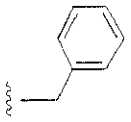

or


The present invention encompasses all compounds described by Formula 1, racemic or diastereoisomeric mixtures, pharmaceutically acceptable salts, prodrugs and active metabolites thereof.

Another aspect of the present invention provides a pharmaceutical composition comprising an effective amount of a compound of Formula 1 and a pharmaceutically acceptable carrier, diluent or excipient.

Also disclosed is~~In another aspect of the present invention, there is provided~~ a use of the compound of Formula 1 as an inhibitor of protein kinase, more particularly, as an inhibitor of cFMS, Flt3, KDR, FGFR1 and Tie2.

In another aspect of the present invention, there is provided the use of a compound as defined above or a pharmaceutical composition as defined above in the manufacture of a medicament for modulating the target kinase function.

In another aspect of the present invention, there is provided a compound as defined above for use as an inhibitor of a protein kinase.

Also disclosed is~~Another aspect of the present invention provides~~ a method of modulating kinase function, the method comprising contacting a cell with a compound of the present invention in an amount sufficient to modulate the enzymatic activity of a given kinase or kinases, such as cFMS, FLT3, KDR, FGFR1, Tie2 or others, thereby modulating the kinase function.

Also disclosed is~~Another aspect of the present invention provides~~ a method of modulating the target kinase function, the method comprising a) contacting a cell with a compound of the present invention in an amount sufficient to modulate the target kinase function, thereby b) modulating the target kinase activity and signaling.

In another aspect of the present invention, there is provided the compound as defined herein for use as an inhibitor of kinases or kinase families in the treatment of diseases or disorders such as: cancer, arthritis, myeloproliferative disorders, cardiac hypertrophy, lung fibrosis, hepatic fibrosis, atherosclerosis, restenosis, glomerulonephritis, psoriasis, lupus, multiple sclerosis, macular degeneration, asthma and reactive synoviotides.

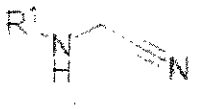
In another aspect of the present invention, there is provided the compound as defiine herein for use in the treatment of: arthritis, tenosynovial giant cell tumour, pigmented villonodular synovitis and other reactive synoviotides, bone metastases formation and progression, acute myeloid leukemia or human cancer by inhibition of cFMS; or acute myeloid leukemia or arthritis by inhibition of Flt3; or arthritis or cancer by VEGF or Tie2 inhibition; or select subsets of cancer, for example breast tumours and gastric cancer by inhibition of FGFR.

In another aspect of the present invention, there is provided the use of a compound as defined herein in a manufacture of a medicament for modulating target kinase function, wherein the medicament is to be contacted to a cell in an amount sufficient to modulate the target kinase function, whereby the target kinase activity and signaling is modulated.

Another aspect of the present invention provides a probe, the probe comprising a compound of Formula 1 labeled with a detectable label or an affinity tag. In other words, the probe comprises a residue of a compound of Formula 1 covalently conjugated to a detectable label. Such detectable labels include, but are not limited

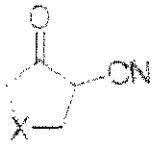
to, a fluorescent moiety, a chemiluminescent moiety, a paramagnetic contrast agent, a metal chelate, a radioactive isotope-containing moiety, or biotin.

In another aspect of the present invention, there is provided a process for preparing a compound as defined herein, wherein m is 0 and R^{2c-f} are H, a compound of formula i-e, comprising the steps of: (a) alkylation of R^1NH_2 with bromoacetonitrile to provide intermediate i-a



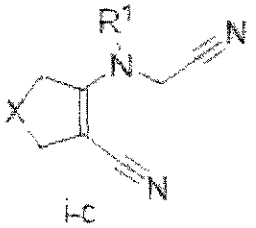
i-a

;



i-b

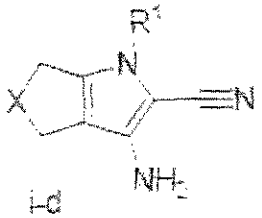
(b) condensation of i-a with in the presence of an acid to provide intermediate i-c



i-c

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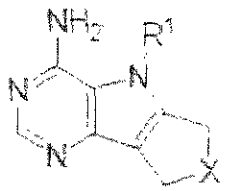
(c) treatment of intermediate i-c with a base to provide intermediate i-d



i-d

;

(d) treatment of intermediate i-d with formamidine acetate in an alcohol to provided a compound of formula i-e



i-e

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The present invention relates to novel kinase inhibitors. The inventors have found these compounds to be effective inhibitors of protein kinases, including members of the receptor tyrosine super family.

Compounds of the present invention may be formulated into a pharmaceutical composition which comprises an effective amount of a compound of Formula 1 with a pharmaceutically acceptable diluent or carrier. For example, the pharmaceutical compositions may be in a conventional pharmaceutical form suitable for oral administration (e.g., tablets, capsules, granules, powders and syrups), parenteral administration (e.g., injections (intravenous, intramuscular, or subcutaneous)), drop infusion preparations, inhalation, eye lotion, topical administration (e.g., ointment), or suppositories. Regardless of the route of administration selected the compounds may be formulated into pharmaceutically acceptable dosage forms by conventional methods known to those skilled in the art.

The phrase "pharmaceutically acceptable" is employed herein to refer to those ligands, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically acceptable carrier" as used herein means a pharmaceutically acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically acceptable carriers include: (1) sugars, such as lactose, glucose, and sucrose; (2) starches, such as corn starch, potato starch, and substituted or unsubstituted β-cyclodextrin; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose, and cellulose acetate; (4)