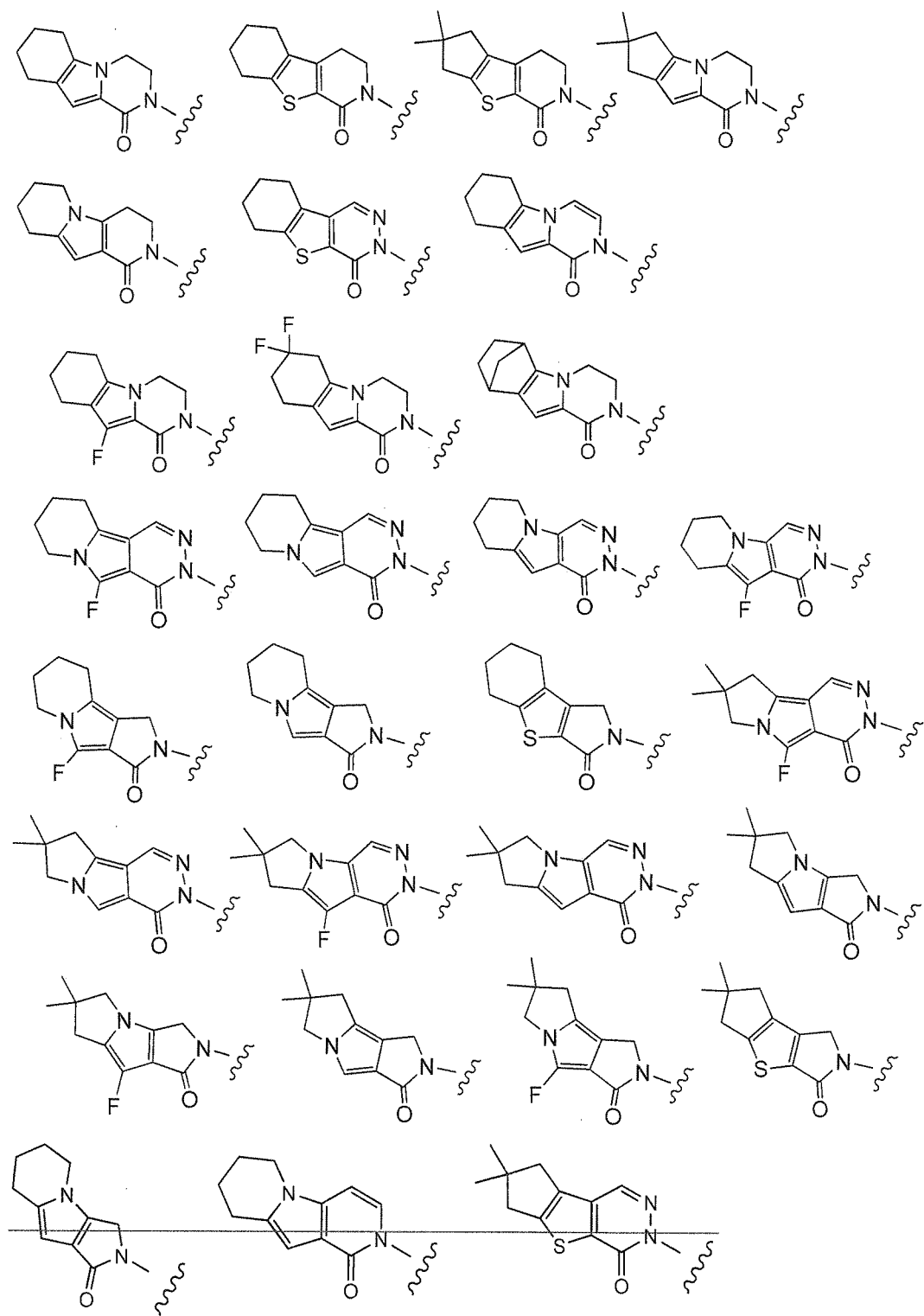


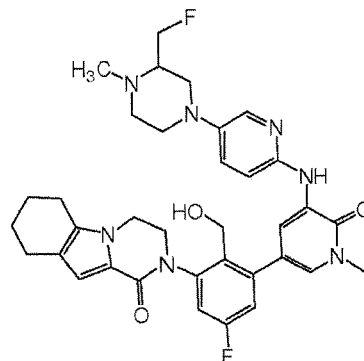


where the wavy line indicates the site of attachment;

5 R^8 is selected from $-CH_3$, $-S(O)_2CH_3$, cyclopropyl, azetidin-3-yl, oxetan-3-yl, and morpholin-4-yl;

X^1 is CR^9 or N, where R^9 is selected from H, F, Cl, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2OH$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-OH$, $-OCH_3$, $-OCH_2CH_3$, and $-OCH_2CH_2OH$;

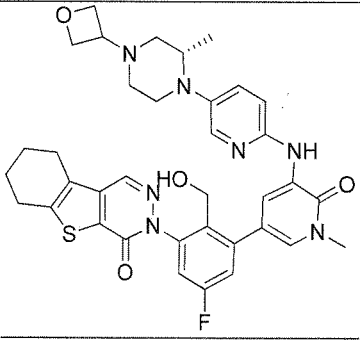
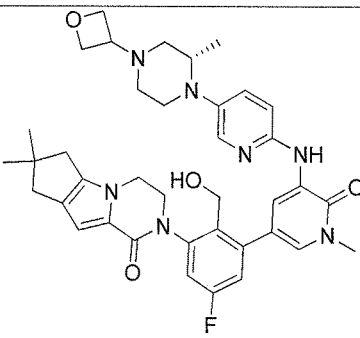
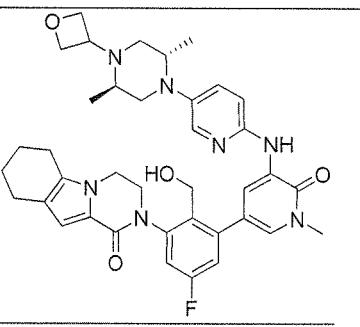
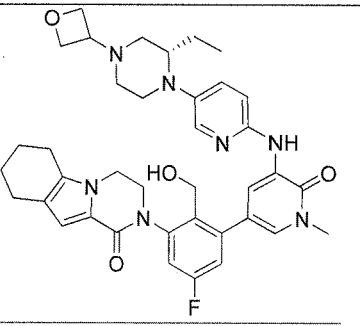
X² is CR¹⁰ or N, where R¹⁰ is selected from H, –CH₃, –CH₂CH₃, and –CH₂CH₂OH; and Y¹ and Y² are independently selected from CH and N, where Y¹ and Y² are not each N₂

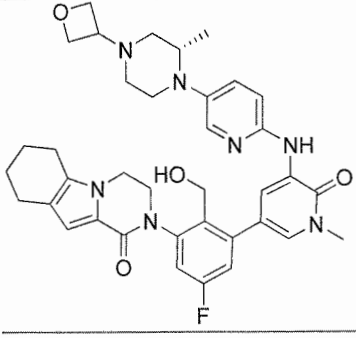
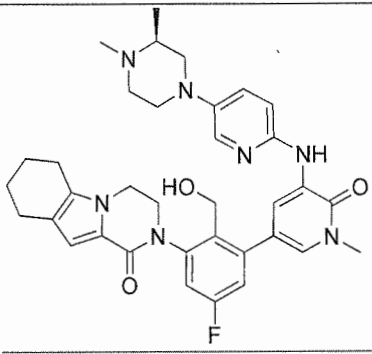
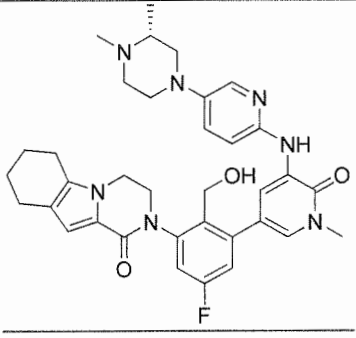
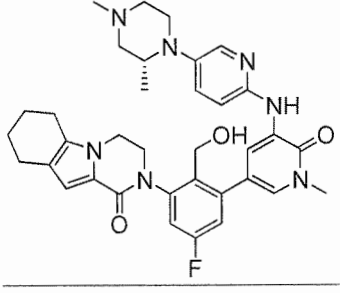


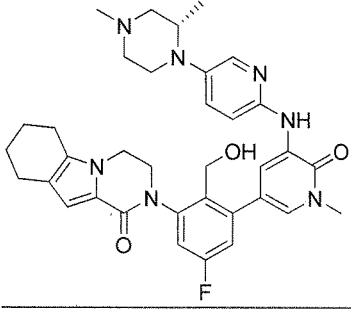
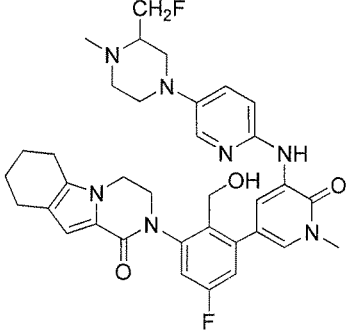
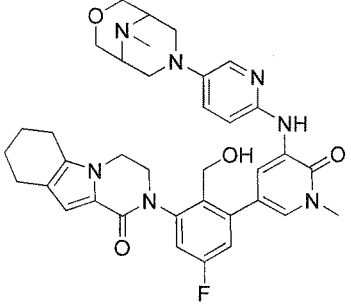
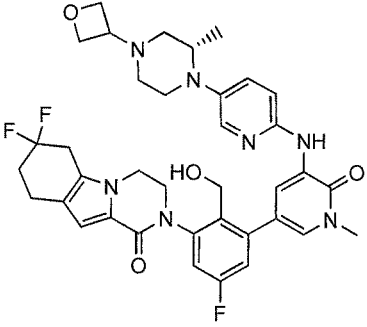
with the proviso that the compound is not

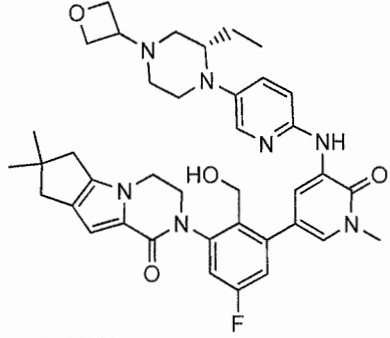
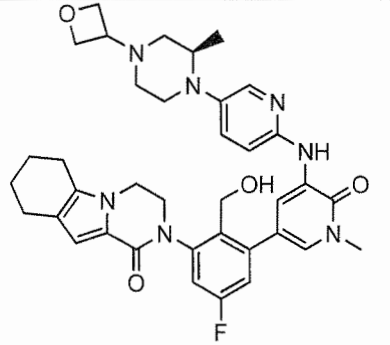
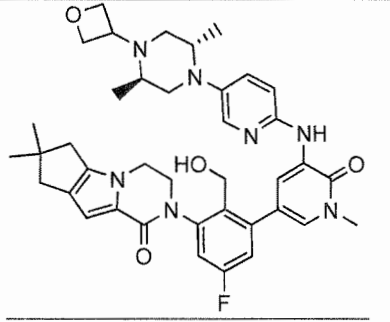
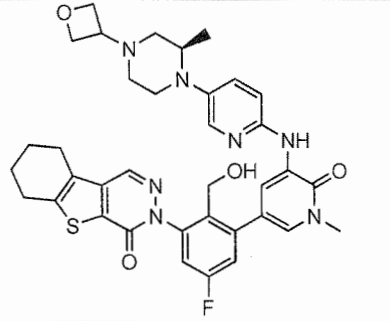
2. The compound of claim 1 wherein X¹ is CR⁹, and R⁹ is H
3. The compound of claim 1 wherein X¹ or X² is N.
4. The compound of claim 1 wherein R⁴ is –CH₂OH.
5. The compound of claim 4 wherein R² is F.
6. The compound of claim 5 wherein R¹ and R³ are H.
7. The compound of claim 1 wherein R⁶ is CH₃.
8. The compound of claim 1 selected from the following Table 1.

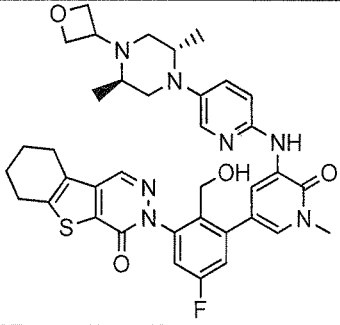
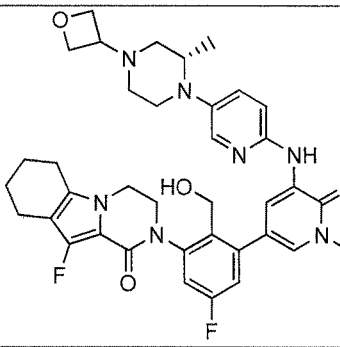
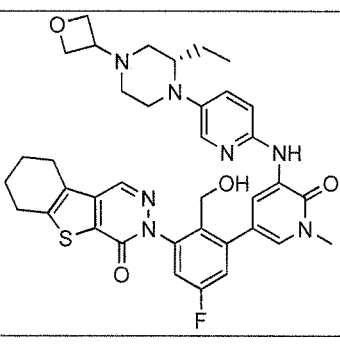
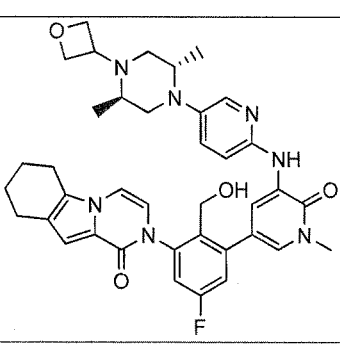
No.	Structure	IUPAC Name
101		(S)-2-(5-fluoro-2-(hydroxymethyl)-3-(1-methyl-5-(5-(2-methyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-3,4,6,7,8,9-hexahydropyrido[3,4-b]indolizin-1(2H)-one

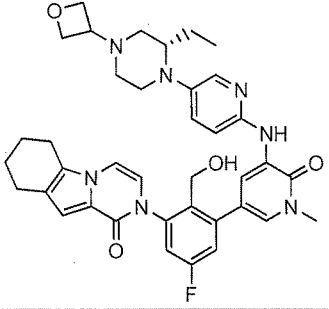
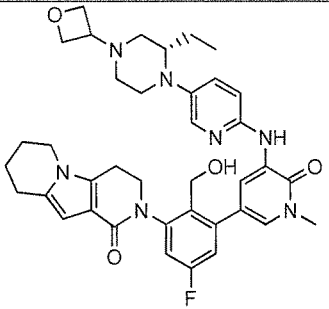
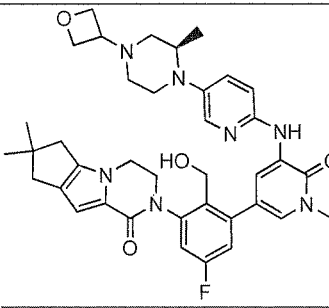
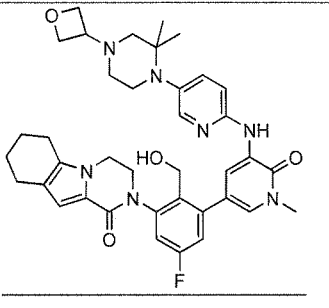
<p><u>102</u></p>		<p>(S)-5-[5-fluoro-2-(hydroxymethyl)-3(1-methyl-5-(5-(2-methyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydropyridin-3-yl)phenyl]-8-thia-4,5-diazatricyclo[7.4.0.0^{2,7}]trideca-1(9),2(7),3-trien-6-one</p>
<p><u>103</u></p>		<p>(2S)-10-[5-fluoro-2-(hydroxymethyl)-3-[1-methyl-5-({5-[2-methyl-4-(oxetan-3-yl)piperazin-1-yl]pyridine-2-yl}amino)-6-oxo-1,6-dihydropyridin-3-yl]phenyl]-4,4-dimethyl-1,10-diazatricyclo[6.4.0.0^{2,6}]dodeca-2(6),7-dien-9-one</p>
<p><u>104</u></p>		<p>2-(3-(5-(5-((2S,5R)-2,5-dimethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>
<p><u>105</u></p>		<p>(S)-2-(3-(5-(5-(2-ethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>

106		<u>(S)-2-(5-fluoro-2-</u> <u>(hydroxymethyl)-3-(1-methyl-5-(5-</u> <u>(2-methyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl)pyridin-2-</u> <u>ylamino)-6-oxo-1,6-</u> <u>dihydropyridin-3-yl)phenyl)-</u> <u>3,4,6,7,8,9-hexahydropyrazino[1,2-</u> <u>a]indol-1(2H)-one</u>
107		<u>(S)-2-(3-(5-(5-(3,4-</u> <u>dimethylpiperazin-1-yl)pyridin-2-</u> <u>ylamino)-1-methyl-6-oxo-1,6-</u> <u>dihydropyridin-3-yl)-5-fluoro-2-</u> <u>(hydroxymethyl)phenyl)-</u> <u>3,4,6,7,8,9-hexahydropyrazino[1,2-</u> <u>a]indol-1(2H)-one</u>
108		<u>(R)-2-(3-(5-(5-(3,4-</u> <u>dimethylpiperazin-1-yl)pyridin-2-</u> <u>ylamino)-1-methyl-6-oxo-1,6-</u> <u>dihydropyridin-3-yl)-5-fluoro-2-</u> <u>(hydroxymethyl)phenyl)-</u> <u>3,4,6,7,8,9-hexahydropyrazino</u> <u>[1,2-α]indol-1(2H)-one</u>
109		<u>(R)-2-(3-(5-(5-(2,4-</u> <u>dimethylpiperazin-1-yl)pyridin-2-</u> <u>ylamino)-1-methyl-6-oxo-1,6-</u> <u>dihydropyridin-3-yl)-5-fluoro-2-</u> <u>(hydroxymethyl)phenyl)-</u> <u>3,4,6,7,8,9-hexahydropyrazino[1,2-</u> <u>a]indol-1(2H)-one</u>

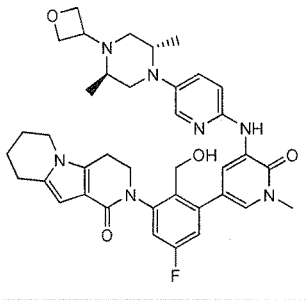
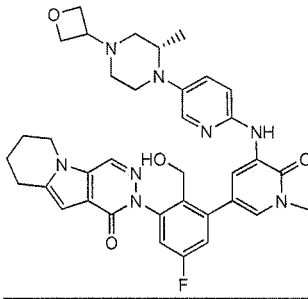
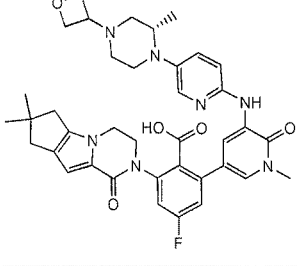
110		<p>(S)-2-(3-(5-(5-(2,4-dimethylpiperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>
111		<p>2-(5-fluoro-3-(5-(5-(3-(fluoromethyl)-4-methylpiperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>
112		<p>2-(5-fluoro-2-(hydroxymethyl)-3-(1-methyl-5-(5-(9-methyl-7-oxa-3,9-diazabicyclo[3.3.1]nonan-3-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>
113		<p>(S)-7,7-difluoro-2-(5-fluoro-2-(hydroxymethyl)-3-(1-methyl-5-(5-(2-methyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>

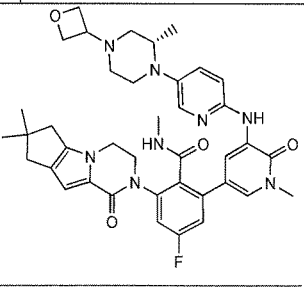
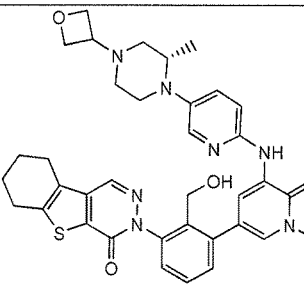
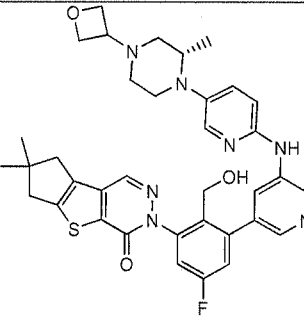
114		<u>2-(3-{5-[5-((S)-2-Ethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-5-fluoro-2-hydroxymethyl-phenyl)-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one</u>
115		<u>(R)-2-(5-fluoro-2-(hydroxymethyl)-3-(1-methyl-5-(5-(2-methyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydro-pyridin-3-yl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</u>
116		<u>2-(3-{5-[5-((2S,5R)-2,5-Dimethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-5-fluoro-2-hydroxymethyl-phenyl)-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one</u>
117		<u>3-(5-Fluoro-2-hydroxymethyl-3-{1-methyl-5-[5-((R)-2-methyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-6-oxo-1,6-dihydro-pyridin-3-yl}-phenyl)-6,7,8,9-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyridazin-4-one</u>

118		<u>3-(3-{5-[5-((2S,5R)-2,5-Dimethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-5-fluoro-2-hydroxymethyl-phenyl)-6,7,8,9-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyridazin-4-one</u>
119		<u>(S)-10-fluoro-2-(5-fluoro-2-(hydroxymethyl)-3-(1-methyl-5-(5-(2-methyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</u>
120		<u>3-(3-{5-[5-((S)-2-Ethyl-4-oxetan-3-yl-piperazin-1-yl)-pyridin-2-ylamino]-1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl}-5-fluoro-2-hydroxymethyl-phenyl)-6,7,8,9-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyridazin-4-one</u>
121		<u>2-(3-(5-(5-((2S,5R)-2,5-dimethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-6,7,8,9-tetrahydropyrazino[1,2-a]indol-1(2H)-one</u>

122		<p>(S)-2-(3-(5-(5-(2-ethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-6,7,8,9-tetrahydropyrazino[1,2-a]indol-1(2H)-one</p>
123		<p>(S)-2-(3-(5-(5-(2-ethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrido[3,4-b]indolizin-1(2H)-one</p>
124		<p>2-(5-Fluoro-2-hydroxymethyl-3-{1-methyl-5-[(R)-2-methyl-4-oxetan-3-ylpiperazin-1-yl]-pyridin-2-ylamino}-6-oxo-1,6-dihydropyridin-3-yl)-phenyl)-7,7-dimethyl-3,4,7,8-tetrahydro-2H,6H-cyclopenta[4,5]pyrrolo[1,2-a]pyrazin-1-one</p>
125		<p>2-(3-(5-(5-(2,2-dimethyl-4-(oxetan-3-yl)piperazin-1-yl)pyridin-2-ylamino)-1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-3,4,6,7,8,9-hexahydropyrazino[1,2-a]indol-1(2H)-one</p>

9. The compound of claim 1 selected from Table 2 the following:

No.	Structure	IUPAC Name
<u>126</u>		<u>2-[3-[5-[[5-[(2S,5R)-2,5-</u> <u>dimethyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl]-2-</u> <u>pyridyl]amino]-1-methyl-6-oxo-</u> <u>3-pyridyl]-5-fluoro-2-</u> <u>(hydroxymethyl)phenyl]-</u> <u>3,4,6,7,8,9-</u> <u>hexahydropyrido[3,4-</u> <u>b]indolizin-1-one</u>
<u>127</u>		<u>2-[5-fluoro-2-</u> <u>(hydroxymethyl)-3-[1-methyl-5-</u> <u>[[5-[(2S)-2-methyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl]-2-</u> <u>pyridyl]amino]-6-oxo-3-</u> <u>pyridyl]phenyl]-6,7,8,9-</u> <u>tetrahydropyridazino[4,5-</u> <u>b]indolizin-1-one</u>
<u>128</u>		<u>2-(7,7-dimethyl-4-oxo-</u> <u>1,2,6,8-</u> <u>tetrahydrocyclopenta[3,4]pyrrol</u> <u>o[3,5-b]pyrazin-3-yl)-4-fluoro-</u> <u>6-[1-methyl-5-[[5-[(2S)-2-</u> <u>methyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl]-2-</u> <u>pyridyl]amino]-6-oxo-3-</u> <u>pyridyl]benzoic acid</u>

129		<u>2-(7,7-dimethyl-4-oxo-</u> <u>1,2,6,8-</u> <u>tetrahydrocyclopenta[3,4]pyrrol</u> <u>o[3,5-b]pyrazin-3-yl)-4-fluoro-</u> <u>N-methyl-6-[1-methyl-5-[[5-</u> <u>[(2S)-2-methyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl]-2-</u> <u>pyridyl]amino]-6-oxo-3-</u> <u>pyridyl]benzamide</u>
130		<u>3-[2-(hydroxymethyl)-3-</u> <u>[1-methyl-5-[[5-[(2S)-2-methyl-</u> <u>4-(oxetan-3-yl)piperazin-1-yl]-</u> <u>2-pyridyl]amino]-6-oxo-3-</u> <u>pyridyl]phenyl]-6,7,8,9-</u> <u>tetrahydrobenzothiopheno[2,3-</u> <u>d]pyridazin-4-one</u>
131		<u>3-[5-fluoro-2-</u> <u>(hydroxymethyl)-3-[1-methyl-5-</u> <u>[[5-[(2S)-2-methyl-4-(oxetan-3-</u> <u>yl)piperazin-1-yl]-2-</u> <u>pyridyl]amino]-6-oxo-3-</u> <u>pyridyl]phenyl]-7,7-dimethyl-</u> <u>6,8-</u> <u>dihydrocyclopenta[3,4]thieno[1,</u> <u>3-d]pyridazin-4-one</u>

10. A pharmaceutical composition comprised of a compound of any one of claims 1 to 9 and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

11. The pharmaceutical composition according to claim 10, further comprising a therapeutic agent.

5 12. A process for making a pharmaceutical composition which comprises combining a compound of any one of claims 1 to 9 with a pharmaceutically acceptable carrier.

13. Use of a pharmaceutical composition of claim 10 in the manufacture of a medicament for 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 wherein the medicament mediates the Bruton's tyrosine kinase.

14. The use of claim 13 wherein the disease or disorder is an immune disorder.

15. The use of claim 14 wherein the immune disorder is rheumatoid arthritis.

5 16. The use of claim 13 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,
10 chronic obstructive pulmonary disease (COPD), psoriasis.

17. The use of claim 13 wherein the disease or disorder is cancer selected from breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx,