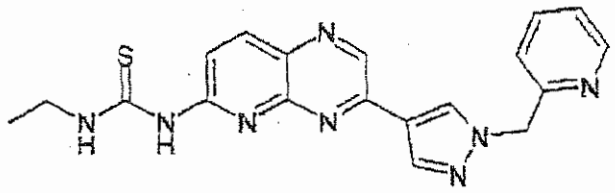
The publication by C. Temple (1968) describes the synthesis and investigation of 6-ethylcarbamate-substituted pyrido[2,3-b]pyrazines as potential antimalarial drugs. No antitumour effect is disclosed or made obvious.

Several PI3K inhibitors (NVP-Bez-235, GDC-0941, XL-147 and others) undergo clinical trials (reviewed by Maira S.M., et al, 2010).

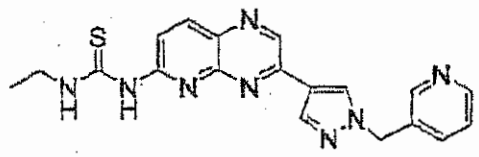
Summary

In a first aspect, there is provided the use for the production of a medicament for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by signal transduction pathways selected from the group consisting of: the PI3K-Akt signal transduction pathway and the ras-Raf-Mek-Erk signal transduction pathway, , wherein the physiological and/or pathophysiological states are selected from the group consisting of malignant tumours, benign tumours, inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, ARC (AIDS related complex), Kaposi's sarcoma, tumours originating from the brain and/or nervous system and/or meninges, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia (BPH), diseases of the immune system, autoimmune diseases, immunodeficiency diseases, colon tumour, gastric tumour, intestinal tumour, pulmonary tumour, pancreatic tumour, ovarian tumour, prostatic tumour, leukaemia, melanoma, hepatic tumour, renal tumour, head tumour, throat tumour, glioma, breast tumour, uterine cancer, endometrial cancer, cervico-uterine carcinoma, brain tumour, adeno-acanthoma, cancer of the bladder, gastric tumour, colorectal tumour, oesophageal cancer, gynaecological tumour, ovarian tumour, cancer of the thyroid, lymphoma, chronic leukaemia, acute leukaemia, restenosis, diabetes, diabetic nephropathy, fibrotic diseases, cystic fibrosis, malignant nephrosclerosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolic diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atherioscierosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischemia, cardiac failure, ischemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, hypertension", , wherein the compound is selected from the group consisting of:

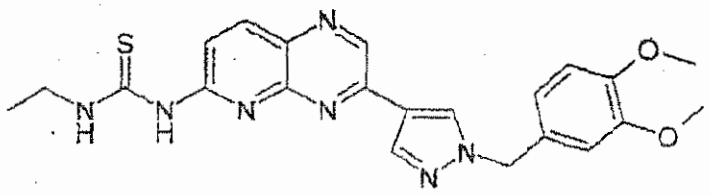
Compound 2: 1-Ethyl-3-[3-(1-pyridin-2-ylmethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



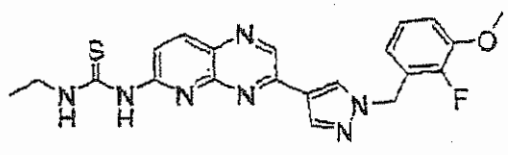
Compound 24: 1-Ethyl-3-[3-(1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



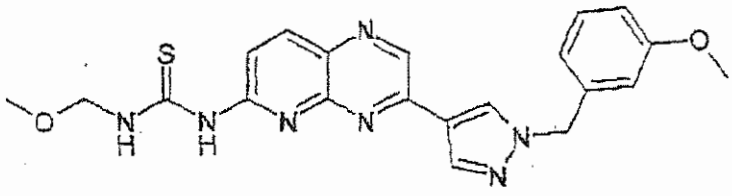
Compound 28: 1-[3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-thiourea



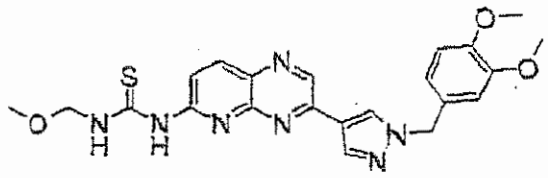
Compound 29: 1-Ethyl-3-[3-[1-(2-fluoro-3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-thiourea



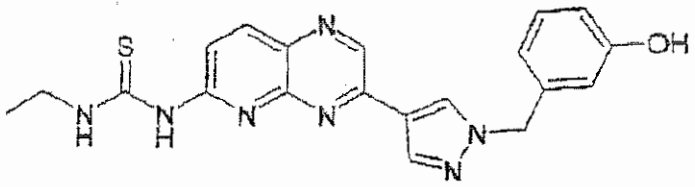
Compound 33: 1-{3-[1-(3-Methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-3-methoxymethyl-thiourea



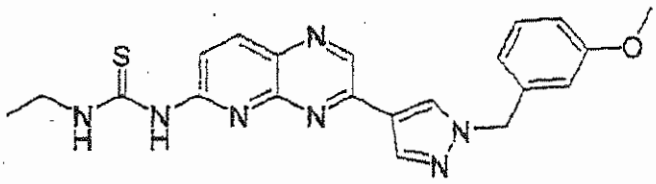
Compound 35: 1-{3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-3-methoxymethyl-thiourea



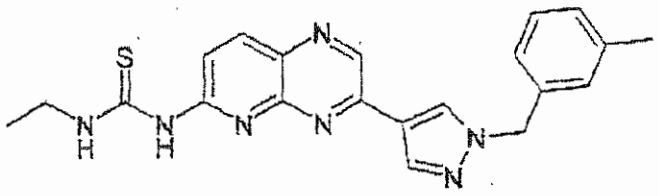
Compound 36: 1-Ethyl-3-{3-[1-(3-hydroxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



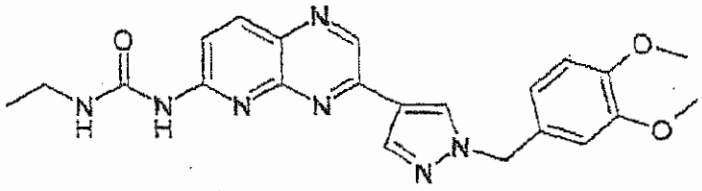
Compound 40: 1-Ethyl-3-{3-[1-(3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



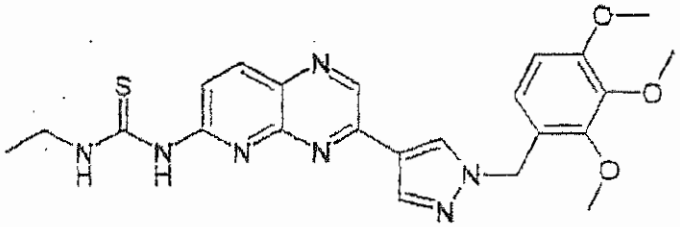
Compound 41: 1-Ethyl-3-{3-[1-(3-methyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



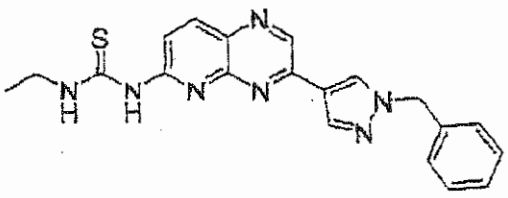
Compound 42: 1-{3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-3-ethyl-urea



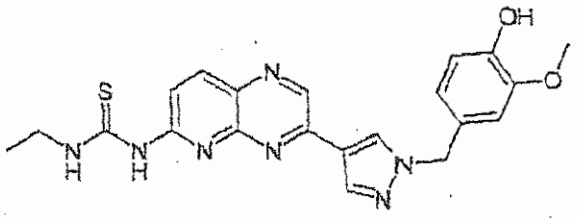
Compound 43: 1-Ethyl-3-{3-[1-(2,3,4-trimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



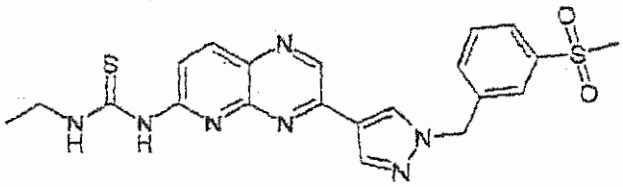
Compound 45: 1-[3-(1-Benzyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-thiourea



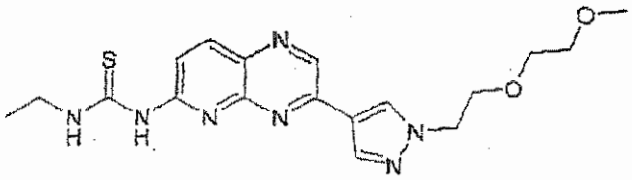
Compound 55: 1-Ethyl-3-{3-[1-(4-hydroxy-3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



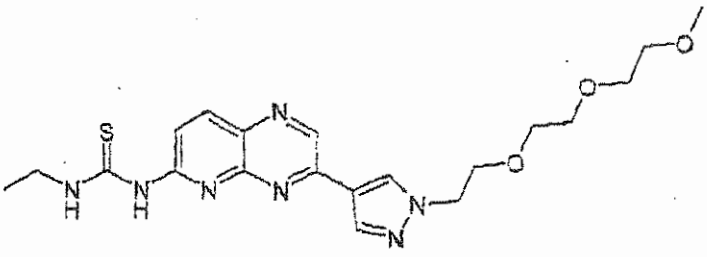
Compound 65: 1-Ethyl-3-{3-[1-(3-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



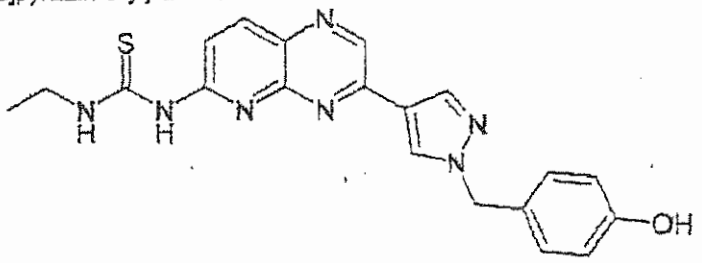
Compound 79: 1-Ethyl-3-(3-{1-[2-(2-methoxy-ethoxy)-ethyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



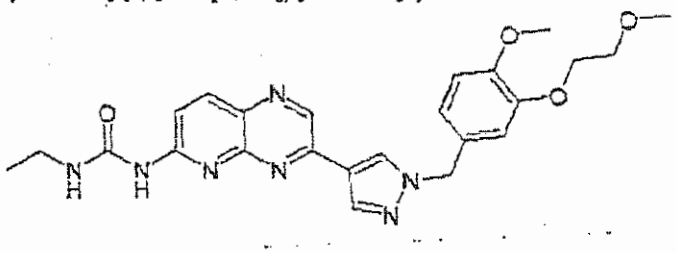
Compound 81: 1-Ethyl-3-[3-(1-{2-[2-(2-methoxy-ethoxy)-ethoxy]-ethyl}-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



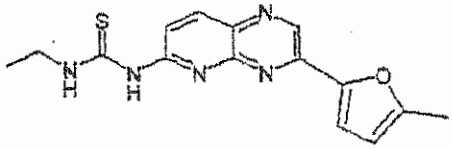
Compound 210: 1-Ethyl-3-{3-[1-(4-hydroxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



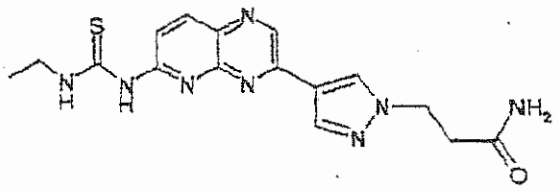
Compound 211: 1-Ethyl-3-(3-[1-[4-methoxy-3-(2-methoxy-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-urea



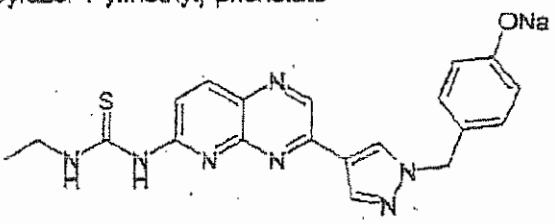
Compound 214: 1-Ethyl-3-[3-(5-methyl-furan-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



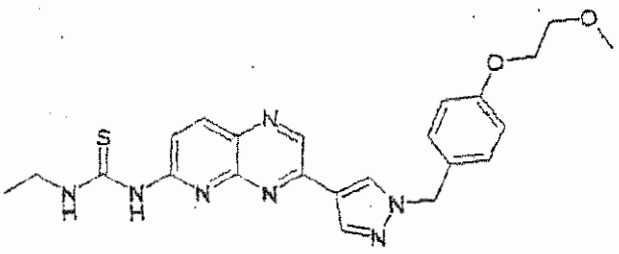
Compound 217: 3-{4-[6-(3-Ethyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl}-propionamide



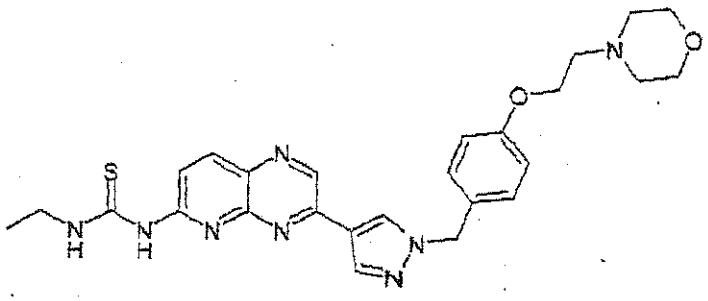
Compound 218: Sodium; 4-{4-[6-(3-ethyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-ylmethyl}-phenolate



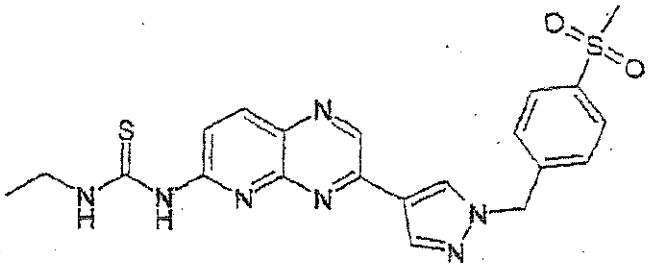
Compound 222: 1-Ethyl-3-(3-{1-[4-(2-methoxy-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



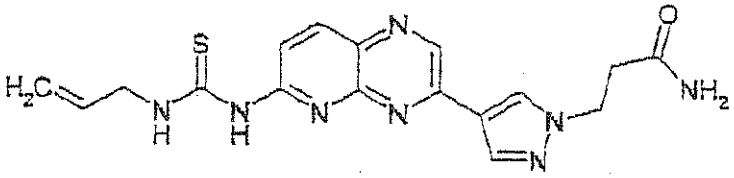
Compound 224: 1-Ethyl-3-(3-{1-[4-(2-morpholin-4-yl-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



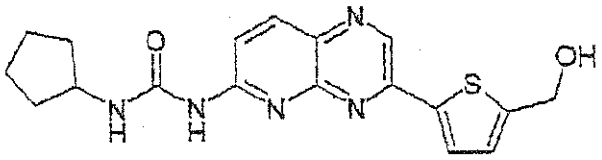
Compound 229: 1-Ethyl-3-(3-[1-(4-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl)-thiourea



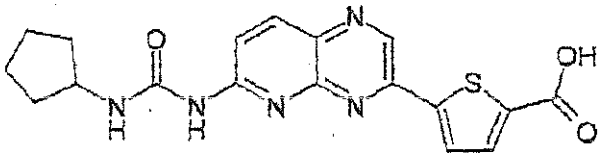
Compound 245: 3-(4-[6-(3- Allyl -thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl)- propionamide



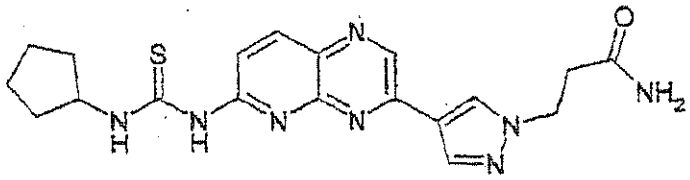
Compound 290: 1-Cyclopentyl-3-[3-(5-hydroxymethyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



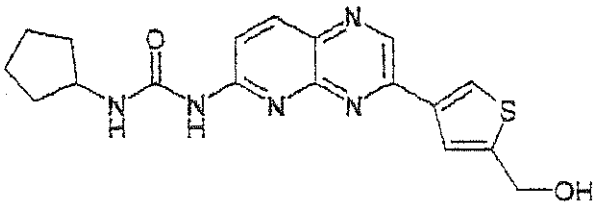
Compound 292: 5-[6-(3-Cyclopentyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-thiophene-2-carboxylic acid



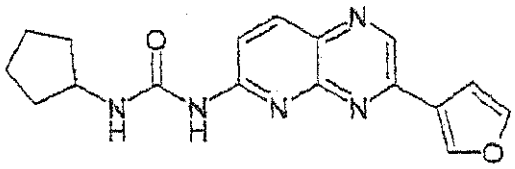
Compound 298: 3-[4-[6-(3- Cyclopentyl -thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl]-propionamide



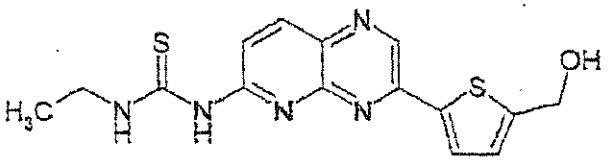
Compound 316: 1- Cyclopentyl -3-[3-(5-hydroxymethyl-thiophen-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



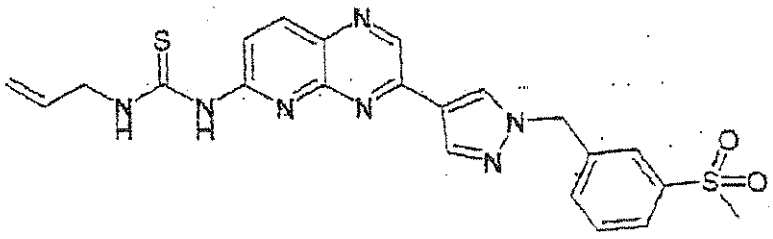
Compound 324: 1- Cyclopentyl -3-(3-furan-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



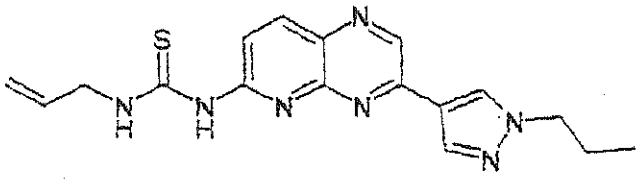
Compound 397: 1-Ethyl-3-[3-(5-hydroxymethyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



Compound 558: 1-Allyl-3-{3-[1-(3-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



Compound 561: 1-Allyl-3-[3-(1-propyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



In a second aspect, there is provided a pyridopyrazine selected from the group consisting of compound 2, 24, 28, **29, 33, 35, 36, 40, 41, 42, 43, 45, 55, 65, 79, 81, 210, 211, 214, 217, 218, 222, 224, 229, 245, 290, 292, 298, 316, 324, 397,559, 561** its physiologically tolerated salts, in the form of its racemates, in the form of its pure enantiomers and/or diastereomers or in the form of mixtures of these enantiomers and/or diastereomers or in the form of its tautomers.

In a third aspect, there is provided a pharmaceutical composition which comprises a pharmaceutically active amount of at the least one compound as defined above, for the treatment or prophylaxis of physiological and/or pathophysiological conditions which can be treated by modulation of the signal transduction pathway or pathways selected from the group consisting of the PI3K-Akt signal transduction pathway and ras-Raf-Mek-Erk signal transduction pathway, wherein the physiological and/or pathophysiological states are selected from the group consisting of malignant tumours, benign tumours, inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, ARC (AIDS related complex), Kaposi's sarcoma, tumours originating from the brain and/or nervous system and/or meninges, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia (BPH), diseases of the immune system, autoimmune diseases, immunodeficiency diseases, colon tumour, gastric tumour, intestinal tumour, pulmonary tumour, pancreatic tumour, ovarian tumour, prostatic tumour, leukaemia, melanoma, hepatic tumour, renal tumour, head tumour, throat tumour, glioma, breast tumour, uterine cancer, endometrial cancer, cervico-uterine carcinoma, brain tumour, adeno-acanthoma, cancer of the bladder, gastric tumour, colorectal tumour, oesophageal cancer, gynaecological tumour, ovarian tumour, cancer of the thyroid, lymphoma, chronic leukaemia, acute leukaemia, restenosis, diabetes, diabetic nephropathy, fibrotic diseases, cystic fibrosis, malignant nephrosclerosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolic diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atherosclerosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischemia, cardiac failure, ischemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, hypertension".

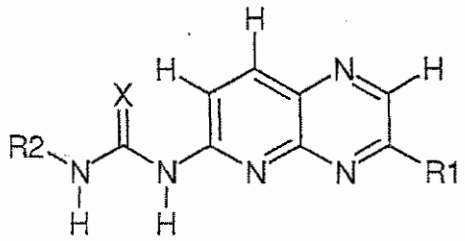
In a fourth aspect, there is provided a pharmaceutical composition comprising a pharmacologically active quantity of at least one compound as defined above.

In a fifth aspect, there is provided a kit comprising a pharmacologically active quantity of at least one compound as defined above and a pharmacologically active quantity of at least one further pharmacologically active substance as defined above.

Description of the invention

The object of the present invention is to provide new compounds which can be used for the treatment or prevention of physiological and/or pathophysiological states in mammals, in particular in humans, which are mediated by signal transduction pathways selected from the group consisting of: the PI3K-Akt signal transduction pathway and the ras-Raf-Mek-Erk signal transduction pathway.

The inventive object was surprisingly achieved in one aspect by preparing a compound according to the general formula **(I)**



(I)

wherein the substituents R1, R2, X have the following meaning:

X O or S

R1

(I) unsubstituted or substituted alkyl, wherein the alkyl group can be substituted with one or more, the same or different F, Cl, Br, I, CF_3, CN, NH_2, NH-alkyl, NH-cycloalkyl, NH-heterocyclyl, NH-aryl, NH-heteroaryl, NH-alkyl-cycloalkyl, NH-alkyl-heterocyclyl, NH-alkyl-aryl, NH-alkyl-heteroaryl, NH-alkyl-NH_2, NH-alkyl-OH, $N(alkyl)_2$, NHC(O)-alkyl, NHC(O)-cycloalkyl, NHC(O)-heterocyclyl, NHC(O)-aryl, NHC(O)-heteroaryl, NHC(O)-alkyl-aryl, NHC(O)-alkyl-heteroaryl, $NHSO_2$-alkyl, $NHSO_2$-cycloalkyl, $NHSO_2$-

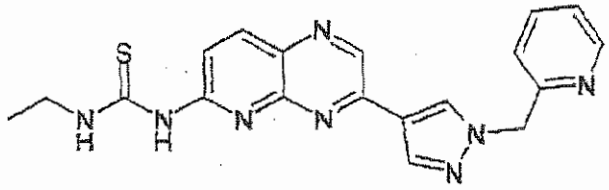
P60072WO_claims_21052013.doc Go

~~Amended~~ Claims

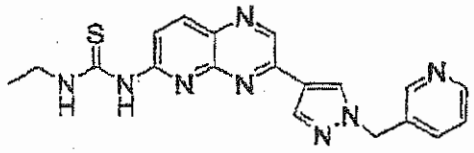
1. Use for the production of a medicament for the treatment or prevention of physiological and/or pathophysiological states in mammals mediated by signal transduction pathways selected from the group consisting of: the PI3K-Akt signal transduction pathway and the ras-Raf-Mek-Erk signal transduction pathway, , wherein the physiological and/or pathophysiological states are selected from the group consisting of malignant tumours, benign tumours, inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, ARC (AIDS related complex), Kaposi's sarcoma, tumours originating from the brain and/or nervous system and/or meninges, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia (BPH), diseases of the immune system, autoimmune diseases, immunodeficiency diseases, colon tumour, gastric tumour, intestinal tumour, pulmonary tumour, pancreatic tumour, ovarian tumour, prostatic tumour, leukaemia, melanoma, hepatic tumour, renal tumour, head tumour, throat tumour, glioma, breast tumour, uterine cancer, endometrial cancer, cervico-uterine carcinoma, brain tumour, adeno-acanthoma, cancer of the bladder, gastric tumour, colorectal tumour, oesophageal cancer, gynaecological tumour, ovarian tumour, cancer of the thyroid, lymphoma, chronic leukaemia, acute leukaemia, restenosis, diabetes, diabetic nephropathy, fibrotic diseases, cystic fibrosis, malignant nephrosclerosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolic diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atherosclerosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischemia, cardiac failure, ischemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, hypertension", , wherein the compound is selected from the group consisting of:

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Received at the EPO on May 24, 2013 08:49:46. Page 4 of 22

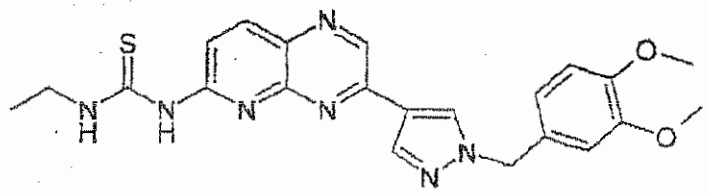
Compound 2: 1-Ethyl-3-[3-(1-pyridin-2-ylmethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



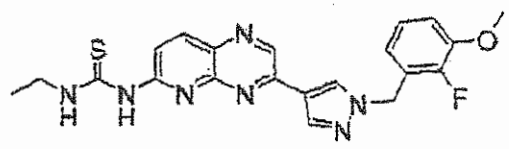
Compound 24: 1-Ethyl-3-[3-(1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



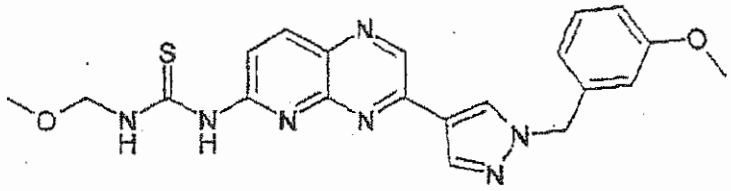
Compound 28: 1-[3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-thiourea



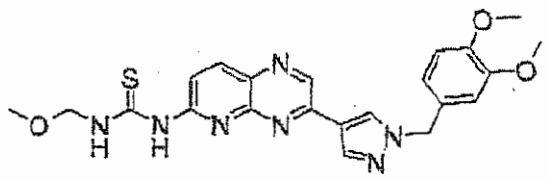
Compound 29: 1-Ethyl-3-[3-[1-(2-fluoro-3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-thiourea



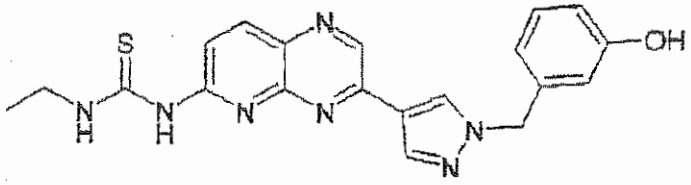
Compound 33: 1-{3-[1-(3-Methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-3-methoxymethyl-thiourea



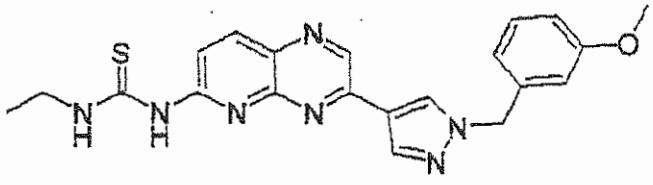
Compound 35: 1-{3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-3-methoxymethyl-thiourea



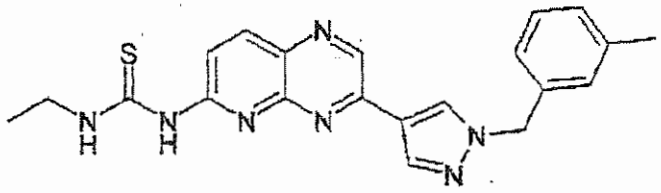
Compound 36: 1-Ethyl-3-{3-[1-(3-hydroxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



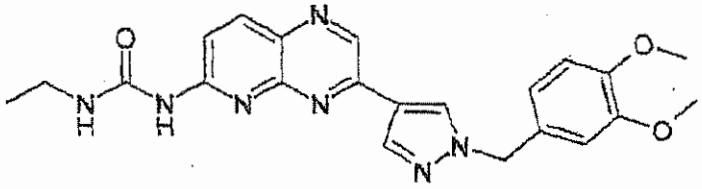
Compound 40: 1-Ethyl-3-{3-[1-(3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



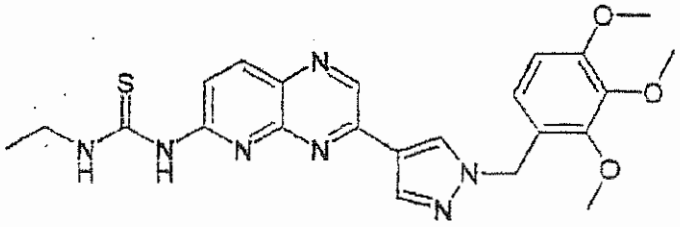
Compound 41: 1-Ethyl-3-[3-[1-(3-methyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-thiourea



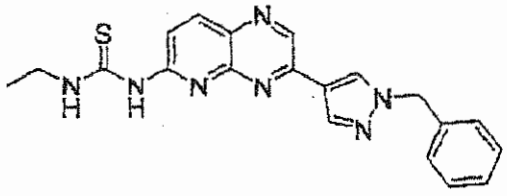
Compound 42: 1-(3-[1-(3,4-Dimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-urea



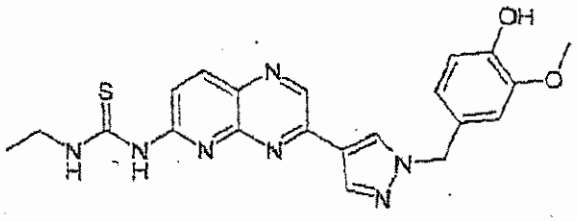
Compound 43: 1-Ethyl-3-{3-[1-(2,3,4-trimethoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



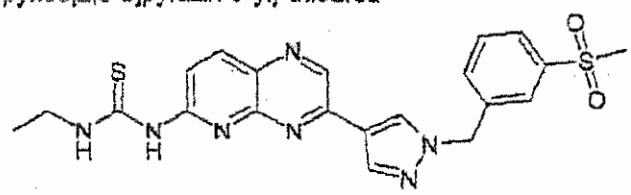
Compound 45: 1-[3-(1-Benzyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-3-ethyl-thiourea



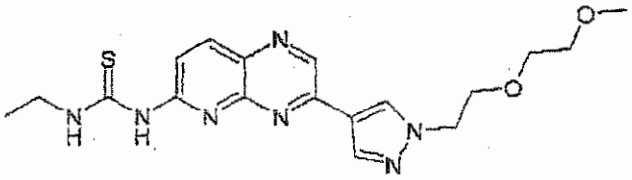
Compound 55: 1-Ethyl-3-{3-[1-(4-hydroxy-3-methoxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



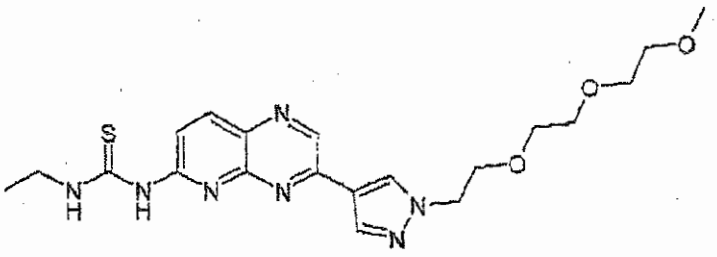
Compound 65: 1-Ethyl-3-{3-[1-(3-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



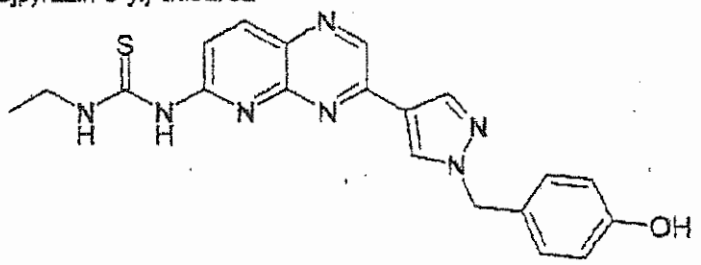
Compound 79: 1-Ethyl-3-(3-{1-[2-(2-methoxy-ethoxy)-ethyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



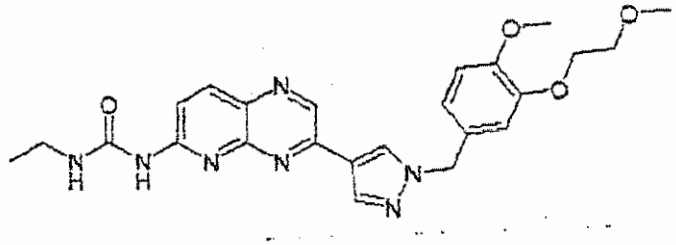
Compound 81: 1-Ethyl-3-[3-(1-{2-[2-(2-methoxy-ethoxy)-ethoxy]-ethyl}-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



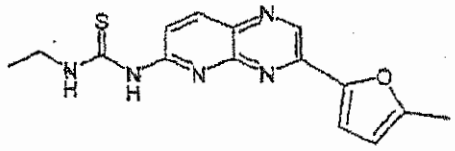
Compound 210: 1-Ethyl-3-{3-[1-(4-hydroxy-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



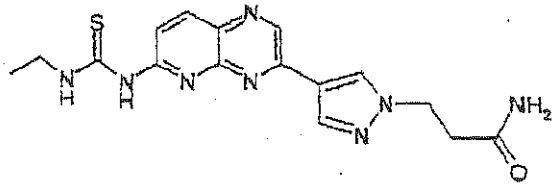
Compound 211: 1-Ethyl-3-(3-{1-[4-methoxy-3-(2-methoxy-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-urea



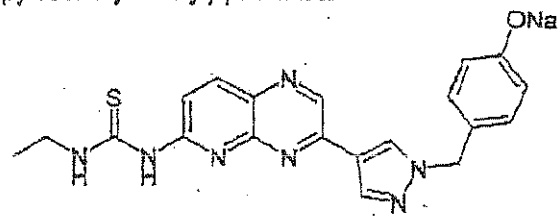
Compound 214: 1-Ethyl-3-[3-(5-methyl-furan-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



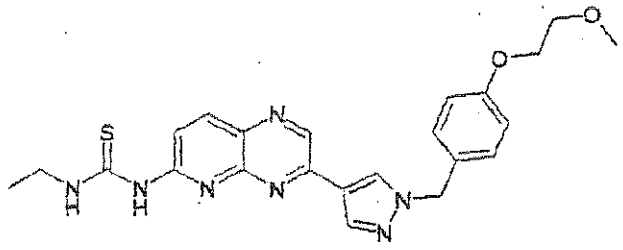
Compound 217: 3-{4-[6-(3-Ethyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl}-propionamide



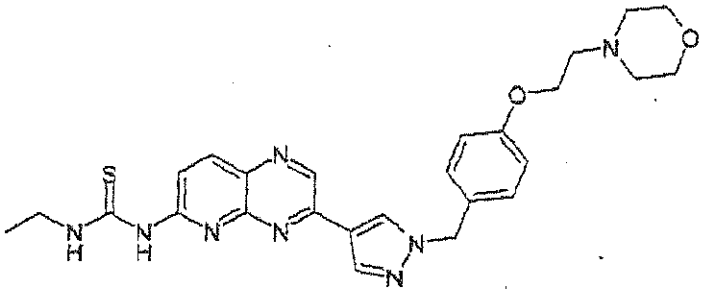
Compound 218: Sodium; 4-{4-[6-(3-ethyl-thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-ylmethyl}-phenolate



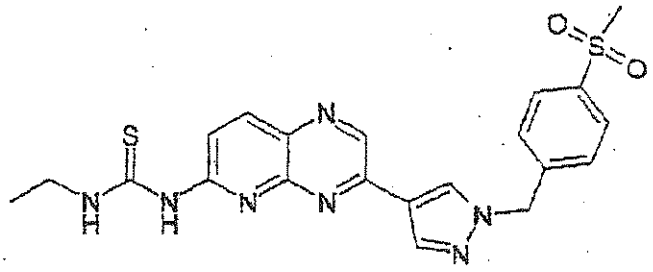
Compound 222: 1-Ethyl-3-(3-{1-[4-(2-methoxy-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



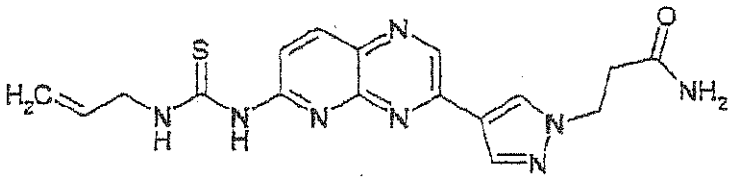
Compound 224: 1-Ethyl-3-(3-{1-[4-(2-morpholin-4-yl-ethoxy)-benzyl]-1H-pyrazol-4-yl}-pyrido[2,3-b]pyrazin-6-yl)-thiourea



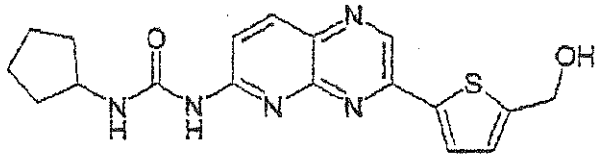
Compound 229: 1-Ethyl-3-{3-[1-(4-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



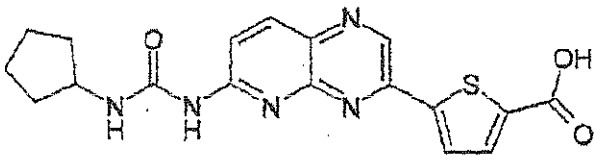
Compound 245: 3-{4-[6-(3- Allyl -thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl}- propionamide



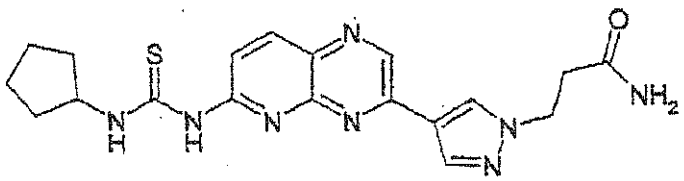
Compound 290: 1-Cyclopentyl-3-[3-(5-hydroxymethyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



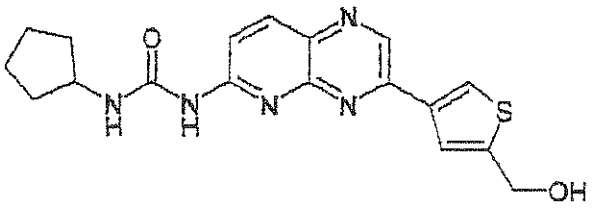
Compound 292: 5-[6-(3-Cyclopentyl-ureido)-pyrido[2,3-b]pyrazin-3-yl]-thiophene-2-carboxylic acid



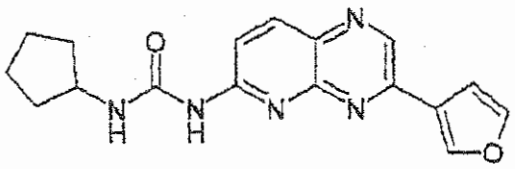
Compound 298: 3-{4-[6-(3- Cyclopentyl -thioureido)-pyrido[2,3-b]pyrazin-3-yl]-pyrazol-1-yl}-propionamide



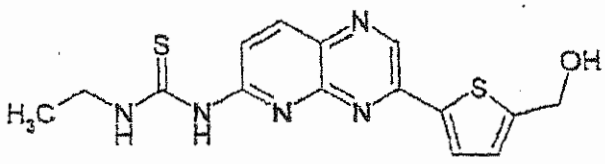
Compound 316: 1- Cyclopentyl -3-[3-(5-hydroxymethyl-thiophen-3-yl)-pyrido[2,3-b]pyrazin-6-yl]-urea



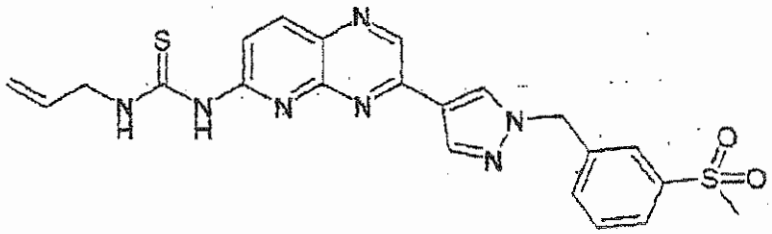
Compound 324: 1- Cyclopentyl -3-(3-furan-3-yl-pyrido[2,3-b]pyrazin-6-yl)-urea



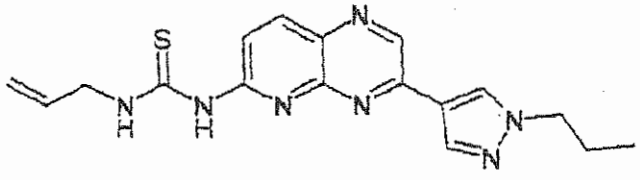
Compound 397: 1-Ethyl-3-[3-(5-hydroxymethyl-thiophen-2-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



Compound 559: 1-Allyl-3-{3-[1-(3-methanesulfonyl-benzyl)-1H-pyrazol-4-yl]-pyrido[2,3-b]pyrazin-6-yl}-thiourea



Compound 561: 1-Allyl-3-[3-(1-propyl-1H-pyrazol-4-yl)-pyrido[2,3-b]pyrazin-6-yl]-thiourea



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2. Use according to claim 1, wherein the treatment or prevention is effected by modulation of the signal transduction pathway or pathways selected from the group consisting of the PI3K-Akt signal transduction pathway and the ras-Raf-Mek-Erk signal transduction pathway.

3. Use according to claim 1 or 2 wherein the modulation of the PI3K-Akt signal transduction pathway and the ras-Raf-Mek-Erk signal transduction pathway is effected by modulation of one or more enzymes selected from the group consisting of lipid kinase, tyrosine kinase, serine/threonine kinase, receptor tyrosine kinase, cytoplasmic tyrosine kinase, cytoplasmic serine/threonine kinase.

4. Use according to Claim 3, wherein the enzyme is selected from the group consisting of PI3K, PI3Kalpha, PI3Kbeta, PI3Kgamma, PI3Kdelta, PI3K-C2alpha, PI3K-C2beta, PI3K-Vps34p.

5. Use according to Claim 3, wherein the enzyme is selected from the group consisting of Erk, Erk1, Erk2.

6. Use according to any one of Claims 1 to 5, wherein one or more enzymes are modulated.

7. Use according to any one of Claims 1 to 6, wherein the modulation is an inhibition.

9. Use according to any one of Claims 1 to 8, wherein the medicament comprises at least one further pharmacologically active substance.

10. Use according to any one of Claims 1 to 9, wherein the medicament is administered before and/or during and/or after treatment with radiation therapy and/or surgery.

11. Use according to Claim 9, wherein the further pharmacologically active substance is selected from the group consisting of DNA topoisomerase I and/or II inhibitors, DNA intercalators, alkylating agents, microtubuli destabilisers, hormone and/or growth factor receptor agonists and/or antagonists, antibodies against growth factors and their receptors, kinase inhibitors, alkylphospholipids, antimetabolites", wherein the further pharmacologically active substance is selected from the group consisting of asparaginase, bleomycin, carboplatin, carmustin, chlorambucil, cisplatin, colaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, doxorubicin(adriamycin), epirubicin, etoposide, 5-fluorouracil, hexamethylmelamine, hydroxurea, Ifosfamide, irinotecan, leucovorin, lomustine, mechlorethamine, 6-mercaptopurine, mesna, methotrexate, mitomycin C, mitoxantrone, prednisolone, prednisone, procarbazine, raloxifene, streptozocin, tamoxifen, thioguanine, topotecan, vinblastine, vincristine, vindesine, aminoglutethimide, L-asparaginase, azathioprine, 5-azacytidine cladribine, busulfan, diethylstilbestrol, 2', 2'-difluorodeoxycytidine, docetaxel, erythrohydroxynonyladenine, ethinylestradiol, 5-fluorodeoxyuridin, 5-fluorodeoxyuridin monophosphate, fludarabine phosphate, fluoxymesterone, flutamide, hydroxyprogesterone caproate, idarubicin, interferon, medroxyprogesterone acetate, megestrol acetate, melphalan, mitotane, paclitaxel, oxaliplatin, pentostatin, N-phosphonoacetyl-L-aspartate (PALA), plicamycin, semustine, teniposide, testosterone propionate, thiotepa, trimethylmelamine, uridine, vinorelbin, epothilone, gemcitabine, Taxotere, BCNU, CCNU, DTIC, 5-fluorouracil, Herceptin, Avastin, Erbitux, Sorafenib, Gleevec, Iressa, Tarceva, rapamycin, perifosine, miltefosine, edelfosine, actinomycin D".

12. Pyridopyrazine selected from the group consisting of compound **2, 24, 28, 29, 33, 35, 36, 40, 41, 42, 43, 45, 55, 65, 79, 81, 210, 211, 214, 217, 218, 222, 224, 229, 245, 290, 292, 298, 316, 324, 397,559, 561** its physiologically tolerated salts, in the form of its racemates, in the form of its pure

enantiomers and/or diastereomers or in the form of mixtures of these enantiomers and/or diastereomers or in the form of its tautomers.

13. A pharmaceutical composition which comprises a pharmacologically active amount of at the least one compound according to claim 12, for the treatment or prophylaxis of physiological and/or pathophysiological conditions which can be treated by modulation of the signal transduction pathway or pathways selected from the group consisting of the PI3K-Akt signal transduction pathway and ras-Raf-Mek-Erk signal transduction pathway, wherein the physiological and/or pathophysiological states are selected from the group consisting of malignant tumours, benign tumours, inflammatory diseases, inflammations, pain, rheumatic diseases, arthritic diseases, HIV infections, neurological or neurodegenerative diseases, rheumatism, arthritis, AIDS, ARC (AIDS related complex), Kaposi's sarcoma, tumours originating from the brain and/or nervous system and/or meninges, dementia, Alzheimer's disease, hyperproliferative diseases, psoriasis, endometriosis, scarring, benign prostatahyperplasia (BPH), diseases of the immune system, autoimmune diseases, immunodeficiency diseases, colon tumour, gastric tumour, intestinal tumour, pulmonary tumour, pancreatic tumour, ovarian tumour, prostatic tumour, leukaemia, melanoma, hepatic tumour, renal tumour, head tumour, throat tumour, glioma, breast tumour, uterine cancer, endometrial cancer, cervico-uterine carcinoma, brain tumour, adeno-acanthoma, cancer of the bladder, gastric tumour, colorectal tumour, oesophageal cancer, gynaecological tumour, ovarian tumour, cancer of the thyroid, lymphoma, chronic leukaemia, acute leukaemia, restenosis, diabetes, diabetic nephropathy, fibrotic diseases, cystic fibrosis, malignant nephrosclerosis, thrombotic microangiopathy syndrome, organ transplant rejection, glomerulopathy, metabolic diseases, solid/fixed tumours, rheumatic arthritis, diabetic retinopathy, asthma, allergies, allergic diseases, chronic obstructive pulmonary diseases, inflammatory bowel disease, fibrosis, atheriosclerosis, heart diseases, cardiovascular diseases, diseases of the myocardium, vascular diseases, angiogenetic diseases, kidney diseases, rhinitis, Grave's disease, focal ischemia, cardiac failure, ischemia, cardiac hypertrophia, renal failure, cardiac myocytic malfunction, high blood pressure, vasoconstriction, stroke, anaphylactic shock, platelet agglutination, skeletomuscular atrophy, obesity, overweight, glucosis homeostasis, congestive

cardiac insufficiency, angina, heart attack, cardiac infarction, hyperglycaemia, hypoglycaemia, hypertension".

14. Pharmaceutical composition comprising a pharmacologically active quantity of at least one compound according to Claim 13.

15. Pharmaceutical composition according to Claim 14, wherein the active substance is present in a unit dose of 0.001 mg to 100 mg per kg body weight of a patient.

16. Pharmaceutical composition according to any one of Claims 14 or 15, wherein the composition further contains at least one pharmaceutically compatible excipient and/or adjuvant.

17. Pharmaceutical composition according to any one of Claims 14 to 16, wherein the composition contains at least one further pharmacologically active substance.

18. Pharmaceutical composition according to Claim 17, wherein the further pharmacologically active substance is selected from the group consisting of DNA topoisomerase I and/or II inhibitors, DNA intercalators, alkylating agents, microtubuli destabilisers, hormone and/or growth factor receptor agonists and/or antagonists, antibodies against growth factors and their receptors, kinase inhibitors, alkylphospholipids, antimetabolites" selected from the group consisting of asparaginase, bleomycin, carboplatin, carmustin, chlorambucil, cisplatin, colaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, doxorubicin(adriamycin), epirubicin, etoposide, 5-fluorouracil, hexamethylmelamine, hydroxurea, ifosfamide, irinotecan, leucovorin, lomustine, mechlorethamine, 6-mercaptopurine, mesna, methotrexate, mitomycin C, mitoxantrone, prednisolone, prednisone, procarbazine, raloxifene, streptozocin, tamoxifen, thioguanine, topotecan, vinblastine, vincristine, vindesine, aminoglutethimide, L-asparaginase, azathioprine, 5-azacytidine cladribine, busulfan, diethylstilbestrol, 2', 2'-difluorodeoxycytidine, docetaxel, erythrohydroxynonyladenine,

ethinylestradiol, 5-fluorodeoxyuridin, 5-fluorodeoxyuridin monophosphate, fludarabine phosphate, fluoxymesterone, flutamide, hydroxyprogesterone caproate, idarubicin, interferon, medroxyprogesterone acetate, megestrol acetate, melphalan, mitotane, paclitaxel, oxaliplatin, pentostatin, N-phosphonoacetyl-L-aspartate (PALA), plicamycin, semustine, teniposide, testosterone propionate, thiotepa, trimethylmelamine, uridine, vinorelbin, epothilone, gemcitabine, Taxotere, BCNU, CCNU, DTIC, 5-fluorouracil, Herceptin, Avastin, Erbitux, Sorafenib, Gleevec, Iressa, Tarceva, rapamycin, perifosine, ,miltefosine, edelfosine, actinomycin D".

19. Kit comprising a pharmacologically active quantity of at least one compound according to Claim 16 and a pharmacologically active quantity of at least one further pharmacologically active substance according to any one of Claims 17 to 18.