



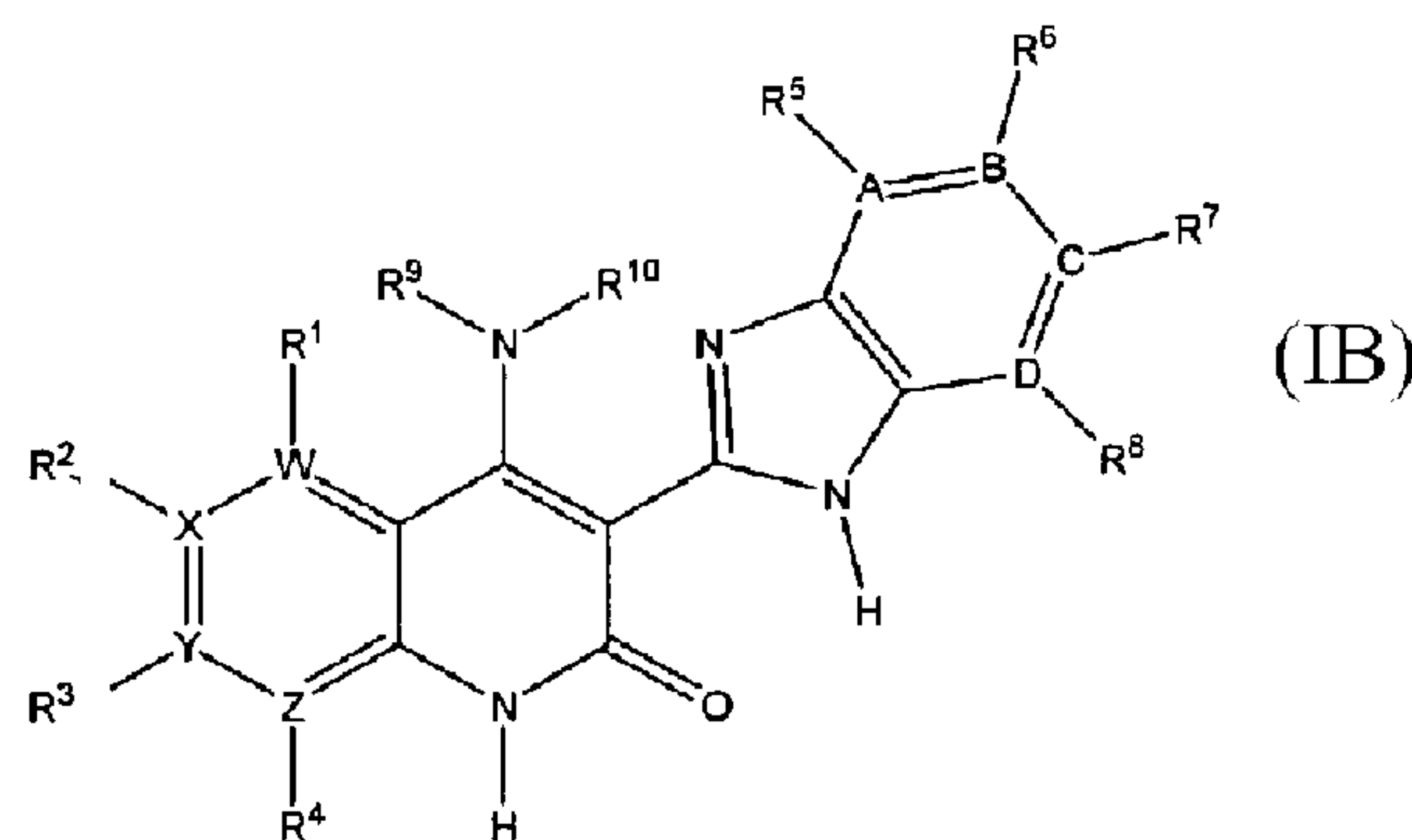
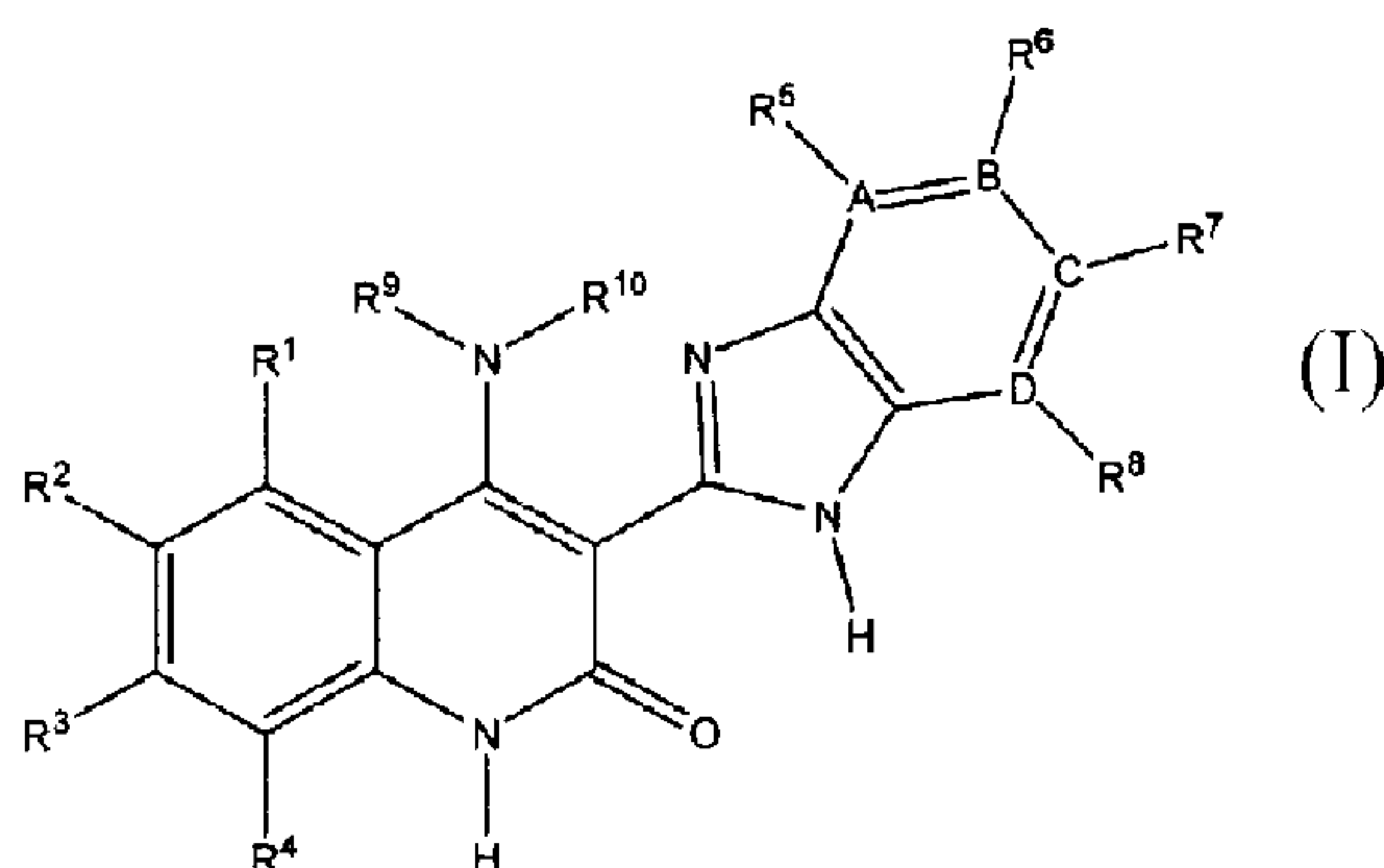
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(54) Titre : QUINOLINONES DE BENZIMIDAZOLE ET LEURS UTILISATIONS

(54) Title: BENZIMIDAZOLE QUINOLINONES AND USES THEREOF



(57) Abrégé/Abstract:

Methods of inhibiting various enzymes and treating various conditions are provided that include administering to a subject a compound of Structure I or IB, a pharmaceutically acceptable salt thereof, a tautomer thereof, or a pharmaceutically acceptable salt of the tautomer. Compounds having the Structure I and IB have the following structures and have the variables described herein. Such compounds may be used to prepare medicaments for use in inhibiting various enzymes and for use in treating conditions mediated by such enzymes.

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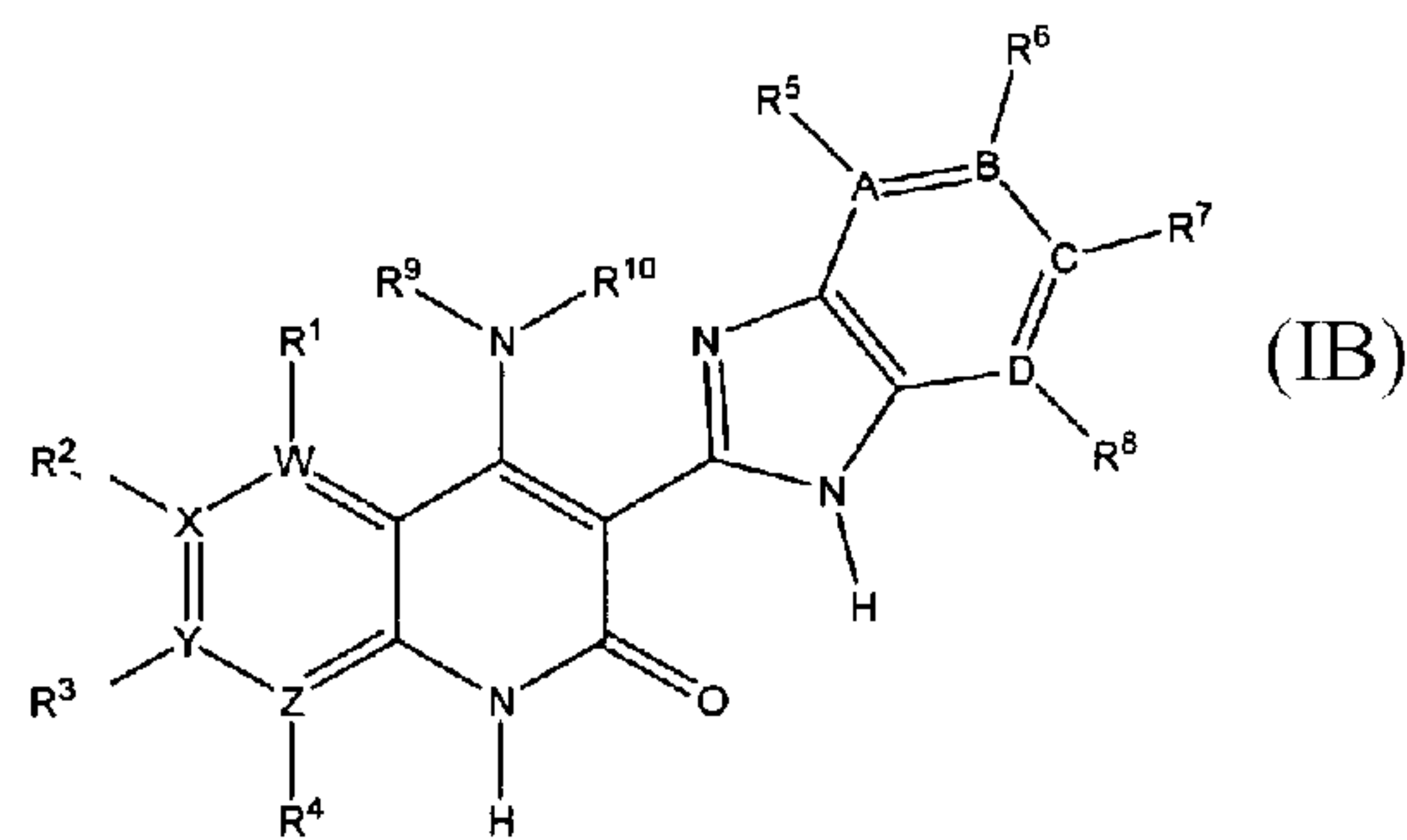
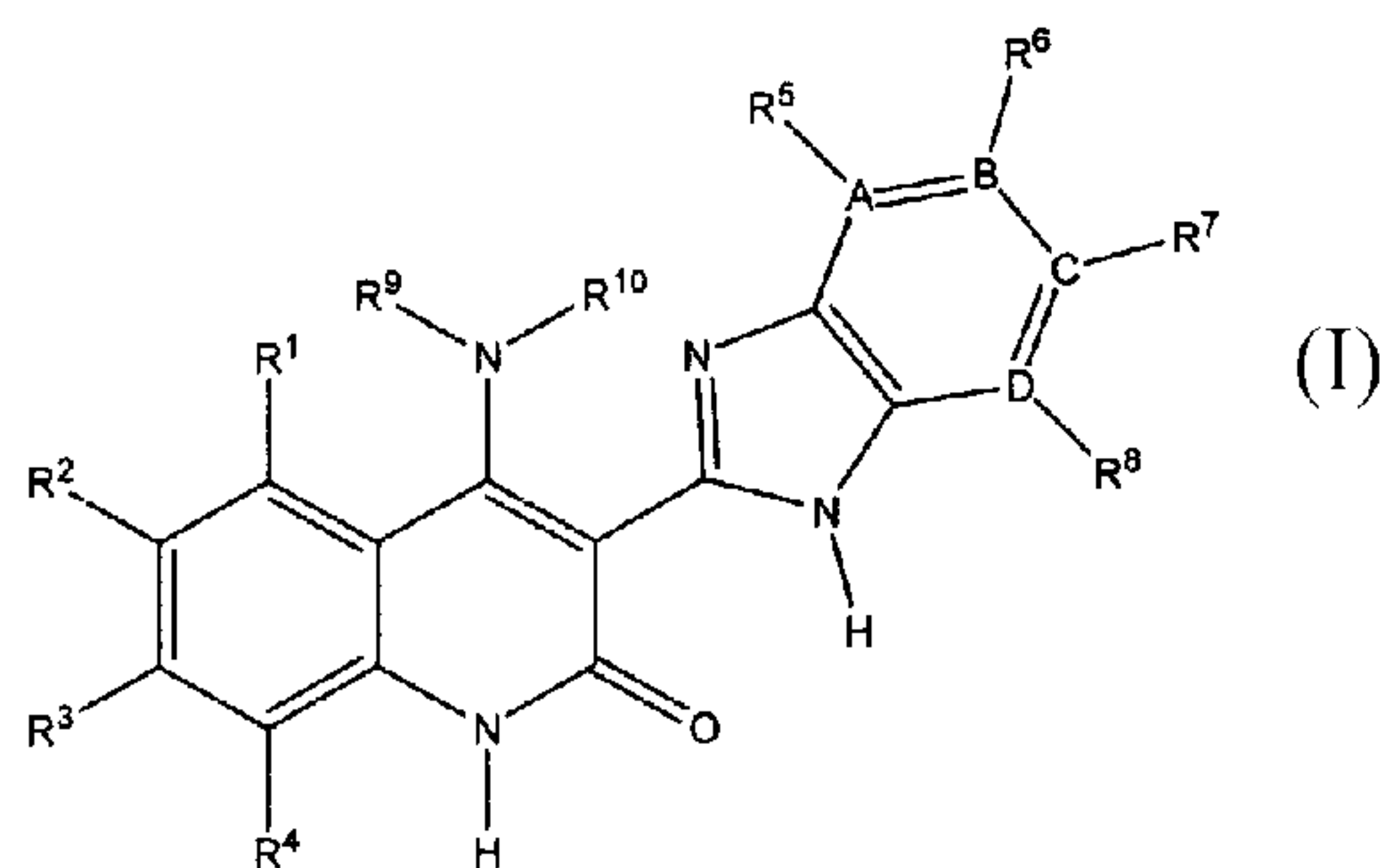
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BENZIMIDAZOLE QUINOLINONES AND USES THEREOF

FIELD OF THE INVENTION

[0001] This invention pertains generally to methods and compositions for treating a variety of patients and cell subjects. More particularly, the present invention provides novel compositions of matter and methods for angiogenesis inhibition, treating cancer, treating diabetes, stimulating insulin-dependent processes, treating Alzheimer's disease, treating bipolar disorder, treating central nervous system disorders, prolonging immune responses, reducing the splitting of centrosomes, blocking DNA repair, modulating cell cycle arrest, and inhibiting enzymes such as serine/threonine kinases and tyrosine kinases. The present invention thus has application in the areas of oncology, diabetes, immunology, and medicinal chemistry.

BACKGROUND OF THE INVENTION

[0002] Capillaries reach into almost all tissues of the human body and supply tissues with oxygen and nutrients as well as removing waste products. Under typical conditions, the endothelial cells lining the capillaries do not divide, and capillaries, therefore, do not normally increase in number or size in a human adult. Under certain normal conditions, however, such as when a tissue is damaged, or during certain parts of the menstrual cycle, the capillaries begin to proliferate rapidly. This process of forming new capillaries from pre-existing blood vessels is known as angiogenesis or neovascularization. See Folkman, J. Scientific American 275, 150-154 (1996). Angiogenesis during wound healing is an example of pathophysiological neovascularization during adult life. During wound healing, the additional capillaries provide a supply of oxygen and nutrients, promote granulation tissue, and aid in waste removal. After termination of the

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healing process, the capillaries normally regress. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999).

[0003] Angiogenesis also plays an important role in the growth of cancer cells. It is known that once a nest of cancer cells reaches a certain size, roughly 1 to 2 mm in diameter, the cancer cells must develop a blood supply in order for the tumor to grow larger as diffusion will not be sufficient to supply the cancer cells with enough oxygen and nutrients. Thus, inhibition of angiogenesis is expected to halt the growth of cancer cells.

[0004] Receptor tyrosine kinases (RTKs) are transmembrane polypeptides that regulate developmental cell growth and differentiation, remodeling and regeneration of adult tissues. Mustonen, T. et al., J. Cell Biology 129, 895-898 (1995); van der Geer, P. et al. Ann Rev. Cell Biol. 10, 251-337 (1994). Polypeptide ligands known as growth factors or cytokines, are known to activate RTKs. Signaling RTKs involves ligand binding and a shift in conformation in the external domain of the receptor resulting in its dimerization. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999); Ullrich, A. et al., Cell 61, 203-212 (1990). Binding of the ligand to the RTK results in receptor trans-phosphorylation at specific tyrosine residues and subsequent activation of the catalytic domains for the phosphorylation of cytoplasmic substrates. Id.

[0005] Two subfamilies of RTKs are specific to the vascular endothelium. These include the vascular endothelial growth factor (VEGF) subfamily and the Tie receptor subfamily. Class V RTKs include VEGFR1 (FLT-1), VEGFR2 (KDR (human), Flk-1 (mouse)), and VEGFR3 (FLT-4). Shibuya, M. et al., Oncogene 5, 519-525 (1990); Terman, B. et al., Oncogene 6, 1677-1683 (1991); Aprelikova, O. et al., Cancer Res. 52, 746-748 (1992).

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[0006] Members of the VEGF subfamily have been described as being able to induce vascular permeability and endothelial cell proliferation and further identified as a major inducer of angiogenesis and vasculogenesis. Ferrara, N. et al., *Endocrinol. Rev.* 18, 4-25 (1997). VEGF is known to specifically bind to RTKs including FLT-1 and Flk-1. DeVries, C. et al., *Science* 255, 989-991 (1992); Quinn, T. et al., *Proc. Natl. Acad. Sci.* 90, 7533-7537 (1993). VEGF stimulates the migration and proliferation of endothelial cells and induces angiogenesis both *in vitro* and *in vivo*. Connolly, D. et al., *J. Biol. Chem.* 264, 20017-20024 (1989); Connolly, D. et al., *J. Clin. Invest.* 84, 1470-1478 (1989); Ferrara, N. et al., *Endocrino. Rew.* 18, 4-25 (1997); Leung, D. et al., *Science* 246, 1306-1309 (1989); Plouet, J. et al., *EMBO J* 8, 3801-3806 (1989).

[0007] Because angiogenesis is known to be critical to the growth of cancer and to be controlled by VEGF and VEGF-RTK, substantial efforts have been undertaken to develop compounds which inhibit or retard angiogenesis and inhibit VEGF-RTK.

[0008] Platelet derived growth factor receptor kinase (PDGFR) is another type of RTK. PDGF expression has been shown in a number of different solid tumors, from glioblastomas to prostate carcinomas. In these various tumor types, the biological role of PDGF signaling can vary from autocrine stimulation of cancer cell growth to more subtle paracrine interactions involving adjacent stroma and angiogenesis. Therefore, inhibiting the PDGFR kinase activity with small molecules may interfere with tumor growth and angiogenesis.

[0009] Tie-2 is a membrane RTK. Upon binding to its ligand, Tie-2 is activated and phosphorylates its downstream signal proteins. Tie-2 kinase activity may then trigger a pathway of cellular response that leads to stabilization of vascular vessels in cancer. Therefore, blocking kinase activity of Tie-2, in synergy with blockage of activity of other angiogenic kinases such

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as VEGF and FGFR1 receptor kinases, may be effective in cutting off the blood supply to cancer cells and in treating the disease.

[0010] FLT-3 is a receptor tyrosine kinase belonging to the PDGF Receptor family expressed on acute myelogenous leukemia (AML) cells in a majority of patients and can be present in wildtype form or have activating mutations that result in constitutively active kinase function. An internal tandem repeat (ITD) mutation is expressed in about 25% of AML patients and has been associated with poor prognosis in AML patients. Levis, M et al Blood 99, 11; 2002.

[0011] c-Kit is another receptor tyrosine kinase belonging to PDGF Receptor family and is normally expressed in hematopoietic progenitor, mast and germ cells. C-kit expression has been implicated in a number of cancers including mast cell leukemia, germ cell tumors, small-cell lung carcinoma, gastrointestinal stromal tumors, acute myelogenous leukemia (AML), neuroblastoma, melanoma, ovarian carcinoma, breast carcinoma. Heinrich, M. C. et al; J. Clin. Onc. 20, 6 1692-1703, 2002 (review article); Smolich, B. D. et al Blood, 97, 5; 1413-1421.

[0012] c-ABL is a tyrosine kinase that was originally identified as an oncogene product from the genome of the Abelson murine leukemia virus. About 90% of chronic myelogenous leukemia (CML), 20-30% of acute lymphoblastic leukemia (ALL) and about 1% of acute myeloblastic leukemia (AML) have a reciprocal translocation between chromosome 9 and 22. The translocation results in the 'Philadelphia' chromosome and is the reason for the expression of a chimeric BCR/ABL transcript.

[0013] FGFR3 is a tyrosine kinase associated with various cancers. Fibroblast growth factor receptor 3 (FGFR3) is a class IV receptor tyrosine kinase. FGFR3 is deregulated due to a t(4,14) translocation in about 15% of multiple myeloma patients. This translocation causes the expression of a functional FGFR3 that can respond to FGF1 in e.g. the bone

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microenvironment. In some cases, activating mutations that make FGFR3 ligand independent have been identified. These activating FGFR3 mutations have been found to cause Ras-like tumor progression and evidence exists that similar signaling pathways are utilized (Chesi et al Blood 2001 97 729-736.).

[0014] Glycogen synthase kinase 3 (GSK-3) is a serine/threonine kinase for which two isoforms, α and β , have been identified. Woodgett, *Trends Biochem. Sci.*, 16:177-81 (1991). Both GSK-3 isoforms are constitutively active in resting cells. GSK-3 was originally identified as a kinase that inhibits glycogen synthase by direct phosphorylation. Upon insulin activation, GSK-3 is inactivated, thereby allowing the activation of glycogen synthase and possibly other insulin-dependent events, such glucose transport. Subsequently, it has been shown that GSK-3 activity is also inactivated by other growth factors that, like insulin, signal through receptor tyrosine kinases (RTKs). Examples of such signaling molecules include IGF-1 and EGF. Saito et al., *Biochem. J.*, 303:27-31 (1994); Welsh et al., *Biochem. J.* 294:625-29 (1993); and Cross et al., *Biochem. J.*, 303:21-26 (1994).

[0015] Agents that inhibit GSK-3 activity are useful in the treatment of disorders that are mediated by GSK-3 activity. In addition, inhibition of GSK-3 mimics the activation of growth factor signaling pathways and consequently GSK-3 inhibitors are useful in the treatment of diseases in which such pathways are insufficiently active. Examples of diseases that can be treated with GSK-3 inhibitors are described below.

[0016] Diabetes mellitus is a serious metabolic disease that is defined by the presence of chronically elevated levels of blood glucose (hyperglycemia). This state of hyperglycemia is the result of a relative or absolute lack of activity of the peptide hormone, insulin. Insulin is produced and secreted by the β cells of the pancreas. Insulin is reported to promote glucose utilization, protein synthesis, and the formation and storage of

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carbohydrate energy as glycogen.¹ Glucose is stored in the body as glycogen, a form of polymerized glucose, which may be converted back into glucose to meet metabolism requirements. Under normal conditions, insulin is secreted at both a basal rate and at enhanced rates following glucose stimulation, all to maintain metabolic homeostasis by the conversion of glucose into glycogen.

[0017] The term diabetes mellitus encompasses several different hyperglycemic states. These states include Type 1 (insulin-dependent diabetes mellitus or IDDM) and Type 2 (non-insulin dependent diabetes mellitus or NIDDM) diabetes. The hyperglycemia present in individuals with Type 1 diabetes is associated with deficient, reduced, or nonexistent levels of insulin that are insufficient to maintain blood glucose levels within the physiological range. Conventionally, Type 1 diabetes is treated by administration of replacement doses of insulin, generally by a parental route. Since GSK-3 inhibition stimulates insulin-dependent processes, it is useful in the treatment of type 1 diabetes.

[0018] Type 2 diabetes is an increasingly prevalent disease of aging. It is initially characterized by decreased sensitivity to insulin and a compensatory elevation in circulating insulin concentrations, the latter of which is required to maintain normal blood glucose levels. Increased insulin levels are caused by increased secretion from the pancreatic beta cells, and the resulting hyperinsulinemia is associated with cardiovascular complications of diabetes. As insulin resistance worsens, the demand on the pancreatic beta cells steadily increases until the pancreas can no longer provide adequate levels of insulin, resulting in elevated levels of glucose in the blood. Ultimately, overt hyperglycemia and hyperlipidemia occur, leading to the devastating long-term complications associated with diabetes, including cardiovascular disease, renal failure and blindness. The exact mechanism(s) causing type 2 diabetes are unknown, but result in impaired glucose transport into skeletal muscle and increased hepatic glucose production, in addition to inadequate insulin response. Dietary modifications are often ineffective, therefore the majority of patients ultimately require pharmaceutical

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intervention in an effort to prevent and/or slow the progression of the complications of the disease. Many patients can be treated with one or more of the many oral anti-diabetic agents available, including sulfonylureas, to increase insulin secretion. Examples of sulfonylurea drugs include metformin for suppression of hepatic glucose production, and troglitazone, an insulin-sensitizing medication. Despite the utility of these agents, 30-40% of diabetics are not adequately controlled using these medications and require subcutaneous insulin injections. Additionally, each of these therapies has associated side effects. For example, sulfonylureas can cause hypoglycemia and troglitazone can cause severe hepatotoxicity. Presently, there is a need for new and improved drugs for the treatment of prediabetic and diabetic patients.

[0019] As described above, GSK-3 inhibition stimulates insulin-dependent processes and is consequently useful in the treatment of type 2 diabetes. Recent data obtained using lithium salts provides evidence for this notion. The lithium ion has recently been reported to inhibit GSK-3 activity. Klein et al., *PNAS* 93:8455-9 (1996). Since 1924, lithium has been reported to have antidiabetic effects including the ability to reduce plasma glucose levels, increase glycogen uptake, potentiate insulin, up-regulate glucose synthase activity and to stimulate glycogen synthesis in skin, muscle and fat cells. However, lithium has not been widely accepted for use in the inhibition of GSK-3 activity, possibly because of its documented effects on molecular targets other than GSK-3. The purine analog 5-iodotubercidin, also a GSK-3 inhibitor, likewise stimulates glycogen synthesis and antagonizes inactivation of glycogen synthase by glucagon and vasopressin in rat liver cells. Fluckiger-Isler et al., *Biochem J.* 292:85-91 (1993); and Massillon et al., *Biochem J.* 299:123-8 (1994). However, this compound has also been shown to inhibit other serine/threonine and tyrosine kinases. Massillon et al., *Biochem J.* 299:123-8 (1994).

[0020] One of the main goals in the management of patients with diabetes mellitus is to achieve blood glucose levels that are as close to normal as possible. In general, obtaining normal postprandial blood glucose

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levels is more difficult than normalizing fasting hyperglycemia. In addition, some epidemiological studies suggest that postprandial hyperglycemia (PPHG) or hyperinsulinemia are independent risk factors for the development of macrovascular complications of diabetes mellitus. Recently, several drugs with differing pharmacodynamic profiles have been developed which target PPHG. These include insulin lispro, amylin analogues, alpha-glucosidase inhibitors and meglitinide analogues. Insulin lispro has a more rapid onset of action and shorter duration of efficacy compared with regular human insulin. In clinical trials, the use of insulin lispro has been associated with improved control of PPHG and a reduced incidence of hypoglycemic episodes. Repaglinide, a meglitinide analogue, is a short-acting insulinotropic agent which, when given before meals, stimulates endogenous insulin secretions and lowers postprandial hyperglycaemic excursions. Both insulin lispro and repaglinide are associated with postprandial hyperinsulinaemia. In contrast, amylin analogues reduce PPHG by slowing gastric emptying and delivery of nutrients to the absorbing surface of the gut. Alpha-glucosidase inhibitors such as acarbose, miglitol and voglibose also reduce PPHG primarily by interfering with the carbohydrate-digesting enzymes and delaying glucose absorption. Yamasaki et al., *Tohoku J Exp Med* 1997;183(3):173-83. The GSK inhibitors of the present invention are also useful, alone or in combination with the agents set forth above, in the treatment of postprandial hyperglycemia as well as in the treatment of fasting hyperglycemia.

[0021] GSK-3 is also involved in biological pathways relating to Alzheimer's disease (AD). The characteristic pathological features of AD are extracellular plaques of an abnormally processed form of the amyloid precursor protein (APP), so called β -amyloid peptide (β -AP) and the development of intracellular neurofibrillary tangles containing paired helical filaments (PHF) that consist largely of hyperphosphorylated tau protein. GSK-3 is one of a number of kinases that have been found to phosphorylate tau protein *in vitro* on the abnormal sites characteristic of PHF tau, and is the only kinase also demonstrated to do this in living cells and in animals. Lovestone

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et al., *Current Biology* 4:1077-86 (1994); and Brownlee et al., *Neuroreport* 8:3251-3255 (1997). Furthermore, the GSK-3 kinase inhibitor, LiCl, blocks tau hyperphosphorylation in cells. Stambolic et al., *Current Biology* 6:1664-8 (1996). Thus GSK-3 activity may contribute to the generation of neurofibrillary tangles and consequently to disease progression. Recently it has been shown that GSK-3 β associates with another key protein in AD pathogenesis, presenilin 1 (PS1). Takashima et al., *PNAS* 95:9637-9641 (1998). Mutations in the PS1 gene lead to increased production of β -AP, but the authors also demonstrate that the mutant PS1 proteins bind more tightly to GSK-3 β and potentiate the phosphorylation of tau, which is bound to the same region of PS1.

[0022] It has also been shown that another GSK-3 substrate, β -catenin, binds to PS1. Zhong et al., *Nature* 395:698-702 (1998). Cytosolic β -catenin is targeted for degradation upon phosphorylation by GSK-3 and reduced β -catenin activity is associated with increased sensitivity of neuronal cells to β -AP induced neuronal apoptosis. Consequently, increased association of GSK-3 β with mutant PS1 may account for the reduced levels of β -catenin that have been observed in the brains of PS1-mutant AD patients and to the disease related increase in neuronal cell-death. Consistent with these observations, it has been shown that injection of GSK-3 antisense but not sense, blocks the pathological effects of β -AP on neurons *in vitro*, resulting in a 24 hour delay in the onset of cell death and increased cell survival at 1 hour from 12 to 35%. Takashima et al., *PNAS* 90:7789-93. (1993). In these latter studies, the effects on cell-death are preceded (within 3-6 hours of β -AP administration) by a doubling of intracellular GSK-3 activity, suggesting that in addition to genetic mechanisms that increase the proximity of GSK-3 to its substrates, β -AP may actually increase GSK-3 activity. Further evidence for a role for GSK-3 in AD is provided by the observation that the protein expression level (but, in this case, not specific activity) of GSK-3 is increased by 50% in postsynaptosomal supernatants of AD vs. normal brain tissue. Pei

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et al., *J. Neuropathol Exp.*, 56:70-78 (1997). Thus, specific inhibitors of GSK-3 should slow the progression of Alzheimer's Disease.

[0023] In addition to the effects of lithium described above, there is a long history of the use of lithium to treat bipolar disorder (manic depressive syndrome). This clinical response to lithium may reflect an involvement of GSK-3 activity in the etiology of bipolar disorder, in which case GSK-3 inhibitors could be relevant to that indication. In support of this notion it was recently shown that valproate, another drug commonly used in the treatment of bipolar disorder, is also a GSK-3 inhibitor. Chen et al., *J. Neurochemistry*, 72:1327-1330 (1999). One mechanism by which lithium and other GSK-3 inhibitors may act to treat bipolar disorder is to increase the survival of neurons subjected to aberrantly high levels of excitation induced by the neurotransmitter, glutamate. Nonaka et al., *PNAS* 95: 2642-2647 (1998). Glutamate-induced neuronal excitotoxicity is also believed to be a major cause of neurodegeneration associated with acute damage, such as in cerebral ischemia, traumatic brain injury and bacterial infection. Furthermore it is believed that excessive glutamate signaling is a factor in the chronic neuronal damage seen in diseases such as Alzheimer's, Huntington's, Parkinson's, AIDS associated dementia, amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS). Thomas, *J. Am. Geriatr. Soc.* 43: 1279-89 (1995). Consequently, GSK-3 inhibitors should provide a useful treatment in these and other neurodegenerative disorders.

[0024] GSK-3 phosphorylates transcription factor NF-AT and promotes its export from the nucleus, in opposition to the effect of calcineurin. Beals et al., *Science* 275:1930-33 (1997). Thus, GSK-3 blocks early immune response gene activation via NF-AT, and GSK-3 inhibitors may tend to permit or prolong activation of immune responses. Thus, GSK-3 inhibitors are believed to prolong and potentiate the immunostimulatory effects of certain cytokines, and such an effect may enhance the potential of those cytokines for tumor immunotherapy or indeed for immunotherapy in general.

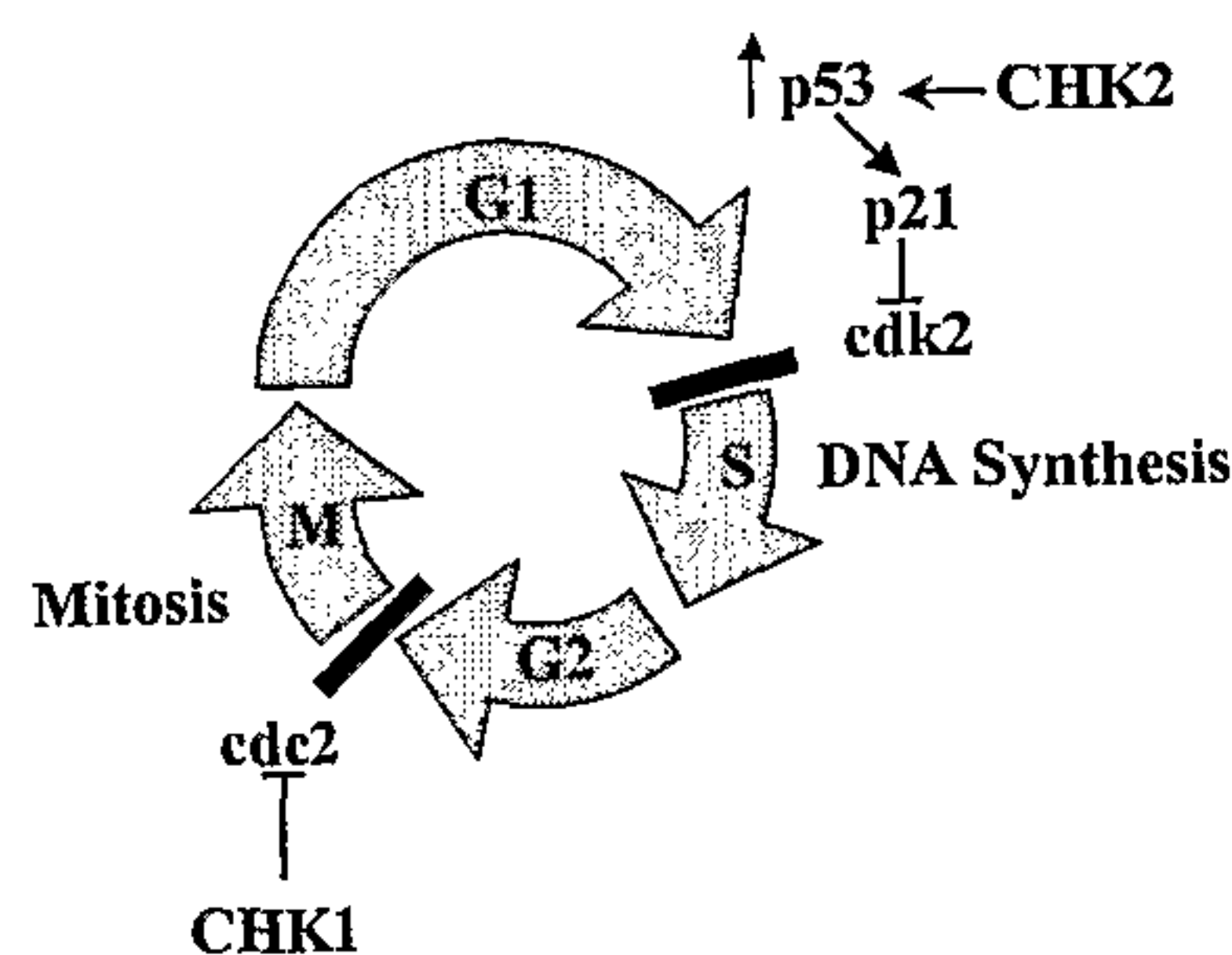
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[0025] Lithium has other biological effects. It is a potent stimulator of hematopoiesis, both *in vitro* and *in vivo*. Hammond et al., *Blood* 55: 26-28 (1980). In dogs, lithium carbonate eliminated recurrent neutropenia and normalized other blood cell counts. Doukas et al. *Exp. Hematol.* 14: 215-221 (1986). If these effects of lithium are mediated through the inhibition of GSK-3, GSK-3 inhibitors may have even broader applications. Since inhibitors of GSK-3 are useful in the treatment of many diseases, the identification of new inhibitors of GSK-3 would be highly desirable.

[0026] NEK-2 is a mammalian serine threonine kinase, which is structurally related to the NimA kinase from the fungus *Aspergillus nidulans*. Mutations in NimA result in G2 phase arrest of cells and overexpression of wt NimA results in premature chromatin condensation, even when ectopically expressed in mammalian cells. Both protein and kinase levels peak in S/G2 phase of the cell cycle. NimA also appears to be required for the localization of cdk1/cyclinB complex to the nucleus and spindle pole body. Histone H3 has been shown to be an *in vitro* substrate for the kinase, and if this is also the case *in vivo*, it may explain the role of the kinase in chromosome condensation. Six NimA kinases have been identified to date in mammals, and of these, NEK-2 appears to be the most closely related to NimA. It's activity is also cell cycle regulated, peaking in S/G2 phase. Overexpression of NEK-2, however, does not affect chromatin condensation but instead results in a pronounced splitting of centrosomes, possibly due to the loss of centriole/centriole adhesion. There is evidence that NEK-2 is regulated by phosphorylation and can interact with protein phosphatase PP1. NEK-2 is ubiquitously expressed and appears to be most abundant in testis. Hyseq cluster 374113, containing only NEK-2 sequences shows dramatic overexpression of NEK-2 in lymph node metastasis (13.3x) and in primary tumor (6.5x). Inhibition of NEK-2 by antisense oligonucleotides inhibited cell proliferation and reduced the capability of cells to grow in soft agar. In addition, increased cell death was observed in these cells both in the presence and absence of cisplatin.

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[0027] Ultraviolet light, ionizing radiation, environmental agents and cytotoxic drugs can result in damage to cellular DNA integrity. When such damage occurs during DNA replication or cell division it is potentially catastrophic and may result in cell death. The cellular response is to arrest the cell cycle at one of two checkpoints (G1/S or G2/M) to either permit DNA repair or initiate apoptosis.

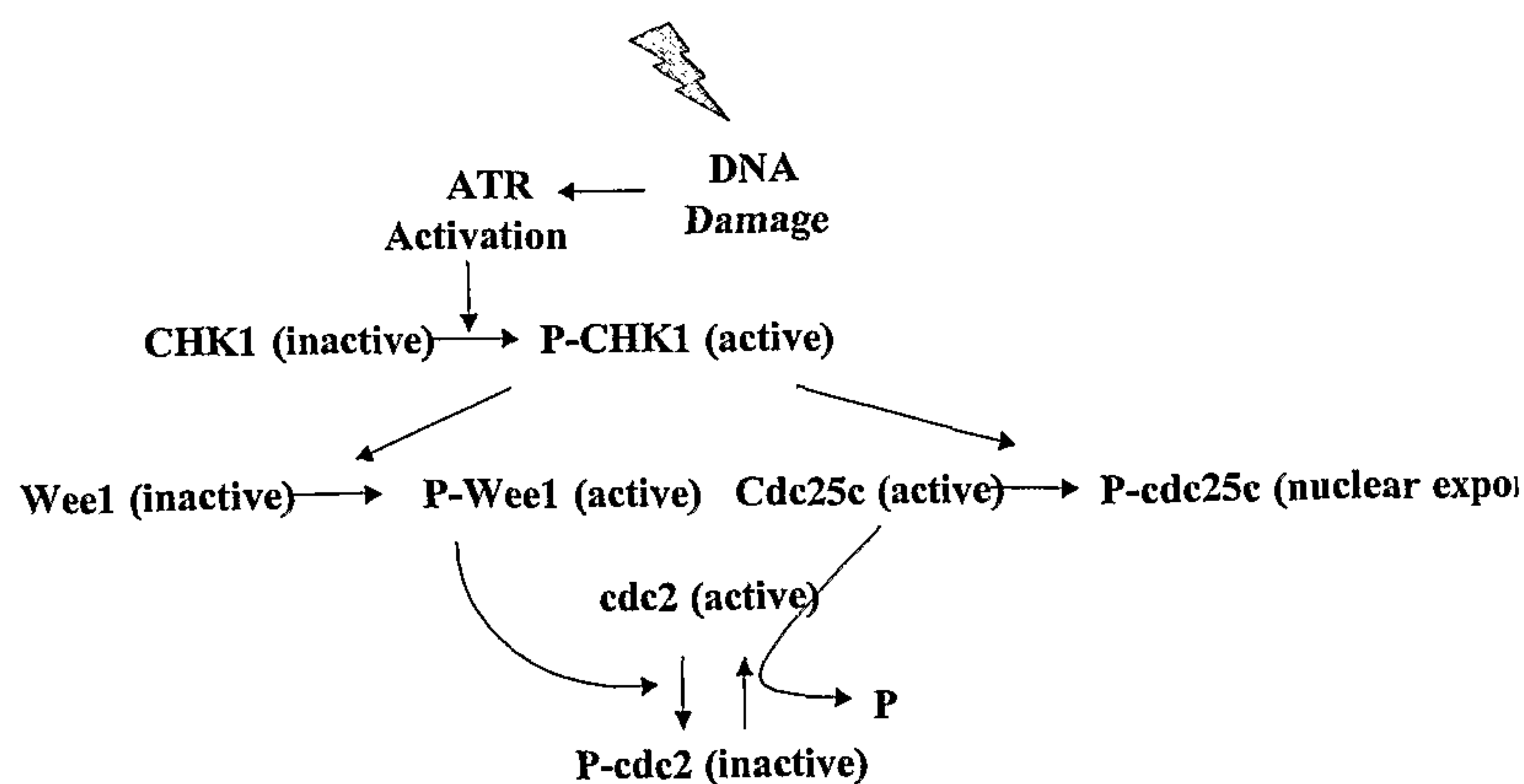


[0028] The G1/S checkpoint is regulated by the p53 transcriptional activator protein and the absence of this critical protein is often an important step in tumorigenesis, thus defining p53 as a tumor suppressor. In fact, nearly 50% of all cancers are p53 defective due to mutation. T. Soussi, *Ann. N.Y. Acad. Sci.*, 910, 121 (2001). In response to DNA damage, checkpoint kinase 2 (CHK-2) phosphorylates p53 and this results in stabilization of the protein and an elevation in p53 levels. A. Hirao et al., *Science*, 287, 1824 (2000). Consequently, negative cell cycle regulators, such as p21Waf1/Cip1, are activated and halt the cell cycle at the G1/S checkpoint. B. Vogelstein et al., *Nature*, 408, 307 (2000).

[0029] The G2/M checkpoint is monitored by the serine/threonine checkpoint kinase 1 (CHK1). Upon DNA damage, the protein kinase ATR (ataxia-telangiectasia mutated - rad53 related kinase) is activated. H. Zhao et al., *Mol. Cell Biol.*, 21, 4129 (2001); Q. Liu et al., *Genes Dev.*, 14, 1448 (2000). ATR-dependent phosphorylation of CHK1 promotes its phosphorylation of Cdc25 and Wee1 and ultimately inactivation of Cdc2. Thus, CHK1 phosphorylation of Cdc25c targets it for nuclear export to the cytoplasm and as a result the Cdc25c phosphatase is rendered unavailable to activate Cdc2 by dephosphorylation. Y. Sanchez et al., *Science*, 277, 1497

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(1997); C. Y. Peng et al., *Science*, 277, 1501 (1997); T. A. Chen et al., *Nature*, 401, 616 (1999); and A. Lopez-Girona et al., *Nature*, 397, 172 (1999). In addition, CHK1 activates the protein kinase Wee1, which phosphorylates and inactivates Cdc2. J. Lee et al. *Mol. Biol. Cell*, 12, 551 (2001); L. L. Parker et al., *Science*, 257, 1955 (1992). These dual pathways thus converge to result in cell cycle arrest. Because cell cycle arrest is a potential mechanism by which tumor cells can overcome the damage induced by cytotoxic agents, abrogation of these checkpoints with novel therapeutic agents should increase the sensitivity of tumors to chemotherapy. The presence of two checkpoints, coupled with the tumor specific abrogation of one of these by p53 mutations in 50% of cancers, can be exploited to design tumor-selective agents. Thus, in p53 minus tumors, therapeutic inhibition of G2/M arrest leaves cancerous cells no options for DNA damage repair and results in apoptosis. Normal cells have wild type p53 and retain an intact G1/S checkpoint. Thus these cells have an opportunity to correct DNA damage and survive. One approach to the design of chemosensitizers that abrogate the G2/M checkpoint is to identify inhibitors of the key G2/M regulatory kinase, CHK1.



[0030] It has been shown that PAR-1, also known as HDAK, a regulator of polarity, is a modulator of Wnt- β -catenin signaling, indicating a link between two important developmental pathways. See Sun, T-Q. et al. *Nature Cell Biology*, 3, 628-636 (2001). An important function of β -catenin, namely its role in cell signaling, has been elucidated in the past few years. β -Catenin

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is the vertebrate homologue of the *Drosophila* segment polarity gene armadillo, an important element in the Wingless/Wnt (Wg/Wnt) signaling pathway. Wingless is a cell–cell signal in *Drosophila* that triggers many key developmental processes, Wnt being the vertebrate homologue. In the absence of a mitotic signal from outside the cell β -catenin is sequestered in a complex with the adenomatous polyposis coli (APC) gene product, a serine threonine glycogen synthetase kinase (GSK-3 β) and an adapter protein axin (or a homologue conductin), enabling phosphorylation and degradation of free β -catenin by the ubiquitin–proteasome system. The function of and interactions between the proteins in the complex was something of a mystery until recently. Axin, a recently recognized component of the complex, acts as a scaffold protein in the multiprotein structure. Formation of an axin regulatory complex is critical for GSK-3 β activity and β -catenin phosphorylation and degradation, since GSK-3 β does not bind directly to β -catenin but requires the presence of axin, which binds to both proteins. This complex formation leads to the maintenance of low levels of free cytoplasmic β -catenin. Residual catenins hold cells together by binding to cadherins, both at the adherens junctions and the actin cytoskeleton.

[0031] When a mitotic signal is delivered by the Wnt pathway, by association of the Wg/Wnt family of secreted glycoproteins and their membrane receptor frizzled, it leads to activation of the dishevelled (Dsh) protein, which is recruited to the cell membrane. The activated Dsh downregulates the protein complex, so that it can no longer phosphorylate β -catenin, which then is not degraded. How exactly Wnt signaling leads to the stabilization of β -catenin remains unclear, although the critical step is possibly the dissociation of GSK-3 β from axin with the help of Dsh. With GSK-3 β no longer bound to axin, it cannot phosphorylate β -catenin, leading to an increase in β -catenin levels. Another proposed model is that inhibition of GSK-3 β activity upon Wnt signaling by Dsh leads to the dephosphorylation of axin, resulting in a reduced efficiency of binding to β -catenin. The release of

β -catenin from the phosphorylation and degradation complex promotes β -catenin stabilization and signaling. The resulting increase in free cytosolic β -catenin then enters the nucleus. This results in an increase of free cytosolic β -catenin which translocates to the nucleus and directly binds the transcription factors Lef and Tcf, leading to the activation of gene expression. Recently, the target genes of these transcription factors have been identified. They are thought to be involved in inhibiting apoptosis and promoting cellular proliferation and migration, and include the *c-myc* oncogene and one of the cell cycle regulators cyclin D1.

[0032] Transformation of adult mammalian cells into malignant tumors is believed to reflect an exaggeration of the Wg/Wnt pathway, at least in some tumors. The PAR-1 gene is involved in Wg/Wnt activity levels as well as production of free β -catenin in the cell. Down regulating of Wg/Wnt has been shown to limit β -catenin, which is involved in anti-apoptosis signaling. Small molecule inhibitors capable of inhibiting PAR-1 such as those disclosed herein, have been shown to be efficacious in cancer cell lines. Screens monitoring PAR-1 (HDAK) inhibition depict effective reduction of Wnt activity, with EC50 values below 10 μ M in cell-based assays. Therefore, a need remains for small molecule inhibitors of the PAR-1, capable of inhibiting Wg/Wnt signaling and β -catenin production in order to reduce growth of tumor cell lines and tumors via stimulation of cellular apoptosis.

[0033] Various indolyl substituted compounds have recently been disclosed in WO 01/29025, WO 01/62251, and WO 01/62252, and various benzimidazolyl compounds have recently been disclosed in WO 01/28993. These compounds are reportedly capable of inhibiting, modulating, and/or regulating signal transduction of both receptor-type and non-receptor tyrosine kinases. Some of the disclosed compounds contain a quinolone fragment bonded to the indolyl or benzimidazolyl group.

[0034] The synthesis of 4-hydroxy quinolone and 4-hydroxy quinoline derivatives is disclosed in a number of references.

For example, Ukrainets et al. have disclosed the synthesis of 3-(benzimidazol-2-yl)-4-hydroxy-2-oxo-1,2-dihydroquinoline. Ukrainets, I. et al., Tet. Lett. 42, 7747-7748 (1995); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 2, 239-241(1992). Ukrainets has also disclosed the synthesis, anticonvulsive and antithyroid activity of other 4-hydroxy quinolones and thio analogs such as 1H-2-oxo-3-(2-benzimidazolyl)-4-hydroxyquinoline. Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 1, 105-108 (1993); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 8, 1105-1108 (1993); Ukrainets, I. et al., Chem. Heterocyclic Comp. 33, 600-604, (1997).

[0035] The synthesis of various quinoline derivatives is disclosed in WO 97/48694. These compounds are disclosed as capable of binding to nuclear hormone receptors and being useful for stimulating osteoblast proliferation and bone growth. The compounds are also disclosed as being useful in the treatment or prevention of diseases associated with nuclear hormone receptor families.

[0036] Various quinoline derivatives in which the benzene ring of the quinolone is substituted with a sulfur group are disclosed in WO 92/18483. These compounds are disclosed as being useful in pharmaceutical formulations and as medicaments.

[0037] Quinolone and coumarin derivatives have been disclosed as having use in a variety of applications unrelated to medicine and pharmaceutical formulations. References that describe the preparation of quinolone derivatives for use in photopolymerizable compositions or for luminescent properties include: U.S. Patent No. 5,801,212 issued to Okamoto et al.; JP 8-29973; JP 7-43896; JP 6-9952; JP 63-258903; EP 797376; and DE 23 63 459.

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[0038] Various quinolinone benzimidazole compounds described as useful in inhibiting angiogenesis and vascular endothelial growth factor receptor tyrosine kinases are disclosed in WO 02/22598 (published on March 21, 2002), WO 02/18383 (published on March 7, 2002), and US 20030028018 A1.

[0040] A continuing need exists for compounds that inhibit the proliferation of capillaries, inhibit the growth of tumors, treat cancer, treat diabetes, stimulate insulin-dependent processes, treat Alzheimer's disease, treat central nervous system disorders, prolong immune responses, reduce the splitting of centrosomes, block DNA repair, modulate cell cycle arrest, and/or inhibit enzymes such as FLT-1 (VEGFR1), VEGFR2 (KDR, Flk-1), VEGFR3, FGFR1, GSK-3, Cdk2, Cdk4, MEK1, CHK2, CK1 ϵ , Raf, c-Kit, c-ABL, p60src, FGFR3, FLT-3, NEK-2, CHK1, Rsk2, PAR-1, Cdc2, Fyn, Lck, Tie-2, PDGFR α , and PDGFR β , and pharmaceutical formulations and medicaments that contain such compounds. A need also exists for methods for administering such compounds, pharmaceutical formulations, and medicaments to patients or subjects in need thereof.

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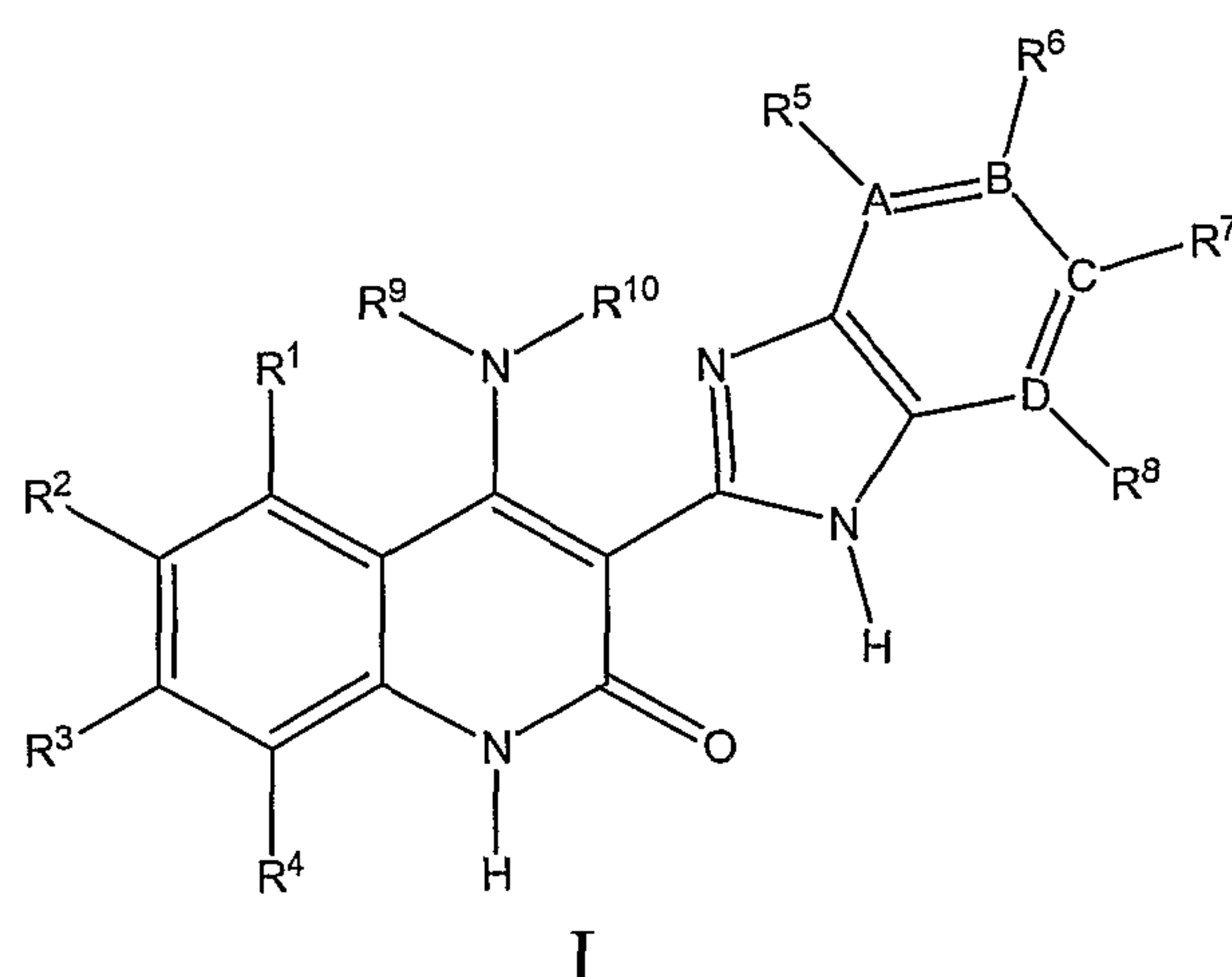
SUMMARY OF THE INVENTION

[0041] The present invention provides methods of inhibiting serine/threonine and tyrosine kinases, and methods of treating biological conditions mediated by serine/threonine and tyrosine kinases. In particular, the present invention provides methods of inhibiting serine/threonine kinases, including glycogen synthase kinase 3 (GSK-3), cyclin dependent kinase 2 (Cdk2), cyclin dependent kinase 4 (Cdk4), MEK1, NEK-2, CHK2, CK1 ϵ , Raf, checkpoint kinase 1 (CHK1), ribosomal S6 kinase 2 (Rsk2), and PAR-1 and methods of inhibiting tyrosine kinases, including cell division cycle 2 kinase (Cdc2 kinase), FYN oncogene kinase related to SRC, FGR, YES (Fyn), lymphocyte-specific protein tyrosine kinase (Lck), c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3 and tyrosine kinase with Ig and EGF homology domains (Tie-2). The present invention also provides methods of treating biological conditions mediated by serine/threonine kinases, including GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, CHK1, Rsk2, and PAR-1, and methods of treating biological conditions mediated by tyrosine kinases, including Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3, Fyn, Lck, and Tie-2. Finally, the present invention provides compounds and pharmaceutical formulations including the compounds that are used in the above methods.

Serine/Threonine Kinase Inhibition

[0042] In one aspect, the present invention provides a method of inhibiting a serine/threonine kinase in a subject and/or a method of treating a biological condition mediated by serine/threonine kinase activity in a subject. The methods include administering to the subject a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. In the method of inhibiting a serine/threonine kinase, the serine/threonine kinase is inhibited in the subject after administration. Structure I has the following formula:

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where:

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted and unsubstituted -S(=O)-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups,

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substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl) groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R² and R³ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-

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alkyl groups, substituted and unsubstituted -S-aryl groups, substituted and unsubstituted -S-aralkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(aryl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(aralkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and

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unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-aryl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-aralkyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted
 and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and
 unsubstituted -N(H)-C(=O)-aryl groups, substituted and
 unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and
 unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and
 unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted
 and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and
 unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and
 unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted
 and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups,
 substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups,
 substituted and unsubstituted -N(alkyl)-S(=O)₂-aryl groups,
 substituted and unsubstituted -N(alkyl)-S(=O)₂-aralkyl groups,
 substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl
 groups, substituted and unsubstituted
 -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂,
 substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups,
 substituted and unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups,
 substituted and unsubstituted -N(H)-C(=O)-N(H)(aryl) groups,
 substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups,
 substituted and unsubstituted -N(H)-C(=O)-N(aryl)₂ groups,
 substituted and unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups,
 substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(aralkyl)
 groups, substituted and unsubstituted -N(H)-C(=O)-N(aralkyl)₂
 groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted and
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl) groups,

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substituted and unsubstituted $-N(H)-C(=O)-N(\text{heterocyclyl})_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(\text{alkyl})(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(\text{heterocyclylalkyl})_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-NH_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(H)(\text{alkyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{alkyl})_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(H)(\text{aryl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{alkyl})(\text{aryl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{aryl})_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(H)(\text{aralkyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{alkyl})(\text{aralkyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{aralkyl})_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(H)(\text{heterocyclyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{alkyl})(\text{heterocyclyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{heterocyclyl})_2$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{alkyl})(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-N(\text{alkyl})-C(=O)-N(\text{heterocyclylalkyl})_2$ groups, substituted and unsubstituted $-C(=O)-\text{alkyl}$ groups, substituted and unsubstituted $-C(=O)-\text{aryl}$ groups, substituted and unsubstituted $-C(=O)-\text{aralkyl}$ groups, substituted and unsubstituted $-C(=O)-\text{heterocyclyl}$ groups, substituted and unsubstituted $-C(=O)-\text{heterocyclylalkyl}$ groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(\text{alkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})_2$ groups, substituted and unsubstituted

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-C(=O)-N(H)(aryl) groups, substituted and unsubstituted
 -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted
 -C(=O)-N(aryl)₂ groups, substituted and unsubstituted
 -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
 -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted
 -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted
 -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted
 -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and
 unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and
 unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted
 and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups,
 substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂
 groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl
 groups, substituted and unsubstituted -C(=O)-O-aryl groups,
 substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or
 substituted and unsubstituted -C(=O)-O-heterocyclylalkyl
 groups;

R⁴ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and
 unsubstituted alkyl groups having from 1 to 12 carbon atoms,
 substituted and unsubstituted alkenyl groups having from 1 to 8
 carbon atoms, substituted and unsubstituted alkynyl groups
 having from 1 to 8 carbon atoms, -SH, substituted and
 unsubstituted -S-alkyl groups, substituted and unsubstituted
 -S(=O)₂-O-alkyl groups, substituted and unsubstituted
 -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl
 groups, -S(=O)₂-NH₂, substituted and unsubstituted
 -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted
 -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted
 alkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl)
 groups, substituted and unsubstituted -N(alkyl)₂ groups,
 substituted and unsubstituted -N(H)-C(=O)-alkyl groups,

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substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted and unsubstituted -C(=O)-O-alkyl groups;

R⁵ and R⁸ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted and unsubstituted -C(=O)-O-alkyl groups; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted

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and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(heterocyclyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -S(=O)₂-N(heterocyclyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -S(=O)₂-N(heterocyclylalkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and

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unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocycl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclalkyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocycl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocycl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocycl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(heterocycl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl)

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groups, substituted and unsubstituted
-C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted and
unsubstituted -C(=O)-O-alkyl groups, substituted and
unsubstituted -C(=O)-O-heterocyclalkyl groups, or substituted and
unsubstituted -C(=O)-O-heterocyclalkyl groups; or R⁶ may be
absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl
groups having from 1 to 12 carbon atoms, substituted and
unsubstituted aryl groups, substituted and unsubstituted aralkyl
groups, substituted and unsubstituted heterocyclalkyl groups,
substituted and unsubstituted heterocyclalkyl groups,
substituted and unsubstituted heterocyclaminoalkyl groups,
substituted and unsubstituted alkoxy groups, or -NH₂, or R⁹ and
R¹⁰ join together to form one or more rings, each having 5, 6, or
7 ring members; and

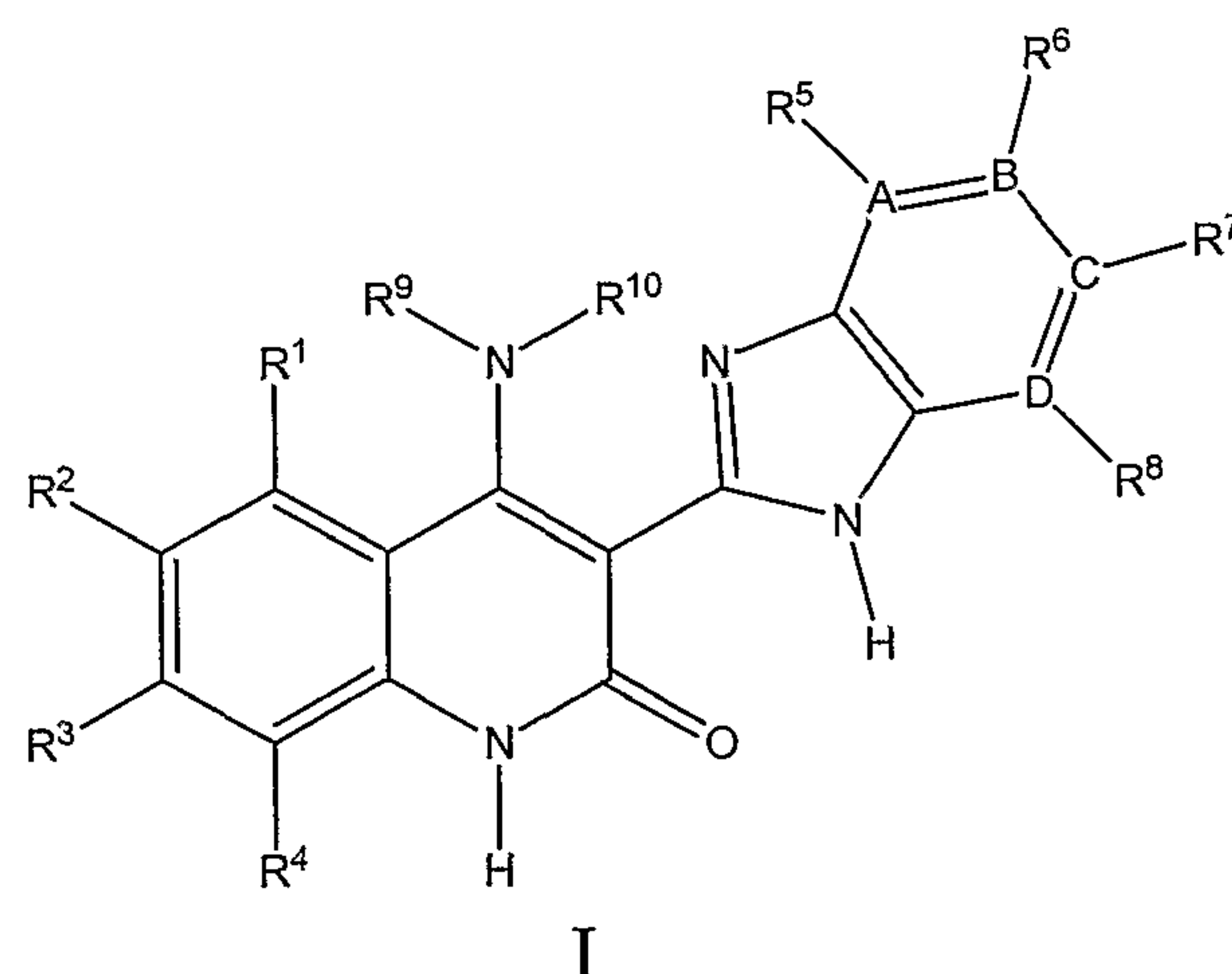
R¹⁰ is -H, or R⁹ and R¹⁰ join together to form one or more rings,
each having 5, 6, or 7 ring members.

[0043] In some embodiments of the method of inhibiting a
serine/threonine kinase using a compound of Structure I, a tautomer of the
compound, a pharmaceutically acceptable salt of the compound, a
pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the
serine/threonine kinase is selected from glycogen synthase kinase 3, cyclin
dependent kinase 2, cyclin dependent kinase 4, MEK1, NEK-2, CHK2, CK1ε,
Raf, checkpoint kinase 1, ribosomal S6 kinase 2, or PAR-1.

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Tyrosine Kinase Inhibition

[0044] In another aspect, the present invention provides a method of inhibiting a tyrosine kinase in a subject and/or a method of treating a biological condition mediated by a tyrosine kinase in a subject. The tyrosine kinase is Cdc2 kinase, Fyn, Lck, c-Kit, p60src, c-ABL, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3, or Tie-2. In some embodiments, the tyrosine kinase is Cdc2 kinase, Fyn, Lck, or Tie-2 and in some other embodiments, the tyrosine kinase is c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3. The methods include administering to the subject a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. In the method of inhibiting a tyrosine kinase, the tyrosine kinase is inhibited in the subject after administration. Structure I has the following formula:



where,

A, B, C, and D are independently selected from carbon or nitrogen;

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R^1 is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl)

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groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclyl})_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})(\text{heterocyclalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclalkyl})_2$ groups, $-\text{CO}_2\text{H}$, substituted and unsubstituted $-C(=O)-\text{O}-\text{alkyl}$ groups, substituted and unsubstituted $-C(=O)-\text{O}-\text{heterocycl}$ groups, or substituted and unsubstituted $-C(=O)-\text{O}-\text{heterocyclalkyl}$ groups;

R^2 and R^3 are independently selected from $-\text{H}$, $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, $-\text{NO}_2$, $-\text{CN}$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, $-\text{SH}$, substituted and unsubstituted $-\text{S}-\text{alkyl}$ groups, substituted and unsubstituted $-\text{S}(=\text{O})_2-\text{O}-\text{alkyl}$ groups, substituted and unsubstituted $-\text{S}(=\text{O})_2-\text{alkyl}$ groups, substituted and unsubstituted $-\text{S}(=\text{O})_2-\text{heterocycl}$ groups, $-\text{S}(=\text{O})_2-\text{NH}_2$, substituted and unsubstituted $-\text{S}(=\text{O})_2-\text{N}(H)(\text{alkyl})$ groups, substituted and unsubstituted $-\text{S}(=\text{O})_2-\text{N}(\text{alkyl})_2$ groups, substituted and unsubstituted $-\text{S}(=\text{O})-\text{alkyl}$ groups, substituted and unsubstituted $-\text{S}(=\text{O})-\text{heterocycl}$ groups, $-\text{OH}$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, $-\text{NH}_2$, substituted and unsubstituted $-\text{N}(H)(\text{alkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})_2$ groups, substituted and unsubstituted $-\text{N}(H)(\text{aryl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})(\text{aryl})$ groups, substituted and unsubstituted $-\text{N}(\text{aryl})_2$

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groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl, substituted and unsubstituted -C(=O)-aralkyl, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and

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unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, C(=O)-O-aryl groups - C(=O)-O-aralkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴ is selected from -H or substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms;

R⁵ and R⁸ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having

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from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted arylalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂,

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substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclylalkyl)_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O-alkyl$ groups, substituted and unsubstituted $-C(=O)-O-heterocyclyl$ groups, or substituted and unsubstituted $-C(=O)-O-heterocyclylalkyl$ groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen;

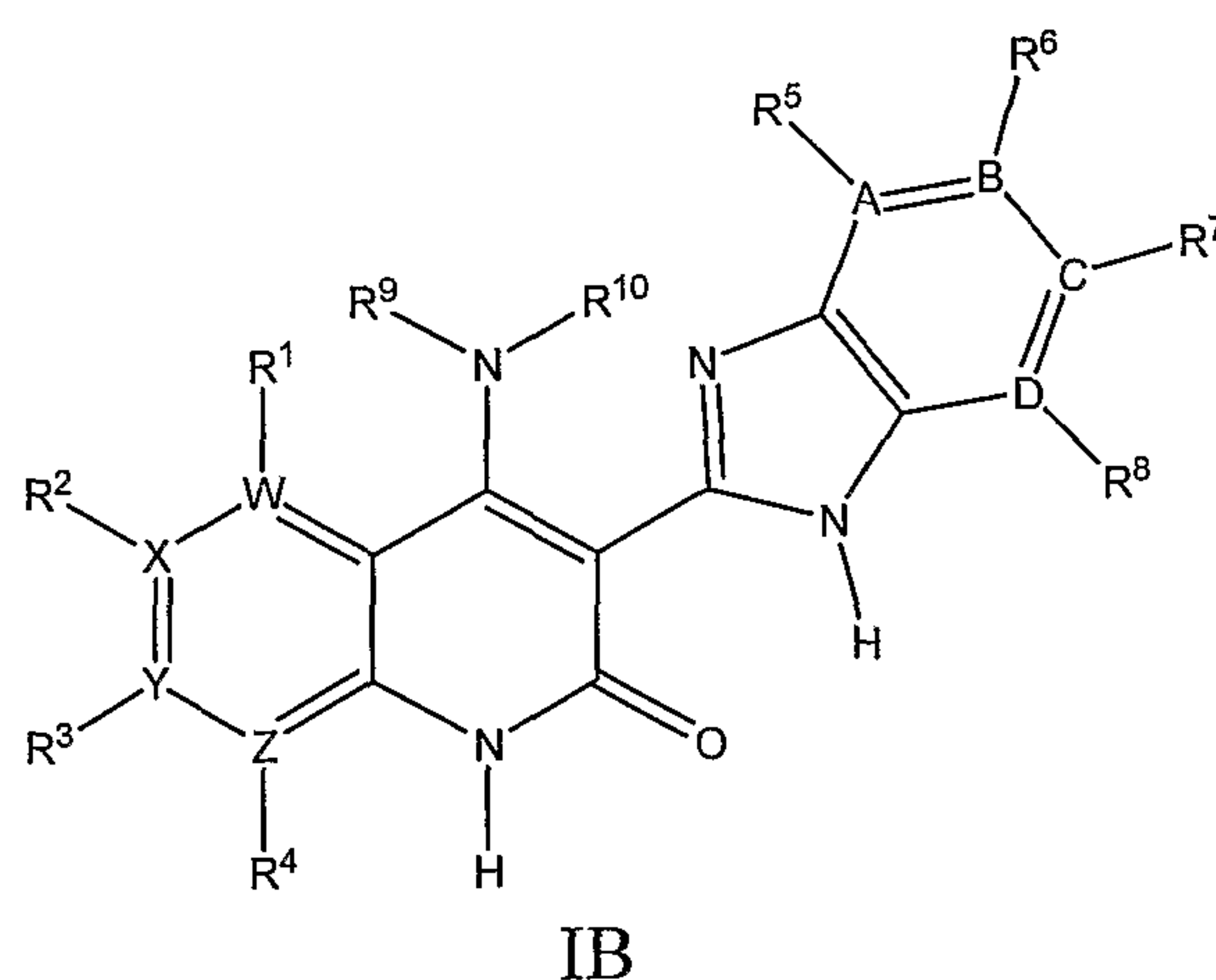
R^9 is selected from $-H$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbons, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, $-NH_2$, or substituted and unsubstituted heterocyclaminoalkyl; and

R^{10} is $-H$.

[0045] The present invention further provides methods of inhibiting serine/threonine kinases and tyrosine kinases and treating biological conditions mediated by such kinases using compounds of Structure IB. In some such embodiments, the invention provides a method of inhibiting GSK-3

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and treating biological conditions mediated by GSK-3 in a subject. The invention also provides the use of a compound of Structure IB in preparing a medicament for use in inhibiting a serine/threonine kinase such as GSK-3 or a tyrosine kinase in a subject and/or for use in treating a biological condition mediated by a serine/threonine kinase such as GSK-3 or a tyrosine kinase. In one aspect, a method of inhibiting a serine/threonine kinase or a tyrosine kinase or treating a biological condition mediated by a serine/threonine kinase or a tyrosine kinase includes administering to the subject a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. In some embodiments, a kinase such as a serine/threonine kinase such as GSK-3 or a tyrosine kinase is inhibited in the subject after administration. Structure IB has the following formula:



where:

A, B, C, and D are independently selected from carbon or nitrogen;

W, X, Y, and Z are independently selected from the group consisting of carbon and nitrogen and at least one of W, X, Y, and Z is a nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having

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from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R¹ may be absent if W is nitrogen;

R² is selected -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, -CO₂H, -OH, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkenyl groups, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted

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-S(=O)₂-heterocyclyl groups, substituted or unsubstituted
 -S(=O)-alkyl groups, substituted or unsubstituted
 -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted
 -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted
 -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted
 -C(=O)-alkyl groups, substituted or unsubstituted
 -C(=O)-heterocyclyl groups, substituted or unsubstituted
 -C(=O)-O-alkyl groups, substituted or unsubstituted
 -N(H)-C(=O)-alkyl groups, substituted or unsubstituted
 -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted
 -N(H)-S(=O)-alkyl groups, substituted or unsubstituted
 -N(H)-S(=O)-heterocyclyl groups, -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted
 -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted
 -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted
 -N(alkyl)-S(=O)-heterocyclyl groups, substituted or unsubstituted
 -N(H)-C(=O)-NH₂, substituted or unsubstituted
 -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or unsubstituted
 -N(alkyl)-C(=O)-N(H)(alkyl) groups, or substituted or unsubstituted
 -N(alkyl)-C(=O)-N(alkyl)₂ groups; or R² and R³ may join together to form a cyclic group when X and Y are both carbon; or R² may be absent if X is nitrogen;

R³ is selected from -H, -F, -Cl, -Br, -I, -OH, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkoxy groups, -CO₂H, -CN, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(cycloalkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted

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aryl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or unsubstituted -C(=O)-N(H)(aryl) groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -NO₂, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, or substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups; or

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R^2 and R^3 may join together to form a cyclic group when X and Y are both carbon; or R^3 may be absent if Y is nitrogen;

R^4 is selected from of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R^4 may be absent if Z is nitrogen;

R^5 is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted

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-S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted
 -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or
 unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl
 groups; or R⁵ may be absent if A is nitrogen;

R⁶ is selected from -H, -Cl, -F, -Br, -OH, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted
 -N(H)(alkyl) groups, substituted or unsubstituted
 -N(H)(heterocyclyl) groups, substituted or unsubstituted
 -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted
 alkoxy groups, substituted or unsubstituted alkyl groups having
 from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl
 groups having from 1 to 8 carbon atoms, substituted or
 unsubstituted alkynyl groups having from 1 to 8 carbon atoms,
 -CN, -NO₂, -OH, -SH, substituted or unsubstituted -S-alkyl
 groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups,
 substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or
 unsubstituted -S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted
 -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or
 unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted
 or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted
 -C(=O)-heterocyclyl groups, substituted or unsubstituted

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-C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups,
 substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups,
 substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or
 substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups;
 or R⁶ may be absent if B is nitrogen;

R⁷ is selected from -H, -Cl, -F, -Br, -OH, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted
 -N(H)(alkyl) groups, substituted or unsubstituted
 -N(H)(heterocyclyl) groups, substituted or unsubstituted
 -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted
 alkoxy groups, substituted or unsubstituted alkyl groups having
 from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl
 groups having from 1 to 8 carbon atoms, substituted or
 unsubstituted alkynyl groups having from 1 to 8 carbon atoms,
 -CN, -NO₂, -OH, -SH, substituted or unsubstituted -S-alkyl
 groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups,
 substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or
 unsubstituted -S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted
 -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or
 unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted
 or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted
 -C(=O)-heterocyclyl groups, substituted or unsubstituted

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-C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups; or R⁷ may be absent if C is nitrogen;

R⁸ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R⁸ may be absent if D is nitrogen;

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R^9 is selected from of substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkoxy groups, $-NH_2$, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members; or

R^{10} is $-H$, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members.

[0046] The invention further provides the use of the compounds of Structure I and IB, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, pharmaceutically acceptable salts of the tautomers, and mixtures thereof in the preparation and manufacture of medicaments for inhibiting any of the serine/threonine kinases or tyrosine kinases or for use in treating any biological conditions mediated by such kinases. In some embodiments, the compounds may be used to prepare medicaments in containers such as vials, ampoules, or other pharmaceutical formulation storage devices and such storage devices may include labels which may include directions for application such as directions for inhibiting a kinase or directions for treating a subject that has a biological condition mediated by a kinase.

[0047] The invention also provides novel compounds of Structure I and IB that may be used to inhibit the kinases described herein or may be used to treat biological conditions mediated by such kinases.

[0048] Further objects, features and advantages of the invention will be apparent from the following detailed description.

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BRIEF DESCRIPTION OF THE DRAWINGS

[0049] FIG. 1 is a graph of tumor growth inhibition in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one in the KM12L4a colon tumor model in *nu/nu* mice.

[0050] FIG. 2 is a graph of inhibition of angiogenesis in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one in the *in vivo* matrigel angiogenesis model.

[0051] FIG. 3 is a graph of tumor growth inhibition in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered intermittently in the PC3 human prostate tumor model in *SCID* mice.

[0052] FIG. 4 is a graph of tumor growth inhibition in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one.

[0053] FIG. 5 is a graph of tumor growth inhibition in the presence of 10 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered in combination with irinotecan in the KM12L4a colon tumor model in *nu/nu* mice.

[0054] FIG. 6 is a graph of tumor growth inhibition in the presence of 50 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered in combination with irinotecan in the KM12L4a colon tumor model in *nu/nu* mice.

[0055] FIG. 7. is a graph of tumor growth inhibition in the presence of 50 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered in combination with trastuzumab in the erbB2-overexpressing ovarian tumor model, SKOV3ip1.

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[0056] FIG. 8 is a graph of tumor growth inhibition in the presence of 50 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered in combination with ZD1839 in the A431 epidermoid tumor model.

[0057] FIGS. 9A and 9B are graphs showing inhibition of VEGF-mediated migration of HUVEC and VEGF-mediated tube formation in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one.

[0058] FIG. 10 is a graph showing inhibition of the sprouting of endothelial cells from rat aortic rings in the presence of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one.

[0059] FIG. 11 is a graph of tumor growth inhibition in the presence of 10, 30, and 70 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one in the MV4-11 (FLT-3 ITD mutant) tumor model in *SCID-NOD* mice.

[0060] FIG. 12 is a graph of tumor growth inhibition starting with different tumor sizes (300, 500, 1000 mm³) in the presence of 30 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one in the MV4-11 (FLT-3 ITD mutant) tumor model in *SCID-NOD* mice.

[0061] FIG. 13 is a graph of tumor growth inhibition in the presence of 30 mg/kg/d 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one administered daily, q.o.d., or 7 days on/7off in the MV4-11 (FLT-3 ITD mutant) tumor model in *SCID-NOD* mice.

DETAILED DESCRIPTION OF THE INVENTION

[0062] The present invention relates to a novel class of compounds which act as inhibitors of serine/threonine kinases and tyrosine kinases, including inhibitors of GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf,

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CHK1, Rsk2, PAR-1, Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Fyn, Lck, and Tie-2. The present invention further relates to the compounds used in these methods. These compounds can be formulated into pharmaceutical formulations that are useful in treating patients with a need for such inhibitors (e.g., those suffering from cancer). The compounds described herein are also useful for reducing capillary proliferation and in the treatment of cancer and other medical or cellular conditions in human and cell subjects.

[0063] The following abbreviations and definitions are used throughout this application:

[0064] "ALS" is an abbreviation that stands for amyotrophic lateral sclerosis.

[0065] "AD" is an abbreviation that stands for Alzheimer Disease.

[0066] "APP" is an abbreviation that stands for amyloid precursor protein.

[0067] "bFGF" is an abbreviation that stands for basic fibroblast growth factor.

[0068] "FGFR1", also referred to as bFGFR, is an abbreviation that stands for a tyrosine kinase that interacts with the fibroblast growth factor FGF.

[0069] "Cdc 2" is an abbreviation that stands for cell division cycle 2.

[0070] "Cdk 2" is an abbreviation that stands for cyclin dependent kinase 2.

[0071] "Cdk 4" is an abbreviation that stands for cyclin dependent kinase 4.

[0072] "Chk 1" is an abbreviation that stands for checkpoint kinase 1.

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[0073] "CK1 ϵ " is a serine/threonine kinase that stands for Casein kinase 1 (epsilon).

[0074] "c-ABL" is an abbreviation for a tyrosine kinase that stands for an oncogene product originally isolated from the Abelson leukemia virus.

[0075] "C-Kit" is also known as stem cell factor receptor or mast cell growth factor receptor.

[0076] "FGF" is an abbreviation for the fibroblast growth factor that interacts with FGFR1.

[0077] "FGFR3" is an abbreviation that stands for the tyrosine kinase fibroblast growth factor receptor 3 that is often expressed in multiple myeloma-type cancers.

[0078] "Flk-1" is an abbreviation that stands for fetal liver tyrosine kinase 1, also known as kinase-insert domain tyrosine kinase or KDR (human), also known as vascular endothelial growth factor receptor-2 or VEGFR2 (KDR (human), Flk-1 (mouse)).

[0079] "FLT-1" is an abbreviation that stands for fms-like tyrosine kinase-1, also known as vascular endothelial growth factor receptor-1 or VEGFR1.

[0080] "FLT-3" is an abbreviation that stands for fms-like tyrosine kinase-3, also known as stem cell tyrosine kinase I (STK I).

[0081] "FLT-4" is an abbreviation that stands for fms-like tyrosine kinase-4, also known as VEGFR3.

[0082] "Fyn" is an abbreviation that stands for FYN oncogene kinase related to SRC, FGR, YES.

[0083] "GSK-3" is an abbreviation that stands for glycogen synthase kinase 3.

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[0084] "p60src" is a tyrosine kinase originally identified as the v-src oncogene of the rous sarcoma virus.

[0085] "PAR-1" is an abbreviation that stands for a kinase also known as disheveled associated kinase, also known as HDAK.

[0086] "Lck" is an abbreviation that stands for lymphocyte-specific protein tyrosine kinase.

[0087] "MEK1" is an abbreviation that stands for a serine threonine kinase in the MAPK (Mitogen activated protein kinase) signal transduction pathway in a module that is formed of the Raf-MEK1-ERK. MEK1 phosphorylates ERK (extracellular regulated kinase).

[0088] "MS" is an abbreviation that stands for multiple sclerosis.

[0089] "NEK-2" is an abbreviation that stands for NIM-A related kinase.

[0090] "NIM-A" is an abbreviation that stands for never in mitosis.

[0091] "PDGF" is an abbreviation that stands for platelet derived growth factor. PDGF interacts with tyrosine kinases PDGFR α and PDGFR β .

[0092] "PHF" is an abbreviation that stands for paired helical filaments.

[0093] "PS 1" is an abbreviation that stands for presenelin 1.

[0094] "Rsk2" is an abbreviation that stands for ribosomal S6 kinase 2.

[0095] "Raf" is a serine/threonine kinase in the MAPK signal transduction pathway.

[0096] "RTK" is an abbreviation that stands for receptor tyrosine kinase.

[0097] "Tie-2" is an abbreviation that stands for tyrosine kinase with Ig and EGF homology domains.

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[0098] "VEGF" is an abbreviation that stands for vascular endothelial growth factor.

[0099] "VEGF-RTK" is an abbreviation that stands for vascular endothelial growth factor receptor tyrosine kinase.

[0100] Generally, reference to a certain element such as hydrogen or H is meant to include all isotopes of that element. For example, if an R group is defined to include hydrogen or H, it also includes deuterium and tritium.

[0101] The phrase "unsubstituted alkyl" refers to alkyl groups that do not contain heteroatoms. Thus the phrase includes straight chain alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. The phrase also includes branched chain isomers of straight chain alkyl groups, including but not limited to, the following which are provided by way of example: $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}(\text{CH}_2\text{CH}_3)_2$, $-\text{C}(\text{CH}_3)_3$, $-\text{C}(\text{CH}_2\text{CH}_3)_3$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)_2$, $-\text{CH}_2\text{C}(\text{CH}_3)_3$, $-\text{CH}_2\text{C}(\text{CH}_2\text{CH}_3)_3$, $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)_3$, $-\text{CH}_2\text{CH}_2\text{C}(\text{CH}_2\text{CH}_3)_3$, $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_2\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, and others. The phrase also includes cyclic alkyl groups such as cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl and such rings substituted with straight and branched chain alkyl groups as defined above. The phrase also includes polycyclic alkyl groups such as, but not limited to, adamantyl norbornyl, and bicyclo[2.2.2]octyl and such rings substituted with straight and branched chain alkyl groups as defined above. Thus, the phrase unsubstituted alkyl groups includes primary alkyl groups, secondary alkyl groups, and tertiary alkyl groups. Unsubstituted alkyl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound. Preferred unsubstituted alkyl groups include straight and branched chain alkyl groups and cyclic alkyl groups

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having 1 to 20 carbon atoms. More preferred such unsubstituted alkyl groups have from 1 to 10 carbon atoms while even more preferred such groups have from 1 to 5 carbon atoms. Most preferred unsubstituted alkyl groups include straight and branched chain alkyl groups having from 1 to 3 carbon atoms and include methyl, ethyl, propyl, and $-\text{CH}(\text{CH}_3)_2$.

[0102] The phrase "substituted alkyl" refers to an unsubstituted alkyl group as defined above in which one or more bonds to a carbon(s) or hydrogen(s) are replaced by a bond to non-hydrogen and non-carbon atoms such as, but not limited to, a halogen atom in halides such as F, Cl, Br, and I; an oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, and ester groups; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfone groups, sulfonyl groups, and sulfoxide groups; a nitrogen atom in groups such as amines, amides, alkylamines, dialkylamines, arylamines, alkylarylamines, diarylamines, N-oxides, imides, and enamines; a silicon atom in groups such as in trialkylsilyl groups, dialkylarylsilyl groups, alkyl diarylsilyl groups, and triarylsilyl groups; and other heteroatoms in various other groups. Substituted alkyl groups also include groups in which one or more bonds to a carbon(s) or hydrogen(s) atom is replaced by a bond to a heteroatom such as oxygen in carbonyl, carboxyl, and ester groups; nitrogen in groups such as imines, oximes, hydrazones, and nitriles. Preferred substituted alkyl groups include, among others, alkyl groups in which one or more bonds to a carbon or hydrogen atom is/are replaced by one or more bonds to fluorine atoms. One example of a substituted alkyl group is the trifluoromethyl group and other alkyl groups that contain the trifluoromethyl group. Other alkyl groups include those in which one or more bonds to a carbon or hydrogen atom is replaced by a bond to an oxygen atom such that the substituted alkyl group contains a hydroxyl, alkoxy, aryloxy group, or heterocycloxy group. Still other alkyl groups include alkyl groups that have an amine, alkylamine, dialkylamine, arylamine, (alkyl)(aryl)amine, diarylamine, heterocyclamine, (alkyl)(heterocycl)amine, (aryl)(heterocycl)amine, or diheterocyclamine group.

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[0103] The phrase “unsubstituted aryl” refers to aryl groups that do not contain heteroatoms. Thus the phrase includes, but is not limited to, groups such as phenyl, biphenyl, anthracenyl, naphthenyl by way of example. Although the phrase “unsubstituted aryl” includes groups containing condensed rings such as naphthalene, it does not include aryl groups that have other groups such as alkyl or halo groups bonded to one of the ring members, as aryl groups such as tolyl are considered herein to be substituted aryl groups as described below. A preferred unsubstituted aryl group is phenyl. Unsubstituted aryl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound, however.

[0104] The phrase “substituted aryl group” has the same meaning with respect to unsubstituted aryl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. However, a substituted aryl group also includes aryl groups in which one of the aromatic carbons is bonded to one of the non-carbon or non-hydrogen atoms described above and also includes aryl groups in which one or more aromatic carbons of the aryl group is bonded to a substituted and/or unsubstituted alkyl, alkenyl, or alkynyl group as defined herein. This includes bonding arrangements in which two carbon atoms of an aryl group are bonded to two atoms of an alkyl, alkenyl, or alkynyl group to define a fused ring system (e.g. dihydronaphthyl or tetrahydronaphthyl). Thus, the phrase “substituted aryl” includes, but is not limited to tolyl, and hydroxyphenyl among others.

[0105] The phrase “unsubstituted alkenyl” refers to straight and branched chain and cyclic groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one double bond exists between two carbon atoms. Examples include, but are not limited to vinyl, $-\text{CH}=\text{C}(\text{H})(\text{CH}_3)$, $-\text{CH}=\text{C}(\text{CH}_3)_2$, $-\text{C}(\text{CH}_3)=\text{C}(\text{H})_2$, $-\text{C}(\text{CH}_3)=\text{C}(\text{H})(\text{CH}_3)$, $-\text{C}(\text{CH}_2\text{CH}_3)=\text{CH}_2$, cyclohexenyl, cyclopentenyl, cyclohexadienyl, butadienyl, pentadienyl, and hexadienyl among others.

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[0106] The phrase “substituted alkenyl” has the same meaning with respect to unsubstituted alkenyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkenyl group includes alkenyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon double bonded to another carbon and those in which one of the non-carbon or non-hydrogen atoms is bonded to a carbon not involved in a double bond to another carbon.

[0107] The phrase “unsubstituted alkynyl” refers to straight and branched chain groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one triple bond exists between two carbon atoms. Examples include, but are not limited to – $\text{C}\equiv\text{C}(\text{H})$, $-\text{C}\equiv\text{C}(\text{CH}_3)$, $-\text{C}\equiv\text{C}(\text{CH}_2\text{CH}_3)$, $-\text{C}(\text{H}_2)\text{C}\equiv\text{C}(\text{H})$, $-\text{C}(\text{H})_2\text{C}\equiv\text{C}(\text{CH}_3)$, and $-\text{C}(\text{H})_2\text{C}\equiv\text{C}(\text{CH}_2\text{CH}_3)$ among others.

[0108] The phrase “substituted alkynyl” has the same meaning with respect to unsubstituted alkynyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkynyl group includes alkynyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon triple bonded to another carbon and those in which a non-carbon or non-hydrogen atom is bonded to a carbon not involved in a triple bond to another carbon.

[0109] The phrase “unsubstituted aralkyl” refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to an aryl group as defined above. For example, methyl ($-\text{CH}_3$) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a phenyl group, such as if the carbon of the methyl were bonded to a carbon of benzene, then the compound is an unsubstituted aralkyl group (*i.e.*, a benzyl group). Thus the phrase includes, but is not limited to, groups such as benzyl, diphenylmethyl, and 1-phenylethyl ($-\text{CH}(\text{C}_6\text{H}_5)(\text{CH}_3)$) among others.

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[0110] The phrase "substituted aralkyl" has the same meaning with respect to unsubstituted aralkyl groups that substituted aryl groups had with respect to unsubstituted aryl groups. However, a substituted aralkyl group also includes groups in which a carbon or hydrogen bond of the alkyl part of the group is replaced by a bond to a non-carbon or a non-hydrogen atom. Examples of substituted aralkyl groups include, but are not limited to, -CH₂C(=O)(C₆H₅), and -CH₂(2-methylphenyl) among others.

[0111] The phrase "unsubstituted heterocyclyl" refers to both aromatic and nonaromatic ring compounds including monocyclic, bicyclic, and polycyclic ring compounds such as, but not limited to, quinuclidyl, containing 3 or more ring members of which one or more is a heteroatom such as, but not limited to, N, O, and S. Although the phrase "unsubstituted heterocyclyl" includes condensed heterocyclic rings such as benzimidazolyl, it does not include heterocyclyl groups that have other groups such as alkyl or halo groups bonded to one of the ring members as compounds such as 2-methylbenzimidazolyl are substituted heterocyclyl groups. Examples of heterocyclyl groups include, but are not limited to: unsaturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridinyl, dihydropyridinyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl etc.), tetrazolyl, (e.g. 1H-tetrazolyl, 2H tetrazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl; condensed unsaturated heterocyclic groups containing 1 to 4 nitrogen atoms such as, but not limited to, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl; unsaturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, oxazolyl, isoxazolyl, oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, morpholinyl; unsaturated condensed heterocyclic

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groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, benzoxazolyl, benzoxadiazolyl, benzoxazinyl (e.g. 2H-1,4-benzoxazinyl etc.); unsaturated 3 to 8 membered rings containing 1 to 3 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolyl, isothiazolyl, thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolodiny; saturated and unsaturated 3 to 8 membered rings containing 1 to 2 sulfur atoms such as, but not limited to, thienyl, dihydrodithiiny, dihydrodithionyl, tetrahydrothiophene, tetrahydrothiopyran; unsaturated condensed heterocyclic rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, benzothiazolyl, benzothiadiazolyl, benzothiazinyl (e.g. 2H-1,4-benzothiazinyl, etc.), dihydrobenzothiazinyl (e.g., 2H-3,4-dihydrobenzothiazinyl, etc.), unsaturated 3 to 8 membered rings containing oxygen atoms such as, but not limited to furyl; unsaturated condensed heterocyclic rings containing 1 to 2 oxygen atoms such as benzodioxolyl (e.g., 1,3-benzodioxolyl, etc.); unsaturated 3 to 8 membered rings containing an oxygen atom and 1 to 2 sulfur atoms such as, but not limited to, dihydrooxathiiny; saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 2 sulfur atoms such as 1,4-oxathiane; unsaturated condensed rings containing 1 to 2 sulfur atoms such as benzothiény, benzodithiiny; and unsaturated condensed heterocyclic rings containing an oxygen atom and 1 to 2 oxygen atoms such as benzoxathiiny. Heterocyclyl group also include those described above in which one or more S atoms in the ring is double-bonded to one or two oxygen atoms (sulfoxides and sulfones). For example, heterocyclyl groups include tetrahydrothiophene oxide and tetrahydrothiophene 1,1-dioxide. Preferred heterocyclyl groups contain 5 or 6 ring members. More preferred heterocyclyl groups include morpholine, piperazine, piperidine, pyrrolidine, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, thiophene, thiomorpholine, thiomorpholine in which the S atom of the thiomorpholine is bonded to one or more O atoms,

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pyrrole, homopiperazine, oxazolidin-2-one, pyrrolidin-2-one, oxazole, quinuclidine, thiazole, isoxazole, furan, and tetrahydrofuran.

[0112] The phrase "substituted heterocyclyl" refers to an unsubstituted heterocyclyl group as defined above in which one or more of the ring members is bonded to a non-hydrogen atom such as described above with respect to substituted alkyl groups and substituted aryl groups. Examples, include, but are not limited to, 2-methylbenzimidazolyl, 5-methylbenzimidazolyl, 5-chlorobenzthiazolyl, N-alkyl piperazinyl groups such as 1-methyl piperazinyl, piperazine-N-oxide, N-alkyl piperazine N-oxides, 2-phenoxy-thiophene, and 2-chloropyridinyl among others. In addition, substituted heterocyclyl groups also include heterocyclyl groups in which the bond to the non-hydrogen atom is a bond to a carbon atom that is part of a substituted and unsubstituted aryl, substituted and unsubstituted aralkyl, or unsubstituted heterocyclyl group. Examples include but are not limited to 1-benzylpiperidinyl, 3-phenylthiomorpholinyl, 3-(pyrrolidin-1-yl)-pyrrolidinyl, and 4-(piperidin-1-yl)-piperidinyl. Groups such as N-alkyl substituted piperazine groups such as N-methyl piperazine, substituted morpholine groups, and piperazine N-oxide groups such as piperazine N-oxide and N-alkyl piperazine N-oxides are examples of some substituted heterocyclyl groups. Groups such as substituted piperazine groups such as N-alkyl substituted piperazine groups such as N-methyl piperazine and the like, substituted morpholine groups, piperazine N-oxide groups, and N-alkyl piperazine N-oxide groups are examples of some substituted heterocyclyl groups that are especially suited as R⁶ or R⁷ groups.

[0113] The phrase "unsubstituted heterocyclylalkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to a heterocyclyl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a heterocyclyl group, such as if the carbon of the methyl were bonded to carbon 2 of pyridine (one of the carbons bonded to the N of the pyridine) or carbons 3

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or 4 of the pyridine, then the compound is an unsubstituted heterocyclalkyl group.

[0114] The phrase "substituted heterocyclalkyl" has the same meaning with respect to unsubstituted heterocyclalkyl groups that substituted aralkyl groups had with respect to unsubstituted aralkyl groups. However, a substituted heterocyclalkyl group also includes groups in which a non-hydrogen atom is bonded to a heteroatom in the heterocycl group of the heterocyclalkyl group such as, but not limited to, a nitrogen atom in the piperidine ring of a piperidinylalkyl group. In addition, a substituted heterocyclalkyl group also includes groups in which a carbon bond or a hydrogen bond of the alkyl part of the group is replaced by a bond to a substituted and unsubstituted aryl or substituted and unsubstituted aralkyl group. Examples include but are not limited to phenyl-(piperidin-1-yl)-methyl and phenyl-(morpholin-4-yl)-methyl.

[0115] The phrase "unsubstituted alkylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an unsubstituted alkyl group as defined above. For example, methyl (-CH₃) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an ethyl group, then the resulting compound is -CH₂-N(H)(CH₂CH₃) which is an unsubstituted alkylaminoalkyl group.

[0116] The phrase "substituted alkylaminoalkyl" refers to an unsubstituted alkylaminoalkyl group as defined above except where one or more bonds to a carbon or hydrogen atom in one or both of the alkyl groups is replaced by a bond to a non-carbon or non-hydrogen atom as described above with respect to substituted alkyl groups except that the bond to the nitrogen atom in all alkylaminoalkyl groups does not by itself qualify all alkylaminoalkyl groups as being substituted. However, substituted alkylaminoalkyl groups does include groups in which the hydrogen bonded to

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the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

[0117] The phrase “unsubstituted dialkylaminoalkyl” refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

[0118] The phrase “substituted dialkylaminoalkyl” refers to an unsubstituted dialkylaminoalkyl group as defined above in which one or more bonds to a carbon or hydrogen atom in one or more of the alkyl groups is replaced by a bond to a non-carbon and non-hydrogen atom as described with respect to substituted alkyl groups. The bond to the nitrogen atom in all dialkylaminoalkyl groups does not by itself qualify all dialkylaminoalkyl groups as being substituted.

[0119] The phrase “unsubstituted alkoxy” refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a carbon atom of an otherwise unsubstituted alkyl group as defined above.

[0120] The phrase “substituted alkoxy” refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a carbon atom of an otherwise substituted alkyl group as defined above.

[0121] The phrase “unsubstituted heterocycloxy” refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom of an otherwise unsubstituted heterocyclyl group as defined above.

[0122] The phrase “substituted heterocycloxy” refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom of an otherwise substituted heterocyclyl group as defined above.

[0123] The phrase “unsubstituted heterocycloxyalkyl” refers to an unsubstituted alkyl group as defined above in which a carbon bond or

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hydrogen bond is replaced by a bond to an oxygen atom which is bonded to an unsubstituted heterocyclyl group as defined above.

[0124] The phrase "substituted heterocycloxyalkyl" refers to an unsubstituted heterocycloxyalkyl group as defined above in which a bond to a carbon or hydrogen group of the alkyl group of the heterocycloxyalkyl group is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups or in which the heterocyclyl group of the heterocycloxyalkyl group is a substituted heterocyclyl group as defined above.

[0125] The phrase "unsubstituted heterocyclalkoxy" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound, and in which another carbon or hydrogen bond of the unsubstituted alkyl group is bonded to an unsubstituted heterocyclyl group as defined above.

[0126] The phrase "substituted heterocyclalkoxy" refers to an unsubstituted heterocyclalkoxy group as defined above in which a bond to a carbon or hydrogen group of the alkyl group of the heterocyclalkoxy group is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups or in which the heterocyclyl group of the heterocyclalkoxy group is a substituted heterocyclyl group as defined above. Further, a substituted heterocyclalkoxy group also includes groups in which a carbon bond or a hydrogen bond to the alkyl moiety of the group may be substituted with one or more additional substituted and unsubstituted heterocycles. Examples include but are not limited to pyrid-2-ylmorpholin-4-ylmethyl and 2-pyrid-3-yl-2-morpholin-4-ylethyl.

[0127] The phrase "unsubstituted arylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or

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hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to at least one unsubstituted aryl group as defined above.

[0128] The phrase “substituted arylaminoalkyl” refers to an unsubstituted arylaminoalkyl group as defined above except where either the alkyl group of the arylaminoalkyl group is a substituted alkyl group as defined above or the aryl group of the arylaminoalkyl group is a substituted aryl group except that the bonds to the nitrogen atom in all arylaminoalkyl groups does not by itself qualify all arylaminoalkyl groups as being substituted. However, substituted arylaminoalkyl groups does include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

[0129] The phrase “unsubstituted heterocyclylaminoalkyl” refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to at least one unsubstituted heterocyclyl group as defined above.

[0130] The phrase “substituted heterocyclylaminoalkyl” refers to unsubstituted heterocyclylaminoalkyl groups as defined above in which the heterocyclyl group is a substituted heterocyclyl group as defined above and/or the alkyl group is a substituted alkyl group as defined above. The bonds to the nitrogen atom in all heterocyclylaminoalkyl groups does not by itself qualify all heterocyclylaminoalkyl groups as being substituted. However, substituted heterocyclylaminoalkyl groups do include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

[0131] The phrase “unsubstituted alkylaminoalkoxy” refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound and in which another carbon or hydrogen bond of the

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unsubstituted alkyl group is bonded to a nitrogen atom which is bonded to a hydrogen atom and an unsubstituted alkyl group as defined above.

[0132] The phrase "substituted alkylaminoalkoxy" refers to unsubstituted alkylaminoalkoxy groups as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if the hydrogen bonded to the amino group is bonded to a non-carbon and non-hydrogen atom and/or if the alkyl group bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all alkylaminoalkoxy groups does not by itself qualify all such groups as substituted alkylaminoalkoxy groups.

[0133] The phrase "unsubstituted dialkylaminoalkoxy" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound and in which another carbon or hydrogen bond of the unsubstituted alkyl group is bonded to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

[0134] The phrase "substituted dialkylaminoalkoxy" refers to an unsubstituted dialkylaminoalkoxy group as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if one or more of the alkyl groups bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all dialkylaminoalkoxy groups does not by itself qualify all such groups as substituted dialkylaminoalkoxy groups.

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[0135] The term "protected" with respect to hydroxyl groups, amine groups, and sulfhydryl groups refers to forms of these functionalities which are protected from undesirable reaction with a protecting group known to those skilled in the art such as those set forth in *Protective Groups in Organic Synthesis*, Greene, T.W.; Wuts, P. G. M., John Wiley & Sons, New York, NY, (3rd Edition, 1999) which can be added or removed using the procedures set forth therein. Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, *t*-butyldimethyl-chlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to methoxymethyl ether, methythiomethyl ether, benzyloxymethyl ether, *t*-butoxymethyl ether, 2-methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1-ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to, benzoylformate, formate, acetate, trichloroacetate, and trifluoroacetate. Examples of protected amine groups include, but are not limited to, amides such as, formamide, acetamide, trifluoroacetamide, and benzamide; imides, such as phthalimide, and dithiosuccinimide; and others. Examples of protected sulfhydryl groups include, but are not limited to, thioethers such as S-benzyl thioether, and S-4-picolyl thioether; substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals; and others.

[0136] A "pharmaceutically acceptable salt" includes a salt with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. As salts of inorganic bases, the invention includes, for example, alkali metals such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. As salts of organic bases, the invention includes, for example, trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. As salts of inorganic acids, the instant invention includes, for example, hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. As salts of organic acids, the instant invention includes, for example,

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formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. As salts of basic amino acids, the instant invention includes, for example, arginine, lysine and ornithine. Acidic amino acids include, for example, aspartic acid and glutamic acid.

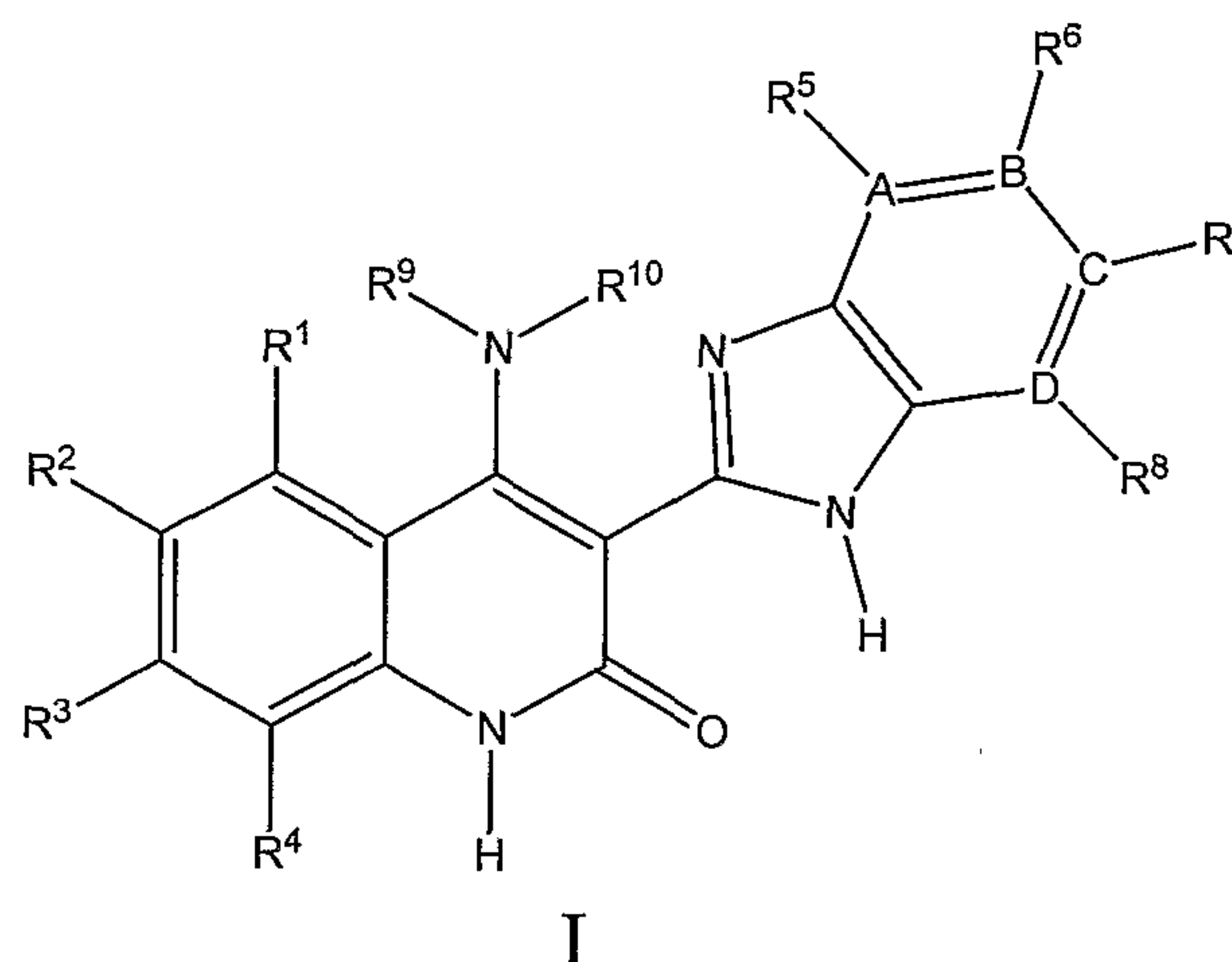
[0137] The present invention provides methods of inhibiting serine/threonine and tyrosine kinases, and methods of treating biological conditions mediated by serine/threonine and tyrosine kinases. In particular, the present invention provides methods of inhibiting serine/threonine kinases, including glycogen synthase kinase 3 (GSK-3), cyclin dependent kinase 2 (Cdk2), cyclin dependent kinase 4 (Cdk4), MEK1, NEK-2, CHK2, CK1 ϵ , Raf, checkpoint kinase 1 (CHK1), ribosomal S6 kinase 2 (Rsk2), and PAR-1 and methods of inhibiting tyrosine kinases, including cell division cycle 2 kinase (Cdc2 kinase), c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3, FYN oncogene kinase related to SRC, FGR, and YES (Fyn), lymphocyte-specific protein tyrosine kinase (Lck), and tyrosine kinase with Ig and EGF homology domains (Tie-2). The present invention also provides methods of treating biological conditions mediated by serine/threonine kinases, including GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, CHK1, Rsk2, and PAR-1, and methods of treating biological conditions mediated by tyrosine kinases, including Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3, Fyn, Lck, and Tie-2.

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Methods Relating to Serine/Threonine Kinases

[0138] In one aspect, the present invention provides a method of inhibiting a serine/threonine kinase in a subject and/or a method of treating a biological condition mediated by serine/threonine kinase activity in a subject. The methods include administering to the subject a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. In the method of inhibiting a serine/threonine kinase, the serine/threonine kinase is inhibited in the subject after administration.

Structure I has the following formula:



where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-

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alkyl groups, substituted and unsubstituted $-S(=O)_2-O$ -alkyl groups, substituted and unsubstituted $-S(=O)_2$ -alkyl groups, substituted and unsubstituted $-S(=O)$ -alkyl groups, $-S(=O)-NH_2$, substituted and unsubstituted $-S(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-S(=O)-N(alkyl)_2$ groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(heterocyclylalkyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)$ -alkyl groups, substituted and unsubstituted $-N(H)-C(=O)$ -heterocyclyl groups, substituted and unsubstituted $-N(H)-C(=O)$ -heterocyclylalkyl groups, substituted and unsubstituted $-N(H)-S(=O)$ -alkyl groups, substituted and unsubstituted $-C(=O)$ -alkyl groups, substituted and unsubstituted $-C(=O)$ -heterocyclyl groups, substituted and unsubstituted $-C(=O)$ -heterocyclylalkyl groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(aralkyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, $-C(=O)-N(H)(heterocyclylalkyl)$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O$ -alkyl groups, substituted and unsubstituted $-C(=O)-O$ -heterocyclyl groups, or substituted and unsubstituted $-C(=O)-O$ -heterocyclylalkyl groups;

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R^2 and R^3 are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-aryl groups, substituted and unsubstituted -S-aralkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(aryl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(aralkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂.

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groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl groups, substituted and unsubstituted -N(H)-S(=O)₂-aralkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-aryl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-aralkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups,

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substituted and unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(aryl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-NH₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(aryl)₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclylalkyl) groups,

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substituted and unsubstituted

-N(alkyl)-C(=O)-N(heterocyclalkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups, substituted and unsubstituted -C(=O)-aralkyl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(heterocycl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-aryl groups, substituted and unsubstituted -C(=O)-O-heterocycl groups, or substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups;

R⁴ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -SH, substituted and

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unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted and unsubstituted -C(=O)-O-alkyl groups;

R⁵ and R⁸ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and

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unsubstituted -C(=O)-N(alkyl)_2 groups, or substituted and unsubstituted -C(=O)-O-alkyl groups; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, - NO_2 , -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-O-alkyl}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-alkyl}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-heterocyclyl}$ groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted $\text{-S(=O)-heterocyclyl}$ groups, $\text{-S(=O)}_2\text{-NH}_2$, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(H)(alkyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)}_2$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(heterocyclyl)}_2$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(H)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(heterocyclylalkyl)}_2$ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH_2 , substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)_2 groups, substituted and

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unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and

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unsubstituted $-C(=O)-N(H)(aralkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(aralkyl)$ groups, substituted and unsubstituted $-C(=O)-N(aralkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclylalkyl)_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O-alkyl$ groups, substituted and unsubstituted $-C(=O)-O-heterocyclyl$ groups, or substituted and unsubstituted $-C(=O)-O-heterocyclylalkyl$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen;

R^9 is selected from $-H$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted alkoxy groups, or $-NH_2$, or R^9 and R^{10} join together to form one or more rings, each having 5, 6, or 7 ring members; and

R^{10} is $-H$, or R^9 and R^{10} join together to form one or more rings, each having 5, 6, or 7 ring members.

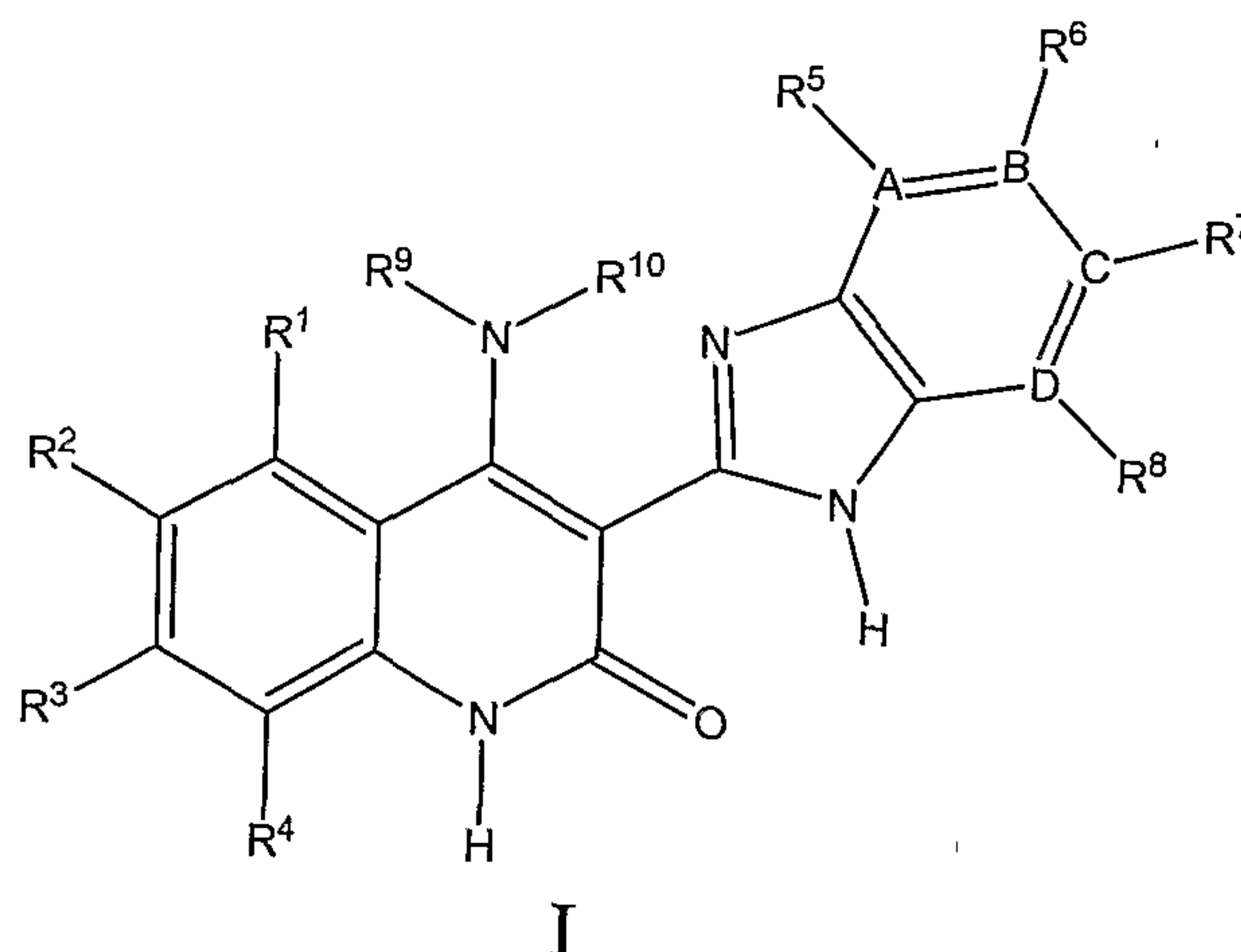
[0139] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject, the serine/threonine kinase is selected from glycogen synthase kinase 3, cyclin

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dependent kinase 2, cyclin dependent kinase 4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, checkpoint kinase 1, ribosomal S6 kinase 2, or disheveled associated kinase (PAR-1).

Methods Relating to Glycogen Synthase Kinase 3

[0140] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the serine/threonine kinase is GSK-3. In some such methods the GSK-3 is inhibited in the subject after administration. Structure I has the following formula:



where:

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl

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groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted and unsubstituted -S(=O)-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, -CO₂H, or substituted and unsubstituted -C(=O)-O-alkyl groups;

R² is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted cycloalkenyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and

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unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-heterocyclyl groups, -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, -CO₂H, or substituted and unsubstituted -C(=O)-O-alkyl groups; or R² and R³ may join together to form a cyclic group;

R³ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms,

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substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted and unsubstituted -S(=O)-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycliloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(cycloalkyl) groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, -NH₂, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups substituted and unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, substituted

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and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted $\text{-C(=O)-heterocyclyl}$ groups, -C(=O)-NH_2 groups, substituted and unsubstituted $\text{-C(=O)-N(H)(alkyl)}$ groups, substituted and unsubstituted -C(=O)-N(alkyl)_2 groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, $\text{-CO}_2\text{H}$, or substituted and unsubstituted -C(=O)-O-alkyl groups, or R^2 and R^3 may join together to form a cyclic group;

R^4 is selected from -H , -F , -Cl , -Br , -I , -CN , -NO_2 , substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -SH , substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-O-alkyl}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-alkyl}$ groups, substituted and unsubstituted -S(=O)-alkyl groups, $\text{-S(=O)}_2\text{-NH}_2$, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(H)(alkyl)}$ groups, substituted and unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)}_2$ groups, -OH , substituted and unsubstituted alkoxy groups, -NH_2 , substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)_2 groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH_2 , substituted and unsubstituted $\text{-C(=O)-N(H)(alkyl)}$ groups, substituted and unsubstituted -C(=O)-N(alkyl)_2 groups, or substituted and unsubstituted -C(=O)-O-alkyl groups;

R^5 is selected from -H , -F , -Cl , -Br , -I , -CN , -NO_2 , substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and

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unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted and unsubstituted -C(=O)-O-alkyl groups; or R⁵ may be absent if A is nitrogen;

R⁶ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, -NH₂, substituted and

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unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted
 -N(alkyl)₂ groups, substituted and unsubstituted
 -N(H)(heterocyclyl) groups, substituted and unsubstituted
 -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-alkyl groups, substituted and unsubstituted
 -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocyclyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and
 unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted
 and unsubstituted -C(=O)-alkyl groups, substituted and
 unsubstituted -C(=O)-heterocyclyl groups, -C(=O)-NH₂,
 substituted and unsubstituted -C(=O)-N(H)(alkyl) groups,
 substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, -CO₂H,
 or substituted and unsubstituted -C(=O)-O-alkyl groups; or R⁶
 may be absent if B is nitrogen;

R⁷ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and
 unsubstituted alkyl groups having from 1 to 8 carbon atoms,
 substituted and unsubstituted alkenyl groups having from 1 to 8
 carbon atoms, substituted and unsubstituted alkynyl groups
 having from 1 to 8 carbon atoms, substituted and unsubstituted
 heterocyclyl groups, substituted and unsubstituted
 heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-
 alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl
 groups, substituted and unsubstituted -S(=O)₂-alkyl groups,
 substituted and unsubstituted -S(=O)₂-heterocyclyl groups,
 substituted and unsubstituted -S(=O)-alkyl groups, substituted
 and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂,
 substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups,

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substituted and unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted and unsubstituted alkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted and unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-alkyl$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-N(H)-S(=O)-alkyl$ groups, substituted and unsubstituted $-N(H)-S(=O)-heterocyclyl$ groups, substituted and unsubstituted $-N(alkyl)-S(=O)-alkyl$ groups, substituted and unsubstituted $-N(alkyl)-S(=O)-heterocyclyl$ groups, substituted and unsubstituted amidine groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-C(=O)-alkyl$ groups, substituted and unsubstituted $-C(=O)-heterocyclyl$ groups, $-CO_2H$, or substituted and unsubstituted $-C(=O)-O-alkyl$ groups; or R^7 may be absent if C is nitrogen;

R^8 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, $-SH$, substituted and unsubstituted $-S-alkyl$ groups, substituted and

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unsubstituted $-S(=O)_2-O$ -alkyl groups, substituted and unsubstituted $-S(=O)_2$ -alkyl groups, substituted and unsubstituted $-S(=O)$ -alkyl groups, $-S(=O)_2-NH_2$, substituted and unsubstituted $-S(=O)_2-N(H)$ (alkyl) groups, substituted and unsubstituted $-S(=O)_2-N$ (alkyl)₂ groups, $-OH$, substituted and unsubstituted alkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)$ (alkyl) groups, substituted and unsubstituted $-N$ (alkyl)₂ groups, substituted and unsubstituted $-N(H)-C(=O)$ -alkyl groups, substituted and unsubstituted $-N(H)-S(=O)_2$ -alkyl groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)$ (alkyl) groups, substituted and unsubstituted $-C(=O)-N$ (alkyl)₂ groups, or substituted and unsubstituted $-C(=O)-O$ -alkyl groups; or R^8 may be absent if D is nitrogen;

R^9 is selected from $-H$, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted alkoxy groups, or $-NH_2$, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members; and

R^{10} is $-H$, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members.

[0141] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject,

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A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups;

R² is selected -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, -CO₂H, -OH, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkenyl groups, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups

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having from 1 to 8 carbon atoms, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups, -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, or substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups; or R² and R³ may join together to form a cyclic group;

R³ is selected from -H, -F, -Cl, -Br, -I, -OH, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkoxy groups, -CO₂H, -CN, substituted or unsubstituted -N(H)(alkyl)

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groups, substituted or unsubstituted -N(H)(cycloalkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or unsubstituted -C(=O)-N(H)(aryl) groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -NO₂, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted

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or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, or substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups; or R² and R³ may join together to form a cyclic group;

R⁴ is selected from of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups;

R⁵ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or

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unsubstituted $-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-S(=O)$ -alkyl groups, $-S(=O)-NH_2$, substituted or unsubstituted $-S(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)-N(alkyl)_2$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)-O$ -alkyl groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)$ -alkyl groups, or substituted or unsubstituted $-N(H)-S(=O)$ -alkyl groups; or R^5 may be absent if A is nitrogen;

R^6 is selected from $-H$, $-Cl$, $-F$, $-Br$, $-OH$, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(H)(heterocyclyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, $-CN$, $-NO_2$, $-OH$, $-SH$, substituted or unsubstituted $-S$ -alkyl groups, substituted or unsubstituted $-S(=O)_2-O$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -heterocyclyl groups, substituted or unsubstituted $-S(=O)$ -alkyl groups, substituted or unsubstituted $-S(=O)$ -heterocyclyl groups, $-S(=O)-NH_2$, substituted or unsubstituted $-S(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)-N(alkyl)_2$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)$ -alkyl groups, substituted or unsubstituted

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-C(=O)-heterocyclyl groups, substituted or unsubstituted
 -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups,
 substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups,
 substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or
 substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups;
 or R⁶ may be absent if B is nitrogen;

R⁷ is selected from -H, -Cl, -F, -Br, -OH, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted
 -N(H)(alkyl) groups, substituted or unsubstituted
 -N(H)(heterocyclyl) groups, substituted or unsubstituted
 -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted
 alkoxy groups, substituted or unsubstituted alkyl groups having
 from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl
 groups having from 1 to 8 carbon atoms, substituted or
 unsubstituted alkynyl groups having from 1 to 8 carbon atoms,
 -CN, -NO₂, -OH, -SH, substituted or unsubstituted -S-alkyl
 groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups,
 substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or
 unsubstituted -S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted
 -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or
 unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted
 or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted

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-C(=O)-heterocyclyl groups, substituted or unsubstituted
 -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl
 groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups,
 substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups,
 substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or
 substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups;
 or R⁷ may be absent if C is nitrogen;

R⁸ is selected from -H, -F, -Cl, -Br, -I, substituted or
 unsubstituted straight or branched chain alkyl groups having
 from 1 to 8 carbon atoms, substituted or unsubstituted
 heterocyclyl groups, substituted or unsubstituted alkenyl groups
 having from 1 to 8 carbon atoms, substituted or unsubstituted
 alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂,
 -OH, -SH, substituted or unsubstituted alkoxy groups,
 substituted or unsubstituted -S-alkyl groups, substituted or
 unsubstituted -S(=O)₂-O-alkyl groups, substituted or
 unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted
 -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted
 -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or
 unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl
 groups; or R⁸ may be absent if D is nitrogen;

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R^9 is selected from substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkoxy groups, $-NH_2$, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members; or

R^{10} is $-H$, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members.

[0142] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject,

R^1 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, and straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-CO_2H$, $-NO_2$, straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted cycloalkenyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups, $-OH$, substituted and unsubstituted alkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, or substituted and unsubstituted $-N(alkyl)_2$ groups;

R^3 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(H)(cycloalkyl)$ groups, substituted and unsubstituted

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-N(H)(heterocyclyl) groups, substituted and unsubstituted
-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted
-N(alkyl)₂ groups, -CO₂H, substituted and unsubstituted
-C(=O)-heterocyclyl groups, substituted and unsubstituted
-C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-
N(H)(alkyl) groups, substituted and unsubstituted
-C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂ groups, substituted and
unsubstituted -C(=O)-N(H)(heterocyclyl) groups, or substituted
and unsubstituted -C(=O)-N(H)(aryl) groups;

R⁴ is selected from -H, -F, -Cl, -Br, -I, and straight and branched
chain alkyl groups having from 1 to 8 carbon atoms;

R⁵ is selected from -H, -F, -Cl, -Br, -I, straight and branched
chain alkyl groups having from 1 to 8 carbon atoms, or
substituted and unsubstituted heterocyclyl groups; or R⁵ may be
absent if A is nitrogen;

R⁶ is selected from -H, -F, -Cl, -Br, substituted and unsubstituted
alkyl groups having from 1 to 8 carbon atoms, substituted and
unsubstituted heterocyclyl groups, -OH, substituted and
unsubstituted alkoxy groups, substituted and unsubstituted
-N(H)(alkyl) groups, substituted and unsubstituted
-N(H)(heterocyclyl) groups, or substituted and unsubstituted
-N(alkyl)(heterocyclyl) groups; or R⁶ may be absent if B is
nitrogen;

R⁷ is selected from -H, -Cl, -F, -Br, substituted and unsubstituted
alkyl groups having from 1 to 8 carbon atoms, -OH, substituted
and unsubstituted alkoxy groups, substituted and unsubstituted
heterocyclyl groups, substituted and unsubstituted -N(H)(alkyl)
groups, substituted and unsubstituted -N(H)(heterocyclyl)

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groups, or substituted and unsubstituted -N(alkyl)(heterocyclyl) groups; or R⁷ may be absent if C is nitrogen; and

R⁸ is selected from -H, -F, -Cl, -Br, -I, straight and branched chain alkyl groups having from 1 to 8 carbon atoms, or substituted and unsubstituted heterocyclyl groups; or R⁸ may be absent if D is nitrogen.

[0143] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, A, B, C, and D are all carbon.

[0144] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0145] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R¹⁰ is -H, and R⁹ is selected from substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted alkoxy groups, or -NH₂.

[0146] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R⁹ is selected from unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups

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wherein the heterocyclyl group is saturated, substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl group is unsaturated, substituted and unsubstituted alkoxy groups, -NH_2 , substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted aminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted and unsubstituted alkyl-(SO_2)-alkyl groups.

[0147] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^{10} is -H , and R^9 is selected from substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, or substituted and unsubstituted aminoalkyl groups.

[0148] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^9 is selected from quinuclidinyl groups, piperidinyl groups, piperidinylalkyl groups, pyrrolidinyl groups, or aminocyclohexyl groups. In some such embodiments, R^9 is a quinuclidinyl group, and in further such embodiments R^9 is a quinuclidin-3-yl group.

[0149] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^9 is selected from monocyclic, bicyclic, or polycyclic saturated heterocyclyl groups.

[0150] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^1 is selected from -H , -F , -Cl , or -CH_3 groups. In

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some such embodiments R^1 is $-H$ or $-F$, and in further such embodiments, R^1 is $-H$.

[0151] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^2 is selected from $-H$, $-Cl$, $-F$, $-Br$, $-I$, $-CH_3$, $-NO_2$, $-OMe$, $-CN$, $-CO_2H$, substituted and unsubstituted 1,2,3,6-tetrahydropyridine groups, substituted and unsubstituted thiophene groups, substituted and unsubstituted imidazole groups, substituted and unsubstituted pyrrole groups, substituted and unsubstituted 3-pyridinyl groups, substituted and unsubstituted 4-pyridinyl groups, phenyl, 2-substituted phenyl groups, 2,4-disubstituted phenyl groups, 4-substituted phenyl groups, 3-substituted phenyl groups, 2,6-disubstituted phenyl groups, 3,4-disubstituted phenyl groups, substituted and unsubstituted dialkylamino groups, or substituted and unsubstituted alkylamino groups.

[0152] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^2 is a substituted and unsubstituted aryl group selected from phenyl, 2-chlorophenyl, 2-methylphenyl, 2-ethylphenyl, 2-hydroxyphenyl, 2-methoxyphenyl, 2-trifluoromethylphenyl, 3-methoxyphenyl, 3-nitrophenyl, 3-carboxyphenyl, 3-acetylphenyl, 3-aminophenyl, 3-hydroxyphenyl, 3-acetamidophenyl, 3-carbomethoxyphenyl, 3-trifluoromethylphenyl, 3-ureidophenyl, 4-chlorophenyl, 4-cyanophenyl, 4-hydroxyphenyl, 4-nitrophenyl, 4-ethylphenyl, 4-methylphenyl, 4-methoxyphenyl, 4-acetylphenyl, 4-acetamidophenyl, 4-carboxyphenyl, 4-formylphenyl, 4-methylthiophenyl, 4-dimethylaminophenyl, 4-carbomethoxyphenyl, 4-carboethoxyphenyl, 4-carboxamidophenyl, 4-(methylsulfonyl)phenyl, 4-trifluoromethylphenyl, 2,4-difluorophenyl, 2-fluoro-4-chlorophenyl, 2,4-dichlorophenyl, 2-amino-4-carbomethoxyphenyl, 2-amino-4-carboxyphenyl, 2,6-difluorophenyl, or 3,4-(methylenedioxy)phenyl.

[0153] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-

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3 activity in a subject, R^2 is selected from $-H$, $-Cl$, $-F$, or $-CH_3$. In some such embodiments R^2 is $-F$.

[0154] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^4 is selected from $-H$ or $-CH_3$. In some such embodiments, R^4 is $-H$.

[0155] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^5 and R^8 are independently selected from $-H$, saturated heterocyclyl groups, or are absent. In some such embodiments, R^5 and R^8 are independently selected from $-H$, or saturated heterocyclyl groups.

[0156] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, A and D are both carbon, R^5 is $-H$, and R^8 is $-H$.

[0157] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^6 and R^7 are independently selected from $-H$, $-F$, $-Cl$, $-OH$, or substituted and unsubstituted heterocyclyl groups. In some such embodiments, R^6 is $-H$ and R^7 is $-H$.

[0158] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, A, B, C, and D are all carbon, and R^5 , R^6 , R^7 , and R^8 are all $-H$.

[0159] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R^3 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-CH_3$, $-OH$, $-CN$, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted alkoxy groups, substituted

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and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or -C(=O)-NH₂ groups.

[0160] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, -CH₃, -CN, -OMe, hydroxyalkylamino groups, dialkylamino groups, dialkylaminoalkylamino groups, alkoxyalkylamino groups, substituted and unsubstituted heterocyclalkylamino groups, acetamidoalkylamino groups, cyanoalkylamino groups, thioalkylamino groups, (methylsulfonyl)alkylamino groups, cycloalkylalkylamino groups, dialkylaminoalkoxy groups, heterocyclalkoxy groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted imidazolyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted pyrrolyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or -C(=O)-NH₂ groups.

[0161] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, R³ is selected from substituted and unsubstituted alkylamino groups or substituted and unsubstituted dialkylamino groups. In some such embodiments, R³ is a dimethylamino group.

[0162] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, A, B, C, and D are all carbon, and R⁴, R⁵, R⁶, R⁷, R⁸, and R¹⁰ are all -H.

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[0163] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, the IC_{50} value of the compound is less than or equal to 10 μ M with respect to GSK-3. In other such embodiments, the IC_{50} value is less than or equal to 1 μ M, is less than or equal to 0.1 μ M, is less than or equal to 0.050 μ M, is less than or equal to 0.030 μ M, is less than or equal to 0.025 μ M, or is less than or equal to 0.010 μ M.

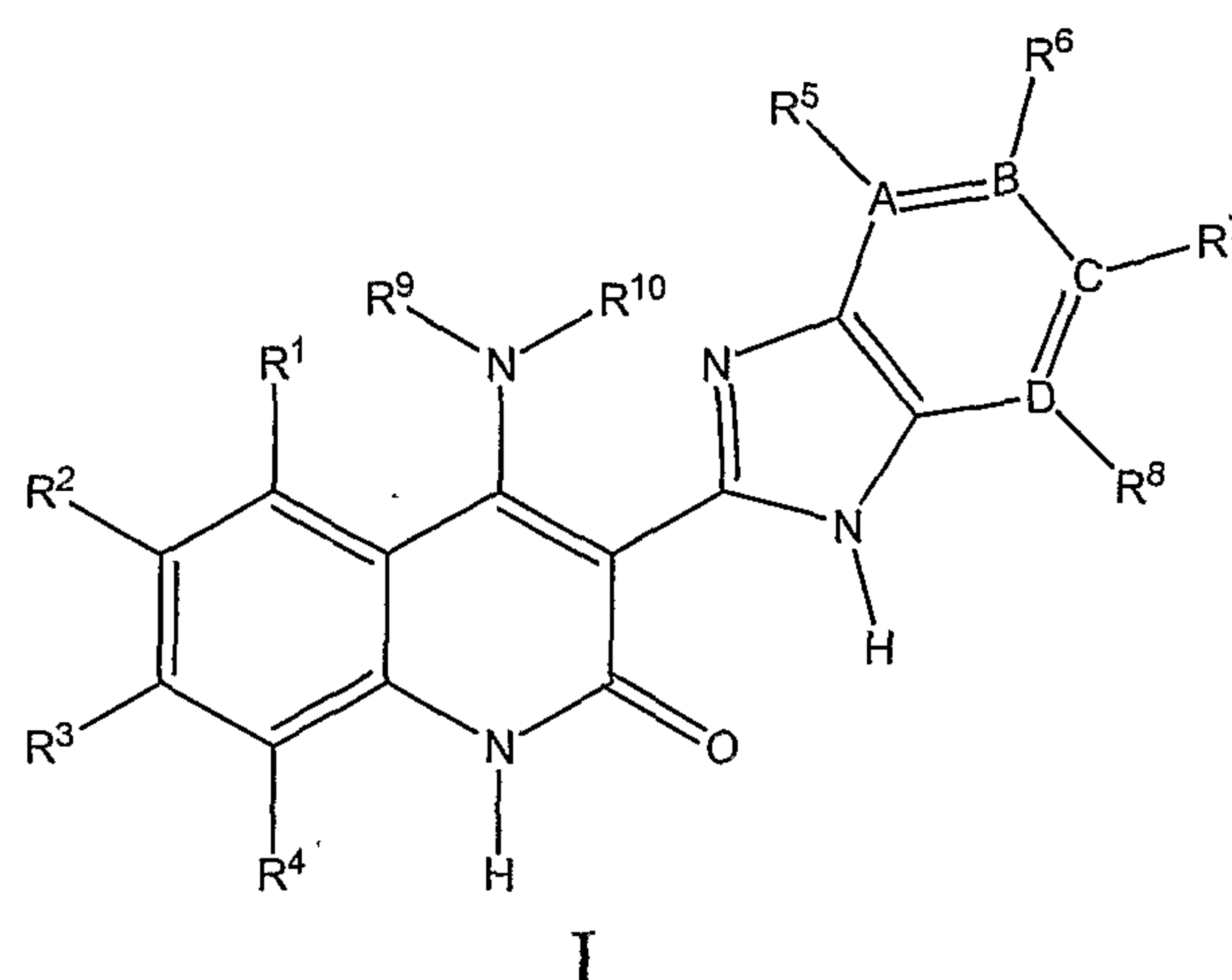
[0164] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject, the subject is a mammal and in some such embodiments is a human.

[0165] In some embodiments of the method of treating a biological condition mediated by GSK-3 activity in a subject, the biological condition is diabetes, and in some such embodiments the biological condition is noninsulin dependent diabetes mellitus (NIDDM). In other such embodiments, the biological condition is Alzheimer's disease or is bipolar disorder.

Methods Relating to Cyclin Dependent Kinase 2

[0166] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the serine/threonine kinase is Cdk2. In some such methods, the Cdk2 is inhibited in the subject after administration. In methods of inhibiting Cdk2, Structure I has the following formula:

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where:

A, B, C, and D are independently selected from carbon or nitrogen;

R^1 , R^4 , R^5 , and R^8 are independently selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^2 and R^3 are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl)

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groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycliloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, or substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted

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heterocycloxy groups, substituted and unsubstituted
heterocyclalkoxy groups, substituted and unsubstituted
-C(=O)-alkyl groups, substituted and unsubstituted
-C(=O)-heterocycl groups, substituted and unsubstituted
-C(=O)-heterocyclalkyl groups; and

R¹⁰ is -H.

[0167] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject,

R² and R³ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, or substituted and unsubstituted -N(aryl)₂ groups;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocycl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups,

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substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, or R⁶ may be absent if B is nitrogen and R⁷ may be absent if C is nitrogen..

[0168] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, A, B, C, and D are all carbon.

[0169] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0170] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R⁹ is selected from -H, substituted and unsubstituted chain alkyl groups having from 1-12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocyclylalkoxy groups.

[0171] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R⁹ is selected from -H, substituted and unsubstituted straight or branched chain alkyl groups having from 1-8 carbon atoms, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocyclylalkoxy groups wherein the heterocyclyl moiety is saturated.

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[0172] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^9 is selected from -H, unsubstituted straight or branched chain alkyl groups having from 1-8 carbon atoms, aminoalkyl groups, alkylaminoalkyl groups, dialkylaminoalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated.

[0173] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^9 is selected from pyrrolidinyl, pyrrolidinylalkyl, piperidinyl, piperidinylalkyl, or quinuclidinyl.

[0174] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^1 is -H.

[0175] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^2 is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbons, substituted and unsubstituted aryl groups, or substituted and unsubstituted pyridinyl groups. In some such embodiments, R^2 is selected from -H, -F, -Cl, -Br, -I, -CN, unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbons, dihalophenyl, carboxyphenyl, aminophenyl, aminocarboxyphenyl, methylcarboxyphenyl, or hydroxyphenyl. In other such embodiments, R^2 is selected from -H, -F, -Cl, -Br, -I, -CN, -CH₃, 2,6-difluorophenyl, 4-carboxyphenyl, 3-aminophenyl, 2-amino-4-methylcarboxyphenyl, 3-methylcarboxyphenyl, or 3-hydroxyphenyl.

[0176] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^3 is selected from the group consisting of -H, -F, -Cl, -Br,

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-I, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups. In some such embodiments, R^3 is selected from -H, -F, -Cl, -Br, -I, unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, aminoalkylamino groups, or substituted aryl groups. In other such embodiments, R^3 is selected from -H, -F, -Cl, -Br, -CH₃, 2-aminopropylamino groups, or 4-carboxamidophenyl, or R^3 is selected from -H, -F, -Cl, -Br, or -CH₃.

[0177] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^4 is -H.

[0178] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^5 or R^8 is -H, or are both -H.

[0179] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, -OH, substituted and unsubstituted -N(alkyl)(piperidinyl), substituted and unsubstituted piperidinyl groups, substituted and unsubstituted morpholinyl groups, or substituted and unsubstituted piperazinyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen. In some such embodiments, R^6 and R^7 are independently selected from -H, -F, -Cl, -OH, substituted and unsubstituted -N(methyl)(4-(N-methylpiperidinyl)), N-morpholinyl groups, or 4-N-methylpiperazinyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen. In other such embodiments, R^6 and R^7 are both -H, and B and C are both carbon.

[0180] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, R^5 and R^8 are both -H, and A and D are both carbon.

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[0181] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, the IC_{50} value of the compound is less than or equal to 10 μM with respect to Cdk2. In other such embodiments, the IC_{50} value is less than or equal to 1 μM , is less than or equal to 0.1 μM , is less than or equal to 0.050 μM , is less than or equal to 0.030 μM , is less than or equal to 0.025 μM , or is less than or equal to 0.010 μM .

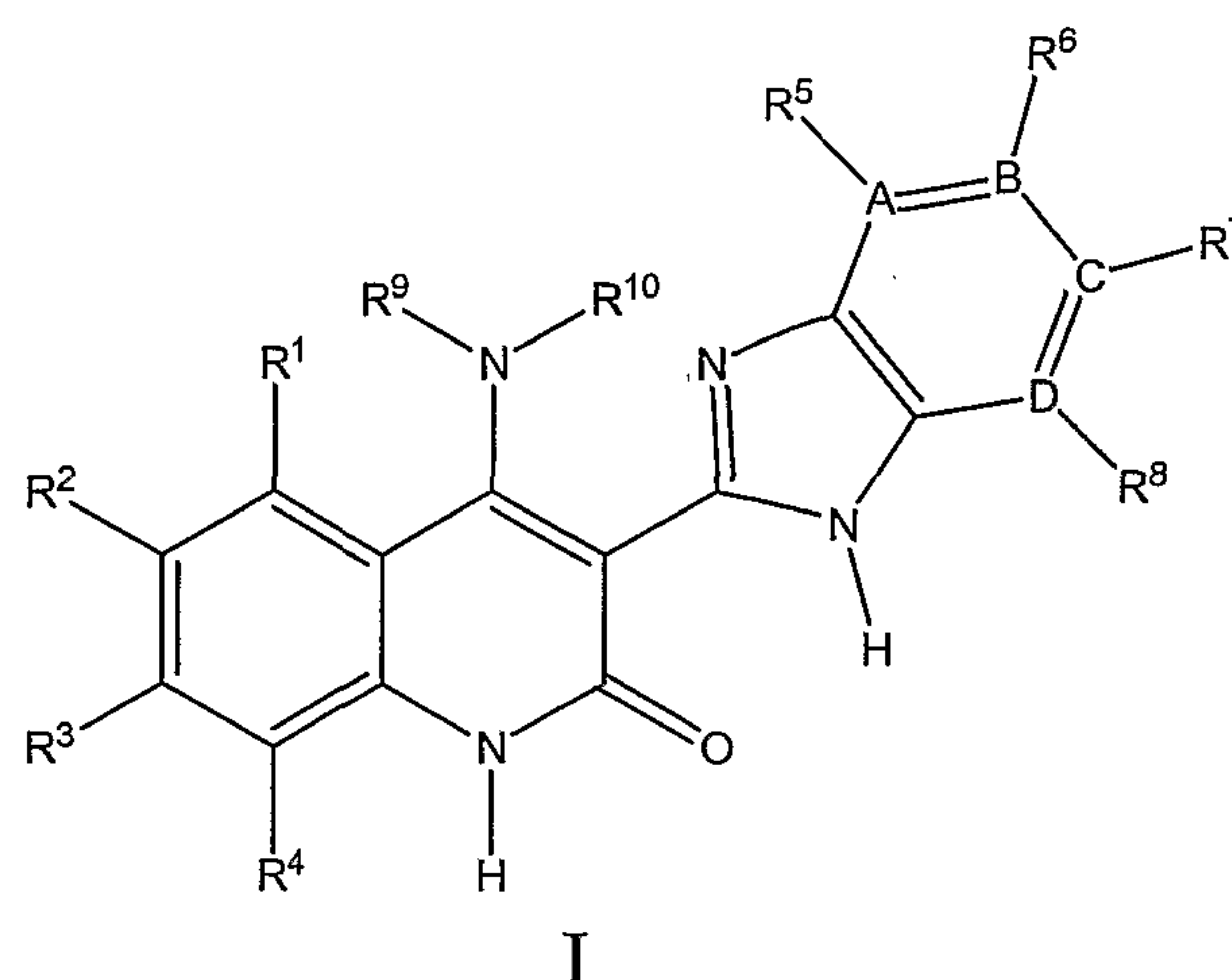
[0182] In some embodiments of the method of inhibiting Cdk2 in a subject and/or the method of treating a biological condition mediated by Cdk2 activity in a subject, the subject is a mammal or is a human.

[0183] In some embodiments of the method of treating a biological condition mediated by Cdk2 activity in a subject, the biological condition is cancer.

Methods Relating to Checkpoint Kinase 1

[0184] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the serine/threonine kinase is CHK1. In some such methods, the CHK1 is inhibited in the subject after administration. In methods of inhibiting CHK1, Structure I has the following formula:

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where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -SH, substituted and unsubstituted -S-alkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted

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-N(alkyl)(heterocyclalkyl) groups, or substituted and unsubstituted -N(heterocyclalkyl)₂ groups;

R² and R³ are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocycl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocycl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aryl) groups, substituted and unsubstituted -S(=O)₂-N(aryl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(aralkyl) groups, substituted and unsubstituted -S(=O)₂-N(aralkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted

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-N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl groups, substituted and unsubstituted -N(H)-S(=O)₂-aralkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-S(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups,

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substituted and unsubstituted $-N(H)-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(H)(aryl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(alkyl)(aryl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(aryl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(H)(aralkyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(alkyl)(aralkyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(aralkyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(H)-C(=O)-N(heterocyclylalkyl)_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-NH_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(H)(alkyl)$ groups substituted and unsubstituted $-N(alkyl)-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(H)(aryl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(alkyl)(aryl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(aryl)_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(H)(aralkyl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(alkyl)(aralkyl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(aralkyl)_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups,

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substituted and unsubstituted

-N(alkyl)-C(=O)-N(heterocyclalkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups, substituted and unsubstituted -C(=O)-aralkyl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(heterocycl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-aryl groups, substituted and unsubstituted -C(=O)-O-heterocycl groups, or substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups;

R⁴ is selected from -H or substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms;

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R^5 and R^8 are independently selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(heterocyclyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -S(=O)₂-N(heterocyclyl)₂ groups, substituted and unsubstituted -S(=O)₂-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -S(=O)₂-N(heterocyclylalkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycloxy

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groups, substituted and unsubstituted heterocyclalkoxy groups, $-\text{NH}_2$, substituted and unsubstituted $-\text{N}(\text{H})(\text{alkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})_2$ groups, substituted and unsubstituted $-\text{N}(\text{H})(\text{aryl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})(\text{aryl})$ groups, substituted and unsubstituted $-\text{N}(\text{aryl})_2$ groups, substituted and unsubstituted $-\text{N}(\text{H})(\text{aralkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})(\text{aralkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{aralkyl})_2$ groups, substituted and unsubstituted $-\text{N}(\text{H})(\text{heterocycl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})(\text{heterocycl})$ groups, substituted and unsubstituted $-\text{N}(\text{heterocycl})_2$ groups, substituted and unsubstituted $-\text{N}(\text{H})(\text{heterocyclalkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})(\text{heterocyclalkyl})$ groups, substituted and unsubstituted $-\text{N}(\text{heterocyclalkyl})_2$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{S}(=\text{O})_2\text{-alkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{S}(=\text{O})_2\text{-heterocycl}$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{S}(=\text{O})_2\text{-heterocyclalkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{C}(=\text{O})\text{-alkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{C}(=\text{O})\text{-heterocycl}$ groups, substituted and unsubstituted $-\text{N}(\text{H})-\text{C}(=\text{O})\text{-heterocyclalkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{C}(=\text{O})\text{-alkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{C}(=\text{O})\text{-heterocycl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{C}(=\text{O})\text{-heterocyclalkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{S}(=\text{O})_2\text{-alkyl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{S}(=\text{O})_2\text{-heterocycl}$ groups, substituted and unsubstituted $-\text{N}(\text{alkyl})-\text{S}(=\text{O})_2\text{-heterocyclalkyl}$ groups, substituted and unsubstituted $-\text{C}(=\text{O})\text{-alkyl}$ groups, substituted and unsubstituted $-\text{C}(=\text{O})\text{-heterocycl}$ groups, substituted and unsubstituted $-\text{C}(=\text{O})\text{-heterocyclalkyl}$ groups, $-\text{C}(=\text{O})\text{-NH}_2$, substituted and unsubstituted $-\text{C}(=\text{O})\text{-N}(\text{H})(\text{alkyl})$ groups, substituted and unsubstituted $-\text{C}(=\text{O})\text{-N}(\text{alkyl})_2$ groups, substituted and

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unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted alkoxy groups, or -NH₂, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members; and

R¹⁰ is -H, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members.

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[0185] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject,

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, or substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups;

R² and R³ are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups,

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substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(aryl)₂ groups, substituted and unsubstituted

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-N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
-N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted and
unsubstituted -N(H)-C(=O)-N(aralkyl)₂ groups, substituted and
unsubstituted -N(H)-C(=O)-N(H)(heterocyclyl) groups,
substituted and unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl)
groups, substituted and unsubstituted
-N(H)-C(=O)-N(heterocyclyl)₂ groups, substituted and
unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups,
substituted and unsubstituted
-N(H)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and
unsubstituted -N(H)-C(=O)-N(heterocyclylalkyl)₂ groups,
substituted and unsubstituted -N(alkyl)-C(=O)-NH₂ groups,
substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl)
groups, substituted and unsubstituted -N(alkyl)-C(=O)-N(H)(aryl)
groups, substituted and unsubstituted
-N(alkyl)-C(=O)-N(H)(aralkyl) groups, substituted and
unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclyl) groups,
substituted and unsubstituted
-N(alkyl)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted and
unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted
-C(=O)-aryl groups, substituted and unsubstituted -C(=O)-aralkyl
groups, substituted and unsubstituted -C(=O)-heterocyclyl
groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl
groups, -C(=O)-NH₂, substituted and unsubstituted
-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted
-C(=O)-N(alkyl)₂ groups, substituted and unsubstituted
-C(=O)-N(H)(aryl) groups, substituted and unsubstituted
-C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted
-C(=O)-N(aryl)₂ groups, substituted and unsubstituted
-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
-C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted
-C(=O)-N(aralkyl)₂ groups, -CO₂H, substituted and unsubstituted

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-C(=O)-O-alkyl groups, substituted and unsubstituted
-C(=O)-O-aryl groups, substituted and unsubstituted
-C(=O)-O-heterocyclyl groups, or substituted and unsubstituted
-C(=O)-O-heterocyclylalkyl groups;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkynyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycliloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups,

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substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted $\text{-C(=O)-heterocyclyl}$ groups, substituted and unsubstituted $\text{-C(=O)-heterocyclylalkyl}$ groups, -C(=O)-NH_2 , substituted and unsubstituted $\text{-C(=O)-N(H)(alkyl)}$ groups, substituted and unsubstituted -C(=O)-N(alkyl)_2 groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(alkyl)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(heterocyclyl)}_2$ groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(alkyl)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(heterocyclylalkyl)}_2$ groups, $\text{-CO}_2\text{H}$, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted $\text{-C(=O)-O-heterocyclyl}$ groups, or substituted and unsubstituted $\text{-C(=O)-O-heterocyclylalkyl}$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0186] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, A, B, C, and D are all carbon.

[0187] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0188] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^{10} is -H , and R^9 is selected from substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups,

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substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, or substituted and unsubstituted heterocyclylaminoalkyl groups.

[0189] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^{10} is $-H$, and R^9 is selected from unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted hydroxyalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, or substituted and unsubstituted aminoalkyl groups. In some such embodiments, R^{10} is $-H$, and R^9 is selected from 2-amino-4-methyl-pentyl, 2-amino-3-methyl-butyl, 2-amino-butyl, 2,2-dimethyl-3-amino-propyl, 1-aminomethyl-propyl, 2-hydroxy-3-amino-propyl, 3-aminopropyl, 2-dimethylamino-ethyl, 2-methylamino-ethyl, 2-hydroxy-ethyl, or 2-amino-ethyl.

[0190] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^{10} is $-H$ and R^9 is selected from substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, or substituted and unsubstituted heterocyclylaminoalkyl groups. In some such embodiments, R^{10} is $-H$ and R^9 is selected from substituted and unsubstituted phenylpropyl groups, substituted and unsubstituted phenylmethyl groups, or substituted and unsubstituted phenyl groups. In other such embodiments, R^{10} is $-H$ and R^9 is selected from phenyl, 4-aminomethyl-phenylmethyl, 2-(2-amino-ethyloxy)-phenylmethyl, 4-(2-amino-ethyloxy)-phenylmethyl, 4-sulfonamido-phenylmethyl, 1-benzyl-2-amino-ethyl, or 2-amino-3-phenyl-propyl.

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[0191] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^{10} is -H and R^9 is selected from substituted and unsubstituted cyclohexyl groups, substituted and unsubstituted cyclohexylalkyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyrrolidinylalkyl groups, substituted and unsubstituted tetrahydrofuranylalkyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted piperidinylalkyl groups, substituted and unsubstituted piperazinylalkyl groups, substituted and unsubstituted morpholinylalkyl groups, or substituted and unsubstituted quinuclidinyl groups. In some such embodiments, R^9 is selected from cyclohexyl, cyclohexylmethyl, 1-cyclohexylethyl, 2-amino-cyclohexyl, 4-amino-cyclohexyl, pyrrolidin-3-yl, 1-methyl-pyrrolidin-3-yl, 1-ethyl-pyrrolidin-2-yl, pyrrolidin-2-ylmethyl, 1-ethyl-pyrrolidin-2-ylmethyl, pyrrolidin-1-ylethyl, 1-methyl-pyrrolidin-2-ylethyl, pyrrolidin-1-ylpropyl, 2-oxo-pyrrolidin-1-ylpropyl, tetrahydrofuran-2-ylmethyl, piperidin-3-yl, 1-ethyl-piperidin-3-yl, piperidin-4-yl, 1-methyl-piperidin-4-yl, 1-benzyl-piperidin-4-yl, piperidin-2-ylmethyl, piperidin-3-ylmethyl, piperidin-4-ylmethyl, piperidin-1-ylethyl, piperidin-2-ylethyl, 4-methyl-piperazin-1-ylpropyl, morpholin-4-ylethyl, morpholin-4-ylpropyl, or quinuclidin-3-yl. In other such embodiments, R^9 is a quinuclidin-3-yl. In further such embodiments R^9 is a piperidin-3-ylmethyl. In other such embodiments, R^9 is selected from pyrrolidin-3-yl, 1-methyl-pyrrolidin-3-yl, or pyrrolidin-2-ylmethyl.

[0192] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^{10} is -H and R^9 is selected from substituted and unsubstituted imidazolylalkyl groups, substituted and unsubstituted pyridinyl groups, substituted and unsubstituted pyridinylalkyl groups, substituted and unsubstituted pyridinylaminoalkyl groups, substituted and unsubstituted pyrimidinylalkyl groups, substituted and unsubstituted pyrazinylalkyl groups, substituted and unsubstituted indolylalkyl groups, substituted and

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unsubstituted benzimidazolylalkyl groups. In some such embodiments, R^{10} is -H and R^9 is selected from 3-(imidazol-1-yl)-propyl, 3-(imidazol-4-yl)-propyl, pyridin-2-yl, pyridin-4-yl, 2-methoxy-pyridin-5-yl, 2-(piperidin-4-yloxy)-pyridin-3-yl, 2-(piperidin-3-yloxy)-pyridin-5-yl, pyridin-3-ylmethyl, pyridin-4-ylmethyl, pyridin-2-ylethyl, pyridin-3-ylethyl, 2-(5-trifluoromethyl-pyridin-2-ylamino)-ethyl, 2-(2-carboxamido-pyridin-5-ylamino)-ethyl, 2-(4-amino-5-nitro-pyridin-2-ylamino)-ethyl, pyridin-2-ylpropyl, pyrazin-2-yl, 2-methyl-4-amino-pyrazin-5-yl, 5-fluoro-indol-3-ylethyl, benzimidazol-2-ylmethyl, benzimidazol-5-ylmethyl, 2-piperidin-4-yl-benzimidazol-5-ylmethyl, and benzimidazol-2-ylethyl.

[0193] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^9 is selected from monocyclic, bicyclic, and polycyclic saturated heterocyclyl groups.

[0194] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^9 and R^{10} join together to form one or more rings, each having 5, 6, or 7 ring members.

[0195] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^1 is selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 4 carbon atoms, substituted and unsubstituted heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocycllyoxy groups, substituted and unsubstituted heterocyclylalkoxy groups, or substituted and unsubstituted -N(H)(alkyl) groups. In some such embodiments, R^1 is selected from -H, -F, -Cl, -CH₃, substituted and unsubstituted piperazinyl groups, -OCH₃, substituted and unsubstituted phenyloxy groups, substituted and unsubstituted piperidinyloxy groups, substituted and unsubstituted quinuclidinyloxy groups, substituted and unsubstituted morpholinylalkoxy

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groups, or $-NCH_3$. In other such embodiments, R^1 is selected from 4-methyl-piperazin-1-yl, 4-ethyl-piperazin-1-yl, 4-amino-phenyloxy, 3-dimethylamino-phenyloxy, 3-acetamido-phenyloxy, 4-acetamido-phenyloxy, or 2-(morpholin-4-yl)-ethyloxy. In still other such embodiments, R^1 is $-H$.

[0196] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 and R^3 are independently selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-NO_2$, $-CN$, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocycliloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(aryl)$ groups, substituted and unsubstituted $-N(alkyl)(aryl)$ groups, substituted and unsubstituted $-N(aryl)_2$ groups, substituted and unsubstituted $-N(H)(aralkyl)$ groups, substituted and unsubstituted $-N(alkyl)(aralkyl)$ groups, substituted and unsubstituted $-N(aralkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(heterocyclylalkyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted and unsubstituted $-N(H)-C(=O)-aryl$ groups, substituted and unsubstituted $-N(H)-C(=O)-aralkyl$ groups, substituted and unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted and unsubstituted

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-N(H)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocycl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocyclalkyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(alkyl)₂ groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(aryl)₂ groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(alkyl)(heterocycl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(heterocycl)₂ groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(heterocyclalkyl)₂ groups, substituted and unsubstituted
 -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups, substituted and unsubstituted
 -C(=O)-aralkyl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted
 -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted
 -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted
 -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted
 -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
 -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, -CO₂H, substituted and unsubstituted
 -C(=O)-O-alkyl groups, substituted and unsubstituted

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-C(=O)-O-aryl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups.

[0197] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted

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-N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted
 -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups,
 substituted and unsubstituted -C(=O)-aralkyl groups, substituted and
 unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted
 -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted
 -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂
 groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted
 and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted
 -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl)
 groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups,
 substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, -CO₂H, or
 substituted and unsubstituted -C(=O)-O-alkyl groups.

[0198] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R² is selected from 2-substituted phenyl groups, 3-substituted phenyl groups, 4-substituted phenyl groups, 2,4-disubstituted phenyl groups, 2,6-disubstituted phenyl groups, substituted or unsubstituted pyrrole groups, substituted and unsubstituted thiophene groups, substituted and unsubstituted tetrahydropyridine groups, or substituted and unsubstituted pyridine groups.

[0199] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R² is a substituted and unsubstituted aryl group selected from phenyl, 2-chlorophenyl, 2-ethylphenyl, 2-hydroxyphenyl, 2-methoxyphenyl, 2-methylphenyl, 2-trifluoromethylphenyl, 3-acetylphenyl, 3-acetamidophenyl, 3-aminophenyl, 3-methoxycarbonylphenyl, 3-carboxyphenyl, 3-hydroxyphenyl, 3-methoxyphenyl, 3-nitrophenyl, 3-trifluoromethylphenyl, 4-acetylphenyl, 4-methoxycarbonylphenyl, 4-carboxamidophenyl, 4-carboxyphenyl, 4-chlorophenyl, 4-cyanophenyl, 4-dimethylaminophenyl, 4-ethylphenyl, 4-formylphenyl, 4-hydroxyphenyl, 4-

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methoxyphenyl, 4-methylthiophenyl, 4-nitrophenyl, 4-(methylsulfonyl)-phenyl, 2,4-difluorophenyl, 2-fluoro-4-chlorophenyl, 2,4-dichlorophenyl, 2-amino-4-methoxycarbonylphenyl, 2-amino-4-carboxyphenyl, or 2,6-difluorophenyl. In some such embodiments, R^2 is selected from 2-hydroxyphenyl, 2-methoxyphenyl, 3-hydroxyphenyl, 3-methoxyphenyl, 3-aminophenyl, 4-cyanophenyl, 4-hydroxyphenyl, and 4-methoxyphenyl.

[0200] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is a substituted and unsubstituted heterocyclyl or heterocyclylalkyl group selected from 1-*tert*-butyloxycarbonyl-pyrrol-2-yl, thiophen-2-yl, thiophen-3-yl, 1,2,5,6-tetrahydropyridin-4-yl, 4-(*tert*-butyloxycarbonyl)-1,2,5,6-tetrahydropyridin-4-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, benzo[1,3]dioxol-5-yl, or benzo[b]thiophen-2-yl. In some such embodiments, R^2 is selected from thiophen-2-yl or thiophen-3-yl. In other such embodiments, R^2 is selected from pyridin-2-yl, pyridin-3-yl, or pyridin-4-yl.

[0201] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is selected from -H, -Cl, -F, -Br, -I, -NO₂, -CN, -CH₃, -OH, -OCH₃, -CO₂H, or -CO₂CH₃. In some such embodiments, R^2 is -Cl.

[0202] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is selected from -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and

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unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted
 -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted
 -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted
 -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl
 groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted
 and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted
 -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
 -N(H)-C(=O)-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂, substituted and
 unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted
 -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted
 -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(H)(aryl)
 groups, or substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups.

[0203] In some embodiments of the method of inhibiting CHK1 in a
 subject and/or the method of treating a biological condition mediated by CHK1
 activity in a subject, R² is selected from -NH₂, substituted and unsubstituted
 -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups,
 substituted and unsubstituted -N(H)(aralkyl) groups, substituted and
 unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted
 -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted
 -N(H)(heterocyclylalkyl) groups, or substituted and unsubstituted
 -N(alkyl)(heterocyclylalkyl) groups. In some such embodiments, R² is
 selected from -NH₂, -N(H)(methyl), -N(methyl)₂, -N(H)(2-methyl-propyl),
 -N(H)(2,2-dimethyl-propyl), -N(H)(2-methyl-butyl), -N(H)(heptyl),
 -N(H)(cyclohexylmethyl), -N(methyl)(isobutyl), -N(methyl)(cyclohexylmethyl),
 -N(H)(benzyl), -N(H)(piperidin-4-yl), -N(H)(pyrrolidin-2-ylmethyl), -N(H)(2-
 dimethylaminomethyl-furan-5-ylmethyl), -N(H)(3-methyl-thiophen-2-ylmethyl),
 -N(H)(3-phenyloxy-thiophen-2-ylmethyl), -N(H)(2-ethyl-5-methyl-imidazol-4-

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ylmethyl), -N(H)(5-methyl-isoxazol-3-ylmethyl), -N(H)(thiazol-2-ylmethyl), -N(H)(pyrazin-2-ylmethyl), or -N(methyl)(1-methyl-piperidin-4-yl).

[0204] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is selected from substituted and unsubstituted -N(H)-C(=O)-alkyl groups, wherein the alkyl moiety is a straight or branched chain alkyl having from 1 to 8 carbon atoms, substituted and unsubstituted -N(H)-C(=O)-cycloalkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, or substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups. In some such embodiments, R^2 is selected from substituted and unsubstituted -N(H)-C(=O)-methyl groups, substituted and unsubstituted -N(H)-C(=O)-cyclohexyl groups, substituted and unsubstituted -N(H)-C(=O)-phenyl groups, substituted and unsubstituted -N(H)-C(=O)-phenylalkyl groups, substituted and unsubstituted -N(H)-C(=O)-furan groups, substituted and unsubstituted -N(H)-C(=O)-thiophenylalkyl groups. In other such embodiments, R^2 is selected from -N(H)-C(=O)-methyl, -N(H)-C(=O)-propyl, -N(H)-C(=O)-isopropyl, -N(H)-C(=O)-benzyloxymethyl, -N(H)-C(=O)-benzylaminomethyl, -N(H)-C(=O)-cyclohexyl groups, -N(H)-C(=O)-4-ethyl-phenyl, -N(H)-C(=O)-4-cyano-phenyl, -N(H)-C(=O)-2-phenyl-ethyl groups, -N(H)-C(=O)-furan-2-yl, -N(H)-C(=O)-thiophen-2-ylmethyl groups, or -N(H)-C(=O)-pyrazin-2-yl.

[0205] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^2 is selected from -N(H)-C(=O)-NH₂, substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted

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-N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups. In some such embodiments, R² is selected from substituted and unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, wherein the alkyl moiety is a straight or branched chain alkyl group having from 1 to 12 carbons, substituted and unsubstituted -N(H)-C(=O)-N(H)(phenyl) groups, or substituted and unsubstituted -N(H)-C(=O)-N(H)(phenylalkyl) groups. In other such embodiments, R² is selected from -N(H)-C(=O)-N(H)(isopropyl), -N(H)-C(=O)-N(H)(heptyl), -N(H)-C(=O)-N(H)(phenyl), -N(H)-C(=O)-N(H)(2-ethoxyphenyl), -N(H)-C(=O)-N(H)(2-methylthiophenyl), -N(H)-C(=O)-N(H)(3-trifluoromethylphenyl), -N(H)-C(=O)-N(H)(3,5-dimethylphenyl), or -N(H)-C(=O)-N(H)(benzyl).

[0206] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups,

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-C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, -CO₂H, or substituted and unsubstituted -C(=O)-O-alkyl groups.

[0207] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups. In some such embodiments, R³ is selected from -H, -F, -Cl, -Br, -CN, -CH₃, -OH, -OCH₃, 2-dimethylaminoethoxy, pyrrolidin-2-ylmethoxy, or 2-oxo-pyrrolidin-1-ylethoxy.

[0208] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R³ is selected from substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups.

[0209] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R³ is selected from 2-substituted phenyl groups, 3-substituted phenyl groups, 4-substituted phenyl groups, 2,4-disubstituted phenyl groups, substituted or unsubstituted pyrrole groups, substituted and unsubstituted thiophene groups, substituted and unsubstituted piperidine groups, substituted and unsubstituted piperazine groups, substituted and unsubstituted morpholine groups, substituted and unsubstituted azepane groups, substituted and unsubstituted pyrrole groups, substituted and unsubstituted imidazole groups, substituted and unsubstituted pyridine groups, or substituted and unsubstituted benzodioxole groups.

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[0210] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^3 is a substituted and unsubstituted aryl group selected from 2-methoxy-phenyl, 2-methylphenyl, 2-trifluoromethyl-phenyl, 3-acetylphenyl, 3-acetamidophenyl, 3-methoxycarbonyl-phenyl, 3-carboxyphenyl, 4-acetylphenyl, 4-carboxamidophenyl, 4-carboxyphenyl, 4-cyanophenyl, 4-formylphenyl, 4-methoxycarbonyl-phenyl, 4-methylsulfonyl-phenyl, 2,4-dichlorophenyl, 2-amino-4-methoxycarbonylphenyl, or 2-amino-4-methoxycarbonyl-phenyl.

[0211] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^3 is a substituted and unsubstituted heterocyclyl group selected from pyrrolidin-1-yl, 3-dimethylamino-pyrrolidin-1-yl, 3-acetamidopyrrolidin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-methylsulfonyl-pyrrolidin-1-yl, 3-trifluoroacetamido-pyrrolidin-1-yl, piperidin-1-yl, 2-hydroxy-piperidin-1-yl, 3-carboxamide-piperidin-1-yl, 3-carboxy-piperidin-1-yl, 3-methoxycarbonyl-piperidin-1-yl, 3-(pyridin-4-yl)-pyrrolidin-3-yl, 4-carboxamido-piperidin-1-yl, 4-carboxy-piperidin-1-yl, 4-ethoxycarbonyl-piperidin-1-yl, 4-methyl-piperazin-1-yl, 4-(pyridin-2-ylmethyl)-piperazin-1-yl, morpholin-4-yl, azepan-1-yl, pyrrol-1-yl, 3-acetyl-pyrrol-1-yl, 3-carboxy-pyrrol-1-yl, imidazol-1-yl, 2-methyl-imidazol-1-yl, 2-ethyl-imidazol-1-yl, 2-isopropyl-imidazol-1-yl, or benzo[1,3]dioxol-5-yl.

[0212] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^3 is selected from $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, or substituted and unsubstituted $-N(heterocyclylalkyl)_2$ groups.

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[0213] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^3 is selected from $-NH_2$, $-N(H)(methyl)$, $-N(H)(2-methylpropyl)$, $-N(H)(2-acetamidoethyl)$, $-N(H)(2-aminoethyl)$, $-N(H)(2-cyanoethyl)$, $-N(H)(2-diethylamino-ethyl)$, $-N(H)(2-dimethylamino-ethyl)$, $-N(H)(2-hydroxyethyl)$, $-N(H)(2-methoxyethyl)$, $-N(H)(2-thioethyl)$, $-N(H)(3-dimethylaminopropyl)$, $-N(H)(3-hydroxypropyl)$, $-N(H)(3-methoxypropyl)$, $-N(H)(2-methylsulfonyl-ethyl)$, $-N(H)(cyclopropyl)$, $-N(H)(4-hydroxy-cyclohexyl)$, $-N(H)(1-hydroxy-cyclohexylmethyl)$, $-N(methyl)_2$, $-N(ethyl)_2$, $-N(methyl)(ethyl)$, $-N(methyl)(2-dimethylamino-ethyl)$, $-N(H)(morpholin-4-ylethyl)$, $-N(H)(pyrrolidin-1-ylethyl)$, $-N(H)(1-methyl-pyrrolidin-2-ylethyl)$, $-N(H)(pyrrolidin-1-ylpropyl)$, $-N(H)(2-oxo-pyrrolidin-1-ylpropyl)$, $-N(H)(piperidin-3-ylmethyl)$, $-N(H)(piperidin-1-ylethyl)$, $-N(H)(pyridin-2-ylmethyl)$, $-N(H)(pyridin-2-ylethyl)$, $-N(H)(pyridin-3-ylethyl)$, or $-N(H)(pyridin-4-ylethyl)$.

[0214] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^3 is selected from substituted and unsubstituted $-C(=O)$ -heterocyclyl groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, or $-CO_2H$. In some such embodiments, R^3 is selected from $-C(=O)$ -morpholin-4-yl, $-C(=O)-NH_2$, $-C(=O)-N(methyl)_2$, or $-CO_2H$.

[0215] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^4 is selected from $-H$ or $-CH_3$. In some such embodiments, R^4 is $-H$.

[0216] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^5 and R^8 are independently selected from $-H$ or saturated heterocyclyl groups, or are absent. In some such embodiments, A and D are both carbon, R^5 is $-H$, and R^8 is $-H$.

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[0217] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-S(=O)_2-NH_2$, substituted and unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted and unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-alkyl$ groups, substituted and unsubstituted $-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-C(=O)-heterocyclylalkyl$ groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O-alkyl$ groups, substituted and unsubstituted $-C(=O)-O-heterocyclyl$ groups, or substituted and unsubstituted $-C(=O)-O-heterocyclylalkyl$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen. In some such embodiments, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, or $-CH_3$.

[0218] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1

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activity in a subject, R^6 and R^7 are independently selected from substituted and unsubstituted heterocyclyl groups or substituted and unsubstituted heterocyclylalkyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0219] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted piperidinylalkyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted thiomorpholinyl groups, substituted and unsubstituted dizaepanyl groups, substituted and unsubstituted oxazepanyl groups, or pyridinylalkyl groups.

[0220] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from 3-(acetyl-methyl-amino)-pyrrolidin-1-yl, 3-diethylamino-pyrrolidin-1-yl, 3-dimethylamino-pyrrolidin-1-yl, 3-(N-oxido-N,N-dimethylamino)-pyrrolidin-1-yl, 3-(pyrrolidin-1-yl)-pyrrolidin-1-yl, 2-(pyrrolidin-1-ylmethyl)-pyrrolidin-1-yl, 4-(piperidin-1-yl)-piperidin-1-yl, 1-acetyl-piperazin-4-yl, 1-carboxymethyl-piperazin-4-yl, 1-methyl-piperazin-4-yl, 1-ethyl-piperazin-4-yl, 1-cyclohexyl-piperazin-4-yl, 1-isopropyl-piperazin-4-yl, morpholin-4-yl, 2-dimethylamino-morpholin-4-yl, 2,6-dimethyl-morpholin-4-yl, 2-dimethylamino-5-methyl-morpholin-4-yl, thiomorpholin-4-yl, thiomorpholin-4-yl 1-oxide 1-methyl-[1,4]dizaepan-1-yl, 2-dimethylaminomethyl-[1,4]oxazepan-4-yl, or pyridin-4-ylmethyl.

[0221] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted

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and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, or substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0222] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R⁶ and R⁷ are independently selected from -OH, substituted and unsubstituted alkoxyalkoxy groups, substituted and unsubstituted pyrrolidinyloxy groups, substituted and unsubstituted tetrahydrofuranyloxy groups, substituted and unsubstituted pyrrolidinylalkoxy groups, substituted and unsubstituted morpholinylalkoxy groups, substituted and unsubstituted pyridinyloxy groups, -NH₂, substituted and unsubstituted -N(H)(pyrrolidinyl) groups, substituted and unsubstituted -N(H)(piperidinyl) groups, substituted and unsubstituted -N(H)(piperidinylalkyl) groups, substituted and unsubstituted -N(H)(pyridinylalkyl) groups, or substituted and unsubstituted -N(alkyl)(piperidinyl) groups.

[0223] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R⁶ and R⁷ are independently selected from -OH, methyloxy, 2-methyloxy-ethyloxy, 4-acetamido-phenyloxy, 1-methyl-pyrrolidin-3-yloxy, pyridin-3-yloxy, 3-(pyrrolidin-1-yl)-propyloxy, tetrahydrofuran-2-ylmethyloxy, 2-(morpholin-4-yl)-ethyloxy, 3-(morpholin-4-yl)-propyloxy, -NH₂, -N(H)(2-(methyloxymethyl)-pyrrolidin-4-yl), -N(H)(piperidin-3-yl), -N(H)(1,3-dimethyl-piperidin-4-yl), -N(H)(1-(ethoxycarbonyl)-piperidin-4-yl), -N(methyl)(1-methylpiperidin-1-yl), -N(H)(piperidin-1-ylethyl), or -N(H)(pyridin-2-ylmethyl). In some such embodiments, R⁶ and R⁷ are independently selected from -H or -N(methyl)(1-methylpiperidin-1-yl).

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[0224] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from $-S(=O)_2-NH_2$, substituted and unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted and unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-alkyl$ groups, substituted and unsubstituted $-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-C(=O)-heterocyclylalkyl$ groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclylalkyl)$ groups, or $-CO_2H$; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0225] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from substituted and unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-pyrrolidinyl$ groups, substituted and unsubstituted $-C(=O)-piperidinyl$ groups, substituted and unsubstituted $-C(=O)-pyrazinyl$ groups, substituted and unsubstituted $-C(=O)-diazabicycloheptanyl$ groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(piperidinyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(pyridinyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(pyrrolidinylalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(H)(piperidinylalkyl)$ groups, or substituted and unsubstituted $-C(=O)-N(alkyl)(piperidinyl)$.

[0226] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, R^6 and R^7 are independently selected from

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-S(=O)₂-N(methyl)₂, -C(=O)-3-amino-pyrrolidin-1-yl, -C(=O)-3-(dimethylcarbamoyl)-pyrrolidin-1-yl, -C(=O)-3-hydroxy-pyrrolidin-1-yl, -C(=O)-4-dimethylamino-piperidin-1-yl, -C(=O)-3-hydroxy-piperidin-1-yl, -C(=O)-4-(piperidin-1-yl)-piperidin-1-yl, -C(=O)-pyridin-3-yl, -C(=O)-piperazin-1-yl, -C(=O)-1-acetyl-piperazin-4-yl, -C(=O)-1-cyclohexyl-piperazin-4-yl, -C(=O)-1-(ethoxycarbonylmethyl)-piperazin-4-yl, -C(=O)-1-hydroxyethyl-piperazin-4-yl, -C(=O)-1-isopropyl-piperazin-4-yl, -C(=O)-1-methyl-piperazin-4-yl, -C(=O)-2-methyl-piperazin-4-yl, -C(=O)-morpholin-4-yl, -C(=O)-2-methyl-2,5-diaza-bicyclo[2.2.1]heptan-5-yl, -C(=O)-N(methyl)(2-dimethylamino-ethyl), -C(=O)-N(ethyl)(2-dimethylamino-ethyl), -C(=O)-N(H)(piperidin-4-yl), -C(=O)-N(H)(piperidin-3-yl), -C(=O)-N(H)(1-ethoxycarbonyl-3-methoxy-piperidin-4-yl), -C(=O)-N(H)(1-aza-bicyclo[2.2.1]heptan-3-yl), -C(=O)-N(H)(2-(pyrrolidin-1-yl)-ethyl), -C(=O)-N(H)(2-(piperidin-1-yl)-ethyl), -C(=O)-N(methyl)(1-methyl-pyrrolidin-3-yl), or -C(=O)-N(methyl)(1-methyl-piperidin-4-yl).

[0227] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, B and C are both carbon and R⁶ is -H and R⁷ is -H.

[0228] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, A, B, C, and D are all carbon, and R⁵, R⁶, R⁷, and R⁸ are all -H.

[0229] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, A, B, C, and D are all carbon, and R⁴, R⁵, R⁶, R⁷, R⁸, and R¹⁰ are all -H.

[0230] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, the IC₅₀ value of the compound is less than or equal to 10

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μM with respect to CHK1. In other such embodiments, the IC_{50} value is less than or equal to $1 \mu\text{M}$, is less than or equal to $0.1 \mu\text{M}$, is less than or equal to $0.050 \mu\text{M}$, is less than or equal to $0.030 \mu\text{M}$, is less than or equal to $0.025 \mu\text{M}$, is less than or equal to $0.010 \mu\text{M}$, or is less than or equal to $0.001 \mu\text{M}$.

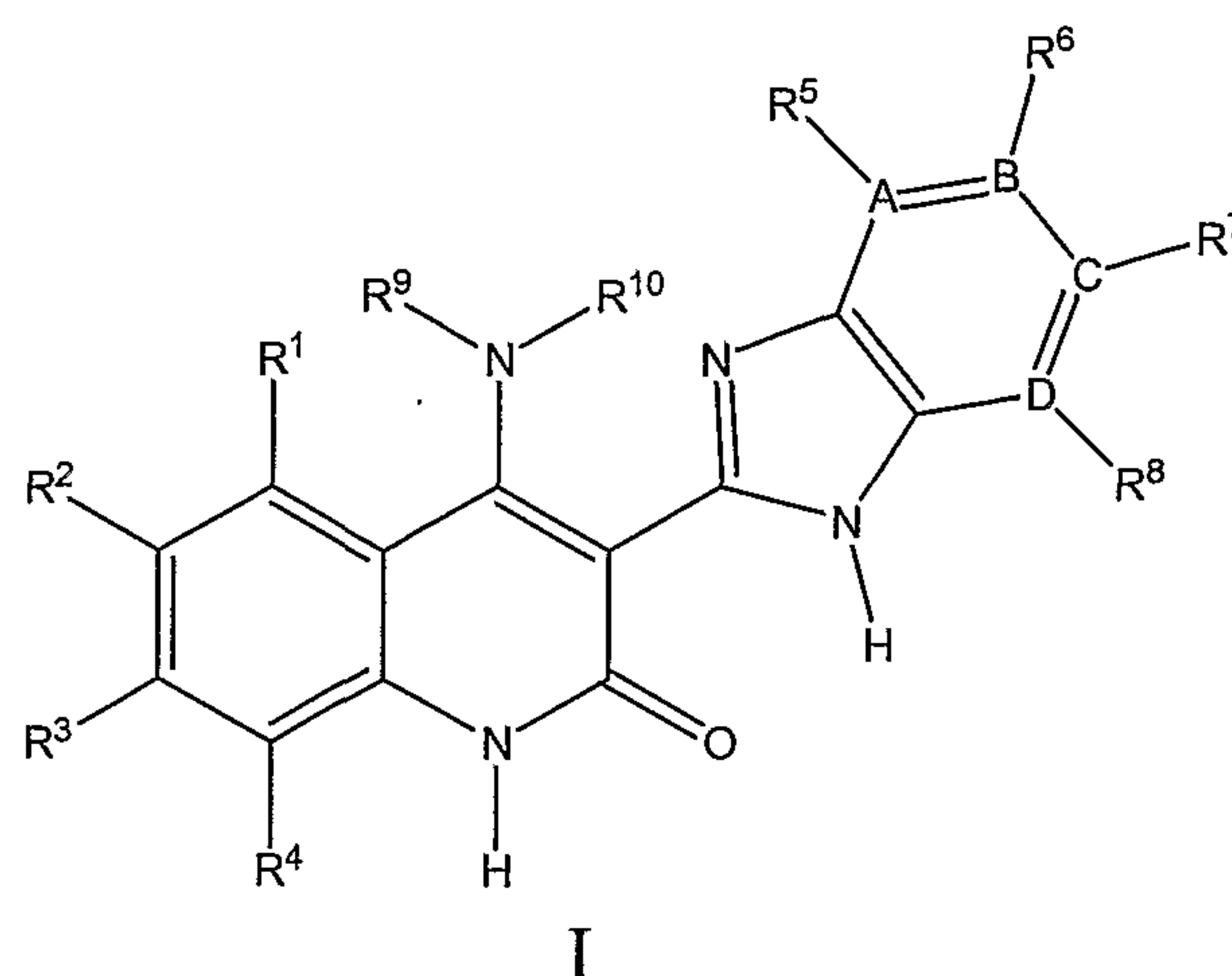
[0231] In some embodiments of the method of inhibiting CHK1 in a subject and/or the method of treating a biological condition mediated by CHK1 activity in a subject, the subject is a mammal or is a human.

[0232] In some embodiments of the method of treating a biological condition mediated by CHK1 activity in a subject, the biological condition is cancer.

Methods Relating to Ribosomal S6 Kinase 2

[0233] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the serine/threonine kinase is Rsk2. In some such methods, the Rsk2 is inhibited in the subject after administration. In methods of inhibiting Rsk2, Structure I has the following formula:

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where:

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and

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unsubstituted -C(=O)-N(alkyl)_2 groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclyl)}$ groups, $\text{-C(=O)-N(H)(heterocyclylalkyl)}$ groups, $\text{-CO}_2\text{H}$, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted $\text{-C(=O)-O-heterocyclyl}$ groups, or substituted and unsubstituted $\text{-C(=O)-O-heterocyclylalkyl}$ groups;

R^2 and R^3 are independently selected from -H , -F , -Cl , -Br , -I , -CN , -NO_2 , substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH , substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-aryl groups, substituted and unsubstituted -S-aralkyl groups, -OH , substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH_2 , substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)_2 groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted $\text{-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-N(H)(heterocyclylalkyl)}$ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted $\text{-N(H)-C(=O)-aralkyl}$ groups, substituted and unsubstituted $\text{-N(H)-C(=O)-heterocyclyl}$ groups, substituted and unsubstituted $\text{-N(H)-C(=O)-heterocyclylalkyl}$ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups, substituted and unsubstituted -C(=O)-aralkyl

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groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclalkyl) groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-aryl groups, substituted and unsubstituted -C(=O)-O-aralkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups; or R² and R³ may join together to form a cyclic group,

R⁴, R⁵, and R⁸ are independently selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen.

R⁶ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -CO₂H, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups,

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substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclyl})$ groups, $-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-O\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclylalkyl}$ groups, substituted and unsubstituted $-C(=O)\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)\text{-heterocyclyl}$ groups, substituted and unsubstituted $-C(=O)\text{-heterocyclylalkyl}$ groups, $-NH_2$, substituted and unsubstituted $-N(H)(\text{alkyl})$ groups, substituted and unsubstituted $-N(H)(\text{heterocyclyl})$ groups, substituted and unsubstituted $-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-N(H)-C(=O)\text{-alkyl}$ groups, substituted and unsubstituted $-N(H)-C(=O)\text{-heterocyclyl}$ groups, or substituted and unsubstituted $-N(H)-C(=O)\text{-heterocyclylalkyl}$ groups;

R^7 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-SH$, substituted and unsubstituted $-S\text{-alkyl}$ groups, $-CO_2H$, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(\text{alkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclyl})$ groups, $-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-O\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclylalkyl}$ groups, substituted and unsubstituted $-C(=O)\text{-alkyl}$ groups, substituted and

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unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, or substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted arylalkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl groups, substituted and unsubstituted -C(=O)-aralkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups; or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members; and

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R^{10} is $-H$, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members.

[0234] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject,

R^1 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups;

R^2 and R^3 are independently selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, or $-CO_2H$; or R^2 and R^3 may join together to form a cyclic group

R^6 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and

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unsubstituted heterocyclalkoxy groups; or R^6 may be absent if B is nitrogen;

R^7 is selected from the group consisting -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocycl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclalkoxy groups; or R^7 may be absent if C is nitrogen.

[0235] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, A, B, C, and D are all carbon.

[0236] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, of A or D is nitrogen, and B and C are both carbon.

[0237] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^{10} is -H and R^9 is selected from -H, substituted and unsubstituted alkyl groups having from 1-12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocyclalkoxy groups.

[0238] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^9 is selected from -H, substituted and unsubstituted straight or branched chain alkyl groups having from 1-12 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted

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aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocyclylalkoxy groups wherein the heterocyclyl moiety is saturated.

[0239] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^{10} is $-H$ and R^9 is selected from $-H$, unsubstituted straight or branched chain alkyl groups having from 1-12 carbon atoms, unsubstituted cycloalkyl groups, alkoxyalkyl groups, aminoalkyl groups, alkylaminoalkyl groups, dialkylaminoalkyl groups, aminocyclohexyl groups, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkoxy groups wherein the heterocyclyl moiety is saturated. In some such embodiments, R^9 is selected from pyrrolidinyl, pyrrolidinylalkyl, piperidinyl, piperidinylalkyl, quinuclidinyl, or aminocyclohexyl groups.

[0240] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^1 is selected from $-H$, $-F$, $-Cl$, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted morpholinylalkyl groups, or substituted and unsubstituted morpholinylalkoxy groups. In some such embodiments, R^1 is selected from $-H$ or $-F$. In other such embodiments, R^1 is $-H$.

[0241] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-NO_2$, $-CH_3$, $-OCH_3$, $-CO_2H$, substituted and unsubstituted aryl groups, or substituted and unsubstituted pyridinyl groups. In some such embodiments, R^2 is selected from $-H$, $-Br$, $-I$, $-CH_3$, $-CO_2H$, $-NH_2$, or 4-hydroxyphenyl.

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[0242] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^3 is selected from -H, -F, -Cl, -Br, -I, -CH₃, -OCH₃, substituted and unsubstituted imidazolyl, substituted and unsubstituted dialkylaminoalkoxy, or substituted and unsubstituted heterocyclalkoxy. In some such embodiments, R^3 is selected from -H or -F.

[0243] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^4 is -H.

[0244] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^5 is -H; or may be absent.

[0245] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^6 is selected from -H, -F, -Cl, -Me, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted morpholinylalkoxy groups, substituted and unsubstituted piperidinyl groups, or substituted and unsubstituted piperazinyl groups; or may be absent.

[0246] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, wherein R^7 is selected from -H, -F, -Me, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted piperidinyl groups, or substituted and unsubstituted piperazinyl groups; or may be absent.

[0247] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, R^8 is -H; or may be absent.

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[0248] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, the IC₅₀ value of the compound is less than or equal to 10 μ M with respect to CHK1. In other such embodiments, the IC₅₀ value is less than or equal to 1 μ M, is less than or equal to 0.1 μ M, is less than or equal to 0.050 μ M, is less than or equal to 0.030 μ M, is less than or equal to 0.025 μ M, is less than or equal to 0.010 μ M, or is less than or equal to 0.001 μ M.

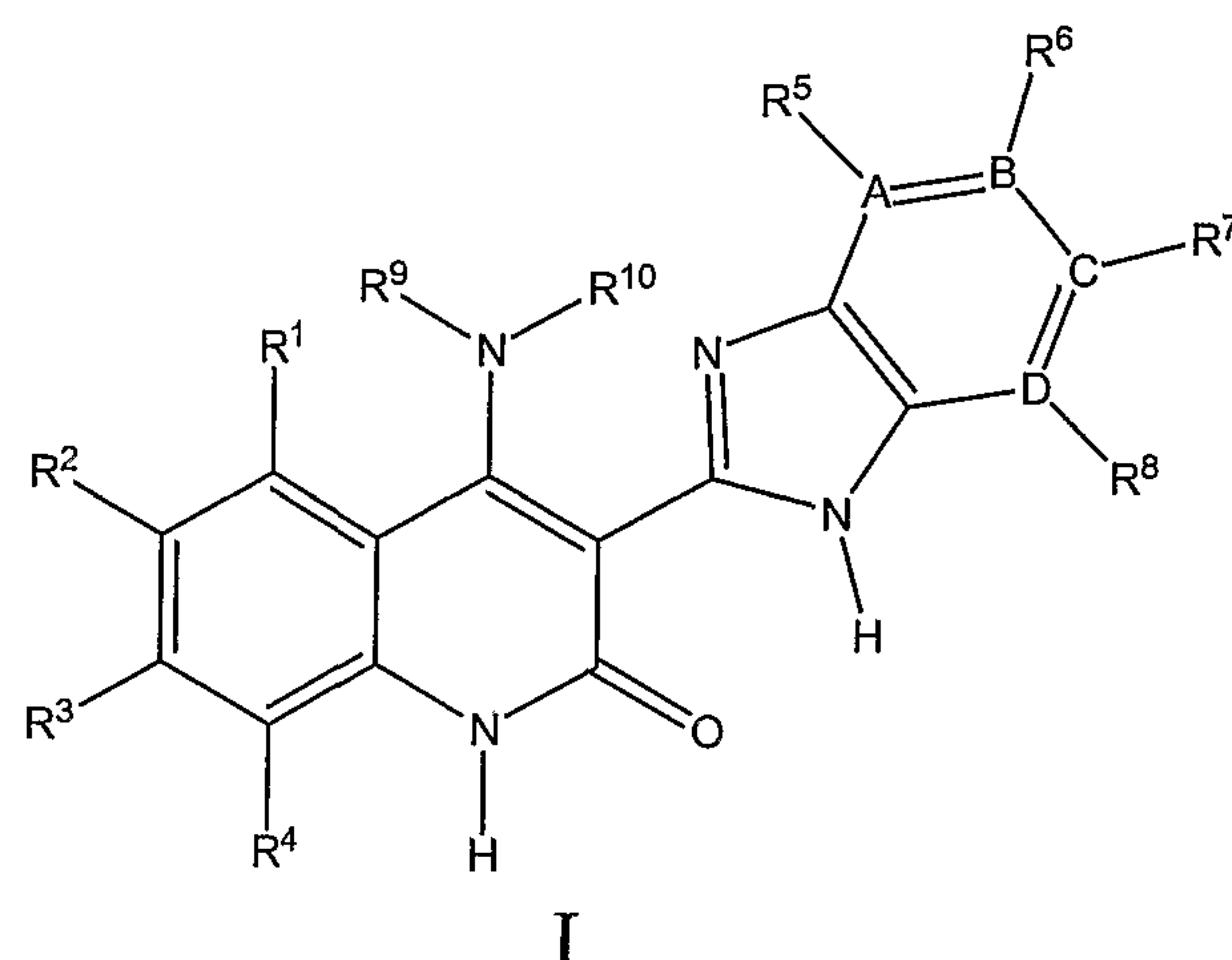
[0249] In some embodiments of the method of inhibiting Rsk2 in a subject and/or the method of treating a biological condition mediated by Rsk2 activity in a subject, the subject is a mammal or is a human.

[0250] In some embodiments of the method of treating a biological condition mediated by Rsk2 activity in a subject, the biological condition is cancer.

Methods Relating to PAR-1

[0251] In some embodiments of the method of inhibiting a serine/threonine kinase in a subject and/or the method of treating a biological condition mediated by serine/threonine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the serine/threonine kinase is PAR-1. In some such methods, the PAR-1 is inhibited in the subject after administration. In methods of inhibiting PAR-1, Structure I has the following formula:

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where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups;

R² is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, -OH, substituted and unsubstituted alkoxy, substituted and unsubstituted heterocycloxy, substituted and unsubstituted heterocyclalkoxy, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl, substituted and unsubstituted -C(=O)-aralkyl, -CO₂H, substituted and

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unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-aryl groups, or substituted and unsubstituted -C(=O)-O-aralkyl groups;

R³ is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-aryl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and

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unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocycl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocycl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl, substituted and unsubstituted -N(H)-S(=O)₂-heterocycl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl, substituted and unsubstituted -C(=O)-aralkyl, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(heterocycl)₂ groups, substituted

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and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-aryl groups, substituted and unsubstituted -C(=O)-O-aralkyl groups, substituted and unsubstituted -C(=O)-O-heterocycl groups, or substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups;

R⁴, R⁵ and R⁸ are independently selected from -H or substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocycl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocycl) groups, substituted and unsubstituted -N(alkyl)(heterocycl) groups, substituted and unsubstituted -N(heterocycl)₂ groups, substituted and unsubstituted -N(H)(heterocyclalkyl) groups, substituted and

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unsubstituted -N(alkyl)(heterocyclalkyl) groups, or substituted and unsubstituted -N(heterocyclalkyl)₂ groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbons, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocyclalkoxy groups; and

R¹⁰ is -H.

[0252] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject,

R³ is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted

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and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and

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unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen.

[0253] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, A, B, C, and D are all carbon.

[0254] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0255] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R⁹ is selected from -H, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups.

[0256] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-

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1 activity in a subject, R^9 is selected from -H, unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted aminoalkyl groups, or substituted and unsubstituted alkylsulfonylalkyl groups.

[0257] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^9 is selected from -H, unsubstituted straight or branched chain alkyl groups of 1-8 carbons, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted alkylsulfonylalkyl groups, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated.

[0258] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^9 is selected from substituted and unsubstituted methylaminoethyl groups, substituted and unsubstituted dimethylaminoethyl groups, substituted and unsubstituted methylsulfonyl groups, substituted and unsubstituted quinuclidinyl groups, substituted and unsubstituted piperazinylalkyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted piperidinylalkyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyrrolidinylalkyl groups, substituted and unsubstituted imidazolylalkyl groups, or substituted and unsubstituted cyclohexyl groups.

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[0259] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^9 is selected from -H, methylaminoethyl, dimethylaminoethyl, methylsulfonyl, 1-aminocyclohexyl, quinuclidinyl, 4-methylpiperazin-1-ylpropyl, 1-benzylpiperidinyl, piperidin-3-yl, piperidin-4-yl, piperidin-3-ylethyl, piperidin-4-ylethyl, imidazol-5-ylethyl, pyrrolidin-1-ylethyl, 1-methylpyrrolidin-2-ylethyl, or pyrrolidin-3-yl. In some such embodiments, R^9 is a quinuclidinyl group. In other such embodiments, R^9 is a quinuclidin-3-yl group. In still other such embodiments, R^9 is -H.

[0260] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^9 is selected from monocyclic, bicyclic, or polycyclic saturated heterocyclyl groups.

[0261] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^1 is selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, or substituted and unsubstituted heterocyclyl groups. In some such embodiments, R^1 is selected from -H, -F, -Cl, or substituted and unsubstituted piperazinyl. In other such embodiments, R^1 is selected from -H, -F, -Cl, or 4-ethylpiperazin-1-yl. In still other such embodiments, R^1 is -H.

[0262] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^2 is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted cycloalkyl groups,

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substituted and unsubstituted aryl groups, or substituted and unsubstituted aralkyl groups.

[0263] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^2 is selected from -H, -Cl, -F, -Br, -I, -CN, substituted and unsubstituted straight or branched chain alkyl having from 1 to 8 carbons, or substituted and unsubstituted phenyl groups.

[0264] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^2 is a substituted and unsubstituted aryl group selected from 2-amino-4-carboxymethylphenyl, 2-methylphenyl, 2-ethylphenyl, 2-methoxyphenyl, 2,4-dichlorophenyl, 2-fluoro-4-chlorophenyl, 2,6-difluorophenyl, 3-methoxyphenyl, 3-carboxyphenyl, 3-acetylphenyl, 3-acetamidophenyl, 3-methylcarboxyphenyl, 4-acetylphenyl, 4-dimethylaminophenyl, 4-cyanophenyl, 4-carboxamidophenyl, 4-carboxyphenyl, 4-methylcarboxyphenyl, 4-methylsulfonylphenyl, or phenyl.

[0265] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^2 is selected from -F, -Cl, -Br, -I, -CN, methyl, methoxy, or -CO₂H. In some such embodiments, R^2 is -Cl.

[0266] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^3 is selected from -H, -F, -Cl, -Br, -I, -CN, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and

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unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, or substituted and unsubstituted -N(H)(heterocyclalkyl) groups.

[0267] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, -I, -CN, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, -OH, unsubstituted straight or branched chain alkoxy groups, dialkylaminoalkoxy groups, or substituted and unsubstituted pyrrolidinylalkoxy groups. In some such embodiments, R³ is selected from -H, -Cl, methoxy, 2-(dimethylamino)ethyl-1-oxy, and pyrrolidin-2-ylmethoxy.

[0268] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R³ is selected from substituted and unsubstituted phenyl groups or substituted and unsubstituted unsaturated heterocycl groups. In some such embodiments, R³ is selected from 2-amino-4-carboxyphenyl, 3-acetamidophenyl, 3-carboxyphenyl, 4-carboxyphenyl, 4-methylsulfonylphenyl, 2-ethyl-imidazol-1-yl, 2-methyl-imidazol-1-yl, imidazol-1-yl, and 3-acetylpyrrol-1-yl.

[0269] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R³ is a saturated heterocycl group. In some such embodiments, R³ a saturated heterocycl group selected from substituted and unsubstituted thiomorpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted piperidinyl groups, or substituted and unsubstituted pyrrolidinyl groups. In other such embodiments,

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R^3 is selected from 3-phenylthiomorpholin-4-yl groups, morpholin-4-yl, 4-methylpiperazin-1-yl groups, 4-methylcarboxypiperidin-1-yl, piperidin-1-yl, 3-dimethylaminopyrrolidin-1-yl, or 3-acetamidopyrrolidin-1-yl.

[0270] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^3 is selected from substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, or substituted and unsubstituted -N(H)(heterocyclalkyl) groups, wherein the heterocyclalkyl moiety is saturated.

[0271] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^3 is selected from substituted and unsubstituted -N(H)(hydroxyalkyl), substituted and unsubstituted -N(H)(aminoalkyl), substituted and unsubstituted -N(H)(dialkylaminoalkyl), substituted and unsubstituted -N(H)(alkylcarboxamidoalkyl), substituted and unsubstituted -N(H)(alkoxyalkyl), substituted and unsubstituted -N(H)(arylsulfonylalkyl), substituted and unsubstituted -N(H)(alkylsulfonylalkyl), substituted and unsubstituted -N(H)(cycloalkyl), substituted and unsubstituted -N(H)(morpholinylalkyl), substituted and unsubstituted -N(H)(piperidinylalkyl), or substituted and unsubstituted -N(H)(pyrrolidinonylalkyl).

[0272] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^3 is selected from -N(H)(2-hydroxyethyl), -N(H)(2-aminoethyl), -N(H)(dimethylaminoethyl), -N(H)(2-diethylaminoethyl), -N(H)(3-dimethylaminopropyl), -N(H)(2-acetamidoethyl), -N(H)(2-methoxyethyl), -N(H)(2-(methylsulfonyl)ethyl), -N(H)(2-(phenylsulfonyl)ethyl), -N(H)(cyclopropyl), -N(methyl)(ethyl), -N(methyl)₂, -N(H)(2-morpholin-4-yl-2-phenylethyl), -N(H)(2-piperidin-1-ylethyl), or -N(H)(3-pyrrolidinon-1-ylpropyl).

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[0273] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^4 is -H.

[0274] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, A and D are both carbon, R^5 is -H, and R^8 is -H.

[0275] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen.

[0276] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -OH, or substituted and unsubstituted heterocyclylalkoxy groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen.

[0277] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, unsubstituted straight or branched chain alkyl groups having from 1 to

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8 carbon atoms, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted pyrrolidinyl groups, -OH, or pyrrolidinylalkoxy; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen. In some such embodiments, R^6 and R^7 are independently selected from -H, -F, methyl, morpholin-4-yl, 4-isopropylpiperazin-1-yl, 4-methylpiperazin-1-yl, -OH; and 3-(pyrrolidin-1-yl)propyl-1-oxy; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen. In other such embodiments, B and C are both carbon and R^6 and R^7 are both -H.

[0278] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, A, B, C, and D are all carbon, and R^5 , R^6 , R^7 , and R^8 are all -H.

[0279] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, the IC_{50} value of the compound is less than or equal to 10 μ M with respect to PAR-1. In other such embodiments, the IC_{50} value is less than or equal to 1 μ M, is less than or equal to 0.1 μ M, is less than or equal to 0.050 μ M, is less than or equal to 0.030 μ M, is less than or equal to 0.025 μ M, or is less than or equal to 0.010 μ M.

[0280] In some embodiments of the method of inhibiting PAR-1 in a subject and/or the method of treating a biological condition mediated by PAR-1 activity in a subject, the subject is a mammal or is a human.

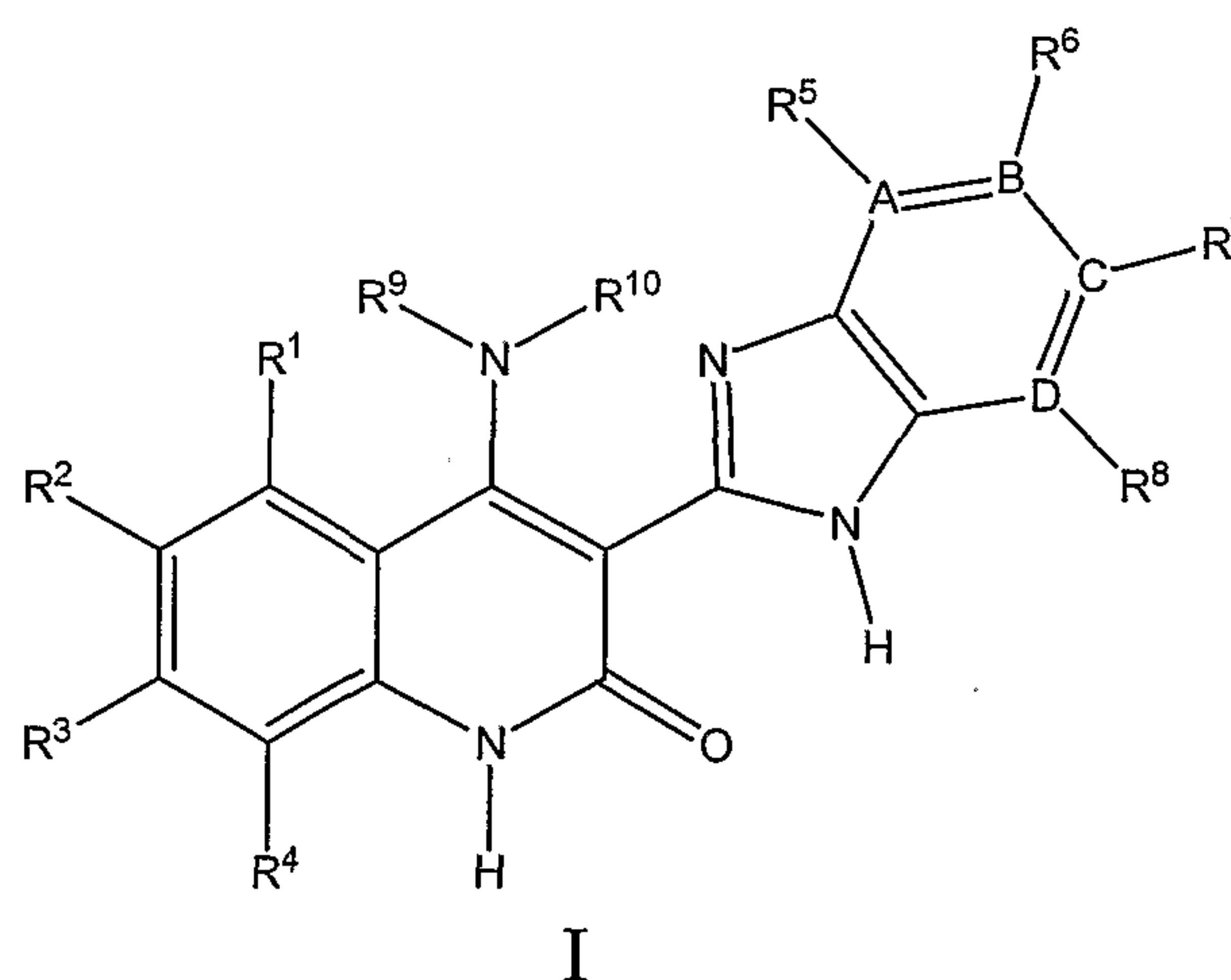
[0281] In some embodiments of the method of treating a biological condition mediated by PAR-1 activity in a subject, the biological condition is controlled by the Wnt pathway and/or is controlled by the planar cell polarity pathway. In some cases, the biological condition is cancer which in some embodiments is caused by aberrant regulation of the Wnt pathway in a mammal such as a human. Thus, in some embodiments, the invention

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provides a method of regulating the Wnt pathway in a subject. In other embodiments, the invention provides a method of modulating the Wnt β -catenin signaling.

Methods Relating to Tyrosine Kinases

[0282] In another aspect, the present invention provides a method of inhibiting a tyrosine kinase in a subject and/or a method of treating a biological condition mediated by a tyrosine kinase in a subject. The tyrosine kinase is Cdc2 kinase, Fyn, Lck, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, FLT-3, or Tie-2. In some embodiments, the tyrosine kinase is Cdc2 kinase, Fyn, Lck, or Tie-2 and in some other embodiments, the tyrosine kinase is c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3. The methods include administering to the subject a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. In the method of inhibiting a tyrosine kinase, the tyrosine kinase is inhibited in the subject after administration. Structure I has the following formula:



where,

A, B, C, and D are independently selected from carbon or nitrogen;

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R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl)

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groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclyl})_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclylalkyl})_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclyl}$ groups, or substituted and unsubstituted $-C(=O)-O\text{-heterocyclylalkyl}$ groups;

R^2 and R^3 are independently selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-NO_2$, $-CN$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-SH$, substituted and unsubstituted $-S\text{-alkyl}$ groups, substituted and unsubstituted $-S(=O)_2\text{-O-alkyl}$ groups, substituted and unsubstituted $-S(=O)_2\text{-alkyl}$ groups, substituted and unsubstituted $-S(=O)_2\text{-heterocyclyl}$ groups, $-S(=O)_2\text{-NH}_2$, substituted and unsubstituted $-S(=O)_2\text{-N(H)(alkyl)}$ groups, substituted and unsubstituted $-S(=O)_2\text{-N(alkyl)}_2$ groups, substituted and unsubstituted $-S(=O)\text{-alkyl}$ groups, substituted and unsubstituted $-S(=O)\text{-heterocyclyl}$ groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(aryl)$ groups, substituted and unsubstituted $-N(alkyl)(aryl)$ groups, substituted and unsubstituted $-N(aryl)_2$

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groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-aryl, substituted and unsubstituted -C(=O)-aralkyl, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and

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unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, C(=O)-O-aryl groups - C(=O)-O-aralkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴ is selected from -H or substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms;

R⁵ and R⁸ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having

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from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted arylalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂,

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substituted and unsubstituted $-C(=O)-N(H)(\text{alkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})(\text{heterocyclyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclyl})_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{alkyl})(\text{heterocyclylalkyl})$ groups, substituted and unsubstituted $-C(=O)-N(\text{heterocyclylalkyl})_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocyclyl}$ groups, or substituted and unsubstituted $-C(=O)-O\text{-heterocyclylalkyl}$ groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen;

R^9 is selected from $-H$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbons, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, $-NH_2$, or substituted and unsubstituted heterocyclylaminoalkyl; and

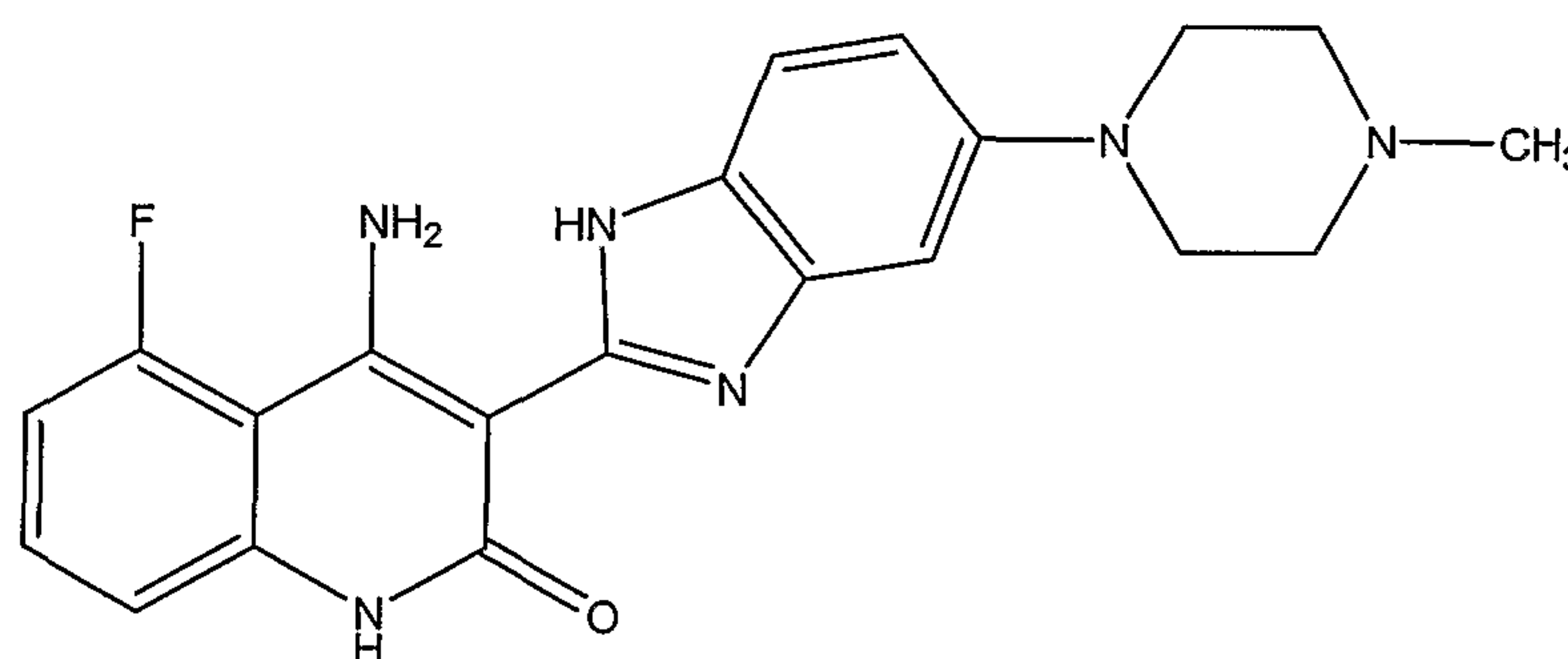
R^{10} is $-H$.

[0283] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt

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of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the tyrosine kinase is FLT-3. In other embodiments, the tyrosine kinase is c-Kit. In still other embodiments, the tyrosine kinase is c-ABL. In still other embodiments, the tyrosine kinase is FGFR3. In still other embodiments, the tyrosine kinase is p60src. In still other embodiments, the tyrosine kinase is VEGFR3. In still other embodiments, the tyrosine kinase is PDGFR α . In other embodiments, the tyrosine kinase is PDGFR β .

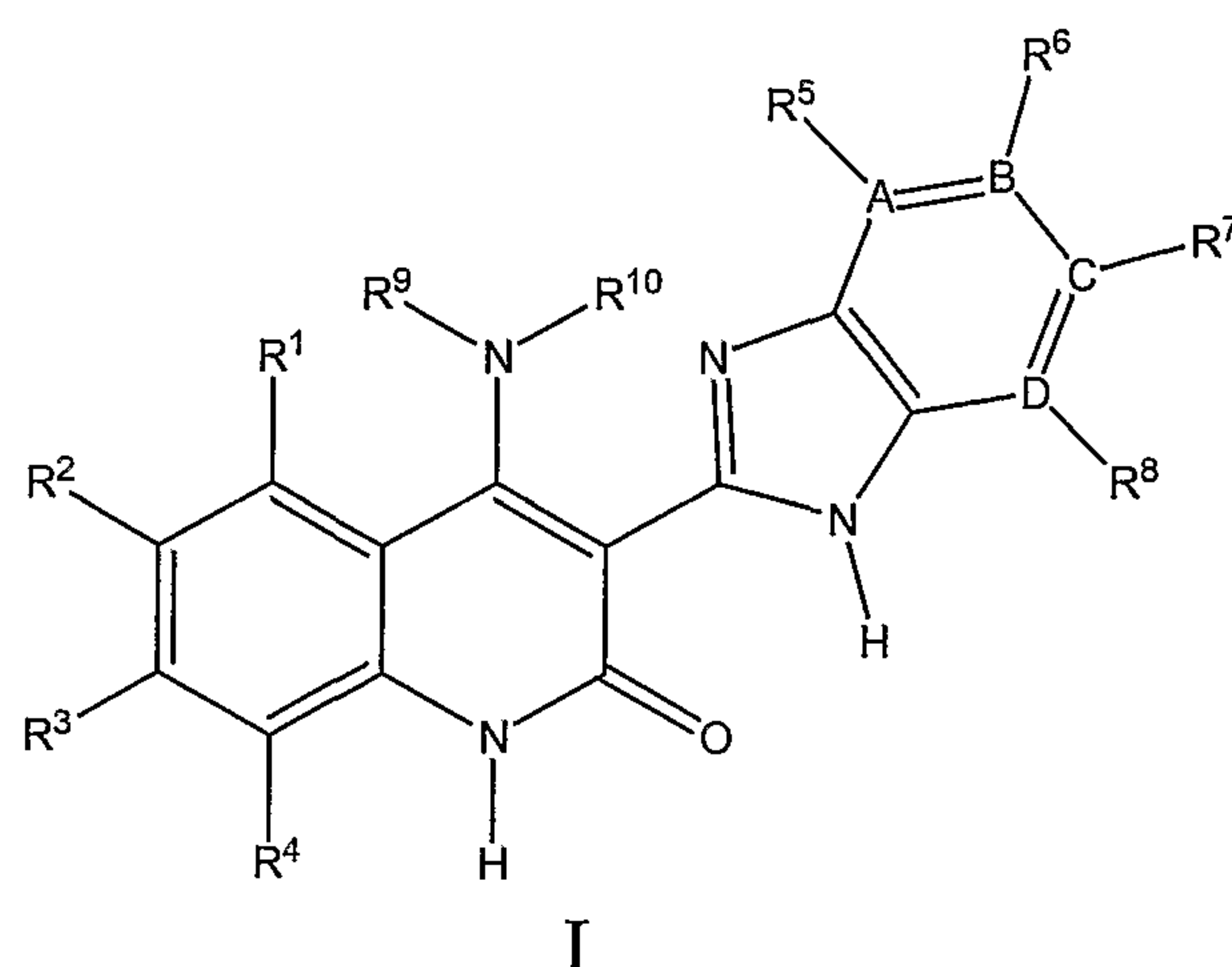
[0284] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the compound of Structure I has the following formula.



Methods Relating to Cell Division Cycle 2 Kinase

[0285] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the tyrosine kinase is Cdc2, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3. In some such methods, the Cdc2 or other kinase is inhibited in the subject after administration. In methods of inhibiting Cdc2, Structure I has the following formula:

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where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups,

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substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R² and R³ are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups,

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substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-aryl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted and unsubstituted -N(H)-C(=O)-aralkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-aryl, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted

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and unsubstituted -C(=O)-aryl, substituted and unsubstituted -C(=O)-aralkyl, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, C(=O)-O-aryl groups - C(=O)-O-aralkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴ is selected from -H or substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms;

R⁵ and R⁸ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted

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and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S-heterocyclyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups,

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substituted and unsubstituted $-C(=O)$ -heterocyclalkyl groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(heterocyclalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(heterocyclalkyl)$ groups, substituted and unsubstituted $-C(=O)-N(heterocyclalkyl)_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O-alkyl$ groups, substituted and unsubstituted $-C(=O)-O-heterocyclyl$ groups, or substituted and unsubstituted $-C(=O)-O-heterocyclalkyl$ groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen;

R^9 is selected from $-H$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbons, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, or $-NH_2$; and

R^{10} is $-H$.

[0286] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, p60src, c-ABL, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject,

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R^1 is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, or substituted and unsubstituted -N(heterocyclylalkyl)₂ groups;

R^2 and R^3 are independently selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted aryloxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(alkyl)(aryl) groups, substituted and unsubstituted -N(aryl)₂ groups, substituted and

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unsubstituted -N(H)(aralkyl) groups, substituted and unsubstituted -N(alkyl)(aralkyl) groups, substituted and unsubstituted -N(aralkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aryl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted and unsubstituted -C(=O)-N(aryl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted and unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups;

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R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(heterocyclylalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups,

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substituted and unsubstituted $-C(=O)-N(\text{heterocyclalkyl})_2$ groups, $-CO_2H$, substituted and unsubstituted $-C(=O)-O\text{-alkyl}$ groups, substituted and unsubstituted $-C(=O)-O\text{-heterocycl}$ groups, or substituted and unsubstituted $-C(=O)-O\text{-heterocyclalkyl}$ groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen.

[0287] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, A, B, C, and D are all carbon.

[0288] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0289] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R^9 is selected from -H, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted alkoxy groups, or $-NH_2$.

[0290] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a

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subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R⁹ is selected from -H, unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted hydroxyalkyl groups, -NH₂, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, or substituted and unsubstituted aminoalkyl groups.

[0291] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R⁹ is selected from -H, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted condensed unsaturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated, or substituted and unsubstituted aminoalkyl groups.

[0292] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R⁹ is selected from 4-aminomethylbenzyl groups, benzimidazolyl groups, quinuclidinyl groups, piperidinyl groups, piperidinylalkyl groups, pyrrolidinyl groups, pyrrolidinylalkyl groups, N-alkylpyrrolidinylalkyl groups, imidazolylalkyl groups, tetrahydrofuranylalkyl groups, aminocyclohexyl groups, hydroxycyclohexyl groups, or 2,2-dimethyl-

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3-aminopropyl groups. In some such embodiments, R^9 is a quinuclidinyl group. In other such embodiments, R^9 is a quinuclidin-3-yl group.

[0293] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R^9 is selected from monocyclic, bicyclic, and polycyclic saturated heterocyclyl groups.

[0294] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, VEGFR3, PDGFR α , PDGFR β , FGFR3, or FLT-3 activity in a subject, R^9 is -H.

[0295] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^1 is selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, or substituted and unsubstituted heterocyclylalkoxy groups.

[0296] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^1 is selected from -H, -F, -Cl, substituted and

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unsubstituted straight or branched chain alkoxy, substituted and unsubstituted piperidinyloxy, substituted and unsubstituted morpholinyl, or substituted and unsubstituted piperazinyl. In some such embodiments, R^1 is selected from $-H$, $-F$, $-Cl$, methoxy, N -methylpiperidin-3-yloxy, N -methylpiperidin-4-yloxy, morpholin-4-yl, N -methylpiperazin-4-yl, or N -ethylpiperazin-4-yl. In other such embodiments, R^1 is $-H$.

[0297] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-NO_2$, $-CN$, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, $-C(=O)-NH_2$, substituted and unsubstituted $-C(=O)-N(H)(aryl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(aryl)$ groups, substituted and unsubstituted $-C(=O)-N(aryl)_2$ groups, substituted and unsubstituted $-C(=O)-N(H)(aralkyl)$ groups, substituted and unsubstituted $-C(=O)-N(alkyl)(aralkyl)$ groups, substituted and unsubstituted $-C(=O)-N(aralkyl)_2$ groups, or $-CO_2H$.

[0298] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^2 is selected from $-H$, $-Cl$, $-F$, $-Br$, $-I$, $-NO_2$, $-CN$, substituted and unsubstituted straight or branched chain alkyl having from 1 to 8 carbons, substituted and unsubstituted phenyl groups, substituted and

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unsubstituted thiophene groups, substituted and unsubstituted 1,2,3,6-tetrahydropyridinyl groups, substituted and unsubstituted pyridinyl groups, substituted and unsubstituted straight or branched chain alkoxy groups, substituted and unsubstituted pyridinylalkoxy groups, substituted and unsubstituted dialkylamino groups, or $-\text{CO}_2\text{H}$.

[0299] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^2 is a substituted and unsubstituted aryl group selected from phenyl, 2-hydroxyphenyl, 2-amino-4-carboxyphenyl, 2, 6-difluorophenyl, 3-methoxyphenyl, 3-carboxyphenyl, 3-acetylphenyl, 3-aminophenyl, 3-hydroxyphenyl, 3-acetamidophenyl, 3-carboxamidophenyl, 4-cyanophenyl, 4-hydroxyphenyl, 4-methoxyphenyl, or 4-carboxyphenyl.

[0300] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^2 is selected from $-\text{H}$, $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, methyl, methoxy, or $-\text{CO}_2\text{H}$. In some such embodiments, R^2 is $-\text{CO}_2\text{H}$.

[0301] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R^3 is selected from $-\text{H}$, $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, $-\text{CN}$, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-\text{OH}$, substituted and unsubstituted

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alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, or substituted and unsubstituted -N(H)(heterocyclylalkyl) groups.

[0302] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, or VEGFR3, PDGFR α , PDGFR β , FLT-3 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, -I, -CN, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted phenyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, unsubstituted straight or branched chain alkoxy groups, dialkylaminoalkoxy groups, substituted and unsubstituted pyrrolidinylalkoxy groups, substituted and unsubstituted pyrrolidinonealkoxy, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, or substituted and unsubstituted -N(H)(pyrrolidinylalkyl) groups.

[0303] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R³ is selected from methoxy, 3-acetamidophenyl groups, 4-carboxamidophenyl groups, 4-carboxyphenyl groups, 2-alkylimidazolyl groups, N-alkylpiperazinyl groups, 3-substituted pyrrolidinyl groups, 4-carboxyamidopiperidinyl groups, dimethylamino groups, or -N(H)(cyclohexylalkyl) groups wherein the cyclohexyl moiety is substituted with hydroxy.

[0304] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a

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subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R³ is selected from -H, -F, -Cl, -Br, methoxy, and dimethylamino groups.

[0305] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R⁴ is selected from -H or -CH₃. In some such embodiments, R⁴ is -H.

[0306] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R⁵ and R⁸ are independently selected from -H, -F, -OH, or saturated heterocyclyl groups; or R⁵ is absent if A is nitrogen; or R⁸ is absent if D is nitrogen. In some such embodiments, A and D are both carbon, R⁵ is -H, and R⁸ is -H.

[0307] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and

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unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, or substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen.

[0308] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -CN, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted straight and branched chain alkoxy groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted pyrrolidinylalkoxy groups, substituted and unsubstituted tetrahydrofuranylalkoxy groups, substituted and unsubstituted morpholinylalkoxy groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(piperidinyl) groups, substituted and unsubstituted -N(alkyl)(piperidinyl) groups, substituted and unsubstituted -N(H)(piperidinylalkyl) groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen.

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[0309] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -CN, substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted piperazinyl groups, substituted and unsubstituted diazepinyl groups, substituted and unsubstituted triazolyl groups, substituted and unsubstituted thiomorpholine 1-oxide groups, substituted and unsubstituted pyridinylalkyl groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted straight and branched chain alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(alkyl)(piperidinyl) groups, substituted and unsubstituted -C(=O)-(morpholin-4-yl) groups, or substituted and unsubstituted -C(=O)-(piperazin-1-yl) groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen. In some such embodiments, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -CN, or -OH; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen. In other such embodiments, B and C are both carbon and R⁶ and R⁷ are both -H.

[0310] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3

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activity in a subject, A, B, C, and D are all carbon, and R^5 , R^6 , R^7 , and R^8 are all -H.

[0311] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, the IC₅₀ value of the compound is less than or equal to 10 μ M with respect to Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3. In other such embodiments, the IC₅₀ value is less than or equal to 1 μ M, is less than or equal to 0.1 μ M, is less than or equal to 0.050 μ M, is less than or equal to 0.030 μ M, is less than or equal to 0.025 μ M, or is less than or equal to 0.010 μ M.

[0312] In some embodiments of the method of inhibiting Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 in a subject and/or the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, the subject is a mammal or is a human.

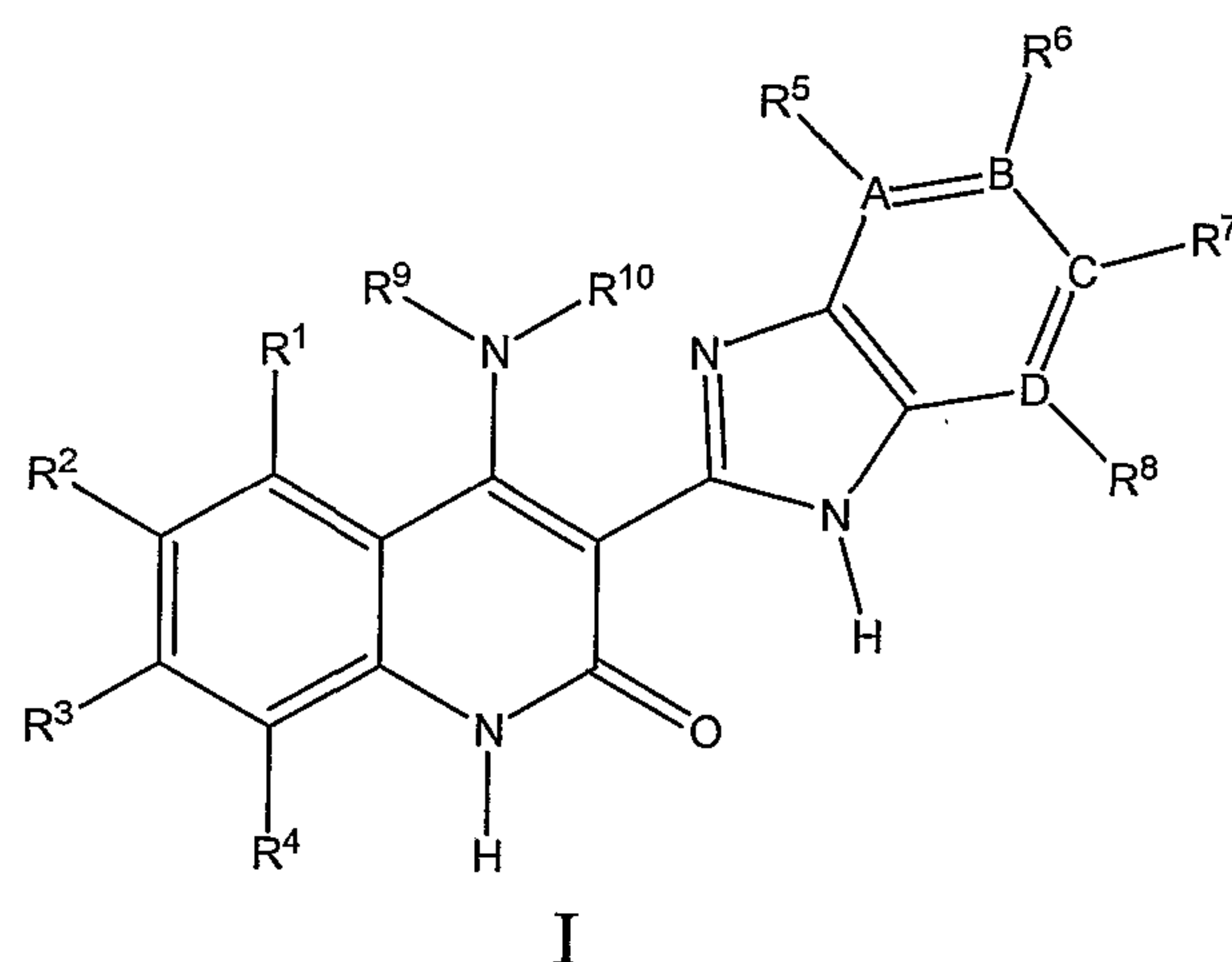
[0313] In some embodiments of the method of treating a biological condition mediated by Cdc2 kinase, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , or FLT-3 activity in a subject, the biological condition is cancer.

Methods Relating to FYN Oncogene Kinase Related to SRC, FGR, YES

[0314] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the tyrosine kinase is Fyn. In some such methods, the Fyn

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is inhibited in the subject after administration. In methods of inhibiting Fyn, Structure I has the following formula:



where:

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ and R³ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

R² is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, or substituted and unsubstituted aralkyl groups;

R⁴ is selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

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R^5 and R^8 are independently selected from $-H$ or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^6 and R^7 are independently selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-SH$, substituted and unsubstituted $-S$ -alkyl groups, $-OH$, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(heterocyclyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(heterocyclylalkyl)_2$ groups, substituted and unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted and unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-N(H)-C(=O)-heterocyclylalkyl$, substituted and unsubstituted $-N(alkyl)-C(=O)-alkyl$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-heterocyclyl$ groups, substituted and unsubstituted $-N(alkyl)-C(=O)-heterocyclylalkyl$, substituted and unsubstituted $-N(H)-S(=O)_2-alkyl$ groups, substituted and unsubstituted $-N(H)-S(=O)_2-heterocyclyl$ groups, substituted and unsubstituted $-N(H)-S(=O)_2-heterocyclylalkyl$ groups, substituted and

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unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclylalkoxy; and

R¹⁰ is -H.

[0315] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -OH, substituted and unsubstituted

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alkoxy groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy, -NH_2 , substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)_2 groups, substituted and unsubstituted $\text{-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-N(alkyl)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-N(heterocyclyl)}_2$ groups, substituted and unsubstituted $\text{-N(H)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-N(alkyl)(heterocyclylalkyl)}$ groups, substituted and unsubstituted $\text{-N(heterocyclylalkyl)}_2$ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted $\text{-N(H)-C(=O)-heterocyclyl}$ groups, substituted and unsubstituted $\text{-N(H)-C(=O)-heterocyclylalkyl}$, substituted and unsubstituted $\text{-N(alkyl)-C(=O)-alkyl}$ groups, substituted and unsubstituted $\text{-N(alkyl)-C(=O)-heterocyclyl}$ groups, substituted and unsubstituted $\text{-N(alkyl)-C(=O)-heterocyclylalkyl}$, -C(=O)-NH_2 , substituted and unsubstituted $\text{-C(=O)-N(H)(alkyl)}$ groups, substituted and unsubstituted -C(=O)-N(alkyl)_2 groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(alkyl)(heterocyclyl)}$ groups, substituted and unsubstituted $\text{-C(=O)-N(H)(heterocyclylalkyl)}$ groups, or substituted and unsubstituted $\text{-C(=O)-N(alkyl)(heterocyclylalkyl)}$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0316] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, A, B, C, and D are all carbon.

[0317] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0318] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^9 is selected from -H , substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbons,

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substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, or substituted and unsubstituted heterocycloxy groups.

[0319] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^9 is selected from $-H$, alkylaminoalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated.

[0320] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^9 is selected from $-H$, substituted and unsubstituted quinuclidinyl groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted N-alkylpiperidinyl groups, substituted and unsubstituted piperidinylalkyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted N-alkyl-pyrrolidinyl, or substituted and unsubstituted pyrrolidinylalkyl groups. In some such embodiments, R^9 is $-H$.

[0321] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^9 is selected from quinuclidin-3-yl, piperidin-3-yl, piperidin-4-yl, N-methylpiperidin-4-yl, 3-piperidinylmethyl, or pyrrolidin-3-yl.

[0322] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^1 and R^3 are independently selected from $-H$ or $-F$. In some such embodiments, R^1 is $-H$.

[0323] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, substituted and

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unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbons, or substituted and unsubstituted aryl groups. In some such embodiments, R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, substituted straight or branched chain alkyl groups having from 1 to 4 carbons, or substituted aryl groups. In other such embodiments, R^2 is selected from $-H$, $-Cl$, $-Br$, and $-I$. In still other such embodiments, R^2 is $-H$.

[0324] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^3 is $-H$.

[0325] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^3 is $-F$.

[0326] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^4 is $-H$.

[0327] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^5 is $-H$; or where B is nitrogen and R^5 is absent.

[0328] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^6 and R^7 are independently selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, $-NH_2$, substituted and unsubstituted $-N(H)(alkyl)$ groups, substituted and unsubstituted $-N(alkyl)_2$ groups, substituted and unsubstituted $-N(H)(heterocyclyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted and unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted and unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted and unsubstituted

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-N(H)-C(=O)-alkyl groups, substituted and unsubstituted
 -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocyclylalkyl, substituted and unsubstituted
 -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocyclyl groups, or substituted and unsubstituted
 -N(alkyl)-C(=O)-heterocyclylalkyl; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0329] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, or substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0330] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, wherein the heterocyclyl moiety is saturated, or substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen. In other such embodiments, R⁶ and R⁷ are independently selected from -H, -F, or -Cl; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen. In other such embodiments, B is carbon and R⁶ is -H; or C is carbon and R⁷ is -H.

[0331] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn

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activity in a subject, R^6 and R^7 are independently selected from substituted and unsubstituted piperazinyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted -N(alkyl)(piperidinyl) groups, or substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0332] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^6 and R^7 are independently selected from 4-alkylpiperazin-1-yl groups, 4-alkyl-2-alkyl-piperazin-1-yl groups, 4-alkyl-3-alkylpiperazin-1-yl groups, morpholin-4-yl groups, 2-dialkylaminoalkyl-5-alkylmorpholin-4-yl groups, 3-dialkylaminopyrrolidin-1-yl groups, 3-dialkylaminoalkylpyrrolidin-1-yl groups, -N(alkyl)(1-alkylpiperidinyl) groups, or -N(alkyl)-C(=O)-alkyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0333] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, R^6 and R^7 are independently selected from 4-methylpiperazin-1-yl groups, 4-ethylpiperazin-1-yl groups, 4-isopropylpiperazin-1-yl groups, 4-methyl-2-methylpiperazin-1-yl groups, 4-ethyl-2-methylpiperazin-1-yl groups, 4-isopropyl-2-methylpiperazin-1-yl groups, 4-cyclobutyl-2-methylpiperazin-1-yl groups, 4-methyl-3-methylpiperazin-1-yl groups, morpholin-4-yl groups, 2-dimethylaminomethyl-5-methylmorpholin-4-yl groups, 3-dimethylaminopyrrolidin-1-yl groups, 3-dimethylaminomethylpyrrolidin-1-yl groups, -N(methyl)(1-methylpiperidin-4-yl) groups, or -N(methyl)-C(=O)-methyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0334] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, the IC_{50} value of the compound is less than or equal to 10

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μM with respect to Fyn. In other such embodiments, the IC_{50} value is less than or equal to $1 \mu\text{M}$, is less than or equal to $0.1 \mu\text{M}$, is less than or equal to $0.050 \mu\text{M}$, is less than or equal to $0.030 \mu\text{M}$, is less than or equal to $0.025 \mu\text{M}$, or is less than or equal to $0.010 \mu\text{M}$.

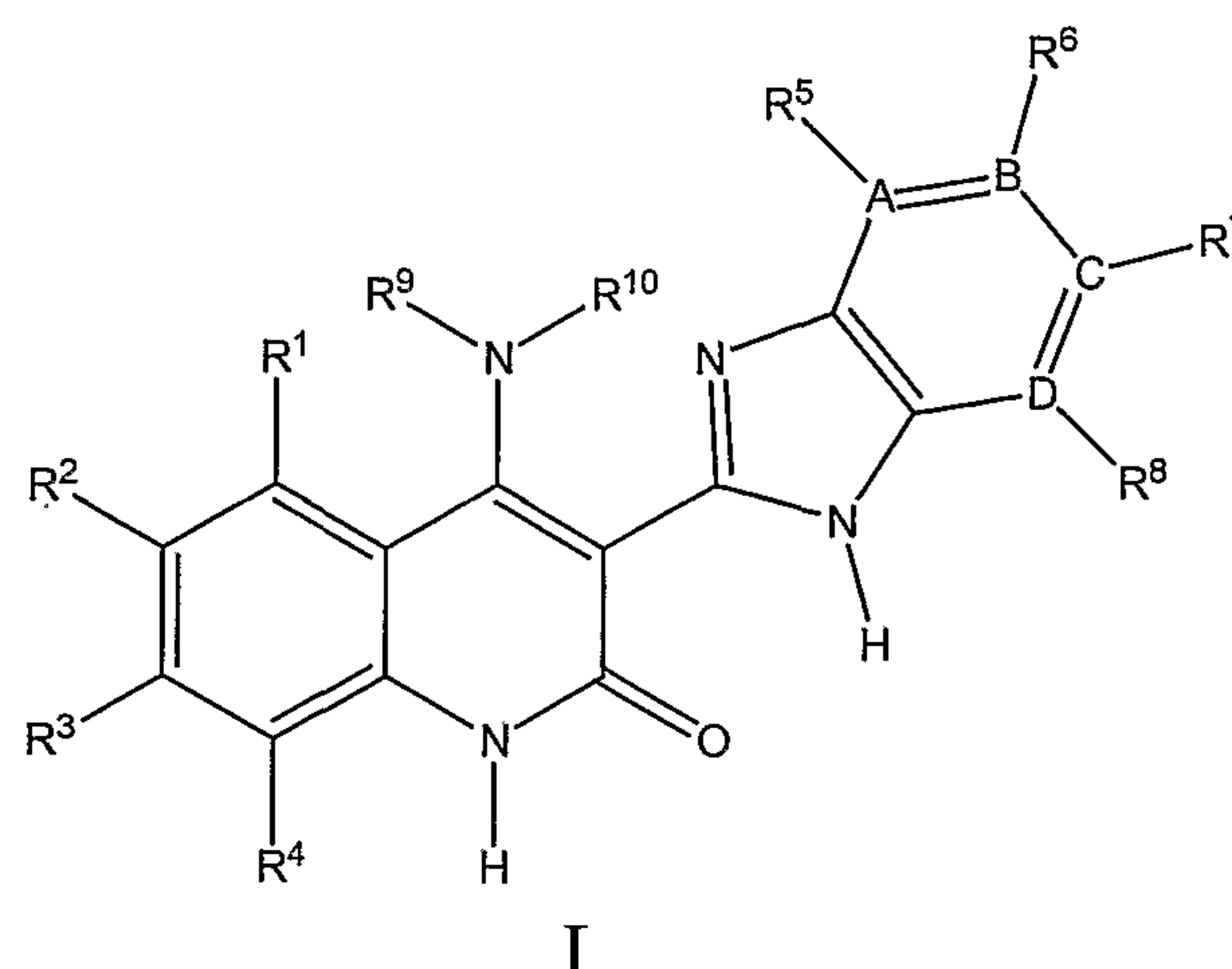
[0335] In some embodiments of the method of inhibiting Fyn in a subject and/or the method of treating a biological condition mediated by Fyn activity in a subject, the subject is a mammal or is a human.

[0336] In some embodiments of the method of treating a biological condition mediated by Fyn activity in a subject, the biological condition is an autoimmune disease, and in some such embodiments the biological condition is rheumatoid arthritis or systemic lupus erythematosus. In other such embodiments, the biological condition is organ transplant rejection.

Methods Relating to Lymphocyte-Specific Protein Tyrosine Kinase

[0337] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the tyrosine kinase is Lck. In some such methods, the Lck is inhibited in the subject after administration. In methods of inhibiting Lck, Structure I has the following formula:

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where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹, R², and R³ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

R⁴ is selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

R⁵ and R⁸ are independently selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and

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unsubstituted heterocyclalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocycl) groups, substituted and unsubstituted -N(alkyl)(heterocycl) groups, substituted and unsubstituted -N(heterocycl)₂ groups, substituted and unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocycl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocycl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocycl groups, substituted and unsubstituted -N(H)-S(=O)₂-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocycl groups, substituted and unsubstituted -N(alkyl)-S(=O)₂-heterocyclalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocycl)

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groups, substituted and unsubstituted

-C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocycl groups, or substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted alkoxy groups, or substituted and unsubstituted heterocycloxy groups; and

R¹⁰ is -H.

[0338] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁶ and R⁷ are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy, substituted and unsubstituted heterocyclalkoxy, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocycl) groups, substituted and unsubstituted -N(alkyl)(heterocycl) groups, substituted and unsubstituted -N(heterocycl)₂ groups, substituted and unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted

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-N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclalkyl, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl, -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, or substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0339] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, A, B, C, and D are all carbon.

[0340] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0341] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁹ is selected from -H, substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbons, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted heterocyclalkyl groups, or substituted and unsubstituted heterocyclalkoxy groups.

[0342] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁹ is selected from -H, aminoalkyl groups, alkylaminoalkyl groups, dialkylaminoalkyl groups, substituted and

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unsubstituted saturated heterocyclyl groups, or substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated. In some such embodiments, R⁹ is selected from quinuclidinyl groups, piperidinyl groups, N-alkylpiperidinyl groups, piperidinylalkyl groups, pyrrolidinyl groups, or pyrrolidinylalkyl groups. In other such embodiments, R⁹ -H.

[0343] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R¹ and R³ are independently selected from -H or -F. In some such embodiments, R¹ is -H.

[0344] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R² is selected from -H, -F, -Cl, -Br, -I, or substituted and unsubstituted straight or branched chain alkyl groups having from 1 to 4 carbons. In some such embodiments, R² is selected from -H, -F, -Cl, -Br, and methyl. In other such embodiments, R² is selected from -H, -Cl, and -Br. In still other such embodiments, R² is -H.

[0345] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R³ is -H.

[0346] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁴ is -H.

[0347] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, A is carbon and R⁵ is -H; or D is carbon and R⁸ is -H. In some such embodiments, both A and D are carbon and both R⁵ and R⁸ are -H.

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[0348] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(H)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, or substituted and unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0349] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, or substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

[0350] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R^6 and R^7 are independently selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 8 carbon

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atoms, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, wherein the heterocyclyl moiety is saturated, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen. In some such embodiments, R⁶ and R⁷ are independently selected from -H, -F, or -Cl; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen. In other such embodiments, B is carbon and R⁶ is -H; or C is carbon and R⁷ is -H.

[0351] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁶ and R⁷ are independently selected from substituted and unsubstituted piperazinyl groups, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted -N(alkyl)(piperidinyl) groups, or substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0352] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁶ and R⁷ are independently selected from 4-alkylpiperazin-1-yl groups, 4-alkyl-2-alkyl-piperazin-1-yl groups, 4-alkyl-3-alkylpiperazin-1-yl groups, morpholin-4-yl groups, 2-dialkylaminoalkyl-5-alkylmorpholin-4-yl groups, 3-dialkylaminopyrrolidin-1-yl groups, 3-dialkylaminoalkylpyrrolidin-1-yl groups, -N(alkyl)(1-alkylpiperidinyl) groups, or -N(alkyl)-C(=O)-alkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0353] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, R⁶ and R⁷ are independently selected from 4-methylpiperazin-1-yl groups, 4-ethylpiperazin-1-yl groups, 4-isopropylpiperazin-1-yl groups, 4-methyl-2-methylpiperazin-1-yl groups, 4-

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ethyl-2-methylpiperazin-1-yl groups, 4-isopropyl-2-methylpiperazin-1-yl groups, 4-cyclobutyl-2-methylpiperazin-1-yl groups, 4-methyl-3-methylpiperazin-1-yl groups, morpholin-4-yl groups, 2-dimethylaminomethyl-5-methylmorpholin-4-yl groups, 3-dimethylaminopyrrolidin-1-yl groups, 3-dimethylaminomethylpyrrolidin-1-yl groups, -N(methyl)(1-methylpiperidin-4-yl) groups, or -N(methyl)-C(=O)-methyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

[0354] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, the IC₅₀ value of the compound is less than or equal to 10 μ M with respect to Lck. In other such embodiments, the IC₅₀ value is less than or equal to 1 μ M, is less than or equal to 0.1 μ M, is less than or equal to 0.050 μ M, is less than or equal to 0.030 μ M, is less than or equal to 0.025 μ M, or is less than or equal to 0.010 μ M.

[0355] In some embodiments of the method of inhibiting Lck in a subject and/or the method of treating a biological condition mediated by Lck activity in a subject, the subject is a mammal or is a human.

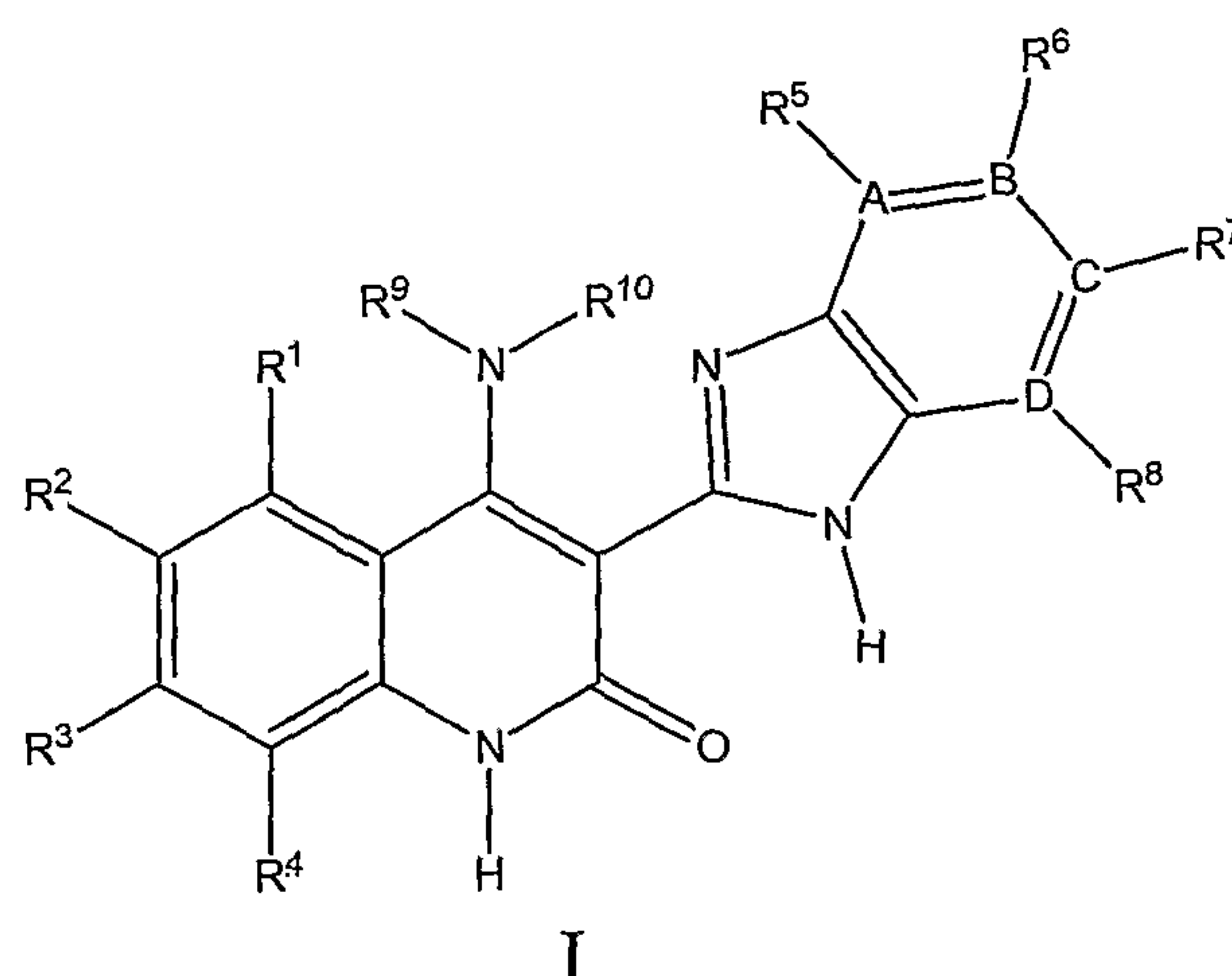
[0356] In some embodiments of the method of treating a biological condition mediated by Lck activity in a subject, the biological condition is an autoimmune disease, and in some such embodiments the biological condition is rheumatoid arthritis or systemic lupus erythematosus. In other such embodiments, the biological condition is organ transplant rejection.

Methods Relating to Tie-2

[0357] In some embodiments of the method of inhibiting a tyrosine kinase in a subject and/or the method of treating a biological condition mediated by tyrosine kinase activity in a subject using a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or

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mixtures thereof, the tyrosine kinase is Tie-2. In some such methods, the Tie-2 is inhibited in the subject after administration. In methods of inhibiting Tie-2, Structure I has the following formula:



where,

A, B, C, and D are independently selected from carbon or nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and

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unsubstituted -N(heterocyclyl)₂ groups, substituted and
 unsubstituted -N(H)-C(=O)-alkyl groups, substituted and
 unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and
 unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted
 -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted and
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted and
 unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted
 and unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted
 and unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups,
 substituted and unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl)
 groups, substituted and unsubstituted
 -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted and
 unsubstituted -C(=O)-O-alkyl groups, substituted and
 unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and
 unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R² is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and
 unsubstituted alkyl groups having from 1 to 12 carbon atoms,
 substituted and unsubstituted alkenyl groups having from 1 to 12
 carbon atoms, substituted and unsubstituted aryl groups,
 substituted and unsubstituted aralkyl groups, substituted and
 unsubstituted heterocyclyl groups, substituted and unsubstituted
 heterocyclylalkyl groups, -OH, substituted and unsubstituted
 alkoxy groups, substituted and unsubstituted heterocyclyloxy
 groups, substituted and unsubstituted heterocyclylalkoxy
 groups, -SH, substituted and unsubstituted -S-alkyl groups,
 -CO₂H, -C(=O)-NH₂, substituted and unsubstituted
 -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted
 -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted
 -C(=O)-N(H)(heterocyclyl) groups, substituted and unsubstituted

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-C(=O)-N(H)(heterocyclalkyl) groups, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclalkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(H)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(heterocyclalkyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, or substituted and unsubstituted -N(H)-S(=O)-alkyl groups; or R² and R³ may join together to form a cyclic group;

R³ and R⁴ are independently selected from -H or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms;

R⁵ is selected from -H, -F, -Cl, -Br, -I, or substituted and unsubstituted straight and branched chain alkyl groups having from 1 to 8 carbon atoms; or R⁵ may be absent if A is nitrogen;

R⁶ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted

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heterocyclalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, substituted and unsubstituted -S(=O)₂-O-alkyl groups, substituted and unsubstituted -S(=O)₂-alkyl groups, substituted and unsubstituted -S(=O)₂-heterocycl groups, substituted and unsubstituted -S(=O)-alkyl groups, substituted and unsubstituted -S(=O)-heterocycl groups, -S(=O)₂-NH₂, substituted and unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted and unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(H)(heterocycl) groups, substituted and unsubstituted -N(alkyl)(heterocycl) groups, substituted and unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(heterocycl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-C(=O)-heterocycl groups, substituted and unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-C(=O)-heterocycl groups, substituted and unsubstituted -N(H)-S(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)-heterocycl groups, substituted and unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted and unsubstituted -N(alkyl)-S(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclalkyl groups -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocycl) groups, -C(=O)-N(H)(heterocyclalkyl) groups, -CO₂H, substituted and

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unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen;

R⁷ is selected from -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, -SH, substituted and unsubstituted -S-alkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, substituted and unsubstituted heterocyclylalkoxy groups, -NH₂, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(aryl) groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclyl) groups, substituted and unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted and unsubstituted -N(alkyl)₂ groups, substituted and unsubstituted -N(heterocyclyl)₂ groups, substituted and unsubstituted -N(H)-C(=O)-alkyl groups, substituted and unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted and unsubstituted -C(=O)-alkyl groups, substituted and unsubstituted -C(=O)-heterocyclylalkyl groups -C(=O)-NH₂, substituted and unsubstituted -C(=O)-N(H)(alkyl) groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, substituted and unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl) groups, -CO₂H, substituted and unsubstituted -C(=O)-O-alkyl groups, substituted and unsubstituted -C(=O)-O-heterocyclyl groups, or substituted and

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unsubstituted -C(=O)-O-heterocyclalkyl groups; or R⁷ may be absent if C is nitrogen;

R⁸ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms; or R⁸ may be absent if D is nitrogen;

R⁹ is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted alkenyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted aryl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, -NH₂, or substituted and unsubstituted heterocyclaminoalkyl; or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members; and

R¹⁰ is -H.

[0358] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject,

R¹ is selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted heterocycl groups, substituted and unsubstituted heterocyclalkyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocycloxy groups, or substituted and unsubstituted heterocyclalkoxy groups;

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R^2 is selected from -H, -F, -Cl, -Br, -I, substituted and unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted and unsubstituted cycloalkenyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy groups, substituted and unsubstituted heterocyclylalkoxy groups;

R^6 is selected from -H, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted and unsubstituted heterocyclyl groups, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyloxy, substituted and unsubstituted heterocyclylalkoxy, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, or substituted and unsubstituted -N(alkyl)(heterocyclyl) groups; or R^6 may be absent if B is nitrogen;

R^7 is selected from -H, -Cl, -F, -Br, substituted and unsubstituted alkyl groups having from 1 to 8 carbon atoms, -OH, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted -N(H)(alkyl) groups, substituted and unsubstituted -N(H)(heterocyclyl) groups, or substituted and unsubstituted -N(alkyl)(heterocyclyl) groups,; or R^7 may be absent if C is nitrogen.

[0359] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, A, B, C, and D are all carbon.

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[0360] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, one of A or D is nitrogen, and B and C are both carbon.

[0361] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^9 is selected from $-H$, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted heterocyclylalkoxy, $-NH_2$, or substituted and unsubstituted heterocyclylaminoalkyl groups.

[0362] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^9 is selected from $-H$, substituted and unsubstituted saturated heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl groups wherein the heterocyclyl moiety is saturated, substituted and unsubstituted alkoxy groups, substituted and unsubstituted heterocyclylalkoxy groups wherein the heterocyclyl moiety is saturated, or substituted and unsubstituted heterocyclylaminoalkyl groups wherein the heterocyclyl moiety is saturated.

[0363] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^9 is selected from $-H$, substituted and unsubstituted cycloalkyl groups, substituted and unsubstituted saturated heterocyclyl groups, or substituted and unsubstituted alkoxy groups. In some such embodiments, R^9 is selected from $-H$ or quinuclidinyl. In other such embodiments, R^9 is $-H$.

[0364] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^1 is selected from $-H$, $-F$, $-Cl$, $-OCH_3$ substituted and

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unsubstituted piperidinyloxy groups, substituted and unsubstituted piperidinylalkoxy groups, substituted and unsubstituted morpholinyloxy groups, or substituted and unsubstituted morpholinylalkoxy groups. In some such embodiments, R^1 is selected from $-H$ or $-Cl$. In other such embodiments, R^1 is $-H$.

[0365] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^2 is selected from $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CH_3$, substituted and unsubstituted pyridinylalkoxy groups.

[0366] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^2 is $-H$.

[0367] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^3 is $-H$.

[0368] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^4 is $-H$.

[0369] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^5 is $-H$ or is absent if A is nitrogen.

[0370] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^6 is selected from $-H$, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted morpholinylalkoxy groups, substituted and unsubstituted pyrrolidinyl groups, substituted and unsubstituted pyrrolidinylalkoxy groups, substituted and unsubstituted piperidinyl groups, substituted and unsubstituted piperidinyloxy groups,

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substituted and unsubstituted piperazinyl groups, or substituted and unsubstituted $-S(=O)_2-N(alkyl)_2$ groups; or may be absent if B is nitrogen.

[0371] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^7 is selected from -H, -F, -Cl, substituted and unsubstituted morpholinyl groups, substituted and unsubstituted pyridinylalkyl groups, or substituted and unsubstituted piperazinyl groups; or may be absent if C is nitrogen.

[0372] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, R^8 is -H or is absent if D is nitrogen.

[0373] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, the IC_{50} value of the compound is less than or equal to 10 μM with respect to Tie-2. In other such embodiments, the IC_{50} value is less than or equal to 1 μM , is less than or equal to 0.1 μM , is less than or equal to 0.050 μM , is less than or equal to 0.030 μM , is less than or equal to 0.025 μM , or is less than or equal to 0.010 μM .

[0374] In some embodiments of the method of inhibiting Tie-2 in a subject and/or the method of treating a biological condition mediated by Tie-2 activity in a subject, the subject is a mammal or is a human.

[0375] In some embodiments of the method of treating a biological condition mediated by Tie-2 activity in a subject, the biological condition is cancer.

[0376] In some embodiments of the method of treating a biological condition mediated by serine/threonine kinase or tyrosine kinase activity in a subject, the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or

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mixtures thereof, is a component of a pharmaceutical formulation or a medicament that includes a pharmaceutically acceptable carrier. In some such embodiments the serine/threonine kinase or tyrosine kinase activity is selected from FLT-1, VEGFR2, VEGFR3, FGFR1, GSK-3, Cdk2, NEK-2, CHK1, Rsk2, PAR-1, Cdc2, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Fyn, Lck, Tie-2, PDGFR α , or PDGFR β activity. In other such embodiments, the serine/threonine kinase or tyrosine kinase activity is selected from GSK-3, Cdk2, CHK1, Rsk2, PAR-1, Cdc2, c-Kit, c-ABL, p60src, FGFR3, VEGFR3, PDGFR α , PDGFR β , FLT-3, Fyn, Lck, or Tie-2 activity. In another such embodiment the serine/threonine kinase activity is CHK1 activity.

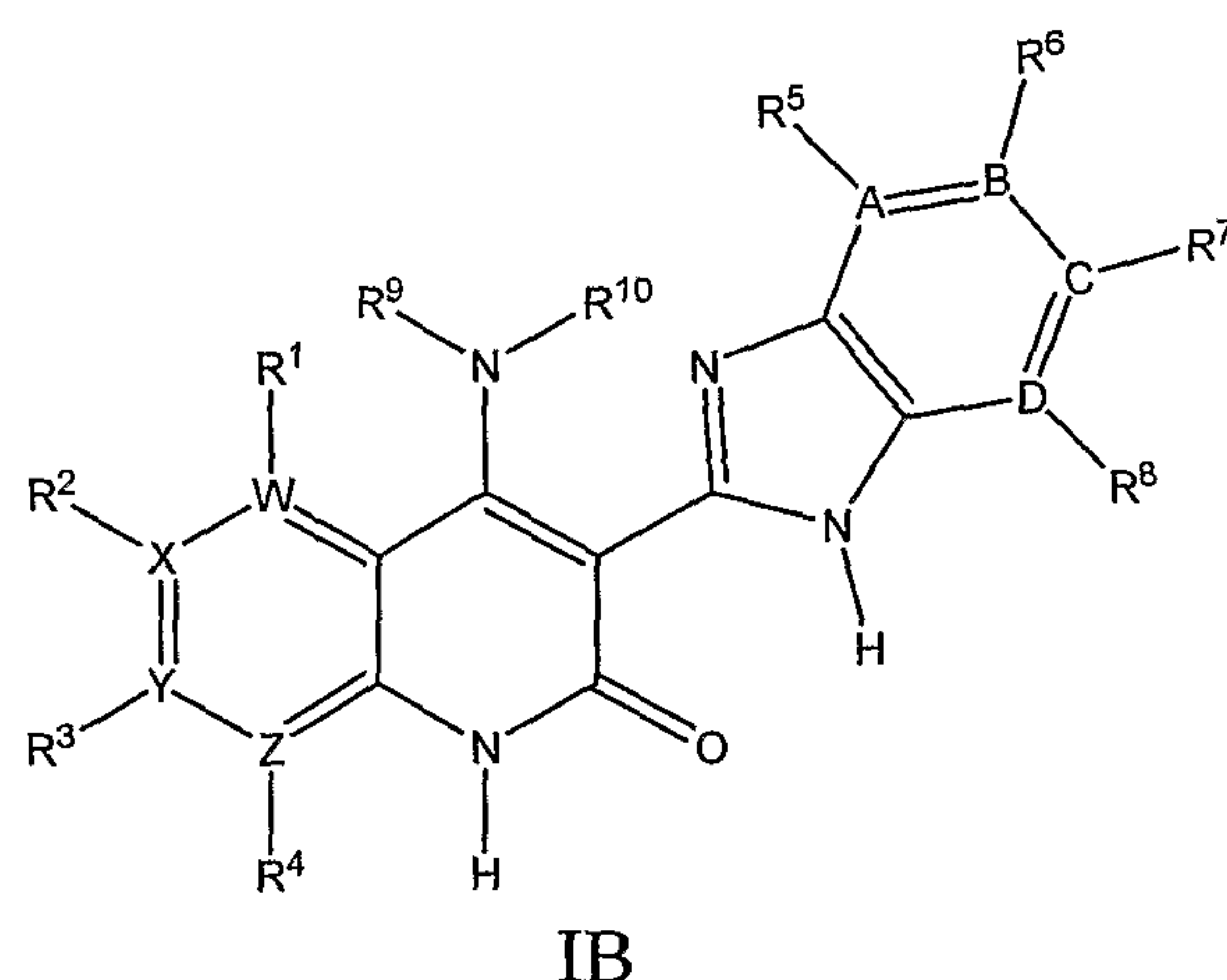
[0377] In other aspects, the invention provides compounds of Structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, pharmaceutically acceptable salts of the tautomers, and mixtures thereof. The invention also provides compounds having any of the R¹ through R¹⁰ values described in the various embodiments described above.

[0378] The invention further provides the use of the compounds of Structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, pharmaceutically acceptable salts of the tautomers, and mixtures thereof in the preparation of medicaments, and in treatment of biological conditions mediated by FLT-1, VEGFR2, VEGFR3, FGFR1, GSK-3, Cdk2, NEK-2, CHK1, Rsk2, PAR-1, Cdc2, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Fyn, Lck, Tie-2, PDGFR α , or PDGFR β activity.

[0379] The present invention further provides methods of inhibiting GSK-3 and treating biological conditions mediated by GSK-3 in a subject using a compound of Structure IB. The invention also provides the use of a compound of Structure IB in preparing a medicament for use in inhibiting GSK-3 in a subject and/or for use in treating a biological condition mediated by GSK-3. In one aspect, a method of inhibiting GSK-3 or treating a biological condition mediated by GSK-3 includes administering to the subject a compound of Structure IB, a tautomer of the compound, a pharmaceutically

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acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof. The invention further provides methods of inhibiting any of the other kinases described herein and methods of treating any of the biological conditions mediated by such kinases using the compounds of Structure IB. In some embodiments, GSK-3 is inhibited in the subject after administration. Structure IB has the following formula:



where:

A, B, C, and D are independently selected from carbon or nitrogen;

W, X, Y, and Z are independently selected from the group consisting of carbon and nitrogen and at least one of W, X, Y, and Z is a nitrogen;

R¹ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted

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-S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted
 -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or
 unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted
 -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl
 groups; or R¹ may be absent if W is nitrogen;

R² is selected -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, -CO₂H, -OH,
 substituted or unsubstituted straight or branched chain alkyl
 groups having from 1 to 8 carbon atoms, substituted or
 unsubstituted cycloalkenyl groups, substituted or unsubstituted
 cycloalkyl groups, substituted or unsubstituted alkoxy groups,
 substituted or unsubstituted -N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted
 heterocyclyl groups, substituted or unsubstituted aryl groups,
 substituted or unsubstituted alkenyl groups having from 1 to 8
 carbon atoms, substituted or unsubstituted alkynyl groups
 having from 1 to 8 carbon atoms, -SH, substituted or
 unsubstituted -S-alkyl groups, substituted or unsubstituted
 -S(=O)₂-O-alkyl groups, substituted or unsubstituted
 -S(=O)₂-alkyl groups, substituted or unsubstituted
 -S(=O)₂-heterocyclyl groups, substituted or unsubstituted
 -S(=O)-alkyl groups, substituted or unsubstituted
 -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or
 unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted
 or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or

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unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted
 -C(=O)-heterocyclyl groups, substituted or unsubstituted
 -C(=O)-O-alkyl groups, substituted or unsubstituted
 -N(H)-C(=O)-alkyl groups, substituted or unsubstituted
 -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted
 -N(H)-S(=O)-alkyl groups, substituted or unsubstituted
 -N(H)-S(=O)-heterocyclyl groups, -N(alkyl)-C(=O)-alkyl groups,
 substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups,
 substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups,
 substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups,
 -N(H)-C(=O)-NH₂, substituted or unsubstituted
 -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted
 -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted
 or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, or
 substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups; or
 R² and R³ may join together to form a cyclic group when X and
 Y are both carbon; or R² may be absent if X is nitrogen;

R³ is selected from -H, -F, -Cl, -Br, -I, -OH, substituted or
 unsubstituted straight or branched chain alkyl groups having
 from 1 to 8 carbon atoms, substituted or unsubstituted alkoxy
 groups, -CO₂H, -CN, substituted or unsubstituted -N(H)(alkyl)
 groups, substituted or unsubstituted -N(H)(cycloalkyl) groups,
 substituted or unsubstituted -N(alkyl)₂ groups, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted
 aryl groups, substituted or unsubstituted -C(=O)-heterocyclyl
 groups, substituted or unsubstituted -C(=O)-alkyl groups,
 substituted or unsubstituted -C(=O)-N(H)(alkyl) groups,
 substituted or unsubstituted -C(=O)-N(alkyl)₂ groups,
 -C(=O)-NH₂ groups, substituted or unsubstituted
 -C(=O)-N(H)(heterocyclyl) groups, substituted or unsubstituted
 -C(=O)-N(H)(aryl) groups, substituted or unsubstituted alkenyl

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groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -NO₂, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, or substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups; or R² and R³ may join together to form a cyclic group when X and Y are both carbon; or R³ may be absent if Y is nitrogen;

R⁴ is selected from of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms,

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-CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R⁴ may be absent if Z is nitrogen;

R⁵ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted

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-N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R⁵ may be absent if A is nitrogen;

R⁶ is selected from -H, -Cl, -F, -Br, -OH, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups,

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substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups; or R⁶ may be absent if B is nitrogen;

R⁷ is selected from -H, -Cl, -F, -Br, -OH, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-heterocyclyl groups,

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substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, or substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups; or R⁷ may be absent if C is nitrogen;

R⁸ is selected from -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkenyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 1 to 8 carbon atoms, -CN, -NO₂, -OH, -SH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-O-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, or substituted or unsubstituted -N(H)-S(=O)-alkyl groups; or R⁸ may be absent if D is nitrogen;

R⁹ is selected from substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkoxy groups, -NH₂, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members; or

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R^{10} is -H, or R^9 and R^{10} join together to form a ring having 5, 6, or 7 ring members.

[0380] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof,

R^1 is selected from -H, -F, -Cl, -Br, -I, or straight or branched chain alkyl groups having from 1 to 8 carbon atoms; or R^1 may be absent if W is nitrogen

R^2 is selected from -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, -CO₂H, -OH, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkenyl groups, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, or substituted or unsubstituted aryl groups; or R^2 may be absent if X is nitrogen;

R^3 is selected from -H, -F, -Cl, -Br, -I, -OH, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkoxy groups, -CO₂H, -CN, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(cycloalkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted

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-C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, or substituted or unsubstituted -C(=O)-N(H)(aryl) groups; or R³ may be absent if Y is nitrogen;

R⁴ is selected from -H, -F, -Cl, -Br, -I, or straight or branched chain alkyl groups having from 1 to 8 carbon atoms; or R⁴ may be absent if Z is nitrogen;

R⁵ is selected from -H, -F, -Cl, -Br, -I, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or substituted or unsubstituted heterocyclyl groups; or R⁵ may be absent if A is nitrogen;

R⁶ is selected from -H, -Cl, -F, -Br, -OH, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted alkoxy groups, or substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms; or R⁶ may be absent if B is nitrogen;

R⁷ is selected from -H, -Cl, -F, -Br, -OH, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted alkoxy groups, or substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms; or R⁷ may be absent if C is nitrogen; and

R⁸ is selected from -H, -F, -Cl, -Br, -I, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or substituted or

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unsubstituted heterocyclyl groups; or R⁸ may be absent if D is nitrogen.

[0381] In some embodiments of the method of inhibiting GSK-3 using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, A, B, C, and D are all carbon. In some such embodiments, R⁵ is -H, R⁶ is -H, R⁷ is -H, and R⁸ is -H

[0382] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, one of A or D is nitrogen, and B and C are both carbon.

[0383] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, W is nitrogen. In some such embodiments, X, Y, and Z are all carbon.

[0384] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, X is nitrogen. In some such embodiments, W, Y, and Z are all carbon.

[0385] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a

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pharmaceutically acceptable salt of the tautomer, or mixtures thereof, Y is nitrogen. In some such embodiments, W, X, and Z are all carbon.

[0386] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, Z is nitrogen. In some such embodiments, W, X, and Y are all carbon.

[0387] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, two of W, X, Y, and Z are nitrogen atoms. In some such embodiments, X and Z are nitrogen atoms and W and Y are carbon atoms.

[0388] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R¹⁰ is – H and R⁹ is selected from substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkoxy groups, –NH₂, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms.

[0389] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a

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pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^9 is selected from substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, unsubstituted alkoxy groups, $-NH_2$, substituted or unsubstituted cycloalkyl groups, unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclylalkyl groups wherein the heterocyclyl group is saturated, substituted or unsubstituted heterocyclylalkyl groups wherein the heterocyclyl group is unsaturated, substituted or unsubstituted aralkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted alkyl-(SO_2)-alkyl groups.

[0390] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^{10} is $-H$ and R^9 is selected from substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted heterocyclylalkyl groups.

[0391] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^9 is selected from quinuclidinyl groups, piperidinyl groups, pyrrolidinyl groups, and aminocyclohexyl groups. In some such embodiments, R^9 is a quinuclidinyl group and in some such embodiments, R^9 is a quinuclidin-3-yl group.

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[0392] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R⁹ is selected from monocyclic, bicyclic, or polycyclic saturated heterocyclyl groups.

[0393] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R¹ is selected from -H, -F, -Cl, or -CH₃ groups. In some such embodiments, R¹ is -H or -F. In other such embodiments, R¹ is -H.

[0394] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R² is selected from -H, -Cl, -F, -Br, -I, -CH₃, -NO₂, -OMe, -CN, -CO₂H, substituted or unsubstituted 1,2,3,6-tetrahydropyridine groups, substituted or unsubstituted thiophene groups, substituted or unsubstituted imidazole groups, substituted or unsubstituted 3-pyridyl groups, substituted or unsubstituted 4-pyridyl groups, 2-substituted phenyl groups, 2,4-disubstituted phenyl groups, 4-substituted phenyl groups, 3-substituted phenyl groups, 2,6-disubstituted phenyl groups, phenyl, substituted or unsubstituted dialkylamino groups, or substituted or unsubstituted alkylamino groups. In some such embodiments, R² is selected from -H, -Cl, -F, or -CH₃. In other such embodiments, R² is -F.

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[0395] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^2 is a substituted or unsubstituted aryl group selected from phenyl, 2-chlorophenyl, 2-methylphenyl, 2-ethylphenyl, 2-hydroxyphenyl, 2-methoxyphenyl, 2-trifluoromethylphenyl, 3-methoxyphenyl, 3-nitrophenyl, 3-carboxyphenyl, 3-acetylphenyl, 3-aminophenyl, 3-hydroxyphenyl, 3-acetamidophenyl, 3-carbomethoxyphenyl, 3-trifluoromethylphenyl, 3-ureidophenyl, 4-chlorophenyl, 4-cyanophenyl, 4-hydroxyphenyl, 4-nitrophenyl, 4-ethylphenyl, 4-methylphenyl, 4-methoxyphenyl, 4-acetylphenyl, 4-acetamidophenyl, 4-carboxyphenyl, 4-formylphenyl, 4-methylthiophenyl, 4-dimethylaminophenyl, 4-carbomethoxyphenyl, 4-carboethoxyphenyl, 4-carboxamidophenyl, 4-(methylsulfonyl)phenyl, 4-trifluoromethylphenyl, 2,4-difluorophenyl, 2-fluoro-4-chlorophenyl, 2,4-dichlorophenyl, 2-amino-4-carbomethoxyphenyl, 2-amino-4-carboxyphenyl, 2,6-difluorophenyl, or 3,4-(methylenedioxy)phenyl.

[0396] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^4 is $-H$ or $-CH_3$. In some such embodiments, R^4 is $-H$.

[0397] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^5 and R^8 are independently selected from $-H$, or saturated heterocyclyl groups, or are absent. In some such embodiments, R^5 and R^8 are independently

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selected from -H or saturated heterocyclyl groups. In some such embodiments R^5 is -H and R^8 is -H.

[0398] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^6 and R^7 are independently selected from -H, -F, -Cl, -OH, or substituted or unsubstituted heterocyclyl groups. In some such embodiments, R^6 is -H and R^7 is -H.

[0399] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^5 is -H, R^6 is -H, R^7 is -H, and R^8 is -H.

[0400] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^3 is selected from -H, -F, -Cl, -Br, -CH₃, -OH, -CN, substituted or unsubstituted alkoxy groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, or -C(=O)-NH₂ groups.

[0401] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-

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3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^3 is selected from -H, -F, -Cl, -Br, -CH₃, -CN, -OMe, hydroxyalkylamino groups, dialkylamino groups, dialkylaminoalkylamino groups, alkoxyalkylamino groups, substituted or unsubstituted heterocyclalkylamino groups, acetamidoalkylamino groups, cyanoalkylamino groups, alkoxyalkylamino groups, thioalkylamino groups, (methylsulfonyl)alkylamino groups, cycloalkylalkylamino groups, dialkylaminoalkoxy groups, heterocyclalkoxy groups, substituted or unsubstituted piperidiny groups, substituted or unsubstituted imidazolyl groups, substituted or unsubstituted morpholiny groups, substituted or unsubstituted pyrroly groups, substituted or unsubstituted pyrrolidiny groups, substituted or unsubstituted piperaziny groups, substituted or unsubstituted aryl groups, substituted or unsubstituted -C(=O)-heterocycl groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, or -C(=O)-NH₂ groups. In some embodiments, R^3 is selected from -H, -F, -Cl, -Br, -CH₃, -OH, -CN, substituted and unsubstituted alkoxy groups, substituted and unsubstituted alkylamino groups, substituted and unsubstituted dialkylamino groups, substituted and unsubstituted heterocycl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted -C(=O)-heterocycl groups, substituted and unsubstituted -C(=O)-N(alkyl)₂ groups, and -C(=O)-NH₂ groups.

[0402] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^3 is selected from substituted or unsubstituted alkylamino groups or substituted or unsubstituted dialkylamino groups. In some such embodiments, R^3 is a dimethylamino group.

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[0403] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, R^4 , R^5 , R^6 , R^7 , R^8 , and R^{10} are all $-H$.

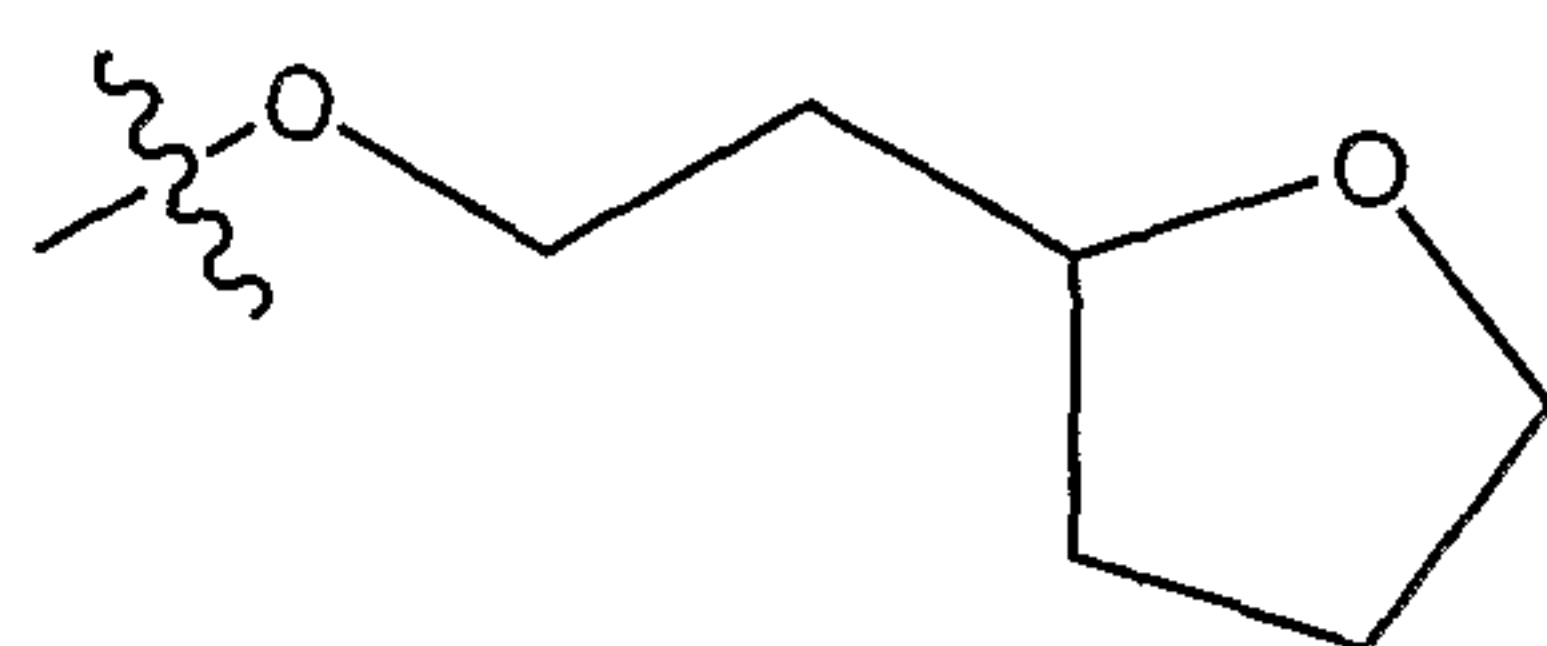
[0404] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the IC_{50} value of the compound is less than or equal to $10\ \mu M$ with respect to GSK-3. In other such embodiments, the IC_{50} value is less than or equal to $1\ \mu M$, is less than or equal to $0.1\ \mu M$, is less than or equal to $0.050\ \mu M$, is less than or equal to $0.030\ \mu M$, is less than or equal to $0.025\ \mu M$, or is less than or equal to $0.010\ \mu M$.

[0405] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or mixtures thereof, the subject is a mammal, and in some embodiments is a human.

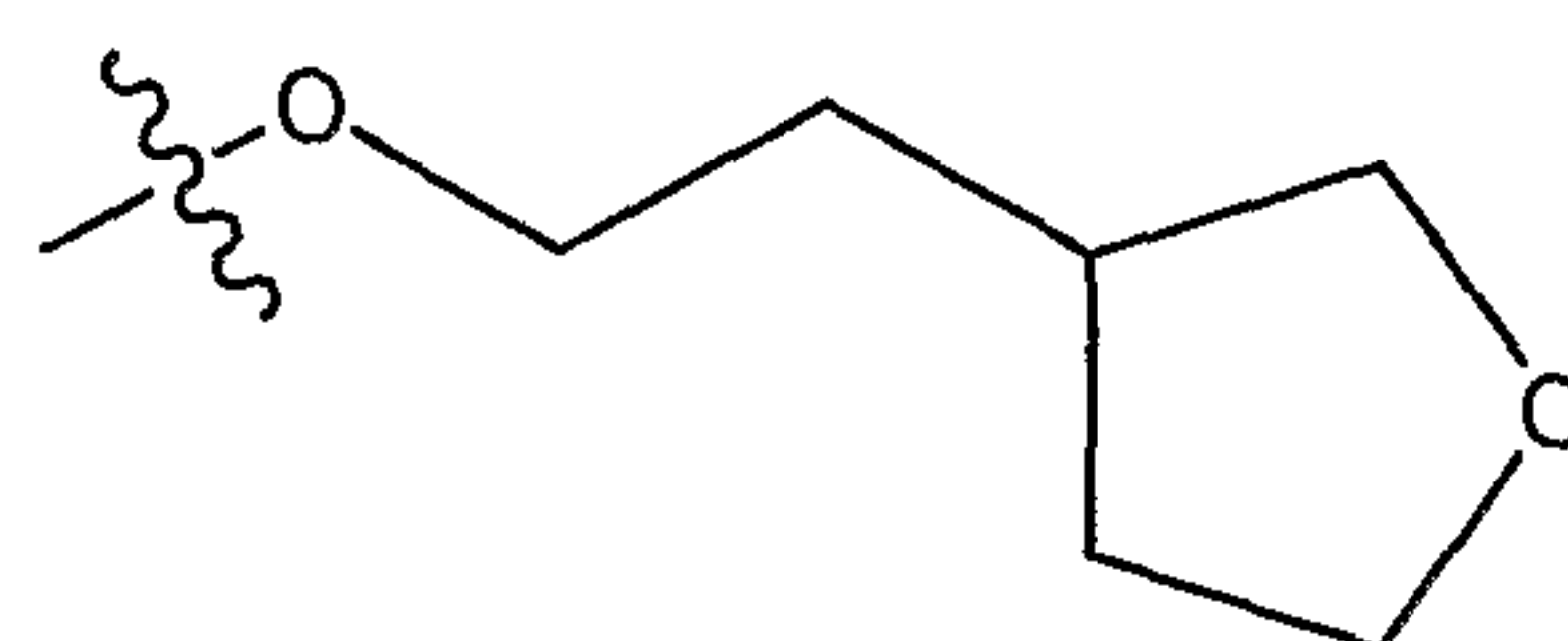
[0406] In some embodiments of the method of inhibiting GSK-3 in a subject and/or the method of treating a biological condition mediated by GSK-3 activity in a subject using a compound of Structure IB, the biological condition is diabetes, and in some such embodiments the biological condition is noninsulin dependent diabetes mellitus (NIDDM). In other such embodiments, the biological condition is Alzheimer's disease or is bipolar disorder.

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[0407] In groups including heterocyclyl groups, the heterocyclyl group may be attached in various ways. For example, in a heterocyclalkoxy group, the heterocyclyl group may be bonded to a methylene carbon of the alkoxy group of the heterocyclalkoxy group through various ring members. By way of non-limiting example, where the heterocyclyl group of the heterocyclalkoxy group is tetrahydrofuran, the group could be represented by the formula $-\text{OCH}_2\text{CH}_2(\text{tetrahydrofuranyl})$ which corresponds to the following two structures:



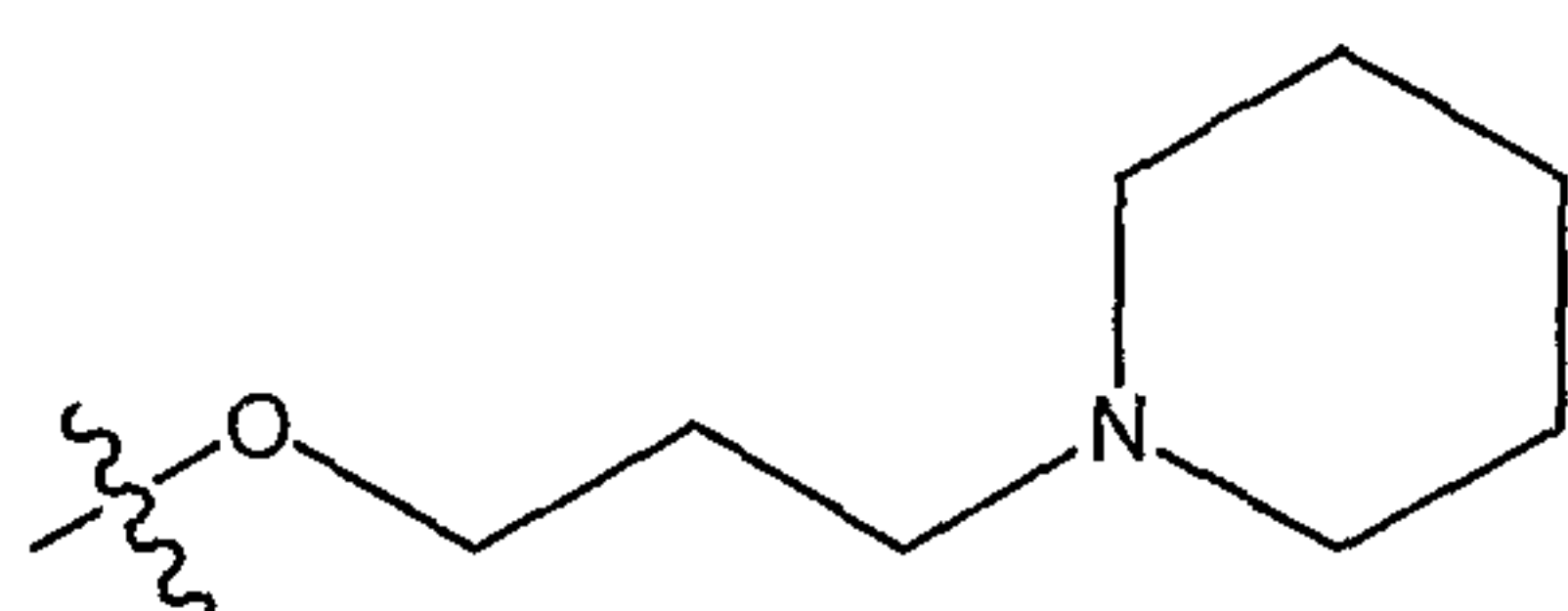
II



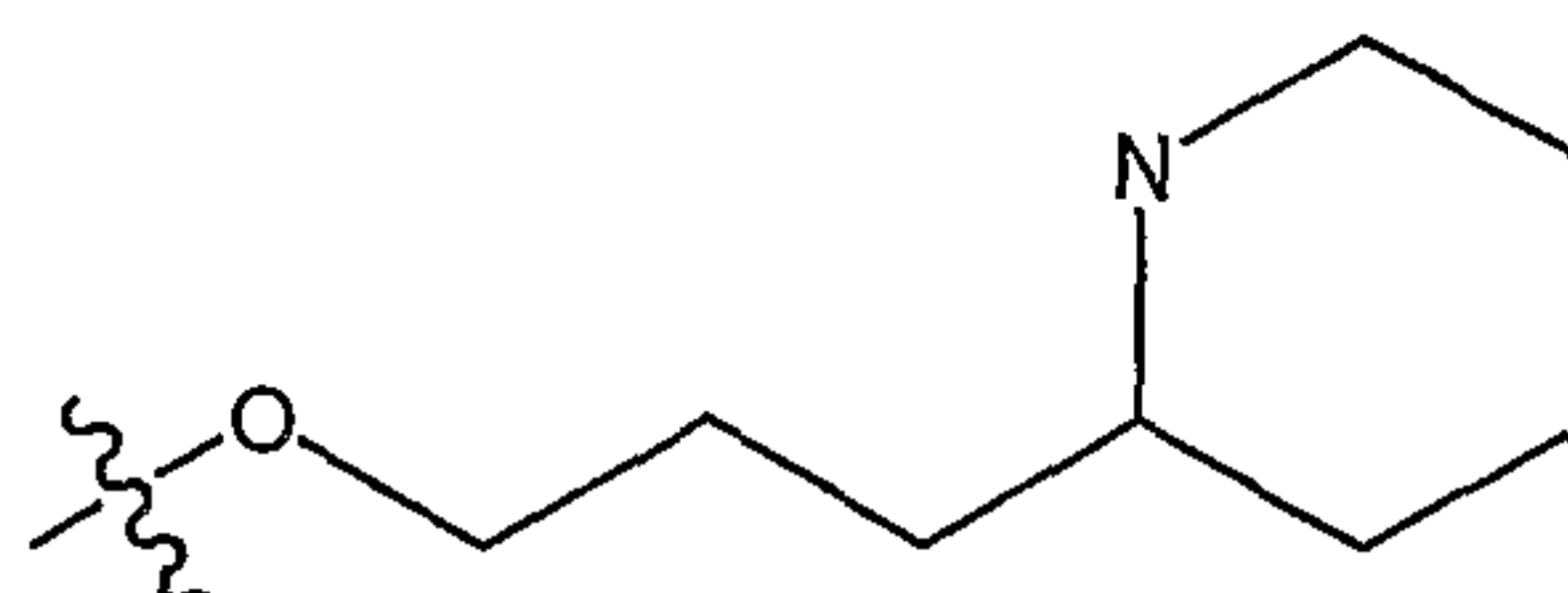
III

where Structure II represents the group that can be referred to as the $-\text{OCH}_2\text{CH}_2(2\text{-tetrahydrofuranyl})$ or $-\text{OCH}_2\text{CH}_2(\text{tetrahydrofuran-2-yl})$ group and Structure III represents the group that can be referred to as the $-\text{OCH}_2\text{CH}_2(3\text{-tetrahydrofuranyl})$ or $-\text{OCH}_2\text{CH}_2(\text{tetrahydrofuran-3-yl})$ group. When the heterocyclyl group is a N-containing heterocycle, such as, but not limited to piperidine, piperazine, morpholine, or pyrrolidine, the heterocycle can be bonded to the methylene carbon through a ring carbon atom or through a nitrogen atom in the ring of the N-containing heterocycle. Both of these are preferred. Where the heterocyclyl group is a piperidine for a $-\text{OCH}_2\text{CH}_2\text{CH}_2(\text{heterocyclyl})$ group, the following structures are possible and preferred:

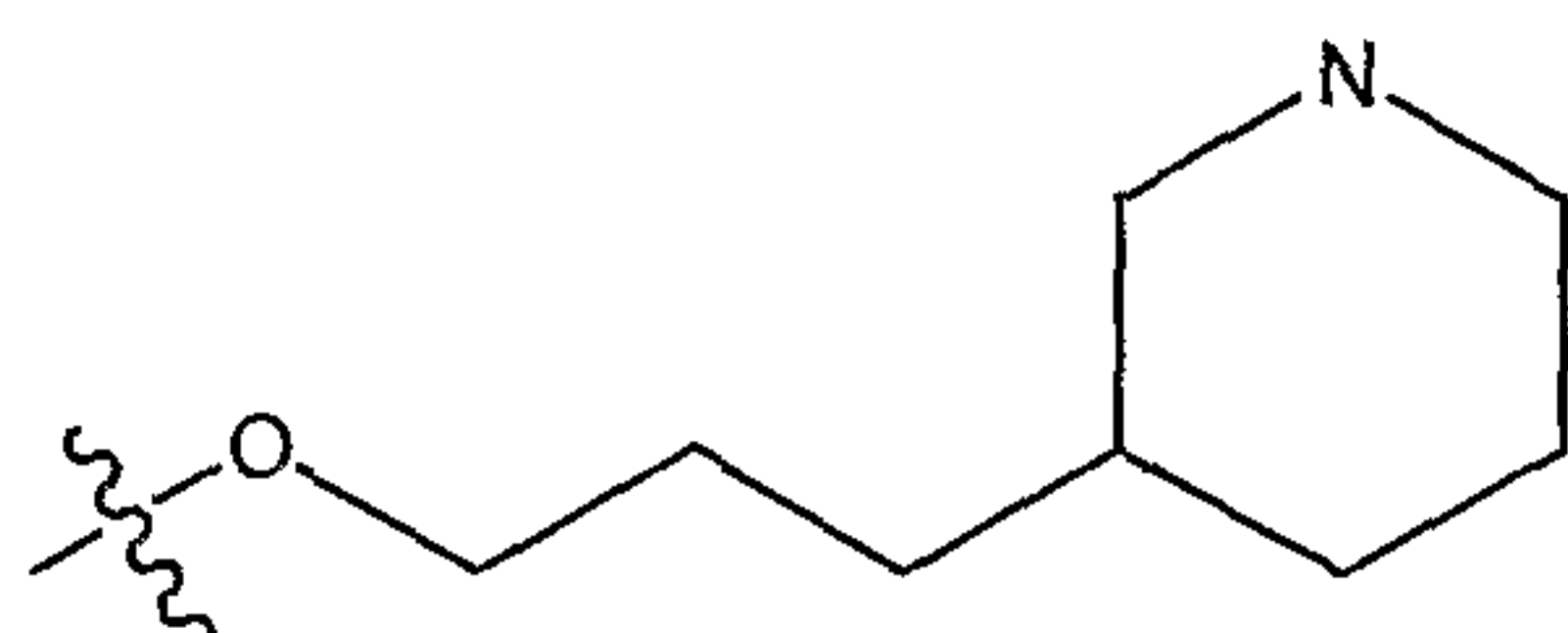
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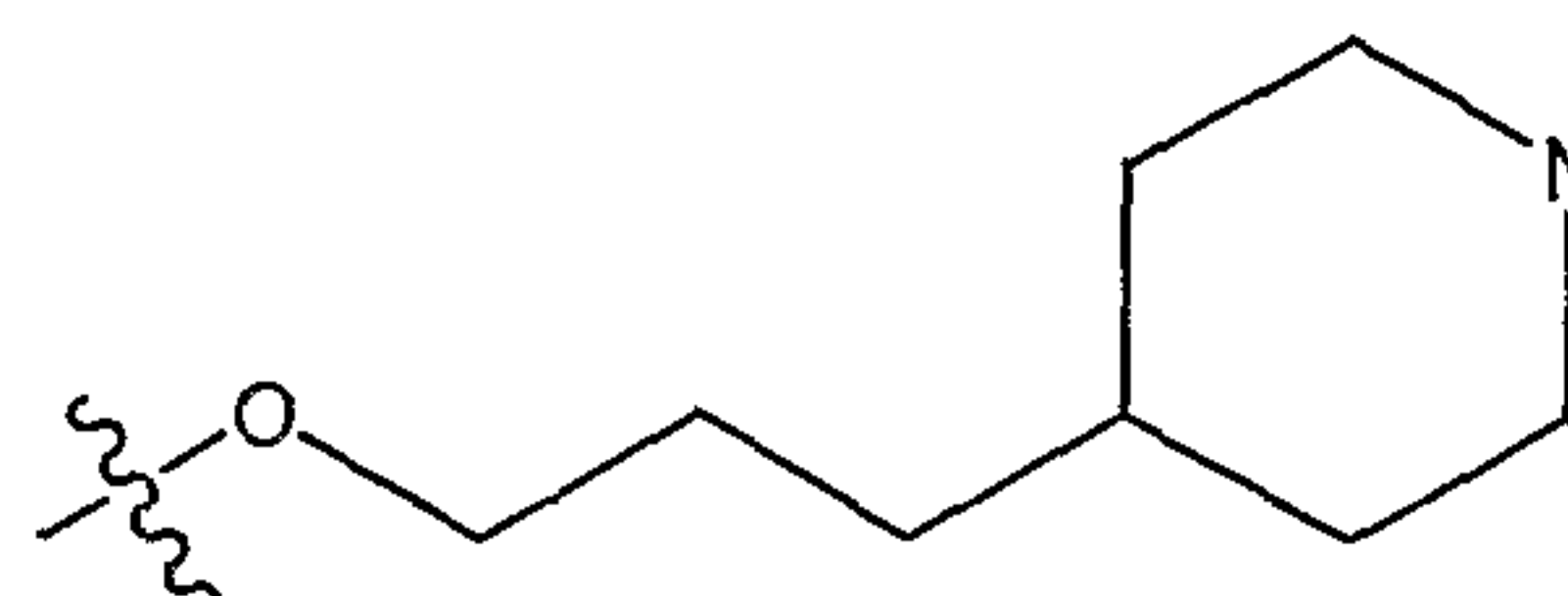
IV



V

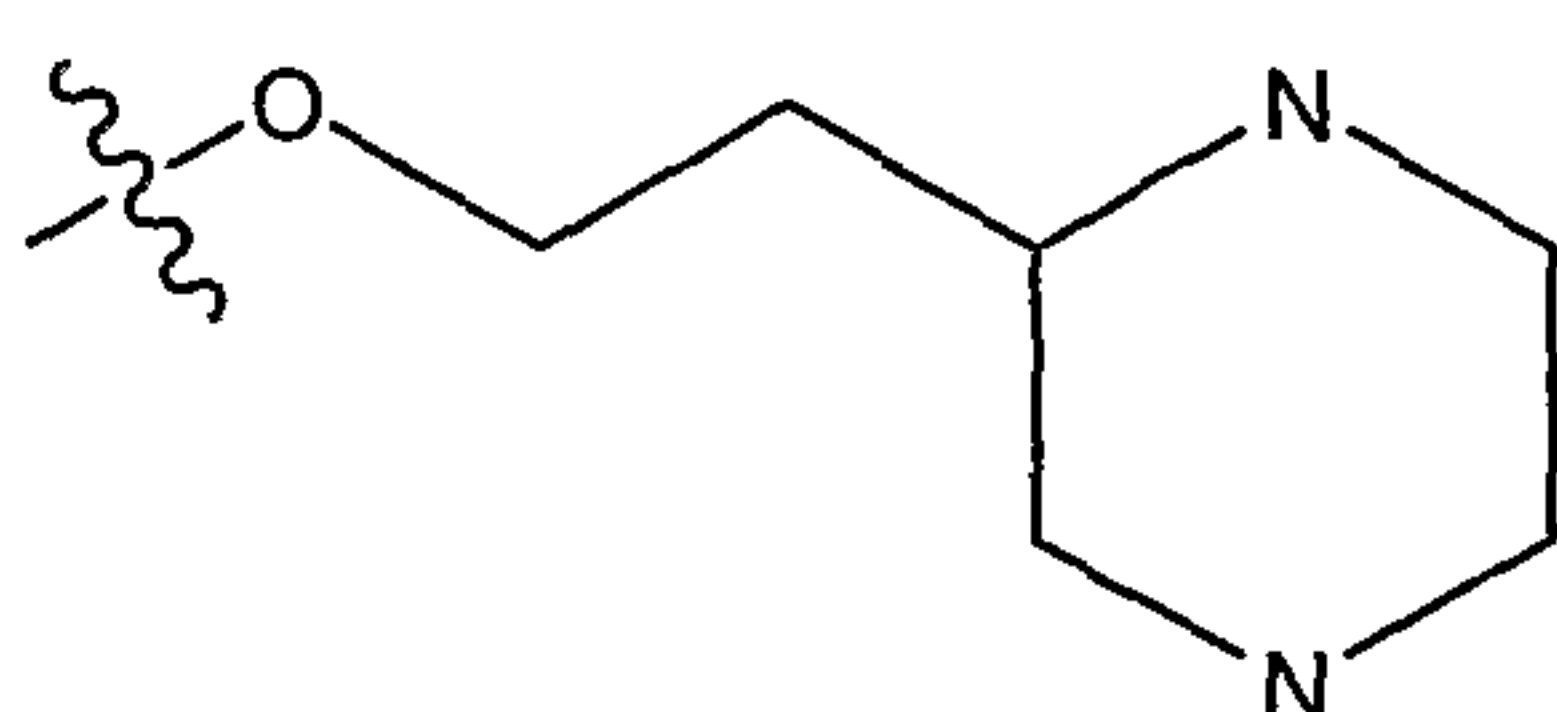


VI

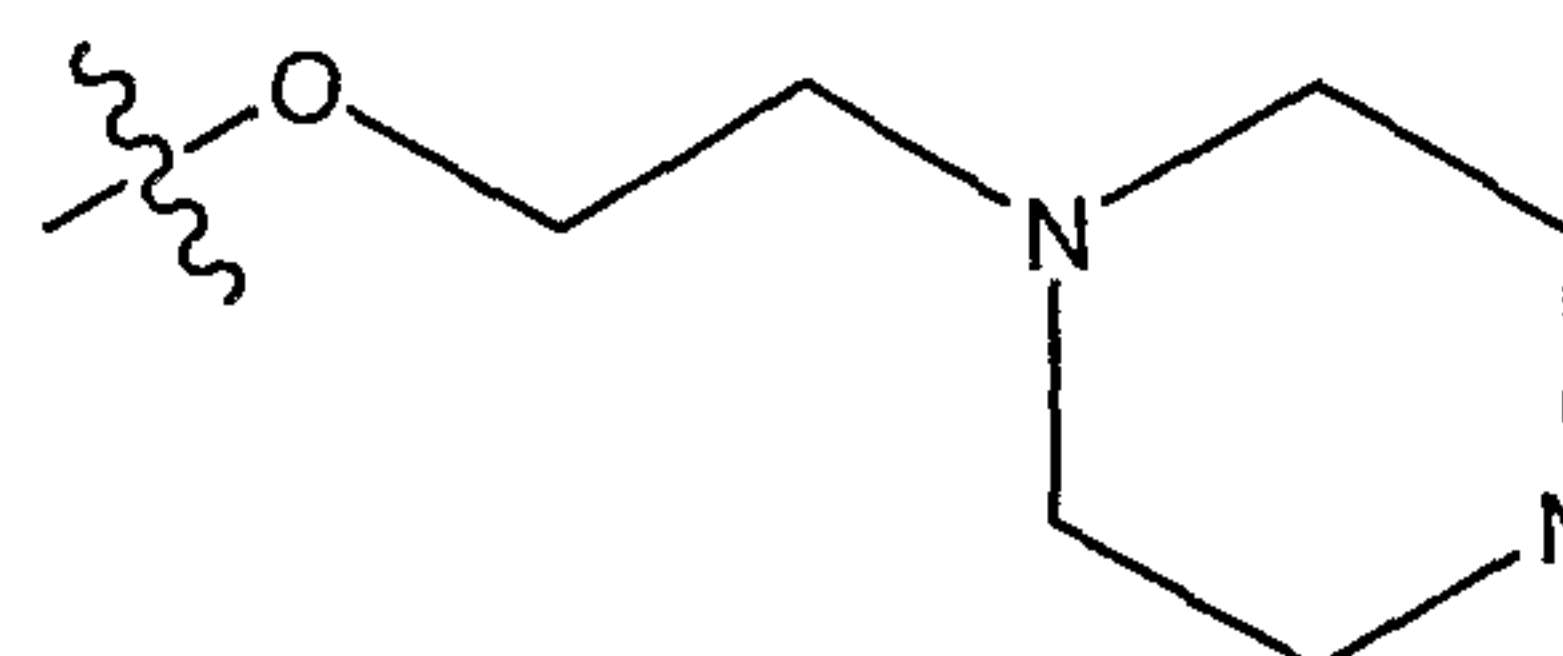


VII

[0408] Structure IV is an example of a $-\text{O}(\text{CH}_2)_3(\text{N-piperidinyl})$ or $-\text{O}(\text{CH}_2)_3(1\text{-piperidinyl})$ or $-\text{O}(\text{CH}_2)_3(\text{piperidin-1-yl})$ group. Structure V is an example of a $-\text{O}(\text{CH}_2)_3(2\text{-piperidinyl})$ or $-\text{O}(\text{CH}_2)_3(\text{piperidin-2-yl})$ group. Structure VI is an example of a $-\text{O}(\text{CH}_2)_3(3\text{-piperidinyl})$ or $-\text{O}(\text{CH}_2)_3(\text{piperidin-3-yl})$ group. Structure VII is an example of a $-\text{O}(\text{CH}_2)_3(4\text{-piperidinyl})$ or $-\text{O}(\text{CH}_2)_3(\text{piperidin-4-yl})$ group. Where the heterocyclyl group is a piperazine for an $-\text{OCH}_2\text{CH}_2(\text{heterocyclyl})$ group, the following structures are possible and preferred:



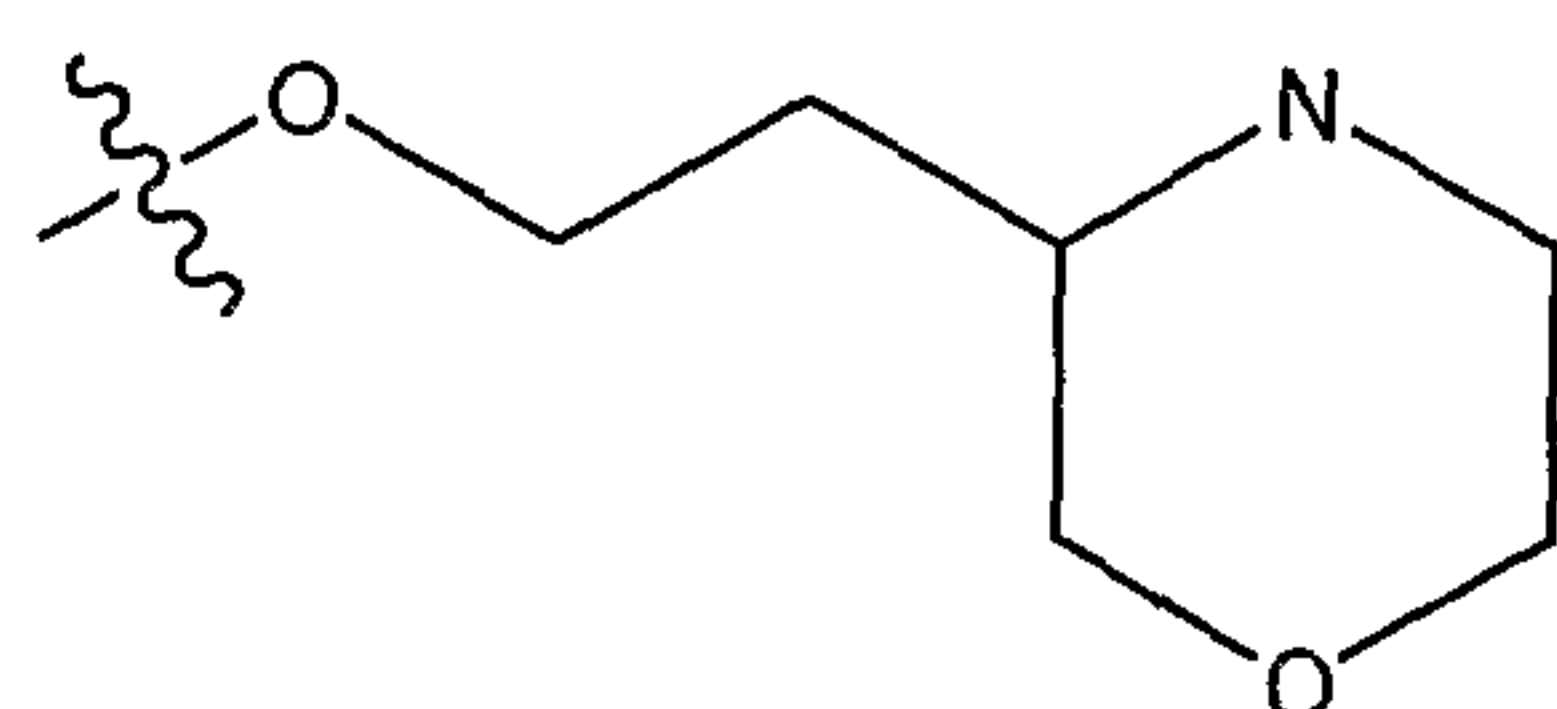
VIII



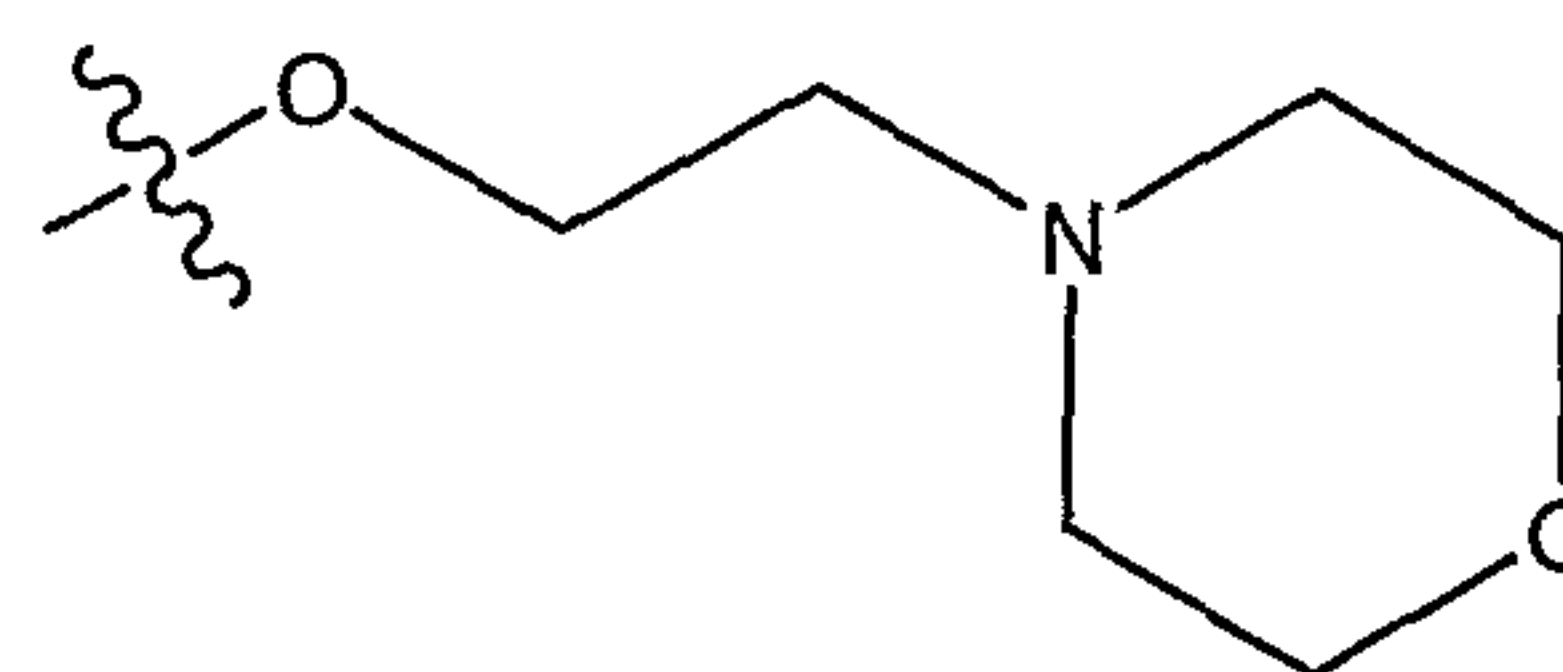
IX

[0409] Structure VIII is an example of a $-\text{O}(\text{CH}_2)_2(2\text{-piperazinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{piperazin-2-yl})$ group, and Structure IX is an example of a $-\text{O}(\text{CH}_2)_2(1\text{-piperazinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{N-piperazinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{piperazin-1-yl})$ group. Where the heterocyclyl group is a morpholine for a $-\text{OCH}_2\text{CH}_2(\text{heterocyclyl})$ group, the following structures are possible and preferred:

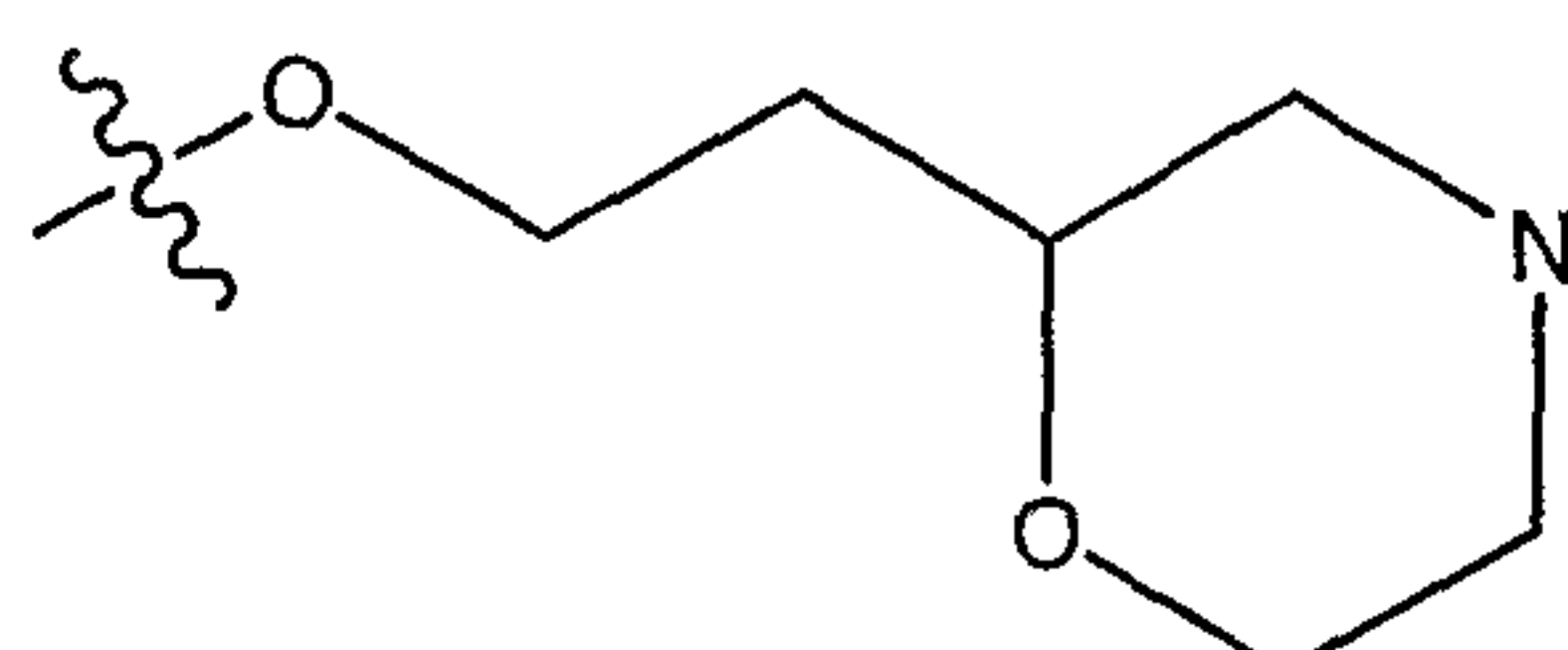
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X



XI

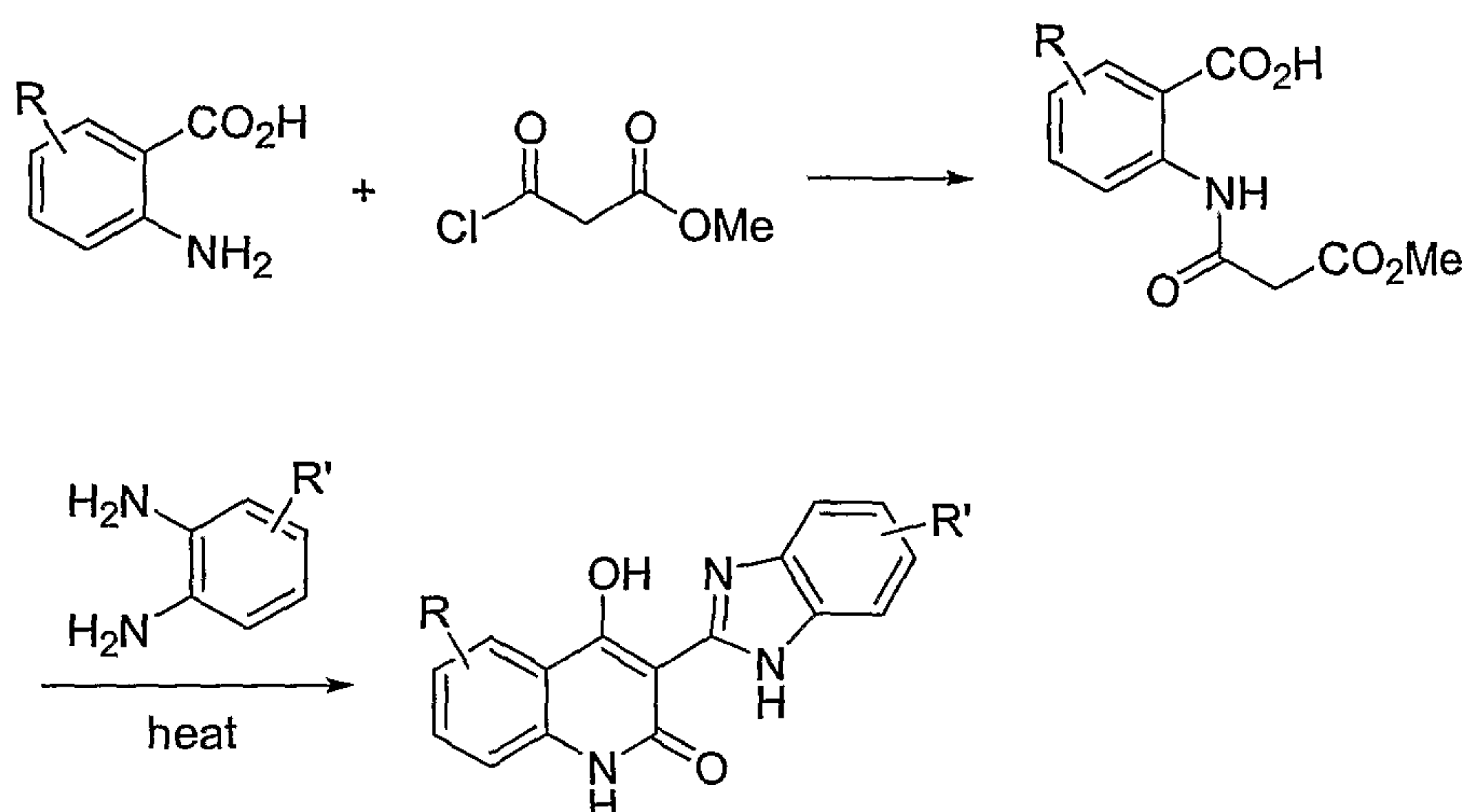


XII

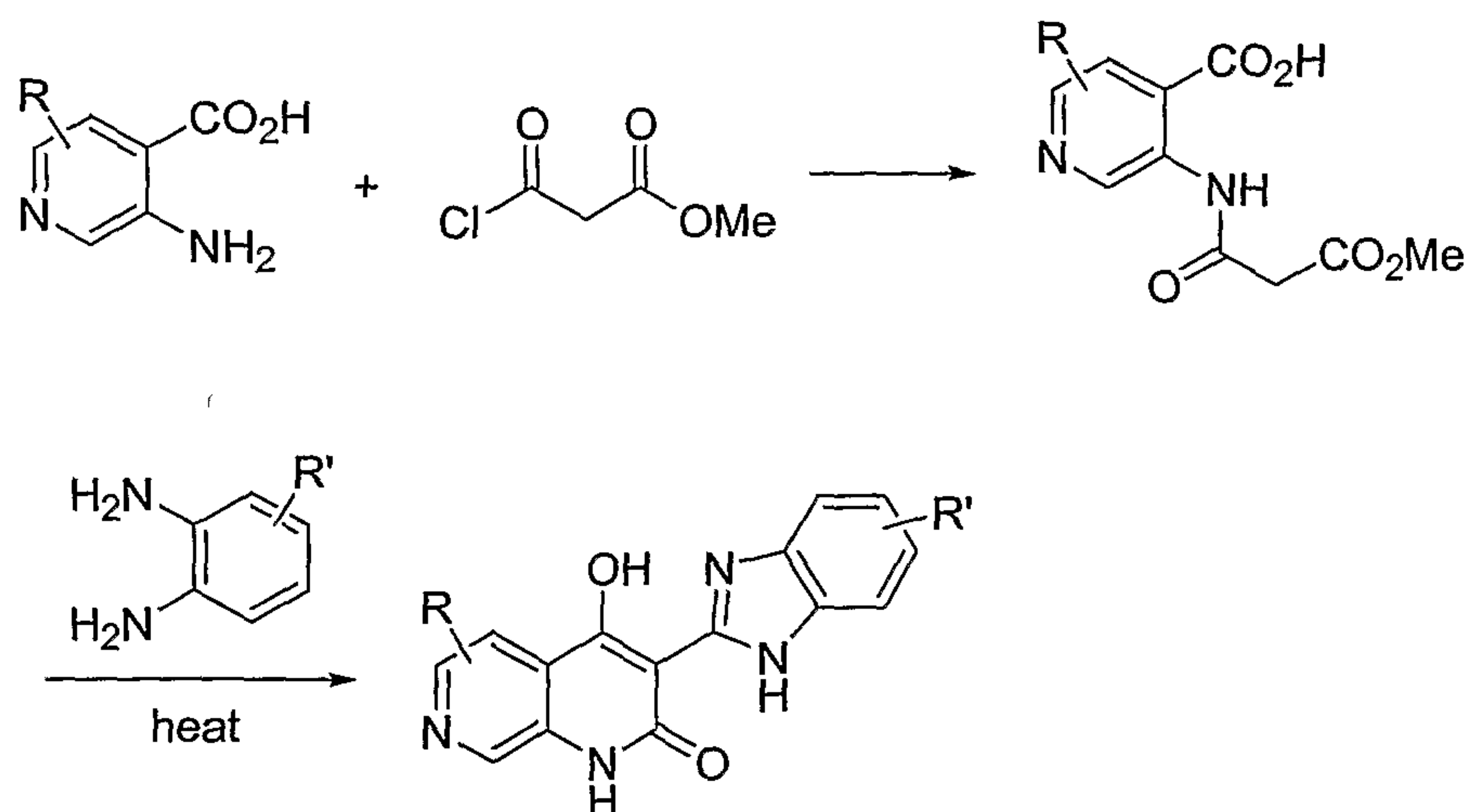
[0410] Structure X is an example of a $-\text{O}(\text{CH}_2)_2(3\text{-morpholinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{morpholin-3-yl})$ group, Structure XI is an example of a $-\text{O}(\text{CH}_2)_2(4\text{-morpholinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{N-morpholinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{morpholin-4-yl})$ group, and Structure XII is an example of a $-\text{O}(\text{CH}_2)_2(2\text{-morpholinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{morpholin-2-yl})$ group. It will be observed that where the heterocyclyl group is a pyrrolidine in a $-\text{OCH}_2\text{CH}_2(\text{heterocyclyl})$ group, the structures available include $-\text{O}(\text{CH}_2)_2(1\text{-pyrrolidinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{N-pyrrolidinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{pyrrolidin-1-yl})$, $-\text{O}(\text{CH}_2)_2(2\text{-pyrrolidinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{pyrrolidin-2-yl})$, and $-\text{O}(\text{CH}_2)_2(3\text{-pyrrolidinyl})$ or $-\text{O}(\text{CH}_2)_2(\text{pyrrolidin-3-yl})$.

[0411] Compounds of Structure I and IB may be synthesized from simple starting molecules as shown in Schemes 1-6 and the Examples. As shown in Scheme 1, hydroxy derivatives of compounds of Structure I may generally be prepared using aromatic compounds substituted with amines and carboxylic acid groups. These compounds may then be converted to compounds of Structure I using the methods described in Schemes 3 and 5 and the Examples. Hydroxy derivatives of heterocyclic analogs of Structure I such as compounds of Structure IB may be similarly prepared using the appropriate heteroaromatic analogs of the compounds as shown in Scheme 2. These may then be converted to heterocyclic analogs of Structure I such as compounds of Structure IB using the methods described in Schemes 4 and 5.

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Scheme 1.

[0412] As shown in Scheme 1, a substituted aromatic compound such as a substituted or unsubstituted 2-aminobenzoic acid may be reacted with an acyl halide such as methyl 2-(chlorocarbonyl)acetate to produce an amide that will react with a substituted or unsubstituted 1,2-diaminobenzene. The resulting product is a 4-hydroxy-substituted analog of a compound of Structure I.

Scheme 2.

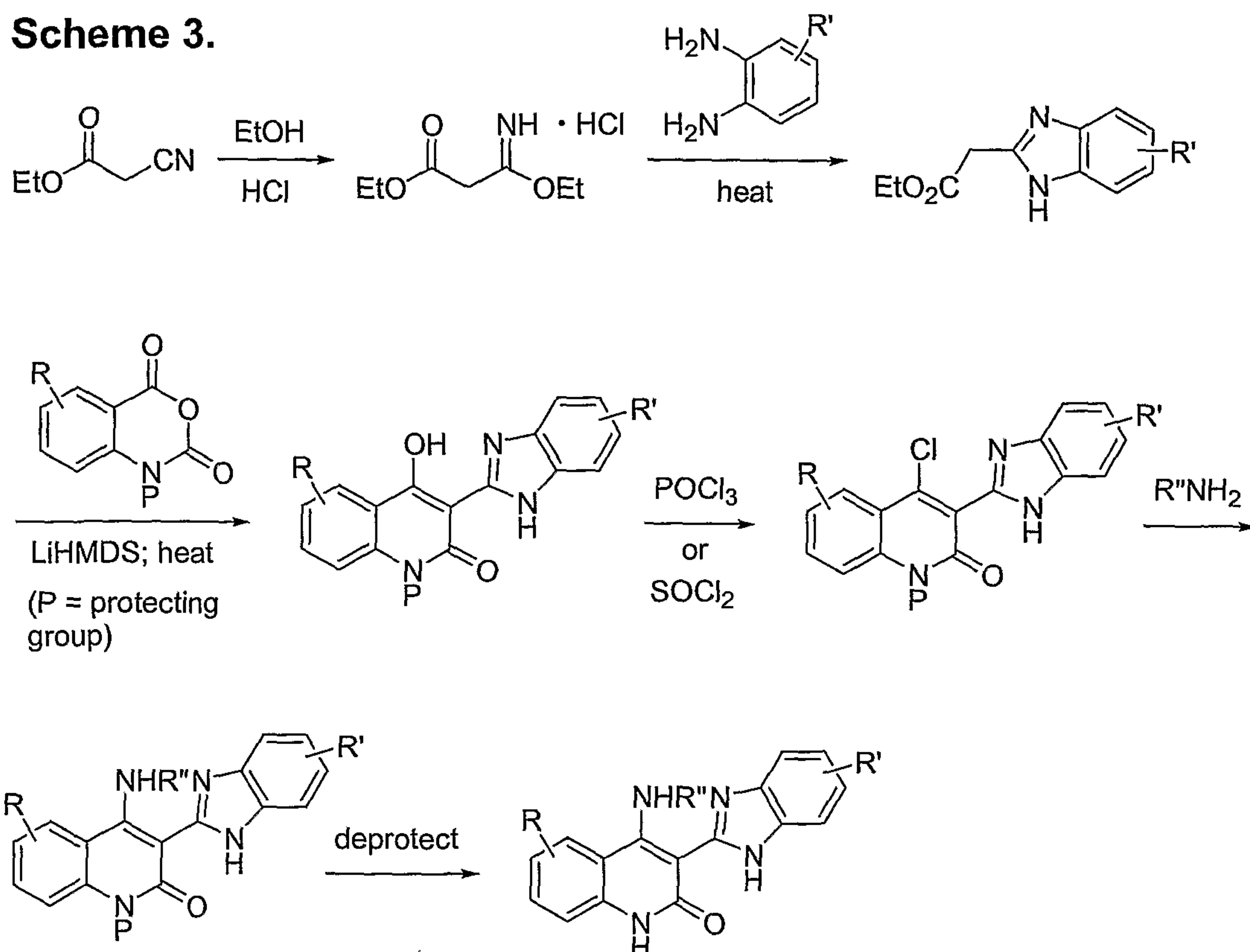
[0413] As shown in Scheme 2, a substituted pyridine such as a substituted or unsubstituted 3-amino-pyridine-4-carboxylic acid may be reacted with an acyl halide such as methyl 2-(chlorocarbonyl)acetate to produce an amide that will react with a substituted or unsubstituted 1,2-

diaminobenzene or a pyridine analog. The resulting product is a 4-hydroxy-substituted heterocyclic analog of a compound of Structure I or IB. The use of starting pyridines with different substitution patterns such as 2-aminonicotinic acid (2-aminopyridine-4-carboxylic acid) provides compounds where the nitrogen is in a different position in the pyridine ring of the final compound. One skilled in the art will recognize that the procedure set forth in Scheme 2 may be modified to produce various 4-hydroxy heterocyclic analogs of compounds of Structure I and IB.

[0414] Scheme 3 illustrates a general synthetic route that allows for the synthesis of various compounds of Structure I. An inspection of Scheme 3 shows that 4-hydroxy substituted analogs of compounds of Structure I may be converted into the 4-chloro derivative by reaction with phosphorus oxychloride or thionyl chloride. The 4-chloro derivative may then be reacted with an appropriate amine such as an alkylamine, a dialkylamine, a heterocyclamine, a cycloalkylamine, an aromatic amine, and the like to produce the corresponding protected compound of Structure I. Deprotection affords the final desired compounds of Structure I.

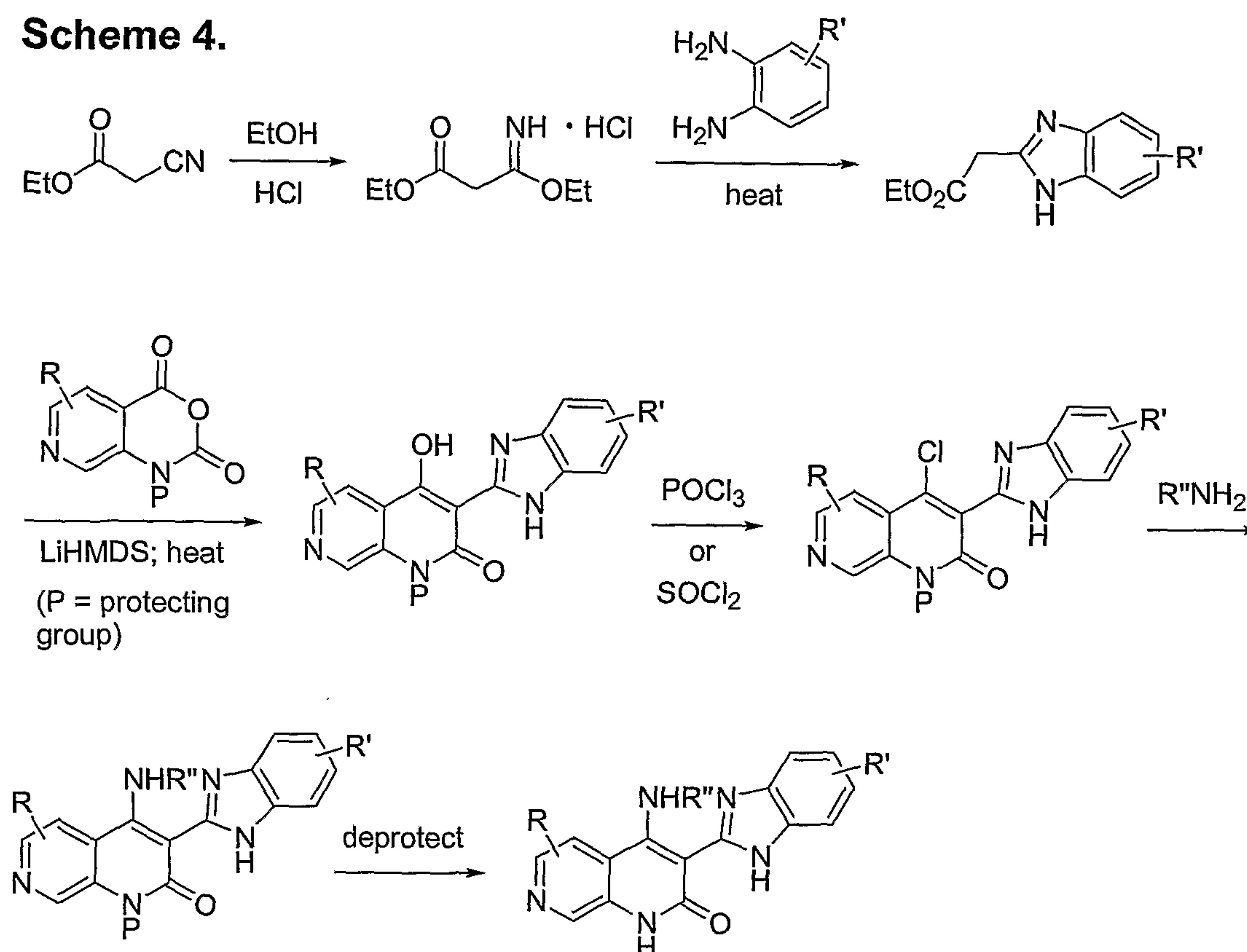
[0415] The various 2-aminobenzoic acid starting materials used to synthesize isatoic anhydrides may be obtained from commercial sources or prepared by methods known to one of skill in the art. General isatoic anhydride synthesis methods are described in *J. Med. Chem.* 1981, 24 (6), 735 and *J. Heterocycl. Chem.* 1975, 12(3), 565.

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Scheme 3.

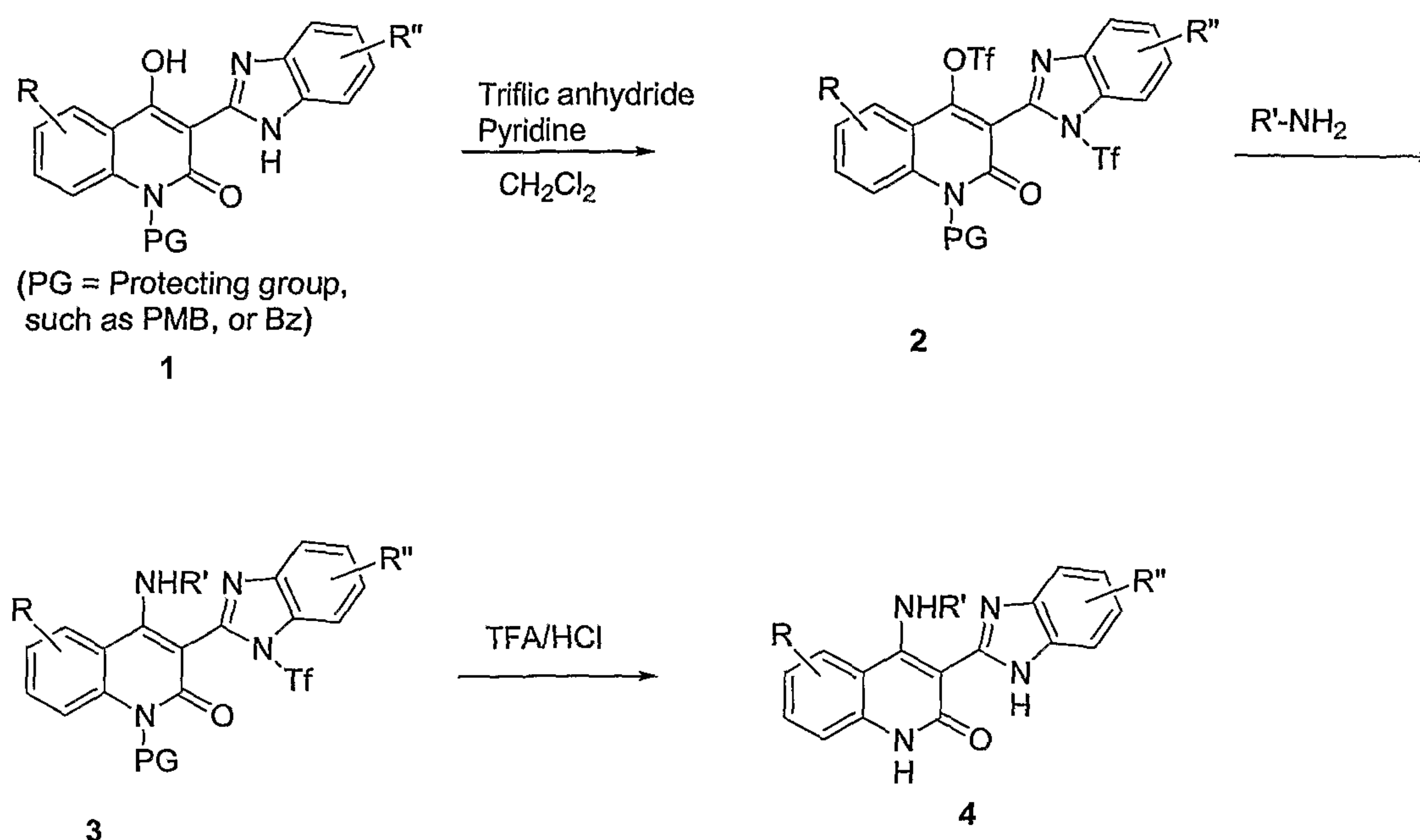
[0416] Scheme 4 illustrates a general synthetic route that allows for the synthesis of various heterocyclic compounds of Structure IB. An inspection of Scheme 4 shows that 4-hydroxy substituted analogs of Structure IB may be converted into the 4-chloro derivative by reaction with phosphorous oxychloride or thionyl chloride. The 4-chloro derivative may then be reacted with an appropriate amine such as an alkylamine, a dialkylamine, a heterocyclamine, a cycloalkylamine, an aromatic amine, and the like to produce the corresponding protected compounds of Structure IB. Deprotection affords the final desired heterocyclic analogs of compounds of Structure I.

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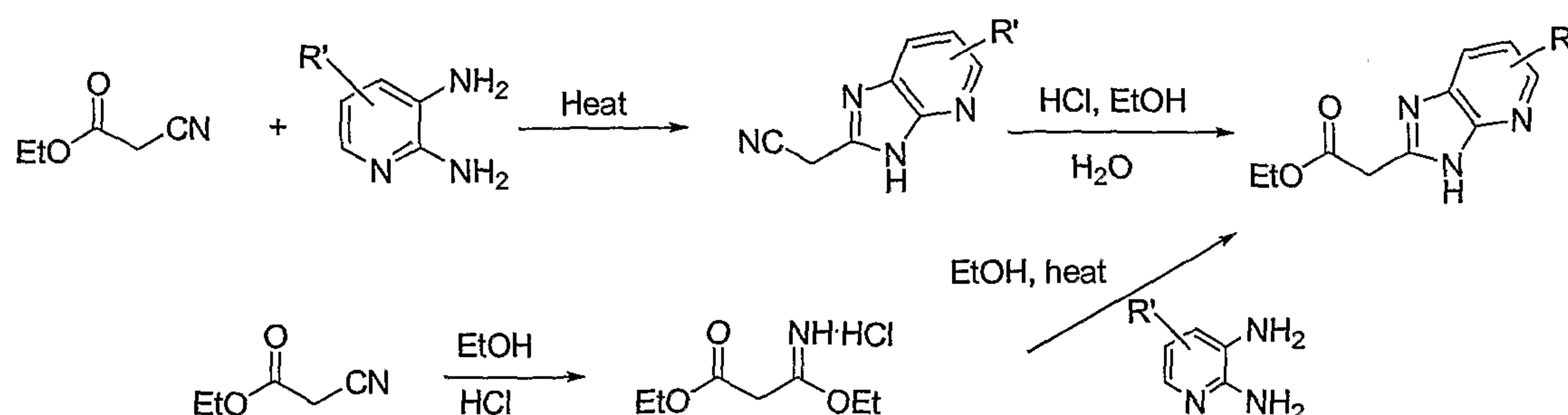
Scheme 4.

[0417] Scheme 5 depicts a general synthetic route that allows for the synthesis of various compounds of Structure I. An inspection of Scheme 5 shows that the hydroxy group of 4-hydroxy substituted analogs of compounds of Structure I may be converted to a leaving group by triflation with triflating agents such as triflic anhydride. The resulting triflates may then be reacted with a wide variety of nitrogen nucleophiles such as 3-aminoquinuclidine and other amines to produce protected analogs of compound of Structure I. Deprotection of the resulting products affords the desired compounds of Structure I. An analogous procedure may be used to prepare heterocyclic compounds of Structure I.

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Scheme 5.

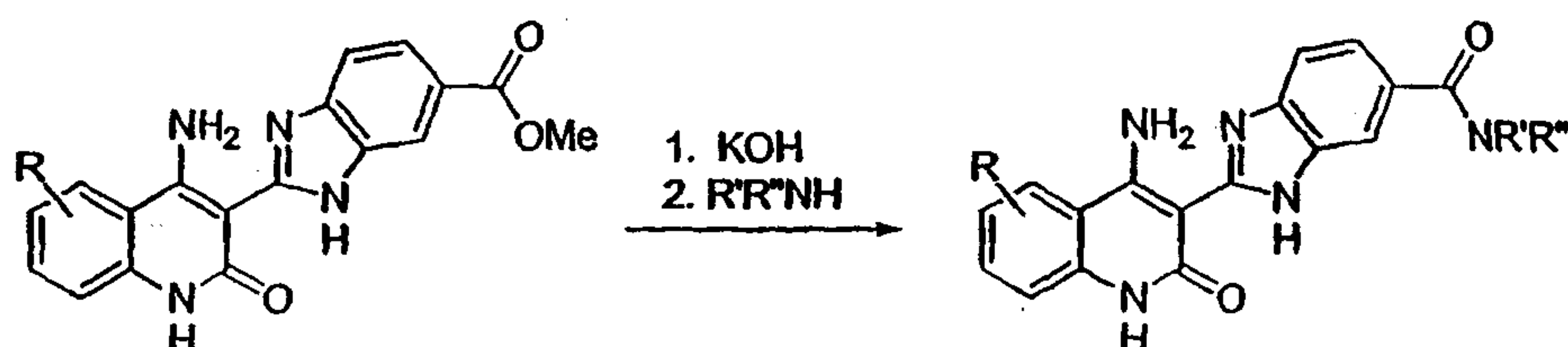
[0418] Heteroaromatic diamines may be simply prepared and used as precursors of compounds of Structure I and IB and heterocyclic analogs of compounds of Structure I and IB where one or more of A, B, C, or D is a nitrogen as shown in Scheme 6.

Scheme 6.

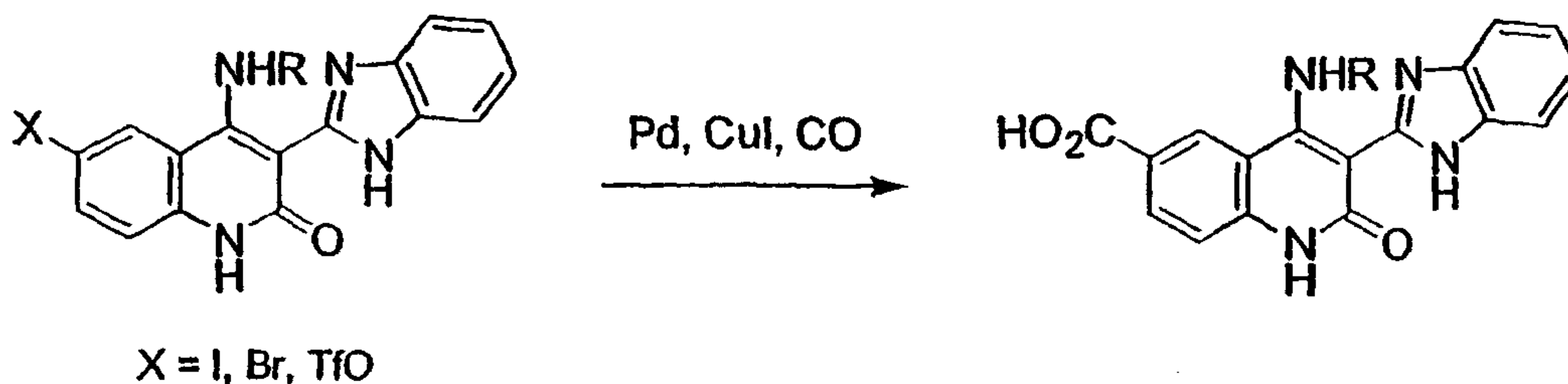
[0419] As shown in Scheme 6, a compound such as ethyl cyanoacetate may be condensed with a substituted or unsubstituted heterocycle containing two ortho amino groups such as substituted or unsubstituted 1,2-diaminopyridine to obtain a substituted or unsubstituted 2-imidazolo[5,4-b]pyridin-2-ylacetate, which may subsequently be hydrolyzed in acidic medium to provide a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetate. As an alternate route, a substituted or unsubstituted

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ethyl 2-imidazo[5,4-b]pyridin-2-ylacetate may be obtained from a compound such as the hydrochloride salt of 3-ethoxy-3-iminopropanoate and a substituted or unsubstituted 1,2-diaminopyridine. Reaction of a substituted or unsubstituted ethyl 2-imidazo[5,4-b]pyridin-2-ylacetates with an appropriate aromatic compound provides compounds of Structure I and heterocyclic analogs of compounds of Structure I where one or more of A, B, C, or D is a nitrogen atom.

Scheme 7.

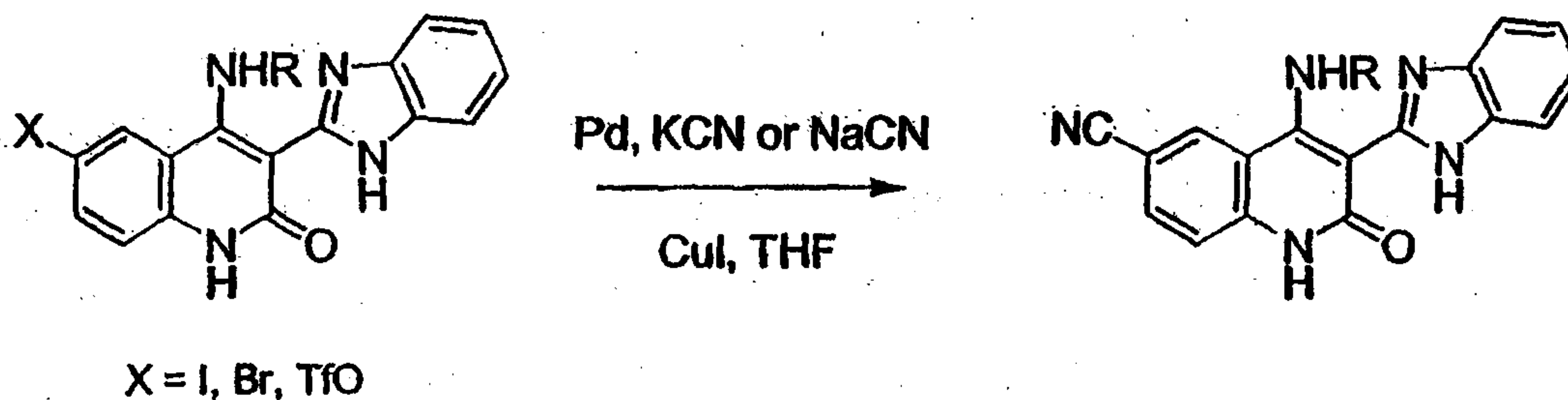
[0420] Introduction of substituents on the benzimidazole ring need not be limited to the early stages of the synthesis and may be accomplished after formation of the quinolinone ring. For example, amides can be obtained by coupling the advanced acid intermediate shown in Scheme 7 with a variety of amine.

Scheme 8.

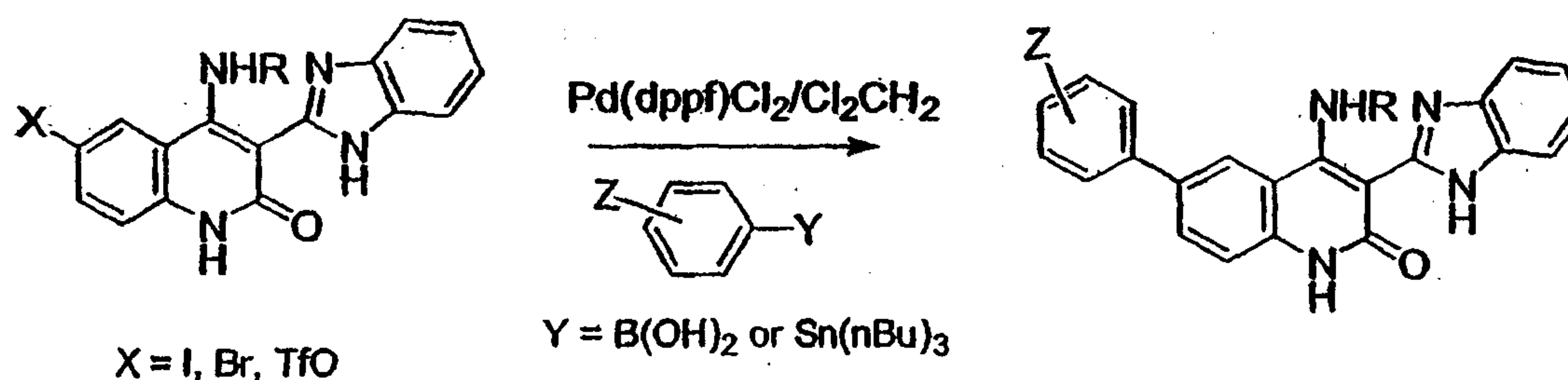
[0421] Conversion of the C-6 or C-7 halides to an acid group was accomplished using procedures in the following references:

Koga, H.; et al., *Tet. Let.*, 1995, 36, 1, 87-90; and Fukuyama, T.; et al., *J. Am. Chem. Soc.*, 1994, 116, 3125-3126.

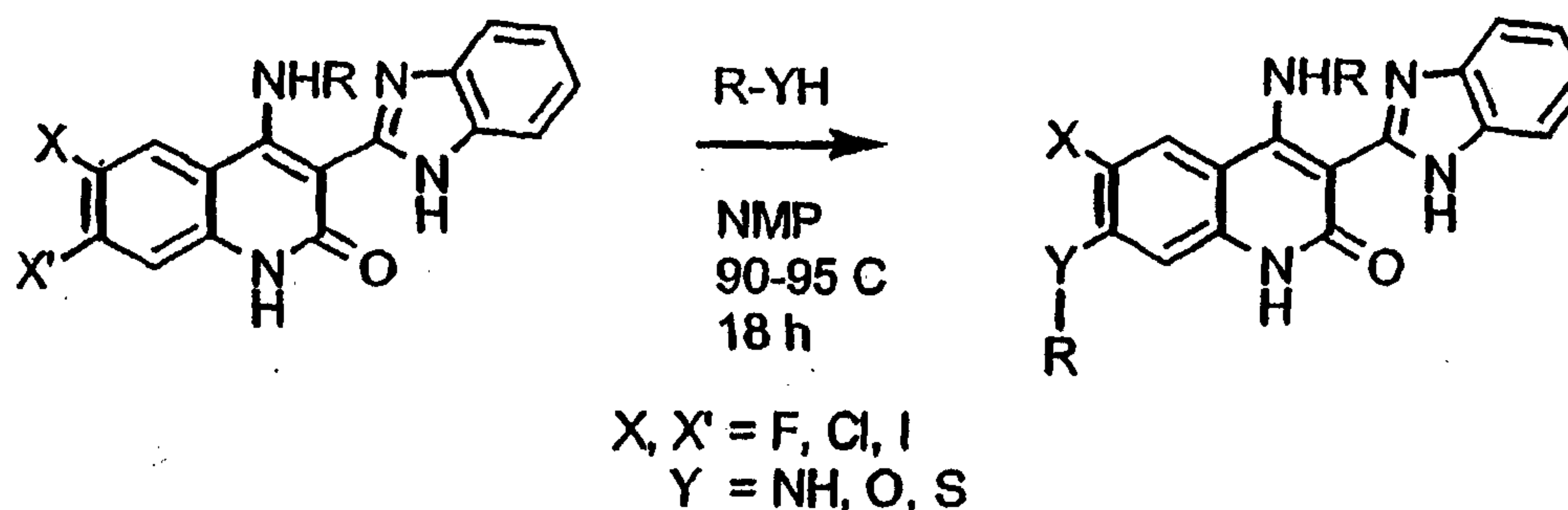
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Scheme 9.

[0422] Conversion of the C-6 or C-7 halides to a cyano group was accomplished using procedures in the following reference:
 Anderson, B.A.; et al., *J. Org. Chem.*, 1998, 63, 8224-828. Preferred reaction conditions for Scheme 9 are described in Method 26 below.

Scheme 10.

[0423] Conversion of the C-6 or C-7 halides to an aryl group was accomplished using standard Suzuki or Stille procedures such as described below.

Scheme 11.

[0424] Additional functionalization using a dihaloquinolone was accomplished as depicted in Scheme 11 by reaction of the dihaloquinolone with nucleophiles such as amines, alcohols and thiols.

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[0425] The compounds of Structure I and IB, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, pharmaceutically acceptable salts of the tautomers, and mixtures thereof may be used to prepare medicaments, that may be used for the purposes described herein, and may be used to treat various biological conditions as described herein.

[0426] Pharmaceutical formulations may include any of the compounds of any of the embodiments described above in combination with a pharmaceutically acceptable carrier such as those described herein.

[0427] The instant invention also provides for compositions which may be prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts tautomers thereof, or mixtures thereof with pharmaceutically acceptable carriers, excipients, binders, diluents or the like to treat or ameliorate a variety of disorders related to the activity of VEGF-RTK, more particularly angiogenesis associated with cancer or related to the activity of FLT-1, VEGFR2, VEGFR3, FGFR1, GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, NEK-2, CHK1, Rsk2, PAR-1, Cdc2, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Fyn, Lck, Tie-2, PDGFR α , and PDGFR β . The compositions of the inventions may be used to create formulations such as medicaments and pharmaceutical formulations that inhibit tyrosine kinases and/or serine/threonine kinases and may be used to treat biological conditions mediated by such kinases. Such compositions can be in the form of, for example, granules, powders, tablets, capsules, syrup, suppositories, injections, emulsions, elixirs, suspensions or solutions. The instant compositions can be formulated for various routes of administration, for example, by oral administration, by nasal administration, by rectal administration, subcutaneous injection, intravenous injection, intramuscular injections, or intraperitoneal injection. The following dosage forms are given by way of example and should not be construed as limiting the instant invention.

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[0428] For oral, buccal, and sublingual administration, powders, suspensions, granules, tablets, pills, capsules, gelcaps, and caplets are acceptable as solid dosage forms. These can be prepared, for example, by mixing one or more compounds of the instant invention, pharmaceutically acceptable salts, tautomers, or mixtures thereof, with at least one additive such as a starch or other additive. Suitable additives are sucrose, lactose, cellulose sugar, mannitol, maltitol, dextran, starch, agar, alginates, chitins, chitosans, pectins, tragacanth gum, gum arabic, gelatins, collagens, casein, albumin, synthetic or semi-synthetic polymers or glycerides. Optionally, oral dosage forms can contain other ingredients to aid in administration, such as an inactive diluent, or lubricants such as magnesium stearate, or preservatives such as paraben or sorbic acid, or anti-oxidants such as ascorbic acid, tocopherol or cysteine, a disintegrating agent, binders, thickeners, buffers, sweeteners, flavoring agents or perfuming agents. Tablets and pills may be further treated with suitable coating materials known in the art.

[0429] Liquid dosage forms for oral administration may be in the form of pharmaceutically acceptable emulsions, syrups, elixirs, suspensions, and solutions, which may contain an inactive diluent, such as water. Pharmaceutical formulations and medicaments may be prepared as liquid suspensions or solutions using a sterile liquid, such as, but not limited to, an oil, water, an alcohol, and combinations of these. Pharmaceutically suitable surfactants, suspending agents, emulsifying agents, may be added for oral or parenteral administration.

[0430] As noted above, suspensions may include oils. Such oil include, but are not limited to, peanut oil, sesame oil, cottonseed oil, corn oil and olive oil. Suspension preparation may also contain esters of fatty acids such as ethyl oleate, isopropyl myristate, fatty acid glycerides and acetylated fatty acid glycerides. Suspension formulations may include alcohols, such as, but not limited to, ethanol, isopropyl alcohol, hexadecyl alcohol, glycerol and propylene glycol. Ethers, such as but not limited to, poly(ethyleneglycol),

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petroleum hydrocarbons such as mineral oil and petrolatum; and water may also be used in suspension formulations.

[0431] For nasal administration, the pharmaceutical formulations and medicaments may be a spray or aerosol containing an appropriate solvent(s) and optionally other compounds such as, but not limited to, stabilizers, antimicrobial agents, antioxidants, pH modifiers, surfactants, bioavailability modifiers and combinations of these. A propellant for an aerosol formulation may include compressed air, nitrogen, carbon dioxide, or a hydrocarbon based low boiling solvent.

[0432] Injectable dosage forms generally include aqueous suspensions or oil suspensions which may be prepared using a suitable dispersant or wetting agent and a suspending agent. Injectable forms may be in solution phase or in the form of a suspension, which is prepared with a solvent or diluent. Acceptable solvents or vehicles include sterilized water, Ringer's solution, or an isotonic aqueous saline solution. Alternatively, sterile oils may be employed as solvents or suspending agents. Preferably, the oil or fatty acid is non-volatile, including natural or synthetic oils, fatty acids, mono-, di- or tri-glycerides.

[0433] For injection, the pharmaceutical formulation and/or medicament may be a powder suitable for reconstitution with an appropriate solution as described above. Examples of these include, but are not limited to, freeze dried, rotary dried or spray dried powders, amorphous powders, granules, precipitates, or particulates. For injection, the formulations may optionally contain stabilizers, pH modifiers, surfactants, bioavailability modifiers and combinations of these.

[0434] For rectal administration, the pharmaceutical formulations and medicaments may be in the form of a suppository, an ointment, an enema, a tablet or a cream for release of compound in the intestines, sigmoid flexure and/or rectum. Rectal suppositories are prepared by mixing one or more

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compounds of the instant invention, or pharmaceutically acceptable salts or tautomers of the compound, with acceptable vehicles, for example, cocoa butter or polyethylene glycol, which is present in a solid phase at normal storing temperatures, and present in a liquid phase at those temperatures suitable to release a drug inside the body, such as in the rectum. Oils may also be employed in the preparation of formulations of the soft gelatin type and suppositories. Water, saline, aqueous dextrose and related sugar solutions, and glycerols may be employed in the preparation of suspension formulations which may also contain suspending agents such as pectins, carbomers, methyl cellulose, hydroxypropyl cellulose or carboxymethyl cellulose, as well as buffers and preservatives.

[0435] Besides those representative dosage forms described above, pharmaceutically acceptable excipients and carriers are generally known to those skilled in the art and are thus included in the instant invention. Such excipients and carriers are described, for example, in "Remingtons Pharmaceutical Sciences" Mack Pub. Co., New Jersey (1991).

[0436] The formulations of the invention may be designed to be short-acting, fast-releasing, long-acting, and sustained-releasing as described below. Thus, the pharmaceutical formulations may also be formulated for controlled release or for slow release.

[0437] The instant compositions may also comprise, for example, micelles or liposomes, or some other encapsulated form, or may be administered in an extended release form to provide a prolonged storage and/or delivery effect. Therefore, the pharmaceutical formulations and medicaments may be compressed into pellets or cylinders and implanted intramuscularly or subcutaneously as depot injections or as implants such as stents. Such implants may employ known inert materials such as silicones and biodegradable polymers.

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[0438] Specific dosages may be adjusted depending on conditions of disease, the age, body weight, general health conditions, sex, and diet of the subject, dose intervals, administration routes, excretion rate, and combinations of drugs. Any of the above dosage forms containing effective amounts are well within the bounds of routine experimentation and therefore, well within the scope of the instant invention.

[0439] A therapeutically effective dose may vary depending upon the route of administration and dosage form. The preferred compound or compounds of the instant invention is a formulation that exhibits a high therapeutic index. The therapeutic index is the dose ratio between toxic and therapeutic effects which can be expressed as the ratio between LD_{50} and ED_{50} . The LD_{50} is the dose lethal to 50% of the population and the ED_{50} is the dose therapeutically effective in 50% of the population. The LD_{50} and ED_{50} are determined by standard pharmaceutical procedures in animal cell cultures or experimental animals.

[0440] "Treating" within the context of the instant invention, means an alleviation of symptoms associated with a disorder or disease, or halt of further progression or worsening of those symptoms, or prevention or prophylaxis of the disease or disorder. For example, within the context of treating patients in need of an inhibitor of VEGF-RTK, successful treatment may include a reduction in the proliferation of capillaries feeding a tumor or diseased tissue, an alleviation of symptoms related to a cancerous growth or tumor, proliferation of capillaries, or diseased tissue, a halting in capillary proliferation, or a halting in the progression of a disease such as cancer or in the growth of cancerous cells. Treatment may also include administering the pharmaceutical formulations of the present invention in combination with other therapies. For example, the compounds and pharmaceutical formulations of the present invention may be administered before, during, or after surgical procedure and/or radiation therapy. The compounds of the invention can also be administered in conjunction with other anti-cancer drugs including those

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used in antisense and gene therapy. Appropriate combinations can be determined by those of skill in the oncology and medicine arts.

[0441] Pharmaceutical formulations and medicaments according to the invention include any of the compounds described above in combination with a pharmaceutically acceptable carrier. Thus, the compounds of the invention may be used to prepare medicaments and pharmaceutical formulations. In some such embodiments, the medicaments and pharmaceutical formulations comprise any of the compounds of any of the embodiments of compounds of Structure I or Structure IB or pharmaceutically acceptable salts thereof. The invention also provides for the use of any of the compounds of any of the embodiments of compounds of Structure I or IB or pharmaceutically acceptable salts thereof for the inhibition of an enzyme such as FLT-1, VEGFR2, VEGFR3, FGFR1, GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, NEK-2, CHK1, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Cdc2, Fyn, Lck, Tie-2, PDGFR α , and PDGFR β , or for the treatment of a disease or condition associated with any of these enzymes as described in greater detail below. The invention also provides the use of any of the compounds of any of the embodiments of compounds of Structure I or IB or pharmaceutically acceptable salts thereof for the manufacture of enzyme inhibition agent such as a tyrosine kinase inhibitor or a serine/threonine kinase inhibitor, a pharmaceutical formulation, or a medicament that inhibits enzymes such as FLT-1, VEGFR2, VEGFR3, FGFR1, GSK-3, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1 ϵ , Raf, NEK-2, CHK1, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, Cdc2, Fyn, Lck, Tie-2, PDGFR α , and PDGFR β or treats a disease or condition associated with any of these enzymes as described in greater detail below.

[0442] A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase includes administering an effective amount of a pharmaceutical formulation, a medicament according to the invention or any of the compounds of any of the embodiments of compounds of Structure I or IB to a patient in need thereof.

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

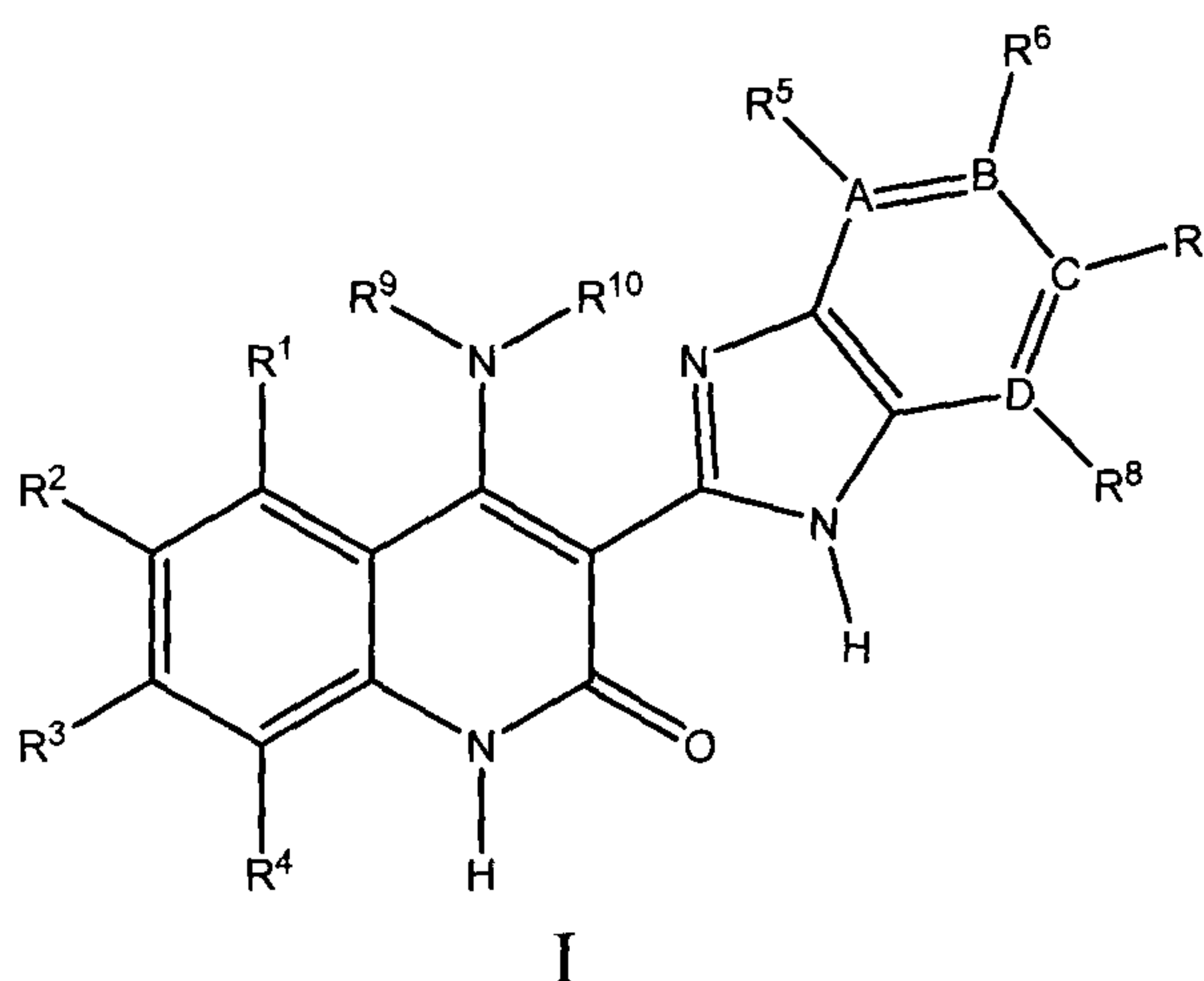
THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

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CLAIMS:

1. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula



wherein,

A, B, C, and D are independently carbon or nitrogen;

R^1 is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups,

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substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -N(heterocyclylalkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl) groups, -CO₂H, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, and substituted or unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R² and R³ are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S-aryl groups, substituted or unsubstituted -S-aralkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted or

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unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or
 unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, substituted or
 unsubstituted $-S(=O)_2-N(H)(aryl)$ groups, substituted or
 unsubstituted $-S(=O)_2-N(alkyl)(aryl)$ groups, substituted or
 unsubstituted $-S(=O)_2-N(aryl)_2$ groups, substituted or
 unsubstituted $-S(=O)_2-N(H)(aralkyl)$ groups, substituted or
 unsubstituted $-S(=O)_2-N(alkyl)(aralkyl)$ groups, substituted or
 unsubstituted $-S(=O)_2-N(aralkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy
 groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted
 arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted
 or unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted or
 unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups,
 substituted or unsubstituted $-N(H)(aryl)$ groups, substituted or
 unsubstituted $-N(alkyl)(aryl)$ groups, substituted or unsubstituted $-N(aryl)_2$ groups,
 substituted or unsubstituted $-N(H)(aralkyl)$ groups, substituted or
 unsubstituted $-N(alkyl)(aralkyl)$ groups, substituted or unsubstituted $-N(aralkyl)_2$
 groups, substituted or unsubstituted $-N(H)(heterocyclyl)$ groups, substituted or
 unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted or
 unsubstituted $-N(heterocyclyl)_2$ groups, substituted or
 unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted or
 unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted or
 unsubstituted $-N(heterocyclylalkyl)_2$ groups, substituted or
 unsubstituted $-N(H)-S(=O)_2-alkyl$ groups, substituted or
 unsubstituted $-N(H)-S(=O)_2-aryl$ groups, substituted or
 unsubstituted $-N(H)-S(=O)_2-aralkyl$ groups, substituted or
 unsubstituted $-N(H)-S(=O)_2-heterocyclyl$ groups, substituted or
 unsubstituted $-N(H)-S(=O)_2-heterocyclylalkyl$ groups, substituted or
 unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted or
 unsubstituted $-N(H)-C(=O)-aryl$ groups, substituted or
 unsubstituted $-N(H)-C(=O)-aralkyl$ groups, substituted or
 unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted or
 unsubstituted $-N(H)-C(=O)-heterocyclylalkyl$ groups, substituted or
 unsubstituted $-N(alkyl)-C(=O)-alkyl$ groups, substituted or

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unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-aryl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-aralkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂,
 substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-NH₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclyl) groups, substituted or

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unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl
 groups, substituted or unsubstituted -C(=O)-aralkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl
 groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, or substituted
 or unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl
 groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl
 groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl
 groups having from 2 to 8 carbon atoms, -SH, substituted or unsubstituted -S-alkyl
 groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or
 unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl

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groups, $-S(=O)_2-NH_2$, substituted or unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(H)-S(=O)-alkyl$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, or substituted or unsubstituted $-C(=O)-O-alkyl$ groups;

R^5 and R^8 are independently $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, $-SH$, substituted or unsubstituted $-S-alkyl$ groups, substituted or unsubstituted $-S(=O)_2-O-alkyl$ groups, substituted or unsubstituted $-S(=O)_2-alkyl$ groups, substituted or unsubstituted $-S(=O)-alkyl$ groups, $-S(=O)_2-NH_2$, substituted or unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(H)-S(=O)-alkyl$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, or substituted or unsubstituted $-C(=O)-O-alkyl$ groups; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^6 and R^7 are independently $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-NO_2$, $-CN$, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl

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groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted or unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted or unsubstituted -S(=O)₂-N(H)(heterocyclyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -S(=O)₂-N(heterocyclyl)₂ groups, substituted or unsubstituted -S(=O)₂-N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -S(=O)₂-N(heterocyclylalkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups, substituted or unsubstituted -N(alkyl)(aryl) groups, substituted or unsubstituted -N(aryl)₂ groups, substituted or unsubstituted -N(H)(aralkyl) groups, substituted or unsubstituted -N(alkyl)(aralkyl) groups, substituted or unsubstituted -N(aralkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -N(heterocyclylalkyl)₂ groups, substituted or unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted or unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted or unsubstituted -N(H)-S(=O)₂-heterocyclylalkyl groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or

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unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclylalkyl groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or
 unsubstituted -C(=O)-O-heterocyclyl groups, or substituted or
 unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R⁶ may be absent if B is
 nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is one of -H, substituted or unsubstituted alkyl groups having from 1 to
 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or
 unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups,
 substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted
 heterocyclylaminoalkyl groups, substituted or unsubstituted alkoxy groups,

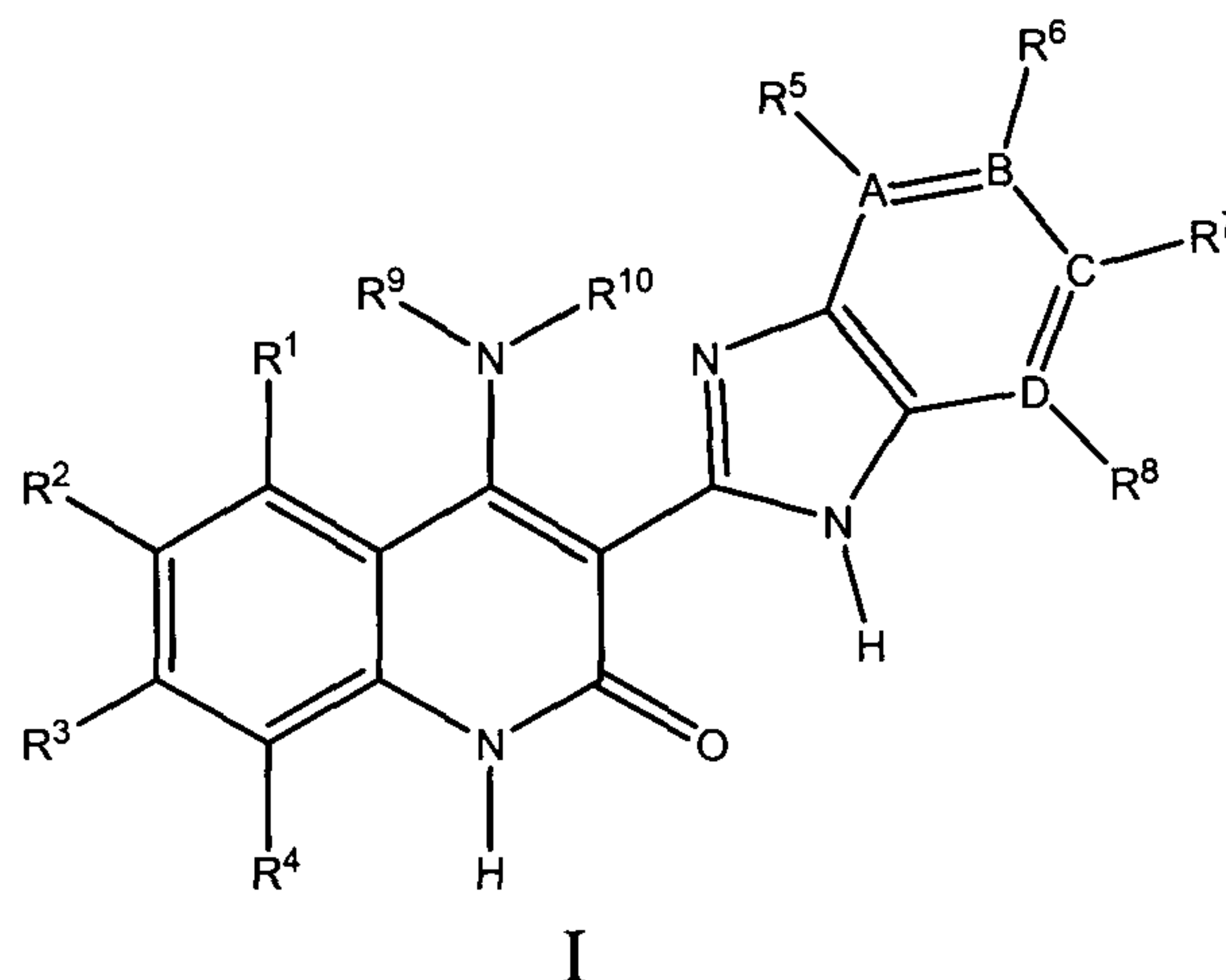
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or -NH₂, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members; and

R¹⁰ is -H, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members.

2. The use according to claim 1, wherein the serine/threonine kinase is glycogen synthase kinase 3, cyclin dependent kinase 2, cyclin dependent kinase 4, checkpoint kinase 1, NEK-2, CHK2, MEK1, CK1ε, Raf, ribosomal S6 kinase 2, or PAR-1.

3. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula and the serine/threonine kinase is glycogen synthase kinase 3



wherein,

A, B, C, and D are independently carbon or nitrogen;

R¹ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups,

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substituted or unsubstituted $-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-S(=O)$ -alkyl groups, $-S(=O)-NH_2$, substituted or unsubstituted $-S(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)$ -alkyl groups, substituted or unsubstituted $-N(H)-S(=O)$ -alkyl groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)-N(H)(aralkyl)$ groups, $-CO_2H$, and substituted or unsubstituted $-C(=O)-O$ -alkyl groups;

R^2 is one of $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-CN$, $-NO_2$, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted cycloalkenyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, $-SH$, substituted or unsubstituted $-S$ -alkyl groups, substituted or unsubstituted $-S(=O)_2-O$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -heterocyclyl groups, substituted or unsubstituted $-S(=O)$ -alkyl groups, substituted or unsubstituted $-S(=O)$ -heterocyclyl groups, $-S(=O)_2-NH_2$, substituted or unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)$ -alkyl groups, substituted or unsubstituted $-N(H)-C(=O)$ -heterocyclyl groups, substituted or unsubstituted $-N(H)-S(=O)$ -alkyl groups, substituted or unsubstituted $-N(H)-S(=O)$ -heterocyclyl groups, $-N(alkyl)-C(=O)$ -alkyl groups,

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substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, -CO₂H, or substituted or unsubstituted -C(=O)-O-alkyl groups; or R² and R³ may join together to form a cyclic group;

R³ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)-NH₂, substituted or unsubstituted -S(=O)-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(cycloalkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, -NH₂, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or

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unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-S(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, -N(H)-C(=O)-NH₂, substituted
 or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, -N(alkyl)-C(=O)-NH₂, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, -C(=O)-NH₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, -CO₂H, and substituted or
 unsubstituted -C(=O)-O-alkyl groups, or R² and R³ may join together to form a
 cyclic group;

R⁴ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted
 straight or branched chain alkyl groups having from 1 to 8 carbon atoms,
 substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms,
 substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, -SH,
 substituted or unsubstituted -S-alkyl groups, substituted or
 unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl
 groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted
 or unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy
 groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl
 groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH₂,
 substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or

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unsubstituted -C(=O)-N(alkyl)_2 groups, or substituted or unsubstituted -C(=O)-O-alkyl groups;

R^5 is one of -H , -F , -Cl , -Br , -I , -CN , -NO_2 , substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -SH , substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-O-alkyl}$ groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-alkyl}$ groups, substituted or unsubstituted -S(=O)-alkyl groups, $\text{-S(=O)}_2\text{-NH}_2$, substituted or unsubstituted $\text{-S(=O)}_2\text{-N(H)(alkyl)}$ groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)}_2$ groups, -OH , substituted or unsubstituted alkoxy groups, -NH_2 , substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)_2 groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)-alkyl groups, -C(=O)-NH_2 , substituted or unsubstituted $\text{-C(=O)-N(H)(alkyl)}$ groups, substituted or unsubstituted -C(=O)-N(alkyl)_2 groups, or substituted or unsubstituted -C(=O)-O-alkyl groups; or R^5 may be absent if A is nitrogen;

R^6 is one of -H , -F , -Cl , -Br , -I , -CN , -NO_2 , substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -SH , substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-O-alkyl}$ groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-alkyl}$ groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-heterocyclyl}$ groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted $\text{-S(=O)-heterocyclyl}$ groups, $\text{-S(=O)}_2\text{-NH}_2$, substituted or unsubstituted $\text{-S(=O)}_2\text{-N(H)(alkyl)}$ groups, substituted or unsubstituted $\text{-S(=O)}_2\text{-N(alkyl)}_2$ groups, -OH , substituted or unsubstituted alkoxy groups, -NH_2 , substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)_2 groups, substituted or unsubstituted $\text{-N(H)(heterocyclyl)}$ groups, substituted or unsubstituted $\text{-N(alkyl)(heterocyclyl)}$ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or

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unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(H)-S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, -CO₂H, or substituted or
 unsubstituted -C(=O)-O-alkyl groups; or R⁶ may be absent if B is nitrogen;

R⁷ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl
 groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl
 groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl
 groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl
 groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or
 unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups,
 substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or
 unsubstituted -S(=O)₂-heterocyclyl groups, substituted or
 unsubstituted -S(=O)-alkyl groups, substituted or
 unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted or
 unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or
 unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy
 groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl)
 groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-S(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-S(=O)-heterocyclyl groups, substituted or

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unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, substituted or unsubstituted amidine groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or unsubstituted -C(=O)-N(H)(alkyl)(heterocyclyl) groups, substituted or unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, -CO₂H, or substituted or unsubstituted -C(=O)-O-alkyl groups; or R⁷ may be absent if C is nitrogen;

R⁸ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)-alkyl groups, -S(=O)₂-NH₂, substituted or unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-S(=O)₂-alkyl groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, or substituted or unsubstituted -C(=O)-O-alkyl groups; or R⁸ may be absent if D is nitrogen;

R⁹ is one of -H, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted alkoxy groups,

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or -NH₂, or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members;
and

R¹⁰ is -H, or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members.

4. The use according to claim 3, wherein

R¹ is one of -H, -F, -Cl, -Br, -I, or straight or branched chain alkyl groups having from 1 to 8 carbon atoms;

R² is one of -H, -F, -Cl, -Br, -I, -CN, -CO₂H, -NO₂, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted cycloalkenyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, or substituted or unsubstituted -N(alkyl)₂ groups;

R³ is one of -H, -F, -Cl, -Br, -I, -CN, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(cycloalkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, -CO₂H, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, -C(=O)-NH₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, or substituted or unsubstituted -C(=O)-N(H)(aryl) groups;

R⁴ is one of -H, -F, -Cl, -Br, -I, or straight or branched chain alkyl groups having from 1 to 8 carbon atoms;

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R^5 is one of -H, -F, -Cl, -Br, -I, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or substituted or unsubstituted heterocyclyl groups; or R^5 may be absent if A is nitrogen;

R^6 is one of -H, -F, -Cl, -Br, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, or substituted or unsubstituted -N(alkyl)(heterocyclyl) groups; or R^6 may be absent if B is nitrogen;

R^7 is one of -H, -Cl, -F, -Br, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, or substituted or unsubstituted -N(alkyl)(heterocyclyl) groups; or R^7 may be absent if C is nitrogen; and

R^8 is -H, -F, -Cl, -Br, -I, straight or branched chain alkyl groups having from 1 to 8 carbon atoms, or substituted or unsubstituted heterocyclyl groups; or R^8 may be absent if D is nitrogen.

5. The use according to claim 3, wherein R^9 is a substituted or unsubstituted straight or branched chain alkyl group having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl group, substituted or unsubstituted aryl group, substituted or unsubstituted aralkyl group, substituted or unsubstituted heterocyclyl group, substituted or unsubstituted heterocyclylalkyl group, substituted or unsubstituted heterocyclylaminoalkyl group, substituted or unsubstituted alkoxy group, or -NH₂.

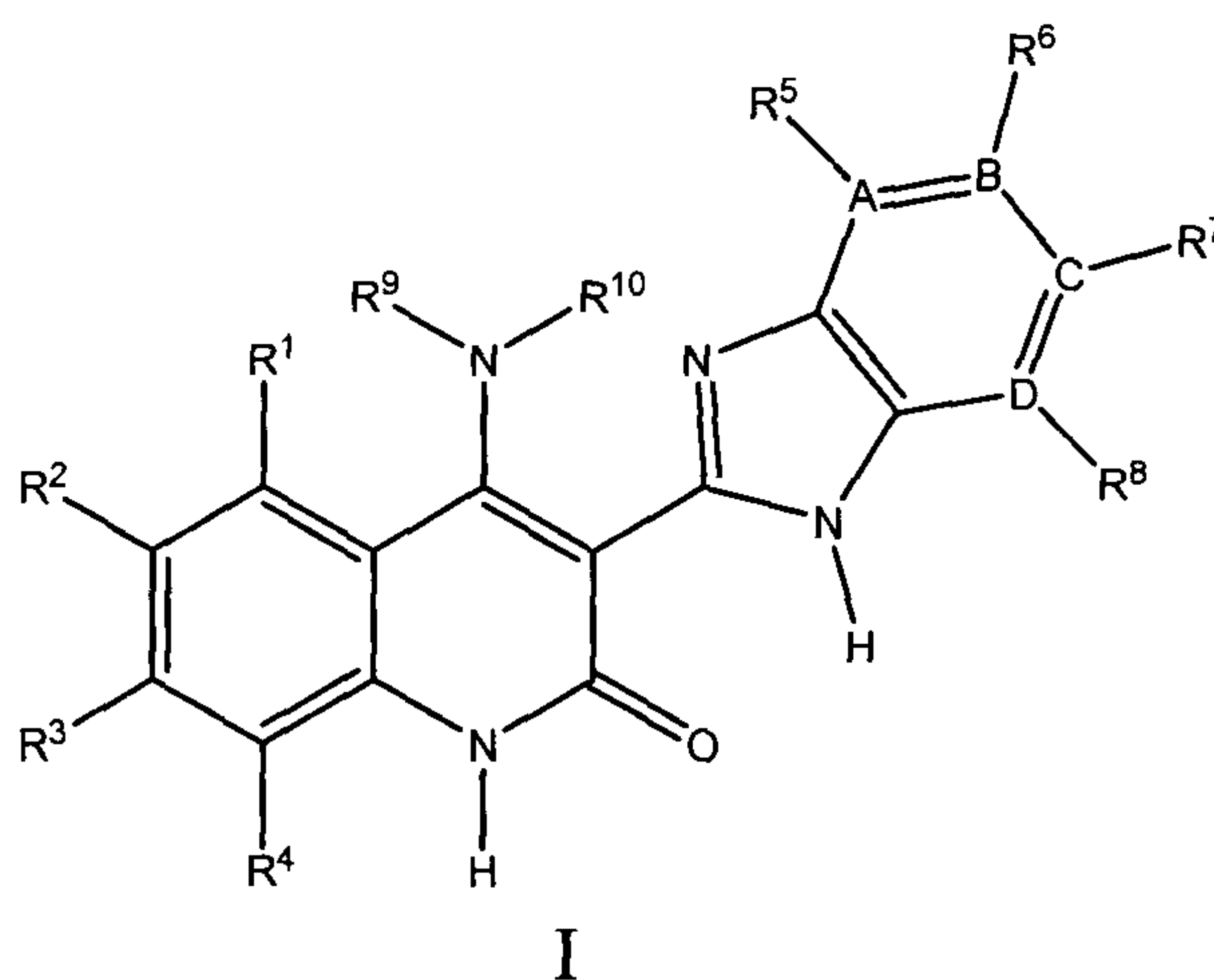
6. The use according to claim 3, wherein R^2 is an -H, -Cl, -F, -Br, -I, -CH₃, -NO₂, -OMe, -CN, -CO₂H, substituted or unsubstituted 1,2,3,6-tetrahydropyridine group, substituted or unsubstituted thiophene group, substituted or unsubstituted imidazole group, substituted or unsubstituted pyrrole group, substituted or unsubstituted 3-pyridinyl group, substituted or unsubstituted 4-pyridinyl group, phenyl, 2-substituted phenyl group, 2,4-disubstituted phenyl

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group, 4-substituted phenyl group, 3-substituted phenyl group, 2,6-disubstituted phenyl group, 3,4-disubstituted phenyl group, substituted or unsubstituted dialkylamino group, or substituted or unsubstituted alkylamino group.

7. The use according to claim 3, wherein R^3 is an -H, -F, -Cl, -Br, -CH₃, -OH, -CN, substituted or unsubstituted aryl group, substituted or unsubstituted heterocyclyl group, substituted or unsubstituted alkoxy group, substituted or unsubstituted alkylamino group, substituted or unsubstituted dialkylamino group, substituted or unsubstituted -C(=O)-heterocyclyl group, substituted or unsubstituted -C(=O)-N(alkyl)₂ group, or -C(=O)-NH₂ group.

8. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula and the serine/threonine kinase is cyclin dependent kinase 2



wherein,

A, B, C, and D are independently carbon or nitrogen;

R^1 , R^4 , R^5 , and R^8 are independently -H or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^2 and R^3 are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or

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unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups, substituted or unsubstituted -N(alkyl)(aryl) groups, substituted or unsubstituted -N(aryl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, or substituted or unsubstituted -N(heterocyclyl)₂ groups;

R⁶ and R⁷ -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -N(heterocyclylalkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, or substituted or unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is -H, substituted or unsubstituted alkyl group having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl group having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl group, substituted or unsubstituted heterocyclylalkyl group, -OH, substituted or unsubstituted alkoxy group, substituted or unsubstituted heterocycloxy group, substituted or unsubstituted heterocyclylalkoxy group, substituted or unsubstituted -C(=O)-alkyl

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group, substituted or unsubstituted -C(=O)-heterocyclyl group, or substituted or unsubstituted -C(=O)-heterocyclylalkyl groups;

R¹⁰ is -H.

9. The use according to claim 8, wherein R⁹ is -H, substituted or unsubstituted straight or branched chain alkyl group having from 1-8 carbon atoms, substituted or unsubstituted saturated heterocyclyl group, substituted or unsubstituted heterocyclylalkyl group wherein the heterocyclyl moiety is saturated, substituted or unsubstituted alkoxy group, or substituted or unsubstituted heterocyclylalkoxy group wherein the heterocyclyl moiety is saturated.

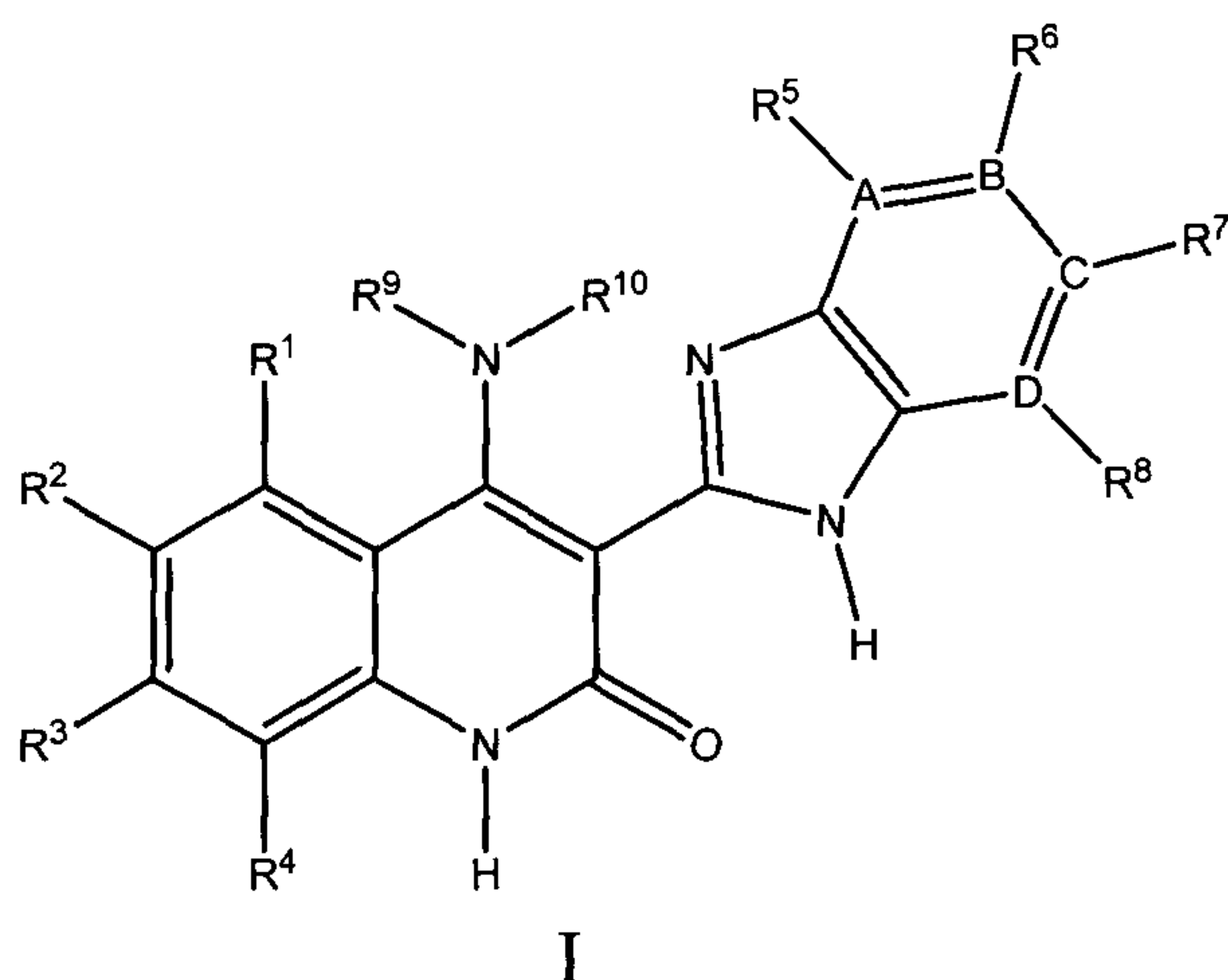
10. The use according to claim 8, wherein R² is -H, -F, -Cl, -Br, -I, -NO₂, -CN, -NH₂, substituted or unsubstituted straight or branched chain alkyl group having from 1 to 8 carbons, substituted or unsubstituted aryl group, or substituted or unsubstituted pyridinyl group.

11. The use according to claim 8, wherein R³ is -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl group having from 1 to 8 carbon atoms, substituted or unsubstituted aryl group, or substituted or unsubstituted aralkyl group.

12. The use according to claim 8, wherein R⁶ and R⁷ are independently -H, -F, -Cl, -Br, -I, -OH, substituted or unsubstituted -N(alkyl)(piperidinyl), substituted or unsubstituted piperidinyl group, substituted or unsubstituted morpholinyl group, substituted or unsubstituted piperazinyl group; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen.

13. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula and the serine/threonine kinase is checkpoint kinase 1

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wherein,

A, B, C, and D are independently carbon or nitrogen;

R¹ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -SH, substituted or unsubstituted -S-alkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, or substituted or unsubstituted -N(heterocyclylalkyl)₂ groups;

R² and R³ are independently -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or

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unsubstituted $-S(=O)_2-O$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-S(=O)_2$ -heterocyclyl groups, substituted or unsubstituted $-S(=O)$ -alkyl groups, substituted or unsubstituted $-S(=O)$ -heterocyclyl groups, $-S(=O)_2-NH_2$, substituted or unsubstituted $-S(=O)_2-N(H)$ (alkyl) groups, substituted or unsubstituted $-S(=O)_2-N$ (alkyl)₂ groups, substituted or unsubstituted $-S(=O)_2-N(H)$ (aryl) groups, substituted or unsubstituted $-S(=O)_2-N$ (alkyl)(aryl) groups, substituted or unsubstituted $-S(=O)_2-N$ (aryl)₂ groups, substituted or unsubstituted $-S(=O)_2-N(H)$ (aralkyl) groups, substituted or unsubstituted $-S(=O)_2-N$ (alkyl)(aralkyl) groups, substituted or unsubstituted $-S(=O)_2-N$ (aralkyl)₂ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)$ (alkyl) groups, substituted or unsubstituted $-N$ (alkyl)₂ groups, substituted or unsubstituted $-N(H)$ (aryl) groups, substituted or unsubstituted $-N$ (alkyl)(aryl) groups, substituted or unsubstituted $-N$ (aryl)₂ groups, substituted or unsubstituted $-N(H)$ (aralkyl) groups, substituted or unsubstituted $-N$ (alkyl)(aralkyl) groups, substituted or unsubstituted $-N$ (aralkyl)₂ groups, substituted or unsubstituted $-N(H)$ (heterocyclyl) groups, substituted or unsubstituted $-N$ (alkyl)(heterocyclyl) groups, substituted or unsubstituted $-N$ (heterocyclyl)₂ groups, substituted or unsubstituted $-N(H)$ (heterocyclylalkyl) groups, substituted or unsubstituted $-N$ (alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted $-N$ (heterocyclylalkyl)₂ groups, substituted or unsubstituted $-N(H)-S(=O)_2$ -alkyl groups, substituted or unsubstituted $-N(H)-S(=O)_2$ -aryl groups, substituted or unsubstituted $-N(H)-S(=O)_2$ -aralkyl groups, substituted or unsubstituted $-N(H)-S(=O)_2$ -heterocyclyl groups, substituted or unsubstituted $-N(H)-S(=O)_2$ -heterocyclylalkyl groups, substituted or unsubstituted $-N(H)-C(=O)$ -alkyl groups, substituted or unsubstituted $-N(H)-C(=O)$ -aryl groups, substituted or

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unsubstituted -N(H)-C(=O)-aralkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-aryl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-aralkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂,
 substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-NH₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(aryl)₂ groups, substituted or

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unsubstituted -N(alkyl)-C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl
 groups, substituted or unsubstituted -C(=O)-aralkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl
 groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, or substituted
 or unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴ is one of -H or substituted or unsubstituted alkyl groups having from 1
 to 12 carbon atoms;

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R^5 and R^8 are independently -H, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups; or R^5 may be absent if A is nitrogen; or R^8 may be absent if D is nitrogen;

R^6 and R^7 are independently -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, substituted or unsubstituted -S(=O)-alkyl groups, substituted or unsubstituted -S(=O)-heterocyclyl groups, -S(=O)₂-NH₂, substituted or unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)₂ groups, substituted or unsubstituted -S(=O)₂-N(H)(heterocyclyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -S(=O)₂-N(heterocyclyl)₂ groups, substituted or unsubstituted -S(=O)₂-N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -S(=O)₂-N(heterocyclylalkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups, substituted or unsubstituted -N(alkyl)(aryl) groups, substituted or unsubstituted -N(aryl)₂ groups, substituted or unsubstituted -N(H)(aralkyl) groups, substituted or unsubstituted -N(alkyl)(aralkyl) groups, substituted or unsubstituted -N(aralkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or

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unsubstituted -N(H)(heterocyclalkyl) groups, substituted or
 unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted or
 unsubstituted -N(heterocyclalkyl)₂ groups, substituted or
 unsubstituted -N(H)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(H)-S(=O)₂-heterocycl groups, substituted or
 unsubstituted -N(H)-S(=O)₂-heterocyclalkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocycl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclalkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocycl groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-heterocyclalkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-alkyl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocycl groups, substituted or
 unsubstituted -N(alkyl)-S(=O)₂-heterocyclalkyl groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocycl groups, substituted or
 unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocycl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocycl) groups, substituted or
 unsubstituted -C(=O)-N(heterocycl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or

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unsubstituted -C(=O)-O-heterocyclyl groups, or substituted or unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R⁶ may be absent if B is nitrogen; or R⁷ may be absent if C is nitrogen;

R⁹ is one of -H, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted alkoxy groups, or -NH₂, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members; and

R¹⁰ is -H, or R⁹ and R¹⁰ join together to form one or more rings, each having 5, 6, or 7 ring members.

14. The use according to claim 13, wherein

R¹ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, or substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups;

R² and R³ are independently -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl

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groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups, substituted or unsubstituted -N(alkyl)(aryl) groups, substituted or unsubstituted -N(aryl)₂ groups, substituted or unsubstituted -N(H)(aralkyl) groups, substituted or unsubstituted -N(alkyl)(aralkyl) groups, substituted or unsubstituted -N(aralkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -N(heterocyclylalkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-aryl groups, substituted or unsubstituted -N(H)-C(=O)-aralkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-alkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-aryl groups, substituted or unsubstituted -N(alkyl)-C(=O)-aralkyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclyl groups, substituted or unsubstituted -N(alkyl)-C(=O)-heterocyclylalkyl groups, -N(H)-C(=O)-NH₂, substituted or unsubstituted -N(H)-C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-N(H)(aryl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)(aryl) groups, substituted or unsubstituted -N(H)-C(=O)-N(aryl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-N(H)(aralkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(alkyl)(aralkyl) groups, substituted or unsubstituted -N(H)-C(=O)-N(aralkyl)₂ groups, substituted or

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unsubstituted -N(H)-C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -N(H)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-N(heterocyclylalkyl)₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-NH₂ groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(alkyl)-C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl
 groups, substituted or unsubstituted -C(=O)-aralkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl
 groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, or substituted
 or unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁶ and R⁷ are independently -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or
 unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or
 unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or
 unsubstituted alkynyl groups having from 2 to 8 carbon atoms, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl
 groups, -S(=O)₂-NH₂, substituted or unsubstituted -S(=O)₂-N(H)(alkyl) groups,

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substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocyclyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted or unsubstituted $-N(heterocyclyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocyclalkyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclalkyl)$ groups, substituted or unsubstituted $-N(heterocyclalkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted or unsubstituted $-N(H)-C(=O)-heterocyclalkyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-heterocyclyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-heterocyclalkyl$ groups, substituted or unsubstituted $-C(=O)-alkyl$ groups, substituted or unsubstituted $-C(=O)-heterocyclyl$ groups, substituted or unsubstituted $-C(=O)-heterocyclalkyl$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)-N(H)(heterocyclyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)(heterocyclyl)$ groups, substituted or unsubstituted $-C(=O)-N(heterocyclyl)_2$ groups, substituted or unsubstituted $-C(=O)-N(H)(heterocyclalkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)(heterocyclalkyl)$ groups, substituted or unsubstituted $-C(=O)-N(heterocyclalkyl)_2$ groups, $-CO_2H$, substituted or unsubstituted $-C(=O)-O-alkyl$ groups, substituted or unsubstituted $-C(=O)-O-heterocyclyl$ groups, or substituted or unsubstituted $-C(=O)-O-heterocyclalkyl$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

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15. The use according to claim 13, wherein R^9 is one of substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, or substituted or unsubstituted heterocyclylaminoalkyl groups.

16. The use according to claim 13, wherein R^9 is one of substituted or unsubstituted cyclohexyl groups, substituted or unsubstituted cyclohexylalkyl groups, substituted or unsubstituted pyrrolidinyl groups, substituted or unsubstituted pyrrolidinylalkyl groups, substituted or unsubstituted tetrahydrofuranylalkyl groups, substituted or unsubstituted piperidinyl groups, substituted or unsubstituted piperidinylalkyl groups, substituted or unsubstituted piperazinylalkyl groups, substituted or unsubstituted morpholinylalkyl groups, or substituted or unsubstituted quinuclidinyl groups.

17. The use according to claim 13, wherein R^1 is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 4 carbon atoms, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, or substituted or unsubstituted -N(H)(alkyl) groups.

18. The use according to claim 13, wherein R^3 is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, or substituted or unsubstituted heterocyclylalkoxy groups.

19. The use according to claim 13, wherein R^6 and R^7 are independently -H, -F, -Cl, -Br, -I, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups,

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substituted or unsubstituted heterocyclalkyl groups, $-S(=O)_2-NH_2$, substituted or unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocycl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocycl)$ groups, substituted or unsubstituted $-N(H)(heterocyclalkyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclalkyl)$ groups, substituted or unsubstituted $-C(=O)-alkyl$ groups, substituted or unsubstituted $-C(=O)-heterocycl$ groups, substituted or unsubstituted $-C(=O)-heterocyclalkyl$ groups, $-C(=O)-NH_2$, substituted or unsubstituted $-C(=O)-N(H)(alkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)-N(H)(heterocycl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)(heterocycl)$ groups, substituted or unsubstituted $-C(=O)-N(H)(heterocyclalkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)(heterocyclalkyl)$ groups, $-CO_2H$, substituted or unsubstituted $-C(=O)-O-alkyl$ groups, substituted or unsubstituted $-C(=O)-O-heterocycl$ groups, or substituted or unsubstituted $-C(=O)-O-heterocyclalkyl$ groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

20. The use according to claim 13, wherein R^6 and R^7 are independently substituted or unsubstituted heterocycl groups or substituted or unsubstituted heterocyclalkyl groups; or R^6 may be absent if B is nitrogen; or R^7 may be absent if C is nitrogen.

21. The use according to claim 13, wherein R^6 and R^7 are independently substituted or unsubstituted pyrrolidinyl groups, substituted or unsubstituted piperidinylalkyl groups, substituted or unsubstituted piperazinyl groups, substituted

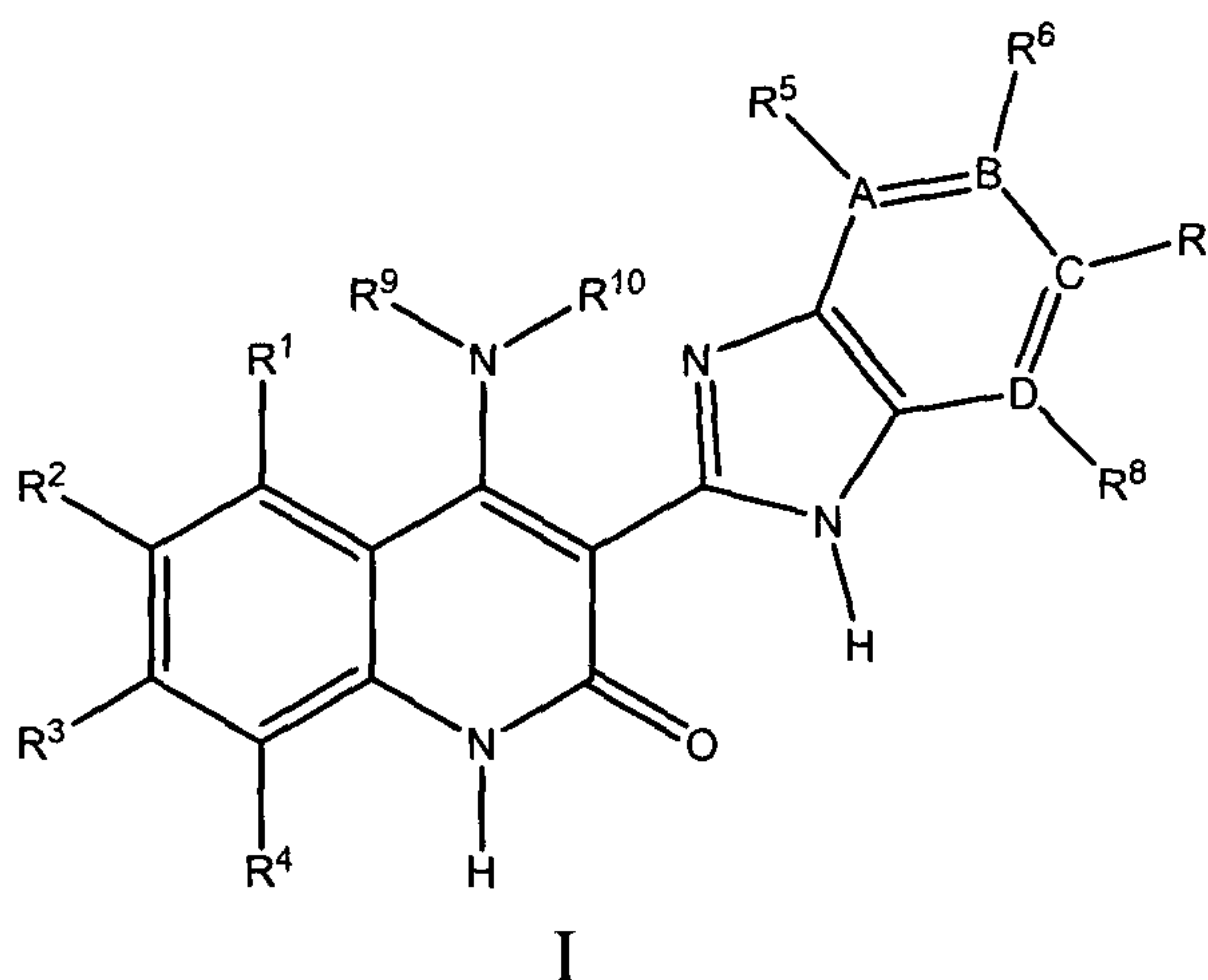
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or unsubstituted morpholinyl groups, substituted or unsubstituted thiomorpholinyl groups, substituted or unsubstituted dizeapanyl groups, substituted or unsubstituted oxazepanyl groups, and pyridinylalkyl groups.

22. The use according to claim 13, wherein the IC_{50} value of the compound is less than or equal to $0.001 \mu M$.

23. The use according to claim 13, wherein the biological condition is cancer.

24. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula and the serine/threonine kinase is ribosomal S6 kinase 2



wherein,

A, B, C, and D are independently carbon or nitrogen;

R^1 is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or

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unsubstituted -N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl)
 groups, -CO₂H, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or
 unsubstituted -C(=O)-O-heterocyclyl groups, or substituted or
 unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R² and R³ are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or
 unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or
 unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or
 unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted
 or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl
 groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or
 unsubstituted -S-aryl groups, substituted or unsubstituted -S-aralkyl groups, -OH,
 substituted or unsubstituted alkoxy groups, substituted or unsubstituted
 heterocyclylloxy groups, substituted or unsubstituted heterocyclylalkoxy
 groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or
 unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups,
 substituted or unsubstituted -N(H)(aralkyl) groups, substituted or
 unsubstituted -N(H)(heterocyclyl) groups, substituted or
 unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -N(H)-C(=O)-alkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-aryl groups, substituted or
 unsubstituted -N(H)-C(=O)-aralkyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclyl groups, substituted or
 unsubstituted -N(H)-C(=O)-heterocyclylalkyl groups, substituted or

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unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl groups, substituted or unsubstituted -C(=O)-aralkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(aryl) groups, substituted or unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl) groups, -CO₂H, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl groups, substituted or unsubstituted -C(=O)-O-aralkyl groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, or substituted or unsubstituted -C(=O)-O-heterocyclylalkyl groups; or R² and R³ may join together to form a cyclic group,

R⁴, R⁵, and R⁸ are independently -H or substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms; or R⁵ may be absent if A is nitrogen; or R⁸ may be absent if D is nitrogen.

R⁶ is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -CO₂H, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, -C(=O)-N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-heterocyclyl groups, substituted or unsubstituted -C(=O)-O-heterocyclylalkyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-heterocyclylalkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(H)(heterocyclyl)

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groups, substituted or unsubstituted -N(H)(heterocyclalkyl) groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocycl groups, or substituted or unsubstituted -N(H)-C(=O)-heterocyclalkyl groups;

R^7 is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocycl groups, substituted or unsubstituted heterocyclalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclalkoxy groups, -SH, substituted or unsubstituted -S-alkyl groups, -CO₂H, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocycl) groups, -C(=O)-N(H)(heterocyclalkyl) groups, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-heterocycl groups, substituted or unsubstituted -C(=O)-O-heterocyclalkyl groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-heterocycl groups, substituted or unsubstituted -C(=O)-heterocyclalkyl groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocycl) groups, substituted or unsubstituted -N(alkyl)(heterocycl) groups, substituted or unsubstituted -N(heterocycl)₂ groups, substituted or unsubstituted -N(H)(heterocyclalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclalkyl) groups, substituted or unsubstituted -N(heterocyclalkyl)₂ groups, substituted or unsubstituted -N(H)-C(=O)-alkyl groups, substituted or unsubstituted -N(H)-C(=O)-heterocycl groups, or substituted or unsubstituted -N(H)-C(=O)-heterocyclalkyl groups; or R^7 may be absent if C is nitrogen;

R^9 is one of -H, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12

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carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted arylalkoxy groups, substituted or unsubstituted heterocyclyoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl groups, substituted or unsubstituted -C(=O)-aralkyl groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, or substituted or unsubstituted -C(=O)-heterocyclylalkyl groups; or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members; and

R¹⁰ is -H, or R⁹ and R¹⁰ join together to form a ring having 5, 6, or 7 ring members.

25. The use according to claim 24, wherein

R¹ is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyoxy groups, or substituted or unsubstituted heterocyclylalkoxy groups;

R² and R³ are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, or -CO₂H; or R² and R³ may join together to form a cyclic group

R⁶ is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or

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unsubstituted heterocycloxy groups, or substituted or unsubstituted heterocyclalkoxy groups; or R⁶ may be absent if B is nitrogen;

R⁷ is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocycl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, or substituted or unsubstituted heterocyclalkoxy groups; or R⁷ may be absent if C is nitrogen.

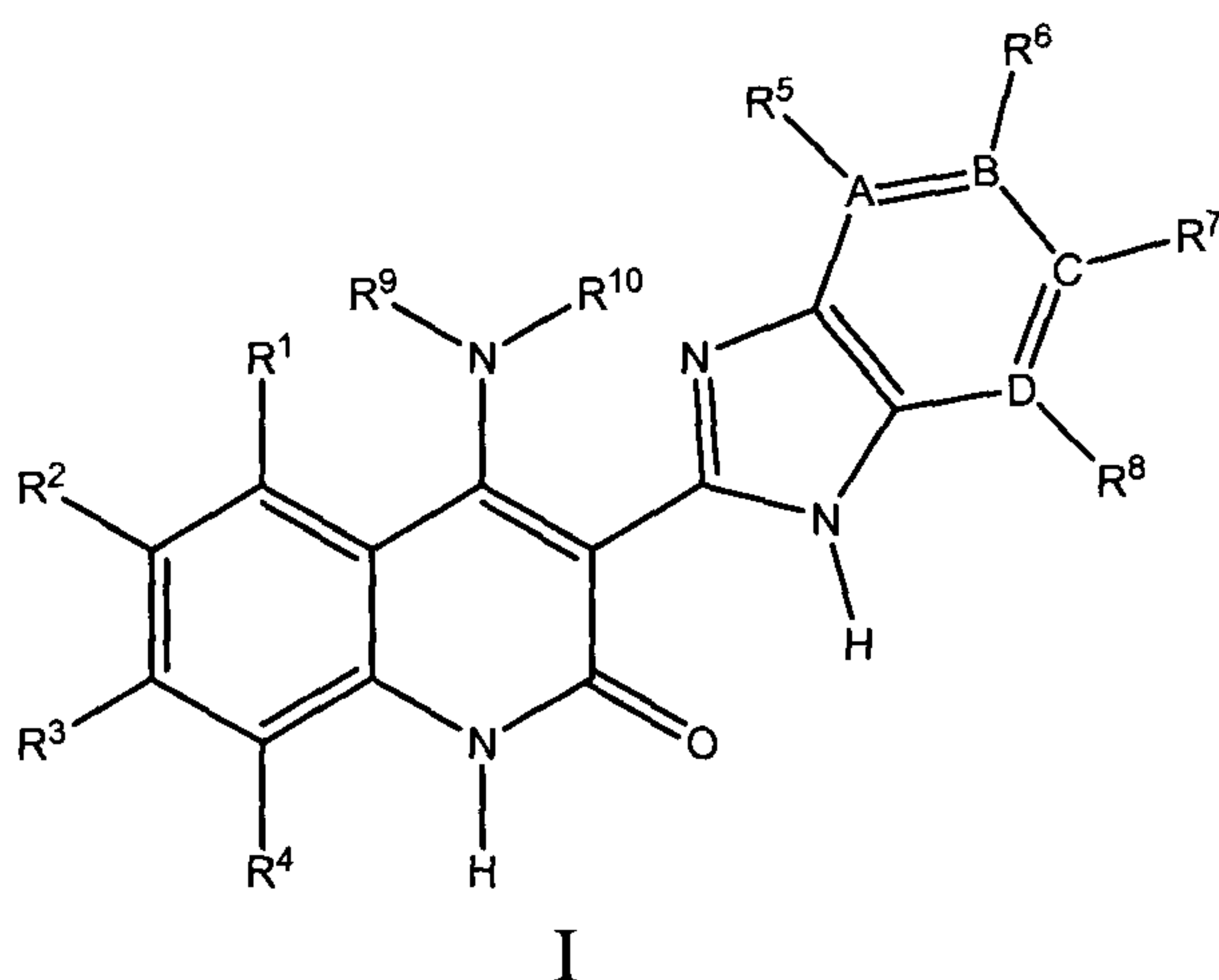
26. The use according to claim 24, wherein R⁹ is one of -H, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted saturated heterocycl groups, substituted or unsubstituted heterocyclalkyl groups wherein the heterocycl moiety is saturated, substituted or unsubstituted alkoxy groups, or substituted or unsubstituted heterocyclalkoxy groups wherein the heterocycl moiety is saturated.

27. The use according to claim 24, wherein R¹ is one of -H, -F, -Cl, substituted or unsubstituted morpholinyl groups, substituted or unsubstituted morpholinylalkyl groups, or substituted or unsubstituted morpholinylalkoxy groups.

28. The use according to claim 24, wherein R² is one of -H, -F, -Cl, -Br, -I, -NO₂, -CH₃, -OCH₃, -CO₂H, substituted or unsubstituted aryl groups, or substituted or unsubstituted pyridinyl groups.

29. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof for inhibiting a serine/threonine kinase in a subject or treating a biological condition mediated by a serine/threonine kinase in a subject, wherein Structure I has the following formula and the serine/threonine kinase is PAR-1

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wherein,

A, B, C, and D are independently carbon or nitrogen;

R^1 is one of -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted heterocyclyl groups, or substituted or unsubstituted heterocyclylalkyl groups;

R^2 is one of -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, -OH, substituted or unsubstituted alkoxy, substituted or unsubstituted heterocyclyloxy, substituted or unsubstituted heterocyclylalkoxy, substituted or unsubstituted -C(=O)-alkyl groups, substituted or unsubstituted -C(=O)-aryl, substituted or unsubstituted -C(=O)-aralkyl, -CO₂H, substituted or unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl groups, or substituted or unsubstituted -C(=O)-O-aralkyl groups;

R^3 is one of -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or unsubstituted -S(=O)₂-O-alkyl groups, substituted or unsubstituted -S(=O)₂-alkyl groups, substituted or unsubstituted -S(=O)₂-heterocyclyl groups, -S(=O)₂-NH₂,

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substituted or unsubstituted $-S(=O)_2-N(H)(alkyl)$ groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, substituted or unsubstituted $-S(=O)-alkyl$ groups, substituted or unsubstituted $-S(=O)-aryl$ groups, substituted or unsubstituted $-S(=O)-heterocyclyl$ groups, $-OH$, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, $-NH_2$, substituted or unsubstituted $-N(H)(alkyl)$ groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)(aryl)$ groups, substituted or unsubstituted $-N(alkyl)(aryl)$ groups, substituted or unsubstituted $-N(aryl)_2$ groups, substituted or unsubstituted $-N(H)(aralkyl)$ groups, substituted or unsubstituted $-N(alkyl)(aralkyl)$ groups, substituted or unsubstituted $-N(aralkyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocyclyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted or unsubstituted $-N(heterocyclyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocyclylalkyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclylalkyl)$ groups, substituted or unsubstituted $-N(heterocyclylalkyl)_2$ groups, substituted or unsubstituted $-N(H)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-alkyl$ groups, substituted or unsubstituted $-N(H)-C(=O)-aryl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-aryl$ groups, substituted or unsubstituted $-N(H)-C(=O)-aralkyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-aralkyl$ groups, substituted or unsubstituted $-N(H)-C(=O)-heterocyclyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-heterocyclyl$ groups, substituted or unsubstituted $-N(H)-C(=O)-heterocyclylalkyl$ groups, substituted or unsubstituted $-N(alkyl)-C(=O)-heterocyclylalkyl$ groups, substituted or unsubstituted $-N(H)-S(=O)_2-alkyl$ groups, substituted or unsubstituted $-N(H)-S(=O)_2-aryl$, substituted or unsubstituted $-N(H)-S(=O)_2-heterocyclyl$ groups, substituted or unsubstituted $-C(=O)-alkyl$ groups, substituted or unsubstituted $-C(=O)-aryl$, substituted or unsubstituted $-C(=O)-aralkyl$, substituted or

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unsubstituted -C(=O)-heterocyclyl groups, substituted or
 unsubstituted -C(=O)-heterocyclylalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclylalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclylalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or unsubstituted -C(=O)-O-aryl
 groups, substituted or unsubstituted -C(=O)-O-aralkyl groups, substituted or
 unsubstituted -C(=O)-O-heterocyclyl groups, or substituted or
 unsubstituted -C(=O)-O-heterocyclylalkyl groups;

R⁴, R⁵ and R⁸ are independently -H or substituted or unsubstituted alkyl
 groups having from 1 to 12 carbon atoms; or R⁵ may be absent if A is nitrogen; or
 R⁸ may be absent if D is nitrogen;

R⁶ and R⁷ are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or
 unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or
 unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or
 unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl
 groups, -SH, substituted or unsubstituted -S-alkyl groups, substituted or
 unsubstituted -S-heterocyclyl groups, -OH, substituted or unsubstituted alkoxy
 groups, substituted or unsubstituted heterocycloxy groups, substituted or
 unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or
 unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups,
 substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or

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unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, or substituted or unsubstituted -N(heterocyclylalkyl)₂ groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is nitrogen;

R⁹ is one of -H, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbons, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, or substituted or unsubstituted heterocyclylalkoxy groups; and

R¹⁰ is -H.

30. The use according to claim 29, wherein

R³ is one of -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocycliloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(aryl) groups, substituted or unsubstituted -N(alkyl)(aryl) groups, substituted or unsubstituted -N(aryl)₂ groups, substituted or unsubstituted -N(H)(aralkyl) groups, substituted or unsubstituted -N(alkyl)(aralkyl) groups, substituted or unsubstituted -N(aralkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(heterocyclyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or

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unsubstituted -N(heterocyclalkyl)₂ groups, substituted or
 unsubstituted -C(=O)-alkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclalkyl groups, substituted or
 unsubstituted -C(=O)-heterocyclalkyl groups, -C(=O)-NH₂, substituted or
 unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or
 unsubstituted -C(=O)-N(aryl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or
 unsubstituted -C(=O)-N(aralkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, substituted or
 unsubstituted -C(=O)-N(H)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(alkyl)(heterocyclalkyl) groups, substituted or
 unsubstituted -C(=O)-N(heterocyclalkyl)₂ groups, -CO₂H, substituted or
 unsubstituted -C(=O)-O-alkyl groups, substituted or
 unsubstituted -C(=O)-O-heterocyclalkyl groups, or substituted or
 unsubstituted -C(=O)-O-heterocyclalkyl groups;

R⁶ and R⁷ are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or
 unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or
 unsubstituted alkenyl groups having from 2 to 12 carbon atoms, substituted or
 unsubstituted heterocyclalkyl groups, substituted or unsubstituted heterocyclalkyl
 groups, -OH, substituted or unsubstituted alkoxy groups, substituted or
 unsubstituted heterocyclalkoxy groups, or substituted or unsubstituted
 heterocyclalkoxy groups; or R⁶ is absent if B is nitrogen; or R⁷ is absent if C is
 nitrogen.

31. The use according to claim 29, wherein R⁹ is one of -H, substituted or
 unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon

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atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted heterocyclyl groups, or substituted or unsubstituted heterocyclylalkyl groups.

32. The use according to claim 29, wherein R^1 is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, or substituted or unsubstituted heterocyclyl groups.

33. The use according to claim 29, wherein R^2 is one of -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted aralkyl groups.

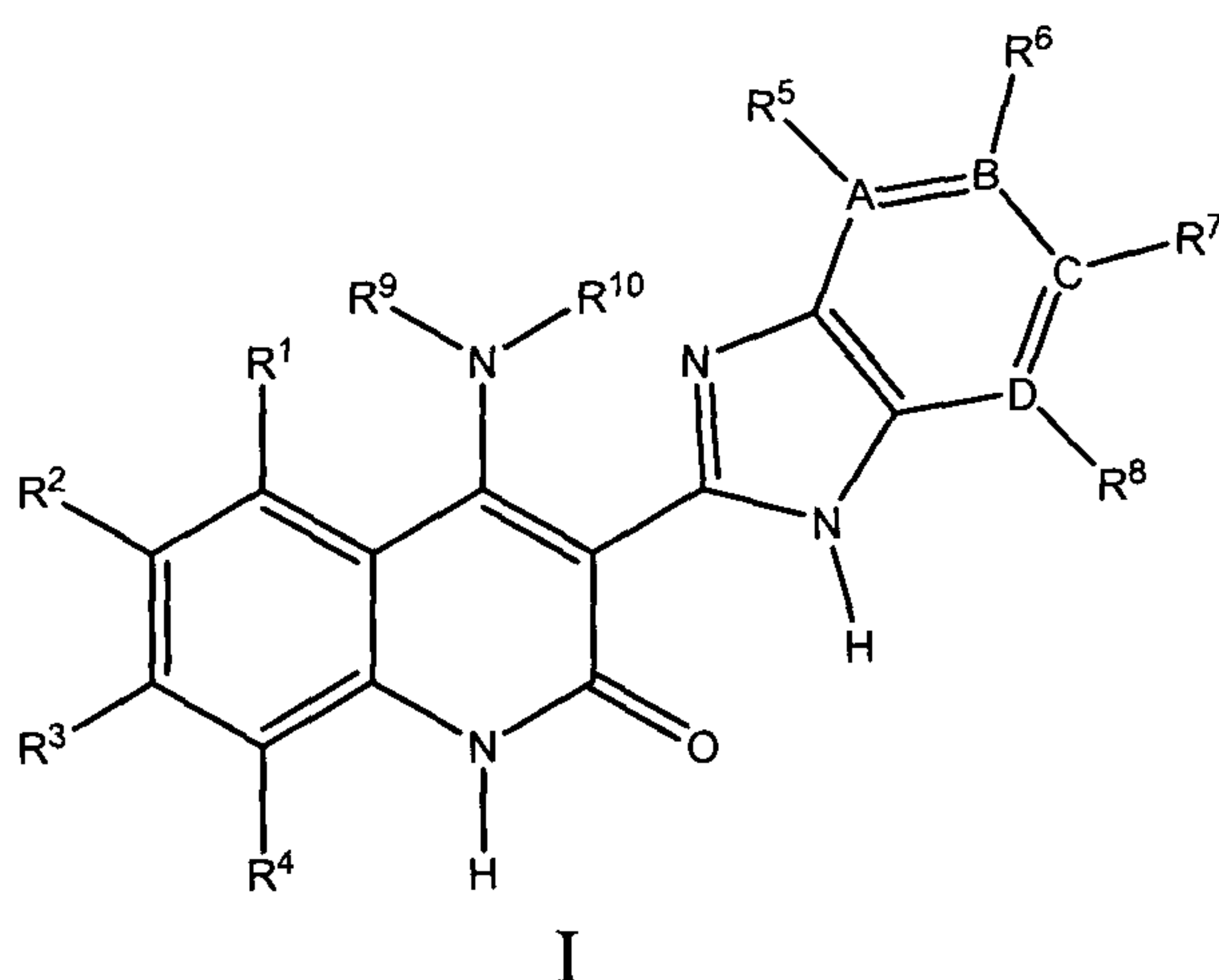
34. The use according to claim 29, wherein R^3 is one of -H, -F, -Cl, -Br, -I, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, or substituted or unsubstituted -N(H)(heterocyclylalkyl) groups.

35. The use according to claim 29, R^6 and R^7 are independently -H, -F, -Cl, -Br, -I, -CN, -NO₂, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, or substituted or unsubstituted heterocyclylalkoxy groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen.

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36. The use according to any of claims 3, 8, 13, 24, or 29, wherein R^9 is one of quinuclidinyl groups, piperidinyl groups, piperidinylalkyl groups, pyrrolidinyl groups, or aminocyclohexyl groups.
37. The use according to any of claims 3 or 13, wherein A, B, C, and D are all carbon, and R^4 , R^5 , R^6 , R^7 , R^8 , and R^{10} are all -H.
38. The use according to any of claims 3, 8, 13, 24, or 29, wherein the IC_{50} value of the compound is less than or equal to $0.1 \mu M$ with respect to the serine/threonine kinase.
39. The use according to any of claims 3, 8, 24, or 29, wherein the biological condition is diabetes.
40. The use according to any of claims 3, 8, 13, 24, or 29, wherein the biological condition is Alzheimer's disease.
41. The use according to claims 1, 3, 8, 13, 24, or 29, wherein administration of the compound to the subject reduces tau phosphorylation.
42. Use of a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof, for treating cancer wherein the cancer is a hematologic cancer, acute myelogenous leukemia, ovarian carcinoma, breast carcinoma, lung cancer, colon cancer, prostate cancer, pituitary cancer, chronic myelogenous leukemia, multiple myeloma, or acute lymphoblastic leukemia, and Structure I has the following formula:

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wherein,

A, B, C, and D are all carbon or one of A or D is nitrogen, and B and C are both carbon;

R¹ is one of -H, -F, -Cl, -Br, -I, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, or substituted or unsubstituted heterocyclylalkoxy groups;

R² is one of -H, -F, -Cl, -Br, -I, -NO₂, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, -NH₂, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, -C(=O)-NH₂, substituted or unsubstituted -C(=O)-N(H)(aryl) groups, substituted or unsubstituted -C(=O)-N(alkyl)(aryl) groups, substituted or unsubstituted -C(=O)-N(aryl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(aralkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)(aralkyl) groups, substituted or unsubstituted -C(=O)-N(aralkyl)₂ groups, or -CO₂H;

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R^3 is one of -H, -F, -Cl, -Br, -I, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted cycloalkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, or substituted or unsubstituted -N(H)(heterocyclylalkyl) groups;

R^4 is one of -H or substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms;

R^5 and R^8 are independently -H, -F, -OH, or saturated heterocyclyl groups; or R^5 is absent if A is nitrogen; or R^8 is absent if D is nitrogen;

R^6 and R^7 are independently -H, -F, -Cl, -Br, -I, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted -S(=O)₂-N(H)(alkyl) groups, substituted or unsubstituted -S(=O)₂-N(alkyl)₂ groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyloxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted -N(H)(alkyl) groups, substituted or unsubstituted -N(alkyl)₂ groups, substituted or unsubstituted -N(H)(heterocyclyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclyl) groups, substituted or unsubstituted -N(H)(heterocyclylalkyl) groups, substituted or unsubstituted -N(alkyl)(heterocyclylalkyl) groups, substituted or unsubstituted -C(=O)-heterocyclyl groups, substituted or unsubstituted -C(=O)-N(H)(alkyl) groups, substituted or unsubstituted -C(=O)-N(alkyl)₂ groups, substituted or unsubstituted -C(=O)-N(H)(heterocyclyl) groups, or substituted or unsubstituted -C(=O)-N(alkyl)(heterocyclyl) groups;

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R^9 is one of -H, substituted or unsubstituted alkyl groups having from 1 to 12 carbon atoms, substituted or unsubstituted alkenyl groups having from 2 to 12 carbons, substituted or unsubstituted aryl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocycloxy groups, -NH₂, or substituted or unsubstituted heterocyclylaminoalkyl; and

R^{10} is -H.

43. The use according to claim 42, wherein R^9 is H.

44. The use according to claim 42, wherein R^1 is one of -H, -F, -Cl, substituted or unsubstituted straight or branched chain alkoxy, substituted or unsubstituted piperidinyloxy, substituted or unsubstituted morpholinyl, or substituted or unsubstituted piperazinyl.

45. The use according to claim 42, wherein R^1 is -F.

46. The use according to claim 42, wherein R^2 is one of -H, -F, -Cl, -Br, -I, methyl, methoxy, or -CO₂H.

47. The use according to claim 42, wherein R^3 is one of -H, -F, -Cl, -Br, methoxy, or dimethylamino.

48. The use according to claim 42, wherein R^4 is -H or -CH₃.

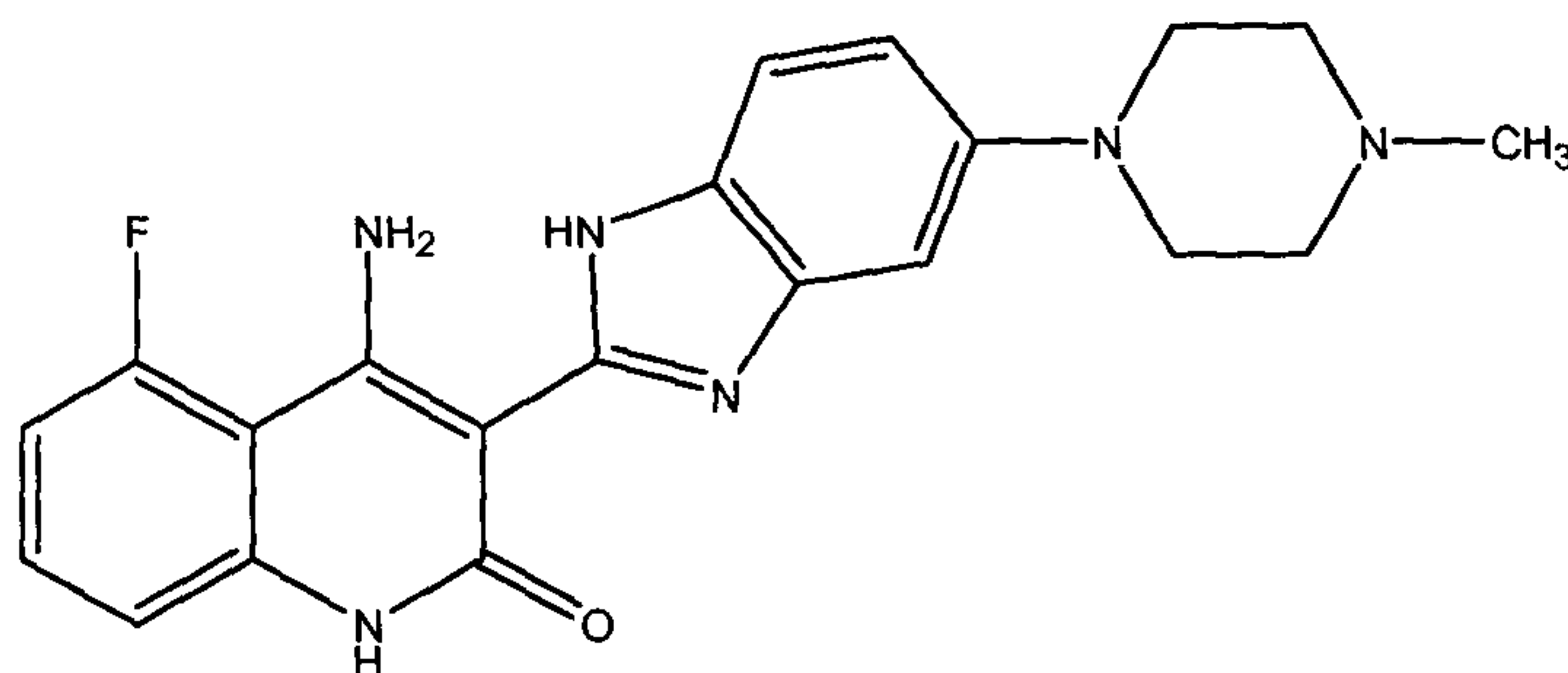
49. The use according to claim 42, wherein R^5 and R^8 are independently -H, -F, -OH, or saturated heterocyclyl groups; or R^5 is absent if A is nitrogen; or R^8 is absent if D is nitrogen.

50. The use according to claim 42, wherein A and D are both carbon, R^5 is -H, and R^8 is -H.

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51. The use according to claim 42, wherein R^6 and R^7 are independently -H, -F, -Cl, -CN, substituted or unsubstituted straight or branched chain alkyl groups having from 1 to 8 carbon atoms, substituted or unsubstituted pyrrolidinyl groups, substituted or unsubstituted morpholinyl groups, substituted or unsubstituted piperazinyl groups, substituted or unsubstituted diazepinyl groups, substituted or unsubstituted triazolyl groups, substituted or unsubstituted thiomorpholine 1-oxide groups, substituted or unsubstituted pyridinylalkyl groups, substituted or unsubstituted $-S(=O)_2-N(alkyl)_2$ groups, -OH, substituted or unsubstituted straight or branched chain alkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclalkoxy groups, substituted or unsubstituted $-N(alkyl)_2$ groups, substituted or unsubstituted $-N(H)(heterocyclyl)$ groups, substituted or unsubstituted $-N(alkyl)(heterocyclyl)$ groups, substituted or unsubstituted $-N(H)(heterocyclalkyl)$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)_2$ groups, substituted or unsubstituted $-C(=O)-N(alkyl)(piperidinyl)$ groups, substituted or unsubstituted $-C(=O)-(morpholin-4-yl)$ groups, or substituted or unsubstituted $-C(=O)-(piperazin-1-yl)$ groups; or R^6 is absent if B is nitrogen; or R^7 is absent if C is nitrogen.

52. The use according to claim 42, wherein the compound has the following formula:



53. The use according to any one of claims 42-52, wherein the cancer is acute myelogenous leukemia, ovarian carcinoma, breast carcinoma, lung cancer, colon cancer, prostate cancer, multiple myeloma, or chronic myelogenous leukemia.

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54. The use according to claim 53, wherein the cancer is acute myelogenous leukemia.
55. The use according to claim 53, wherein the cancer is breast carcinoma.
56. The use according to claim 53, wherein the cancer is colon cancer.
57. The use according to claim 53, wherein the cancer is prostate cancer.
58. The use according to claim 53, wherein the cancer is multiple myeloma.
59. A compound, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof, wherein the compound is 4-amino-5-fluoro-3-(5-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one.
60. A pharmaceutical composition, comprising the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 59 and a pharmaceutically acceptable carrier.
61. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 59 in cancer treatment.
62. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 59 as an anti-cancer agent.
63. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 59 in preparation of a medicament for treating cancer.

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64. A compound, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt of the tautomer, or a mixture thereof, wherein the compound is 4-amino-5-fluoro-3-[5-(4-methyl-4-oxidopiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one.

65. A pharmaceutical composition, comprising the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 64 and a pharmaceutically acceptable carrier.

66. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 64 in cancer treatment.

67. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 64 as an anti-cancer agent.

68. Use of the compound, the tautomer, the pharmaceutically acceptable salt of the compound, the pharmaceutically acceptable salt of the tautomer, or the mixture thereof of claim 64 in preparation of a medicament for treating cancer.

69. Use of 4-amino-5-fluoro-3-(5-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one, a tautomer of 4-amino-5-fluoro-3-(5-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one, a pharmaceutically acceptable salt of 4-amino-5-fluoro-3-(5-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one, a pharmaceutically acceptable salt of the tautomer of 4-amino-5-fluoro-3-(5-piperazin-1-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one, 4-amino-5-fluoro-3-[5-(4-methyl-4-oxidopiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one, a tautomer of 4-amino-5-fluoro-3-[5-(4-methyl-4-oxidopiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one, a pharmaceutically acceptable salt of 4-amino-5-fluoro-3-[5-(4-methyl-4-oxidopiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one, a

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pharmaceutically acceptable salt of the tautomer of 4-amino-5-fluoro-3-[5-(4-methyl-4-oxidopiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one, or a mixture thereof in cancer treatment.

Fig. 1

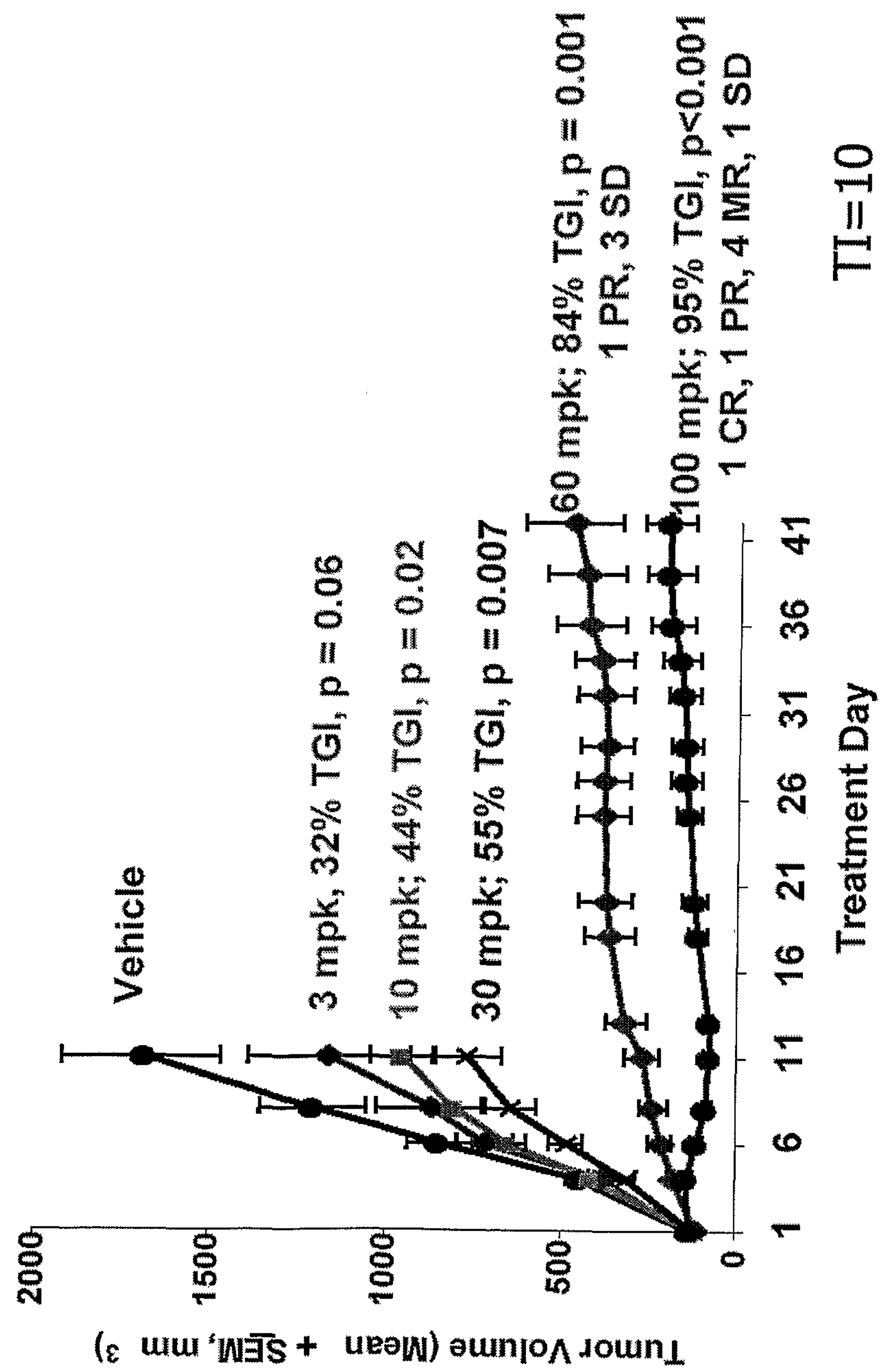


FIG. 2

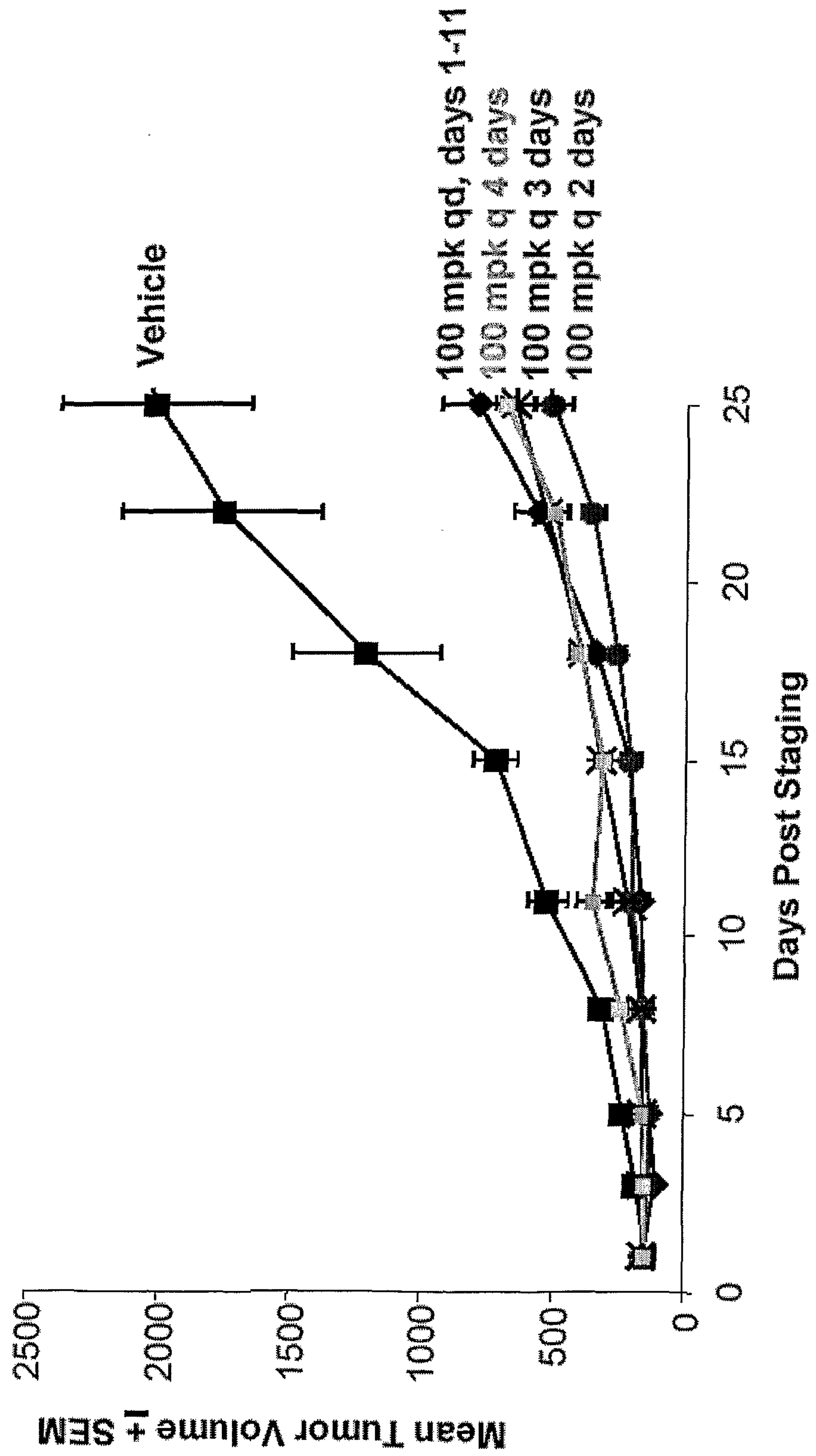
FIG. 3

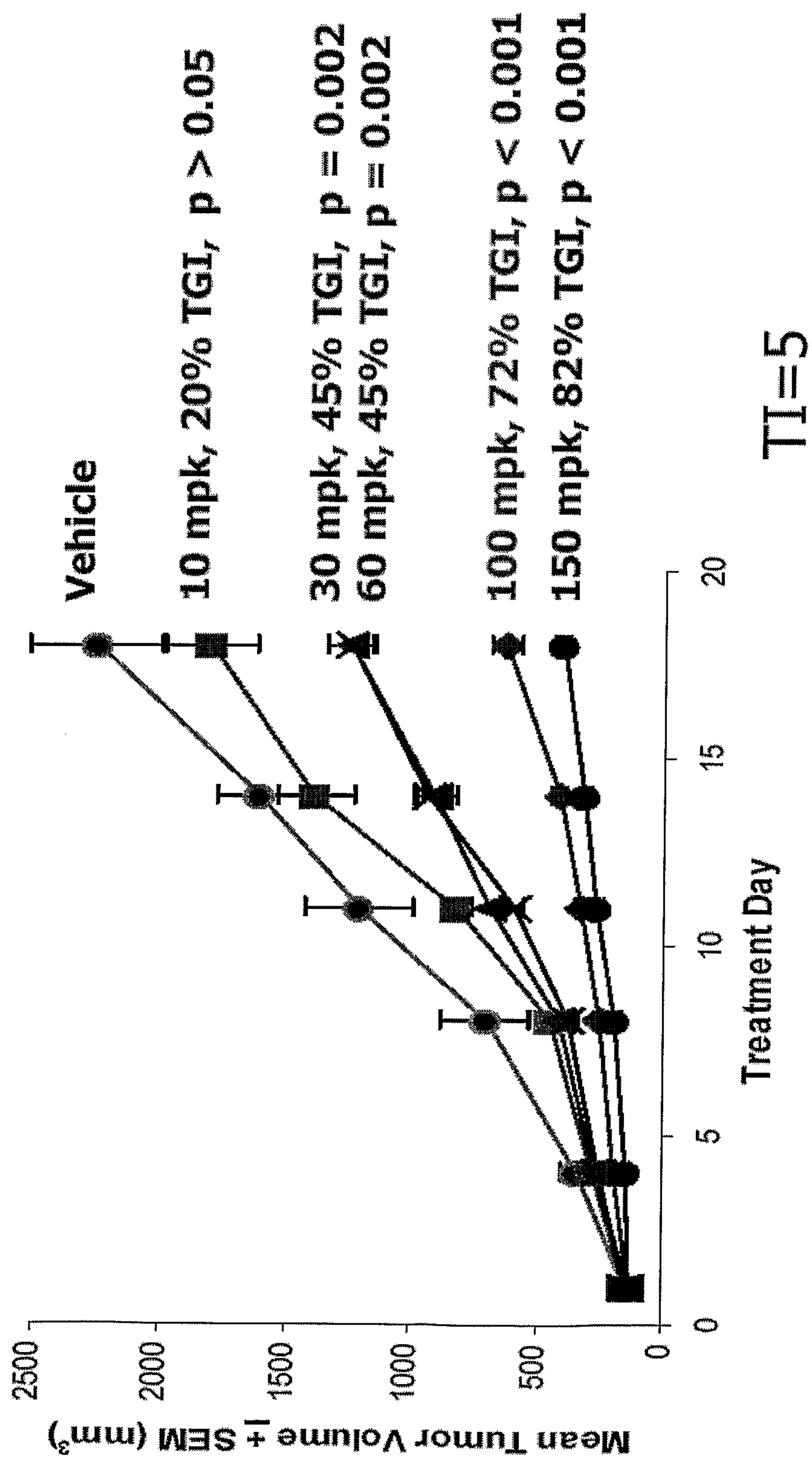
FIG. 4

FIG. 5

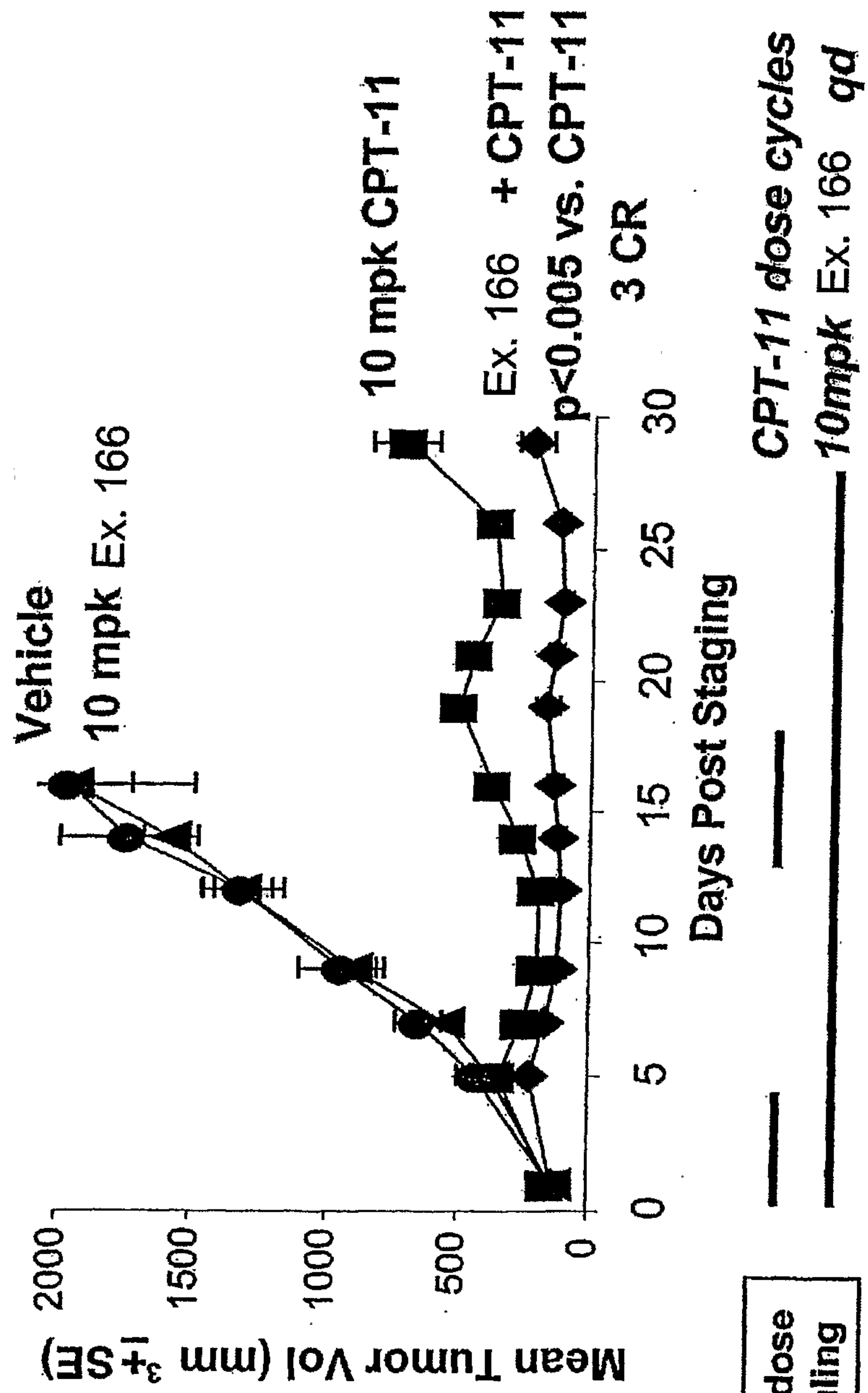


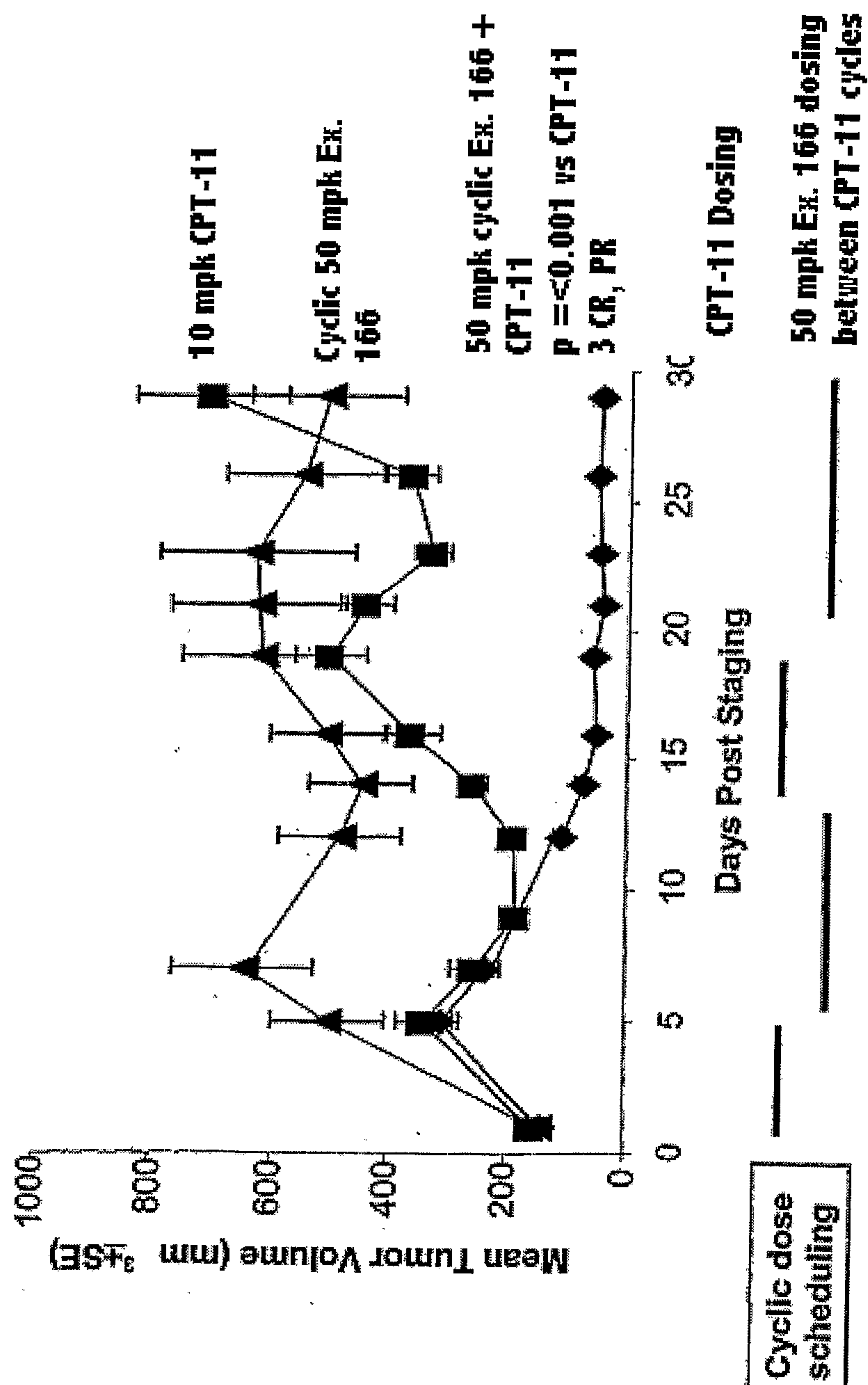
FIG. 6

FIG. 7

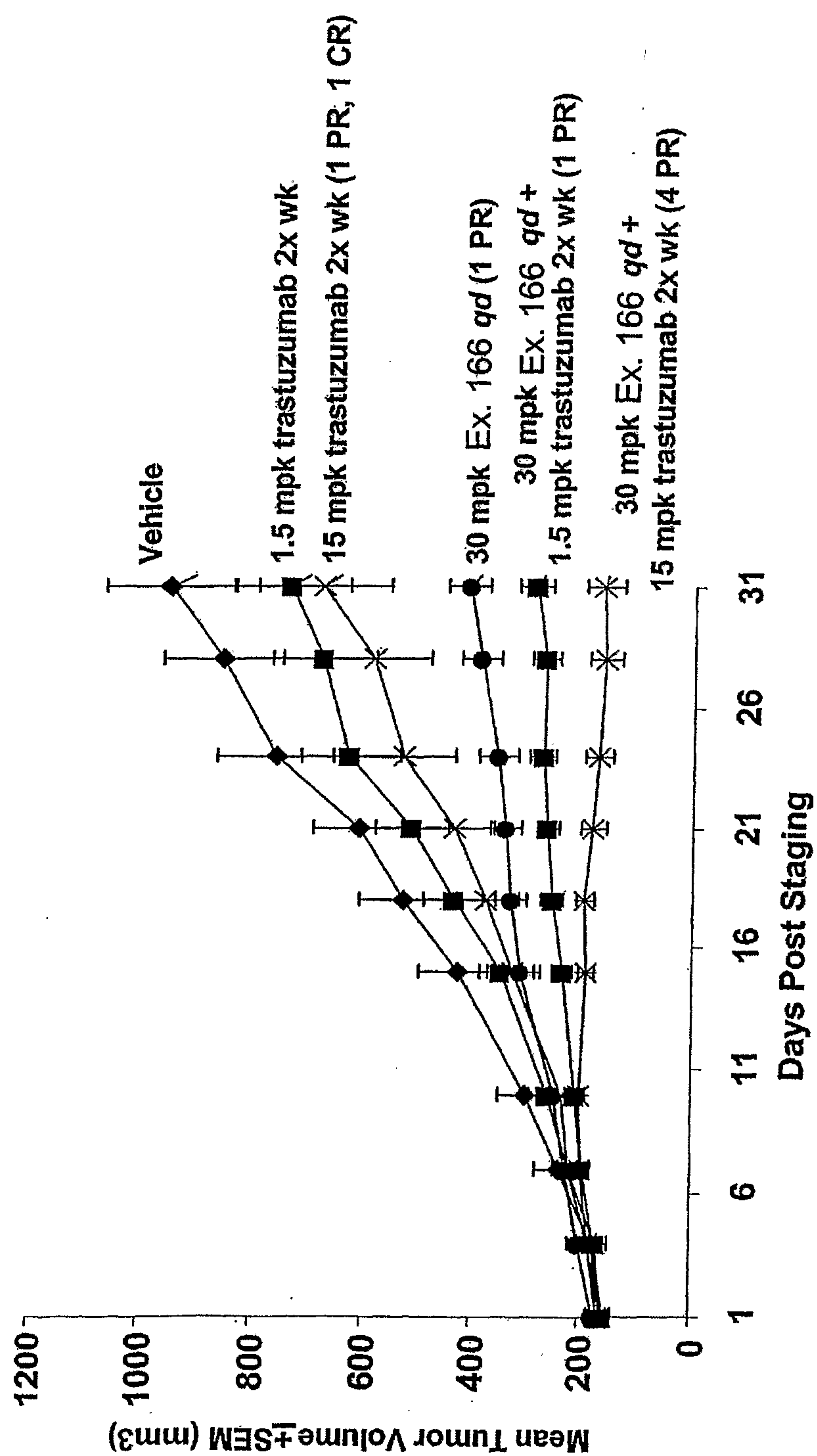


FIG. 8

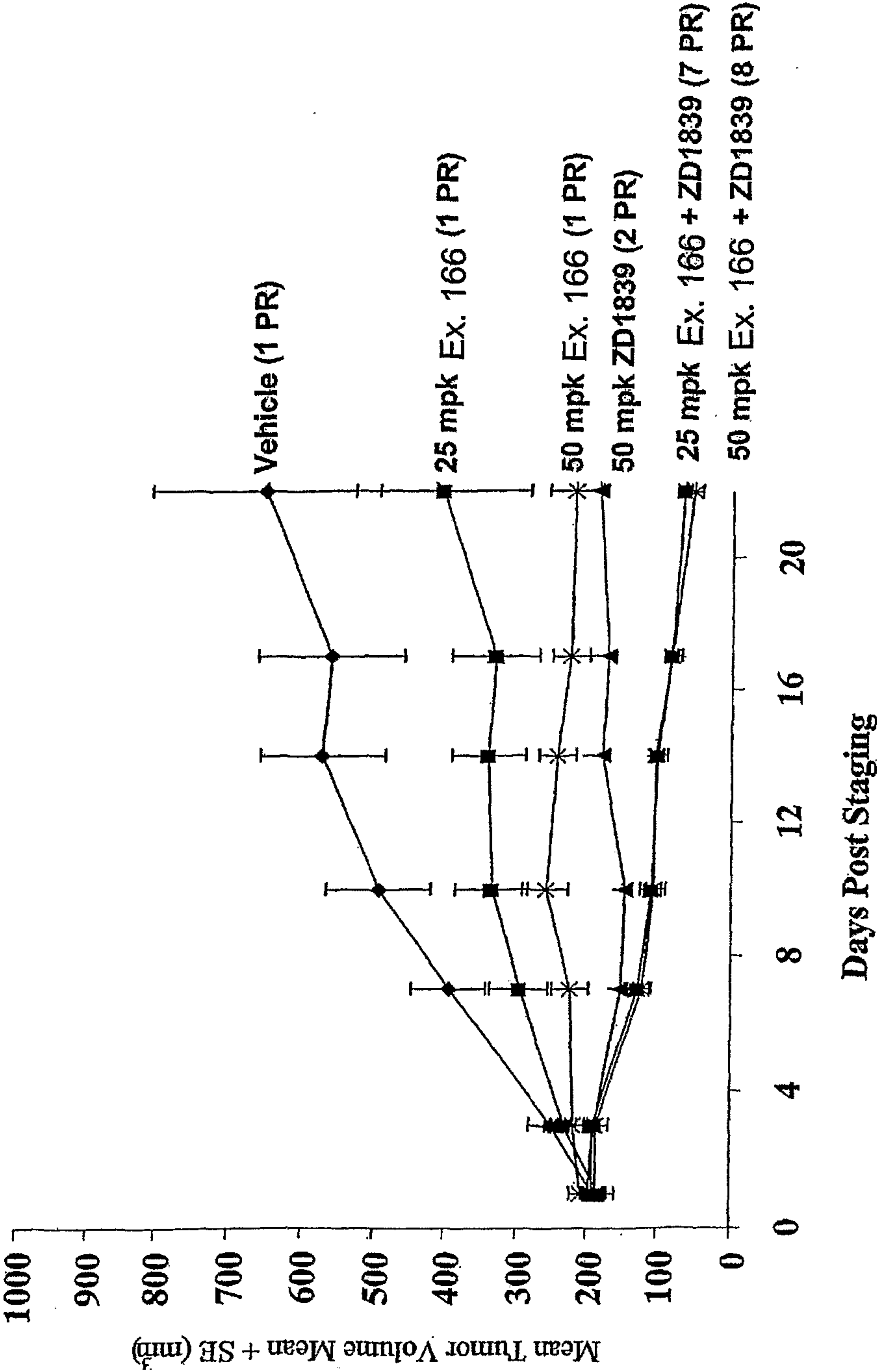


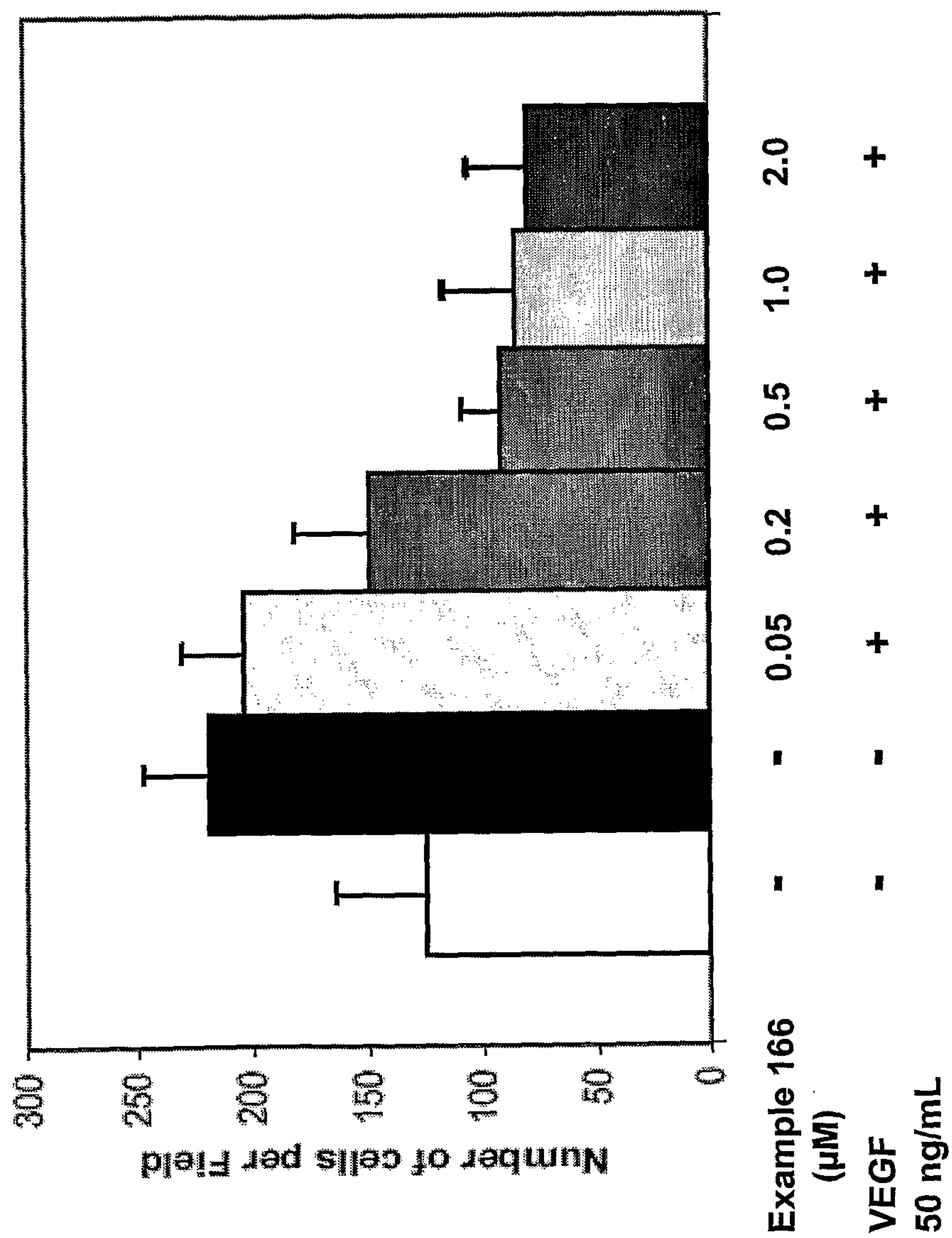
FIG. 9A

FIG. 9B

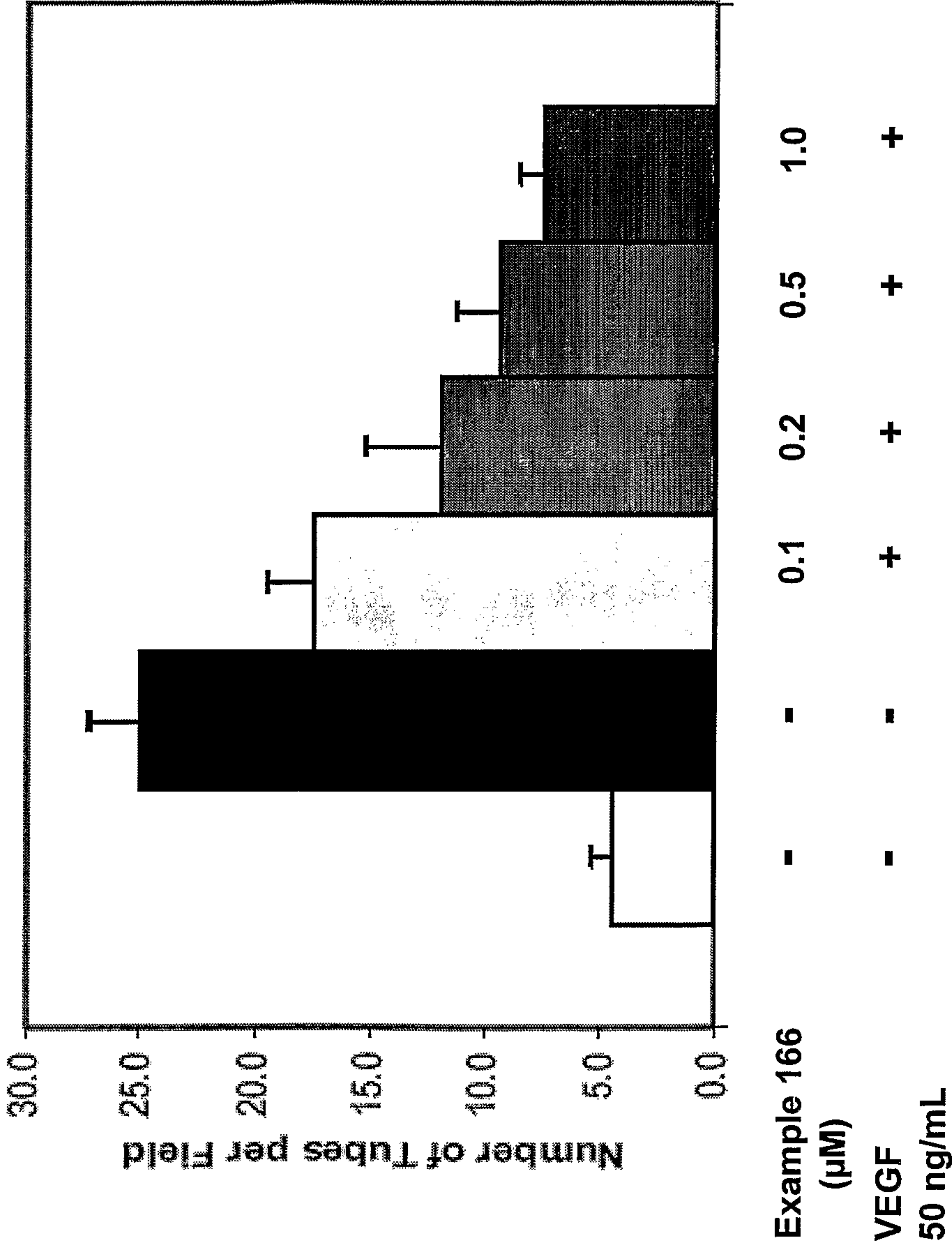


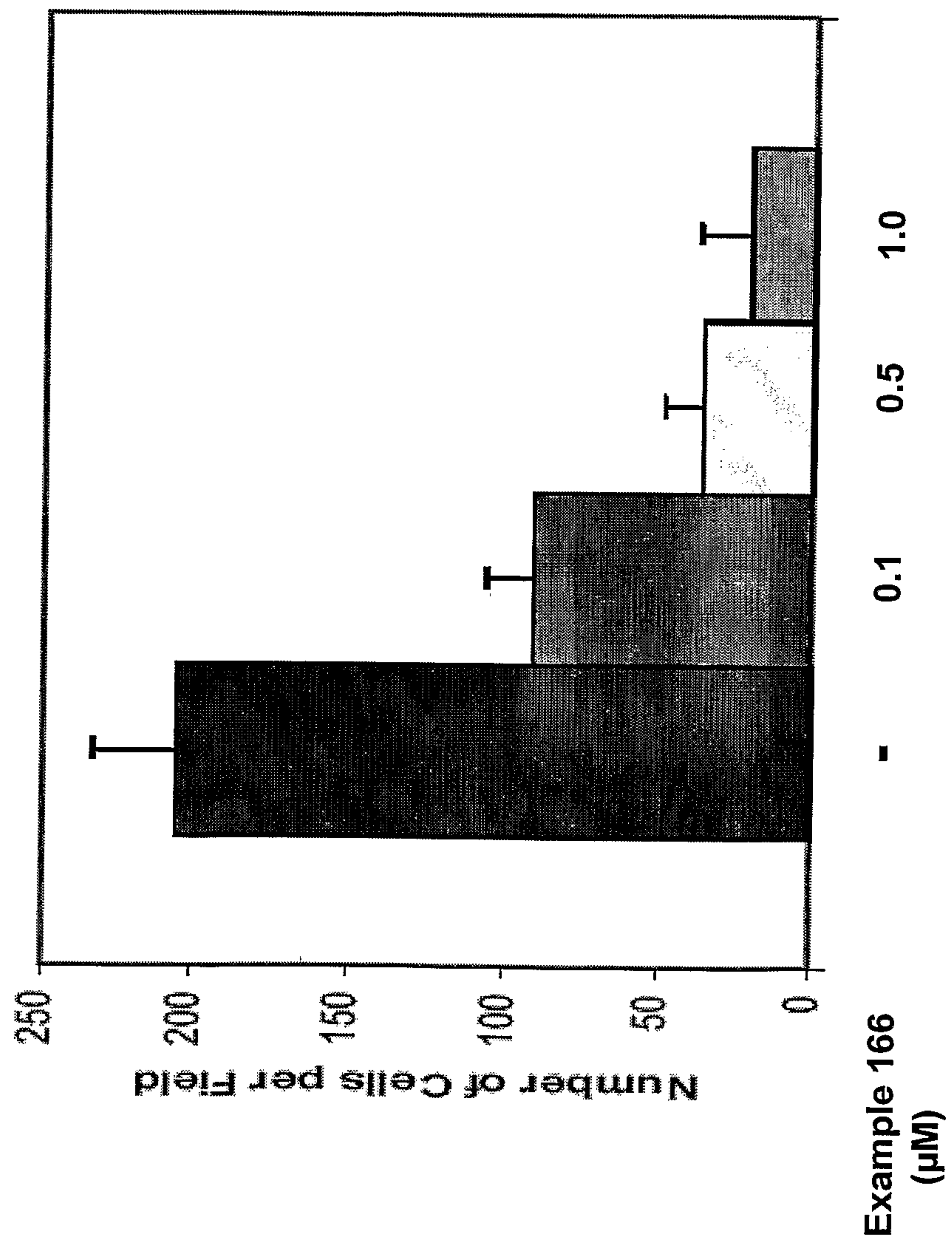
FIG. 10

FIG. 11

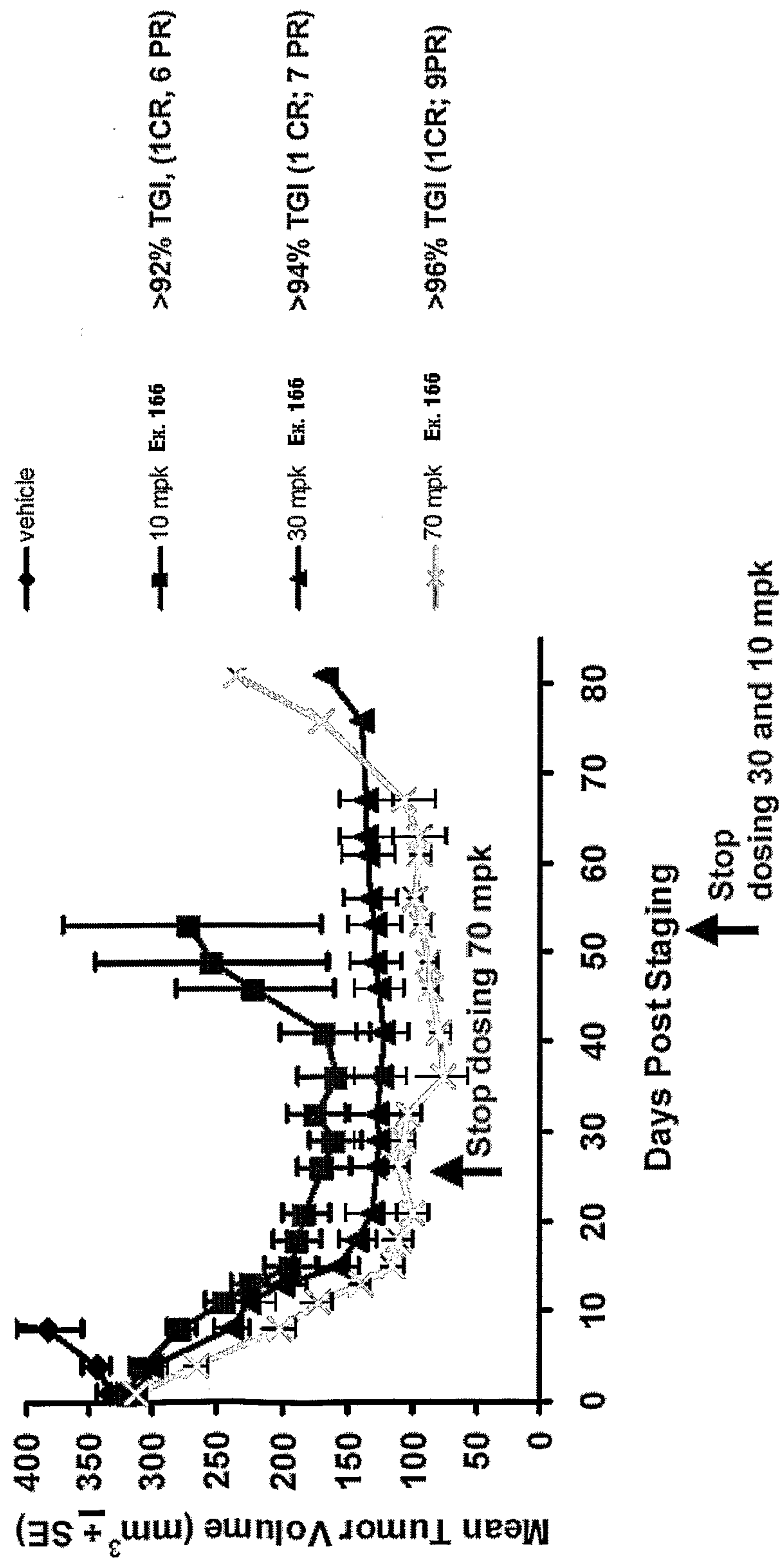


FIG. 12

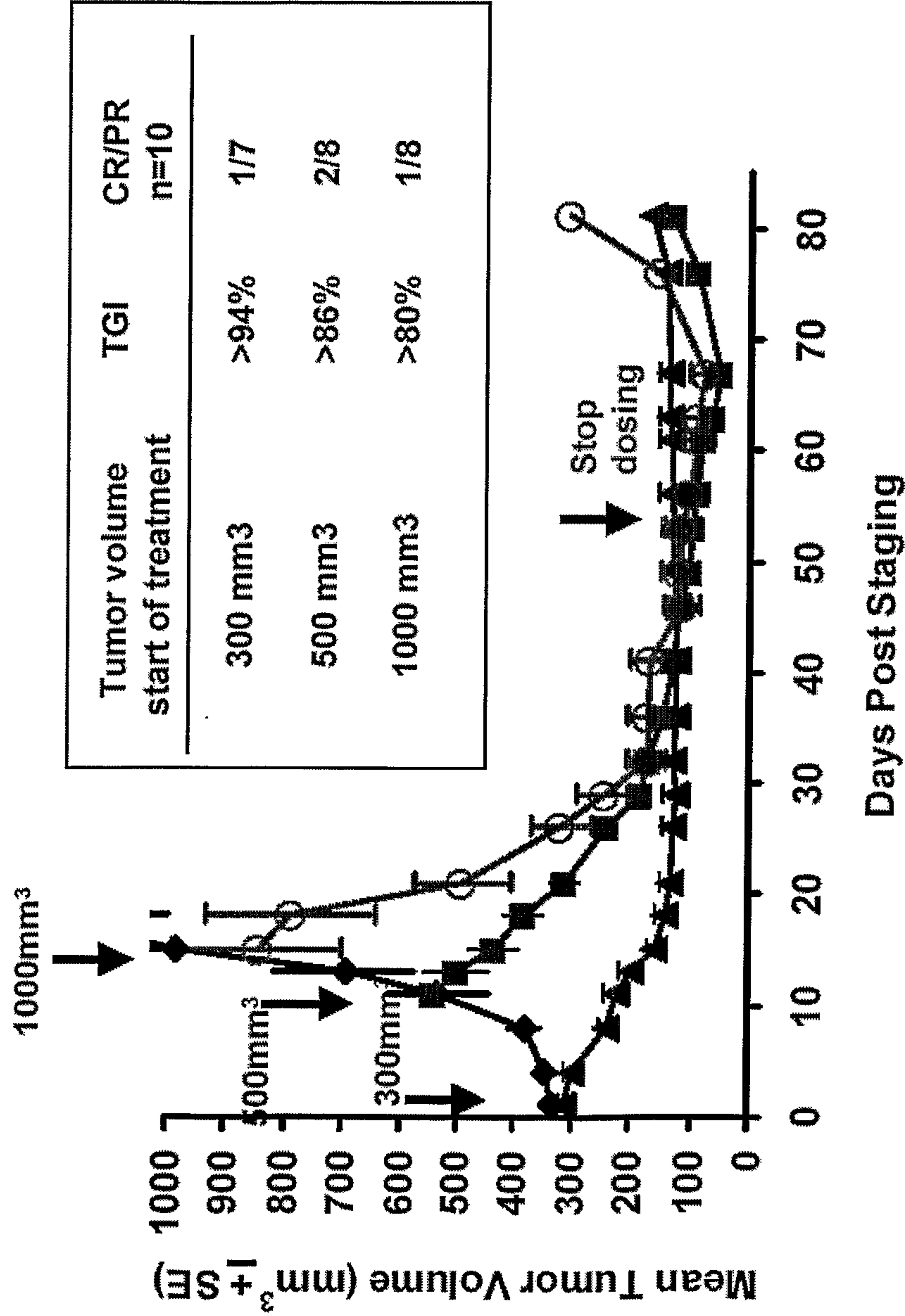
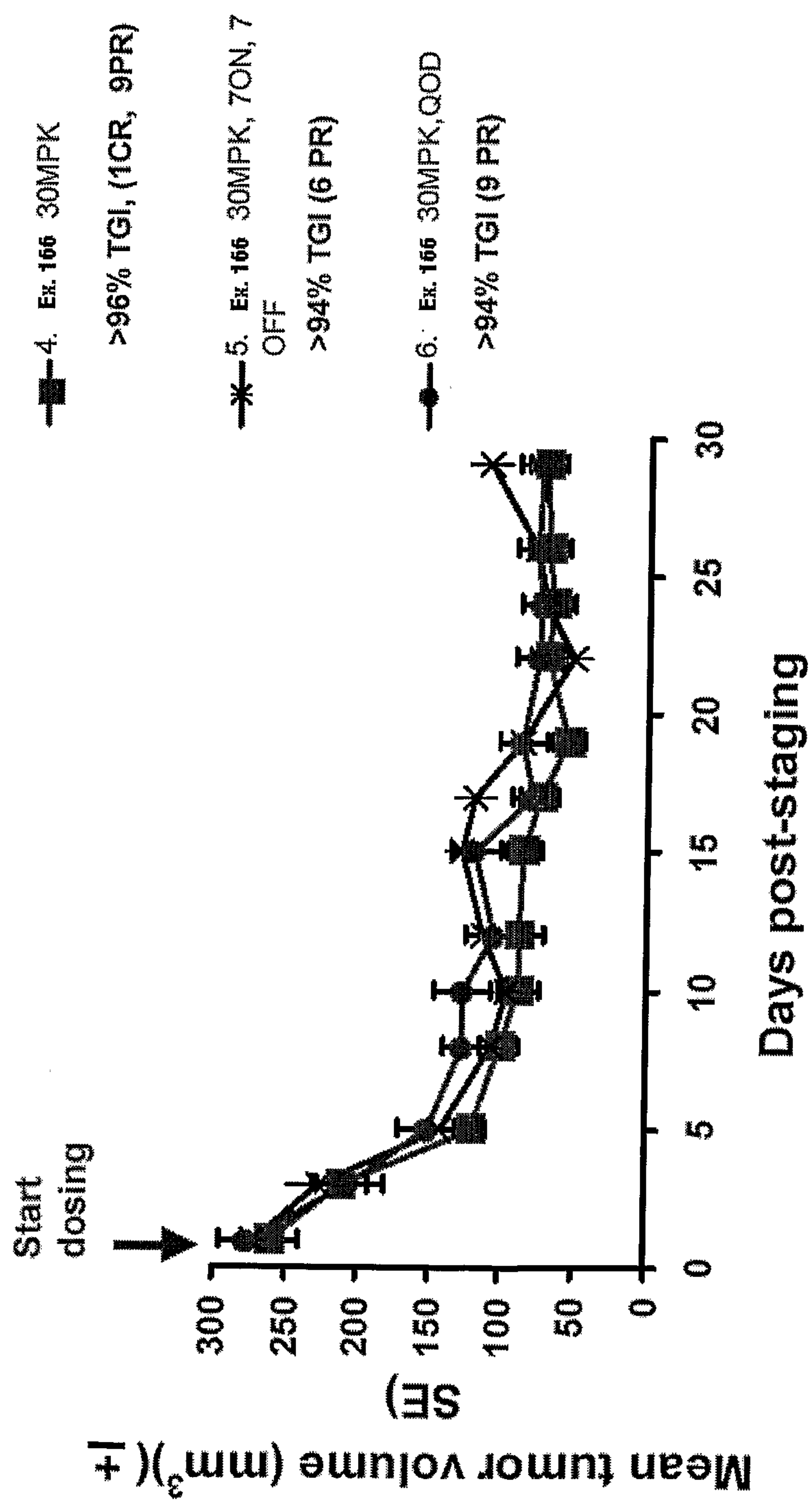
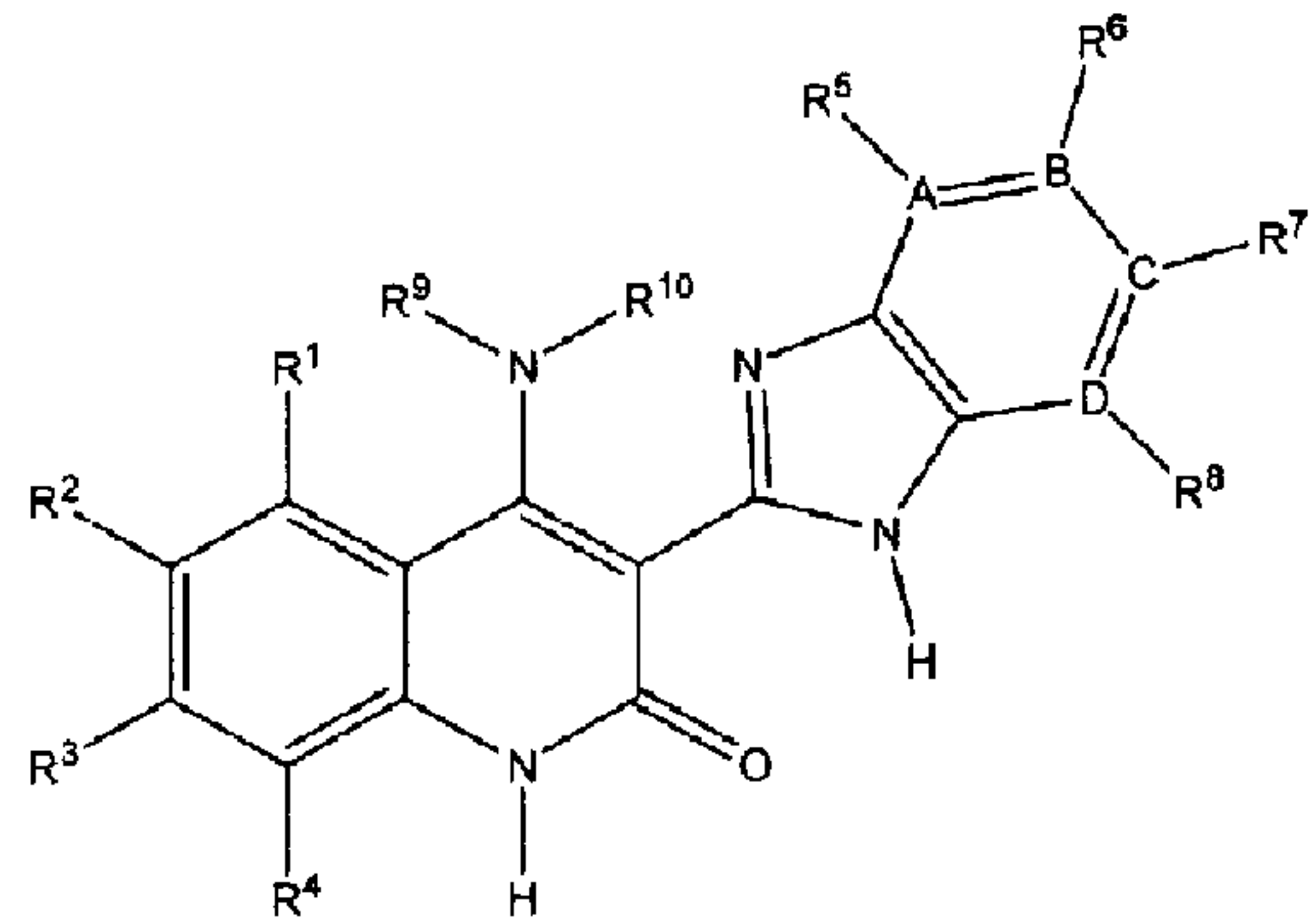
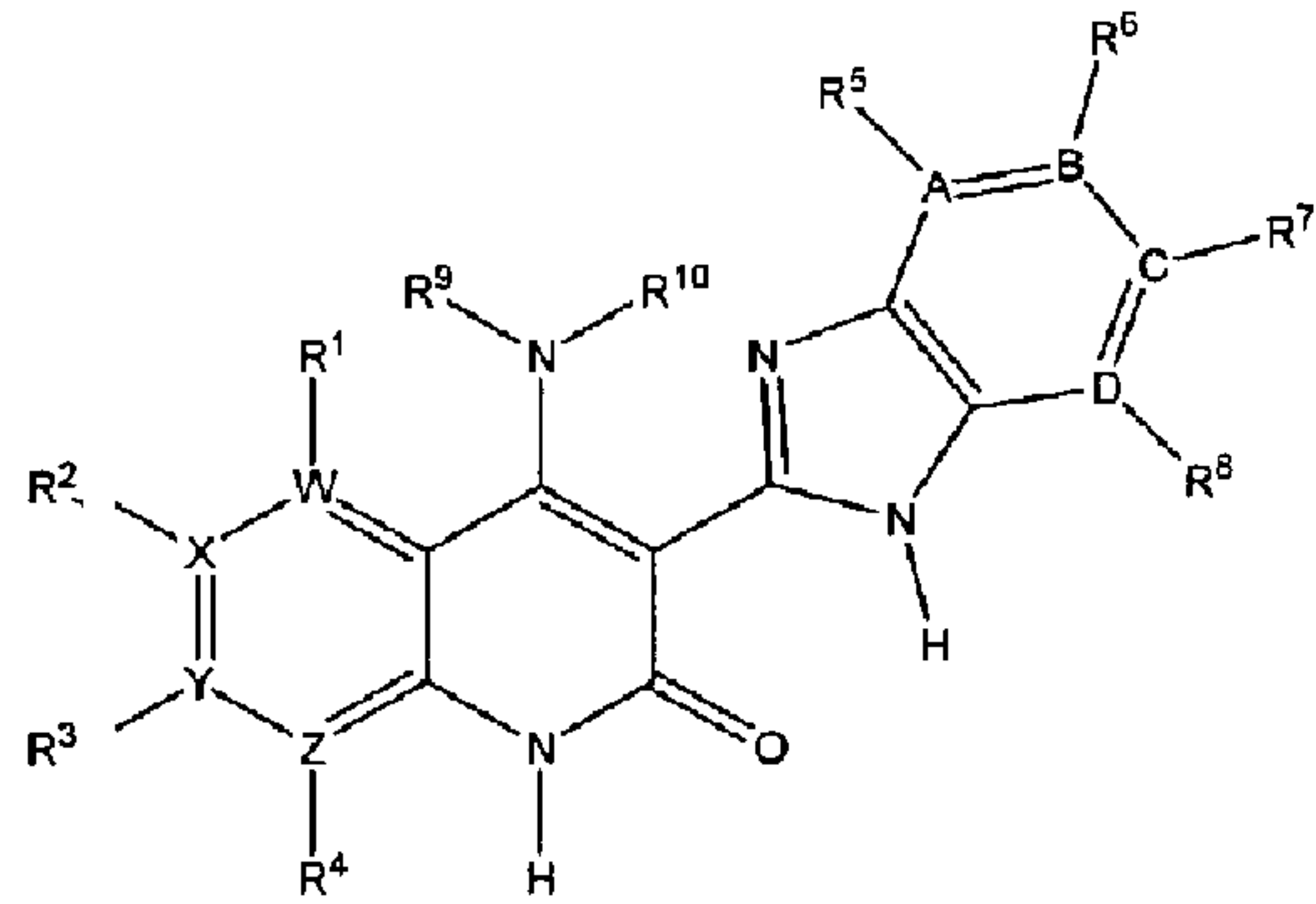


FIG. 13





(I)



(IB)