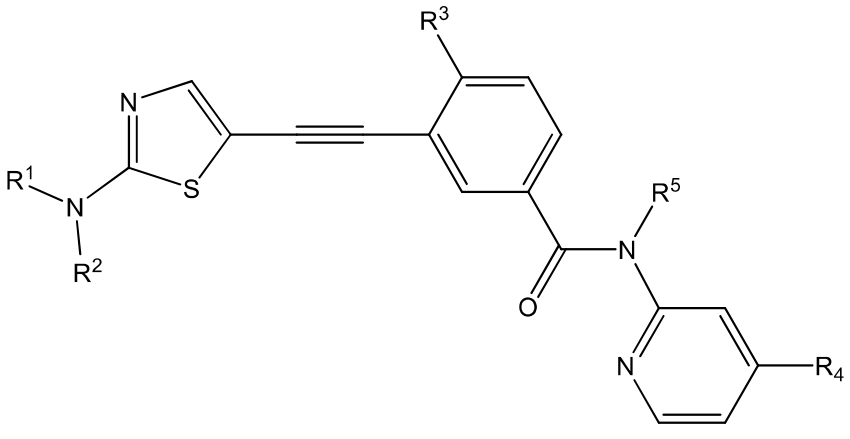
[0007a] In one aspect, the present disclosure refers to a compound of one of the following formulae (Ig) or (Ih):



(Ig), or

(Ih),

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is H;

R^2 is -C(O)R^8 or –C(O)NR^9R^{10};

each R^3 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, halogen, or OH;

each R^4 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, halogen, -OH, CN, -$(C(R^6)_2)_p$-heterocycloalkyl wherein the heterocycloalkyl comprises a 4- to 7-membered ring and 1 to 3 heteroatoms selected from N, O, and S , or -$(C(R^6)_2)_p$-heteroaryl wherein the heteroaryl comprises a 5- or 6-membered ring and 1 to 3 heteroatoms selected from N, O, and S, and wherein the heterocycloalkyl or heteroaryl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, -NH_2, (C_1-C_6) alkylamino, and (C_1-C_6) dialkylamino;

R^5 is H, (C_1-C_6) alkyl, or (C_1-C_6) haloalkyl;

each R^6 is independently H or (C_1-C_6) alkyl;

R^8 is (C_2-C_6) alkyl, (C_3-C_7) cycloalkyl, (C_2-C_6) alkenyl, (C_1-C_3) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, and S;

R^9 is H, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_3-C_7) cycloalkyl, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S;

R^{10} is H, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_3-C_7) cycloalkyl, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S, wherein the

cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, -NH_2, (C_1-C_6) alkylamino, (C_1-C_6) dialkylamino, and -OH, and wherein the (C_1-C_6) alkyl is optionally substituted with one or more R^{11};

or R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocycloalkyl ring comprising 1 to 3 heteroatom selected from N, O, and S, optionally substituted with one or more substituent each independently selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-NH_2, -$(CH_2)_q$-(C_1-C_6) alkylamino, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, -OH, and 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with one or more (C_1-C_6) alkyl;

R^{11} is (C_1-C_6) alkoxy, -OH, -NH_2, (C_1-C_6) alkylamino, (C_1-C_6) dialkylamino, 5- or 6-membered heteroaryl comprising 1 to 3 heteroatoms selected from N, O, or S, or 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S, wherein the heterocycloalkyl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl and OH; and

each p and q is independently 0, 1 or 2.

[0007b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

[0007c] In another aspect, the present disclosure refers to a compound that is selected from the group consisting of:

3-((2-(3,3-dimethylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)-3-((2-ureidothiazol-5-yl)ethynyl)benzamide;

methyl (5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)carbamate;

4-methyl-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-morpholinoethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-ethyl-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(dimethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(dimethylamino)ethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-(pyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-((1-methylpiperidin-4-yl)methyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxy-2-methylpropyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-cyclopropylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(3-hydroxypyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(2-(pyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-((1-methylpyrrolidin-2-yl)methyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxy-2-methylpropyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(4-hydroxycyclohexyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-hydroxy-3-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)azetidine-1-carboxamide;

4-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperidine-1-carboxamide;

4-methyl-3-((2-(3-(pyridin-4-ylmethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-(2-hydroxyethyl)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

4-methyl-3-((2-(3-methyl-3-(2-(methylamino)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-4-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-((2-(3-(4-aminobutyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-3-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(4-aminocyclohexyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

2-((dimethylamino)methyl)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)morpholine-4-carboxamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)morpholine-4-carboxamide;

3-((2-(3-(3-aminopropyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-acetyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-((2-(3-(2-aminoethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylazetidin-3-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-(dimethylamino)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)pyrrolidine-1-carboxamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)-4-(4-methylpiperazin-1-yl)piperidine-1-carboxamide;

2-fluoro-5-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

2-fluoro-N-(4-(trifluoromethyl)pyridin-2-yl)-5-((2-ureidothiazol-5-yl)ethynyl)benzamide;

3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-fluoro-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(pyrrolidin-1-ylmethyl)-3-(trifluoromethyl)phenyl)benzamide;

N-(2-methoxy-3-(trifluoromethyl)phenyl)-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylbenzamide;

N-(4-cyano-3-(trifluoromethyl)phenyl)-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylbenzamide;

3-((2-(cyclopropanecarboxamido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(cyclopropanecarboxamido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-((4-methylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)benzamide;

3-((2-acetamidothiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-pivalamidothiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

N-(4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-4-yl)ureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(4-methyl-3-((2-(3-methyl-3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3,3-dimethylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-3-(trifluoromethoxy)benzamide;

N-(4-methyl-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-(dimethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-(diethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-hydroxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide; and

N-(4-fluoro-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

or a pharmaceutically acceptable salt thereof.

[0008] A second example of the disclosure relates to a method of treating a c-Kit-mediated disease or disorder. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0008a] In yet another aspect, the present disclosure refers to use of the compound a, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for-treating a c-Kit-mediated disease or disorder,-wherein said cKit-mediated disease or disorder is selected from cell proliferative disorder, a fibrotic disorder, a metabolic disorder, multiple sclerosis, asthma, an allergic reaction, inflammatory arthritis, and mastocytosis.

[0009] Another example of the disclosure relates to a method of preventing a c-Kit-mediated disease or disorder. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0010] Another example of the disclosure relates to a method of inhibiting c-Kit. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0011] Another example of the disclosure relates to a method of treating a disease or disorder associated with inhibiting c-Kit. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0012] Another example of the disclosure relates to a method of preventing a disease or disorder associated with inhibiting c-Kit. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0013] Another example of the disclosure relates to a method of treating cancer. The method comprises administering to a patient in need thereof an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0014] Another example of the disclosure is directed to pharmaceutical compositions comprising a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof and a pharmaceutically acceptable carrier. The pharmaceutical acceptable carrier may further include an excipient, diluent, or surfactant.

[0015] Another example of the present disclosure relates to a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, for use in the manufacture of a medicament for treating a disease associated with inhibiting c-Kit.

[0016] Another example of the present disclosure relates to a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, for use in the manufacture of a medicament for preventing a disease associated with inhibiting c-Kit.

[0017] Another example of the present disclosure relates to the use of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, in the treatment of a disease associated with inhibiting c-Kit.

[0018] Another example of the present disclosure relates to the use of a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, in the prevention of a disease associated with inhibiting c-Kit.

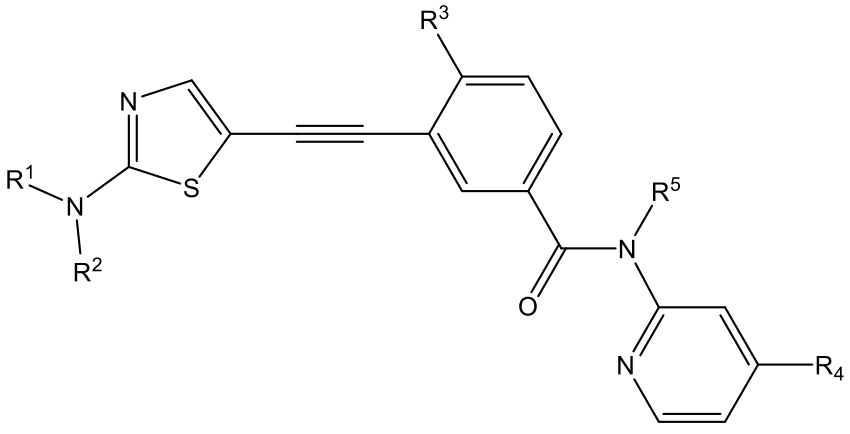
[0019] The present disclosure further provides methods of treating or preventing a disease or disorder associated with modulation of c-Kit including, cancer, metastasis, inflammation and auto-immune pathogenesis, comprising administering to a patient suffering from at least one of said diseases or disorder a compound of Formula (I), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

[0020] The present disclosure provides inhibitors of c-Kit that are therapeutic agents in the treatment of diseases such as cancer, metastasis, inflammation and auto-immune pathogenesis.

[0021] The present disclosure provides agents with novel mechanisms of action toward c-Kit enzymes in the treatment of various types of diseases including cancer and cell proliferative disorders, multiple sclerosis, asthma, mastocytosis, inflammatory disorders, allergic reactions, fibrotic disorders, auto-immune pathogenesis and metabolic disorders. Ultimately the present disclosure provides the medical community with a novel pharmacological strategy for the treatment of diseases and disorders associated with c-Kit.

CLAIMS

1. A compound of one of the following formulae (Ig) or (Ih):



(Ig), or

(Ih),

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is H;

R^2 is -C(O)R^8 or –C(O)NR^9R^{10};

each R^3 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, halogen, or OH;

each R^4 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, halogen, -OH, CN, -$(C(R^6)_2)_p$-heterocycloalkyl wherein the heterocycloalkyl comprises a 4- to 7-membered ring and 1 to 3 heteroatoms selected from N, O, and S , or -$(C(R^6)_2)_p$-heteroaryl wherein the heteroaryl comprises a 5- or 6-membered ring and 1 to 3 heteroatoms selected from N, O, and S, and wherein the heterocycloalkyl or heteroaryl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, -NH_2, (C_1-C_6) alkylamino, and (C_1-C_6) dialkylamino;

R^5 is H, (C_1-C_6) alkyl, or (C_1-C_6) haloalkyl;

each R^6 is independently H or (C_1-C_6) alkyl;

R^8 is (C_2-C_6) alkyl, (C_3-C_7) cycloalkyl, (C_2-C_6) alkenyl, (C_1-C_3) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, and S;

R^9 is H, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_3-C_7) cycloalkyl, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S;

R^{10} is H, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_3-C_7) cycloalkyl, or 4 to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, -NH_2, (C_1-C_6) alkylamino, (C_1-C_6) dialkylamino, and -OH, and wherein the (C_1-C_6) alkyl is optionally substituted with one or more R^{11};

or R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocycloalkyl ring comprising 1 to 3 heteroatom selected from N, O, and S, optionally substituted with one or more substituent each independently selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-NH_2, -$(CH_2)_q$-(C_1-C_6) alkylamino, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, -OH, and 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with one or more (C_1-C_6) alkyl;

R^{11} is (C_1-C_6) alkoxy, -OH, -NH_2, (C_1-C_6) alkylamino, (C_1-C_6) dialkylamino, 5- or 6-membered heteroaryl comprising 1 to 3 heteroatoms selected from N, O, or S, or 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms selected from N, O, or S, wherein the heterocycloalkyl is optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl and OH; and

each p and q is independently 0, 1 or 2.

2. The compound of claim 1, wherein R^5 is H.

3. The compound of claim 1, wherein R^4 is (C_1-C_6) haloalkyl.

4. The compound of claim 1, wherein R^4 is CF_3.

5. The compound of claim 1, wherein R^3 is methyl.

6. The compound of claim 1, wherein R^2 is –C(O)NR^9R^{10}.

7. The compound of claim 1, wherein

R^2 is –C(O)NR^9R^{10}; wherein

R^9 is (C_1-C_6) alkyl and R^{10} is (C_1-C_6) alkyl or (C_1-C_6) alkyl substituted with one R^{11}, optionally wherein R^{11} is –OH; or

R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycloalkyl ring comprising 1 to 3 heteroatom selected from N, O, and S, optionally substituted with one or more substituents each independently

selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, OH, or 6-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with (C_1-C_6) alkyl.

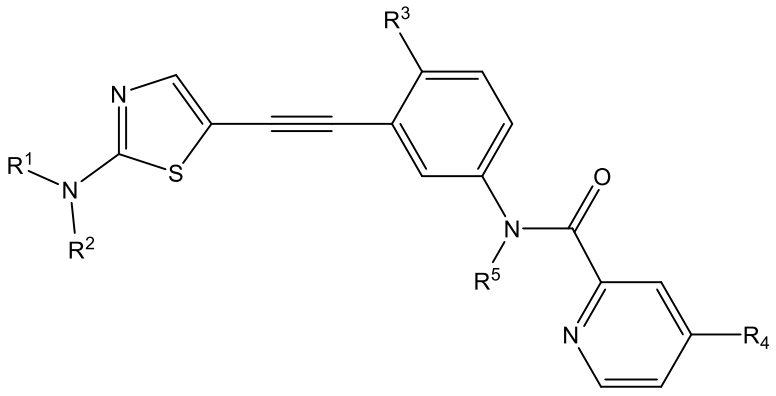
8. The compound of claim 7, wherein R^9 is (C_1-C_6) alkyl and R^{10} is (C_1-C_6) alkyl substituted with one R^{11}.

9. The compound of claim 8, wherein R^{11} is -OH.

10. The compound of claim 7, wherein R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycloalkyl ring comprising 1 to 3 heteroatom selected from N, O, and S, optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, OH, or 6-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with (C_1-C_6) alkyl.

11. The compound of claim 7, wherein R^9 and R^{10} together with the nitrogen atom to which they are attached form a heterocycloalkyl ring that is azetidinyl, morpholinyl, piperidinyl, or piperazinyl, and which is optionally substituted with one or more substituent each independently selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, -OH, and 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with one or more (C_1-C_6) alkyl.

12. The compound of claim 1, wherein the compound has a structure that is:



(Ih),

or a pharmaceutically acceptable salt thereof, wherein

R^2 is –C(O)NR^9R^{10}

R^3 is (C_1-C_6) alkyl or halogen;

R^4 is (C_1-C_6) haloalkyl;

R^5 is H;

R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4- to 6-membered heterocycloalkyl ring comprising 1 to 3 heteroatom selected from N, O, and S, optionally substituted with one or more substituents each independently selected from (C_1-C_6) alkyl, (C_1-C_6) hydroxyalkyl, -$(CH_2)_q$-(C_1-C_6) dialkylamino, -C(O)(C_1-C_6) alkyl, OH, or 6-membered heterocycloalkyl comprising 1 to 3 heteroatom selected from N, O, and S, and optionally substituted with (C_1-C_6) alkyl; and

q is 0, 1 or 2.

13. A compound that is selected from the group consisting of:

3-((2-(3,3-dimethylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)-3-((2-ureidothiazol-5-yl)ethynyl)benzamide;

methyl (5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)carbamate;

4-methyl-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-morpholinoethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-ethyl-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(dimethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(dimethylamino)ethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-(pyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-((1-methylpiperidin-4-yl)methyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxy-2-methylpropyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-cyclopropylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-(3-hydroxypyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(2-(pyrrolidin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-((1-methylpyrrolidin-2-yl)methyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-hydroxy-2-methylpropyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(4-hydroxycyclohexyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-hydroxy-3-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)azetidine-1-carboxamide;

4-methyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperidine-1-carboxamide;

4-methyl-3-((2-(3-(pyridin-4-ylmethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-(2-hydroxyethyl)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

4-methyl-3-((2-(3-methyl-3-(2-(methylamino)ethyl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-4-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-((2-(3-(4-aminobutyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-3-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(4-aminocyclohexyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

2-((dimethylamino)methyl)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)morpholine-4-carboxamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)morpholine-4-carboxamide;

3-((2-(3-(3-aminopropyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-acetyl-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)piperazine-1-carboxamide;

3-((2-(3-(2-aminoethyl)ureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-(3-methyl-3-(1-methylazetidin-3-yl)ureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-(dimethylamino)-N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)pyrrolidine-1-carboxamide;

N-(5-((2-methyl-5-((4-(trifluoromethyl)pyridin-2-yl)carbamoyl)phenyl)ethynyl)thiazol-2-yl)-4-(4-methylpiperazin-1-yl)piperidine-1-carboxamide;

2-fluoro-5-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

2-fluoro-N-(4-(trifluoromethyl)pyridin-2-yl)-5-((2-ureidothiazol-5-yl)ethynyl)benzamide;

3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-fluoro-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(pyrrolidin-1-ylmethyl)-3-(trifluoromethyl)phenyl)benzamide;

N-(2-methoxy-3-(trifluoromethyl)phenyl)-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylbenzamide;

N-(4-cyano-3-(trifluoromethyl)phenyl)-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylbenzamide;

3-((2-(cyclopropanecarboxamido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

3-((2-(cyclopropanecarboxamido)thiazol-5-yl)ethynyl)-4-methyl-N-(4-((4-methylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)benzamide;

3-((2-acetamidothiazol-5-yl)ethynyl)-4-methyl-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

4-methyl-3-((2-pivalamidothiazol-5-yl)ethynyl)-N-(4-(trifluoromethyl)pyridin-2-yl)benzamide;

N-(4-methyl-3-((2-(3-methyl-3-(1-methylpiperidin-4-yl)ureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(4-methyl-3-((2-(3-methyl-3-(2-(4-methylpiperazin-1-yl)ethyl)ureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3,3-dimethylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-3-(trifluoromethoxy)benzamide;

N-(4-methyl-3-((2-(3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-(dimethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-(diethylamino)ethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-hydroxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)-4-methylphenyl)-4-(trifluoromethyl)picolinamide;

N-(3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide; and

N-(4-fluoro-3-((2-(3-(2-methoxyethyl)-3-methylureido)thiazol-5-yl)ethynyl)phenyl)-4-(trifluoromethyl)picolinamide;

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

15. Use of the compound according to any one of claims 1-13, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for-treating a c-Kit-mediated disease or disorder,-wherein said cKit-mediated disease or disorder is selected from cell proliferative disorder, a fibrotic disorder, a metabolic disorder, multiple sclerosis, asthma, an allergic reaction, inflammatory arthritis, and mastocytosis.

16. The use of claim 15, wherein said cell proliferative disorder is cancer, optionally wherein

said cancer is selected from the group consisting of leukemia, mast cell tumor, small cell lung cancer, testicular cancer, cancer of the gastrointestinal tract, cancer of the central nervous system, cancer of the female genital tract, sarcoma of neuroectodermal origin, and Schwann cell neoplasia associated with neurofibromatosis; or

said cancer is selected from the group consisting of small cell lung carcinoma, acute myeloid leukemia (AML), neuroblastoma, malignant melanomas, colorectal cancer,systemic mastocytosis (SM), and gastrointestinal stromal tumors (GISTs).