Title: 3-(lH-PYRROLO[2,3-B]PYRIDIN-2-YL)-lH-PYRAZOLE[4,3-B]PYRIDINES AND THERAPEUTIC USES THEREOF

Abstract: 4-Azaindazole compounds for treating various diseases and pathologies are disclosed. More particularly, the present disclosure concerns the use of a 4-azaindazole compound or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

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RELATED APPLICATIONS

[001] This application claims the benefit of U.S. Provisional Application Nos. 62/200,275, filed August 3, 2015, and 62/354,021, filed June 23, 2016, which are incorporated herein by reference in their entirety.

BACKGROUND

Technical Field

[002] This disclosure relates to inhibitors of one or more proteins in the Wnt pathway, including inhibitors of one or more Wnt proteins, and compositions comprising the same. More particularly, it concerns the use of a 4-azaindazole compound or salts or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

Background

[003] The Wnt growth factor family includes more than 10 genes identified in the mouse and at least 19 genes identified in the human. Members of the Wnt family of signaling molecules mediate many short-and long-range patterning processes during invertebrate and vertebrate development. The Wnt signaling pathway is known for its role in the inductive interactions that regulate growth and differentiation, and it also plays roles in the homeostatic maintenance of post-embryonic tissue integrity. Wnt stabilizes cytoplasmic β-catenin, which stimulates the expression of genes including c-myc, c jun, fra-1, and cyclin D1. In addition, misregulation of Wnt signaling can cause developmental defects and is implicated in the genesis of several human cancers. The Wnt pathway has also been implicated in the maintenance of stem or progenitor cells in a growing list of adult tissues including skin, blood, gut, prostate, muscle, and the nervous system.
The present disclosure provides methods and reagents, involving contacting a cell with an agent, such as a 4-azaindazole compound, in a sufficient amount to antagonize a Wnt activity, e.g., to reverse or control an aberrant growth state or correct a genetic disorder due to mutations in Wnt signaling components.

Some embodiments disclosed herein include Wnt inhibitors containing a 4-azaindazole core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

One embodiment disclosed herein includes a compound having the structure of Formula I:

![Chemical structure](attachment:image.png)

as well as prodrugs and pharmaceutically acceptable salts thereof.

In some embodiments of Formula (I):

- $R^1$ and $R^2$ are independently selected from the group consisting of $H$ and halide;
- $R^3$ is selected from the group consisting of -heteroaryl optionally substituted with 1-4 $R^6$ and -heterocyclyl optionally substituted with 1-10 $R^7$;
- $R^5$ is selected from the group consisting of $H$, -heteroaryl optionally substituted with 1-4 $R^8$, -heterocyclyl optionally substituted with 1-10 $R^9$, and -aryl optionally substituted with 1-5 $R^{10}$;

- each $R^6$ is independently selected from the group consisting of halide, -(C1-6 alkyl), -(C2-6 alkenyl), -(C2-6 alkynyl), -(C1-4 alkyne), -I, -heterocyclyl optionally substituted with 1-10 $R^{11}$, -(C2-4 alkenylene), -I, heterocyclyl optionally substituted with 1-10 $R^{11}$, -(C2-4 alkynylene), -I, heterocyclyl optionally substituted with 1-10 $R^{11}$, -(C1-4 alkyne), -I, carbocyclyl optionally substituted with 1-12 $R^{12}$, -(C2-4 alkenylene), -I, carbocyclyl optionally substituted with 1-12 $R^{12}$, -(C2-4 alkynylene), -I, carbocyclyl optionally substituted with 1-12 $R^{12}$, -(C1-4 alkyne), -I, aryl optionally substituted with 1-5 $R^{13}$, -(C2-4 alkenylene), -I, aryl optionally substituted with 1-5 $R^{13}$, -(C2-4 alkynylene), -I, aryl optionally substituted with 1-5 $R^{13}$, -NHC (=(O)R^{14}, -NR^{15}R^{16}, -(C1-6
alkylene)NR<sup>17</sup>R<sup>18</sup>, -(C<sub>2-6</sub> alkenylene)NR<sup>17</sup>R<sup>18</sup>, -(C<sub>2-6</sub> alkynylene)NR<sup>17</sup>R<sup>18</sup> and -(C<sub>M</sub> alkylene)pOR<sup>24</sup>;

- each R<sup>7</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, and -CN;
- each R<sup>8</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, -OCH<sub>3</sub>, -CN, and -C(=0)R<sup>19</sup>;
- each R<sup>9</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, -CN, and -OCH<sub>3</sub>;
- each R<sup>10</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, -CN,-(C<sub>1-6</sub> alkenylene)pNH<sub>0</sub>R<sup>19</sup>, -(C<sub>2-6</sub> alkenylene)pNHSO<sub>2</sub>R<sup>19</sup>, -(C<sub>2-6</sub> alkenylene)pNHSO<sub>2</sub>R<sup>19</sup>, -NR<sup>15</sup>(C<sub>1-6</sub> alkenylene)NR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>(C<sub>7</sub>-<sub>6</sub> alkenylene)NR<sup>15</sup>R<sup>16</sup>, -(C<sub>1-5</sub> alkenylene)NR<sup>15</sup>R<sup>16</sup>, -(C<sub>1-5</sub> alkenylene)NR<sup>15</sup>R<sup>16</sup>, -(C<sub>2-6</sub> alkenylene)pNR<sup>15</sup>R<sup>16</sup>, -(C<sub>2-6</sub> alkylene)pNR<sup>15</sup>R<sup>16</sup>, -(C<sub>2-6</sub> alkylene)pNR<sup>15</sup>R<sup>16</sup>, and -OR<sup>27</sup>;
- each R<sup>11</sup> is independently selected from the group consisting of amino, -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, and -CN;
- each R<sup>12</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, and -CN;
- each R<sup>13</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), halide, -CF<sub>3</sub>, and -CN;
- each R<sup>14</sup> is independently selected from the group consisting of -(C<sub>1-4</sub> alkyl), -(C<sub>1-4</sub> haloalkyl), -(C<sub>2-9</sub> alkenyl), -(C<sub>2-9</sub> alkynyl), -heteroaryl optionally substituted with 1-4 R<sup>20</sup>, -aryl optionally substituted with 1-5 R<sup>21</sup>, -CH<sub>2</sub>aryl optionally substituted with 1-5 R<sup>21</sup>, -carbocyclyl optionally substituted with 1-12 R<sup>22</sup>, -CF<sub>3</sub>carbocyclyl optionally substituted with 1-12 R<sup>22</sup>, -(C<sub>1-4</sub> alkenylene)pNR<sup>25</sup>R<sup>26</sup>, -(C<sub>2-4</sub> alkenylene)pNR<sup>25</sup>R<sup>26</sup>, -(C<sub>2-4</sub> alkenylene)pNR<sup>25</sup>R<sup>26</sup>, -heterocyclyl optionally substituted with 1-10 R<sup>23</sup>, and -CF<sub>3</sub>heterocyclyl optionally substituted with 1-10 R<sup>23</sup>;
- each R<sup>15</sup> is independently selected from the group consisting of H, -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), and -(C<sub>2-4</sub> alkynyl);
- each R<sup>16</sup> is independently selected from the group consisting of H, -(C<sub>1-4</sub> alkyl), -(C<sub>2-4</sub> alkenyl), -(C<sub>2-4</sub> alkynyl), -CFharyl optionally substituted with 1-5 R<sup>21</sup>, and -CH<sub>2</sub>carbocyclyl optionally substituted with 1-12 R<sup>22</sup>;
- each R<sup>17</sup> is independently selected from the group consisting of H, -(C<sub>1-4</sub> alkyl), -(C<sub>2-6</sub> alkenyl), and -(C<sub>2-6</sub> alkynyl);
each R₁ is independently selected from the group consisting of H, -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), -CF₃aryl optionally substituted with 1-5 R²¹ and -CH₂carbocyclyl optionally substituted with 1-12 R²²;

each R₁ is independently selected from the group consisting of -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), and -(C₂₋₆ alkynyl);

each R² is independently selected from the group consisting of -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), halide, -CF₃, and -CN;

each R³ is independently selected from the group consisting of -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), halide, -CF₃, and -CN;

each R₄ is independently selected from the group consisting of -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), halide, -CF₃, and -CN;

each R₅ is independently selected from the group consisting of -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), halide, -CF₃, and -CN;

R²⁴ is selected from the group consisting of H, -(C₁₋₆ alkyl), -(C₂₋₆ alkenyl), -(C₂₋₆ alkynyl), -(C₁₋₆ alkenylene)ₚₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗₗ₇
R³ is selected from the group consisting of -heteroaryl optionally substituted with 1-4 R⁶ and -heterocyclyl optionally substituted with 1-10 R⁷;

R³ is selected from the group consisting of H, -heteroaryl optionally substituted with 1-4 R⁸, -heterocyclyl optionally substituted with 1-10 R⁹, and -aryl optionally substituted with 1-5 R¹⁰;

each R⁶ is independently selected from the group consisting of halide, -(Ci-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), -(C₁-4 alkylene)ₚ heterocyclyl optionally substituted with 1-10 R¹¹, -(C₂-4 alkynylene)ₚ heterocyclyl optionally substituted with 1-10 R¹¹, -(C₁-4 alkylene)ₚ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-4 alkynylene)ₚ carbocyclyl optionally substituted with 1-12 R¹², -(C₁-4 alkylene)ₚ aryl optionally substituted with 1-5 R¹³, -(C₂-4 alkylene)ₚ aryl optionally substituted with 1-5 R¹³, -NHC(=0)R ¹⁴, -NR ¹⁵R ¹⁶, -(Ci-6 alkylene)NR ¹⁷R ¹⁸, -(C₂₆ alkylene)NR ¹⁷R ¹⁸, and -(C₂₆ alkylene)NR ¹⁷R ¹⁸, -OR ²⁴;

each R⁷ is independently selected from the group consisting of -(C₁-4 alkyl), -(C₂-4 alkynyl), -(C₂-4 alkenyl), halide, -CF₃, and -CN;

each R⁸ is independently selected from the group consisting of -(Ci-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -OCH₃, -CN, and -(=O)R ¹⁹;

each R⁹ is independently selected from the group consisting of -(Ci-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -CN, and -OCH₃;

each R¹⁰ is independently selected from the group consisting of -(Ci-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -(Ci-6 alkylene)ₚ NHSO₂R ²⁰, -(C₂-6 alkynylene)ₚ NHSO₂R ²⁰, -(C₂-6 alkylene)ₚ NHSO₂R ²⁰, -(C₂-6 alkynylene)ₚ NHSO₂R ²⁰, -NR ¹⁵(Ci-6 alkylene)NR ¹⁵R ¹⁶, -NR ¹⁵(C₂₆ alkylene)NR ¹⁵R ¹⁶, -(Ci-6 alkylene)ₚ NR ¹⁵R ¹⁶, -(C₂-6 alkylene)ₚ NR ¹⁵R ¹⁶, -(C₂-6 alkylene)ₚ NR ¹⁵R ¹⁶, -(C₂-6 alkylene)ₚ NR ¹⁵R ¹⁶, -(C₂-6 alkylene)ₚ NR ¹⁵R ¹⁶, and -OR ²⁷;

each R¹¹ is independently selected from the group consisting of amino, -(C₁-4 alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN;

each R¹² is independently selected from the group consisting of -(C₁-4 alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN;

each R¹³ is independently selected from the group consisting of -(C₁-4 alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN;

each R¹⁴ is independently selected from the group consisting of -(C₁-9 alkyl), -(C₂-9 alkenyl), -(C₂-9 alkynyl), -heteroaryl optionally substituted with 1-4 R²⁰, -aryl optionally substituted with 1-5 R²¹, -CF₃aryl optionally substituted with 1-5 R²¹, -carbocyclyl optionally
substituted with 1-12 $R_{12}^{22}$, -CF$_3$carbocyclyl optionally substituted with 1-12 $R_{12}^{22}$, -(CM alkylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$, -(C$_2$-$\gamma$ alkylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$, -(C$_2$-$\gamma$ alkynylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$, -heterocyclyl optionally substituted with 1-10 R$_{10}^{23}$, and -CF$_3$heterocyclyl optionally substituted with 1-10 R$_{10}^{23}$;

each $R_{15}^6$ is independently selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$-6 alkenyl), and -(C$_2$$\gamma$-alkynyl);

each $R_{16}^6$ is independently selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$-6 alkenyl), -(C$_2$-6 alkynyl), -CH$_2$aryl optionally substituted with 1-5 R$_{15}^{21}$, and -CF$_3$heterocyclyl optionally substituted with 1-12 R$_{12}^{22}$;

each $R_{17}^6$ is independently selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$-6 alkenyl), and -(C$_2$-6 alkynyl);

each $R_{18}^6$ is independently selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$-6 alkenyl), -(C$_2$-6 alkynyl), -CF$_3$aryl optionally substituted with 1-5 R$_{15}^{21}$ and -CH$_2$carbocyclyl optionally substituted with 1-12 R$_{12}^{22}$;

each $R_{19}^6$ is independently selected from the group consisting of -(C$_6$-alkyl), -(C$_2$$\gamma$-alkenyl), and -(C$_2$$\gamma$-alkynyl);

each $R_{20}^6$ is independently selected from the group consisting of -(C$_{1-4}$ alkyl), -(C$_{2-4}$ alkynyl), -(C$_2$-4 alkynyl), halide, -CF$_3$, and -CN;

each $R_{21}^6$ is independently selected from the group consisting of -(CM alkyl), -(C$_2$-4 alkenyl), -(C$_2$-4 alkynyl), halide, -CF$_3$, and -CN;

each $R_{22}^6$ is independently selected from the group consisting of -(CM alkyl), -(C$_2$-4 alkenyl), -(C$_2$-4 alkynyl), halide, -CF$_3$, and -CN;

each $R_{23}^6$ is independently selected from the group consisting of -(CM alkyl), -(C$_2$-4 alkenyl), -(C$_2$-4 alkynyl), halide, -CF$_3$, and -CN;

$R_{24}^6$ is selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$-6 alkenyl), -(C$_2$-6 alkynyl), -(CM alkylene)$_p$heterocyclyl optionally substituted with 1-10 R$_{10}^{23}$, -(C$_2$-4 alkylene)$_p$heterocyclyl optionally substituted with 1-10 R$_{10}^{23}$, -(C$_2$-4 alkynylene)$_p$heterocyclyl optionally substituted with 1-10 R$_{10}^{23}$, -(C$_1$-4 alkylene)$_p$carbocyclyl optionally substituted with 1-12 R$_{12}^{22}$, -(C$_2$-4 alkylene)$_p$carbocyclyl optionally substituted with 1-12 R$_{12}^{22}$, -(C$_1$-4 alkylene)$_p$aryl optionally substituted with 1-5 R$_{15}^{21}$, -(C$_2$-4 alkylene)$_p$aryl optionally substituted with 1-5 R$_{15}^{21}$, -(C$_6$-alkylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$, -(C$_2$$\gamma$-alkenylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$, and -(C$_2$$\gamma$-alkynylene)$_p$NR$_{10}^{25}$R$_{26}^{25}$;

each $R_{25}^6$ is independently selected from the group consisting of H, -(C$_6$-alkyl), -(C$_2$$\gamma$-alkenyl), and -(C$_2$-6 alkynyl);
each R\textsuperscript{26} is independently selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), and -(C\textsubscript{2-6} alkylnyl);

R\textsuperscript{27} is selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), -(C1-4 alkylene)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{33}, -(C2-4 alkenylene)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{33}, -(Ci-6 alkylene)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, -(C2-6 alkenylene)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, and -(C\textsubscript{2-6} alkylnylene)\textsubscript{p}NR\textsuperscript{25}R\textsuperscript{26}; and each p is independently an integer of 0 or 1.

[009] Some embodiments include stereoisomers and pharmaceutically acceptable salts of a compound of Formula (I).

[010] Some embodiments include pro-drugs of a compound of Formula (I).

[011] Some embodiments of the present disclosure include pharmaceutical compositions comprising a compound of Formula (I) and a pharmaceutically acceptable carrier, diluent, or excipient.

[012] Other embodiments disclosed herein include methods of inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins by administering to a patient affected by a disorder or disease in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, cell cycling and mutations in Wnt signaling components, a compound according to Formula (I). Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation and correct a genetic disorder due to mutations in Wnt signaling components.

[013] Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, osteochondrodysplasia, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, osteoporosis - pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Mullerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X
syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Nome disease, and Rett syndrome.

[014] Some embodiments of the present disclosure include methods to prepare compounds of Formula (I).

[015] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the disclosure, as claimed.

DETAILED DESCRIPTION

[016] Provided herein are compositions and methods for inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins. Other Wnt inhibitors and methods for using the same are disclosed in U.S. Application Ser. Nos. 12/852,706; 12/968,505; 13/552,188; 13/800,963; 13/855,874; 13/887,177 13/938,691; 13/938,692; 14/019,103; 14/019,147; 14/019,940; 14/149,948; 14/178,749; 14/331,427; 14/334,005; and 14/664,571 and U.S. Provisional Application Ser. Nos. 61/232,603; 61/288,544; 61/305,459; 61/620,107; 61/642,915; 61/750,221; 61/968,350; 62/047,324; 62/047,371; 62/047,395; 62/047,401; 62/047,406; 62/047,438; 62/047,509; 62/047,575; 62/047,567, all of which are incorporated by reference in their entirety herein.

[017] Some embodiments provided herein relate to a method for treating a disease or disorder including, but not limited to, cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, osteoarthritis, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG), familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Mullerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alphathalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

[018] In some embodiments, non-limiting examples of bone and cartilage diseases which can be treated with the compounds and compositions provided herein include bone spur
(osteophytes), craniosynostosis, fibrodysplasia ossificans progressiva, fibrous dysplasia, giant cell tumor of bone, hip labral tear, meniscal tears, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), osteochondritis dissecans, osteochondroma (bone tumor), osteopetrosis, relapsing polychondritis, and Salter-Harris fractures.

[019] In some embodiments, pharmaceutical compositions are provided that are effective for treatment of a disease of an animal, e.g., a mammal, caused by the pathological activation or mutations of the Wnt pathway. The composition includes a pharmaceutically acceptable carrier and a compound as described herein.

Definitions

[020] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this disclosure belongs. All patents, applications, published applications, and other publications are incorporated by reference in their entirety. In the event that there is a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

[021] As used herein, "alkyl" means a branched, or straight chain chemical group containing only carbon and hydrogen, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl and neo-pentyl. Alkyl groups can either be unsubstituted or substituted with one or more substituents. In some embodiments, alkyl groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

[022] As used herein, "alkenyl" means a straight or branched chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon double bond, such as ethenyl, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like. In various embodiments, alkenyl groups can either be unsubstituted or substituted with one or more substituents. Typically, alkenyl groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[023] "Exocyclic double bond" means a carbon-carbon double bond connected to and hence external to, a ring structure.

[024] As used herein, "alkynyl" means a straight or branched chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon triple bond, such as ethynyl, 1-propynyl, 1-butynyl, 2-butynyl, and the like. In various embodiments, alkynyl groups can either be unsubstituted or substituted with one or more substituents. Typically, alkynyl
groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[025] As used herein, "alkylene" means a bivalent branched, or straight chain chemical group containing only carbon and hydrogen, such as methylene, ethylene, n-propylene, iso-propylene, n-butylene, iso-butylene, sec-butylene, tert-butylene, n-pentylene, iso-pentylene, sec-pentylene and neo-pentylene. Alkylene groups can either be unsubstituted or substituted with one or more substituents. Alkylene groups can be saturated or unsaturated (e.g., containing -C=C- or -C=C- subunits), at one or several positions. In some embodiments, alkylene groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

[026] As used herein, "alkenylene" means a bivalent branched, or straight chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon double bond, such as ethylene, 1-propenylene, 2-propenylene, 2-methyl-1-propenylene, 1-butene, 2-butene, and the like. In various embodiments, alkenylene groups can either be unsubstituted or substituted with one or more substituents. Typically, alkenylene groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[027] As used herein, "alkynylene" means a bivalent branched, or straight chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon triple bond, such as ethynylene, 1-propynylene, 1-butynylene, 2-butynylene, and the like. In various embodiments, alkynylene groups can either be unsubstituted or substituted with one or more substituents. Typically, alkynylene groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[028] As used herein, "carbocyclyl" means a cyclic ring system containing only carbon atoms in the ring system backbone, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cyclohexenyl. Carbocyclyls may include multiple fused rings. Carbocyclyls may have any degree of saturation provided that at least one ring in the ring system is not aromatic. Carbocyclyl groups can either be unsubstituted or substituted with one or more substituents. In some embodiments, carbocyclyl groups include 3 to 10 carbon atoms, for example, 3 to 6 carbon atoms.

[029] As used herein, "aryl" means a mono-, bi-, tri- or polycyclic group with only carbon atoms present in the ring backbone having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic. Aryl groups can either be unsubstituted or substituted with one or more
substituents. Examples of aryl include phenyl, naphthyl, tetrahydronaphthyl, 2,3-dihydro-lH-indenyl, and others. In some embodiments, the aryl is phenyl.

[030] As used herein, "aryllkylene" means an aryl-alkylene- group in which the aryl and alkylene moieties are as previously described. In some embodiments, aryllkylene groups contain a Ci-4alkylene moiety. Exemplary aryllkylene groups include benzyl and 2-phenethyl.

[031] As used herein, the term "heteroaryl" means a mono-, bi-, tri- or polycyclic group having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic, and at least one ring in the system contains one or more heteroatoms independently selected from the group consisting of N, O, and S. Heteroaryl groups can either be unsubstituted or substituted with one or more substituents. Examples of heteroaryl include thienyl, pyridinyl, furyl, oxazolyl, oxadiazolyl, pyrrolyl, imidazolyl, triazolyl, thiodiazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrranyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thiazolyl benzothienyl, benzo[diazolyl, benzofuranyl, benzimidazolyl, benzotriazolyl, cinnolinyl, indazolyl, indolyl, isoquinolinyl, isothiazolyl, naphthyridinyl, purinyl, thienopyridinyl, pyrido[2,3-<f]pyrimidinyl, pyrrolo[2,3-6]pyridinyl, quinazolinyl, quinolinyl, thieno[2,3-c]pyridinyl, pyrazolo[3,4-6]pyridinyl, pyrazolo[3,4-c]pyridinyl, pyrazolo[4,3-c]pyridine, pyrazolo[4,3-6]pyridinyl, tetrazolyl, chromane, 2,3-dihydrobenzo[b][1,4]dioxine, benzo[d][1,3]dioxole, 2,3-dihydrobenzofuran, tetrahydroquinoline, 2,3-dihydrobenzo[6][1,4]oxathine, and others. In some embodiments, the heteroaryl is selected from thiienyl, pyridinyl, furyl, pyrazolyl, imidazolyl, pyranyl, pyrazinyl, and pyrimidinyl.

[032] As used herein, "halo", "halide" or "halogen" is a chloro, bromo, fluoro, or iodo atom radical. In some embodiments, a halo is a chloro, bromo or fluoro. For example, a halide can be fluoro.

[033] As used herein, "haloalkyl" means a hydrocarbon substituent, which is a linear or branched, alkyl, alkenyl or alkynyl substituted with one or more chloro, bromo, fluoro, and/or iodo atom(s). In some embodiments, a haloalkyl is a fluoroalkyls, wherein one or more of the hydrogen atoms have been substituted by fluoro. In some embodiments, haloalkyls are of 1 to about 3 carbons in length (e.g., 1 to about 2 carbons in length or 1 carbon in length). The term "haloalkylene" means a diradical variant of haloalkyl, and such diradicals may act as spacers between radicals, other atoms, or between a ring and another functional group.

[034] As used herein, "heterocycl" means a nonaromatic cyclic ring system comprising at least one heteroatom in the ring system backbone. Heterocycls may include
multiple fused rings. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of heterocyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydrofuryl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others. In some embodiments, the heterocyclyl is selected from azetidinyl, morpholinyl, piperazinyl, pyrrolidinyl, and tetrahydropyridinyl.

[035] As used herein, "monocyclic heterocyclyl" means a single nonaromatic cyclic ring comprising at least one heteroatom in the ring system backbone. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of heterocyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydrofuryl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others.

[036] The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more non-hydrogen atoms of the molecule. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. Substituents can include, for example, -(C1-9 alkyl) optionally substituted with one or more of hydroxyl, -Nth, -NH(C1-3 alkyl), and -N(C1-3 alkyl)2; -C1-9 haloalkyl; a halide; a hydroxyl; a carboxyl [such as -C(O)OR, and -C(0)R]; a thiocarbonyl [such as -C(S)OR, -C(0)SR, and -C(S)R]; -C1-9 alkoyloxy] optionally substituted with one or more of halide, hydroxyl, -Nth, -NH(C1-3 alkyl), and -N(C1-3 alkyl)2; -OPO(OH)2; a phosphonate [such as -PO(OH)2 and -PO(OR)2]; -OPO(OR)2; -NRR'; -C(0)NRR'; -C(NR)NR'R'; a cyano; a nitro; an azido; -SH; -S-R; -OS02(OR); a
sulfonate [such as -SO₂(OH) and -SO₂(OR)]; -SCHR'R''; and -SO₂R; in which each occurrence of R, R' and R'' are independently selected from H; -(C₁₋₅ alkyl); C₆₋₁₀ aryl optionally substituted with from 1-3R'''; 5-10 membered heteroaryl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'''; and 3-8 membered heterocyclcyl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'''; wherein each R''' is independently selected from -(C₁₋₅ alkyl), -(C₁₋₅ haloalkyl), a halide (e.g., F), a hydroxyl, -C(0)OR, -C(0)R, -(C₁₋₅ alkoxyl), -NRR', -C(0)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and -(C₁₋₅ alkyl). In some embodiments, the substituent is selected from -(C₁₋₅ alkyl), -(C₁₋₅ haloalkyl), a halide (e.g., F), a hydroxyl, -C(0)OR, -C(0)R, -(C₁₋₅ alkoxyl), -NRR', -C(0)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and -(C₁₋₅ alkyl).

[037] As used herein, when two groups are indicated to be "linked" or "bonded" to form a "ring", it is to be understood that a bond is formed between the two groups and may involve replacement of a hydrogen atom on one or both groups with the bond, thereby forming a carbocyclyl, heterocyclyl, aryl, or heteroaryl ring. The skilled artisan will recognize that such rings can and are readily formed by routine chemical reactions. In some embodiments, such rings have from 3-7 members, for example, 5 or 6 members.

[038] The skilled artisan will recognize that some structures described herein may be resonance forms or tautomers of compounds that may be fairly represented by other chemical structures, even when kinetically, the artisan recognizes that such structures are only a very small portion of a sample of such compound(s). Such compounds are clearly contemplated within the scope of this disclosure, though such resonance forms or tautomers are not represented herein.

[039] The compounds provided herein may encompass various stereochemical forms. The compounds also encompass diastereomers as well as optical isomers, e.g., mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art. Unless otherwise indicated, when a disclosed compound is named or depicted by a structure without specifying the stereochemistry and has one or more chiral centers, it is understood to represent all possible stereoisomers of the compound.

[040] The term "administration" or "administering" refers to a method of providing a dosage of a compound or pharmaceutical composition to a vertebrate or invertebrate, including
a mammal, a bird, a fish, or an amphibian, where the method is, e.g., orally, subcutaneously, intravenously, intralymphatic, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonaryrily, vaginally, rectally, ontologically, neuro-otologically, intraocularly, subconjunctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intra-abdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracistermally, intravascularly, intraventricularly, intrariosously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic device. The method of administration can vary depending on various factors, e.g., the components of the pharmaceutical composition, the site of the disease, the disease involved, and the severity of the disease.

[041] A "diagnostic" as used herein is a compound, method, system, or device that assists in the identification or characterization of a health or disease state. The diagnostic can be used in standard assays as is known in the art.

[042] The term "mammal" is used in its usual biological sense. Thus, it specifically includes humans, cattle, horses, monkeys, dogs, cats, mice, rats, cows, sheep, pigs, goats, and non-human primates, but also includes many other species.

[043] The term "pharmaceutically acceptable carrier", "pharmaceutically acceptable diluent" or "pharmaceutically acceptable excipient" includes any and all solvents, cosolvents, complexing agents, dispersion media, coatings, isotonic and absorption delaying agents and the like which are not biologically or otherwise undesirable. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. In addition, various adjuvants such as are commonly used in the art may be included. These and other such compounds are described in the literature, e.g., in the Merck Index, Merck & Company, Rahway, NJ. Considerations for the inclusion of various components in pharmaceutical compositions are described, e.g., in Gilman et al. (Eds.) (2010); Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 12th Ed., The McGraw-Hill Companies.

[044] The term "pharmaceutically acceptable salt" refers to salts that retain the biological effectiveness and properties of the compounds provided herein and, which are not biologically or otherwise undesirable. In many cases, the compounds provided herein are capable
of forming acid and/or base salts by virtue of the presence of amino and/or carboxyl groups or groups similar thereto. Many such salts are known in the art, for example, as described in WO 87/05297. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases. Inorganic bases from which salts can be derived include, for example, sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum, and the like; particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like, specifically such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

[045] "Solvate" refers to the compound formed by the interaction of a solvent and a compound as provided herein or a salt thereof. Suitable solvates are pharmaceutically acceptable solvates including hydrates.

[046] "Patient" as used herein, means a human or a non-human mammal, e.g., a dog, a cat, a mouse, a rat, a cow, a sheep, a pig, a goat, a non-human primate, or a bird, e.g., a chicken, as well as any other vertebrate or invertebrate. In some embodiments, the patient is a human.

[047] A "therapeutically effective amount" of a compound as provided herein is one which is sufficient to achieve the desired physiological effect and may vary according to the nature and severity of the disease condition, and the potency of the compound. "Therapeutically effective amount" is also intended to include one or more of the compounds of Formula I in combination with one or more other agents that are effective to treat the diseases and/or conditions described herein. The combination of compounds can be a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Advances in Enzyme Regulation* (1984), 22, 27-55, occurs when the effect of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the
compounds. It will be appreciated that different concentrations may be employed for prophylaxis than for treatment of an active disease. This amount can further depend upon the patient's height, weight, sex, age and medical history.

[048] A therapeutic effect relieves, to some extent, one or more of the symptoms of the disease.

[049] "Treat," "treatment," or "treating," as used herein refers to administering a compound or pharmaceutical composition as provided herein for therapeutic purposes. The term "therapeutic treatment" refers to administering treatment to a patient already suffering from a disease thus causing a therapeutically beneficial effect, such as ameliorating existing symptoms, ameliorating the underlying metabolic causes of symptoms, postponing or preventing the further development of a disorder, and/or reducing the severity of symptoms that will or are expected to develop.

[050] "Drug-eluting" and/or controlled release as used herein refers to any and all mechanisms, e.g., diffusion, migration, permeation, and/or desorption by which the drug(s) incorporated in the drug-eluting material pass therefrom over time into the surrounding body tissue.

[051] "Drug-eluting material" and/or controlled release material as used herein refers to any natural, synthetic or semi-synthetic material capable of acquiring and retaining a desired shape or configuration and into which one or more drugs can be incorporated and from which incorporated drug(s) are capable of eluting over time.

[052] "Elutable drug" as used herein refers to any drug or combination of drugs having the ability to pass over time from the drug-eluting material in which it is incorporated into the surrounding areas of the body.

Compounds

[053] The compounds and compositions described herein can be used as anti-proliferative agents, e.g., anti-cancer and anti-angiogenesis agents, and/or as inhibitors of the Wnt signaling pathway, e.g., for treating diseases or disorders associated with aberrant Wnt signaling. In addition, the compounds can be used as inhibitors of one or more kinases, kinase receptors, or kinase complexes. Such compounds and compositions are also useful for controlling cellular proliferation, differentiation, and/or apoptosis.

[054] Some embodiments of the present disclosure include compounds of Formula I:
or salts, pharmaceutically acceptable salts, or prodrugs thereof.

[055] In some embodiments, $R^1$ and $R^2$ are independently selected from the group consisting of H and halide (e.g., F, Cl, Br, I).

[056] In some embodiments, $R^1$ is H, and $R^2$ is F.

[057] In some embodiments, $R^1$ is F, and $R^2$ is H.

[058] In some embodiments, $R^1$ and $R^2$ are both H.

[059] In some embodiments, $R^1$ and $R^2$ are both F.

[060] In some embodiments, $R^3$ is selected from the group consisting of $-\text{heteroaryl}$ optionally substituted with 1-4 (e.g., 1-3, 1-2, 1) $R^6$ and $-\text{heterocyclyl}$ optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R^7$.

[061] In some embodiments, $R^3$ is selected from the group consisting of $-\text{heteroaryl}$ optionally substituted with 1-2 (e.g., 1) $R^6$ and $-\text{heterocyclyl}$ optionally substituted with 1-2 (e.g., 1) $R^7$.

[062] In some embodiments, the heteroaryl of $R^3$ is selected from the group consisting of $-\text{pyridinyl}$, $-\text{pyrimidinyl}$, $-\text{pyrazolyl}$, $-\text{imidazolyl}$, $-\text{thiazolyl}$, and $-\text{oxazolyl}$.

[063] In some embodiments, the heteroaryl of $R^3$ is selected from the group consisting of $-\text{pyridin-3-yl}$, $-\text{pyrimidin-5-yl}$, $-\text{pyrazol-4-yl}$, $-\text{imidazol-5-yl}$, $-\text{thiazol-2-yl}$, $-\text{thiazol-5-yl}$, $-\text{oxazol-2-yl}$, and $-\text{oxazol-5-yl}$.

[064] In some embodiments, the $-\text{heterocyclyl}$ of $R^3$ is selected from the group consisting of $-\text{tetrahydropyridinyl}$ and $-\text{piperidinyl}$.

[065] In some embodiments, the $-\text{heterocyclyl}$ of $R^3$ is selected from the group consisting of $-\text{1,2,3,6-tetrahydropyridinyl}$ and $-\text{piperidin-4-yl}$.

[066] In some embodiments, $R^3$ is $-\text{pyridinyl}$ optionally substituted with 1 $R^6$.

[067] In some embodiments, $R^3$ is $-\text{pyridin-3-yl}$ optionally substituted with 1 $R^6$.

[068] In some embodiments, $R^3$ is $-\text{pyrimidinyl}$ optionally substituted with 1 $R^6$.

[069] In some embodiments, $R^3$ is $-\text{pyrimidin-5-yl}$ optionally substituted with 1 $R^6$. 

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In some embodiments, R^3 is -pyrazolyl optionally substituted with 1 R^6.

In some embodiments, R^3 is -pyrazolyl substituted with 1 R^6.

In some embodiments, R^3 is -pyrazolyl substituted with 1 methyl.

In some embodiments, R^3 is -pyrazolyl optionally substituted with 2 R^6.

In some embodiments, R^3 is -pyrazolyl substituted with 2 R^6.

In some embodiments, R^3 is -pyrazolyl substituted with 1 methyl and 1 - CH_2OH.

In some embodiments, R^3 is -pyrazol-4-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is -pyrazol-4-yl substituted with 1 R^6.

In some embodiments, R^3 is -pyrazol-4-yl substituted with 1 methyl.

In some embodiments, R^3 is -pyrazol-4-yl optionally substituted with 2 R^6.

In some embodiments, R^3 is -pyrazol-4-yl substituted with 2 R^6.

In some embodiments, R^3 is -pyrazol-4-yl substituted with 1 methyl and 1 - CH_2OH.

In some embodiments, R^3 is -imidazolyl optionally substituted with 1-2 R^6.

In some embodiments, R^3 is -imidazolyl substituted with 1-2 R^6.

In some embodiments, R^3 is -imidazolyl substituted with 1-2 methyls.

In some embodiments, R^3 is -imidazolyl substituted with 1 methyl.

In some embodiments, R^3 is -imidazolyl substituted with 2 methyls.

In some embodiments, R^3 is -imidazolyl substituted with 1 methyl and 1-2 R^6.

In some embodiments, R^3 is -imidazol-5-yl optionally substituted with 1-2 R^6.

In some embodiments, R^3 is -imidazol-5-yl substituted with 1-2 R^6.

In some embodiments, R^3 is -imidazol-5-yl substituted with 1 methyl.

In some embodiments, R^3 is -imidazol-5-yl substituted with 2 methyls.

In some embodiments, R^3 is -imidazol-5-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is -thiazolyl optionally substituted with 1 R^6.

In some embodiments, R^3 is -thiazol-2-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is -thiazol-2-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is thiazol-5-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is oxazolyl optionally substituted with 1 R^6.

In some embodiments, R^3 is oxazol-2-yl optionally substituted with 1 R^6.

In some embodiments, R^3 is oxazol-5-yl optionally substituted with 1 R^6.

In some embodiments, R^5 is selected from the group consisting of H, heteroaryl optionally substituted with 1-4 (e.g., 1-3, 1-2, 1) R^8, heterocyclyl optionally...
substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) \(R^9\), and -aryl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) \(R^{10}\).

[0099] In some embodiments, \(R^5\) is selected from the group consisting of H, -heteroaryl optionally substituted with 1-2 (e.g., 1) \(R^8\), -heterocyclyl optionally substituted with 1-2 (e.g., 1) \(R^9\), and -phenyl optionally substituted with 1-2 (e.g., 1) \(R^{10}\).

[0100] In some embodiments, \(R^5\) is H.

[0101] In some embodiments, \(R^5\) is -heteroaryl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0102] In some embodiments, \(R^5\) is -heterocyclyl optionally substituted with 1-2 (e.g., 1) \(R^9\).

[0103] In some embodiments, \(R^5\) is -piperidinyl optionally substituted with 1-2 (e.g., 1) \(R^9\).

[0104] In some embodiments, \(R^5\) is -piperazinyl optionally substituted with 1-2 (e.g., 1) \(R^9\).

[0105] In some embodiments, \(R^5\) is -aryl optionally substituted with 1-2 (e.g., 1) \(R^{10}\).

[0106] In some embodiments, \(R^5\) is -phenyl optionally substituted with 1-2 (e.g., 1) \(R^{10}\).

[0107] In some embodiments, \(R^5\) is -pyridinyl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0108] In some embodiments, \(R^5\) is -pyridin-3-yl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0109] In some embodiments, \(R^5\) is -pyridin-4-yl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0110] In some embodiments, \(R^5\) is -pyridin-5-yl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0111] In some embodiments, \(R^5\) is -imidazolyl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0112] In some embodiments, \(R^5\) is -imidazolyl substituted with 1-2 (e.g., 1) \(R^8\).

[0113] In some embodiments, \(R^5\) is -imidazolyl substituted with 1\(R^8\).

[0114] In some embodiments, \(R^5\) is -imidazolyl substituted with 1 methyl.

[0115] In some embodiments, \(R^5\) is -imidazol-l-yl optionally substituted with 1-2 (e.g., 1) \(R^8\).

[0116] In some embodiments, \(R^5\) is -imidazol-l-yl substituted with 1-2 (e.g., 1) \(R^8\).
In some embodiments, R<sub>5</sub> is -imidazol-1-yl substituted with 1 R<sub>8</sub>.

In some embodiments, R<sub>5</sub> is -imidazol-1-yl substituted with 1 methyl.

In some embodiments, R<sub>5</sub> is -furanyl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>.

In some embodiments, R<sub>5</sub> is -furan-2-yl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>.

In some embodiments, R<sub>5</sub> is -furan-3-yl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>.

In some embodiments, R<sub>5</sub> is -thiophenyl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>, and each R<sub>8</sub> is independently halide.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) F.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) Cl.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>, and each R<sub>8</sub> is independently -(C<sub>1</sub>-alkyl).

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) R<sub>8</sub>, and each R<sub>8</sub> is independently -(C<sub>2</sub>-alkyl).

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) methyls.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) -CF<sub>3</sub>.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-2 (e.g., 1) -CN.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-C(=0)R<sub>19</sub>.

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-C(=0)R<sub>19</sub>, and R<sub>19</sub> is -(C<sub>1</sub>-alkyl).

In some embodiments, R<sub>5</sub> is -thiophen-2-yl optionally substituted with 1-C(=0)R<sub>19</sub>, and R<sub>19</sub> is -(C<sub>4</sub>-alkyl).
In some embodiments, R^5 is thiophen-2-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is -(C_i-2 alkyl).

In some embodiments, R^5 is thiophen-2-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is methyl.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) R^8.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) R^8 and each R^8 is independently halide.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) F.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) Cl.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) R^8, and each R^8 is independently -(C_i-3 alkyl).

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) R^8, and each R^8 is independently -(C_i-2 alkyl).

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) methyls.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) -CF_3.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-2 (e.g., 1) -CN.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-C(=0)R^{19}.

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is -(C_i-2 alkyl).

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is -(C_i-4 alkyl).

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is -(C_i-2 alkyl).

In some embodiments, R^5 is thiophen-3-yl optionally substituted with 1-C(=0)R^{19}, and R^{19} is methyl.

In some embodiments, R^5 is selected from the group consisting of:
In some embodiments, R⁵ is -phenyl optionally substituted with 1-2 (e.g., 1) R¹⁰, and each R¹⁰ is independently halide.

In some embodiments, R⁵ is -phenyl optionally substituted with 1-2 (e.g., 1) F.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -(CM alkylene)NHSO₂R¹⁹.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -(CM alkylene)NHSO₂R¹⁹.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -(Ci₂ alkylene)NHSO₂R¹⁹.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -CH₂NHSO₂R¹⁹.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -CH₂NHSO₂R¹⁹, R¹⁹ is -(CM alkyl).

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -CH₂NHSO₂R¹⁹, R¹⁹ is -(Ci₂ alkyl).

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -CH₂NHSO₂R¹⁹, R¹⁹ is methyl.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is F and the other R¹⁰ is -CH₂NHSO₂R¹⁹, R¹⁹ is -(Ci₂ alkyl).

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is F and the other R¹⁰ is -CH₂NHSO₂R¹⁹, R¹⁹ is methyl.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -NR₁⁵(Ci⁶ alkylene)NR₁⁵R¹⁶.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -NR₁⁵(Ci⁷ alkylene)NR₁⁵R¹⁶.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R¹⁰, one R¹⁰ is halide and the other R¹⁰ is -NR₁⁵(Ci⁸ alkylene)NR₁⁵R¹⁶.
[0166] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NR^15(Ci-alkylene)NR^15R^16.

[0167] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NR^15CH_2CH_2NR^15R^16.

[0168] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NHCH_2CH_2NR^15R^16.

[0169] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NHCH_2CH_2NR^15R^16, and R^15 and R^16 are independently selected from -(Ci-alkyl).

[0170] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NHCH_2CH_2NR^15R^16, and R^15 and R^16 are independently selected from - (Ci-1-alkyl).

[0171] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NHCH_2CH_2NR^15R^16, and R^15 and R^16 are independently selected from - (Ci-2alkyl).

[0172] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -NHCH_2CH_2NR^15R^16, and both R^15 and R^16 are methyls.

[0173] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is F and the other R^10 is -NHCH_2CH_2NR^15R^16, and R^15 and R^16 are independently selected from - (Ci-2alkyl).

[0174] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is F and the other R^10 is -NHCH_2CH_2NR^15R^16, and both R^15 and R^16 are methyls.

[0175] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -OR^27.

[0176] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -OCH_2CH_2NR^25R^26.

[0177] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -OCH_2CH_2NR^25R^26, and R^25 and R^26 are independently -(Ci-2alkyl).

[0178] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is halide and the other R^10 is -OCH_2CH_2NR^25R^26, and R^25 and R^26 are both methyl.

[0179] In some embodiments, R^5 is -phenyl optionally substituted with 2 R^10, one R^10 is F and the other R^10 is -OCH_2CH_2NR^25R^26, and R^25 and R^26 are both methyl.
In some embodiments, R⁵ is -phenyl optionally substituted with 2 R₁⁰, one R₁⁰ is halide and the other R₁⁰ is -OC₄H₄heterocyclyl optionally substituted with 1-2 (e.g., 1) R²³.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R₁⁰, one R₁⁰ is F and the other R₁⁰ is -OCH₂CH₂heterocyclyl optionally substituted with 1-2 (e.g., 1) R²³.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R₁⁰, one R₁⁰ is halide and the other R₁⁰ is -OH.

In some embodiments, R⁵ is -phenyl optionally substituted with 2 R₁⁰, one R₁⁰ is halide and the other R₁⁰ is -OMe.

In some embodiments, R⁵ is selected from the group consisting of:

- piperidin-1-yl optionally substituted with 1-2 (e.g., 1) R⁹.
- piperidin-1-yl optionally substituted with 1-2 (e.g., 1) R⁹, and each R⁹ is independently halide.
- piperazin-1-yl optionally substituted with 1-2 (e.g., 1) R⁹.
- piperazin-1-yl optionally substituted with 1CI₃ alkyl.
- piperazin-1-yl optionally substituted with 1 methyl.
- morpholinyl optionally substituted with 1-2 (e.g., 1) R⁹.

And:

- and
In some embodiments, R^5 is morpholin-1-yl optionally substituted with 1-2 (e.g., 1) R^9.

In some embodiments, R^5 is selected from the group consisting of:

![Diagram](image)

and...

In some embodiments, each R^6 is independently selected from the group consisting of halide, -(Cⁱ alkyl), -(C₂ᵦ alknyl), -(C₂₋₄ alkenylenyl), -(Cⁱ₋₄ alkylene), pherocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₂₋₄ alkenylenyl), pherocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₂₋₄ alkynylene), pherocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₁₋₄ alkynylene), carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁², -(CM alkylene), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkylene), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₁₋₄ alkylene), carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₂₋₄ alkenylenyl), carbocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₁₋₄ alkenylenyl), carbocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₁₋₄ alkenylenyl), carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(C₁₋₄ alkenylenyl), carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R₁¹, -(CM alkylene), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenylenyl), arenyl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R₁³, -(C₂₋₄ alkenyleny
NR^15R^16, -(C_1-6 alkylene)NR^17R^18, -(C_2-6 alkenylene)NR^17R^18, -(C_2-6 alkynylene)NR^17R^18, and -(C_1-4 alkylene) p OR^{24}.

[0196] In some embodiments, each R^6 is independently selected from the group consisting of F, Cl, -(C1-3 alkyl), -heterocyclyl optionally substituted with 1-2 (e.g., 1) R^11, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) R^{11}, -carbocycyl optionally substituted with 1-2 (e.g., 1) R^{12}, -CH2carbocycyl optionally substituted with 1-2 (e.g., 1) R^{12}, -aryl optionally substituted with 1-2 (e.g., 1) R^{12}, -CH2aryl optionally substituted with 1-2 (e.g., 1) R^{12}, -NHC (=0)R^{14}, -NR^15R^16, -CH_2NR^17R^18, and -OR^{24}.

[0197] In some embodiments, each R^6 is independently selected from the group consisting of F, Cl, -(C1-3 alkyl), -heterocyclyl optionally substituted with 1-2 (e.g., 1) R^11, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) R^{11}, -carbocycyl optionally substituted with 1-2 (e.g., 1) R^{12}, -CFhheterocyclyl optionally substituted with 1-2 (e.g., 1) R^{12}, -aryl optionally substituted with 1-2 (e.g., 1) R^{12}, -CH2aryl optionally substituted with 1-2 (e.g., 1) R^{12}, -NHC (=0)R^{14}, -NR^15R^16, -CH_2NR^17R^18, -CH_2OR^{24}, and -OR^{24}.

[0198] In some embodiments, each R^6 is independently selected from the group consisting of F, -Me, -heterocyclyl optionally substituted with 1-2 (e.g., 1) halides, -heterocyclyl optionally substituted with 1-2 (e.g., 1) methyls, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -CFhheterocyclyl optionally substituted with with 1-2 (e.g., 1) halides, -aryl optionally substituted with 1-2 (e.g., 1) halides, -aryl optionally substituted with 1-2 (e.g., 1) halides, -aryl optionally substituted with 1-2 (e.g., 1) halides, -aryl optionally substituted with 1-2 (e.g., 1) halides, -NHC (=0)R^{14}, -Nf, -NHMe, -NHEt, -NHP, -NMe_2, -CH_2NMe_2, -CFhNHMe, -CFhNHMe, -CFhNHMe, -CFhNHMe, -CFhNHCFhphenyl, -CFhNHCFhcarbocyclyl, -CFhOH, and -OR^{24}.

[0199] In some embodiments, R^6 is selected from the group consisting of -(C1-3 alkyl), -CFhheterocyclyl optionally substituted with 1-2 R^{11}, -NHC (=0)R^{14}, -NR^15R^16, -CH_2NR^17R^18, -CFhOH, and -OR^{24}.

[0200] In some embodiments, at least one R^6 is -(C1-3 alkyl).

[0201] In some embodiments, at least one R^6 is -(C2-alkyl).

[0202] In some embodiments, at least one R^6 is -Me.

[0203] In some embodiments, at least one R^6 is halide.

[0204] In some embodiments, at least one R^6 is F.

[0205] In some embodiments, at least one R^6 is -(C1-4 alkylene)heterocyclyl optionally substituted with 1-2 R^{11}. 

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In some embodiments, at least one $R^6$ is -(C1-3 alkylene)heterocyclyl optionally substituted with 1-2 $R^{11}$.

In some embodiments, at least one $R^6$ is -(C1-2 alkylene)heterocyclyl optionally substituted with 1-2 $R^{11}$.

In some embodiments, at least one $R^6$ is -CF$_3$pyrrolidinyl optionally substituted with 1-2 $R^{11}$.

In some embodiments, $R^6$ is -CF$_3$pyrrolidinyl optionally substituted with 1-2 $R^{11}$, and each $R^{11}$ is independently halide.

In some embodiments, $R^6$ is -CF$_3$pyrrolidinyl optionally substituted with 1-2 F.

In some embodiments, $R^6$ is -CH$_2$pyrrolidinyl substituted with 1-2 F.

In some embodiments, $R^6$ is -CH$_2$pyrrolidinyl substituted with 2 F.

In some embodiments, at least one $R^6$ is -CF$_3$piperidinyl optionally substituted with 1-2 $R^{11}$.

In some embodiments, $R^6$ is -CF$_3$piperidinyl optionally substituted with 1-2 $R^{11}$, and each $R^{11}$ is independently halide.

In some embodiments, $R^6$ is -CH$_2$piperidinyl optionally substituted with 1-2 $R^{11}$, and each $R^{11}$ is independently halide.

In some embodiments, $R^6$ is -CH$_2$piperidinyl optionally substituted with 1-2 F.

In some embodiments, $R^6$ is -(C1-4 alkylene)carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{12}$.

In some embodiments, at least one $R^6$ is -(C1-3 alkylene)carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{12}$.

In some embodiments, at least one $R^6$ is -(C1-2 alkylene)carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{12}$.

In some embodiments, at least one $R^6$ is -CH$_2$carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{12}$.
In some embodiments, R^6 is -Cttcarbocyclyl optionally substituted with 1-2 alkyl.

In some embodiments, at least one R^6 is -Cttaryl optionally substituted with 1-2 alkyl.

In some embodiments, at least one R^6 is -Cttphenyl optionally substituted with 1-2 alkyl.

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(C2-5 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-9 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C8 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-7 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-6 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-5 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(C1-5 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-4 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(CM alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-3 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(C1-3 alkyl).

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C1-2 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(C1-2 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -CF_3.

In some embodiments, at least one R^6 is -NHC(=0)R^14 and R^14 is -(C2-5 alkyl).

In some embodiments, R^6 is -NHC(=0)R^14 and R^14 is -(C2-5 alkyl).
In some embodiments, at least one R6 is -NHC(=0)R14 and R14 is -(C3-4 alkyl).

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -aryl optionally substituted with 1-2 (e.g., 1) R21.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -phenyl optionally substituted with 1-2 (e.g., 1) R21.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -CH2aryl optionally substituted with 1-2 (e.g., 1) R21.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -CH2phenyl optionally substituted with 1-2 (e.g., 1) R21.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -heteroaryl optionally substituted with 1-2 (e.g., 1) R20.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -carbocyclyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -cyclopropyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -cyclobutyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -cyclopentyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -cyclohexyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -Cf2carbocyclyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NHC(=0)R14, R14 is -Ct2cyclopropyl optionally substituted with 1-2 (e.g., 1) R22.

In some embodiments, at least one R6 is -NR15R16.

In some embodiments, at least one R6 is -NR15R16, and R15 and R16 are independently selected from the group consisting of H and -(C3-4 alkyl).

In some embodiments, at least one R6 is -NR15R16, and R15 and R16 are independently selected from the group consisting of H and -(C4-5 alkyl).

In some embodiments, at least one R6 is -NR15R16, and R15 and R16 are independently selected from the group consisting of H and -(C1-4 alkyl).
In some embodiments, at least one $R^6$ is $-NR^5R_{16}$, and $R^{15}$ and $R^{16}$ are independently selected from the group consisting of H and -(C1-4 alkyl).

In some embodiments, at least one $R^6$ is $-NR^5R_{16}$, and $R^{15}$ and $R^{16}$ are independently selected from the group consisting of H and -(C1-2 alkyl).

In some embodiments, at least one $R^6$ is $-HR^5R_{16}$, and $R^{15}$ and $R^{16}$ are independently selected from the group consisting of H and methyl.

In some embodiments, at least one $R^6$ is $-NH2$.

In some embodiments, $R^6$ is $-NH2$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-(\text{CM} \text{alkyl})$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-(\text{C}1_{3} \text{alkyl})$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-(\text{C}1_{2} \text{alkyl})$.

In some embodiments, $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-(\text{CM} \text{alkyl})$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CH}_2\text{aryl}$ optionally substituted with 1-2 (e.g., 1) $R^{21}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CH}_2\text{phenyl}$ optionally substituted with 1-2 (e.g., 1) $R^{21}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CH}_2\text{carbocyclyl}$ optionally substituted with 1-2 (e.g., 1) $R^{22}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CTetcyclopropyl}$ optionally substituted with 1-2 (e.g., 1) $R^{22}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CH}_2\text{cyclobutyl}$ optionally substituted with 1-2 (e.g., 1) $R^{22}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CH}_2\text{Cyclopentyl}$ optionally substituted with 1-2 (e.g., 1) $R^{22}$.

In some embodiments, at least one $R^6$ is $-NHR^{16}$ and $R^{16}$ is $-\text{CTetcyclohexyl}$ optionally substituted with 1-2 (e.g., 1) $R^{22}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, at least one $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.

In some embodiments, $R^6$ is $-\text{alkylene}NR^{17}R^{18}$.
In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and methyl.

In some embodiments, $R_6$ is -CH$_2$NHR$_{17}$R$_{18}$, and R$_{17}$ and R$_{18}$ are independently selected from the group consisting of H and methyl.

In some embodiments, at least one $R_6$ is -CH$_2$NH$_2$.

In some embodiments, $R_6$ is -CH$_2$NH$_2$.

In some embodiments, at least one $R_6$ is -CH$_2$NMe$_2$.

In some embodiments, $R_6$ is -CH$_2$NMe$_2$.

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -(C1-$n$ alkyl).

In some embodiments, R$_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -(C1-$n$ alkyl).

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$aryl optionally substituted with 1-2 (e.g., 1) $R_{21}$.

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$phenyl optionally substituted with 1-2 (e.g., 1) $R_{21}$.

In some embodiments, $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$phenyl optionally substituted with 1-2 (e.g., 1) $R_{21}$.

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$carbocycle optionally substituted with 1-2 (e.g., 1) $R_{22}$.

In some embodiments, at least one $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$cyclopropyl optionally substituted with 1-2 (e.g., 1) $R_{22}$.

In some embodiments, $R_6$ is -CH$_2$NHR$_{18}$ and R$_{18}$ is -CH$_2$cyclopropyl optionally substituted with 1-2 (e.g., 1) $R_{22}$.
[0305] In some embodiments, at least one $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclobutyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0306] In some embodiments, $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclobutyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0307] In some embodiments, at least one $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclopentyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0308] In some embodiments, $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclopentyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0309] In some embodiments, at least one $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclohexyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0310] In some embodiments, $R^6$ is -CH$_2$NHR$^{18}$ and $R^{18}$ is -CH$_2$cyclohexyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0311] In some embodiments, at least one $R^6$ is -OR$^{24}$.

[0312] In some embodiments, at least one $R^6$ is -OH.

[0313] In some embodiments, $R^6$ is -OH.

[0314] In some embodiments, at least one $R^6$ is -(C1-alkylene)OR$^{24}$.

[0315] In some embodiments, $R^6$ is -(C1-alkylene)OR$^{24}$.

[0316] In some embodiments, $R^6$ is -(C1-3 alkylene)OR$^{24}$.

[0317] In some embodiments, $R^6$ is -(C1-alkylene)OR$^{24}$.

[0318] In some embodiments, $R^6$ is -CH$_2$OR$^{24}$.

[0319] In some embodiments, $R^6$ is -CH$_2$OH.

[0320] In some embodiments, at least one $R^6$ is -OR$^{24}$ and $R^{24}$ is -(C1-3 alkyl).

[0321] In some embodiments, at least one $R^6$ is -OR$^{24}$ and $R^{24}$ is -(C1-2 alkyl).

[0322] In some embodiments, at least one $R^6$ is -OMe.

[0323] In some embodiments, $R^6$ is -OMe.

[0324] In some embodiments, at least one $R^6$ is -OR$^{24}$ and $R^{24}$ is -heterocyclyl optionally substituted with 1-2 (e.g., 1) $R^{23}$.

[0325] In some embodiments, $R^6$ is -OR$^{24}$ and $R^{24}$ is -heterocyclyl optionally substituted with 1-2 (e.g., 1) $R^{23}$.

[0326] In some embodiments, at least one $R^6$ is -OR$^{24}$ and $R^{24}$ is -carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.

[0327] In some embodiments, $R^6$ is -OR$^{24}$ and $R^{24}$ is -carbocyclyl optionally substituted with 1-2 (e.g., 1) $R^{22}$.
In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \(-(\text{CM alkylene})\text{heterocyclyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{23} \).

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \(-(\text{CH2CH2})\text{heterocyclyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{23} \).

In some embodiments, \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \(-(\text{CH}_2\text{CH}_2)\text{heterocyclyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{23} \).

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \(-(\text{CM alkylene})\text{NR}^{25}\text{R}^{26} \) and \( R^{25} \) and \( R^{26} \) are independently \(-\text{(C}_4\text{-alkyl)} \).

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2\text{CH}_2)\text{NR}^{25}\text{R}^{26} \) and \( R^{25} \) and \( R^{26} \) are independently \-(\text{C}1-2\text{-alkyl}) \).

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2\text{CH}_2)\text{NMe}_2 \).

In some embodiments, \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2\text{CH}_2)\text{NMe} \).

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{C}1\text{-alkenyl}) \) optionally substituted with 1-2 (e.g., 1) \( R^{21} \), and each \( R^{21} \) is independently halide.

In some embodiments, at least one \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2\text{CH}_2)\text{phenyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{21} \), and each \( R^{21} \) is independently halide.

In some embodiments, \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2\text{CH}_2)\text{phenyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{21} \), and each \( R^{21} \) is independently halide.

In some embodiments, \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2)\text{phenyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{21} \), and each \( R^{21} \) is independently halide.

In some embodiments, \( R^6 \) is \(-\text{OR}^{24} \) and \( R^{24} \) is \-(\text{CH}_2)\text{phenyl} \) optionally substituted with 1-2 (e.g., 1) \( R^{21} \), and each \( R^{21} \) is independently halide.

In some embodiments, each \( R^7 \) is independently selected from the group consisting of \-(\text{C}1-4\text{-alkyl}), -(\text{C}2-4\text{-alkenyl}), -(\text{C}2-4\text{-alkynyl}), \text{halide}, -\text{CF3}, \) and -\text{CN}.

In some embodiments, each \( R^7 \) is independently selected from the group consisting of methyl, \( F, \text{Cl}, -\text{CF3}, \) and -\text{CN}.

In some embodiments, at least one \( R^7 \) is \-(\text{CM alkyl}) \).

In some embodiments, at least one \( R^7 \) is \-(\text{CM alkyl}) \).

In some embodiments, at least one \( R^7 \) is \-(\text{CM alkyl}) \).

In some embodiments, at least one \( R^7 \) is methyl.

In some embodiments, at least one \( R^7 \) is halide.

In some embodiments, at least one \( R^7 \) is F.
In some embodiments, each R³ is independently selected from the group consisting of -(C₁-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -OCH₃, -CN, and -C(=0)R₁⁹.

In some embodiments, each R⁸ is independently selected from the group consisting of methyl, F, Cl, -CF₃, -OCH₃, -CN, and -C(=0)Me.

In some embodiments, at least one R⁸ is halide.

In some embodiments, at least one R⁸ is F.

In some embodiments, at least one R⁸ is -(C₁-4 alkyl).

In some embodiments, at least one R⁸ is -(C₁-3 alkyl).

In some embodiments, at least one R⁸ is -(C₁-2 alkyl).

In some embodiments, at least one R⁸ is methyl.

In some embodiments, R⁸ is methyl.

In some embodiments, at least one R⁸ is -C(=0)(C₁-3 alkyl).

In some embodiments, at least one R⁸ is -C(=0)Me.

In some embodiments, R⁸ is -C(=0)Me.

In some embodiments, each R⁹ is independently selected from the group consisting of -(C₁₆ alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -CN, and -OCH₃.

In some embodiments, each R⁹ is independently selected from the group consisting of methyl, F, Cl, -CF₃, -CN, and -OCH₃.

In some embodiments, each R¹⁰ is independently selected from the group consisting of -(C₁-6 alkyl), -(C₂-6 alkenyl), -(C₂-6 alkynyl), halide, -CF₃, -CN, -(C₁-6 alkylene)pNHS₀₂R¹⁹, -(C₂-6 alkenylene)pNHS₀₂R¹⁹, -(C₂-6 alkynylene)pNHS₀₂R¹⁹, -NR¹⁵(C₁-6 alkylene)NR¹⁵R¹⁶, -NR¹⁵(C₂₆ alkylene)NR¹⁵R¹⁶, -NR¹⁵(C₂₆ alkynylene)NR¹⁵R¹⁶, -(C₁-6 alkylene)pNR¹⁵R¹⁶, -(C₂-6 alkenylene)pNR¹⁵R¹⁶, -(C₂-6 alkynylene)pNR¹⁵R¹⁶, and -OR²⁷.

In some embodiments, each R¹¹ is independently selected from the group consisting of amino, -(C₁₆ alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN.

In some embodiments, each R¹¹ is independently selected from the group consisting of amino, methyl, F, Cl, -CF₃, and -CN.

In some embodiments, each R¹² is independently selected from the group consisting of -(C₁-4 alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN.

In some embodiments, each R¹² is independently selected from the group consisting of methyl, F, Cl, -CF₃, and -CN.

In some embodiments, each R¹³ is independently selected from the group consisting of -(C₁-4 alkyl), -(C₂-4 alkenyl), -(C₂-4 alkynyl), halide, -CF₃, and -CN.
In some embodiments, each R\textsuperscript{13} is independently selected from the group consisting of methyl, F, Cl, -CF\textsubscript{3}, and -CN.

In some embodiments, each R\textsuperscript{14} is independently selected from the group consisting of-(Ci-9 alkyl), -(Ci-zhaloalkyl), -(C2 ≡ alkenyl), -(C2 ≡ alkynyl), -heteroaryl optionally substituted with 1-4 (e.g., 1-3, 1-2, 1) R\textsuperscript{20}, -aryl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R\textsuperscript{21}, -CH\textsubscript{2}aryl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R\textsuperscript{21}, -carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{22}, -CH\textsubscript{2}carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{22}, -(CM alkylene)\textsubscript{p}NR\textsubscript{25}R\textsubscript{26}, -(C2 ≡ alkenylene)\textsubscript{p}NR\textsubscript{25}R\textsubscript{26}, -(C2 ≡ alkyne)\textsubscript{p}NR\textsubscript{25}R\textsubscript{26}, -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{23}, and -Cffheterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{23}.

In some embodiments, each R\textsuperscript{15} is independently selected from the group consisting of H, -(C\textsubscript{16} alkyl), -(C\textsubscript{26} alkkenyl), and -(C\textsubscript{26} alkynyl).

In some embodiments, each R\textsuperscript{16} is independently selected from the group consisting of H, -(C\textsubscript{16} alkyl), -(C\textsubscript{26} alkkenyl), -(C\textsubscript{26} alkynyl), -CH\textsubscript{2}aryl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R\textsuperscript{21}, and -Cttcarbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{22}.

In some embodiments, each R\textsuperscript{17} is independently selected from the group consisting of H, -(Ci-ealkyl), -(C2 ≡ alkenyl), and -(C2 ≡ alkynyl).

In some embodiments, each R\textsuperscript{18} is independently selected from the group consisting of H, -(Ci-ealkyl), -(C2 ≡ alkenyl), -(C2 ≡ alkynyl), -Cttaryl optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) R\textsuperscript{21} and -Cttcarbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R\textsuperscript{22}.

In some embodiments, each R\textsuperscript{19} is independently selected from the group consisting of-(Ci-6 alkyl), -(C2 ≡ alkenyl), and -(C2 ≡ alkynyl).

In some embodiments, each R\textsuperscript{20} is independently selected from the group consisting of-(Ci-4 alkyl), -(C2 ≡ alkenyl), -(C2 ≡ alkynyl), halide, -CF\textsubscript{3}, and -CN.

In some embodiments, each R\textsuperscript{20} is independently selected from the group consisting of methyl, F, Cl, -CF\textsubscript{3}, and -CN.

In some embodiments, each R\textsuperscript{21} is independently selected from the group consisting of-(Ci-4 alkyl), -(C\textsubscript{24} alkenyl), -(C\textsubscript{24} alkynyl), halide, -CF\textsubscript{3}, and -CN.

In some embodiments, each R\textsuperscript{21} is independently selected from the group consisting of methyl, F, Cl, -CF\textsubscript{3}, and -CN.
In some embodiments, each $R_{22}$ is independently selected from the group consisting of -(Ci-4 alkyl), -(C2-4 alkenyl), -(C2-4 alkylnyl), halide, -CF3, and -CN.

In some embodiments, each $R_{22}$ is independently selected from the group consisting of methyl, F, Cl, -CF3, and -CN.

In some embodiments, each $R_{23}$ is independently selected from the group consisting of -(Ci-4 alkyl), -(C2-4 alkenyl), -(C2-4 alkylnyl), halide, -CF3, and -CN.

In some embodiments, each $R_{23}$ is independently selected from the group consisting of methyl, F, Cl, -CF3, and -CN.

In some embodiments, $R_{24}$ is selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), -(C2-6 alkylnyl), -(C1-4 alkylene), heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{21}$, -(C2-4 alkenylene) heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{23}$, -(C2-4 alkylnylene) heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2), 1) $R_{22}$, -(C2-4 alkenylene) carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{22}$, -(C2-4 alkenylene) carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{22}$, -(C2-4 alkylnylene) arylicarbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{22}$, -(C2-4 alkylnylene) aromatic optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) $R_{22}$, -(C2-4 alkylidene) NR$^{25}$R$^{26}$, -(C2-4 alkylnylene) NR$^{25}$R$^{26}$, and -(C2-4 alkynylene) NR$^{25}$R$^{26}$.

In some embodiments, each $R_{25}$ is independently selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), -(C2-6 alkylnyl).

In some embodiments, each $R_{26}$ is independently selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), -(C2-6 alkylnyl).

In some embodiments, $R_{27}$ is selected from the group consisting of H, -(Ci-6 alkyl), -(C2-6 alkenyl), -(C2-6 alkylnyl), -(C1-4 alkylene), heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{21}$, -(C2-4 alkenylene) heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{23}$, -(C2-4 alkylnylene) heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) $R_{23}$, -(C2-4 alkylnylene) NR$^{25}$R$^{26}$, -(C2-4 alkylnylene) NR$^{25}$R$^{26}$, and -(C2-6 alkynylene) NR$^{25}$R$^{26}$.

In some embodiments, each $p$ is independently an integer of 0 or 1.

In some embodiments, $p$ is 0.

In some embodiments, $p$ is 1.
Illustrative compounds of Formula (I) are shown in Table 1.

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Administration and Pharmaceutical Compositions

[0391] Some embodiments include pharmaceutical compositions comprising: (a) a therapeutically effective amount of a compound provided herein, or its corresponding enantiomer, diastereoisomer or tautomer, or pharmaceutically acceptable salt; and (b) a pharmaceutically acceptable carrier.

[0392] The compounds provided herein may also be useful in combination (administered together or sequentially) with other known agents.

[0393] Non-limiting examples of diseases which can be treated with a combination of a compound of Formula (I) and other known agents are colorectal cancer, ovarian cancer, retinitis pigmentosa, macular degeneration, diabetic retinopathy, idiopathic pulmonary fibrosis/pulmonary fibrosis, and osteoarthritis.

[0394] In some embodiments, colorectal cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: 5-Fluorouracil (5-FU), which can be administered with the vitamin-like drug leucovorin (also called folinic acid); capecitabine (XELODA®), irinotecan (CAMPOSTAR®), oxaliplatin (ELOXATIN®). Examples of
combinations of these drugs which could be further combined with a compound of Formula (I) are FOLFOX (5-FU, leucovorin, and oxaliplatin), FOLFIRI (5-FU, leucovorin, and irinotecan), FOLFOXIRI (leucovorin, 5-FU, oxaliplatin, and irinotecan) and CapeOx (Capecitabine and oxaliplatin). For rectal cancer, chemo with 5-FU or capecitabine combined with radiation may be given before surgery (neoadjuvant treatment).

[0395] In some embodiments, ovarian cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Topotecan, Liposomal doxorubicin (DOXIL®), Gemcitabine (GEMZAR®), Cyclophosphamide (CYTOXAN®), Vinorelbine (NAVELBINE®), Ifosfamide (IFEX®), Etoposide (VP-16), Altretamine (HEXALEN®), Capecitabine (XELODA®), Irinotecan (CPT-11, CAMPTOSAR®), Melphalan, Pemtrexed (ALIMTA®) and Albumin bound paclitaxel (nab-paclitaxel, ABRAXANE®). Examples of combinations of these drugs which could be further combined with a compound of Formula (I) are TIP (paclitaxel [Taxol], ifosfamide, and cisplatin), VelP (vinblastine, ifosfamide, and cisplatin) and VIP (etoposide [VP-16], ifosfamide, and cisplatin).

[0396] In some embodiments, a compound of Formula (I) can be used to treat cancer in combination with any of the following methods: (a) Hormone therapy such as aromatase inhibitors, LHRH [luteinizing hormone-releasing hormone] analogs and inhibitors, and others; (b) Ablation or embolization procedures such as radiofrequency ablation (RFA), ethanol (alcohol) ablation, microwave thermotherapy and cryosurgery (cryotherapy); (c) Chemotherapy using alkylating agents such as cisplatin and carboplatin, oxaliplatin, mechlorethamine, cyclophosphamide, chlorambucil and ifosfamide; (d) Chemotherapy using anti-metabolites such as azathioprine and mercaptopurine; (e) Chemotherapy using plant alkaloids and terpenoids such as vinca alkaloids (i.e. Vincristine, Vinblastine, Vinorelbine and Vindesine) and taxanes; (f) Chemotherapy using podophyllotoxin, etoposide, teniposide and docetaxel; (g) Chemotherapy using topoisomerase inhibitors such as irinotecan, topotecan, amsacrine, etoposide, etoposide phosphate, and teniposide; (h) Chemotherapy using cytotoxic antibiotics such as actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and mitomycin; (i) Chemotherapy using tyrosine-kinase inhibitors such as Imatinib mesylate (GLEEVEC®, also known as STI-571), Gefitinib (Iressa, also known as ZD1839), Erlotinib (marketed as TARCEVA®), Bortezomib (VELCADE®), tamoxifen, tofacitinib, crizotinib, Bcl-2 inhibitors (e.g. obatoclax in clinical trials, ABT-263, and Gossypol), PARP inhibitors (e.g. Iniparib, Olaparib in clinical trials), PI3K inhibitors (e.g. perifosine in a phase III trial), VEGF Receptor 2 inhibitors (e.g. Apatinib), AN-152, (AEZS-108), Braf inhibitors (e.g. vemurafenib, dabrafenib and LGX818), MEK inhibitors (e.g. trametinib and MEK162), CDK
inhibitors, (e.g. PD-033299 1), salinomycin and Sorafenib; (j) Chemotherapy using monoclonal antibodies such as Rituximab (marketed as MABThera® or RITUXAN®), Trastuzumab (Herceptin also known as ErbB2), Cetuximab (marketed as ERBITUX®), and Bevacizumab (marketed as AVASTIN®); and (k) radiation therapy.

In some embodiments, diabetic retinopathy can be treated with a combination of a compound of Formula (I) and one or more of the following natural supplements: Bilberry, Butcher's broom, Ginkgo, Grape seed extract, and Pycnogenol (Pine bark).

In some embodiments, idiopathic pulmonary fibrosis/pulmonary fibrosis can be treated with a combination of one of the following drugs: pirfenidone (pirfenidone was approved for use in 2011 in Europe under the brand name Esbriet®), prednisone, azathioprine, N-acetylcysteine, interferon-γ 1b, bosentan (bosentan is currently being studied in patients with IPF, [The American Journal of Respiratory and Critical Care Medicine (2011), 184(1), 92-9]), Nintedanib (BIBF 1120 and Vargatef), QAX576 [British Journal of Pharmacology (2011), 163(1), 141-172], and anti-inflammatory agents such as corticosteroids.

In some embodiments, a compound of Formula (I) can be used to treat idiopathic pulmonary fibrosis/pulmonary fibrosis in combination with any of the following methods: oxygen therapy, pulmonary rehabilitation and surgery.

In some embodiments, a compound of Formula (I) can be used to treat osteoarthritis in combination with any of the following methods: (a) Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, aspirin and acetaminophen; (b) physical therapy; (c) injections of corticosteroid medications; (d) injections of hyaluronic acid derivatives (e.g. Hyalgan, Synvisc); (e) narcotics, like codeine; (f) in combination with braces and/or shoe inserts or any device that can immobilize or support your joint to help you keep pressure off it (e.g., splints, braces, shoe inserts or other medical devices); (g) realigning bones (osteotomy); (h) joint replacement (arthroplasty); and (i) in combination with a chronic pain class.

In some embodiments, macular degeneration can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Bevacizumab (Avastin®), Ranibizumab (Lucentis®), Pegaptanib (Macugen), Afiblercept (Eylea®), verteporfin (Visudyne®) in combination with photodynamic therapy (PDT) or with any of the following methods: (a) in combination with laser to destroy abnormal blood vessels (photocoagulation); and (b) in combination with increased vitamin intake of antioxidant vitamins and zinc.
In some embodiments, retinitis pigmentosa can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: UF-021 (Ocuseva™), vitamin A palmitate and pikachurin or with any of the following methods: (a) with the Argus® II retinal implant; and (b) with stem cell and/or gene therapy.

Administration of the compounds disclosed herein or the pharmaceutically acceptable salts thereof can be via any of the accepted modes of administration, including, but not limited to, orally, subcutaneously, intravenously, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, ontologically, neurootologically, intraocularly, subconjunctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intra-abdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracisternally, intravascularly, intraventricularly, intrasosseously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic devices. In some embodiments, the administration method includes oral or parenteral administration.

Compounds provided herein intended for pharmaceutical use may be administered as crystalline or amorphous products. Pharmaceutically acceptable compositions may include solid, semi-solid, liquid, solutions, colloidal, liposomes, emulsions, suspensions, complexes, coacervates and aerosols. Dosage forms, such as, e.g., tablets, capsules, powders, liquids, suspensions, suppositories, aerosols, implants, controlled release or the like. They may be obtained, for example, as solid plugs, powders, or films by methods such as precipitation, crystallization, milling, grinding, supercritical fluid processing, coacervation, complex coacervation, encapsulation, emulsification, complexation, freeze drying, spray drying, or evaporative drying. Microwave or radio frequency drying may be used for this purpose. The compounds can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills (tablets and or capsules), transdermal (including electrotransport) patches, implants and the like, for prolonged and/or timed, pulsed administration at a predetermined rate.

The compounds can be administered either alone or in combination with a conventional pharmaceutical carrier, excipient or the like. Pharmaceutically acceptable excipients include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, self-emulsifying drug delivery systems (SEDDS) such as d-a-tocopherol polyethylene glycol 1000
succinate, surfactants used in pharmaceutical dosage forms such as Tweens, poloxamers or other similar polymeric delivery matrices, serum proteins, such as human serum albumin, buffer substances such as phosphates, tris, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium-chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethyl cellulose, polyacrylates, waxes, polyethylene -poly oxypolyene -block polymers, and wool fat. Cyclodextrins such as α-, β, and γ-cyclodextrin, or chemically modified derivatives such as hydroxyalkylcyclodextrins, including 2- and 3-hydroxypropyl -P-cyclodextrins, or other solubilized derivatives can also be used to enhance delivery of compounds described herein. Dosage forms or compositions containing a compound as described herein in the range of 0.005% to 100% with the balance made up from non-toxic carrier may be prepared. The contemplated compositions may contain 0.00 1%-100% of a compound provided herein, in one embodiment 0.1-95%, in another embodiment 75-85%, in a further embodiment 20-80%. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington: The Science and Practice of Pharmacy, 22nd Edition (Pharmaceutical Press, London, UK. 2012).

[0406] In one embodiment, the compositions will take the form of a unit dosage form such as a pill or tablet and thus the composition may contain, along with a compound provided herein, a diluent such as lactose, sucrose, dicalcium phosphate, or the like; a lubricant such as magnesium stearate or the like; and a binder such as starch, gum acacia, polyvinylpyrrolidone, gelatin, cellulose, cellulose derivatives or the like. In another solid dosage form, a powder, marume, solution or suspension (e.g., in propylene carbonate, vegetable oils, PEG's, poloxamer 124 or triglycerides) is encapsulated in a capsule (gelatin or cellulose base capsule). Unit dosage forms in which one or more compounds provided herein or additional active agents are physically separated are also contemplated; e.g., capsules with granules (or tablets in a capsule) of each drug; two-layer tablets; two-compartment gel caps, etc. Enteric coated or delayed release oral dosage forms are also contemplated.

[0407] Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc. a compound provided herein and optional pharmaceutical adjuvants in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) to form a solution, colloid, liposome, emulsion, complexes, coacervate or suspension. If desired, the pharmaceutical composition can also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, co-solvents, solubilizing agents, pH buffering agents
and the like (e.g., sodium acetate, sodium citrate, cyclodextrin derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine olate, and the like).

[0408] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 50 mg/Kg in humans.

[0409] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 20 mg/Kg in humans.

[0410] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.50 mg/Kg to about 19 mg/Kg in humans.

[0411] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.75 mg/Kg to about 18 mg/Kg in humans.

[0412] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.0 mg/Kg to about 17 mg/Kg in humans.

[0413] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.25 mg/Kg to about 16 mg/Kg in humans.

[0414] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.50 mg/Kg to about 15 mg/Kg in humans.

[0415] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.75 mg/Kg to about 14 mg/Kg in humans.

[0416] In some embodiments, the unit dosage of compounds of Formula (I) is about 2.0 mg/Kg to about 13 mg/Kg in humans.

[0417] In some embodiments, the unit dosage of compounds of Formula (I) is about 3.0 mg/Kg to about 12 mg/Kg in humans.

[0418] In some embodiments, the unit dosage of compounds of Formula (I) is about 4.0 mg/Kg to about 11 mg/Kg in humans.

[0419] In some embodiments, the unit dosage of compounds of Formula (I) is about 5.0 mg/Kg to about 10 mg/Kg in humans.

[0420] In some embodiments, the compositions are provided in unit dosage forms suitable for single administration.

[0421] In some embodiments, the compositions are provided in unit dosage forms suitable for twice a day administration.

[0422] In some embodiments, the compositions are provided in unit dosage forms suitable for three times a day administration.

[0423] Injectables can be prepared in conventional forms, either as liquid solutions, colloid, liposomes, complexes, coacervate or suspensions, as emulsions, or in solid forms suitable
for reconstitution in liquid prior to injection. The percentage of a compound provided herein
contained in such parenteral compositions is highly dependent on the specific nature thereof, as
well as the activity of the compound and the needs of the patient. However, percentages of active
ingredient of 0.01% to 10% in solution are employable, and could be higher if the composition is
a solid or suspension, which could be subsequently diluted to the above percentages.

[0424] In some embodiments, the composition will comprise about 0.1-10% of the
active agent in solution.

[0425] In some embodiments, the composition will comprise about 0.1-5% of the
active agent in solution.

[0426] In some embodiments, the composition will comprise about 0.1-4% of the
active agent in solution.

[0427] In some embodiments, the composition will comprise about 0.15-3% of the
active agent in solution.

[0428] In some embodiments, the composition will comprise about 0.2-2% of the
active agent in solution.

[0429] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-96 hours.

[0430] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-72 hours.

[0431] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-48 hours.

[0432] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-24 hours.

[0433] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-12 hours.

[0434] In some embodiments, the compositions are provided in dosage forms
suitable for continuous dosage by intravenous infusion over a period of about 1-6 hours.

[0435] In some embodiments, these compositions can be administered by
intravenous infusion to humans at doses of about 5 mg/m² to about 300 mg/m².

[0436] In some embodiments, these compositions can be administered by
intravenous infusion to humans at doses of about 5 mg/m² to about 200 mg/m².

[0437] In some embodiments, these compositions can be administered by
intravenous infusion to humans at doses of about 5 mg/m² to about 100 mg/m².
In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 10 mg/m² to about 50 mg/m².

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 50 mg/m² to about 200 mg/m².

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 75 mg/m² to about 175 mg/m².

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 100 mg/m² to about 150 mg/m².

It is to be noted that concentrations and dosage values may also vary depending on the specific compound and the severity of the condition to be alleviated. It is to be further understood that for any particular patient, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

In one embodiment, the compositions can be administered to the respiratory tract (including nasal and pulmonary) e.g., through a nebulizer, metered-dose inhalers, atomizer, misters, aerosol, dry powder inhaler, insufflator, liquid instillation or other suitable device or technique.

In some embodiments, aerosols intended for delivery to the nasal mucosa are provided for inhalation through the nose. For optimal delivery to the nasal cavities, inhaled particle sizes of about 5 to about 100 microns are useful, with particle sizes of about 10 to about 60 microns being preferred. For nasal delivery, a larger inhaled particle size may be desired to maximize impaction on the nasal mucosa and to minimize or prevent pulmonary deposition of the administered formulation. In some embodiments, aerosols intended for delivery to the lung are provided for inhalation through the nose or the mouth. For delivery to the lung, inhaled aerodynamic particle sizes of about less than 10 µm are useful (e.g., about 1 to about 10 microns). Inhaled particles may be defined as liquid droplets containing dissolved drug, liquid droplets containing suspended drug particles (in cases where the drug is insoluble in the suspending medium), dry particles of pure drug substance, drug substance incorporated with excipients, liposomes, emulsions, colloidal systems, coacervates, aggregates of drug nanoparticles, or dry particles of a diluent which contain embedded drug nanoparticles.

In some embodiments, compounds of Formula (I) disclosed herein intended for respiratory delivery (either systemic or local) can be administered as aqueous formulations, as
non-aqueous solutions or suspensions, as suspensions or solutions in halogenated hydrocarbon propellants with or without alcohol, as a colloidal system, as emulsions, coacervates, or as dry powders. Aqueous formulations may be aerosolized by liquid nebulizers employing either hydraulic or ultrasonic atomization or by modified micropump systems (like the soft mist inhalers, the Aerodose® or the AERx® systems). Propellant-based systems may use suitable pressurized metered-dose inhalers (pMDIs). Dry powders may use dry powder inhaler devices (DPIs), which are capable of dispersing the drug substance effectively. A desired particle size and distribution may be obtained by choosing an appropriate device.

[0446] In some embodiments, the compositions of Formula (I) disclosed herein can be administered to the ear by various methods. For example, a round window catheter (e.g., U.S. Pat. Nos. 6,440,102 and 6,648,873) can be used.

[0447] Alternatively, formulations can be incorporated into a wick for use between the outer and middle ear (e.g., U.S. Pat. No. 6,120,484) or absorbed to collagen sponge or other solid support (e.g., U.S. Pat. No. 4,164,559).

[0448] If desired, formulations of the disclosure can be incorporated into a gel formulation (e.g., U.S. Pat. Nos. 4,474,752 and 6,911,211).

[0449] In some embodiments, compounds of Formula (I) disclosed herein intended for delivery to the ear can be administered via an implanted pump and delivery system through a needle directly into the middle or inner ear (cochlea) or through a cochlear implant stylet electrode channel or alternative prepared drug delivery channel such as but not limited to a needle through temporal bone into the cochlea.

[0450] Other options include delivery via a pump through a thin film coated onto a multichannel electrode or electrode with a specially imbedded drug delivery channel (pathways) carved into the thin film for this purpose. In other embodiments the acidic or basic solid compound of Formula (I) can be delivered from the reservoir of an external or internal implanted pumping system.

[0451] Formulations of the disclosure also can be administered to the ear by intratympanic injection into the middle ear, inner ear, or cochlea (e.g., U.S. Pat. No. 6,377,849 and Ser. No. 11/337,815).

[0452] Intratympanic injection of therapeutic agents is the technique of injecting a therapeutic agent behind the tympanic membrane into the middle and/or inner ear. In one embodiment, the formulations described herein are administered directly onto the round window membrane via transtympanic injection. In another embodiment, the ion channel modulating agent auris-acceptable formulations described herein are administered onto the round window.
membrane via a non-transtympanic approach to the inner ear. In additional embodiments, the formulation described herein is administered onto the round window membrane via a surgical approach to the round window membrane comprising modification of the crista fenestrae cochleae.

[0453] In some embodiments, the compounds of Formula (I) are formulated in rectal compositions such as enemas, rectal gels, rectal foams, rectal aerosols, suppositories, jelly suppositories, or retention enemas, containing conventional suppository bases such as cocoa butter or other glycerides, as well as synthetic polymers such as polyvinylpyrrolidone, PEG (like PEG ointments), and the like.

[0454] Suppositories for rectal administration of the drug (either as a solution, colloid, suspension or a complex) can be prepared by mixing a compound provided herein with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt or erode/dissolve in the rectum and release the compound. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, poloxamers, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol. In suppository forms of the compositions, a low-melting wax such as, but not limited to, a mixture of fatty acid glycerides, optionally in combination with cocoa butter, is first melted.

[0455] Solid compositions can be provided in various different types of dosage forms, depending on the physicochemical properties of the compound provided herein, the desired dissolution rate, cost considerations, and other criteria. In one of the embodiments, the solid composition is a single unit. This implies that one unit dose of the compound is comprised in a single, physically shaped solid form or article. In other words, the solid composition is coherent, which is in contrast to a multiple unit dosage form, in which the units are incoherent.

[0456] Examples of single units which may be used as dosage forms for the solid composition include tablets, such as compressed tablets, film-like units, foil-like units, wafers, lyophilized matrix units, and the like. In one embodiment, the solid composition is a highly porous lyophilized form. Such lyophilizates, sometimes also called wafers or lyophilized tablets, are particularly useful for their rapid disintegration, which also enables the rapid dissolution of the compound.

[0457] On the other hand, for some applications the solid composition may also be formed as a multiple unit dosage form as defined above. Examples of multiple units are powders, granules, microparticles, pellets, mini-tablets, beads, lyophilized powders, and the like. In one embodiment, the solid composition is a lyophilized powder. Such a dispersed lyophilized system
comprises a multitude of powder particles, and due to the lyophilization process used in the formation of the powder, each particle has an irregular, porous microstructure through which the powder is capable of absorbing water very rapidly, resulting in quick dissolution. Effervescent compositions are also contemplated to aid the quick dispersion and absorption of the compound.

[0458] Another type of multiparticulate system which is also capable of achieving rapid drug dissolution is that of powders, granules, or pellets from water-soluble excipients which are coated with a compound provided herein so that the compound is located at the outer surface of the individual particles. In this type of system, the water-soluble low molecular weight excipient may be useful for preparing the cores of such coated particles, which can be subsequently coated with a coating composition comprising the compound and, for example, one or more additional excipients, such as a binder, a pore former, a saccharide, a sugar alcohol, a film-forming polymer, a plasticizer, or other excipients used in pharmaceutical coating compositions.

[0459] Also provided herein are kits. Typically, a kit includes one or more compounds or compositions as described herein. In certain embodiments, a kit can include one or more delivery systems, e.g., for delivering or administering a compound as provided herein, and directions for use of the kit (e.g., instructions for treating a patient). In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with cancer. In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with one or more of hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma, ovarian cancer, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG), familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Mullerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.
Methods of Treatment

[0460] The compounds and compositions provided herein can be used as inhibitors and/or modulators of one or more components of the Wnt pathway, which may include one or more Wnt proteins, and thus can be used to treat a variety of disorders and diseases in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, and cell cycling. Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation, to correct a genetic disorder, and/or to treat a neurological condition/disorder/disease due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, mycotic and viral infections, bone and cartilage diseases, neurological conditions/diseases such as Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), motor neuron disease, multiple sclerosis or autism, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG), familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Mullerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

[0461] The compounds and compositions described herein can be used to treat tendinopathy includes all tendon pathologies (tendinitis, tendinosis and paratenonitis) localized in and around the tendons and is characterized by pain, swelling and impaired performance due to the degeneration of the tendon’s collagen in response tendon overuse, often referred to as tendinosis. Tendinopathy may be categorized into two histopathologic entities - tendonitis, which results from acute injury to the tendon accompanied by intratendinous inflammation, and more commonly, tendinosis, which is a degenerative response to repetitive microtrauma resulting from overuse. Tendinosis may be accompanied by paratenonitis, an inflammatory condition of the lining of the tendon.
With respect to cancer, the Wnt pathway is known to be constitutively activated in a variety of cancers including, for example, colon cancer, hepatocellular carcinoma, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer and leukemias such as CML, CLL and T-ALL. Accordingly, the compounds and compositions described herein may be used to treat these cancers in which the Wnt pathway is constitutively activated. In certain embodiments, the cancer is chosen from hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma and ovarian cancer.

Other cancers can also be treated with the compounds and compositions described herein.

More particularly, cancers that may be treated by the compounds, compositions and methods described herein include, but are not limited to, the following:

1) Breast cancers, including, for example ER+ breast cancer, ER- breast cancer, her2+ breast cancer, her2+ breast cancer, stromal tumors such as fibroadenomas, phyllodes tumors, and sarcomas, and epithelial tumors such as large duct papillomas; carcinomas of the breast including in situ (noninvasive) carcinoma that includes ductal carcinoma in situ (including Paget's disease) and lobular carcinoma in situ, and invasive (infiltrating) carcinoma including, but not limited to, invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, colloid (mucinous) carcinoma, tubular carcinoma, and invasive papillary carcinoma; and miscellaneous malignant neoplasms. Further examples of breast cancers can include luminal A, luminal B, basal A, basal B, and triple negative breast cancer, which is estrogen receptor negative (ER-), progesterone receptor negative, and her2 negative (her2-). In some embodiments, the breast cancer may have a high risk Oncotype score.

2) Cardiac cancers, including, for example sarcoma, e.g., angiosarcoma, fibrosarcoma, rhabdomyosarcoma, and liposarcoma; myxoma; rhabdomyoma; fibroma; lipoma and teratoma.

3) Lung cancers, including, for example, bronchogenic carcinoma, e.g., squamous cell, undifferentiated small cell, undifferentiated large cell, and adenocarcinoma; alveolar and bronchiolar carcinoma; bronchial adenoma; sarcoma; lymphoma; chondromatous hamartoma; and mesothelioma.

4) Gastrointestinal cancer, including, for example, cancers of the esophagus, e.g., squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, and lymphoma; cancers of the stomach, e.g., carcinoma, lymphoma, and leiomyosarcoma; cancers of the pancreas, e.g., ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, and vipoma; cancers of the small bowel, e.g., adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma,
leiomyoma, hemangioma, lipoma, neurofibroma, and fibroma; cancers of the large bowel, e.g., adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, and leiomyoma.

[0469] 5) Genitourinary tract cancers, including, for example, cancers of the kidney, e.g., adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, and leukemia; cancers of the bladder and urethra, e.g., squamous cell carcinoma, transitional cell carcinoma, and adenocarcinoma; cancers of the prostate, e.g., adenocarcinoma, and sarcoma; cancer of the testis, e.g., seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, and lipoma.

[0470] 6) Liver cancers, including, for example, hepatoma, e.g., hepatocellular carcinoma; cholangiocarcinoma; hepatoblastoma; angiosarcoma; hepatocellular adenoma; and hemangioma.

[0471] 7) Bone cancers, including, for example, osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors.

[0472] 8) Nervous system cancers, including, for example, cancers of the skull, e.g., osteoma, hemangioma, granuloma, xanthoma, and osteitis deformans; cancers of the meninges, e.g., meningioma, meningiosarcoma, and gliomatosis; cancers of the brain, e.g., astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendrogioma, schwannoma, retinoblastoma, and congenital tumors; and cancers of the spinal cord, e.g., neurofibroma, meningioma, glioma, and sarcoma.

[0473] 9) Gynecological cancers, including, for example, cancers of the uterus, e.g., endometrial carcinoma; cancers of the cervix, e.g., cervical carcinoma, and pre tumor cervical dysplasia; cancers of the ovaries, e.g., ovarian carcinoma, including serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma, granulosa theca cell tumors, Sertoli Leydig cell tumors, dysgerminoma, and malignant teratoma; cancers of the vulva, e.g., squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, and melanoma; cancers of the vagina, e.g., clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, and embryonal rhabdomyosarcoma; and cancers of the fallopian tubes, e.g., carcinoma.

[0474] 10) Hematologic cancers, including, for example, cancers of the blood, e.g., acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, and myelodysplastic...
syndrome, Hodgkin's lymphoma, non-Hodgkin's lymphoma (malignant lymphoma) and Waldenstrom's macroglobulinemia.

[0475] 11) Skin cancers and skin disorders, including, for example, malignant melanoma and metastatic melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, and scleroderma.

[0476] 12) Adrenal gland cancers, including, for example, neuroblastoma.

[0477] Cancers may be solid tumors that may or may not be metastatic. Cancers may also occur, as in leukemia, as a diffuse tissue. Thus, the term "tumor cell," as provided herein, includes a cell afflicted by any one of the above identified disorders.

[0478] A method of treating cancer using a compound or composition as described herein may be combined with existing methods of treating cancers, for example by chemotherapy, irradiation, or surgery (e.g., oophorectomy). In some embodiments, a compound or composition can be administered before, during, or after another anticancer agent or treatment.

[0479] The compounds and compositions described herein can be used as anti-angiogenesis agents and as agents for modulating and/or inhibiting the activity of protein kinases, thus providing treatments for cancer and other diseases associated with cellular proliferation mediated by protein kinases. For example, the compounds described herein can inhibit the activity of one or more kinases. Accordingly, provided herein is a method of treating cancer or preventing or reducing angiogenesis through kinase inhibition.

[0480] In addition, and including treatment of cancer, the compounds and compositions described herein can function as cell-cycle control agents for treating proliferative disorders in a patient. Disorders associated with excessive proliferation include, for example, cancers, scleroderma, immunological disorders involving undesired proliferation of leukocytes, and restenosis and other smooth muscle disorders. Furthermore, such compounds may be used to prevent de-differentiation of post-mitotic tissue and/or cells.

[0481] Diseases or disorders associated with uncontrolled or abnormal cellular proliferation include, but are not limited to, the following:

- a variety of cancers, including, but not limited to, carcinoma, hematopoietic tumors of lymphoid lineage, hematopoietic tumors of myeloid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system and other tumors including melanoma, seminoma and Kaposi’s sarcoma.
- a disease process which features abnormal cellular proliferation, e.g., benign prostatic hyperplasia, familial adenomatosis polyposis, neurofibromatosis, atherosclerosis, arthritis, glomerulonephritis, restenosis following angioplasty or
vascular surgery, inflammatory bowel disease, transplantation rejection, endotoxic shock, and fungal infections. Fibrotic disorders such as skin fibrosis; scleroderma; progressive systemic fibrosis; lung fibrosis; muscle fibrosis; kidney fibrosis; glomerulosclerosis; glomerulonephritis; hypertrophic scar formation; uterine fibrosis; renal fibrosis; cirrhosis of the liver, liver fibrosis; fatty liver disease (FLD); adhesions, such as those occurring in the abdomen, pelvis, spine or tendons; chronic obstructive pulmonary disease; fibrosis following myocardial infarction; pulmonary fibrosis; fibrosis and scarring associated with diffuse/interstitial lung disease; central nervous system fibrosis, such as fibrosis following stroke; fibrosis associated with neuro-degenerative disorders such as Alzheimer's Disease or multiple sclerosis; fibrosis associated with proliferative vitreoretinopathy (PVR); restenosis; endometriosis; ischemic disease and radiation fibrosis.

- defective apoptosis-associated conditions, such as cancers (including but not limited to those types mentioned herein), viral infections (including but not limited to herpesvirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including but not limited to systemic lupus erythematosus, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, autoimmune mediated glomerulonephritis, inflammatory bowel disease and autoimmune diabetes mellitus), neuro-degenerative disorders (including but not limited to Alzheimer's disease, lung disease, amyotrophic lateral sclerosis, retinitis pigmentosa, Parkinson's disease, AIDS-related dementia, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including but not limited to chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including but not limited to osteoporosis and arthritis), tendinopathies such as tendinitis and tendinosis, aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.

- genetic diseases due to mutations in Wnt signaling components, such as polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG), familial exudative vitreoretinopathy, retinal angiogenesis,

The compounds and compositions described herein can be used to treat neurological conditions, disorders and/or diseases caused by dysfunction in the Wnt signaling pathway. Non-limiting examples of neurological conditions/disorders/diseases which can be treated with the compounds and compositions provided herein include Alzheimer's disease, aphasia, apraxia, arachnoiditis, ataxia telangiectasia, attention deficit hyperactivity disorder, auditory processing disorder, autism, alcoholism, Bell's palsy, bipolar disorder, brachial plexus injury, Canavan disease, carpal tunnel syndrome, causalgia, central pain syndrome, central pontine myelinolysis, centronuclear myopathy, cephalic disorder, cerebral aneurysm, cerebral arteriosclerosis, cerebral atrophy, cerebral gigantism, cerebral palsy, cerebral vasculitis, cervical spinal stenosis, Charcot-Marie-Tooth disease, Chiari malformation, chronic fatigue syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic pain, Coffin-Lowry syndrome, complex regional pain syndrome, compression neuropathy, congenital facial palsy, corticobasal degeneration, cranial arteritis, cranosynostosis, Creutzfeldt-Jakob disease, cumulative trauma disorder, Cushing's syndrome, cytomegalic inclusion body disease (CIBD), Dandy-Walker syndrome, Dawson disease, de Morsier's syndrome, Dejerine-Klumpke palsy, Dejerine-Sottas disease, delayed sleep phase syndrome, dementia, dermatomyositis, developmental dyspraxia, diabetic neuropathy, diffuse sclerosis, Dravet syndrome, dysautonomia, dyscalculia, dysgraphia, dyslexia, dystonia, empty sella syndrome, encephalitis, encephalopathy, encephalotrigeminal angiomatosis, encopresis, epilepsy, Erb's palsy, erythromelalgia, essential tremor, Fabry's disease, Fahr's syndrome, familial spastic paralysis, febrile seizure, Fisher syndrome, Friedreich's ataxia, fibromyalgia, Foville's syndrome, Gaucher's disease, Gerstmann's syndrome, giant cell arteritis, giant cell inclusion disease, globoid cell leukodystrophy, gray matter heterotopia, Guillain-Barre syndrome, HTLV-1 associated myelopathy, Hallervorden-Spatz disease, hemifacial spasm, hereditary spastic paraplegia, heredopathia atactica polyneuritiformis, herpes zoster oticus, herpes zoster, Hirayama syndrome, holoprosencephaly, Huntington's disease, hydranencephaly, hydrocephalus, hypercortisolism, hypoxia, immune-mediated encephalomyelitis, inclusion body

The compounds and compositions may also be useful in the inhibition of the development of invasive cancer, tumor angiogenesis and metastasis.

In some embodiments, the disclosure provides a method for treating a disease or disorder associated with aberrant cellular proliferation by administering to a patient in need of such treatment an effective amount of one or more of the compounds of Formula (I), in combination (simultaneously or sequentially) with at least one other agent.

In some embodiments, the disclosure provides a method of treating or ameliorating in a patient a disorder or disease selected from the group consisting of: cancer, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), degenerative disc disease, bone/osteoporotic fractures, bone or cartilage disease, and osteoarthritis, the method comprising administering to the patient a therapeutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof.

In some embodiments, the pharmaceutical composition comprises a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In some embodiments, the method of treats a disorder or disease in which aberrant Wnt signaling is implicated in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the disorder or disease is cancer.

In some embodiments, the disorder or disease is systemic inflammation.

In some embodiments, the disorder or disease is metastatic melanoma.

In some embodiments, the disorder or disease is fatty liver disease.

In some embodiments, the disorder or disease is liver fibrosis.
In some embodiments, the disorder or disease is tendon regeneration. 

In some embodiments, the disorder or disease is diabetes.

In some embodiments, the disorder or disease is degenerative disc disease.

In some embodiments, the disorder or disease is osteoarthritis.

In some embodiments, the disorder or disease is diabetic retinopathy.

In some embodiments, the disorder or disease is pulmonary fibrosis.

In some embodiments, the disorder or disease is idiopathic pulmonary fibrosis (IPF).

In some embodiments, the disorder or disease is degenerative disc disease.

In some embodiments, the disorder or disease is rheumatoid arthritis.

In some embodiments, the disorder or disease is scleroderma.

In some embodiments, the disorder or disease is a mycotic or viral infection.

In some embodiments, the disorder or disease is a bone or cartilage disease.

In some embodiments, the disorder or disease is Alzheimer's disease.

In some embodiments, the disorder or disease is osteoarthritis.

In some embodiments, the disorder or disease is lung disease.

In some embodiments, the disorder or disease is tendinitis.

In some embodiments, the disorder or disease is tendinosis.

In some embodiments, the disorder or disease is paratenonitis.

In some embodiments, the disorder or disease is degeneration of the tendon's collagen.

In some embodiments, the disorder or disease is tendinopathy.

In some embodiments, the disorder or disease is a genetic disease caused by mutations in Wnt signaling components, wherein the genetic disease is selected from: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Mullerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrman syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alphathalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

In some embodiments, the patient is a human.
In some embodiments, the cancer is chosen from: hepatocellular carcinoma, colon cancer, breast cancer, pancreatic cancer, chronic myeloid leukemia (CML), chronic myelomonocytic leukemia, chronic lymphocytic leukemia (CLL), acute myeloid leukemia, acute lymphocytic leukemia, Hodgkin lymphoma, lymphoma, sarcoma and ovarian cancer.

In some embodiments, the cancer is nasopharyngeal cancer.

In some embodiments, the cancer is neuroblastoma.


In some embodiments, the cancer is hepatocellular carcinoma.

In some embodiments, the cancer is colon cancer.

In some embodiments, the cancer is colorectal cancer.

In some embodiments, the cancer is breast cancer.

In some embodiments, the cancer is pancreatic cancer.

In some embodiments, the cancer is chronic myeloid leukemia (CML).

In some embodiments, the cancer is chronic myelomonocytic leukemia.

In some embodiments, the cancer is chronic lymphocytic leukemia (CLL).

In some embodiments, the cancer is acute myeloid leukemia.

In some embodiments, the cancer is acute lymphocytic leukemia.

In some embodiments, the cancer is Hodgkin lymphoma.

In some embodiments, the cancer is lymphoma.

In some embodiments, the cancer is sarcoma.

In some embodiments, the cancer is ovarian cancer.

In some embodiments, the cancer is lung cancer - non-small cell.

In some embodiments, the cancer is lung cancer - small cell.

In some embodiments, the cancer is multiple myeloma.

In some embodiments, the cancer is nasopharyngeal cancer.

In some embodiments, the cancer is neuroblastoma.
In some embodiments, the cancer is osteosarcoma.

In some embodiments, the cancer is penile cancer.

In some embodiments, the cancer is pituitary tumors.

In some embodiments, the cancer is prostate cancer.

In some embodiments, the cancer is retinoblastoma.

In some embodiments, the cancer is rhabdomyosarcoma.

In some embodiments, the cancer is salivary gland cancer.

In some embodiments, the cancer is skin cancer - basal and squamous cell.

In some embodiments, the cancer is skin cancer - melanoma.

In some embodiments, the cancer is small intestine cancer.

In some embodiments, the cancer is stomach (gastric) cancers.

In some embodiments, the cancer is testicular cancer.

In some embodiments, the cancer is thymus cancer.

In some embodiments, the cancer is thyroid cancer.

In some embodiments, the cancer is uterine sarcoma.

In some embodiments, the cancer is vaginal cancer.

In some embodiments, the cancer is vulvar cancer.

In some embodiments, the cancer is Wilms tumor.

In some embodiments, the cancer is laryngeal or hypopharyngeal cancer.

In some embodiments, the cancer is kidney cancer.

In some embodiments, the cancer is Kaposi sarcoma.

In some embodiments, the cancer is gestational trophoblastic disease.

In some embodiments, the cancer is gastrointestinal stromal tumor.

In some embodiments, the cancer is gastrointestinal carcinoïd tumor.

In some embodiments, the cancer is gallbladder cancer.

In some embodiments, the cancer is eye cancer (melanoma and lymphoma).

In some embodiments, the cancer is Ewing tumor.

In some embodiments, the cancer is esophagus cancer.

In some embodiments, the cancer is endometrial cancer.

In some embodiments, the cancer is colorectal cancer.

In some embodiments, the cancer is cervical cancer.

In some embodiments, the cancer is brain or spinal cord tumor.

In some embodiments, the cancer is bone metastasis.

In some embodiments, the cancer is bone cancer.
In some embodiments, the cancer is bladder cancer.

In some embodiments, the cancer is bile duct cancer.

In some embodiments, the cancer is anal cancer.

In some embodiments, the cancer is adrenal cortical cancer.

In some embodiments, the disorder or disease is a neurological condition, disorder or disease, wherein the neurological condition/disorder/disease is selected from: Alzheimer's disease, frontotemporal dementias, dementia with Lewy bodies, prion diseases, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, amyotrophic lateral sclerosis (ALS), inclusion body myositis, autism, degenerative myopathies, diabetic neuropathy, other metabolic neuropathies, endocrine neuropathies, orthostatic hypotension, multiple sclerosis and Charcot-Marie-Tooth disease.

In some embodiments, the compound of Formula (I) inhibits one or more proteins in the Wnt pathway.

In some embodiments, the compound of Formula (I) inhibits signaling induced by one or more Wnt proteins.

In some embodiments, the Wnt proteins are chosen from: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11 and WNT16.

In some embodiments, the compound of Formula (I) inhibits a kinase activity.

In some embodiments, the method treats a disease or disorder mediated by the Wnt pathway in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula (I) inhibits one or more Wnt proteins.

In some embodiments, the method treats a disease or disorder mediated by kinase activity in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the disease or disorder comprises tumor growth, cell proliferation, or angiogenesis.
In some embodiments, the method inhibits the activity of a protein kinase receptor, the method comprises contacting the receptor with an effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method prevents or reduces angiogenesis in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method prevents or reduces abnormal cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient, the method comprises administering to the patient a pharmaceutical composition comprising one or more of the compounds of claim 1 in combination with a pharmaceutically acceptable carrier and one or more other agents.

Moreover, the compounds and compositions, for example, as inhibitors of the cyclin-dependent kinases (CDKs), can modulate the level of cellular RNA and DNA synthesis and therefore are expected to be useful in the treatment of viral infections such as HIV, human papilloma virus, herpes virus, Epstein-Barr virus, adenovirus, Sindbis virus, pox virus and the like.

Compounds and compositions described herein can inhibit the kinase activity of, for example, CDK/cyclin complexes, such as those active in the G0 or G1 stage of the cell cycle, e.g., CDK2, CDK4, and/or CDK6 complexes.

Evaluation of Biological Activity

The biological activity of the compounds described herein can be tested using any suitable assay known to those of skill in the art, see, e.g., WO 2001/053268 and WO 2005/009997. For example, the activity of a compound may be tested using one or more of the test methods outlined below.

In one example, tumor cells may be screened for Wnt independent growth. In such a method, tumor cells of interest are contacted with a compound (i.e. inhibitor) of interest,
and the proliferation of the cells, e.g. by uptake of tritiated thymidine, is monitored. In some embodiments, tumor cells may be isolated from a candidate patient who has been screened for the presence of a cancer that is associated with a mutation in the Wnt signaling pathway. Candidate cancers include, without limitation, those listed above.

[0592] In another example, one may utilize in vitro assays for Wnt biological activity, e.g. stabilization of β-catenin and promoting growth of stem cells. Assays for biological activity of Wnt include stabilization of β-catenin, which can be measured, for example, by serial dilutions of a candidate inhibitor composition. An exemplary assay for Wnt biological activity contacts a candidate inhibitor with cells containing constitutively active Wnt/p-catenin signaling. The cells are cultured for a period of time sufficient to stabilize β-catenin, usually at least about 1 hour, and lysed. The cell lysate is resolved by SDS PAGE, then transferred to nitrocellulose and probed with antibodies specific for β-catenin.

[0593] In a further example, the activity of a candidate compound can be measured in a Xenopus secondary axis bioassay (Leyns, L. et al. Cell (1997), 88(6), 747-756).

[0594] To further illustrate this disclosure, the following examples are included. The examples should not, of course, be construed as specifically limiting the disclosure. Variations of these examples within the scope of the claims are within the purview of one skilled in the art and are considered to fall within the scope of the disclosure as described, and claimed herein. The reader will recognize that the skilled artisan, armed with the present disclosure, and skill in the art is able to prepare and use the disclosure without exhaustive examples.

**EXAMPLES**

**Compound preparation**

[0595] The starting materials used in preparing the compounds of the disclosure are known, made by known methods, or are commercially available. It will be apparent to the skilled artisan that methods for preparing precursors and functionality related to the compounds claimed herein are generally described in the literature. The skilled artisan given the literature and this disclosure is well equipped to prepare any of the compounds.

[0596] It is recognized that the skilled artisan in the art of organic chemistry can readily carry out manipulations without further direction, that is, it is well within the scope and practice of the skilled artisan to carry out these manipulations. These include reduction of carbonyl compounds to their corresponding alcohols, oxidations, acylations, aromatic substitutions, both electrophilic and nucleophilic, etherifications, esterification and saponification and the like. These manipulations are discussed in standard texts such as March's Advanced
The skilled artisan will readily appreciate that certain reactions are best carried out when other functionality is masked or protected in the molecule, thus avoiding any undesirable side reactions and/or increasing the yield of the reaction. Often the skilled artisan utilizes protecting groups to accomplish such increased yields or to avoid the undesired reactions. These reactions are found in the literature and are also well within the scope of the skilled artisan. Examples of many of these manipulations can be found for example in T. Greene and P. Wuts Protective Groups in Organic Synthesis, 4th Ed., John Wiley & Sons (2007), incorporated herein by reference in its entirety.

Trademarks used herein are examples only and reflect illustrative materials used at the time of the disclosure. The skilled artisan will recognize that variations in lot, manufacturing processes, and the like, are expected. Hence the examples, and the trademarks used in them are non-limiting, and they are not intended to be limiting, but are merely an illustration of how a skilled artisan may choose to perform one or more of the embodiments of the disclosure.

(¾) nuclear magnetic resonance spectra (NMR) were measured in the indicated solvents on a Bruker NMR spectrometer (Avance TM DRX300, 300 MHz for ¾ or Avance TM DRX500, 500 MHz for ¾) or Varian NMR spectrometer (Mercury 400BB, 400 MHz for ¾). Peak positions are expressed in parts per million (ppm) downfield from tetramethylsilane. The peak multiplicities are denoted as follows, s, singlet; d, doublet; t, triplet; q, quartet; ABq, AB quartet; quin, quintet; sex, sextet; sep, septet; non, nonet; dd, doublet of doublets; ddd, doublet of doublets of doublets; d/ABq, doublet of AB quartet; dt, doublet of triplets; td, triplet of doublets; dq, doublet of quartets; m, multiplet.

The following abbreviations have the indicated meanings:

AC2O = acetic anhydride
B³⁻-Me2S = borane dimethyl sulfide complex
B(i-Pr)₃ = triisopropyl borate
(Boc)₂O = di-tert-butyl dicarbonate
brine = saturated aqueous sodium chloride
tBuOK = potassium tert-butoxide
CDCl₃ = deuterated chloroform
CD3OD = deuterated methanol
Cy3P = tricyclohexylphosphine
DCAD = di-(4-chlorobenzyl)azodicarboxylate
DCE = dichloroethane
DCM = dichloromethane
DEAD = diethyl azodicarboxylate
DHP = dihydropyran
DIPEA = diisopropylethylamine
DMAP = 4-dimethylaminopyridine
DMF = N,N-dimethylformamide
DMSO-d6 = deuterated dimethylsulfoxide
ESIMS = electron spray mass spectrometry
EtOAc = ethyl acetate
EtOH = ethanol
HCl = hydrochloric acid
HOAc = acetic acid
K2CO3 = potassium carbonate
KOAc = potassium acetate
LC/MS = liquid chromatography-mass spectrometry
LDA = lithium diisopropylamide
MeOH = methanol
MgSO4 = magnesium sulfate
MPLC = Medium pressure liquid chromatography
MsCl = methanesulfonyl chloride or mesyl chloride
NaBH4 = sodium borohydride
NaBH(OAc)3 = sodium triacetoxyborohydride
NaCNBu4 = sodium cyanoborohydride
NaHCO3 = sodium bicarbonate
NaH2P04 = monosodium phosphate
Na2HPC>4 = disodium phosphate
NaIC>4 = sodium periodate
NaOH = sodium hydroxide
Na2SC>4 = sodium sulfate
NMR = nuclear magnetic resonance
ON = overnight

Pcb(dba)$_3$ = tris(dibenzylideneacetone)dipalladium(0)

Pd(dppf)Cl$_2$ = 1,1'-bis(diphenylphosphino)ferrocenylpalladium(II) chloride

Pd(PPh$_3$)$_4$ = tetrakis(triphenylphosphine)palladium(0)

PE = petroleum ether

Pin$_2$B$_2$ = bis(pinacolato)diboron

PPh$_3$ = triphenylphosphine

prep-HPLC = preparative High-performance liquid chromatography

r.t = room temperature

SEM-C1 = 2-(trimethylsilyl)ethoxymethyl chloride

TBAF = tetra-n-butylammonium fluoride

TEA = triethylamine

TFA = trifluoroacetic acid

THF = tetrahydrofuran

THP = tetrahydropyran

TLC = thin layer chromatography

p-TsOH = p-toluenesulfonic acid

XPhos = 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

[0601] The following example schemes are provided for the guidance of the reader, and collectively represent an example method for making the compounds provided herein. Furthermore, other methods for preparing compounds of the disclosure will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. The skilled artisan is thoroughly equipped to prepare these compounds by those methods given the literature and this disclosure. The compound numberings used in the synthetic schemes depicted below are meant for those specific schemes only, and should not be construed as or confused with same numberings in other sections of the application. Unless otherwise indicated, all variables are as defined above.
General procedure

Compounds of Formula (I) of the present disclosure can be prepared as depicted in Scheme 1a.

Scheme 1a

1) R^3-Y (Y = Br, -B(OH)₂, or boronate)

2) deprotection

III

(X = Br, -B(OH)₂, or boronate ester)

IV

Conditions A (R^* = R⁵): 1) Suzuki coupling; 2) deprotection

Conditions B (R^* = Br or Cl): 1) Suzuki coupling; 2) R^5-Y' (VII, Y' = -B(OH)₂ or boronate ester), Suzuki coupling; 3) deprotection

V

VI

Compound I, wherein PG is a protecting group such as THP, undergoes Suzuki coupling with Compound II to provide Compound III. In certain embodiments, Compound I (X = Br) undergoes Suzuki coupling with Compound II (Y = -B(OH)₂ or boronate ester) to provide Compound III after removal of the protecting group. In other embodiments, Compound I (X = Br) is first converted to the corresponding boronic acid or boronate ester (not shown), which in turn undergoes Suzuki coupling with Compound II (Y = Br) to provide Compound III after removal of the protecting group. Treatment of Compound III with KOH and BOC₂ affords the protected iodide IV.

In certain embodiments, when R^* is R⁵ (e.g., a six-membered ring), Suzuki coupling between iodide (IV) and boronic acid (V) followed by removal of the protecting groups affords the desired bi-heteroaryl product VI (see, for example, conditions A above).

In other embodiments, when R^* is Br or Cl, the resultant Suzuki product can further undergo a second Suzuki coupling to install the R⁵ substituent. In some cases, this procedure is useful when the R⁵ substituent is a five-membered ring. In these embodiments,
removal of the protecting groups affords the desired bi-heteroaryl product VI. See, for example, conditions B above.

[0606] Compounds of Formula (I) of the present disclosure can be prepared as depicted in Scheme 1.

Scheme 1

[0607] Scheme 1 describes a method for preparation of 3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine compounds (IX) by either converting the lH-pyrazolo[4,3-b]pyridine (I) to the tributylstannane (II) followed by Migita-Kosugi-Stille coupling to form (III) with various bromo compounds or by reacting (I) directly with various boronic acids (VIII) using Suzuki coupling to produce compound (III) analogs. Compounds (III) are then deprotected before iodination of (IV) with iodine and sodium periodate to produce compound (V) analogs. The 3-iodo-lH-pyrazolo[4,3-b]pyridine (V) nitrogen is then protected with Boc followed by Suzuki coupling with the Boc protected (lH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (VII) to form the protected 3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine compounds (VIII). Final deprotection of the pyrazole nitrogen yields the desired substituted 3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine compounds (IX).
Alternatively, compounds of Formula (I) of the present disclosure can be prepared as depicted in Scheme 2.

**Scheme 2**


**Illustrative Compound Examples**

Preparation of intermediates (XVII) and (XVIII) are depicted below in Scheme 3.

**Scheme 3**

**Step 1**

A suspension of 6-bromo-2-methyl-3-nitropyridine (XIV) (250 g, 1.15 mol, 1.00 eq) and NH₄Cl (300 g, 5.61 mol, 4.88 eq) in EtOH (3.50 L) and water (150 mL) was heated
with stirring to 65°C. To this mixture was added Fe (130 g, 2.33 mol, 2.02 eq) and HCl (15.3 g, 419 mmol, 0.36 eq). The suspension was then heated to 80°C for another 3 h. The reaction was cooled to 25°C and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure to yield a residue that was taken up in EtOAc (1 L x 3) and washed with brine. The organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure to give 6-bromo-2-methylpyridin-3-amine (XV) as brown solid (373 g, 1.99 mol, 86.7% yield) which was used for the next step without any purification. 1H NMR (DMSO-d6, 400 MHz) δ ppm 6.01 (dd, J = 2.3, 7.9 Hz, 2H), 7.03 (d, J = 8.2 Hz, 1H); ESIMS found for C6H5BrN3 m/z 186.8 (M+H).

**Step 2**

[0612] To a suspension 6-bromo-2-methylpyridin-3-amine (XV) (186 g, 994 mmol, 1.00 eq) and KOAc (115 g, 1.17 mol, 1.18 eq) in CHCl3 (3.50 L) was added Ac2O (405 g, 3.97 mol, 3.99 eq) and the suspension was stirred at 25°C for 1 h and then heated at 60-70°C to reflux for an additional 2 h. After cooling the suspension to 25°C, isopentyl nitrate (233 g, 1.99 mol, 2.00 eq) and 18-crown-6 (21 g, 79.5 mmol, 0.08 eq) was added and the suspension heated to reflux for 12 h. After cooling to 25°C, the suspension was filtered and the filtrate was concentrated under reduced pressure to yield a residue that was treated with a suspension of potassium carbonate (450 g) in a solution of methanol and water (450 mL) at 0°C for 3 h. The suspension was concentrated under reduced pressure to yield a residue that was extracted with EtOAc (1000 mL x 3) and washed with brine. The organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure to give 5-bromo-1H-pyrazolo[4,3-b]pyridine (XVI) (405 g, crude) as yellow solid. The crude product was used for the next step without any purification. 1H NMR (DMSO-d6, 400 MHz) δ ppm 7.49 (d, J = 8.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 8.27 (s, 1H); ESIMS found for C6H4BrN3 m/z 198.1 (M+H).

**Step 3**

[0613] To a solution of 5-bromo-1H-pyrazolo[4,3-b]pyridine (XVI) (200 g, 1.01 mol, 1.00 eq) in DCM (1.60 L), THF (1.60 L) and DMF (100 mL) at 25°C was added p-TsOH (19.2 g, 101 mmol, 0.10 eq). The reaction solution was stirred at 25°C for 6 h. The solvent was removed under vacuum. 10% NaHCO3 (1.5 L) and EtOAc (1.5 L) was added to the residue and the residue was washed with EtOAc (500 mL x 3). The layers were separated and the organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure to give 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[4,3-b]pyridine (XVII) (347 g, crude) as yellow
oil. The crude product was used for the next step without any purification. ESIMS found for CnHi2BrN3O mlz 281.7 (M+H).

Step 4

[0614] To a suspension of 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-lH-pyrazolo[4,3-b]pyridine (XVII) (260 g, 923 mmol, 1.00 eq) in 1,4-dioxane (3.0 L) was added LiCl (235 g, 5.54 mol, 6.0 eq), Cy3P (25.9 g, 92.3 mmol, 0.10 eq), bis(tributyltin) (643 g, 1.11 mol, 1.2 eq) and Pd2(dba)3 (42.3 g, 46.2 mmol, 0.05 eq) under Nitrogen. The resulting suspension was sealed in a pressure tube and heated at 100 °C for 4 hrs. The suspension was filtered through Celite. The filter cake was washed with EtOAc (200 mL x 3). The crude product was purified by column chromatography (PE/EtOAc = 4/1) to obtain the 1-tetrahydro-2H-pyran-2-yl)-5-(tributylstannyl)-1H-pyrazolo[4,3-b]pyridine (XVIII) (306 g, 621 mmol, 67.3% yield) as a yellow oil. ESIMS found for C2H3BrN2OSn mlz 494.2 (M+H).

[0615] Preparation of intermediate N-(5-bromopyridin-3-yl)pivalamide (XXI) is depicted below in Scheme 4.

![Scheme 4](image)

Step 1

[0616] To a solution of 3-amino-5-bromo pyridine (XIX) (1.0 g, 5.78 mmol) in dry pyridine (10 mL) was added pivaloyl chloride (XX) (769 mg, 6.38 mmol). The reaction mixture was stirred at room temperature for 3 h. The reaction was poured into an ice water/saturated aqueous NaHCO3 mixture and stirred for 30 min. The precipitate was filtered, washed with cold water and dried at room temperature to yield N-(5-bromopyridin-3-yl)pivalamide (XXI) as an off-white solid (1.082 g, 4.22 mmol, 73.1% yield). ¾ NMR (DMSO-δ6, 500 MHz) δ ppm 1.23 (s, 9H), 8.37 (d, J=2Hz, 1H), 8.39 (t, J=2Hz, 1H), 8.80 (d, J=2Hz, 1H), 9.58 (brs, 1H); ESIMS found C10H13BrN2O mlz 258.9 (Br91M+H).

[0617] The following intermediates were prepared in accordance with the procedure described in the above Scheme 4.
[0618] N-(5-Bromopyridin-3-yl)isobutyramide (XXII): Off-white solid, (71\% yield). ¾ NMR (CDCl$_3$) δ ppm 8.55-8.35 (m, 3H), 7.32 (s, 1H), 2.59-2.48 (m, 1H), 1.28-1.27 (d, 6H); ESIMS found C$_5$H$_9$BrN$_2$O $m/z$ 242.9 (Br$^{79}$M+H).

[0619] N-(5-Bromopyridin-3-yl)propionamide (XXIII): Off white solid (92\% yield). ¾ NMR (DMSO-d$_6$) δ ppm 1.09 (t, $J$=7.54 Hz, 3H), 2.36 (q, $J$=7.54 Hz, 2H), 8.36 (m, 2H), 8.65 (d, $J$=2.07 Hz, 1H), 10.26 (s, 1H); ESIMS found C$_8$H$_8$BrN$_2$O $m/z$ 231.1 (Br$^{81}$M+H).

[0620] N-(5-Bromopyridin-3-yl)butyramide (XXIV): Yellow solid (2.1 g, 8.64 mmol, 88.8\% yield). ¾ NMR (CD$_3$OD, 400 MHz) δ ppm 1.02 (t, $J$=7.2 Hz, 3H), 1.74 (sxt, $J$=7.2Hz, 2H), 2.40 (t, $J$=7.2Hz, 2H), 8.35 (d, $J$=2Hz, 1H), 8.46 (t, $J$=2Hz, 1H), 8.63 (d, $J$=2Hz, 1H); ESIMS found C$_8$H$_8$BrN$_2$O $m/z$ 243.1 (Br$^{79}$M+H).

[0621] N-(5-Bromopyridin-3-yl)pentanamide (XXV): Yellow solid (2.0 g, 7.78 mmol, 85.3\% yield). ¾ NMR (CD$_3$OD, 400 MHz) δ ppm 0.98 (t, $J$=7.4Hz, 3H), 1.43 (sxt, $J$=7.4Hz, 2H), 1.70 (quin, $J$=7.4Hz, 2H), 2.43 (t, $J$=7.6Hz, 2H), 8.35 (s, 1H), 8.45 (d, $J$=2Hz, 1H), 8.64 (d, $J$=2Hz, 1H); ESIMS found C$_{10}$H$_9$BrN$_2$O $m/z$ 256.9 (Br$^{79}$M+H).

XXVI
N-(5-Bromopyridin-3-yl)-3-methylbutanamide (XXVI): Off white solid, (67% yield), ¾ NMR (CDCl$_3$, 500 MHz) δ ppm 8.55-8.42 (m, 3H), 7.62 (s, IH), 2.31-2.18 (m, 3H), 1.02-1.01 (d, J = 6Hz, 6H); ESIMS found C$_{10}$H$_{13}$BrN$_2$O mlz 258.9 (Br$_{8}^{1}$M+H).

N-(5-Bromopyridin-3-yl)-3,3-dimethylbutanamide (XXVII): Yellow solid (1.7 g, 6.27 mmol, 78.6% yield). ¾ NMR (CD$_3$OD, 400 MHz) δ ppm 1.10 (s, 9H), 2.29 (s, 2H), 8.36 (d, J=1.6Hz, IH), 8.46 (d, J=2.0Hz, IH), 8.64 (d, J=2.0Hz, IH); ESIMS found C$_n$H$_m$BrN$_2$O mlz 273.1 ((Br$_{8}^{1}$M+H).

N-(5-Bromopyridin-3-yl)-2-phenylacetamide (XXVIII): White solid (2.5 g, 8.59 mmol, 77.9% yield). ¾ NMR (CDCl$_3$, 400 MHz) δ ppm 3.76 (s, 2H), 7.26-7.45 (m, 5H), 7.57 (brs, IH), 8.33 (s, IH), 8.37 (s, 2H); ESIMS found C$_{13}$H$_n$BrN$_2$O mlz 292.8 (Br$_{8}^{1}$M+H).

N-(5-Bromopyridin-3-yl)benzamide (XXIX): White solid (2.7 g, 9.74 mmol, 60% yield). ¾ NMR (CDCl$_3$, 400 MHz) δ ppm 7.40-7.52 (m, 2H), 7.52-7.62 (m, IH), 7.86 (d, J=7.2Hz, 2H), 8.39 (d, J=1.6Hz, IH), 8.46 (s, IH), 8.55 (d, J=1.6Hz, IH), 8.57 (d, J=2.0Hz, IH); ESIMS found C$_{12}$H$_n$BrN$_2$O mlz 278.8 (Br$_{8}^{1}$M+H).

N-(5-Bromopyridin-3-yl)cyclopropanecarboxamide (XXX): Off-white solid, (83% yield), ¾ NMR (CDCl$_3$, 500 MHz) δ ppm 8.46-8.39 (m, 3H), 7.54 (bs, IH), 1.56-1.50 (m, 2H), 1.13-1.07 (m, 2H), 0.96-0.90 (m, 2H); ESIMS found C$_9$H$_n$BrN$_2$O mlz 240.9 (Br$_{8}^{1}$M+H).
N-(5-Bromopyridin-3-yl)cyclobutanecarboxamide (XXXI): Yellow solid (2.1 g, 6.27 mmol, 86.6% yield). ¾ NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm 1.80-1.99 (m, 1H), 1.99-2.15 (m, 1H), 2.16-2.30 (m, 2H), 2.30-2.45 (m, 2H), 3.25-3.35 (m, 1H), 8.34 (d, J=2.0Hz, 1H), 8.47 (s, 1H), 8.64 (d, J=2.0Hz, 1H); ESIMS found C<sub>10</sub>H<sub>11</sub>BrN<sub>2</sub>O m/z 257.1 (Br<sup>81</sup>M+H).

N-(5-Bromopyridin-3-yl)cyclopentanecarboxamide (XXXII): Yellow solid (1.9 g, 7.06 mmol, 80.2% yield). ¾ NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm 1.57-1.74 (m, 2H), 1.74-1.91 (m, 4H), 1.91-2.07 (m, 2H), 2.77-2.92 (m, 1H), 8.34 (d, J=1.6Hz, 1H), 8.45 (s, 1H), 8.65 (d, J=2.0Hz, 1H); ESIMS found C<sub>n</sub>H<sub>13</sub>BrN<sub>2</sub>O m/z 271.1 (Br<sup>81</sup>M+H).

N-(5-bromopyridin-3-yl)cyclohexanecarboxamide (XXXIII): Yellow solid (2.0 g, 7.06 mmol, 84.3% yield). ¾ NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm 1.19-1.46 (m, 3H), 1.46-1.63 (m, 2H), 1.74 (d, J=11.6Hz, 1H), 1.88 (s, J=14.0Hz, 4H), 2.40 (tt, J=11.6Hz, J=3.6Hz, 1H), 8.34 (d, J=2.0Hz, 1H), 8.44 (t, J=2.0Hz, 1H), 8.64 (d, J=2.0Hz, 1H); ESIMS found C<sub>12</sub>H<sub>19</sub>BrN<sub>2</sub>O m/z 285.1 (Br<sup>81</sup>M+H).

N-(5-bromopyridin-3-yl)-2-cyclohexylacetamide (XXXIV): Yellow solid (261 mg, 0.878 mmol, 84.4% yield). ESIMS found C<sub>14</sub>H<sub>19</sub>BrN<sub>2</sub>O m/z 297A (Br<sup>81</sup>M+H).

Preparation of intermediate 5-bromo-N,N-dimethylpyridin-3-amine (XXXVI) is depicted below in Scheme 5.
Step 1

To a solution of 3,5-dibromopyridine (XXXV) (2.37 g, 10.0 mmol) in dry DMF (20.0 mL) was added K₂CO₃ (4.5 g, 33 mmol) and dimethylamino hydrochloride (1.79 g, 22 mmol). The mixture was heated overnight at 200°C in a sealed tube. The solution was cooled to room temperature and excess DMF was removed under vacuum. The residue was partitioned between EtOAc and water. The organic phase was separated. The aqueous phase was washed with EtOAc and the combined organic phases were dried over MgSO₄, and concentrated to afford 5-bromo-N,N-dimethylpyridin-3-amine (XXXVI) as an off-white solid (1.78 g, 8.85 mmol, 88% yield).

¾ NMR (DMSO-d₆, 500 MHz) δ ppm 2.94 (s, 6H), 7.25 (t, J=2Hz, 1H), 7.91 (d, J=2Hz, 1H), 8.07 (d, J=2Hz, 1H); ESIMS found C₇H₃BrN₂ mlz 201.1 (M+H).

Steps 1

Preparation of intermediate 5-bromo-N-isopropylpyridin-3-amine (XXXVII) is depicted below in Scheme 6.

To a solution of 5-bromopyridin-3-amine (XIX) (535 mg, 3.09 mmol) in MeOH (62 mL) was added acetone (296 µL, 4.02 mL). The pH was adjusted to 4 using HOAc and stirred for 30 min. NaCNB₃ (272 mg, 4.33 mmol) was added and stirred at room temperature overnight. The MeOH was removed under vacuum and the residue was partitioned between EtOAc and saturated aqueous NaHCO₃. The organic layer was dried over MgSO₄ and evaporated under vacuum. The crude product was purified on a silica gel column (100% hexane → 90:10 hexane:EtOAc) to produce 5-bromo-N-isopropylpyridin-3-amine (XXXVII) as an oil which slowly solidified into an off-white solid (309 mg, 1.44 mmol, 47% yield).

¾ NMR (DMSO-d₆, 500 MHz) δ ppm 1.12 (d, J=6.3Hz, 6H), 3.55-3.59 (m, 1H), 6.03 (d, J=7.9Hz, 1H), 7.25 (t, J=2Hz, 1H), 7.91 (d, J=2Hz, 1H), 8.07 (d, J=2Hz, 1H); ESIMS found C₇H₅BrN₂ mlz 201.1 (M+H).
7.05-7.06 (m, 1H), 7.75 (d, J=2Hz, 1H), 7.90 (d, J=2Hz, 1H); ESIMS found C₈H₉BrN₂ mlz 215.1 (M+H).

[0635] Preparation of intermediate 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (XXXIX) is depicted below in Scheme 7.

Scheme 7

Steps 1

[0636] Preparation of 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (XXXIX) was performed following the procedure listed in Scheme 6, Step 1. Brown oil (1.20 g, 5.59 mmol, 45% yield). ¾ NMR (DMSO-D₆, 500 MHz) δ ppm 2.15 (s, 6H), 3.43 (s, 2H), 7.94 (s, 1H), 8.47 (d, J=1.1Hz, 1H), 8.59 (d, J=2.2Hz, 1H); ESIMS found C₈H₉BrN₂ mlz 215 (M⁺Br⁺) and 217 (M⁺Br⁺+H).

[0637] Preparation of intermediate 3-bromo-5-((3,3-difluoropyrrolidin-1-y1)methyl)pyridine (XL) is depicted below in Scheme 8.

Scheme 8

Steps 1

[0638] To a mixture of 5-bromopyridine-3-carbaldehyde (XXXVIII) (6.00 g, 32.26 mmol, 1.0 eq), 3,3-difluoropyrrolidine (5.56 g, 38.71 mmol, 1.20 eq) and TEA (5.39 mL, 38.71 mmol, 1.2 eq) in DCE (200 mL) was stirred at room temperature for 30 min, then added sodium triacetoxyborohydride (10.25 g, 48.38 mmol, 1.50 eq) in one portion at room temperature under N₂. The mixture was stirred at room temperature for 6 h. TLC showed the reaction was complete. The reaction was quenched with IN NaOH (100 mL), extracted with DCE (100 mL x 2). The combined organic layers were washed with brine (100 mL), dried and concentrated. The residue was purified by silica gel chromatography (column height: 50 mm, diameter: 50 mm, 300-400
mesh silica gel, DCM/MeOH=30/l → 20/l) to give 3-bromo-5-((3,3-difluoropyrrolidin-l-yilmethyl) pyridine (XL): Yellow oil (8.00 g, 28.9 mmol, 89.5% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 2.30 (spt, J=7.2Hz, 2H), 2.75 (t, J=6.8Hz, 2H), 2.91 (t, J=13.2Hz, 2H), 7.85 (s, IH), 8.45 (s, IH), 8.59 (d, J=2Hz, IH); ESIMS found for C₁₉H₁₂BrF₂N₂ mlz 277.0 (M+H).

[0639] The following intermediates were prepared in accordance with the procedure described in the above Schemes 6-8.

**XLII**

3-Bromo-5-(piperidin-l-yilmethyl)pyridine (XLII): Brown liquid (13.1 g, 94% yield). ¾ NMR (DMSO-Ç tf , 400 MHz) δ ppm 1.36-1.39 (m, 2H), 1.46-1.51 (m, 4H), 2.31-2.32 (m, 4H), 3.46 (s, 2H), 7.94 (s, IH), 8.47 (d, J=2Hz, IH), 8.58 (d, J=3Hz, IH); ESIMS found for C₁₉H₁₂BrN₂ mlz 257.0 (M+H).

**XLIII**

N-((5-Bromopyridin-3-yl)methyl)ethanamine (XLIII): Golden liquid (1.29 g, 6.00 mmol, 60% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.14 (t, J=7.2Hz, 3H), 2.67 (q, J=7.2Hz, 2H), 3.79 (s, 2H), 7.85 (t, J=2Hz, IH), 8.46 (d, J=1.6Hz, IH), 8.56 (d, J=2.4Hz, IH); ESIMS found for C₈H₁₆BrN₂ mlz 215.1 (M+H).

**XLIV**

N-Benzyl- 1-(5-bromopyridin-3-yl)methanamine (XLIV): Yellow oil (8.0 g, 28.9 mmol, 89.5% yield). ¾ NMR (DMSO-J₁, 400 MHz) δ ppm 3.71 (s, 2H), 3.74 (s, 2H), 7.18-
7.28 (m, 1H), 7.28-7.40 (m, 4H), 8.04 (s, 1H), 8.52 (s, 1H), 8.58 (s, 1H); ESIMS found for C$_{13}$H$_{13}$BrN$_2$ mlz 277.1 (M+H).

[0644] Preparation of intermediate tert-butyl (5-bromopyridin-3-yl)methyl (cyclopentylmethyl)carbamate (XLIX) is depicted below in Scheme 9.

![Scheme 9](image)

**Step 1**

[0645] To a solution of 5-bromonicotinaldehyde (XXXVIII) (2.0 g, 10.8 mmol, 1 eq) in MeOH (20 mL) was added NaBH$_4$ (2.4 g, 64.9 mmol, 6 eq) and the reaction mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo and the residue was diluted in water (15 mL), the aqueous phase was extracted with DCM (10 mL x 3). The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo to afford (5-bromopyridin-3-yl)methanol (XLV) (1.8 g, 9.57 mmol, 90.0% yield) as a colorless oil. $^1$H NMR (CDCl$_3$, 500 MHz) δ ppm 4.73 (s, 2H), 7.90 (s, 1H), 8.47 (s, 1H), 8.57 (s, 1H). ESIMS found for C$_{8}$H$_{6}$BrNO mlz 188.0 (M+H).

**Step 2**

[0646] To a stirred solution of (5-bromopyridin-3-yl)methanol (XLV) (1.60 g, 8.5 mmol, 1 eq), phthalimide (1.24 g, 8.5 mmol, 1 eq) and PPI$_{13}$ (3.33 g, 12.75 mmol, 1.5 eq) in anhydrous THF (15 mL) was added DEAD (2.21 g, 12.75 mmol, 1.5 eq) dropwise at 0°C under N$_2$. Then the reaction mixture was stirred at room temperature for 6 h. The mixture was washed with saturated NaHCO$_3$ solution (15 mL), water (15 mL) and brine (15 mL) subsequently. The organic layers were dried over MgSO$_4$, concentrated under reduced pressure, the resultant residue
was purified by flash chromatography on silica gel (PE:EtOAc = 4:1) to give 2-((5-bromopyridin-3-yl)methyl)isoindoline-1,3-dione (XLVI) (2.5 g, 7.88 mmol, 82.3% yield) as a white solid. ESIMS found for C_{14}H_{7}BrN_{2} m/z 317.1 (M+H).

Step 3

[0647] A solution of 2-((5-bromopyridin-3-yl)methyl)isoindoline-1,3-dione (XLVI) (1.9 g, 6.0 mmol, 1 eq) and hydrazine hydrate (2.0 g, 40 mmol, 6 eq) in EtOH (20 mL) was heated at 70°C for 3 h. The mixture was filtered through a Celite® pad and the filtrate was concentrated in vacuo to give crude product. ESIMS found for C_{14}H_{9}BrN_{2} m/z 347.1 (M+H).

Step 4

[0648] A solution of (5-bromopyridin-3-yl)methanamine (XLVII) (1.30 g, 5.8 mmol, 1.0 eq), cyclopentanecarbaldehyde (0.57 g, 5.8 mmol, 1.0 eq) and TEA (0.60 g, 5.8 mmol, 1.0 eq) in MeOH (15 mL) was stirred at room temperature for 2 h. Then NaBH₄CN (1.98 g, 34.6 mmol, 6.0 eq) was added and the mixture was stirred at the same temperature for another 3 h. The solvent was removed under reduced pressure and the residue was diluted in water (20 mL) and extracted with DCM (10 mL x 3), combined organic layers were dried over MgSO₄ and concentrated in vacuo to give 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl)methanamine (XLVIII) (1.23 g, 4.57 mmol, 79.3% yield) as a yellow oil. ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.07-1.23 (m, 2H), 1.47-1.67 (m, 4H), 1.70-1.84 (m, 2H), 2.02 (spt, J=7.6Hz. IH), 2.53 (d, J=7.2Hz, 2H), 3.80 (s, 2H), 7.86 (s, IH), 8.47 (s, IH), 8.56 (d, J=2.0Hz, IH); ESIMS found for C_{12}H_{14}BrN_{2} m/z 269.1 (M+H).

Step 5

[0649] To a solution of 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl) methanamine (XLVIII) (1.00 g, 3.7 mmol, 1 eq) and TEA (0.93 g, 9.2 mmol, 2.5 eq) in DCM (20 mL) was added portion wise Boc₂O (0.85 g, 4.0 mmol, 1.1 eq) at 0°C, the reaction mixture was stirred at room temperature for 1 h. The mixture was washed with water (10 mL), brine (10 mL), the organic layer was separated, dried over MgSO₄ and concentrated in vacuo to give tert-butyl
(5-bromopyridin-3-yl)methyl(cyclopentylmethyl) carbamate (XLIX) (1.25 g, 3.38 mmol, 91.9% yield) as a white solid. ESIMS found for C_{17}H_{25}BrN_{2}O_{2} m/z 369.1 (M+H).

[0650] Preparation of intermediate 3-bromo-5-(cyclohexyloxy)pyridine (LII) is depicted below in Scheme 10.

![Scheme 10](image)

**Step 1**

[0651] To a solution of 5-bromopyridin-3-ol (L) (523 mg, 3.01 mmol) in THF (30 mL) cooled to 0°C were added triphenylphosphine (867 mg, 3.31 mmol) and cyclohexanol (LI) (331 mg, 3.31 mmol) followed by (£)-bis(4-chlorobenzyl) diazene-1,2-dicarboxylate (1.21 g, 3.31 mmol), added portion wise. The reaction mixture was then stirred at 25°C overnight. The reaction was worked-up with an EtOAc-NaHCO_3 extraction and the solid filtered off. The solvent was removed and the residue was purified by ISCO (20% EtOAc-hexanes) to give 3-bromo-5-(cyclohexyloxy)pyridine (LII) (209 mg, 0.82 mmol, 27.2% yield) as a yellow oil. ½ NMR (DMSO-d_6, 500 MHz) δ ppm 1.21 - 1.31 (m, 1 H) 1.34 - 1.48 (m, 4 H) 1.49 - 1.57 (m, 1 H) 1.70 (br dd, J=9.74, 4.25 Hz, 2 H) 1.88 - 1.96 (m, 2 H) 2.50 (dt, J=3.70, 1.72 Hz, 5 H) 4.46 - 4.54 (m, 1 H) 7.72 (t, J=2.20 Hz, 1 H) 8.24 (d, J=1.92 Hz, 1 H) 8.27 (d, J=2.47 Hz, 1 H).

[0652] The following intermediate was prepared in accordance with the procedure described in the above Scheme 10.

![LIII](image)

[0653] tert-Butyl 4-((5-bromopyridin-3-yl)oxy)piperidine-1-carboxylate (LIII): Yellow oil (244 mg, 0.683 mmol, 23.2% yield). ESIMS found for C_{17}H_{25}BrN_{2}O_{3} m/z 358.3 (M+H).
Preparation of intermediate 3-(benzyloxy)-5-bromopyridine (LV) is depicted below in Scheme 11.

**Scheme 11**

**Step 1**
To a solution of 5-bromopyridin-3-ol (L) (174 mg, 1.0 mmol) in DMF (3 inL) was added potassium carbonate (415 mg, 3.0 mmol). The slurry was heated at 90°C for 1 h and then cooled to 25°C. The (bromomethyl)benzene (LIV) (171 mg, 1.0 mmol) was added and the mixture was stirred at 25°C overnight. The reaction was worked-up using a saturated sodium bicarbonate and EtOAc extraction. The product was purifed by ISCO column (40-100% EtOAc-hexanes). The 3-(benzyloxy)-5-bromopyridine (LV) (105 mg, 0.398 mmol, 39.8 % yield) was obtained as yellow oil. ESIMS found for C_{12}H_{10}BrNO mlz 266.1 (M+H).

The following intermediates were prepared in accordance with the procedure described in the above Scheme 11.

**LVI**

3-Bromo-5-(2-(pyrrolidin-1-yl)ethoxy)pyridine (LVI): Yellow oil (97 mg, 0.358 mmol, 15.56% yield). ESIMS found for C_{14}H_{15}BrN_2O mlz 272.2 (M+H).

**LVII**

2-((5-Bromopyridin-3-yl)oxy)-N,N-dimethylethan-1 -amine (LVII): Yellow oil (97 mg, 0.396 mmol, 28.9% yield). ESIMS found for C_{9}H_{13}BrN_2O mlz 245.1 (M+H).
LVIII

[0659] L-(2-(3-Bromo-5-fluorophenoxy)ethyl)pyrrolidine (LVIII): Yellow oil (370 mg, 1.284 mmol, 85.8% yield). ESIMS found for C₁₂H₁₅BrFNO \text{mlz} 289.0 (M+H).

LIX

[0660] 2-(3-Bromo-5-fluorophenoxy)-N,N-dimethylethan-l-amine (LIX): Yellow oil (364 mg, 1.389 mmol, 50.2% yield). ESIMS found for C₁₀H₁₃BrFNO \text{mlz} 263.9 (M+H).

[0661] Preparation of intermediate tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXI) is depicted below in Scheme 12.

![Scheme 12](image)

Step 1

[0662] To a solution of 2-(1-(fert-butoxycarbonyl)piperidin-4-yl)acetic acid (LX) (3.4 g, 13.97 mmol) in DCM (10 inL) was added DMF (1 mL). The solution was cooled in ice-water to 0°C. Oxalyl chloride (1.835 mL, 20.96 mmol) was then added dropwise. The mixture was stirred for 1 h at 25°C. The organic volatile was then removed under vacuum. The residue was dissolved in DCM (10 mL). DMAP (0.17 g, 1.397 mmol) and 5-bromopyridin-3-amine (XIX) (2.418 g, 13.97 mmol) were added to the solution and cooled to 0°C. DIPEA (4.88 ml, 27.9 mmol) was then added dropwise and the mixture was stirred for 2 h at 25°C. The reaction was worked-up with DCM and saturated NaHCCl. The product was purified by ISCO (0-100% EtOAc-hexanes). The tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXI) (2.82 g, 7.08 mmol, 50.7 % yield) was obtained as a yellow oil. ESIMS found for C₁₇H₂₄BrN₃O₃ \text{mlz} 343.1 (M-56).

[0663] The following intermediate was prepared in accordance with the procedure described in the above Scheme 12.
N-(5-Bromopyridin-3-yl)-2-(dimethylamino)acetamide (LXII): Yellow oil (528 mg, 2.05 mmol, 19.0% yield). ESIMS found for C_{13}H_{12}BrN_{3}O mlz 259.3 (M+H).

Preparation of intermediate tert-butyl (1-(6-chloropyrazin-2-yl)azetidin-3-yl)carbamate (LXV) is depicted below in Scheme 13.

Scheme 13

Step 1

To a solution of tert-butyl azetidin-3-ylcarbamate hydrochloride (LXIII) (2 g, 9.58 mmol) in dry DMF (19.2 mL) was added DIPEA (8.37 ml, 47.9 mmol). To this mixture was added 2,6-dichloropyrazine (LXIV) (1.428 g, 9.58 mmol) and the reaction was stirred at 95°C for 3 h. The reaction was quenched with water (20 mL) and extracted with EtOAc. The organic layer was dried over anhydrous Na_{2}SO_{4}, filtered and concentrated. The residue was purified by silica gel column chromatography (40 g) (100% hexanes → hexanes:EtOAc 1:1) to yield tert-butyl (1-(6-chloropyrazin-2-yl)azetidin-3-yl)carbamate (LXV) (2.2882 g, 8.04 mmol, 84 % yield) as a white solid. ESIMS found for C_{12}H_{17}CIN_{4}O_{2} mlz 285.1 (M+H).

Preparation of intermediate N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)methanesulfonamide (LXIX) is depicted below in Scheme 14.
Step 1

A solution of 3-bromo-5-fluorobenzonitrile (LXVI) (44.0 g, 220.0 mmol, 1.0 eq) was dissolved in THF (30 mL). BH₄-Me₂S (33.43 g, 440.0 mmol, 2.0 eq) was added to the solution at 20°C. Then it was stirred at 80°C for 2 h, HCl (6 N, 100 mL) was added to the mixture slowly at 20°C. The mixture was stirred at 80°C for 1 h, then it was washed with EtOAc (300 mL). The water phase was basified with 50% aqueous NaOH and it was extracted with EtOAc (300 mL x 3). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated in vacuo to produce 3-bromo-5-fluoro-phenyl)methanamine (LXVII) (24.0 g, 117.62 mmol, 53.5% yield). ¾ NMR (CDCl₃, 300 MHz) ppm 3.86 (s, 2H), 7.01 (d, J=8Hz, IH), 7.12 (d, J=8Hz, IH), 7.28 (s, IH); ESIMS found C₇H₇BrFN mlz 203.9 (Br⁺M+H).

Step 2

A solution of (3-bromo-5-fluoro-phenyl)methanamine (LXVII) (23.0 g, 112.7 mmol, 1.0 eq) was dissolved in DCM (15 mL), TEA (34.22 g, 338.2 mmol, 3.0 eq) was added to the mixture. Then MsCl (13.44 g, 117.3 mmol, 1.04 eq) was added slowly to the solution at 0°C. It was stirred at 0-30°C for 2 h. The reaction was washed with water and extracted with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated to give N-(3-bromo-5-fluorobenzyl)methanesulfonamide (LXVIII) (34.0 g, 102.44 mmol, 90.9% yield, 85% purity) as an oil. ¾ NMR (CDCl₃, 300 MHz) ppm 2.88 (s, 3H), 4.24 (d, J=4.5Hz, 2H), 6.99 (d, J=9Hz, IH), 7.13 (dt, J=8.1Hz, J=2Hz, IH), 7.25 (s, IH); ESIMS found C₈H₉BrFN=S mlz 282.0 (Br⁺M+H).

Step 3

A solution of N-(3-bromo-5-fluorobenzyl)methanesulfonamide (LXVIII) (34.0 g, 102.4 mmol, 1.0 eq) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (52.02 g, 204.9 mmol, 2.0 eq) KOAc (20.11 g, 204.9 mmol, 2.0 eq) was dissolved in dioxane (20 mL). Then Pd(dppf)Cl₂ (7.60 g, 10.2 mmol, 0.1 eq) was added to the mixture. It was stirred at 90°C for 2 h. Then the solvent was removed to get the residue which was purified by silica gel column (PE:EtOAc = 10:1 → 100% EtOAc) to get N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)methanesulfonamide (LXIX) (30.0 g, crude). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.37 (s, 12H), 2.92 (s, 3H), 4.34 (d, J=6.3Hz, 2H), 7.19 (dt, J=9.3Hz, J=2.1Hz, IH), 7.44 (dd, J=8.7Hz, J=2.4Hz, IH), 7.54 (s, IH); ESIMS found C₁₉H₂₁BFNO₅ mlz 330.1 (M⁺H).
Preparation of intermediate N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl) methanesulfonamide (LXXIII) is depicted below in Scheme 15.

**Scheme 15**

**Step 1**

To mixture of 1,3-dibromo-5-fluorobenzene (LXX) (100 g, 393 mmol) and N,N'-dimethylthene-1,2-diamine (173 g, 1.97 mol, 214 mL) was added t-BuOK (88 g, 787 mmol) in one portion at 25°C under N2. The mixture was stirred at 25°C for 30 min, then heated to 110°C and stirred for 11.5 h. The mixture was cooled to 25°C and concentrated in reduced pressure at 45°C. The residue was purified by silica gel chromatography (column height: 250 mm, diameter: 100 mm, 100-200 mesh silica gel, PE/EtOAc = 2:1, Rf = 0.6) to give N^1^-bromo-5-fluorophenyl)-N^2^-dimethylthene-1,2-diamine (LXXI) (30 g, 114.9 mmol, 29.2% yield) as a yellow oil. ESIMS found for C11H14BrFN2 m/z 261.1 (M+H).

**Step 2**

To a mixture of N^1^-S-bromo-S-fluorophenyl^-N^2^-dimethylthene-1^-diamine (LXXI) (30 g, 114 mmol) in DCM (200 mL) was added (Boc)_2O (37.6 g, 172 mmol), TEA (34.8 g, 344 mmol) and DMAP (7 g, 57.4 mmol) in one portion at 25°C under N2. The mixture was stirred at 25°C for 12 h. The mixture was concentrated in reduced pressure at 45°C. The residue was purified by silica gel chromatography (column height: 250 mm, diameter: 100 mm, 100-200 mesh silica gel, PE/EtOAc = 2:1, Rf = 0.43) to give tert-butyl (3-bromo-5-fluorophenyl)(2-(dimethylamino)ethyl)carbamate (LXXII) (20 g, 55.4 mmol, 48.2% yield) as yellow oil. ¾ NMR (CDCl3, 400 MHz) δ ppm 1.43 (s, 9H), 2.21 (s, 6H), 2.41 (t, J=7Hz, 2H), 3.67 (t, J=7.2Hz, 2H), 6.96 (d, J=9.6Hz, IH), 7.06 (d, J=6Hz, IH), 7.22 (s, IH); ESIMS found for C15H22BrFN2O2 m/z 361.0 (M+H).

**Step 3**

To a mixture of tert-butyl (3-bromo-5-fluorophenyl)(2-(dimethylamino)ethyl)carbamate (LXXII) (19 g, 52.6 mmol) and bis(pinacolato) diboron (20 g, 78.9 mmol) in dioxane (60 mL) was added Pd(dpff)Cl2 (3.8 g, 5.26 mmol) and KOAc (30.9 g, 315.6 mmol) in
one portion at 25°C under N₂. The mixture was stirred at 25°C for 30 min, then heated to 110°C and stirred for 11.5 h. The mixture was cooled to 25°C and concentrated in reduced pressure at 45°C. The residue was purified by silica gel chromatography (column height: 250 mm, diameter: 100 mm, 100-200 mesh silica gel, PE/EtOAc = 1:1, Rf = 0.24) to give tert-butyl (2-(dimethylamino)ethyl)(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]carbamate (LXXIII) (15 g, 36.7 mmol, 69.8% yield) as yellow oil. ESIMS found for C21H34BFN2O4 mlz 327.2 (M+H as the boronic acid).

[0675] Preparation of intermediate (1-(fert-butoxycarbonyl)-4-(3-fluorophenyl)boronic acid (LXXVIII) is depicted below in Scheme 16

Scheme 16

Step 1

[0676] To a solution of 4-bromo-IH-pyrrolo[2,3-b]pyridine (LXXIV) (5 g, 25.4 mmol, 1 eq.), DMAP (311 mg, 2.55 mmol, 0.1 eq.) and TEA (5.3 mL, 38 mmol, 3 eq.) in DCM (100 mL) was added B0C2O (7.2 mL, 31 mmol, 1.2 eq.) at 0°C. The reaction was warmed to room temperature and stirred for 2 h. Water (100 mL) was added and extracted with DCM (x 2). Removal solvents gave tert-butyl 4-bromo-IH-pyrrolo[2,3-b]pyridine-l-carboxylate (LXXV) as a colorless oil (6.95 g, 23.4 mmol, 92.1% yield). 1H NMR (CDCl₃, 400 MHz) δ ppm 1.60 (s, 9H), 6.50 (d, J=4Hz, 1H), 7.31 (d, J=5.2Hz, 1H), 7.63 (d, J=4Hz, 1H), 8.23 (d, J=5.2Hz, 1H); ESIMS found for C12H13BrN2O2 mlz 297.1 (M+H).

Step 2

[0677] To a solution of tert-butyl 4-bromo-IH-pyrrolo[2,3-b]pyridine-l-carboxylate (LXXV) (1.5 g, 5.1 mmol, 1.0 eq) and (3-fluorophenyl)boronic acid (LXXVI) (1.07 g, 7.65 mmol, 1.1 eq) in a mixture solvent of dioxane (18 mL) and water (6 mL) was added K3PO4 (2.11 g, 15.3 mmol, 2.5 eq). The suspension was purged with nitrogen (x 3) followed by addition of Pd(dppf)Cl2 (373 mg, 0.51 mmol, 0.1 eq). The reaction was stirred at 60°C for 5 h. The suspension was poured into water (10 mL) and extracted with EtOAc (10 mL x 3). The combined
organic layer was washed with brine (5 mL), dried over Na2SO4 and concentrated under reduced pressure. Then the crude product was purified by column chromatography on silica gel to afford tert-butyl 4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (XLXXVII) as a white solid (1.37 g, 4.39 mmol, 86.0% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.69 (s, 9H), 6.68 (d, J=4Hz, 1H), 7.17 (dt, J=2Hz, J=8.4Hz, 1H), 7.25 (d, J=4.8Hz, 1H), 7.35 (d, J=12Hz, 1H), 7.41-7.53 (m, 2H), 7.70 (d, J=4Hz, 1H), 8.57 (d, J=4.8Hz, 1H); ESIMS found for C₁₈H₁₇FN₂O₂ m/z 313.1 (M+H).

Step 3

To a solution of tert-butyl 4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXVII) (1.37 g, 4.4 mmol, 1.0 eq) and triisopropyl borate (2.06 g, 10.9 mmol, 2.5 eq) in THF (10 mL), was added dropwise LDA (2 M, 5.45 mL, 10.9 mmol, 2.5 eq) at -78°C under N₂. The reaction was stirred at this temperature for 5 h. The reaction was acidified with IN HCl at -45°C until pH < 2. The aqueous phase was extracted with EtOAc (20 mL x 3). The combined organic phase was washed with cooled IN NaOH (50 mL x 2). The aqueous was added ice and acidified with IN HCl. The cloud solution was extracted with EtOAc (x 2). The organic phase was separated and dried with Na2SO4. The solvent was removed under reduced pressure to give crude (1-(tert-butoxycarbonyl)-4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXVIII) as a brown solid (0.98 g, 2.75 mmol, 62.5% yield). ESIMS found for C₁₈H₁₈BFN₂O₄ m/z 357.0 (M+H).

The following intermediate was prepared in accordance with the procedure described in the above Scheme 16.
(l-(tert-Butoxycarbonyl)-4-(4-fluorophenyl)-lH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXIX): White solid (580 mg, 1.63 mmol, 37.0% yield). ¾ NMR (DMSO-δ, 400 MHz) δ ppm 1.60 (s, 9H), 7.36 (d, J=4.8Hz, 1H), 7.41 (t, J=8.8Hz, 2H), 7.78 (dd, J=5.6Hz, J=9.2Hz, 2H), 8.36 (s, 2H), 8.42 (d, J=5.2Hz, 2H); ESIMS found for C₁₈H₁₈BFN₂O₂ mlz 357.0 (M+H).

Preparation of intermediate (1-(fert-butoxycarbonyl)-lH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXXII) is depicted below in Scheme 17

Step 1

To a solution of 1H-pyrrolo[2,3-b]pyridine (LXXX) (2.0 g, 16.9 mmol, 1 eq.), DMAP (103 mg, 0.84 mmol, 0.05 eq.) and TEA (12.7 mL, 50.7 mmol, 3 eq.) in DCM (30 mL) was added BOC₂O (4.7 mL, 18.6 mmol, 1.1 eq.) at 0°C. The reaction was warmed to room temperature and stirred for 2 h. Water (50 mL) was added and extracted with DCM (x 2). Removal solvents gave tert-butyl 1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXI) as a yellow oil (3.4 g, 15.6 mmol, 92.2% yield). ESIMS found for C₁₂H₁₄N₂O₂ mlz 219.1 (M+H).
Step 2

[0683] To a solution of tert-butyl 1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXI) (1.1 g, 5.0 mmol, 1.0 eq) and triisopropyl borate (2.0 g, 11.0 mmol, 2.2 eq) in THF (20 mL), was added dropwise LDA (2 M, 5.0 mL, 10.0 mmol, 2.0 eq) at -78°C under N₂. The reaction was stirred at this temperature for 5 h. The reaction was acidified with IN HCl at -45°C until pH < 2. The aqueous phase was extracted with EtOAc (20 mL x 3). The combined organic phase was washed with cooled IN NaOH (50 mL x 2). The aqueous was added ice and acidified with IN HCl. The cloud solution was extracted with EtOAc (x 2). The organic phase was separated and dried with Na₂SO₄. The solvent was removed under reduced pressure to give crude (1-(feri-butoxycarbonyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXXII) as a white solid (0.89 g, 3.39 mmol, 67.9% yield). ESIMS found for C₁₂H₁₅BN₂O₄ mlz 263.1 (M+H).

[0684] Preparation of intermediate (1-(fert-butoxycarbonyl)-4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXXVI) is depicted below in Scheme 18

Scheme 18

Step 1

[0685] A solution of tert-butyl 4-bromo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXV) (2 g, 6.8 mmol, 1.0 eq), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-y1)-1,3,2-dioxaborolane (2.07 g, 8.16 mmol, 1.0 eq), KOAc (1.99 g, 20.4 mmol, 3 eq) in dioxane (25 mL) was degassed (x 3) with a water pump. Pd(dppf)Cl₂ (246 mg, 0.34 mmol, 0.05 eq) was then added quickly in one portion under nitrogen. The reaction was stirred at 90°C for 6 h. Water (100 mL) was added and extracted with EtOAc (x 3). Flash chromatography (PE:EtOAc 20:1) gave fert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXIII) as a green oil (2.0 g, 5.82 mmol, 86.4%). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.39 (s, 12H), 1.67 (s, 9H), 6.93 (d, J =4Hz, 1H), 7.54 (d, J =4.8Hz, 1H), 7.65 (d, J =4Hz, 1H), 8.51 (d, J =4.4Hz, 1H); ESIMS found for C₁₂H₂₅BN₂O₄ mlz 345.1 (M+H).
Step 2

The solution of tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXIII) (890 mg, 2.59 mmol, 1.0 eq), 2-bromopyridine (LXXXIV) (410 mg, 2.59 mmol, 1.0 eq), K$_2$CO$_3$ (1.07 g, 7.77 mmol, 3 eq) in dioxane/water (11 mL 10:1) was degassed (x 3) with a water pump. Pd(dppf)Cl$_2$ (95 mg, 0.13 mmol, 0.05 eq) was added quickly in one portion under nitrogen. The reaction was stirred at 90°C for 5 h. Water (10 mL) was added and extracted with EtOAc (x 3). Flash chromatography gave tert-butyl 4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXV) as a yellow solid (420 mg, 1.42 mmol, 54.9%). ¾ NMR (CDCl$_3$, 400 MHz) δ ppm 1.69 (s, 9H), 7.10 (d, J=4Hz, IH), 7.36 (t, J=6Hz, IH), 7.58 (d, J=5.2Hz, IH), 7.72 (d, J=4Hz, IH), 7.80 - 7.86 (m, 2H), 8.62 (d, J=4.8Hz, IH), 8.82 (d, J=4.4Hz, IH); ESIMS found for C$_{17}$H$_{17}$N$_3$O$_2$ mlz 318.2 (M+Na).
To a solution of \textit{tert}-butyl 4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (LXXXV) (1.91 g, 6.5 mmol, 1.0 eq) and triisopropyl borate (3.05 g, 16.2 mmol, 2.5 eq) in THF (30 mL), was added dropwise LDA (2 M, 8.1 mL, 16.2 mmol, 2.5 eq) at -78°C under N2. The reaction was stirred at this temperature for 5 h. The reaction was acidified with IN HCl at -45°C until pH < 2. The aqueous phase was extracted with EtOAc (20 mL x 3). The combined organic phase was washed with cooled IN NaOH (50 mL x 2). The aqueous was added ice and acidified with IN HCl. The cloud solution was extracted with EtOAc (x 2). The organic phase was separated and dried with Na2SO4. The solvent was removed under reduced pressure to give crude (1-(teri-butoxycarbonyl)-4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (LXXXVI) as a white solid (1.31 g, 3.86 mmol, 59.4% yield). ESIMS found for C17H18BN3O4 m/z 362.1 (M+Na).

Preparation of intermediate (1-(fert-butoxycarbonyl)-4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCI) is depicted below in Scheme 19

\begin{center}
\includegraphics[width=\textwidth]{Scheme_19.png}
\end{center}

Scheme 19

Step 1

A solution of 4-bromo-1H-pyrrolo[2,3-b]pyridine (LXXIV) (10 g, 50.8 mmol, 1.0 eq) in anhydrous THF (150 mL) was degassed (x 3) with a water pump, then cooled to 0°C under Ar. NaH (60% in mineral oil) (2.436 g, 60.9 mmol, 1.2 eq) was added portion wise slowly under Ar. The reaction was stirred at 0°C for 30 min. (2-(chloromethoxy)ethyl)trimethylsilane (10.15 g, 60.9 mmol, 1.2 eq) was added dropwise slowly. The reaction was
stirred at room temperature for 2.5 h. The reaction mixture was added water (2 mL) then was concentrated in vacuo and water (50 mL) was added and extracted with EtOAc (x 3). The organic layer was washed with brine and dried over Na2SO4. Flash chromatography (PE:ETOAc=10:1) gave 4-bromo-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (LXXXVII) as a yellow oil (14.38 g, 43.9 mmol, 86.6% yield). ESIMS found for C_{15}H_{19}BrN_{2}OSi m/z 327.0 (M+H).

**Step 2**

[0690] A solution of 4-bromo-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (LXXXVII) (3.27 g, 10 mmol, 1.0 eq), 1-methylpiperazine (2 g, 20 mmol, 2.0 eq), tBuOK (2.24 g, 20 mmol, 1.0 eq), Pd_{2}(dba)_{3} (915 mg, 1.0 mmol, 0.1 eq), XPhos (953 mg, 2 mmol, 0.2 eq), and toluene (50 mL) was degassed (x 3) with a water pump. The reaction was stirred at 110°C for overnight. The reaction mixture was concentrated in vacuo and water (50 mL) was added and extracted with DCM (x 3). The organic layer was washed with brine and dried over Na2SO4. Flash chromatography (DCM:MeOH=40:1) gave 4-(4-methylpiperazin-l-yl)-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (LXXXVIII) as a yellow oil (2.81 g, 8.1 mmol, 81.1% yield). ESIMS found for C_{18}H_{12}N_{4}OSi m/z 347.3 (M+H).

**Step 3**

[0691] A solution of 4-(4-methylpiperazin-l-yl)-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (LXXXVIII) (2.4 g, 6.92 mmol, 1.0 eq), ethane-1,2-diamine (1.25 g, 20.76 mmol, 3.0 eq), TBAF (5.43 g, 20.76 mmol, 3.0 eq) and anhydrous THF (50 mL) was degassed (x 3) with a water pump. Then the reaction was stirred at 80°C for overnight. The reaction mixture was concentrated in vacuo and DCM (200 mL) was added. The organic layer was washed with brine and dried over Na2SO4. Flash chromatography (DCM:MeOH=30:1) gave 4-(4-methylpiperazin-l-yl)-IH-pyrrolo[2,3-b]pyridine (LXXXIX) as a yellow solid (1.2 g, 5.55 mmol, 80.2% yield). ESIMS found for C_{12}H_{10}N_{4} m/z 217.1 (M+H).

**Step 4**

[0692] To a solution of 4-(4-methylpiperazin-l-yl)-IH-pyrrolo[2,3-b]pyridine (LXXXIX) (1.2 g, 5.55 mmol, 1 eq.), DMAP (68 mg, 0.56 mmol, 0.1 eq.) and DIPEA (1.9 mL, 11.1 mmol, 2 eq.) in DCM (50 mL) was added Boc_{2}O (2.42 g, 11.1 mmol, 2.0 eq.) at 0°C. The reaction was warmed to room temperature and stirred overnight. The reaction mixture was concentrated in vacuo. Flash chromatography with (DCM:MeOH=30:1) gave tert-butyl 4-(4-
methylpiperazin-1-yl)-IH-pyrrolo[2,3-b]pyridine-1-carboxylate (XC) as a yellow oil (980 mg, 3.10 mmol, 55.8% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.65 (s, 9H), 2.37 (s, 3H), 2.61 (t, J=4.8 Hz, 4H), 3.42 (t, J=4.8 Hz, 4H), 6.47 (d, J=4 Hz, 1H), 6.55 (d, J=5.2 Hz, 1H), 7.47 (d, J=4 Hz, 1H), 8.28 (d, J=5.6 Hz, 1H); ESIMS found for C₁₁H₁₄N₄O₂ mlz 317.2 (M+H).

Step 5

To a solution of fert-butyl 4-(4-methylpiperazin-1-yl)-IH-pyrrolo[2,3-b]pyridine-1-carboxylate (XC) (1.05 g, 3.3 mmol, 1.0 eq) and triisopropyl borate (1.57 g, 8.4 mmol, 2.5 eq) in THF (30 mL), was added dropwise LDA (2 M, 4.2 mL, 8.4 mmol, 2.5 eq) at -78°C under N₂. The reaction was stirred at this temperature for 5 h. The reaction was acidified with IN HCl at -45°C until pH < 2. The aqueous phase was extracted with EtOAc (50 mL x 3). The combined organic phase was washed with cooled IN NaOH (50 mL x 2). The aqueous was added ice and acidified with IN HCl. The cloud solution was extracted with EtOAc (x 2). The organic phase was separated and dried with Na₂SO₄. The solvent was removed under reduced pressure to give crude (l-(tert-butoxycarbonyl)-4-(4-methylpiperazin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCI) as a white solid (732 mg, 2.03 mmol, 61.6% yield). ESIMS found for C₁₇H₂₅BN₄O₄ mlz 361.1 (M+H).

The following intermediate was prepared in accordance with the procedure described in the above Scheme 19.
(1-(fert-Butoxycarbonyl)-4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCII): White solid (580 mg, 1.68 mmol, 56.0% yield). ESIMS found C17H24BN3O4 mlz 346.1 (M+H).

Preparation of intermediate (4-(pyridin-3-yl)-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCV) is depicted below in Scheme 20.

Scheme 20

Step 1

To a solution of 4-bromo-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (LXXXVII) (5.0 g, 15.3 mmol, 1.0 eq) and pyridin-3-ylboronic acid (XCIII) (2.44 g, 19.9 mmol, 1.3 eq) in a mixture solvent of dioxane (60 mL) and water (20 mL) was added K3PO4 (8.1 g, 38.2 mmol, 2.5 eq). The suspension was purged with nitrogen (x 3) followed by addition of Pd(dppf)Cl2 (894 mg, 1.22 mmol, 0.08 eq). The reaction was stirred at 60°C for 5 h. The suspension was cooled and poured into water (100 mL) and extracted with EtOAc (150 mL x 3). The combined organic layer was washed with brine (100 mL), dried over Na2SO4, and concentrated under reduced pressure. Then the residue was purified by silica gel chromatography (column height: 25 cm, diameter: 10 cm, 100-200 mesh silica gel) to afford 4-(pyridin-3-yl)-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (XCIV) as a yellow oil (4.97 g, 15.3 mmol, 99.9% yield). ESIMS found for C18H22N3OSi mlz 326.0 (M+H).

Step 2

To a solution of 4-(pyridin-3-yl)-l-((2-(trimethylsilyl)ethoxy)methyl)-IH-pyrrolo[2,3-b]pyridine (XCIV) (3.8 g, 11.7 mmol, 1.0 eq) and triisopropyl borate (7.68 g, 40.6 mmol, 3.5 eq) in THF (65 mL), was added dropwise LDA (2 M, 23.3 mL, 46.7 mmol, 4.0 eq) at -78°C under N2. The reaction was stirred at this temperature for 30 min. The reaction was quench with buffer pH=7, then warmed to 25°C and extracted with EtOAc (100 mL x 3), washed with brine (50 mL), and dried with Na2SO4. The solvent was removed under reduced pressure to give
crude (4-(pyridin-3-yl)-1-(2-(trimethylsilyl)ethoxy)methyl)-H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCV) as a yellow solid (3.7 g, 10.0 mmol, 85.8% yield). ¾ NMR (DMSO-ð¾, 400 MHz) δ ppm -0.12 (s, 9H), 0.79 (t, J=8Hz, 2H), 3.49 (dt, J=4.8Hz, J=8Hz, 2H), 5.97 (s, 2H), 7.36 (dd, J=3.2Hz, J=8Hz, 2H), 7.75 (dd, J=4.8Hz, J=8Hz, IH), 8.36 (d, J=8Hz, IH), 8.44 (d, J=4.8Hz, IH), 8.77 (dd, J=1.6Hz, J=4.8Hz, IH), 9.08 (d, J=1.6Hz, IH); ESIMS found for C18H24BN3O3S1 mlz 370.1 (M+H).

[0699] The following intermediates were prepared in accordance with the procedure described in the above Scheme 20.

\[
\text{XCVI}
\]

(4-(2-Fluorophenyl)-1-(2-(trimethylsilyl)ethoxy)methyl)-H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCVI): Yellow solid (5.3 g, 13.7 mmol, 95.9% yield). ¾ NMR (acetone-ð¾, 400 MHz) δ ppm 0.00 (s, 9H), 1.00 (dt, J=2.8Hz, J=8.4Hz, 2H), 3.71 (t, J=8.4Hz, 2H), 6.11 (s, 2H), 7.16 (d, J=1.6Hz, IH), 7.29 (dd, J=1.6Hz, J=5.2Hz, IH), 7.38 - 7.50 (m, 2H), 7.57 - 7.65 (m, IH), 7.69 - 7.77 (m, IH), 8.50 (d, J=4.8Hz, IH); ESIMS found C19H24BFN2O3S1 mlz 387.1 (M+H).

\[
\text{XCVII}
\]
(4-(Pyridin-4-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCVII): Yellow solid (8.0 g, 21.7 mmol, 70.5% yield). ¾ NMR (acetone-Δ, 400 MHz) δ ppm 0.06 (s, 9H), 1.06 (dt, J = 2.8Hz, J = 8.4Hz, 2H), 3.76 (dt, J = 2.8Hz, J = 8.4Hz, 2H), 6.21 (s, 2H), 7.53 (s, IH), 7.58 (d, J = 5.2Hz, IH), 8.25 (d, J = 6.4Hz, 2H), 8.33 (brs, 2H), 8.65 (d, J = 5.2Hz, IH), 9.10 (d, J = 6Hz, IH); ESIMS found C_{8}H_{4}BN_{3}O_{3}S_{1} mlz 370.2 (M+H).

[0702] Preparation of intermediate (1-(tert-butoxycarbonyl)-4-(3-((tert-butoxycarbonyl)(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (Cl) is depicted below in Scheme 21.

![Scheme 21](image)

**Step 1**

[0703] To a solution of tert-butyl (2-(dimethylamino)ethyl)(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate (LXXIII) (5.0 g, 12.2 mmol, 1.0 eq), 4-chloro-1H-pyrrolo[2,3-b]pyridine (XCVIII) (2.06 g, 13.5 mmol, 1.1 eq) and K2CO3 (3.4 g, 24.5 mmol, 2.0 eq), Pd(dppf)Cl2 (896 mg, 1.22 mmol, 0.1 eq) in dioxane (100 mL) was de-gassed and then heated to 80°C for 12 h under N2. The suspension was poured into water (150 mL) and extracted with EtOAc (200 mL x 2). The combined organic layers was washed with brine (100 mL), dried over Na2SO4 and concentrated under reduced pressure to give the crude product which was purified by silica gel (PE:EtOAc = 30:1) to give tert-butyl (2-(dimethylamino)ethyl)(3-fluoro-5-(1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)carbamate (XCIX) (3.6 g, 9.06 mmol, 74.0% yield) as yellow oil. ESIMS found for C_{22}H_{27}FN_{4}O_{2} mlz 399.1 (M+H).

**Step 2**

[0704] To a solution of tert-butyl (2-(dimethylamino)ethyl)(3-fluoro-5-(1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)carbamate (XCIX) (4.0 g, 10.0 mmol, 1.0 eq) and BOC2O (6.5 g, 30.0 mmol, 3.0 eq) in DCM (20 mL) was added Et$_3$N (5.6 mL, 40.0 mmol, 4.0 eq) in one portion at 20°C under N2. The mixture was stirred at 20°C for 12 h. The aqueous phase was
extracted with DCM (50 mL x 4). The combined organic phase was washed with brine (10 mL x 2), dried with anhydrous Na₂SO₄, filtered and concentrated in vacuum to give fert-butyl 4-(3-((fert-butoxycarbonyl)(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridine-l-carboxylate (C) as a yellow solid (2.0 g, 4.0 mmol, 40.0% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.49 (s, 9H), 1.70 (s, 9H), 2.27 (s, 6H), 2.52 (brs, 2H), 3.80 (t, J=6.4Hz, 2H), 6.71 (d, J=4Hz, 1H), 7.13 (d, J=10Hz, 1H), 7.20 (d, J=8.8Hz, 1H), 7.24 (d, J=5.2Hz, 1H), 7.38 (s, 1H), 7.71 (d, J=4.4Hz, 1H), 8.58 (d, J=4.8Hz, 1H); ESIMS found for C₂₇H₃₅FN₄O₄ mlz 499.1 (M+H).

**Step 3**

To a solution of fert-butyl 4-(3-((teri-butoxycarbonyl)(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridine-l-carboxylate (C) (1.5 g, 3.01 mmol, 1.0 eq) in THF (20 mL) was added trisopropyl borate (1.98 g, 10.5 mmol, 3.5 eq) at -30°C, then the solution was cooled to -78°C. LDA (2 M, 6 mL, 12.0 mmol, 4 eq) was added dropwise under N₂. The reaction was stirred at this temperature for 30 min. The reaction was quench with buffer solution (pH=7), then warmed to 25°C and extracted with EtOAc (40 mL x 3), washed with brine (10 mL), dried with Na₂SO₄, filtered and concentrated to afford the crude product (1-(teri-butoxycarbonyl)-4-(3-((fert-butoxycarbonyl)(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (CI) as a yellow solid (1.5 g, 2.77 mmol, 91.9% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.49 (s, 9H), 2.28 (s, 6H), 2.54 (t, J=6.4Hz, 2H), 3.82 (t, J=6.4Hz, 2H), 6.72 (s, 1H), 7.11 (d, J=9.6Hz, 1H), 7.17 (d, J=3.6Hz, 1H), 7.32 (d, J=8.8Hz, 1H), 7.43 (s, 1H), 7.46 (s, 1H), 8.39 (d, J=3.2Hz, 1H); ESIMS found for C₂₇H₃₆BFN₄O₆ mlz 543.2 (M+H).

The following intermediates were prepared in accordance with the procedure described in the above Scheme 21.
(l-(tert-Butoxycarbonyl)-4-(furan-3-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (CI): Yellow solid (2.0 g, 6.10 mmol, 57.5% yield). ESIMS found C_{16}H_{17}BN_{2}O_{5} m/z 229.0 (M+H-Boc).

Example 1.

Preparation of 5-(pyridin-3-yl)-3-(4-(pyridin-3-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine (88) is depicted below in Scheme 22.

Steps 1

A mixture of 1-(tetrahydro-2H-pyran-2-yl)-5-(tributylstannyl)-lH-pyrazolo[4,3-b]pyridine (XVIII) (25 g, 50.8 mmol, 1.0 eq), 3-bromopyridine (CIV) (8.8 g, 55.9 mmol, 1.10 eq) and Pd(PPh3)4 (2.35 g, 2.03 mmol, 0.04 eq) in dioxane (150 mL) was degassed and purged with N2 (3 x), and then the mixture was stirred at 105°C for 16 h under a N2 atmosphere. The reaction mixture was concentrated and the residue was purified by column chromatography.
(SiO₂, PE/EtOAc) to give 5-(pyridin-3-yl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[4,3-b]pyridine (CV) as a yellow oil (6.4 g, 22.8 mmol, 44.9% yield). ESIMS found for C₁₉H₁₈N₄O₂ mlz 281.1 (M+H).

**Step 2**

[0711] To a solution of 5-(pyridin-3-yl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo [4,3-b]pyridine (CV) (3.1 g, 11.1 mmol, 1.0 eq) in EtOAc (10 mL) was added HCl/EtOAc (4 M, 100 mL) and the mixture was stirred at 10°C for 16 h. The reaction mixture was concentrated to yield crude 5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine (CVI) as a yellow solid (1.9 g, 9.68 mmol, 87.6% yield) which was used for next step without further purification. ESIMS found for C₁₁H₇IN₄ mlz 197.0 (M+H).

**Steps 3**

[0712] To a solution of 5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine (CVI) (g, mmol, 1.0 eq) and KOH (3.5 g, 17.8 mmol, 5.0 eq) in DMF (50 mL) was added I₂ (3.4 g, 26.8 mmol, 1.5 eq) and the mixture was stirred at 15°C for 4 h. The reaction mixture was quenched by addition saturated aqueous Na₂S₂O₃ (50 mL), and acidified with 1 N HCl to pH=6. The suspension was filtered and the filtrate cake was dried under reduced pressure to give 3-iodo-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine (CVII) as a yellow oil (4.8 g, 14.9 mmol, 83.5% yield) which was used for next step without further purification. ESIMS found for C₁₁H₇IN₄ mlz 322.9 (M+H).

**Steps 4**

[0713] To a solution of 3-iodo-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine (CVII) (2.0 g, 6.2 mmol, 1.0 eq), Boc₂O (1.49 g, 6.83 mmol, 1.1 eq) and TEA (1.73 mL, 12.4 mmol, 2.0 eq) in DCM (100 mL) was added DMAP (76 mg, 0.62 mmol, 0.1 eq) and the mixture was stirred at 15°C for 4 h. The reaction was concentrated and the residue was purified by column chromatography (SiO₂, PE/EtOAc) to give tert-butyl 3-iodo-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine-1-carboxylate (CVIII) as a yellow solid (2.1 g, 4.97 mmol, 80.1% yield). ¾ NMR (CDCl₃, 400 MHz) δ ppm 1.74 (s, 9H), 7.46 (dd, J=5.2Hz, J=8Hz, IH), 7.99 (d, J=8.8Hz, IH), 8.50 (d, J=8.4Hz, 2H), 8.70 (d, J=3.6Hz, IH), 9.31 (s, IH); ESIMS found for C₁₉H₁₉N₅O₂ mlz 423.0 (M+H).
Steps 5

[0714] A mixture of tert-butyl 3-iodo-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine-1-carboxylate (CVIII) (80 mg, 0.19 mmol, 1.0 eq), (1-(tert-butoxycarbonyl)-4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)boronic acid (XCV) (70.7 mg, 0.21 mmol, 1.1 eq), Pd(dppf)Cl₂ (14 mg, 0.19 mmol, 0.1 eq), and K3PO4 (80 mg, 0.38 mmol, 2.0 eq) in dioxane (10 mL) and water (1 inL) was stirred at 90°C for 16 h. The mixture was filtered and the filtrate was concentrated to give the tert-butyl 3-(1-(tert-butoxycarbonyl)-4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine-1-carboxylate (CIX) as a yellow solid (60 mg, 0.10 mmol, 53.7% yield) which was used in the next step directly. ESIMS found for C33H31N7O4 mlz 590.3 (M+). 

Step 6

[0715] A mixture of tert-butyl 3-(1-(tert-butoxycarbonyl)-4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine-1-carboxylate (CIX) (60 mg, 0.10 mmol, 1.0 eq) in HCl/EtOAc (4 M, 50 mL) was stirred at 20°C for 16 h. The mixture was filtered and the filtrate was concentrated. The residue was purified by acid prep-HPLC to give 5-(pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine (88) as an off-white solid (6.5 mg, 0.017 mmol, 16.4% yield). ¾ NMR (400 MHz, DMSO-d₆) δ ppm 7.34 (br d, J=4.85 Hz, 1 H), 7.59 (br dd, J=7.72, 5.07 Hz, 1 H), 7.64 - 7.72 (m, 1 H), 7.87 (s, 1 H), 8.12 - 8.19 (m, 1 H), 8.20 - 8.27 (m, 1 H), 8.34 (br d, J=8.16 Hz, 1 H), 8.38 (br d, J=5.07 Hz, 1 H), 8.58 (br d, J=7.72 Hz, 1 H), 8.68 (br d, J=3.53 Hz, 1 H), 8.75 (br d, J=4.19 Hz, 1 H), 9.09 (br s, 1 H), 9.43 (br s, 1 H), 12.51 (br s, 1 H), 13.73 (br s, 1 H); ESIMS found for C23H15N7 mlz 390.0 (M+). 

[0716] The following compounds were prepared in accordance with the procedures described herein. See, for example, Schemes 1a and 1-22.

[0718] ¾ NMR (400 MHz, DMSO-<i>d</i><sub>6</i>) δ ppm 7.34 (d, <i>J</i>=5.04 Hz, 1 H), 7.37 - 7.45 (m, 1 H), 7.65 - 7.76 (m, 3 H), 7.77 - 7.83 (m, 1 H), 7.92 - 7.96 (m, 1 H), 8.18 - 8.24 (m, 1 H), 8.24 - 8.32 (m, 1 H), 8.36 (d, <i>J</i>=4.39 Hz, 1 H), 8.74 - 8.85 (m, 2 H), 9.51 (s, 1 H), 12.57 (s, 1 H), 13.83 (br s, 1 H); ESIMS found for C<sub>24</sub>H<sub>15</sub>FN<sub>6</sub> mlz 407.1 (M+1).

[0719] N-(5-(3-(4-(3-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide 8.

[0720] ¾ NMR (400 MHz, DMSO-<i>d</i><sub>6</i>) δ ppm 1.27 (br s, 9 H), 7.26 - 7.38 (m, 2 H), 7.58 - 7.73 (m, 2 H), 7.79 (br d, <i>J</i>=6.17 Hz, 1 H), 7.83 (br s, 1 H), 8.04 (br d, <i>J</i>=8.82 Hz, 1 H), 8.20 - 8.29 (m, 1 H), 8.35 (br d, <i>J</i>=4.85 Hz, 1 H), 8.81 (br s, 1 H), 8.97 (br s, 1 H), 9.08 (br s, 1 H), 9.58 (br s, 1 H), 12.47 (br s, 1 H), 13.77 (br s, 1 H); ESIMS found for C<sub>29</sub>H<sub>24</sub>FN<sub>7</sub>O mlz 506.1 (M+1).

[0721] 3-(4-(3-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine 15.

[0722] ¾ NMR (400 MHz, DMSO-<i>d</i><sub>6</sub>) δ ppm 1.39 (br d, <i>J</i>=2.87 Hz, 2 H), 1.42 - 1.62 (m, 4 H), 2.34 - 2.44 (m, 2 H), 3.58 (s, 2 H), 7.29 (br d, <i>J</i>=4.85 Hz, 1 H), 7.34 - 7.44 (m, 1 H), 7.65 - 7.73 (m, 2 H), 7.77 (br d, <i>J</i>=7.06 Hz, 1 H), 7.86 (br s, 1 H), 8.17 (br d, <i>J</i>=9.04 Hz, 1 H), 8.20 - 8.27 (m, 1 H), 8.35 (br d, <i>J</i>=5.07 Hz, 1 H), 8.40 - 8.49 (m, 1 H), 8.54 - 8.65 (m, 1 H), 9.31 (s, 1 H), 12.47 (br s, 1 H), 13.77 (br s, 1 H); ESIMS found for C<sub>30</sub>H<sub>26</sub>FN<sub>7</sub>O mlz 504.2 (M+1).
33.


[0724] ¾ NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm 2.58 (br s, 3 H), 7.21 (br d, \(J=6.39\) Hz, 1 H), 7.37 - 7.50 (m, 3 H), 7.72 (br s, 1 H), 7.78 (br d, \(J=8.82\) Hz, 1 H), 7.88 (br dd, \(J=8.27, 5.40\) Hz, 2 H), 8.22 (br d, \(J=10.14\) Hz, 1 H), 8.28 - 8.35 (m, 1 H), 8.52 (br d, \(J=3.67\) Hz, 1 H), 8.35 (br s, 1 H), 12.39 (br s, 1 H); ESIMS found for C29H17FN6 mlz 421.0 (M+1).

39.


[0726] ¾ NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm 7.33 - 7.43 (m, 3 H), 7.57 - 7.63 (m, 2 H), 7.65 - 7.73 (m, 1 H), 7.87 (d, \(J=1.54\) Hz, 1 H), 8.01 (br dd, \(J=8.60, 5.51\) Hz, 2 H), 8.09 (br d, \(J=7.28\) Hz, 2 H), 8.19 (d, \(J=8.82\) Hz, 1 H), 8.34 (d, \(J=8.82\) Hz, 1 H), 8.39 (d, \(J=5.29\) Hz, 1 H), 9.26 (br s, 1 H), 9.30 (br s, 1 H), 9.41 (br s, 1 H), 11.05 (br s, 1 H), 12.80 (br s, 1 H), 14.00 (br s, 1 H); ESIMS found for C31H20FN7O mlz 526.1 (M+1).

54.

NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm 2.17 - 2.30 (m, 2 H), 2.70 - 2.79 (m, 2 H), 2.93 (br t, \(J=13.34\) Hz, 2 H), 3.79 (br s, 2 H), 7.02 (br d, \(J=3.75\) Hz, 1 H), 7.27 - 7.38 (m, 1 H), 7.42 - 7.51 (m, 2 H), 7.85 - 7.90 (m, 1 H), 7.97 (br dd, \(J=7.06, 2.43\) Hz, 1 H), 8.15 - 8.24 (m, 1 H), 8.33 (br d, \(J=1.10\) Hz, 1 H), 8.63 (br s, 1 H), 9.35 (br s, 1 H), 12.44 (br s, 1 H), 13.73 (br s, 1 H); ESIMS found for C29H22F3N7 mlz 526.1 (M+1).

\[\text{55}\]

3-(4-(4-Fluorophenyl)-1H-pyrrolo [2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine 55.

NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm 7.39 (d, \(J=5.09\) Hz, 1 H), 7.44 - 7.53 (m, 2 H), 7.92 (d, \(J=1.57\) Hz, 1 H), 7.99 - 8.06 (m, 2 H), 8.23 - 8.28 (m, 1 H), 8.28 - 8.33 (m, 1 H), 8.40 (d, \(J=5.09\) Hz, 1 H), 9.31 (s, 1 H), 9.64 (s, 2 H), 12.87 (br s, 1 H), 13.96 (br s, 1 H); ESIMS found for C23H14FN7 mlz 408.1 (M+1).

\[\text{58}\]

N-(5-(3-(4-(2-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-3-methylbutanamide 58.

NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm 0.99 (d, \(J=6.62\) Hz, 6 H), 2.09 - 2.20 (m, 1 H), 2.29 (d, \(J=7.28\) Hz, 2 H), 7.21 (dd, \(J=5.07, 1.10\) Hz, 1 H), 7.38 - 7.48 (m, 2 H), 7.52 - 7.60 (m, 2 H), 7.80 (td, \(J=7.83, 1.54\) Hz, 1 H), 8.01 (d, \(J=8.82\) Hz, 1 H), 8.23 (d, \(J=8.82\) Hz, 1 H), 8.35 (d, \(J=4.63\) Hz, 1 H), 8.72 - 8.78 (m, 1 H), 8.81 (d, \(J=2.20\) Hz, 1 H), 9.03 (d, \(J=1.98\) Hz, 1 H), 10.22 (s, 1 H), 12.38 (br s, 1 H), 13.74 (br s, 1 H); ESIMS found for C29H24FN7O mlz 506.2 (M+1).
1-(5-(3-(4-(2-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 69.

\[\text{HNMR (400 MHz, DMSO-}d_6\text{)} \delta \text{ ppm} \]

2.18 (s, 6 H), 3.52 (s, 2 H), 7.20 (br d, \(J=4.89\) Hz, 1 H), 7.42 - 7.53 (m, 2 H), 7.56 - 7.67 (m, 2 H), 7.79 (br dd, \(J=8.90, 7.53\) Hz, 1 H), 8.13 - 8.19 (m, 1 H), 8.19 - 8.24 (m, 1 H), 8.35 (br d, \(J=4.69\) Hz, 1 H), 8.40 (br d, \(J=1.56\) Hz, 1 H), 8.57 (br d, \(J=1.56\) Hz, 1 H), 9.28 (br d, \(J=1.96\) Hz, 1 H), 12.42 (br s, 1 H), 13.72 (br s, 1 H); ESIMS found for C\(_{27}\)H\(_{22}\)FN\(_7\) m/z 464.1 (M+1).

N-(5-(3-(4-(2-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide 76.

\[\text{\textsuperscript{1}H NMR (400 MHz, DMSO-}d_6\text{)} \delta \text{ ppm} \]

0.85 - 0.95 (m, 4 H), 1.83 - 1.92 (m, 1 H), 7.21 (dd, \(J=4.85, 1.10\) Hz, 1 H), 7.40 - 7.49 (m, 2 H), 7.53 - 7.65 (m, 2 H), 7.77 - 7.85 (m, 1 H), 8.01 (d, \(J=8.82\) Hz, 1 H), 8.22 (d, \(J=8.82\) Hz, 1 H), 8.35 (d, \(J=4.85\) Hz, 1 H), 8.71 (t, \(J=1.98\) Hz, 1 H), 8.81 (d, \(J=2.20\) Hz, 1 H), 9.03 (d, \(J=1.76\) Hz, 1 H), 10.55 (s, 1 H), 12.39 (s, 1 H), 13.74 (s, 1 H); ESIMS found for C\(_{28}\)H\(_{20}\)F\(_7\)O m/z 490.1 (M+1).
N-Benzyl-1-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine 80.

¾ NMR (400 MHz, DMSO-d_6) δ ppm 4.26 (br d, J=5.07 Hz, 2 H), 4.39 (br d, J=4.63 Hz, 2 H), 5.90 (s, 1 H), 7.32 (br d, J=5.07 Hz, 1 H), 7.38 - 7.46 (m, 2 H), 7.46 - 7.56 (m, 2 H), 7.60 (br d, J=7.72 Hz, 2 H), 7.62 - 7.70 (m, 2 H), 7.83 (br t, J=7.72 Hz, 1 H), 8.21 (br d, J=8.82 Hz, 1 H), 8.39 - 8.46 (m, 1 H), 8.54 (br d, J=8.82 Hz, 1 H), 8.92 (br s, 1 H), 9.02 (br s, 1 H), 9.54 (dd, J=9.48, 1.98 Hz, 1 H), 9.95 (br s, 2 H), 12.68 (br s, 1 H); ESIMS found for C_{32}H_{24}F_{18}N_{10} m/z 526.2 (M+).

3-(4-(2-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 84.

¾ NMR (400 MHz, DMSO-d_6) δ ppm 7.22 - 7.28 (m, 1 H), 7.46 - 7.58 (m, 3 H), 7.60 - 7.65 (m, 1 H), 7.73 (s, 1 H), 7.79 - 7.86 (m, 1 H), 8.01 - 8.08 (m, 1 H), 8.22 (d, J=8.77 Hz, 1 H), 8.36 (d, J=4.60 Hz, 1 H), 8.48 - 8.58 (m, 2 H), 8.70 - 8.77 (m, 1 H), 12.47 (s, 1 H), 13.77 (s, 1 H); ESIMS found for C_{24}H_{13}F_{16}N_{10} m/z 407.0 (M+).

5-(Pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 88.

¾ NMR (400 MHz, DMSO-d_6) δ ppm 7.34 (br d, J=4.85 Hz, 1 H), 7.59 (br dd, J=7.72, 5.07 Hz, 1 H), 7.64 - 7.72 (m, 1 H), 7.87 (s, 1 H), 8.12 - 8.19 (m, 1 H), 8.20 - 8.27 (m, 1 H), 8.34 (br d, J=8.8 Hz, 1 H), 8.38 (br d, J=5.07 Hz, 1 H), 8.58 (br d, J=7.72 Hz, 1 H), 8.68 (br d, J=3.53 Hz, 1 H), 8.75 (br d, J=4.19 Hz, 1 H), 9.09 (br s, 1 H), 9.43 (br s, 1 H), 12.51 (br s, 1 H), 13.73 (br s, 1 H); ESIMS found for C_{23}H_{15}N_{17} m/z 390.0 (M+).
[0743] N,N-Dimethyl-5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine 91.

[0744] ¾ NMR (400 MHz, DMSO-\text{d}_{6}) \delta ppm 2.99 (s, 6 H), 7.29 (br d, J=5.29 Hz, 1 H), 7.59 - 7.67 (m, 1 H), 7.79 (br s, 1 H), 7.82 (br s, 1 H), 8.12 - 8.23 (m, 3 H), 8.25 - 8.31 (m, 1 H), 8.37 (br d, J=4.85 Hz, 1 H), 8.68 (br s, 1 H), 8.74 (br d, J=4.41 Hz, 1 H), 9.06 (br s, 1 H), 12.51 (br s, 1 H); ESIMS found for C_{29}H_{28}N_{8} mlz 433.2 (M+).

[0745] N-Isopropyl-5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine 96.

[0746] ¾ NMR (400 MHz, DMSO-\text{d}_{6}) \delta ppm 1.21 (d, J=6.39 Hz, 6 H), 3.77 - 3.85 (m, 1 H), 7.40 (br d, J=5.07 Hz, 1 H), 7.79 (br d, J=1.98 Hz, 1 H), 7.82 - 7.92 (m, 1 H), 8.13 (br d, J=2.21 Hz, 1 H), 8.20 (br d, J=8.82 Hz, 1 H), 8.28 - 8.38 (m, 2 H), 8.42 (d, J=4.85 Hz, 1 H), 8.51 - 8.59 (m, 1 H), 8.78 (s, 1 H), 8.82 (br d, J=5.07 Hz, 1 H), 9.20 (br d, J=1.10 Hz, 1 H), 12.64 (br s, 1 H), 13.98 (br s, 1 H); ESIMS found for C_{25}H_{22}N_{8} mlz 447.02 (M+).

[0747] 3-(4-(Pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine 102.

[0748] ¾ NMR (400 MHz, DMSO-\text{d}_{6}) \delta ppm 7.36 (br d, J=4.85 Hz, 1 H), 7.73 (br dd, J=8.27, 4.96 Hz, 1 H), 7.95 (s, 1 H), 8.21 (br dd, J=3.86, 1.21 Hz, 2 H), 8.22 - 8.31 (m, 2 H),
8.34 - 8.43 (m, 2 H), 8.69 - 8.84 (m, 3 H), 9.11 (br s, 1 H), 12.53 (br s, 1 H); ESIMS found for C23H15N7 ml/z 390.1 (M+).

[0749] 5-(5-(((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 110.

[0750] 34 NMR (400 MHz, DMSO-d6) δ ppm 2.18 - 2.30 (m, 2 H), 2.76 (br t, J=6.84 Hz, 2 H), 2.96 (br t, J=13.34 Hz, 2 H), 3.82 (s, 2 H), 7.34 (d, J=5.07 Hz, 1 H), 7.67 (dd, J=7.72, 5.29 Hz, 1 H), 7.90 (d, J=1.76 Hz, 1 H), 8.18 - 8.27 (m, 2 H), 8.32 (dt, J=7.94, 1.65 Hz, 1 H), 8.38 (d, J=5.07 Hz, 1 H), 8.50 (br t, J=1.76 Hz, 1 H), 8.62 (br d, J=1.76 Hz, 1 H), 8.75 (dd, J=4.63, 1.76 Hz, 1 H), 9.14 (d, J=2.20 Hz, 1 H), 9.33 (d, J=2.20 Hz, 1 H), 12.55 (br d, J=0.66 Hz, 1 H), 13.77 (s, 1 H); ESIMS found for C28H22F2N8 ml/z 509.1 (M+).

[0751] 5-(3-(4-(Pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine 115.

[0752] 34 NMR (400 MHz, DMSO-d6) δ ppm 5.50 (s, 2 H), 7.37 (d, J=4.82 Hz, 1 H), 7.73 (s, 1 H), 7.90 - 7.96 (m, 3 H), 7.98 (d, J=8.77 Hz, 1 H), 8.05 (d, J=2.63 Hz, 1 H), 8.16 - 8.22 (m, 2 H), 8.39 (d, J=5.26 Hz, 1 H), 8.56 (s, 1 H), 8.82 (d, J=6.14 Hz, 2 H), 12.52 (s, 1 H), 13.73 (br s, 1 H); ESIMS found for C23H16N8 ml/z 405.0 (M+).
[0753] 5-(4-Methylpyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine 117.

[0754] ¼ NMR (400 MHz, DMSO-d$_6$) $\delta$ ppm 2.60 (s, 3 H), 7.33 (br d, $J$=4.85 Hz, 1 H), 7.47 (br d, $J$=5.73 Hz, 1 H), 7.73 - 7.90 (m, 4 H), 8.23 (br d, $J$=9.04 Hz, 2 H), 8.38 (br d, $J$=4.63 Hz, 1 H), 8.52 (br d, $J$=5.07 Hz, 1 H), 8.73 - 8.81 (m, 2 H), 12.56 (br s, 1 H), 13.82 (br s, 1 H); ESIMS found for C$_{24}$H$_{17}$N$_7$ mlz 404.1 (M$^+$).

![Chemical structure](image)

[0755] 5-(5-(Piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine 127.

[0756] ¼ NMR (400 MHz, DMSO-d$_6$) $\delta$ ppm 1.23 (br s, 2 H), 1.32 - 1.41 (m, 2 H), 1.47 (br s, 3 H), 2.37 (br s, 3 H), 3.59 (br s, 2 H), 7.36 (br d, $J$=3.53 Hz, 1 H), 7.91 (br s, 3 H), 8.21 (br dd, $J$=18.63, 8.71 Hz, 2 H), 8.40 (br d, $J$=3.31 Hz, 1 H), 8.45 (br s, 1 H), 8.59 (br s, 1 H), 8.83 (br s, 2 H), 9.32 (br s, 1 H), 12.56 (br s, 1 H), 13.77 (br s, 1 H); ESIMS found for C$_{36}$H$_{28}$N$_8$ mlz 487.1 (M$^+$).

![Chemical structure](image)

[0757] 1-Cyclopentyl-N-((5-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl) methanamine 137.

[0758] ¼ NMR (400 MHz, DMSO-d$_6$) $\delta$ ppm 1.26 - 1.37 (m, 2 H), 1.45 - 1.66 (m, 4 H), 1.77 - 1.87 (m, 2 H), 2.23 - 2.32 (m, 1 H), 3.00 (br d, $J$=1.98 Hz, 2 H), 4.45 (br s, 2 H), 7.58 (br d, $J$=4.63 Hz, 1 H), 8.00 (s, 1 H), 8.29 - 8.41 (m, 2 H), 8.51 (br d, $J$=4.85 Hz, 1 H), 8.60 (br d, $J$=5.73 Hz, 2 H), 9.11 (br s, 1 H), 9.21 (br d, $J$=5.07 Hz, 2 H), 9.52 (br s, 1 H), 9.73 (br s, 1 H), 9.80 (br s, 2 H), 12.88 (br s, 1 H), 14.17 (br s, 1 H); ESIMS found for C$_{50}$H$_{38}$N$_8$ mlz 501.1 (M$^+$).
[0759] 5-(4-Methylpyridin-3-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 173.

[0760] ¾ NMR (400 MHz, DMSO-\(d_6\)) δ ppm 1.62 - 1.74 (m, 6 H), 2.62 (s, 3 H), 3.43 (br d, J=5.95 Hz, 4 H), 6.44 (d, J=5.51 Hz, 1 H), 7.45 (d, J=4.85 Hz, 1 H), 7.57 (d, J=1.10 Hz, 1 H), 7.78 (d, J=8.82 Hz, 1 H), 7.96 (d, J=5.51 Hz, 1 H), 8.19 (d, J=8.82 Hz, 1 H), 8.52 (d, J=4.85 Hz, 1 H), 8.77 (s, 1 H), 11.94 (s, 1 H), 13.58 (s, 1 H); ESIMS found for C\(_{24}\)H\(_{23}\)N\(_7\) m/z 410.1 (M+).

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[0761] N,N-Dimethyl-1-(5-(3\(^4\)piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine 181.

[0762] ¾ NMR (400 MHz, DMSO-\(d_6\)) δ ppm 1.67 - 1.75 (m, 2 H), 1.75 - 1.87 (m, 4 H), 2.24 (br s, 6 H), 3.44 - 3.55 (m, 4 H), 3.55 - 3.65 (m, 2 H), 6.45 (d, J=5.48 Hz, 1 H), 7.71 (s, 1 H), 7.98 (d, J=5.67 Hz, 1 H), 8.18 (s, 2 H), 8.52 (br s, 1 H), 8.59 (s, 1 H), 9.36 (br d, J=1.17 Hz, 1 H), 11.93 (br s, 1 H), 13.55 (br s, 1 H); ESIMS found for C\(_{26}\)H\(_{28}\)N\(_8\) m/z 453.2 (M+).

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[0763] 3-(4-(Piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine 183.
\[ \text{NMR (400 MHz, DMSO-d}_6\text{) } \delta \text{ ppm } 1.36 - 1.45 \text{ (m, 2 H), 1.48 - 1.59 } \text{ (m, 4 H), 1.66 - 1.74 } \text{ (m, 2 H), 1.76 - 1.84 } \text{ (m, 4 H), 2.34 - 2.42 } \text{ (m, 4 H), 3.51 } \text{ (ddd, J=4.80, 3.03, 1.43 Hz, 4 H), 3.60 } \text{ (s, 2 H), 6.45 } \text{ (d, J=5.51 Hz, 1 H), 7.71 } \text{ (d, J=2.21 Hz, 1 H), 7.98 } \text{ (d, J=5.51 Hz, 1 H), 8.18 } \text{ (d, J=2.21 Hz, 2 H), 8.48 } \text{ (br t, J=2.09 Hz, 1 H), 8.59 } \text{ (d, J=1.76 Hz, 1 H), 9.34 } \text{ (d, J=2.43 Hz, 1 H), 11.96 } \text{ (br s, 1 H), 13.57 } \text{ (s, 1 H); ESIMS found for C}_{28}H_{32}N_8 \text{ m/z 493.1 (M+).} \]

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\[ \text{N-(5-((3-((4-(Piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide} \text{ 187.} \]

\[ \text{NMR (400 MHz, DMSO-d}_6\text{) } \delta \text{ ppm } 0.94 } \text{ (t, J=7.28 Hz, 3 H), 1.38 } \text{ (dq, J=14.83, 7.48 Hz, 2 H), 1.66 } \text{ (dt, J=14.88, 7.55 Hz, 2 H), 1.77 } \text{ (br s, 5 H), 2.44 - 2.49 } \text{ (m, 2 H), 3.96 } \text{ (br s, 4 H), 6.83 } \text{ (d, J=7.50 Hz, 1 H), 7.78 } \text{ (d, J=1.98 Hz, 1 H), 7.99 } \text{ (d, J=7.28 Hz, 1 H), 8.19 } \text{ (d, J=8.82 Hz, 1 H), 8.25 - 8.32 } \text{ (m, 1 H), 9.03 } \text{ (br s, 1 H), 9.25 } \text{ (br s, 1 H), 9.39 } \text{ (s, 1 H), 10.93 } \text{ (br s, 1 H), 12.92 } \text{ (s, 1 H), 14.04 } \text{ (br s, 1 H); ESIMS found for C}_{28}H_{32}N_0 \text{ m/z 495.2 (M+).} \]

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\[ 5-((3,3-\text{Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl}-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine} \text{ 194.} \]

\[ \text{NMR (400 MHz, DMSO-d}_6\text{) } \delta \text{ ppm } 1.59 - 1.85 } \text{ (m, 6 H), 2.21 - 2.37 } \text{ (m, 2 H), 2.35 - 2.37 } \text{ (m, 1 H), 2.72 - 2.81 } \text{ (m, 2 H), 2.89 - 3.00 } \text{ (m, 3 H), 3.51 } \text{ (br s, 4 H), 3.79 } \text{ (br d, J=5.07 Hz, 2 H), 6.41 - 6.50 } \text{ (m, 1 H), 7.72 } \text{ (s, 1 H), 7.92 - 8.01 } \text{ (m, 1 H), 8.09 - 8.24 } \text{ (m, 2 H), 8.51 } \text{ (br s, 1 H), 8.60 } \text{ (br d, J=12.35 Hz, 1 H), 9.38 } \text{ (br d, J=1.54 Hz, 1 H), 11.97 } \text{ (br s, 1 H), 13.63 } \text{ (br s, 1 H); ESIMS found for C}_{28}H_{32}F_2N_8 \text{ m/z 515.2 (M+).} \]

[0770] ¾ NMR (400 MHz, DMSO-\textit{d}_6) δ ppm 1.66 - 1.73 (m, 2 H), 1.75 - 1.84 (m, 4 H), 3.46 - 3.56 (m, 4 H), 6.45 (d, \textit{J}=5.73 Hz, 1 H), 7.73 (d, \textit{J}=1.10 Hz, 1 H), 7.98 (d, \textit{J}=5.51 Hz, 1 H), 8.24 (s, 2 H), 9.29 (s, 1 H), 9.66 (s, 2 H), 11.98 (s, 1 H); ESIMS found for C_{23}H_{21}N_{7} mlz 397.1 (M+1).

[0771] 3-(4-(Piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 196.

[0772] ¾ NMR (400 MHz, DMSO-\textit{d}_6) δ ppm 1.67 - 1.77 (m, 2 H), 1.78 - 1.88 (m, 4 H), 3.45 - 3.60 (m, 4 H), 6.45 (d, \textit{J}=5.73 Hz, 1 H), 7.49 (ddd, \textit{J}=7.44, 4.69, 1.10 Hz, 1 H), 7.81 (d, \textit{J}=1.32 Hz, 1 H), 7.98 (d, \textit{J}=5.29 Hz, 1 H), 8.02 (td, \textit{J}=7.72, 1.76 Hz, 1 H), 8.19 (d, \textit{J}=8.82 Hz, 1 H), 8.54 (d, \textit{J}=8.82 Hz, 1 H), 8.62 (d, \textit{J}=7.94 Hz, 1 H), 8.74 (ddd, \textit{J}=4.80, 1.82, 0.66 Hz, 1 H), 11.97 (br s, 1 H), 13.57 (s, 1 H); ESIMS found for C_{23}H_{21}N_{7} mlz 396.1 (M+1).

[0773] 3-Methyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide 226.
[0774] ¾ NMR (400 MHz, DMSO-d$_6$) δ ppm 0.99 (d, $J$=6.62 Hz, 6 H), 2.18 (dq, $J$=13.59, 6.64 Hz, 1 H), 2.43 (d, $J$=7.06 Hz, 2 H), 2.88 (s, 3 H), 3.31 - 3.45 (m, 2 H), 3.63 - 3.73 (m, 2 H), 3.85 - 3.98 (m, 2 H), 4.55 - 4.71 (m, 2 H), 6.97 (d, $J$=7.28 Hz, 1 H), 7.70 (br d, $J$=1.54 Hz, 1 H), 8.15 - 8.25 (m, 2 H), 8.25 - 8.33 (m, 1 H), 9.23 (br d, $J$=1.54 Hz, 1 H), 9.36 (s, 1 H), 9.49 (s, 1 H), 11.17 (br s, 1 H), 12.83 (br s, 1 H), 14.16 (br s, 1 H); ESIMS found for C$_{28}$H$_{31}$N$_9$O $m/z$ 510.1 (M$^+$).

[0775] N-(5-(3-(4-(4-Methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide

232.

[0776] ¾ NMR (400 MHz, DMSO-d$_6$) δ ppm 1.35 (s, 9 H), 2.87 (s, 3 H), 3.59 - 3.73 (m, 2 H), 3.80 - 3.95 (m, 2 H), 4.58 - 4.73 (m, 2 H), 6.99 (d, $J$=7.28 Hz, 1 H), 7.75 (br d, $J$=1.76 Hz, 1 H), 8.18 - 8.30 (m, 2 H), 8.35 (d, $J$=8.82 Hz, 1 H), 9.37 (br dd, $J$=8.71, 1.21 Hz, 2 H), 9.61 (br s, 1 H), 10.30 (br s, 1 H), 11.27 (s, 1 H), 12.84 (br s, 1 H), 14.15 (br s, 1 H); ESIMS found for C$_{28}$H$_{31}$N$_9$O $m/z$ 510.1 (M$^+$).

[0777] N-(5-(3-(4-(4-Methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide

235.

[0778] ¾ NMR (400 MHz, DMSO-d$_6$) δ ppm 2.71 (s, 3 H), 3.23 - 3.38 (m, 2 H), 3.62 (br s, 2 H), 3.82 - 3.96 (m, 2 H), 4.54 - 4.72 (m, 2 H), 6.98 (br d, $J$=7.28 Hz, 1 H), 7.54 - 7.65 (m, 2 H), 7.65 - 7.73 (m, 1 H), 7.79 (br d, $J$=1.54 Hz, 1 H), 8.14 - 8.21 (m, 2 H), 8.23 (br d, $J$=8.82 Hz, 1 H), 8.35 (br d, $J$=9.04 Hz, 1 H), 9.33 (br s, 1 H), 9.38 (br s, 1 H), 9.59 (br s, 1 H), 11.12 (br s, 1 H), 11.35 (br s, 1 H), 13.06 (br s, 1 H), 14.14 (br s, 1 H); ESIMS found for C$_{30}$H$_{27}$N$_9$O $m/z$ 530.2 (M$^+$).
[0779] 3,3-Dimethyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide 240.

[0780] ¹H NMR (400 MHz, DMSO-d₆) δ ppm 1.08 (s, 9 H), 2.41 (s, 2 H), 2.87 (s, 3 H), 3.61 - 3.72 (m, 2 H), 3.83 - 3.98 (m, 2 H), 4.58 - 4.72 (m, 2 H), 6.99 (br d, J=7.28 Hz, 1 H), 7.78 (br d, J=1.76 Hz, 1 H), 8.14 - 8.24 (m, 2 H), 8.33 (d, J=8.82 Hz, 1 H), 9.13 (br d, J=1.76 Hz, 1 H), 9.31 (br d, J=1.54 Hz, 1 H), 9.37 (br s, 1 H), 10.85 (br s, 1 H), 11.33 (s, 1 H), 12.97 (br s, 1 H); ESIMS found for C₂₉H₃₃N₉O mlz 524.2 (M+).

[0781] 5-(Pyridin-3-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine 256.

[0782] ¹H NMR (400 MHz, DMSO-d₆) δ ppm 7.16 - 7.24 (m, 1 H), 7.70 (s, 1 H), 7.86 - 7.99 (m, 2 H), 8.16 - 8.22 (m, 1 H), 8.23 - 8.35 (m, 2 H), 8.80 - 8.88 (m, 1 H), 9.00 - 9.09 (m, 1 H), 9.63 (br s, 1 H), 12.50 (br s, 1 H), 13.87 (br s, 1 H); ESIMS found for C₁₈H₁₂N₆ mlz 313.1 (M+).

[0783] N-((5-(3-(1H-Pyrrolo [2,3-b]pyridin-2-yl) IH-pyrazolo [4,3-b]pyridin-5 -yl)pyridin-3-yl)methyl)ethanamine 258.

[0784] ¹H NMR (400 MHz, DMSO-d₆) δ ppm 1.31 (t, J=7.28 Hz, 3 H), 3.02 - 3.15 (m, 2 H), 4.39 - 4.47 (m, 2 H), 7.40 (dd, J=7.83, 5.40 Hz, 1 H), 7.96 (d, J=1.32 Hz, 1 H), 8.27 -
8.33 (m, 1H), 8.33 - 8.38 (m, 1H), 8.41 (dd, J=5.29, 1.32 Hz, 1H), 8.51 (br d, J=7.94 Hz, 1H),
8.96 (br d, J=1.76 Hz, 1H), 9.32 (s, 1H), 9.65 (d, J=1.98 Hz, 1H), 9.76 (br s, 2H), 13.02 (br s, 1H),
14.14 (br s, 1H); ESIMS found for C_{21}H_{19}N_{7} mlz 370.1 (M+).
[0789] 5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 278.

[0790] ¾ NMR (400 MHz, DMSO-d<sub>6</sub>) δ ppm 2.62 - 2.77 (m, 2 H), 3.69 (br t, J=7.28 Hz, 2 H), 3.98 (br t, J=12.35 Hz, 2 H), 4.81 (s, 2 H), 7.48 (dd, J=7.83, 5.62 Hz, 1 H), 8.04 (s, 1 H), 8.30 - 8.39 (m, 2 H), 8.45 (dd, J=5.51, 1.10 Hz, 1 H), 8.64 (d, J=7.28 Hz, 1 H), 9.05 (d, J=1.54 Hz, 1 H), 9.48 (s, 1 H), 9.71 (d, J=1.76 Hz, 1 H), 13.22 (br s, 1 H), 14.27 (br s, 1 H); ESIMS found for C<sub>23</sub>H<sub>19</sub>F<sub>2</sub>N<sub>7</sub> mlz 432 (M+1).

279


[0792] ¾ NMR (400 MHz, DMSO-d<sub>6</sub>) δ ppm 7.44 (dd, J=7.94, 5.5 Hz, 1 H), 7.86 (s, 1 H), 8.25 - 8.30 (m, 1 H), 8.30 - 8.36 (m, 1 H), 8.41 (dd, J=5.51, 1.10 Hz, 1 H), 8.57 (d, J=7.94 Hz, 1 H), 9.31 (s, 1 H), 9.71 (s, 2 H), 13.23 (br s, 1 H), 14.15 (br s, 1 H); ESIMS found for C<sub>17</sub>H<sub>11</sub>N<sub>7</sub> mlz 314.0 (M+1).

315

[0793] 5-(3-(4-(Furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine 315.

[0794] ¾ NMR (400 MHz, METHANOL-<sup>δ</sup>) δ ppm 3.30 (s, 6H), 7.28 (d, J=1.10 Hz, 1 H), 7.76 (d, J=6.39 Hz, 1 H), 7.87 - 7.93 (m, 1 H), 8.14 (s, 1 H), 8.23 (d, J=2.65 Hz, 1 H), 8.24 - 8.32 (m, 2 H), 8.37 (d, J=6.39 Hz, 1 H), 8.61 - 8.66 (m, 1 H), 8.68 (s, 1 H), 8.88 (s, 1 H); ESIMS found for C<sub>24</sub>H<sub>19</sub>N<sub>7</sub>O mlz 422 A (M+1).
N-(5-(3-(4-(Furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide 318.

$\frac{1}{4}$ NMR (400 MHz, METHANOL-$d^4$) $\delta$ ppm 3.91 (s, 2 H), 7.23 - 7.32 (m, 2 H), 7.36 (br t, $J=7.50$ Hz, 2 H), 7.44 (br d, $J=7.28$ Hz, 2 H), 7.76 (d, $J=6.17$ Hz, 1 H), 7.81 (t, $J=1.54$ Hz, 1 H), 8.07 (s, 1 H), 8.20 (d, $J=9.04$ Hz, 1 H), 8.30 (d, $J=8.82$ Hz, 1 H), 8.35 (br d, $J=6.17$ Hz, 1 H), 8.72 (s, 1 H), 9.19 (br s, 1 H), 9.36 (s, 1 H), 9.64 (s, 1 H); ESIMS found for C$_{30}$H$_{21}$N$_{7}$O$_{2}$ mlz 512.1 (M+).

N-Isopropyl-5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pyridin-3-amine 348.

$\frac{1}{4}$ NMR (400 MHz, DMSO-$d_6$) $\delta$ ppm 1.26 (d, $J=6.14$ Hz, 6 H), 3.83 - 3.94 (m, 1 H), 6.97 - 7.02 (m, 1 H), 7.53 (d, $J=4.82$ Hz, 1 H), 7.69 (dd, $J=2.85, 1.97$ Hz, 1 H), 7.98 - 8.04 (m, 1 H), 8.13 (d, $J=1.75$ Hz, 1 H), 8.22 (d, $J=8.77$ Hz, 1 H), 8.29 - 8.33 (m, 2 H), 8.38 (d, $J=3.51$ Hz, 1 H), 8.46 (s, 1 H), 8.79 (s, 1 H), 12.11 (br s, 2 H), 13.84 (br s, 1 H); ESIMS found for C$_{25}$H$_{21}$N$_{7}$S mlz 452.1 (M+).

5-(Pyridin-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 354.
[0800] ¾ NMR (400 MHz, DMSO-\(d_6\)) δ ppm 7.06 (dd, \(J=3.42, 1.21\) Hz, 1 H), 7.63 (d, \(J=5.51\) Hz, 1 H), 7.71 - 7.78 (m, 1 H), 8.08 (d, \(J=3.97\) Hz, 1 H), 8.32 - 8.39 (m, 2 H), 8.42 (d, \(J=3.75\) Hz, 1 H), 8.46 (d, \(J=9.04\) Hz, 1 H), 8.85 (d, \(J=6.84\) Hz, 2 H), 9.05 (br d, \(J=6.39\) Hz, 2 H), 12.36 (br s, 1 H), 14.02 (br s, 1 H); ESIMS found for C\(_{22}\)H\(_{14}\)N\(_{8}\)S mlz 395.0 (M+1).

363


[0802] ¾ NMR (400 MHz, DMSO-\(d_6\)) δ ppm 6.93 (br d, \(J=1.32\) Hz, 1 H), 7.44 (d, \(J=5.26\) Hz, 1 H), 7.64 (d, \(J=3.07\) Hz, 1 H), 7.96 (d, \(J=3.95\) Hz, 1 H), 8.20 - 8.33 (m, 3 H), 8.41 (d, \(J=3.95\) Hz, 1 H), 9.30 (s, 1 H), 9.65 (s, 2 H); ESIMS found for C\(_{21}\)H\(_{13}\)N\(_{7}\)S mlz 396.0 (M+1).

459

[0803] N-(5-(3-(4-(3-(2-(Dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide 459.

[0804] ¾ NMR (400 MHz, DMSO-\(d_6\)) δ ppm 2.74 - 2.88 (m, 6 H), 3.21 - 3.29 (m, 2 H), 3.46 - 3.55 (m, 2 H), 6.40 - 6.51 (m, 1 H), 6.90 (dt, \(J=9.10, 1.63\) Hz, 1 H), 6.98 (s, 1 H), 7.27 (br d, \(J=4.85\) Hz, 1 H), 7.49 - 7.63 (m, 2 H), 7.64 - 7.72 (m, 1 H), 7.84 (br d, \(J=1.98\) Hz, 1 H), 7.96 - 8.07 (m, 2 H), 8.10 (br d, \(J=9.04\) Hz, 1 H), 8.30 (br d, \(J=8.82\) Hz, 1 H), 8.35 (br d, \(J=4.85\) Hz, 1 H), 9.04 (br d, \(J=1.76\) Hz, 1 H), 9.18 (br d, \(J=2.21\) Hz, 1 H), 9.26 (br d, \(J=1.76\) Hz, 1 H), 9.88 (br s, 2 H), 10.77 (br s, 1 H), 12.52 (br s, 1 H), 13.88 (br s, 1 H); ESIMS found for C\(_{35}\)H\(_{30}\)FN\(_{9}\)O mlz 612.1 (M+1).
[0805] N1-(3-Fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N2,N2-dimethylethane-1,2-diamine 466.

[0806] ¾ NMR (400 MHz, DMSO-d6) δ ppm 2.82 (br d, J=2.2 1 Hz, 6 H), 3.27 (br d, J=5.73 Hz, 2 H), 3.57 (br d, J=7.28 Hz, 2 H), 6.64 - 6.75 (m, 1 H), 6.95 (br d, J=9.92 Hz, 1 H), 7.02 (s, 1 H), 7.34 (d, J=5.07 Hz, 1 H), 7.91 (d, J=1.32 Hz, 1 H), 8.34 - 8.42 (m, 2 H), 8.42 - 8.49 (m, 1 H), 8.80 (d, J=6.39 Hz, 2 H), 9.89 (d, J=6.39 Hz, 2 H), 10.44 (br s, 1 H), 12.71 (br s, 1 H), 14.13 (br s, 1 H); ESIMS found for C35H38FN9 mlz 604. (M+1).

[0807] N1-(3-(2-(5-(((Cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-4-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine 473.

[0808] ¾ NMR (400 MHz, DMSO-d6) δ ppm 1.19 - 1.34 (m, 2 H), 1.45 - 1.55 (m, 2 H), 1.55 - 1.67 (m, 2 H), 1.73 - 1.87 (m, 2 H), 2.16 - 2.28 (m, 1 H), 2.83 (br d, J=4.19 Hz, 6 H), 2.89 - 3.02 (m, 2 H), 3.25 - 3.35 (m, 2 H), 4.32 (br d, J=1.54 Hz, 2 H), 6.61 - 6.70 (m, 1 H), 6.86 - 6.95 (m, 1 H), 7.01 (br s, 1 H), 7.28 (br d, J=4.85 Hz, 1 H), 7.85 (br d, J=1.54 Hz, 1 H), 8.18 (br d, J=9.04 Hz, 1 H), 8.26 - 8.41 (m, 2 H), 8.87 (s, 1 H), 9.21 - 9.34 (m, 1 H), 9.54 (s, 1 H), 12.51 (br d, J=1.10 Hz, 1 H), 13.89 (br s, 1 H); ESIMS found for C35H38FN9 mlz 604. (M+1).
518

5-(5-(Benzyloxy)pyridin-3-yl)-3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 518.

\[ \text{\textit{NMR} (400 MHz, DMSO-\textit{d}_6) \delta ppm 5.32 (s, 2 H), 7.07 (td, } J = 8.60, 2.43 \text{ Hz, } 1 \text{ H), 7.34 (d, } J = 5.07 \text{ Hz, } 1 \text{ H), 7.37 - 7.47 (m, 3 H), 7.47 - 7.52 (m, 2 H), 7.53 - 7.61 (m, 1 H), 7.64 - 7.71 (m, 1 H), 7.79 (d, } J = 7.72 \text{ Hz, } 1 \text{ H), 7.87 (d, } J = 1.54 \text{ Hz, } 1 \text{ H), 8.26 (s, 2 H), 8.38 (d, } J = 5.07 \text{ Hz, } 1 \text{ H), 8.45 (br s, } 1 \text{ H), 8.60 (br d, } J = 2.20 \text{ Hz, } 1 \text{ H), 9.15 (s, } 1 \text{ H), 12.66 (br s, } 1 \text{ H), 13.89 (br s, } 1 \text{ H); ESIMS found for } C_{33}H_{2i}FN_0 m/z 513.1 (M+). \]

533

5-(3-(4-(4-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol 533.

\[ \text{\textit{NMR} (400 MHz, METHANOL-\textit{d}^4) \delta ppm 7.50 (t, } J = 8.82 \text{ Hz, } 2 \text{ H), 7.71 (d, } J = 6.17 \text{ Hz, } 1 \text{ H), 8.05 - 8.14 (m, 3 H), 8.21 (d, } J = 8.82 \text{ Hz, } 1 \text{ H), 8.27 - 8.34 (m, 1 H), 8.40 (d, } J = 2.21 \text{ Hz, } 1 \text{ H), 8.45 (br d, } J = 6.17 \text{ Hz, } 1 \text{ H), 8.78 (s, } 1 \text{ H), 9.16 (s, } 1 \text{ H); ESIMS found for } C_{42}H_{5}FN_0 m/z 423.1 (M+). \]

563

N,N-Dimethyl-2-(((5-(3-(4-pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine 563.
¾ NMR (400 MHz, DMSO-$d_6$) δ ppm 2.53 - 2.58 (m, 2 H), 2.90 (br s, 6 H), 4.60 - 4.73 (m, 2 H), 7.45 (br d, $J=5.07$ Hz, 1 H), 7.84 (br dd, $J=1.76$ Hz, 1 H), 7.99 (br dd, $J=8.16$, 5.07 Hz, 1 H), 8.22 - 8.35 (m, 2 H), 8.44 (br d, $J=5.07$ Hz, 1 H), 8.49 (br s, 1 H), 8.60 (br d, $J=2.43$ Hz, 1 H), 8.70 (br d, $J=8.60$ Hz, 1 H), 8.94 (br d, $J=4.4$ Hz, 1 H), 9.21 (s, 1 H), 9.31 (s, 1 H), 10.55 (br s, 1 H), 12.75 (br s, 1 H), 14.01 (br s, 1 H); ESIMS found for C$_{23}$H$_{27}$N$_7$ m/z 402.2 (M+).

578

3-(4-(Pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)-ethoxy) pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine 578.

¾ NMR (400 MHz, DMSO-$d_6$) δ ppm 1.71 (br s, 4 H), 2.63 (br s, 4 H), 2.95 (br t, $J=5.26$ Hz, 2 H), 4.28 (br t, $J=5.48$ Hz, 2 H), 7.37 (d, $J=4.82$ Hz, 1 H), 7.91 (br d, $J=4.82$ Hz, 2 H), 7.94 (s, 1 H), 8.16 - 8.19 (m, 1 H), 8.22 (s, 2 H), 8.40 (dd, $J=4.60$, 2.41 Hz, 1 H), 8.42 (br s, 1 H), 8.83 (br d, $J=3.5$ Hz, 2 H), 9.05 (s, 1 H), 12.57 (br s, 1 H); ESIMS found for C$_{26}$H$_{28}$N$_8$ m/z 503.1 (M+).

601

3-(4-(Piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine 601.

¾ NMR (400 MHz, DMSO-$d_6$) δ ppm 1.64 (br d, $J=0.66$ Hz, 1 H), 1.71 (br d, $J=0.66$ Hz, 1 H), 1.79 (br s, 4 H), 2.18 (br s, 2 H), 3.07 (br dd, $J=6.39$, 3.31 Hz, 2 H), 3.19 - 3.30 (m, 1 H), 3.40 (br d, $J=10.80$ Hz, 2 H), 3.64 (br s, 2 H), 3.92 (br s, 4 H), 6.78 - 6.91 (m, 1 H), 7.46 (br d, $J=8.60$ Hz, 1 H), 7.77 (br s, 1 H), 7.97 (br d, $J=6.62$ Hz, 1 H), 8.05 - 8.13 (m, 1 H), 9.07 (br s, 1 H), 9.18 (br s, 1 H), 13.04 (br s, 1 H), 13.76 (s, 1 H); ESIMS found for C$_{23}$H$_{27}$N$_7$ m/z 402.2 (M+).
3-(4-(4-Methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine 635.

¾ NMR (400 MHz, DMSO- d6) δ ppm 2.87 (s, 3 H), 3.29 - 3.39 (m, 2 H), 3.60 - 3.69 (m, 2 H), 3.84 - 3.95 (m, 2 H), 4.63 (br d, J = 13.89 Hz, 2 H), 6.99 (d, J = 7.28 Hz, 1 H), 7.73 (s, 1 H), 7.87 (d, J = 8.82 Hz, 1 H), 8.11 (d, J = 8.82 Hz, 1 H), 8.18 (d, J = 7.28 Hz, 1 H), 8.54 (s, 2 H), 11.39 (br s, 1 H), 12.91 (br s, 1 H), 13.83 (br s, 1 H); ESIMS found for C21H21N9 m/z 400.1 (M+).

5-(1-Methyl-1H-pyrazol-4-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine 652.

¾ NMR (400 MHz, DMSO- d6) δ ppm 3.95 (s, 3 H), 7.47 (dd, J = 7.72, 5.51 Hz, 1 H), 7.77 (s, 1 H), 7.81 (d, J = 8.82 Hz, 1 H), 8.11 (d, J = 8.82 Hz, 1 H), 8.27 (s, 1 H), 8.43 (br d, J = 5.29 Hz, 1 H), 8.55 (br d, J = 7.72 Hz, 1 H), 8.66 (s, 1 H), 13.08 (br s, 1 H), 13.94 (br s, 1 H); ESIMS found for C17H13N7 m/z 316.0 (M+).

N-(5-(3-(4-(Furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide 689.

¾ NMR (400 MHz, METHANOL- d4) δ ppm 1.53 - 1.68 (m, 2 H), 2.03 - 2.13 (m, 2 H), 2.24 - 2.36 (m, 1 H), 2.61 (d, J = 6.84 Hz, 2 H), 2.99 - 3.10 (m, 2 H), 3.43 (br d,
J = 13.01 Hz, 2 H), 7.29 (d, J = 3.75 Hz, 1 H), 7.81 (d, J = 3.53 Hz, 1 H), 8.04 (br d, J = 6.17 Hz, 1 H),
8.16 (s, 1 H), 8.17 - 8.22 (m, 1 H), 8.28 (d, J = 8.82 Hz, 1 H), 8.48 (br d, J = 6.39 Hz, 1 H), 8.80 (s, 1 H), 9.35 (br d, J = 1.98 Hz, 1 H), 9.39 (br s, 1 H), 9.41 (br s, 1 H); ESIMS found for C20H26N5O2
mlz 519.1 (M+1).

[0825] 5-(5-(Cyclohexyloxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo [2,3-b]pyridin-2-yl)-1H-pyrazolo [4,3-b]pyridine 703.

[0826] 3¹ NMR (400 MHz, DMSO-d₆) δ ppm 1.25 - 1.36 (m, 1 H), 1.37 - 1.49 (m, 2 H), 1.56 (q, J = 9.50 Hz, 3 H), 1.76 (br d, J = 7.45 Hz, 2 H), 2.00 - 2.11 (m, 2 H), 4.73 - 4.82 (m, 1 H), 7.09 (br s, 1 H), 7.66 (d, J = 5.70 Hz, 1 H), 7.76 (br s, 1 H), 8.12 (d, J = 3.51 Hz, 1 H), 8.25 - 8.35 (m, 2 H), 8.35 - 8.41 (m, 2 H), 8.63 (br s, 1 H), 8.65 (br s, 1 H), 9.20 (s, 1 H), 12.45 (br s, 1 H), 13.89 (br s, 1 H); ESIMS found for C28H4N6O5S mlz 493.1 (M+1).

[0827] 5-(5-(Piperidin-4-yloxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo [2,3-b]pyridin-2-yl)-1H-pyrazolo [4,3-b]pyridine 704.

[0828] 3¹ NMR (400 MHz, DMSO-d₆) δ ppm 1.95 - 2.08 (m, 2 H), 2.19 - 2.31 (m, 2 H), 3.08 - 3.20 (m, 2 H), 3.27 - 3.38 (m, 2 H), 5.05 - 5.13 (m, 1 H), 7.14 (br d, J = 1.75 Hz, 1 H), 7.71 (br d, J = 5.26 Hz, 1 H), 7.79 (br s, 1 H), 8.18 (br d, J = 3.95 Hz, 1 H), 8.25 - 8.33 (m, 2 H), 8.36 - 8.46 (m, 2 H), 8.62 (br s, 1 H), 8.71 (br s, 1 H), 9.13 (br s, 2 H), 9.23 (s, 1 H), 12.60 (br s, 1 H), 13.95 (br s, 1 H); ESIMS found for C27H31N7OS mlz 494.0 (M+1).

Example 2.

[0829] The screening assay for Wnt activity is described as follows. Reporter cell lines can be generated by stably transducing cancer cell lines (e.g., colon cancer) or primary cells
(e.g., IEC-6 intestinal cells) with a lentiviral construct that includes a Wnt-responsive promoter driving expression of the firefly luciferase gene.

[0830] SW480 colon carcinoma cells were transduced with a lentiviral vector expressing luciferase with a human Sp5 promoter consisting of a sequence of eight TCF/LEF binding sites. SW480 cells stably expressing the Sp5-Luc reporter gene and a hygromycin resistance gene were selected by treatment with 150 µg/mL of hygromycin for 7 days. These stably transduced SW480 cells were expanded in cell culture and used for all further screening activities. Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 10-point dose-response curves starting from 10 µM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 384-well white solid bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.1%. For Sp5-Luc reporter gene assays, the cells were plated at 4,000 cells/well in 384-well plates with medium containing 1% fetal bovine serum and incubated overnight at 37°C and 5% CO₂. Following incubation, 20 µl of BrightGlo luminescence reagent (Promega) was added to each well of the 384-well assay plates. The plates were placed on an orbital shaker for 2 min and then luminescence was quantified using the Envision (Perkin Elmer) plate reader. Readings were normalized to DMSO only treated cells, and normalized activities were utilized for EC50 calculations using the dose-response log (inhibitor) vs. response -variable slope (four parameters) nonlinear regression feature available in GraphPad Prism 5.0 (or Dotmatics). For EC50 of >10 µM, the percent inhibition at 10 µM is provided.

[0831] Table 2 shows the measured activity for representative compounds of Formula I as described herein.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>&gt;10 (47.3%)</td>
<td>96</td>
<td>0.255</td>
<td>226</td>
<td>3.447</td>
<td>363</td>
<td>&gt;10 (29.8%)</td>
</tr>
<tr>
<td>8</td>
<td>&gt;10 (14.3%)</td>
<td>102</td>
<td>&gt;10 (9.5%)</td>
<td>232</td>
<td>3.835</td>
<td>459</td>
<td>1.499</td>
</tr>
<tr>
<td>15</td>
<td>&gt;10 (8.0%)</td>
<td>110</td>
<td>&gt;10 (47.7%)</td>
<td>235</td>
<td>6.095</td>
<td>466</td>
<td>&gt;10 (8.6%)</td>
</tr>
<tr>
<td>33</td>
<td>&gt;10 (16.2%)</td>
<td>115</td>
<td>&gt;10 (24.4%)</td>
<td>240</td>
<td>3.912</td>
<td>473</td>
<td>4.668</td>
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<tr>
<td>39</td>
<td>&gt;10 (0%)</td>
<td>117</td>
<td>&gt;10 (11.8%)</td>
<td>256</td>
<td>&gt;10 (47.0%)</td>
<td>518</td>
<td>&gt;10 (16.7%)</td>
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<tr>
<td>54</td>
<td>&gt;10 (10.2%)</td>
<td>127</td>
<td>&gt;10 (5.8%)</td>
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<td>3.777</td>
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<td>0.310</td>
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<td>55</td>
<td>&gt;10 (32.0%)</td>
<td>137</td>
<td>&gt;10 (19.5%)</td>
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<td>2.363</td>
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<td>578</td>
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</tr>
<tr>
<td>69</td>
<td>&gt;10 (8.3%)</td>
<td>181</td>
<td>&gt;10 (41.4%)</td>
<td>278</td>
<td>0.104</td>
<td>601</td>
<td>&gt;10 (5.5%)</td>
</tr>
<tr>
<td>76</td>
<td>&gt;10 (37.3%)</td>
<td>183</td>
<td>&gt;10 (6.5%)</td>
<td>279</td>
<td>&gt;10 (8.0%)</td>
<td>635</td>
<td>&gt;10 (13.4%)</td>
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<tr>
<td>80</td>
<td>&gt;10 (29.0%)</td>
<td>187</td>
<td>&gt;10 (14.3%)</td>
<td>315</td>
<td>&gt;10 (6.6%)</td>
<td>652</td>
<td>2.260</td>
</tr>
<tr>
<td>84</td>
<td>&gt;10 (3.0%)</td>
<td>194</td>
<td>5.274</td>
<td>318</td>
<td>&gt;10 (3.4%)</td>
<td>689</td>
<td>&gt;10 (10.9%)</td>
</tr>
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</table>

**Table 2.**
Example 3.

Representative compounds were screened using the following assay procedure to assess the effect on cell viability as described below.

Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 8-point dose-response curves from 10 µM to 0.0045 µM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 96-well clear bottom, black-walled plates (Corning-Costar).

Approximately 2 x 10^3 SW480 colon cancer cells were seeded into each well and allowed to incubate in the presence or absence of compound for four days at 37°C/5% CO2. Eight replicates of DMSO-treated cells served as controls and cells treated with compound were performed in duplicate.

After incubation, 20 µL of CellTiter-Blue (Promega) was added to each well allowed to incubate for approximately 3 hours. This reagent was a buffered solution which contains resazurin, metabolically active cells were able to reduce resazurin (blue) into resorufin (pink) which was highly fluorescent. This measured fluorescence was used as a readout for cell viability.

After incubation, the plates were read at Ex 560 nm Em 590 run (Cytation 3, BioTek). Dose-response curves were generated and EC50 concentration values were calculated using non-linear regression curve fit in the GraphPad Prism (San Diego, CA) or Dotmatics’ Studies Software (Bishops Stortford, UK). For EC50 of >10 µM, the percent inhibition at 10 µM is provided.

Table 3 shows the activity of representative compounds of Formula I as provided herein.

<table>
<thead>
<tr>
<th>Table 3.</th>
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</thead>
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<tr>
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<tr>
<td>Compound</td>
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<tr>
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<td>91</td>
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</tbody>
</table>

**Example 4.**

Representative compounds were screened using primary human fibroblasts (derived from IPF patients) treated with TGF-β1 to determine their ability to inhibit the fibrotic process.

**Human Fibroblast Cell Culture:** Primary human fibroblasts derived from IPF patients (LL29 cells) [Xiaoqiu Liu, et.al., "Fibrotic Lung Fibroblasts Show Blunted Inhibition by cAMP Due to Deficient cAMP Response Element-Binding Protein Phosphorylation", *Journal of Pharmacology and Experimental Therapeutics* (2005), 315(2), 678-687; Watts, K. L., et.al., "RhoA signaling modulates cyclin D1 expression in human lung fibroblasts; implications for idiopathic pulmonary fibrosis", *Respiratory Research* (2006), 7(1), 88] were obtained from American Type Culture Collection (ATCC) and expanded in F12 medium supplemented with 15% Fetal Bovine Serum and Penicillin/Streptomycin.

**Compound Screening:** Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:2, 11-point dose-response curves from 10 µM to 1.87 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 384-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.1%. LL29 cells are plated at 1,500 cells/well in 80 µL/well F12 medium supplemented with 1% Fetal Bovine Serum. One hour after addition of the cells, TGF-β1 (Peprotech: 20 ng/mL) was added to the plates to induce fibrosis (ref. 1 and 2 above). Wells treated with TGF-β1 and containing DMSO were used as controls. Cells were incubated at 37°C and 5% CO2 for 4 days. Following incubation for 4 days, SYTOX green nucleic acid stain (Life Technologies [Thermo Fisher Scientific]) was added to the wells at a final concentration of 1 µM and incubated at room temperature for 30 min. Cells were then fixed using 4% formaldehyde (Electron Microscopy Sciences), washed 3 times with PBS followed by blocking and permeabilization using 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS. Cells were then stained with antibody specific to a-smooth...
muscle actin (aSMA; Abeam) (ref. 1 and 2 above) in 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS, and incubated overnight at 4°C. Cells were then washed 3 times with PBS, followed by incubation with Alexa Flor-647 conjugated secondary antibody (Life Technologies [Thermo Fisher Scientific]) and DAPI at room temperature for 1 hour. Cells were then washed 3 times with PBS and plates were sealed for imaging. aSMA staining was imaged by excitation at 630 nm and emission at 665 nm and quantified using the Compartmental Analysis program on the CellInsight CX5 (Thermo Scientific). Dead or apoptotic cells were excluded from analysis based on positive SYTOX green staining. % of total cells positive for aSMA were counted in each well and normalized to the average of 11 wells treated with TGF-β1 on the same plate using Dotmatics’ Studies Software. The normalized averages (fold change over untreated) of 3 replicate wells for each compound concentration were used to create dose-responses curves and EC50 values were calculated using non-linear regression curve fit in the Dotmatics’ Studies Software. For EC50 of >10 µM, the percent inhibition at 10 µM is provided.

Table 4 shows the activity of representative compounds of Formula I as provided herein.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50 (µM)</th>
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<td>8</td>
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<tr>
<td>91</td>
<td>2.190</td>
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</table>

Example 5.

Representative compounds were screened using primary human mesenchymal stem cells (hMSCs) to determine their ability to induce chondrogenesis (process by which cartilage is developed).
**Human Mesenchymal Stem Cell Culture:** Primary human mesenchymal stem cells (hMSCs) were purchased from Lonza (Walkersville, MD) and expanded in Mesenchymal Stem Cell Growth Media (Lonza). Cells between passage 3 and 6 were used for the experiments.

**Compound Screening:** Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 6-point dose-response curves from 2700 nM to 10 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 96-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.03%. hMSCs were plated at 20,000 cells/well in 250 µL/well Incomplete Chondrogenic Induction Medium (Lonza; DMEM, dexamethasone, ascorbate, insulin-transferrin-selenium [ITS supplement], gentamycin-amphotericin [GA-1000], sodium pyruvate, proline and L-glutamine). TGF-β3 (10 ng/mL) was used as a positive control for differentiation while negative control wells were treated with 75 nL DMSO for normalization and calculating EC50 values. Cells were incubated at 37°C and 5% CO2 for 6 days. To image chondrogenic nodules, the cells were fixed using 4% formaldehyde (Electron Microscopy Sciences), and stained with 2 µg/mL Rhodamine B (Sigma-Aldrich) and 20 µM Nile Red (Sigma-Aldrich) [Johnson K., et.al, A Stem Cell-Based Approach to Cartilage Repair, *Science*, (2012). 336(6082), 717-721]. The nodules imaged (4 images per well at 4X magnification) by excitation at 531 nm and emission at 625 nm and quantified using the CellInsight CX5 (Thermo Scientific). Number of nodules in each well was normalized to the average of 3 DMSO treated wells on the same plate using Excel (Microsoft Inc.). The normalized averages (fold change over DMSO) of 3 replicate wells for each compound concentration were calculated. Due to solubility limitations of some of the compounds, curve fitting was incomplete leading to inaccurate EC50 determinations.

Using TGF-β3 as a positive control, the concentration of representative compounds required to induce 50% levels of chondrogenesis is reported. In addition, the maximum activity of each compound and the respective dose that each compound reached maximum chondrogenesis activity is reported. Table 5 shows the activity of representative compounds as provided herein.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conc (nM) of Max. activity</th>
<th>Max. Activity as % TGF-β3 activity</th>
<th>Conc (nM) of 50% TGF-β3 activity</th>
<th>Compound</th>
<th>Conc (nM) of Max. activity</th>
<th>Max. Activity as % TGF-β3 activity</th>
<th>Conc (nM) of 50% TGF-β3 activity</th>
</tr>
</thead>
<tbody>
<tr>
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<td>62</td>
<td>900</td>
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</table>

Table 5.
Example 6. Representative compounds were screened using the following assay procedure to determine their ability to inhibit IL-6 and therefore demonstrate their anti-inflammatory properties.

**Human Monocyte Cell Culture:** Human monocyte cell line (THP-1 cells; Catalog # TIB-202, ATCC, Manassas, VA) were cultured in Roswell Park Memorial Institute (RPMI) 1640 Medium (Catalog # 21870-100, Buffalo, NY) with 1% L-glutamine, 1% HEPES, 1% Sodium Pyruvate, 2% Sodium Bicarbonate supplemented with 100 units/mL penicillin, 50 µg/mL streptomycin, 2-mercaptoethanol (0.05mM) [basal medium] and 10% fetal bovine serum (Catalog # 16140089, Life Technologies, Carlsbad, CA) at 37°C and 5% CO₂.

**Compound Screening:** THP-1 cells were cultured in basal media with 1% FBS for 24 hours before the start of the assay. Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 10-point dose-response curves starting from 10 µM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 384-well white low volume assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.1%. THP-1 cells were plated at 5000 cells/well in the 384-well plates and incubated at 37°C for 2 h. 500 ng/mL of LPS was added after 2 hours and cells were incubated for another 22 hours at 37°C. Plates were spun in a centrifuge for 1 minute at 10,000 rpm and a mixture of anti-IL6 XL665, and anti-IL6 Cryptate diluted in reconstitution buffer (Cisbio Inc.) was added to each well. Following incubation for 3hrs at room temperature, Homogeneous Time-Resolved Fluorescence (HTRF) was measured using the Envision (Perkin Elmer) at 665 nm and 620 nM. The ratio of fluorescence at 665 nm to 620 nm was used as a readout for IL6 quantification. All samples were processed in duplicate. Readings were normalized to DMSO treated cells and normalized activities were utilized for EC₅₀ calculations using the dose-response log (inhibitor) vs. response -
variable slope (four parameters) nonlinear regression feature available in GraphPad Prism 5.0 (or Dotmatics). For EC50 of >10 µM, the percent inhibition at 10 µM is provided.

Table 6 shows the activity of representative compounds of Formula I as provided herein.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
<th>Compound</th>
<th>EC50 (µM)</th>
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</tr>
<tr>
<td>8</td>
<td>&gt;10 (13.7%)</td>
<td>102</td>
<td>&gt;10 (23.9%)</td>
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<td>3.427</td>
<td>459</td>
<td>0.009</td>
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<tr>
<td>54</td>
<td>&gt;10 (34.8%)</td>
<td>127</td>
<td>&gt;10 (50.2%)</td>
<td>258</td>
<td>&gt;10 (4.6%)</td>
<td>533</td>
<td>&gt;10 (37.1%)</td>
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<tr>
<td>55</td>
<td>&gt;10 (14.1%)</td>
<td>137</td>
<td>&gt;10 (40.8%)</td>
<td>265</td>
<td>0.653</td>
<td>563</td>
<td>&gt;10 (20.3%)</td>
</tr>
<tr>
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<td>0.100</td>
<td>173</td>
<td>0.967</td>
<td>275</td>
<td>0.157</td>
<td>578</td>
<td>&gt;10 (27.0%)</td>
</tr>
<tr>
<td>69</td>
<td>1.076</td>
<td>181</td>
<td>&gt;10 (29.2%)</td>
<td>278</td>
<td>0.107</td>
<td>601</td>
<td>3.495</td>
</tr>
<tr>
<td>76</td>
<td>&gt;10 (42.2%)</td>
<td>183</td>
<td>&gt;10 (18.2%)</td>
<td>279</td>
<td>0.003</td>
<td>635</td>
<td>&gt;10 (8.4%)</td>
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<tr>
<td>80</td>
<td>&gt;10 (18.2%)</td>
<td>187</td>
<td>0.340</td>
<td>315</td>
<td>0.418</td>
<td>652</td>
<td>0.046</td>
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<td>84</td>
<td>0.006</td>
<td>194</td>
<td>6.945</td>
<td>318</td>
<td>&gt;10 (46.6%)</td>
<td>689</td>
<td>3.342</td>
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<tr>
<td>88</td>
<td>&gt;10 (38.7%)</td>
<td>195</td>
<td>&gt;10 (26.0%)</td>
<td>348</td>
<td>1.347</td>
<td>703</td>
<td>0.303</td>
</tr>
<tr>
<td>91</td>
<td>&gt;10 (36.3%)</td>
<td>196</td>
<td>&gt;10 (46.5%)</td>
<td>354</td>
<td>1.615</td>
<td>704</td>
<td>0.106</td>
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</table>
WHAT IS CLAIMED IS:

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

![Chemical Structure]

wherein:

R₁ and R₂ are independently selected from the group consisting of H and halide;

R³ is selected from the group consisting of -heteroaryl optionally substituted with 1-4 R⁶ and -heterocyclyl optionally substituted with 1-10 R⁷;

R⁵ is selected from the group consisting of H, -heteroaryl optionally substituted with 1-4 R⁸, -heterocyclyl optionally substituted with 1-10 R⁹, and -aryl optionally substituted with 1-5 R¹⁰;

each R⁶ is independently selected from the group consisting of halide, -(C₁-6 alkyl), -(C₂-6 alkenyl), -(C₁-4 alkenylene), R₆₇ heterocyclyl optionally substituted with 1-10 R¹¹, -(C₂-4 alkenylene)₂₆ R₆₇ heterocyclyl optionally substituted with 1-10 R¹¹, -(C₂-4 alkynylene)₈₇ R₆₇ heterocyclyl optionally substituted with 1-10 R¹¹, -(C₁-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-4 alkynylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₁-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₁-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₁-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₁-4 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substituted with 1-12 R¹², -(C₂-6 alkylene)₉₇ carbocyclyl optionally substated with 1-5 R¹³, -(C₂-4 alkenylene)₉₇ aryl optionally substituted with 1-5 R¹³, -(C₂-4 alkenylene)₉₇ aryl optionally substituted with 1-5 R¹³, -(C₂-4 alkynylene)₉₇ aryl optionally substituted with 1-5 R¹³, -(C₁-6 alkylene)NR °R¹⁸, -(C₂-6 alkylene)NR °R¹⁸, -(C₂-6 alkylene)NR °R¹⁸, -(C₂-6 alkylene)NR °R¹⁸, and -(C₁-4 alkylene)₉₇ OR°;
each R^10 is independently selected from the group consisting of -(C\_i\_6 alkyl), -(C\_2\_6 alkenyl), -(C\_2\_6 alkynyl), halide, -CF\_3, -CN, -(C\_i\_6 alkylene)p\_NH\_2 R^9, -(C\_2\_6 alkenylene)p\_NH\_2 R^9, -(C\_2\_6 alkynylene)p\_NH\_2 R^9, -(C\_2\_6 alkynylene)p\_NR^5 R^16, -(C\_2\_6 alkynylene)p\_NR^5 R^16, -(C\_2\_alkynylene)p\_NR^5 R^16, and -OR^27;

each R^11 is independently selected from the group consisting of amino, -(C\_1\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), halide, -CF\_3, and -CN;

each R^12 is independently selected from the group consisting of -(C\_1\_4 alkyl), -(C\_2\_4 alkenyl), -(C\_2\_alkynyl), halide, -CF\_3, and -CN;

each R^13 is independently selected from the group consisting of -(C\_1\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), halide, -CF\_3, and -CN;

each R^14 is independently selected from the group consisting of -(C\_1\_4 alkyl), -(C\_M haloalkyl), -(C\_2\_9 alkyl), -(C\_2\_9 alkynyl), -heteroaryl optionally substituted with 1-4 R^20, -aryl optionally substituted with 1-5 R^21, -CF\_naryl optionally substituted with 1-5 R^21, -carbocyclyl optionally substituted with 1-12 R^22, -CH\_2carbocyclyl optionally substituted with 1-12 R^22, -(C\_r\_alkylene)p\_NR^5 R^26, -(C\_2\_4 alkynylene)p\_NR^5 R^26, -(C\_2\_4 alkynylene)p\_NR^5 R^26, -heterocyclyl optionally substituted with 1-10 R^23, and -CF\_nheterocyclyl optionally substituted with 1-10 R^23;

each R^15 is independently selected from the group consisting of H, -(C\_i\_4 alkyl), -(C\_2\_4 alkynyl), and -(C\_2\_4 alkynyl);

each R^16 is independently selected from the group consisting of H, -(C\_i\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), -CH\_2aryl optionally substituted with 1-5 R^23, and -CH\_2carbocyclyl optionally substituted with 1-12 R^22;

each R^17 is independently selected from the group consisting of H, -(C\_i\_4 alkyl), -(C\_2\_4 alkynyl), and -(C\_2\_4 alkynyl);

each R^18 is independently selected from the group consisting of H, -(C\_i\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), -CH\_2aryl optionally substituted with 1-5 R^23, and -CF\_nhcarbocyclyl optionally substituted with 1-12 R^22;

each R^19 is independently selected from the group consisting of -(C\_i\_4 alkyl), -(C\_2\_4 alkynyl), and -(C\_2\_4 alkynyl);

each R^20 is independently selected from the group consisting of -(C\_1\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), halide, -CF\_3, and -CN;

each R^21 is independently selected from the group consisting of -(C\_1\_4 alkyl), -(C\_2\_4 alkynyl), -(C\_2\_4 alkynyl), halide, -CF\_3, and -CN.
each R\textsuperscript{22} is independently selected from the group consisting of -\((\text{Ci-4 alkyl})\), -\((\text{C2-4 alkenyl})\), halide, -\text{CF3}, and -\text{CN};

each R\textsuperscript{23} is independently selected from the group consisting of -\((\text{C1-4 alkyl})\), -\((\text{C2-4 alkenyl})\), halide, -\text{CF3}, and -\text{CN};

R\textsuperscript{24} is selected from the group consisting of H, -\((\text{C1-6 alkyl})\), -\((\text{C2-6 alkenyl})\), -\((\text{C1-4 alkylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C2-4 alkenylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C2-4 alkynylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C1-4 alkylene})\)\textsubscript{p} carbocyclyl optionally substituted with 1-12 R\textsuperscript{22}, -\((\text{C2-4 alkenylene})\)\textsubscript{p} carbocyclyl optionally substituted with 1-12 R\textsuperscript{22}, -\((\text{C1-4 alkynylene})\)\textsubscript{p} carbocyclyl optionally substituted with 1-12 R\textsuperscript{22}, -\((\text{C2-4 alkynylene})\)\textsubscript{p} aryl optionally substituted with 1-5 R\textsuperscript{21}, -\((\text{C2-4 alkenylene})\)\textsubscript{p} aryl optionally substituted with 1-5 R\textsuperscript{21}, -\((\text{C2-4 alkynylene})\)\textsubscript{p} aryl optionally substituted with 1-5 R\textsuperscript{21}, -\((\text{C1-6 alkenylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, -\((\text{C2-4 alkenylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, and -\((\text{C2-4 alkynylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26};

each R\textsuperscript{25} is independently selected from the group consisting of H, -\((\text{C1-6 alkyl})\), -\((\text{C2-6 alkenyl})\), and -\((\text{C2-6 alkynyl})\);

each R\textsuperscript{26} is independently selected from the group consisting of H, -\((\text{C1-6 alkyl})\), -\((\text{C2-6 alkenyl})\), and -\((\text{C2-6 alkynyl})\);

R\textsuperscript{27} is selected from the group consisting of H, -\((\text{C1-6 alkyl})\), -\((\text{C2-6 alkenyl})\), -\((\text{C1-4 alkenylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C2-4 alkenylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C2-4 alkynylene})\)\textsubscript{p} heterocyclyl optionally substituted with 1-10 R\textsuperscript{25}, -\((\text{C1-6 alkenylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, -\((\text{C2-6 alkenylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}, and -\((\text{C2-6 alkynylene})\)\textsubscript{p} NR\textsuperscript{25}R\textsuperscript{26}; and

each p is independently an integer of 0 or 1.

2. The compound of claim 1, wherein R\textsuperscript{1} and R\textsuperscript{2} are H.
3. The compound of any of claims 1-2, wherein R\textsuperscript{1} is H, and R\textsuperscript{2} is F.
4. The compound of any of claims 1-3, wherein R\textsuperscript{3} is -pyridinyl optionally substituted with 1 R\textsuperscript{6}.
5. The compound of any of claims 1-4, wherein R\textsuperscript{3} is -pyrinderin-3-yl optionally substituted with 1 R\textsuperscript{6}.
6. The compound of any of claims 1-5, wherein R\textsuperscript{3} is -pyrimidinyl optionally substituted with 1 R\textsuperscript{6}.
7. The compound of any of claims 1-6, wherein R\textsuperscript{3} is -pyrimidine-5-yl optionally substituted with 1 R\textsuperscript{6}.

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8. The compound of any of claims 1-7, wherein R3 is -pyrazolyl optionally substituted with 1 R6.

9. The compound of any of claims 1-8, wherein R3 is -imidazolyl substituted with 1-2 R6.

10. The compound of any of claims 1-9, wherein R6 is selected from the group consisting of -((C1-3 alkyl), -(C1-3 heterocyclyl) optionally substituted with 1-2 R11, -NHC(=0)R14, -NR15R16, -CH2NR17R18, and -OR24.

11. The compound of any of claims 1-10, wherein R6 is -(C1-3 alkyl).

12. The compound of any of claims 1-11, wherein each R6 is -(C1-3 alkyl).

13. The compound of any of claims 1-12, wherein R11 is halide.

14. The compound of any of claims 1-13, wherein R14 is selected from the group consisting of -(C1-5 alkyl), -phenyl optionally substituted with 1-2 R21, -G-phenyl optionally substituted with 1-2 R21, and -carbocyclyl optionally substituted with 1-2 R22.

15. The compound of any of claims 1-14, wherein R15 and R16 are independently selected from H and -(C1-3 alkyl).

16. The compound of any of claims 1-15, wherein R17 and R18 are independently selected from H and -(C1-3 alkyl).

17. The compound of any of claims 1-16, wherein R24 is selected from the group consisting of H, -(C1-3 alkyl), -(C1-3 heterocyclyl) optionally substituted with 1-2 R23, -(C1-3 heterocyclyl) optionally substituted with 1-2 R23, -(C1-3 heterocyclyl) optionally substituted with 1-2 R23, -(CH2)aryl optionally substituted with 1-2 R22, -(CH2)aryl optionally substituted with 1-2 R22, and -(CH2)aryl optionally substituted with 1-2 R22.

18. The compound of any of claims 1-17, wherein the -phenyl and -carbocyclyl are both unsubstituted.

19. The compound of any of claims 1-18, wherein R5 is -phenyl optionally substituted with 1-2 R10.

20. The compound of any of claims 1-19, wherein R10 is one halide.

21. The compound of any of claims 1-20, wherein one R10 is halide and one R10 is -CH2NHSO3R19.

22. The compound of any of claims 1-21, wherein R10 is -(C1-3 alkyl).

23. The compound of any of claims 1-22, wherein one R10 is halide and one R10 is -NHCH2CH2NR15R16.
24. The compound of any of claims 1-23, wherein R\textsuperscript{15} and R\textsuperscript{16} are independently selected from H and -(C\textsubscript{1}-3 alkyl).

25. The compound of any of claims 1-24, wherein R\textsuperscript{5} is -heteroaryl optionally substituted with 1-2 R\textsuperscript{8}.

26. The compound of any of claims 1-25, wherein R\textsuperscript{5} is selected from the group consisting of -pyridinyl optionally substituted with 1-2 R\textsuperscript{8}, -imidazolyl optionally substituted with 1-2 R\textsuperscript{8}, -furanyl optionally substituted with 1-2 R\textsuperscript{8}, and -thiophenyl optionally substituted with 1-2 R\textsuperscript{8}.

27. The compound of any of claims 1-26, wherein R\textsuperscript{8} is selected from the group consisting of halide, -(C\textsubscript{1}-3 alkyl), and - C(=0)R\textsuperscript{19}, and R\textsuperscript{19} is -(C\textsubscript{1}-2 alkyl).

28. The compound of any of claims 1-27, wherein R\textsuperscript{5} is -heterocyclyl optionally substituted with 1-2 R\textsuperscript{9}.

29. The compound of any of claims 1-28, wherein R\textsuperscript{5} is selected from the group consisting of -piperidinyl optionally substituted with 1-2 R\textsuperscript{9} and -piperazinyl optionally substituted with 1-2 R\textsuperscript{9}.

30. The compound of any of claims 1-29, wherein R\textsuperscript{9} is -(C\textsubscript{1}-3 alkyl).

31. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)propionamide [1];

N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [2];

5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [3];

3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [4];

3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [5];

N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)methyl)ethanamine [6];

5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [7];

N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [8];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [9];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [10];
N-(5-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [11];
5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [12];
1-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [13];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [14];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [15];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [16];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [17];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [18];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [19];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropane carboxamide [20];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarb oxamide [21];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecar boxamide [22];
N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecar boxamide [23];
N-benzyl-1-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [24];
1-cyclopentyl-N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [25];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [26];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [27];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [28];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [29];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [30];
5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [31];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [32];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [33];
N-((5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [34];
5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [35];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [36];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [37];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [38];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [39];
5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)N-isopropylpyridin-3-amine [40];
1-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [41];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [42];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [43];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [44];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [45];

3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [46];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [47];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [48];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [49];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [50];

N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [51];

N-benzyl-1-{((5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [52];

1-cyclopentyl-N-((5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [53];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(4-fluorophenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [54];

3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [55];

3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [56];

N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [57];

N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [58];

5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [59];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [60];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [61];
N-((5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [62];
5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [63];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [64];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutryamide [65];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [66];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [67];
5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [68];
1-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [69];
3-(4-(2-fluorophenyl)-1H-pyrazolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [70];
3-(4-(2-fluorophenyl)-1H-pyrazolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [71];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [72];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [73];
3-(4-(2-fluorophenyl)-1H-pyrazolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [74];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [75];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [76];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [77];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [78];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [79];
N-benzyl-l-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [80];
1-cyclopentyl-N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [81];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [82];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [83];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [84];
N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [85];
3-methyl-N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [86];
5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [87];
5-(pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [88];
5-(4-methylpyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [89];
N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [90];
N,N-dimethyl-5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [91];
N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [92];
N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [93];
2-phenyl-N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [94];
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [95];
N-isopropyl-5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [96];
N,N-dimethyl-1-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [97];
3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [102];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [98];
3,3-dimethyl-N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [100]; or a pharmaceutically acceptable salt thereof.

32. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [103];
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [104];
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [105];
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [106];
N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [107];
N-benzyl-1-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [108];
1-cyclopentyl-N-(5-(3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [109];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [110]; 3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-IH-pyrazolo[4,3-b]pyridine [111]; 5-(pyridin-2-yl)-3-(4-(pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [112]; N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [113]; 3-methyl-N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [114]; 5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [115]; 5-(pyridin-3-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [116]; 5-(4-methylpyridin-3-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [117]; N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methylethanamine [118]; N,N-dimethyl-5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [119]; N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [120]; N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [121]; 2-phenyl-N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [122]; N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [123]; N-isopropyl-5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [124]; N,N-dimethyl-1-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [125]; 3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-pyrrolidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [126];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [127];

3,3-dimethyl-N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [128];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [129];

5-(pyridin-4-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [130];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [131];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [132];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [133];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [134];

N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [135];

N-benzyl-1-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [136];

1-cyclopentyl-N-(5-(3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [137];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [138];

3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-IH-pyrazolo[4,3-b]pyridine [139];

5-(pyridin-2-yl)-3-(4-(pyridin-4-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [140];

N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [141];

3-methyl-N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [142];

5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [143];
3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [144];
5-(4-methylpyridin-3-yl)-3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [145];
N-((5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [146];
N,N-dimethyl-5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [147];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [148];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [149];
2-phenyl-N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [150];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [151];
N-isopropyl-5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [152];
N,N-dimethyl-1-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [153];
3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [154];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [155];
3,3-dimethyl-N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [156];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [157];
3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [158];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [159];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [160];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [161];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [162];
N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [163];
N-benzyl-1-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [164];
1-cyclopentyl-N-(5-(3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [165];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [166];
3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-IH-pyrazolo[4,3-b]pyridine [167];
5-(pyridin-2-yl)-3-(4-(pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [168];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [169];
3-methyl-N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [170];
5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [171];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-3-yl)-IH-pyrazolo[4,3-b]pyridine [172];
5-(4-methylpyridin-3-yl)-3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [173];
N-((5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [174];
N,N-dimethyl-5-((3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [175];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [176];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [177];
2-phenyl-N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [178];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [179];
N-isopropyl-5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [180];
N,N-dimethyl-1-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [181];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-lH-pyrazolo[4,3-b]pyridine [182];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-lH-pyrazolo[4,3-b]pyridine [183];
3,3-dimethyl-N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [184];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [185];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-lH-pyrazolo[4,3-b]pyridine [186];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [187];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [188];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [189];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [190];
N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [191];
N-benzyl-1-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [192];
l-cyclopentyl-N-(5-(3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [193];
5-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine [194];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-IH-pyrazolo[4,3-b]pyridine [195];
3-(4-(piperidin-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [196];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [197];
3-methyl-N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [198];
5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [199]; and
3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [200]; or a pharmaceutically acceptable salt thereof.

33. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [201];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [202];
N,N-dimethyl-5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)pyridin-3-amine [203];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [204];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [205];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)2-phenylacetamide [206];
N-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [207];
N-isopropyl-5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)propionamide [208];
N,N-dimethyl-1-(5-(3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [209];
3-(4-(4-methyl-IH-imidazol-1-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-yl)methyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [210];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [211];
3,3-dimethyl-N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [212];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [213];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [214];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [215];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [216];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [217];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [218];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [219];
N-benzyl-1-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl) methanamine [220];
1-cyclopentyl-N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [221];
5-(5-(3-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [222];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [223];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [224];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [225];
3-methyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)butanamide [226];
5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [227];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [228];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [229];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [230];
N,N,N-dimethyl-5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)amine [231];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [232];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [233];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [234];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [235];
N-isopropyl-5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)methanamine [236];
N,N,N-dimethyl-1-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [237];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [238];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [239];
3,3-dimethyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [240];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [241];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [242];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [243];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [244];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [245];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [246];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [247];
N-benzyl-1-(5-(3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [248];
1-cyclopentyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [249];
5-(5-(3-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine [250];
3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-lH-pyrazolo[4,3-b]pyridine [251];
3-(4-(4-methylpiperazin-1-yl)-lH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine [252];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [253];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [254];
5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [255];
5-(pyridin-3-yl)-3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine [256];
5-(4-methylpyridin-3-yl)-3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridine [257];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [258];
5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [259];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [260];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [261];
N-(5-(3-(lH-pyrrolo[2,3-b]pyridin-2-yl)-lH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [262];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [263];
5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [264];
l-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [265];
5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [266];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [267];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [268];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [269];
5-(pyridin-4-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [270];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [271];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [272];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [273];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [274];
N-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [275];
l-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N-benzylmethanamine [276];
l-(5-(3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N-(cyclopentylmethyl)methanamine [277];
5-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [278];
5-(pyrimidin-5-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [279];
5-(pyridin-2-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [280];
N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo-[2,3-b]pyridin-2-yl)-IH-pyrazolo-[4,3-b]pyridin-5-yl)propionamide [281];
3-methyl-N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [282];
5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [283];
5-(pyridin-3-yl)-3-(4-(methylpyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [284];
5-(4-methylpyridin-3-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [285];
N-((5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [286];
N,N-dimethyl-5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [287];
N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [288];
N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [289];
2-phenyl-N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [290];
N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [291];
N-isopropyl-5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [292];
N,N-dimethyl-I-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [293];
5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [294];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [295];
3,3-dimethyl-N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [296];
N-(5-(3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [297];
5-(pyridin-4-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,^b]pyridine [298];
N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [299]; and
N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [300]; or a pharmaceutically acceptable salt thereof.

34. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [301];
N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [302];
N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [303];
N-benzyl-l-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [304];
1-cyclopentyl-N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)methyl)methanamine [305];
5-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [306];
5-(pyrimidin-5-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [307];
5-(pyridin-2-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [308];
N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [309];
N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [310];
5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [311];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [312];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [313];
N-((5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [314];
5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [315];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [316];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [317];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [319];
5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [320];
1-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [321];
3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [322];
3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [323];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [324];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [325];
3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [326];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [327];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [328];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [329];
N-(5-(3-(4-(furan-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [330];
N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [331];
N-benzyl-1-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [332];
1-cyclopentyl-N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [333];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo [4,3-b]pyridine [334];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [335];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [336];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [337];
3-methyl-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [338];
5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [339];
5-(pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [340];
5-(4-methylpyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [341];
N-((5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [342];
N,N,N-dimethyl-5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [343];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [344];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [345];
2-phenyl-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [346];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamid [347];
N-isopropyl-5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [348];
N,N-dimethyl-l-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [349];
5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [350];
5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [351];
3,3-dimethyl-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [352];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [353];
5-(pyridin-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [354];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [355];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [356];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [357];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [358];
N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [359];
N-benzyl-l-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [360];
l-cyclopentyl-N-((5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [361];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [362];
5-(pyrimidin-5-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [363];
5-(pyridin-2-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [364];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [365];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [366];
5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [367];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [368];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [369];
N-((5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [370];
5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [371];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [372];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [373];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [374];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [375];
5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [376];
1-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [377];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [378];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [379];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [380];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [381];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [382];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [383];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [384];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [385];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [386];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [387];
N-benzyl-1-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pyridin-3-yl)methanamine [388];
l-cyclopentyl-N-((5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [389];
5-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [390];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [391];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [392];
N-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [393];
3-methyl-N-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [394];
5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [395];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-3-yl)-1H-pyrazolo[4,3-b]pyridine [396];
5-(4-methylpyridin-3-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [397];
N-((5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [398];
N,N-dimethyl-5-(3-(4-(5-methylthiophen-2-yl)pyridin-3-yl)pyridin-5-yl)pyridin-3-amine [399]; and
N-(5-(3-(4-(5-methylthiophen-2-yl)pyridin-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [400]; or a pharmaceutically acceptable salt thereof.

35. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [401];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [402];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [403];
N-isopropyl-5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [404];
N,N-dimethyl-1-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [405];
3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [406];
3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [407];
3,3-dimethyl-N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butanamide [408];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [409];
3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [410];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [411];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [412];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutane carboxamide [413];
N-(5-(3-(4-(5-methylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentane carboxamide [414];
N-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [415];
N-benzyl-1-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [416];
l-cyclopentyl-N-((5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [417];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [418];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [419];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [420];
N-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [421];
N-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [421];
l-(5-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [419];
l-(5-(2-(5-(pyrimidin-5-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [420];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
l-(5-(2-(5-(3-(4-(5-acetyltiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [422];
1-(5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [432];
1-(5-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [433];
1-(5-(2-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [434];
1-(5-(2-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [435];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [436];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [437];
1-(5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [438];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [439];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [440];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [441];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [442];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [443];
1-(5-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [444];
1-(5-(2-(5-(5-((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [445];
1-(5-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [446];
1-(5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [447];
1-(5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [448];
N-(5-(3-(4-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)propionamide [449];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-3-methylbutanamide [450];
N^1-(3-(2-(5-(5-aminopyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N,N-dimethylethane-1,2-diamine [451];
N^1-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [452];
N^1-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N,N-dimethylethane-1,2-diamine [453];
N^1-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pivalamide [454];
N^1-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N,N-dimethylethane-1,2-diamine [455];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pivalamide [456];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)isobutyramide [457];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)phenylacetamide [458];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)benzamide [459];
N^1-(3-fluoro-5-(2-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrazolo[2,3-b]pyridin-4-yl)-N,N-dimethylethane-1,2-diamine [460];
N^1-(3-(2-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [461];
N^1-(3-fluoro-5-(2-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [462];
N^1-(3-fluoro-5-(2-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [463];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-3-methylbutanamide [464];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)butyramide [465];
N₁-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N₂,N₂-dimethylethane-1,2-diamine [466];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [467];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)cyclopropanecarboxamide [468];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)cyclobutanecarboxamide [469];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)cyclopentanecarboxamide [470];
N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)cyclohexanecarboxamide [471];
N₁-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N₂,N₂-dimethylethane-1,2-diamine [472];
N₁-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N₂,N₂-dimethylethane-1,2-diamine [473];
N₁-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)propionamide [474];
N₁-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)propionamide [475];
N₁-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N₂,N₂-dimethylethane-1,2-diamine [476];
N₁-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)propionamide [477];
N₁-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)propionamide [478];
N₁-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)propionamide [479];
N₁-(3-fluoro-5-(2-(5-(pyrimidin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [480];
N₁-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [481];
N₁-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [482];
N-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [483];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-3-yl)pyridin-3-yl)pivalamide [484];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isoctylamide [485];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [486];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)benzamide [487];
N-(3-fluoro-5-(2-(5-(5-((isopropylamino)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [488];
N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [489];
N-(3-fluoro-5-(2-(5-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [490];
N-(3-fluoro-5-(2-(5-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [491];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-3-yl)-3,3-dimethylbutanamide [492];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [493];
N-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [494];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [495];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropane carboxamide [496];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [497];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [498];
N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-1H-pyrrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [499]; and
N-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [500]; or a pharmaceutically acceptable salt thereof.

36. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [501];
N-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [502];
N-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [503];
N-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [504];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [505];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [506];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(IH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridine [507];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-IH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridine [508];
5-(1,2-dimethyl-IH-imidazol-5-yl)-3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [509];
1-(6-(3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [510];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [511];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [512];
N-(5-(3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pypidin-3-yl)-2-(piperidin-4-ylo)acetamide [513];
3-(4-(3-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [514];
2-((5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [515];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [516];
5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-ol [517];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [518];
2-cyclohexyl-N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [519];
3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [520];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [521];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [522];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [523];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [524];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [525];
1-(6-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [526];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [527];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [528];
N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [529];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [530];
2-((5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [531];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [532];
5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [533];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [534];
2-cyclohexyl-N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [535];
3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [536];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [537];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [538];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [539];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [540];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [541];
1-(6-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)-N,N-dimethylethanediamine [542];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [543];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [544];
N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-(piperidin-4-yl)acetamide [545];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [546];
2-((5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [547];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [548];
5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [549];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [550];
2-cyclohexyl-N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [551];
3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [552];
5-(piperdin-4-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [553];
3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [554];
5-(1H-pyrazol-4-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [555];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [556];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [557];
1-(6-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [558];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [559];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [560];
2-(piperidin-4-yl)-N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [561];
3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [562];
N,N-dimethyl-2-((5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [563];
5-(5-methoxypyridin-3-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [564];
5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [565];
5-(pyrazin-2-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [566];
2-cyclohexyl-N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [567];
5-(pyrazin-2-yl)-3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [568];
5-(piperidin-4-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [569];
3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [570];
5-(1H-pyrazol-4-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [571];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [572];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [573];
1-(6-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [574];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [575];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [576];
2-(piperidin-4-yl)-N-(5-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [577];
3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [578];
N,N-dimethyl-2-((5-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [579];
5-(5-methoxypyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [580];
5-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [581];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [582];
2-cyclohexyl-N-(5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [583];
5-(pyrazin-2-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [584];
5-(piperidin-4-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [585];
3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [586];
5-(1H-pyrazol-4-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [587];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [588];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [589];
1-(6-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [590];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [591];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [592];
2-(piperidin-4-yl)-N-(5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [593];
3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [594];
N,N-dimethyl-2-((5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [595];
5-(5-methoxy)pyridin-3-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [596];
5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [597];
5-(5-(benzxyloxy)pyridin-3-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [598];
2-cyclohexyl-N-(5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [599]; and
5-(pyrazin-2-yl)-3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [600]; or a pharmaceutically acceptable salt thereof.

37. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:

3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [601];
3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [602];
3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [603];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [604];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [605];
1-(6-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [606];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [607];
3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [608];
N-(5-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [609];
3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [610];
N,N-dimethyl-2-((5-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [611];
5-(5-methoxypyridin-3-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [612];
5-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [613];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [614];
2-cyclohexyl-N-(5-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [615];
3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [616];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [617];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [618];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [619];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [620];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [621];
1-(6-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [622];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [623];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [624];
N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [625];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [626];
N,N-dimethyl-2-((5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [627];
5-(5-methoxypyridin-3-yl)-3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [628];
5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [629];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [630];
2-cyclohexyl-N-(5-(3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [631];
3-(4-(4-methyl-1H-imidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [632];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [633];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [634];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [635];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [636];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [637];
1-(6-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [638];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [639];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yl)oxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [640];
N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-5-yl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [641];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [642];
N,N-dimethyl-2-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [643];
5-(5-methoxy)pyridin-3-yl)-3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [644];
5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [645];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [646];
2-cyclohexyl-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [647];
3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [648];
5-(piperidin-4-yl)-3-(1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [649];
3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [650];
5-(IH-pyrazol-4-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [651];
5-((4-methyl-IH-pyrazol-4-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [652];
5-((1,2-dime1h-IH-imidazol-5-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [653];
1-(6-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [654];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [655];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [656];
N-(5-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [657];
5-(5-((2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [658];
2-((5-((3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [659];
5-(5-methoxypyridin-3-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [660];
5-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [661];
5-(5-(benzyloxy)pyridin-3-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [662];
N-(5-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-cyclohexylacetamide [663];
5-(pyrazin-2-yl)-3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [664];
5-(piperidin-4-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [665];
5-(1,2,3,6-tetrahydropyridin-4-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [666];
5-(IH-pyrazol-4-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [667];
5-(1-methyl-IH-pyrazol-4-yl)-3-(4-(thiophen-3-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [668];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [669];
1-(6-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [670];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [671];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [672];
2-(piperidin-4-yl)-N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [673];
5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [674];
N,N-dimethyl-2-((5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [675];
5-(5-methoxypyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [676];
5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [677];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [678];
2-cyclohexyl-N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [679];
5-(pyrazin-2-yl)-3-(4-(miophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [680];
3-(4-(furanyl-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [681];
3-(4-(furanyl-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [682];
3-(4-(furanyl-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [683];
3-(4-(furanyl-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [684];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(furanyl-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [685];
1-(6-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)azetidin-3-amine [686];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [687];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [688];
N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-2-(piperidin-4-yloxy)acetamide [689];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [690];
2-((5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [691];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [692];
5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-ol [693];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [694];
2-cyclohexyl-N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [695];
3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [696];
5-(piperidin-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [697];
5-(1,2,3,6-tetrahydropyridin-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [698];
5-(1H-pyrazol-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [699]; and
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [700]; or a pharmaceutically acceptable salt thereof.

38. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [701];
1-(6-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [702];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [703];

4-(6-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [702];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [703];

2-(piperidin-4-yl)-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [705];

5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [706];

N,N-dimethyl-2-((5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [707];

5-(5-methoxypyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [708];

5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [709];

5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [710];

2-cyclohexyl-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [711];

5-(pyrazin-2-yl)-3-(4-(miophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [712];

3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [713];

3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [714];

3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [715];

3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [716];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [717];

1-(6-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [718];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [719];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo [4,3-b]pyridine [720];
N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [721];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [722];
2-((5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethanol-1-amine [723];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [724];
5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [725];
5-(5-benzyl oxy)pyridin-3-yl)-3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [726];
2-cyclohexyl-N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [727];
3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [728];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [729];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [730];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [731];
5-(1-methyl-1H-pyrazol-4-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [732];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [733];
1-(6-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [734];
5-(5-cyclohexyloxy)pyridin-3-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [735];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [736];
N-(5-((3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [737];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [738];
N,N-dimethyl-2-((5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [739];
5-(5-methoxy pyridin-3-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [740];
5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [741];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [742];
2-cyclohexyl-N-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [743];
3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [744];
1-(5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [745];
1-(5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [746];
1-(5-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [747];
1-(5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [748];
1-(5-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [749];
1-(5-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [750];
1-(5-(2-(5-(3-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [751];
1-(5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [752];
N-(5-(3-(4-(5-acetylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [753];

1-(5-(2-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [754];

1-(5-(2-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [755];

1-(5-(2-(5-(methoxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [756];

1-(5-(2-(5-(5-hydroxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [757];

1-(5-(2-(5-(5-methoxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [758];

N-(5-(3-(4-(5-acetylthiophen-2-yl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-cyclohexylacetamide [759];

1-(5-(2-(5-(pyrazin-2-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [760];

N-(3-fluoro-5-(2-(5-(piperidin-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [761];

N-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [762];

N-(3-(2-(5-(IH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)thiophen-2-yl)ethan-1-one [763];

N-(3-fluoro-5-(2-(5-(l-methyl-lH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [764];

N-(3-(2-(5-(1,2-dimethyl-lH-imidazol-5 -yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [765];

N-(3-(2-(5-(IH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [766];

N-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [767];

N-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [768];

N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [769];
N-(3-fluoro-5-(2-(pyrrolidin-1-yloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [770];
N-(3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [771];
N-(3-fluoro-5-(2-(5-(methoxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methanesulfonamide [772];
N-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N,N-dimethylethane-1,2-diamine [773];
N-(3-fluoro-5-(2-(5-(5-(benzyloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorobenzyl)methanesulfonamide [774];
2-cyclohexyl-N-(5-(3-(4-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-IH-pyrazolo[4,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [775];
N-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)benzyl)methane sulfonamide [776];
N1-(3-fluoro-5-(2-(5-(piperidin-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N2,N2-dimethylethane-1,2-diamine [777];
N1-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N2,N2-dimethylethane-1,2-diamine [778];
N1-(3-(2-(5-(IH-pyrazol-4-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine [779];
N1-(3-fluoro-5-(2-(5-(l-methyl-lH-pyrazol-4-yl)-lH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N,N-dimethylethane-1,2-diamine [780];
N1-(3-(2-(5-(1,2-dimethyl-IH-imidazol-5-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine [781];
N1-(3-(2-(5-(benzyloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N,N-dimethylethane-1,2-diamine [782];
N1-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine [783];
N1-(3-fluoro-5-(2-(5-(piperidin-4-yl)acetamide [784];
N-(5-(3-(4-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-2-(piperidin-4-yl)acetamide [785];
N1-(3-fluoro-5-(2-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N2,N2-dimethylethane-1,2-diamine [786];
N₁-(3-(2-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N₂,N₂-dimethylethane-1,2-diamine [787];
N₁-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N₂,N₂-dimethylethane-1,2-diamine [788];
5-(3 -(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [789];
N₁-(3-(2-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenyl)-N₂,N₂-dimethylethane-1,2-diamine [790];
2-cyclohexyl-N-(5-(3-(4-(3-(2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [791];
N₁-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenyl)-N₂,N₂-dimethylethane-1,2-diamine [792];
N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [793];
N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [794];
5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [795];
2-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrrolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [796];
2-(3-fluoro-5-(2-(5-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [797];
2-(3-(2-(5-(5-((ethy lamino)methyl)pyridin-3-yl)-1H-pyrrolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [798];
5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [799]; and
N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [800]; or a pharmaceutically acceptable salt thereof.

39. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [801];
N-(5-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [802];
N-(5-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [803];
5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-yl)pyridin-3-yl)benzamide [804];
2-(3-fluoro-5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [805];
2-(3-fluoro-5-((pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [806];
2-(3-fluoro-5-((pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [807];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [809];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [810];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [811];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [812];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [813];
N-(5-(3-((2-(dimethylamino)ethoxy)-5-fluorophenyl)pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrrozolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [814];
2-(3-(2-((benzylamino)methyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [815];
2-(3-(2-((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [816];
2-(3-(2-(3-fluoro-5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [817];
2-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)pyridin-3-yl)-1H-pyrrozolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [818];
2-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [819];
2-(3-fluoro-5-(2-(5-(pip eridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [820];
2-(3-fluoro-5-(2-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [821];
2-(2-(1-(1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [822];
2-(3-fluoro-5-(2-(1-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [823];
2-(3-fluoro-5-(2-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [824];
1-(6-(3-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [825];
2-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [826];
2-(3-fluoro-5-(2-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [827];
N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [828];
2-(3-fluoro-5-(2-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [829];
2-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [830];
2-(3-fluoro-5-(2-(5-(methoxy)pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [831];
5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [832];
2-(3-(2-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [833];
2-cyclohexyl-N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [834];
2-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenoxy)-N,N-dimethylethan-1-amine [835];
2-(3-fluoro-5-(2-(5-(pyrazin-2-yl)IH-pyrazolo[4,3-b]pyridin-3-yl)phenoxy)-N,N-dimethylethan-1-amine [836];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [837];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [838];
5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-amine [839];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [840];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [841];
N-((5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methylethanamine [842];
5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [843];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [844];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [845];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)2-phenylacetamide [846];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [847];
5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [848];
1-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [849];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [850];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [851];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [852];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [853];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [854];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [855];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [856];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [857];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [858];
N-benzyl-1-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [859];
1-cyclopentyl-N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methylmethanamine [860];
5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [861];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [862];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [863];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [864];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [865];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [866];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [867];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [868];
1-(6-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [869];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [870];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [871];
N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [872];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [873];
2-((5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethanol-1-amine [874];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-IH-pyrazolo[4,3-b]pyridine [875];
5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [876];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridine [877];
2-cyclohexyl-N-(5-(3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [878];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyridin-4-yl)-IH-pyrazolo[4,3-b]pyridine [879];
3-(4-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-IH-pyrazolo[4,3-b]pyridine [880];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [881];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrrolo[2,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [882];
3-(2-(5-(5-aminopyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrazolo[2,3-b]pyridin-4-yl)-5-fluorophenol [883];
3-fluoro-5-(2-(5-(pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenol [884];
3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)phenol [885];
3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [886];
3-(2-(5-(dimethylamino)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-IH-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [887];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [888];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [889];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [890];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [891];
3-fluoro-5-(2-(5-(isopropylamino)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [892];
3-(2-(5-(dimethylamino)methyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [893];
3-fluoro-5-(2-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [894];
3-fluoro-5-(2-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-IH-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [895];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [896];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [897];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [898];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [899]; and
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [900]; or a pharmaceutically acceptable salt thereof.

40. The compound of any of claims 1-30, wherein the compound of Formula I is selected from the group consisting of:
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-IH-pyrazolo[4,3-b]pyridin-2-yl)-IH-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [901];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)cyclohexanecarboxamide [902];
3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [903];
3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [904];
3-fluoro-5-(2-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [905];
3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [906];
3-fluoro-5-(2-(5-((pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)- phenol [907];
3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [908];
3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorphenol [909];
3-fluoro-5-(2-(5-(l-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [910];
3-(2-(5-(l,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [911];
3-(2-(5-((6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [913];
3-(2-(5-(5-cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [914];
3-fluoro-5-(2-(5-(3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [915];
N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-2-(piperidin-4-yl)acetamide [916];
3-fluoro-5-(2-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [917];
3-(2-(5-((dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [918];
3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [919];
5-(3-(4-(3-fluoro-5-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [920];
3-(2-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-fluorophenol [921];
2-cyclohexyl-N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [922];
3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [923];
3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)phenol [924];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)propionamide [925];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-3-methylbutanamide [926];
5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-3-yl)pyridin-3-amine [927];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [928];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [929];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)methylethanamine [930];
5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [931];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pivalamide [932];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)isobutyramide [933];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)2-phenylacetamide [934];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)benzamide [935];
5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)-N-isopropylpyridin-3-amine [936];

1-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [937];

3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [938];

3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [939];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [940];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)butyramide [941];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)pentanamide [942];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [943];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [944];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [945];

N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [946];

N-benzyl-1-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methanamine [947];

1-cyclopentyl-N-((5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [948];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [949];

3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[4,3-b]pyridine [950];

3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [951];

3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[4,3-b]pyridine [952];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [953];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [954];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[4,3-b]pyridine [955];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [956];
1-(6-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[3-b]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [957];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [958];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [959];
N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [960];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yloxy)pyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [961];
2-((5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [962];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[4,3-b]pyridine [963];
5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-ol [964];
5-(5-(benzyloxy)pyridin-3-yl)-3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine [965];
2-cyclohexyl-N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [966];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[4,3-b]pyridine [967];
3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[4,3-b]pyridine [968];
2-(dimethylamino)-N-(5-(3-(4-(3-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [969];
2-(dimethylamino)-N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [970];
2-(dimethylamino)-N-(5-(3-(4-(2-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [971];
2-(dimethylamino)-N-(5-(3-(4-(pyridin-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [972];
2-(dimethylamino)-N-(5-(3-(4-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [973];
2-(dimethylamino)-N-(5-(3-(4-(pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [974];
2-(dimethylamino)-N-(5-(3-(4-(piperidin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [975];
2-(dimethylamino)-N-(5-(3-(4-(4-methylimidazol-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [976];
2-(dimethylamino)-N-(5-(3-(4-(4-methylpiperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [977];
2-(dimethylamino)-N-(5-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [978];
2-(dimethylamino)-N-(5-(3-(4-(thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [979];
2-(dimethylamino)-N-(5-(3-(4-(furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [980];
2-(dimethylamino)-N-(5-(3-(4-(thiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [981];
2-(dimethylamino)-N-(5-(3-(4-(5-fluorothiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [982];
2-(dimethylamino)-N-(5-(3-(4-(5-methylthiophen-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [983];
N-(5-(3-(IH-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)-2-(dimethylamino)acetamide [984];
2-(dimethylamino)-N-(5-(3-(4-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [985];
2-(dimethylamino)-N-(5-(3-(4-(3-(2-(dimethylamino)ethylamino)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [986];
2-(dimethylamino)-N-(5-(3-(4-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [987];
2-(dimethylamino)-N-(5-(3-(4(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [988];
2-(dimethylamino)-N-(5-(3-(4-(3-fluoro-5-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [989]; and
2-(dimethylamino)-N-(5-(3-(4-(3-fluoro-5-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridin-5-yl)pyridin-3-yl)acetamide [990]; or a pharmaceutically acceptable salt thereof.

41. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any of claims 1-40, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

42. A method of treating or ameliorating in a patient a disorder or disease selected from the group consisting of: cancer, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), degenerative disc disease, bone/osteoporotic fractures, bone or cartilage disease, and osteoarthritis, the method comprising administering to the patient a therapeutically effective amount of a compound according to any one of claims 1-40, or a pharmaceutically acceptable salt thereof.

43. A method of claim 42, wherein the disorder or disease is cancer.

44. A method of claim 42, wherein the disorder or disease is pulmonary fibrosis.

45. A method of claim 42, wherein the disorder or disease is idiopathic pulmonary fibrosis (IPF).

46. A method of claim 42, wherein the disorder or disease is degenerative disc disease.

47. A method of claim 42, wherein the disorder or disease is a bone/osteoporotic fracture.

48. A method of claim 42, wherein the disorder or disease is a bone or cartilage disease.

49. A method of claim 42, wherein the disorder or disease is osteoarthritis.

50. The method of claim 42, wherein the patient is a human.

51. The method of claim 43, wherein the cancer is selected from the group consisting of: colon cancer, colorectal cancer, leukemia, breast cancer, skin cancer, prostate cancer, stomach (gastric) cancer, lung cancer, pancreatic cancer, and liver (hepatic) cancer.
52. The method of claim 42, wherein the compound inhibits one or more proteins in the Wnt pathway.

53. The method of claim 42, wherein the compound inhibits signaling induced by one or more Wnt proteins.

54. The method of claim 52, wherein the Wnt proteins are selected from the group consisting of: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

55. The method of claim 53, wherein the Wnt proteins are selected from the group consisting of: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

56. The method of claim 42, wherein the compound inhibits a kinase activity.
### A. CLASSIFICATION OF SUBJECT MATTER

**IPC(8):** A61K 31/4162, 31/4188, 31/437 (2016.01)

根据国际专利分类（IPC）或两者兼顾的国家分类和IPC分类

### B. FIELDS SEARCHED

- **Minimum documentation searched (classification system followed by classification symbols):**
  - IPC(8): A61K 31/4162, 31/4188, 31/437; C07D 403/14 (2016.01)
  - CPC: A61K 31/4162, 31/4188, 31/437; C07D 403/14

- **Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched:**

  - **Electronic data base consulted during the international search (name of data base and, where practicable, search terms used):**
    - PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google Scholar; Pubmed; EBSCO; SureChemBL; KC, Wallace, Cao, Chiruta, Hood, pyrazolo[4,3-b]pyridine, pyrrolo[2,3-B]pyridine, benzodiazepine, imidazole, indole, indole, pyrrole, fluoro, pyridine, 3-(1H-pyrrolo[2,3-B]pyridin-2-yl)-1H-pyrazolo[4,3-b]pyridine, 7-azaindole

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
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<tbody>
<tr>
<td>Y</td>
<td>US 2009/0247504 A 1 (CHURCHER, I et al) 1 October 2009; abstract; paragraphs [0001], [0013], [0023], [0028], [0035], [0053], [0061]; claim 3</td>
<td>1-3, 4/1-3</td>
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<tr>
<td>Y</td>
<td>PIERSANTI, et al. Synthesis of benzo[1,2-d:3,4-d']dilimidazole and 1H-pyrazolo[4,3-b]pyridine as putative A2A receptor antagonists. Organic and Biomolecular Chemistry, Vol. 5, 2007, pp. 2567-2571; page 2567, column 1, paragraph 1; page 2568, scheme 2</td>
<td>1-3, 4/1-3</td>
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<tr>
<td>Y</td>
<td>US 7,943,616 B2 (COX, PJ et al) May 17, 2011; abstract; column 283, lines 1-10</td>
<td>1-3, 4/1-3</td>
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<tr>
<td>Y</td>
<td>WO 2013/030138 A1 (F. HOFFMANN-LA ROCHE AG) 7 March 2013; abstract; page 1, lines 10-15; page 767, lines 10-20</td>
<td>3, 4/3</td>
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* Special documents are listed in the continuation of Box C.

**See patent family annex.**

- **T** later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- **Y** document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- **V** document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- **X** document member of the same patent family

- **“A”** document defining the general state of the art which is not considered to be of particular relevance
- **“E”** earlier application or patent but published on or after the international filing date
- **“L”** document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- **“O”** document referring to an oral disclosure, use, exhibition or other means
- **“P”** document published prior to the international filing date but later than the priority date claimed

**Date of actual completion of the international search:**

15 September 2016 (15.09.2016)

**Date of mailing of the international search report:**

07 OCT 2016

**Name and mailing address of the ISA:**

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

**Facsimile No.** 571-273-8300

**Authorized officer:** Shane Thomas

**PCT Helpdesk:** 571-272-4300
**PCT OIS:** 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)
INTERNATIONAL SEARCH REPORT

Box No. I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. □ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. □ Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. □ Claims Nos.: 5-56
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. □ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. □ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. □ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. □ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant’s protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.