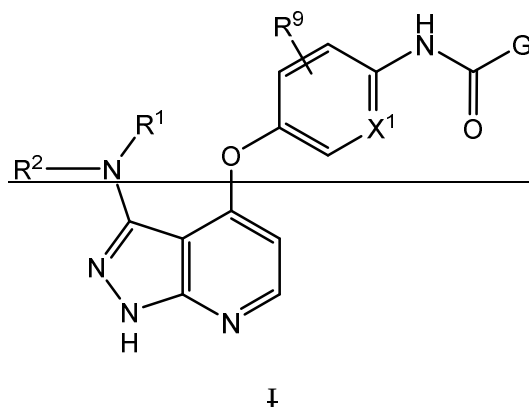


~~What is claimed is:~~

1. A compound of Formula I



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

- X^1 is CH or N;
- R^1 is hydrogen or C1-C6 alkyl;
- R^2 is
 - (a) hydrogen,
 - (b) C1-C6 alkyl,
 - (c) hydroxyC1-C6 alkyl,
 - (d) dihydroxyC2-C6 alkyl,
 - (e) C1-C6 fluoroalkyl optionally substituted with OH,
 - (f) (di-C1-C6 alkoxy)C2-C6 alkyl,
 - (g) (C1-C6 alkoxy)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH,
 - (h) Cyc¹;
 - (i) Cyc²;
 - (j) (hetCyc¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH,
 - (k) (Ar¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH,
 - (l) (hetAr¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH, or
 - (m) (HOSO₃)C1-C6 alkyl;
- Cyc¹ is a 3-4 membered cycloalkyl ring optionally substituted with 1-2 substituents independently selected from halogen, hydroxy, C1-C3 alkyl, hydroxyC1-C3 alkyl, C1-C3 alkoxy,

~~(C1-C3 alkoxy)C1-C3 alkyl and R'R''NC(=O);~~

~~— R' and R'' are independently hydrogen or C1-C6 alkyl;~~

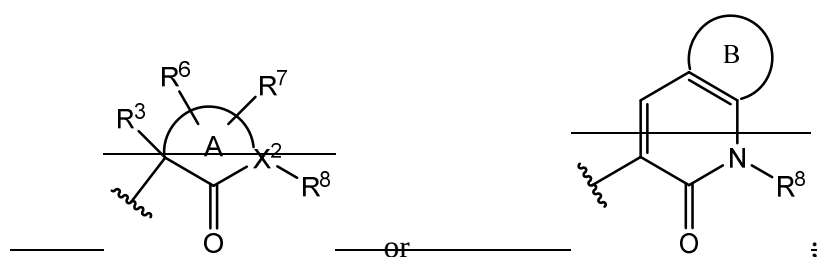
~~— Cyc² is a 5-membered cycloalkyl ring substituted with 1-2 substituents independently selected from C1-C3 alkyl, (C1-C3 alkoxy)C1-C6 alkyl and hydroxyC1-C3 alkyl;~~

~~— hetCyc¹ is a 5-6 membered saturated heterocyclic ring having 1-2 ring heteroatoms independently selected from O, N, S and SO₂, wherein said ring is optionally substituted with oxo;~~

~~— Ar¹ is phenyl;~~

~~— hetAr¹ is pyridyl;~~

~~— G is~~



~~— X² is C or N;~~

~~— Ring A, including the atoms at the points of attachment, is a 5-6 membered heterocyclic ring optionally having an additional 1-2 ring nitrogen atoms when X² is N and having one ring nitrogen atom when X² is C;~~

~~— R³ is hydrogen, methyl, or absent;~~

~~— R⁶ is hydrogen, halogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl or hetCyc², provided that when R⁶ is halogen and is on the ring carbon atom adjacent to the carbon linked to the NHC(=O) moiety of Formula I, then R⁶ is not halogen, and~~

~~— R⁷ is hydrogen, C1-C6 alkyl, oxo or thioxo,~~

~~— or optionally when R⁶ and R⁷ are on the same carbon atom, R⁶ and R⁷ together with the carbon atom to which they are attached form a cyclopropyl ring;~~

~~— hetCyc² is a 4-6 membered saturated heterocyclic ring having a ring nitrogen atom and optionally substituted with C1-C6 alkyl;~~

~~— Ring B, including the atoms at the points of attachment, is a 6-membered saturated carbocyclic optionally substituted with oxo or a 6-membered aromatic carbocyclic ring optionally~~

~~substituted with OH;~~

~~— R^8 is Ar^2 , $hetAr^2$, C3-C6 cycloalkyl, $hetCyc^3$ or C1-C6 alkyl;~~

~~— Ar^2 is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;~~

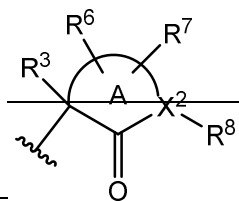
~~— $hetAr^2$ is a 5-6 membered heteroaryl having 1-2 ring nitrogen atoms and optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;~~

~~— $hetCyc^3$ is a 5-6 membered heterocyclic ring having a ring oxygen atom;~~

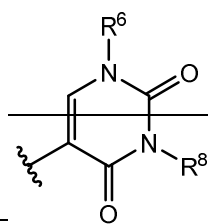
~~and~~

~~— R^9 is hydrogen or halogen.~~

~~— 2. A compound of claim 1, wherein G is~~



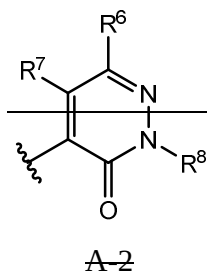
~~— 3. A compound of claim 2, wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having one additional ring nitrogen atom, and R^7 is oxo, wherein G has the formula A-1~~



~~— A-1~~

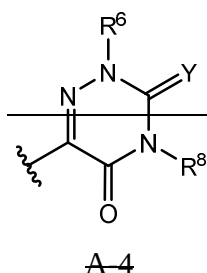
~~wherein R^6 is C1-C6 alkyl, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl or $hetCyc^2$.~~

~~4. A compound of claim 2, wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having an additional ring nitrogen atom, and R^7 is hydrogen, wherein G has the formula A-2~~



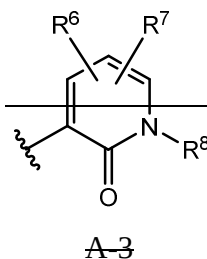
~~wherein R^6 is hydrogen, C1-C6 alkyl, or C3-C6 cycloalkyl and R^7 is hydrogen.~~

~~5. A compound of claim 2, wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having two additional ring nitrogen atoms, and R^7 is oxo or thiooxo, wherein G has the formula A-4~~



~~wherein Y is O or S and R^6 is C1-C6 alkyl.~~

~~6. A compound of claim 2, wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring, wherein G has the formula A-3~~

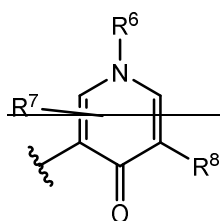


~~wherein;~~

~~— R⁶ is halogen, C1-C6 alkyl, C1-C6 alkoxy, or C3-C6 cycloalkyl, provided that when R⁶ on the ring carbon atom adjacent to the carbon linked to the NHC(=O) moiety of Formula I, then R⁶ is not halogen; and~~

~~— R⁷ is hydrogen.~~

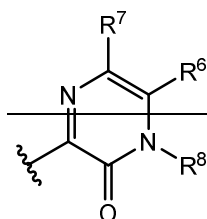
~~— 7. A compound of claim 2, wherein X² is C, R³ is absent, Ring A is a 6 membered heterocyclic ring having a ring nitrogen atom, wherein G has the formula A-5~~



~~A-5~~

~~wherein R⁶ is C1-C6 alkyl and R⁷ is hydrogen.~~

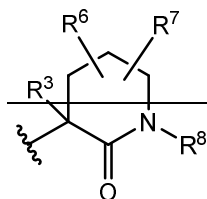
~~— 8. A compound of claim 2, wherein X² is N, R³ is absent, Ring A is a 6 membered heterocyclic ring having two additional ring nitrogen atoms, wherein G has the formula A-6~~



~~A-6~~

~~R⁶ and R⁷ are hydrogen.~~

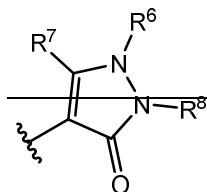
~~— 9. A compound of claim 2, wherein R³ is hydrogen or methyl, and Ring A is a 6 membered heterocyclic ring having a ring nitrogen atom, wherein G has the formula~~



~~A-7~~

wherein R^6 and R^7 are hydrogen, or R^6 and R^7 are on the same carbon atom and R^6 and R^7 together with the carbon atom to which they are attached form a cyclopropyl ring.

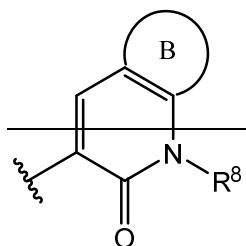
10. A compound of claim 2, wherein X^2 is N, R^3 is absent, Ring A is a 5-membered heterocyclic ring having an additional ring nitrogen atom, wherein G has the formula A-8



A-8

wherein R^6 is C1-C6 alkyl and R^7 is hydrogen or C1-C6 alkyl.

11. A compound of claim 1, wherein G is



12. A compound of claim 11, wherein Ring B is a 6-membered saturated carbocyclic optionally substituted with oxo.

13. A compound of claim 11, wherein Ring B is a 6-membered aromatic carbocyclic ring optionally substituted with OH.

14. A compound according to any one of claims 1-13, wherein R^2 is hydrogen.

15. A compound according to any one of claims 1-13, wherein R^2 is C1-C6 alkyl.

16. A compound according to any one of claims 1-13, wherein R^2 is hydroxyC1-C6 alkyl.

- 17. A compound according to any one of claims 1-13, wherein R^2 is dihydroxyC2-C6 alkyl.
- 18. A compound according to any one of claims 1-13, wherein R^2 is C1-C6 fluoroalkyl optionally substituted with OH.
- 19. A compound according to any one of claims 1-13, wherein R^2 is (di-C1-C6 alkoxy)C2-C6 alkyl.
- 20. A compound according to any one of claims 1-13, wherein R^2 is (C1-C6 alkoxy)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH.
- 21. A compound according to any one of claims 1-13, wherein R^2 is Cyc¹.
- 22. A compound according to any one of claims 1-13, wherein R^2 is Cyc².
- 23. A compound according to any one of claims 1-13, wherein R^2 is (hetCyc¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH.
- 24. A compound according to any one of claims 1-13, wherein R^2 is (Ar¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH.
- 25. A compound according to any one of claims 1-13, wherein R^2 is (hetAr¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH.
- 26. A compound according to any one of claims 1-13, wherein R^2 is (HOSO₂)C1-C6 alkyl.
- 27. A compound according to any one of claims 1-26, wherein R^8 is Ar².

— 28. A compound according to claim 27, wherein Ar² is phenyl optionally substituted with one or more halogens.

— 29. A compound according to any one of claims 1-26, wherein R⁸ is hetAr².

— 30. A compound according to any one of claims 1-26, wherein R⁸ is C3-C6 cycloalkyl.

— 31. A compound according to any one of claims 1-26, wherein R⁸ is hetCyc³.

— 32. A compound according to any one of claims 1-26, wherein R⁸ is C1-C6 alkyl.

— 33. A compound according to any one of claims 1-32, wherein X¹ is CH.

— 34. A compound according to any one of claims 1-32, wherein X¹ is N.

— 35. A compound according to any one of claims 1-32, wherein R⁹ is hydrogen.

— 36. A compound according to any one of claims 1-32, wherein R⁹ is halogen.

— 37. A compound according to claim 36, wherein R⁹ is fluoro.

— 38. A compound according to any one of claims 1-37, wherein R¹ is hydrogen.

— 39. A compound according to claim 1, selected from Examples 1-201.

40. A compound according to claim 1, wherein: X¹ is CH or N;

R¹ is hydrogen or C1-C6 alkyl;

R² is

(a) hydrogen,

(b) C1-C6 alkyl,

(c) hydroxyC1-C6 alkyl,

(d) ~~dihydroxyC2-C6 alkyl,~~
 (e) ~~C1-C6 fluoroalkyl optionally substituted with OH,~~
 (g) ~~(C1-C6 alkoxy)C1-C6 alkyl wherein said alkyl portion is optionally substituted with~~
 OH,

(h) ~~Cyc¹,~~

(i) ~~Cyc²,~~

(j) ~~(hetCyc¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH,~~

(k) ~~(Ar¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH,~~

(l) ~~(hetAr¹)C1-C6 alkyl wherein said alkyl portion is optionally substituted with OH, or~~

(m) ~~(HOSO₃)C1-C6 alkyl;~~

~~Cyc¹ is a 3-4 membered cycloalkyl ring optionally substituted with 1-2 substituents independently selected from halogen, hydroxy, hydroxyC1-C3 alkyl, C1-C3 alkoxy, (C1-C3 alkoxy)C1-C3 alkyl, and R'R''NC(=O);~~

~~R' and R'' are independently selected from C1-C6 alkyl;~~

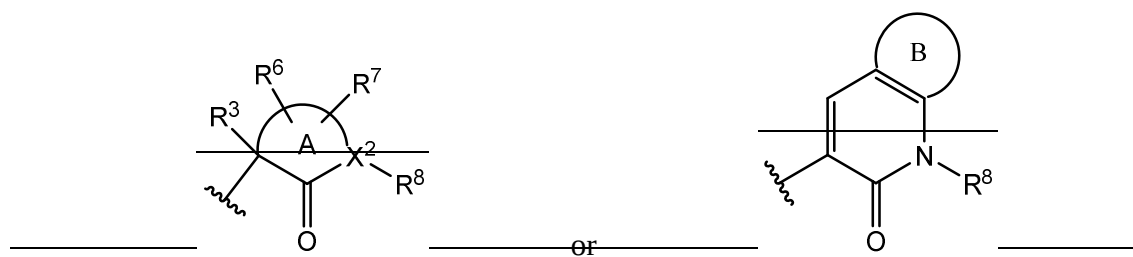
~~Cyc² is a 5-membered cycloalkyl ring substituted with 1-2 substituents independently selected from C1-C3 alkyl, (C1-C3 alkoxy)C1-C3 alkyl and hydroxyC1-C3 alkyl;~~

~~hetCyc¹ is a 5-6 membered saturated heterocyclic ring having 1-2 ring heteroatoms independently selected from O, N and SO₂, wherein said ring is optionally substituted with oxo;~~

~~Ar¹ is phenyl;~~

~~hetAr¹ is pyridyl;~~

~~G is~~



~~X² is C or N;~~

~~Ring A, including the atoms at the points of attachment, is a 5-6 membered heterocyclic ring optionally having an additional 1-2 ring nitrogen atoms when X² is N and having one ring nitrogen atom when X² is C;~~

~~R³ is hydrogen or absent;~~

~~R⁶ is hydrogen, halogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl or hetCyc², provided that when R⁶ is halogen and is on the ring carbon atom adjacent to the carbon linked to the NHC(=O) moiety of Formula I, then R⁶ is not halogen;~~

~~R⁷ is hydrogen, C1-C6 alkyl, oxo or thioxo;~~

~~hetCyc² is a 4 membered saturated heterocyclic ring having a ring nitrogen atom substituted with C1-C6 alkyl;~~

~~Ring B, including the atoms at the points of attachment, is a 6 membered saturated carbocyclic optionally substituted with oxo or a 6 membered aromatic carbocyclic ring optionally substituted with OH;~~

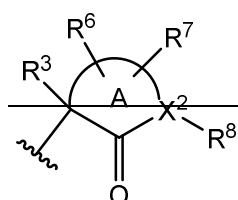
~~R⁸ is Ar², hetAr², C3-C6 cycloalkyl, hetCyc³ or C1-C6 alkyl;~~

~~Ar² is phenyl optionally substituted with one or more substituents independently selected from halogen;~~

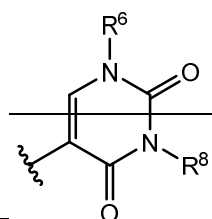
~~hetAr² is a 5-6 membered heteroaryl having 1-2 ring nitrogen atoms and optionally substituted with one or more substituents independently selected from C1-C2 alkyl; and~~

~~R⁹ is hydrogen or halogen.~~

~~41. The compound according to claim 40, wherein G is~~



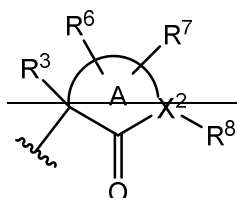
~~wherein X² is N, R³ is absent, Ring A is a 6 membered heterocyclic ring having one additional ring nitrogen atom, and R⁷ is oxo, such that G has the formula A-1~~



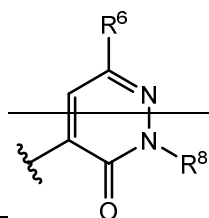
~~A-1~~

wherein R^6 is C1-C6 alkyl, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl or hetCyc².

42. The compound according to claim 40, wherein G is



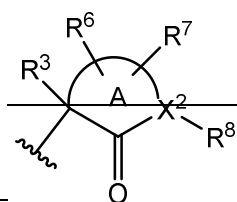
wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having an additional ring nitrogen atom, and R^7 is hydrogen, such that G has the formula A-2



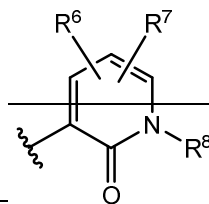
A-2

wherein R^6 is hydrogen, C1-C6 alkyl, or C3-C6 cycloalkyl, and R^7 is hydrogen.

43. The compound according to claim 40, wherein G is



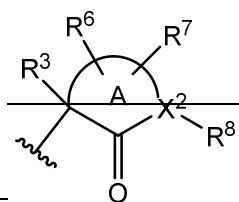
wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring, such that G has the formula A-3



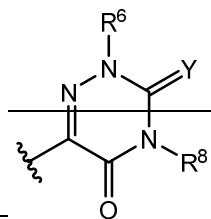
A-3

wherein R^6 is halogen, C1-C6 alkyl, C1-C6 alkoxy, or C3-C6 cycloalkyl, R^7 is hydrogen, provided that when R^6 is on the ring carbon atom adjacent to the carbon linked to the $\text{NHC}(=\text{O})$ moiety of Formula II, then R^6 is not halogen.

44. The compound according to claim 40, wherein G is



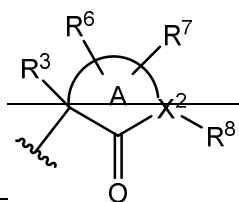
wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having two additional ring nitrogen atoms, and R^7 is oxo or thiooxo, such that G has the formula A-4



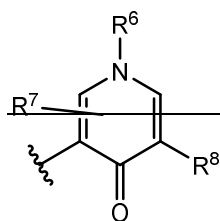
A-4

wherein Y is O or S, R^6 is C1-C6 alkyl.

45. The compound according to claim 40, wherein G is



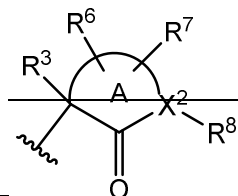
wherein X^2 is C, R^3 is absent, Ring A is a 6-membered heterocyclic ring having a ring nitrogen atom, such that G has the formula A-5



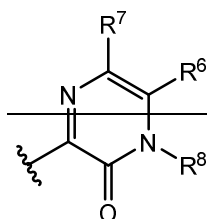
A-5

wherein R^6 is C1-C6 alkyl, and R^7 is hydrogen.

46. The compound according to claim 40, wherein G is



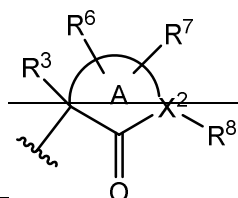
wherein X^2 is N, R^3 is absent, Ring A is a 6-membered heterocyclic ring having two additional ring nitrogen atoms, such that G has the formula A-6



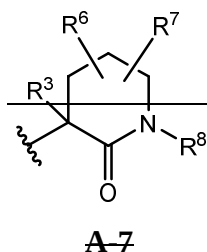
A-6

wherein R^6 and R^7 are hydrogen.

47. The compound according to claim 40, wherein G is

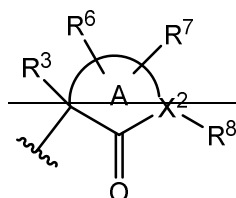


wherein X^2 is N, R^3 is hydrogen or methyl, and Ring A is a 6-membered heterocyclic ring having a ring nitrogen atom, such that G has the formula A-7

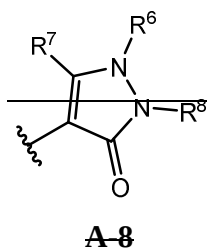


wherein R^6 and R^7 are hydrogen.

48. The compound according to claim 40, wherein G is

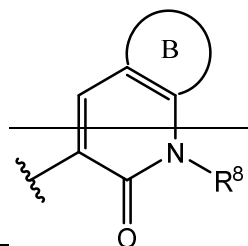


wherein X^2 is N, R^3 is absent, Ring A is a 5-membered heterocyclic ring having an additional ring nitrogen atom, such that G has the formula A-8

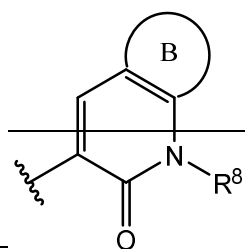


wherein R^6 is C1-C6 alkyl, and R^7 is hydrogen or C1-C6 alkyl.

49. The compound according to claim 40, wherein G is



50. The compound according to claim 40, wherein G is



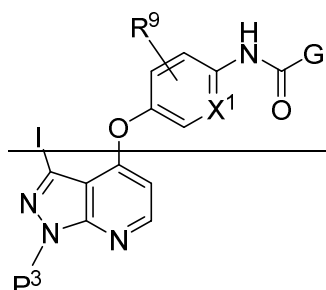
wherein Ring B is a 6-membered saturated carbocyclic optionally substituted with oxo.

~~51. The compound according to claim 40, wherein the compound is a compound of Example No. 2, 3, 4, 5, 6, 7, 8, 12, 13, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 67, 68, 69, 70, 71, 72, 73, 75, 76, 77, 79, 80, 81, 84, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 128, 142, 144, 145, 146, 147, 148, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 166, 167, 168, 169, 170, 171, 172, 173, 179, 181, 182, 183, 184, 185, 186, 187, 189, 191, 192, 193, 194, 195, 196, or 197, or a pharmaceutically acceptable salt or solvate thereof.~~

~~52. A pharmaceutical composition, comprising a compound of Formula I as defined in any one of claims 1 to 51 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.~~

~~53. A process for preparing a compound according to claim 1, comprising:~~

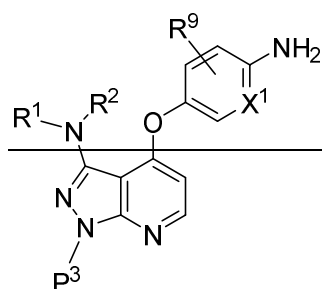
~~(a) reacting a compound having the formula~~



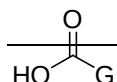
wherein X^1 , G, and R^9 are as defined in claim 1 and P^3 is an amino protecting group, with a reagent

having the formula R^1R^2NH , wherein R^1 and R^2 are as defined in claim 1 and wherein if the R^2 moiety contains a hydroxyl group then the hydroxyl group is optionally protected with a hydroxyl protecting group, in the presence of copper(I) iodide and either in the presence of a base and 1H-pyrrole-2-carboxylic acid, or in the presence of a ligand and a base, followed by removal of the amino protecting group and removal of the hydroxyl group, if present; or

—— (b) reacting a compound having the formula:



wherein R^9 and X^1 are as defined in claim 1, P^3 is an amino protecting group, and R^1 and R^2 are as defined in claim 1, wherein if the R^2 moiety contains a hydroxyl group then the hydroxyl group is optionally protected with a hydroxyl protecting group, with a reagent having the formula



wherein G is as defined in claim 1, in the presence of coupling reagents, followed by removal of the amino protecting group and removal of the hydroxyl group, if present; and

—— optionally forming a pharmaceutically acceptable salt thereof.

54. A method for treating cancer in a patient in need thereof, the method comprising administering to the patient an effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 52.

55. A method of treating a patient identified or diagnosed as having a TAM associated cancer, a c-Met associated cancer, or both, the method comprising administering to a patient identified or diagnosed as having a TAM associated cancer, a c-Met associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

~~56. A method of treating a patient having a cancer, the method comprising:~~

~~(a) identifying the patient as having a TAM-associated cancer, a c-Met-associated cancer, or both; and~~

~~(b) administering to the patient identified as having a TAM-associated cancer, a c-Met-associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~57. A method of decreasing the risk of developing a metastasis or an additional metastasis in a patient identified or diagnosed as having a TAM-associated cancer, a c-Met-associated cancer, or both, the method comprising administering to a patient identified or diagnosed as having a TAM-associated cancer, a c-Met-associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~58. A method of decreasing the risk of developing a metastasis or an additional metastasis in a patient having a cancer, the method comprising:~~

~~(a) identifying the patient as having a TAM-associated cancer, a c-Met-associated cancer, or both; and~~

~~(b) administering to the patient identified as having a TAM-associated cancer, a c-Met-associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~59. A method of decreasing migration and/or invasion of a cancer cell in a patient identified or diagnosed as having a TAM-associated cancer a c-Met-associated cancer, or both, the method comprising administering to a patient identified or diagnosed as having a TAM-associated cancer, a c-Met-associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~60. A method of decreasing migration and/or invasion of a cancer cell in a patient having~~

a cancer, the method comprising:

(a) identifying the patient as having a TAM-associated cancer, a c-Met-associated cancer, or both; and

(b) administering to the patient identified as having a TAM-associated cancer, a c-Met-associated cancer, or both, a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

61. The method of any one of claims 54-60, wherein the method further includes administering to the patient at least one additional anticancer agent.

62. The method of claim 61, wherein the at least one additional anticancer agent or therapy is selected from the group consisting of: an immune checkpoint inhibitor, a kinase inhibitor, a chemotherapy, radiation, and surgery.

63. The method of any one of claims 54-60, wherein the patient was previously treated with at least one additional anticancer agent and the previous treatment with the at least one additional anticancer agent was unsuccessful.

64. The method of claim 63, wherein the patient previously developed resistance to one or more of the at least one additional anticancer agent.

65. The method of any one of claims 61, 63, or 64, wherein the at least one additional anticancer agent is selected from the group consisting of: a chemotherapeutic agent, a PI 3-kinase inhibitor, an EGFR inhibitor, a HER2/neu inhibitor, an FGFR inhibitor, an ALK inhibitor, an IGF1R inhibitor, a VEGFR inhibitor, a PDGFR inhibitor, a glucocorticoid, a BRAF inhibitor, a MEK inhibitor, a HER4 inhibitor, a MET inhibitor, a RAF inhibitor, an Akt inhibitor, a FTL-3 inhibitor, and a MAP kinase pathway inhibitor.

66. The method of claim 65, wherein the at least one additional anticancer agent comprises a kinase inhibitor, and the patient previously developed resistance to the kinase inhibitor.

67. The method of claim 66, wherein the kinase inhibitor is selected from the group

consisting of: ~~bozitinib, 1-(6,7-Dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-[7(S)-(1-pyrrolidinyl)-6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl]-1H-1,2,4-triazole-3,5-diamine, crizotinib, foretinib, (N-[4-(2-Amino-3-chloropyridin-4-yloxy)-3-fluorophenyl]-4-ethoxy-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide, amuvatinib, BMS-796302, cabozantinib, glesatinib, 2-(4-Fluorophenyl)-N-[3-fluoro-4-(3-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yloxy)phenyl]-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide, N-[4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]-4-ethoxy-1-(4-fluoro-2-methylphenyl)-1H-pyrazole-3-carboxamide hydrochloride, gilteritinib, [3-(2-[[3-Fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino]-5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)phenyl]acetonitrile, duberminatinib, trans-4-[2-(Butylamino)-5-[4-[(4-methylpiperazin-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidin-7-yl]cyclohexanol, 3-[3-[4-(Morpholin-4-yl)methyl]-1H-pyrrol-2-ylmethylene]-2-oxo-2,3-dihydro-1H-indol-5-ylmethyl]thiazolidine-2,4-dione hydrochloride, sunitinib, 12A11, Mab173, YW327.6S2, D9, E8, merestinib, [3-(2-[[3-Fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino]-5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)phenyl]acetonitrile, duberminatinib, N-[4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]-4-ethoxy-1-(4-fluoro-2-methylphenyl)-1H-pyrazole-3-carboxamide hydrochloride, crizotinib, capmatinib, NVP-BVU972, AMG-337, bozitinib, glumetinib, savolitinib, and tepotinib.~~

68. The method of claim 64, wherein the at least one additional anticancer agent comprises dexamethasone, and the patient previously developed resistance to dexamethasone.

69. The method of claim 64, wherein the at least one additional anticancer agent comprises cytarabine, and the patient previously developed resistance to cytarabine.

70. The method of claim 64, wherein the at least one additional anticancer agent comprises imatinib, and the patient previously developed resistance to imatinib.

71. The method of claim 64, wherein the at least one additional anticancer agent comprises lapatinib, and the patient previously developed resistance to lapatinib.

72. The method of claim 64, wherein the at least one additional anticancer agent comprises

cetuximab, and the patient previously developed resistance to cetuximab.

73. The method of claim 64, wherein the at least one additional anticancer agent comprises erlotinib, and the patient previously developed resistance to erlotinib.

74. The method of claim 64, wherein the at least one additional anticancer agent comprises alpelisib, and the patient previously developed resistance to alpelisib.

75. The method of claim 64, wherein the at least one additional anticancer agent comprises cisplatin, and the patient previously developed resistance to cisplatin.

76. The method of claim 64, wherein the at least one additional anticancer agent comprises sunitinib, and the patient previously developed resistance to sunitinib.

77. The method of claim 64, wherein the at least one additional anticancer agent comprises metformin, and the patient previously developed resistance to metformin.

78. The method of claim 64, wherein the at least one additional anticancer agent comprises an anti PD1 antibody, and the patient previously developed resistance to the anti PD1 antibody.

79. The method of claim 64, wherein the at least one additional anticancer agent comprises docetaxel, and the patient previously developed resistance to docetaxel.

80. The method of claim 64, wherein the at least one additional anticancer agent comprises an EGFR inhibitor, and the patient previously developed resistance to the EGFR inhibitor.

81. The method of claim 64, wherein the at least one additional anticancer agent comprises crizotinib, and the patient previously developed resistance to crizotinib.

82. The method of claim 64, wherein the at least one additional anticancer agent comprises

~~capmatinib, and the patient previously developed resistance to capmatinib.~~

83. The method of claim 64, wherein the at least one additional anticancer agent comprises NVP-BVU972, and the patient previously developed resistance to NVP-BVU972.

84. The method of claim 64, wherein the at least one additional anticancer agent comprises AMG 337, and the patient previously developed resistance to AMG 337.

85. The method of claim 64, wherein the at least one additional anticancer agent comprises bozitinib, and the patient previously developed resistance to AMG 337.

86. The method of claim 64, wherein the at least one additional anticancer agent comprises glumetinib, and the patient previously developed resistance to glumetinib.

87. The method of claim 64, wherein the at least one additional anticancer agent comprises savolitinib, and the patient previously developed resistance to savolitinib.

88. The method of claim 64, wherein the at least one additional anticancer agent comprises tepotinib, and the patient previously developed resistance to tepotinib.

89. A method of selecting a treatment for a patient identified or diagnosed as having a TAM-associated cancer, a c-Met-associated cancer, or both, the method selecting a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of claim 52 for the patient identified or diagnosed as having a TAM-associated cancer, a c-Met-associated cancer, or both.

90. A method of selecting a treatment for a patient, the method comprising:

(a) identifying the patient as having a TAM-associated cancer, a c-Met-associated cancer, or both; and

(b) selecting a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of claim 52 for the patient identified as having a TAM-

~~associated cancer, a c-Met-associated cancer, or both.~~

~~91. The method of any one of claims 55-90, wherein the subject is identified or diagnosed as having a TAM-associated cancer.~~

~~92. The method of any one of claims 55-90, wherein the subject is identified or diagnosed as having both a TAM-associated cancer and a c-Met-associated cancer.~~

~~93. The method of any one of claims 55-90, wherein the subject is identified or diagnosed as having a c-Met-associated cancer.~~

~~94. The method of claim 91 or 92, wherein the TAM-associated cancer is selected from the group consisting of: gastrointestinal stromal tumor (GIST), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), B-cell chronic myeloid leukemia (B-CLL), lung cancer, glioblastoma, breast cancer, colorectal cancer, gastric cancer, glioma, pancreatic cancer, esophageal cancer, mantle cell lymphoma, melanoma, squamous cell skin cancer, prostate cancer, endometrial cancer, ovarian cancer, oral squamous cell carcinoma, thyroid cancer, bladder cancer, renal cancer, schwannoma, mesothelioma, Kaposi's sarcoma, osteosarcoma, rhabdomyosarcoma, erythroid leukemia, colon cancer, liver cancer, renal cell carcinoma, pituitary adenoma, urinary tract cancer, kidney cancer, colon cancer, head and neck cancer, brain cancer, and non-small cell lung cancer.~~

~~95. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having overexpression of a TAM kinase.~~

~~96. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having ectopic expression of a TAM kinase.~~

~~97. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of a TYRO3 protein.~~

~~98. The method of claim 97, wherein the TAM-associated cancer is selected from the group~~

consisting of: acute myeloid leukemia (AML), multiple myeloma, lung cancer, melanoma, prostate cancer, endometrial cancer, thyroid cancer, schwannoma, pancreatic cancer, and brain cancer.

99. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of an AXL protein.

100. The method of claim 99, wherein the TAM-associated cancer is selected from the group consisting of: gastrointestinal stromal tumor (GIST), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), B-cell chronic myeloid leukemia (B-CLL), lung cancer, glioblastoma, breast cancer, colorectal cancer, gastric cancer, pancreatic cancer, prostate cancer, oesophageal cancer, melanoma, squamous cell skin cancer, endometrial cancer, ovarian cancer, oral squamous cell carcinoma, thyroid cancer, bladder cancer, renal cancer, schwannoma, mesothelioma, osteosarcoma, erythroid leukemia, colon cancer, liver cancer, renal cell carcinoma, kidney cancer, non-small cell lung cancer, and triple negative metastatic breast cancer.

101. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of a MER protein.

102. The method of claim 101, wherein the TAM-associated cancer is selected from the group consisting of: acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), B-cell chronic myeloid leukemia (B-CLL), T-cell acute lymphoblastic leukemia (T-ALL), lung cancer, glioma, melanoma, prostate cancer, schwannoma, mantle cell lymphoma, rhabdomyosarcoma, pancreatic cancer, breast cancer, gastric cancer, pituitary adenoma, urinary tract cancer, kidney cancer, liver cancer, colon cancer, and breast cancer.

103. The method of claim 91 or 92, wherein the TAM-associated cancer is a cancer having a chromosomal translocation that results in the expression of a TMEM87B-MERTK fusion protein or an AXL-MBIP fusion protein.

104. The method of claim 92 or 93, wherein the subject is identified or diagnosed as having

~~a c-Met associated cancer.~~

~~105. The method of claim 104, wherein the c-Met associated cancer is a cancer having a mutation that increases the activity of a c-Met kinase.~~

~~106. The method of claim 105, wherein the mutation that increases the activity of a c-Met kinase results in one or more amino acid substitutions in the c-Met kinase.~~

~~107. The method of claim 104, wherein the c-Met associated cancer is a cancer having a mutation that increases the expression of c-Met in a mammalian cell.~~

~~108. The method of claim 104, wherein the c-Met associated cancer is a cancer having a mutation that confers increased half-life of c-Met kinase in a mammalian cell.~~

~~109. The method of claim 108, wherein the mutation that confers increased half-life of c-Met kinase in a mammalian cell is a mutation that results in c-Met exon 14 skipping during mRNA splicing.~~

~~110. The method of claim 104, wherein the c-Met associated cancer is a cancer having a MET gene amplification.~~

~~111. The method of claim 110, wherein the c-Met associated cancer is a c-Met associated cancer that has resistance to a Type I c-Met inhibitor.~~

~~112. The method of any one of claims 104-111, wherein the c-Met associated cancer is selected from the group of gastrointestinal cancer (GI), gastric cancer, colorectal adenocarcinoma, colorectal carcinoma (CRC), non-small cell lung cancer (NSCLC), hepatocellular carcinoma (HCC), hereditary papillary renal carcinoma (HPRC), papillary renal carcinoma, melanoma, gastric adenocarcinoma, appendiceal adenocarcinoma, duodenal adenocarcinoma, pancreatic adenocarcinoma, lung adenocarcinoma, thyroid papillary carcinoma, thyroid medullary carcinoma, Ewing sarcoma, prostate adenocarcinoma, squamous cell carcinoma of the head and~~

~~neck and cervix, renal cell carcinoma, pheochromocytoma and composite pheochromocytoma, ovarian serous carcinoma, ovarian clear cell carcinoma, ovarian mixed carcinoma, peritoneal serous carcinoma, breast ductal adenocarcinoma, uterine leiomyosarcoma, uterine endometrioid adenocarcinoma, uterine malignant mixed mullerian tumor, glioblastoma, anaplastic glioma, oligodendroglioma, desmoplastic small round cell tumor, squamous cell carcinoma of rectum, salivary gland carcinoma, heart angiosarcoma, gastrointestinal stromal tumor, invasive thymoma, and spindle sarcoma.~~

~~113. A method of selecting a treatment for a patient identified or diagnosed as having a cancer, the method comprising:~~

- ~~(a) administering at least one additional anticancer agent to the patient;~~
- ~~(b) after (a), detecting increased expression, level, and/or activity of a TAM kinase and/or a c-Met kinase in a cancer cell or an immune cell from the patient; and~~
- ~~(c) after (b), selecting a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of claim 52 for the patient.~~

~~114. A method of treating a patient identified or diagnosed as having a cancer, the method comprising:~~

- ~~(a) administering to the patient identified or diagnosed as having a cancer one or more doses of at least one additional anticancer agent;~~
- ~~(b) after (a), detecting an increase in the expression, level, and/or activity of a TAM kinase and/or a c-Met kinase in a cancer cell or an immune cell from the patient; and~~
- ~~(c) after (b), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~115. A method of treating a patient identified or diagnosed as having a cancer, the method comprising:~~

- ~~(a) detecting an increase in the expression, level, and/or activity of a TAM kinase and/or c-Met kinase in a cancer cell or an immune cell from a patient identified or diagnosed as having a cancer and previously administered one or more doses of at least one additional anticancer agent;~~

and

(b) after (a), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 of a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 116. A method of treating a patient identified or diagnosed as having a cancer that has been previously administered one or more doses of at least one additional anticancer agent and has been identified as having a cancer cell or an immune cell that has increased expression, level, and/or activity of a TAM kinase and/or a c-Met kinase, the method comprising administering a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52 to the patient.

117. A method of treating a patient identified or diagnosed as having a cancer, the method comprising:

(a) selecting a patient identified or diagnosed as having increased expression, level, and/or activity of a TAM kinase and/or a c-Met kinase in a cancer cell or an immune cell; and

(b) after (a), administering to the selected patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 118. A method treating a patient identified or diagnosed as having a cancer, the method comprising:

(a) selecting a patient identified or diagnosed as having a cancer that has been previously administered one or more doses of at least one additional anticancer agent and identified as having a cancer cell or an immune cell having increased expression, level, and/or activity of a TAM kinase and/or a c-Met kinase; and

(b) after (a), administering to the selected patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

119. The method of any one of claims 113-115, wherein an increased expression, level,

~~and/or activity of a TAM kinase is detected in a cancer cell or an immune cell.~~

~~120. The method of claim 116-118, wherein the patient is identified or diagnosed as having a cancer cell or an immune cell having increased expression, level, and/or activity of a TAM kinase.~~

~~121. The method of any one of claims 113-115, wherein an increased expression, level, and/or activity of a TAM kinase and a c-Met kinase are detected in a cancer cell or an immune cell.~~

~~122. The method of any one of claims 116-118, wherein the patient is identified or diagnosed as having a cancer cell or an immune cell having increased expression, level, and/or activity of a TAM kinase and a c-Met kinase.~~

~~123. The method of any one of claims 113-115, wherein an increased expression, level, and/or activity of a c-Met kinase is detected in a cancer cell or an immune cell.~~

~~124. The method of any one of claims 116-118, wherein the patient is identified or diagnosed as having a cancer cell or an immune cell having increased expression, level, and/or activity of a c-Met kinase.~~

~~—— 125. The method of any one of claims 113-115 and 119-122, wherein the increased expression, level, and/or activity of a TAM kinase in a cancer cell or an immune cell results from a chromosomal translocation that results in the expression of a TMEM87B-MERTK fusion protein or an AXL-MBIP fusion protein.~~

~~—— 126. A method of treating a patient identified or diagnosed as having a TAM-associated cancer, the method comprising:~~

~~(a) administering to the patient identified or diagnosed as having a TAM-associated cancer one or more doses of a TAM kinase inhibitor;~~

~~(b) after (a), detecting resistance of the TAM-associated cancer in the patient to the TAM~~

kinase inhibitor; and

(c) after (b), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 127. A method of treating a patient identified or diagnosed as having a TAM-associated cancer, the method comprising:

(a) detecting resistance of the TAM-associated cancer in the patient to a TAM kinase inhibitor that was previously administered to the patient; and

(b) after (a), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 128. A method of treating a patient identified or diagnosed as having a TAM-associated cancer and determined to have previously developed resistance to a TAM kinase inhibitor, the method comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 129. A method of treating a patient identified or diagnosed as having a c-Met-associated cancer, the method comprising:

(a) administering to the patient identified or diagnosed as having a c-Met-associated cancer one or more doses of a c-Met kinase inhibitor;

(b) after (a), detecting resistance of the c-Met-associated cancer in the patient to the c-Met kinase inhibitor; and

(c) after (b), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 130. A method of treating a patient identified or diagnosed as having a c-Met-associated

cancer, the method comprising:

(a) detecting resistance of the c-Met associated cancer in the patient to a c-Met kinase inhibitor that was previously administered to the patient; and

(b) after (a), administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 131. A method of treating a patient identified or diagnosed as having a c-Met associated cancer and determined to have previously developed resistance to a c-Met kinase inhibitor, the method comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

——— 132. The method of claim 131, wherein the c-Met inhibitor is a type I c-Met inhibitor.

133. The method of claim 113, wherein step (c) further comprises administering to the patient at least one additional anticancer agent.

——— 134. The method of claim 114, wherein step (c) further comprises administering to the patient the at least one additional anticancer agent.

——— 135. The method of claim 115, wherein step (b) further comprises administering to the patient the at least one additional anticancer agent.

——— 136. The method of claim 116, wherein the method further comprises administering to the patient the at least one additional anticancer agent.

——— 137. The method of claim 119, wherein step (b) further comprises administering to the patient at least one additional anticancer agent.

——— 138. The method of claim 118, wherein step (b) further comprises administering to the

~~patient the at least one additional anticancer agent.~~

~~—— 139. The method of claim 126, wherein step (c) further comprises administering to the patient at least one additional anticancer agent.~~

~~—— 140. The method of claim 127, wherein step (b) further comprising administering to the patient at least one additional anticancer agent.~~

~~—— 141. The method of claim 128, wherein the method further comprises administering to the patient at least one additional anticancer agent.~~

~~—— 142. The method of claim 129, wherein step (c) further comprises administering to the patient at least one additional anticancer agent.~~

~~—— 143. The method of claim 130, wherein step (b) further comprises administering to the patient at least one additional anticancer agent.~~

~~—— 144. The method of claim 131, further comprising administering to the patient at least one additional anticancer agent.~~

~~—— 145. The method of any one of claims 126-128, wherein the TAM associated cancer is selected from the group consisting of: gastrointestinal stromal tumor (GIST), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), B-cell chronic myeloid leukemia (B-CLL), lung cancer, glioblastoma, breast cancer, colorectal cancer, gastric cancer, glioma, pancreatic cancer, oesophageal cancer, mantle cell lymphoma, melanoma, squamous cell skin cancer, prostate cancer, endometrial cancer, ovarian cancer, oral squamous cell carcinoma, thyroid cancer, bladder cancer, renal cancer, schwannoma, mesothelioma, Kaposi's sarcoma, osteosarcoma, rhabdomyosarcoma, erythroid leukemia, colon cancer, liver cancer, renal cell carcinoma, pituitary adenoma, urinary tract cancer, kidney cancer, colon cancer, head and neck cancer, brain cancer, and non-small cell lung cancer.~~

~~146. The method of any one of claims 126-128 and 145, wherein the TAM associated~~

~~cancer is a cancer having overexpression of a TAM kinase.~~

~~147. The method of any one of claims 126-128 and 145, wherein the TAM-associated cancer is a cancer having ectopic expression of a TAM kinase.~~

~~148. The method of any one of claims 126-128 and 145, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of a TYRO3 protein.~~

~~149. The method of claim 148, wherein the TAM-associated cancer is selected from the group consisting of: acute myeloid leukemia (AML), multiple myeloma, lung cancer, melanoma, prostate cancer, endometrial cancer, thyroid cancer, schwannoma, pancreatic cancer and brain cancer.~~

~~150. The method of any one claims 126-128 and 145, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of an AXL protein.~~

~~151. The method of claim 150, wherein the TAM-associated cancer is selected from the group consisting of: gastrointestinal stromal tumor (GIST), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), B-cell chronic myeloid leukemia (B-CLL), lung cancer, glioblastoma, breast cancer, colorectal cancer, gastric cancer, pancreatic cancer, prostate cancer, oesophageal cancer, melanoma, squamous cell skin cancer, endometrial cancer, ovarian cancer, oral squamous cell carcinoma, thyroid cancer, bladder cancer, renal cancer, schwannoma, mesothelioma, osteosarcoma, erythroid leukemia, colon cancer, liver cancer, renal cell carcinoma, kidney cancer, non-small cell lung cancer, and triple-negative metastatic breast cancer.~~

~~152. The method of any one claims 126-128 and 145, wherein the TAM-associated cancer is a cancer having overexpression or ectopic expression of a MER protein.~~

~~153. The method of claim 152, wherein the TAM-associated cancer is selected from the~~

~~group consisting of: acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), B-cell chronic myeloid leukemia (B-CLL), T cell acute lymphoblastic leukemia (T-ALL), lung cancer, glioma, melanoma, prostate cancer, schwannoma, mantle cell lymphoma, rhabdomyosarcoma, pancreatic cancer, breast cancer, gastric cancer, pituitary adenoma, urinary tract cancer, kidney cancer, liver cancer, colon cancer, and breast cancer.~~

~~154. The method of any one of claims 126-128 and 145, wherein the TAM-associated cancer is a cancer having a chromosomal translocation that results in the expression of a TMEM87B-MERTK fusion protein or a AXL-MBIP fusion protein.~~

~~155. The method of any one of claims 129-131, wherein the c-Met-associated cancer is a cancer having a mutation that increases the activity of a c-Met kinase.~~

~~156. The method of claim 155, wherein the mutation that increases the activity of a c-Met kinase results in one or more amino acid substitutions in the c-Met kinase.~~

~~157. The method of any one of claims 129-131, wherein the c-Met-associated cancer is a cancer having a mutation that increases the expression of c-Met in a mammalian cell.~~

~~158. The method of any one of claims 129-131, wherein the c-Met-associated cancer is a cancer having a mutation that confers increased half-life of c-Met kinase in a mammalian cell.~~

~~159. The method of claim 158, wherein the mutation that confers increased half-life of c-Met kinase in a mammalian cell is a mutation that results in c-Met exon 14 skipping during mRNA splicing.~~

~~160. The method of any one of claims 129-131, wherein the c-Met-associated cancer is a cancer having a MET gene amplification.~~

~~161. The method of claim 160, wherein the c-Met-associated cancer is a cancer that is~~

resistant to a Type I c-Met inhibitor.

~~162. The method of any one of claims 129-131 and 155-161, wherein the c-Met associated cancer is selected from the group of gastrointestinal cancer (GI), gastric cancer, colorectal adenocarcinoma, colorectal carcinoma (CRC), non-small cell lung cancer (NSCLC), hepatocellular carcinoma (HCC), hereditary papillary renal carcinoma (HPRC), papillary renal carcinoma, melanoma, gastric adenocarcinoma, appendiceal adenocarcinoma, duodenal adenocarcinoma, pancreatic adenocarcinoma, lung adenocarcinoma, thyroid papillary carcinoma, thyroid medullary carcinoma, Ewing sarcoma, prostate adenocarcinoma, squamous cell carcinoma of the head and neck and cervix, renal cell carcinoma, pheochromocytoma and composite pheochromocytoma, ovarian serous carcinoma, ovarian clear cell carcinoma, ovarian mixed carcinoma, peritoneal serous carcinoma, breast ductal adenocarcinoma, uterine leiomyosarcoma, uterine endometrioid adenocarcinoma, uterine malignant mixed müllerian tumor, glioblastoma, anaplastic glioma, oligodendroglioma, desmoplastic small round cell tumor, squamous cell carcinoma of rectum, salivary gland carcinoma, heart angiosarcoma, gastrointestinal stromal tumor, invasive thymoma, and spindle sarcoma.~~

~~——— 163. The method of any one of claims 113-116, 118, and 133-144, wherein the at least one additional anticancer agent is selected from the group consisting of: an immune checkpoint inhibitor, a chemotherapeutic agent, a PI-3 kinase inhibitor, an EGFR inhibitor, a HER2/neu inhibitor, an FGFR inhibitor, an ALK inhibitor, an IGF1R inhibitor, a VEGFR inhibitor, a PDGFR inhibitor, a glucocorticoid, a BRAF inhibitor, a MEK inhibitor, a HER4 inhibitor, a c-Met inhibitor, a RAF inhibitor, an Akt inhibitor, a FTL-3 inhibitor, and a MAP kinase pathway inhibitor.~~

~~——— 164. The method of claim 163, wherein the MET inhibitor is a Type I c-Met inhibitor.~~

~~165. The method of any one of claims 113-116, 118, and 133-144, wherein the at least one additional anticancer agent comprises a kinase inhibitor.~~

~~166. The method of claim 165, wherein the kinase inhibitor is selected from the group~~

consisting of: ~~bozitinib, 1-(6,7-Dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-[7(S)-(1-pyrrolidinyl)-6,7,8,9-tetrahydro-5H-benzocycloheptene-2-yl]-1H-1,2,4-triazole-3,5-diamine, crizotinib, foretinib, (N-[4-(2-Amino-3-chloropyridin-4-yloxy)-3-fluorophenyl]-4-ethoxy-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide, amuvatinib, BMS-796302, cabozantinib, glesatinib, (4-Fluorophenyl)-N-[3-fluoro-4-(3-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yloxy)phenyl]-1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide, N-[4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]-4-ethoxy-1-(4-fluoro-2-methylphenyl)-1H-pyrazole-3-carboxamide hydrochloride, gilteritinib, [3-(2-[[3-Fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino]-5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)phenyl]acetonitrile, duberminatinib, trans-4-[2-(Butylamino)-5-[4-[(4-methylpiperazin-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidin-7-yl]cyclohexanol, 3-[3-[4-(Morpholin-4-yl)methyl]-1H-pyrrol-2-ylmethylene]-2-oxo-2,3-dihydro-1H-indol-5-ylmethyl]thiazolidine-2,4-dione hydrochloride, sunitinib, 12A11, Mab173, YW327.6S2, D9, E8, merestinib, [3-(2-[[3-Fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino]-5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)phenyl]acetonitrile, N-[4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]-4-ethoxy-1-(4-fluoro-2-methylphenyl)-1H-pyrazole-3-carboxamide hydrochloride, capmatinib, NVP-BVU972, AMG-337, glumetinib, savolitinib, and tepotinib.~~

167. The method of any one of claims 113-116, 118, and 133-144, wherein the at least one additional anticancer agent is selected from the group consisting of: dexamethasone, cytarabine, imatinib, lapatinib, cetuximab, erlotinib, alpelisib, cisplatin, sunitinib, metformin, an anti-PD1 antibody, and docetaxel.

168. The method of any one of claims 113-116, 118, and 133-144, wherein the at least one additional anticancer agent is an EGFR inhibitor.

169. A method of decreasing immune tolerance in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.

170. A method of inhibiting angiogenesis in a subject in need thereof, the method

~~comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52.~~

~~——— 171. A method of suppressing resistance to a therapeutic agent in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of (i) a compound of any one of claims 1-51 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 52, and (ii) the therapeutic agent, wherein the therapeutic agent is selected from the group consisting of a chemotherapeutic agent, a PI-3 kinase inhibitor, an EGFR inhibitor, a HER2/neu inhibitor, an FGFR inhibitor, an ALK inhibitor, an IGF1R inhibitor, a VEGFR inhibitor, a PDGFR inhibitor, a glucocorticoid, a BRAF inhibitor, a MEK inhibitor, a HER4 inhibitor, a c-Met inhibitor, a RAF inhibitor, an Akt inhibitor, a FTL-3 inhibitor, and a MAP kinase pathway inhibitor.~~

~~——— 172. The method of claim 171, wherein the c-Met inhibitor is a Type I c-Met inhibitor.~~

~~——— 173. The method of claim 171, wherein (i) the compound of any one of claims 1-36 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 37, and (ii) the therapeutic agent, are administered to the subject at substantially the same time.~~

~~——— 174. The method of claim 173, wherein (i) the compound of any one of claims 1-36 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 37, and (ii) the therapeutic agent, are formulated in a single dosage form.~~

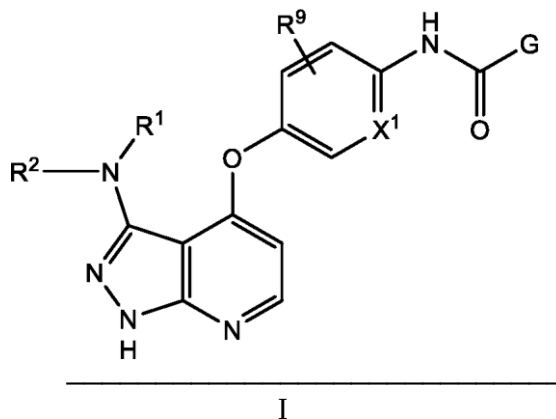
~~——— 175. The method of claim 171, wherein (i) the compound of any one of claims 1-36 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 37, is administered to the subject prior to administration of (ii) the therapeutic agent to the subject.~~

~~——— 176. The method of claim 171, wherein (ii) the therapeutic agent is administered to the subject prior to administration of (i) the compound of any one of claims 1-36 or a~~

~~pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 37, to the subject.~~

CLAIMS

1. A compound of Formula I



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

X¹ is CH or N;

R¹ is hydrogen or C1-C6 alkyl;

R² is

(a) hydrogen,

(b) C 1-C6 alkyl,

(c) hydroxyC 1-C6 alkyl,

(d) dihydroxyC2-C6 alkyl,

(e) C1-C6 fluoroalkyl optionally substituted with OH,

(f) (di-C1-C6 alkoxy)C2-C6 alkyl-,

(g) (C1-C6 alkoxy)C 1-C6 alkyl- wherein said alkyl portion is optionally substituted with

OH,

(h) Cyc¹,

(i) Cyc²,

(j) (hetCyc¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH,

(k) (Ar¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH,

(l) (hetAr¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH, or

(m) (HOS03)C 1-C6 alkyl-;

Cyc¹ is a 3-4 membered cycloalkyl ring optionally substituted with 1-2 substituents

independently selected from halogen, hydroxy, C1-C3 alkyl, hydroxyC1-C3 alkyl, C1-C3 alkoxy, (C1-C3 alkoxy)C1-C3 alkyl- and $R'R''NC(=O)-$;

R' and R'' are independently hydrogen or C1-C6 alkyl;

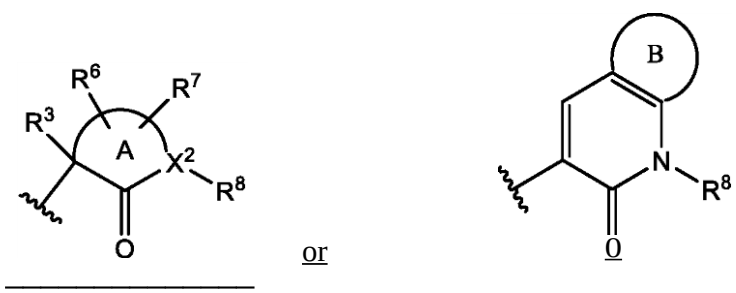
Cyc^2 is a 5-membered cycloalkyl ring substituted with 1-2 substituents independently selected from C1-C3 alkyl, (C1-C3 alkoxy)C1-C3 alkyl- and hydroxyC1-C3 alkyl-;

$hetCyc^1$ is a 5-6 membered saturated heterocyclic ring having 1-2 ring heteroatoms independently selected from O, N, S and SO_2 , wherein said ring is optionally substituted with oxo;

Ar^1 is phenyl;

$hetAr^1$ is pyridyl;

G is



X^2 is C or N;

Ring A, including the atoms at the points of attachment, is a 5-6 membered heterocyclic ring optionally having an additional 1-2 ring nitrogen atoms when X^2 is N and having one ring nitrogen atom when X^2 is C;

R^3 is hydrogen, methyl, or absent;

R^6 is hydrogen, halogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl- or $hetCyc^2$, provided that when R^6 is on the ring carbon atom adjacent to the carbon linked to the $-NHC(=O)-$ moiety of Formula I, then R^6 is not halogen, and

R^7 is hydrogen, C1-C6 alkyl, oxo or thioxo,

or optionally when R^6 and R^7 are on the same carbon atom, R^6 and R^7 together with the carbon atom to which they are attached form a cyclopropyl ring;

$hetCyc^2$ is a 4-6 membered saturated heterocyclic ring having a ring nitrogen atom and optionally substituted with C1-C6 alkyl;

Ring B, including the atoms at the points of attachment, is a 6-membered saturated

R⁸ is Ar², hetAr², C3-C6 cycloalkyl, hetCyc³ or C1-C6 alkyl;
Ar² is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;
hetAr² is a 5-6 membered heteroaryl having 1-2 ring nitrogen atoms and optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;
hetCyc³ is a 5-6 membered heterocyclic ring having a ring oxygen atom;
and
R⁹ is hydrogen or halogen.


A-1

387

4. A compound according to any one of claims 1-3 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein R^2 is hydroxyC1-C6 alkyl.

5. A compound according to any one of claims 1-4 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein R^8 is Ar^2 .

6. A compound according to claim 5 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein Ar^2 is phenyl optionally substituted with one or more halogens.

7. A compound according to any one of claims 1-6 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein X^1 is CH.

8. A compound according to any one of claims 1-7 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein R^9 is halogen.

9. A compound according to claim 8 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein R^9 is fluoro.

10. A compound according to any one of claims 1-9 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen.

11. A compound according to claim 1, selected from
N-(3-fluoro-4-((3-((2-hydroxyethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;
N-(3-fluoro-4-((3-((2-methoxyethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;
N-(3-fluoro-4-((3-((1-hydroxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-

4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-hydroxy-2-methylpropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((2-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((2-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((3-hydroxy-2,2-dimethylpropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(S)-N-(4-((3-((2,3-dihydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(4-((3-((cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(4-((3-((3,3-difluorocyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(R)-N-(4-((3-((2,3-dihydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1r,3r)-3-methoxycyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1s,3s)-3-methoxycyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1s,3s)-3-hydroxy-1-methylcyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(methoxymethyl)cyclopropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-methoxyethyl)(methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(methoxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(methoxymethyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4-methoxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((tetrahydrofuran-2-yl)methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-(((1,1-dioxidotetrahydrothiophen-3-yl)methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-((1,3-dimethoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((cis-2-(methoxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((tetrahydrofuran-3-yl)methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((2-oxopiperidin-4-yl)methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-(((1s,3s)-3-(dimethylcarbamoyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-((1,3-dihydroxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4-hydroxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((3-hydroxy-3-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-hydroxyethyl)(methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1r,3r)-3-(hydroxymethyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1s,3s)-3-(hydroxymethyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((3-hydroxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((3-hydroxy-2,3-dimethylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4-hydroxy-2-methylpentan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-6-methyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-hydroxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-6-methyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4-hydroxy-1-methoxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((3,3,3-trifluoro-2-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-((1,3-dihydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-hydroxy-3-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-hydroxy-3-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4-hydroxy-1-methoxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-hydroxy-4-methoxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-

4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(4-((3-((2,2-difluoro-3-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(4-((3-((4,4-difluoro-1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((4,4,4-trifluoro-1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(hydroxymethyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1S,2R)-2-(hydroxymethyl)-1-methylcyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(hydroxymethyl)cyclopropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((cis-2-(hydroxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-(hydroxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((2-hydroxy-1-phenylethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((1-hydroxy-2-(hydroxymethyl)butan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-hydroxy-1-(pyridin-3-yl)ethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-hydroxy-1-(pyridin-4-yl)ethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

N-(3-fluoro-4-((3-((2-hydroxy-1-(tetrahydro-2H-pyran-4-yl)ethyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydro-2H-pyridazine-4-carboxamide;

pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2,5-dioxo-1-phenyl-1,2,5,6, 7,8-hexahydroquinoline-3-carboxamide;

N-(3-fluoro-4-(3-iodo-1-(4-methoxybenzyl)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2,5-dioxo-1,2,5,6, 7,8-hexahydroquinoline-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(3-fluoro-4-(3-((1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-(3-((1-(hydroxymethyl)cyclobutyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-(3-((1-hydroxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

2-(4-fluorophenyl)-N-(5-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)(methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)(methyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-(3-((2-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(S)-N-(3-fluoro-4-((3-((2-hydroxypropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

N-(3-fluoro-4-((3-((2-hydroxy-2-methylpropyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

N-(3-fluoro-4-((3-(((2R,3S)-3-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

N-(3-fluoro-4-((3-(((2R,3R)-3-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(R)-N-(3-fluoro-4-((3-((3-hydroxy-3-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(3-fluoro-4-((3-((3-hydroxy-3-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-1-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-1-(cyclopropylmethyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-4-ethoxy-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-

yl)oxy)phenyl)-1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-1-methyl-3-oxo-2,3-dihydro-1H-pyrazole-4-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-(1-methylazetidin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-3-cyclopentyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-1-cyclobutyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-3-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-3-(1-methyl-1H-pyrazol-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1-(pentan-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1,3-diisopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-3-cyclohexyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(R)-3-(4-chlorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;
(S)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-3-(tetrahydro-2H-pyran-4-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

N-(3-fluoro-4-(3-(((R)-1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxopiperidine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-4-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-3-oxo-3,4-dihydropyrazine-2-carboxamide;

(R)-6-cyclopropyl-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-6-isopropyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(S)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(R)-1-cyclopropyl-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-

yl)oxy)phenyl)-1-(5-fluoropyridin-2-yl)-2,5-dioxo-1,2,5,6, 7,8-hexahydroquinoline-3-carboxamide;

(R)-5-(4-fluorophenyl)-N-(5-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-1-methyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-1-(4-fluorophenyl)-N-(5-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-1-isopropyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-1-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-1-methyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-1-methyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-5-cyclopropyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-1-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-5-bromo-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(3-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-5-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-5-(4-chlorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-1-isopropyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(S)-1-ethyl-N-(3-fluoro-4-(3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-

b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-5-(2,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-3-(3,4-difluorophenyl)-1-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-5-chloro-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-1-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-3-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-4-(3,4-difluorophenyl)-2-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(R)-4-(3,4-difluorophenyl)-2-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(S)-4-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(R)-4-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(S)-2-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(R)-2-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-

carboxamide;

(S)-3-(3,4-difluorophenyl)-1-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(S)-1-cyclopropyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

N-(3-fluoro-4-((3-(((R)-1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-(4-fluorophenyl)-6-oxo-5-azaspiro[2.5]octane-7-carboxamide;

N-(3-fluoro-4-((3-(((R)-1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-3-methyl-2-oxopiperidine-3-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-5-hydroxy-2-oxo-1-phenyl-1,2-dihydroquinoline-3-carboxamide;

(R)-2-(4-fluorophenyl)-N-(5-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-2-(4-fluorophenyl)-N-(5-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-6-methyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-3-(4-fluorophenyl)-N-(5-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(R)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(S)-3-cyclopentyl-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-1-ethyl-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(S)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-

carboxamide;

(S)-1-(cyclopropylmethyl)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-1-cyclobutyl-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-3-(3,4-difluorophenyl)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

1-ethyl-N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-((3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-(2-hydroxyethyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-6-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-1-cyclobutyl-N-(3-fluoro-4-(3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-(3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

(S)-N-(3-fluoro-4-(3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-4-(4-fluorophenyl)-2-isopropyl-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carboxamide;

N-(4-(3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(4-(3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-5-(4-fluorophenyl)-1-methyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

N-(4-(3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-6-isopropyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(5-(3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-5-(4-fluorophenyl)-1-methyl-4-oxo-1,4-dihydropyridine-3-carboxamide;

N-(5-(3-((4,4-difluorobutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-N-(3-fluoro-4-(3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

N-(3-fluoro-4-(3-((1-methoxy-2-methylpropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-3-(3,4-difluorophenyl)-N-(4-(3-((1-ethoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(S)-N-(4-(3-((1-ethoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-1-(4-fluorophenyl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(S)-N-(4-(3-((1-ethoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-5-(4-fluorophenyl)-1-isopropyl-N-(5-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-4-oxo-1,4-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-6-isopropyl-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-2-(4-fluorophenyl)-6-isopropyl-N-(5-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-5-cyclopropyl-1-(4-fluorophenyl)-N-(5-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-1-(4-fluorophenyl)-N-(5-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)pyridin-2-yl)-5-methyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-1-(cyclopropylmethyl)-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-1-ethyl-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-4-ethoxy-N-(3-fluoro-4-((3-((1-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

N-(3-fluoro-4-((3-((1-(2-hydroxypropan-2-yl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

2-((4-(2-fluoro-4-(2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamido)phenoxy)-1H-pyrazolo[3,4-b]pyridin-3-yl)amino)-2-methylpropyl hydrogen sulfate;

(S)-N-(3-fluoro-4-((3-((3-hydroxy-3-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((3-hydroxy-3-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1S,2R)-2-(hydroxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(3-fluoro-4-((3-(((1R,2S)-2-(hydroxymethyl)cyclopentyl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((4-hydroxy-1-methoxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((4-hydroxy-1-methoxy-2-methylbutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxy-3-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxy-3-methoxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxy-4-methoxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(3-fluoro-4-((3-((1-hydroxy-4-methoxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(R)-N-(4-((3-((4,4-difluoro-1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

(S)-N-(4-((3-((4,4-difluoro-1-hydroxybutan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-2-(4-fluorophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxamide;

N-(4-((3-amino-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(3-fluoro-4-((3-(methylamino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

N-(4-((3-(ethylamino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)-3-fluorophenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-5-isopropyl-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-5-ethyl-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-1,2-dihydropyridine-3-carboxamide;

(R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-1-(4-fluorophenyl)-2-oxo-5-propyl-1,2-dihydropyridine-3-carboxamide;

and stereoisomers, tautomers and pharmaceutically acceptable salts thereof.

12. A compound according to claim 1 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein:

X¹ is CH or N;

R¹ is hydrogen or C1-C6 alkyl;

R² is

(a) hydrogen,

(b) C1-C6 alkyl,

(c) hydroxyC1-C6 alkyl,

(d) dihydroxyC2-C6 alkyl,

(e) C1-C6 fluoroalkyl optionally substituted with OH,

(g) (C1-C6 alkoxy)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH,

(h) Cyc¹,

(i) Cyc²,

(j) (hetCyc¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH,

(k) (Ar¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH,

(l) (hetAr¹)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH, or

(m) (HOS03)C1-C6 alkyl-;

Cyc¹ is a 3-4 membered cycloalkyl ring optionally substituted with 1-2 substituents independently selected from halogen, hydroxy, hydroxyC1-C3 alkyl, C1-C3 alkoxy, (C1-C3 alkoxy)C1-C3 alkyl-, and R'R''NC(=O)-;

R' and R'' are independently selected from C1-C6 alkyl;

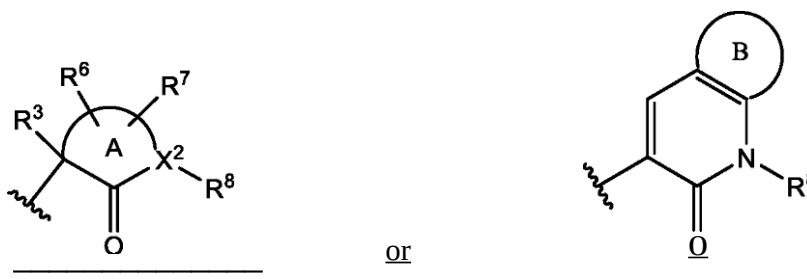
Cyc² is a 5-membered cycloalkyl ring substituted with 1-2 substituents independently selected from C1-C3 alkyl, (C1-C3 alkoxy)C1-C3 alkyl- and hydroxyC1-C3 alkyl-;

hetCyc¹ is a 5-6 membered saturated heterocyclic ring having 1-2 ring heteroatoms independently selected from O, N and S02, wherein said ring is optionally substituted with oxo;

Ar¹ is phenyl;

hetAr¹ is pyridyl;

G is



X² is C or N;

Ring A, including the atoms at the points of attachment, is a 5-6 membered heterocyclic ring optionally having an additional 1-2 ring nitrogen atoms when X² is N and having one ring nitrogen atom when X² is C;

R³ is hydrogen or absent;

R⁶ is hydrogen, halogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl- or hetCyc², provided that when R⁶ is on the ring carbon atom adjacent to the carbon linked to the -NHC(=O)- moiety of Formula I, then R⁶ is not halogen;

R⁷ is hydrogen, C1-C6 alkyl, oxo or thioxo;

hetCyc² is a 4 membered saturated heterocyclic ring having a ring nitrogen atom substituted with C1-C6 alkyl;

Ring B, including the atoms at the points of attachment, is a 6-membered saturated carbocyclic optionally substituted with oxo or a 6-membered aromatic carbocyclic ring optionally substituted with OH;

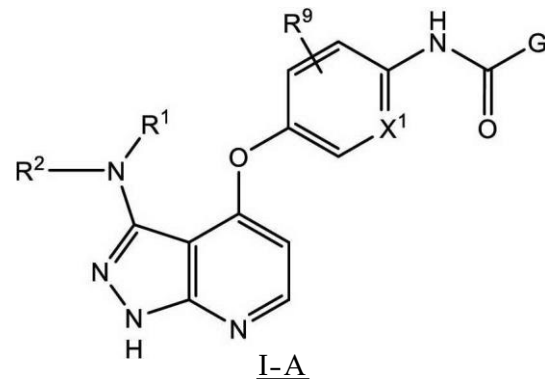
R⁸ is Ar², hetAr², C3-C6 cycloalkyl, hetCyc³ or C1-C6 alkyl;

Ar² is phenyl optionally substituted with one or more substituents independently selected from halogen;

hetAr² is a 5-6 membered heteroaryl having 1-2 ring nitrogen atoms and optionally substituted with one or more substituents independently selected from C1-C2 alkyl; and

R⁹ is hydrogen or halogen.

13. A compound of Formula I-A



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

X¹ is CH or N;

R¹ is hydrogen or C1-C6 alkyl;

R² is

(a) hydrogen,

(b) C1-C6 alkyl,

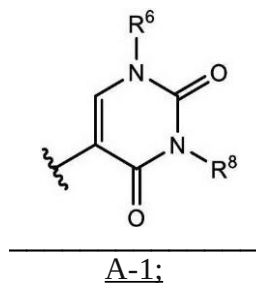
(c) hydroxyC1-C6 alkyl,

(g) (C1-C6 alkoxy)C1-C6 alkyl- wherein said alkyl portion is optionally substituted with OH, or

(h) Cyc¹;

Cyc¹ is a 3-4 membered cycloalkyl ring optionally substituted with 1-2 substituents independently selected from halogen, hydroxy, C1-C3 alkyl, hydroxyC1-C3 alkyl, C1-C3 alkoxy, (C1-C3 alkoxy)C1-C3 alkyl- and R'R''NC(=O)-;

X² is N, R³ is absent, Ring J is a 6-membered heterocyclic ring having one additional ring nitrogen atom, and R⁷ is oxo, wherein G has the formula A-1.



R⁶ is C1-C6 alkyl, hydroxyC1-C6 alkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)C1-C6 alkyl- or hetCyc²;

hetCyc² is a 4-6 membered saturated heterocyclic ring having a ring nitrogen atom and

optionally substituted with C1-C6 alkyl;

R⁸ is Ar², hetAr², C3-C6 cycloalkyl, hetCyc³ or C1-C6 alkyl;

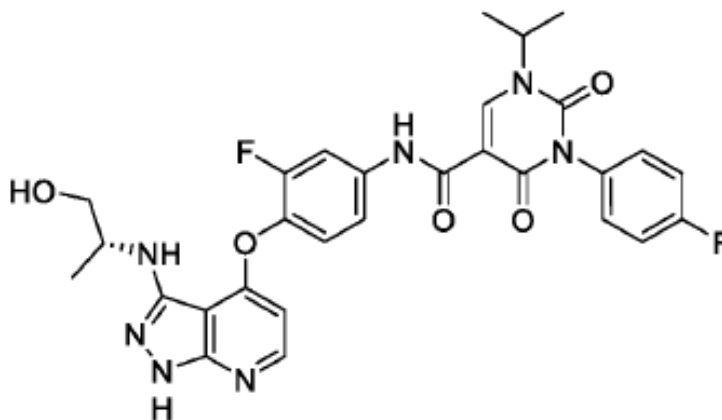
Ar² is phenyl optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;

hetAr² is a 5-6 membered heteroaryl having 1-2 ring nitrogen atoms and optionally substituted with one or more substituents independently selected from halogen, C1-C2 alkyl and C1-C2 alkoxy;

hetCyc³ is a 5-6 membered heterocyclic ring having a ring oxygen atom; and

R⁹ is hydrogen or halogen.

14. (R)-N-(3-fluoro-4-((3-((1-hydroxypropan-2-yl)amino)-1H-pyrazolo[3,4-b]pyridin-4-yl)oxy)phenyl)-3-(4-fluorophenyl)-1-isopropyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide having the structure



or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition, comprising a compound of Formula I as defined in any one of claims 1 to 14 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

16. A compound of any one of claims 1-14 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 15, for use in the treatment of cancer in a patient in need thereof.

17. Use of a compound of any one of claims 1-14 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a patient in need thereof.

18. Use of claim 17, wherein the medicament further includes at least one additional anticancer agent to be administered to the patient.

19. Use of claim 18, wherein the at least one additional anticancer agent or therapy is selected from the group consisting of: an immune checkpoint inhibitor, a kinase inhibitor, a chemotherapy, radiation, and surgery.

20. Use of claim 18, wherein the at least one additional anticancer agent is selected from the group consisting of: a chemotherapeutic agent, a PI-3 kinase inhibitor, an EGFR inhibitor, a HER2/neu inhibitor, an FGFR inhibitor, an ALK inhibitor, an IGFIR inhibitor, a VEGFR inhibitor, a PDGFR inhibitor, a glucocorticoid, a BRAF inhibitor, a MEK inhibitor, a HER4 inhibitor, a MET inhibitor, a RAF inhibitor, an Akt inhibitor, a FTL-3 inhibitor, and a MAP kinase pathway inhibitor.

21. Use of any one of claims 17-20, wherein the subject is identified or diagnosed as having a TAM-associated cancer.

22. Use of claim 21, wherein the TAM-associated cancer is selected from the group consisting of: gastrointestinal stromal tumor (GIST), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myeloid leukemia (CML), B-cell chronic myeloid leukemia (B-CLL), lung cancer, glioblastoma, breast cancer, colorectal cancer, gastric cancer, glioma, pancreatic cancer, esophageal cancer, mantle cell lymphoma, melanoma, squamous cell skin cancer, prostate cancer, endometrial cancer, ovarian cancer, oral squamous cell carcinoma, thyroid cancer, bladder cancer, renal cancer, schwannoma, mesothelioma, Kaposi's sarcoma, osteosarcoma, rhabdomyosarcoma, erythroid leukemia, colon cancer, liver cancer, renal cell carcinoma, pituitary adenoma, urinary tract cancer, kidney cancer, head and neck cancer, brain cancer, and non-small cell lung cancer.

23. The use of claim 18, wherein the additional anticancer agent is an immune checkpoint inhibitor.
24. The use of claim 23, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.
25. The use of claim 24, wherein the anti-PD1 antibody is pembrolizumab.
26. The use of claim 18, wherein the additional anticancer agent is a VEGF inhibitor.
27. The use of claim 26, wherein the VEGF inhibitor is axitinib.
28. The use according to any one of claims 23 to 27, wherein the cancer is lung cancer.
29. The use according to any one of claims 23 to 27, wherein the cancer is gastric cancer.
30. The use according to any one of claims 23 to 27, wherein the cancer is renal cancer.
31. The use according to any one of claims 23 to 27, wherein the cancer is melanoma.