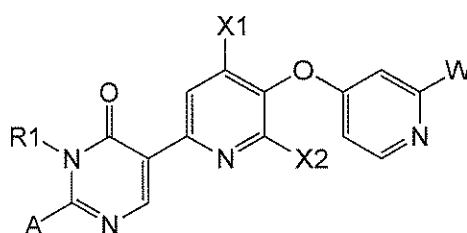


Summary of the Invention

[0011] In one aspect, the present disclosure provides compounds of the Formula I—are described:

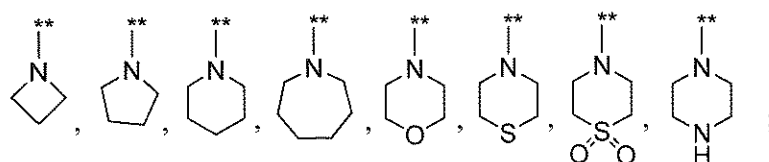


Formula I

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

A is taken from the group consisting of $-N(R_2)R_3$ and G;

G is selected from the group consisting of



and wherein the symbol (**) is the point of attachment to the pyrimidine ring;

each G moiety may be further substituted with one, two, or three R4 moieties;

W is C5-C6heteroaryl, phenyl, $-NHC(O)R_6$, $-NHC(O)R_7$, $-NHC(O)N(R_8)R_9$ or $-C(O)N(R_8)R_9$, and wherein each C5-C6heteroaryl or phenyl is optionally substituted by one, two, or three R5 moieties;

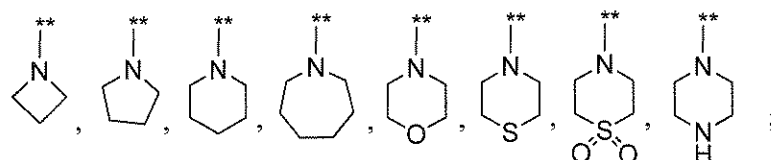
X1 and X2 are individually and independently hydrogen or C1-C6 alkyl;

R1 is hydrogen, C1-C6 alkyl, deuterio-C1-C6 alkyl wherein the alkyl chain is partially or completely deuterated, or branched C3-C8 alkyl;

R2 is hydrogen, C1-C6 alkyl, deuterio-C1-C6 alkyl wherein the alkyl chain is partially or completely deuterated, branched C3-C8 alkyl, C3-C8 cycloalkyl, fluoroC1-C6alkyl wherein the alkyl is fully or partially fluorinated, $-(CH_2)_m-OR_8$, or a 3-8 membered heterocyclic ring, wherein each alkylene is optionally substituted with C1-C4 alkyl;

R3 is hydrogen, C1-C6 alkyl, deuterio-C1-C6 alkyl wherein the alkyl chain is partially or completely deuterated, branched C3-C8 alkyl, C3-C8 cycloalkyl, fluoroC1-C6alkyl wherein the alkyl is fully or partially fluorinated or a 3-8 membered heterocyclic ring;

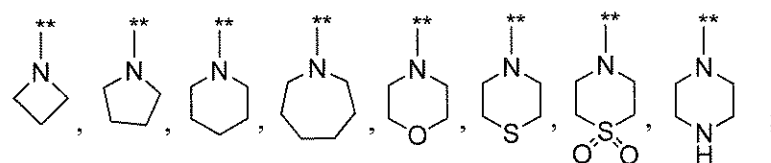
each R4 is individually and independently hydrogen, halogen, C1-C6 alkyl, fluoro-C1-C6 alkyl wherein the alkyl chain is partially or completely fluorinated, branched C3-C8



wherein the symbol (**) is the point of attachment to the pyrimidine ring;

and wherein each G moiety may be further substituted with one, two, or three R₄ moieties.

[0117] In one embodiment, the compound of Formula Id is a compound wherein: R₁ is methyl and G is selected from the group consisting of



wherein the symbol (**) is the point of attachment to the pyrimidine ring;

and wherein each G moiety may be further substituted with one, two, or three R₄ moieties.

[0118] In one embodiment, the compound of Formula Id is a compound wherein: R₅ is hydrogen, C₁-C₆ alkyl, deuterio-C₁-C₆ alkyl wherein the alkyl chain is partially or completely deuterated, branched C₃-C₈ alkyl, halogen, cyano, fluoro-C₁-C₆ alkyl wherein the alkyl chain is partially or completely fluorinated, $-(CH_2)_m-C(O)NR_8(R_9)$, $-(CH_2)_m-C(O)R_7$, $-(CH_2)_m-OR_8$, $-(CH_2)_m-NR_8(R_9)$, or $-(CH_2)_m-R_7$, wherein each alkylene is optionally substituted with C₁-C₄ alkyl.

[0119] In one embodiment, the compound of Formula Id is a compound wherein: R₅ is hydrogen, C₁-C₆ alkyl, or deuterio-C₁-C₆ alkyl wherein the alkyl chain is partially or completely deuterated, or branched C₃-C₈ alkyl.

[0120] In one embodiment, the compound of Formula Id is a compound wherein: R₅ is C₁-C₆ alkyl, or deuterio-C₁-C₆ alkyl wherein the alkyl chain is partially or completely deuterated.

[0121] In one embodiment, the compound of Formula Id is a compound wherein: R₅ is C₁-C₆ alkyl.

[0122] In ~~another aspect~~~~some embodiments~~, the ~~present disclosure provides~~~~invention~~ comprises a compound selected from the group consisting of 2-(ethylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one, 2-(dimethylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one, 2-(isopropylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-

pyran-4-yl)amino)pyrimidin-4(3H)-one, 2-(tert-butylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one, 5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)-2-(neopentylamino)pyrimidin-4(3H)-one, and 2-(3,3-difluoropyrrolidin-1-yl)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.

[0122a] In a further aspect, the present disclosure provides a compound 2-(ethylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.

[0122b] In another aspect, the present disclosure provides a compound 2-(isopropylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.

[0122c] In a further aspect, the present disclosure provides a compound 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.

[0123] In certain embodiments, the ~~invention~~present disclosure comprises a method of treating mammalian disease at least partially mediated by the kinase activity of c-FMS, PDGFR- β , or c-KIT kinases, wherein the kinase is a wildtype form, a mutant oncogenic form, an aberrant fusion protein form or a polymorph thereof, the method comprising administering to a mammal in need thereof an effective amount of a compound of formula I.

[0123a] In one aspect, the present disclosure provides a pharmaceutical composition, comprising a compound as disclosed herein and a pharmaceutically acceptable carrier.

[0124] In other embodiments, the ~~present invention~~present disclosure comprises a pharmaceutical composition, comprising a compound of formula I and a pharmaceutically acceptable carrier.

[0125] In certain embodiments, the composition comprises an additive selected from adjuvants, excipients, diluents, or stabilizers.

[0126] In some embodiments, the ~~invention~~present disclosure includes a method of treating cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic

cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia, the method comprising administering to a patient in need thereof an effective amount of a compound of formula I.

[0127] In some embodiments, the ~~invention~~present disclosure includes a method of treating glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone, the method comprising administering to a patient in need thereof an effective amount of a compound of formula I.

[0128] In certain embodiments of the present methods, the compound is administered orally, parenterally, by inhalation, or subcutaneously.

[0129] In some embodiments, the ~~invention~~present disclosure provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, in the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases,

solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia, the method comprising administering to a patient in need thereof an effective amount of a compound of formula I.

[0130] In some embodiments, the ~~invention~~present disclosure provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, in the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone, the method comprising administering to a patient in need thereof an effective amount of a compound of formula I.

[0130a] In one aspect, the present disclosure provides a use of a compound as disclosed herein in the manufacture of a medicament for the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia.

[0131] In some embodiments, the ~~invention~~present disclosure provides for the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia.

[0131a] In one aspect, the present disclosure provides a use of a compound as disclosed herein in the manufacture of a medicament for the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone.

[0132] In certain embodiments, the invention present disclosure provides for the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone.

[0132a] In one aspect, the present disclosure provides a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia.

[0132b] In another aspect, the present disclosure provides a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone.

[0133] The details of the invention are set forth in the accompanying description below. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, illustrative methods and materials are now described. Other features, objects, and advantages of the invention will be apparent from the description and from the claims. In the specification and the appended claims, the singular forms also include the plural unless the context clearly dictates otherwise. Unless defined

17. The composition of claim 16 further comprising an additive selected from adjuvants, excipients, diluents, or stabilizers.
18. The compound 2-(isopropylamino)-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.
19. A pharmaceutical composition, comprising the compound of claim 18 and a pharmaceutically acceptable carrier.
20. The composition of claim 19 further comprising an additive selected from adjuvants, excipients, diluents, or stabilizers.
21. The compound 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one.
22. A pharmaceutical composition, comprising the compound of claim 21 and a pharmaceutically acceptable carrier.
23. The composition of claim 22 further comprising an additive selected from adjuvants, excipients, diluents, or stabilizers.
24. A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
25. The composition of claim 24 further comprising an additive selected from adjuvants, excipients, diluents, or stabilizers.
26. Use of of a compound of claim 1 in the manufacture of a medicament for the treatment of~~A method of treating~~ cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia,~~the method comprising administering to a patient in need thereof an effective amount of a compound of claim 1.~~

27. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of A method of treating glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone, the method comprising administering to a patient in need thereof an effective amount of a compound of claim 1.
28. The method use of any one of claims 26 or 27, wherein the compound is to be administered orally, parenterally, by inhalation, or subcutaneously.
- ~~29. The method of claim 27, wherein the compound is administered orally, parenterally, by inhalation, or subcutaneously.~~
- ~~30. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia.~~
- ~~31. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone.~~
3229. AUse of a compound of claim 1, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for the treatment of cancer, gastrointestinal stromal tumors, hyperproliferative diseases, metabolic diseases, neurodegenerative diseases, solid tumors, melanomas, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, renal cancers, hepatic cancers, osteosarcomas, multiple myelomas, cervical carcinomas, metastasis of primary tumor sites, cancers that are metastatic to bone, papillary thyroid carcinoma, non-small cell lung cancer, colonic cancers, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune

nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, mastocytosis, or mast cell leukemia.

3330. ~~A Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for the treatment of glioblastomas, breast cancers, pancreatic cancers, metastasis of primary tumor sites, or cancers that are metastatic to bone.~~