-yl, 5-acetyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-2-yl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-2-yl, and 1-methyl-5-(5-(4-methylpiperazin-1-yl)pyridin-2-yl).
25

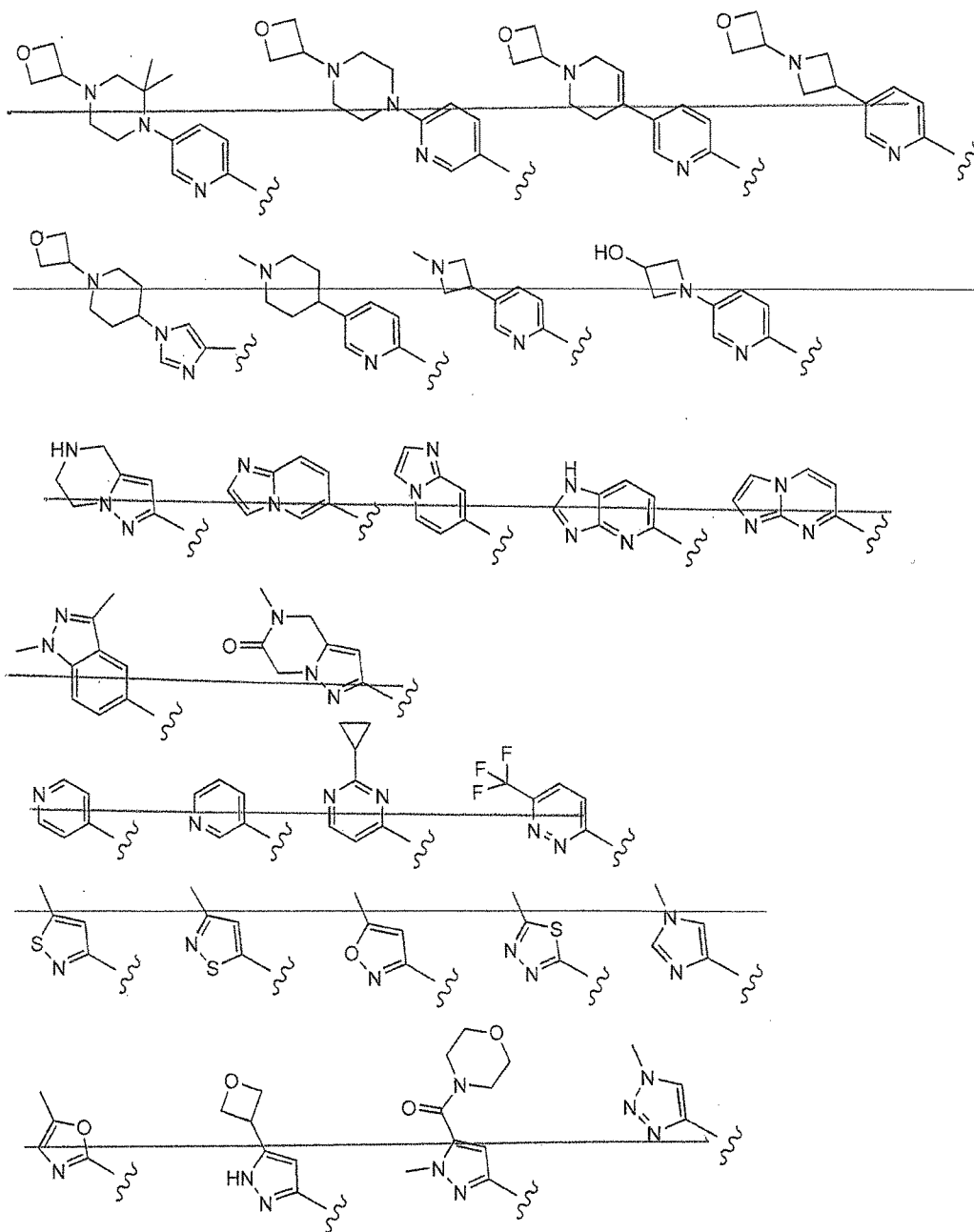
7. — The compound of claim 1 wherein R^5 is (C₄-C₂₀ heteroaryl)-(C₂-C₂₀ heterocyclyl) where heteroaryl is optionally substituted pyridinyl and heterocyclyl is optionally substituted piperazinyl.

8. — The compound of claim 1 wherein R^5 is phenyl, optionally substituted with
30 one or more groups selected from F, Cl, -CH₃, -S(O)₂CH₃, cyclopropyl, azetidiny, oxetanyl, and morpholine.

9. — The compound of claim 1 wherein R^5 is selected from the structures:

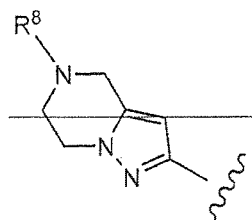






where the wavy line indicates the site of attachment.

10. The compound of claim 1 wherein R^5 is:



5

where R^8 is selected from H, CH_3 , CH_2OCH_3 , CH_2CH_3 , $\text{CH}(\text{CH}_3)_2$, $\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_2\text{CH}_2\text{OCH}_3$, CH_2F , CHF_2 , CF_3 , CH_2CF_3 , CH_2CHF_2 , $\text{CH}(\text{CH}_3)\text{CN}$,

~~C(CH₃)₂CN, CH₂CN, C(O)CH₃, C(O)CH₂CH₃, C(O)CH(CH₃)₂, NH₂, NHCH₃,
N(CH₃)₂, OH, OCH₃, OCH₂CH₃, OCH₂CH₂OH, cyclopropyl, and oxetanyl.~~

112. The compound of claim 1 wherein R⁶ is CH₃.

123. The compound of claim 1 wherein Y¹ is CH and Y² is N.

5 134. The compound of claim 1 wherein Y¹ is N and Y² is CH.

145. The compound of claim 1 wherein Y¹ and Y² are each CH.

156. The compound of claim 1 wherein Y¹ and Y² are each CH, and R⁶ is CH₃.

16. The compound of claim 1 selected from Table 1.

17. The compound of claim 1 selected from Table 2

10 7. A compound selected from:

2-{4-Hydroxymethyl-1'-methyl-5'-[5-(4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6'-oxo-1',6'-dihydro-[3,3']bipyridinyl-5-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

15 2-{3'-Hydroxymethyl-1-methyl-5-[5-(4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{3'-Hydroxymethyl-1-methyl-5-[5-((S)-2-methyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

20 2-[3'-Hydroxymethyl-1-methyl-5-(5-methyl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

25 2-[3'-Hydroxymethyl-1-methyl-6-oxo-5-(pyrimidin-4-ylamino)-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[4-Hydroxymethyl-1'-methyl-5'-(5-methyl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6'-oxo-1',6'-dihydro-[3,3']bipyridinyl-5-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

30 2-{3'-Hydroxymethyl-1-methyl-5-[5-((R)-2-methyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{5-[5-((2S,5R)-2,5-Dimethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(5-oxetan-3-yl-4,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrazin-2-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{5-[5-((S)-2-Ethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[5-(6,7-Dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-2-ylamino)-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[5-(2,6-Dimethyl-pyrimidin-4-ylamino)-3'-hydroxymethyl-1-methyl-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(2-methyl-pyrimidin-4-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-[3'-Hydroxymethyl-1-methyl-5-(6-methyl-pyrimidin-4-ylamino)-6-oxo-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one;

2-{3-Hydroxymethyl-4-[6-(imidazo[1,2-a]pyridin-7-ylamino)-4-methyl-5-oxo-4,5-dihydro-pyrazin-2-yl]-pyridin-2-yl}-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one; and

2-[3'-Hydroxymethyl-1-methyl-6-oxo-5-(pyrazin-2-ylamino)-1,6-dihydro-[3,4']bipyridinyl-2'-yl]-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one.

~~188.~~ A pharmaceutical composition comprised of a compound of any one of claims 1 to ~~17~~ 7 and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

~~199.~~ The pharmaceutical composition according to claim ~~188~~, further comprising a therapeutic agent.

~~2010.~~ A process for making a pharmaceutical composition which comprises combining a compound of any one of claims 1 to 17 with a pharmaceutically acceptable carrier.

~~21~~11. The pharmaceutical composition of claim ~~18~~8 for use in the treatment of a disease or disorder selected from immune disorders, cancer, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders, and mediated by Bruton's tyrosine kinase.

5 ~~22~~12. The pharmaceutical composition of claim ~~21~~11 wherein the disease or disorder is an immune disorder.

~~23~~13. The pharmaceutical composition of claim ~~22~~12 wherein the immune disorder is rheumatoid arthritis.

10 ~~24~~14. The pharmaceutical composition of claim ~~21~~11 wherein the disease or disorder is systemic and local inflammation, arthritis, inflammation related to immune suppression, organ transplant rejection, allergies, ulcerative colitis, Crohn's disease, dermatitis, asthma, systemic lupus erythematosus, Sjögren's Syndrome, multiple sclerosis, scleroderma/systemic sclerosis, idiopathic thrombocytopenic purpura (ITP), anti-neutrophil cytoplasmic antibodies (ANCA) vasculitis, chronic obstructive pulmonary disease (COPD),
15 psoriasis.

~~25~~15. The pharmaceutical composition of claim ~~21~~11 wherein the disease or disorder is cancer selected from 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, multiple myeloma, acute myelogenous leukemia, chronic myelogenous leukemia, lymphocytic leukemia, chronic lymphoid leukemia (CLL), myeloid leukemia, oral cavity and pharynx, non-Hodgkin lymphoma, melanoma, and villous colon adenoma.

2616. The pharmaceutical composition of claim 24-11 further comprising an additional therapeutic agent selected from an anti-inflammatory agent, an immunomodulatory agent, chemotherapeutic agent, an apoptosis-enhancer, 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.

2717. A kit for treating a condition mediated by Bruton's tyrosine kinase, comprising:

- a) a pharmaceutical composition of claim 188; and
- b) instructions for use.

2818. Use of a pharmaceutical composition of claim 18-8 in the manufacture of a medicament for the treatment of immune disorders, cancer, cardiovascular disease, viral infection, inflammation, metabolism/endocrine function disorders and neurological disorders; and wherein the medicament mediates the Bruton's tyrosine kinase.