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(54) **Title:** FUROPYRIDIN AND FUROPYRIMIDIN, INHIBITORS OF PI4K, FOR USE IN THE TREATMENT OF PARASITE INFECTION AND MALARIA

(57) **Abstract:** The present invention relates to novel compounds having valuable properties, in particular those which can be used for the preparation of medicaments as well as methods of their use and manufacture. Said compounds are particularly useful as PI4K inhibitors and for the treatment or prevention of PI4K-related disorders such as protozoan infections like malaria and virus infections.

TITLE OF THE INVENTION

FUROPYRIDIN AND FUROPYRIMIDIN, INHIBITORS OF PI4K, FOR USE IN THE TREATMENT OF PARASITE INFECTION AND MALARIA

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to novel compounds having valuable properties, in particular those which can be used for the preparation of medicaments as well as methods of their use and manufacture. Said compounds are particularly useful as PI4K inhibitors and for the treatment or prevention of PI4K-related disorders such as protozoan infections like malaria and virus infections.

Description of the Related Art

Malaria represents a major global health burden with an estimated 229 million new cases and nearly 409 000 deaths in 2019, mostly affecting young children and pregnant women (World Malaria Report 2020; World Health Organization: Geneva, Switzerland, 2020.). It is a vector-borne infectious disease caused by the hematoprotozoan parasite of genus Plasmodium (Phillips, M. A. et al., Malaria.Nat. Rev. Dis. Prim. 2017, 3, 17050). According to data from the World Health Organization (WHO), Plasmodium falciparum was responsible for the vast majority of malaria related morbidity and mortality in sub-Saharan Africa.

Currently, the WHO recommends artemisinin-based combination therapy (ACT). Additionally, vector control measures are key players in relieving the malarial burden. However, reports of emerging resistance toward ACTs (Dondorp, A. M et al., Artemisinin Resistance in Plasmodium falciparum Malaria. N. Engl. J. Med. 2009, 361, 455−467) illustrate the necessity of a new generation of drugs to combat resistance and improve standard of care for millions of affected patients. In recent years, research has identified novel druggable target structures, which can affect plasmodium viability. The

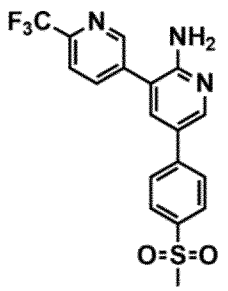
availability of a limited number of validated drug targets such as dihydrofolate reductase, cytochrome c-oxidoreductases, and hemozoin formation are a promising starting point for the development of new anti-malaria compounds and emphasizes the need to expand chemical matter toward more efficacious drugs with novel modes of action and multistage antiparasitic activity.

Within this context, Plasmodium kinases are attractive targets for new generation anti-malarials as both protein and lipid kinases are involved in key signaling pathways at various stages of the parasite lifecycle and have had some level of genetic or phenotypic validation (Arendse, L. B. et al., Plasmodium Kinases as Potential Drug Targets for Malaria: Challenges and Opportunities, ACS Infect Dis. 2021, 7(3):518-534. doi: 10.1021/acsinfecdis.0c00724).

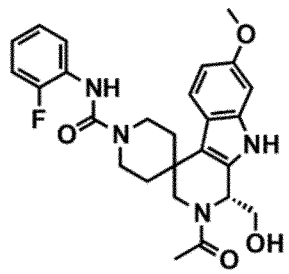
For example, lipid kinases are important in all stages of the Plasmodium lifecycle; this includes phosphatidylinositol-4-kinase (PI4K) that catalyzes the conversion of phosphatidylinositol (PI) to phosphatidylinositol-4-phosphate (PI4P). Phosphatidylinositol 4-kinase type III beta (PI4KIIIβ) is a ubiquitous eukaryotic enzyme that phosphorylates lipids to regulate intracellular signaling and trafficking. Imidazopyrazines are known inhibitors of PI4Ks. In blood stages of malaria, imidazopyrazines block a late step in parasite development by disrupting plasma membrane ingression around developing daughter merozoites. This likely stems from altered phosphatidylinositol 4-phosphate (PI4P) pools and disrupted Rab11A-mediated membrane trafficking. (McNamara, C. W. et al., Targeting Plasmodium PI(4)K to Eliminate Malaria. Nature 2013, 504 (7479), 248−253). Plasmodium PI4K is therefore important for signal transduction and membrane trafficking and has been shown to be a validated drug target for prevention, treatment, and elimination of malaria.

Several agents were recently reported as being Plasmodium PI4K inhibitors and the 2-aminopyridine MMV390048 had reached Phase IIa clinical trials (Paquet, T. et al., Antimalarial Efficacy of MMV390048, an Inhibitor of

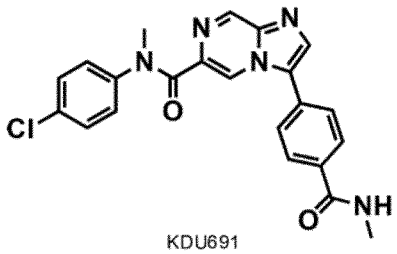
Plasmodium Phosphatidylinositol 4-Kinase. Sci. Transl. Med. 2017, 9 (387), 1−14) and further related compounds is shown below (PvPI4K, Pv = Plasmodium vivax).



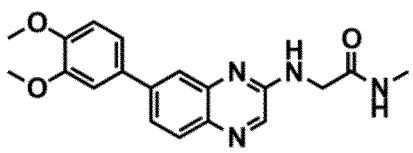
MMV390048
*Pv*PI4K - 3.4 nM



BRD73842
*Pv*PI4K - 21 nM



KDU691
*Pv*PI4K - 1.5 nM



BQR695
*Pv*PI4K - 3.5 nM

While PI4K has been identified as a useful target for protozoan infection treatment, human PI4K is also well-known to be hijacked by viruses. In particular human PI4KIIIβ, is an important host-target for viruses such as RNA viruses [PMID: 20510927; PMID: 33022924]. Therefore, PI4K inhibitors show great potential for the treatment of PI4K-related disorders such as virus or malaria infections.

RELEVANT PRIOR ART

WO 2012 025187 A1 discloses heterocyclic compounds useful as inhibitors of Syk that can be employed for the treatment of rheumatoid arthritis and/ or systemic lupus.

WO 2013 117285 A1 discloses heterocyclic compounds useful as inhibitors of TBK1 and IKKε that can be employed for the treatment of cancer and inflammatory diseases.

WO 2013 124025 A1 discloses heterocyclic compounds useful as inhibitors of Syk that can be employed for the treatment of rheumatoid arthritis and/ or systemic lupus.

WO 2017 003995 A1 discloses heterocyclic compounds useful as TBK/IKKε inhibitors.

WO 2011 086531 A1 and **WO 2013 121387 A1** disclose the use of aminopyridine derivatives in the manufacture of medicaments for preventing or treating malaria. Specifically, the disclosure relates to aminopyridine derivatives useful for the inhibition of malaria parasite proliferation.

While many new compounds are in development, the need for a broader pallet of effective drugs targeting PI4K is high in order to allow for combination therapies to suppress the development of resistance to single compounds. Additionally, several lead structures, which have demonstrated acceptable PI4K inhibition require high dosages in order to be effective *in vivo*. The constant development and improvement of compounds is necessary to adapt biophysical properties of compounds to increase bio-availability as well as tolerability in clinical settings. Therefore, it has been the object of the present invention to overcome the disadvantages associated with the state-of-the-art as explained above and provide alternatives with high efficacy.

SUMMARY OF THE INVENTION

One aspect of the present invention concerns compounds according to formula (I) useful in the prevention and/or treatment of PI4K-related disorders such as malaria or viral infections. The present invention further relates to pharmaceutical compositions comprising said compounds.

In another aspect, the present invention provides compounds of formula (I), which are suitable as PI4K inhibitors. Said compounds preferably inhibit Plasmodium PI4K and significantly reduce growth.

In certain embodiments, the present invention provides compounds of formula (I), which are selective PI4K inhibitors. In certain embodiments, the present

invention provides compounds of formula (I), which are selective for Plasmodium PI4K.

In certain embodiments, the present invention provides compounds of formula (I), which inhibit human PI4K, more preferably human PI4KIIIβ.

In certain embodiments, the present invention provides compounds of formula (I), for use in the prevention and/or treatment of virus infections, most preferably virus infections caused by RNA viruses.

In further embodiments, the invention relates to pharmaceutical composition for use in the prevention and/or treatment of PI4K-related disorders, comprising at least one compound of formula (I).

In another aspect, the present invention provides methods for the treatment and/or prevention of malaria comprising administering a compound of formula (I). In another aspect, the present invention provides compounds which are able to modulate, especially inhibit the activity of IP4K in a disease state in mammals.

For convenience, certain terms employed in the specification, examples, and appended embodiments are collected here and provide definitions of the various chemical moieties that make up the compounds according to the invention and are intended to apply uniformly through-out the specification and embodiments, unless an otherwise expressly set out definition provides a broader definition.

The term "pharmaceutically acceptable salts or complexes" refers to salts or complexes of the compounds according to the invention. Examples of such salts include, but are not restricted, to base addition salts formed by reaction of compounds of the invention with organic or inorganic bases such as hydroxide, carbonate or bicarbonate of a metal cation such as those selected

in the group consisting of alkali metals (sodium, potassium or lithium), alkaline earth metals (e.g. calcium or magnesium). Also comprised are salts which are formed from acid addition, salts formed with inorganic acids (e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, and the like), as well as salts formed with organic acids such as acetic acid, oxalic acid, tartaric acid, succinic acid, malic acid, fumaric acid, maleic acid, ascorbic acid, benzoic acid, tannic acid, palmoic acid, alginic acid, polyglutamic acid, naphthalene sulfonic acid, naphthalene disulfonic acid, and poly-galacturonic acid.

"Pharmaceutically active compounds" refers to any compound that upon administration to the recipient, is capable of providing directly or indirectly, the activity disclosed herein. The term "indirectly" also encompasses prodrugs which may be converted to the active form of the drug via endogenous enzymes or metabolism. The prodrug is a derivative of the compounds according to the invention and presenting anti-malarial activity that has a chemically or metabolically decomposable group, and a compound that may be converted into a pharmaceutically active compound according to the invention *in vivo* by solvolysis under physiological conditions. The prodrug is converted into a compound according to the present invention by a reaction with an enzyme, gastric acid or the like under a physiological condition in the living body, e.g., by oxidation, reduction, hydrolysis or the like, each of which is carried out enzymatically. These compounds can be produced from compounds of the present invention according to well-known methods.

The term "solvates" of the compounds is taken to mean adductions of inert solvent molecules onto the compounds which form owing to their mutual attractive force. Solvates are, for example, mono- or dihydrates or alkoxides.

The term "indirectly" also encompasses metabolites of compounds according to the invention.

The term "metabolite" refers to all molecules derived from any of the compounds according to the present invention in a cell or organism, preferably mammal.

The term "malaria" includes disease and conditions related to an infection with Plasmodium.

As used herein, "treatment" and "treating" and the like generally mean obtaining a desired pharmacological and physiological effect. The effect may be prophylactic in terms of preventing or partially preventing a disease, symptom or condition thereof and/or may be therapeutic in terms of a partial or complete cure of a disease, condition, symptom or adverse effect attributed to the disease. The term "treatment" as used herein covers any treatment of a disease in a mammal, particularly a human, and includes: (a) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; (b) inhibiting the disease, i.e., arresting its development; or relieving the disease, i.e., causing regression of the disease and/or its symptoms or conditions. The term "effective amount" includes "prophylaxis-effective amount" as well as "treatment-effective amount".

The term "prophylaxis-effective amount" refers to a concentration of compound of this invention that is effective in inhibiting, decreasing the likelihood of the disease by malarial parasites, or preventing malarial infection or preventing the delayed onset of the disease by malarial parasites, when administered before infection, i.e., before, during and/or slightly after the exposure period to malarial parasites.

The term "prophylaxis" includes causal prophylaxis, i.e., antimalarial activity comprising preventing the pre-erythrocytic development of the parasite, suppressive prophylaxis, i.e. antimalarial activity comprising suppressing the development of the blood stage infection and terminal prophylaxis, i.e.

antimalarial activity comprising suppressing the development of intra-hepatic stage infection. This term includes primary prophylaxis (i.e. preventing initial infection) where the antimalarial compound is administered before, during and/or after the exposure period to malarial parasites and terminal prophylaxis (i.e. to prevent relapses or delayed onset of clinical symptoms of malaria) when the antimalarial compound is administered towards the end of and/or slightly after the exposure period to malarial parasites but before the clinical symptoms. Further, this term includes suppression of dormant forms of the parasite in the liver (intrahepatic or pre-erythrocytic stage) as well as the activation and elimination of dormant forms (wake-up-and-kill concept). Typically, against *P. falciparum* infections, suppressive prophylaxis is used whereas against *P. ovale*, *P. vivax* or a combination of *P. falciparum* and *P. vivax*, terminal prophylaxis is used. Suppression of dormant stages is particularly useful against *P. ovale* and *P. vivax*.

The expression "effective amount" denotes the amount of a medicament or of a pharmaceutical active ingredient which causes in a tissue, system, animal or human a biological or medical response which is sought or desired, for example, by a researcher or physician.

Likewise, the term "treatment-effective amount" or "therapeutically effective amount" refers to an amount of compound which, compared with a corresponding subject who has not received this amount, has the following consequence: improved treatment, healing, prevention or elimination of a disease, syndrome, condition, complaint, disorder or side-effects or also the reduction in the advance of a disease, complaint or disorder.

The expression "treatment-effective amount" or "therapeutically effective amount" also encompasses the amounts which are effective for increasing normal physiological function and are necessary for effective treatment of a disease such as a malaria infection e.g. leading to a reduction in parasite

numbers in blood following microscopic examination when administered after infection has occurred.

The expression "PI4K-related disorders" refer to disorders affected by PI4K interactions such as inhibition or overexpression of PI4K caused by for example pathogens, genetic predisposition, usage of PI4K for viral replication, as well as disorders treatable and/or preventable by inhibition of PI4K of the patient or of parasites such as Plasmodium. Examples for PI4K-related disorders are, but not limited to, viral infections such as infections caused by RNA viruses or protozoan infections such as malaria.

The term "subject" as used herein refers to mammals. For examples, mammals contemplated by the present invention include humans and the like.

The term "pharmaceutically acceptable carrier, adjuvant, or excipient " refers to a nontoxic carrier, adjuvant, or excipient that does not destroy the pharmacological activity of the compound with which it is formulated. Pharmaceutically acceptable carriers, adjuvants or excipient that are used in the compositions of this invention include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene- polyoxypropylene-block polymers, polyethylene glycol and wool fat.

A "pharmaceutically acceptable derivative" means any non-toxic salt, ester, salt of an ester or other derivative of a compound of this invention that, upon administration to a recipient, is capable of providing, either directly or indirectly,

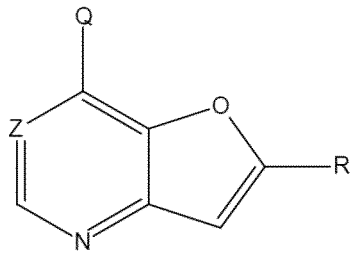
a compound of this invention or an inhibitory active metabolite or residue thereof.

A wavy line at the end of a bond line, generally appearing perpendicular to the bond line, has the same meaning as a wavy line that bisects a bond line.

DETAILED DESCRIPTION OF THE INVENTION

The aim of the present invention was the development of novel compounds useful for inhibition of PI4K and the treatment of PI4K-related disorders such as malaria or viral infections in order to extend, offer alternatives and improve limited treatment options for physicians and vets thereby ensuring highly effective treatments for patients.

Surprisingly, it has been discovered that compounds according to the present invention are inhibitors of PI4K, which is found in multiple organisms.
The present invention provides a compound of formula (I)



(I)

or a pharmaceutically acceptable solvate, salt, tautomer or stereoisomer thereof for use in the prevention and/or treatment of PI4K-related disorders, wherein:

R denotes AR1 or HT1;

AR1 denotes phenyl, which is unsubstituted or substituted by

- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN and/or NO_2 (preferably Alk2, OAlk2, Hal and/or Cyc); and/or
- a substituent selected from a group comprising:

A, NH_2, OH, $(CR^aR^b)_n$HetCyc1, $(CR^aR^b)_n$HetAr1, $(CR^aR^b)_n$Aryl, $(CR^aR^b)_nCO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nCO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nCO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COCyc, $(CR^aR^b)_n$COA, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_n$CONHA, $(CR^aR^b)_nCONH(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_nCONH(CR^aR^b)_m$HetAr1, $(CR^aR^b)_nCONH(R^aR^b)_m$Aryl, $(CR^aR^b)_n$CONHCyc, $(CR^aR^b)_n$COOA, $(CR^aR^b)_n$COOH, $(CR^aR^b)_nCOO(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_nCOO(CR^aR^b)_m$HetAr1, $(CR^aR^b)_nCOO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COOCyc, $(CR^aR^b)_nNHCO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nNHCO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nNHCO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$NHCOCyc, $(CR^aR^b)_n$NHCOA, $(CR^aR^b)_nS(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nS(R^aR^b)_m$HetAr1, $(CR^aR^b)_nS(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SA, $(CR^aR^b)_nSO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nSO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nSO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SOA, $(CR^aR^b)_nSO_2(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nSO_2(R^aR^b)_m$HetAr1, $(CR^aR^b)_nSO_2(R^aR^b)_m$Aryl, $(CR^aR^b)_nSO_2$Cyc, $(CR^aR^b)_nSO_2$A, $(CR^aR^b)_n$SOA(NH), $(CR^aR^b)_n$SOCyc(NH), $(CR^aR^b)_n$SOAryl(NH), $(CR^aR^b)_n$SOHetCyc1(NH), $(CR^aR^b)_n$SOHetAr1(NH), $(CR^aR^b)_n$SOA(NA), $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_n$SOCyc(NA), $(CR^aR^b)_n$SOAryl(NA), $(CR^aR^b)_n$SOHetCyc1(NA), $(CR^aR^b)_n$SOHetAr1(NA), $(CR^aR^b)_n$SOA(NCyc), $(CR^aR^b)_n$SOCyc(NCyc), $(CR^aR^b)_n$SOAryl(NCyc), $(CR^aR^b)_n$SOHetCyc1(NCyc), $(CR^aR^b)_n$SOHetAr1(NCyc), $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2$NHA, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or

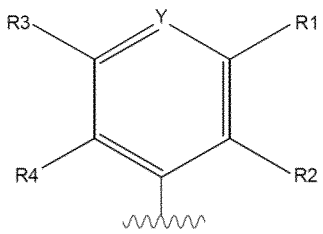
monosubstituted by at least one Hal, Alk2 or OAlk2 group;

HT1 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle with 3 to 9 carbon atoms and 1, 2, 3 or 4 N, O and/or S atoms, wherein said heterocycle is unsubstituted or substituted by

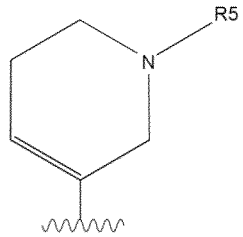
- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN, =O and/or NO_2(preferably Alk2, OAlk2, Hal and/or Cyc); and/or
- a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$,

$(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

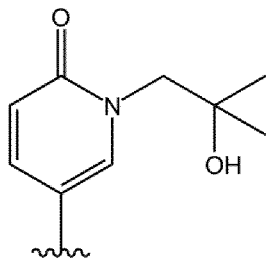
Q denotes a structure according to formula (II), (III), or (XII)



(II)



(III)



(XII)

R^1 and R^5 denote, independently from each other, AR2 or HT2;

R^2, R^3 and R^4 denote, independently from each other, H, Hal or CAlk2;

Y denotes CH, CHal, CAlk2, $CCHal_3$ or N;

AR2 denotes phenyl, which is unsubstituted or substituted by

- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN and/or NO_2 (preferably Alk2, OAlk2, Hal, and/or Cyc); and/or
- a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$,

$(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

HT2 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle with 3 to 9 carbon atoms and 1, 2, 3 or 4 N, O and/or S atoms, wherein said heterocycle is unsubstituted or substituted by

- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN, =O and/or NO_2 (preferably Alk2, OAlk2, Hal, and/or Cyc); and/or
- a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONR^{Cyc3}R^{Cyc4}$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$,

$(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

A denotes linear or branched alkyl having 1, 2, 3, 4, 5, or 6 carbon atoms, wherein:

- one or two non-adjacent CH_2 groups may be replaced by O, NAlk2 or NH; and/or
- 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal; and/or
- one hydrogen may be replaced by OH or NH_2 or a cyclic alkyl having 3, 4, 5 or 6 carbon atoms, which is mono- di or trisubstituted by Hal, OH, Alk2, NHAlk2, $N(Alk2)_2$ and/or NH_2;

Alk1 denotes linear or branched alkyl having 1, 2, 3, 4, 5, or 6 carbon atoms, wherein - one or two CH_2 groups may be replaced by O, NAlk2 or NH; and/or

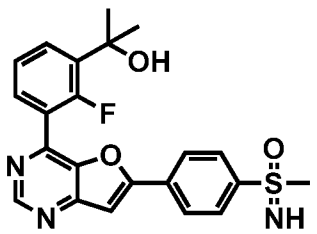
		- 1 hydrogen may be replaced by OH, NHAlk2, $N(Alk2)_2$ or NH_2; and/or - 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal;
	Alk2	denotes linear or branched alkyl having 1 to 6 carbon atoms, wherein 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal;
	Aryl	denotes phenyl, which is unsubstituted or mono-, di- or trisubstituted Hal, Alk2, OAlk2, OH, NH_2, Cyc or HetAr2, HetCyc2;
	HetCyc1	denotes a mono- or bicyclic optionally bridged saturated or unsaturated 4- to 10-membered heterocycle having 1 or 2 heteroatoms selected from N, O, S and/or Si, wherein said heterocycle may be unsubstituted or mono-or disubstituted by Hal, OH, A, Aryl, HetAr2, SO_2Alk2 and/or =O;
	HetCyc2	denotes a mono- or bicyclic optionally bridged saturated or unsaturated 4- to 10-membered heterocycle having 1 or 2 heteroatoms selected from N, O, S and/or Si, wherein said heterocycle may be unsubstituted or mono-or disubstituted by Hal, OH, A, SO_2Alk1 and/or =O;
	Cyc	denotes cyclic alkyl having 3 to 6 carbon atoms, wherein 1, 2 or 3 hydrogens may be replaced by Hal and 1 additional hydrogen may be replaced by HetCyc2, HetAr2, Aryl, Alk2, NH_2 and/or OH;
	Hal	denotes F or Cl;
	HetAr1	denotes a mono- or bicyclic aromatic 4- to 12-membered heterocycle having 1, 2, 3 or 4 N, O and/or S atoms, said heterocycle being unsubstituted or mono- or disubstituted Hal, Alk2, SOAlk2, SO_2Alk2, HetCyc2, OH or NH_2;
	HetAr2	denotes a mono- or bicyclic aromatic 4- to 12-membered heterocycle having 1, 2, 3 or 4 N, O and/or S atoms, said

	heterocycle being unsubstituted or mono- or disubstituted Hal, Alk2, SOAlk2, SO_2Alk2, OH or NH_2
R^a and R^b	denote each, independently from each other, H, Alk2 or Cyc; or R^a and R^b together represent $-(CH_2)_x-$ with x= 2, 3, 4 or 5, thus forming together with the carbon atom they are attached to a (3-, 4-, 5- or 6- membered) cycloalkyl ring;
R^{Cyc1} and R^{Cyc2}	together form $-(CH_2)_x-$ with x= 3 or 4, thus forming together with the atoms they are attached to a (5- or 6-membered) ring, wherein 1, or 2 H atoms, in $-(CH_2)_x-$ may be independently replaced by Hal or Alk1;
$R^{Cyc3}$and R^{Cyc4}	together form $-(CH_2)_x-$ with x= 3, 4 or 5, thus forming together with the nitrogen atom they are attached to a (4-, 5- or 6-membered) ring, wherein 1, or 2 H atoms, in $-(CH_2)_x-$ may be independently replaced by Hal or Alk1;
n	denotes 0, 1 or 2 (preferably 0 or 1);
m	denotes 0 or 1 (preferably 0); and
Z	denotes CH, CHal, CAlk2, $CCHal_3$ or N (preferably CH or N).

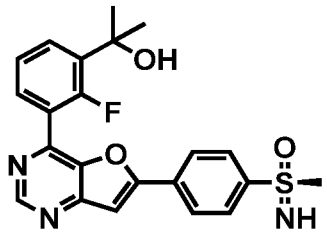
The compounds of formula (I) according to the present invention may – also depending on the nature of substituents they may bear – have one or more centers of chirality. They may accordingly occur in various enantiomeric and diastereomeric forms, as the case may be, and be in racemic or optically active form. The invention, therefore, also relates to the optically active forms, enantiomers, racemates, diastereomers, mixtures thereof in all ratios, collectively: “stereoisomers”. It may be desirable to use a specific stereoisomer, e.g. one specific enantiomer or diastereomer of a certain compound. In these cases, a compound according to the present invention obtained as a racemate or even intermediates thereof – may be separated into the stereoisomeric (enantiomeric, diastereoisomeric) compounds by chemical or physical measures known to the person skilled in the art. The compounds

of the invention which have one or more centers of chirality and which occur as racemates or as mixtures of enantiomers or diastereoisomers can for example be fractionated or resolved by methods known per se into their optically pure or enriched isomers, i.e. enantiomers or diastereomers. The separation of the compounds of the invention can take place by chromatographic methods, e.g. column separation on chiral or nonchiral phases, or by recrystallization from an optionally optically active solvent or by use of an optically active acid or base or by derivatization with an optically active reagent such as, for example, an optically active alcohol, and subsequent elimination of the radical. Another approach that may be applied to obtain one or more specific stereoisomers of a compound of the present invention in an enriched or pure form makes use of stereoselective synthetic procedures, e.g. applying starting material in a stereoisomerically enriched or pure form (for instance using the pure or enriched (R)- or (S)-enantiomer of a particular starting material bearing a chiral center) or utilizing chiral reagents or catalysts, in particular enzymes.

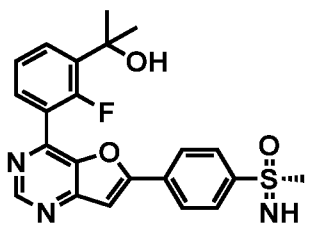
Examples of compounds according to the present invention, which have a stereogenic center are:



Racemic mixture (D203)



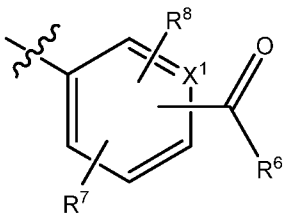
(*S*)-enantionmer (D209)



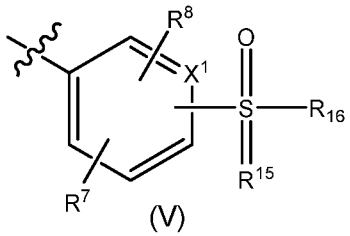
(*R*)-enantiomer (D210)

In this specific example the sulfur atom represents the stereocenter, in other examples of the present invention the compounds may of course have other or additional stereocenters located at a different atom e.g. at a carbon atom. As shown above, in case a compound with one or more stereocenter(s) is shown without specifying the stereoconfiguration at the stereocenter(s) this refers to a mixture of the corresponding stereoisomers.

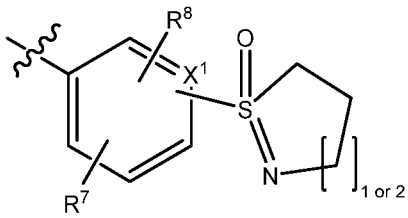
In a certain embodiment of the present invention residue R of a compound according to formula (I) denotes a structure according to formula (IV), (V), (Va) or (VI)



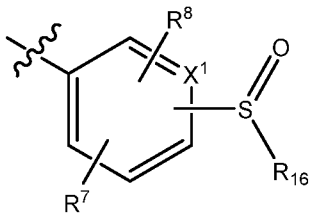
(IV)



(V)



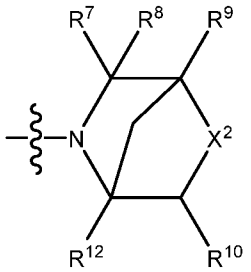
(Va)



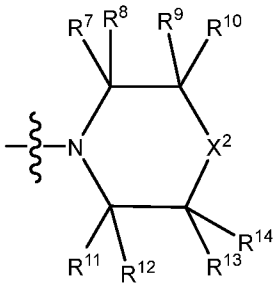
(VI)

wherein

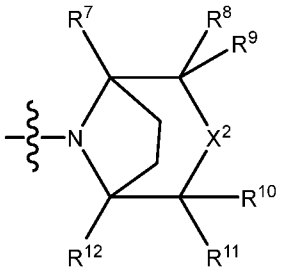
R^6 denotes OH, A or Cyc (preferably OH, cyclopropyl, OCH_3, OCF_3, $OCHF_2$, CH_3, C_2H_5, CH_2F, CHF_2, OC_2H_5, O*i*Pr, O*t*Bu, NH_2, $NHCH_3$, $N(CH_3)_2$, $N(C_2H_5)_2$, $N(iPr)_2$, $N(CH_3)(nPr)$ or $N(CH_3)(tBu)$) or a substituent according to formula (VII) to (X)



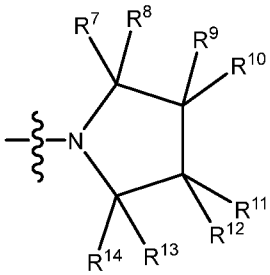
(VII)



(VIII)



(IX)



(X)

wherein

R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} denote each, independently from each other, H, OH, Hal, CH_3, C_2H_5, $CHal_3$, OCH_3, $OCHal_3$, $OCHal_2$, OCH_2Hal, CH_2Hal and/or $CHHal_2$;

R^{15} denotes NR^{17} or O;

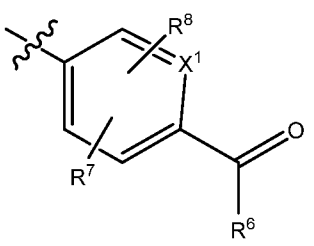
R^{16} denotes A or Cyc;

R^{17} denotes H, Alk1 or cyclic alkyl having 3 to 6 carbon atoms, wherein 1, 2 or 3 hydrogens of said cyclic alkyl group may be replaced by Hal;

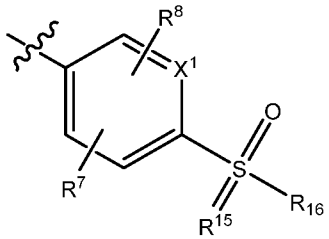
X^1 denotes N or CH; and

X^2 denotes NH, NAlk1 or O.

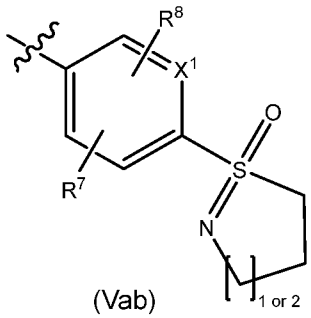
For the avoidance of doubt, residues R^7, R^8 COR^6, $SOR^{16}(NR^{15})$ and SOR^{16} of formulas (IV), (V), and (VI) and the cyclic S-residue of formula (Va) as shown above may be attached to each of the carbon atoms of the aromatic ring. In important embodiments residues COR^6, $SOR^{16}(NR^{15})$ and SOR^{16} are attached in para-position to the carbon atom, which connects residue R with the annulated ring system (the furo pyrimidine residue), as shown in formulas (IVb)-(VIb) below,



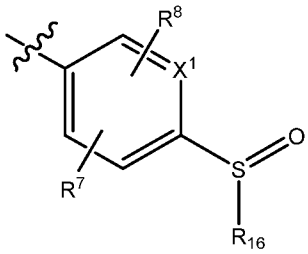
(IVb)



(Vb)



(Vab)

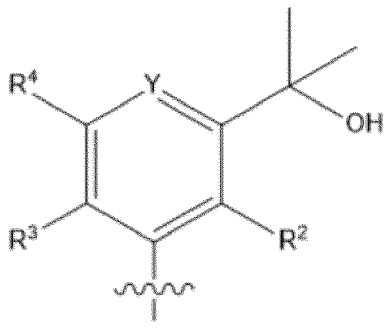


(VIb)

and residues R^7 and R^8 are each preferably attached in ortho- or meta-position to the carbon atom which connects residue R with the annulated ring system.

Another embodiment of the present invention relates to a compound according to formula (I) as defined above, wherein Q denotes a structure according to formula (II).

Another particular embodiment concerns a compound according to formula (I) as defined above, wherein Q denotes a residue according to formula (XI)



(XI)

wherein

Y denotes N or CH;

and one or two of the residues R^2, R^3 and R^4 independently represent, Hal, CH_3, $CHal_3$, OCH_3, $OCHal_3$, $OCHHal_2$, OCH_2Hal, CH_2Hal and/or $CHHal_2$ and the remaining of said residue(s) represent H.

In such an embodiment R^2 and R^4 preferably represent independently from one another, a residue selected from F, CH_3, CF_3, OCH_3, OCF_3, $OCHF_2$, OCH_2F, CH_2F and/or CHF_2 and R^3 denotes H. In another important embodiment of a residue according to formula (XI) as described above R^2 represents, a residue selected from F, CH_3, CF_3, OCH_3, OCF_3, $OCHF_2$, OCH_2F, CH_2F and/or CHF_2 and R^3 and R^4 denote H. In further important embodiment of said residue R^4 represents, a residue selected from F, CH_3, CF_3, OCH_3, OCF_3, $OCHF_2$, OCH_2F, CH_2F and/or CHF_2 and R^3 and R^2 denote H.

A further particular embodiment concerns a compound according to formula (I), wherein Z denotes N.

In the context of the present invention “hydroxyalkyl” represents a linear or branched hydrocarbon residue with 1, 2, 3, 4, 5 or 6 carbon atoms (preferably 1, 2, 3 or 4 carbon atoms), which is substituted with one or two (preferably one) hydroxy groups. Examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2- (hydroxymethyl)-3-hydroxypropyl, preferably 2-hydroxypropan-2-yl, 1-hydroxyethyl, 2-hydroxy2-methylpropyl and the like.

Throughout the invention, all residues which occur more than once may be identical or different, i.e. are independent of one another. For example in “$(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$” or “$(CR^aR^b)_nSO_2NA_2$” each instance of R^a, R^b and A may have a different meanig (within the scope of the corresponding definition).

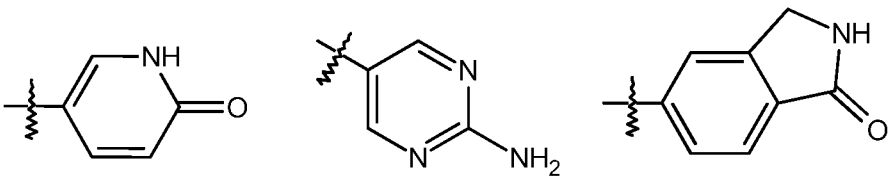
In particular important embodiments A represents a linear or branched alkyl group having 1, 2, 3 or 4 carbon atoms, wherein (as applicable) one or two non-adjacent CH_2 groups may be replaced by O, NCH_3, NC_2H_5, N*i*Pr or NH; and/or 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal on/or one hydrogen may be replaced by OH, NH_2 or a cyclic alkyl group having 3, 4, 5, or 6 carbon atoms, wherein said cyclic alkyl group may be mono or disubstituted by Hal, Alk2 NHAlk2 $(NAlk2)_2$ and/or NH_2.

AR1 denotes preferably 3,4,5-trimethoxyphenyl or phenyl, which is substituted by

- one or two residue(s) selected from Hal, CH_3, $CHal_3$ and/or OCH_3; and
- one residue selected from: $CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, ($(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$,

$(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group.

HT1 denotes preferably pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, isoindolyl, bezoimidazoyl, indazolyl or one of following residues:

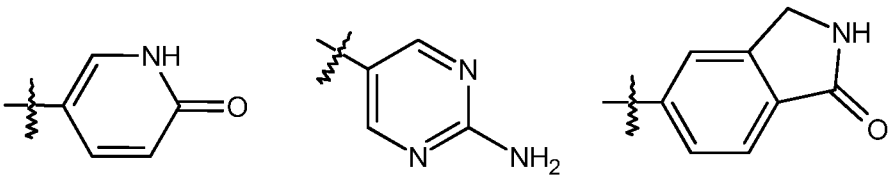


each of said residues, independently from one another unsubstituted or substituted by (following optional substituents, which may be attached to a carbon atom or another atom under the provisio that a proper valency of said atom results, are not shown in the residues depicted above):

- 1, 2 or 3 substituents independently selected from: A, Hal; and/or
- a substituent selected from a group comprising:
  NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$,

$(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

HT2 denotes preferably pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, isoindolyl, benzoimidazoyl, indazolyl (most preferably pyridinyl) or one of following residues:



each of said residues, independently from one another unsubstituted or substituted by (following optional substituents, which may be attached to a carbon atom or another atom under the provisio that a proper valency of said atom results, are not shown in the residues depicted above):

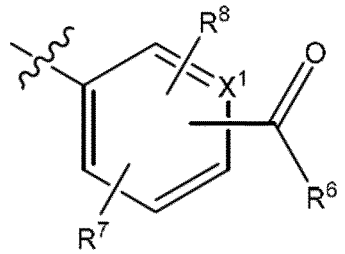
- 1, 2 or 3 substituents independently selected from: A, Hal; and/or
- a substituent selected from a group comprising:

NH_2, OH, $(CR^aR^b)_n$HetCyc1, $(CR^aR^b)_n$HetAr1, $(CR^aR^b)_n$Aryl, $(CR^aR^b)_n$CO$(R^aR^b)_m$HetCyc1, $(CR^aR^b)_n$CO$(R^aR^b)_m$HetAr1, $(CR^aR^b)_n$CO$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COCyc, $(CR^aR^b)_n$COA, $(CR^aR^b)_n$CONA_2, $(CR^aR^b)_n$CONH_2, $(CR^aR^b)_n$CONHA, $(CR^aR^b)_n$CONH$(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_n$CONH$(CR^aR^b)_m$HetAr1, $(CR^aR^b)_n$CONH$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$CONHCyc, $(CR^aR^b)_n$COOA, $(CR^aR^b)_n$COOH, $(CR^aR^b)_n$COO$(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_n$COO$(CR^aR^b)_m$HetAr1, $(CR^aR^b)_n$COO$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COOCyc, $(CR^aR^b)_n$NHCO$(R^aR^b)_m$HetCyc1, $(CR^aR^b)_n$NHCO$(R^aR^b)_m$HetAr1, $(CR^aR^b)_n$NHCO$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$NHCOCyc, $(CR^aR^b)_n$NHCOA, $(CR^aR^b)_n$S$(R^aR^b)_m$HetCyc1, $(CR^aR^b)_n$S$(R^aR^b)_m$HetAr1, $(CR^aR^b)_n$S$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SA, $(CR^aR^b)_n$SO$(R^aR^b)_m$HetCyc1, $(CR^aR^b)_n$SO$(R^aR^b)_m$HetAr1, $(CR^aR^b)_n$SO$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SOA, $(CR^aR^b)_n$S$O_2$$(R^aR^b)_m$HetCyc1, $(CR^aR^b)_n$S$O_2$$(R^aR^b)_m$HetAr1, $(CR^aR^b)_n$S$O_2$$(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SO_2Cyc, $(CR^aR^b)_n$SO_2A, $(CR^aR^b)_n$SOA(NH), $(CR^aR^b)_n$SOCyc(NH), $(CR^aR^b)_n$SOAryl(NH), $(CR^aR^b)_n$SOHetCyc1(NH), $(CR^aR^b)_n$SOHetAr1(NH), $(CR^aR^b)_n$SOA(NA), $(CR^aR^b)_n$S$OR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_n$SOCyc(NA), $(CR^aR^b)_n$SOAryl(NA), $(CR^aR^b)_n$SOHetCyc1(NA), $(CR^aR^b)_n$SOHetAr1(NA), $(CR^aR^b)_n$SOA(NCyc), $(CR^aR^b)_n$SOCyc(NCyc), $(CR^aR^b)_n$SOAryl(NCyc), $(CR^aR^b)_n$SOHetCyc1(NCyc), $(CR^aR^b)_n$SOHetAr1(NCyc), $(CR^aR^b)_n$S$O_2$$NA_2$, $(CR^aR^b)_n$S$O_2$$NH_2$, $(CR^aR^b)_n$SO_2NHA, $(CR^aR^b)_n$$POA_2$,

and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group.

Cyc denotes preferably cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

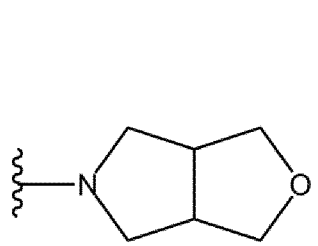
In a specific embodiment of the present invention residue R of a compound according to formula (I) denotes a structure according to formula (IV)



(IV) ;

wherein

R^6 is Alk1, Alk2, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, -OH, $-OCH_3$, $-OC(CH_3)_3$,



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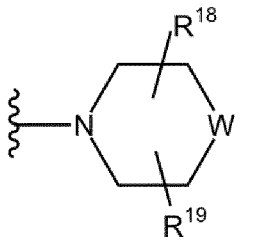

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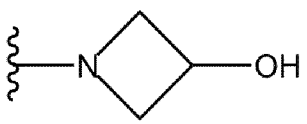

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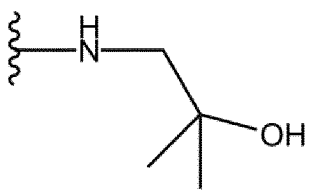

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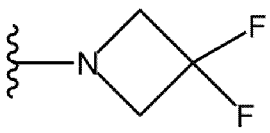

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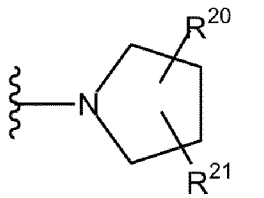

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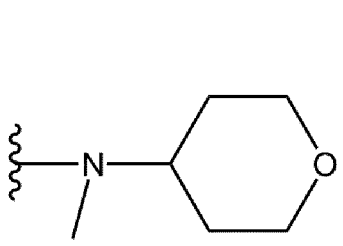
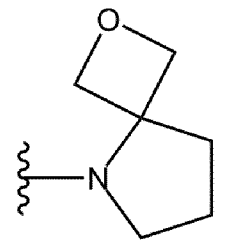
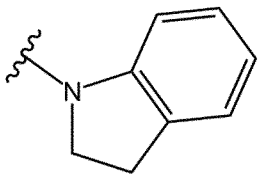
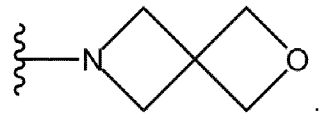
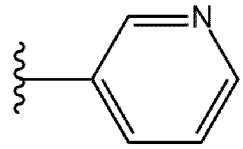

, 
, 
or 
;

R^7, R^8 is each independently selected from H, Hal, Alk1, or Alk2;

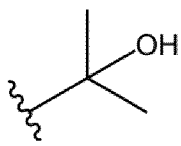
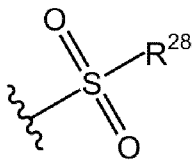
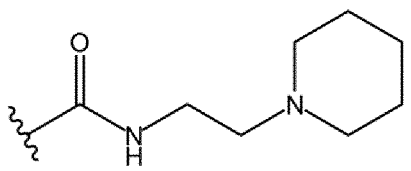
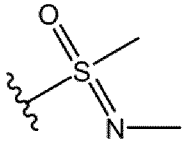
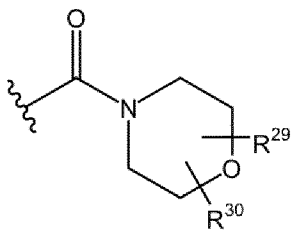
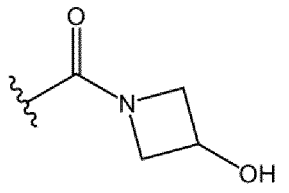
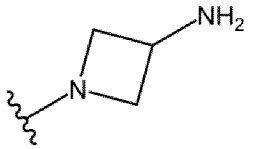
R^{18}, R^{19} is each independently selected from H, Hal, Alk1, Alk2, or are taken together form a cycloalkyl ring;

R^{20}, R^{21} is each independently selected from H, -Hal, -$CHal_3$, -CH_3, -$C((CH_3)_2OH)$, or 
;

W is O, NR^{18}, or $CR^{18}R^{19}$;

X^1 is CR^7 or N.

In this specific embodiment of the present invention residue Q of the compound denotes a structure according to formula (II) above, wherein

R^1 is H, Hal, 
, 
, 
, 
, 
, 
, 
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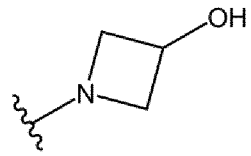
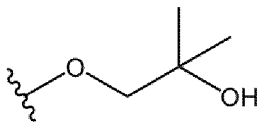
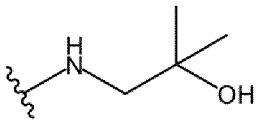
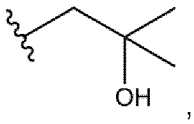
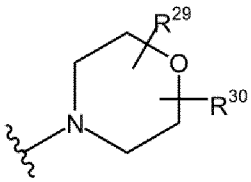
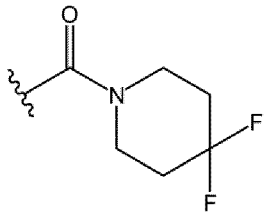
 ,

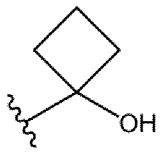
 ,

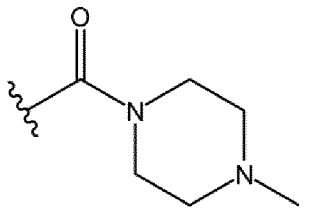
 ,

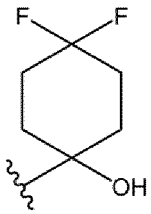
 ,

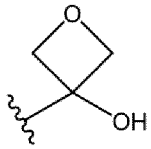
 ,

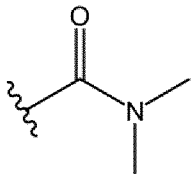
 ,

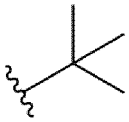
 ,

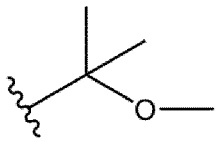
 ,

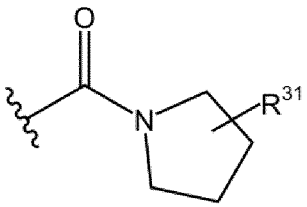
 ,

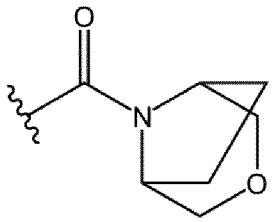
 ,

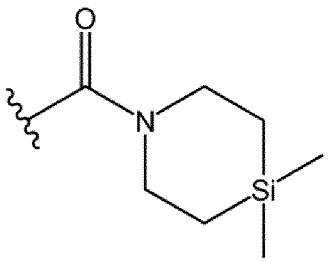
 ,

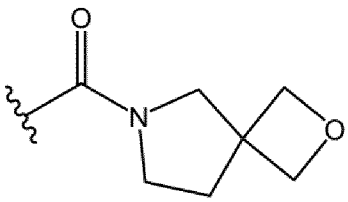
 ,

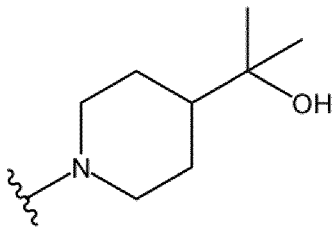
 ,

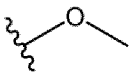
 ,

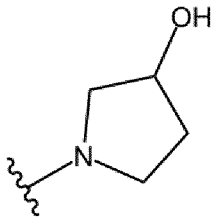
 ,

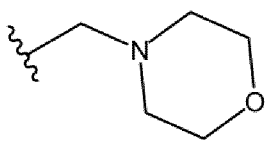
 ,

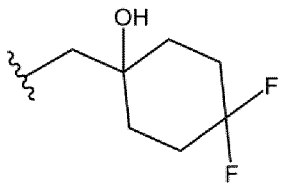
 ,

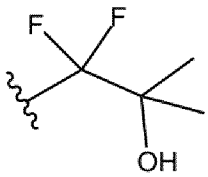
 ,

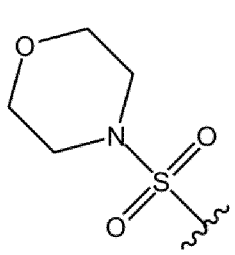
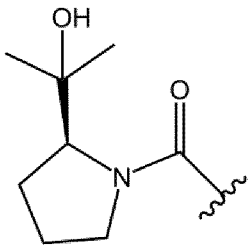
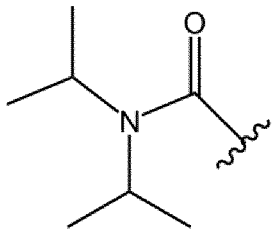
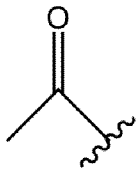
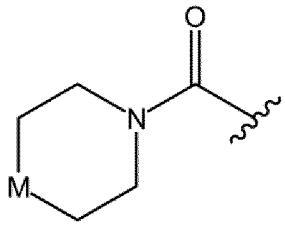
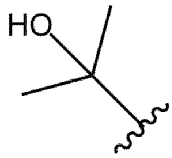
 ,

 ,

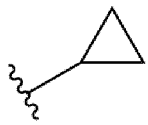
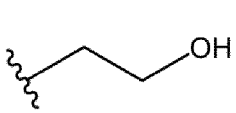
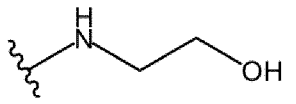
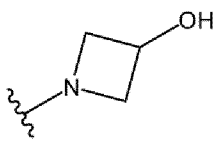
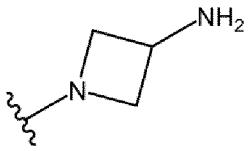
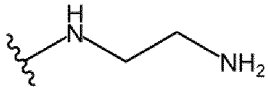
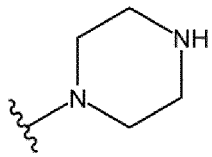
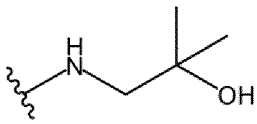
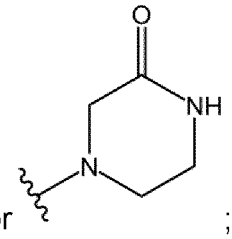
 ,

 , or

 ;

R^3 is H, Hal,  ,  ,  ,  ,  , or  ;

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,  ,  ,  ,  ,  ,  ,  ,  , or  ;

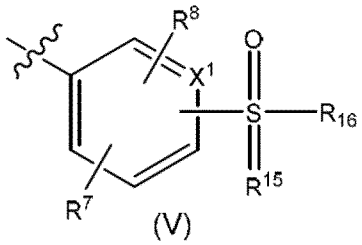
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

In a specific embodiment of the present invention residue R of a compound according to formula (I) denotes a structure according to formula (V)



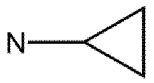
(V)

;

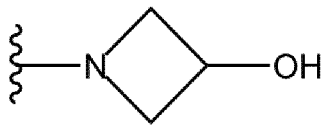
wherein

X^1 is CR^7 or N;

R^7, R^8 is each independently selected from H, Hal, $-CH_3$, or $-CHal_3$;

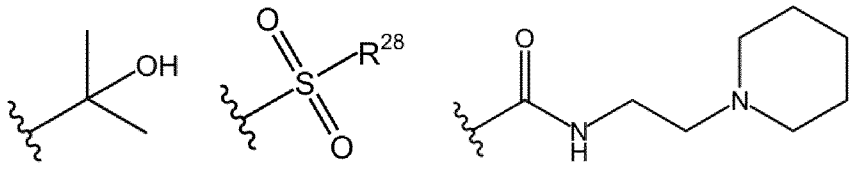
R^{15} is O, NH, or 

;

R^{16} is Alk1, $-NH_2$, $-N(CH_3)_2$, Alk2, or 

; and

In this specific embodiment of the present invention residue Q of the compound denotes a structure according to formula (II) above, wherein

R^1 is H, Hal, 

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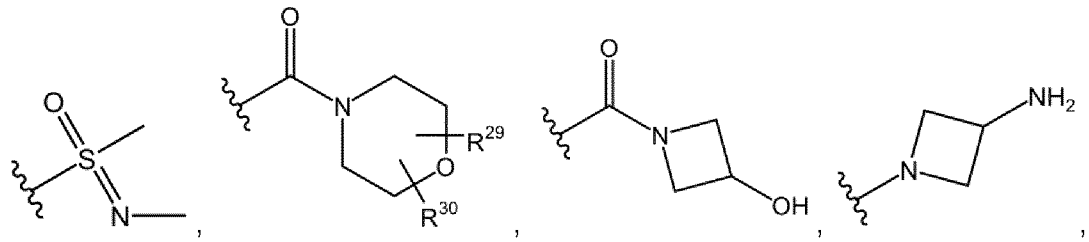

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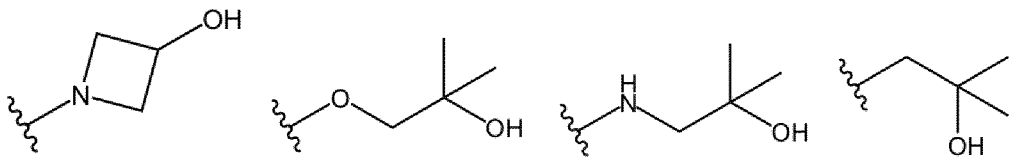

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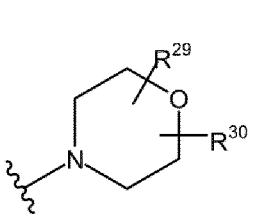
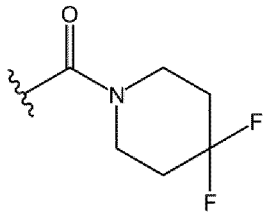
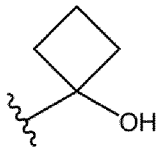
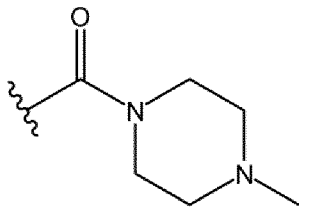
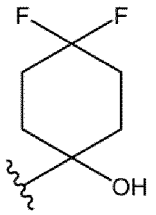
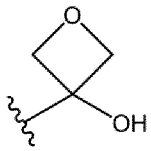
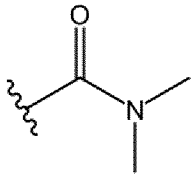
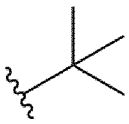
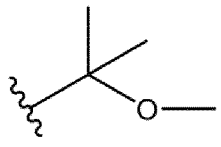
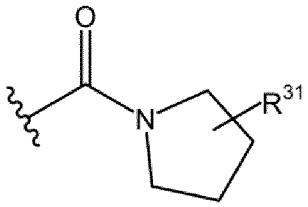
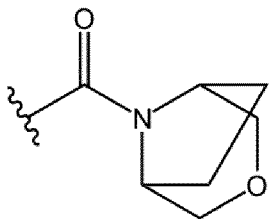
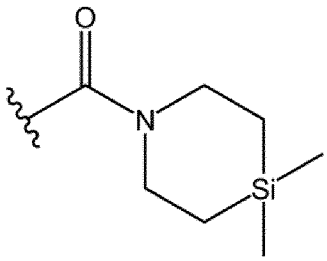
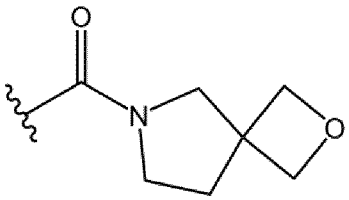
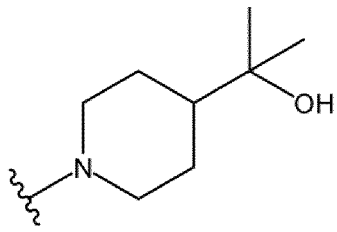
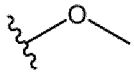
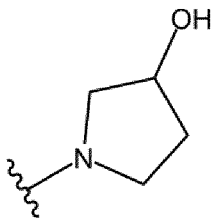
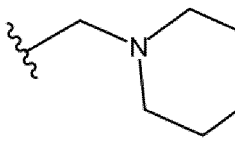
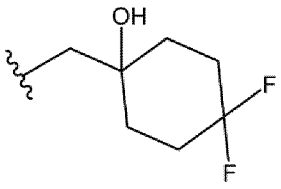
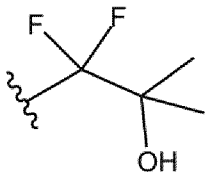
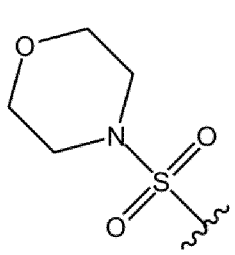
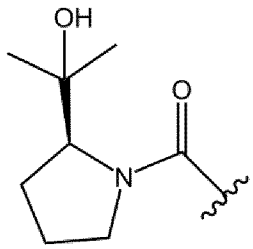
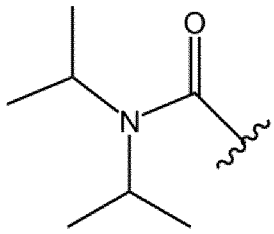
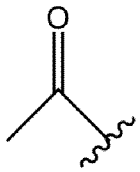
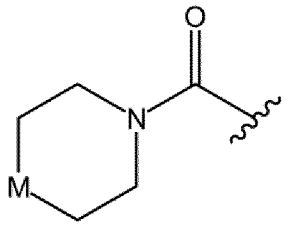
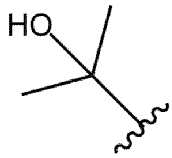
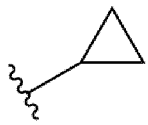
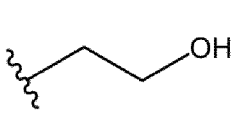
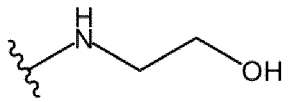
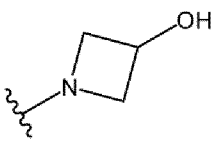
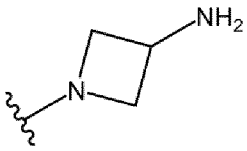
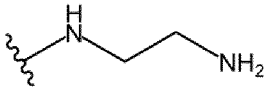
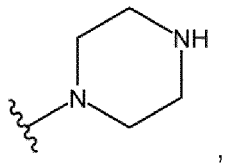
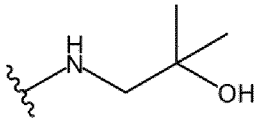
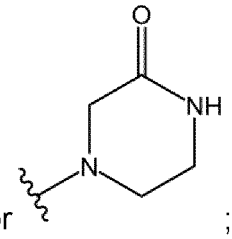




















, or ;

R^3 is H, Hal,  ,  ,  ,  ,  , or  ;

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,  ,  ,  ,  ,  ,  ,  ,  , or  ;

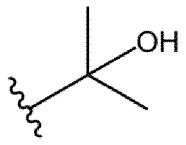
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

Further, in a preferred embodiment of the present invention residue R of a compound according to formula (I) denotes the structure according to formula (V) above and residue Q has the sas the structure according to formula (II), wherein

R^1 is selected from H, Alk1, Alk2, or 

;

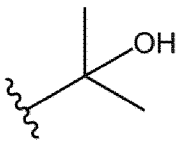
R^2, R^3, R^4, R^7, R^8 is each independently selected from H or Hal;

R^{15} is O or NH;

R^{16} is -CH_3 or Alk1; and

Y is CH or CHal. In some embodiments, the $SOR^{15}R^{16}$ group of formula (V) is ortho to the linkage of formula (I). In some embodiments, R^3 and R^4 are H. In some embodiments, X^1 is CH.

Further, in a preferred embodiment of the present invention residue R of a compound according to formula (I) denotes the structure according to formula (V) above and residue Q has the sas the structure according to formula (II), wherein

R^1 is selected from Alk1 or 

;

R^2, R^3, R^4, R^7, R^8 is each independently selected from H or Hal;

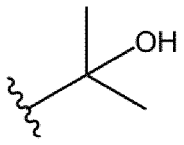
R^{15} is NH;

R^{16} is -CH_3 or Alk1;

X^1 is CH; and

Y is CH. In some embodiments, the $SOR^{15}R^{16}$ group of formula V is ortho to the linkage of formula I. In some embodiments, R^3 and R^4 are H. In some embodiments, X^1 is CH.

Further, in a preferred embodiment of the present invention residue R of a compound according to formula (I) denotes the structure according to formula (V) above and residue Q has the sas the structure according to formula (II), wherein

R^1 is 

;

R^{15} is NH;

R^{16} is $-CH_3$;

X^1 is CH; and

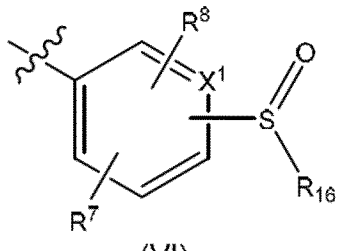
Y is CH. In some embodiments, the $SOR^{15}R^{16}$ group of formula V is ortho to the linkage of formula I. In some embodiments, R^3 and R^4 are H. In some embodiments, X^1 is CH.

In a very specific embodiment, the compound of the present invention is selected from:

D203	(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ6-sulfanone
D209	(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D210	(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone

.

In a specific embodiment of the present invention residue R of a compound according to formula (I) denotes a structure according to formula (VI)



(VI)

;

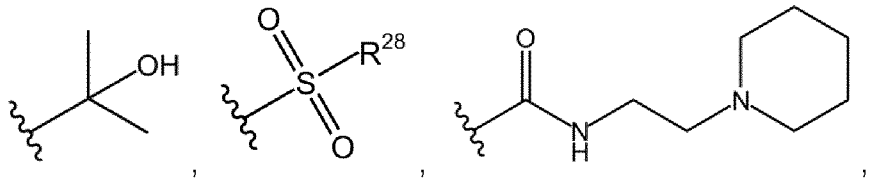
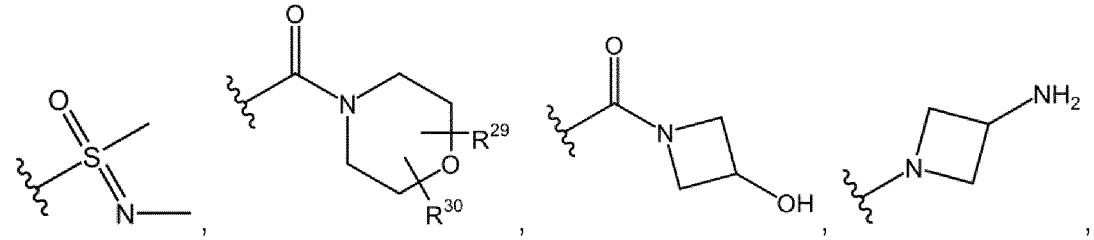
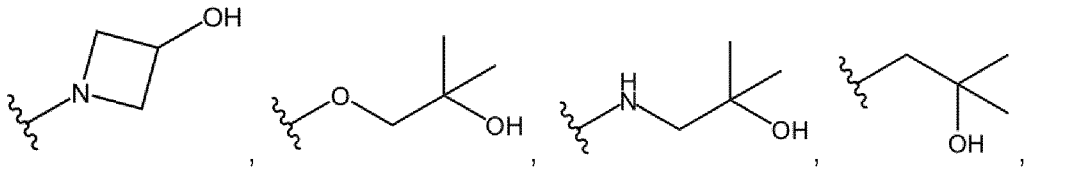
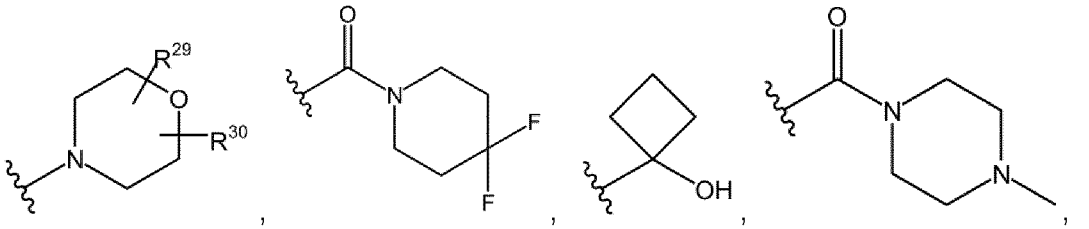
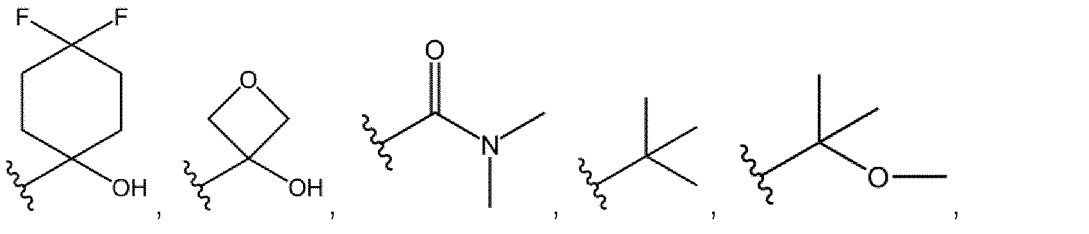
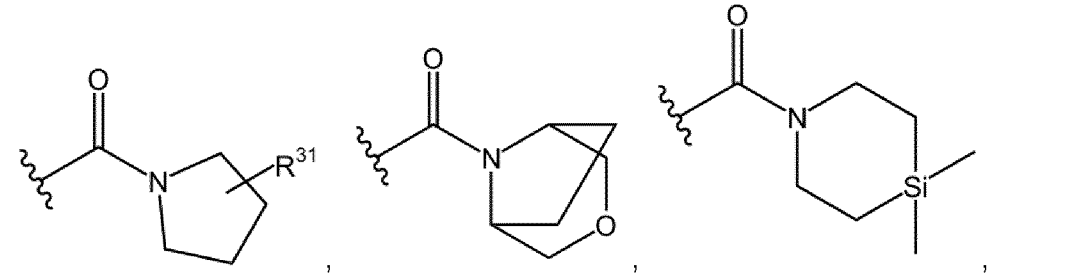
wherein

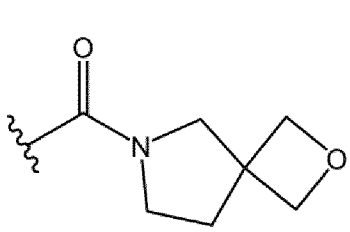
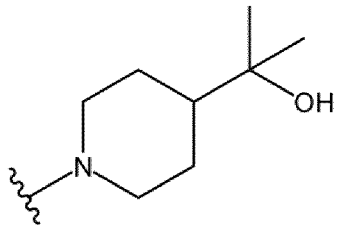
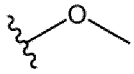
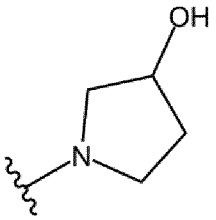
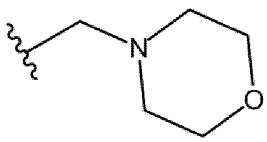
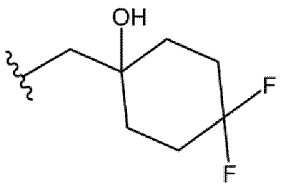
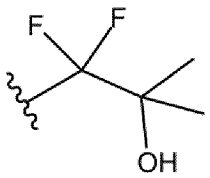
R^7, R^8 is each independently selected from H, Hal, or $CHal_3$; and

R^{16} is CH_3 or $CHal_3$; and

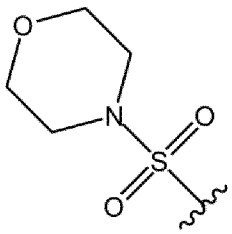
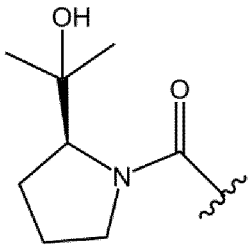
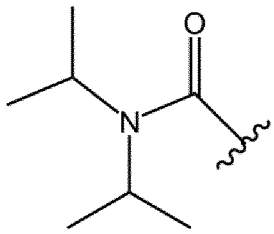
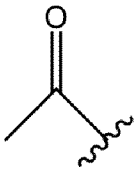
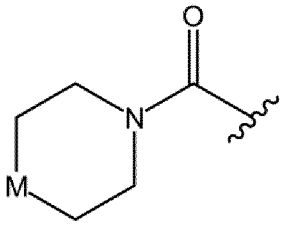
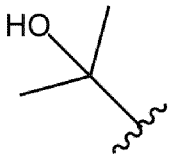
X^1 is CR^7 or N.

In this specific embodiment of the present invention residue Q of the compound denotes a structure according to formula (II) above, wherein

R^1 is H, Hal,  ,  ,  ,  ,  ,  ,

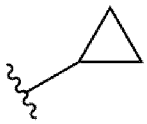
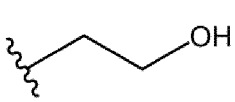
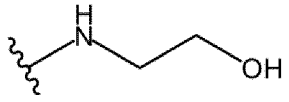
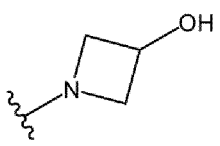
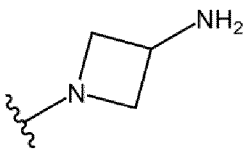
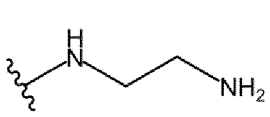
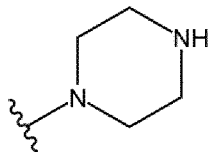








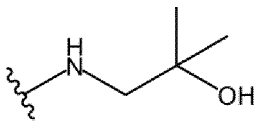
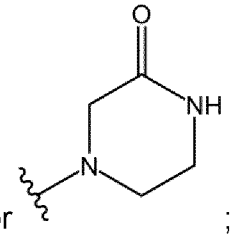
R^3 is H, Hal,

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,

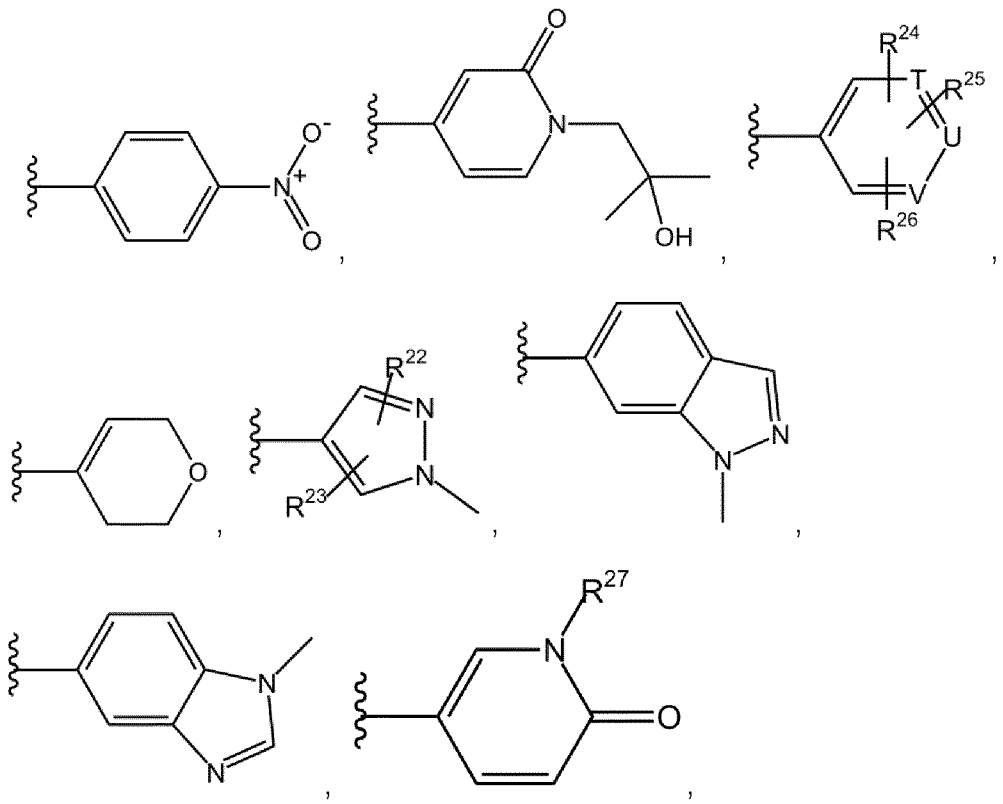
R^{29}, R^{30} is each independently selected from H or CH_3;

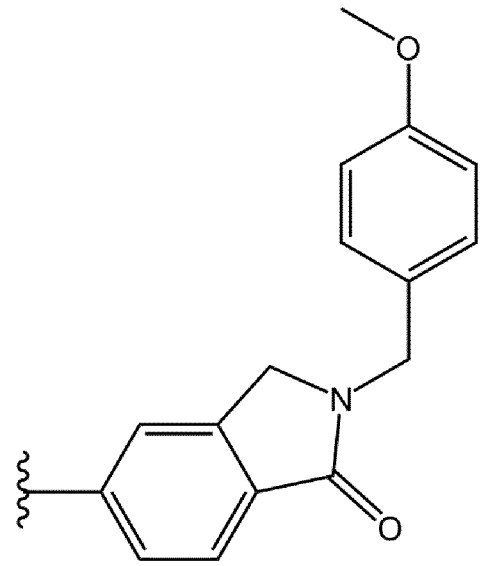
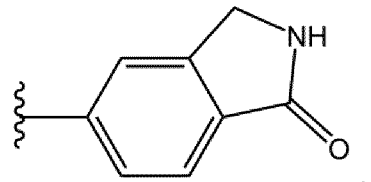
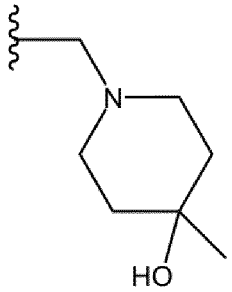
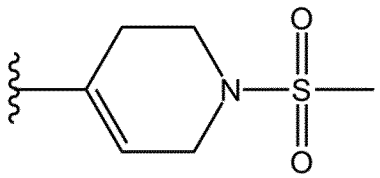
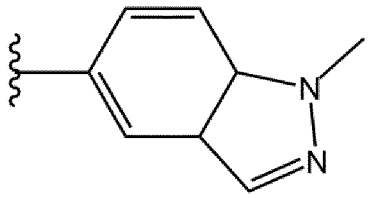
R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

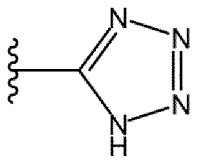
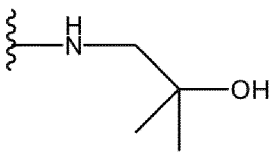
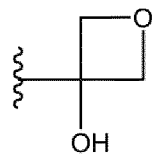
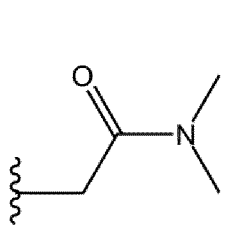
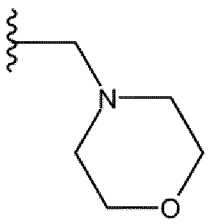
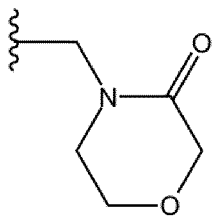
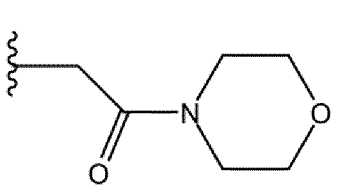
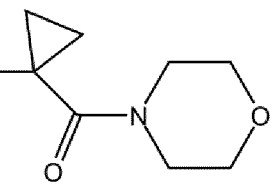
In a specific embodiment of the present invention residue R of a compound according to formula (I) denotes a structure selected from the following:



R^{22}, R^{23} is each independently selected from H or CH_3;

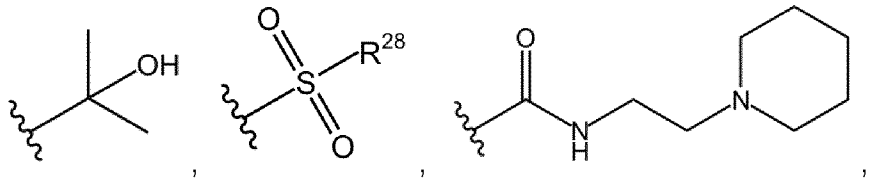
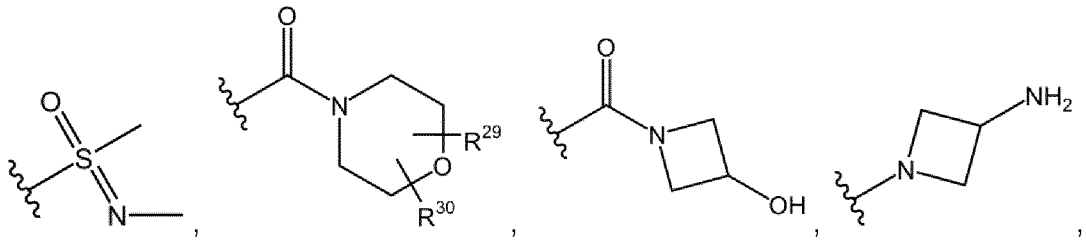
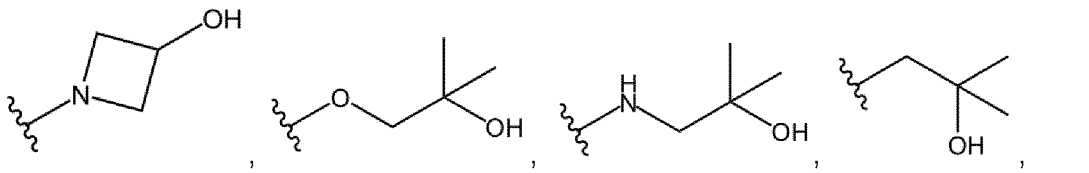
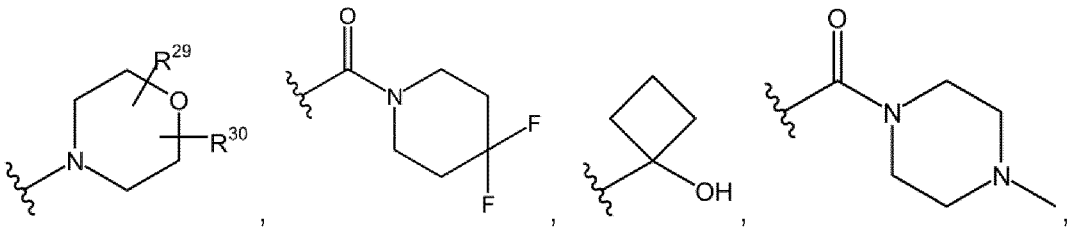
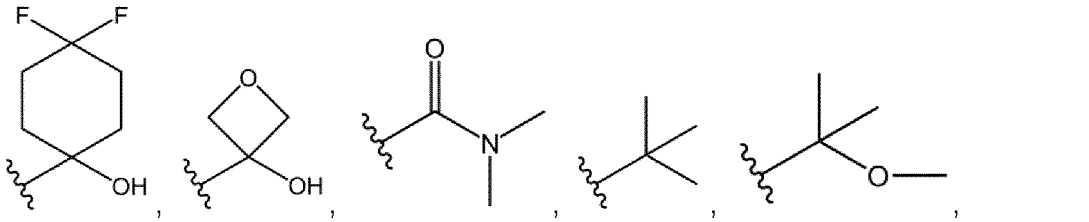
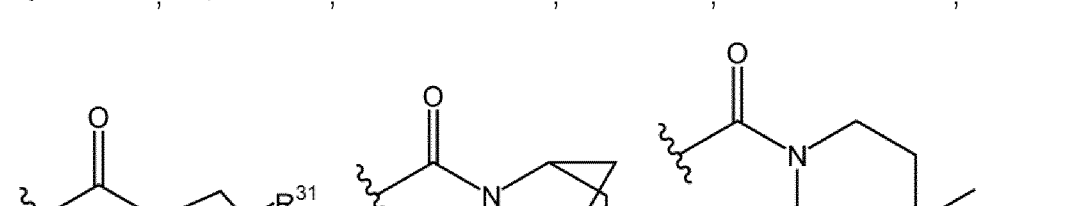
R^{24}, R^{25}, R^{26} is each independently selected from H, -OCH_3, -NH_2, -$CH_2C((CH_3)_2OH)$, -$C((CH_3)_2OH)$, -$PO(CH_3)_2$, -$C(CH_3)_2OH$, -SCH_3, -$CH(CH_3OH)$,

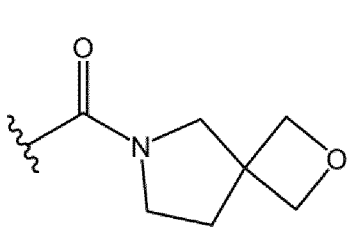
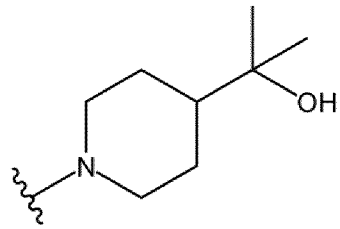
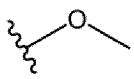
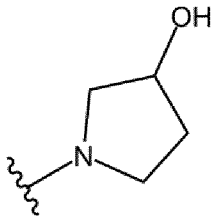
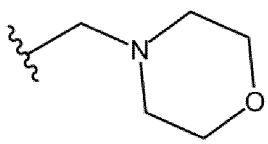
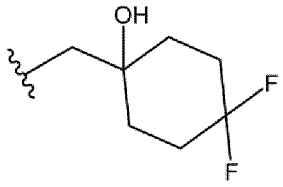
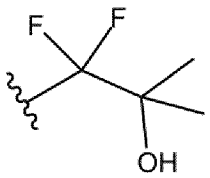









R^{27} is $-CH_3$ or $-C((CH_3)_2OH)$; and

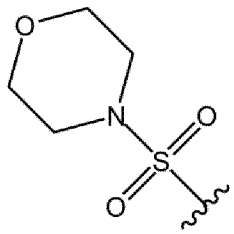
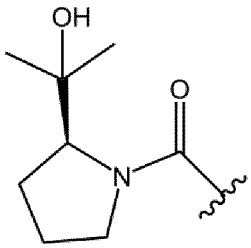
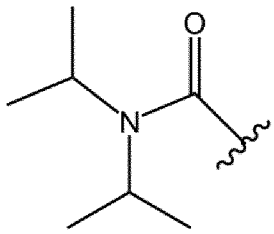
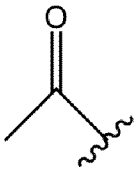
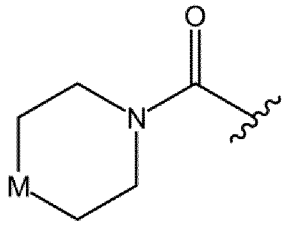
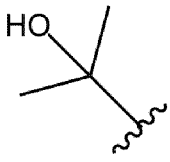
T, U, V is each independently selected from N or CR^{24}.

In this specific embodiment of the present invention residue Q of the compound denotes a structure according to formula (II) above, wherein

R^1 is H, Hal,  ,  ,  ,  ,  , 

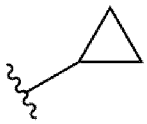
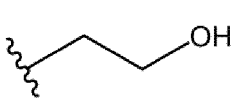
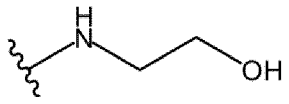
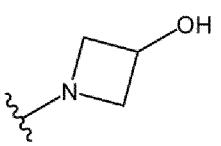
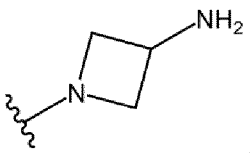
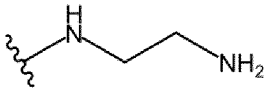
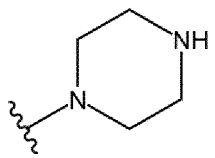
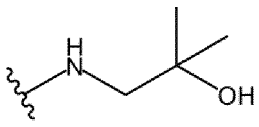
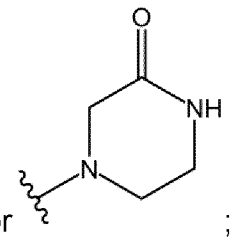








R^3 is H, Hal,

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,

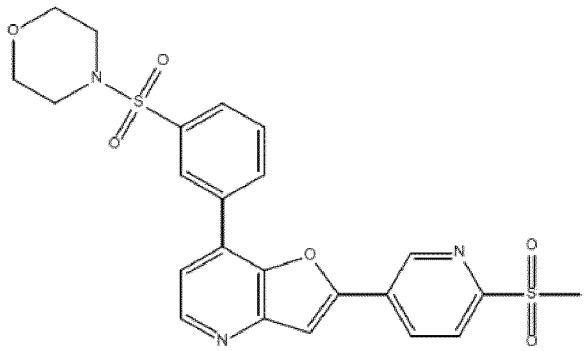
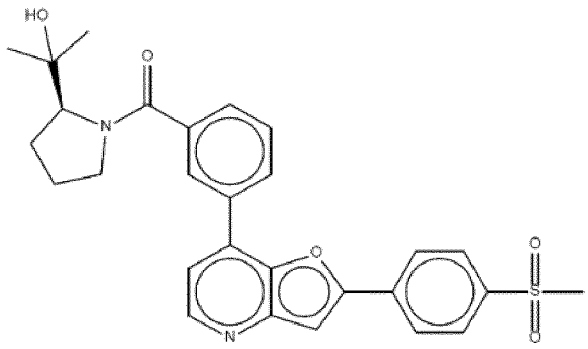
R^{29}, R^{30} is each independently selected from H or CH_3;

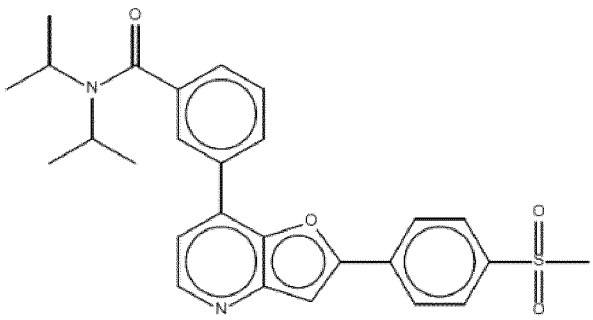
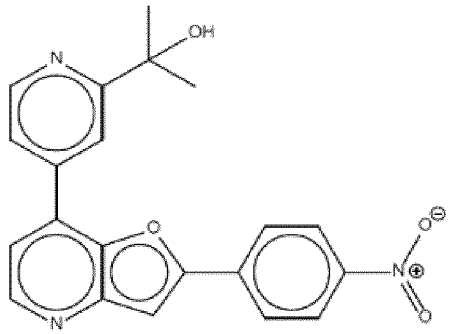
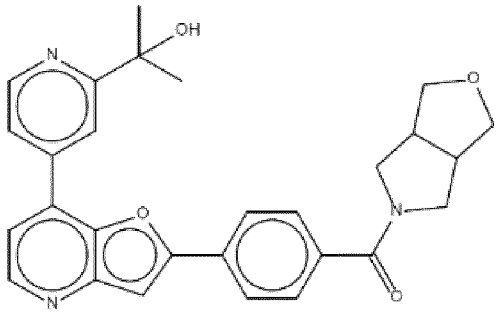
R^{31} is H or $CHal_3$;

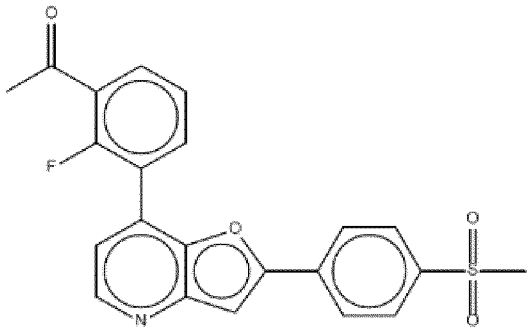
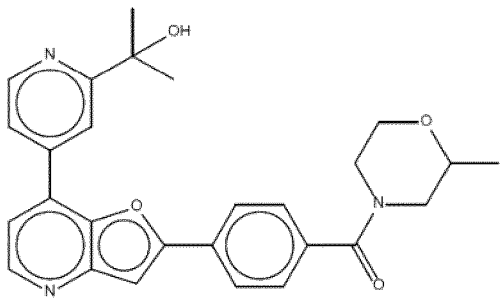
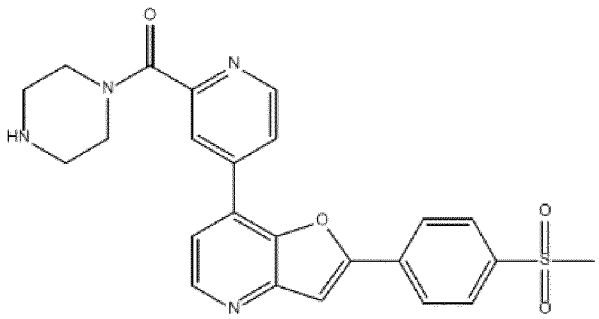
M is NH or O; and

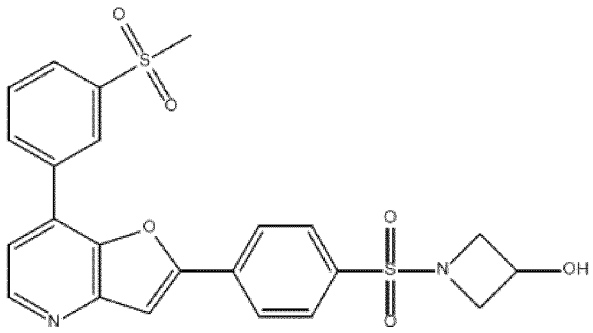
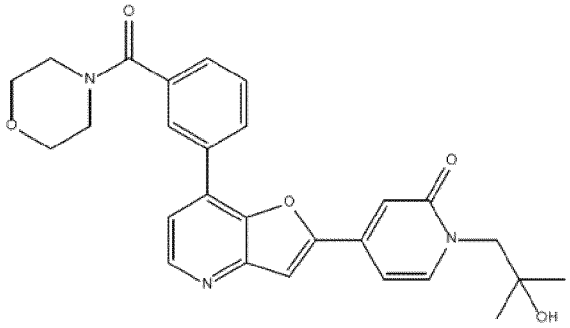
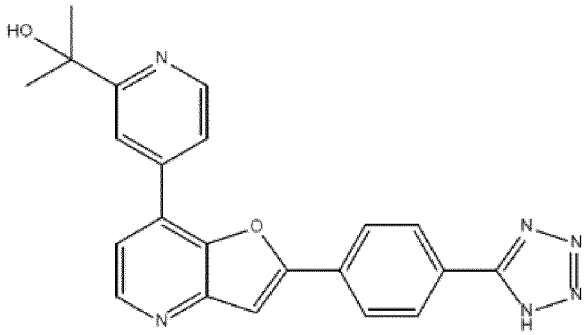
Y is N, CH, or CHal.

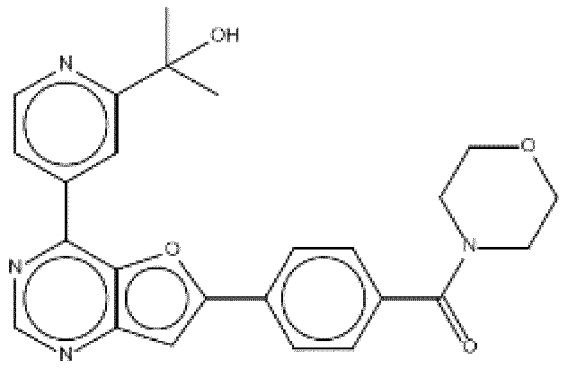
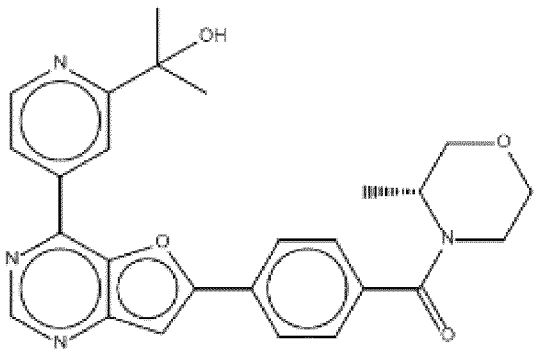
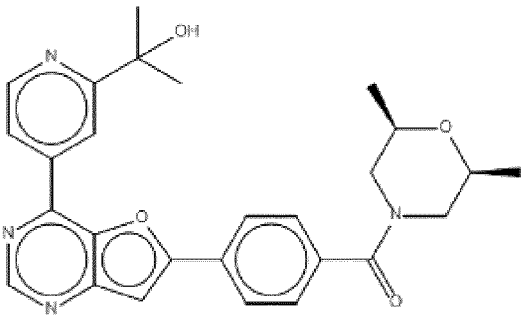
A very specific embodiment concerns a compound according to the present invention selected from following group:

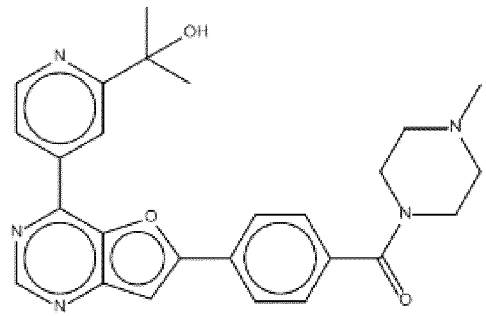
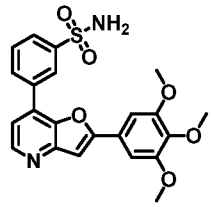
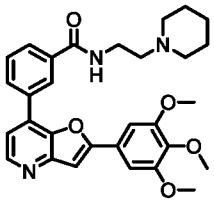
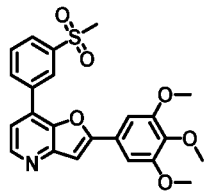
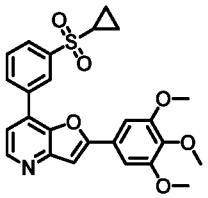
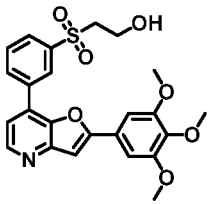
Comp.	Structure	Name
C9		2-(6-Methanesulfonyl-pyridin-3-yl)-7-[3-(morpholine-4-sulfonyl)-phenyl]-furo[3,2-b]pyridine
C28		[(S)-2-(1-Hydroxy-1-methyl-ethyl)-pyrrolidin-1-yl]-{3-[2-(4-methanesulfonyl-phenyl)-furo[3,2-b]pyridin-7-yl]-phenyl}-methanone

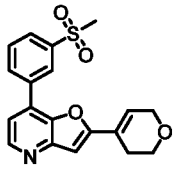
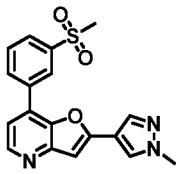
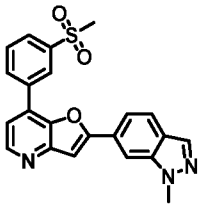
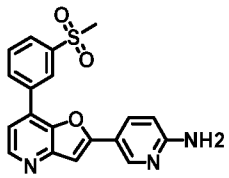
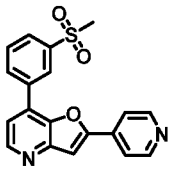
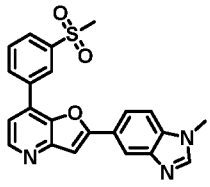
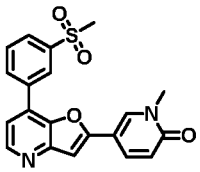
C29		N,N-Diisopropyl-3-[2-(4-methanesulfonyl-phenyl)-furo[3,2-b]pyridin-7-yl]-benzamide
C43		2-{4-[2-(4-nitrophenyl)furo[3,2-b]pyridin-7-yl]pyridin-2-yl}propan-2-ol
C45		2-{4-[2-(4-{hexahydro-1H-furo[3,4-c]pyrrole-5-carbonyl}phenyl)furo[3,2-b]pyridin-7-yl]pyridin-2-yl}propan-2-ol

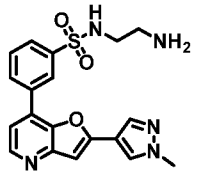
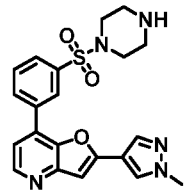
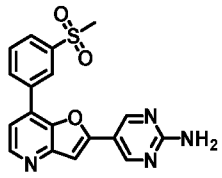
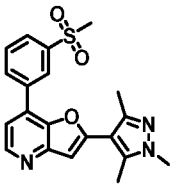
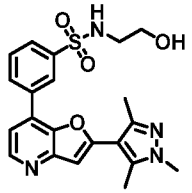
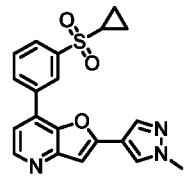
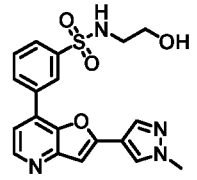
C46		1-{2-fluoro-3-[2-(4-methanesulfonylphenyl)furo[3,2-b]pyridin-7-yl]phenyl}ethan-1-one
C50		2-(4-{2-[4-(2-methylmorpholine-4-carbonyl)phenyl]furo[3,2-b]pyridin-7-yl}pyridin-2-yl)propan-2-ol
C56		1-{4-[2-(4-methanesulfonylphenyl)furo[3,2-b]pyridin-7-yl]pyridine-2-carbonyl}piperazine

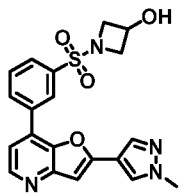
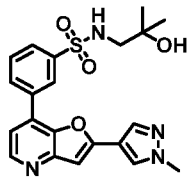
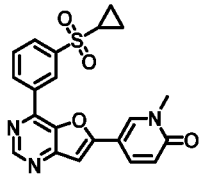
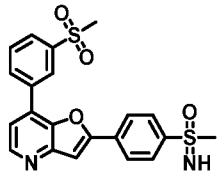
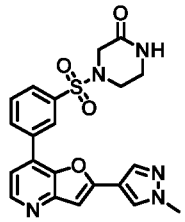
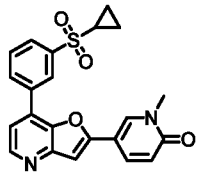
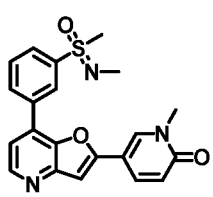
C58		1-((4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)sulfonyl)azetidin-3-ol
C63		1-(2-Hydroxy-2-methyl-propyl)-4-{7-[3-(morpholine-4-carbonyl)-phenyl]-furo[3,2-b]pyridin-2-yl}-1H-pyridin-2-one
C66		2-(4-(2-(4-(1H-tetrazol-5-yl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol

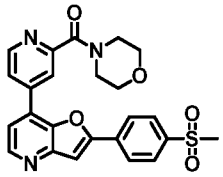
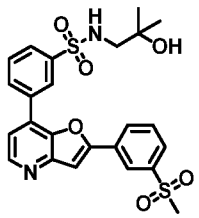
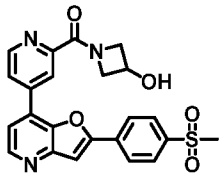
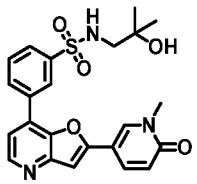
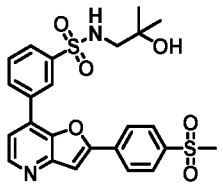
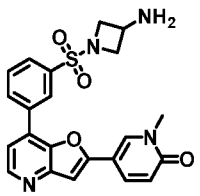
C74		(4-{4-[2-(1-Hydroxy-1-methyl-ethyl)-pyridin-4-yl]-furo[3,2-d]pyrimidin-6-yl}-phenyl)-morpholin-4-yl-methanone
C75		(4-{4-[2-(1-Hydroxy-1-methyl-ethyl)-pyridin-4-yl]-furo[3,2-d]pyrimidin-6-yl}-phenyl)-((R)-3-methyl-morpholin-4-yl)-methanone
C76		2-[4-(6-{4-[(2R,6S)-2,6-dimethylmorpholine-4-carbonyl]phenyl}furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl]propan-2-ol

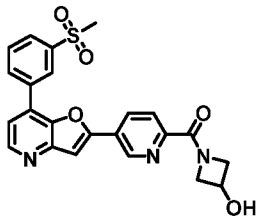
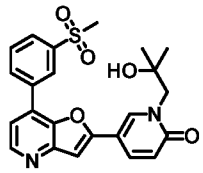
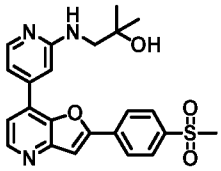
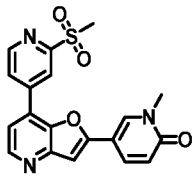
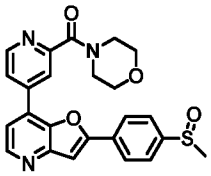
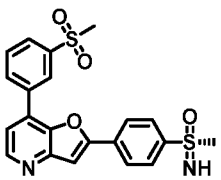
C77		2-(4-{6-[4-(4-methylpiperazine-1-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}pyridin-2-yl)propan-2-ol
D1		3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D2		N-(2-(piperidin-1-yl)ethyl)-3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzamide
D3		7-(3-(methylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine
D4		7-(3-(cyclopropylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine
D5		2-((3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)ethan-1-ol

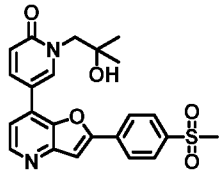
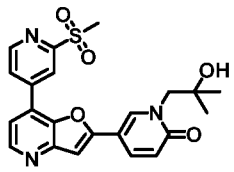
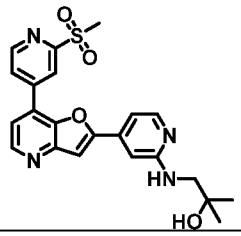
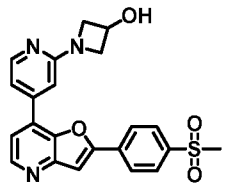
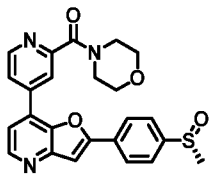
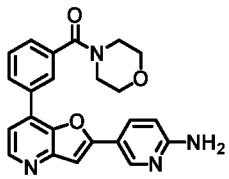
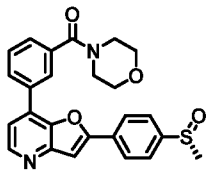
D6		2-(3,6-dihydro-2H-pyran-4-yl)-7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridine
D7		2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridine
D8		2-(1-methyl-1H-indazol-6-yl)-7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridine
D9		5-(7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridin-2-yl)pyridin-2-amine
D10		7-(3-(methylsulfonyl)phenyl) -2-(pyridin-4-yl)furo[3,2-b]pyridine
D11		2-(1-methyl-1H-benzo[d]imidazol-5-yl)-7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridine
D12		1-methyl-5-(7-(3-(methylsulfonyl)phenyl) furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one

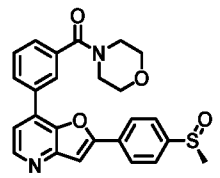
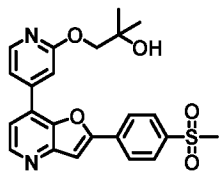
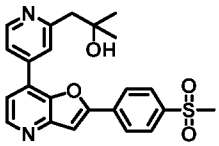
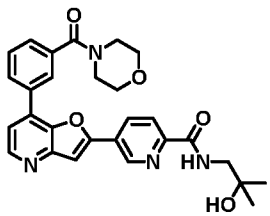
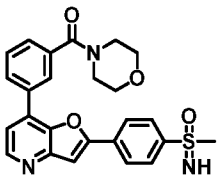
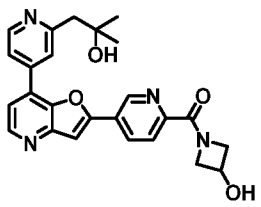
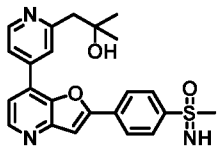
D13		N-(2-aminoethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D14		2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(piperazin-1-ylsulfonyl)phenyl)furo[3,2-b]pyridine
D15		5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyrimidin-2-amine
D16		7-(3-(methylsulfonyl)phenyl)-2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine
D17		N-(2-hydroxyethyl)-3-(2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D18		7-(3-(cyclopropylsulfonyl)phenyl)-2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine
D19		N-(2-hydroxyethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide

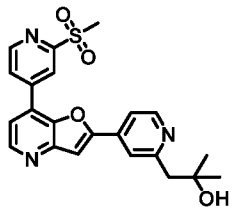
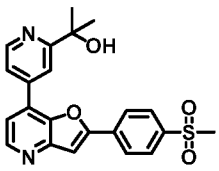
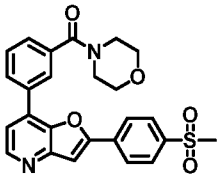
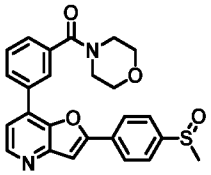
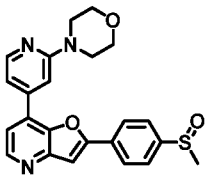
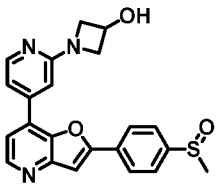
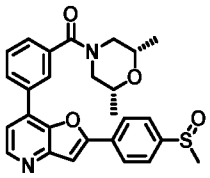
D20		1-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)azetidin-3-ol
D21		N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D22		5-(4-(3-(cyclopropylsulfonyl)phenyl)furo[3,2-d]pyrimidin-6-yl)-1-methylpyridin-2(1H)-one
D23		imino(methyl)(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone
D24		4-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)piperazin-2-one
D25		5-(7-(3-(cyclopropylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one
D26		5-(7-(3-(N,S-dimethylsulfonimidoyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one

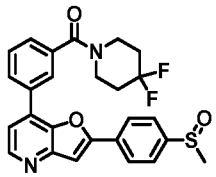
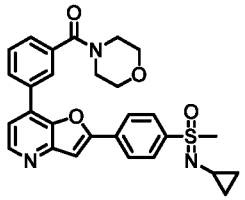
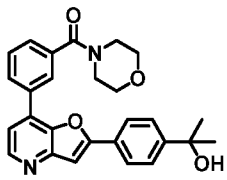
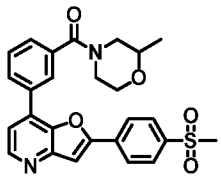
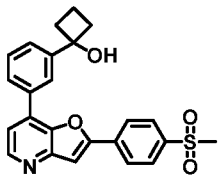
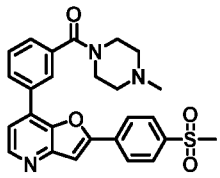
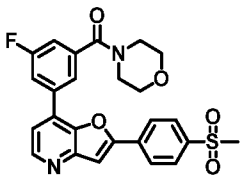
D27		(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D28		N-(2-hydroxy-2-methylpropyl)-3-(2-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D29		(3-hydroxyazetidin-1-yl)(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D30		N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D31		N-(2-hydroxy-2-methylpropyl)-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D32		5-(7-(3-((3-aminoazetidin-1-yl)sulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one

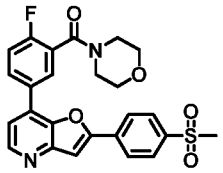
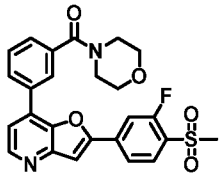
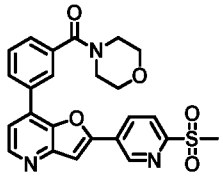
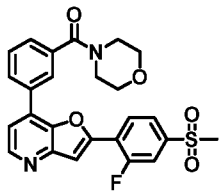
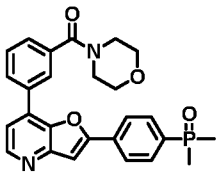
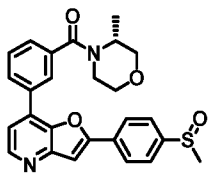
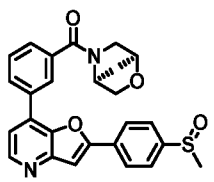
D33		(3-hydroxyazetidin-1-yl)(5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)methanone
D34		2-methyl-1-(5-(7-(3-(2-methyl-2l7-propa-1,2-dien-2-yl)phenyl)furo[3,2-b]pyridin-2-yl)-2-methylenepyridin-1(2H)-yl)propan-2-ol
D35		2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)amino)propan-2-ol
D36		1-methyl-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one
D37		(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D38		(R)-imino(methyl)(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone

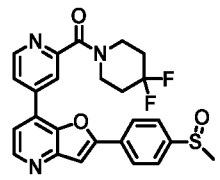
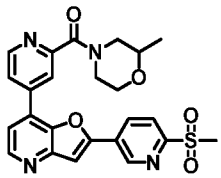
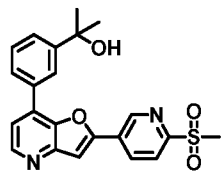
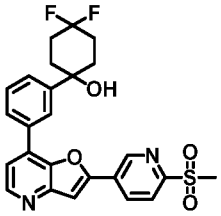
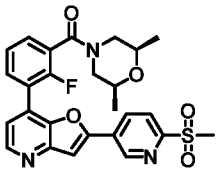
D39		1-(2-hydroxy-2-methylpropyl)-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2(1H)-one
D40		1-(2-hydroxy-2-methylpropyl)-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one
D41		2-methyl-1-((4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)amino)propan-2-ol
D42		1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol
D43		(R)-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D44		(3-(2-(6-aminopyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D45		(R)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone

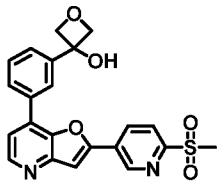
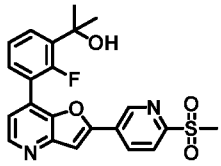
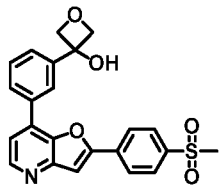
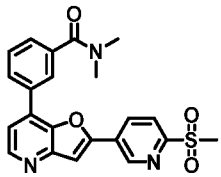
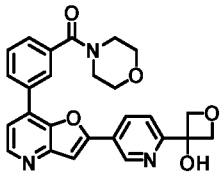
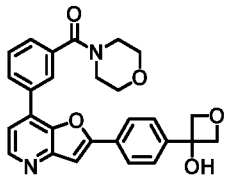
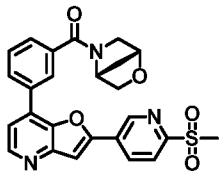
D46		(S)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D47		2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)oxy)propan-2-ol
D48		2-methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D49		N-(2-hydroxy-2-methylpropyl)-5-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)picolinamide
D50		imino(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone
D51		(5-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)(3-hydroxyazetidin-1-yl)methanone
D52		(4-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone

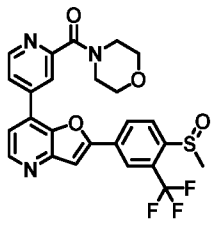
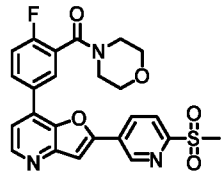
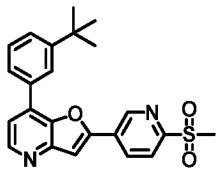
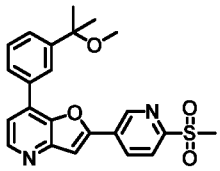
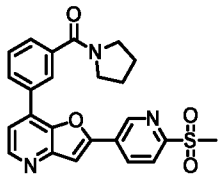
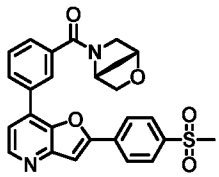
D53		2-methyl-1-(4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)propan-2-ol
D54		2-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D55		(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D56		(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D57		2-(4-(methylsulfinyl)phenyl)-7-(2-morpholinopyridin-4-yl)furo[3,2-b]pyridine
D58		1-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol
D59		((2R,6S)-2,6-dimethylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

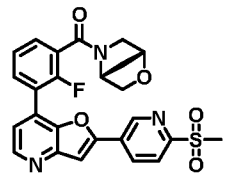
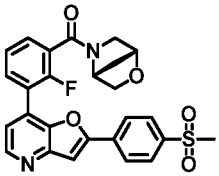
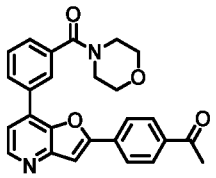
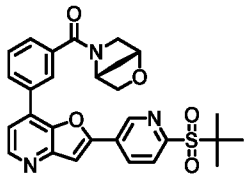
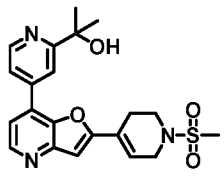
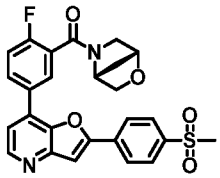
D60		(4,4-difluoropiperidin-1-yl)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D61		(cyclopropylimino)(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ^6-sulfanone
D62		(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D63		(2-methylmorpholino)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D64		1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)cyclobutan-1-ol
D65		(4-methylpiperazin-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D66		(3-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone

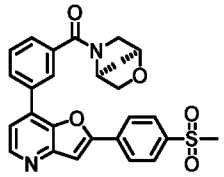
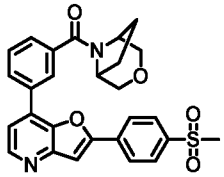
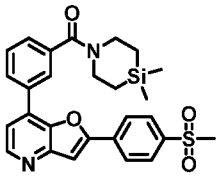
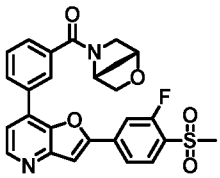
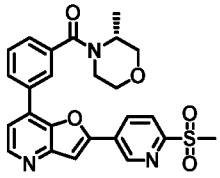
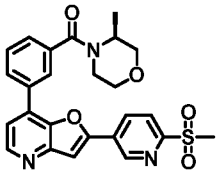
D67		(2-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D68		(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D69		(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D70		(3-(2-(2-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D71		(3-(2-(4-(dimethylphosphoryl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D72		((R)-3-methylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D73		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfinyl)phenyl)f

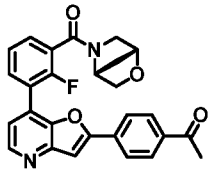
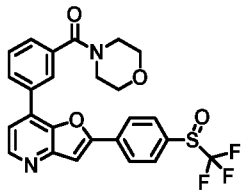
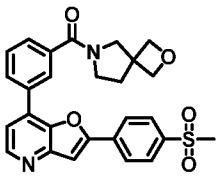
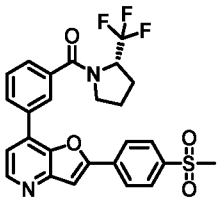
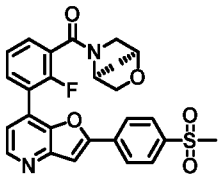
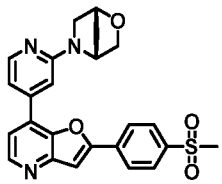
		uro[3,2-b]pyridin-7-yl)phenyl)methanone
D74		(4,4-difluoropiperidin-1-yl)(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D75		(2-methylmorpholino)(4-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D76		2-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D77		4,4-difluoro-1-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)cyclohexan-1-ol
D78		((2S,6R)-2,6-dimethylmorpholino)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

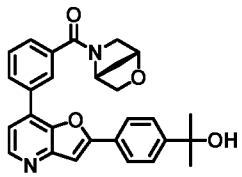
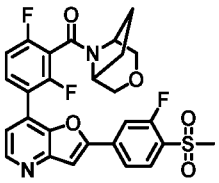
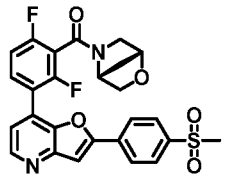
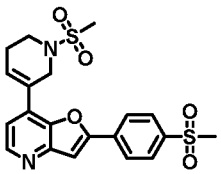
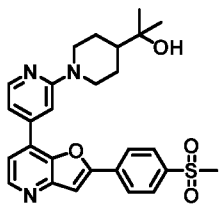
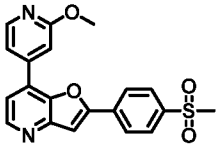
D79		3-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol
D80		2-(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D81		3-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol
D82		N,N-dimethyl-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)benzamide
D83		(3-(2-(6-(3-hydroxyoxetan-3-yl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D84		(3-(2-(4-(3-hydroxyoxetan-3-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D85		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

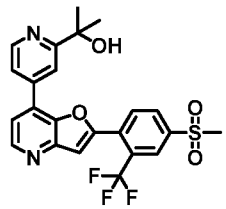
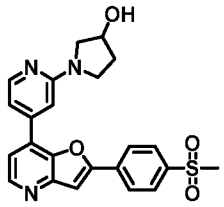
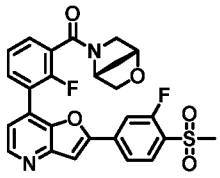
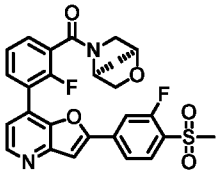
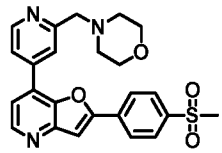
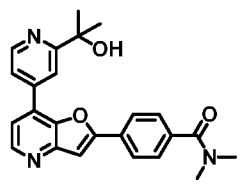
D86		(4-(2-(4-(methylsulfinyl)-3-(trifluoromethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D87		(2-fluoro-5-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D88		7-(3-(tert-butyl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine
D89		7-(3-(2-methoxypropan-2-yl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine
D90		(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(pyrrolidin-1-yl)methanone
D91		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

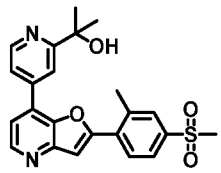
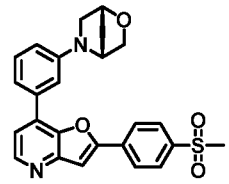
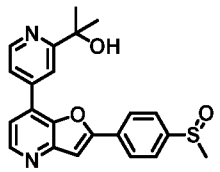
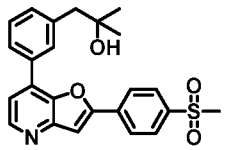
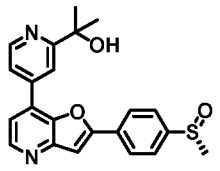
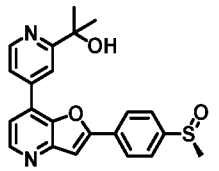
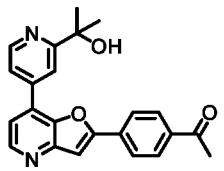
D92		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D93		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D94		1-(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one
D95		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(tert-butylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D96		2-(4-(2-(1-(methylsulfonyl)-1,2,3,6-tetrahydropyridin-4-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D97		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

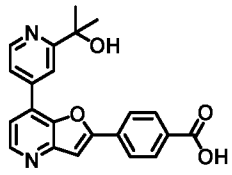
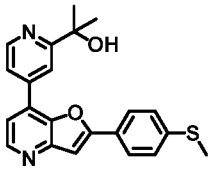
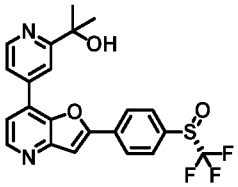
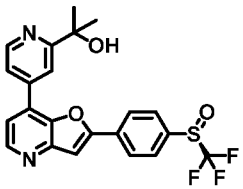
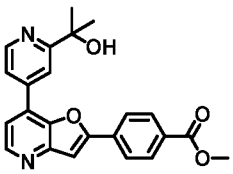
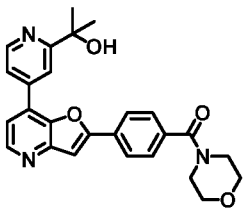
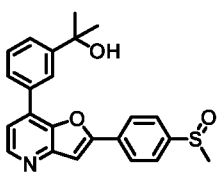
D98		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D99		(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D100		(4,4-dimethyl-1,4-azasilinan-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D101		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D102		(R)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D103		(S)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

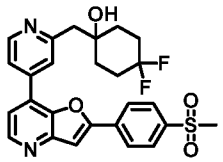
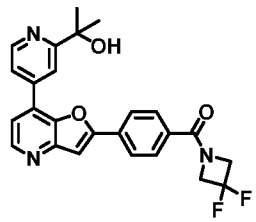
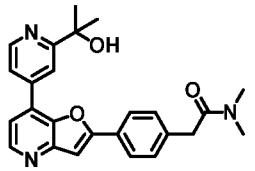
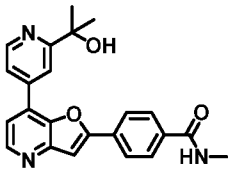
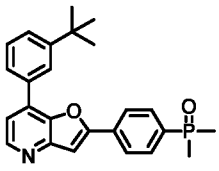
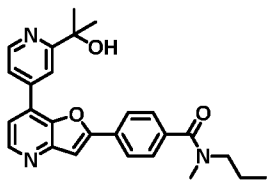
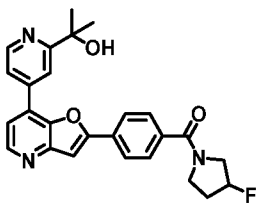
D104		1-(4-(7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-carbonyl)-2-fluorophenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one
D105		morpholino(3-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D106		(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-oxa-6-azaspiro[3.4]octan-6-yl)methanone
D107		(S)-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone
D108		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D109		7-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)pyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine

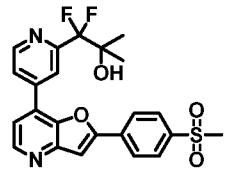
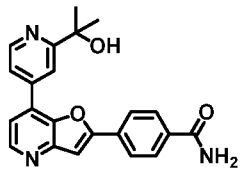
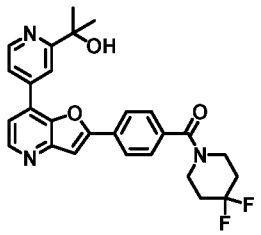
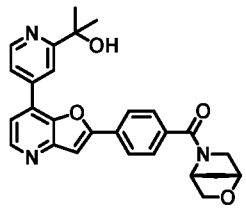
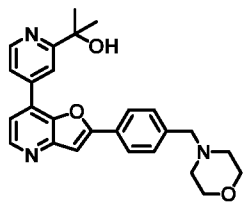
D110		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D111		(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(2,6-difluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D112		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D113		7-(1-(methylsulfonyl)-1,2,5,6-tetrahydropyridin-3-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D114		2-(1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)piperidin-4-yl)propan-2-ol
D115		7-(2-methoxypyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine

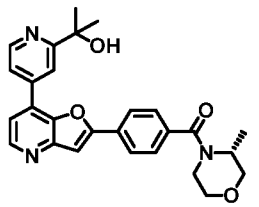
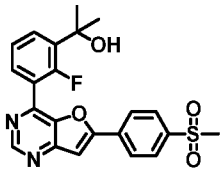
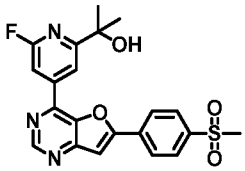
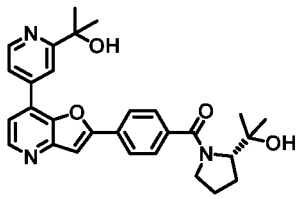
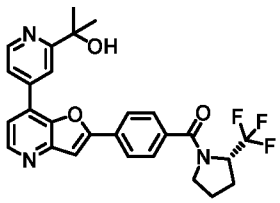
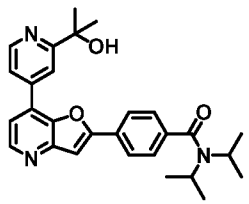
D116		2-(4-(2-(4-(methylsulfonyl)-2-(trifluoromethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D117		1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)pyrrolidin-3-ol
D118		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D119		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D120		2-(4-(methylsulfonyl)phenyl)-7-(2-(morpholinomethyl)pyridin-4-yl)furo[3,2-b]pyridine
D121		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-dimethylbenzamide

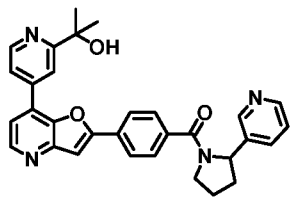
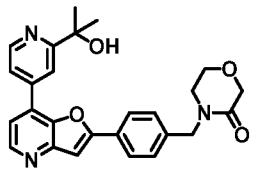
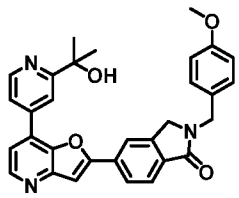
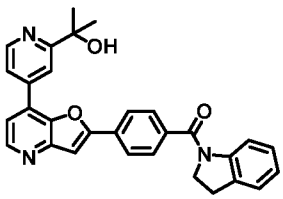
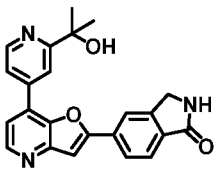
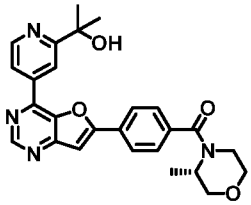
D122		2-(4-(2-(2-methyl-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D123		7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)phenyl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D124		2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D125		2-methyl-1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D126		(R)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D127		(S)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D128		1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one

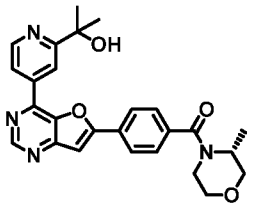
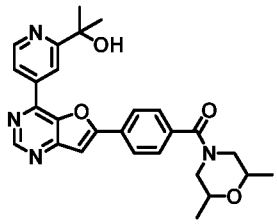
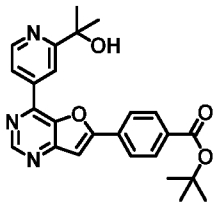
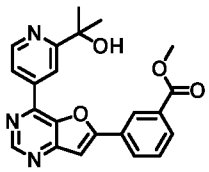
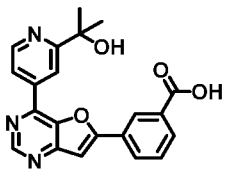
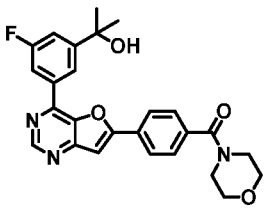
D129		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoic acid
D130		2-(4-(2-(4-(methylthio)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D131		(S)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D132		(R)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D133		methyl 4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoate
D134		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D135		2-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol

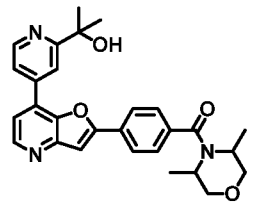
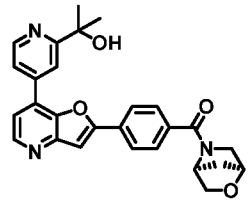
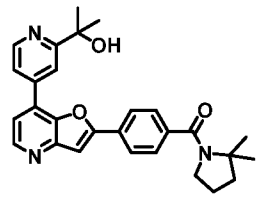
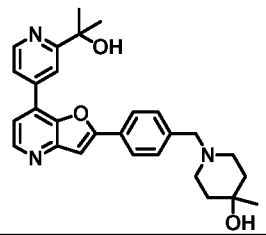
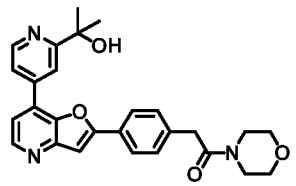
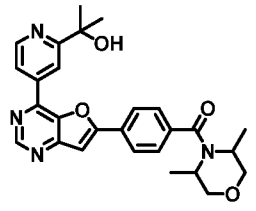
D136		4,4-difluoro-1-((4-(2-(4-(methylsulfonyl)phenyl) furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methyl)cyclohexan-1-ol
D137		(3,3-difluoroazetidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D138		2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-N,N-dimethylacetamide
D139		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methylbenzamide
D140		(4-(7-(3-(tert-butyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)dimethylphosphine oxide
D141		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-propylbenzamide
D142		(3-fluoropyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-

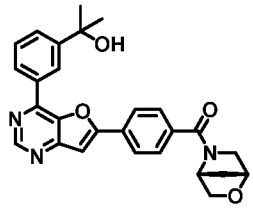
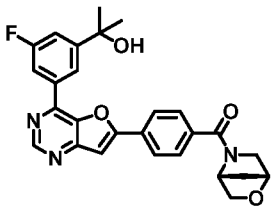
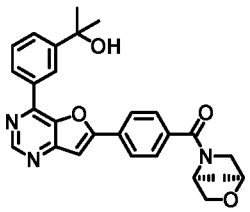
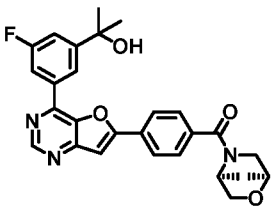
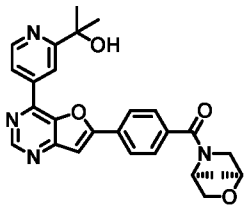
		b]pyridin-2-yl)phenyl)methanone
D143		1,1-difluoro-2-methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D144		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide
D145		(4,4-difluoropiperidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D146		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D147		2-(4-(2-(4-(morpholinomethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol

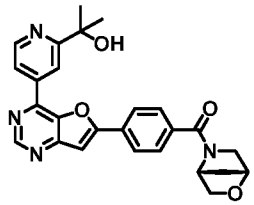
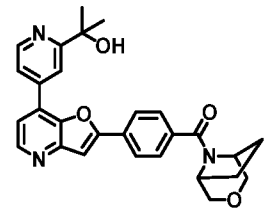
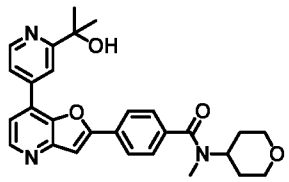
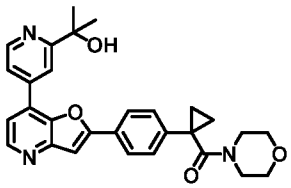
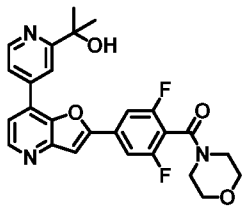
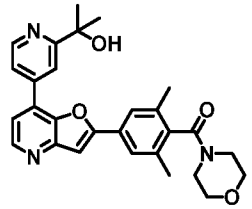
D148		(R)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(3-methylmorpholino)methanone
D149		2-(2-fluoro-3-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)phenyl)propan-2-ol
D150		2-(6-fluoro-4-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl)propan-2-ol
D151		(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)methanone
D152		(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone
D153		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-diisopropylbenzamide

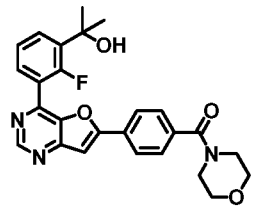
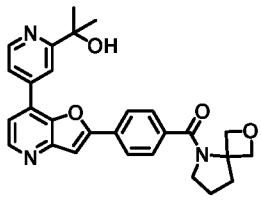
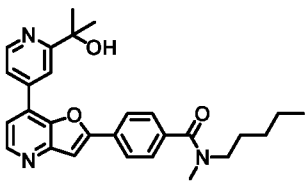
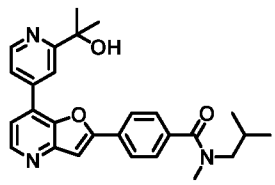
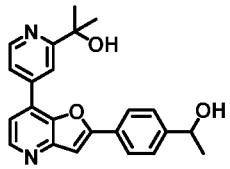
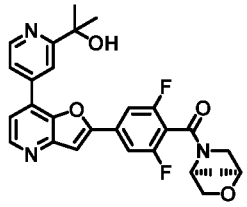
D154		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(pyridin-3-yl)pyrrolidin-1-yl)methanone
D155		4-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)morpholin-3-one
D156		5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2-(4-methoxybenzyl)isoindolin-1-one
D157		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(indolin-1-yl)methanone
D158		5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)isoindolin-1-one
D159		(S)-(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone

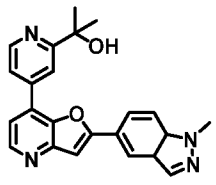
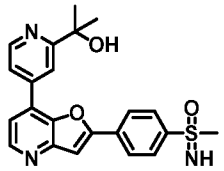
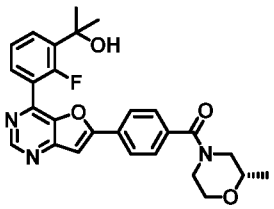
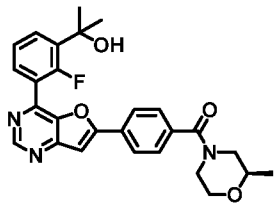
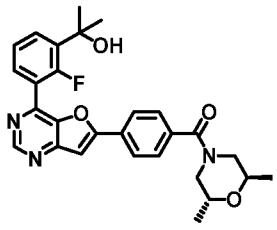
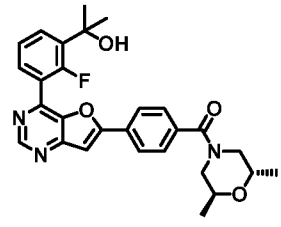
D160		(R)-(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D161		(2,6-dimethylmorpholino)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D162		tert-butyl 4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoate
D163		methyl 3-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoate
D164		3-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoic acid
D165		(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone

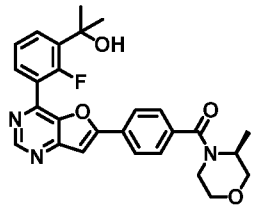
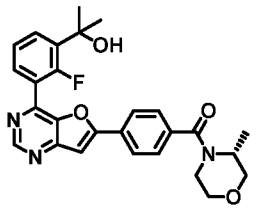
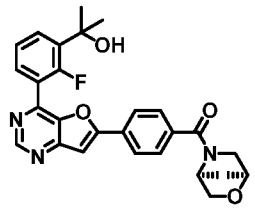
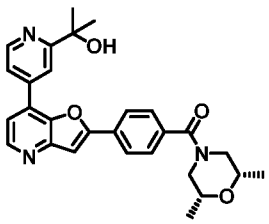
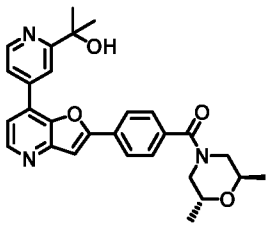
D166		(3,5-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D167		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D168		(2,2-dimethylpyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D169		1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)-4-methylpiperidin-4-ol
D170		2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-1-morpholinoethan-1-one
D171		(3,5-dimethylmorpholino)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone

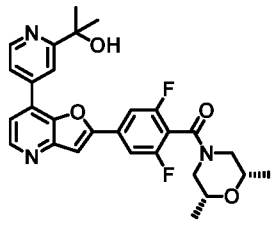
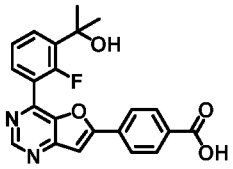
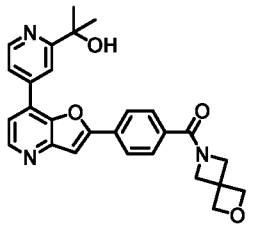
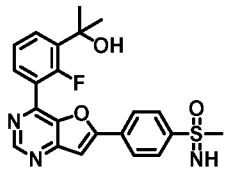
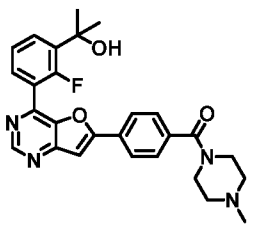
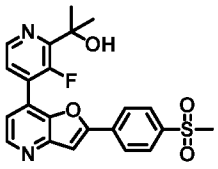
D172		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D173		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D174		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D175		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D176		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone

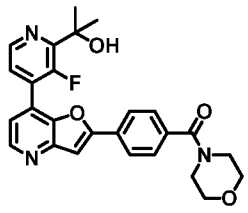
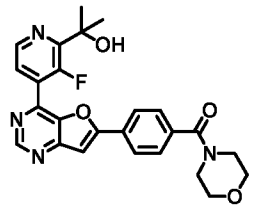
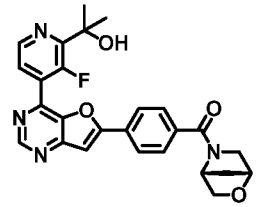
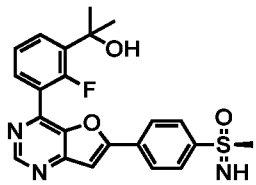
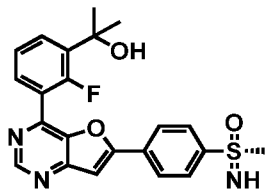
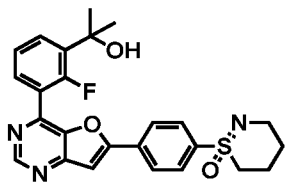
D177		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D178		(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D179		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)benzamide
D180		(1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)(morpholino)methanone
D181		(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D182		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2,6-dimethylphenyl)(morpholino)methanone

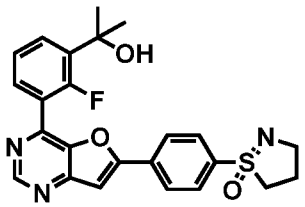
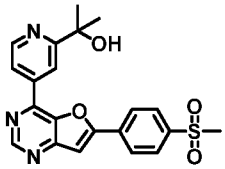
D183		(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone
D184		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-oxa-5-azaspiro[3.4]octan-5-yl)methanone
D185		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-pentylbenzamide
D186		4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-isobutyl-N-methylbenzamide
D187		2-(4-(2-(4-(1-hydroxyethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D188		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone

D189		2-(4-(2-(1-methyl-3a,7a-dihydro-1H-indazol-5-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D190		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone
D191		(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(2-methylmorpholino)methanone
D192		(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(2-methylmorpholino)methanone
D193		((2R,6R)-2,6-dimethylmorpholino)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D194		((2S,6S)-2,6-dimethylmorpholino)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone

D195		(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D196		(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D197		((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D198		((2R,6S)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D199		((2R,6R)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone

D200		(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)((2R,6S)-2,6-dimethylmorpholino)methanone
D201		4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)benzoic acid
D202		(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone
D203		(4-(4-[2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ6-sulfanone
D204		(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(4-methylpiperazin-1-yl)methanone
D205		2-(3-fluoro-4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol

D206		(4-(7-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D207		(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone
D208		((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D209		(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D210		(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D211		1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide

D212		1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-4,5-dihydro-3H-isothiazole 1-oxide
D213		2-(4-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl)propan-2-ol;

Surprisingly, *in vitro* studies show that small amounts of compounds according to the present invention are potent PI4K inhibitors.

These versatile PI4K inhibitory properties make the compounds according to the present invention ideal candidates for treatment and/or prevention of PI4K-related disorders such as, but not limited to, protozoan infections and viral infections.

Surprisingly, small amounts of the compounds according to the present invention are sufficient to decrease Plasmodium viability and reduce growth. Additional data suggests a high inhibitory potential of said compounds on Plasmodium PI4K activity. The present invention, therefore, also relates to the use of the compounds according to the invention for treatment and/or prevention of protozoan infections such as malaria.

The compounds according to the present invention inhibit PI4K of protozoans such as, but not limited to, *Plasmodium ssp*, *Toxoplasma ssp*, *Babesia ssp*, *Cryptosporidium ssp.*

Human PI4K is a well-known druggable-target for the treatment and prevention of virus infections. Surprisingly, the disclosed compounds were additionally

found to inhibit human PI4KIIIβ, an important target for viruses such as but not limited to RNA viruses.

Therefore, in some embodiments of the present invention relates to the use of the compounds according to the invention for treatment and/or prevention of PI4K-related disorder selected from the list of protozoan infections and viral infections. In a preferred embodiment, said PI4K-related disorder is a protozoan infection, more preferably malaria.

Viral infections can be caused by viruses such as RNA or DNA viruses. In a preferred embodiment, the compounds according to the present invention are used for the treatment and/or prevention of virus infections caused by RNA viruses.

In a preferred embodiment said virus infection is caused by viruses selected from the families orthomyxoviridae, adenoviridae, paramyxoviridae, and coronaviridae. Virus of the orthomyxoviridae family include the influenza A virus, influenza B virus, influenza C virus, the infectious salmon anemia virus (isavirus), Thogoto Virus, and Dhori Virus. Members of the adenoviridae family include human adenovirus A, B, C, D, E, and F; bovine adenovirus A, B, and C; canine adenovirus; equine adenovirus A and B; murine adenovirus A; ovine adenovirus A and B; porcine adenovirus A, B, and C; and tree shrew adenovirus. Members of the paramyxoviridae family include bovine parainfluenza virus 3 (BPIV-3), human parainfluenza virus 1 (HPIV-1), human parainfluenza virus 3 (HPIV-3); sendai virus (murine parainfluenza virus 1); simian parainfluenza virus 10 (SPIV-10), bovine respiratory syncytial virus (BRSV), human respiratory syncytial virus (HRSV), pneumonia virus of mice (PVM), canine distemper virus (CDV), dolphin distemper virus (DMV), measles virus (MeV), Peste des petits ruminants virus (PPRV), phocine (seal) distemper virus (PDV), porpoise distemper virus, rinderpest virus (RPV), avian paramyxovirus 2 (APMV-2), avian paramyxovirus 3 (APMV-3), avian paramyxovirus 4 (APMV-4), avian paramyxovirus 5 (APMV-5), avian

paramyxovirus 6 (APMV-6), avian paramyxovirus 7 (APMV-7), avian paramyxovirus 8 (APMV-8), avian paramyxovirus 9 (APMV-9), human parainfluenza virus 2 (HPIV-2), human parainfluenza virus 4a (HPIV-4a), human parainfluenza virus 4b (HPIV-4-b), mumps virus, newcastle disease virus (avian paramyxovirus 1) (NDV; APMV-1), porcine rubulavirus, simian parainfluenza virus 5 (SV-5), and simian parainfluenza virus 41 (SV-41). Members of the coronaviridae family include infectious bronchitis virus, bovine coronavirus, canine coronviarus, feline coronavirus, human coronavirus, and SARS-coronavirus, SAR2-Coronavirus-2, MERS-CoV. In a more preferred embodiment, the compounds according to the present invention are used for treatment and/or prevention of SARS-CoV2.

INDUSTRIAL APPLICATION

COMPOSITIONS

The present invention further relates to pharmaceutical compositions for use in prevention and/or treatment of PI4K-related disorders comprising at least one compound according to formula (I) of the present invention.

In another particular embodiment, a pharmaceutical formulation is provided containing at least one derivative according to the present invention and a pharmaceutically acceptable carrier, diluent or excipient thereof.

In some embodiments the present invention further relates to pharmaceutical compositions for use in prevention and/or treatment of PI4K-related disorders, comprising at least one compound of formula (I) according to the present invention, wherein the PI4K-related disorders are selected from the list of protozoan infections and viral infections. In a preferred embodiment said protozoan infection is malaria. In another preferred embodiment, said viral infection is caused by an RNA virus.

In a preferred embodiment the present invention relates to pharmaceutical compositions for use in prevention and/or treatment of PI4K-related disorders selected from the list of protozoan and viral infections. In some embodiments said PI4K-related disorder is malaria. In some embodiments said PI4K-related disorder is a viral infection.

COMBINATION

According to the present invention, a compound according to formula (I) or a pharmaceutical composition thereof can be administered alone or in combination with a further active ingredient (a co-agent) such as a pharmaceutically active compound useful in the treatment and/or prevention of PI4K-related disorders.

Therefore, the present invention further also refers to a pharmaceutical composition comprising at least one compound of formula (I) and at least one further active ingredient (co-agent), which is different from formula (I). In certain embodiments said co-agent is an antimalarial agent, which is different from formula (I). Preferably, said further active ingredient (the antimalarial co-agent) is selected from: Pyronaridine (free base or tetraphosphate salt), quinacrine, chloroquine, ferroquine, primaquine, tafenoquine, doxycycline, atovaquone, proguanil, cycloguanil, cabamiquine (free base or succinate salt), cipargamin, ganaplacide, sulfadoxine, pyrimethamine, artemisinin, dihydrodroartemisinin, artesunic acid, artesunate, arterolane, artefenomel, lumefantrine, DSM 265 (CAS Number: 1282041-94-4), (OC-6-21)-[4-[[2-(1,1-Difluoroethyl)-5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-7-yl]amino]phenyl]pentafluorosulfur, SAR121 (CAS Number : 2260904-47-8), Benzamide, 5-[2-[3-[[(aminoiminomethyl)amino]carbonyl]-5-(trifluoromethyl)phenyl]ethynyl]-N-2-pyridinyl-2-(trifluoromethyl), INE963 (CAS number 2640567-43-5), 4-Piperidinol, 4-(aminomethyl)-1-[5-[2-methoxy-6-(1-methylethyl)-3-pyridinyl]imidazo[2,1-b]-1,3,4-thiadiazol-2-yl], ZY19489 (CAS Number: 1821293-40-6), 2,4-Pyrimidinediamine, N2-(4-cyclopropyl-5-fluoro-6-methyl-2-pyridinyl)-5-[(3R)-3,4-dimethyl-1-piperazinyl]-N4-(1,5-dimethyl-1H-

pyrazol-3-yl) and GSK701 (Cas Number : 2366983-10-8) Methanone, [(3R)-3-(4-fluorophenyl)-1-pyrrolidinyl.

In another embodiments the pharmaceutical composition comprises at least one compound of formula (I) and at least one additional antiviral agent (a antiviral co-agent) different from formula (I).

An antiviral co-agents according to the present invention can be any antiviral agent known in the art such as but not limited to antivirals selected from: Abacavir, Acyclovir (Aciclovir), Adefovir, Amantadine, Ampligen, Amprenavir (Agenerase), Umifenovir (Arbidol), Atazanavir,Atripla, Baloxavir marboxil (Xofluza), Biktarvy, Boceprevir, Bulevirtide, Cidofovir, Cobicistat (Tybost, Combivir, Daclatasvir (Daklinza), Darunavir, Delavirdine, Descovy, Didanosine, Docosanol, Dolutegravir, Doravirine (Pifeltro), Edoxudine, Efavirenz, Elvitegravir, Emtricitabine, Enfuvirtide, Ensitrelvir, Entecavir, Etravirine (Intelence), Famciclovir, Fomivirsen, Fosamprenavir, Foscarnet, Ganciclovir (Cytovene), Ibacitabine, Ibalizumab (Trogarzo), Idoxuridine, Imiquimod, Imunovir, Indinavir, Lamivudine, Letermovir (Prevymis), Lopinavir, Loviride, Maraviroc, Methisazone, Moroxydine, Nelfinavir, Nevirapine, Nexavir formerly (Kutapressin), Nitazoxanide, Norvir, Oseltamivir (Tamiflu),Penciclovir, Peramivir, Penciclovir, Peramivir (Rapivab), Pleconaril, Podophyllotoxin, Raltegravir, Remdesivir, Ribavirin, Rilpivirine (Edurant), Rilpivirine, Rimantadine, Ritonavir, Saquinavir, Simeprevir (Olysio), Sofosbuvir, Stavudine, Taribavirin (Viramidine), Telaprevir, Telbivudine (Tyzeka),Tenofovir alafenamide, Tenofovir disoproxil, Tipranavir,Trifluridine, Trizivir, Tromantadine, Truvada, Umifenovir, Valaciclovir (Valtrex), Valganciclovir (Valcyte), Vicriviroc, Vidarabine ,Zalcitabine, Zanamivir (Relenza) and Zidovudine.

ADMINISTRATION

The invention encompasses the administration of an compounds according to the invention or of a pharmaceutical formulation thereof, wherein said

compounds or the pharmaceutical formulation thereof is administered to an individual prior to, simultaneously or sequentially with other therapeutic regimens or co-agents useful in the treatment of malaria or viral infections (e.g., multiple drug regimens), in an effective amount. Compounds according to the present invention or the pharmaceutical formulations thereof that are administered simultaneously with said co-agents can be administered in the same or different composition(s) and by the same or different route(s) of administration.

In further embodiments, the present invention relates to a method for preventing or treating of PI4K-related disorders, wherein the method comprises the following step:

(i) providing at least one compound and/or a composition according to the present invention; and

(ii) administering an effective amount of said at least one compound or said composition to a patient in need thereof.

In a preferred embodiment said PI4K-related disorder is selected from the list of protozoan infections and viral infection, more preferably a viral infection caused by an RNA virus and most preferably malaria.

Further preferred embodiments listed above also apply to the method according to the present invention.

The invention furthermore relates to medicaments comprising at least one compound of formula (I) and/or pharmaceutically acceptable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants for the treatment and/or prevention of PI4K-related disorders.

Pharmaceutical compositions can be administered in the form of dosage units which comprise a predetermined amount of active ingredient per dosage unit. Such a unit can comprise, for example, 0.5 mg to 1 g, preferably 1 mg to 700

mg, particularly preferably 5 mg to 100 mg, of a compound according to the invention, depending on the condition treated, the method of administration and the age, weight and condition of the patient, or pharmaceutical formulations can be administered in the form of dosage units which comprise a predetermined amount of active ingredient per dosage unit. Preferred dosage unit formulations are those which comprise a daily dose or part-dose, as indicated above, or a corresponding fraction thereof of an active ingredient. Furthermore, pharmaceutical formulations of this type can be prepared using a process which is generally known in the pharmaceutical art.

Pharmaceutical compositions can be adapted for administration via any desired suitable method, for example by oral (including buccal or sublingual), rectal, nasal, topical (including buccal, sublingual or transdermal), vaginal or parenteral (including subcutaneous, intramuscular, intravenous or intradermal) methods. Such formulations can be prepared using all processes known in the pharmaceutical art by, for example, combining the active ingredient with the excipient(s) or adjuvant(s).

In some embodiments, the administration according to the method of the present invention takes place oral, including buccal or sublingual, rectal, nasal, topical, including buccal, sublingual or transdermal, vaginal or parenteral, including subcutaneous, intramuscular, intravenous or intradermal.

Pharmaceutical compositions adapted for oral administration can be administered as separate units, such as, for example, capsules or tablets; powders or granules; solutions or suspensions in aqueous or non-aqueous liquids; edible foams or foam foods; or oil-in-water liquid emulsions or water-in-oil liquid emulsions.

Thus, for example, in the case of oral administration in the form of a tablet or capsule, the active-ingredient component can be combined with an oral, non-toxic and pharmaceutically acceptable inert excipient, such as, for example,

ethanol, glycerol, water and the like. Powders are prepared by comminuting the compound to a suitable fine size and mixing it with a pharmaceutical excipient comminuted in a similar manner, such as, for example, an edible carbohydrate, such as, for example, starch or mannitol. A flavor, preservative, dispersant and dye may likewise be present.

Capsules are produced by preparing a powder mixture as described above and filling shaped gelatin shells therewith. Glidants and lubricants, such as, for example, highly disperse silicic acid, talc, magnesium stearate, calcium stearate or polyethylene glycol in solid form, can be added to the powder mixture before the filling operation. A disintegrant or solubilize, such as, for example, agar-agar, calcium carbonate or sodium carbonate, may likewise be added in order to improve the availability of the medicament after the capsule has been taken.

In addition, if desired or necessary, suitable binders, lubricants and disintegrants as well as dyes can likewise be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars, such as, for example, glucose or beta-lactose, sweeteners made from maize, natural and synthetic rubber, such as, for example, acacia, tragacanth or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. The lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride and the like. The disintegrants include, without being restricted thereto, starch, methylcellulose, agar, bentonite, xanthan gum and the like. The tablets are formulated by, for example, preparing a powder mixture, granulating or dry-pressing the mixture, adding a lubricant and a disintegrant and pressing the entire mixture to give tablets. A powder mixture is prepared by mixing the compound comminuted in a suitable manner with a diluent or a base, as described above, and optionally with a binder, such as, for example, carboxymethylcellulose, an alginate, gelatin or polyvinylpyrrolidone, a dissolution retardant, such as, for example, paraffin, an absorption accelerator,

such as, for example, a quaternary salt, and/or an absorbent, such as, for example, bentonite, kaolin or dicalcium phosphate. The powder mixture can be granulated by wetting it with a binder, such as, for example, syrup, starch paste, acacia mucilage or solutions of cellulose or polymer materials and pressing it through a sieve. As an alternative to granulation, the powder mixture can be run through a tableting machine, giving lumps of non-uniform shape, which are broken up to form granules. The granules can be lubricated by addition of stearic acid, a stearate salt, talc or mineral oil in order to prevent sticking to the tablet casting molds. The lubricated mixture is then pressed to give tablets. The compounds according to the invention can also be combined with a free-flowing inert excipient and then pressed directly to give tablets without carrying out the granulation or dry-pressing steps. A transparent or opaque protective layer consisting of a shellac sealing layer, a layer of sugar or polymer material and a gloss layer of wax may be present. Dyes can be added to these coatings in order to be able to differentiate between different dosage units.

Oral liquids, such as, for example, solution, syrups and elixirs, can be prepared in the form of dosage units so that a given quantity comprises a prespecified amount of the compound. Syrups can be prepared by dissolving the compound in an aqueous solution with a suitable flavor, while elixirs are prepared using a non-toxic alcoholic vehicle. Suspensions can be formulated by dispersion of the compound in a non-toxic vehicle. Solubilizers and emulsifiers, such as, for example, ethoxylated isostearyl alcohols and polyoxyethylene sorbitol ethers, preservatives, flavor additives, such as, for example, peppermint oil or natural sweeteners or saccharin, or other artificial sweeteners and the like, can likewise be added. The dosage unit formulations for oral administration can, if desired, be encapsulated in microcapsules. The formulation can also be prepared in such a way that the release is extended or retarded, such as, for example, by coating or embedding of particulate material in polymers, wax and the like.

The compounds of formula (I) and salts, solvates and physiologically functional derivatives thereof can also be administered in the form of liposome delivery systems, such as, for example, small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from various phospholipids, such as, for example, cholesterol, stearylamine or phosphatidylcholines.

The compounds of the formula (I) and the salts, solvates and physiologically functional derivatives thereof can also be delivered using a delivery reagent such as monoclonal antibodies, nucleic acids or nanoparticles as individual carriers to which the compound molecules are coupled or enclosed. The compounds can also be coupled to soluble polymers as targeted medicament carriers. Such polymers may encompass polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidophenol, polyhydroxy-ethylaspartamidophenol or polyethylene oxide polylysine, substituted by palmitoyl radicals. The compounds may furthermore be coupled to a class of biodegradable polymers which are suitable for achieving controlled release of a medicament, for example polylactic acid, poly-epsilon-capro- lactone, polyhydroxybutyric acid, polyorthoesters, polyacetals, polydihy- droxypyrans, polycyanoacrylates and crosslinked or amphipathic block co- polymers of hydrogels.

Pharmaceutical compositions adapted for transdermal administration can be administered as independent plasters for extended, close contact with the epidermis of the recipient. Thus, for example, the active ingredient can be delivered from the plaster by iontophoresis, as described in general terms in Pharmaceutical Research, 3(6), 318 (1986). Pharmaceutical compounds adapted for topical administration can be formulated as ointments, creams, suspensions, lotions, powders, solutions, pastes, gels, sprays, aerosols or oils.

For the treatment of the eye or other external tissue, for example mouth and skin, the formulations are preferably applied as topical ointment or cream. In

the case of formulation to give an ointment, the active ingredient can be employed either with a paraffinic or a water-miscible cream base. Alternatively, the active ingredient can be formulated to give a cream with an oil-in-water cream base or a water-in-oil base.

Pharmaceutical compositions adapted for topical application to the eye include eye drops, in which the active ingredient is dissolved or suspended in a suitable carrier, in particular an aqueous solvent.

Pharmaceutical compositions adapted for topical application in the mouth encompass lozenges, pastilles and mouthwashes.

Pharmaceutical compositions adapted for rectal administration can be administered in the form of suppositories or enemas.

Pharmaceutical compositions adapted for nasal administration in which the carrier substance is a solid comprise a coarse powder having a particle size, for example, in the range 20-500 microns, which is administered in the manner in which snuff is taken, i.e. by rapid inhalation via the nasal passages from a container containing the powder held close to the nose. Suitable formulations for administration as nasal spray or nose drops with a liquid as carrier substance encompass active-ingredient solutions in water or oil. Pharmaceutical formulations adapted for administration by inhalation encompass finely particulate dusts or mists, which can be generated by various types of pressurized dispensers with aerosols, nebulizers or insufflators.

Pharmaceutical compositions adapted for vaginal administration can be administered as pessaries, tampons, creams, gels, pastes, foams or spray formulations.

Pharmaceutical compositions adapted for parenteral administration include aqueous and non-aqueous sterile injection solutions comprising antioxidants, buffers, bacteriostatics and solutes, by means of which the formulation is rendered isotonic with the blood of the recipient to be treated; and aqueous and non-aqueous sterile suspensions, which may comprise suspension media and thickeners. The formulations can be administered in single-dose or multidose containers, for example sealed ampoules and vials, and stored in freeze-dried (lyophilized) state, so that only the addition of the sterile carrier liquid, for example water for injection purposes, immediately before use is necessary. Injection solutions and suspensions prepared in accordance with the recipe can be prepared from sterile powders, granules and tablets.

It goes without saying that, in addition to the above particularly mentioned constituents, the compositions may also comprise other agents usual in the art with respect to the particular type of formulation; thus, for example, formulations which are suitable for oral administration may comprise flavors.

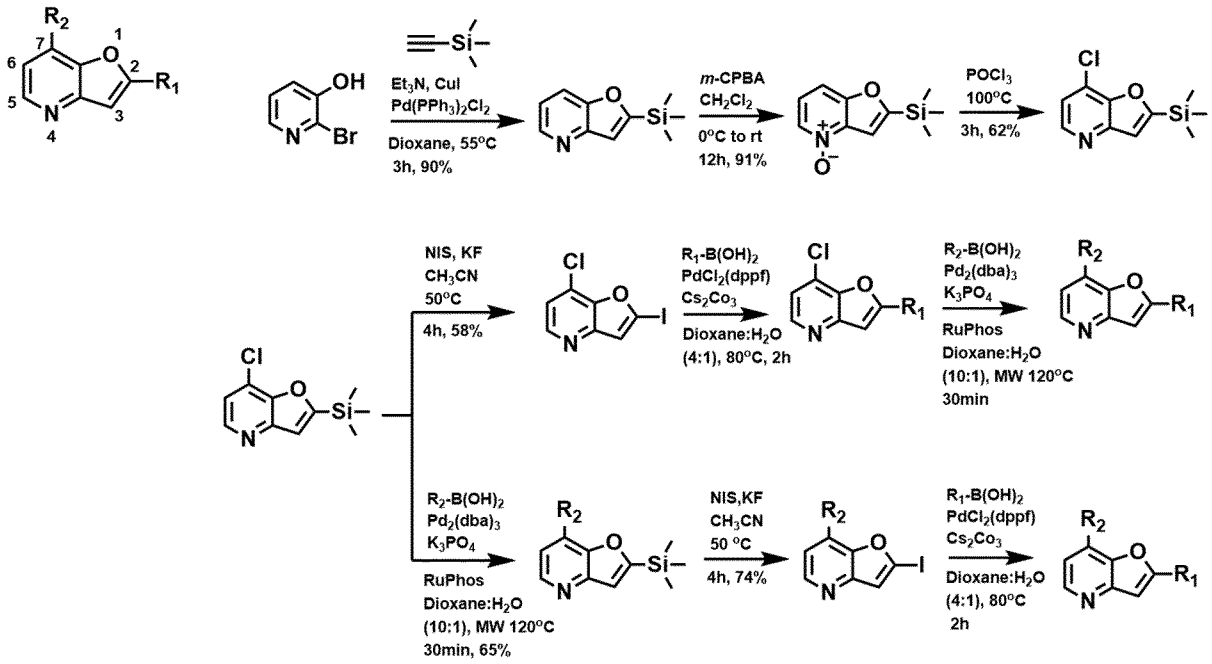
A therapeutically effective amount of a compound of the formula (I) depends on a number of factors, including, for example, the age and weight of the subjects such as animals and humans, the precise condition that requires treatment, and its severity, the nature of the formulation and the method of administration, and is ultimately determined by the treating doctor or vet. However, an effective amount of a compound according to the invention is generally in the range from 0.01 to 100 mg/kg of body weight of the recipient (mammal) per day and particularly typically in the range from 1 to 100 mg/kg of body weight per day. Thus, the actual amount per day for an adult mammal weighing 70 kg is usually between 70 and 700 mg, where this amount can be administered as a single dose per day or usually in a series of part-doses (such as, for example, two, three, four, five or six) per day, so that the total daily dose is the same. An effective amount of a salt or solvate or of a physiologically functional derivative thereof can be determined as the fraction of the effective amount of the compound according to the invention perse. It can be assumed

that similar doses are suitable for the treatment of other conditions mentioned above.

PREPARATION OF REACTANTS AND COMPOUNDS ACCORDING TO THE INVENTION

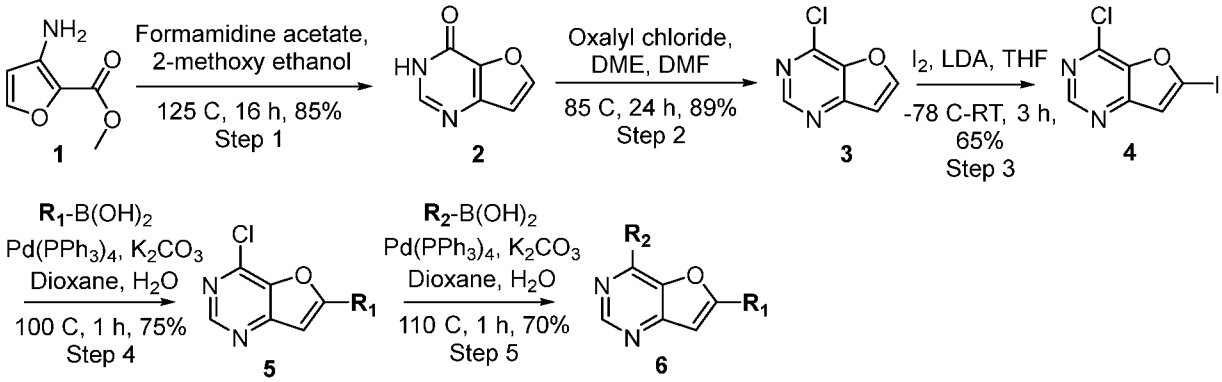
Compounds and derivatives thereof according to the present invention can be prepared from readily available starting materials using methods and procedures known to the skilled person. It will be appreciated that where typical or preferred experimental conditions (i.e. reaction temperatures, time, moles of reagents, solvents etc.) are given, other experimental conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvents used, but such conditions can be determined by the person skilled in the art, using routine optimization procedures.

A general synthetic approach for obtaining compounds of Formula (I) is depicted in Scheme 1 below. Compounds and derivatives according to Formula (I), whereby the substituent Z is carbon (C), may be prepared following the synthetic pathway as outlined in Scheme 1 below.



Scheme 1: General synthesis of furo-pyridine core

A general synthetic approach for obtaining compounds of Formula (I) is depicted in Scheme 1 below. Compounds and derivatives according to Formula (I), whereby the substituent Z is nitrogen (N), may be prepared following the synthetic pathway as outlined in Scheme 2 below.



Scheme 2: General synthesis of furo-pyrimidine core

If the above synthetic methods are not applicable to obtain furo-pyridine or furo-pyrimidine derivatives and/or necessary intermediates according to the invention, suitable methods of preparation known by a person skilled in the art should be used. In general, the synthesis pathways for any individual furo-pyridine or furo-pyrimidine derivative will depend on the specific substituents of each molecule and upon the ready availability of intermediates necessary; again, such factors being appreciated by those of ordinary skill in the art.

Further examples illustrating different synthesis strategies to obtain compounds or reactants according to the present invention can be found in the examples disclosed below.

EXAMPLES

HPLC:

LC purity traces were performed using one of the following methods:

Method 1:

Using a Kinetex 2.6 µM C-18 column, 2 µL injection volume, flow 0.7 mL/min; gradient: 15-100% B in 1.2 min (hold 3.3 min), 100-15% in 0.3 min (hold 1.2 min) (Mobile phase A: 10 mM buffer (Ammonium acetate/acetic acid) in H_2O and Mobile phase B: 10 mM buffer (Ammonium acetate/acetic acid) in Methanol).

Method 2:

Using a Kinetex 1.7 µM C-18 column, 1 µL injection volume, flow 1.2 mL/min; gradient: 5-100% B in 1.5 min (hold 0.4 min), 100-5% in 0.3 min (hold 0.5 min) (Mobile phase A: 0.1% formic acid in H2O and Mobile phase B: 0.1% formic acid in Acetonitrile).

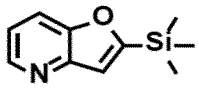
The invention will be illustrated, but not limited, by reference to the specific embodiments described in the following examples.

Unless otherwise specified, all starting materials are obtained from commercial suppliers and used without further purifications. Unless otherwise specified, all temperatures are expressed in °C and all reactions are conducted at rt. Compounds were purified by either silica chromatography or preparative HPLC.

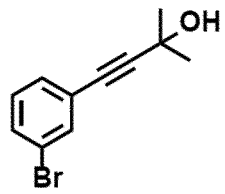
Unless stated otherwise all structures indicated below, where no specific stereochemistry is indicated, refer to mixtures of the stereoisomers (preferably a racemic mixture of the stereoisomers).

Example 1: Synthesis of reactants and compounds according to the invention following General Procedure 1

General Procedure 1: Sonogashira Cross-Coupling Reaction (GP1)



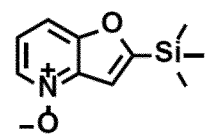
Synthesis of 2-(trimethylsilyl)furo[3,2-b]pyridine ((building block)). To a stirred solution of 2-bromo-3- hydroxypyridine (10.0 g, 57.5 mmol) in 1,4-dioxane (115 mL) were added copper(I) iodide (1.1 g, 5.6 mmol), Bis(triphenylphosphine)palladium (II) dichloride (2 g, 2.9 mmol), Triethylamine (40.1 mL, 287.4 mmol) and degassed for 15 min. Ethynyltrimethylsilane (15.9 mL, 114.9 mmol) was then added in a single portion and the reaction was heated to 55°C for 20 h. The reaction mixture was then washed through a pad of celite using ethyl acetate. It was then concentrated under reduced pressure to yield a thick brown oil as a crude product mixture. The residue was subjected to column chromatography on silica gel using hexane/ethyl acetate 9.5:0.5 v/v ratio initially and slowly increased to hexane/ethyl acetate 8:2 v/v ratio to elute 2- (trimethylsilyl)furo[3,2-b]pyridine in 90% yield as amber oil. Anal. RP-HPLC tR = 2.700 min (method 1, purity 94%); LC-MS ESI: m/z 192.1 [M+H]+ (anal. calcd for C10H14NOSi+: m/z = 192.1).



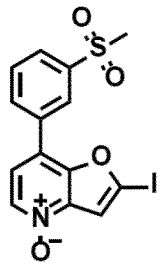
4-(3-bromophenyl)-2-methylbut-3-yn-2-ol ((building block)). According to GP1: Yield 36%. 1H NMR (300 MHz, CDCl3) δ = 7.60 (t, J = 1.7 Hz, 1H), 7.46 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.40-7.34 (m, 1H), 7.23-7.15 (m, 1H), 1.64 (s, 6H); Anal. RP-HPLC tR = 1.106 min (method 2, purity 99%); LC-MS ESI: m/z = 223.0 [M-OH] + (anal. calcd for C11H11BrO+: m/z = 238.0).

<u>Example 2: Synthesis of reactants and compounds according to the invention following General Procedure 2</u>

General Procedure 2: N-Oxidation Reaction (GP2).

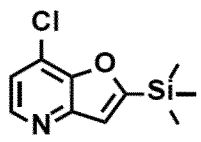


Synthesis of 2-(trimethylsilyl)furo[3,2-b]pyridine 4-oxide **(**(building block)**)**. To a stirred solution of furo[3,2- b]pyridin-2-yl(trimethyl)silane (4.2 g, 22.2 mmol) in dichloromethane (80 mL) was carefully added 3-chloroperbenzoic acid (9.6 g, 55.4 mmol) in small portions at 0 °C under nitrogen atmosphere. The reaction mixture turned into clear yellow color and after stirring at room temperature for approximately 45 min, a large amount of white precipitate had formed in the reaction mixture. The excess mCPBA was quenched by the addition of sat. NaHSO3 (100 mL). The contents of the flask were then transferred to a separating funnel and the aqueous and organic layers were separated. The aqueous layer was extracted with additional portions of dichloromethane (2 × 100 mL). The combined organic layers were then washed with Sat. NaHCO3 (2 × 150 mL) to remove the mCPBA. The organic layer was then isolated, dried over MgSO4 and finally concentrated, affording 2-(trimethylsilyl)furo[3,2-b]pyridine 4-oxide, in 93% yield as brown oil. Anal. RP-HPLC tR = 0.871 min (method 2, purity 99%); LC-MS ESI: m/z 208.1 [M+H]+ (anal. calcd for C10H14NO2Si+: m/z = 208.1).



2-iodo-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine 4-oxide ((building block)). According to GP2: Yield 48%. Anal. RP-HPLC tR = 0.784 min (method 2, purity 78%); LC-MS ESI: m/z = 415.9 [M+H]+ (anal. calcd for C14H10INO4S+: m/z = 414.9).

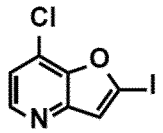
Synthesis of 7-chloro-2-(trimethylsilyl)furo[3,2-b]pyridine ((building block)).



7-chloro-2-(trimethylsilyl)furo[3,2-b]pyridine. Trimethyl-(4-oxidofuro[3,2-b]pyridin-4-ium-2- yl)silane (0.5 g, 2.4 mmol) was added to toluene (16.1 mL). Phosphorus oxychloride (0.5 mL, 4.8 mmol) was then carefully added to the reaction mixture, which was heated to 95°C for 2 h. The excess phosphorus oxychloride was carefully quenched by the drop-wise addition of cooled (0°C) sat. NaHCO3. Once fully quenched, the reaction mixture was transferred to a separating funnel. The product was extracted using ethyl acetate (2 × 100 mL). After separating the layers, the organic layer was dried over MgSO4, filtered and concentrated, yielding a brown oil as a crude product mixture. The residue was subjected to column chromatography on silica gel using hexane/ethyl acetate 9:1 v/v ratio initially and slowly increased to hexane/ethyl acetate 6:4 v/v ratio to elute 7-chloro-2-(trimethylsilyl)furo[3,2-b]pyridine, in 44% yield as amber oil. Anal. RP-HPLC tR = 3.197 min (method 1, purity 99%); LC- MS ESI: m/z 226.0 [M+H]+ (anal. calcd for C10H13ClNOSi+: m/z = 226.1).

Example 3: Synthesis of reactants and compounds according to the invention following General Procedure 3

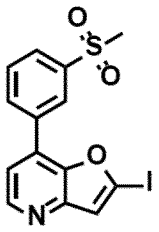
General Procedure 3: Iodination Reaction (GP3)



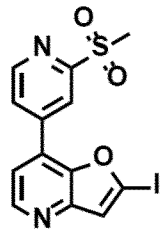
Synthesis of 7-chloro-2-iodofuro[3,2-b]pyridine ((building block)). To a stirred solution of (7-chlorofuro[3,2- b]pyridin-2-yl)-trimethylsilane (6.0 g, 26.6 mmol) in acetonitrile (150 mL) were added N- iodosuccinimide (29.9 g, 132.9 mmol), potassium fluoride (1.9 g, 31.9 mmol) under nitrogen atmosphere and heated at 55 °C for 24 h. The excess N-iodosuccinimide was quenched by the addition of sat. Na2S2O3 (150 mL). The content of the flask was transferred to a separating funnel and the product was extracted using ethyl acetate (2 × 200 mL). The combined organic layers were washed with sat. NaHCO3 (2 × 100 mL), dried over MgSO4 and concentrated. The residue was subjected to column chromatography on silica gel using hexane/ethyl acetate 9:1 v/v ratio

initially and slowly increased to hexane/ethyl acetate 2:8 v/v ratio to elute 7-chloro- 2-iodofuro[3,2-b]pyridine, in 91% yield as yellow solid. Anal. RP-HPLC tR = 1.189 min (method 2, purity 99%); LC-MS ESI: m/z 279.9 [M+H]+ (anal. calcd for C7H4ClINO+: m/z = 279.9).

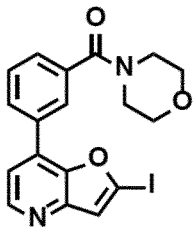
Manufacturing examples



2-iodo-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (building block). According to GP3: Yield 74%. Anal. RP-HPLC tR = 2.547 min (method 1, purity 98%); LC-MS ESI: m/z = 399.8 [M+H]+ (anal. calcd for C14H11INO3S+: m/z = 400.0).

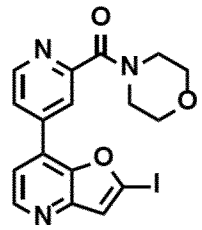


2-iodo-7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridine ((building block)). According to GP3: Yield 80%. Anal. RP-HPLC tR = 0.886 min (method 1, purity 91%); LC-MS ESI: m/z = 399.8 [M]+ (anal. calcd for C13H9IN2O3S+: m/z = 399.9).

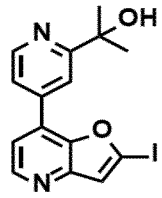


(3-(2-iodofuro[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone ((building block)). According to GP3: Yield 87%. Anal. RP-HPLC tR = 0.924 min (method

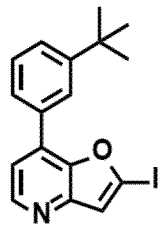
2, purity 98%); LC-MS ESI: m/z = 434.9 [M+H]+ (anal. calcd for C18H16IN2O3+: m/z = 435.0).



(4-(2-iodofuro[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone ((building block)). According to GP3: Yield 56%. Anal. RP-HPLC tR = 0.885 min (method 2, purity 86%); LC-MS ESI: m/z = 436.0 [M+H]+ (anal. calcd for C17H15IN3O3+: m/z = 436.0).



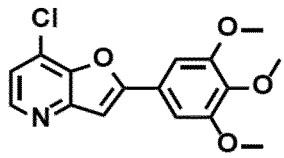
2-(4-(2-iodofuro[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol ((building block)). According to GP3: Yield 48%. Anal. RP-HPLC tR = 2.001 min (method 1, purity 99%); LC-MS ESI: m/z = 380.9 [M+H]+ (anal. calcd for C15H14IN2O2+: m/z = 381.0).



7-(3-tert-butylphenyl)-2-iodofuro[3,2-b]pyridine ((building block)). According to GP3: Yield 68%. Anal. RP-HPLC tR = 1.375 min (method 2, purity 92%); LC-MS ESI: m/z = 378.3 [M+H]+ (anal. calcd for C17H17INO+: m/z = 378.0).

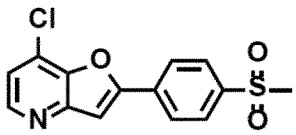
Example 4: Synthesis of reactants and compounds according to the invention following General Procedure 4

General Procedure 4: Suzuki Cross-Coupling Reaction (GP4)

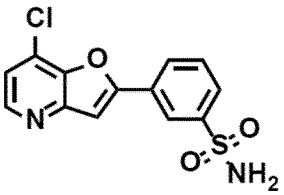


Synthesis of 7-chloro-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine ((building block)). To a stirred solution of 7-chloro-2-iodofuro[3,2-b]pyridine (1.2 g, 4.3 mmol) in 1,4-dioxane (15 mL) were added (1,1'-Bis(triphenylphosphino)ferrocene)palladium(II) dichloride (0.3 g, 0.4 mmol), cesium carbonate (4.2 g, 12.9 mmol), (3,4,5-trimethoxyphenyl)boronic acid (1.1 g, 5.2 mmol), deionized water (3 mL) and degassed for 10 minutes. The resulting reaction mixture was heated at 80 °C for 2 h. 1,4-dioxane was evaporated from the reaction mixture in vacuo. The resulting residue was dissolved in ethyl acetate (50 mL) and washed with water (3 x 50 mL), dried over MgSO4 and concentrated in vacuo to give a brown solid. The residue was subjected to column chromatography on silica gel using hexane/ethyl acetate 8:2 v/v ratio initially and slowly increased to hexane/ethyl acetate 6:4 v/v ratio to elute 7-chloro-2-(3,4,5- trimethoxyphenyl)furo[3,2-b]pyridine in 71% yield as yellow solid. Anal. RP-HPLC tR = 2.850 min (method 1, purity 98%); LC-MS ESI: m/z 320.0 [M+H]+ (anal. calcd for C16H15ClNO4+: m/z = 320.1).

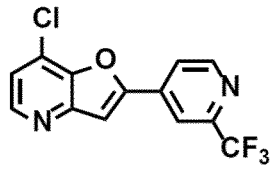
Manufacturing examples



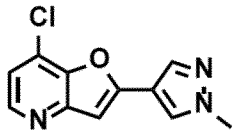
7-chloro-2-(4-methylsulfonylphenyl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 70%. Anal. RP-HPLC tR = 0.971 min (method 2, purity 94%); LC-MS ESI: m/z = 307.9 [M+H]+ (anal. calcd for C14H11ClNO3S+: m/z = 308.1).



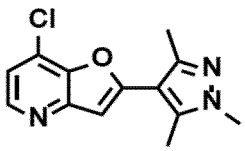
3-(7-chlorofuro[3,2-b]pyridin-2-yl)benzenesulfonamide (building block). Synthesis according to GP4: Yield 53%. Anal. RP-HPLC tR = 2.479 min (method 1, purity 98%); LC-MS ESI: m/z = 308.8 [M+H]+ (anal. calcd for C13H10ClN2O3S+: m/z = 309.1).



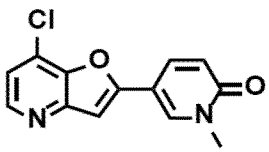
7-chloro-2-(2-(trifluoromethyl)pyridin-4-yl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 82%. Anal. RP-HPLC tR = 2.743 min (method 1, purity 97%); LC-MS ESI: m/z = 298.8 [M+H]+ (anal. calcd for C13H7ClF3N2O+: m/z = 299.0).



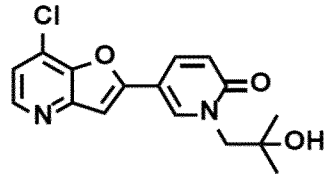
7-chloro-2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 45%. Anal. RP-HPLC tR = 0.830 min (method 2, purity 83%); LC-MS ESI: m/z = 234.0 [M+H]+ (anal. calcd for C11H9ClN3O+: m/z = 234.0).



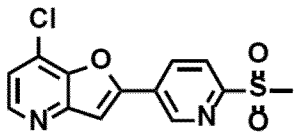
7-chloro-2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 62%. Anal. RP-HPLC tR = 3.219 min (method 1, purity 96%); LC-MS ESI: m/z = 262.0 [M+H]+ (anal. calcd for C13H13ClN3O+: m/z = 262.1).



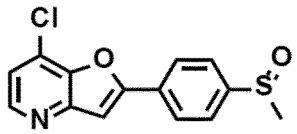
5-(7-chlorofuro[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one (building block). Synthesis according to GP4: Yield 62%. Anal. RP-HPLC tR = 2.636 min (method 1, purity 97%); LC-MS ESI: m/z = 261.0 [M+H]+ (anal. calcd for C13H10ClN2O2+: m/z = 261.0).



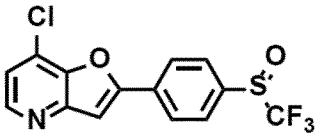
5-(7-chlorofuro[3,2-b]pyridin-2-yl)-1-(2-hydroxy-2-methylpropyl)pyridin-2(1H)-one (building block). Synthesis according to GP4: Yield 65%. Anal. RP-HPLC tR = 0.840 min (method 1, purity 80%); LC-MS ESI: m/z = 319.0 [M+H]+ (anal. calcd for C16H16ClN2O3+: m/z = 319.1).



7-chloro-2-(6-methylsulfonylpyridin-3-yl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 55%. Anal. RP-HPLC tR = 2.362 min (method 1, purity 85%); LC-MS ESI: m/z = 308.9 [M+H]+ (anal. calcd for C13H10ClN2O3S+: m/z = 309.0).

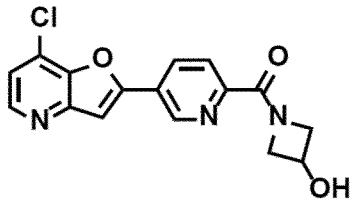


7-chloro-2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 50%. Anal. RP-HPLC tR = 1.016 min (method 2, purity 86%); LC-MS ESI: m/z = 291.9 [M+H]+ (anal. calcd for C14H11ClNO2S+: m/z = 292.0).

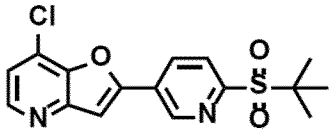


7-chloro-2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 84%. Anal. RP-HPLC tR = 2.622

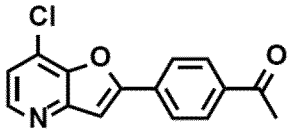
min (method 1, purity 96%); LC-MS ESI: m/z = 346.0 [M+H]+ (anal. calcd for C14H8ClF3NO2S+: m/z = 346.0).



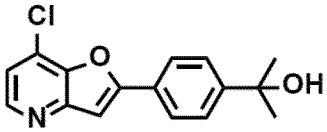
(5-(7-chlorofuro[3,2-b]pyridin-2-yl)pyridin-2-yl)(3-hydroxyazetidin-1-yl)methanone (building block). Synthesis according to GP4: Yield 16%. Anal. RP-HPLC tR = 0.861 min (method 1, purity 96%); LC-MS ESI: m/z = 329.1 [M]+ (anal. calcd for C16H12ClN3O3+: m/z = 329.1).



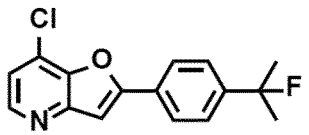
2-(6-(tert-butylsulfonyl)pyridin-3-yl)-7-chlorofuro[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 84%. Anal. RP-HPLC tR = 1.118 min (method 1, purity 96%); LC-MS ESI: m/z = 350.1 [M]+ (anal. calcd for C16H15ClN2O3S+: m/z = 350.1).



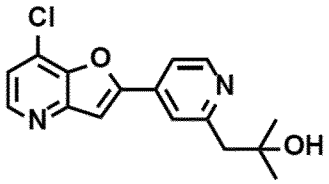
1-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)ethan-1-one (building block). Synthesis according to GP4: Yield 94%. Anal. RP-HPLC tR = 1.125 min (method 1, purity 94%); LC-MS ESI: m/z = 272.1 [M+H]+ (anal. calcd for C15H11ClNO2+: m/z = 272.1).



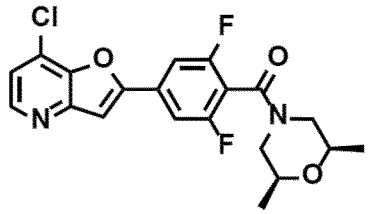
2-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)propan-2-ol (building block). Synthesis according to GP4: Yield 54%. Anal. RP-HPLC tR = 1.042 min (method 1, purity 93%); LC-MS ESI: m/z = 288.0 [M+H]+ (anal. calcd for C16H15ClNO2+: m/z = 288.1).



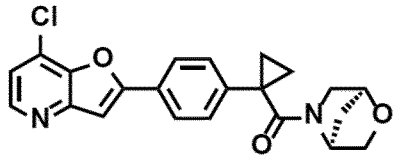
7-chloro-2-(4-(2-fluoropropan-2-yl)phenyl)furo[3,2-b]pyridine (building block). Synthesis according to GP4: Yield 57%. Anal. RP-HPLC tR = 1.260 min (method 1, purity 77%); LC-MS ESI: m/z = 290.1 [M+H]+ (anal. calcd for C16H14ClFNO+: m/z = 290.1).



1-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)pyridin-2-yl)-2-methylpropan-2-ol (building block). Synthesis according to GP4: Yield 87%. Anal. RP-HPLC tR = 0.732 min (method 1, purity 99%); LC-MS ESI: m/z = 303.0 [M+H]+ (anal. calcd for C16H16ClN2O2+: m/z = 303.1).

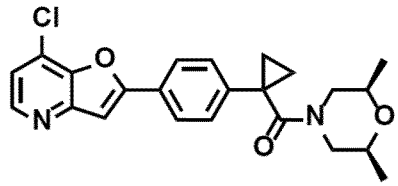


(4-(7-chlorofuro[3,2-b]pyridin-2-yl)-2,6-difluorophenyl)((2S,6R)-2,6-dimethylmorpholino)methanone (building block). Synthesis according to GP4: Yield 54% as a yellow solid. Anal. RP-HPLC tR = 1.146 min (method 2, purity 87%); LC-MS ESI: m/z = 407.1 [M+H]+ (anal. calcd for C20H18ClF2N2O3+: m/z = 407.1).



((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(1-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)methanone (building block). Synthesis according to GP4: Yield 60% as a light yellow solid. Anal. RP-HPLC tR =

1.013min (method 2, purity 99%); LC-MS (ESI): m/z = 395.1 [M+H]+ (anal. calcd for C22H20ClN2O3+: m/z = 395.1).



(1-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)((2S,6R)-2,6-dimethylmorpholino)methanone (building block). Synthesis according to GP4: Yield 69% as a light yellow solid. Anal. RP-HPLC tR = 1.154 min (method 2, purity 94%); LC-MS (ESI): m/z = 411.2 [M+H]+ (anal. calcd for C23H24ClN2O3+: m/z = 411.2).

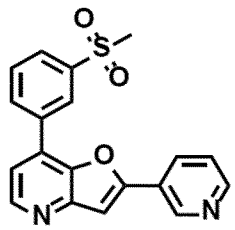
5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyrimidin-2-amine (D15). Synthesis according to GP4: Yield 45%. 1H NMR (300 MHz, DMSO-d6) δ = 8.89 (s, 2H), 8.72 (d, J = 1.9 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.48 (dt, J = 7.8, 1.4 Hz, 1H), 8.09 (d, J = 1.6 Hz, 1H), 7.92 (t, J = 7.8 Hz, 1H), 7.71(d, J = 5.1 Hz, 1H), 7.56 (s, 1H), 7.26 (s, 2H), 3.35 (s, 3H); Anal. RP-HPLC tR = 2.571 min (method1, purity 98%); LC-MS ESI: m/z = 366.9 [M+H]+ (anal. calcd for C18H15N4O3S+: m/z = 367.1).

2-(3,6-dihydro-2H-pyran-4-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (D6). Synthesis according to GP4: Yield 32%. 1H NMR (300 MHz, DMSO-d6) δ = 8.62 (t, J = 1.6 Hz, 1H), 8.59 (d, J = 5.1 Hz, 1H), 8.41 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.89 (t, J = 7.9 Hz, 1H), 7.71 (d, J = 5.1 Hz,1H), 7.17 (s, 1H), 6.99 (s, 1H), 4.33-4.32 (m, 2H), 3.87 (t, J = 5.5 Hz, 2H), 3.32 (s, 3H), 2.56-2.53(m, 2H); Anal. RP-HPLC tR = 0.875 min (method 2, purity 97%); LC-MS ESI: m/z = 356.0 [M+H]+ (anal. calcd for C19H18NO4S+: m/z = 356.1).

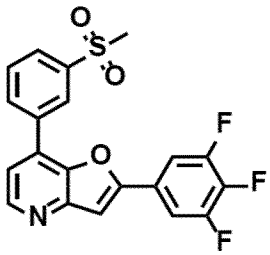
2-(1-methyl-1H-indazol-6-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (D8). Synthesis according to GP4: Yield 30%. 1H NMR (300 MHz, DMSO-d6) δ = 8.97 (t, J = 1.8 Hz, 1H), 8.66 (d, J = 5.1 Hz, 1H), 8.50 (dt, J = 8.0, 1.4 Hz, 1H), 8.29 (d, J = 1.4 Hz, 1H), 8.19-8.07 (m, 2H), 8.03-7.75 (m, 5H),4.17 (s,

3H), 3.40 (s, 3H); Anal. RP-HPLC tR = 3.135 min (method 1, purity 95%); LC-MS ESI: m/z= 404.0 [M+H]+ (anal. calcd for C22H18N3O3S+: m/z = 404.1).

7-(3-(methylsulfonyl)phenyl)-2-(pyridin-4-yl)furo[3,2-b]pyridine (D10). Synthesis according to GP4: Yield 44%. 1H NMR (300 MHz, DMSO-d6) δ = 8.81-8.75 (m, 2H), 8.74-8.68 (m, 2H), 8.55-8.47 (m, 1H),8.16-8.09 (m, 2H), 8.02-7.90 (m, 3H), 7.85 (d, J = 5.1 Hz, 1H), 3.36 (s, 3H); Anal. RP-HPLC tR =2.924 min (method 1, purity 95%); LC-MS ESI: m/z = 351.0 [M+H]+ (anal. calcd for C19H15N2O3S+:m/z = 351.1).

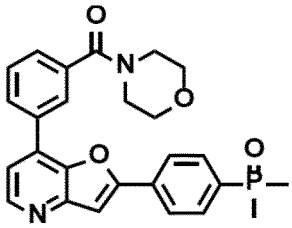


7-(3-(methylsulfonyl)phenyl)-2-(pyridin-3-yl)furo[3,2-b]pyridine. Synthesis according to GP4: Yield 49%. 1H NMR (300 MHz, DMSO-d6) δ = 9.27 (dd, J = 2.3, 0.9 Hz, 1H), 8.76-8.63 (m, 3H), 8.51(ddd, J = 7.8, 1.9, 1.1 Hz, 1H), 8.40 (dt, J = 8.1, 1.9 Hz, 1H), 8.12 (ddd, J = 7.9, 1.9, 1.1 Hz, 1H),8.00-7.89 (m, 2H), 7.80 (d, J = 5.1 Hz, 1H), 7.61 (ddd, J = 8.0, 4.8, 0.9 Hz, 1H), 3.36 (s, 3H); Anal.RP-HPLC tR = 2.959 min (method 1, purity 99%); LC-MS ESI: m/z = 351.0 [M+H]+ (anal. calcd for C19H15N2O3S+: m/z = 351.1).



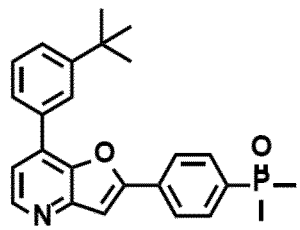
7-(3-(methylsulfonyl)phenyl)-2-(3,4,5-trifluorophenyl)furo[3,2-b]pyridine. Synthesis according to GP4: Yield 36%. 1H NMR (300 MHz, DMSO-d6) δ = 8.76-8.62 (m, 2H), 8.49 (d, J = 7.9 Hz, 1H), 8.20-8.06 (m, 2H), 8.00-7.74 (m, 4H), 7.66 (q, J = 8.8 Hz, 1H), 3.36 (s, 3H); Anal. RP-HPLC tR =1.067 min

(method 2, purity 98%); LC-MS ESI: m/z = 404.0 [M+H]+ (anal. calcd for C20H13F3NO3S+: m/z = 404.1).



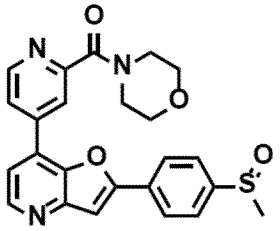
(3-(2-(4-(dimethylphosphoryl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone. Synthesis according to GP4: Yield 47%. 1H NMR (300 MHz, DMSO- d6+TFA) δ = 8.71 (d, J = 5.2 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.22-8.12 (m, 3H), 8.02-7.92 (m,3H), 7.78 (dd, J = 16.7, 6.7 Hz, 2H), 7.65 (d, J = 7.7 Hz, 1H), 3.58 (d, J = 38.3 Hz, 8H), 1.75 (s, 3H),1.70 (s, 3H); Anal. RP-HPLC tR = 0.935 min (method 2, purity 99%); LC-MS ESI: m/z = 461.1 [M+H]+ (anal. calcd for C26H26N2O4P+: m/z = 461.2).

2-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D54). Synthesis according to GP4: Yield 26% as an amorphous off-white solid. 1H NMR (300 MHz, CDCl3): δ = 8.76 (d, J = 5.1 Hz, 1H), 8.26 (d, J = 5.05 Hz, 1H), 8.47 (s, 1H), 7.64 (d, J = 8.5 Hz, 2H), 8.03 (s,1H), 7.95 (dd, J = 5.1 Hz, J = 1.7 Hz,1 H), 7.79 (d, J = 5.05 Hz, 1H), 5.45 (bs, 1H, OH), 3.20 (s, 2H),3.29 (s, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.828 min (method 2, purity 99%); LC-MS ESI: m/z= 409.0 [M+H]+ (anal. calcd for C22H21N2O4S+: m/z = 409.1).

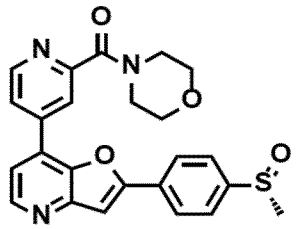


(4-(7-(3-(tert-butyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)dimethylphosphine oxide. Synthesis according to GP4: Yield 15%. 1H NMR (300 MHz, DMSO-d6) δ = 8.61 (d, J = 5.1 Hz, 1H), 8.20- 8.11 (m, 3H), 7.95 (dd, J = 11.0, 8.3 Hz, 2H), 7.91-7.85 (m, 2H), 7.66 (d, J = 5.1 Hz, 1H), 7.63-7.56 (m, 2H), 1.73 (s, 3H),

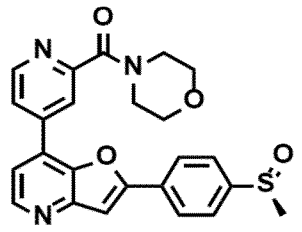
1.69 (s, 3H), 1.42 (s, 9H); Anal. RP-HPLC tR = 2.742 min (method 1, purity 99%); LC-MS ESI: m/z = 404.1 [M+H]+ (anal. calcd for C25H27NO2P+: m/z = 404.2).



(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone. Synthesis according to GP4: Yield 40% as an off white solid. 1H NMR (CDCl3+MeOD-d4) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.56 (d, J = 5.1 Hz, 1H), 8.20 (s, 1H), 7.97-8.03 (m,3H), 7.72 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 5.1 Hz, 1H), 7.39 (s, 1H), 4.23 (s, 3H), 3.32 (t, J = 7.1 Hz,1H), 2.74 (t, J = 3.4 Hz, 5H), 2.28 (t, J = 8.3 Hz, 1H), 1.89-2.00 (m, 1H); Anal. RP-HPLC tR = 0.815 min (method 2, purity 99%); LC-MS ESI: m/z = 448.0 [M+H]+ (anal. calcd for C24H22N3O4S+: m/z= 448.1).



(R)-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone. Synthesis according to GP4 (stereoisomer derived via chiral HPLC starting rom rac material described above) : Yield 15%. 1H NMR (300 MHz, CDCl3) δ = 8.85 (d, J = 5.1 Hz, 1H), 8.70 (d, J = 5.1 Hz, 1H), 8.34 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 8.03-7.97 (m,1H), 7.82 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 5.6 Hz, 2H), 3.82 (m, J = 29.5 Hz, 8H), 2.79 (s, 3H); Anal.RP-HPLC tR = 0.832 min (method 2, purity 99%); LC-MS ESI: m/z = 448.0 [M+H]+ (anal. calcd for C24H22N3O4S+: m/z = 448.1).



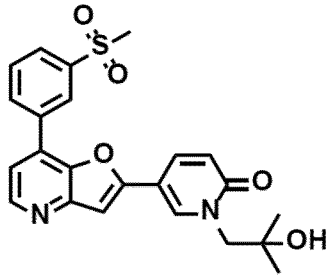
(S)-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2yl)(morpholino)methanone. Synthesis according to GP4 ((stereoisomer derived via chiral HPLC starting rom rac material described above)): Yield 13%. Anal. RP-HPLC tR = 0.832 min (method 2, purity 99%); LC-MS ESI: m/z = 448.0 [M+H]+ (anal. calcd for C24H22N3O4S+: m/z = 448.1).

(3-(2-(6-aminopyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D44). Synthesis according to GP4: Yield 73%. 1H NMR (300 MHz, DMSO-d6) δ = 8.57 (dd, J = 2.5, 0.7 Hz, 1H), 8.51 (d, J = 5.1 Hz, 1H), 8.17 (dt, J = 7.8, 1.6 Hz, 1H), 8.08 (t, J = 1.7 Hz, 1H), 7.94 (dd, J = 8.7,2.5 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.61-7.51 (m, 2H), 7.39 (s, 1H), 6.65-6.45 (m, 3H), 3.63 (s,8H); Anal. RP-HPLC tR = 0.667 min (method 2, purity 99%); LC-MS ESI: m/z = 401.1 [M+H]+ (anal. calcd for C23H21N4O3+: m/z = 401.2).

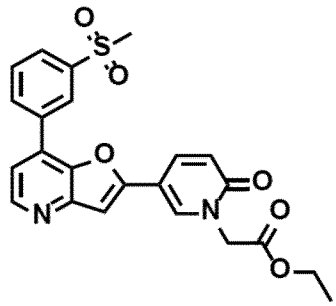
2-methyl-1-((4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)amino)propan-2-ol (D41). Synthesis according to GP4: Yield 57% as a yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.98-8.88 (m, 2H), 8.72 (d, J = 5.1 Hz, 1H), 8.12 (dd, J = 5.1, 1.7 Hz, 2H), 7.55 (d, J = 5.1 Hz,1H), 7.41 (s, 1H), 7.04 (s, 1H), 6.98 (dd, J = 5.4, 1.3 Hz, 1H), 5.29 (t, J = 5.8 Hz, 1H), 3.45 (d, J =5.9 Hz, 2H), 3.34 (s, 3H), 1.31 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.709 min (method 2, purity 95%); LC-MS ESI: m/z = 439.0 [M+H]+ (anal. calcd for C22H23N4O4S+: m/z = 439.1).

1-(2-hydroxy-2-methylpropyl)-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one (D40). Synthesis according to GP4: Yield

53% as a yellow solid. 1H NMR (300 MHz, CDCl3) δ = 9.14-9.10 (m, 1H), 8.91 (d, J = 5.1 Hz, 1H), 8.65 (d, J = 5.1 Hz, 1H), 8.36 (d, J = 2.5 Hz, 1H),8.01 (dd, J = 5.1, 1.7 Hz, 1H), 7.74 (dd, J = 9.5, 2.6 Hz, 1H), 7.51 (d, J = 5.2 Hz, 1H), 7.05 (s, 1H), 6.73 (d, J = 9.5 Hz, 1H), 4.18 (s, 2H), 3.36 (s, 3H), 1.33 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.802 min (method 2, purity 98%); LC-MS ESI: m/z = 440.0 [M+H]+ (anal. calcd for C22H22N3O5S+: m/z = 440.1).

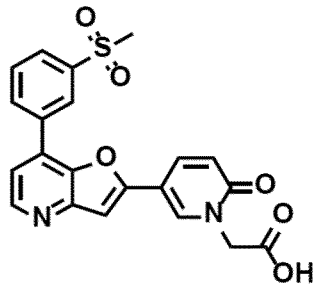


1-(2-hydroxy-2-methylpropyl)-5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2- yl)pyridin-2(1H)-one. Synthesis according to GP4: Yield 14% as a yellow solid. 1H NMR (300 MHz, DMSO- d6) δ = 8.65 (t, J = 1.8 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.47-8.42 (m, 1H), 8.35 (d, J = 2.6 Hz, 1H), 8.11 (d, J = 7.7 Hz, 1H), 8.06 (dd, J = 9.5, 2.6 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 5.1 Hz, 1H), 7.47 (s, 1H), 6.62 (d, J = 9.5 Hz, 1H), 4.03 (s, 2H), 3.36 (s, 3H), 1.14 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.830 min (method 2, purity 99%); LC-MS ESI: m/z = 439.1 [M+H]+ (anal. calcd for C23H23N2O5S+: m/z = 439.1).



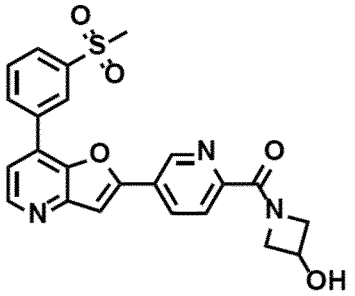
ethyl 2-(5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-2-oxopyridin-1(2H)- yl)acetate (building block). Synthesis according to GP4: Yield 39% as an off-white solid. 1H NMR (300 MHz, DMSO-d6) δ= 8.67 (t, J = 1.8 Hz, 1H),

8.61 (d, J = 5.1 Hz, 1H), 8.47 (dt, J = 7.9, 1.2 Hz, 1H), 8.43 (d, J = 2.6Hz, 1H), 8.16-8.07 (m, 2H), 7.91 (t, J = 7.9 Hz, 1H), 7.72 (d, J = 5.1 Hz, 1H), 7.50 (s, 1H), 6.66 (d,J = 9.6 Hz, 1H), 4.82 (s, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.35 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); Anal.RP-HPLC tR = 0.885 min (method 2, purity 97%); LC-MS ESI: m/z = 453.0 [M+H]+ (anal. calcd for C23H21N2O6S+: m/z = 453.1).

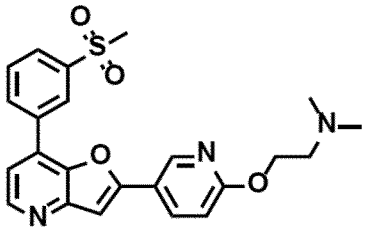


2-(5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-2-oxopyridin-1(2H)-yl)acetic acid (building block). Yield 57% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (s, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.47 (d, J = 7.9 Hz, 1H), 8.42 (d, J = 2.5 Hz, 1H), 8.14-8.07 (m, 2H), 7.92 (t, J = 7.8 Hz, 1H), 7.71 (d, J = 5.1 Hz, 1H), 7.48 (s, 1H), 6.64 (d, J = 9.5 Hz, 1H), 4.72 (s, 2H), 3.35 (s, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 2.763 min (method 1, purity 99%); LC-MS ESI: m/z = 425.0 [M+H]+ (anal. calcd for C21H17N2O6S+: m/z = 425.1).

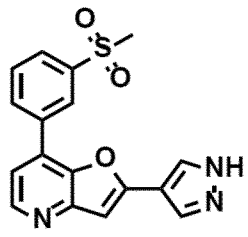
1-((4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)sulfonyl)azetidin-3-ol (C58). Synthesis according to GP4: Yield 14% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.71 (d, J = 5.2 Hz, 2H), 8.51 (dt, J = 7.6, 1.3 Hz, 1H), 8.34 (d, J = 8.5 Hz, 2H), 8.14 (dt, J = 8.0, 1.3 Hz, 1H), 8.06 (s, 1H), 8.00-7.91 (m, 3H), 7.83 (d, J = 5.1 Hz, 1H), 5.72 (s, 1H), 4.31 (s, 1H), 4.01-3.92 (m, 2H), 3.41 (dd, J = 8.7, 5.7 Hz, 2H), 3.37 (s, 3H); Anal. RP-HPLC tR = 0.927 min (method 2, purity 99%); LC-MS ESI: m/z = 485.0 [M+H]+ (anal. calcd for C23H21N2O6S2+: m/z = 485.1).



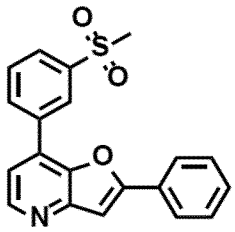
(3-hydroxyazetidin-1-yl)(5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)methanone (D33). Synthesis according to GP4: Yield 53% as a brown solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.30 (d, J = 1.8 Hz, 1H), 8.69 (q, J = 2.7, 1.9 Hz, 2H), 8.52 (dd, J = 8.2, 2.0 Hz, 2H), 8.16-8.04 (m, 3H), 7.95 (t, J = 7.8 Hz, 1H), 7.83 (s, 1H), 5.73 (d, J = 6.2 Hz, 1H), 4.81 (dd, J = 10.8, 6.1 Hz,1H), 4.54 (h, J = 6.2 Hz, 1H), 4.33 (td, J = 11.8, 11.1, 5.7 Hz, 2H), 3.84 (dd, J = 10.8, 4.3 Hz, 1H),3.36 (s, 3H); Anal. RP-HPLC tR = 0.837 min (method 2, purity 99%); LC-MS ESI: m/z = 450.0 [M+H]+ (anal. calcd for C23H20N3O5S+: m/z = 450.1).



N,N-dimethyl-2-((5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2- yl)oxy)ethan-1-amine. Synthesis according to GP4: Yield 55%. 1H NMR (400 MHz, DMSO-d6) δ = 8.84 (d, J = 2.5 Hz, 1H), 8.69 (t, J = 1.5 Hz, 1H), 8.62 (d, J = 5.1 Hz, 1H), 8.50-8.47 (m, 1H), 8.30 (dd, J =8.7 Hz & 2.5 Hz, 1H), 8.12-8.09 (m, 1H), 7.93 (t, J = 7.8 Hz, 1H), 7.73 (d, J = 5.1 Hz, 1H), 7.70 (s, 1H), 6.99 (d, J = 8.7 Hz, 1H), 4.43 (t, J = 5.8 Hz, 2H), 3.34 (s, 3H), 2.65 (t, J = 5.8 Hz, 2H), 2.22 (s, 6H); Anal. RP-HPLC tR = 0.687 min (method 2, purity 97%); LC-MS ESI: m/z = 438.0 [M+H]+ (anal. calcd for C23H24N3O4S+: m/z = 438.2).

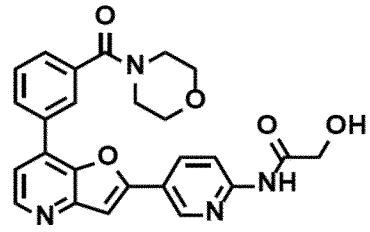


7-(3-(methylsulfonyl)phenyl)-2-(1H-pyrazol-4-yl)furo[3,2-b]pyridine. Synthesis according to GP4: Yield 28%. 1H NMR (300 MHz, DMSO-d6) δ = 13.38 (s, 1H), 8.71 (s, 1H), 8.56 (d, J = 5.2 Hz, 1H), 8.46 (d, J = 8.1 Hz, 1H), 8.24 (s, 2H), 8.09 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.67 (d, J = 5.2 Hz, 1H), 7.28 (s, 1H), 3.35 (s, 3H); Anal. RP-HPLC tR = 0.727 min (method 2, purity 99%); LC-MS ESI: m/z = 340.0 [M+H]+ (anal. calcd for C17H14N3O3S+: m/z = 340.1).

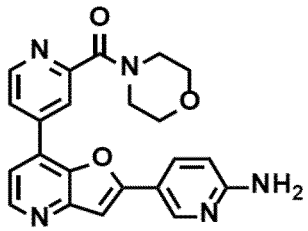


7-(3-(methylsulfonyl)phenyl)-2-phenylfuro[3,2-b]pyridine. Synthesis according to GP4: Yield 36%. 1H NMR (300 MHz, DMSO-d6) δ = 8.72 (s, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 8.1 Hz, 1H), 8.13-8.05 (m, 3H), 7.94 (t, J = 7.9 Hz, 1H), 7.78-7.75 (m, 2H), 7.60-7.47 (m, 3H), 3.35 (s, 3H); Anal.RP-HPLC tR = 0.995 min (method 2, purity 99%); LC-MS ESI: m/z = 350.0 [M+H]+ (anal. calcd for C20H16NO3S+: m/z = 350.1).

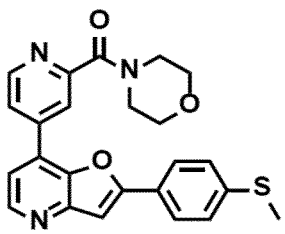
5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2-amine (D9). Synthesis according to GP4: Yield 59%. 1H NMR (300 MHz, DMSO-d6) δ = 8.70 (s, 1H), 8.62 (d, J = 2.2 Hz, 1H), 8.51 (d, J = 5.1 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.99 (m, 2H), 7.65 (d, J = 5.1 Hz,1H), 7.42 (s, 1H), 6.50-6.55 (m, 3H), 3.34 (s, 3H); Anal. RP-HPLC tR = 0.644 min (method 2, purity 99%); LC-MS ESI: m/z = 366.0 [M+H]+ (anal. calcd for C19H16N3O3S+: m/z = 366.1).



2-hydroxy-N-(5-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2- yl)acetamide. Synthesis according to GP4: Yield 30%. 1H NMR (300 MHz, DMSO-d6) δ = 10.01 (s, 1H), 8.97 (dd, J = 2.4, 0.8 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.40 (dd, J = 8.8, 2.4 Hz, 1H), 8.30-8.18 (m, 2H), 8.11 (t, J = 1.7 Hz, 1H), 7.78-7.69 (m, 2H), 7.66-7.57 (m, 1H), 5.75-5.69 (m, 2H), 4.10 (d, J = 6.0 Hz, 2H), 3.63 (s, 8H); Anal. RP-HPLC tR = 0.803 min (method 2, purity 99%); LC-MS ESI: m/z = 459.0 [M+H]+ (anal. calcd for C25H23N4O5+: m/z = 459.2).



(4-(2-(6-aminopyridin-3-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone. Synthesis according to GP4: Yield 4% as a yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.83 (d, J = 5.0 Hz, 1H), 8.57-8.54 (m, 2H), 8.32-8.30 (m, 1H), 8.18 (dd, J = 5.2, 1.8 Hz, 1H), 8.01 (dd, J = 8.8,2.4 Hz, 1H), 7.64 (d, J = 5.2 Hz, 1H), 7.23 (s, 1H), 6.70 (d, J = 8.7 Hz, 1H), 3.84 (br. s, 4H), 3.72-3.64 (m, 4H). The two NH signals were not observed due to the deuterated solvent; Anal. RP- HPLC tR = 0.653 min (method 2, purity 99%); LC-MS ESI: m/z = 402.1 [M+H]+ (anal. calcd for C22H20N5O3+: m/z = 402.2)



(4-(2-(4-(methylthio)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone (building block). Synthesis according to GP4: Yield 85% as a yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.84-8.76 (m, 1H), 8.63 (d, J = 5.2 Hz, 1H), 8.31-8.29 (m, 1H), 8.03 (dd, J = 5.2, 1.8 Hz, 1H), 7.85-7.80 (m, 2H), 7.46(d , J = 5.2 Hz, 1H), 7.39-7.32 (m, 2H), 7.30 (s, 1H), 3.96-3.65 (m, 8H), 2.55 (s, 3H); Anal. RP-HPLC tR = 1.028 min (method 2, purity 98%); LC-MS ESI: m/z = 432.0 [M+H]+ (anal. calcd for C24H22N3O3S+: m/z = 432.1).

(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D56). Synthesis according to GP4: Yield 78% as a yellow solid. 1H NMR (300 MHz, CDCl3+MeOD-d4) δ = 8.63 (d, J = 5.1 Hz, 1H), 8.14-7.97 (m, 4H), 7.77 (d, J = 8.5 Hz, 2H), 7.66 (t, J = 7.7 Hz, 1H), 7.55 (d, J = 7.7Hz, 1H), 7.44-7.42 (m, 2H), 3.73 (br. s, 8H), 2.78 (s, 3H); Anal. RP-HPLC tR = 0.842 min (method2, purity 99%); LC-MS ESI: m/z = 447.0 [M+H]+ (anal. calcd for C25H23N2O4S+: m/z = 447.1).

(R)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D45). Synthesis according to GP4 (stereoisomer derived via chiral HPLC starting from rac material (D56)): Yield 25%. 1H NMR (300 MHz, CDCl3) δ = 8.64 (d, J = 5.0 Hz, 1H), 8.12-8.00 (m, 4H), 7.82-7.75 (m, 2H), 7.67 (t, J = 7.7 Hz, 1H), 7.56 (dt, J = 7.7, 1.4 Hz, 1H), 7.47-7.39 (m, 2H), 3.73 (s, 8H), 2.79 (s, 3H); Anal. RP-HPLC tR = 0.836 min(method 2, purity 99%); LC-MS ESI: m/z = 447.0 [M+H]+ (anal. calcd for C25H23N2O4S+: m/z = 447.1).

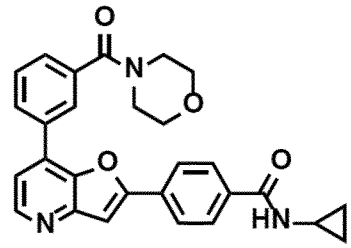
(S)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D46). Synthesis according to GP4 (stereoisomer derived via chiral HPLC starting from rac material (D56): Yield 25%. 1H NMR (300 MHz, CDCl3) δ = 8.64 (s, 1H), 8.15-8.00 (m, 4H), 7.82-7.74 (m, 2H), 7.68 (t, J = 7.7 Hz, 1H), 7.57 (dt, J = 7.7, 1.4 Hz, 1H), 7.46 (d, J = 5.1 Hz, 2H), 3.73 (s, 8H), 2.79 (s, 3H); Anal. RP-HPLC tR = 0.837 min

(method 2, purity 99%); LC-MS ESI: m/z = 447.0 [M+H]+ (anal. calcd for C25H23N2O4S+: m/z = 447.1).

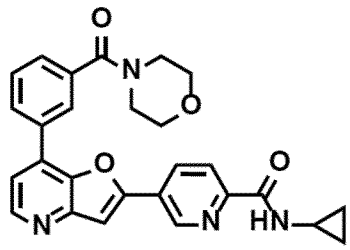
(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone (D27). Synthesis according to GP4: Yield 67%. 1H NMR (300 MHz, DMSO-d6) δ = 8.87 (d, J = 5.1 Hz, 1H), 8.72 (d, J = 5.0 Hz, 1H), 8.34-8.22 (m, 4H), 8.11 (d, J = 8.6 Hz, 2H), 8.05(s, 1H), 7.85 (d, J = 5.1 Hz, 1H), 3.82-3.42 (m, 8H), 3.26 (s, 3H); Anal. RP-HPLC tR = 0.872 min(method 2, purity 99%); LC-MS ESI: m/z = 464.0 [M+H]+ (anal. calcd for C24H22N3O5S+: m/z = 464.0).

(3-(2-(4-(3-hydroxyoxetan-3-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D84). Synthesis according to GP4: Yield 31% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.60 (d, J = 5.1 Hz, 1H), 8.21 (d, J = 8.1 Hz, 1H), 8.10 (s, 1H), 8.04 (d, J= 8.4 Hz, 2H), 7.81-7.70 (m, 4H), 7.62 (m, 2H), 6.49 (s, 1H), 4.82 (d, J = 6.6 Hz, 2H), 4.73 (d, J =6.6 Hz, 2H), 3.63 (s, 8H); Anal. RP-HPLC tR = 1.030 min (method 2, purity 97%); LC-MS ESI: m/z= 457.1 [M+H]+ (anal. calcd for C27H25N2O5+: m/z = 457.2).

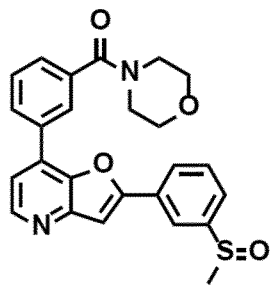
(3-(2-(6-(3-hydroxyoxetan-3-yl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D83). Synthesis according to GP4: Yield 37% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.29 (d, J = 2.0 Hz, 1H), 8.63 (d, J = 5.1 Hz, 1H), 8.39 (dd, J = 8.2, 2.2Hz, 1H), 8.25 (d, J = 7.9 Hz, 1H), 8.12 (s, 1H), 7.90 (s, 1H), 7.78-7.67 (m, 3H), 7.61 (d, J = 7.7 Hz,1H), 6.69 (s, 1H), 4.97 (d, J = 6.1 Hz, 2H), 4.70 (d, J = 6.1 Hz, 2H), 3.64 (s, 8H); Anal. RP-HPLC tR= 2.385 min (method 1, purity 99%); LC-MS ESI: m/z = 458.1 [M+H]+ (anal. calcd for C26H24N3O5+: m/z = 458.2).



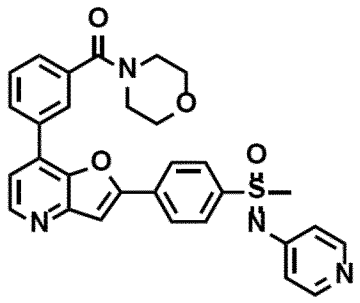
N-cyclopropyl-4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)benzamide. Synthesis according to GP4: Yield 51%. 1H NMR (300 MHz, DMSO-d6) δ = 8.62 (d, J = 5.1 Hz, 1H), 8.57 (d, J = 4.2 Hz, 1H), 8.20 (ddd, J = 7.8, 1.9, 1.2 Hz, 1H), 8.14-8.04 (m, 3H), 7.99 (d, J = 8.5 Hz, 2H),7.86 (s, 1H), 7.77-7.57 (m, 3H), 3.64 (s, 8H), 2.87 (tt, J = 7.7, 3.9 Hz, 1H), 0.77-0.55 (m, 4H); Anal. RP-HPLC tR = 0.913 min (method 2, purity 99%); LC-MS ESI: m/z = 468.1 [M+H]+ (anal. calcd for C28H26N3O4+: m/z = 468.2).



N-cyclopropyl-5-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)picolinamide. Synthesis according to GP4: Yield 10% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.22 (d, J = 1.6 Hz, 1H), 8.83 (d, J = 4.9 Hz, 1H), 8.66 (d, J = 5.0 Hz, 1H), 8.54 (dd, J = 8.2, 2.2 Hz, 1H), 8.23 (d, J= 7.9 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H), 8.09 (d, J = 17.4 Hz, 2H), 7.77-7.68 (m, 2H), 7.61 (d, J =7.7 Hz, 1H), 3.58 (m, 8H), 2.95 (q, J = 6.0 Hz, 1H), 0.76-0.65 (m, 4H); Anal. RP-HPLC tR = 1.003min (method 2, purity 99%); LC-MS ESI: m/z = 469.1 [M+H]+ (anal. calcd for C27H25N4O4+: m/z= 469.2).



(3-(2-(3-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone. Synthesis according to GP4: Yield 47%. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (d, J = 5.0 Hz, 1H), 8.27- 8.09 (m, 4H), 7.88 (s, 1H), 7.82-7.57 (m, 5H), 3.63 (s, 8H), 2.85 (s, 3H); Anal. RP-HPLC tR = 0.845min (method 2, purity 99%); LC-MS ESI: m/z = 447.0 [M+H]+ (anal. calcd for C25H23N2O4S+: m/z = 447.1).

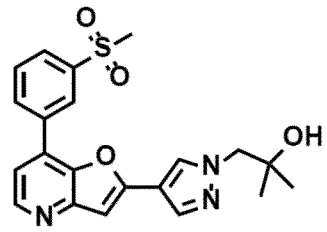


methyl(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)(pyridin-4- ylimino)-λ6-sulfanone. Synthesis according to GP4: Yield 14% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.66 (d, J = 4.8 Hz, 1H), 8.36 (br. s, 2H), 8.32-8.15 (m, 4H), 8.08-8.04 (m, 2H),7.76-7.70 (m, 3H), 7.61 (d, J = 7.7 Hz, 1H), 7.14 (br. s, 2H), 3.80 (s, 3H), 3.63 (br. s, 8H); Anal.RP-HPLC tR = 2.312 min (method 1, purity 99%); LC-MS ESI: m/z = 539.1 [M+H]+ (anal. calcd for C30H27N4O4S+: m/z = 539.2).

(3-(2-(2-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D70). Synthesis according to GP4: Yield 31% as a light brown solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.66 (d, J = 5.0 Hz, 1H), 8.25-8.12 (m, 2H), 8.06 (m, 4H), 7.74(dd, J = 8.5, 6.5 Hz, 2H), 7.61 (m,1H), 3.63 (s, 8H), 3.39 (s, 3H); Anal. RP-HPLC tR = 2.424min (method 1, purity 99%); LC-MS ESI: m/z = 481.1 [M+H]+ (anal. calcd for C25H22FN2O5S+: m/z = 481.1).

(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D68). Synthesis according to GP4: Yield 23% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (d, J = 5.0 Hz,

1H), 8.27-7.98 (m, 6H), 7.75 (t, J = 7.0 Hz, 2H), 7.61 (d, J = 7.7 Hz, 1H), 3.63 (br. s, 8H), 3.39 (s, 3H); Anal. RP-HPLC tR = 2.414 min (method 1, purity 99%); LC-MS ESI: m/z = 481.1 [M+H]+ (anal. calcd for C25H22FN2O5S+: m/z = 481.1).

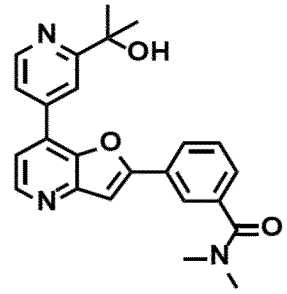


2-methyl-1-(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1H-pyrazol-1- yl)propan-2-ol. Synthesis according to GP4: Yield 76% as an off white solid. 1H NMR (300 MHz, DMSO- d6) δ = 8.66 (t, J = 1.7 Hz, 1H), 8.57 (d, J = 5.1 Hz, 1H), 8.48-8.42 (m, 1H), 8.29 (d, J = 0.8 Hz, 1H), 8.13-8.07 (m, 1H), 8.05 (d, J = 0.7 Hz, 1H), 7.91 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 5.2 Hz, 1H), 7.31 (s, 1H), 4.78 (s, 1H), 4.12 (s, 2H), 3.35 (s, 3H), 1.12 (s, 6H); Anal. RP-HPLC tR = 0.794 min (method 2, purity 99%); LC-MS ESI: m/z = 412.1 [M+H]+ (anal. calcd for C21H22N3O4S+: m/z = 412.1).

2-(4-(2-(4-(methylsulfonyl)-2-(trifluoromethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D116). Synthesis according to GP4: Yield 18%. 1H NMR (300 MHz, DMSO-d6) δ = 8.77 (d, J = 5.0 Hz, 1H), 8.71 (d, J = 5.1 Hz, 1H), 8.45-8.35 (m, 3H), 8.27 (d, J = 1.6 Hz, 1H), 7.86 (dd, J = 5.0, 1.7Hz, 1H), 7.83-7.76 (m, 2H), 5.30 (s, 1H), 3.42 (s, 3H), 1.51 (s, 6H); Anal. RP-HPLC tR = 0.954 min (method 2, purity 99%); LC-MS ESI: m/z = 477.1 [M+H]+ (anal. calcd for C23H20F3N2O4S+: m/z = 477.1).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-dimethylbenzamide (D121). Synthesis according to GP4: Yield 12%. 1H NMR (300 MHz, DMSO-d6) δ = 8.75 (d, J= 5.2 Hz, 1H), 8.67 (d, J = 5.1 Hz, 1H), 8.43 (s, 1H), 8.12 (d, J = 8.1 Hz, 2H), 7.96 (d, J = 5.2 Hz, 1H), 7.86 (s, 1H), 7.74 (d, J = 5.1 Hz, 1H), 7.59 (d, J = 8.1 Hz, 2H), 5.42 (s, 1H), 2.99 (d, J = 12.7

Hz, 6H), 1.55 (s, 6H); Anal. RP-HPLC tR = 1.350 min (method 2, purity 99%); LC-MS ESI: m/z = 402.2 [M+H]+ (anal. calcd for C24H24N3O3+: m/z = 402.2).

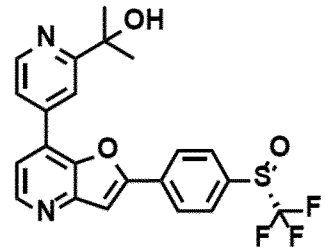


3-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-dimethylbenzamide. Synthesis according to GP4: Yield 17% as a white solid. 1H NMR (300 MHz, DMSO- d6) δ = 8.75 (d, J = 5.7 Hz, 1H), 8.66 (d, J = 5.1 Hz, 1H), 8.43 (d, J = 1.0 Hz, 1H), 8.13 (dt, J = 7.8,1.3 Hz, 1H), 8.07 (t, J = 1.4 Hz, 1H), 7.93 (dd, J = 5.1, 1.8 Hz, 1H), 7.88 (s, 1H), 7.73 (d, J = 5.1Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.51 (dt, J = 7.6, 1.2 Hz, 1H), 5.39 (s, 1H), 3.00 (d, J = 20.3 Hz,6H), 1.55 (s, 6H); Anal. RP-HPLC tR = 2.458 min (method 1, purity 99%); LC-MS ESI: m/z = 402.1 [M+H]+ (anal. calcd for C24H24N3O3+: m/z = 402.2).

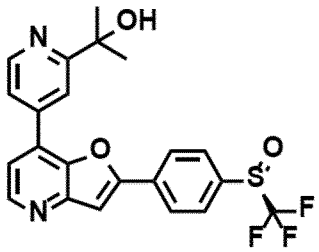
2-(4-(2-(2-methyl-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. (D122) Synthesis according to GP4: Yield 10%. 1H NMR (300 MHz, DMSO-d6) δ = 8.73 (dd, J = 5.1, 3.3 Hz, 2H), 8.44 (d, J = 1.4 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 7.99 (s, 1H), 7.91 (dd, J = 5.2, 1.8 Hz, 2H), 7.80(d, J = 5.1 Hz, 1H), 7.75 (s, 1H), 5.39 (s, 1H), 3.28 (s, 3H), 2.75 (s, 3H), 1.53 (s, 6H); Anal. RP-HPLC tR = 1.412 min (method 2, purity 99%); LC-MS ESI: m/z = 423.2 [M+H]+ (anal. calcd for C23H23N2O4S+: m/z = 423.1).

1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one (D128). Synthesis according to GP4: Yield 16%. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.1 Hz, 1H), 8.69 (d, J = 5.0 Hz, 1H), 8.48 (d, J = 1.8 Hz, 1H), 8.21 (d, J = 8.3 Hz, 2H), 8.12 (d, J = 8.3 Hz, 2H), 8.01 – 7.91 (m, 2H), 7.78 (d, J = 5.0 Hz, 1H), 5.42 (s, 1H), 2.65 (s, 3H), 1.56

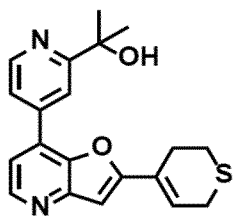
(s, 6H); Anal. RP-HPLC tR = 0.916 min (method 2, purity 99%); LC-MS ESI: m/z = 373.1 [M+H]+ (anal. calcd for C23H21N2O3+: m/z = 373.2).



(S)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan- 2-ol. Synthesis according to GP4: Yield 34%. 1H NMR (300 MHz, DMSO-d6) δ = 8.73 (dd, J = 14.3, 5.1 Hz, 2H), 8.47 (d, J = 1.7 Hz, 1H), 8.38 (d, J = 8.5 Hz, 2H), 8.13-8.00 (m, 3H), 7.97 (dd, J = 5.2, 1.8 Hz, 1H), 7.80 (d, J = 5.1 Hz, 1H), 5.43 (s, 1H), 1.55 (s, 6H); Anal. RP-HPLC tR = 1.004 min (method 2, purity 99%); LC-MS ESI: m/z = 447.1 [M+H]+ (anal. calcd for C22H18F3N2O3S+: m/z = 447.1).



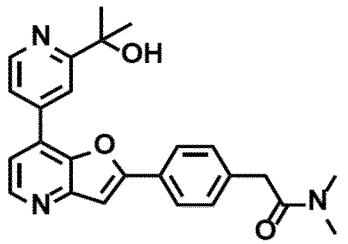
(R)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. Synthesis according to GP4: Yield 47%. Anal. RP-HPLC tR = 1.006 min (method 2, purity 99%); LC- MS ESI: m/z = 447.1 [M+H]+ (anal. calcd for C22H18F3N2O3S+: m/z = 447.1).



2-(4-(2-(3,6-dihydro-2H-thiopyran-4-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (building block). Synthesis according to GP4: Yield 67% as a white solid. Anal. RP-HPLC tR = 1.450 min (method 2, purity 96%); LC-MS ESI: m/z = 353.1 [M+H]+ (anal. calcd for C20H21N2O2S+: m/z = 353.1).

2-(4-(2-(4-(1H-tetrazol-5-yl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (C66). Synthesis according to GP4: Yield 14% as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.79- 8.75 (m, 1H), 8.65 (d, J = 5.1 Hz, 1H), 8.51 – 8.46 (m, 1H), 8.15 (q, J = 8.7 Hz, 4H), 7.96 (dd, J =5.2, 1.8 Hz, 1H), 7.77 (s, 1H), 7.72 (d, J = 5.1 Hz, 1H), 5.44 (s, 1H), 1.57 (s, 6H). The NH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.831 min (method 2, purity 97%); LC-MS ESI: m/z = 399.1 [M+H]+ (anal. calcd for C22H19N6O2+: m/z = 399.2).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methylbenzamide (D139).Synthesis according to GP4: Yield 26% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.6 Hz, 1H), 8.67 (d, J = 5.1 Hz, 1H), 8.57 (q, J = 4.2 Hz, 1H), 8.49-8.44 (m, 1H), 8.15 (d, J = 8.5 Hz, 2H), 8.02 (d, J = 8.5 Hz, 2H), 7.95 (dd, J = 5.1, 1.8 Hz, 1H), 7.89 (s, 1H), 7.76 (d, J = 5.1 Hz,1H), 5.42 (s, 1H), 2.82 (d, J = 4.5 Hz, 3H), 1.56 (s, 6H); Anal. RP-HPLC tR = 0.802 min (method 2, purity 98%); LC-MS ESI: m/z = 388.2 [M+H]+ (anal. calcd for C23H22N3O3+: m/z = 388.2).



2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-N,N-dimethylacetamide. Synthesis according to GP4: Yield 24% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.47 (s, 1H), 8.00 (d, J = 8.1 Hz,2H), 7.94 (dd, J = 5.1, 1.3 Hz, 1H), 7.71 (m, 2H), 7.41 (d, J = 8.1 Hz, 2H), 5.41 (s, 1H), 3.79 (s, 2H), 3.03 (s, 3H), 2.85 (s, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.851 min (method 2, purityn99%); LC-MS ESI: m/z = 416.2 [M+H]+ (anal. calcd for C25H26N3O3+: m/z = 416.2).

(3,3-difluoroazetidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D137). Synthesis according to GP4: Yield 23% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.1 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.43 (s, 1H), 8.16 (d, J = 8.3 Hz,2H), 7.96 (d, J = 5.3 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 5.0 Hz, 1H), 5.41 (s, 1H), 4.70 (m, 4H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.915 min (method 2, purity 99%); LC-MS ESI: m/z =450.1 [M+H]+ (anal. calcd for C25H22F2N3O3+: m/z = 450.2).

2-(4-(2-(4-(methylthio)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D130). Synthesis according to GP4: Yield 33% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.63 (d, J = 5.1 Hz, 1H), 8.44 (s, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.96-7.92 (m, 1H), 7.72 (s, 1H), 7.70 (d, J = 5.1 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 5.40 (s, 1H), 2.56 (s, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR = 1.030min (method 2, purity 99%); LC-MS ESI: m/z = 377.1 [M+H]+ (anal. calcd for C22H21N2O2S+: m/z = 377.1).

7-(3-(tert-butyl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine (D88). Synthesis according to GP4: Yield 64% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.39 (d, J = 2.0 Hz, 1H), 8.70- 8.61 (m, 2H), 8.23 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 4.2 Hz, 2H), 7.92 (d, J = 6.9 Hz, 1H), 7.72 (d, J = 5.0 Hz, 1H), 7.65-7.54 (m, 2H), 3.34 (s, 3H), 1.41 (s, 9H); Anal. RP-HPLC tR = 1.538 min (method2, purity 99%); LC-MS ESI: m/z = 407.1 [M+H]+ (anal. calcd for C23H23N2O3S+: m/z = 407.1).

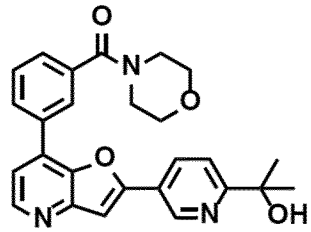
2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (racemic mixture) (D124). Synthesis according to GP4: Yield 24%. 1H NMR (300 MHz, CDCl3) δ = 8.89 (d, J = 5.4 Hz, 1H), 8.75 (d, J = 5.2 Hz, 1H), 8.22 (s, 1H), 8.09 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 5.5 Hz, 1H), 7.84 (d, J = 8.1 Hz, 2H), 7.64-7.53 (m, 2H), 2.82 (s, 3H), 1.78 (s, 6H); Anal. RP-HPLC tR = 0.775 min (method 2, purity 99%); LC-MS ESI: m/z = 393.1 [M+H]+ (anal. calcd for C22H21N2O3S+: m/z = 393.1).

(S)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D127). Synthesis according to GP4. Yield 30% as light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.68 (d, J = 5.0 Hz, 1H), 8.47 (d, J = 1.8 Hz, 1H), 8.26 (d, J = 8.2 Hz, 2H), 8.00-7.84(m, 4H), 7.77 (d, J = 5.1 Hz, 1H), 5.42 (s, 1H), 2.82 (s, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR =0.738min (method 2, purity 99%); LC-MS ESI: m/z = 393.1 [M+H]+ (anal. calcd for C22H21N2O3S+: m/z = 393.1). Separation of the (*S*)-enantiomer starting from racemic mixture (D124) was performed using the following method with a Waters 2545 Quaternary gradient Module with MassLynx Software (Version 4.1), Waters 2424 ELS Detector, Waters 2767 Sample Manager and a Chiralpak IC 5µM, (20 mm x 250 mm) Chiral Column; Isocratic Elution: Hexane/CH_2Cl_2/EtOH (50:25:25).

(R)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D126). Synthesis according to GP4: Yield 30% as light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.68 (d, J = 5.0 Hz, 1H), 8.47 (d, J = 1.8 Hz, 1H), 8.26 (d, J = 8.2 Hz, 2H), 8.00-7.84(m, 4H), 7.77 (d, J = 5.1 Hz, 1H), 5.42 (s, 1H), 2.82 (s, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR =0.777min (method 2, purity 99%); LC-MS ESI: m/z = 393.1 [M+H]+ (anal. calcd for C22H21N2O3S+:m/z = 393.1). Separation of the (*R*)-enantiomers starting from racemic mixture (D124) was performed using the following method with a Waters 2545 Quaternary gradient Module with MassLynx Software (Version 4.1), Waters 2424 ELS Detector, Waters 2767 Sample Manager and a Chiralpak IC 5µM, (20 mm x 250 mm) Chiral Column; Isocratic Elution: Hexane/CH_2Cl_2/EtOH (50:25:25).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-propylbenzamide (D141). Synthesis according to GP4: Yield 15%. 1H NMR (300 MHz, CDCl3) δ = 8.80 (d, J = 5.2 Hz, 1H), 8.68 (d, J = 5.2 Hz, 1H), 8.11 (s, 1H), 7.97-7.90 (m, 2H), 7.86 (dd, J = 5.3, 1.6 Hz, 1H),7.52 (dd, J = 8.9, 6.4

Hz, 3H), 7.44 (s, 1H), 3.53 (s, 1H), 3.24 (s, 1H), 3.04 (d, J = 32.8 Hz, 3H),1.71 (s, 8H), 0.90 (d, J = 61.3 Hz, 3H); Anal. RP-HPLC tR = 0.938 min (method 2, purity 99%); LC- MS ESI: m/z = 430.2 [M+H]+ (anal. calcd for C26H287N3O3+: m/z = 430.2).

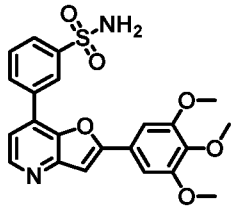


(3-(2-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone. Synthesis according to GP4: Yield 19% as a brown solid. 1H NMR (300 MHz, DMSO-d6): δ = 9.13 (d, J = 1.7 Hz, 1H), 8.62 (d, J = 5.0 Hz, 1H), 8.35 (dd, J = 8.4 Hz, J = 2.1 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 8.11 (s, 1H), 7.85 (s,1H), 7.82 (s, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.67 (d, J = 5.0 Hz, 1H), 7.60 (d, J = 5.0 Hz, 1H), 3.63 (bs, 8H), 1.76 (s, -OH, 1H), 1.49 (s, 6H); Anal. RP-HPLC tR = 0.934 min (method 2, purity 99%); LC-MS ESI: m/z = 444.2 [M+H]+ (anal. calcd for C26H26N3O4+: m/z = 444.2).

1-(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one (D94). Synthesis according to GP4: Yield 21% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.64 (d, J = 5.1 Hz, 1H), 8.22 (dt, J = 7.8, 1.3 Hz, 1H), 8.12 (dd, J = 10.0, 1.9 Hz, 5H), 7.95 (s, 1H), 7.74 (t, J = 7.7 Hz, 1H), 7.69 (d, J = 5.1 Hz, 1H), 7.61 (dt, J = 7.7, 1.3 Hz, 1H), 3.64 (br. s, 8H), 2.64 (s, 3H); Anal. RP-HPLC tR = 1.204 min (method 2, purity 99%); LC-MS ESI: m/z = 427.1 [M+H]+ (anal. calcd for C26H23N2O4+: m/z = 427.2).

Example 5: Synthesis of reactants and compounds according to the invention following General Procedure 5

General Procedure 5: Microwave Mediated Suzuki Cross-Coupling Reaction (GP5)



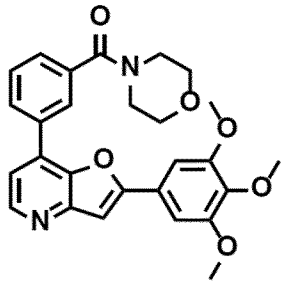
3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide (D1). To a solution of 7-chloro-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine (100 mg, 0.27 mmol) in 1,4-dioxane (1 mL) in 10 mL microwave vial, (3-sulfamoylphenyl)boronic acid (137 mg, 0.68 mmol), tris(dibenzylideneacetone)dipalladium(0) (28.6 mg, 0.03 mmol), dicyclohexyl(2',6'-diisopropoxy-[1,1'-biphenyl]-2-yl)phosphane (43.8 mg, 0.09 mmol) and tripotassium phosphate (199 mg, 0.94 mmol) were added and degassed using N2 for 5 min. Deionized water (0.2 mL) was then added and the reaction mixture was stirred for an additional 5 min. The mixture was microwaved in dynamic mode at 125 °C, 250 watts, 17.5 bar for 30 min. 1,4-dioxane was removed under reduced pressure and the residue purified by column chromatography on silica gel using hexane/ethyl acetate 8:2 v/v ratio initially and slowly increased to hexane/ethyl acetate 9.5:0.5 v/v ratio to elute 3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide in 23% yield as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.88 (s, 1H), 8.63 (d, J = 5.1 Hz, 1H), 8.32 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 7.7 Hz, 1H), 7.94-7.68 (m, 3H), 7.43 (d, J = 32.8 Hz, 4H), 3.94 (s, 6H), 3.75 (s, 3H); Anal. RP-HPLC tR = 2.600 min (method 1, purity 98%); LC-MS ESI: m/z = 441.0 [M+H]+ (anal. calcd for C22H21N2O6S+: m/z = 441.1).

Manufacturing examples

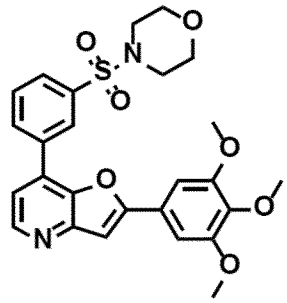
N-(2-(piperidin-1-yl)ethyl)-3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzamide (D2). Synthesis according to GP5: Yield 44%. 1H NMR (300 MHz, DMSO-d6) δ = 8.81 (s, 1H), 8.60 (d, J = 5.1 Hz, 2H), 8.27 (d, J = 8.1 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.76-7.70 (m, 3H), 7.37 (s, 2H), 3.93 (s, 6H), 3.75 (s, 3H), 3.46-3.37 (m, 2H), 2.51-2.37 (m, 6H), 1.56-1.46 (m, 4H), 1.43-1.33 (m,

2H); Anal.RP-HPLC tR = 0.831 min (method 2, purity 99%); LC-MS ESI: m/z = 516.0 [M+H]+ (anal. calcd for C30H34N3O5+: m/z = 516.3).

7-(3-(methylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine (D3). Synthesis according to GP5: Yield 68%. 1H NMR (300 MHz, DMSO-d6) δ = 8.91 (s, 1H), 8.62 (d, J = 5.1 Hz, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.92 (t, J = 7.9 Hz, 1H), 7.80-7.76 (m, 2H), 7.36 (s, 2H), 3.93 (s, 6H), 3.74 (s, 3H), 3.34 (m, 3H); Anal. RP-HPLC tR = 1.059 min (method 2, purity 99%); LC-MS ESI: m/z = 440.0 [M+H]+ (anal. calcd for C23H22NO6S+: m/z = 440.1).



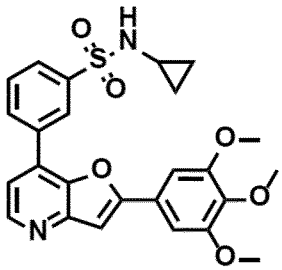
morpholino(3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 64%. 1H NMR (300 MHz, DMSO-d6) δ = 8.59 (d, J = 5.1 Hz, 1H), 8.29 (s, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.75-7.66 (m, 3H), 7.58 (d, J = 7.9 Hz, 1H), 7.33 (s, 2H), 3.92 (s, 6H), 3.74 (s, 3H), 3.62-3.50 (m, 8H); Anal. RP-HPLC tR = 2.743 min (method 1, purity 99%); LC-MS ESI: m/z = 475.0 [M+H]+ (anal. calcd for C27H27N2O6+: m/z = 475.2).



7-(3-(morpholinosulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine. Synthesis according to GP5: Yield 56%. 1H NMR (300 MHz, DMSO-d6) δ = 8.68 (s, 1H), 8.62 (d, J = 5.1 Hz, 1H), 8.48-8.45 (m, 1H), 7.96-7.92 (m, 2H), 7.80-7.76 (m, 2H), 7.34 (s, 2H), 3.92 (s, 6H), 3.74 (s, 3H), 3.63

(s, 4H), 2.96 (s, 4H); Anal. RP-HPLC tR = 1.080 min (method 2, purity 99%); LC-MS ESI: m/z = 511.0 [M+H]+ (anal. calcd for C26H27N2O7S+: m/z = 511.2).

7-(3-(cyclopropylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine (D4). Synthesis according to GP5: Yield 53%. 1H NMR (300 MHz, DMSO-d6) δ = 8.87 (s, 1H), 8.62 (d, J = 5.1 Hz, 1H), 8.45 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.92 (t, J = 7.8 Hz, 1H), 7.81-7.76 (m, 2H), 7.36 (s, 2H) 3.93 (s, 6H), 3.74 (s, 3H), 3.07-2.98 (s, 1H), 1.22-1.04 (m, 4H); Anal. RP-HPLC tR = 1.081 min (method 2, purity 97%); LC-MS ESI: m/z = 466.0 [M+H]+ (anal. calcd for C25H24NO6S+: m/z = 466.1).



N-cyclopropyl-3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide. Synthesis according to GP5: Yield 15%. 1H NMR (300 MHz, DMSO-d6) δ = 8.85 (s, 1H), 8.62 (d, J = 5.1 Hz, 1H), 8.38 (d, J = 7.9 Hz, 1H), 8.04-7.97 (m, 2H), 7.88 (t, J = 7.9 Hz, 1H), 7.81 (s, 1H), 7.75 (d, J = 5.1 Hz, 1H), 7.37 (s, 2H), 3.93 (s, 6H), 3.74 (s, 3H), 2.19-2.15 (m, 1H), 0.52-0.38 (m, 4H); Anal. RP-HPLC tR = 1.090 min (method 2, purity 98%); LC-MS ESI: m/z = 481.0 [M+H]+ (anal. calcd for C25H25N2O6S+: m/z = 481.1).

2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine. (D7) Synthesis according to GP5: Yield 40%. 1H NMR (300 MHz, DMSO-d6) δ = 8.64 (s, 1H), 8.56 (d, J = 5.0 Hz, 1H), 8.45 (d, J = 7.8 Hz, 1H), 8.32 (s, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.03 (s, 1H), 7.90 (t, J = 7.8 Hz, 1H), 7.66 (d,J = 5.0 Hz, 1H), 7.26 (s, 1H), 3.94 (s, 3H), 3.35 (s, 3H); Anal. RP-HPLC tR = 0.794 min (method 2, purity 96%); LC-MS ESI: m/z = 354.0 [M+H]+ (anal. calcd for C18H16N3O3S+: m/z = 354.1).

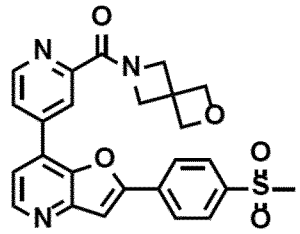
1-methyl-5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one (D12). Synthesis according to GP5: Yield 73%. 1H NMR (300 MHz, DMSO-d6) δ = 8.73 (t, J = 1.8 Hz, 1H), 8.58 (d, J = 5.1 Hz, 1H), 8.47-8.44 (m, 1H), 8.41 (d, J = 2.6 Hz, 1H), 8.11-8.08 (m, 1H), 8.04 (dd, J = 9.5 Hz & 2.6 Hz, 1H), 7.91 (t, J = 8.1 Hz, 1H), 7.70 (d, J = 5.2 Hz, 1H), 7.46 (s, 1H), 6.59 (d, J = 9.5 Hz, 1H), 3.56 (s, 3H), 3.36 (s, 3H); Anal. RP-HPLC tR = 0.800 min (method 2, purity 98%); LC-MS ESI: m/z = 381.0 [M+H]+ (anal. calcd for C20H17N2O4S+: m/z = 381.1).

5-(7-(3-(cyclopropylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one (D25). Synthesis according to GP5: Yield 52%. 1H NMR (300 MHz, DMSO-d6) δ = 8.68 (t, J = 1.8 Hz, 1H), 8.59 (d, J = 5.1 Hz, 1H), 8.47 (dt, J = 7.9, 1.4 Hz, 1H), 8.41 (d, J = 2.6 Hz, 1H), 8.11-8.01 (m, 2H), 7.92 (t, J = 7.8 Hz, 1H), 7.70 (d, J = 5.1 Hz, 1H), 7.47 (s, 1H), 6.60 (d, J = 9.5 Hz, 1H), 3.57 (s, 3H), 3.05 (tt, J = 7.9, 4.8 Hz, 1H), 1.28-1.06 (m, 4H); Anal. RP-HPLC tR = 0.866 min (method 2, purity 99%); LC-MS ESI: m/z = 407.0 [M+H]+ (anal. calcd for C22H19N2O4S+: m/z = 407.1).

N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)furo[3,2- b]pyridin-7-yl)benzenesulfonamide (D30). Synthesis according to GP5: Yield 26%. 1H NMR (300 MHz, DMSO- d6) δ = 8.66 (t, J = 1.8 Hz, 1H), 8.59 (d, J = 5.1 Hz, 1H), 8.45 (d, J = 2.6 Hz, 1H), 8.36 (dt, J = 7.8, 1.4 Hz, 1H), 8.06 (dd, J = 9.5, 2.6 Hz, 1H), 7.96 (dt, J = 7.9, 1.3 Hz, 1H), 7.85 (t, J = 7.8 Hz, 1H), 7.65 (d, J = 5.1 Hz, 2H), 7.47 (s, 1H), 6.60 (d, J = 9.5 Hz, 1H), 4.42 (s, 1H), 3.58 (s, 3H), 2.71 (s, 2H), 1.07 (s, 6H); Anal. RP-HPLC tR = 0.808 min (method 2, purity 99%); LC-MS ESI: m/z = 454.1 [M+H]+ (anal. calcd for C23H24N3O5S+: m/z = 454.1).

5-(7-(3-((3-aminoazetidin-1-yl)sulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin- 2(1H)-one (D32). Synthesis according to GP5: Yield 25%. 1H NMR (300 MHz, DMSO-d6) δ = 8.60 (d, J = 5.1 Hz, 1H), 8.57 (q, J = 1.4 Hz,

1H), 8.48 (dt, J = 6.4, 2.1 Hz, 1H), 8.39 (d, J = 2.6 Hz, 1H), 8.03 (dd, J =9.5, 2.6 Hz, 1H), 7.98-7.93 (m, 2H), 7.71 (d, J = 5.2 Hz, 1H), 7.48 (s, 1H), 6.61 (d, J = 9.5 Hz, 1H), 4.00-3.89 (m, 2H), 3.56 (s, 3H), 3.56-3.47 (m, 1H), 3.38 (dd, J = 8.0, 6.6 Hz, 2H); Anal. RP-HPLC tR = 0.667 min (method 2, purity 96%); LC-MS ESI: m/z = 437.1 [M+H]+ (anal. calcd for C22H21N4O4S+: m/z = 437.1).

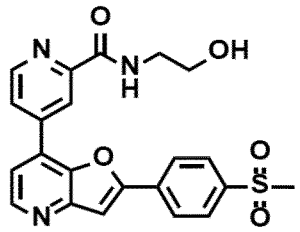


(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone. Synthesis according to GP4: Yield 52% as a white solid. 1H NMR (300 MHz, CDCl3) δ = 8.90 (d, J = 5.0 Hz, 1H), 8.82 (m, 1H), 8.72 (d, J = 5.6 Hz, 1H), 8.12-8.19(m, 4H), 8.01 (dd, J = 5.1, 1.9 Hz, 1H), 7.85 (s, 1H), 7.78 (d, J = 5.4 Hz, 1H), 5.00 (br. s, 2H), 4.86-4.91 (m, 4H), 4.45 (br. s, 2H), 3.12 (s, 3H); Anal. RP-HPLC tR = 0.909 min (method 2, purity 99%); LC-MS ESI: m/z = 476.0 [M+H]+ (anal. calcd for C25H22N3O5S+: m/z = 476.1).

2-methyl-1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol (D125). Synthesis according to GP5: Yield 35% as a light pink solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.62 (d, J = 5.0 Hz, 1H), 8.28 (d, J = 8.3 Hz, 2H), 8.09 (d, J = 8.3 Hz, 2H), 8.00 (d, J = 10.8 Hz, 2H), 7.90 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 4.9 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H), 4.44 (s, 1H), 3.30 (s, 3H), 2.82 (s, 2H), 1.18 (s, 6H); Anal. RP-HPLC tR = 1.011 min (method 2, purity 99%); LC-MS ESI: m/z = 422.1 [M+H]+ (anal. calcd for C24H24NO4S+: m/z = 422.1).

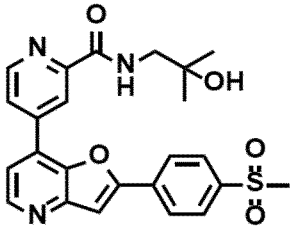
7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)phenyl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (D123). Synthesis according to GP5: Yield 5% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.86 (d,

J = 6.1 Hz, 1H), 8.36 (d, J = 8.4 Hz, 2H), 8.24-8.10 (m, 4H), 7.56-7.34 (m, 3H), 6.94 (dd, J = 5.5, 2.9 Hz, 1H), 4.70 (d, J = 13.5 Hz, 2H), 3.81 (q, J = 7.2 Hz, 2H), 3.63 (d, J = 9.1 Hz, 1H), 3.29 (s, 3H), 3.16 (s, 1H), 2.05-1.90 (m, 2H); Anal. RP-HPLC tR = 1.552 min (method 2, purity 97%); LC-MS ESI: m/z = 447.1 [M+H]+ (anal. calcd for C25H23N2O4S+: m/z = 447.1).



N-(2-hydroxyethyl)-4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)picolinamide. Synthesis according to GP5: Yield 14%. 1H NMR (300 MHz, DMSO-d6) δ = 8.92 (dd, J = 5.1, 0.8 Hz, 1H), 8.82 (t, J = 5.9 Hz, 1H), 8.78 (dd, J = 1.9, 0.8 Hz, 1H), 8.73 (d, J = 5.1 Hz, 1H), 8.36 (dd, J = 5.1,1. Hz, 1H), 8.31 (d, J = 8.6 Hz, 2H), 8.12 (d, J = 8.5 Hz, 2H), 8.05 (s, 1H), 7.89 (d, J = 5.1 Hz, 1H), 4.84 (t, J = 5.4 Hz, 1H), 3.60 (q, J = 5.7 Hz, 2H), 3.47 (q, J = 5.9 Hz, 2H), 3.31 (s, 3H); Anal. RP-HPLC tR = 0.856 min (method 2, purity 99%); LC-MS ESI: m/z = 438.0 [M+H]+ (anal. calcd for C22H20N3O5S+: m/z = 438.1).

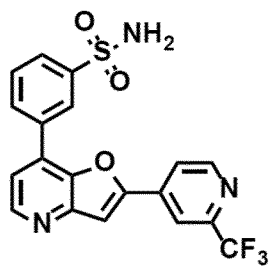
(3-hydroxyazetidin-1-yl)(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2- yl)methanone (D29). Synthesis according to GP5: Yield 9%. 1H NMR (300 MHz, DMSO-d6) δ = 8.88 (d, J = 5.1 Hz, 1H), 8.78-8.65 (m, 2H), 8.28 (t, J = 7.3 Hz, 3H), 8.11 (d, J = 8.1 Hz, 2H), 8.03 (s, 1H), 7.84 (d,J = 5.1 Hz, 1H), 5.74 (s, 1H), 4.84 (dd, J = 10.7, 6.6 Hz, 1H), 4.56 (s, 1H), 4.36 (td, J = 11.8, 11.3, 5.5 Hz, 2H), 3.88 (dd, J = 11.0, 4.2 Hz, 1H), 3.32 (s, 3H); Anal. RP-HPLC tR = 0.851 min (method2, purity 99%); LC-MS ESI: m/z = 450.0 [M+H]+ (anal. calcd for C23H20N3O5S+: m/z = 450.1).



N-(2-hydroxy-2-methylpropyl)-4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7- yl)picolinamide. Synthesis according to GP5: Yield 18%. 1H NMR (300 MHz, DMSO-d6) δ = 8.94 (dd, J = 5.1, 0.8 Hz, 1H), 8.79 (dd, J = 1.9, 0.8 Hz, 1H), 8.73 (d, J = 5.1 Hz, 1H), 8.61 (t, J = 6.0 Hz, 1H),8.38 (dd, J = 5.1, 1.9 Hz, 1H), 8.31 (d, J = 8.5 Hz, 2H), 8.11 (d, J = 8.6 Hz, 2H), 8.05 (s, 1H), 7.90 (d, J = 5.1 Hz, 1H), 4.76 (s, 1H), 3.37 (d, J = 6.1 Hz, 2H), 3.31 (s, 3H), 1.17 (s, 6H); Anal. RP-HPLC tR = 0.925 min (method 2, purity 99%); LC-MS ESI: m/z = 466.1 [M+H]+ (anal. calcd for C24H24N3O5S+: m/z = 466.1).

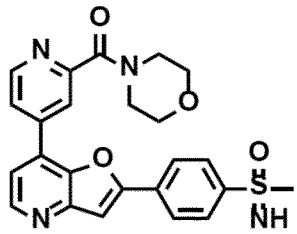
N-(2-hydroxy-2-methylpropyl)-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7- yl)benzenesulfonamide (D31). Synthesis according to GP5: Yield 44%. 1H NMR (300 MHz, DMSO-d6) δ = 8.69 (d, J = 5.1 Hz, 1H), 8.61 (t, J = 1.7 Hz, 1H), 8.37 (ddd, J = 7.8, 1.9, 1.1 Hz, 1H), 8.32-8.27 (m, 2H),8.12-8.07 (m, 2H), 8.03 (s, 1H), 7.99 (ddd, J = 7.9, 1.8, 1.1 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.74 (d, J = 5.1 Hz, 1H), 7.66 (s, 1H), 4.44 (s, 1H), 3.29 (s, 3H), 2.73 (s, 2H), 1.07 (s, 6H); Anal. RP-HPLC tR = 0.947 min (method 2, purity 99%); LC-MS ESI: m/z = 501.1 [M+H]+ (anal. calcd for C24H25N2O6S2+: m/z = 501.1).

N-(2-hydroxy-2-methylpropyl)-3-(2-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7- yl)benzenesulfonamide (D28). Synthesis according to GP5: Yield 9%. 1H NMR (300 MHz, DMSO-d6) δ = 8.68 (d, J = 5.1 Hz, 1H), 8.60 (t, J = 1.8 Hz, 1H), 8.52 (t, J = 1.8 Hz, 1H), 8.37 (ddt, J = 7.0, 5.3, 1.3 Hz, 2H), 8.08-7.94 (m, 3H), 7.86 (td, J = 7.8, 4.8 Hz, 2H), 7.73 (d, J = 5.1 Hz, 1H), 4.41 (s, 1H), 3.35 (s, 3H), 2.72 (s, 2H), 1.07 (s, 6H); Anal. RP-HPLC tR = 0.925 min (method 2, purity 99%); LC-MS ESI: m/z = 501.0 [M+H]+ (anal. calcd for C24H25N2O6S2+: m/z = 501.1).

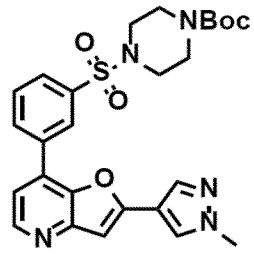


3-(2-(2-(trifluoromethyl)pyridin-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide. Synthesis according to GP5: Yield 29%. 1H NMR (300 MHz, DMSO-d6) δ = 8.96 (d, J = 5.2 Hz, 1H), 8.82- 8.63 (m, 2H), 8.50 (d, J = 1.2 Hz, 1H), 8.43-8.22 (m, 3H), 8.03 (ddd, J = 7.9, 1.9, 1.1 Hz, 1H), 7.94-7.72 (m, 2H), 7.53 (s, 2H); Anal. RP-HPLC tR = 2.576 min (method 1, purity 99%); LC-MS ESI: m/z = 420.0 [M+H]+ (anal. calcd for C19H13F3N3O3S+: m/z = 420.1).

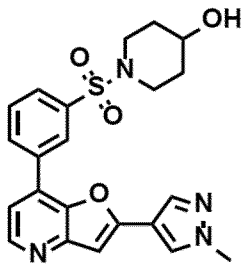
imino(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone (D50). Synthesis according to GP5: Yield 88% as a light yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.65 (d, J = 5.1 Hz, 1H), 8.18-8.00 (m, 6H), 7.67 (t, J = 7.7 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.51(s, 1H), 7.47 (d, J = 5.1 Hz, 1H), 3.73 (br. s, 8H), 3.16 (s, 3H), 2.10 (s, 1H); Anal. RP-HPLC tR =0.809 min (method 2, purity 99%); LC-MS ESI: m/z = 462.0 [M+H]+ (anal. calcd for C25H24N3O4S+:m/z = 462.2).



imino(methyl)(4-(7-(2-(morpholine-4-carbonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)- λ6-sulfanone. Synthesis according to GP5: Yield 23% as a yellow powder. 1H NMR (CDCl3+MeOD-d4) δ = 8.80 (d, J = 4.9 Hz, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.26 (s, 1H), 8.11-8.19 (m, 4H), 7.99 (dd, J = 5.0, 1.7 Hz, 1H), 7.54-7.80 (m, 2H), 3.82 (br s, 4H), 3,72 (br s, 4H), 1.98 (s, 3H). The NH signal wasnot observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.780 min (method 2, purity 95%); LC-MS ESI: m/z = 463.0 [M+H]+ (anal. calcd for C24H23N4O4S+: m/z = 463.1).



tert-butyl 4-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)piperazine-1-carboxylate (building block). Synthesis according to GP5: Yield 55%. Anal. RP-HPLC tR = 1.054 min (method 2, purity 93%); LC-MS ESI: m/z = 524.1 [M+H]+ (anal. calcd for C26H30N5O5S+:



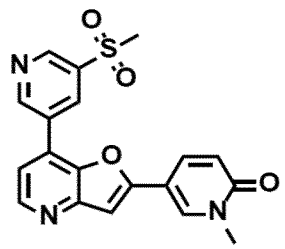
1-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)piperidin-4-ol. Synthesis according to GP5: Yield 10%. 1H NMR (300 MHz, MeOD-d4) δ = 8.59-8.45 (m, 2H), 8.32 (d, J = 7.8 Hz, 1H), 8.17 (s, 1H), 8.04-7.80 (m, 3H), 7.57 (d, J = 5.3 Hz, 1H), 7.07 (s, 1H), 4.00 (s, 3H), 3.69 (s, 1H), 3.46 (d, J = 9.5 Hz, 2H), 2.95 (td, J = 9.1, 8.7, 4.6 Hz, 2H), 1.93 (d, J = 12.1 Hz, 2H), 1.72-1.52 (m, 2H); Anal. RP-HPLC tR = 0.815 min (method 2, purity 96%); LC-MS ESI: m/z = 439.0 [M+H]+ (anal. calcd for C22H23N4O4S+: m/z = 439.1).

7-(3-(cyclopropylsulfonyl)phenyl)-2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine (D18). Synthesis according to GP5: Yield 18%. 1H NMR (300 MHz, DMSO-d6) δ = 8.57 (d, J = 8.4 Hz, 2H), 8.45 (d, J = 7.9 Hz, 1H), 8.33 (s, 1H), 8.13-7.99 (m, 2H), 7.91 (t, J = 7.9 Hz, 1H), 7.65 (d, J = 5.1 Hz, 1H), 7.26 (s, 1H), 3.95 (s, 3H), 3.03 (s, 1H), 1.30-1.02 (m, 4H); Anal. RP-HPLC tR = 0.848 min (method2, purity 95%); LC-MS ESI: m/z = 380.0 [M+H]+ (anal. calcd for C20H18N3O3S+: m/z = 380.1).

1-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)azetidin-3-ol (D20). Synthesis according to GP5: Yield 29%. 1H NMR (300 MHz, DMSO-d6) δ = 8.57 (d, J = 5.1 Hz, 1H), 8.53- 8.42 (m, 2H), 8.29 (s, 1H), 8.05-7.91 (m, 3H), 7.66 (d, J = 5.1 Hz, 1H), 7.27 (s, 1H), 5.77 (d, J = 6.1 Hz, 1H), 4.34 (h, J = 6.0 Hz, 1H), 4.00 (dd, J = 8.4, 6.6 Hz, 2H), 3.94 (s, 3H), 3.47 (dd, J = 8.4, 5.7 Hz, 2H); Anal. RP-HPLC tR = 0.779 min (method 2, purity 99%); LC-MS ESI: m/z = 411.0 [M+H]+ (anal. calcd for C20H19N4O4S+: m/z = 411.1).

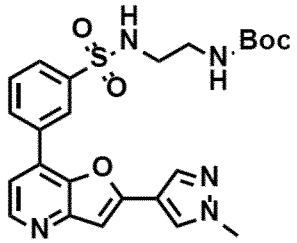
N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7- yl)benzenesulfonamide (D21). Synthesis according to GP5: Yield 47%. 1H NMR (300 MHz, DMSO-d6) δ = 8.56 (t, J = 3.6 Hz, 2H), 8.34 (d, J = 4.4 Hz, 2H), 8.05 (s, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.84 (t, J = 7.8Hz, 1H), 7.73-7.54 (m, 2H), 7.27 (s, 1H), 4.45 (s, 1H), 3.94 (s, 3H), 2.72 (d, J = 6.5 Hz, 2H), 1.08 (s, 6H); Anal. RP-HPLC tR = 0.795 min (method 2, purity 99%); LC-MS ESI: m/z = 427.0 [M+H]+ (anal. calcd for C21H23N4O4S+: m/z = 427.1).

4-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)piperazin-2-one (D24). Synthesis according to GP5: Yield 20%. 1H NMR (300 MHz, DMSO-d6) δ = 8.57 (d, J = 5.1 Hz, 1H), 8.49- 8.39 (m, 2H), 8.31 (s, 1H), 8.12-7.88 (m, 4H), 7.63 (d, J = 5.1 Hz, 1H), 7.28 (s, 1H), 3.95 (s, 3H), 3.68 (s, 2H), 3.25 (t, J = 2.6 Hz, 2H), 3.10 (m, 2H); Anal. RP-HPLC tR = 0.783 min (method 2, purity 99%); LC-MS ESI: m/z = 438.0 [M+H]+ (anal. calcd for C21H20N5O4S+: m/z = 438.1).

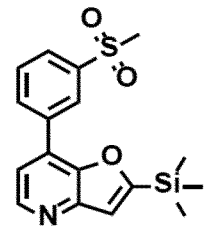


1-methyl-5-(7-(5-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one. Synthesis according to GP5: Yield 18%. 1H NMR (300 MHz,

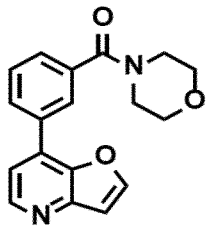
DMSO-d6) δ = 9.63 (d, J = 2.2 Hz, 1H), 9.23 (d, J = 2.2 Hz, 1H), 9.03 (t, J = 2.2 Hz, 1H), 8.63 (d, J = 5.1 Hz, 1H), 8.45 (d, J = 2.6 Hz, 1H), 8.05 (dd, J = 9.5, 2.6 Hz, 1H), 7.81 (d, J = 5.1 Hz, 1H), 7.50 (s, 1H), 6.60 (d, J = 9.5 Hz, 1H), 3.57 (s, 3H),3.48 (s, 3H); Anal. RP-HPLC tR = 2.436 min (method 1, purity 97%); LC-MS ESI: m/z = 382.2 [M+H]+ (anal. calcd for C19H16N3O4S+: m/z = 382.1).



tert-butyl (2-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonamido)ethyl)carbamate (building block). Synthesis according to GP5: Yield 65%. Anal. RP-HPLC tR = 0.922 min (method 2, purity 96%); LC-MS ESI: m/z = 498.3 [M+H]+ (anal. calcd for C24H28N5O5S+: m/z = 498.2).



7-(3-(methylsulfonyl)phenyl)-2-(trimethylsilyl)furo[3,2-b]pyridine (building block). Synthesis according to GP5: Yield 65%. Anal. RP-HPLC tR = 2.804 min (method 1, purity 93%); LC-MS ESI: m/z = 345.8 [M+H]+ (anal. calcd for C17H20NO3SSi+: m/z = 346.1).



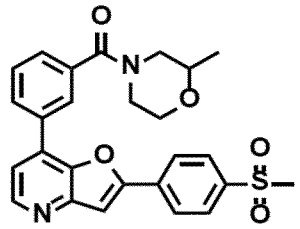
(3-(furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (building block). Synthesis according to GP5: Yield 12% as an orange solid. Anal. RP-HPLC tR

= 2.282 min (method 1, purity 95%); LC-MS ESI: m/z = 309.1 [M+H]+ (anal. calcd for C18H17N2O3+: m/z = 309.1).

7-(3-(methylsulfonyl)phenyl)-2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine (D16). Synthesis according to GP5: Yield 35%. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (t, J = 1.8 Hz, 1H), 8.58 (d, J = 5.1 Hz, 1H), 8.38 (dt, J = 7.8, 1.4 Hz, 1H), 8.12-8.07 (m, 1H), 7.90 (t, J = 7.9 Hz, 1H), 7.62 (d, J = 5.1 Hz, 1H), 7.06 (s, 1H), 3.76 (s, 3H), 3.31 (s, 3H), 2.53 (s, 3H), 2.39 (s, 3H); Anal. RP-HPLC tR = 2.632 min (method 1, purity 96%); LC-MS ESI: m/z = 381.9 [M+H]+ (anal. calcd for C20H20N3O3S+: m/z = 382.1).

N-(2-hydroxyethyl)-3-(2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide (D17). Synthesis according to GP5: Yield 34%. 1H NMR (300 MHz, DMSO-d6) δ = 8.58 (d, J = 5.1 Hz, 1H), 8.51 (t, J = 1.6 Hz, 1H), 8.32-8.25 (m, 1H), 7.99-7.93 (m, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.71 (s, 1H), 7.58 (d, J = 5.1 Hz, 1H), 7.07 (s, 1H), 4.68 (t, J = 5.5 Hz, 1H), 3.76 (s, 3H), 3.39 (q, J = 6.0 Hz, 2H), 2.85 (q, J = 6.0 Hz, 2H), 2.53 (s, 3H), 2.39 (s, 3H); Anal. RP-HPLC tR = 2.205 min (method 1, purity 98%); LC-MS ESI: m/z = 426.9 [M+H]+ (anal. calcd for C21H23N4O4S+: m/z = 427.1).

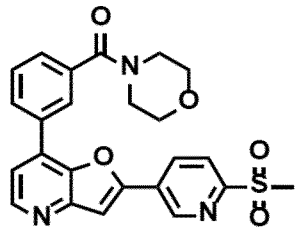
N-(2-hydroxyethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide (D19). Synthesis according to GP5: Yield 32%. 1H NMR (300 MHz, DMSO-d6) δ = 8.56- 8.50 (m, 2H), 8.35-8.28 (m, 2H), 8.02 (d, J = 0.7 Hz, 1H), 7.97-7.91 (m, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.76 (t, J = 5.9 Hz, 1H), 7.57 (d, J = 5.1 Hz, 1H), 7.24 (s, 1H), 4.71 (t, J = 5.5 Hz, 1H), 3.92 (s, 3H), 3.40 (q, J = 6.1 Hz, 2H), 2.89 (q, J = 6.1 Hz, 2H); Anal. RP-HPLC tR = 0.729 min (method 2, purity 97%); LC-MS ESI: m/z = 399.2 [M+H]+ (anal. calcd for C19H19N4O4S+: m/z = 399.1).



(2-methylmorpholino)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D63). Synthesis according to GP5: Yield 33%. 1H NMR (300 MHz, DMSO-d6+TFA) δ = 8.74 (d, J = 5.3 Hz, 1H), 8.34-8.23 (m, 3H), 8.16-8.09 (m, 3H), 8.06 (s, 1H), 7.85 (d, J = 5.3 Hz, 1H), 7.77 (t, J = 7.7 Hz, 1H), 7.65 (dt, J = 7.7, 1.4 Hz, 1H), 4.60-3.36 (m, 5H), 3.31 (s, 3H), 3.13- 2.58 (m, 1H), 1.29-0.95 (m, 4H); Anal. RP-HPLC tR = 2.440 min (method 1, purity 99%); LC-MS ESI: m/z = 477.1 [M+H]+ (anal. calcd for C26H25N2O5S+: m/z = 477.1).

1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)cyclobutan-1-ol (D64). Synthesis according to GP5: Yield 8%. 1H NMR (300 MHz, CDCl3) δ = 8.67 (s, 1H), 8.26 (t, J = 1.7 Hz, 1H), 8.14-8.04 (m, 4H), 7.93 (dt, J = 7.7, 1.5 Hz, 1H), 7.73 (dt, J = 7.9, 1.4 Hz, 1H), 7.65 (t, J = 7.7 Hz,1H), 7.54 (s, 2H), 3.13 (s, 3H), 2.78-2.65 (m, 2H), 2.58-2.44 (m, 2H), 2.24-2.08 (m, 1H), 1.93-1.77 (m, 1H), 1.28 (s, 1H); Anal. RP-HPLC tR = 1.016 min (method 2, purity 99%); LC-MS ESI: m/z = 420.0 [M+H]+ (anal. calcd for C24H22NO4S+: m/z = 420.1).

2- methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2- ol (D48). Synthesis according to GP5: Yield 28% as an off white solid. 1H NMR (300 MHz, CDCl3) δ = 8.78 (d, J = 5.3 Hz, 1H), 8.72 (d, J = 5.0 Hz, 2H), 8.11-8.05 (m, 3H), 7.87-7.79 (m, 2H), 7.53-7.47 (m, 2H),3.16 (s, 3H), 3.12 (s, 3H), 1.34 (s, 6H); Anal. RP-HPLC tR = 0.771 min (method 2, purity 99%); LC-MS ESI: m/z = 423.0 [M+H]+ (anal. calcd for C23H23N2O4S+: m/z = 423.1).



(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone. Synthesis according to GP5: Yield 10%. 1H NMR (300 MHz, CDCl3) δ = 8.89 (d, J = 5.1 Hz, 1H), 8.76 (d, J = 5.3 Hz, 1H), 8.39 (s, 1H), 8.16 (s, 4H), 8.03 (d, J = 5.0 Hz,1H), 7.74 (s, 1H), 7.69 (s, 1H), 3.98 – 3.72 (m, 8H), 3.14 (s, 3H); Anal. RP-HPLC tR = 2.345 min(method 1, purity 96%); LC-MS ESI: m/z = 464.0 [M+H]+ (anal. calcd for C24H22N3O5S+: m/z = 464.1).

(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D62). Synthesis according to GP5: Yield 40% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.59 (d, J = 5.0 Hz, 1H), 8.20 (d, J = 7.7 Hz, 1H), 8.11 (s, 1H), 7.94 (d, J= 8.1 Hz, 2H), 7.78-7.54 (m, 6H), 3.64 (br. s, 8H), 1.47 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 2.519 min (method 1, purity 99%); LC-MS ESI: m/z = 443.1 [M+H]+ (anal. calcd for C27H27N2O4+: m/z = 443.2).

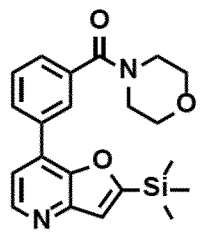
2-(4-(methylsulfinyl)phenyl)-7-(2-morpholinopyridin-4-yl)furo[3,2-b]pyridine (D57). Synthesis according to GP5: Yield 6% as a light yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.64 (d, J = 4.9 Hz, 1H), 8.42 (d, J = 5.1 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 7.43-7.41 (m, 2H), 7.23-7.21(m, 2H), 3.92-3.83 (m, 4H), 3.68-3.61 (m, 4H), 2.78 (s, 3H); Anal. RP-HPLC tR = 0.811 min(method 2, purity 99%); LC-MS ESI: m/z = 420.0 [M+H]+ (anal. calcd for C23H22N3O3S+: m/z = 420.1).

1-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol (D58).

Synthesis according to GP5: Yield 12% as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 5.0 Hz, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.23-8.20 (m, 2H), 7.91-7.87 (m, 3H), 7.72 (d, J = 5.1 Hz,1H), 7.32 (d, J = 5.2 Hz, 1H), 7.08 (s, 1H), 5.70 (d, J = 5.0 Hz, 1H), 4.72-4.59 (m, 1H), 4.35-4.22 (m, 2H), 3.87-3.77 (m, 2H), 2.83 (s, 3H); Anal. RP-HPLC tR = 0.685 min (method 2, purity 99%); LC-MS ESI: m/z = 406.0 [M+H]+ (anal. calcd for C22H20N3O3S+: m/z = 406.1).

1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol (D42). Yield 26% as a yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.59 (d, J = 4.9 Hz, 1H), 8.26-8.16 (m,3H), 8.12-8.07 (m, 2H), 7.71-7.58 (m, 2H), 7.28 (dd, J = 5.5, 1.5 Hz, 1H), 7.09-7.04 (m, 1H), 4.45-4.33 (m, 2H), 3.95-3.90 (m, 2H), 3.19 (s, 3H); Anal. RP-HPLC tR = 0.715 min (method 2, purity 99%); LC-MS ESI: m/z = 422.0 [M+H]+ (anal. calcd for C22H20N3O4S+: m/z = 422.1).

(cyclopropylimino)(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2- yl)phenyl)-λ6-sulfanone (D61). Synthesis according to GP5: Yield 18% as a white solid. 1H NMR (300 MHz, CDCl3) δ = 8.45 (s, 1H), 7.84 (m, 6H), 7.46 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 7.7 Hz, 1H), 7.23 (d, J = 4.8 Hz, 1H), 7.04 (d, J = 9.4 Hz, 1H), 3.52 (s, 8H), 2.93 (s, 3H), 2.25-2.17 (m, 1H), 0.46-0.16 (m, 4H); Anal. RP-HPLC tR = 2.493 min (method 1, purity 95%); LC-MS ESI: m/z = 502.1 [M+H]+ (anal. calcd for C28H28N3O4S+: m/z = 502.2).



morpholino(3-(2-(trimethylsilyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (building block). Synthesis according to GP5: Yield 78%; Anal. RP-HPLC tR = 2.552 min (method 1, purity 96%); LC-MS ESI: m/z = 381.1 [M+H]+ (anal. calcd for C21H25N2O3Si+: m/z = 381.2).

2-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol (D76). Synthesis according to GP5: Yield 13%. 1H NMR (300 MHz, CDCl3) δ = 9.25 (dd, J = 2.2, 0.8 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.42 (dd, J = 8.2, 2.2 Hz, 1H), 8.26 (t, J = 1.9 Hz, 1H), 8.21 (dd, J = 8.3, 0.8 Hz,1H), 7.89 (dt, J = 7.6, 1.5 Hz, 1H), 7.72-7.54 (m, 4H), 3.30 (s, 3H), 1.73 (s, 6H); Anal. RP-HPLC tR = 0.986 min (method 2, purity 99%); LC-MS ESI: m/z = 409.0 [M+H]+ (anal. calcd for C22H21N2O4S+: m/z = 409.1).

3-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol (D79). Synthesis according to GP5: Yield 18%. 1H NMR (300 MHz, DMSO-d6+TFA) δ = 9.45 (d, J = 2.1 Hz, 1H), 8.77 – 8.71 (m, 2H), 8.52 (t, J = 1.8 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 8.17 (s, 1H), 8.12 (dt, J = 7.8, 1.4 Hz, 1H), 7.90 (d, J = 5.3 Hz, 1H), 7.88-7.83 (m, 1H), 7.70 (t, J = 7.8 Hz, 1H), 4.91 (d, J = 6.5 Hz, 2H), 4.82 (d, J = 6.5 Hz, 2H), 3.36 (s, 3H); Anal. RP-HPLC tR = 2.343 min (method 1, purity 97%); LC-MS ESI: m/z = 423.0 [M+H]+ (anal. calcd for C22H19N2O5S+: m/z = 423.1).

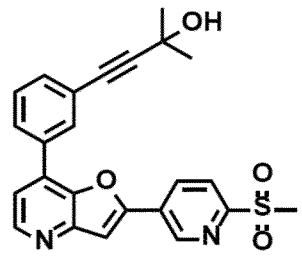
2-(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol (D80). Synthesis according to GP5: Yield 11%. 1H NMR (300 MHz, CDCl3) δ = 9.23 (s, 1H), 8.72 (s, 1H), 8.45-8.36 (m, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.76 (s, 1H), 7.63 (dd, J = 15.5, 8.7 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 3.31 (s, 3H), 1.78 (s, 6H), 1.28 (s, 1H); Anal. RP-HPLC tR = 2.458 min (method 1, purity 99%); LC-MS ESI: m/z = 427.0 [M+H]+ (anal. calcd for C22H20FN2O4S+: m/z = 427.1).

3-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol (D81). Synthesis according to GP5: Yield 15%. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (d, J = 5.1 Hz, 1H), 8.53 (t, J = 1.8 Hz, 1H), 8.34-8.28 (m, 2H), 8.12-8.05 (m, 3H), 8.01 (s, 1H), 7.83 (ddd, J = 7.8, 1.9, 1.2 Hz, 1H), 7.77 (d, J = 5.1 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 4.95-4.89 (m, 2H), 4.86-4.80 (m, 2H), 3.30 (s, 3H);

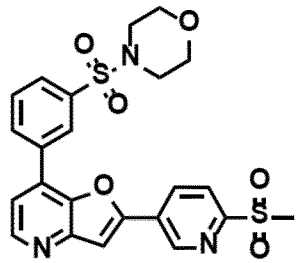
Anal. RP-HPLC tR = 1.199 min (method 2, purity 99%); LC-MS ESI: m/z = 422.1 [M+H]+ (anal. calcd for C23H20NO5S+: m/z = 4212.1).

N,N-dimethyl-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)benzamide (D82). Synthesis according to GP5: Yield 30%. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (dd, J = 2.2, 0.8 Hz, 1H), 8.70-8.64 (m, 2H), 8.24 (dd, J = 8.2, 0.9 Hz, 2H), 8.14 (s, 1H), 8.12-8.10 (m, 1H), 7.77-7.69 (m, 2H), 7.61 (dt, J = 7.7, 1.4 Hz, 1H), 3.36 (s, 3H), 3.04 (s, 6H); Anal. RP-HPLC tR = 2.381 min (method 1, purity 99%); LC-MS ESI: m/z = 422.0 [M+H]+ (anal. calcd for C22H20N3O4S+: m/z = 422.1).

(2-fluoro-5-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D87). Synthesis according to GP5: Yield 28%. 1H NMR (300 MHz, CDCl3) δ = 9.26 (d, J = 2.0 Hz, 1H), 8.71 (d, J = 5.1 Hz, 1H), 8.44 (dd, J = 8.2, 2.1 Hz, 1H), 8.25 (d, J = 8.2 Hz, 1H), 8.10 (ddd, J = 14.9, 5.8, 2.6 Hz, 2H), 7.68 (s, 1H), 7.53 (d, J = 5.1 Hz, 1H), 7.39 (t, J = 8.7 Hz, 1H), 3.95-3.80 (m, 4H), 3.72 (d, J = 5.0 Hz, 2H), 3.47 (d, J = 5.1 Hz, 2H), 3.32 (s, 3H); Anal. RP-HPLC tR = 2.377 min (method 1, purity 99%); LC-MS ESI: m/z = 482.0 [M+H]+ (anal. calcd for C24H21FN3O5S+: m/z = 482.1).



2-methyl-4-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)but-3-yn-2- ol. Synthesis according to GP5: Yield 19%. 1H NMR (300 MHz, MeOD-d4) δ = 9.35 (dd, J = 2.2, 0.8 Hz, 1H), 8.69-8.60 (m, 2H), 8.24 (dd, J = 8.3, 0.8 Hz, 1H), 8.14-8.05 (m, 2H), 7.82 (s, 1H), 7.70-7.58 (m, 3H), 3.32 (s, 3H), 1.63 (s, 6H); Anal. RP-HPLC tR = 1.046 min (method 2, purity 96%); LC-MS ESI: m/z = 433.1 [M+H]+ (anal. calcd for C24H21N2O4S+: m/z = 433.1).



2-(6-(methylsulfonyl)pyridin-3-yl)-7-(3-(morpholinosulfonyl)phenyl)furo[3,2-b]pyridine. Synthesis according to GP5: Yield 11%. 1H NMR (300 MHz, DMSO-d6) δ = 9.41 (d, J = 2.3 Hz, 1H), 8.73 (d, J = 5.0 Hz, 1H), 8.68 (dd, J = 8.3, 2.1 Hz, 1H), 8.51 (d, J = 11.1 Hz, 2H), 8.23 (d, J = 8.3 Hz, 1H), 8.17 (s, 1H), 7.96 (d, J = 5.8 Hz, 2H), 7.84 (d, J = 5.1 Hz, 1H), 3.67 (t, J = 4.7 Hz, 4H), 3.36 (s, 3H), 3.01 (t, J = 4.7 Hz, 4H); Anal. RP-HPLC tR = 2.416 min (method 1, purity 98%); LC-MS ESI: m/z = 500.0 [M+H]+ (anal. calcd for C23H22N3O6S2+: m/z = 500.1).

4,4-difluoro-1-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)cyclohexan-1-ol (D77). Synthesis according to GP5: Yield 24% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.43 (s, 1H), 8.67 (d, J = 5.4 Hz, 2H), 8.30 (s, 1H), 8.21 (d, J = 8.1 Hz, 1H), 8.14 (s,1H), 8.02 (d, J = 7.1 Hz, 1H), 7.77-7.56 (m, 3H), 5.40 (s, 1H), 3.35 (s, 3H), 2.41-1.77 (m, 8H); Anal. RP-HPLC tR = 1.089 min (method 2, purity 99%); LC-MS ESI: m/z = 485.1 [M+H]+ (anal. calcd for C25H23F2N2O4S+: m/z = 485.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(methylsulfonyl)pyridin-3- yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone.(D85) Synthesis according to GP5: Yield 36% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (d, J = 1.6 Hz, 1H), 8.73-8.59 (m, 2H), 8.23 (m, 3H), 8.14 (s, 1H), 7.81-7.62 (m, 3H), 4.98-4.47 (m, 2H), 3.97-3.75 (m, 2H), 3.72-3.53 (m, 2H), 3.35 (s, 3H), 2.02-1.79 (m, 2H); Anal. RP-HPLC tR = 2.343 min (method 1, purity 99%); LC-MS ESI: m/z = 476.0 [M+H]+ (anal. calcd for C25H22N3O5S+: m/z = 476.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D97). Synthesis according to GP5: Yield10%. 1H NMR (300 MHz, DMSO-d6) δ = 8.78 (d, J = 5.5 Hz, 1H), 8.44-8.29 (m, 3H), 8.27 (dd, J =6.4, 2.4 Hz, 1H), 8.16-8.06 (m, 3H), 7.94 (dd, J = 5.6, 2.5 Hz, 1H), 7.64 (q, J = 8.7 Hz, 1H), 5.02-4.69 (m, 1H), 4.47 (d, J = 98.7 Hz, 1H), 3.94-3.65 (m, 2H), 3.61-3.34 (m, 2H), 3.31 (s, 3H), 1.99-1.79 (m, 2H); Anal. RP-HPLC tR = 0.917 min (method 2, purity 99%); LC-MS ESI: m/z = 493.1 [M+H]+ (anal. calcd for C26H22FN2O5S+: m/z = 493.1).

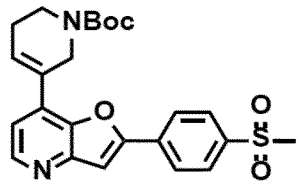
((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2- b]pyridin-7-yl)phenyl)methanone. (D98) Synthesis according to GP5: Yield 15%. 1H NMR (300 MHz, DMSO- d6) δ = 8.83 (d, J = 5.7 Hz, 1H), 8.36 (d, J = 1.9 Hz, 1H), 8.35-8.23 (m, 3H), 8.15 (d, J = 1.9 Hz,1H), 8.13 (s, 2H), 8.03 (d, J = 5.6 Hz, 1H), 7.84-7.74 (m, 2H), 4.82 (d, J = 71.4 Hz, 1H), 4.56 (d, J= 29.6 Hz, 1H), 3.97-3.53 (m, 3H), 3.41 (d, J = 10.8 Hz, 1H), 3.31 (s, 3H), 2.03-1.75 (m, 2H); Anal. RP-HPLC tR = 0.895 min (method 2, purity 99%); LC-MS ESI: m/z = 475.1 [M+H]+ (anal. calcd for C26H23N2O5S+: m/z = 475.1).

((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2- b]pyridin-7-yl)phenyl)methanone (D73). Synthesis according to GP5: Yield 32% as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (d, J = 5.0 Hz, 1H), 8.28-8.15 (m, 4H), 7.91-7.82 (m, 3H), 7.75-7.67 (m, 3H), 4.95-4.48 (m, 2H), 3.97-3.54 (m, 3H), 3.40 (d, J = 10.8 Hz, 1H), 2.82 (s, 3H), 2.00-1.74 (m, 2H); Anal. RP-HPLC tR = 0.975 min (method 2, purity 99%); LC-MS ESI: m/z = 459.1 [M+H]+ (anal. calcd for C26H23N2O4S+: m/z = 459.1).

((R)-3-methylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone.(D72) Synthesis according to GP5: Yield 29% as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (d, J = 5.1 Hz, 1H), 8.20

(m, 3H), 8.07 (s, 1H), 7.91-7.82 (m, 3H), 7.74 (t, J =7.7 Hz, 1H), 7.68 (d, J = 5.1 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 4.02-3.31 (m, 7H), 2.82 (s, 3H), 1.30(d, J = 6.8 Hz, 3H); Anal. RP-HPLC tR = 1.033 min (method 2, purity 99%); LC-MS ESI: m/z = 461.1 [M+H]+ (anal. calcd for C26H25N2O4S+: m/z = 461.2).

morpholino(3-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone.(D105) Synthesis according to GP5: Yield 8%. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (d, J = 5.1 Hz, 1H), 8.36-8.30 (m, 2H), 8.25 (dt, J = 7.9, 1.5 Hz, 1H), 8.10 (d, J = 1.4 Hz, 2H), 8.07 (s,1H), 8.01 (s, 1H), 7.79-7.71 (m, 2H), 7.65-7.59 (m, 1H), 3.65 (s, 8H); Anal. RP-HPLC tR = 2.537 min (method 1, purity 99%); LC-MS ESI: m/z = 501.1 [M+H]+ (anal. calcd for C25H20F3N2O4S+: m/z = 501.1).

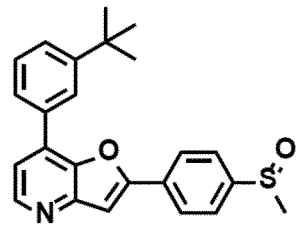


tert-butyl 5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)-3,6-dihydropyridine- 1(2H)-carboxylate (building block). Synthesis according to GP5: Yield 81%; Anal. RP-HPLC tR = 2.558 min (method 1, purity 95%); LC-MS ESI: m/z = 455.1 [M+H]+ (anal. calcd for C24H27N2O5S+: m/z = 455.2).

7-(2-methoxypyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (D115). Synthesis according to GP5: Yield 67%. 1H NMR (300 MHz, DMSO-d6) δ = 8.69 (d, J = 5.5 Hz, 1H), 8.44 (d, J = 5.4 Hz, 1H), 8.28 (d, J = 8.3 Hz, 2H), 8.12 (d, J = 8.3 Hz, 2H), 8.02 (s, 1H), 7.78 (d, J = 5.1 Hz, 1H), 7.72 (dd, J = 5.4, 1.5 Hz, 1H), 7.52 (t, J = 1.0 Hz, 1H), 3.98 (d, J = 0.8 Hz, 3H), 3.30 (s, 3H); Anal. RP-HPLC tR = 2.471 min (method 1, purity 99%); LC-MS ESI: m/z = 381.0 [M+H]+ (anal. calcd for C20H17N2O4S+: m/z = 381.1).

2-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol (D135). Synthesis according to GP5: Yield 51%. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (d, J = 5.3 Hz, 1H), 8.34 (t, J = 1.8 Hz, 1H), 8.29-8.22 (m, 2H),

8.00-7.94 (m, 1H), 7.93 (s, 1H), 7.91-7.85 (m, 2H), 7.76 (d, J = 5.3 Hz, 1H), 7.69 (dt, J = 7.9, 1.4 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 2.83 (s, 3H), 1.56 (s, 6H); Anal. RP-HPLC tR = 2.518 min (method 1, purity 99%); LC-MS ESI: m/z = 392.0 [M+H]+ (anal. calcd for C23H22NO3S+: m/z = 392.1).



7-(3-(tert-butyl)phenyl)-2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridine. Synthesis according to GP5: Yield 40%. 1H NMR (300 MHz, CDCl3) δ = 8.64 (s, 1H), 8.16 (d, J = 7.0 Hz, 3H), 7.96-7.89 (m, 1H), 7.86 (d, J = 7.7 Hz, 3H), 7.81-7.68 (m, 2H), 7.64 (t, J = 7.8 Hz, 1H), 2.83 (s, 3H), 1.53-1.40 (m, 9H); Anal. RP-HPLC tR = 2.779 min (method 1, purity 99%); LC-MS ESI: m/z = 390.0 [M+H]+ (anal. calcd for C24H24NO2S+: m/z = 390.2).

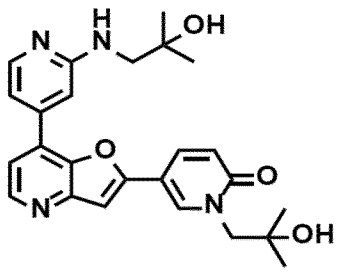
(4,4-difluoropiperidin-1-yl)(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2- yl)methanone (D74). Synthesis according to GP5: Yield 48% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.92-8.83 (m, 1H), 8.70 (d, J = 5.1 Hz, 1H), 8.36-8.29 (m, 1H), 8.31-8.19 (m, 3H), 7.94 (s, 1H), 7.87 (d, J = 8.6 Hz, 2H), 7.81 (d, J = 5.1 Hz, 1H), 3.87-3.79 (m, 2H), 3.63-3.55 (m, 2H), 2.82 (s, 3H), 2.20 – 2.01 (m, 4H); Anal. RP-HPLC tR = 1.134 min (method 2, purity 99%); LC-MS ESI: m/z = 482.1 [M+H]+ (anal. calcd for C25H22F2N3O3S+: m/z = 482.1).

4,4-difluoro-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2- yl)methyl)cyclohexan-1-ol (D136). Synthesis according to GP5: Yield 14%.1H NMR (300 MHz, DMSO-d6+TFA) δ = 9.07 (d, J = 6.1 Hz, 1H), 8.84 (d, J = 5.1 Hz, 1H), 8.67 (s, 1H), 8.61 (dd, J = 6.3, 1.7 Hz, 1H), 8.36 (d, J = 8.3 Hz, 2H), 8.13 (d, J = 2.3 Hz, 2H), 8.09 (s, 1H), 7.94 (d, J = 5.1 Hz, 1H), 3.30 (d, J = 2.5 Hz, 5H), 2.21-1.62 (m, 8H); Anal. RP-HPLC tR = 0.960 min (method

2, purity 99%); LC-MS ESI: m/z = 499.1 [M+H]+ (anal. calcd for C26H25F2N2O4S+: m/z = 499.2).

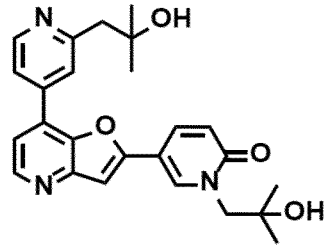
1,1-difluoro-2-methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2- yl)propan-2-ol (D143). Synthesis according to GP5: Yield 20%. 1H NMR (300 MHz, DMSO-d6+TFA) δ = 8.94 (d, J= 5.1 Hz, 1H), 8.81-8.74 (m, 1H), 8.37 (dd, J = 1.8, 0.8 Hz, 1H), 8.35-8.29 (m, 2H), 8.22 (dd, J = 5.2, 1.7 Hz, 1H), 8.16-8.10 (m, 2H), 8.09 (s, 1H), 7.89 (d, J = 5.5 Hz, 1H), 3.30 (s, 3H), 1.33 (d, J = 1.4 Hz, 6H); Anal. RP-HPLC tR = 2.451 min (method 1, purity 99%); LC-MS ESI: m/z = 459.1 [M+H]+ (anal. calcd for C23H21F2N2O4S+: m/z = 459.1).

1- methyl-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one (D36) Synthesis according to GP5: Yield 23% as an olive green solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.04 (dd, J = 5.1, 0.8 Hz, 1H), 8.80 (dd, J = 1.8, 0.8 Hz, 1H), 8.65 (d, J = 5.2 Hz, 1H), 8.51 (dd, J = 5.1, 1.8 Hz, 1H), 8.47 (d, J = 2.6 Hz, 1H), 8.07 (dd, J = 9.5, 2.6 Hz, 1H), 7.85 (d, J = 5.1 Hz, 1H), 7.52 (s, 1H), 6.61 (d, J = 9.5 Hz, 1H), 3.58 (s, 3H), 3.41 (s, 3H); Anal. RP-HPLC tR = 0.786 min (method 2, purity 97%); LC-MS ESI: m/z = 382.0 [M+H]+ (anal. calcd for C19H16N3O4S+: m/z = 382.1).

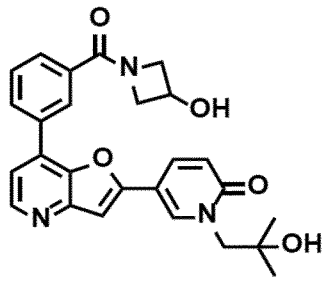


1-(2-hydroxy-2-methylpropyl)-5-(7-(2-((2-hydroxy-2-methylpropyl)amino)pyridin-4- yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one. Synthesis according to GP5: Yield 25%. 1H NMR (300 MHz, DMSO-d6) δ = 8.54 (d, J = 5.1 Hz, 1H), 8.39 (d, J = 2.6 Hz, 1H), 8.17-7.99 (m, 2H), 7.51 (d, J = 5.1 Hz, 1H), 7.41 (s, 1H), 7.31-7.21 (m, 1H), 7.07 (dd, J = 5.4, 1.5 Hz, 1H), 6.60 (dd, J = 10.6, 5.3 Hz, 2H), 4.85 (s, 1H), 4.67 (s, 1H), 4.04 (s, 2H), 3.33 (d,

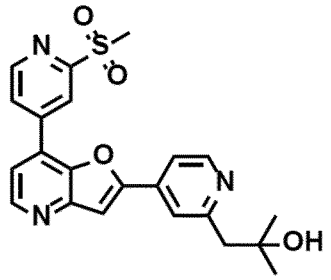
J = 5.8 Hz, 2H), 1.17 (s, 6H), 1.12 (s, 6H); Anal. RP-HPLC tR = 0.670 min (method 2, purity 99%); LC-MS ESI: m/z = 449.1 [M+H]+ (anal. calcd for C25H29N4O4+: m/z = 449.2).



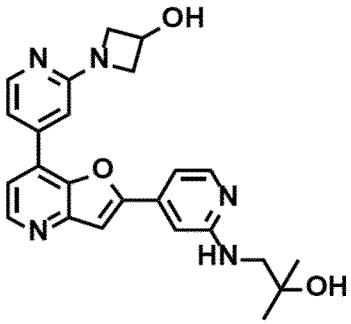
1-(2-hydroxy-2-methylpropyl)-5-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2- b]pyridin-2-yl)pyridin-2(1H)-one. Synthesis according to GP5: Yield 37% as a bright yellow solid. 1H NMR (300 MHz, CDCl3): δ = 8.76 (s, 1H), 8.26 (s, 1H), 8.15 (s, 1H), 7.64 (d, J = 9.2 Hz, 2H), 7.36 (s, 1H), 6.99 (s, 1H), 6.66 (d, J = 9.3 Hz, 2H), 4.17 (s, 2H), 3.20 (s, 2H), 1.35 (s, 6H), 1.32 (s, 6H). The OH signals were not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.720 min (method 2, purity 99%); LC-MS ESI: m/z = 434.1 [M+H]+ (anal. calcd for C25H28N3O4+: m/z = 434.2).



1-(2-hydroxy-2-methylpropyl)-5-(7-(3-(3-hydroxyazetidine-1-carbonyl)phenyl)furo[3,2- b]pyridin-2-yl)pyridin-2(1H)-one. Synthesis according to GP4: Yield 25% as a yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.71 (d, J = 5.0 Hz, 1H), 8.47 (d, J = 5.2 Hz, 1H), 8.13 (d, J = 5.1 Hz, 1H), 7.78 (dt, J = 5.2, 1.6 Hz, 2H), 7.57 (s, 1H), 7.48 (d, J = 5.1 Hz, 1H), 7.45 (s, 1H), 7.04 (dd, J = 5.5, 1.4 Hz, 1H), 7.01 (s, 1H), 5.56 (br. s, 1H), 3.49 (s, 5H), 3.46 (d, J = 5.9 Hz, 2H), 1.32 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.745 min (method 2, purity 99%); LC-MS ESI: m/z = 460.0 [M+H]+ (anal. calcd for C26H26N3O5+: m/z = 460.2).



2-methyl-1-(4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)propan-2-ol. Synthesis according to GP5: Yield 49% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.06 (d, J = 5.1 Hz, 1H), 8.85-8.81 (m, 1H), 8.75 (d, J = 5.1 Hz, 1H), 8.68 (d, J = 5.2 Hz, 1H), 8.50 (dd, J = 5.1, 1.7 Hz, 1H), 8.06 (s, 1H), 7.97 (d, J = 5.1 Hz, 1H), 7.89 (s, 1H), 7.84 (dd, J = 5.2, 1.6 Hz, 1H), 4.70 (s, 1H), 3.40 (s, 3H), 2.96 (s, 2H), 1.16 (s, 6H); Anal. RP-HPLC tR = 0.723 min (method 2, purity 97%); LC-MS ESI: m/z = 424.0 [M+H]+ (anal. calcd for C22H22N3O4S+: m/z = 424.1).



1-(4-(2-(2-((2-hydroxy-2-methylpropyl)amino)pyridin-4-yl)furo[3,2-b]pyridin-7-yl)pyridin-2- yl)azetidin-3-ol. Synthesis according to GP5: Yield 20% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.55 (d, J = 5.1 Hz, 1H), 8.36 (d, J = 2.2 Hz, 1H), 8.33 (s, 1H), 8.21 (d, J = 7.9 Hz, 1H), 8.04 (dd, J = 9.5, 2.5 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 5.1 Hz, 1H), 7.43 (s, 1H), 6.61 (d, J = 9.5 Hz, 1H), 4.61-4.49 (m, 2H), 4.37-4.25 (m, 1H), 4.20-4.12 (m, 1H), 4.07-3.99 (m, 2H), 3.91-3.80 (m, 1H), 3.17 (s, 2H), 1.13 (s, 6H); Anal. RP-HPLC tR = 0.745 min (method 2, purity 95%); LC-MS ESI: m/z = 432.1 [M+H]+ (anal. calcd for C24H26N5O3+: m/z = 432.2).

N-(2-hydroxy-2-methylpropyl)-5-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2- yl)picolinamide (D49). Synthesis

according to GP5: Yield 31% as a white solid. 1H NMR (300 MHz, CDCl3) δ = 9.11 (s, 1H), 8.67 (d, J = 5.1 Hz, 1H), 8.41 (t, J = 6.1 Hz, 1H), 8.33-8.29 (m, 2H), 8.11-8.09 (m, 1H), 8.02 (br. s, 1H), 7.68 (t, J = 7.7 Hz, 1H), 7.58 (m, 2H), 7.50 (d, J = 5.1 Hz, 1H), 3.74 (br. s, 8H), 3.53 (d, J = 6.4 Hz, 2H) 1.31 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.890 min (method 2, purity 99%); LC-MS ESI: m/z = 501.1 [M+H]+ (anal. calcd for C28H29N4O5+: m/z = 501.2)

(4-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone (D52). Synthesis according to GP5: Yield 31% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.71 (dd, J = 15.7, 4.8 Hz, 2H), 8.28-8.25 (m, 2H), 8.11-8.09 (m, 3H), 7.97 (s, 1H), 7.91 (d, J = 4.7 Hz, 1 H), 7.74 (d, J = 4.7 Hz, 1H), 4.74 (s, 1H), 4.34 (s, 1H), 3.13 (s, 3H), 3.01 (s, 2H), 1.20 (s, 6H); Anal. RP-HPLC tR = 0.706 min (method 2, purity 99%); LC-MS ESI: m/z = 422.0 [M+H]+ (anal. calcd for C23H24N3O3S+: m/z = 422.2).

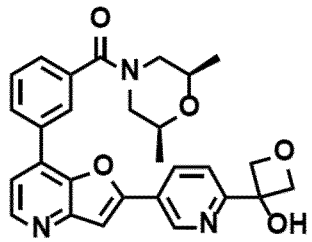
2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)oxy)propan-2-ol (D47). Synthesis according to GP5: Yield 45% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.66 (d, J = 5.0 Hz, 1H), 8.40 (d, J = 5.3 Hz, 1H), 8.26 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 8.4 Hz, 2H), 8.00 (s, 1H), 7.77 (d, J = 5.0 Hz, 1H), 7.73-7.68 (m, 1H), 7.48 (s, 1H), 4.65 (s, 1H), 4.16 (s, 2H), 3.29 (s, 3H), 1.25 (s, 6H); Anal. RP-HPLC tR = 0.986 min (method 2, purity 99%); LC- MS ESI: m/z = 439.0 [M+H]+ (anal. calcd for C23H23N2O5S+: m/z = 439.1).

(5-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)(3- hydroxyazetidin-1-yl)methanone (D51). Synthesis according to GP5: Yield 44% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.31 (d, J = 1.7 Hz, 1H), 8.75 (d, J = 5.2 Hz, 1H), 8.70 (d, J = 5.0 Hz, 1H), 8.55 (dd, J = 8.3, 2.2 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 8.09-8.03 (m, 2H), 7.94 (dd, J = 5.2, 1.5 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 5.74 (d, J = 6.5 Hz, 1H), 4.87-4.77 (m,

1H), 4.74 (s, 1H), 4.62-4.49 (m, 1H), 4.38-4.29 (m, 2H), 3.85 (dd, J = 10.5, 3.8 Hz, 1H), 3.01 (s, 2H), 1.20 (s, 6H); Anal. RP-HPLC tR = 0.717 min (method 2, purity 98%); LC-MS ESI: m/z = 445.1 [M+H]+ (anal. calcd for C25H25N4O4+: m/z = 445.2).

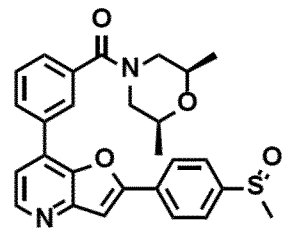
1-(2-hydroxy-2-methylpropyl)-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7- yl)pyridin-2(1H)-one (D39). Synthesis according to GP5: Yield 12% as a white solid. 1H NMR (300 MHz, DMSO- d6) δ = 8.77 (d, J = 2.7 Hz, 1H), 8.57 (d, J = 5.1 Hz, 1H), 8.38 (d, J = 8.6 Hz, 2H), 8.19 (dd, J = 9.6, 2.8 Hz, 1H), 8.10 (d, J = 8.5 Hz, 2H), 7.97 (s, 1H), 7.60 (d, J = 5.1 Hz, 1H), 6.66 (d, J = 9.5 Hz, 1H), 5.05 (s, 1H), 4.11 (s, 2H), 3.30 (s, 3H), 1.21 (s, 6H); Anal. RP-HPLC tR = 2.792 min (method 1, purity 97%); LC-MS ESI: m/z = 439.1 [M+H]+ (anal. calcd for C23H23N2O5S+: m/z = 439.1).

(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone (D55). Synthesis according to GP5: Yield 51%. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 5.0 Hz, 1H), 8.24 (ddt, J = 9.3, 7.8, 1.7 Hz, 3H), 8.14-8.05 (m, 3H), 8.00 (s, 1H), 7.78-7.66 (m, 2H), 7.61 (dt, J = 7.7, 1.3 Hz, 1H), 3.64 (s, 8H), 3.29 (3H); Anal. RP-HPLC tR = 0.902 min (method 2, purity 97%); LC-MS ESI: m/z = 463.1 [M+H]+ (anal. calcd for C25H23N2O5S+: m/z = 463.1).

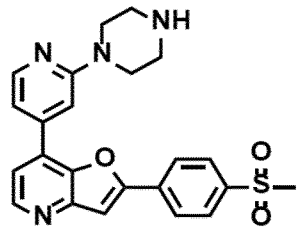


((2S,6R)-2,6-dimethylmorpholino)(3-(2-(6-(3-hydroxyoxetan-3-yl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 18% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.29 (s, 1H), 8.64 (d, J = 5.5 Hz, 1H), 8.39 (d, J = 10.1 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.12 (s, 1H), 7.89 (s, 1H), 7.82-7.65 (m, 3H), 7.59 (d, J = 7.4 Hz, 1H), 6.69 (s, 1H), 4.97 (d, J = 6.1 Hz, 2H), 4.70 (d, J = 6.1 Hz, 2H), 4.45 (br. s, 1H), 4.06

(br. s, 1H), 3.59 (br. s, 3H), 2.89 (br. s, 1H),1.16 (br. m, 6H); LC-MS ESI: m/z = 486.2 [M+H]+ (anal. calcd for C28H28N3O5+: m/z = 486.2).



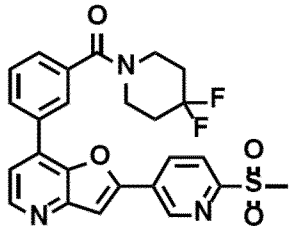
((2S,6R)-2,6-dimethylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 47% as a yellow solid. 1H NMR (300 MHz, CDCl3) δ = 8.63 (d, J = 5.1 Hz, 1H), 8.15-7.97 (m, 4H), 7.77 (d, J = 8.5 Hz, 2H), 7.66 (t, J = 7.7 Hz, 1H), 7.53 (dt, J = 7.6, 1.3 Hz, 1H), 7.45-7.37 (m, 2H), 4.61 (br. s, 1H), 3.63 (br. s, 3H), 2.90 (br. s, 1H), 2.77 (s, 3H), 2.61 (br. s, 1H), 1.19 (br. m, 6H); Anal. RP-HPLC tR = 0.929 min (method 2, purity 96%); LC-MS ESI: m/z = 475.0 [M+H]+ (anal. calcd for C27H27N2O4S+: m/z = 475.2).



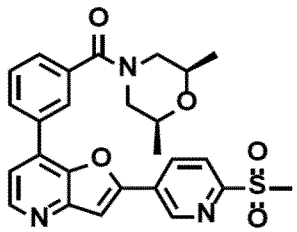
2-(4-(methylsulfonyl)phenyl)-7-(2-(piperazin-1-yl)pyridin-4-yl)furo[3,2-b]pyridine. Synthesis according to GP5: Yield 71% as a light yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.61 (d, J = 5.1 Hz, 1H), 8.41 (d, J = 4.8 Hz, 1H), 8.22-8.18 (m, 2 H), 8.11-8.07 (m, 2H), 7.69-7.67 (m, 2H) 7.517.49 (m, 1H), 7.43 (dd, J = 5.3, 1.3 Hz, 1H), 3.94-3.91 (m, 4H), 3.37-3.33 (m, 4H), 3.18 (s, 3H). The NH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.717 min (method 2, purity 96%); LC-MS ESI: m/z = 435.0 [M+H]+ (anal. calcd for C23H23N4O3S+: m/z = 435.2).

2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)amino)propan-2-ol (D35). Synthesis according to GP5: Yield 26% as a yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.62 (d, J = 5.1 Hz, 1H), 8.29 (d, J = 8.7 Hz, 2H), 8.17 (dd, J = 5.5, 0.8 Hz, 1H), 8.13 (d, J = 8.6 Hz, 2H), 7.70

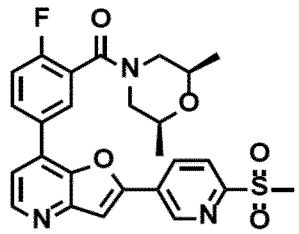
(s, 1H), 7.67 (d, J = 5.2 Hz, 1H), 7.32 (d, J = 0.7 Hz, 1H), 7.21 (dd, J = 5.5, 1.6 Hz, 1H), 3.46 (s, 2H), 3.21 (s, 3H), 1.31 (s, 6H). The OH and NH signals was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.713 min (method 2, purity 99%); LC-MS ESI: m/z = 438.0 [M+H]+ (anal. calcd for C23H24N3O4S+: m/z = 438.2)



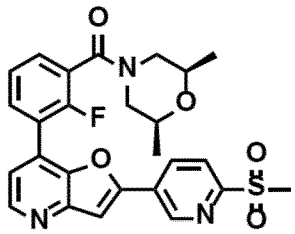
(4,4-difluoropiperidin-1-yl)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 38%. 1H NMR (300 MHz, DMSO-d6) δ = 9.47- 9.38 (m, 1H), 8.76-8.61 (m, 2H), 8.33-8.08 (m, 4H), 7.80-7.60 (m, 3H), 3.65 (s, 4H), 3.35 (s, 3H), 2.03 (d, J = 28.6 Hz, 4H); Anal. RP-HPLC tR = 1.032 min (method 2, purity 99%); LC-MS ESI: m/z = 498.1 [M+H]+ (anal. calcd for C25H22F2N3O4S+: m/z = 498.1).



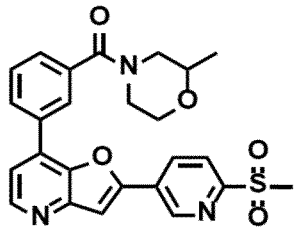
((2S,6R)-2,6-dimethylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 32% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (d, J = 2.0 Hz, 1H), 8.72-8.65 (m, 2H), 8.30-8.26 (m, 1H), 8.25-8.21 (m, 1H), 8.14 (s, 1H), 8.11 (t, J = 1.6 Hz, 1H), 7.80-7.67 (m, 2H), 7.61 (d, J = 7.7 Hz, 1H), 4.42 (br. s, 1H), 3.75 -3.43 (m, 3H), 3.36 (s, 3H), 2.92 (br. s, 2H), 1.10 (s, 6H); Anal. RP-HPLC tR = 1.106 min (method 2, purity 99%); LC-MS ESI: m/z = 492.1 [M+H]+ (anal. calcd for C26H26N3O5S+: m/z = 492.2).



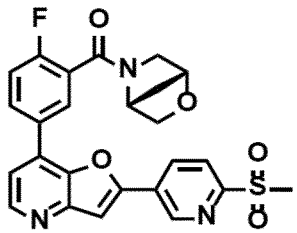
((2S,6R)-2,6-dimethylmorpholino)(2-fluoro-5-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2- b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 34%. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (dd, J = 2.2, 0.8 Hz, 1H), 8.73-8.62 (m, 2H), 8.35 (ddd, J = 8.7, 5.1, 2.4 Hz, 1H), 8.25-8.10 (m, 3H), 7.74 (d, J = 5.1 Hz, 1H), 7.60 (t, J = 9.0 Hz, 1H), 4.47 (d, J = 13.0 Hz, 1H), 3.58 (s,2H), 3.36 (s, 4H), 2.90 (dd, J = 13.1, 10.7 Hz, 1H), 2.62-2.53 (m, 1H), 1.23-1.15 (m, 3H), 1.02 (d, J = 6.2 Hz, 3H); Anal. RP-HPLC tR = 2.427 min (method 1, purity 98%); LC-MS ESI: m/z = 510.1 [M+H]+ (anal. calcd for C26H25FN3O5S+: m/z = 510.1).



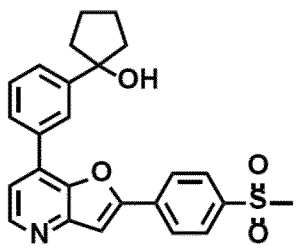
((2S,6R)-2,6-dimethylmorpholino)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2- b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 25%. 1H NMR (300 MHz, DMSO- d6) δ = 9.34 (dd, J = 2.2, 0.8 Hz, 1H), 8.71 (d, J = 5.0 Hz, 1H), 8.59 (dd, J = 8.2, 2.2 Hz, 1H), 8.22-8.12 (m, 2H), 7.98 (td, J = 7.4, 1.9 Hz, 1H), 7.67-7.51 (m, 3H), 4.44 (d, J = 13.0 Hz, 1H), 3.62-3.39 (m, 3H), 3.33 (s, 3H), 2.90 (t, J = 11.8 Hz, 1H), 2.60-2.52 (m, 1H), 1.16 (d, J = 6.2 Hz, 3H), 1.05 (d, J = 6.1 Hz, 3H); Anal. RP-HPLC tR = 2.392 min (method 1, purity 99%); LC-MS ESI: m/z = 510.1 [M+H]+ (anal. calcd for C26H25FN3O5S+: m/z = 510.1).



(2-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 45% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.41 (d, J = 1.5 Hz, 1H), 8.70-8.63 (m, 2H), 8.26 (d, J = 8.0 Hz, 1H), 8.24-8.20 (m,1H), 8.13 (s, 1H), 8.10 (t, J = 1.4 Hz, 1H), 7.79-7.69 (m, 2H), 7.64-7.57 (m, 1H), 4.35 (br.s, 1H), 3.83 (br. s, 2H), 3.61-3.41 (m, 3H), 3.35 (s, 3H), 2.98 (br. s, 1H), 1.09 (br. s, 3H); Anal. RP-HPLC tR = 1.116 min (method 2, purity 99%); LC-MS ESI: m/z = 478.1 [M+H]+ (anal. calcd for C25H24N3O5S+: m/z = 478.1).



((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-5-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 4%. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (d, J = 2.2 Hz, 1H), 8.68 (dd, J = 9.0, 3.5 Hz, 2H), 8.38-8.28 (m, 1H), 8.24-8.18 (m, 2H), 8.13 (s, 1H), 7.75 (dd, J = 5.1, 2.2 Hz, 1H), 7.60 (q, J = 8.8 Hz, 1H), 4.96 (s, 0.5H), 4.71 (s, 0.5H), 4.61 (s, 0.5H), 4.29 (s, 0.5H), 3.85 (dd, J = 20.2, 7.9 Hz, 1.5H), 3.68 (d, J = 7.3 Hz, 0.5H), 3.57-3.50 (m, 1H), 3.43 (s, 1H), 3.35 (s, 3H), 1.96-1.80 (m, 2H); Anal. RP-HPLC tR = 2.301 min (method 1, purity 99%); LC-MS ESI: m/z = 494.1 [M+H]+ (anal. calcd for C25H21FN3O5S+: m/z = 494.1).



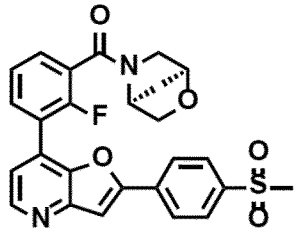
1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)cyclopentan-1-ol. Synthesis according to GP5: Yield 19%. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (d, J = 5.0 Hz, 1H), 8.28- 8.22 (m, 2H), 8.17-8.08 (m, 3H), 7.98 (d, J = 6.3 Hz, 2H), 7.76-7.56 (m, 3H), 6.48 (s, 1H), 2.79 (d, J = 8.0 Hz, 2H), 2.56 (s, 4H), 2.10-1.98 (m, 2H); Anal. RP-HPLC tR = 1.287 min (method 2, purity 96%); LC-MS ESI: m/z = 416.1 [M-OH]+ (anal. calcd for C25H23NO4S+: m/z = 433.1).

(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D99). Synthesis according to GP5: Yield 48%. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 5.0 Hz, 1H), 8.28-8.21 (m, 3H), 8.17 (d, J = 1.7 Hz, 1H), 8.13-8.06 (m, 2H), 8.00 (s, 1H), 7.85-7.62 (m, 3H), 4.58 (s, 1H), 4.03 (m, 1H), 3.69 (s, 4H), 3.29 (s, 3H), 1.92 (s, 4H); Anal. RP-HPLC tR= 0.964 min (method 2, purity 98%); LC-MS ESI: m/z = 489.2 [M+H]+ (anal. calcd for C27H25N2O5S+: m/z = 489.2).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone.(D101) Synthesis according to GP5: Yield 40%. 1H NMR (300 MHz, DMSO-d6) δ = 8.67 (d, J = 5.0 Hz, 1H), 8.28-8.12 (m, 3H), 8.09-7.98 (m, 3H), 7.73 (t, J = 6.8 Hz, 3H), 4.92 (s, 0.5H), 4.69 (s, 0.5H), 4.59 (s, 0.5H), 4.51 (s, 0.5H), 3.95-3.86 (m, 1H), 3.81 (s, 0.5H), 3.71-3.54 (m, 1.5H), 3.41 (s, 4H), 1.99-1.76 (m, 2H); Anal. RP-HPLC tR = 0.928 min (method 2, purity 99%); LC-MS ESI: m/z = 493.1 [M+H]+ (anal. calcd for C26H22FN2O5S+: m/z = 493.1).

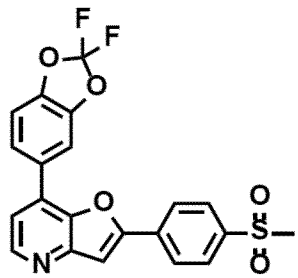
(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-oxa-6-azaspiro[3.4]octan-6-yl)methanone (D106). Synthesis according to GP5: Yield 21%. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 4.6 Hz, 1H), 8.29-8.17 (m, 4H), 8.12-8.07 (m, 2H), 7.98 (s, 1H), 7.78-7.68 (m, 3H), 4.65 (d, J = 6.0 Hz, 1H), 4.52-4.43 (m, 3H), 3.76 (d, J = 9.6 Hz, 2H), 3.55 (s, 2H), 3.28 (d, J =1.3 Hz, 3H), 2.19 (q, J = 7.5 Hz, 2H); Anal. RP-HPLC tR = 0.900 min (method

2, purity 99%); LC- MS ESI: m/z = 489.1 [M+H]+ (anal. calcd for C27H25N2O5S+: m/z = 489.2).

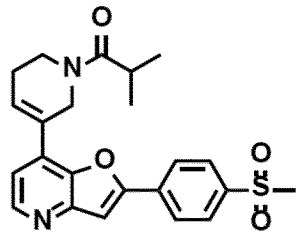


((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D108). Synthesis according to GP5: Yield 40%. 1H NMR (300 MHz, DMSO-d6) δ = 8.68 (dd, J = 5.0, 2.1 Hz, 1H), 8.18 (dd, J = 8.5, 1.8 Hz, 2H), 8.07 (dd, J = 8.6, 1.7 Hz, 2H), 8.01 (d, J = 1.3 Hz, 1H), 7.99-7.89 (m, 1H), 7.73-7.63 (m, 1H), 7.60-7.50 (m, 2H), 4.95 (s, 0.5H), 4.69 (d, J = 13.9 Hz, 1H), 4.35 (s, 0.5H), 3.83-3.68 (m, 2H), 3.53 (d, J = 11.3 Hz, 1H), 3.41 (s, 1H), 3.28 (s, 3H), 1.88 (d, J = 16.8 Hz, 2H); Anal. RP-HPLC tR = 0.907 min (method 2, purity 99%); LC-MS ESI: m/z = 493.1 [M+H]+ (anal. calcd for C26H22FN2O5S+: m/z = 493.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D112). Synthesis according to GP5: Yield 21%. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.23 (dd, J = 8.5, 2.5 Hz, 2H), 8.15-8.01 (m, 4H), 7.70 (d, J = 5.9 Hz, 1H), 7.62-7.46 (m, 1H), 4.86 (d, J = 77.1 Hz, 1H), 4.71- 4.37 (m, 1H), 3.88-3.69 (m, 2H), 3.62-3.32 (m, 2H), 3.29 (s, 3H), 1.92 (d, J = 10.7 Hz, 2H); Anal. RP-HPLC tR = 0.936 min (method 2, purity 99%); LC-MS ESI: m/z = 511.1 [M+H]+ (anal. calcd for C27H25F2N2O5S+: m/z = 511.1).

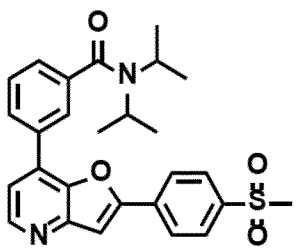


7-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine. Synthesis according to GP5: Yield 56%. 1H NMR (300 MHz, DMSO-d6) δ = 8.63 (d, J = 5.1 Hz, 1H), 8.28 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 1.7 Hz, 1H), 8.09 (d, J = 8.3 Hz, 2H), 8.04-7.97 (m, 2H), 7.70-7.64 (m, 2H), 3.28 (s, 3H); Anal. RP-HPLC tR = 1.195 min (method 2, purity 99%); LC-MS ESI: m/z = 430.1 [M+H]+ (anal. calcd for C21H14F2NO5S+: m/z = 430.1).

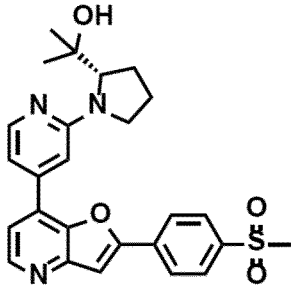


2-methyl-1-(5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)-3,6-dihydropyridin- 1(2H)-yl)propan-1-one. Synthesis according to GP5: Yield 18%. 1H NMR (300 MHz, DMSO-d6) δ = 8.53 (d, J = 5.1 Hz, 1H), 8.28 (d, J = 8.3 Hz, 2H), 8.08 (d, J = 8.3 Hz, 2H), 7.92 (s, 1H), 7.49-7.32 (m, 1H), 7.06 (s, 1H), 4.65 (d, J = 15.6 Hz, 2H), 3.73 (d, J = 6.8 Hz, 2H), 3.29 (s, 3H), 3.03 (d, J = 13.6 Hz, 1H), 2.41 (d, J = 5.4 Hz, 1H), 1.18-0.90 (m, 6H); Anal. RP-HPLC tR = 1.234 min (method 2, purity 99%); LC-MS ESI: m/z = 425.1 [M+H]+ (anal. calcd for C23H25N2O4S+: m/z = 425.2).

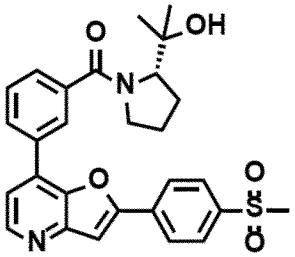
2-(4-(methylsulfonyl)phenyl)-7-(2-(morpholinomethyl)pyridin-4-yl)furo[3,2-b]pyridine (D120). Synthesis according to GP5: Yield 8%. 1H NMR (300 MHz, CDCl3) δ = 9.01-8.92 (m, 2H), 8.79-8.73 (m, 1H), 8.23 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.4 Hz, 4H), 7.90 (s, 1H), 4.52 (s, 2H), 4.19 (s, 4H), 3.64 (s, 4H) 3.15 (s, 3H); Anal. RP-HPLC tR = 0.871 min (method 2, purity 99%); LC-MS ESI: m/z = 450.1 [M+H]+ (anal. calcd for C24H24N3O4S+: m/z = 450.2).



N,N-diisopropyl-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)benzamide. Synthesis according to GP5: Yield 9% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.91 (d, J = 6.2 Hz, 1H), 8.38 (d, J = 7.9 Hz, 2H), 8.29 (d, J = 7.7 Hz, 1H), 8.23-8.16 (m, 2H), 8.12 (s, 2H), 8.09 (s,1H), 7.76 (t, J = 7.6 Hz, 1H), 7.58 (d, J = 7.2 Hz, 1H), 3.69 (s, 2H), 3.28 (s, 3H), 1.18 (m, 12H); Anal. RP-HPLC tR = 1.420 min (method 2, purity 99%); LC-MS ESI: m/z = 477.2 [M+H]+ (anal. calcd for C27H29N2O4S+: m/z = 477.2).

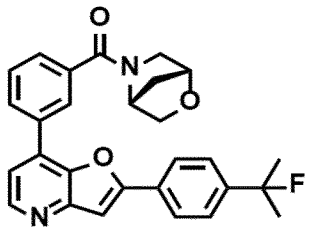


(S)-2-(1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)pyrrolidin-2-yl)propan-2-ol. Synthesis according to GP5. Yield 14% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.85 (d, J = 5.4 Hz, 1H), 8.38 (d, J = 8.1 Hz, 2H), 8.25 (s, 1H), 8.11 (d, J = 7.1 Hz, 4H), 7.99 (d, J = 5.6 Hz, 2H), 7.56 (s, 1H), 4.31 (s, 1H), 3.78 (s, 2H), 3.25 (s, 3H), 2.26-1.91 (m, 3H), 1.29 (s, 3H), 1.15 (s, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 1.035 min (method 2, purity 99%); LC-MS ESI: m/z = 478.1 [M+H]+ (anal. calcd for C26H28N3O4S+: m/z = 478.2).

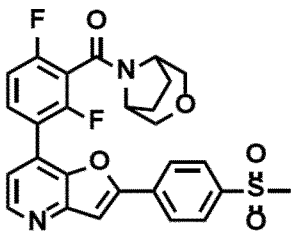


(S)-(2-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5. Yield 23% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.92 (d, J = 6.1 Hz, 1H), 8.38 (d, J = 6.9 Hz, 3H), 8.31 (d, J = 7.8 Hz, 1H),

8.20 (d, J = 7.2 Hz, 2H), 8.14 (d, J = 7.2 Hz, 2H), 7.85 (d, J = 7.6 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 4.35 (t, J = 6.7 Hz, 1H), 3.68-3.54 (m, 1H), 3.49-3.47(m, 1H), 3.28 (s, 3H), 1.99-1.82 (m, 3H), 1.71- 1.58 (m, 1H), 1.16 (d, J = 12.8 Hz, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 1.342 min (method 2, purity 99%); LC-MS ESI: m/z = 505.1 [M+H]+ (anal. calcd for C28H29N2O5S+: m/z = 505.2).

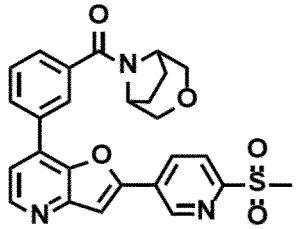


((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(2-fluoropropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 24% as a light yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.82 (d, J = 5.7 Hz, 1H), 8.40-8.22 (m, 2H), 8.14- 8.10 (m, 3H), 7.95-7.93 (m, 1H), 7.81-7.79 (m, 2H), 7.65 (d, J = 8.3 Hz, 2H), 4.97-4.42 (m, 2H), 3.96-3.50 (m, 3H), 3.40 (d, J = 11.4 Hz, 1H), 2.01-1.76 (m, 2H), 1.70 (d, J = 22.2 Hz, 6H); Anal. RP-HPLC tR = 1.061 min (method 2, purity 96%); LC-MS ESI: m/z = 457.2 [M+H]+ (anal. calcd for C28H26FN2O3+: m/z = 457.2).



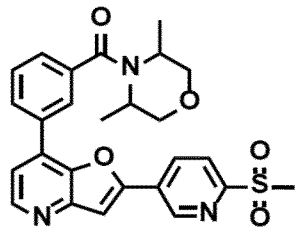
(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(2,6-difluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5. Yield 16% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.80 (d, J = 5.2 Hz, 1H), 8.25 (d, J = 8.1 Hz, 2H), 8.16-8.02 (m, 4H), 7.78 (t, J = 4.6 Hz, 1H), 7.52 (q, J = 8.0, 7.6 Hz, 1H), 4.64 (s, 1H), 3.94-3.91 (m, 1H), 3.78-3.56 (m, 3H), 3.51 (dd, J = 11.3, 6.2 Hz, 1H), 3.27 (s, 3H), 2.05-1.80 (m, 4H); Anal. RP-HPLC tR = 0.990 min (method 2, purity 99%); LC-MS ESI: m/z = 525.1 [M+H]+ (anal. calcd for C27H23F2N2O5S+: m/z = 525.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D110). Synthesis according to GP5: Yield 28% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.85 (d, J = 6.2 Hz, 1H), 8.33 (m, 2H), 8.14 (d, J = 6.1 Hz, 1H), 8.08 (d, J = 8.4 Hz, 2H), 7.90 (s, 1H), 7.88-7.76 (m, 2H), 7.71 (d, J = 8.3 Hz, 2H), 4.99-4.40 (m, 2H), 3.98-3.34 (m, 4H), 1.98-1.75 (m, 2H), 1.47 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.883 min (method 2, purity 99%); LC-MS ESI: m/z = 455.2 [M+H]+ (anal. calcd for C28H27N2O4+: m/z = 455.2).



(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 13% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (d, J = 1.6 Hz, 1H), 8.70-8.65 (m, 2H), 8.28 (dt, J = 7.6, 1.4 Hz, 1H), 8.24-8.20 (m, 1H), 8.18 (m, 1H), 8.14 (s, 1H), 7.81-7.64 (m, 3H), 4.59 (s, 1H), 4.04 (s, 1H), 3.57-63 (m, 5H), 3.35 (s, 3H), 1.92 (s, 3H); Anal. RP-HPLC tR = 0.921 min (method 2, purity 98%); LC-MS ESI: m/z = 490.1 [M+H]+ (anal. calcd for C26H24N3O5S+: m/z = 490.1).

1-(4-(7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-carbonyl)-2-fluorophenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one (D104). Synthesis according to GP5: Yield 48% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.70-8.64 (m, 1H), 8.09 (m, 4H), 7.95 (d, J = 9.4 Hz, 2H), 7.69 (dt, J =14.9, 7.7 Hz, 1H), 7.61-7.50 (m, 2H), 4.96-4.67 (m, 2H), 3.80-3.32 (m, 4H), 2.63 (s, 3H), 1.97-1.81 (m, 2H); Anal. RP-HPLC tR = 2.455 min (method 1, purity 99%); LC-MS ESI: m/z = 457.1 [M+H]+ (anal. calcd for C27H22FN2O4+: m/z = 457.1).



(3,5-dimethylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone. Synthesis according to GP5: Yield 9% as a white solid. 1H NMR (300 MHz, CDCl3) δ = 9.26 (s, 1H), 8.71 (s, 1H), 8.49-8.41 (m, 1H), 8.23 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 7.80 (s, 1H), 7.77-7.50 (m, 3H), 4.22 (s, 1H), 3.98-3.86 (m, 1H), 3.81-3.62 (m, 3H), 3.52 (dd, J = 11.3, 5.5 Hz, 1H), 3.30 (s, 3H) 1.46 (d, J = 7.0 Hz, 4H), 1.34 (d, J = 6.3 Hz, 2H); Anal. RP-HPLC tR = 0.957 min (method 2, purity 99%); LC-MS ESI: m/z = 492.1 [M+H]+ (anal. calcd for C26H26N3O5S+: m/z = 492.2).

(S)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D103). Synthesis according to GP5: Yield 54% as a white solid. 1H NMR (300 MHz, CDCl3) δ = 9.26 (s, 1H), 8.71 (br. s, 1H), 8.45 (d, J = 7.5 Hz, 1H), 8.24 (d, J = 7.9 Hz, 1H), 8.11 (d, J = 6.8 Hz, 1H), 8.03 (s, 1H), 7.83 (s, 1H), 7.80-7.53 (m, 3H), 4.03-3.40 (m, 7H), 3.30 (s, 3H), 1.43 (d, J = 6.7 Hz, 3H); Anal. RP-HPLC tR = 0.917 min (method 2, purity 99%); LC-MS ESI: m/z = 478.1 [M+H]+ (anal. calcd for C25H24N3O5S+: m/z = 478.1).

(R)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D102). Synthesis according to GP5: Yield 40% as an off white solid. 1H NMR (300 MHz, CDCl3) δ = 9.25 (s, 1H), 8.70 (s, 1H), 8.43 (d, J = 7.7 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 8.10 (d, J =7.5 Hz, 1H), 8.01 (s, 1H), 7.79-7.53 (m, 4H), 3.68 (m, 7H), 3.30 (s, 3H), 1.43 (d, J = 6.7 Hz, 3H); Anal. RP-HPLC tR = 0.916 min (method 2, purity 99%); LC-MS ESI: m/z = 478.1 [M+H]+ (anal. calcd for C25H24N3O5S+: m/z = 478.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(tert-butylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D95). Synthesis according to GP5: Yield 9% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.45 (s, 1H), 8.72-8.60 (m, 2H), 8.34-8.09 (m, 4H), 7.83-7.62 (m, 3H), 4.97-4.46 (m, 2H), 4.00-3.39 (m, 4H), 2.03-1.70 (m, 2H), 1.35 (s, 9H); Anal. RP-HPLC tR =1.183 min (method 2, purity 97%); LC-MS ESI: m/z = 518.2 [M+H]+ (anal. calcd for C28H28N3O5S+: m/z = 518.2).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D93). Synthesis according to GP5: Yield 51% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.68 (dd, J = 5.0, 2.1 Hz, 1H), 8.18 (dd, J = 8.6, 1.7 Hz, 2H), 8.07 (dd, J = 8.6, 1.6 Hz, 2H), 8.02 (d, J = 1.2 Hz, 1H), 7.94 (qd, J = 7.9, 1.6 Hz, 1H), 7.74-7.63 (m, 1H), 7.60-7.50 (m, 2H), 5.08-4.31 (m, 2H), 3.87-3.65 (m, 2H), 3.58-3.31 (m, 2H), 3.28 (s, 3H), 1.97-1.79 (m, 2H); Anal. RP-HPLC tR = 1.009 min (method 2, purity 99%); LC-MS ESI: m/z = 493.1 [M+H]+ (anal. calcd for C26H22FN2O5S+: m/z = 493.1)

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D92). Synthesis according to GP5: Yield 50% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.40-9.32 (m, 1H), 8.72 (dd, J = 5.0, 2.4 Hz, 1H), 8.57 (td, J = 7.7, 7.2, 2.0 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H), 8.16 (s, 1H), 7.98 (qd, J = 7.6, 1.8 Hz, 1H), 7.76-7.64 (m, 1H), 7.64-7.51 (m, 2H) 5.06-4.19 (m, 2H), 3.86-3.65 (m, 2H), 3.56-3.25 (m, 2H), 3.33 (s, 3H), 1.96-1.76 (m, 2H); Anal. RP-HPLC tR = 0.956 min (method 2, purity 99%); LC-MS ESI: m/z = 494.1 [M+H]+ (anal. calcd for C26H21FN3O5S+: m/z = 494.1).

((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D91). Synthesis according to GP5: Yield 33% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 5.0 Hz, 1H), 8.30-8.06 (m, 6H), 8.00 (s, 1H),

7.73 (p, J = 9.6, 8.7 Hz, 3H), 4.97-4.44 (m, 2H), 3.97-3.86 (m, 1H), 3.85-3.51 (m, 2H), 3.40 (d, J = 10.7 Hz, 1H), 3.29 (s, 3H), 2.00-1.70 (m, 2H); Anal. RP-HPLC tR = 0.967min (method 2, purity 99%); LC-MS ESI: m/z = 475.0 [M+H]+ (anal. calcd for C26H23N2O5S+: m/z = 475.1).

(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(pyrrolidin-1-yl)methanone (D90). Synthesis according to GP5: Yield 29% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.42 (d, J = 1.7 Hz, 1H), 8.74-8.62 (m, 2H), 8.27-8.20 (m, 3H), 8.14 (s, 1H), 7.74 (m, 3H), 3.53 (br. s, 4H), 3.36 (s, 3H), 1.89 (m, 4H); Anal. RP-HPLC tR = 0.968 min (method 2, purity 98%); LC- MS ESI: m/z = 448.1 [M+H]+ (anal. calcd for C24H22N3O4S+: m/z = 448.1).

7-(3-(2-methoxypropan-2-yl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine (D89). Synthesis according to GP5: Yield 15% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 9.41 (s, 1H), 8.72-8.61 (m, 2H), 8.24 (d, J = 8.2 Hz, 1H), 8.15 (d, J = 9.1 Hz, 2H), 8.01 (d, J = 6.4 Hz, 1H), 7.73 (d, J = 4.9 Hz, 1H), 7.62 (dt, J = 10.7, 6.4 Hz, 2H), 3.35 (s, 3H), 3.10 (s, 3H), 1.57 (s, 6H); Anal.RP-HPLC tR = 1.114 min (method 2, purity 99%); LC-MS ESI: m/z = 423.1 [M+H]+ (anal. calcd for C23H23N2O4S+: m/z = 423.1).

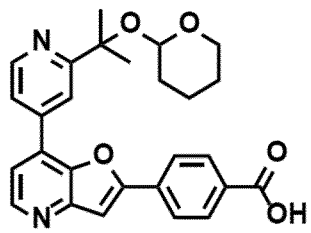
imino(methyl)(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone (D23). Synthesis according to GP9: Yield 30%. 1H NMR (300 MHz, DMSO-d6) δ = 8.75 (t, J = 1.8 Hz, 1H), 8.71 (d, J = 5.1 Hz, 1H), 8.50 (ddd, J = 7.9, 1.9, 1.1 Hz, 1H), 8.32 (d, J = 8.6 Hz, 2H), 8.16 (d, J = 8.6 Hz,2H), 8.13 (dd, J = 1.9, 1.1 Hz, 1H), 8.05 (s, 1H), 7.95 (t, J = 7.8 Hz, 1H), 7.84 (d, J = 5.1 Hz, 1H),3.42 (s, 3H), 3.37 (s, 3H); Anal. RP-HPLC tR = 0.831 min (method 2, purity 96%); LC-MS ESI: m/z= 427.0 [M+H]+ (anal. calcd for C21H19N2O4S2+: m/z = 427.1).

2-(1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)piperidin-4-yl)propan-2-ol (D114). Synthesis according to GP5: Yield 40%

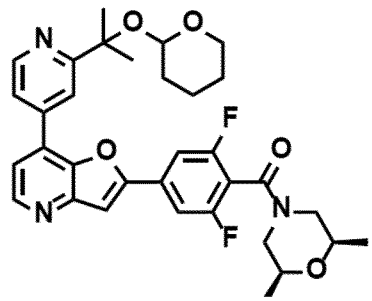
as a light yellow solid. 1H NMR (300 MHz, DMSO- d6) δ = 8.77 (d, J = 5.1 Hz, 1H), 8.28 (d, J = 8.3 Hz, 2H), 8.21 (d, J = 6.6 Hz, 1H), 8.15-8.06 (m,3H), 8.01 (s, 1H), 7.90 (d, J = 5.1 Hz, 1H), 7.56 (d, J = 6.7 Hz, 1H), 4.41 (d, J = 12.9 Hz, 2H), 3.29 (s, 3H), 3.22 (d, J = 12.4 Hz, 2H), 1.92 (d, J = 11.6 Hz, 2H), 1.67-1.60 (m, 1H), 1.50-1.38 (m, 2H),1.09 (s, 6H); Anal. RP-HPLC tR = 2.524 min (method 1, purity 98%); LC-MS ESI: m/z = 492.1 [M+H]+ (anal. calcd for C27H30N3O4S+: m/z = 492.2).

7-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)pyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (D109). Synthesis according to GP5: Yield 46% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.70-8.62 (m, 1H), 8.31 (d, J = 5.2 Hz, 1H), 8.25 (d, J = 8.6 Hz,2H), 8.11 (d, J = 8.6 Hz, 2H), 8.00 (s, 1H), 7.75 (d, J = 5.0 Hz, 1H), 7.27 (dd, J = 5.3, 1.4 Hz, 1H),7.19 (s, 1H), 5.00 (s, 1H), 4.73 (s, 1H), 3.88-3.82 (m, 1H), 3.76 (d, J = 7.3 Hz, 1H), 3.65-3.54 (m,1H), 3.39 (d, J = 9.9 Hz, 1H), 3.29 (s, 3H), 2.04-1.87 (m, 2H); Anal. RP-HPLC tR = 0.749 min (method 2, purity 99%); LC-MS ESI: m/z = 448.1 [M+H]+ (anal. calcd for C24H22N3O4S+: m/z = 448.1).

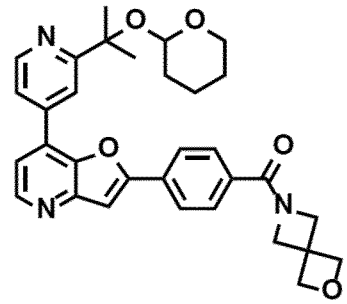
1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)pyrrolidin-3-ol (D117). Synthesis according to GP5: Yield 27% as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.79 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 8.4 Hz, 2H), 8.22 (d, J = 6.8 Hz, 1H), 8.15-8.07 (m, 3H), 7.93 (d, J = 5.1 Hz, 1H), 7.77 (s, 1H), 7.58 (d, J = 6.8 Hz, 1H), 4.57 (s, 1H), 3.86-3.73 (m, 3H), 3.61 (d, J = 10.5 Hz, 1H), 3.29 (s, 3H), 2.28-1.98 (m, 2H); Anal. RP-HPLC tR = 0.744 min (method 2, purity 100%); LC- MS ESI: m/z = 436.1 [M+H]+ (anal. calcd for C23H22N3O4S+: m/z = 436.1).



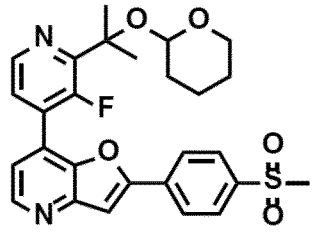
4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2- yl)benzoic acid (building block). Synthesis according to GP5: Yield 49% as a yellow solid. Anal. RP-HPLC tR = 1.081 min (method 2, purity 99%); LC-MS ESI: m/z 459.1 [M+H]+ (anal. calcd for C27H27N2O5+: m/z = 459.2).



(2,6-difluoro-4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)((2S,6R)-2,6-dimethylmorpholino)methanone (building block). Synthesis according to GP5: Yield 53% as a yellow oil. Anal. RP-HPLC tR = 1.262 min (method 2, purity 92%); LC-MS ESI: m/z 508.2 [M-OTHP]+ (anal. calcd for C33H36F2N3O5+: m/z = 592.3).

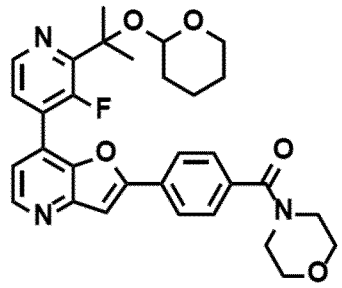


(2-oxa-6-azaspiro[3.3]heptan-6-yl)(4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (building block). Synthesis according to GP5: Yield 39% as a yellow oil. Anal. RP-HPLC tR = 1.026 min (method 2, purity 59%); LC-MS ESI: m/z 540.2 [M+H]+ (anal. calcd for C32H34N3O5+: m/z = 540.3).



7-(3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine (building block). Synthesis

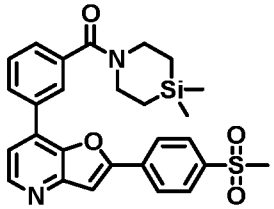
according to GP5: Yield 43% as a yellow oil. Anal. RP-HPLC tR = 1.158 min (method 2, purity 96%); LC-MS ESI: m/z 511.1 [M+H]+ (anal. calcd for C27H28FN2O5S+: m/z = 511.2).



(4-(7-(3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone (building block). Synthesis according to GP5: Yield 20% as a yellow oil. Anal. RP-HPLC tR = 1.139 min (method 2, purity 62%); LC-MS ESI: m/z 546.2 [M+H]+ (anal. calcd for C31H33FN3O5S+: m/z = 546.2).

Example 6: Synthesis of reactants and compounds according to the invention following General Procedure 6

General Procedure 6: Amide Coupling Formation Using EDC and DMAP (GP6)

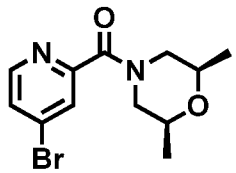


Synthesis of (4,4-dimethyl-1,4-azasilinan-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone (D100). To a stirred solution of 3-(2-(1-methyl-1H-pyrazol-4- yl)furo[3,2-b]pyridin-7-yl)benzoic acid (50 mg, 0.16 mmol) in dichloromethane (4 mL) were added DMAP (19.1 mg, 0.16 mmol) and EDC (30 mg, 0.16 mmol) and stirred for 5 min at room temperature. To this reaction mixture, 4,4-dimethyl-1,4-azasilinane (21 mg, 0.16 mmol) was added and stirred at room temperature overnight. Deionized water (8 mL) was added, and the reaction mixture

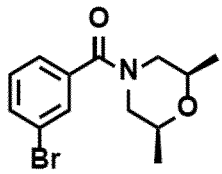
extracted with dichloromethane (20 mL). The organic layer was washed with brine (2 x 10 mL), dried over MgSO4, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using hexane/ethyl acetate 8:2 v/v ratio initially and slowly increased to hexane/ethyl acetate 5:5 v/v ratio to afford (4,4-dimethyl-1,4-azasilinan-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone in 46% yield as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.66 (d, J = 5.0 Hz, 1H), 8.24 (t, J = 11.1 Hz, 3H), 8.16-8.04 (m, 3H), 8.01 (s, 1H), 7.73 (t, J = 7.3 Hz, 2H),7.59 (d, J = 7.6 Hz, 1H), 3.83 (s, 2H), 3.58 (s, 2H), 3.29 (s, 3H), 0.87 (s, 2H), 0.72 (s, 2H), 0.12 (s, 6H); Anal. RP-HPLC tR = 2.619 min (method 1, purity 99%); LC-MS ESI: m/z = 505.1 [M+H]+ (anal. calcd for C27H29N2O4SiS+: m/z = 505.2).

Manufacturing examples

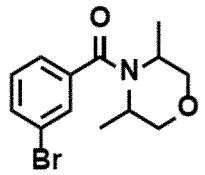
(S)-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone (D107). Synthesis according to GP6: Yield 22%. 1H NMR (300 MHz, DMSO-d6) δ = 8.79 (d, J = 5.5 Hz, 1H), 8.32 (dd, J = 9.1, 2.4 Hz, 4H), 8.13 (d, J = 1.9 Hz, 1H), 8.10(d, J = 1.1 Hz, 2H), 7.97 (d, J = 5.5 Hz, 1H), 7.84-7.75 (m, 2H), 5.11 (s, 1H), 3.65 (d, J = 36.5 Hz, 2H), 3.31 (s, 3H), 2.27 (s, 1H), 2.12-1.88 (m, 3H); Anal. RP-HPLC tR = 1.091 min (method 2, purity 99%); LC-MS ESI: m/z = 515.1 [M+H]+ (anal. calcd for C26H22F3N2O4S+: m/z = 515.1).



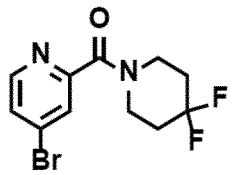
(4-bromopyridin-2-yl)((2S,6R)-2,6-dimethylmorpholino)methanone (building block), Synthesis according to GP6: Yield 68%. Anal. RP-HPLC tR = 0.999 min (method 2, purity 97%); LC-MS ESI: m/z = 299.0 [M+H]+ (anal. calcd for C12H16BrN2O2+: m/z = 299.0).



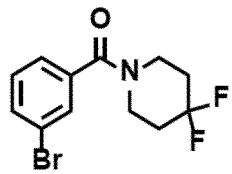
(3-bromophenyl)((2S,6R)-2,6-dimethylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 96%. Anal. RP-HPLC tR = 1.655 min (method 2, purity 99%); LC-MS ESI: m/z = 298.0 [M+H]+ (anal. calcd for C13H17BrN2O2+: m/z = 298.0).



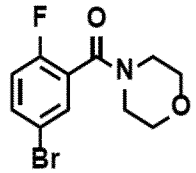
(3-bromophenyl)(3,5-dimethylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 41%. Anal. RP-HPLC tR = 0.966 min (method 2, purity 99%); LC-MS ESI: m/z = 298.0 [M+H]+ (anal. calcd for C13H17BrN2O2+: m/z = 298.0).



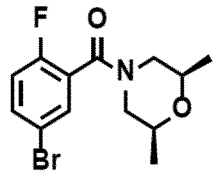
(4-bromopyridin-2-yl)(4,4-difluoropiperidin-1-yl)methanone, (building block): Synthesis according to GP6: Yield 80%. Anal. RP-HPLC tR = 1.046 min (method 2, purity 99%); LC-MS ESI: m/z = 305.0 [M+H]+ (anal. calcd for C11H12BrF2N2O+: m/z = 305.0).



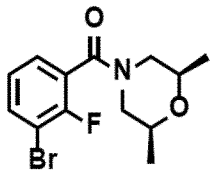
(3-bromophenyl)(4,4-difluoropiperidin-1-yl)methanone, (building block): Synthesis according to GP6: Yield 97%. Anal. RP-HPLC tR = 1.191 min (method 2, purity 100%); LC-MS ESI: m/z = 304.0 [M+H]+ (anal. calcd for C12H13BrF2NO+: m/z = 304.0).



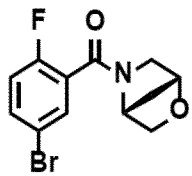
(5-bromo-2-fluorophenyl)(morpholino)methanone, (building block): Synthesis according to GP6: Yield 88%. Anal. RP- HPLC tR = 1.098 min (method 2, purity 99%); LC-MS ESI: m/z = 288.0 [M+H]+ (anal. calcd for C11H12BrFNO2+: m/z = 288.0).



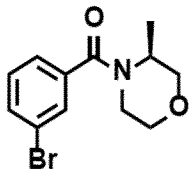
(5-bromo-2-fluorophenyl)((2S,6R)-2,6-dimethylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 98%. Anal. RP-HPLC tR = 1.105 min (method 2, purity 100%); LC-MS ESI: m/z = 316.0 [M+H]+ (anal. calcd for C13H16BrFNO2+: m/z = 316.0).



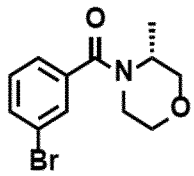
(3-bromo-2-fluorophenyl)((2S,6R)-2,6-dimethylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 97%. Anal. RP-HPLC tR = 1.105 min (method 2, purity 100%); LC-MS ESI: m/z = 316.0 [M+H]+ (anal. calcd for C13H16BrFNO2+: m/z = 316.0).



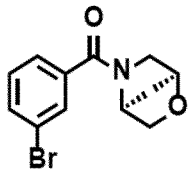
((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(5-bromo-2-fluorophenyl)methanone, (building block): Synthesis according to GP6: Yield 96%. Anal. RP-HPLC tR = 0.827 min (method 2, purity 99%); LC-MS ESI: m/z = 300.0 [M+H]+ (anal. calcd for C12H12BrFNO2+: m/z = 300.0).



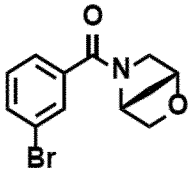
(S)-(3-bromophenyl)(3-methylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 92%. Anal. RP-HPLC tR = 0.897 min (method 2, purity 97%); LC-MS ESI: m/z = 284.0 [M+H]+ (anal. calcd for C12H15BrNO2+: m/z = 284.0).



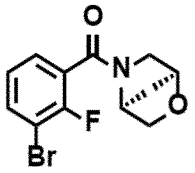
(R)-(3-bromophenyl)(3-methylmorpholino)methanone, (building block): Synthesis according to GP6: Yield 93%. Anal. RP-HPLC tR = 2.268 min (method 1, purity 99%); LC-MS ESI: m/z = 284.0 [M+H]+ (anal. calcd for C12H15BrNO2+: m/z = 284.0).



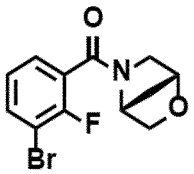
((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-bromophenyl)methanone, (building block): Synthesis according to GP6: Yield 87%. Anal. RP-HPLC tR = 0.813 min (method 2, purity 90%); LC-MS ESI: m/z = 282.0 [M+H]+ (anal. calcd for C12H13BrNO2+: m/z = 282.0).



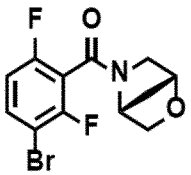
((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-bromophenyl)methanone, (building block): Synthesis according to GP6: Yield 99%. Anal. RP-HPLC tR = 0.810 min (method 2, purity 100%); LC-MS ESI: m/z = 282.0 [M+H]+ (anal. calcd for C12H13BrNO2+: m/z = 282.0).



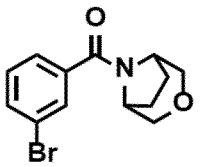
((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-bromo-2-fluorophenyl)methanone, (building block): Synthesis according to GP6: Yield 92%. Anal. RP-HPLC tR = 0.817 min (method 2, purity 100%); LC-MS ESI: m/z = 300.0 [M+H]+ (anal. calcd for C12H12BrFNO2+: m/z = 300.0).



((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-bromo-2-fluorophenyl)methanone, (building block): Synthesis according to GP6: Yield 95%. Anal. RP-HPLC tR = 0.819 min (method 2, purity 100%); LC-MS ESI: m/z = 300.0 [M+H]+ (anal. calcd for C12H12BrFNO2+: m/z = 300.0).



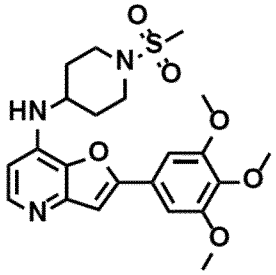
((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-bromo-2,6-difluorophenyl)methanone, (building block): Synthesis according to GP6: Yield 74%. Anal. RP-HPLC tR = 0.824 min (method 2, purity 99%); LC-MS ESI: m/z = 318.0 [M+H]+ (anal. calcd for C12H10BrF2NO +: m/z = 318.0).



(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(3-bromophenyl)methanone, (building block): Synthesis according to GP6: Yield 89%. Anal. RP-HPLC tR = 2.193 min (method 1, purity 100%); LC-MS ESI: m/z = 296.0 [M+H]+ (anal. calcd for C13H15BrNO2+: m/z = 296.0).

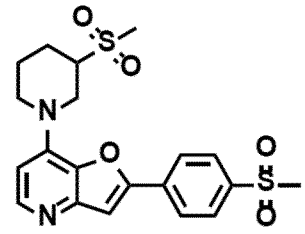
Example 7: Synthesis of reactants and compounds according to the invention following General Procedure 7

General Procedure 7: Buchwald-Hartwig Cross-Coupling Reaction (GP7)

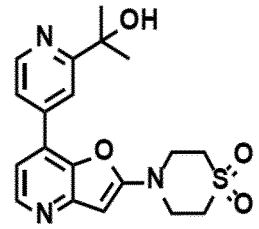


Synthesis of N-(1-(methylsulfonyl)piperidin-4-yl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-amine. To a stirred solution of 7-chloro-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine (120 mg, 0.38 mmol) in toluene (3 mL) were added tris(dibenzylideneacetone)dipalladium(0) (29 mg, 0.03 mmol), 1-(methylsulfonyl)piperidin-4-amine (68 mg, 0.38 mmol), sodium tert-butoxide (61 mg, 0.63 mmol), BINAP (39 mg, 0.06 mmol) and degassed for 10 min. The resulting reaction mixture was heated at 85 °C for 12 h. Toluene was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed-phase silica gel using water/methanol 9.5:0.5 v/v ratio initially and slowly increased to water/methanol 7:3 v/v ratio to afford N-(1-(methylsulfonyl)piperidin-4-yl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-amine in 42% yield as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.03 (d, J = 5.5 Hz, 1H), 7.44 (s, 1H), 7.28 (s, 2H), 6.59 (dd, J = 20.7, 7.0 Hz, 2H), 3.91 (s, 6H), 3.73 (s, 3H), 3.66 (d, J = 11.8 Hz, 2H), 2.90 (s, 5H), 2.11 (d, J = 11.9 Hz, 2H), 1.64 (q, J = 11.6, 11.2 Hz, 2H); Anal. RP-HPLC tR = 2.326 min (method 1, purity 97%); LC-MS ESI: m/z = 462.0 [M+H]+ (anal. calcd for C22H28N3O6S+: m/z = 462.1).

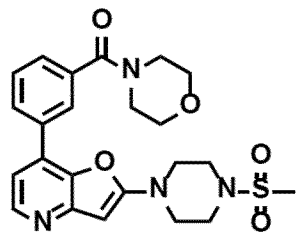
Manufacturing examples



2-(4-(methylsulfonyl)phenyl)-7-(3-(methylsulfonyl)piperidin-1-yl)furo[3,2-b]pyridine. Synthesis according to GP7: Yield 45% as a light yellow solid. 1H NMR (400 MHz, CDCl3+MeOD-d4) δ = 8.26-8.19 (m, 2H), 8.16 (d, J = 6.3 Hz, 1H), 8.09-8.03 (m, 2H), 7.45 (s, 1H), 6.84 (d, J = 6.3 Hz, 1H), 5.16-5.10 (m, 1H), 4.29-4.26 (m,1H), 3.67 (dd, J = 13.4, 10.7 Hz, 1H), 3.52-3.44 (m, 1H), 3.35-3.28 (m, 1H), 3.15 (s, 3H), 3.01 (s, 3H), 2.42-2.36 (m, 1H), 2.14-1.99 (m, 2H), 1.91-1.81 (m, 1H); Anal. RP-HPLC tR = 0.645 min (method 1, purity 99%); LC-MS ESI: m/z = 435.0 [M+H]+ (anal. calcd for C20H23N2O5S2+: m/z = 435.1).



4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)thiomorpholine 1,1- dioxide. Synthesis according to GP7: Yield 21%. 1H NMR (300 MHz, DMSO-d6+TFA) δ = 8.86 (d, J = 5.6 Hz, 1H), 8.48 (d, J = 1.8 Hz, 1H), 8.44 (d, J = 6.6 Hz, 1H), 8.15 (dd, J = 5.6, 1.7 Hz, 1H), 7.69 (d, J = 6.6 Hz, 1H), 6.46 (s, 1H), 4.17 (dd, J = 6.6, 3.9 Hz, 4H), 3.43 (t, J = 5.3 Hz, 4H), 1.60 (s, 6H); Anal. RP-HPLC tR = 0.511 min (method 2, purity 99%); LC-MS ESI: m/z = 388.1 [M+H]+ (anal. calcd for C19H22N3O4S+: m/z = 388.1).

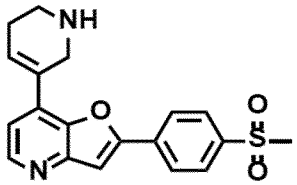


(3-(2-(4-(methylsulfonyl)piperazin-1-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone. Synthesis according to GP7: Yield 30%.

1H NMR (300 MHz, CDCl3) δ = 8.34 (d, J = 5.4 Hz, 1H), 7.90 (dt, J = 9.5, 1.7 Hz, 2H), 7.59 (td, J = 7.6, 0.8 Hz, 1H), 7.49 (dt, J = 7.6, 1.4 Hz, 1H), 7.11 (d, J = 5.5 Hz, 1H), 5.84 (s, 1H), 3.88-3.61 (m, 8H), 3.57 (dd, J = 6.4, 3.7 Hz, 4H), 3.42 (dd, J = 6.3, 3.7 Hz, 4H), 2.84 (s, 3H); Anal. RP-HPLC tR = 2.145 min (method 1, purity 98%); LC-MS ESI: m/z = 471.1 [M+H]+ (anal. calcd for C23H27N4O5S+: m/z = 471.1).

Example 8: Synthesis of reactants and compounds according to the invention following General Procedure 8

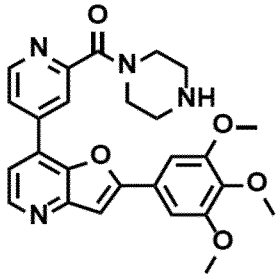
General Procedure 8: N-Boc Deprotection Reaction (GP8)



Synthesis of 2-(4-(methylsulfonyl)phenyl)-7-(1,2,5,6-tetrahydropyridin-3-yl)furo[3,2- b]pyridine. 4 M Hydrochloric acid in 1,4-dioxane solution (2 mL, 57.6 mmol) was added to tert-butyl 5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)-3,6-dihydropyridine-1(2H)- carboxylate (320 mg, 0.7 mmol) and stirred for 1 h at room temperature. Excess hydrochloric acid solution was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed-phase silica gel using water/methanol 9.5:0.5 v/vratio initially and slowly increased to water/methanol 7:3 v/v ratio to afford 2-(4- (methylsulfonyl)phenyl)-7-(1,2,5,6-tetrahydropyridin-3-yl)furo[3,2-b]pyridine in 81 % yield as a white solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.58 (d, J = 5.3 Hz, 1H), 8.32-8.25 (m, 2H), 8.17- 8.10 (m, 2H), 7.71 (s, 1H), 7.46 (d, J = 5.3 Hz, 1H), 7.22 (dt, J = 4.1, 2.3 Hz, 1H), 4.43 (q, J = 2.2Hz, 2H), 3.54 (t, J = 6.2 Hz, 2H), 3.21 (s, 3H), 2.89-2.78 (m, 2H); Anal. RP-HPLC tR = 0.579 min (method 2, purity 99%); LC-MS ESI: m/z = 355.1 [M+H]+ (anal. calcd for C19H19N2O3S+: m/z = 355.1).

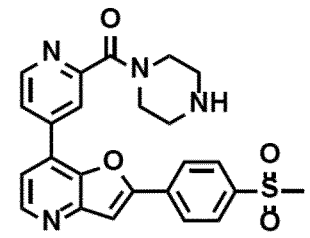
Manufacturing examples

2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(piperazin-1-ylsulfonyl)phenyl)furo[3,2-b]pyridine (D14). Synthesis according to GP8: Yield 57%. 1H NMR (300 MHz, DMSO-d6) δ = 8.57 (d, J = 5.4 Hz, 1H), 8.39 (s, 2H), 8.30 (s, 1H), 8.00 (s, 1H), 7.90 (s, 2H), 7.62 (d, J = 5.1 Hz, 1H), 7.27 (s, 1H), 3.94 (s, 3H), 2.91 (s, 4H), 2.76 (d, J = 5.0 Hz, 4H); Anal. RP-HPLC tR = 0.669 min (method 2, purity 99%); LC- MS ESI: m/z = 424.0 [M+H]+ (anal. calcd for C21H22N5O3S+: m/z = 424.1).



piperazin-1-yl(4-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone. Synthesis according to GP8: Yield 40%. 1H NMR (300 MHz, DMSO-d6) δ = 8.85 (d, J = 5.2 Hz, 1H), 8.67 (d, J = 5.1 Hz, 1H), 8.59 (d, J = 1.1 Hz, 1H), 8.23 (dd, J = 5.2 Hz & 1.8 Hz, 1H), 7.83-7.81 (m, 2H), 7.38 (s, 2H), 3.94 (s, 6H), 3.85-3.75 (s, 7H), 3.17-3.09 (m, 5H); Anal. RP-HPLC tR =0.706 min (method 2, purity 99%); LC-MS ESI: m/z = 475.0 [M+H]+ (anal. calcd for C26H27N4O5+:m/z = 475.1).

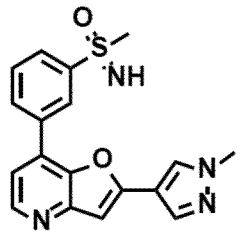
N-(2-aminoethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide (D13). Synthesis according to GP8: Yield 53%. 1H NMR (600 MHz, DMSO-d6) δ = 8.56 (d, J = 5.0 Hz, 1H), 8.52 (d, J = 1.9 Hz, 1H), 8.35-8.31 (m, 2H), 8.03 (s, 1H), 7.97-7.94 (m, 1H),7.85 (t, J = 7.9 Hz, 1H), 7.59 (d, J = 5.0 Hz, 1H), 7.26 (s, 1H), 3.94 (s, 3H), 2.84 (t, J = 6.5 Hz, 2H), 2.58 (t, J = 6.5 Hz, 2H); Anal. RP-HPLC tR = 0.620 min (method 2, purity 99%); LC-MS ESI: m/z = 398.0 [M+H]+ (anal. calcd for C19H20N5O3S+: m/z = 398.1).



(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(piperazin-1-yl)methanone. Synthesis according to GP8: Yield 45%. 1H NMR (300 MHz, DMSO-d6) δ = 8.86 (d, J = 6.0 Hz, 1H), 8.71 (d, J = 5.1 Hz, 1H), 8.29 (d, J = 8.7 Hz, 2H), 8.23-8.22 (m, 2H), 8.10 (d, J = 8.7 Hz, 2H), 8.03 (s, 1H), 7.84 (d, J = 5.1 Hz, 1H), 3.65 (s, 2H), 3.40 (s, 2H), 3.29 (s, 3H), 2.82 (s, 2H), 2.72 (s, 2H); Anal. RP-HPLC tR = 0.670 min (method 2, purity 99%); LC-MS ESI: m/z = 463.1 [M+H]+ (anal. calcd for C24H23N4O4S+: m/z = 463.1).

Example 9: Synthesis of reactants and compounds according to the invention following General Procedure 9

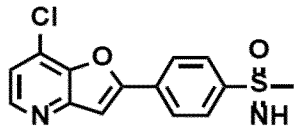
General Procedure 9: Sulfoximine Formation (GP9)



Synthesis of imino(methyl)(3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)- λ6-sulfanone. To a stirred solution of 2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(methylthio)phenyl)furo[3,2-b]pyridine (100 mg, 0.31 mmol) in methanol (1 mL) were added phenyl-l3-iodanediyl diacetate (251 mg, 0.78 mmol), ammonium acetate (48 mg, 0.62 mmol) and the solution was stirred at room temperature for 2 h. Excess solvent was evaporated from the reaction mixture in vacuo. Residue was purified by column chromatography on silica gel using hexane/ethyl acetate 5:5 v/v ratio initially and slowly increased to ethyl acetate/methanol 9.5:0.5 v/v ratio to afford imino(methyl)(3-(2-(1-methyl-1H-pyrazol-4- yl)furo[3,2-b]pyridin-7-yl)phenyl)-λ6-sulfanone in 61% yield as a

white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.71 (t, J = 1.8 Hz, 1H), 8.56 (d, J = 5.1 Hz, 1H), 8.35 (s, 2H), 8.22-8.00 (m, 2H), 7.85 (t, J = 7.8 Hz, 1H), 7.64 (d, J = 5.1 Hz, 1H), 7.26 (s, 1H), 4.43 (s, 1H), 3.94 (s, 3H), 3.18 (s, 3H); Anal. RP-HPLC tR = 2.917 min (method 1, purity 95%); LC-MS ESI: m/z = 353.0 [M+H]+ (anal. calcd for C18H17N4O2S+: m/z = 353.1).

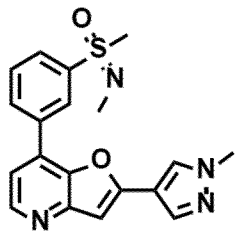
Manufacturing examples



(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone, (building block): Synthesis according to GP9: Yield 37%. Anal. RP-HPLC tR = 0.849 min (method 2, purity 97%); LC-MS ESI: m/z = 306.9 [M+H]+ (anal. calcd for C14H12ClN2O2S+: m/z = 307.0).

<u>Example 10: Synthesis of reactants and compounds according to the invention following General Procedure 10</u>

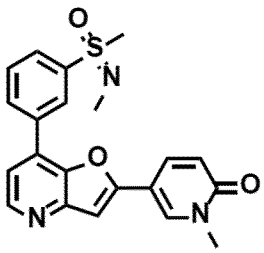
General Procedure 10: N-Methylation of Sulfoximine (GP10)



Synthesis of methyl(3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)(methylimino)-λ6-sulfanone. To a stirred solution imino(methyl)(3-(2-(1-methyl- 1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)-λ6-sulfanone (40 mg, 0.11 mmol) in formic acid (0.3 mL, 7.82 mmol) was added formaldehyde (6.88 µl, 0.25 mmol) and stirred at 105 °C for 36 h. After complete consumption of starting material, formic acid was evaporated from the reaction mixture in vacuo. Residue was purified by column chromatography on silica gel using hexane/ethyl acetate 5:5 v/v ratio initially and slowly increased to ethyl

acetate/methanol 9.5:0.5 v/v ratio to afford methyl(3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)(methylimino)-λ6-sulfanone in 23% yield as a yellow solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.56 (d, J = 4.2 Hz, 2H), 8.44-8.29 (m, 2H), 8.01 (d, J = 13.2 Hz, 2H), 7.89 (t, J = 7.9 Hz, 1H), 7.64 (d, J = 5.2 Hz, 1H), 7.26 (s, 1H), 3.95 (s, 3H), 3.24 (s, 3H), 2.58 (s, 3H); Anal. RP-HPLC tR = 0.733 min (method 2, purity 97%); LC-MS ESI: m/z = 367.1 [M+H]+ (anal. calcd for C19H19N4O2S+: m/z = 367.1).

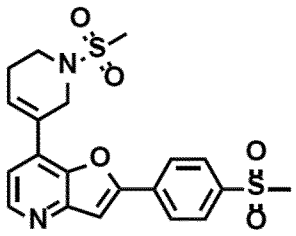
Manufacturing examples



5-(7-(3-(N,S-dimethylsulfonimidoyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)- one. Synthesis according to GP10: Yield 34%. 1H NMR (300 MHz, DMSO-d6) δ = 8.66 (s, 1H), 8.58 (d, J = 5.1 Hz, 1H), 8.40 (dd, J = 8.6, 2.0 Hz, 2H), 8.10-7.95 (m, 2H), 7.88 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 5.1 Hz, 1H), 7.46 (s, 1H), 6.59 (d, J = 9.5 Hz, 1H), 3.57 (s, 3H), 3.25 (s, 3H), 2.56 (s, 3H); Anal. RP- HPLC tR = 0.757 min (method 2, purity 98%); LC-MS ESI: m/z = 394.0 [M+H]+ (anal. calcd for C21H20N3O3S+: m/z = 394.1).

<u>Example 11: Synthesis of reactants and compounds according to the invention following General Procedure 11</u>

General Procedure 11: N-Mesylate Reaction (GP11)



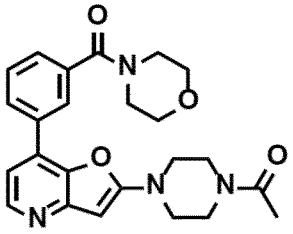
Synthesis of 7-(1-(methylsulfonyl)-1,2,5,6-tetrahydropyridin-3-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine. To a stirred solution of 2-(4-methylsulfonylphenyl)-7-(1,2,3,6-tetrahydropyridin-5-yl)furo[3,2-b]pyridine (130 mg, 0.37 mmol) in dichloromethane (10 mL) at 0 °C was added triethylamine (0.15 mL, 1.1 mmol) and the solution was stirred at 0 °C for 5 min. Finally, methanesulfonyl chloride (0.03 mL, 0.44 mmol) was added dropwise and continued to stir for 5 min at 0 °C. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. Residue was purified by column chromatography on silica gel using hexane/ethyl acetate 5:5 v/v ratio initially and slowly increased to ethyl acetate/methanol 9.8:0.2 v/v ratio to afford 7-(1-(methylsulfonyl)-1,2,5,6-tetrahydropyridin-3-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine in 24% yield as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.54 (d, J = 5.1 Hz, 1H), 8.28 (d, J = 8.5 Hz, 2H), 8.09 (d, J = 8.5 Hz, 2H), 7.93 (s, 1H), 7.37 (d, J = 5.1 Hz, 1H), 7.15-7.00 (m, 1H), 4.35 (d, J = 2.3 Hz, 2H), 3.43 (t, J = 5.8 Hz, 2H), 3.30 (s, 3H), 3.05 (s, 3H), 2.60 (s, 2H); Anal. RP-HPLC tR = 2.310 min (method 1, purity 99%); LC- MS ESI: m/z = 433.0 [M+H]+ (anal. calcd for C20H21N2O5S2+: m/z = 433.1).

Manufacturing examples

2-(4-(2-(1-(methylsulfonyl)-1,2,3,6-tetrahydropyridin-4-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D96). Synthesis according to GP11: Yield 17% as a beige gum. 1H NMR (300 MHz, DMSO-d6): δ = 8.84 (d, J = 5.6 Hz, 1H), 8.71 (d, J = 5.0 Hz, 1H), 8.60 (s, 1H), 8.31 (d, J = 5.6 Hz, 1H), 7.90 (d, J = 5.0 Hz, 1H), 7.30 (s, 1H), 6.77 (m, 1H), 4.01 (m, 2H), 3.44 (t, J = 5.8 Hz, 2H), 2.98 (s, 3H), 2.70 (m, 2H), 1.63 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP- HPLC tR = 0.788 min (method 2, purity 99%); LC-MS ESI: m/z = 414.1 [M+H]+ (anal. calcd for C21H24N3O4S+: m/z = 414.2).

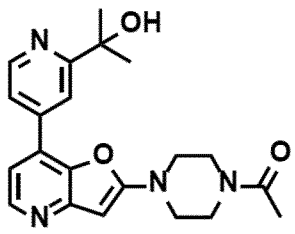
Example 12: Synthesis of reactants and compounds according to the invention following General Procedure 12

General Procedure 12: Acetylation Reaction (GP12)



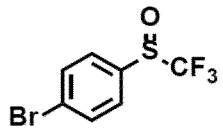
Synthesis of 1-(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)piperazin-1- yl)ethan-1-one. To a stirred solution of [3-(2-iodofuro[3,2-b]pyridin-7-yl)phenyl]-morpholin- 4-ylmethanone (125 mg, 0.29 mmol) in toluene (2mL) was added 1-acetylpiperazine (110.7 mg, 0.86 mmol) and the solution was stirrred at room temperature for 5 min. To this reaction mixture, p-toluenesulfonic acid monohydrate (11 mg, 0.06 mmol) was added and continued to stir at 100 °C for 4 days. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed-phase silica gel using water/methanol 9.5:0.5 v/v ratio initially and slowly increased to water/methanol 3:7 v/v ratio to afford 1-[4-[7-[3-(morpholine- 4-carbonyl)phenyl]furo[3,2-b]pyridin-2-yl]piperazin-1-yl]ethanone in 12% yield as a brown oil. 1H NMR (300 MHz, DMSO-d6) δ = 8.29 (d, J = 5.3 Hz, 1H), 8.04 (dt, J = 7.8, 1.5 Hz, 1H), 7.92 (t, J = 1.7 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.53 (dt, J = 7.7, 1.4 Hz, 1H), 7.25 (d, J = 5.3 Hz, 1H), 5.91 (s, 1H), 3.68-3.58 (m, 8H), 3.48-3.33 (m, 8H), 2.07 (s, 3H); Anal. RP-HPLC tR = 2.130 min (method 1, purity 96%); LC-MS ESI: m/z = 435.2 [M+H]+ (anal. calcd for C24H27N4O4+: m/z = 435.2).

Manufacturing examples



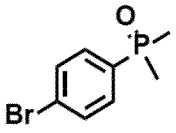
1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)piperazin-1-yl)ethan- 1-one. Synthesis according to GP12: Yield 10%. 1H NMR (300 MHz, CDCl3) δ = 8.70 (dd, J = 5.2, 0.9 Hz, 1H), 8.39 (d, J = 5.4 Hz, 1H), 7.89 (dd, J = 1.7, 0.9 Hz, 1H), 7.65 (dd, J = 5.2, 1.7 Hz, 1H), 7.16 (d,J = 5.4 Hz, 1H), 5.81 (s, 1H), 3.81 (d, J = 5.3 Hz, 2H), 3.73-3.62 (m, 2H), 3.53-3.40 (m, 4H), 2.18 (s, 3H), 2.03 (s, 1H), 1.64 (s, 6H); Anal. RP-HPLC tR = 2.155 min (method 1, purity 99%); LC-MS ESI: m/z = 381.2 [M+H]+ (anal. calcd for C21H25N4O3+: m/z = 381.2).

Synthesis of 1-bromo-4-((trifluoromethyl)sulfinyl)benzene, (building block):



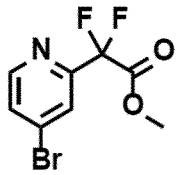
1-bromo-4-((trifluoromethyl)sulfinyl)benzene. To a stirred solution of 1-bromo-4- trifluoromethylthiobenzene (250 mg, 0.97 mmol) in trifluoroacetic acid (2 mL, 0.97 mmol) were added 15 mass % aqueous solution of hydrogen peroxide (33.1 mg, 0.97 mmol) dropwise slowly during 10-15 min at room temperature (Reaction is strongly exothermic). Hydrogen peroxide was added at such a rate that the temperature was kept in the range 25-28°C inside the flask. The reaction mixture was stirred overnight at room temperature. When the reaction mixture showed complete conversion of starting material, contents were poured into water, neutralized with solid NaHCO3 to pH = 6-7 and then extracted with ethyl acetate (4 x 30 mL). The organic phase was washed with water (4 x 20 mL), dried with MgSO4, evaporated in vacuo to afford 1-bromo-4-(trifluoromethylsulfinyl)benzene in 69% yield as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 7.96 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H); Anal. RP-HPLC tR = 1.092 min (method 2, purity 99%); LC-MS ESI: m/z = 272.9 [M+H]+ (anal. calcd for C7H5BrF3OS+: m/z = 272.9).

Synthesis of (4-bromophenyl)dimethylphosphine oxide, (building block):



(4-bromophenyl)dimethylphosphine oxide. To a stirred solution of 1,4-dibromobenzene (350 mg, 1.48 mmol) in acetonitrile (3 mL) were added methylphosphonoylmethane (121.6 mg, 1.56 mmol), tetrakis(triphenylphosphine)palladium (128.6 mg, 0.11 mmol) and the solution was stirred at room temperature for 5 min. Triethylamine (0.31 mL, 2.23 mmol) was then added and the solution was stirred at 90 °C for 12 h. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed-phase silica gel using water/methanol 9.5:0.5 v/v ratio initially and slowly increased to water/methanol 4:6 v/v ratio to afford 1- bromo-4-dimethylphosphorylbenzene in 43% yield as an off white solid. Anal. RP-HPLC tR = 0.822 min (method 2, purity 89%); LC-MS ESI: m/z = 232.9 [M+H]+ (anal. calcd for C8H11BrOP+: m/z = 233.0).

Synthesis of methyl 2-(4-bromopyridin-2-yl)-2,2-difluoroacetate, (building block):

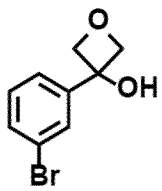


methyl 2-(4-bromopyridin-2-yl)-2,2-difluoroacetate. To a stirred solution of 2,4-dibromopyridine (700 mg, 2.95 mmol) in DMSO (3 mL) were added copper (187.8 mg, 2.95 mmol), methyl bromodifluoroacetate (558.4 mg, 2.95 mmol) and the reaction mixture was degassed for 15 min. The reaction mixture was then stirred at 50 °C for 10 min. Temperature was slowly increased to 70 °C over 10 min. Finally, the reaction mixture was cooled down to 50 °C and continued to stir for 2 h. When the reaction mixture showed complete conversion of starting material, it was cooled to room temperature and ethyl acetate (20 mL) was added. 1.27 M KH2PO4 (20 mL) was added slowly

keeping internal temperature below 30 °C. The mixture was stirred at room temperature for 30 min before filtering through celite. The filtrate was washed with ethyl acetate (2 x 15 mL). The bi-phasic filtrate layers were separated. The organic layer was washed with deionized water (1 x 10 mL) and brine (1 x 10 mL). The organic layer was concentrated to give a yellow oil. The residue was purified by column chromatography on silica gel using hexane/ethyl acetate 8:2 v/v ratio initially and slowly increased to hexane/ethyl acetate 1:9 v/v ratio to afford methyl 2-(4-bromopyridin-2-yl)-2,2- difluoroacetate in 60% yield as a pale-yellow oil. Anal. RP-HPLC tR = 1.009 min (method 2, purity 95%); LC-MS ESI: m/z = 266.0 [M+H]+ (anal. calcd for C8H7BrF2NO2+: m/z = 266.0).

Example 13: Synthesis of reactants and compounds according to the invention following General Procedure 13

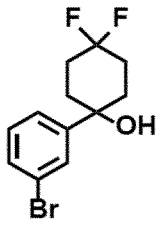
General Procedure 13: Lithiation Reaction (GP13)



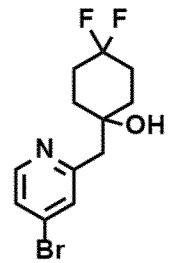
Synthesis of 3-(3-bromophenyl)oxetan-3-ol, (building block): To a -78 °C solution of 1,3-dibromobenzene (1 g,4.24 mmol) was added n-butyllithium solution, 2.5 M in hexane (1.76 mL, 19.08 mmol) keeping the temperature below -70 °C. The resulting reaction mixture was stirred at -78 °C for 30 min followed by addition of the 3-oxetanone (336 mg, 4.66 mmol). Upon completion, the reaction was quenched with saturated NH4Cl and allowed to warm to room temperature. The reaction mixture was diluted with ethyl acetate (20 mL). The content of the flask was transferred to a separating funnel and the product was extracted using ethyl acetate (2 × 100 mL). The combined organic layers were collected, dried over MgSO4 and concentrated. The residue was purified by column chromatography on silica gel using hexane/ethyl acetate 8:2 v/v ratio initially and slowly increased to hexane/ethyl

acetate 5:5 v/v ratio to afford 3-(3- bromophenyl)oxetan-3-ol in 49% yield as a clear oil. 1H NMR (300 MHz, CDCl3) δ = 7.79 (t, J = 1.9 Hz, 1H), 7.58 (ddd, J = 7.7, 1.8, 1.0 Hz, 1H), 7.50 (ddd, J = 8.0, 2.1, 1.1 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 4.92-4.88 (m, 4H).

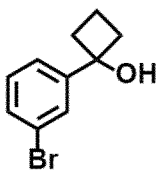
Manufacturing examples



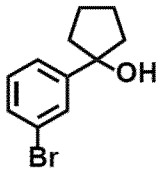
1-(4-bromopyridin-2-yl)-4,4-difluorocyclohexan-1-ol, (building block): According to GP13: Yield 57%. 1H NMR (300 MHz, CDCl3) δ = 7.69 (t, J = 1.8 Hz, 1H), 7.44 (m, 2H), 7.28 (s, 1H), 2.43-2.03 (m, 6H), 1.91-1.85 (m, 2H).



1-((4-bromopyridin-2-yl)methyl)-4,4-difluorocyclohexan-1-ol, (building block): According to GP13: Yield 57%. Anal. RP-HPLC tR = 0.335 min (method 1, purity 99%); LC-MS ESI: m/z = 306.0 [M+H]+ (anal. calcd for C12H15BrF2NO+: m/z = 306.0).



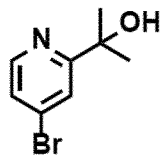
1-(3-bromophenyl)cyclobutan-1-ol, (building block): According to GP13: Yield 61%. Anal. RP-HPLC tR = 0.995 min (method 1, purity - low UV absorption); LC-MS ESI: m/z = 209.0 [M-OH]+ (anal. calcd for C10H11BrO+: m/z = 226.0).



1-(3-bromophenyl)cyclopentan-1-ol, (building block): According to GP13: Yield 65%. Anal. RP-HPLC tR = 1.375 min (method 1, purity 83%); LC-MS ESI: m/z = 241.1 [M+H]+ (anal. calcd for C11H14BrO+: m/z = 241.0).

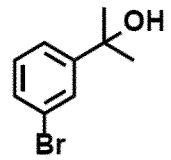
Example 14: Synthesis of reactants and compounds according to the invention following General Procedure 14

General Procedure 14: Grignard Reaction (GP14)

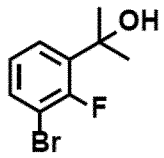


Synthesis of 2-(4-bromopyridin-2-yl)propan-2-ol, (building block): A solution of methyl 4-bromopyridine-2- carboxylate (3 g, 13.89 mmol) in anhydrous tetrahydrofuran (30 mL) was slowly added to a stirred solution of methylmagnesium bromide, 3 M in diethyl ether (8.3 mL, 72.33 mmol) in tetrahydrofuran (60 mL) at 0 °C under inert atmosphere. After 1 h at 0 °C the cooling bath was removed, and the mixture was stirred at 25 °C for 2 h. The reaction was quenched with saturated aqueous NaHCO3, then partitioned between ethyl acetate and deionized water. The aqueous layer was extracted with ethyl acetate (2 x 100 mL). The combined extracts were washed with deionized water (1 x 50 mL), brine (1 x 50 mL), then dried over MgSO4, filtered and evaporated to afford 2-(4-bromopyridin-2-yl)propan-2-ol in 97% yield as amber oil. 1H NMR (300 MHz, CDCl3) δ = 8.37 (d, J = 5.3 Hz, 1H), 7.64-7.59 (m, 1H), 7.41 (dd, J = 5.3, 1.8 Hz,1H), 1.57 (s, 6H); Anal. RP-HPLC tR = 0.866 min (method 2, purity 99%); LC-MS ESI: m/z = 216.0 [M+H]+ (anal. calcd for C8H11BrNO+: m/z = 216.0).

Manufacturing examples



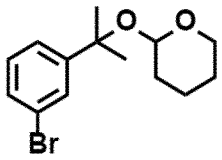
2-(3-bromophenyl)propan-2-ol, (building block): According to GP14: Yield 98%. 1H NMR (300 MHz, CDCl3) δ = 7.66 (t, J = 1.9 Hz, 1H), 7.39 (tdd, J = 8.0, 1.9, 1.1 Hz, 2H), 7.20 (t, J = 7.8 Hz, 1H), 1.57 (s, 6H).



2-(3-bromo-2-fluorophenyl)propan-2-ol, (building block): According to GP14: Yield 77%. 1H NMR (300 MHz, CDCl3) δ = 7.56 (td, J = 7.7, 1.7 Hz, 1H), 7.48 (ddd, J = 8.0, 6.3, 1.7 Hz, 1H), 7.04 (t, J = 7.9 Hz,
1H), 2.05 (br s, 1H), 1.67 (d, J = 1.2 Hz, 6H); Anal. RP-HPLC tR = 1.004 min (method 2, purity 99%); LC-MS ESI: m/z = 215.0 [M-OH]+ (anal. calcd for C9H10BrFO+: m/z = 232.0).

<u>Example 15: Synthesis of reactants and compounds according to the invention following General Procedure 15</u>

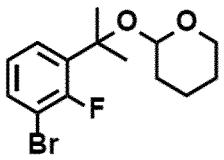
General procedure 15: O-THP Protection (GP15)



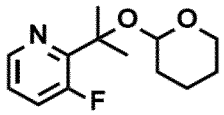
2-((2-(3-bromophenyl)propan-2-yl)oxy)tetrahydro-2H-pyran, (building block): To a solution of 2-(4-bromopyridin-2-yl)propan-2-ol (1.03 g, 4.77 mmol) in dry dichloromethane (80 mL) were added 3,4-dihydro-2H-pyran (0.87mL, 9.53 mmol) and pyridinium p-toluenesulfonate (0.24 g, 0.95 mmol). The resulting mixture was stirred at room temperature for 48 h. Then the mixture was poured

into water and extracted with dichloromethane (3 x 5 mL), the combined organic layers were dried, filtered and concentrated. The residue was purified by Teledyne ISCO CombiFlash system eluting a gradient of petroleum ether/ethyl acetate 9:1 v/v ratio on a silica column to give 4-bromo-2-[2-(oxan-2-yloxy)propan-2-yl]pyridine (711 mg, 2.37 mmol) in a 50% yield as a colorless oil, which was used directly in the next step without any further purification. Anal. RP-HPLC tR = 1.167 min (method 2, purity 99%); LC-MS ESI: m/z 300.1 [M+H]+ (anal. calcd for C13H18BrNO2+: m/z = 300.1).

Manufacturing examples

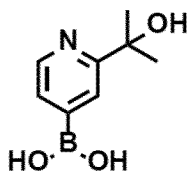


2-((2-(3-bromo-2-fluorophenyl)propan-2-yl)oxy)tetrahydro-2H-pyran, (building block): According to GP15: Yield 64% as a colorless oil. Anal. RP-HPLC tR = 1.328 min (method 2, purity 79%); LC-MS ESI: m/z 232.0 [M-OTHP]+ (anal. calcd for C9H10BrFO+: m/z = 232.0).



3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridine, (building block): According to GP15: Yield 64% as a pale yellow oil. Anal. RP-HPLC tR = 1.001 min (method 2, purity 70%); LC-MS ESI: m/z 240.2 [M+H]+ (anal. calcd for C13H19FNO2+: m/z = 240.1).

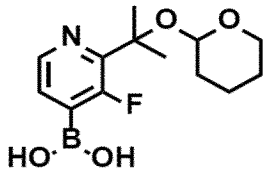
Synthesis of (2-(2-hydroxypropan-2-yl)pyridin-4-yl)boronic acid, (building block):



(2-(2-hydroxypropan-2-yl)pyridin-4-yl)boronic acid. To a solution of 2-(4-bromopyridin-2- yl)propan-2-ol (3.5 g, 16.2 mmol) in 1,4-dioxane (75 mL) at room temperature under nitrogen environment was added with bis(triphenylphosphine)palladium (II) dichloride (1.4 g, 1.94 mmol) and the solution was stirred at 45 °C for 15 min. This was followed by the addition of bis(pinacolato)diboron (1.03 g, 40.49 mmol) and the resulting mixture was heated to 100 °C for 15 min. Finally, the reaction mixture was cooled down to 95 °C and was added with potassium acetate (4.77 g, 48.59 mmol) followed by triethylamine (6.77 mL, 48.59 mmol). The reaction mixture was heated to 100 °C and stirred for 5 h under a nitrogen environment. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed- phase silica gel using water/methanol 9.5:0.5 v/v ratio initially and slowly increased to water/methanol 5:5 v/v ratio to give desired product as beige oil. The oil was then triturated with pentane, hexane, and hexane/ethyl acetate to afford (2-(2-hydroxypropan-2-yl)pyridin-4-yl)boronic acid in 87% yield as light brown powder. LC-MS ESI: m/z 182.2 [M+H]+ (anal. calcd for C8H13BNO3+: m/z = 182.1).

Synthesis of (3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)boronic acid

Manufacturing examples

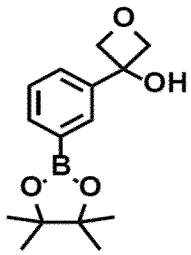


(3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)boronic acid, (building block): 3-fluoro-2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridine (1.5 g, 6.29 mmol) was dissolved in tetrahydrofuran (40 mL), cooled down to -78°C and nBuli solution (10.07 mL, 25.18 mmol) was then added to a stirring solution in a drop-wise fashion. The reaction was stirred at -78°C for

45 min, after which time triisopropyl borate (1.74 mL, 7.55 mmol) was added to and the reaction mixture was kept at 0 °C for another 45 min. The reaction was then quenched by addition of methanol (5 mL). The excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on C18 reversed-phase silica gel using water/methanol 9.5:0.5 v/v ratio initially and slowly increased to water/methanol 5:5 v/v ratio to give desired product as an off white solid in 85% yield. Anal. RP-HPLC tR = 0.768 min (method 2, purity 100%); LC-MS ESI: m/z = 284.2 [M+H]+ (anal. calcd for C13H20BrFNO4+: m/z = 284.2).

Example 16: Synthesis of reactants and compounds according to the invention following General Procedure 16

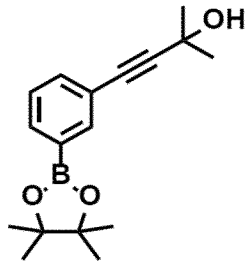
General Procedure 16: Miyaura Borylation Reaction (GP16)



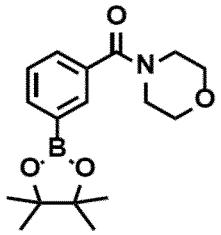
Synthesis of 3-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxetan-3-ol, (building block): To a stirred solution of 3-(3-bromophenyl)oxetan-3-ol (330 mg, 1.44 mmol) in 1,4-dioxane (15 mL) at room temperature under nitrogen environment were added bis(pinacolato)diboron (731.7 mg, 2.88 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (58.8 mg, 0.07 mmol) and continued to stir at room temperature for 15 min. This was followed by the addition of potassium acetate (212.1 mg, 2.16 mmol) and the resulting mixture was heated to 85 °C and continued to stir for 14 h. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to column chromatography on silica gel using hexane/ethyl acetate 9.5:0.5 v/v ratio initially and slowly increased to hexane/ethyl acetate 8:2 v/v ratio to afford 3-(3-(4,4,5,5-tetramethyl-1,3,2-

dioxaborolan-2-yl)phenyl)oxetan-3-ol in 61% yield as a clear oil. 1H NMR (300 MHz, CDCl3) δ = 8.02 (s, 1H), 7.81 (dt, J = 7.2, 1.3 Hz, 1H), 7.70 (ddd, J = 7.9, 1.9, 1.2 Hz, 1H), 7.49-7.43 (m, 1H), 5.03-4.99 (m, 2H), 4.95-4.91 (m, 2H), 1.38 (s, 12H).

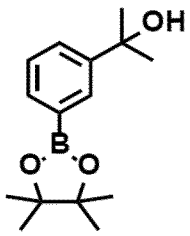
Manufacturing examples



2-methyl-4-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]but-3-yn-2-ol, (building block): According to GP16: Yield 67%. Anal. RP-HPLC tR = 1.223 min (method 2, purity 88%); LC-MS ESI: m/z = 269.2 [M-OH]+ (anal. calcd for C17H23BO3+: m/z = 286.2).

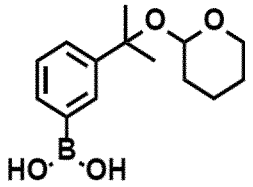


morpholino(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanone, (building block): According to GP16: Yield 91%. Anal. RP-HPLC tR = 2.401 min (method 1, purity 99%); LC-MS ESI: m/z = 318.1 [M+H]+ (anal. calcd for C17H25BNO4+: m/z = 318.2).

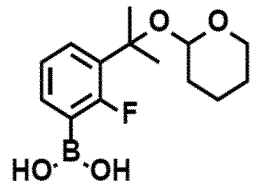


2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-2-ol, (building block): According to GP16: Yield 60%. 1H NMR (300 MHz, CDCl3) δ

= 7.95-7.92 (m, 1H), 7.72 (dt, J = 7.3, 1.2 Hz, 1H), 7.63 (ddd, J = 7.9, 2.1, 1.3 Hz, 1H), 7.38 (ddd, J = 7.9, 7.3, 0.6 Hz, 1H), 1.62 (s, 6H), 1.37 (s, 12H).

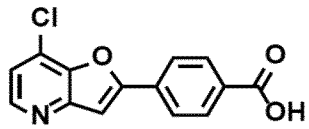


(3-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)phenyl)boronic acid, (building block): According to GP16: Yield 93% as white solid. Anal. RP-HPLC tR = 0.495 min (method 2, purity 93%); LC-MS ESI: m/z 265.2 [M+H]+ (anal. calcd for C14H22BO4+: m/z = 265.2).



(2-fluoro-3-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)phenyl)boronic acid, (building block): According to GP16: Yield 96% as light brown solid. LC-MS ESI: m/z 265.1 [M-OH]+ (anal. calcd for C13H20BFNO4+: m/z = 282.1).

Synthesis of 4-(7-chlorofuro[3,2-b]pyridin-2-yl)benzoic acid

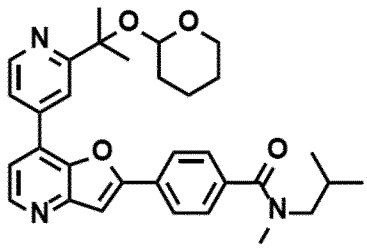


4-(7-chlorofuro[3,2-b]pyridin-2-yl)benzoic acid, (building block): To a stirred suspension of methyl 4-(7- chlorofuro[3,2-b]pyridin-2-yl)benzoate (5 g, 17.38 mmol) in 1,4-dioxane (16 mL) at room temperature, was slowly added lithium hydroxide monohydrate (2.19 mg, 52.14 mmol) in deionized water (4 mL). The reaction mixture was stirred at 70 °C for 5 h, after which LC-MS indicated the reaction was completed. The reaction mixture was cooled to room temperature and the pH adjusted to 2-3 using 2 N HCl aqueous solution. During this time the reaction mixture became milky and after stirring for 1h, a precipitate formed. The precipitate was filtered and washed with water (2 x 10 mL). The

filtrate was then dried to afford 4-(7- chlorofuro[3,2-b]pyridin-2-yl)benzoic acid (4.4 g, 14.79 mmol) in 85% as an off white solid, which was used directly in the next step without further purification. Anal. RP-HPLC tR = 0.994 min (method 2, purity 92%); LC-MS ESI: m/z 274.1 [M+H]+ (anal. calcd for C14H9ClNO3+: m/z = 274.0).

Example 17: Synthesis of reactants and compounds according to the invention following General Procedure 17

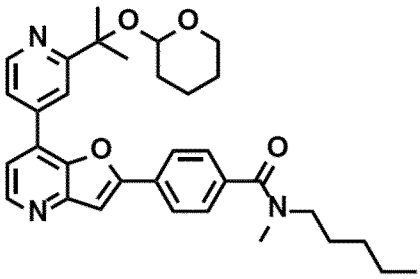
General Procedure 17: Amide Formation Using TBTU, DIPEA and DMAP (GP17)



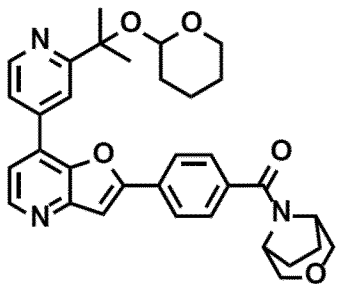
N-isobutyl-N-methyl-4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide, (building block): To a suspension of the 4-(7-(2-(2-((tetrahydro-2H- pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoic acid (142 mg, 0.31 mmol) in dichloromethane (4 mL) and N,N-dimethylformamide (1 mL) was added N-ethyl-N- isopropyl-propan-2-amine ((DIPEA), 0.16 mL, 0.93 mmol), 4-(dimethylamino)pyridine ((DMAP), 3.8 mg, 0.03 mmol), N,2-dimethylpropan-1-amine (32.4 mg, 0.37 mmol) and O-(benzotriazol-1-yl)- N,N,N',N'-tetramethyluronium tetrafluoroborate ((TBTU)119.3 mg, 0.37 mmol). The reaction mixture was stirred at 50 °C for 24 h. After complete consumption of starting material, excess solvent was evaporated from the reaction mixture in vacuo. The residue was subjected to flash chromatography ISCO Teledyne using ethyl acetate/methanol 9.9:0.1 v/v ratio initially and slowly increased to ethyl acetate/methanol 9.5:5 v/v to afford N-isobutyl-N-methyl-4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide (100 mg, 0.19 mmol) in 81% as a yellow oil, which was used in

the next step without further purification. Anal. RP-HPLC tR = 1.241 min (method 2, purity 99%); LC-MS ESI: m/z 528.3 [M+H]+ (anal. calcd for C32H38N3O4+: m/z = 528.3).

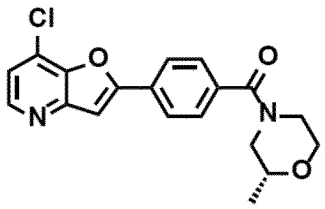
Manufacturing examples



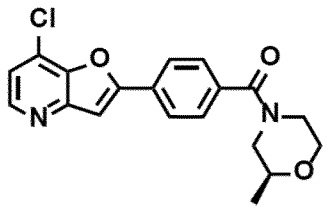
N-methyl-N-pentyl-4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide, (building block): According to GP17: Yield 30% as a brown solid. Anal. RP-HPLC tR = 1.300 min (method 2, purity 92%); LC-MS ESI: m/z 542.3 [M+H]+ (anal. calcd for C33H40N3O4+: m/z = 542.3).



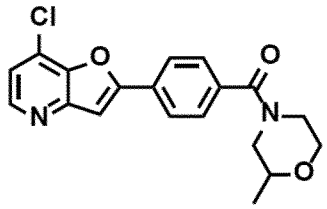
(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(4-(7-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone, (building block): According to GP17: Yield 31% as a yellow solid. Anal. RP-HPLC tR = 1.346 min (method 2, purity 98%); LC-MS ESI: m/z 554.2 [M+H]+ (anal. calcd for C33H36N3O5+: m/z = 554.3).



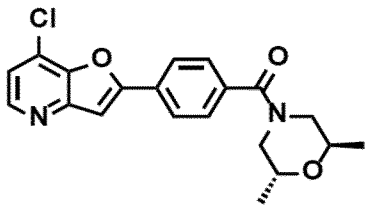
(R)-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(2-methylmorpholino)methanone, (building block): According to GP17: Yield 63% as a yellow solid. Anal. RP-HPLC tR = 1.018 min (method 2, purity 99%); LC-MS (ESI): m/z = 357.1 [M+H]+ (anal. calcd for C19H18ClN2O3+: m/z = 357.1).



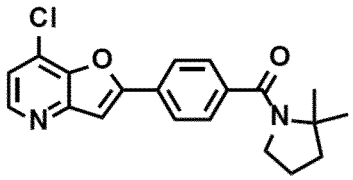
(S)-(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(2-methylmorpholino)methanone, (building block): According to GP17: Yield 76% as a yellow solid. Anal. RP-HPLC tR = 1.010 min (method 2, purity 99%); LC-MS (ESI): m/z = 357.1 [M+H]+ (anal. calcd for C19H18ClN2O3+: m/z = 357.1).



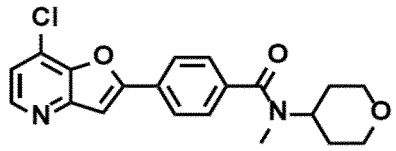
(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(2-methylmorpholino)methanone, (building block): According to GP17: Yield 68% as a yellow solid. Anal. RP-HPLC tR = 1.010 min (method 2, purity 99%); LC-MS (ESI): m/z = 357.1 [M+H]+ (anal. calcd for C19H18ClN2O3+: m/z = 357.1).



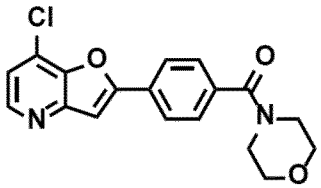
(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)((2R,6R)-2,6-dimethylmorpholino)methanone, (building block): According to GP17: Yield 51% as a yellow solid. Anal. RP-HPLC tR = 1.051 min (method 2, purity 92%); LC-MS (ESI): m/z = 371.1 [M+H]+ (anal. calcd for C20H20ClN2O3+: m/z = 371.1).



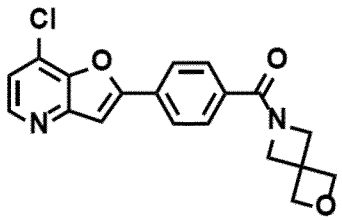
(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(2,2-dimethylpyrrolidin-1-yl)methanone, (building block): According to GP17. Yield 50% as a yellow solid. Anal. RP-HPLC tR = 1.187 min (method 2, purity 98%); LC-MS (ESI): m/z = 355.1 [M+H]+ (anal. calcd for C20H20ClN2O2+: m/z = 355.1).



4-(7-chlorofuro[3,2-b]pyridin-2-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)benzamide, (building block): According to GP17: Yield 88% as a yellow solid. Anal. RP-HPLC tR = 1.136 min (method 2, purity 95%); LC-MS (ESI): m/z = 371.1 [M+H]+ (anal. calcd for C20H20ClN2O3+: m/z = 371.1).



(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone, (building block): According to GP17: Yield 70% as a yellow solid. Anal. RP-HPLC tR = 1.079 min (method 2, purity 95%); LC-MS (ESI): m/z = 343.1 [M+H]+ (anal. calcd for C18H16ClN2O3+: m/z = 343.1).



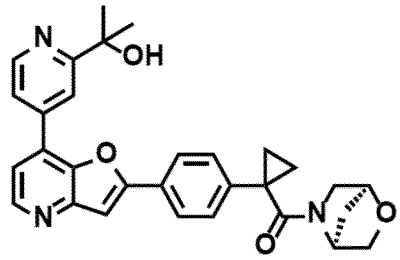
(4-(7-chlorofuro[3,2-b]pyridin-2-yl)phenyl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone, (building block): According to GP17: Yield 69% as a yellow solid. Anal. RP-HPLC tR = 0.930 min (method 2, purity 89%); LC-MS (ESI): m/z = 355.1 [M+H]+ (anal. calcd for C19H16ClN2O3+: m/z = 355.1).

Example 18: Synthesis of reactants and compounds according to the invention following General Procedure 18

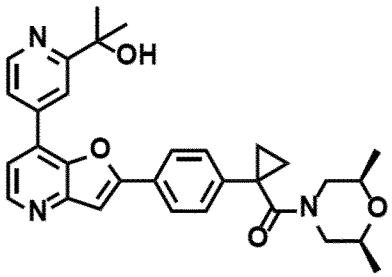
General Procedure 18: O-THP Deprotection (GP18)

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-isobutyl-N-methylbenzamide (D186). A hydrogen chloride solution (0.47 mL, 1.9 mmol) in 1,4-dioxane (4 N) was added to a solution of N-isobutyl-N-methyl-4-(7-(2-(2-((tetrahydro-2H-pyran-2- yl)oxy)propan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide (100 mg, 0.19 mmol) in dichloromethane (4 mL) at room temperature. The reaction was stirred at room temperature for 1 h, after which LC-MS confirmed product formation and consumption of the starting material. Amberlyst A-21 was added, and reaction mixture was stirred for 30 min. The reaction mixture was then filtered, and the filtrate was concentrated in vacuo and purified by Teledyne ISCO CombiFlash system eluting a reverse phase solvent gradient of methanol/deionized water on a C18 column. Compound was then passed through ion-exchange resin to afford 4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-isobutyl-N-methylbenzamide (58 mg, 0.13 mmol) in 68% as a yellow solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.54 (d, J = 1.8 Hz, 1H), 8.16 (d, J = 7.9 Hz, 2H), 7.98 (dd, J = 5.2, 1.7 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 7.64-7.54 (m, 3H), 3.45 (d, J = 7.6 Hz, 1H), 3.23 (d, J = 7.6 Hz, 1H), 3.12 and 3.04 (s and s, 3H), 2.26-1.93 (m, 1H), 1.68 (s, 6H), 1.04 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.985 min (method 2, purity 99%); LC-MS ESI: m/z = 444.2 [M+H]+ (anal. calcd for C27H30N3O3+: m/z = 444.2).

Manufacturing examples

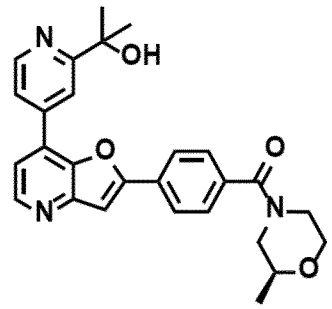


((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)methanone. According to GP18: Yield 26% as a light yellow solid. 1H NMR (600 MHz, DMSO-d6) δ = 8.74 (d, J = 5.0 Hz, 1H), 8.64 (d, J = 5.0 Hz, 1H), 8.46 (s, 1H), 8.02 (t, J = 8.0 Hz, 2H), 7.94 (d, J = 5.0 Hz, 1H), 7.73 (dd, J = 16.5, 5.0 Hz, 2H), 7.38 (dd, J = 20.9, 8.0 Hz, 2H), 5.41 (s, 1H), 4.76 (s, 0.5H), 4.56 (s, 0.5H), 4.48 (d, J = 11.5 Hz, 1H), 3.71-3.62 (m, 1H), 3.46 (d, J = 7.3 Hz, 0.5H), 3.38 (d, J = 11.6 Hz, 0.5H), 3.17 (dd, J = 8.7, 3.3 Hz, 1H), 3.05 (q, J = 10.3 Hz, 1H), 1.68 (p, J = 10.2 Hz, 2H), 1.55 (s, 6H), 1.45-1.40 (m, 1H), 1.35 (t, J = 8.1 Hz, 1H), 1.26 (tt, J = 11.3, 5.3 Hz, 1H), 1.18-1.13 (m, 1H); Anal. RP-HPLC tR = 0.856 min (method 2, purity 99%); LC-MS ESI: m/z = 496.2 [M+H]+ (anal. calcd for C30H30N3O4+: m/z = 496.2).

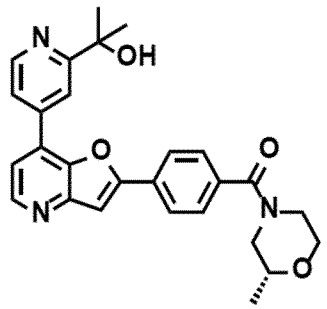


((2S,6R)-2,6-dimethylmorpholino)(1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2- b]pyridin-2-yl)phenyl)cyclopropyl)methanone. According to GP18: Yield 21% as a white solid. 1H NMR (600 MHz, DMSO-d6) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.64 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 1.8 Hz, 1H), 8.00 (d, J = 8.1 Hz, 2H), 7.91 (dd, J = 5.1, 1.8 Hz, 1H), 7.70-7.63 (m, 2H), 7.36 (d, J = 8.1 Hz, 2H), 5.18 (s, 1H), 4.07 (s, 2H), 3.33 (s, 2H), 2.47-2.40 (m, 2H), 1.57 (s, 6H), 1.39 (q, J = 4.6, 4.1 Hz, 2H), 1.28 (q, J = 4.6 Hz, 2H), 1.01 (d, J = 6.1 Hz, 6H); Anal.

RP-HPLC tR = 0.956 min (method 2, purity 99%); LC-MS ESI: m/z = 512.4 [M+H]+ (anal. calcd for C31H34N3O4+: m/z = 512.3).

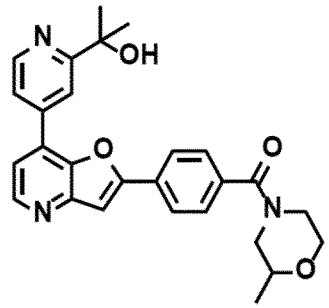


(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2- methylmorpholino)methanone. According to GP18: Yield 64% as an amorphous solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.71 (d, J = 5.1 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 1.8 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.94 (dd, J = 5.2, 1.8 Hz, 1H), 7.71 (d, J = 5.1 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.56 (s, 1H), 4.48 (m, 1H), 3.89 (m, 1H), 3.67-3.49 (m, 4H), 2.99 (s, 1H), 1.64 (s, 6H), 1.42 m, 1H), 1.16 (s, 3H); Anal. RP-HPLC tR = 0.852 min (method 2, purity 96%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C27H28N3O4+: m/z = 458.2).



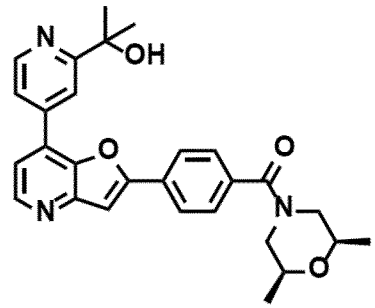
(R)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2- methylmorpholino)methanone. According to GP18: Yield 26% as an amorphous brown solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.71 (d, J = 5.2 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 1.8 Hz, 1H), 8.13 (d, J = 8.2 Hz, 2H), 7.94 (dd, J = 5.1, 1.9 Hz, 1H), 7.72 (d, J = 5.1 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.56 (s, 1H), 4.46 (s, 1H), 3.89 (m, 1H), 3.65-3.51 (m, 4H), 3.03 (s, 1H), 1.64 (s, 6H), 1.57-1.50 (m, 1H), 1.16 (s, 3H); Anal. RP-HPLC tR = 0.853

min (method 2, purity 96%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C27H28N3O4+: m/z = 458.2).



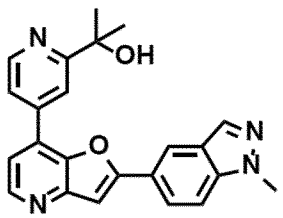
(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-methylmorpholino)methanone. According to GP18: Yield 88% as a yellow solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.71 (d, J = 5.2 Hz, 1H), 8.64-8.57 (d, J = 6.0 Hz, 1H), 8.49 (s, 1H), 8.12 (d, J = 6.0 Hz, 2H), 7.93 (dt, J = 5.2, 1.5 Hz, 1H), 7.71 (d, J = 6.0 Hz, 1H), 7.59 (d, J = 6.0 Hz, 2H), 7.55 (s, 1H), 4.46 (br s, 1H), 3.87-3.81 (m, 1H), 3.58 (br s, 3H), 3.33-3.31 (m, 1H), 3.02 (s, 1H), 1.63 (s, 6H), 1.22-1.03 (m, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.854 min (method 2, purity 99%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C27H28N3O4+: m/z = 458.2).

((2R,6R)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D199). According to GP18: Yield 43% as a pale yellow solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.71 (d, J = 5.1 Hz, 1H), 8.60 (dd, J = 5.0, 1.2 Hz, 1H), 8.49 (s, 1H), 8.13 (d, J = 7.8 Hz, 2H), 7.94 (dd, J = 5.1, 1.8 Hz, 1H), 7.72 (d, J = 5.1 Hz, 1H), 7.60-7.57 (m, 2H), 7.56 (s, 1H), 4.11 (s, 1H), 3.97 (s, 1H), 3.83 (s, 1H), 3.60-3.45 (m, 2H), 3.21 (s, 1H), 1.60 (s, 6H), 1.26 (s, 3H), 1.10 (s, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.876 min (method 2, purity 96%); LC-MS ESI: m/z = 472.2 [M+H]+ (anal. calcd for C28H30N3O4+: m/z = 472.2).



((2S,6R)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2- b]pyridin-2-yl)phenyl)methanone. According to GP18: Yield 24% as an off white solid. 1H NMR (600 MHz, DMSO-d6) δ = 8.69 (d, J = 49.3 Hz, 2H), 8.41 (s, 1H), 8.11 (s, 2H), 7.89 (d, J = 48.8 Hz, 2H), 7.72 (s, 1H), 7.57 (s, 2H), 5.39 (s, 1H, OH), 4.37 (s, 1H), 3.49 (d, J = 67.4 Hz, 4H), 2.84 (s, 1H), 1.53 (s, 6H), 1.06 (d, J = 90.3 Hz, 6H); Anal. RP-HPLC tR = 0.895 min (method 2, purity 99%); LC-MS ESI: m/z = 472.2 [M+H]+ (anal. calcd for C28H30N3O4+: m/z = 472.2).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone (D190). According to GP18: Yield 50% as a brown solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.66 (d, J = 5.1 Hz, 1H), 8.54 (d, J = 1.7 Hz, 1H), 8.29 (d, J = 8.3 Hz, 2H), 8.18 (d, J = 8.3 Hz, 2H), 7.97 (dd, J = 5.2, 1.7 Hz, 1H), 7.78 (d, J = 5.1 Hz, 1H), 7.71 (s, 1H), 3.37 (s, 1H), 3.23 (s, 3H), 1.68 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.750 min (method 2, purity 99%); LC-MS ESI: m/z = 408.1 [M+H]+ (anal. calcd for C22H22N3O3S+: m/z = 408.1)



2-(4-(2-(1-methyl-1H-indazol-5-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. According to GP18: Yield 46% as a yellow solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.57 (d, J = 5.3 Hz, 2H), 8.45 (s, 1H), 8.15 (s,

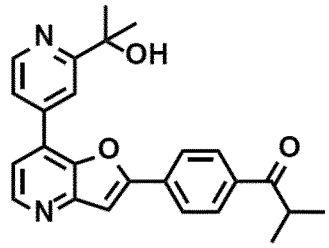
1H), 8.06 (dd, J = 8.9, 1.6 Hz, 1H), 7.98 (dt, J = 5.1, 1.4 Hz, 1H), 7.72-7.66 (dd, J = 12.0, 8.0 Hz, 2H), 7.41 (s, 1H), 4.12 (s, 3H), 1.70 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.881 min (method 2, purity 99%); LC-MS ESI: m/z = 385.2 [M+H]+ (anal. calcd for C23H21N4O2+: m/z = 385.2).

((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D188). According to GP18: Yield 40% as an off white solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.74-8.69 (m, 1H), 8.64 (dd, J = 5.1, 2.3 Hz, 1H), 8.46 (ddd, J = 7.4, 1.9, 0.9 Hz, 1H), 7.92 (dd, J = 5.2, 1.6 Hz, 1H), 7.83-7.78 (m, 2H), 7.77-7.74 (m, 1H), 7.69 (d, J = 8.3 Hz, 1H), 4.69 (m, 1H), 3.97-3.72 (m, 2H), 3.66-3.44 (m, 2H), 3.35- 3.28 (m, 2H), 2.04-1.92 (m, 2H), 1.63 (d, J = 1.4 Hz, 6H); Anal. RP-HPLC tR = 0.855 min (method 2, purity 97%); LC-MS ESI: m/z = 492.2 [M+H]+ (anal. calcd for C H F N O +: m/z = 492.2).

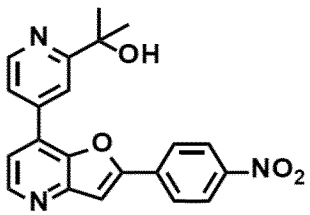
2-(4-(2-(4-(1-hydroxyethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D187). According to GP18: Yield 44% as a brown solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.73-8.69 (m, 1H), 8.56 (d, J = 5.1 Hz, 1H), 8.48 (dd, J = 1.8, 0.8 Hz, 1H), 8.02-7.95 (m, 2H), 7.93 (m, 1H), 7.67 (d, J = 5.2 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.41 (s, 1H), 4.88 (q, J = 6.6 Hz, 1H), 1.64 (s, 6H), 1.46(d, J = 6.6 Hz, 3H). The OH signal was not observed due to the deuterated solvent; Anal. RP- HPLC tR = 0.839 min (method 2, purity 99%); LC-MS ESI: m/z = 375.2 [M+H]+ (anal. calcd for C23H23N2O3+: m/z = 375.2).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-pentylbenzamide (D185). According to GP18: Yield 52% as a brown solid. 1H NMR (400 MHz, MeOD- d4) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.54 (d, J = 1.7 Hz, 1H), 8.16 (d, J = 8.1Hz, 2H), 7.99 (dd, J = 5.3, 1.8 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 7.64-7.54 (m, 3H), 3.59 (t, J = 7.6Hz, 1H), 3.37 (t, J = 7.6 Hz, 1H), 3.11 and 3.03 (s and s, 3H), 1.77-1.62 (m, 2H), 1.68 (s, 6H), 1.44 (m, 2H), 1.20 (m, 2H), 1.03-0.80 (m, 3H). The OH signal was not observed

due to the deuterated solvent; Anal. RP-HPLC tR = 1.048 min (method 2, purity 98%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C28H32N3O3+: m/z = 458.2).



1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-2-methylpropan-1-one. According to GP18: Yield 52% as a brown solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.64 (d, J = 5.2 Hz, 1H), 8.53 (dd, J = 10.5, 3.2 Hz, 1H), 8.17 (d, J = 5.6 Hz, 3H), 8.13 (s, 2H), 7.97 (dt, J = 5.3, 1.4 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 7.64 (s, 1H), 3.71 (d, J = 6.8 Hz, 1H), 1.69 (s, 6H), 1.24 (dd, J = 7.0, 2.1 Hz, 6H); Anal. RP-HPLC tR = 1.050 min (method 2, purity 99%); LC-MS ESI: m/z = 401.2 [M+H]+ (anal. calcd for C25H25N2O3+: m/z = 401.2).



2-(4-(2-(4-nitrophenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. According to GP18: Yield 20% as a yellow solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.77 (d, J = 5.2 Hz, 1H), 8.69 (d, J = 5.1 Hz, 1H), 8.54 (d, J = 1.8 Hz, 1H), 8.43 (d, J = 8.8 Hz, 2H), 8.30 (d, J = 8.7 Hz, 2H), 7.99 (dd, J = 5.3, 1.8 Hz, 1H), 7.81 (d, J = 5.1 Hz, 1H), 7.78 (s, 1H), 7.70-7.63 (m, 1H), 7.58 (m, 1H), 1.69 (s, 6H); Anal. RP-HPLC tR = 2.497 min (method 1, purity 99%); LC-MS ESI: m/z = 376.1 [M+H]+ (anal. calcd for C21H18N3O4+: m/z = 376.1).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2,6-dimethylphenyl)(morpholino)methanone (D182). According to GP18: Yield

53% as a yellow solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.62 (d, J = 5.2 Hz, 1H), 8.58 (s, 1H), 7.95 (dd, J = 5.1, 1.6 Hz, 1H), 7.82 (s, 2H), 7.74 (dd, J = 5.2, 1.4 Hz, 1H), 7.52 (d, J = 1.6 Hz, 1H), 3.86 (t, J = 5.0 Hz, 2H), 3.82 (t, J = 5.0 Hz, 2H), 3.65 (t, J = 4.8 Hz, 2H), 3.29 (t, J = 4.9 Hz, 2H), 2.39 (s,6H), 1.69 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP- HPLC tR = 0.861 min (method 2, purity 99%); LC-MS ESI: m/z = 472.2 [M+H]+ (anal. calcd for C28H30N3O4+: m/z = 472.2).

(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone (D181). According to GP18: Yield 30% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.76 (d, J = 5.1 Hz, 1H), 8.71 (d, J = 5.0 Hz, 1H), 8.45 (d, J = 1.8 Hz, 1H), 8.05 (s, 1H), 7.99-7.89 (m, 3H), 7.82 (d, J = 5.1 Hz, 1H), 5.43 (s, 1H), 3.72-3.65 (m, 4H), 3.56 (t, J = 4.7 Hz, 2H), 3.35 (t, J = 4.7 Hz, 2H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.887 min (method 2, purity 100%); LC-MS ESI: m/z = 480.2 [M+H]+ (anal. calcd for C26H24F2N3O4+: m/z = 480.2).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)benzamide (D179). According to GP18: Yield 41% as a yellow solid. 1HN MR (400 MHz, MeOD-d4) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.56-8.51 (m, 1H), 8.17 (d, J = 8.0 Hz, 2H), 7.99 (dd, J = 5.2, 1.8 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 7.61 (d, J = 7.2 Hz, 3H), 4.02 (m, 2H), 3.57 (m, 2H), 3.19 (m, 1H), 3.00 (br s, 3H), 1.99 (s, 2H), 1.74 (s, 2H), 1.68 (s, 6H). The OH signal was not observed due to the deuterated solvent. Anal. RP-HPLC tR = 0.861 min (method 2, purity 99%); LC-MS ESI: m/z = 472.2 [M+H]+ (anal. calcd for C28H30N3O4+: m/z = 472.2).

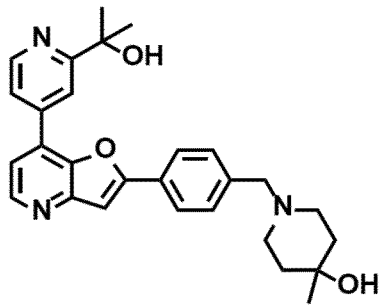
(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2- b]pyridin-2-yl)phenyl)methanone (D178). According to GP18: Yield 47% as a yellow solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.71 (d, J = 5.1 Hz, 1H), 8.60 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 1.7 Hz, 1H), 8.16-8.11 (m, 2H), 7.94 (dd, J = 5.2, 1.8 Hz, 1H), 7.72 (d, J = 5.1 Hz, 1H), 7.69-7.66 (m, 2H), 7.56 (s,

1H), 4.65 (s, 1H), 4.04 (s, 1H), 3.71 (t, J = 65.9 Hz, 4H), 2.10-1.97 (m, 4H), 1.64 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 1.120 min (method 2, purity 99%); LC-MS ESI: m/z = 470.2 [M+H]+ (anal. calcd for C28H28N3O4+: m/z= 470.2).

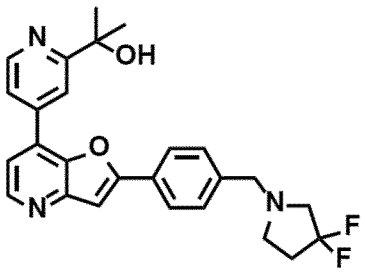
(1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)(morpholino)methanone (D180). According to GP18: Yield 35% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.64 (d, J = 5.3 Hz, 1H), 8.49- 8.41 (m, 1H), 8.02 (d, J = 8.2 Hz, 2H), 7.93 (dd, J = 5.1, 1.7 Hz, 1H), 7.76-7.69 (m, 2H), 7.33 (d, J = 8.2 Hz, 2H), 5.41 (s, 1H), 3.45 (s,8H), 1.55 (s, 6H), 1.39 (t, J = 3.3 Hz, 2H), 1.31-1.25 (m, 2H); Anal. RP-HPLC tR = 0.894 min (method 2, purity 99%); LC-MS ESI: m/z = 484.2 [M+H]+ (anal. calcd for C29H30N3O4+: m/z = 484.2).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone (D134). According to GP18: Yield 78% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.67 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 1.8 Hz, 1H),8.14 (d, J = 8.1 Hz, 2H), 7.96 (dd, J = 5.2, 1.7 Hz, 1H), 7.88 (s, 1H), 7.75 (d, J = 5.0 Hz, 1H), 7.60(d, J = 8.1 Hz, 2H), 5.41 (s, 1H), 3.62 (s, 8H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.828 min (method2, purity 99%); LC-MS ESI: m/z = 444.2 [M+H]+ (anal. calcd for C26H26N3O4+: m/z = 444.2).

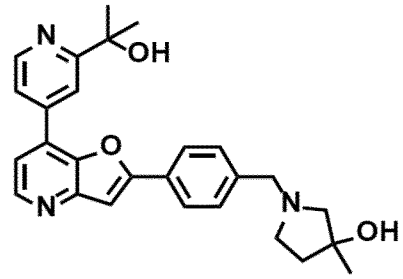
2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-1-morpholinoethan-1-one (D170). According to GP18: Yield 44% as a yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.70 (m, 1H), 8.49 (m, 2H), 7.98 (d, J = 8.1 Hz, 3H), 7.69 (s, 1H), 7.50-7.34 (m, 3H), 3.88 (s, 2H), 3.65 (m, 4H), 3.59 (m, 4H), 1.68 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.839 min (method 2, purity 99%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C27H28N3O4+: m/z = 458.2).



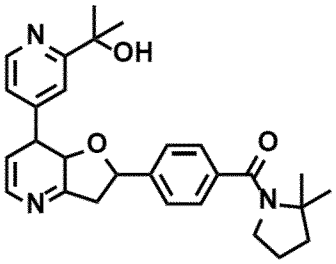
1-[[4-[7-[2-(2-hydroxypropan-2-yl)pyridin-4-yl]furo[3,2-b]pyridin-2-yl]phenyl]methyl]-4-methylpiperidin-4-ol. According to GP18: Yield 14% as off white solid. 1H NMR (600 MHz, DMSO-d6) δ = 8.71 (d, J = 5.0 Hz, 1H), 8.60 (d, J = 5.0 Hz, 1H), 8.44 (s, 1H), 7.98 (d, J = 7.8 Hz, 2H), 7.92-7.87 (m, 1H), 7.68 (d, J = 6.2 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 5.38 (s, 1H, OH), 4.06 (s, 1H, OH), 3.52 (s, 2H), 2.38 (s, 4H), 1.51 (s, 6H), 1.45 (t, J = 5.6 Hz, 4H), 1.07 (s, 3H); Anal. RP-HPLC tR = 2.271 min (method 1, purity 99%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C28H32N3O3+: m/z = 458.2).



2-(4-(2-(4-((3,3-difluoropyrrolidin-1-yl)methyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. According to GP18: Yield 34% as a light purple solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.75 (dd, J = 5.1, 0.8 Hz, 1H), 8.64 (d, J = 5.1 Hz, 1H), 8.47 (dd, J = 1.8, 0.8 Hz, 1H), 8.04 (d, J = 8.2 Hz, 2H), 7.94 (dd, J = 5.2, 1.8 Hz, 1H), 7.76-7.69 (m, 2H), 7.50 (d, J = 8.2 Hz, 2H), 5.41 (s, 1H), 3.71 (s, 2H), 2.90 (t, J = 13.3 Hz, 2H), 2.73 (t, J = 6.9 Hz, 2H), 2.28 (td, J = 15.2, 7.4 Hz, 2H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.791 min (method 2, purity 99%); LC-MS ESI: m/z = 450.2 [M+H]+ (anal. calcd for C26H26F2N3O2+: m/z = 450.2).

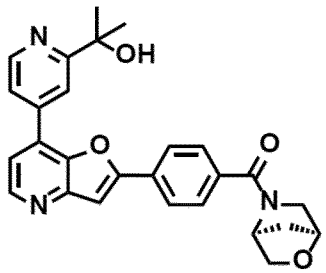


1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)-3-methylpyrrolidin-3-ol. According to GP18: Yield 39% as a light yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.72 (dd, J = 5.2, 0.8 Hz, 1H), 8.57 (d, J = 5.2 Hz, 1H), 8.49 (dd, J = 1.9, 0.9 Hz, 1H), 8.04-7.97 (m, 2H), 7.94 (dd, J = 5.2, 1.8 Hz, 1H), 7.69 (d, J = 5.2 Hz, 1H), 7.58-7.50 (m, 2H), 7.43 (s, 1H), 3.76 (d, J = 2.9 Hz, 2H), 2.98-2.84 (m, 1H), 2.76-2.63 (m, 2H), 2.60 (d, J = 10.1 Hz, 1H), 1.96-1.83 (m, 2H), 1.66 (s, 6H), 1.36 (s, 3H); Anal. RP-HPLC tR = 0.662 min (method 2, purity 99%); LC-MS ESI: m/z = 444.2 [M+H]+ (anal. calcd for C27H30N3O3+: m/z = 444.2).



((2,2-dimethylpyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)-2,3,7,7a-tetrahydrofuro[3,2-b]pyridin-2-yl)phenyl)methanone. According to GP18: Yield 13% as a yellow solid. 1H NMR (400 MHz, MeOD-d4) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.63 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.17-8.11 (m, 2H), 7.99 (d, J = 5.2 Hz, 1H), 7.76 (dd, J = 5.2, 1.4 Hz, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.58 (s, 1H), 3.50 (t, J = 6.6 Hz, 2H), 1.96 (t, J = 6.7 Hz, 2H), 1.88 (q, J = 6.6 Hz, 2H), 1.68 (d, J = 1.4 Hz, 6H), 1.63 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 1.008 min (method 2, purity 99%); LC-MS ESI: m/z = 456.2 [M+H]+ (anal. calcd for C28H30N3O3+: m/z = 456.2).

(3,5-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2- yl)phenyl)methanone (D166). According to GP18: Yield 15% as a pale yellow solid. 1H NMR (600 MHz, MeOD-d4) δ = 8.70 (d, J = 5.2 Hz, 1H), 8.60-8.57 (m, 1H), 8.50-8.46 (m, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.93 (dd, J = 5.2, 1.8 Hz, 1H), 7.70 (d, J = 5.1 Hz, 1H), 7.64-7.59 (m, 2H), 7.58-7.52 (m, 2H), 4.13 (br s, H), 3.94-3.84 (m, 1H), 3.74 (d, J = 11.7 Hz, 2H), 3.66 (dd, J = 11.6, 3.8 Hz, 2H), 1.64 (s, 6H), 1.39 (d, J = 6.9 Hz, 6H); Anal. RP-HPLC tR = 0.900 min (method 2, purity 95%); LC-MS ESI: m/z = 472.2 [M+H]+ (anal. calcd for C28H30N3O4+: m/z = 472.2).



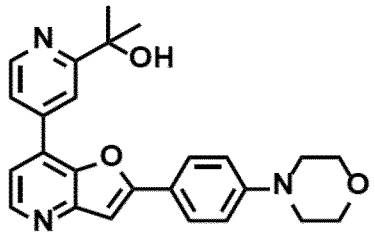
((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4- yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D167). According to GP18: Yield 35% as a light yellow solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.76 (d, J = 5.1 Hz, 1H), 8.67 (d, J = 5.1 Hz, 1H), 8.44 (d, J = 13.0 Hz, 1H), 8.14 (t, J = 9.1 Hz, 2H), 8.01-7.88 (m, 2H), 7.79-7.63 (m, 3H), 5.45 (s, 1H), 4.64(dd, J = 108.5, 71.8 Hz, 2H), 3.95-3.51 (m, 3H), 3.23 (dd, J = 48.3, 7.5 Hz, 1H), 1.99-1.75 (m, 2H),1.55 (s, 6H); Anal. RP-HPLC tR = 0.813 min (method 2, purity 99%); LC-MS ESI: m/z = 456.2 [M+H]+ (anal. calcd for C27H26N3O4+: m/z = 456.2).

5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)isoindolin-1-one (D158). According to GP18: Yield 25% as a yellow solid. 1H NMR (600 MHz, DMSO-d6) δ = 8.73 (d, J = 5.1 Hz, 1H), 8.67 (s, 1H), 8.65 (d, J = 5.0 Hz, 1H), 8.40 (d, J = 1.8 Hz, 1H), 8.23 (s, 1H), 8.15 (dd, J = 7.9, 1.5 Hz, 1H), 7.94 (dd, J = 5.0, 1.8 Hz, 1H), 7.90 (s, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.72 (d, J = 5.0 Hz, 1H), 5.38 (s, 1H), 4.46 (s, 2H), 1.52 (s, 6H); Anal. RP-HPLC tR = 2.372

min (method 1, purity 95%); LC-MS ESI: m/z = 386.1 [M+H]+ (anal. calcd for C23H20N3O3+: m/z = 386.2).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(indolin-1-yl)methanone (D157). According to GP18: Yield 13% as a yellow solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.81 (d, J = 5.3 Hz, 1H), 8.72 (d, J = 5.0 Hz, 1H), 8.53 (s, 1H), 8.20 (d, J = 8.0 Hz, 2H), 8.13 (d, J = 6.6 Hz, 2H), 7.97 (s, 1H), 7.81 (dd, J = 14.9, 6.6 Hz, 3H), 7.68-7.53 (m, 3H), 7.31 (d, J =7.5 Hz, 1H), 4.08 (t, J = 8.3 Hz, 2H), 3.12 (t, J = 8.3 Hz, 2H), 1.59 (s, 6H); Anal. RP-HPLC tR = 2.591 min (method 1, purity 98%); LC-MS ESI: m/z = 476.1 [M+H]+ (anal. calcd for C30H26N3O3+: m/z = 476.2).

5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2-(4-methoxybenzyl)isoindolin-1-one (D156). According to GP18: Yield 18% as a yellow solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.75 (d, J = 5.1 Hz, 1H), 8.68 (dd, J = 5.1, 1.4 Hz, 1H), 8.45 (s, 1H), 8.26-8.18 (m, 2H), 7.97 (d, J = 4.9 Hz, 1H), 7.93 (d, J = 1.4 Hz, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 5.1 Hz, 1H), 7.26 (d, J = 8.3 Hz, 2H), 6.98-6.90 (m, 2H), 5.45 (s, 1H), 4.70 (s, 2H), 4.45 (s, 2H), 3.74 (d, J = 1.5 Hz, 3H), 1.55 (s, 6H); Anal. RP-HPLC tR = 2.591 min (method 1, purity 95%); LC-MS ESI: m/z = 506.2 [M+H]+ (anal. calcd for C31H28N3O4+: m/z = 506.2).



2-(4-(2-(4-morpholinophenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. According to GP18: Yield 29% as a yellow solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.74 (d, J = 5.1 Hz, 1H), 8.57 (dd, J = 5.2, 1.6 Hz, 1H), 8.45 (s, 1H), 7.92 (dt, J = 7.1, 1.8 Hz, 3H), 7.64 (dd, J = 5.2, 1.7 Hz, 1H), 7.52 (d, J = 1.8 Hz, 1H), 7.13-7.04 (m, 2H), 5.43 (d, J = 1.7 Hz, 1H), 3.76 (t, J = 4.7 Hz, 4H), 3.25 (t, J = 4.9 Hz, 4H), 1.54 (d, J = 1.6 Hz, 6H); Anal. RP-HPLC tR = 1.083

min (method 2, purity 99%); LC-MS ESI: m/z = 416.2 [M+H]+ (anal. calcd for C25H26N3O3+: m/z = 416.2).

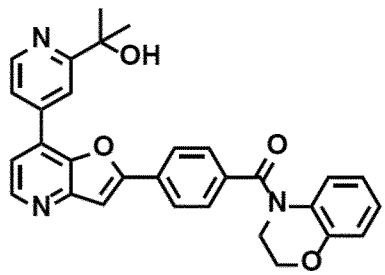
4-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)morpholin-3-one (D155). According to GP18: Yield 19% as white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.75 (d, J = 5.1 Hz, 1H), 8.66 (d, J = 5.1 Hz, 1H), 8.48 (s, 1H), 8.07 (d, J = 7.9 Hz, 2H), 7.96 (d, J = 5.0 Hz, 1H), 7.79 (s, 1H), 7.75 (d, J = 5.1 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 5.46 (s, 1H, OH), 4.64 (s, 2H), 4.16 (s, 2H), 3.85 (t, J = 5.1 Hz, 2H), 3.31 (s, 2H), 1.55 (s, 6H); Anal. RP-HPLC tR = 2.405 min (method 1, purity 99%); LC-MS ESI: m/z = 444.1 [M+H]+ (anal. calcd for C26H26N3O4+: m/z = 444.2).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(pyridin-3-yl)pyrrolidin-1-yl)methanone (D154). According to GP18: Yield 14% as white solid. 1H NMR (400 MHz, CDCl3) δ = 8.77 (d, J = 5.2 Hz, 1H), 8.68 (q, J = 5.5 Hz, 2H), 8.54 (d, J = 5.0 Hz, 1H), 8.52 – 8.26 (m, 1H), 8.06 (d, J = 10.7 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.82 (d, J = 5.1 Hz, 1H), 7.75 (d, J = 8.1 Hz, 3H), 7.53 – 7.29 (m, 3H), 5.35 (t, J = 6.8 Hz, 1H, OH), 4.11 – 3.70 (m, 2H), 2.60 – 2.34 (m, 2H), 2.03 (dd, J = 34.9, 9.3 Hz, 3H), 1.69 (d, J = 8.0 Hz, 6H); Anal. RP-HPLC tR = 2.036 min (method 1, purity 99%); LC-MS ESI: m/z = 505.2 [M+H]+ (anal. calcd for C31H29N4O3+: m/z = 505.2).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-diisopropylbenzamide (D153). According to GP18: Yield 23% as a pale yellow solid. 1H NMR (400 MHz, CDCl3) δ = 8.98 (s, 1H), 8.74 (s, 1H), 8.35 (s, 1H), 8.08 (s, 1H), 7.96 (d, J = 7.8 Hz, 2H), 7.69 (d, J = 19.9 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 3.81 (s, 2H), 1.83 (s, 6H), 1.57 (s, 6H), 1.25 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 1.048min (method 2, purity 99%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C28H32N3O3+: m/z = 458.2).

(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone (D152). According to GP18: Yield 28% as pale yellow solid. 1H NMR (400 MHz, CDCl3) δ = 8.92 (d, J = 5.3 Hz, 1H), 8.75 (d, J = 5.2 Hz, 1H), 8.26 (s, 1H), 8.00 (t, J = 7.9 Hz, 3H), 7.74 (d, J = 7.9 Hz, 2H), 7.63 (d, J = 5.3 Hz, 1H), 7.59 (s, 1H), 5.17 (s, 1H, OH), 3.69 (t, J = 8.1 Hz, 1H), 3.59 (s, 2H), 2.21 (q, J = 14.4, 10.9 Hz, 3H), 1.95 (s, 1H), 1.79 (s, 6H); Anal. RP-HPLC tR = 1.029 min (method 2, purity 99%); LC-MS ESI: m/z = 496.1 [M+H]+ (anal. calcd for C27H25F3N3O3+: m/z = 496.2).

(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)methanone (D151). According to GP18: Yield 23% as pale yellow solid. 1H NMR (400 MHz, CDCl3) δ = 8.83 (d, J = 5.3 Hz, 1H), 8.71 (d, J = 5.1 Hz, 1H), 8.15 (s, 1H), 7.98 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 5.3 Hz, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 5.2 Hz, 1H), 7.49 (s, 1H), 4.43 (d, J = 10.2 Hz, 1H), 3.66 (s, 1H), 3.50 (s, 1H), 2.25 (s, 1H), 1.92 (s,1H), 1.74 (s, 8H), 1.28 (d, J = 10.9 Hz, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.929 min (method 2, purity 97%); LC-MS ESI: m/z = 486.2 [M+H]+ (anal. calcd for C29H32N3O4+: m/z = 486.2).



(2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone. According to GP18: Yield 10% as an off white solid. 1H NMR (400 MHz, CDCl3) δ = 8.81 (d, J = 4.9 Hz, 1H), 8.71 (d, J = 4.9 Hz, 1H), 8.10 (s, 1H),7.93 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 4.8 Hz, 1H), 7.68 (d, J = 7.9 Hz, 2H), 7.56-7.51 (m, 1H), 7.47(s, 1H),

7.28 (s, 1H), 7.03 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.67 (s, 1H), 4.46 (t, J = 4.6Hz, 2H), 4.09 (t, J = 4.5 Hz, 2H), 1.72 (d, J = 1.5 Hz, 6H), 1.28 (s, 1H, OH); Anal. RP-HPLC tR = 1.041 min (method 2, purity 98%); LC-MS ESI: m/z = 492.2 [M+H]+ (anal. calcd for C30H26N3O4+: m/z = 492.2).

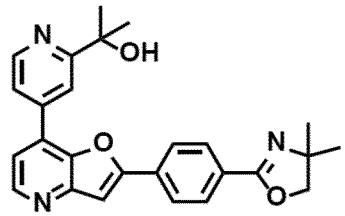
(R)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(3-methylmorpholino)methanone (148). According to GP18: Yield 24% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.75 (d, J = 5.2 Hz, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.44 (s, 1H), 8.14 (d, J = 8.3Hz, 2H), 7.96 (d, J = 5.2 Hz, 1H), 7.89 (s, 1H), 7.75 (d, J = 5.2 Hz, 1H), 7.58 (d, J = 8.3 Hz, 2H), 5.44 (s, 1H), 3.81 (s, 1H), 3.63-3.57 (m, 2H), 3.51-3.37 (m, 2H), 1.55 (s, 6H), 1.27 (d, J = 6.4 Hz, 3H), 1.04 (d, J = 5.2 Hz, 2H); Anal. RP-HPLC tR = 1.030 min (method 2, purity 99%); LC-MS ESI: m/z = 458.2 [M+H]+ (anal. calcd for C27H28N3O4+: m/z = 457.2).

2-(4-(2-(4-(morpholinomethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D147). According to GP18: Yield 6%. 1H NMR (400 MHz, DMSO-d6) δ = 8.75 (d, J = 5.1 Hz, 1H), 8.65 (d, J = 5.1 Hz, 1H), 8.48 (s, 1H), 8.04 (d, J = 7.9 Hz, 2H), 7.95 (d, J = 5.3 Hz, 1H), 7.77-7.71 (m, 2H),7.51 (d, J = 7.9 Hz, 2H), 5.45 (s, 1H, OH), 3.60 (t, J = 4.5 Hz, 4H), 3.55 (s, 2H), 2.40 (d, J = 4.5 Hz,4H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.909 min (method 2, purity 99%); LC-MS ESI: m/z = 430.2 [M+H]+ (anal. calcd for C26H28N3O3+: m/z = 430.2).

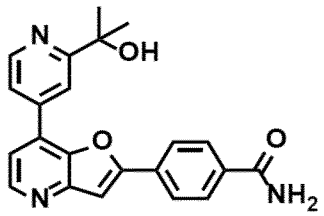
((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D146). According to GP18: Yield 14% as a yellow solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.76 (d, J = 5.1 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.44 (d, J = 11.2 Hz, 1H), 8.14 (t, J = 9.3 Hz, 2H), 8.02-7.95 (m, 1H), 7.91 (s, 1H), 7.80-7.70 (m, 2H), 7.68 (d, J = 8.3 Hz, 1H), 5.46 (br. s, 1H), 4.64 (m, 2H), 3.98-3.50 (m, 5H), 3.29 (m, 1H), 2.01-1.71 (m, 2H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.871 min (method 2,

purity 99%); LC-MS ESI: m/z = 456.2[M+H]+ (anal. calcd for C27H26N3O4+: m/z = 456.2).

(4,4-difluoropiperidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone (D145). According to GP18: Yield 14% as an off white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.76 (d, J = 5.9 Hz, 1H), 8.67 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 1.8 Hz, 1H), 8.14 (d, J= 8.4 Hz, 2H), 7.99-7.94 (m, 1H), 7.90 (s, 1H), 7.75 (d, J = 5.0 Hz, 1H), 7.64 (d, J = 8.5 Hz, 2H), 5.44 (s, 1H), 3.60 (m, 4H), 2.08 (m, 4H), 1.55 (s, 6H); Anal. RP-HPLC tR = 1.064 min (method 2, purity 99%); LC-MS ESI: m/z = 478.2[M+H]+ (anal. calcd for C27H26F2N3O3+: m/z = 478.2).



2-(4-(2-(4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol. According to GP18: Yield 11% as a white solid. 1H NMR (400 MHz, DMSO-d6) δ= 8.76 (d, J = 5.1 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.47 (s, 1H), 8.17 (d, J = 8.6 Hz, 2H), 8.02 (d, J= 8.6 Hz, 2H), 7.96 (dd, J = 5.1, 1.8 Hz, 1H), 7.93 (s, 1H), 7.77 (d, J = 5.1 Hz, 1H), 5.46 (s, 1H), 4.16 (s, 2H), 1.56 (s, 6H), 1.32 (s, 6H); Anal. RP-HPLC tR = 0.990 min (method 2, purity 99%); LC-MS ESI: m/z = 428.2 [M+H]+ (anal. calcd for C26H26N3O3+: m/z = 428.2).

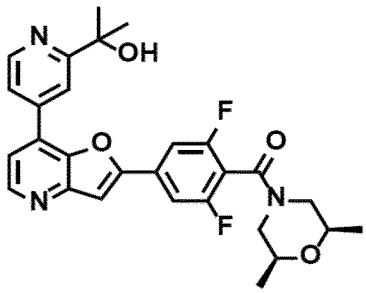


4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide (D144). According to GP18: Yield 10% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.77 (dd, J = 5.1, 0.7 Hz, 1H), 8.69 (d, J = 5.1 Hz, 1H),

8.48 (dd, J = 1.7, 0.7 Hz, 1H), 8.19-8.03 (m, 4H), 7.96 (dd, J = 5.2, 1.8 Hz, 1H), 7.92 (s, 1H), 7.77 (d, J = 5.1 Hz, 1H), 7.48 (br. s, 2H), 5.43 (s, 1H), 1.56 (s, 6H); Anal. RP-HPLC tR = 0.759 min (method 2, purity 99%); LC-MS ESI: m/z = 374.1 [M+H]+ (anal. calcd for C22H20N3O3+: m/z = 374.1).

4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoic acid (D129). According to GP18: Yield 31% as beige solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.77 (d, J = 5.1 Hz, 1H), 8.70 (d, J = 5.0 Hz, 1H), 8.47 (s, 1H), 8.20 (d, J = 8.3 Hz, 2H), 8.11 (d, J = 8.2 Hz, 2H), 8.00-7.93 (m, 2H), 7.78 (d, J = 5.1 Hz, 1H), 5.43 (s, 1H, OH), 1.56 (s, 6H); Anal. RP-HPLC tR = 2.447 min (method 1, purity 99%); LC-MS ESI: m/z = 375.1 [M+H]+ (anal. calcd for C22H19N2O4+: m/z = 375.1).

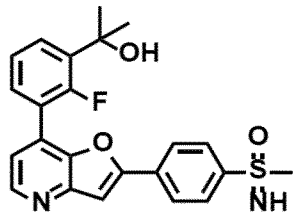
(3-fluoropyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2- yl)phenyl)methanone (D142). According to GP18: Yield 23% as a white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.67 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 1.7 Hz, 1H), 8.17- 8.10 (m, 2H), 7.96 (dd, J = 5.1, 1.8 Hz, 1H), 7.89 (s, 1H), 7.73 (dd, J = 10.7, 7.0 Hz, 3H), 5.41 (s, 2H), 3.86-3.50 (m, 4H), 2.20 (d, J = 8.8 Hz, 2H), 1.55 (s, 6H); Anal. RP-HPLC tR = 0.869 min(method 2, purity 99%); LC-MS ESI: m/z = 446.2 [M+H]+ (anal. calcd for C26H25FN3O3+: m/z = 446.2).



(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)((2S,6R)-2,6-dimethylmorpholino)methanone. According to GP18: Yield 38% as a yellow solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.76 (dd, J = 5.2, 0.8 Hz, 1H), 8.68 (d, J = 5.1 Hz, 1H), 8.50 (dd, J = 1.8, 0.8 Hz, 1H), 7.96 (dd, J = 5.2, 1.8 Hz, 1H), 7.83 (d, J = 1.7 Hz, 1H), 7.81-7.77 (m, 2H), 7.73 (s,

1H), 4.64-4.48 (m, 2H), 3.73-3.57 (m, 2H), 3.44 (d, J = 13.3 Hz, 1H), 2.96 (dd, J = 13.3, 10.6 Hz, 1H), 2.65 (dd, J = 13.2, 10.7 Hz, 1H), 1.68 (s, 6H), 1.27 (d, J = 6.2 Hz, 3H), 1.12 (d, J = 6.2 Hz, 3H); Anal. RP-HPLC tR = 0.992 min (method 2, purity 99%); LC-MS ESI: m/z = 508.2 [M+H]+ (anal. calcd for C28H28F2N3O4+: m/z = 508.2).

(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone (D202). According to GP18: Yield 30% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.76 (d, J = 5.2 Hz, 1H), 8.68 (d, J = 5.0 Hz, 1H), 8.46 (d, J = 1.8 Hz, 1H), 8.15 (d, J = 8.4 Hz, 2H), 7.96 (dd, J = 5.1, 1.8 Hz, 1H), 7.91 (s, 1H), 7.84-7.79 (m, 2H), 7.76 (d, J = 5.1 Hz, 1H), 5.14 (s, 1H), 4.13 (d, J = 4.4 Hz, 2H), 3.93 (s, 2H), 3.86 (d, J = 11.3 Hz, 2H), 3.62 (d, J = 4.3 Hz, 2H), 1.56 (s, 6H); Anal. RP-HPLC tR = 0.995 min (method 2, purity 99%); LC-MS ESI: m/z = 456.2 [M+H]+ (anal. calcd for C27H26N3O4+: m/z = 456.2).



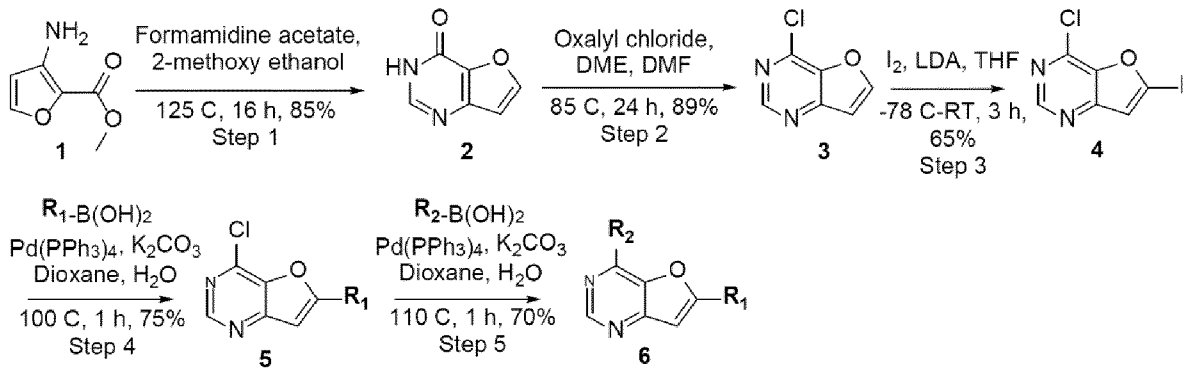
(4-(7-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone. According to GP18: Yield 36% as a light brown solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.65 (d, J = 5.0 Hz, 1H), 8.22-8.02 (m, 4H), 7.98 (s, 1H), 7.91-7.77 (m, 1H), 7.74-7.62 (m, 1H), 7.51-7.36 (m, 2H), 5.49 (s, 1H), 3.18 (s, 3H), 1.59 (s, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.892 min (method 2, purity 100%); LC-MS ESI: m/z = 425.1 [M+H]+ (anal. calcd for C23H22FN2O3S+: m/z = 425.1).

2-(3-fluoro-4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol (D205). According to GP18: Yield 46% as an off white solid. 1H NMR (300 MHz, MeOD-d4) δ = 8.69 (d, J = 5.1 Hz, 1H), 8.61 (dd, J = 4.9,

0.9 Hz, 1H), 8.26-8.18 (m, 2H), 8.14-8.07 (m, 2H), 7.83 (t, J = 5.0 Hz, 1H), 7.75 (s, 1H), 7.63 (dd, J = 5.1, 1.1 Hz, 1H), 3.20 (s, 3H), 1.73 (d, J = 1.5 Hz, 6H). The OH signal was not observed due to the deuterated solvent; Anal. RP-HPLC tR = 0.984 min (method 2, purity 99%); LC-MS ESI: m/z = 427.1 [M+H]+ (anal. calcd for C22H20FN2O4S+: m/z = 427.1).

(4-(7-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone (D206). According to GP18: Yield 59% as an off white solid. 1H NMR (300 MHz, DMSO-d6) δ = 8.74-8.45 (m, 2H), 8.07 (dd, J = 18.9, 8.0 Hz, 2H), 7.91 (s, 1H), 7.85 (t, J = 4.9 Hz, 1H), 7.69-7.48 (m, 3H), 5.45 (s, 1H), 3.63 (br s, 8H), 1.62 (s, 6H); Anal. RP-HPLC tR = 0.962 min (method 2, purity 99%); LC-MS ESI: m/z = 462.1 [M+H]+ (anal. calcd for C26H25FN3O4+: m/z = 462.2).

Example 19: Synthesis of furo-pyrimidine core:



Step-1: A mixture of methyl 3-aminothiophene-2-carboxylate (5 g, 0.035 mol), formamidine acetate (7.3 g, 0.070 g) and 2-methoxy ethanol (50 mL) was stirred and heated to reflux for 3 hours. The mixture was cooled to ambient temperature and water (50 ml) was added. The resultant solid was isolated, washed thoroughly with water and with diethyl ether and dried under vacuum to get furo[3,2-d]pyrimidin-4(3H)-one 2 (4.1 g, 85.06%). LCMS: Calculated for C6H6N6O2 136.11, Observed 137.1 (M+H), RT. 0.934 min, 94.28% (Max). 1H NMR (400 MHz, DMSO-d6): δ 12.60 (s, 1 H), 8.23 (d, J = 1.60 Hz, 1 H), 8.07 (s, 1 H), 6.99 (d, J = 2.00 Hz, 1 H).

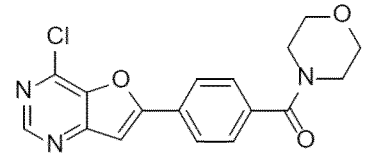
Step-2: Furo[3,2-d]pyrimidin-4(3H)-one 2 (4.1 g) was taken in thionylchloride (20 ml) and DMF (0.2 ml). Stirred at reflux for 5 h. After the completion of the reaction, the reaction mixture was concentrated to remove thionylchloride, was added water, extracted using dichloromethane and dried with anhydrous sodium sulphate. After concentrated under vacuum, trituration was carried out with hexane to get 4-chlorofuro[3,2-d]pyrimidine 3 (4.1 g, 89.1%). LCMS: Calculated for C6H3ClN2O 154.55, Observed 155.1 (M+H), RT. 1.41 min, 97.42% (Max). 1H NMR (400 MHz, DMSO-d6): δ 8.92 (s, 1 H), 8.68 (d, J = 2.40 Hz, 1 H), 7.40 (d, J = 2.00 Hz, 1 H).

Step-3: To a stirred solution of 4-chlorofuro[3,2-d]pyrimidine 3 (2 g, 0.013 mol) in THF at -78°C, was added dropwise n-butyl lithium1.6 M solution in THF (12.1 ml, 0.019 mol) over a period of 15 minutes. After 2h stirring at -78 °C, was added ICl (1.01 ml, 0.019 mol) dropwise and allowed to stir at room temperature for 30 minutes. The reaction mixture is poured into water and extracted three times with ethyl acetate. The combined organic phases are washed with 10% sodiumthiosulphate solution, dried over sodium sulphate and after filtration, dried under reduced pressure. The solid obtained was washed with diethyl ether and dried to get 4-chloro- 6-iodofuro[3,2-d]pyrimidine 4 (2 g, 55.2%) as reddish orange solid. LCMS: Calculated for C6H2ClIN2O 280.45, Observed 280.9 (M+H), RT. 1.94 min, 95.31% (Max). 1H NMR (400 MHz, DMSO-d6): δ 8.85 (s, 1 H), 7.72 (s, 1 H).

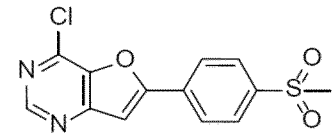
General procedure for step 4:

To a stirred solution of 4-chloro-6-iodofuro[3,2-d]pyrimidine (0.285 mmol), R1-B(OH)2 (67.0 mg, 0.285 mmol) in 1,4-Dioxane (3 ml) and Water (1.00 ml) and added K2CO3 (0.571 mmol). The reaction mixture was then degassed for 5 min followed by addition of Pd(PPh3)4 (0.029 mmol). The reaction mixture was stirred for about 3h at 90^0C. The solvent was evaporated to get compound 5 as crude mixture which was taken as is for next step.

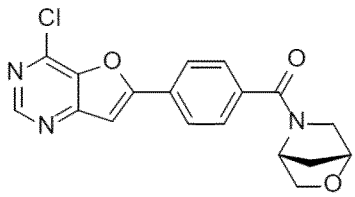
Manufacturing examples



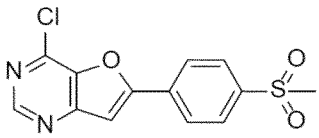
4-(4-{4-chlorofuro[3,2-d]pyrimidin-6-yl}benzoyl)morpholine, (building block): LCMS: Calculated 343.77; Observed 344.0(M+H).



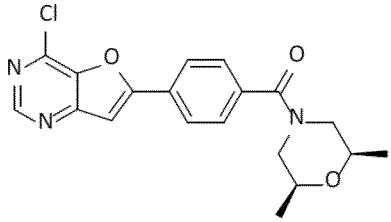
4-chloro-6-(4-methanesulfonylphenyl)furo[3,2-d]pyrimidine, (building block): LCMS: Calculated for C13H9ClN2O3S, Exact Mass: 308.73, Observed 309.1(M+H).



(1R,4R)-5-(4-{4-chlorofuro[3,2-d]pyrimidin-6-yl}benzoyl)-2-oxa-5-azabicyclo[2.2.1]heptane, (building block): LCMS: Calculated for C18H14ClN3O3, Exact mass 355.07, Observed 356.0 (M+H).



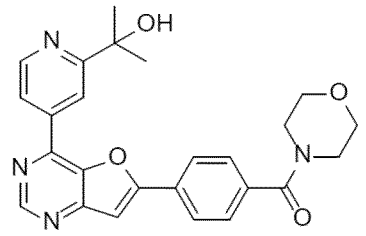
4-chloro-6-(4-methanesulfonylphenyl)furo[3,2-d]pyrimidine, (building block): LCMS: Calculated for C21H18FN304S 308.0, Observed 309.0 (M+H).



(2R,6S)-4-(4-{4-chlorofuro[3,2-d]pyrimidin-6-yl}benzoyl)-2,6-dimethylmorpholine (building block): LCMS: Calculated for C19H18ClN3O3 371.82, 372.0 (M+H).

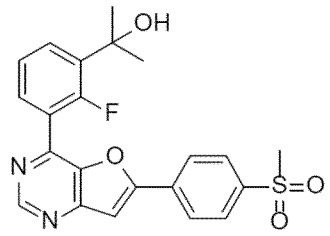
General procedure for step 5:

To a stirred solution of compound 5 (0.233 mmol), R2-B(OH)2 (0.233 mmol) in 1,4-Dioxane (4 ml) and Water (1 ml) added potassium carbonate (0.465 mmol). The reaction mixture was then degassed for 5 min followed by addition of Pd(PPh3)4 (0.029 mmol) and stirred for about 16 h at 110°C. The resulting residue was purified by preparative- HPLC to get compound 6.



2-(4-{6-[4-(morpholine-4-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}pyridin-2-yl)propan-2- ol: 1H NMR (400 MHz, DMSO-d6): δ 8.38 (s, 1H), 8.20 (s, 1H), 8.03 (d, J = 5.60 Hz, 1H), 7.72- 7.70 (m, 1H), 7.50 (d, J = 8.40 Hz, 2H), 6.90 (s, 3H), 3.01-2.52 (m, 8H), 0.90 (s, 6H). LCMS: Calculated for C25H24N4O4 343.77, Observed 444.49(M+H).

Manufacturing examples



2-{2-fluoro-3-[6-(4-methanesulfonylphenyl)furo[3,2-d]pyrimidin-4-yl]phenyl}propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.20 (s, 1 H), 8.28 (d, J = 8.40 Hz, 2 H), 8.15 (d, J = 8.80 Hz, 2 H), 8.10 (s, 1 H),7.95-7.91 (m, 1 H), 7.84-7.80 (m, 1 H), 7.46 (t, J = 7.60 Hz, 1 H), 5.50 (s, 1 H), 3.31 (s, 3 H),

1.62(s, 6 H). LCMS: Calculated for C22H19FN2O4S, Molecular Weight: 426.1, Observed 427.1 (M+H).

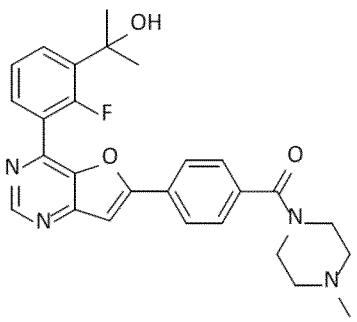
(4-{4-[2-fluoro-3-(2-hydroxypropan-2-yl)phenyl]furo[3,2-d]pyrimidin-6-yl}phenyl)(imino)methyl-λ⁶-sulfanone (D203). Synthesis according to GP4: Yield 35% as off-white solid. ^{1}H NMR 300 MHz, MeOD-d_4) δ = 9.13 (s, 1H), 8.29 (d, J = 8.3 Hz, 2H), 8.23 (d, J = 8.4 Hz, 2H), 7.96 (t, J = 7.5 Hz, 1H), 7.83 (t, J = 6.7 Hz, 1H), 7.78 (s, 1H), 7.45 (t, J = 7.7 Hz, 1H), 3.43 (s, 3H), 1.73 (s, 6H); Anal. RP-HPLC t_R = 2.4 min (method 2, purity 96.9%); LC-MS: m/z = 426.2 $[M+H]^+$ (anal. calcd for $C_{22}H_{20}FN_3O_3S^+$: m/z = 426.1). Separation of the (S)- and (R)-enantiomer (D209 and D210, respectively) was performed using the following method with a Waters 2545 Quaternary gradient Module with MassLynx Software (Version 4.1), Waters 2424 ELS Detector, Waters 2767 Sample Manager and a Chiralpak IC 5µM, (20 mm x 250 mm) Chiral Column. Isocratic Elution: Hexane/CH_2Cl_2/EtOH (50:25:25) D209 t_R = 20.18 min (purity 100 %), D210 t_R = 29.02 min (purity 100 %).

(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone (D209). Synthesis: See D203 above. Yield 43%. ^{1}H NMR (300 MHz, MeOD-d_4) δ = 9.11 (s, 1H), 8.19 (q, J = 8.4 Hz, 4H), 7.95 (t, J = 7.8 Hz, 1H), 7.80 (d, J = 7.1 Hz, 1H), 7.71 (s, 1H), 7.44 (t, J = 7.7 Hz, 1H), 3.23 (s, 3H), 1.72 (s, 6H); Anal. RP-HPLC t_R = 2.34 min (method 2, purity 100 %); LC-MS: m/z = 426.2 $[M+H]^+$ (anal. calcd for $C_{22}H_{20}FN_3O_3S^+$: m/z = 426.1).

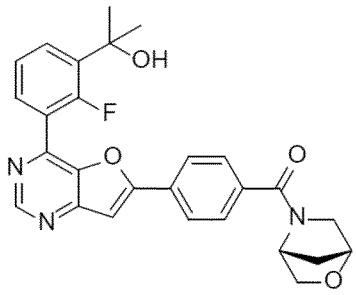
(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone (D210). Synthesis: See D203 above. Yield 46%. ^{1}H NMR (300 MHz, DMSO-d_6) δ = 9.25 (s, 1H), 8.29 (overlapping s, 2H), 8.22-8.09 (m, 3H), 7.99 (t, J = 7.8 Hz, 1H), 7.88 (t, J = 6.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 5.59 (s, 1H), 3.20 (s, 3H), 1.68 (s, 6H) ; Anal. RP-HPLC t_R = 2.34 min (method 2, purity 99%); LC-MS: m/z = 426.2 $[M+H]^+$ (anal. calcd for $C_{22}H_{20}FN_3O_3S^+$: m/z = 426.1).

1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide (D211). Yield 32%. ^{1}H NMR (300 MHz, MeOH-d_4) δ = 9.10 (s, 1H), 8.22 (t, *J* = 6.4 Hz, 4H), 7.95 (t, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.1 Hz, 1H), 7.72 (s, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 3.63 (t, *J* = 11.4 Hz, 1H), 3.46 (d, *J* = 13.3 Hz, 1H), 3.36 – 3.21 (m, 3H), 2.47 (s, 1H), 2.28 (d, *J* = 14.2 Hz, 1H), 1.88 (d, *J* = 12.5 Hz, 1H), 1.82 (s, 1H), 1.71 (s, 6H), 1.62 (s, 1H) ; Anal. RP-HPLC t_R = 2.61 min (method 2, purity 100%); LC-MS: *m/z* = 466.2 $[M+H]^+$ (anal. calcd for $C_{25}H_{24}FN_3O_3S^+$: *m/z* = 466.2).

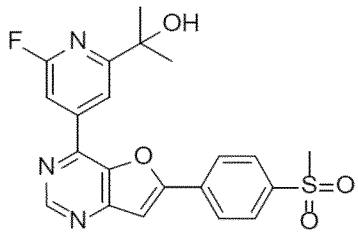
1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-4,5-dihydro-3H-isothiazole 1-oxide (D212). Yield 49%. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.23 (2s, 2H), 8.18 – 8.01 (m, 3H), 7.93 (t, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.0 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 5.52 (s, 1H), 3.84 (dt, *J* = 11.1, 5.8 Hz, 1H), 3.77 – 3.64 (m, 1H), 3.59 – 3.39 (m, 2H), 2.27 (s, 2H), 1.61 (s, 6H) ; Anal. RP-HPLC t_R = 0.76 min (method 2, purity 100%); LC-MS: *m/z* = 452.1 $[M+H]^+$ (anal. calcd for $C_{24}H_{22}FN_3O_3S^+$: *m/z* = 452.1).



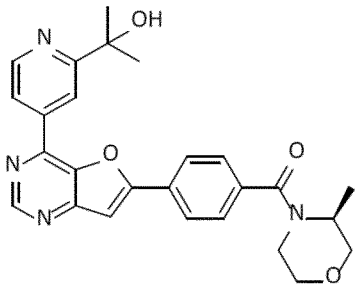
2-(2-fluoro-3-{6-[4-(4-methylpiperazine-1-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}phenyl)propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.81 (s, 1H), 9.18 (s, 1H), 8.12 (d, J = 8.00 Hz, 2H), 7.98 (s, 1H), 7.93-7.80 (m, 1H), 7.67 (d, J = 8.00 Hz, 2H), 7.45 (t, J = 8.00 Hz, 1H), 3.13 (s, 4H), 2.84 (s, 4H), 1.62 (s, 6H). LCMS: Calculated for C26H27FN4O3 474.5, Observed 475.2 (M+H).



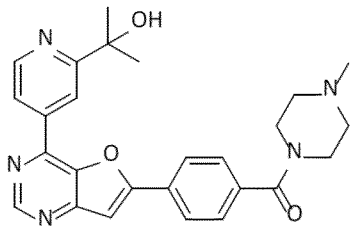
2-[2-fluoro-3-(6-{4-[(1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-carbonyl]phenyl}furo[3,2-d]pyrimidin-4-yl)phenyl]propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.14 (s, 1H), 8.08 (d, J = 8.40 Hz, 2H), 7.95-7.91 (m, 1H), 7.81-7.78 (m, 2H), 7.71 (d, J = 8.00 Hz, 2H), 7.43 (t, J = 7.60 Hz, 1H), 5.21 (s, 1H), 4.63 (s, 2H), 3.88 (d, J = 7.20 Hz, 1H), 3.75 (s, 1H), 3.54 (dd, J = 1.20, 11.00 Hz, 1H), 3.35 (d, J = 9.60 Hz, 1H), 1.92 (d, J = 8.80 Hz, 1H), 1.83 (s, 1H), 1.64 (s, 6H). LCMS: Calculated for C27H24FN3O4, Exact mass 473.18, Observed 474.2 (M+H).



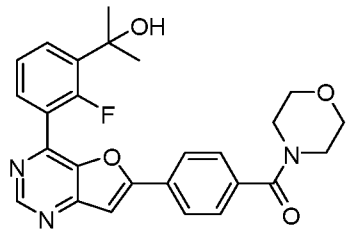
2-{6-fluoro-4-[6-(4-methanesulfonylphenyl)furo[3,2-d]pyrimidin-4-yl]pyridin-2-yl}propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.27 (s, 1H), 8.78 (s, 1H), 8.45 (d, J = 8.00 Hz, 2H), 8.19 (d, J = 7.20 Hz, 3H), 7.97 (s, 1H), 7.65-7.56 (m, 1H), 5.69 (s, 1H), 3.44 (s, 3H), 1.53 (s, 6H). LCMS:Calculated for C21H18FN304S 427.45, Observed 428.0 (M+H).



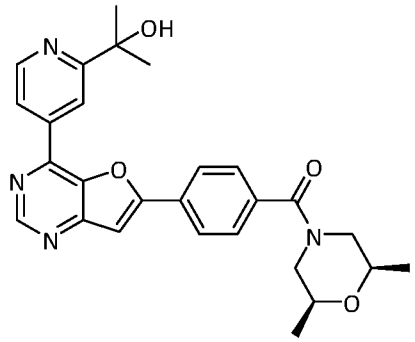
2-[4-(6-{4-[(3S)-3-methylmorpholine-4-carbonyl]phenyl}furo[3,2-d]pyrimidin-4-yl)pyridin- 2-yl]propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.23 (s, 1 H), 8.85-8.83 (m, 1 H), 8.56-8.56 (m, 1 H), 8.35-8.33 (m, 1 H), 8.08-8.06 (m, 1 H), 7.63-7.61 (m, 3 H), 7.38 (s, 1 H), 4.88 (s, 1 H), 3.95 (s, 1 H), 3.72-3.69 (m, 2 H), 3.58-3.45 (m, 2 H), 1.72 (s, 6 H), 1.44 (d, J = 6.80 Hz, 3 H). LCMS: Calculated for C26H26N4O4 458.52, Observed 459.1 (M+H).



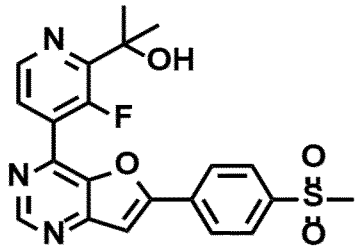
2-(4-{6-[4-(4-methylpiperazine-1-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}pyridin-2- yl)propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.20 (s, 1 H), 8.84-8.83 (m, 2 H), 8.32-8.26 (m, 3 H), 7.99 (s, 1 H), 7.64 (d, J = 8.40 Hz, 2 H), 5.50 (s, 1 H), 3.66 (s, 2 H), 3.32-3.36 (m, 2 H), 2.38 (S, 3 H), 2.33-2.34 (m, 1 H), 2.22 (s, 3 H), 1.55 (s, 6 H). LCMS: Calculated for C26H27N5O3 457.53, Observed 458.1 (M+H).



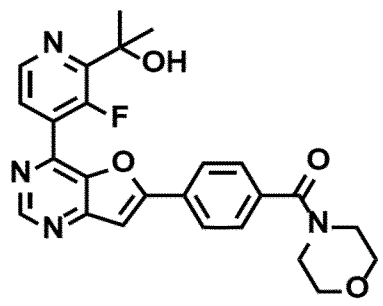
2-(2-fluoro-3-{6-[4-(morpholine-4-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}phenyl)propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.16 (s, 1 H), 8.09 (d, J = 8.40 Hz, 2 H), 7.93 (d, J = 6.00 Hz, 2 H), 7.81 (s, 1 H), 7.63 (d, J = 8.00 Hz, 2 H), 7.45 (t, J = 8.0 Hz, 1 H), 5.50 (s, 1 H), 3.65 (s, 8 H), 1.61 (s, 6 H). LCMS: Calculated for C26H24FN3O4 461.493, Observed 462.1 (M+H).



2-[4-(6-{4-[(2R,6S)-2,6-dimethylmorpholine-4-carbonyl]phenyl}furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl]propan-2-ol: 1H NMR (400 MHz, DMSO-d6): δ 9.21 (s, 1H), 8.84-8.82 (m, 2H), 8.33-8.27 (m, 3H), 7.99 (s, 1H), 7.66 (d, J = 8.40 Hz, 2H), 5.50 (s, 1H), 4.43-4.40 (m, 1H), 3.59-3.50 (m, 2H), 3.44-3.27 (m, 1H), 2.68-2.56 (m, 1H), 1.55 (s, 6H), 1.40-1.10 (m, 6H). LCMS: Calculated for C27H28N4O4 472.55, Observed 473.3 (M+H).

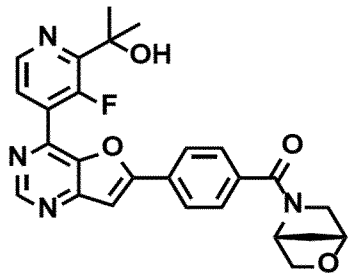


2-(3-fluoro-4-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl)propan-2- ol. Yield 51% as a white solid. 1H NMR (300 MHz, MeOD-d4) δ = 9.22 (s, 1H), 8.64 (dd, J = 4.9, 1.1 Hz, 1H), 8.37-8.26 (m, 2H), 8.21-8.11 (m, 2H), 7.95 (t, J = 4.9 Hz, 1H), 7.83 (s, 1H), 3.21 (s, 3H), 1.75 (d, J = 1.4 Hz, 6H); Anal. RP-HPLC tR = 0.959 min (method 2, purity 99%); LC-MS ESI: m/z = 428.1 [M+H]+ (anal. calcd for C21H19FN3O4S+: m/z = 428.1).



(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone. Yield 24% as a white solid. 1H NMR (300

MHz, MeOD-d4) δ = 9.12 (s, 1H), 8.60 (d, J = 4.9 Hz, 1H), 8.10 (s, 2H), 7.89 (dd, J = 4.8, 4.8 Hz, 1H), 7.61 (s, 3H),3.77 (s, 4H), 3.64 (s, 2H), 3.48 (s, 2H), 1.71 (s, 6H); Anal. RP-HPLC tR = 0.941 min (method 2, purity 99%); LC-MS ESI: m/z = 463.2 [M+H]+ (anal. calcd for C25H24FN4O4+: m/z = 463.2).



((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone. Yield 27% as a white solid. 1H NMR (300 MHz, MeOD-d4) δ = 9.17 (s, 1H), 8.63 (dd, J = 4.8, 1.0 Hz, 1H), 8.15 (d, J = 9.9, 8.2 Hz, 2H), 7.93 (dd, J = 4.8, 4.8 Hz, 1H), 7.80-7.66 (m, 3H), 4.79-4.40 (m, 2H), 4.02 (dd, J = 10.1, 7.7 Hz, 1H), 3.94-3.78 (m, 1H), 3.68-3.60 (m, 1H), 3.57-3.35 (m, 1H), 2.12-1.88 (m, 2H), 1.74 (s, 6H); Anal. RP-HPLC tR = 0.920 min (method 2, purity 100%); LC-MS ESI: m/z = 475.2 [M+H]+ (anal. calcd for C26H24FN4O4+: m/z = 475.2).

BIOLOGICAL ACTIVITY

Example 20

In vitro P. falciparum Assay

Compounds were screened against sensitive (NF54) strains of *P. falciparum in vitro* using the modified [3H]hypoxanthine incorporation assay. (Vennerstrom, J. L.; Arbe-Barnes, S.; Brun, R.; Charman, S. A.; Chiu, F. C. K.; Chollet, J.; Dong, Y.; Dorn, A.; Hunziker, D.; Matile, H.; McIntosh, K.; Padmanilayam, M.; Tomas, J. S.; Scheurer, C.; Scorneaux, B.; Tang, Y.; Urwyler, H.; Wittlin, S. and Charman, W. N. Identification of an Antimalarial

Synthetic Trioxolane Drug Development Candidate. Nature, 2004, 430, 900-904.).

Compound concentrations at which growth of *P. falciparum* was inhibited by 50% compared to untreated controls was measured in nM (IC_{50}).

Table 1: Growth inhibition of *P. falciparum* by compounds according to the present invention

Compound ID	***In vitro P. falciparum* growth inhibition IC_{50} (nM)**
D34	B
D35	A
D54	A
D63	B
D64	A
D77	A
D81	B
D84	C
C9	A
D93	A
D96	B
D100	B
D101	B
D105	B
D106	B
D109	B
D12	A
D113	B
D114	A
D116	C
D120	B
D122	B

D129	A
D132	A
D137	A
D140	C
D143	A
C28	B
C29	B
D149	A
D150	B
D152	B
D154	A
D155	B
D157	B
D158	A
D166	A
D134	A
D167	A
D179	A
D180	A
D182	A
C43	B
D183	A
C45	B
C46	B
D186	A
D189	B
D197	A
C50	A
D200	A
D203	A
D204	A

D209	A
D210	A
D211	A
D212	A
D213	B

IC50: <10nM= A, 10-50nM=B, >50nM=C

These data illustrate the potency of compounds according to the present invention in inhibiting growth of P. falciparum and underline the usefulness as anti-malaria drugs.

Example 21

Data presented in example 20 indicates a substantial impact of the compounds according to the present invention on growth of plasmodia. In order to further examine the underlying mechanisms responsible for inhibition of growth, the compounds were tested for inhibitory properties of plasmodium PI4K, a recently identified drug target for anti-malaria medication.

In order to test the impact of the compounds according to the present invention, *in vitro* assays were performed analyzing concentrations at which PI4K is inhibited. IC_{50} measurements were recorded.

The lipid kinase reaction is performed by incubating lipid substrate (PI:3PS or PIP2:3PS) with a recombinant enzyme and ATP, and the kinase activity is measured using the ADP-Glo™ Kinase Assay. First, the kinase reaction is terminated, and any ATP remaining after the reaction is depleted, leaving only ADP. Then the Kinase Detection Reagent is added to convert ADP to ATP, which is used in a coupled luciferin/luciferase reaction. The luminescent output is measured and is correlated with kinase activity. The assays can be performed in 96- or 384-well plates and can be used for enzyme characterization, inhibitor screening or compound profiling. Results measuring the effect of compounds on P. vivax PI4K are reported in table 2

Table 2: Inhibitory properties on PvPI4K

Compound ID	*In vitro P. vivax* PI4K enzymatic inhibition IC_{50} (nM)
D34	D
D35	B
D54	B
D132	B
D137	A
D12	A
C56	B
D14	B
C58	C
D29	C
D33	B
D39	C
D41	C
C63	D
D59	C
D134	A
C66	A

IC50: <50nM= A, 50-100nM=B, 100-500nM=C, >500=D

These data illustrate the potency of compounds according to the present invention in inhibiting PfPI4K and provide an explanation for the discovered plasmodium growth inhibition as described in example 20.

Example 22

To further test the impact of compounds according to the present invention on human PI4Kβ, HuPI4Kβ (human PI4Kβ) inhibition was tested for selected compounds and contrasted with the results for inhibiting PfNF54 strains as described in example 20.

Table 3: Inhibitory properties of compounds

Compound ID	PfNF54 IC_{50} (nM)	HuP14Kβ IC_{50} (nM)
D54	A	+++
D114	A	+++
D149	A	+
D183	A	+
D197	A	+
D12	B	++
C56	C	-
D7	C	++
D27	C	-
D43	B	-
D50	A	+
D124	A	++
C74	B	-
C75	A	-
C76	A	-
C77	B	-
Reference Compound MMV390048	B	-

IC50 (PfNF54): <10nM= A, 10-50nM=B, >50nM

IC50 (HuP14Kβ): <50nM= +++, 50-100nM=++, 100-500nM=+, >500=-

As illustrated in table 3, several compounds showed high potency to inhibit human PI4K in addition to plasmodium derived protein. However, some compounds, in particular comprising a furo-pyrimidine core structure showed low inhibitory properties in regard to human-derived PI4K, while strongly inhibiting plasmodia growth.

Example 23

Further compounds according to the present invention have been tested for growth inhibition of NF54 strains in order to evaluate the concentration required to reduce Plasmodium viability.

H3D - *In vitro* antiplasmodial activity

Test samples were screened for in vitro antiplasmodial activity against a chloroquine sensitive (CQS) strain (NF54) of the malaria parasite P. falciparum. Continuous in vitro cultures of asexual erythrocyte stages of P. falciparum were maintained using a modified version of the method of Trager and Jensen (1976).1 Quantitative assessment of antiplasmodial activity in vitro was determined via the parasite lactate dehydrogenase assay using a modified method described by Makler (1993). The test samples were tested in triplicate on two separate occasions. Further dilutions were prepared in complete medium on the day of the experiment. Samples were tested as a suspension if not completely dissolved. Chloroquine and artesunate were used as reference drugs.

A full dose-response were performed starting at a concentration of 3000 nM, which is then serially diluted 2-fold in complete medium to give 10 concentrations; with the lowest concentration being approximately 6 nM. The same dilution techniques were used for all samples. References were tested at a starting concentration of 1000 ng/mL. The highest concentration of solvent to which the parasites were exposed has no measurable effect on the parasite viability (data not shown).

Table 4: Inhibitory properties of compounds on *Plasmodium* growth

Compound ID	H3D NF54 IC50
D1	C
D2	B
D3	B
D4	B
D5	B

D6	C
D7	C
D8	C
D9	A
D10	A
D11	C
D12	B
D13	B
D14	A
D15	B
D16	A
D17	B
D18	A
D19	A
D20	A
D21	A
D22	C
D23	A
D24	B
D25	A
D26	C
D27	C
D28	A
D29	B
D30	A
D31	A
D32	A
D33	A
D34	A
D35	A
D36	C
D37	C
D38	A
D39	B
D40	B
D41	A
D42	A
D43	B
D44	B
D45	A
D46	B
D47	B
D48	A
D49	C
D50	A
D51	A

D52	A
D53	B
D54	A
D55	B
D56	A
D57	A
D58	A
D59	A
D60	B
D61	C
D62	B
D63	A
D64	A
D65	A
D66	A
D67	A
D68	A
D69	C
D70	C
D71	C
D72	A
D73	A
D74	C
D75	C
D76	A
D77	A
D78	C
D79	A
D80	A
D81	A
D82	A
D83	B
D84	A
D85	A
D86	A
D87	B
D88	A
D89	A
D90	A
D91	A
D92	A
D93	A
D94	C
D95	A
D96	A
D97	A

D98	A
D99	A
D100	B
D101	B
D102	C
D103	B
D104	B
D105	B
D106	B
D107	C
D108	A
D109	B
D110	C
D111	A
D112	A
D113	B
D114	A
D115	B
D116	B
D117	A
D118	A
D119	B
D120	B
D121	A
D122	A
D123	B
D124	A
D125	A
D126	A
D127	A
D128	B
D129	A
D130	B
D131	C
D132	A
D133	B
D134	A
D135	A
D136	C
D137	A
D138	B
D139	A
D140	B
D141	A
D142	A
D143	A

D144	A
D145	A
D146	A
D147	B
D148	A
D149	A
D150	C
D151	A
D152	A
D153	B
D154	A
D155	B
D156	B
D157	B
D158	A
D159	B
D160	B
D161	A
D162	A
D163	A
D164	A
D165	A
D166	A
D167	A
D168	B
D169	C
D170	A
D171	C
D172	A
D173	A
D174	A
D175	A
D176	A
D177	A
D178	A
D179	A
D180	A
D181	A
D182	A
D183	A
D184	B
D185	A
D186	A
D187	A
D188	A
D189	A

D190	A
D191	A
D192	A
D193	A
D194	A
D195	A
D196	A
D197	A
D198	A
D199	A
D200	A
D201	A
D202	A
D203	A
D204	A
D205	A
D206	A
D207	A
D208	A
D209	A
D210	A
D212	A

IC50: <15nM= A, 15-50nM=B, >50nM=C

The data presented above further provide clear evidence for the use of the compounds according to the present invention for the treatment and/or prevention of malaria. Concentrations as low as >1nM were able to inhibit Plasmodium growth by 50%.

***In vitro P. vivax* liver-stage Assay**

Compound efficacy against *P. vivax* liver-stage schizonts and hypnozoites is evaluated in infected primary human hepatocytes (PHHs). Compound screening is performed in 384-well plates, in a 12-point dose response, from 50 µM. All compounds are tested in radical cure mode (RCM).

PHHs are seeded onto 384-well plates two days prior to *P. vivax* sporozoite infection. In RCM, compounds are added to the culture for three days, from day 5 post infection, in duplicate wells. Nigericin and a PI4K inhibitor (KDU691) are used as positive controls in each assay, while solvent (DMSO) without

added compound serves as a negative control. Daily medium changes are performed, and the culture is fixed on day twelve post infection to ensure complete parasite clearance. Fixed cells are permeabilized and stained with an anti-UIS4 primary antibody and a fluorescent secondary antibody. Liver-stage schizonts and hypnozoites are then quantified by High Content Imaging.

Reference

Roth, A., et al. A comprehensive model for assessment of liver stage therapies targeting Plasmodium vivax and Plasmodium falciparum. Nat. Commun. 2018, 9(1), 1837. doi.org/10.1038/s41467-018-04221-9.

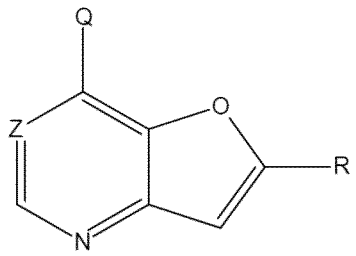
Table 5

Compound ID/Structure	*Pv* Hypnozoite IC_{50} (nM)	*Pv* Schizont IC_{50} (nM)
D54	A	A
D149	A	A
D183	A	A
D201	B	A
D203	B	A
D213	C	A

IC50: <15nM=A, 15-50nM=B, >50nM=C

CLAIMS

1. A compound according to formula (I)



(I)

or a pharmaceutically acceptable solvate, salt, tautomer or stereoisomer thereof for use in the prevention and/or treatment of PI4K-related disorders, wherein:

R denotes AR1 or HT1;

AR1 denotes phenyl, which is unsubstituted or substituted by

- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN and/or NO_2; and/or
- a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$,

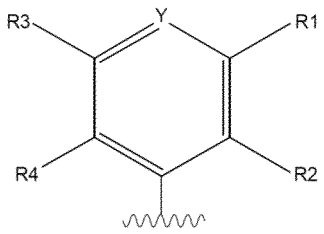
$(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

HT1 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle with 3 to 9 carbon atoms and 1, 2, 3 or 4 N, O and/or S atoms, wherein said heterocycle is unsubstituted or substituted by

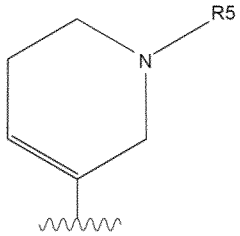
- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN, =O and/or NO_2; and/or
- a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$,

$(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

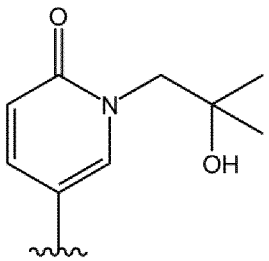
Q denotes a structure according to formula (II), (III), or (XII)



(II)



(III)



(XII)

R^1 and R^5	denote, independently from each other, AR2 or HT2;	
R^2, R^3 and R^4	denote, independently from each other, H, Hal or CAlk2;	
Y	denotes CH, CHal, CAlk2, $CCHal_3$ or N;	
AR2	denotes phenyl, which is unsubstituted or substituted by	
	-	1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN and/or NO_2; and/or
	-	a substituent selected from a group comprising: A, NH_2, OH, $(CR^aR^b)_nHetCyc1$, $(CR^aR^b)_nHetAr1$, $(CR^aR^b)_nAryl$, $(CR^aR^b)_nCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nCO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOCyc$, $(CR^aR^b)_nCOA$, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_nCONHA$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCONH(CR^aR^b)_mHetAr1$, $(CR^aR^b)_nCONH(R^aR^b)_mAryl$, $(CR^aR^b)_nCONHCyc$, $(CR^aR^b)_nCOOA$, $(CR^aR^b)_nCOOH$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetCyc1$, $(CR^aR^b)_nCOO(CR^aR^b)_mHetAr1$,

$(CR^aR^b)_nCOO(R^aR^b)_mAryl$, $(CR^aR^b)_nCOOCyc$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nNHCO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nNHCO(R^aR^b)_mAryl$, $(CR^aR^b)_nNHCOCyc$, $(CR^aR^b)_nNHCOA$, $(CR^aR^b)_nS(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nS(R^aR^b)_mHetAr1$, $(CR^aR^b)_nS(R^aR^b)_mAryl$, $(CR^aR^b)_nSA$, $(CR^aR^b)_nSO(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO(R^aR^b)_mAryl$, $(CR^aR^b)_nSOA$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetCyc1$, $(CR^aR^b)_nSO_2(R^aR^b)_mHetAr1$, $(CR^aR^b)_nSO_2(R^aR^b)_mAryl$, $(CR^aR^b)_nSO_2Cyc$, $(CR^aR^b)_nSO_2A$, $(CR^aR^b)_nSOA(NH)$, $(CR^aR^b)_nSOCyc(NH)$, $(CR^aR^b)_nSOAryl(NH)$, $(CR^aR^b)_nSOHetCyc1(NH)$, $(CR^aR^b)_nSOHetAr1(NH)$, $(CR^aR^b)_nSOA(NA)$, $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_nSOCyc(NA)$, $(CR^aR^b)_nSOAryl(NA)$, $(CR^aR^b)_nSOHetCyc1(NA)$, $(CR^aR^b)_nSOHetAr1(NA)$, $(CR^aR^b)_nSOA(NCyc)$, $(CR^aR^b)_nSOCyc(NCyc)$, $(CR^aR^b)_nSOAryl(NCyc)$, $(CR^aR^b)_nSOHetCyc1(NCyc)$, $(CR^aR^b)_nSOHetAr1(NCyc)$, $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2NHA$, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or monosubstituted by at least one Hal, Alk2 or OAlk2 group;

HT2 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle with 3 to 9 carbon atoms and 1, 2, 3 or 4 N, O and/or S atoms, wherein said heterocycle is unsubstituted or substituted by

- 1, 2 or 3 substituents independently selected from: Alk2, OAlk2, Hal, Cyc, CN, =O and/or NO_2; and/or
- a substituent selected from a group comprising:

A, NH_2, OH, $(CR^aR^b)_n$HetCyc1, $(CR^aR^b)_n$HetAr1, $(CR^aR^b)_n$Aryl, $(CR^aR^b)_nCO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nCO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nCO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COCyc, $(CR^aR^b)_n$COA, $(CR^aR^b)_nCONA_2$, $(CR^aR^b)_nCONH_2$, $(CR^aR^b)_n$CONHA, $(CR^aR^b)_nCONH(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_nCONH(CR^aR^b)_m$HetAr1, $(CR^aR^b)_nCONH(R^aR^b)_m$Aryl, $(CR^aR^b)_n$CONHCyc, $(CR^aR^b)_n$COOA, $(CR^aR^b)_n$COOH, $(CR^aR^b)_nCOO(CR^aR^b)_m$HetCyc1, $(CR^aR^b)_nCOO(CR^aR^b)_m$HetAr1, $(CR^aR^b)_nCOO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$COOCyc, $(CR^aR^b)_nNHCO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nNHCO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nNHCO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$NHCOCyc, $(CR^aR^b)_n$NHCOA, $(CR^aR^b)_nS(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nS(R^aR^b)_m$HetAr1, $(CR^aR^b)_nS(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SA, $(CR^aR^b)_nSO(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nSO(R^aR^b)_m$HetAr1, $(CR^aR^b)_nSO(R^aR^b)_m$Aryl, $(CR^aR^b)_n$SOA, $(CR^aR^b)_nSO_2(R^aR^b)_m$HetCyc1, $(CR^aR^b)_nSO_2(R^aR^b)_m$HetAr1, $(CR^aR^b)_nSO_2(R^aR^b)_m$Aryl, $(CR^aR^b)_nSO_2$Cyc, $(CR^aR^b)_nSO_2$A, $(CR^aR^b)_n$SOA(NH), $(CR^aR^b)_n$SOCyc(NH), $(CR^aR^b)_n$SOAryl(NH), $(CR^aR^b)_n$SOHetCyc1(NH), $(CR^aR^b)_n$SOHetAr1(NH), $(CR^aR^b)_n$SOA(NA), $(CR^aR^b)_nSOR^{Cyc1}(NR^{Cyc2})$, $(CR^aR^b)_n$SOCyc(NA), $(CR^aR^b)_n$SOAryl(NA), $(CR^aR^b)_n$SOHetCyc1(NA), $(CR^aR^b)_n$SOHetAr1(NA), $(CR^aR^b)_n$SOA(NCyc), $(CR^aR^b)_n$SOCyc(NCyc), $(CR^aR^b)_n$SOAryl(NCyc), $(CR^aR^b)_n$SOHetCyc1(NCyc), $(CR^aR^b)_n$SOHetAr1(NCyc), $(CR^aR^b)_nSO_2NA_2$, $(CR^aR^b)_nSO_2NH_2$, $(CR^aR^b)_nSO_2$NHA, $(CR^aR^b)_nPOA_2$, and an azaspirocycle, which is unsubstituted or

monosubstituted by at least one Hal, Alk2 or OAlk2 group;

A denotes linear or branched alkyl having 1, 2, 3, 4, 5, or 6 carbon atoms, wherein:
- one or two non-adjacent CH_2 groups may be replaced by O, NAlk2 or NH; and/or
- 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal; and/or
- one hydrogen may be replaced by OH or NH_2 or a cyclic alkyl having 3, 4, 5 or 6 carbon atoms, which is mono- di or trisubstituted by Hal, OH, Alk2, NHAlk2, $N(Alk2)_2$ and/or NH_2;

Alk1 denotes linear or branched alkyl having 1, 2, 3, 4, 5, or 6 carbon atoms, wherein - one or two CH_2 groups may be replaced by O, NAlk2 or NH; and/or
- 1 hydrogen may be replaced by OH, NHAlk2, $N(Alk2)_2$ or NH_2; and/or
- 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal;

Alk2 denotes linear or branched alkyl having 1 to 6 carbon atoms, wherein 1, 2, 3, 4 or 5 hydrogens may be replaced by Hal;

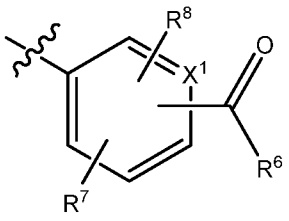
Aryl denotes phenyl, which is unsubstituted or mono-, di- or trisubstituted Hal, Alk2, OAlk2, OH, NH_2, Cyc or HetAr2, HetCyc2;

HetCyc1 denotes a mono- or bicyclic optionally bridged saturated or unsaturated 4- to 10-membered heterocycle having 1 or 2 heteroatoms selected from N, O, S and/or Si, wherein said heterocycle may be unsubstituted or mono-or disubstituted by Hal, OH, A, Aryl, HetAr2, SO_2Alk2 and/or =O;

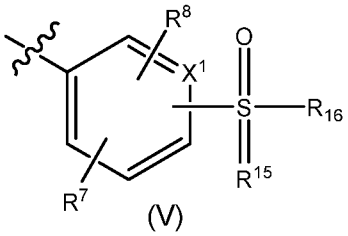
HetCyc2 denotes a mono- or bicyclic optionally bridged saturated or unsaturated 4- to 10-membered heterocycle having 1 or 2 heteroatoms selected from N, O, S and/or Si, wherein said

	heterocycle may be unsubstituted or mono-or disubstituted by Hal, OH, A, SO_2Alk1 and/or =O;
Cyc	denotes cyclic alkyl having 3 to 6 carbon atoms, wherein 1, 2 or 3 hydrogens may be replaced by Hal and 1 additional hydrogen may be replaced by HetCyc2, HetAr2, Aryl, Alk2, NH_2 and/or OH;
Hal	denotes F or Cl;
HetAr1	denotes a mono- or bicyclic aromatic 4- to 12-membered heterocycle having 1, 2, 3 or 4 N, O and/or S atoms, said heterocycle being unsubstituted or mono- or disubstituted Hal, Alk2, SOAlk2, SO_2Alk2, HetCyc2, OH or NH_2;
HetAr2	denotes a mono- or bicyclic aromatic 4- to 12-membered heterocycle having 1, 2, 3 or 4 N, O and/or S atoms, said heterocycle being unsubstituted or mono- or disubstituted Hal, Alk2, SOAlk2, SO_2Alk2, OH or NH_2
R^a and R^b	denote each, independently from each other, H, Alk2 or Cyc; or R^a and R^b together represent $-(CH_2)_x-$ with x= 2, 3, 4 or 5, thus forming together with the carbon atom they are attached to a (3-, 4-, 5- or 6- membered) cycloalkyl ring;
R^{Cyc1} and R^{Cyc2}	together form $-(CH_2)_x-$ with x= 3 or 4, thus forming together with the atoms they are attached to a (5- or 6-membered) ring, wherein 1, or 2 H atoms, in $-(CH_2)_x-$ can be independently replaced by Hal or Alk1;
n	denotes 0, 1 or 2;
m	denotes 0 or 1; and
Z	denotes CH, CHal, CAlk2, $CCHal_3$ or N.

2. A compound according to claim 1, wherein R denotes a structure according to formula (IV), (V), (Va) or (VI)



(IV)



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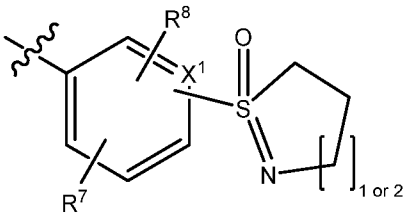
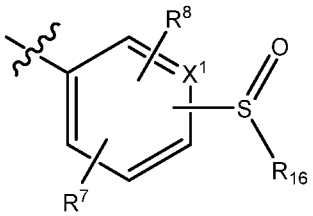


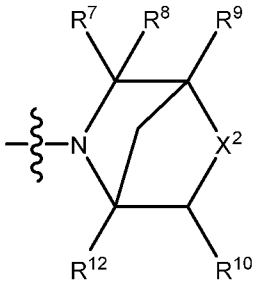
(Va)



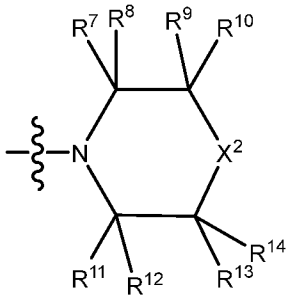
(VI)

wherein

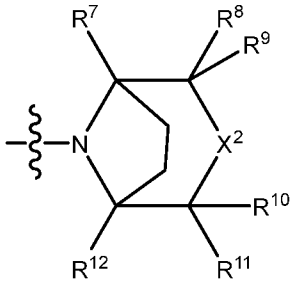
R^6 denotes OH, A or Cyc or a substituent according to formula (VII) to (X)



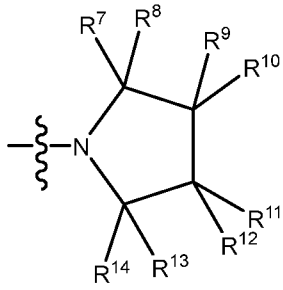
(VII)



(VIII)



(IX)



(X)

wherein

R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} denote each, independently from each other, H, OH, Hal, CH_3, C_2H_5, $CHal_3$, OCH_3, $OCHal_3$, $OCHal_2$, OCH_2Hal, CH_2Hal and/or $CHHal_2$;

R^{15} denotes NR^{17} or O;

R^{16} denotes A or Cyc;

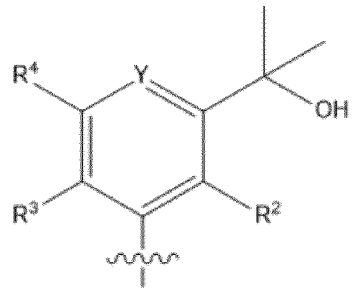
R^{17} denotes H, Alk1 or cyclic alkyl having 3 to 6 carbon atoms, wherein 1, 2 or 3 hydrogens of said cyclic alkyl group may be replaced by Hal;

X^1 denotes N or CH; and

X^2 denotes NH, NAlk1 or O.

3. A compound according to claim 1 or 2, wherein Q denotes a structure according to formula (II).

4. A compound according to any of claim 1, 2 or 3, wherein Q denotes a structure according to formula (XI)



(XI)

wherein one or two of the residues R^2, R^3 and R^4 independently represent, Hal, CH_3, $CHal_3$, OCH_3, $OCHal_3$, $OCHHal_2$, OCH_2Hal, CH_2Hal and/or $CHHal_2$ and the remaining residue(s) represent H.

5. A compound according to any of claim 1, 2, 3 or 4, wherein Z denotes N.

6. A compound according to claim 1 selected from following group:

Compound	**Name**
C9	2-(6-Methanesulfonyl-pyridin-3-yl)-7-[3-(morpholine-4-sulfonyl)-phenyl]-furo[3,2-b]pyridine
C28	[(S)-2-(1-Hydroxy-1-methyl-ethyl)-pyrrolidin-1-yl]-{3-[2-(4-methanesulfonyl-phenyl)-furo[3,2-b]pyridin-7-yl]-phenyl}-methanone

C29	N,N-Diisopropyl-3-[2-(4-methanesulfonyl-phenyl)-furo[3,2-b]pyridin-7-yl]-benzamide
C43	2-{4-[2-(4-nitrophenyl)furo[3,2-b]pyridin-7-yl]pyridin-2-yl}propan-2-ol
C45	2-{4-[2-(4-{hexahydro-1H-furo[3,4-c]pyrrole-5-carbonyl}phenyl)furo[3,2-b]pyridin-7-yl]pyridin-2-yl}propan-2-ol
C46	1-{2-fluoro-3-[2-(4-methanesulfonylphenyl)furo[3,2-b]pyridin-7-yl]phenyl}ethan-1-one
C50	2-(4-{2-[4-(2-methylmorpholine-4-carbonyl)phenyl]furo[3,2-b]pyridin-7-yl}pyridin-2-yl)propan-2-ol
C56	1-{4-[2-(4-methanesulfonylphenyl)furo[3,2-b]pyridin-7-yl]pyridine-2-carbonyl}piperazine
C58	1-((4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)sulfonyl)azetidin-3-ol
C63	1-(2-Hydroxy-2-methyl-propyl)-4-{7-[3-(morpholine-4-carbonyl)-phenyl]-furo[3,2-b]pyridin-2-yl}-1H-pyridin-2-one
C66	2-(4-(2-(4-(1H-tetrazol-5-yl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
C74	(4-{4-[2-(1-Hydroxy-1-methyl-ethyl)-pyridin-4-yl]-furo[3,2-d]pyrimidin-6-yl}-phenyl)-morpholin-4-yl-methanone
C75	(4-{4-[2-(1-Hydroxy-1-methyl-ethyl)-pyridin-4-yl]-furo[3,2-d]pyrimidin-6-yl}-phenyl)-((R)-3-methyl-morpholin-4-yl)-methanone
C76	2-[4-(6-{4-[(2R,6S)-2,6-dimethylmorpholine-4-carbonyl]phenyl}furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl]propan-2-ol
C77	2-(4-{6-[4-(4-methylpiperazine-1-carbonyl)phenyl]furo[3,2-d]pyrimidin-4-yl}pyridin-2-yl)propan-2-ol
D1	3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide

D2	N-(2-(piperidin-1-yl)ethyl)-3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)benzamide
D3	7-(3-(methylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine
D4	7-(3-(cyclopropylsulfonyl)phenyl)-2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridine
D5	2-((3-(2-(3,4,5-trimethoxyphenyl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)ethan-1-ol
D6	2-(3,6-dihydro-2H-pyran-4-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D7	2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D8	2-(1-methyl-1H-indazol-6-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D9	5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2-amine
D10	7-(3-(methylsulfonyl)phenyl)-2-(pyridin-4-yl)furo[3,2-b]pyridine
D11	2-(1-methyl-1H-benzo[d]imidazol-5-yl)-7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D12	1-methyl-5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one
D13	N-(2-aminoethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D14	2-(1-methyl-1H-pyrazol-4-yl)-7-(3-(piperazin-1-ylsulfonyl)phenyl)furo[3,2-b]pyridine
D15	5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyrimidin-2-amine
D16	7-(3-(methylsulfonyl)phenyl)-2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine
D17	N-(2-hydroxyethyl)-3-(2-(1,3,5-trimethyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide

D18	7-(3-(cyclopropylsulfonyl)phenyl)-2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridine
D19	N-(2-hydroxyethyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D20	1-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)azetidin-3-ol
D21	N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D22	5-(4-(3-(cyclopropylsulfonyl)phenyl)furo[3,2-d]pyrimidin-6-yl)-1-methylpyridin-2(1H)-one
D23	imino(methyl)(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone
D24	4-((3-(2-(1-methyl-1H-pyrazol-4-yl)furo[3,2-b]pyridin-7-yl)phenyl)sulfonyl)piperazin-2-one
D25	5-(7-(3-(cyclopropylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one
D26	5-(7-(3-(N,S-dimethylsulfonimidoyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one
D27	(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D28	N-(2-hydroxy-2-methylpropyl)-3-(2-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D29	(3-hydroxyazetidin-1-yl)(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D30	N-(2-hydroxy-2-methylpropyl)-3-(2-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide

D31	N-(2-hydroxy-2-methylpropyl)-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)benzenesulfonamide
D32	5-(7-(3-((3-aminoazetidin-1-yl)sulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)-1-methylpyridin-2(1H)-one
D33	(3-hydroxyazetidin-1-yl)(5-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)methanone
D34	2-methyl-1-(5-(7-(3-(2-methyl-2l7-propa-1,2-dien-2-yl)phenyl)furo[3,2-b]pyridin-2-yl)-2-methylenepyridin-1(2H)-yl)propan-2-ol
D35	2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)amino)propan-2-ol
D36	1-methyl-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one
D37	(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D38	(R)-imino(methyl)(4-(7-(3-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone
D39	1-(2-hydroxy-2-methylpropyl)-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2(1H)-one
D40	1-(2-hydroxy-2-methylpropyl)-5-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2(1H)-one
D41	2-methyl-1-((4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)amino)propan-2-ol
D42	1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol
D43	(R)-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone

D44	(3-(2-(6-aminopyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D45	(R)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D46	(S)-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D47	2-methyl-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)oxy)propan-2-ol
D48	2-methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D49	N-(2-hydroxy-2-methylpropyl)-5-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)picolinamide
D50	imino(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ6-sulfanone
D51	(5-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)(3-hydroxyazetidin-1-yl)methanone
D52	(4-(7-(2-(2-hydroxy-2-methylpropyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone
D53	2-methyl-1-(4-(7-(2-(methylsulfonyl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)pyridin-2-yl)propan-2-ol
D54	2-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D55	(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D56	(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D57	2-(4-(methylsulfinyl)phenyl)-7-(2-morpholinopyridin-4-yl)furo[3,2-b]pyridine
D58	1-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)azetidin-3-ol

D59	((2R,6S)-2,6-dimethylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D60	(4,4-difluoropiperidin-1-yl)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D61	(cyclopropylimino)(methyl)(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)-λ^6-sulfanone
D62	(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D63	(2-methylmorpholino)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D64	1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)cyclobutan-1-ol
D65	(4-methylpiperazin-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D66	(3-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D67	(2-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D68	(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D69	(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D70	(3-(2-(2-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D71	(3-(2-(4-(dimethylphosphoryl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone

D72	((R)-3-methylmorpholino)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D73	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D74	(4,4-difluoropiperidin-1-yl)(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D75	(2-methylmorpholino)(4-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methanone
D76	2-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D77	4,4-difluoro-1-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)cyclohexan-1-ol
D78	((2S,6R)-2,6-dimethylmorpholino)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D79	3-(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol
D80	2-(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D81	3-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)oxetan-3-ol
D82	N,N-dimethyl-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)benzamide
D83	(3-(2-(6-(3-hydroxyoxetan-3-yl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D84	(3-(2-(4-(3-hydroxyoxetan-3-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone

D85	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D86	(4-(2-(4-(methylsulfinyl)-3-(trifluoromethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)(morpholino)methanone
D87	(2-fluoro-5-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(morpholino)methanone
D88	7-(3-(tert-butyl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine
D89	7-(3-(2-methoxypropan-2-yl)phenyl)-2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridine
D90	(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)(pyrrolidin-1-yl)methanone
D91	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D92	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D93	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D94	1-(4-(7-(3-(morpholine-4-carbonyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one
D95	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(6-(tert-butylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D96	2-(4-(2-(1-(methylsulfonyl)-1,2,3,6-tetrahydropyridin-4-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol

D97	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-5-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D98	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D99	(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D100	(4,4-dimethyl-1,4-azasilinan-1-yl)(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D101	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D102	(R)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D103	(S)-(3-methylmorpholino)(3-(2-(6-(methylsulfonyl)pyridin-3-yl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D104	1-(4-(7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptane-5-carbonyl)-2-fluorophenyl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one
D105	morpholino(3-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D106	(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-oxa-6-azaspiro[3.4]octan-6-yl)methanone
D107	(S)-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone
D108	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone

D109	7-(2-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)pyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D110	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(3-(2-(4-(2-hydroxypropan-2-yl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D111	(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(2,6-difluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D112	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D113	7-(1-(methylsulfonyl)-1,2,5,6-tetrahydropyridin-3-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D114	2-(1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)piperidin-4-yl)propan-2-ol
D115	7-(2-methoxypyridin-4-yl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D116	2-(4-(2-(4-(methylsulfonyl)-2-(trifluoromethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D117	1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)pyrrolidin-3-ol
D118	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D119	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2-fluoro-3-(2-(3-fluoro-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)methanone
D120	2-(4-(methylsulfonyl)phenyl)-7-(2-(morpholinomethyl)pyridin-4-yl)furo[3,2-b]pyridine
D121	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-dimethylbenzamide

D122	2-(4-(2-(2-methyl-4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D123	7-(3-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)phenyl)-2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridine
D124	2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D125	2-methyl-1-(3-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D126	(R)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D127	(S)-2-(4-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D128	1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)ethan-1-one
D129	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoic acid
D130	2-(4-(2-(4-(methylthio)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D131	(S)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D132	(R)-2-(4-(2-(4-((trifluoromethyl)sulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D133	methyl 4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzoate
D134	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D135	2-(3-(2-(4-(methylsulfinyl)phenyl)furo[3,2-b]pyridin-7-yl)phenyl)propan-2-ol
D136	4,4-difluoro-1-((4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)methyl)cyclohexan-1-ol

D137	(3,3-difluoroazetidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D138	2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-N,N-dimethylacetamide
D139	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methylbenzamide
D140	(4-(7-(3-(tert-butyl)phenyl)furo[3,2-b]pyridin-2-yl)phenyl)dimethylphosphine oxide
D141	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-propylbenzamide
D142	(3-fluoropyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D143	1,1-difluoro-2-methyl-1-(4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D144	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzamide
D145	(4,4-difluoropiperidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D146	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D147	2-(4-(2-(4-(morpholinomethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D148	(R)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(3-methylmorpholino)methanone
D149	2-(2-fluoro-3-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)phenyl)propan-2-ol
D150	2-(6-fluoro-4-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl)propan-2-ol

D151	(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)methanone
D152	(S)-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(trifluoromethyl)pyrrolidin-1-yl)methanone
D153	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N,N-diisopropylbenzamide
D154	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-(pyridin-3-yl)pyrrolidin-1-yl)methanone
D155	4-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)morpholin-3-one
D156	5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2-(4-methoxybenzyl)isoindolin-1-one
D157	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(indolin-1-yl)methanone
D158	5-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)isoindolin-1-one
D159	(S)-(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D160	(R)-(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D161	(2,6-dimethylmorpholino)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D162	tert-butyl 4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoate
D163	methyl 3-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoate
D164	3-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)benzoic acid

D165	(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone
D166	(3,5-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D167	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D168	(2,2-dimethylpyrrolidin-1-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D169	1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)benzyl)-4-methylpiperidin-4-ol
D170	2-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)-1-morpholinoethan-1-one
D171	(3,5-dimethylmorpholino)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D172	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D173	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D174	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D175	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-5-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D176	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone

D177	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D178	(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D179	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)benzamide
D180	(1-(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)cyclopropyl)(morpholino)methanone
D181	(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D182	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-2,6-dimethylphenyl)(morpholino)methanone
D183	(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone
D184	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-oxa-5-azaspiro[3.4]octan-5-yl)methanone
D185	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-methyl-N-pentylbenzamide
D186	4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)-N-isobutyl-N-methylbenzamide
D187	2-(4-(2-(4-(1-hydroxyethyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D188	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D189	2-(4-(2-(1-methyl-3a,7a-dihydro-1H-indazol-5-yl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D190	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(imino)(methyl)-λ6-sulfanone

D191	(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(2-methylmorpholino)methanone
D192	(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(2-methylmorpholino)methanone
D193	((2R,6R)-2,6-dimethylmorpholino)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D194	((2S,6S)-2,6-dimethylmorpholino)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D195	(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D196	(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(3-methylmorpholino)methanone
D197	((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D198	((2R,6S)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D199	((2R,6R)-2,6-dimethylmorpholino)(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)methanone
D200	(2,6-difluoro-4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)((2R,6S)-2,6-dimethylmorpholino)methanone
D201	4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)benzoic acid
D202	(4-(7-(2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(2-oxa-6-azaspiro[3.3]heptan-6-yl)methanone
D203	(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ6-sulfanone

D204	(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(4-methylpiperazin-1-yl)methanone
D205	2-(3-fluoro-4-(2-(4-(methylsulfonyl)phenyl)furo[3,2-b]pyridin-7-yl)pyridin-2-yl)propan-2-ol
D206	(4-(7-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-b]pyridin-2-yl)phenyl)(morpholino)methanone
D207	(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)(morpholino)methanone
D208	((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(4-(4-(3-fluoro-2-(2-hydroxypropan-2-yl)pyridin-4-yl)furo[3,2-d]pyrimidin-6-yl)phenyl)methanone
D209	(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D210	(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D211	1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-3,4,5,6-tetrahydro-1,2-thiazine 1-oxide;
D212	1-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)-4,5-dihydro-3H-isothiazole 1-oxide; and
D213	2-(4-(6-(4-(methylsulfonyl)phenyl)furo[3,2-d]pyrimidin-4-yl)pyridin-2-yl)propan-2-ol.

7. A compound according to any of claims 1 to 6, wherein the PI4K-related disorder is selected from the list of protozoan infections and viral infection.

8. A compound according to claim 7, wherein the protozoan infection is malaria.

9. A compound according to claim 7, wherein the viral infection is an RNA viral infection.

10. A pharmaceutical composition for use in the prevention and/or treatment of PI4K-related disorders, comprising at least one compound of formula (I) according to any of claims 1 to 6.

11. A pharmaceutical composition according to claim 10 further comprising a pharmaceutically acceptable carrier, diluent or excipient thereof.

12. A pharmaceutical composition according to claim 10 or 11, wherein the PI4K-related disorder is malaria.

13. A pharmaceutical composition according to any of claims 10, 11 or 12, further comprising at least one antimalarial agent different from formula (I).

14. A pharmaceutical composition according to claim 10 or 11, wherein the PI4K-related disorder is a viral infection caused by an RNA virus.

15. A pharmaceutical composition according to claim 14 further comprising at least one antiviral agent different from formula (I).

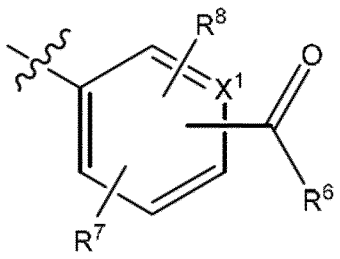
16. A method for preventing or treating of PI4K-related disorders, wherein the method comprises the following step:

(i) providing at least one compound according to any of claims 1 to 6 and/or a pharmaceutical composition according to any of claims 10 to 15; and

(ii) administering an effective amount of said at least one compound or said composition to a patient in need thereof.

17. A method according to claim 16, wherein the PI4K-related disorder is malaria.

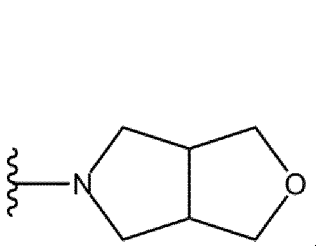
18. The compound according to claim 1, wherein R has a structure of formula (IV):



(IV) ;

wherein

R^6 is Alk1, Alk2, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, -OH, $-OCH_3$, $-OC(CH_3)_3$,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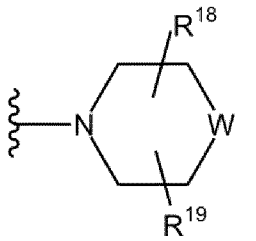
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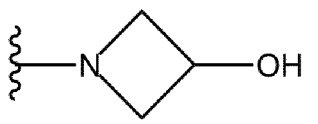
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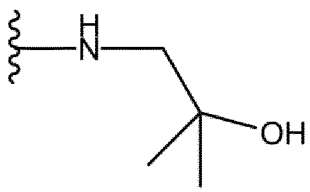
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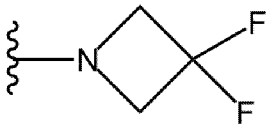
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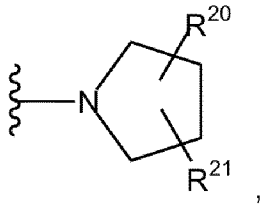
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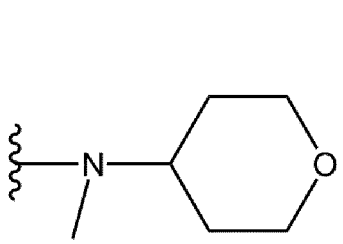
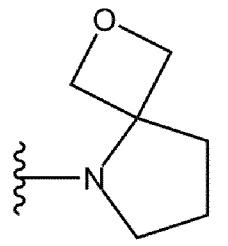
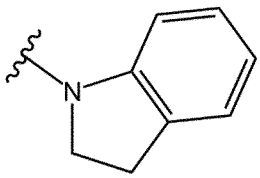
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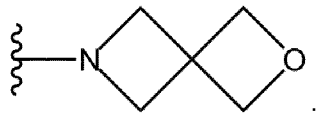
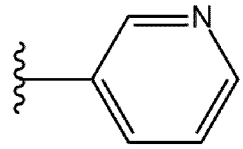

;

R^7, R^8 is each independently selected from H, Hal, Alk1, or Alk2;

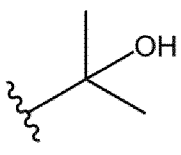
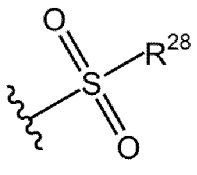
R^{18}, R^{19} is each independently selected from H, Hal, Alk1, Alk2, or are taken together form a cycloalkyl ring;

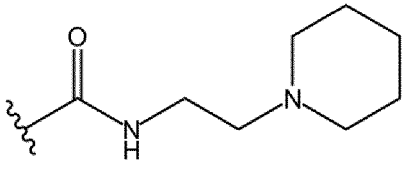
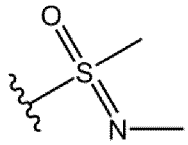
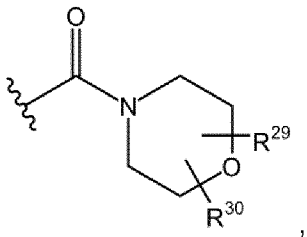
R^{20}, R^{21} is each independently selected from H, -Hal, -$CHal_3$, -CH_3, -$C((CH_3)_2OH)$, or  ;

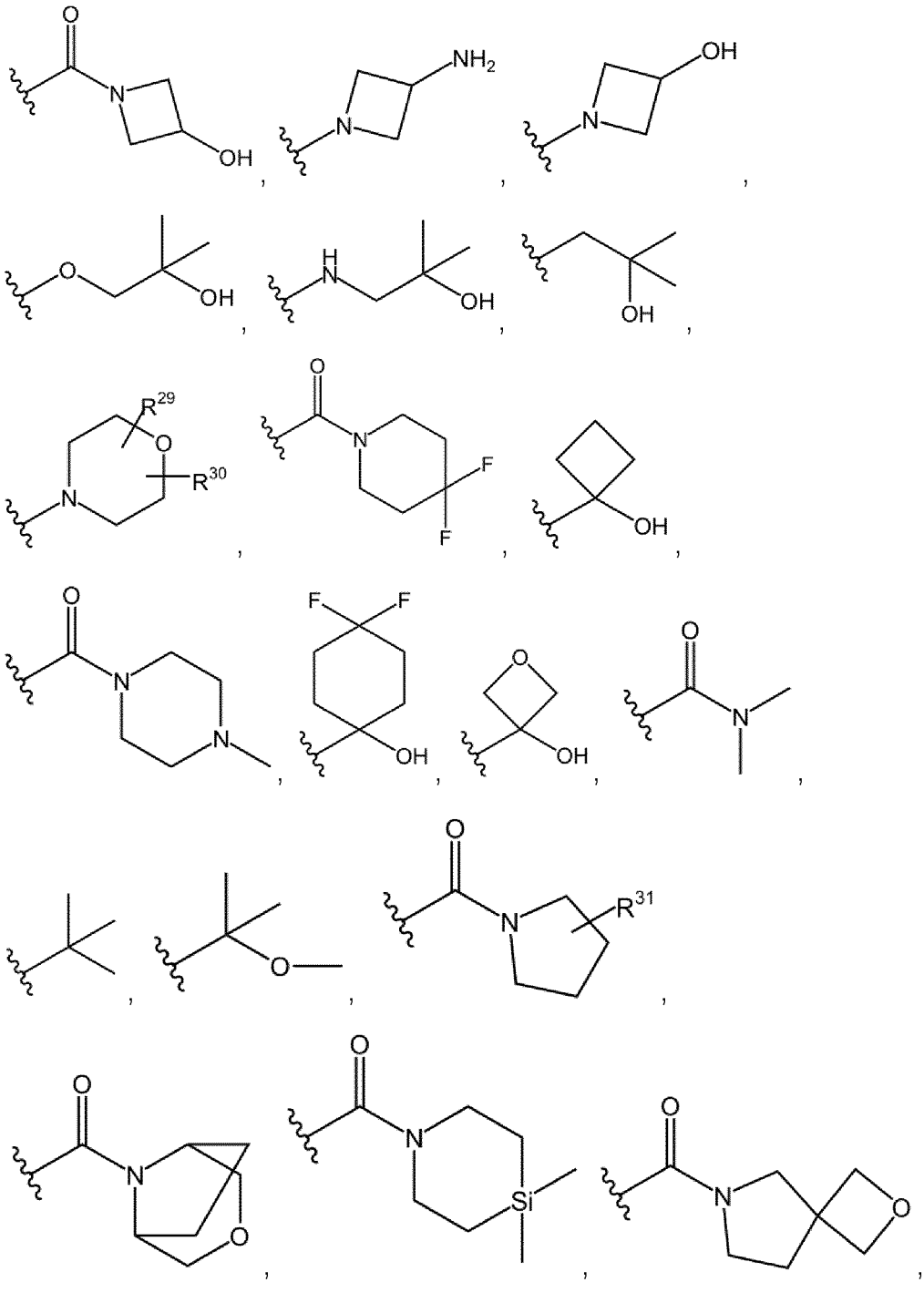
W is O, NR^{18}, or $CR^{18}R^{19}$;

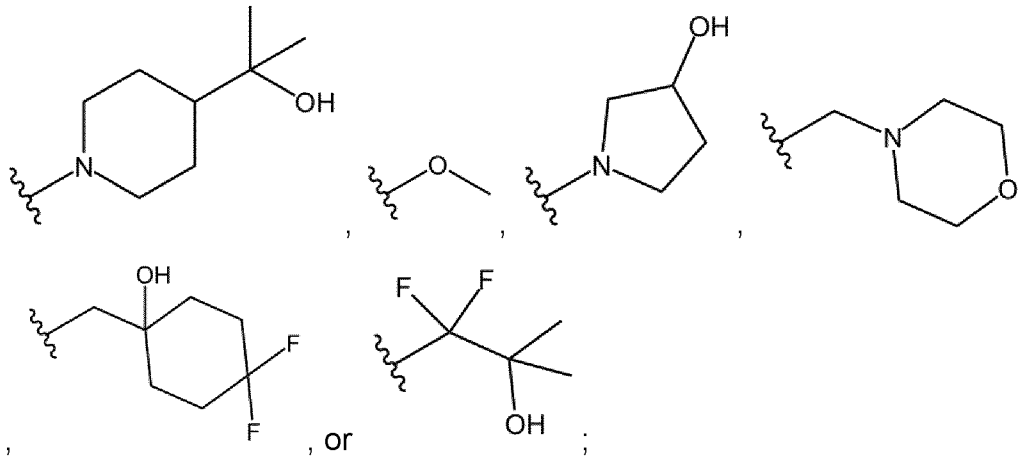
X^1 is CR^7 or N; and

wherein Q is formula II and

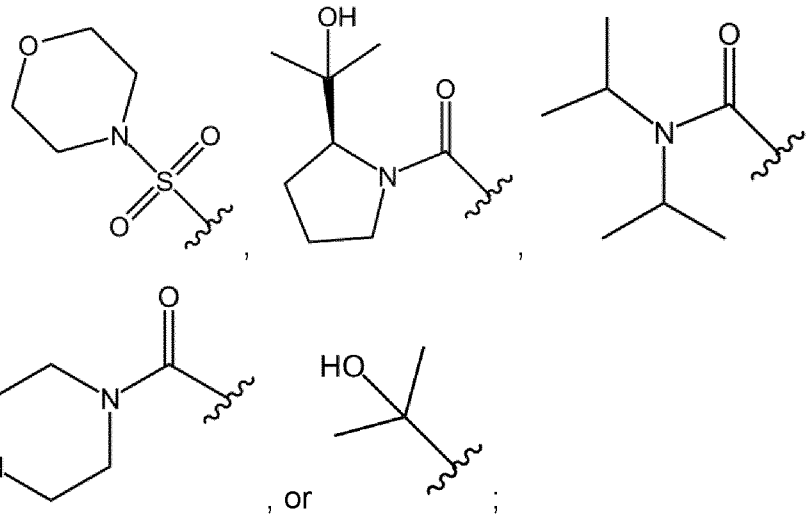
R^1 is H, Hal,  ,  ,

 ,  ,  ,



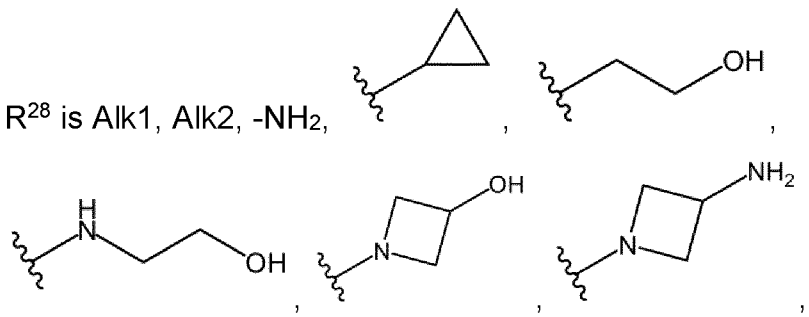


, or ;

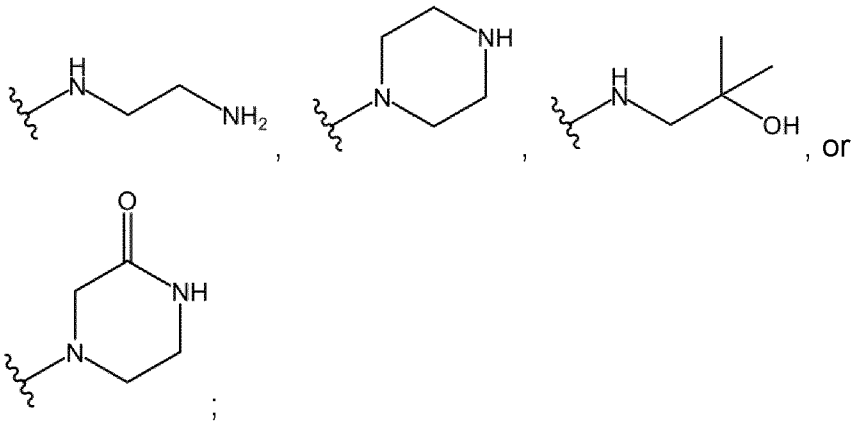


R^3 is H, Hal, , or ;

R^2, R^4 is each independently selected from H or Hal;



R^{28} is Alk1, Alk2, -NH_2, , , , , ,



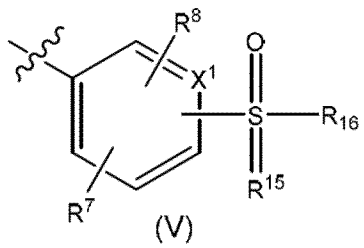
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

19. The compound according to claim 1, wherein R has a structure of formula (V):

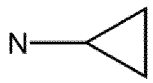


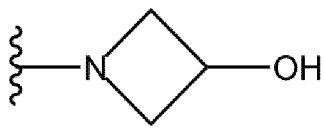
(V)

;

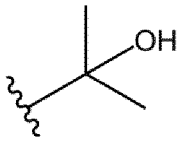
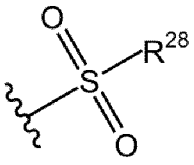
X^1 is CR^7 or N;

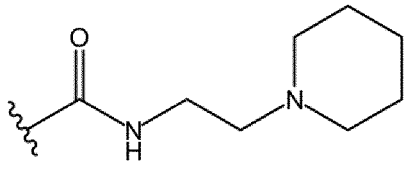
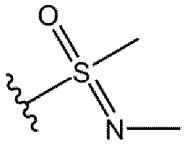
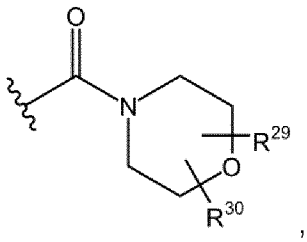
R^7, R^8 is each independently selected from H, Hal, $-CH_3$, or $-CHal_3$;

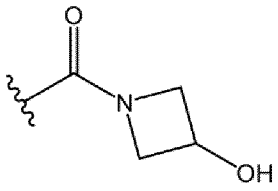
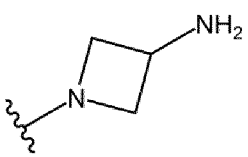
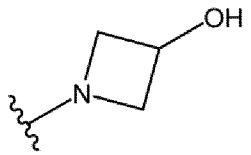
R^{15} is O, NH, or  ;

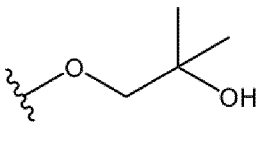
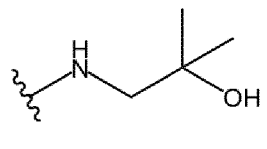
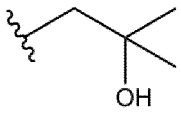
R^{16} is Alk1, $-NH_2$, $-N(CH_3)_2$, Alk2, or  ; and

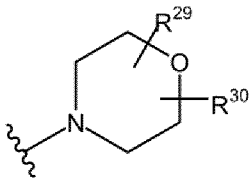
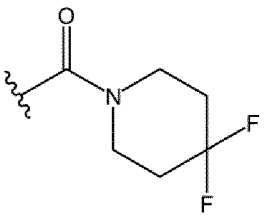
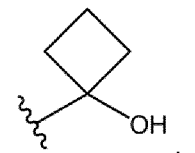
wherein Q is formula II and

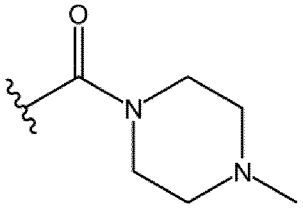
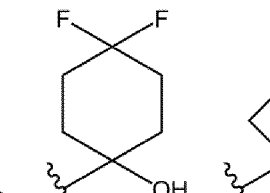
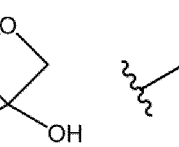
R^1 is H, Hal,  ,  ,

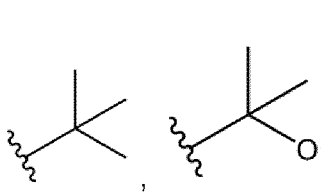
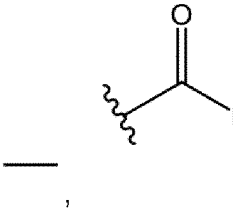
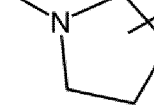
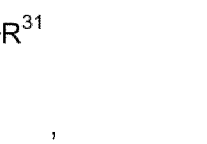
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,  ,

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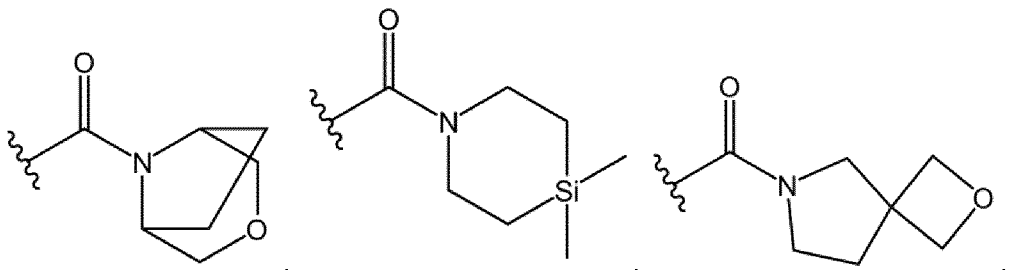

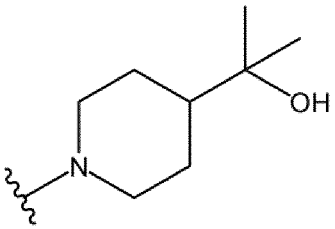
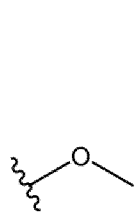
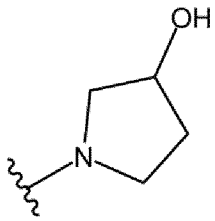
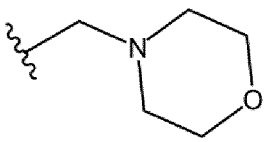
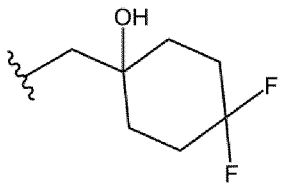
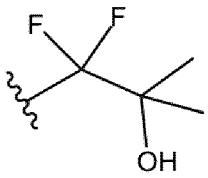

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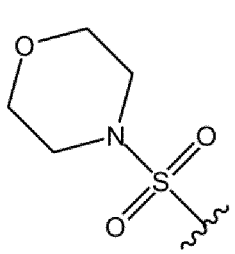
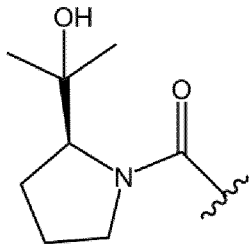
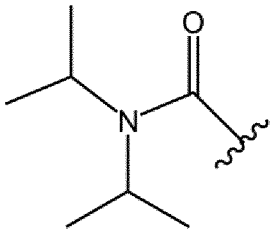
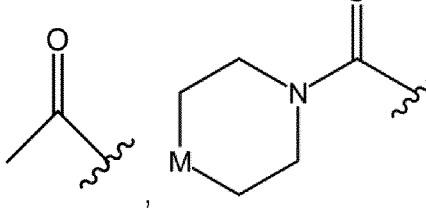
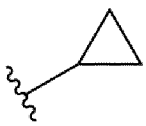
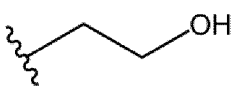




R^3 is H, Hal,

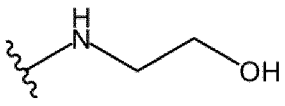
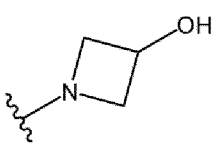
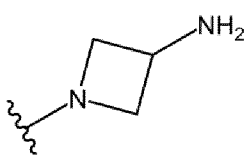


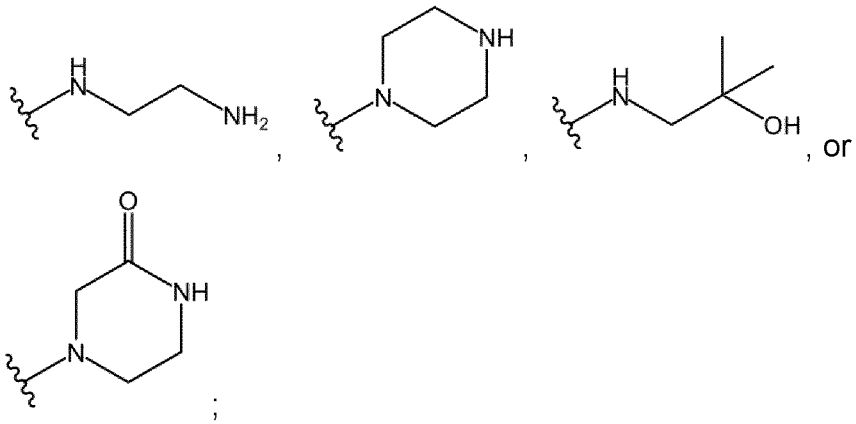
, or ;

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,



;

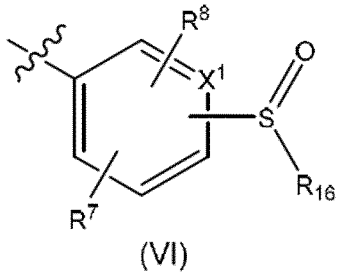
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

20. The compound according to claim 1, wherein R has a structure of formula (VI):



(VI)

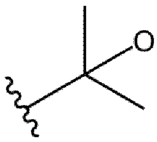
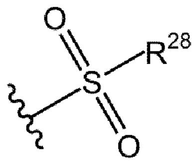
;

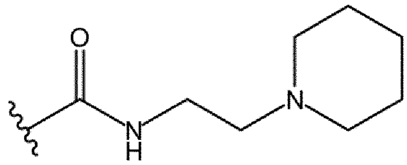
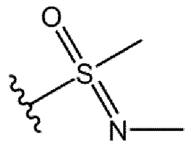
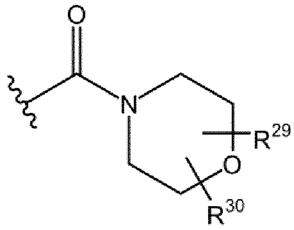
R^7, R^8 is each independently selected from H, Hal, or $CHal_3$; and

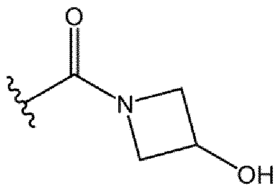
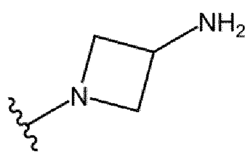
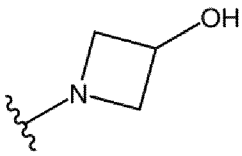
R^{16} is CH_3 or $CHal_3$;

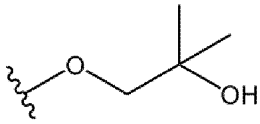
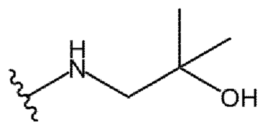
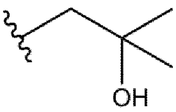
X^1 is CR^7 or N;

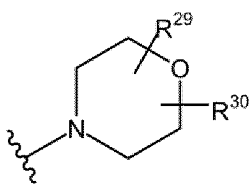
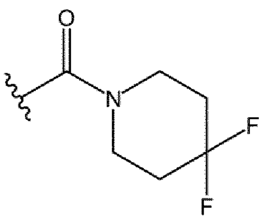
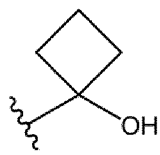
wherein Q is formula II and

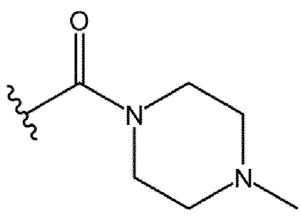
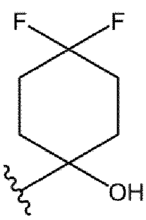
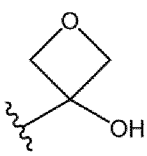
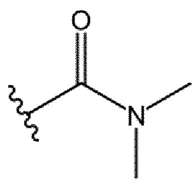
R^1 is H, Hal,  ,  ,

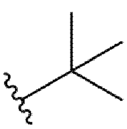
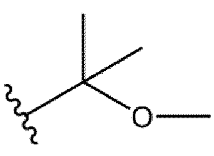
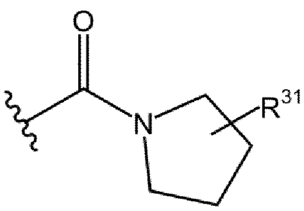
 ,  ,  ,

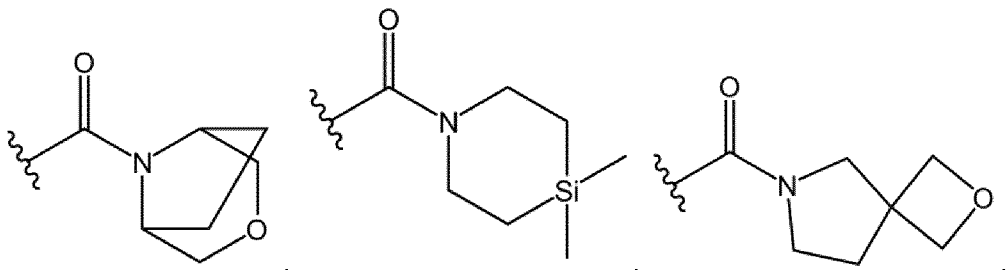
 ,  ,  ,

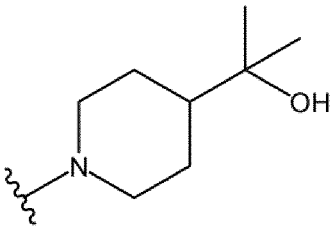
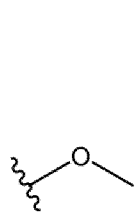
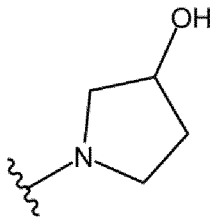
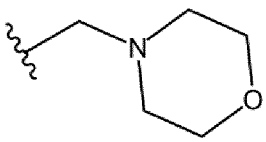
 ,  ,  ,

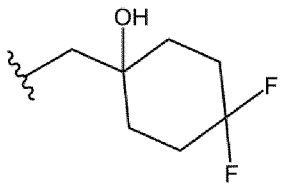
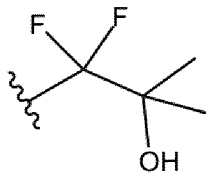
 ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,

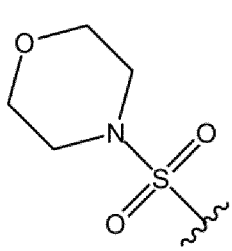
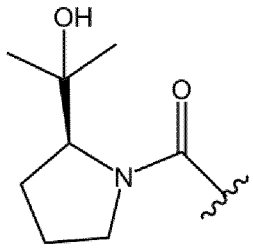
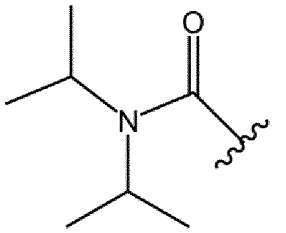


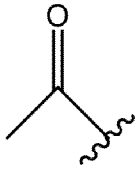
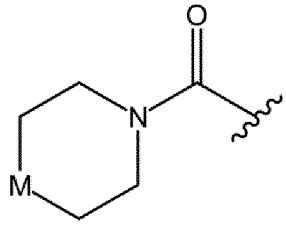
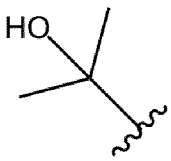





, or ;

R^3 is H, Hal,

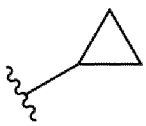
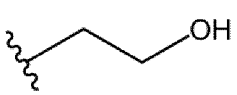




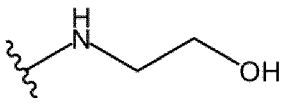
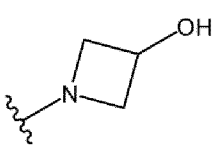
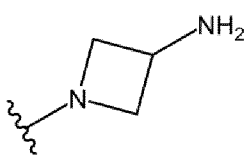




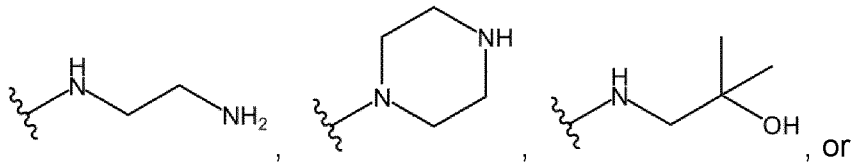
, or ;

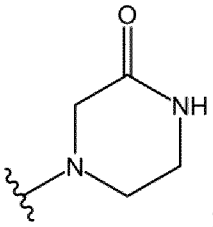
R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, -NH_2,


, or


;

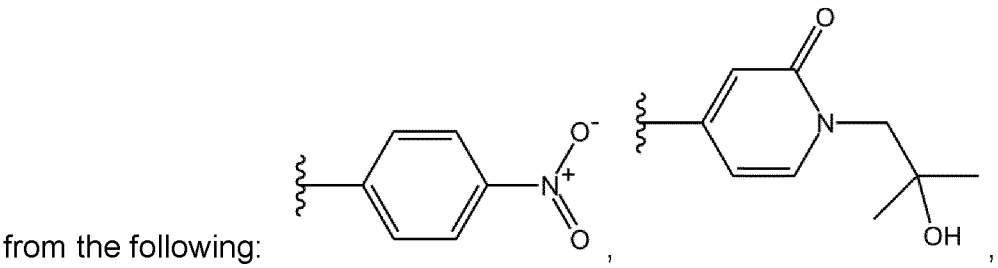
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

21. The compound according to claim 1, wherein R has a structure selected from the following: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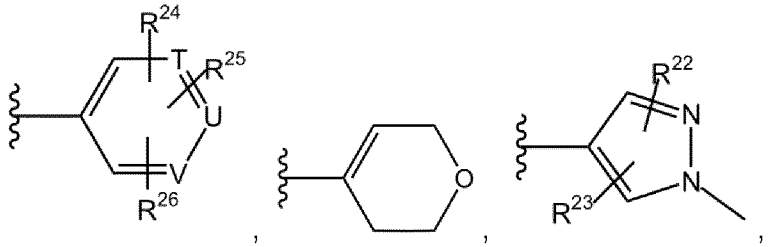
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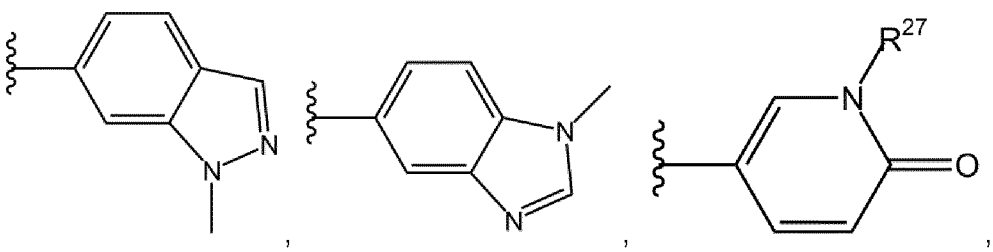
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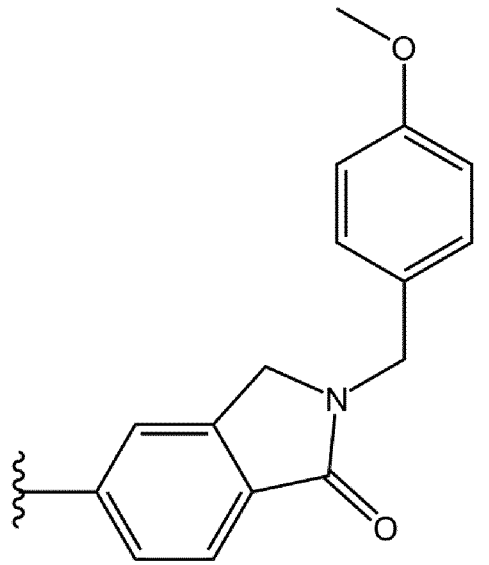
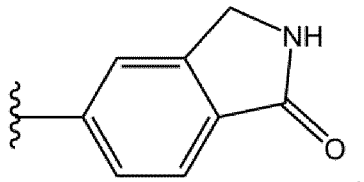
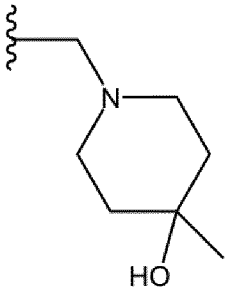
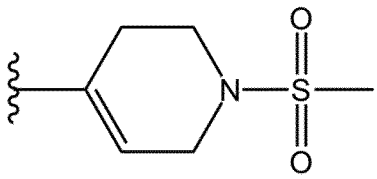
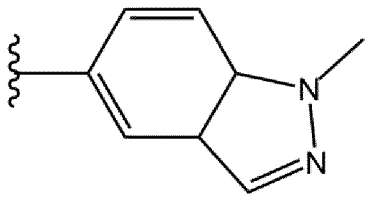
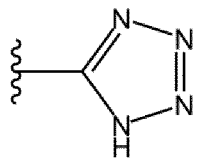
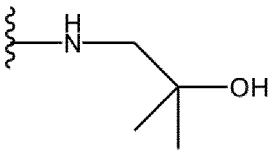
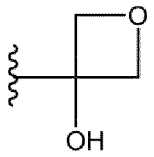
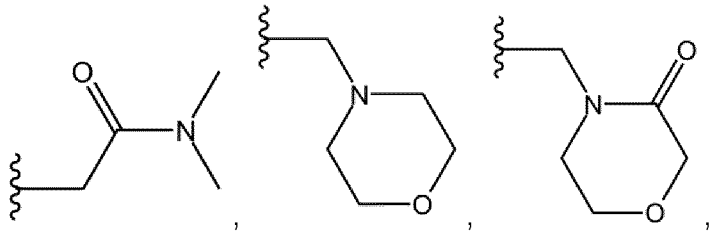
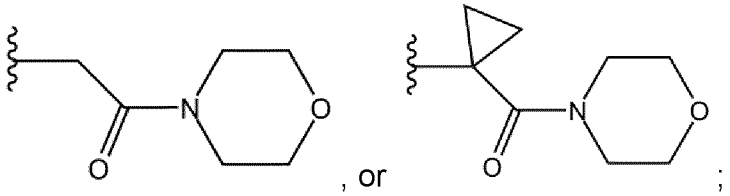






;

R^{22}, R^{23} is each independently selected from H or CH_3;

R^{24}, R^{25}, R^{26} is each independently selected from H, -OCH_3, -NH_2, -$CH_2C((CH_3)_2OH)$, -$C((CH_3)_2OH)$, -$PO(CH_3)_2$, -$C(CH_3)_2OH$, -SCH_3, -$CH(CH_3OH)$,

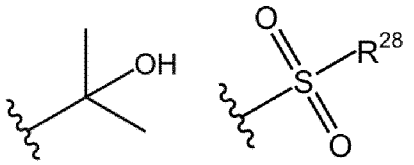
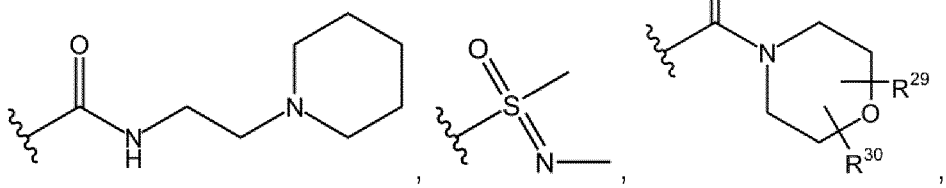
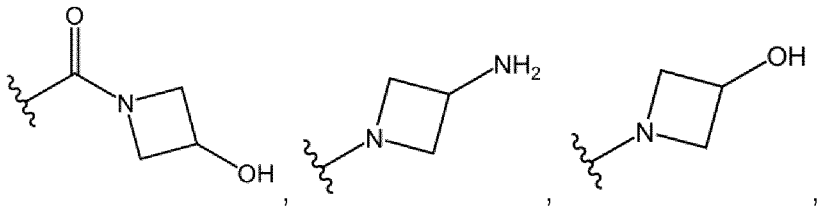
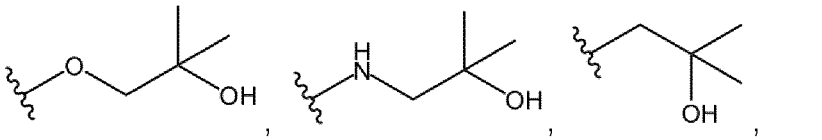
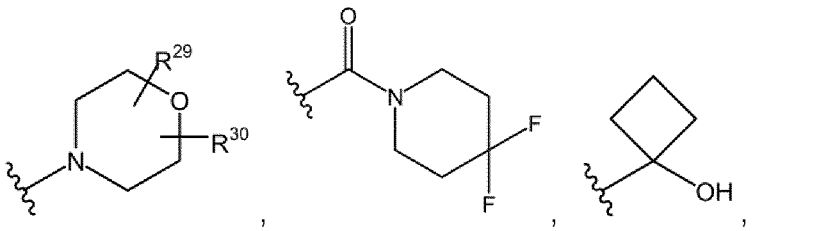
, or ;

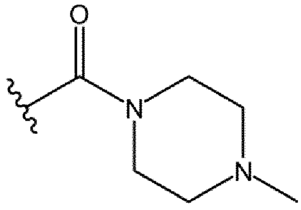
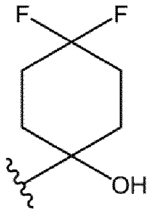
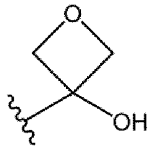
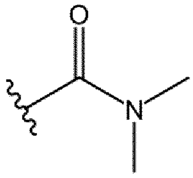
R^{27} is -CH_3 or -$C((CH_3)_2OH)$;

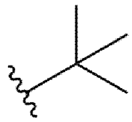
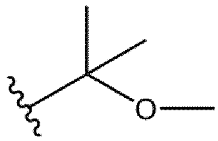
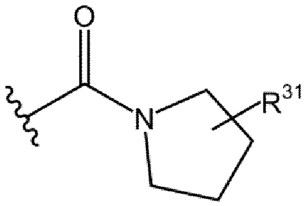
T, U, V is each independently selected from N or CR^{24}; and

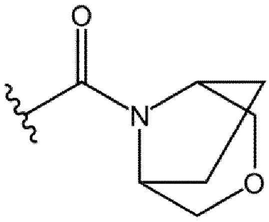
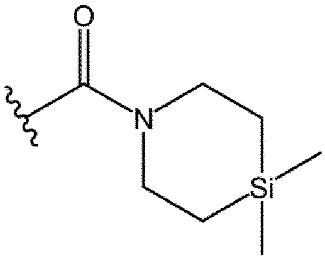
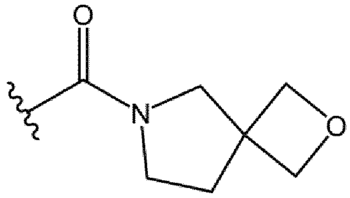
wherein Q is formula II and

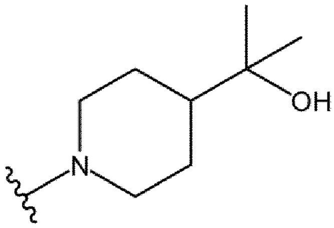
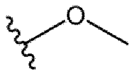
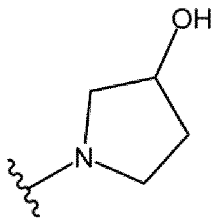
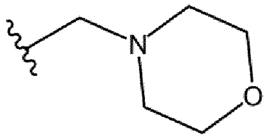
R^1 is H, Hal,

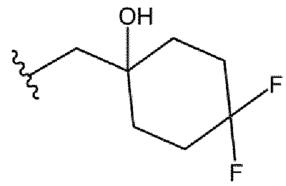
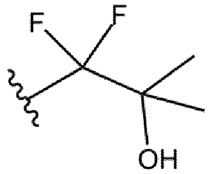






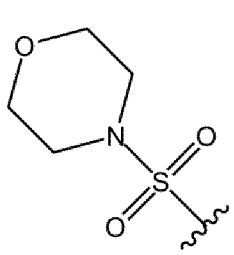
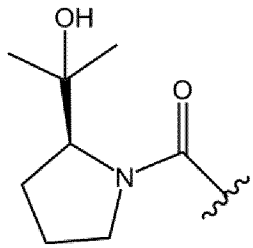
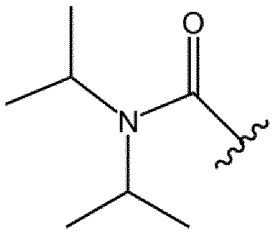
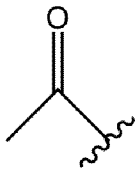
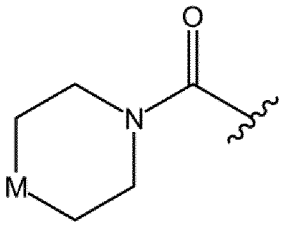
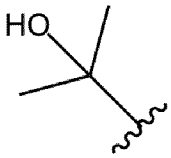
 ,  ,  ,  ,

 ,  ,  ,

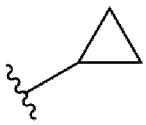
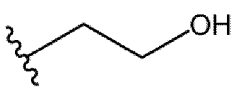
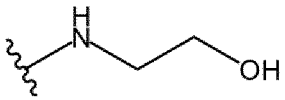
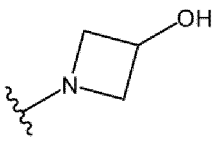
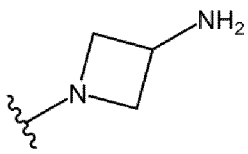
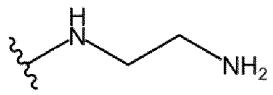
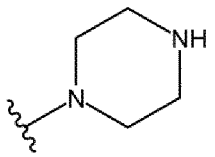
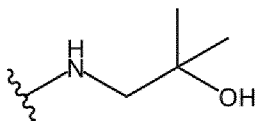
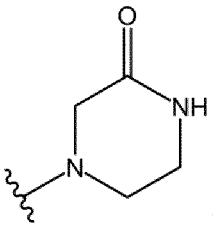
 ,  ,  ,

 ,  ,  , 

,  , or  ;

R^3 is H, Hal,  ,  ,  ,  ,  ,  ;

R^2, R^4 is each independently selected from H or Hal;

R^{28} is Alk1, Alk2, $-NH_2$,  ,  ,  ,  ,  ,  ,  ,  , or  ;

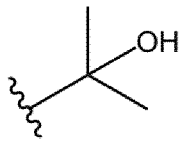
R^{29}, R^{30} is each independently selected from H or CH_3;

R^{31} is H or $CHal_3$;

M is NH or O; and

Y is N, CH, or CHal.

22. The compound according to claim 19, wherein

R^1 is selected from H, Alk1, Alk2, or 

;

R^2, R^3, R^4, R^7, R^8 is each independently selected from H or Hal;

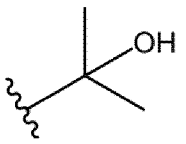
R^{15} is O or NH;

R^{16} is $-CH_3$ or Alk1; and

Y is CH or CHal.

23. The compound of claim 22, wherein the $SOR^{15}R^{16}$ group of formula V is ortho to the linkage of formula I.

24. The compound according to claim 22, wherein

R^1 is selected from Alk1 or 

;

R^2, R^3, R^4, R^7, R^8 is each independently selected from H or Hal;

R^{15} is NH;

R^{16} is $-CH_3$ or Alk1;

X^1 is CH; and

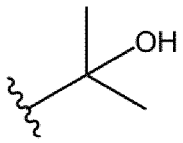
Y is CH.

25. The compound of claim 24, wherein the $SOR^{15}R^{16}$ group of formula V is ortho to the linkage of formula I.

26. The compound of claim 25, wherein R^3 and R^4 are H.

27. The compound according to claim 26, wherein X^1 is CH.

28. The compound according to claim 27, wherein

R^1 is  ;

R^{15} is NH;

R^{16} is $-CH_3$;

X^1 is CH; and

Y is CH.

29. The compound according to claim 28, wherein the compound is selected from the group consisting of:

D203	(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ6-sulfanone
D209	(S)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone
D210	(R)-(4-(4-(2-fluoro-3-(2-hydroxypropan-2-yl)phenyl)furo[3,2-d]pyrimidin-6-yl)phenyl)(imino)(methyl)-λ⁶-sulfanone

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2023/071761

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/519 A61K45/06 A61P31/14 A61P33/06
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/124025 A1 (MERCK PATENT GMBH [DE]) 29 August 2013 (2013-08-29) cited in the application paragraph [0298]; claim 1; example all -----	1-5,7,8, 10-12, 16-29
X	BRUNSCHWIG CHRISTEL ET AL: "UCT943, a Next-Generation Plasmodium falciparum PI4K Inhibitor Preclinical Candidate for the Treatment of Malaria", PHARMACOLOGY, vol. 62, no. 9, 27 August 2018 (2018-08-27), XP093089818, DOI: 10.1128/AAC.00012 compound MMV048 and UCT943 ----- -/--	1-29

[x] Further documents are listed in the continuation of Box C.

[x] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 October 2023	19/10/2023

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Bareyt, Sébastian

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2023/071761

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KONG D ET AL: "Inhibition profiles of phosphatidylinositol 3-kinase inhibitors against PI3K superfamily and human cancer cell line panel JFCR39", EUROPEAN JOURNAL OF CANCER, ELSEVIER, AMSTERDAM NL, vol. 46, no. 6, 1 April 2010 (2010-04-01), pages 1111-1121, XP026971003, ISSN: 0959-8049 [retrieved on 2010-02-01] compounds GDC-0941 -----	1-29
A	CASE W. MCNAMARA ET AL: "Targeting Plasmodium PI(4)K to eliminate malaria", CLEO: APPLICATIONS AND TECHNOLOGY 2019 SAN JOSE, CALIFORNIA UNITED STATES 5-10 MAY 2019, vol. 504, no. 7479, 27 November 2013 (2013-11-27), pages 248-253, XP055316473, DOI: 10.1038/nature12782 cited in the application -----	1-29
X	IVANA MEJDROVÁ ET AL: "Highly Selective Phosphatidylinositol 4-Kinase III&bgr; Inhibitors and Structural Insight into Their Mode of Action", JOURNAL OF MEDICINAL CHEMISTRY, vol. 58, no. 9, 14 May 2015 (2015-05-14), pages 3767-3793, XP055206384, ISSN: 0022-2623, DOI: 10.1021/acs.jmedchem.5b00499 compound KAI407 and KAI715 -----	1-7, 9-11, 13-29
X,P	LING DAWSON B. ET AL: "A Pyridyl-Furan Series Developed from the Open Global Health Library Block Red Blood Cell Invasion and Protein Trafficking in Plasmodium falciparum through Potential Inhibition of the Parasite's PI4KIIIB Enzyme", ACS INFECTIOUS DISEASES, vol. 9, no. 9, 28 August 2023 (2023-08-28) , pages 1695-1710, XP093089808, US ISSN: 2373-8227, DOI: 10.1021/acsinfecdis.3c00138 Retrieved from the Internet: URL:https://pubs.acs.org/doi/pdf/10.1021/acsinfecdis.3c00138> compounds WEHI-518 -----	1-29

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2023/071761

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2013124025 A1	29-08-2013	AR 090105 A1	22-10-2014
		AU 2013224420 A1	02-10-2014
		CA 2863717 A1	29-08-2013
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		JP 2015508085 A	16-03-2015
		TW 201336850 A	16-09-2013
		US 2015038527 A1	05-02-2015
		WO 2013124025 A1	29-08-2013