demonstrated by biopsy samples obtained from different progressing metastases within each patient (Wardelmann, E., et al. *Lancet Oncol.* **2005**, *6*, pg. 249-251; Fletcher, J.A. and Rubin, B.P., *Curr. Opin in Genetics & Develop.*, **2007**, *17*, pg. 3-7). This complex c-KIT mutational heterogeneity within individual patients underscores an unmet medical need to identify inhibitors of c-KIT kinase that are effective across a broad spectrum of c-KIT primary and secondary mutations. Such a broad spectrum c-KIT inhibitor would be of high therapeutic value in the treatment of refractory GIST patients.

Summary of the Invention

[0005] The present ~~invention~~disclosure discloses the unexpected utility of compounds that inhibit c-KIT kinase across a broad range of c-KIT mutations, including complex occurrences of primary mutations (*KIT* exon 9 or 11) and secondary *KIT* mutations (exons 13, 14, 17 and 18) that may arise in individual, refractory GIST patients. Also unexpected is the utility of compounds of the present ~~invention~~disclosure to inhibit the problematic exon 17 D816V c-KIT mutation, for which there is currently no effective therapy. D816 mutations in c-KIT have been demonstrated to cause mastocytosis, mast cell leukemia, seminomas, dysgerminomas, lymphomas, and intracranial teratomas (Ning, A.Q, Li, J., and Arceci, R.J. *Leuk Lymphoma*, **2001**, *41*, pg. 513-522; Beghini, A., et al. *Blood*, **2000**, *95*, pg. 726-727; Tian, Q., et al. *Am J. Pathol.* **1999**, *154*, pg. 1643-1647; Nagata, H., et al. *Proc. Natl. Acad. Sci. USA*, **1995**, *92*, 10560-10564; Longley, B.J., et al. *Nat. Genet.*, **1996**, *12*, pg. 312-314). The present ~~invention~~disclosure also discloses new compounds for the treatment of diseases caused by c-KIT mutation, including new compounds for the treatment of refractory GIST, mast cell leukemia, or mastocytosis.

[0006] ~~One aspect of the present invention provides~~Disclosed is a method of treating a disease caused by the kinase activity of c-KIT, oncogenic forms thereof, aberrant fusion proteins thereof or polymorphs thereof, comprising the administration of a compound of formula Ia

each R10 is independently and individually selected from the group consisting of CO_2H, CO_2C1-C6alkyl, CO-N(R4)$_2$, OH, C1-C6alkoxy, C1-C6alkyl, and -N(R4)$_2$;

each R17 is taken from the group comprising phenyl, naphthyl, pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, oxetanyl, azetadinyl, tetrahydrofuranyl, oxazolinyl, oxazolidinyl, pyranyl, thiopyranyl, tetrahydropyranyl, dioxalinyl, pyrrolidinyl, and piperidinyl;

wherein R17 can be further substituted with one or more Z2 or Z3 moieties;

wherein two R3 or R4 moieties are independently and individually taken from the group consisting of C1-C6alkyl and branched C3-C6alkyl, hydroxyalkyl, and alkoxyalkyl and are attached to the same nitrogen atom, said moieties may cyclize to form a C3-C7 heterocyclyl ring; and k is 1 or 2; n is 0-6; p is 1-4; q is 2-6; r is 0 or 1; t is 1-3.

[0007] In one ~~embodiment~~example, the ~~invention~~present disclosure provides a method of treating a disease caused by the kinase activity of c-KIT, oncogenic forms thereof, aberrant fusion proteins thereof or polymorphs thereof, wherein c-KIT contains a missense mutatation, insertion mutation, or a deletion mutation encoded by exons comprising Exon 9, Exon 11, Exon 13, Exon 14, Exon 17, or Exon 18, presenting either individually or in combination, comprising the administration of a compound of formula Ia or a pharmaceutically acceptable salt thereof.

[0008] Also disclosed is ~~A second aspect of the present invention provides~~ a method of treating a disease selected from gastrointestinal stromal tumors, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, melanoma, renal cancers, hepatic cancers, cervical carcinomas, metastasis of primary tumor sites, papillary thyroid carcinoma, non-small cell lung cancer, mesothelioma, hypereosinophilic syndrome, colonic cancers, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, teratomas, mastocytosis, or mast cell leukemia, said method comprising administering a therapeutically effective amount of a compound of Formula Ia, or a pharmaceutically acceptable salt thereof, to a patient.

In one aspect, there is provided a pharmaceutical composition comprising a compound as described herein or a salt thereof, together with a pharmaceutically acceptable carrier, said carrier including an additive selected from the group including adjuvants, excipients, diluents, and stablilizers.

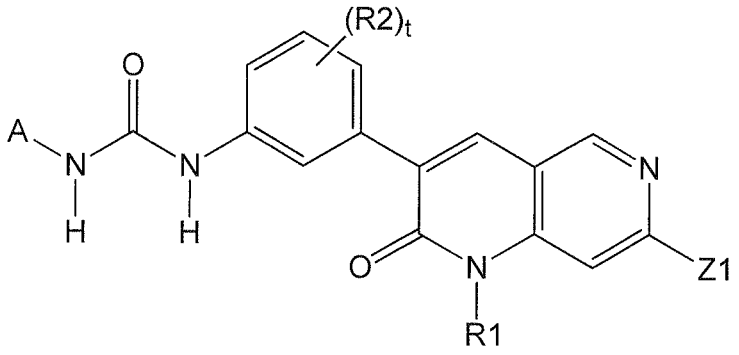
[0009] ~~A third aspect of the present invention provides~~Also disclosed is a pharmaceutical composition comprising a compound of Formula Ia, or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable carrier, with the proviso that the compound is not 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-

methylphenyl)-3-(naphthalen-1-yl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,3-difluorophenyl)urea, 1-(2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, or 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(2,3-difluorophenyl)urea.

In one aspect, there is provided use of a compound of Formula Ia or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a disease caused by the kinase activity of c-KIT, oncogenic forms thereof, or polymorphs thereof.

[0010] ~~A fourth aspect of the present invention provides~~Also disclosed is use of a compound of Formula Ia or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a disease selected from gastrointestinal stromal tumors, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, melanoma, renal cancers, hepatic cancers, cervical carcinomas, metastasis of primary tumor sites, papillary thyroid carcinoma, non-small cell lung cancer, mesothelioma, hypereosinophilic syndrome, colonic cancers, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, teratomas, mastocytosis, or mast cell leukemia.

[0011] ~~A fifth aspect of the present invention provides~~Also disclosed is a compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof,

wherein R17 can be further substituted with one or more Z2 or Z3 moieties;

wherein two R3 or R4 moieties are independently and individually taken from the group consisting of C1-C6alkyl and branched C3-C6alkyl, hydroxyalkyl, and alkoxyalkyl and are attached to the same nitrogen atom, said moieties may cyclize to form a C3-C7 heterocyclyl ring;

and k is 1 or 2; n is 0-6; p is 1-4; q is 2-6; r is 0 or 1; t is 1-3;

with the proviso that the compound is not 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(naphthalen-1-yl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,3-difluorophenyl)urea, 1-(2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, or 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(2,3-difluorophenyl)urea.

[0012] In any of the foregoing aspects:

[0013] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: A is phenyl; or a pharmaceutically acceptable salt thereof.

[0014] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: A is naphthyl; or a pharmaceutically acceptable salt thereof.

[0015] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: A is benzothienyl; or a pharmaceutically acceptable salt thereof.

[0016] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: R1 is taken from the group consisting of C1-C4alkyl, branched C3-C5alkyl, and C3-C5carbocyclyl; or a pharmaceutically acceptable salt thereof.

[0017] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: R1 is C1-C4alkyl; or a pharmaceutically acceptable salt thereof.

[0018] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: R1 is branched C3-C5alkyl; or a pharmaceutically acceptable salt thereof.

[0019] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: R1 is C3-C5carbocyclyl; or a pharmaceutically acceptable salt thereof.

[0020] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is selected from the group consisting of -NH(R4) and -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0021] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NH(R4); or a pharmaceutically acceptable salt thereof.

[0022] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NH(R4) and R4 is H or C1-C6alkyl; or a pharmaceutically acceptable salt thereof.

[0023] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NH(R4) and R4 is H; or a pharmaceutically acceptable salt thereof.

[0024] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NH(R4) and R4 is C1-C6alkyl; or a pharmaceutically acceptable salt thereof.

[0025] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0026] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NR4COR8; or a pharmaceutically acceptable salt thereof.

[0027] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0028] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is hydrogen, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, -N(R4)2, or R5; or a pharmaceutically acceptable salt thereof.

[0029] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is C1-C6alkyl; or a pharmaceutically acceptable salt thereof.

[0030] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is branched C3-C7alkyl; or a pharmaceutically acceptable salt thereof.

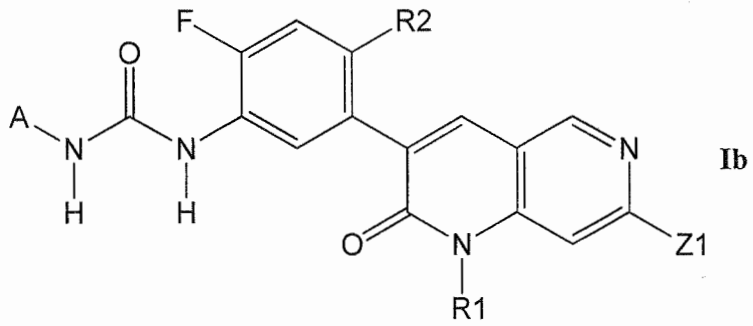
[0031] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is C3-C8carbocyclyl; or a pharmaceutically acceptable salt thereof.

[0032] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is -N(R4)2; or a pharmaceutically acceptable salt thereof.

[0033] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: Z1 is -NHCOR8 and R8 is R5; or a pharmaceutically acceptable salt thereof.

[0034] In one ~~embodiment~~example, the compound of Formula Ia is a compound wherein: each R2 is independently hydrogen, methyl, or halogen and t is 2; or a pharmaceutically acceptable salt thereof.

[0035] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib



Ib

wherein:

R2 is hydrogen, methyl, or halogen; or a pharmaceutically acceptable salt thereof.

[0036] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: R2 is hydrogen; or a pharmaceutically acceptable salt thereof.

[0037] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: R2 is methyl; or a pharmaceutically acceptable salt thereof.

[0038] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: R2 is halogen; or a pharmaceutically acceptable salt thereof.

[0039] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is C1-C4alkyl, branched C3-C5alkyl, or C3-C5carbocyclyl, R2 is hydrogen, methyl, or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0040] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is C1-C4alkyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0041] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is ethyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0042] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is ethyl, R2 is methyl or halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0043] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is ethyl, R2 is methyl, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0044] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is phenyl, R1 is ethyl, R2 is halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0045] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is C1-C4alkyl, branched C3-C5alkyl, or C3-C5carbocyclyl, R2 is hydrogen, methyl, or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0046] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is C1-C4alkyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0047] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is ethyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0048] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is ethyl, R2 is methyl or halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0049] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is ethyl, R2 is methyl, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0050] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is naphthyl, R1 is ethyl, R2 is halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0051] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is C1-C4alkyl, branched C3-C5alkyl, or C3-C5carbocyclyl, R2 is hydrogen, methyl, or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0052] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is C1-C4alkyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0053] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is ethyl, R2 is methyl or halogen, and Z1 is -NH(R4) or -NHCOR8; or a pharmaceutically acceptable salt thereof.

[0054] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is ethyl, R2 is methyl or halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0055] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is ethyl, R2 is methyl, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0056] In one ~~embodiment~~example, the compound of Formula Ia is a compound of Formula Ib wherein: A is benzothienyl, R1 is ethyl, R2 is halogen, Z1 is -NH(R4) and R4 is methyl; or a pharmaceutically acceptable salt thereof.

[0057] In some ~~embodiments~~examples, the present ~~invention~~disclosure provides a method treating a disease caused by c-KIT kinase comprising gastrointestinal stromal tumors, ovarian cancer, melanoma, cervical carcinomas, acute myeloid leukemia, germ cell tumors of the seminoma

yl)azetidine-1-carboxamide, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-iodophenyl)-3-phenylurea, and 1-(5-(1-ethyl-7-((1-methyl-1H-pyrazol-4-yl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea; or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided a compound selected from the group consisting of

1-(4-chloro-3-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2-fluoro-4-methyl-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2,4-difluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, 1-(3-chlorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(3-fluoro-phenyl)-urea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(2-fluoro-phenyl)-urea, 1-(4-chloro-3-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(4-chloro-5-(7-(2-(dimethylamino)ethylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(7-(3-(dimethylamino)propylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(benzo[b]thiophen-3-yl)-3-(4-chloro-5-(1-ethyl-7-

(methylamino)-2-oxo-1,2,4a,8a-tetrahydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(4-chloro-3-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(4-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2-fluorophenyl)urea, 1-(5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(2-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(3-methoxypropylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(2,4-difluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-fluorophenyl)urea, 1-(2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-methylphenyl)-3-(3-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-2-oxo-7-(tetrahydro-2H-pyran-4-ylamino)-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, (S)-1-(4-chloro-5-(1-ethyl-7-(1-methoxypropan-2-ylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-(cyclopropylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(3-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(1-methylpiperidin-4-ylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-2-oxo-7-(THF-3-ylamino)-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-(methylsulfonyl)ethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(1-methylpyrrolidin-3-ylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(4-bromo-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-bromo-5-(1-ethyl-7-(2-(methylsulfonyl)ethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(5-(7-acetamido-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, 1-(5-(7-acetamido-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3,5-difluorophenyl)urea, 1-(4-bromo-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-

methylphenyl)-3-(3-fluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea, 1-(3,5-difluorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea, 1-(2,5-difluorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea, 1-(2,5-difluorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2,4a,8a-tetrahydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(3,5-difluorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2,4a,8a-tetrahydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, N-(3-(2-bromo-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-2-cyanoacetamide,N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-2-cyanoacetamide, 1-(5-(7-acetamido-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, N-(3-(2-chloro-5-(3-(3,5-difluorophenyl)ureido)-4-fluorophenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,5-difluorophenyl)urea, 1-(3-chloro-5-fluorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea, 3-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-chloro-5-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluoro-5-methylphenyl)urea, methyl (3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)carbamate, N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-2-methoxyacetamide, 2-cyano-N-(3-(2,4-difluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, 1-(4-cyano-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-fluorophenyl)urea, N-(1-ethyl-3-(4-fluoro-5-(3-(3-fluorophenyl)ureido)-2-methylphenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-3-hydroxyazetidine-1-carboxamide, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, (R)-N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-3-(dimethylamino)pyrrolidine-1-carboxamide, (S)-N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)pyrrolidine-2-carboxamide, N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-

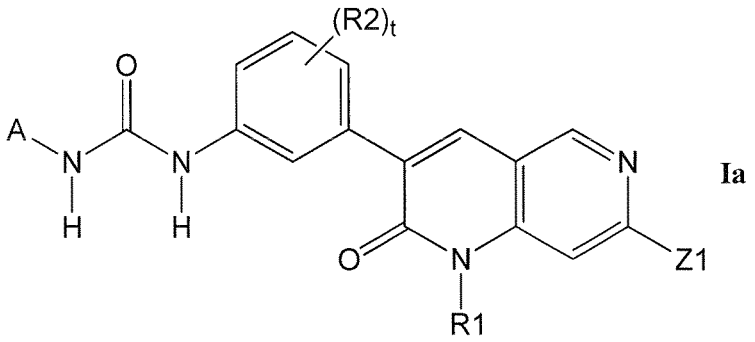
fluorophenyl)-3-(4-fluoro-3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluoro-5-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(4-fluoro-3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-(4-fluoro-3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-cyanophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-((3-morpholinopropyl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(4-fluoro-3-((4-methylpiperazin-1-yl)methyl)phenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-((dimethylamino)methyl)-4-fluorophenyl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(4-fluoro-3-(morpholinomethyl)phenyl)urea, (S)-N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-3-(dimethylamino)pyrrolidine-1-carboxamide, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(4-fluoro-3-(pyrrolidin-1-ylmethyl)phenyl)urea, 3-(3-(2-chloro-4-fluoro-5-(3-(3-fluorophenyl)ureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(2-chloro-4-fluoro-5-(3-(3-fluorophenyl)ureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, N-(1-ethyl-3-(4-fluoro-5-(3-(4-fluoro-3-((4-methylpiperazin-1-yl)methyl)phenyl)ureido)-2-methylphenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)formamide, 3-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-3-(dimethylamino)azetidine-1-carboxamide, 3-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 3-(3-(5-(3-(benzo[b]thiophen-3-yl)ureido)-4-fluoro-2-methylphenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 3-(3-(2-bromo-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 3-(1-ethyl-3-(4-fluoro-5-(3-(3-fluorophenyl)ureido)-2-methylphenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(2-chloro-4-fluoro-5-(3-(4-fluoro-3-(morpholinomethyl)phenyl)ureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)formamide, 3-(3-(5-(3-(3,5-difluorophenyl)ureido)-4-fluoro-2-methylphenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide, N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide, 1-(5-(1-ethyl-7-((6-methylpyridin-3-yl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 3-(3-(2,4-difluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 3-(dimethylamino)-N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-

naphthyridin-3-yl)-2-fluoro-4-iodophenyl)-3-phenylurea, and 1-(5-(1-ethyl-7-((1-methyl-1H-pyrazol-4-yl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea.

[0058] In some ~~embodiments~~examples, the present ~~invention~~disclosure comprises a compound selected from the group consisting of 1-(4-chloro-3-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2-fluoro-4-methyl-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2,4-difluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, 1-(3-chlorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(3-fluoro-phenyl)-urea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(2-fluoro-phenyl)-urea, 1-(4-chloro-3-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(4-chloro-5-(7-(2-(dimethylamino)ethylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(7-(3-(dimethylamino)propylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-

Claims

1. ~~A method of treating a disease caused by the kinase activity of c-KIT, oncogenic forms thereof, or polymorphs thereof, comprising the administration of~~Use of a compound of formula Ia



Ia

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease caused by the kinase activity of c-KIT, oncogenic forms thereof, or polymorphs thereof wherein:

A is selected from the group consisting of phenyl, naphthyl, and benzothienyl;

G1 is a heteroaryl taken from the group consisting of pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, pyridinyl, and pyrimidinyl;

G4 is a heterocyclyl taken from the group consisting of oxetanyl, azetadinyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, oxazolidinyl, imidazolonyl, pyranyl, tetrahydropyranyl, dioxalinyl, piperidinyl, and morpholinyl;

when A has one or more substitutable sp2-hybridized carbon atom, each respective sp2 hybridized carbon atom may be optionally substituted with a Z3 substituent;

Z1 is selected from the group consisting of -NH(R4), and -NHCOR8;

in the event that Z1 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z2 is independently and individually selected from the group consisting of hydrogen, C1-C6alkyl, C3-C8carbocyclyl, C1-C6 alkoxy, hydroxyl, hydroxyC1-C6alkyl-, cyano, $(R3)_2N$-, and $-(CH_2)_nR5$;

each R8 is independently and individually selected from the group consisting of hydrogen, C1-C6alkyl, branched C3-C7alkyl, fluoroalkyl wherein the alkyl moiety is partially or fully fluorinated, C3-C8carbocyclyl, Z3-substituted phenyl, Z3-substituted G1, Z3-substituted G1-C1-C6alkyl, Z2-substituted G4, Z2-substituted G4-C1-C6alkyl, C1-C6alkoxy, C1-C6alkoxyC1-C6alkyl, cyanoC1-C6alkyl, -$N(R4)_2$, and R5;

each R10 is independently and individually selected from the group consisting of CO_2H, CO_2C1-C6alkyl, CO-$N(R4)_2$, OH, C1-C6alkoxy, C1-C6alkyl, and -$N(R4)_2$;

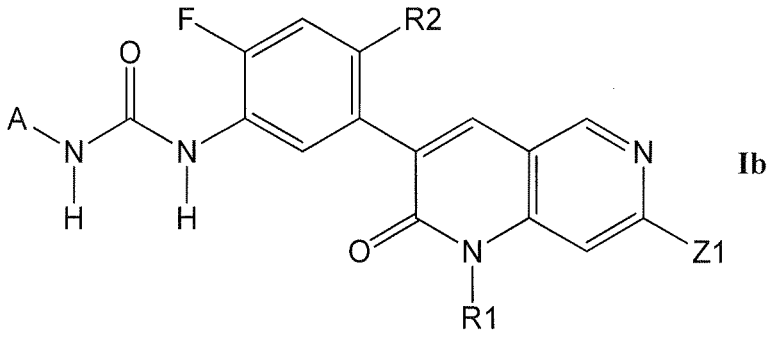
each R17 is taken from the group comprising phenyl, naphthyl, pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, oxetanyl, azetadinyl, tetrahydrofuranyl, oxazolinyl, oxazolidinyl, pyranyl, thiopyranyl, tetrahydropyranyl, dioxalinyl, pyrrolidinyl, and piperidinyl;

wherein R17 can be further substituted with one or more Z2 or Z3 moieties;

wherein two R3 or R4 moieties are independently and individually taken from the group consisting of C1-C6alkyl and branched C3-C6alkyl, hydroxyalkyl, and alkoxyalkyl and are attached to the same nitrogen atom, said moieties may cyclize to form a C3-C7 heterocyclyl ring;

and k is 1 or 2; n is 0-6; p is 1-4; q is 2-6; r is 0 or 1; t is 1-3.

2. The ~~method~~ use of claim 1 wherein the compound of Formula Ia is a compound of Formula Ib



Ib

or a pharmaceutically acceptable salt thereof,

wherein:

A is phenyl, R1 is linear or branched C1-C4alkyl, R2 is methyl or halogen, Z1 is -NH(R4) or -NHCOR8.

3. The ~~method~~ use of claim 1 wherein the the kinase activity of c-KIT, oncogenic forms thereof, or polymorphs thereof, wherein c-KIT contains a missense mutatation, insertion mutation, or a deletion mutation encoded by exons comprising Exon 9, Exon 11, Exon 13, Exon 14, Exon 17, or Exon 18, presenting either individually or in combination, comprising the administration of a compound of formula Ia or a pharmaceutically acceptable salt thereof.

4. The ~~method~~ use of claim 1 wherein the disease is selected from gastrointestinal stromal tumors, ovarian cancer, melanoma, cervical carcinomas, acute myeloid leukemia, germ cell tumors of the seminoma or dysgerminoma, teratomas, mastocytosis, or mast cell leukemia.

5. The ~~method~~ use of claim 1 wherein the compound is selected from the group consisting of 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(naphthalen-1-yl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,3-difluorophenyl)urea, 1-(2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, 1-(4-chloro-2-fluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(2,3-difluorophenyl)urea, 1-(4-chloro-3-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2-fluoro-4-methyl-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2,4-difluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-(3-

dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(2-chloro-4-fluoro-5-(3-(4-fluoro-3-(morpholinomethyl)phenyl)ureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)formamide, 3-(3-(5-(3-(3,5-difluorophenyl)ureido)-4-fluoro-2-methylphenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-1-isopropyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide, N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide, 1-(5-(1-ethyl-7-((6-methylpyridin-3-yl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 3-(3-(2,4-difluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, 3-(dimethylamino)-N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)azetidine-1-carboxamide,

1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-iodophenyl)-3-phenylurea, and 1-(5-(1-ethyl-7-((1-methyl-1H-pyrazol-4-yl)amino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea.

6. The ~~method~~ use of claim 5 wherein the compound is selected from the group consisting of

1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(naphthalen-1-yl)urea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,3-difluorophenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(3-fluoro-phenyl)-urea, 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea,

1-(benzo[b]thiophen-3-yl)-3-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2,4a,8a-tetrahydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-

1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea, 3-(3-(2-chloro-4-fluoro-5-(3-phenylureido)phenyl)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea, N-(1-ethyl-3-(4-fluoro-5-(3-(3-fluorophenyl)ureido)-2-methylphenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, N-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)acetamide, and 3-(1-ethyl-3-(4-fluoro-2-methyl-5-(3-phenylureido)phenyl)-2-oxo-1,2-dihydro-1,6-naphthyridin-7-yl)-1,1-dimethylurea.

7. The ~~method~~ use of claim 5 wherein the compound is 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-(naphthalen-1-yl)urea.

8. The ~~method~~ use of claim 5 wherein the compound is 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(2,3-difluorophenyl)urea.

9. The ~~method~~ use of claim 5 wherein the compound is 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea.

10. The ~~method~~ use of claim 5 wherein the compound is 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea.

11. The ~~method~~ use of claim 5 wherein the compound is 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)urea.

12. The ~~method~~ use of claim 5 wherein the compound is 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(3-fluoro-phenyl)-urea.

13. The ~~method~~ use of claim 5 wherein the compound is 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea.

14. The ~~method~~ use of claim 5 wherein the compound is 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea.

15. The ~~method~~ use of claim 5 wherein the compound is 1-(4-chloro-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea.

16. A compound selected from the group consisting of

1-(4-chloro-3-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-(3-cyanophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2-fluoro-4-methyl-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(2,4-difluoro-5-(1-methyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)-3-phenylurea, 1-(3-chlorophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(3-cyanophenyl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea, 1-(benzo[b]thiophen-3-yl)-3-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2,4-difluorophenyl)urea,

1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-chloro-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-2-fluoro-5-(1-isopropyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)phenyl)-3-phenylurea, 1-(5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluoro-4-methylphenyl)-3-phenylurea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(3-fluoro-phenyl)-urea, 1-[4-chloro-5- (1-ethyl-7-methylamino-2-oxo-1,2-dihydro-[1,6]naphthyridin-3-yl)-2-fluoro-phenyl]-3-(2-fluoro-phenyl)-urea, 1-(4-chloro-3-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(1-ethyl-7-(2-methoxyethylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-(3-fluorophenyl)urea, 1-(4-chloro-5-(7-(2-(dimethylamino)ethylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-chloro-5-(7-(3-(dimethylamino)propylamino)-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(4-bromo-5-(1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-2-fluorophenyl)-3-phenylurea, 1-(benzo[b]thiophen-3-yl)-3-(4-chloro-5-(1-ethyl-7-