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(71) Applicant *(for all designated States except US)*: **GALAPAGOS NV** [BE/BE]; Industriepark Mechelen Noord, Generaal De Wittelaan L11/A3, B-2800 Mechelen (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MENET, Christel, Jeanne, Marie** [FR/BE]; Galapagos NV, Generaal De Wittelaan L11/A3, B-2800 Mechelen (BE). **BLANC, Javier** [ES/BE]; Galapagos NV, Generaal De Wittelaan L11/A3, B-2800 Mechelen (BE). **HODGES, Alastair, James** [GB/GB]; Biofocus DPI Ltd., Chesterford Research Park, Saffron Walden Essex CB10 1XL (GB). **BURLI, Roland, Werner** [CH/GB]; Biofocus DPI Ltd, Chesterford Research Park, Saffron Walden Essex CB10 1XL (GB). **BRECCIA, Perla** [IT/GB]; Biofocus DPI Ltd, Chesterford Research Park, Saffron Walden Essex CB10 1XL (GB). **BLACKABY, Wesley, Peter** [GB/GB]; Biofocus DPI Ltd., Chesterford Research Park, Saffron Walden Essex CB10 1XL (GB). **VAN ROMPAEY, Luc, Juliaan, Corina** [BE/BE]; Galapagos NV, Generaal De Wittelaan L11/A3, B-2800 Mechelen (BE). **FLETCHER, Stephen, Robert** [GB/FR]; Galapagos SASU, 102 Avenue Gaston Roussel, B-93230 Romainville (BE).

(74) Agent: **NICHOL, Maria**; Galapagos NV, Chesterford Research Park, Saffron Walden Essex CB10 1XL (GB).

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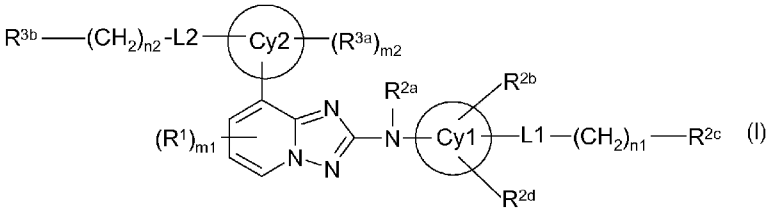
(54) **Title**: [1, 2, 4] TRIAZOLO [1, 5-A] PYRIDINES AS JAK INHIBITORS



(57) **Abstract**: Novel [1,2,4]triazolo[1,5-a]pyridine compounds are disclosed that have a Formula represented by the following: (I). The compounds may be prepared as pharmaceutical compositions, and may be used for the prevention and treatment of a variety of conditions in mammals including humans, including by way of non-limiting example, joint disease, inflammation, and others.

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[1 , 2 , 4] TRIAZOLO [1 , 5-A] PYRIDINES AS JAK INHIBITORS

FIELD OF THE INVENTION

[0001] The present invention relates to compounds that are inhibitors of JAK, a family of tyrosine kinases that are involved in the modulation of the degradation of cartilage, joint degeneration and diseases involving such degradation and/or inflammation. The present invention also provides methods for the production of these compounds, pharmaceutical compositions comprising these compounds, methods for the prevention and/or treatment of diseases involving cartilage degradation, bone and/or joint degradation, conditions involving inflammation or immune responses, endotoxin-driven disease states, cancer, and organ transplant rejection; and/ or methods for the prevention and/or treatment of diseases involving cartilage degradation, joint degradation and/or inflammation by administering a compound of the invention.

[0002] Janus kinases (JAKs) are cytoplasmic tyrosine kinases that transduce cytokine signaling from membrane receptors to STAT transcription factors. Four JAK family members are described, JAK1, JAK2, JAK3 and TYK2. Upon binding of the cytokine to its receptor, JAK family members auto- and/or transphosphorylate each other, followed by phosphorylation of STATs that then migrate to the nucleus to modulate transcription. JAK-STAT intracellular signal transduction serves the interferons, most interleukins, as well as a variety of cytokines and endocrine factors such as EPO, TPO, GH, OSM, LIF, CNTF, GM-CSF, PRL Vainchenker W. *et al.* (2008).

[0003] The combination of genetic models and small molecule JAK inhibitor research revealed the therapeutic potential of several JAKs. JAK3 is validated by mouse and human genetics as an immune-suppression target (O'Shea J. *et al.* (2004)). JAK3 inhibitors were successfully taken into clinical development, initially for organ transplant rejection but later also in other immuno-inflammatory indications such as rheumathoid arthritis (RA), psoriasis and Crohn's disease (http://clinicaltrials.gov/).

[0004] TYK2 is a potential target for immuno-inflammatory diseases, being validated by human genetics and mouse knock-out studies (Levy D. and Loomis C. (2007)).

[0005] JAK1 is a novel target in the immuno-inflammatory disease area. JAK1 heterodimerizes with the other JAKs to transduce cytokine-driven pro-inflammatory signaling. Therefore, inhibition of JAK1 and/or other JAKs is expected to be of therapeutic benefit for a range of inflammatory conditions as well as for other diseases driven by JAK-mediated signal transduction.

BACKGROUND OF THE INVENTION

[0006] Cartilage is an avascular tissue of which chondrocytes are the main cellular component. The chondrocytes in normal articular cartilage occupy approximately 5% of the tissue volume, while the extra-cellular matrix makes up the remaining 95% of the tissue. The chondrocytes secrete the components of the matrix, mainly proteoglycans and collagens, which in turn supply the chondrocytes with an environment suitable for their survival under mechanical stress. In cartilage, collagen type II, together

with the protein collagen type IX, is arranged in solid fibril-like structures which provide cartilage with great mechanical strength. The proteoglycans can absorb water and are responsible for the resilient and shock absorbing properties of the cartilage.

[0007] One of the functional roles of cartilage in the joint is to allow bones to articulate on each other smoothly. Loss of articular cartilage, therefore, causes the bones to rub against each other leading to pain and loss of mobility. The degradation of cartilage can have various causes. In inflammatory arthritides, as rheumatoid arthritis for example, cartilage degradation is caused by the secretion of proteases (e.g. collagenases) by inflamed tissues (the inflamed synovium for example). Cartilage degradation can also be the result of an injury of the cartilage, due to an accident or surgery, or exaggerated loading or 'wear and tear'. The ability of cartilage tissue to regenerate after such insults is limited. Chondrocytes in injured cartilage often display reduced cartilage synthesizing (anabolic) activity and / or increased cartilage degrading (catabolic) activity.

[0008] The degeneration of cartilage is the hallmark of various diseases, among which rheumatoid arthritis and osteoarthritis are the most prominent. Rheumatoid arthritis (RA) is a chronic joint degenerative disease, characterized by inflammation and destruction of the joint structures. When the disease is unchecked, it leads to substantial disability and pain due to loss of joint functionality and even premature death. The aim of an RA therapy, therefore, is not only to slow down the disease but to attain remission in order to stop the joint destruction. Besides the severity of the disease outcome, the high prevalence of RA (~ 0.8% of the adults are affected worldwide) means a high socio-economic impact. (For reviews on RA, we refer to Smolen and Steiner (2003); Lee and Weinblatt (2001); Choy and Panayi (2001); O'Dell (2004) and Firestein (2003)).

[0009] Osteoarthritis (also referred to as OA, or wear-and-tear arthritis) is the most common form of arthritis and is characterized by loss of articular cartilage, often associated with hypertrophy of the bone and pain. The disease mainly affects hands and weight-bearing joints such as knees, hips and spines. This process thins the cartilage. When the surface area has disappeared due to the thinning, a grade I osteoarthritis is reached; when the tangential surface area has disappeared, grade II osteoarthritis is reached. There are further levels of degeneration and destruction, which affect the deep and the calcified cartilage layers that border with the subchondral bone. For an extensive review on osteoarthritis, we refer to Wieland *et al.*, 2005.

[0010] The clinical manifestations of the development of the osteoarthritis condition are: increased volume of the joint, pain, crepitation and functional disability that lead to pain and reduced mobility of the joints. When disease further develops, pain at rest emerges. If the condition persists without correction and/or therapy, the joint is destroyed leading to disability. Replacement surgery with total prosthesis is then required.

[0011] Therapeutic methods for the correction of the articular cartilage lesions that appear during the osteoarthritic disease have been developed, but so far none of them have been able to mediate the regeneration of articular cartilage *in situ* and *in vivo*.

[0012] Osteoarthritis is difficult to treat. At present, no cure is available and treatment focuses on relieving pain and preventing the affected joint from becoming deformed. Common treatments include the use of non-steroidal anti-inflammatory drugs (NSAIDs). Although dietary supplements such as chondroitin and glucosamine sulphate have been advocated as safe and effective options for the treatment of osteoarthritis, a recent clinical trial revealed that both treatments did not reduce pain associated to osteoarthritis. (Clegg *et al.*, 2006). Taken together, no disease modifying osteoarthritic drugs are available.

[0013] In severe cases, joint replacement may be necessary. This is especially true for hips and knees. If a joint is extremely painful and cannot be replaced, it may be fused. This procedure stops the pain, but results in the permanent loss of joint function, making walking and bending difficult.

[0014] Another possible treatment is the transplantation of cultured autologous chondrocytes. Here, chondral cellular material is taken from the patient, sent to a laboratory where it is expanded. The material is then implanted in the damaged tissues to cover the tissue's defects.

[0015] Another treatment includes the intra-articular instillation of Hylan G-F 20 (e.g. Synvisc®, Hyalgan®, Artz®), a substance that improves temporarily the rheology of the synovial fluid, producing an almost immediate sensation of free movement and a marked reduction of pain.

[0016] Other reported methods include application of tendinous, periosteal, fascial, muscular or perichondral grafts; implantation of fibrin or cultured chondrocytes; implantation of synthetic matrices, such as collagen, carbon fiber; administration of electromagnetic fields. All of these have reported minimal and incomplete effects, resulting in a poor quality tissue that can neither support the weighted load nor allow the restoration of an articular function with normal movement.

[0017] Stimulation of the anabolic processes, blocking catabolic processes, or a combination of these two, may result in stabilization of the cartilage, and perhaps even reversion of the damage, and therefore prevent further progression of the disease. Various triggers may stimulate anabolic stimulation of chondrocytes. Insulin-like growth factor-I (IGF-I) is the predominant anabolic growth factor in synovial fluid and stimulates the synthesis of both proteoglycans and collagen. It has also been shown that members of the bone morphogenetic protein (BMP) family, notably BMP2, BMP4, BMP6, and BMP7, and members of the human transforming growth factor-ß (TGF-ß) family can induce chondrocyte anabolic stimulation (Chubinskaya and Kuettner, 2003). A compound has recently been identified that induces anabolic stimulation of chondrocytes (US 6,500,854; EP 1 391 211). However, most of these compounds show severe side effects and, consequently, there is a strong need for compounds that stimulate chondrocyte differentiation without these side effects.

[0018] Vandeghinste *et al.* (WO 2005/124342) discovered JAK1 as a target whose inhibition might have therapeutic relevance for several diseases including OA. JAK1 belongs to the Janus kinase (JAK) family of cytoplasmic tyrosine kinases, involved in cytokine receptor-mediated intracellular signal transduction. The JAK family consists of 4 members: JAK1, JAK2, JAK3 and TYK2. JAKs are recruited to cytokine receptors, upon binding of the cytokine, followed by heterodimerization of the cytokine receptor and a shared receptor subunit (common gamma-c chain, gp130). JAKs are then activated by

auto- and/or transphosphorylation by another JAK, resulting in phosphorylation of the receptors and recruitment and phosphorylation of members of the signal transducer and activator of transcription (STATs). Phosphorylated STATs dimerize and translocate to the nucleus where they bind to enhancer regions of cytokine-responsive genes. Knockout of the JAK1 gene in mice demonstrated that JAK1 plays essential and nonredundant roles during development: JAK1-/- mice died within 24h after birth and lymphocyte development was severely impaired. Moreover, JAK1 -/- cells were not, or less, reactive to cytokines that use class II cytokine receptors, cytokine receptors that use the gamma-c subunit for signaling and the family of cytokine receptors that use the gp130 subunit for signaling (Rodig *et al.,* 1998).

[0019] Various groups have implicated JAK-STAT signaling in chondrocyte biology. Li *et al.* (2001) showed that Oncostatin M induces MMP and TIMP3 gene expression in primary chondrocytes by activation of JAK/STAT and MAPK signaling pathways. Osaki *et al.* (2003) showed that interferon-gamma mediated inhibition of collagen II in chondrocytes involves JAK-STAT signaling. IL1-beta induces cartilage catabolism by reducing the expression of matrix components, and by inducing the expression of collagenases and inducible nitric oxide synthase (NOS2), which mediates the production of nitric oxide (NO). Otero *et al.*, (2005) showed that leptin and IL1-beta synergistically induced NO production or expression of NOS2 mRNA in chondrocytes, and that that was blocked by a JAK inhibitor. Legendre *et al.* (2003) showed that IL6/IL6Receptor induced downregulation of cartilage-specific matrix genes collagen II, aggrecan core and link protein in bovine articular chondrocytes, and that this was mediated by JAK/STAT signaling. Therefore, these observations suggest a role for JAK kinase activity in cartilage homeostasis and therapeutic opportunities for JAK kinase inhibitors.

[0020] JAK family members have been implicated in additional conditions including myeloproliferative disorders (O'Sullivan *et al*, 2007, Mol Immunol. 44(10):2497-506), where mutations in JAK2 have been identified. This indicates that inhibitors of JAK in particular JAK2 may also be of use in the treatment of myeloproliferative disorders. Additionally, the JAK family, in particular JAK1, JAK2 and JAK3, has been linked to cancers, in particular leukaemias *e.g.* acute myeloid leukaemia (O'Sullivan *et al*, 2007, Mol Immunol. 44(10):2497-506; Xiang *et al.*, 2008, "Identification of somatic *JAK1* mutations in patients with acute myeloid leukemia" Blood First Edition Paper, prepublished online December 26, 2007; DOI 10.1182/blood-2007-05-090308) and acute lymphoblastic leukemia (Mullighan *et al*, 2009) or solid tumours *e.g.* uterine leiomyosarcoma (Constantinescu *et al.*, 2007, Trends in Biochemical Sciences 33(3): 122-131), prostate cancer (Tam *et al.*, 2007, British Journal of Cancer, 97, 378 – 383) These results indicate that inhibitors of JAK, in particular of JAK1 and/or JAK2, may also have utility in the treatment of cancers (leukaemias and solid tumours e.g. uterine leiomyosarcoma, prostate cancer).

[0021] In addition, Castleman's disease, multiple myeloma, mesangial proliferative glomerulonephritis, psoriasis, and Kaposi's sarcoma are likely due to hypersecretion of the cytokine IL-6, whose biological effects are mediated by intracellular JAK-STAT signaling (Tetsuji Naka, Norihiro Nishimoto and Tadamitsu Kishimoto, Arthritis Res 2002, 4 (suppl 3):S233-S242). This result shows that inhibitor of JAK, may also find utility in the treatment of said diseases.

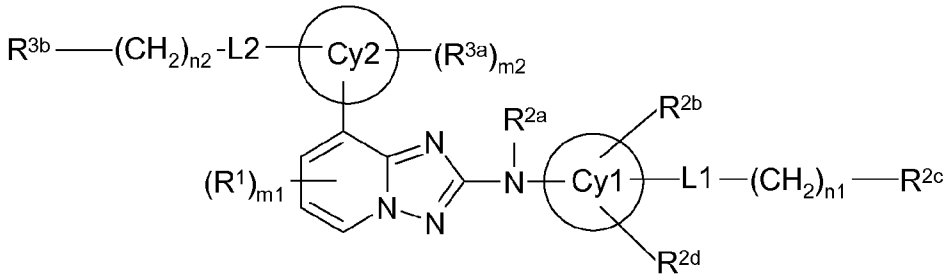
[0022] A link with autoimmune diseases has been established for JAK3 and Tyk2. Mutations in JAK3 but also in the upstream signaling components gamma-c receptor chain and IL7 receptor account in aggregate for ~70% of cases of human severe combined immunodeficiency ('OShea *et al.*, 2004). Note that JAK1 cooperates with JAK3 in transducing signals from the gamma-c receptor chain. Tyk2 polymorphisms are seen in systemic lupus erythematosus (SLE) (O'Sullivan *et al*, 2007, Mol Immunol. 44(10):2497-506). Hence, targeting the JAK family may provide a therapeutic opportunity in the immuno-inflammation area.

[0023] The current therapies are not satisfactory and therefore there remains a need to identify further compounds that may be of use in the treatment of diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). The present invention therefore provides compounds, methods for their manufacture and a pharmaceutical comprising a compound of the invention together with a suitable pharmaceutical carrier. The present invention also provides for the use of a compound of the invention in the preparation of a medicament for the treatment of degenerative joint diseases.

SUMMARY OF THE INVENTION

[0024] The present invention is based on the discovery that inhibitors of JAK are useful for the treatment of diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). The present invention also provides methods for the production of these compounds, pharmaceutical compositions comprising these compounds and methods for treating diseases involving cartilage degradation, joint degradation and/or inflammation by administering a compound of the invention.

[0025] Accordingly, in a first aspect of the invention, substituted bicycloheteroaryl compounds are disclosed according to Formula (I):



I

wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$, -$N(R^{4a})$-, -$CON(R^{4a})$-, -$SO_2N(R^{4a})$-, -$N(R^{4a})CO$-, or -$N(R^{4a})SO_2$-;

each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, substituted or unsubstituted amino, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, substituted or unsubstituted amino, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted –O-aryl, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, substituted or unsubstituted amino, substituted or unsubstituted amido, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, C_1-C_6alkyl, substituted C_1-C_6alkyl, C_3-C_7 cycloalkyl, or substituted C_3-C_7 cycloalkyl;

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts, or solvates thereof or the solvates of the pharmaceutically acceptable salts.

[0026] In a further aspect of the invention, 1,2,4-triazolo[1,5-a]pyridine compounds are disclosed that are capable of capable of modulating the activity of JAK *in vivo,* having a Formula (I) above.

[0027] In a further aspect, the present invention provides pharmaceutical compositions comprising a compound of the invention, and a pharmaceutical carrier, excipient or diluent. In this aspect of the invention, the pharmaceutical composition can comprise one or more of the compounds described herein. Moreover, the compounds of the invention useful in the pharmaceutical compositions and treatment methods disclosed herein, are all pharmaceutically acceptable as prepared and used.

[0028] In a further aspect of the invention, this invention provides a method of treating a mammal susceptible to or afflicted with a condition from among those listed herein, and particularly, such condition as may be associated with aberrant JAK activity, for example diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection), which method comprises administering a therapeutically effective amount of a compound of the invention or a pharmaceutical composition thereof. Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). In a particular embodiment the present invention provides a method for treating conditions selected from inflammation, such as rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), inflammatory bowel diseases (e.g. Crohn's disease, colitis), endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), and organ transplant rejection; and cartilage, bone and/or joint degradation or degeneration, such as osteoarthritis, which method comprises administering an effective amount of one or more of the pharmaceutical compositions or compounds herein described.

[0029] In a further aspect, the present invention provides a method of treating a mammal susceptible to or afflicted with proliferative disorders, in particular cancer, (e.g. solid tumours), leukaemias, multiple myeloma or psoriasis.

[0030] In a further aspect, the present invention provides a compound of the invention for use in the treatment or prevention of a condition selected from those listed herein, particularly such conditions as may be associated with aberrant JAK activity such as diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). In a specific embodiment, the condition is selected from inflammation, such as rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), inflammatory bowel diseases (e.g. Crohn's disease, colitis), endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), and organ transplant rejection; and cartilage, bone and/or joint degradation or degeneration, such as osteoarthritis.

[0031] In a further aspect, the present invention provides a compound of the invention for use in the treatment or prevention of proliferative disorders, in particular cancer, (e.g. solid tumours), leukaemias, multiple myeloma or psoriasis.

[0032] In yet another method of treatment aspect, this invention provides a method for treating a mammal susceptible to or afflicted with a condition that is causally related to abnormal JAK activity as described herein, which method comprises administering an effective condition-treating or condition-preventing amount of one or more of the pharmaceutical compositions or compounds herein described.

[0033] In a further aspect, the present invention provides a compound of the invention for use in the treatment or prevention of a condition that is causally related to abnormal JAK activity.

[0034] In additional aspects, this invention provides methods for synthesizing the compounds of the invention, with representative synthetic protocols and pathways disclosed later on herein.

[0035] Accordingly, it is a principal object of this invention to provide a novel series of compounds, which can modify the activity of JAK and thus avert or treat any maladies that may be causally related thereto.

[0036] It is further an object of this invention to provide a series of compounds that can treat or alleviate maladies or symptoms of same, such as cartilage and/or bone degradation and related inflammation, and joint diseases, that may be causally related to the activity of JAK.

[0037] A still further object of this invention is to provide pharmaceutical compositions that may be used in the treatment or prevention of a variety of disease states, including the diseases associated with JAK activity such as diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). In a specific embodiment the condition is selected from inflammation, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), and organ transplant rejection; and cartilage, bone and/or joint degradation or degeneration, such as osteoarthritis or cancers (e.g. solid tumours or leukaemias).

[0038] Other objects and advantages will become apparent to those skilled in the art from a consideration of the ensuing detailed description.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0039] The following terms are intended to have the meanings presented therewith below and are useful in understanding the description and intended scope of the present invention.

[0040] When describing the invention, which may include compounds, pharmaceutical compositions containing such compounds and methods of using such compounds and compositions, the following terms, if present, have the following meanings unless otherwise indicated. It should also be understood that when described herein any of the moieties defined forth below may be substituted with a variety of substituents, and that the respective definitions are intended to include such substituted moieties within their scope as set out below. Unless otherwise stated, the term "substituted" is to be defined as set out below. It should be further understood that the terms "groups" and "radicals" can be considered interchangeable when used herein.

[0041] The articles "a" and "an" may be used herein to refer to one or to more than one (i.e. at least one) of the grammatical objects of the article. By way of example "an analogue" means one analogue or more than one analogue.

[0042] 'Acyl' refers to a radical $-C(O)R^{20}$, where R^{20} is hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylmethyl, 4-10 membered heterocycloalkyl, aryl, arylalkyl, 5-10 membered

heteroaryl or heteroarylalkyl as defined herein. Representative examples include, but are not limited to, formyl, acetyl, cyclohexylcarbonyl, cyclohexylmethylcarbonyl, benzoyl and benzylcarbonyl. Exemplary 'acyl' groups are –C(O)H, –C(O)-C_1-C_8 alkyl, –C(O)-$(CH_2)_t$(C_6-C_{10} aryl), –C(O)-$(CH_2)_t$(5-10 membered heteroaryl), –C(O)-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and –C(O)-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4.

[0043] 'Substituted Acyl' refers to a radical -C(O)R^{21}, wherein R^{21} is independently

- C_1-C_8 alkyl, substituted with halo or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, arylalkyl, 5-10 membered heteroaryl or heteroarylalkyl, each of which is substituted with unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0044] 'Acylamino' refers to a radical -NR^{22}C(O)R^{23}, where R^{22} is hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, arylalkyl, 5-10 memberd heteroaryl or heteroarylalkyl and R^{23} is hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, arylalkyl, 5-10 membered heteroaryl or heteroarylalkyl, as defined herein. Exemplary 'acylamino' include, but are not limited to, formylamino, acetylamino, cyclohexylcarbonylamino, cyclohexylmethyl-carbonylamino, benzoylamino and benzylcarbonylamino. Exemplary 'acylamino' groups are –$NR^{21'}$C(O)-C_1-C_8 alkyl, –$NR^{21'}$C(O)-$(CH_2)_t$(C_6-C_{10} aryl), –$NR^{21'}$C(O)-$(CH_2)_t$(5-10 membered heteroaryl), –$NR^{21'}$C(O)-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and –$NR^{21'}$C(O)-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4, each $R^{21'}$ independently represents H or C_1-C_8 alkyl.

[0045] 'Substituted Acylamino' refers to a radical -NR^{24}C(O)R^{25}, wherein:

R^{24} is independently

- H, C_1-C_8 alkyl, substituted with halo or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, arylalkyl, 5-10 membered heteroaryl or heteroarylalkyl, each of which is substituted with unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy; and

R^{25} is independently

- H, C_1-C_8 alkyl, substituted with halo or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, arylalkyl, 5-10 membered heteroaryl or heteroarylalkyl, each of which is substituted with unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxyl;

provided at least one of R^{24} and R^{25} is other than H.

[0046] 'Alkoxy' refers to the group –OR^{26} where R^{26} is C_1-C_8 alkyl. Particular alkoxy groups are methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, tert-butoxy, sec-butoxy, n-pentoxy, n-hexoxy, and 1,2-dimethylbutoxy. Particular alkoxy groups are lower alkoxy, i.e. with between 1 and 6 carbon atoms. Further particular alkoxy groups have between 1 and 4 carbon atoms.

[0047] 'Substituted alkoxy' refers to an alkoxy group substituted with one or more of those groups recited in the definition of "substituted" herein, and particularly refers to an alkoxy group having 1 or more substituents, for instance from 1 to 5 substituents, and particularly from 1 to 3 substituents, in particular 1 substituent, selected from the group consisting of amino, substituted amino, C_6-C_{10} aryl, -O-aryl, carboxyl, cyano, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, halogen, 5-10 membered heteroaryl, hydroxyl, nitro, thioalkoxy, thio-O-aryl, thiol, alkyl-S(O)-, aryl–S(O)-, alkyl–$S(O)_2$- and aryl-$S(O)_2$-. Exemplary 'substituted alkoxy' groups are –O-$(CH_2)_t$(C_6-C_{10} aryl), –O-$(CH_2)_t$(5-10 membered heteroaryl), –O-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and –O-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. Particular exemplary 'substituted alkoxy' groups are OCF_3, OCH_2CF_3, OCH_2Ph, OCH_2-cyclopropyl, OCH_2CH_2OH, $OCH_2CH_2NMe_2$.

[0048] 'Alkoxycarbonyl' refers to a radical -C(O)-OR^{27} where R^{27} represents an C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, 4-10 membered heterocycloalkylalkyl, aralkyl, or 5-10 membered heteroarylalkyl as defined herein. Exemplary "alkoxycarbonyl" groups are C(O)O-C_1-C_8 alkyl, –C(O)O-$(CH_2)_t$(C_6-C_{10} aryl), –C(O)O-$(CH_2)_t$(5-10 membered heteroaryl), –C(O)O-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and –C(O)O-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 1 to 4.

[0049] 'Substituted Alkoxycarbonyl' refers to a radical -C(O)-OR^{28} where R^{28} represents:

- C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} cycloalkylalkyl, or 4-10 membered heterocycloalkylalkyl, each of which is substituted with halo, substituted or unsubstituted amino, or hydroxy; or
- C_6-C_{10} aralkyl, or 5-10 membered heteroarylalkyl, each of which is substituted with unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxyl.

[0050] 'Alkyl' means straight or branched aliphatic hydrocarbon having 1 to 20 carbon atoms. Particular alkyl has 1 to 12 carbon atoms. More particular is lower alkyl which has 1 to 6 carbon atoms. A further particular group has 1 to 4 carbon atoms. Exemplary straight chained groups include methyl, ethyl n-propyl, and n-butyl. Branched means that one or more lower alkyl groups such as methyl, ethyl, propyl or butyl is attached to a linear alkyl chain, exemplary branched chain groups include isopropyl, iso-butyl, t-butyl and isoamyl.

[0051] 'Substituted alkyl' refers to an alkyl group as defined above substituted with one or more of those groups recited in the definition of "substituted" herein, and particularly refers to an alkyl group having 1 or more substituents, for instance from 1 to 5 substituents, and particularly from 1 to 3 substituents, in particular 1 substituent, selected from the group consisting of acyl, acylamino, acyloxy (-O-acyl or –$OC(O)R^{20}$), alkoxy, alkoxycarbonyl, alkoxycarbonylamino (-NR''-alkoxycarbonyl or -NH-C(O)-OR^{27}), amino, substituted amino, aminocarbonyl (carbamoyl or amido or –C(O)-NR''_2), aminocarbonylamino (-NR''-C(O)-NR''_2), aminocarbonyloxy (-O-C(O)-NR''_2), aminosulfonyl,

sulfonylamino, aryl, -O-aryl, azido, carboxyl, cyano, cycloalkyl, halogen, hydroxy, heteroaryl, nitro, thiol, -S-alkyl, –S-aryl, -S(O)-alkyl,–S(O)-aryl, $–S(O)_2$-alkyl, and $-S(O)_2$-aryl. In a particular embodiment 'substituted alkyl' refers to a C_1-C_8 alkyl group substituted with halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR'''SO_2R''$, $-SO_2NR''R'''$, $-C(O)R''$, $-C(O)OR''$, $-OC(O)R''$, $-NR'''C(O)R''$, $-C(O)NR''R'''$, $-NR''R'''$, or $-(CR'''R'''')_mOR'''$; wherein each R'' is independently selected from H, C_1-C_8 alkyl, $-(CH_2)_t(C_6$-C_{10} aryl), $-(CH_2)_t$(5-10 membered heteroaryl), $-(CH_2)_t(C_3$-C_{10} cycloalkyl), and $-(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. Each of R''' and R'''' independently represents H or C_1-C_8 alkyl.

[0052] 'Amino' refers to the radical $-NH_2$.

[0053] 'Substituted amino' refers to an amino group substituted with one or more of those groups recited in the definition of 'substituted' herein, and particularly refers to the group $-N(R^{33})_2$ where each R^{33} is independently selected from:

- hydrogen, C_1-C_8 alkyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, or C_3-C_{10} cycloalkyl; or
- C_1-C_8 alkyl, substituted with halo or hydroxy; or
- $-(CH_2)_t(C_6$-C_{10} aryl), $-(CH_2)_t$(5-10 membered heteroaryl), $-(CH_2)_t(C_3$-C_{10} cycloalkyl) or $-(CH_2)_t$(4-10 membered heterocycloalkyl) wherein t is an integer between 0 and 8, each of which is substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy; or
- both R^{33} groups are joined to form an alkylene group.

When both R^{33} groups are hydrogen, $-N(R^{33})_2$ is an amino group. Exemplary 'substituted amino' groups are $–NR^{33'}$-C_1-C_8 alkyl, $–NR^{33'}$-$(CH_2)_t(C_6$-C_{10} aryl), $–NR^{33'}$-$(CH_2)_t$(5-10 membered heteroaryl), $–NR^{33'}$-$(CH_2)_t(C_3$-C_{10} cycloalkyl), and $–NR^{33'}$-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4, each $R^{33'}$ independently represents H or C_1-C_8 alkyl; and any alkyl groups present, may themselves be substituted by halo, substituted or unsubstituted amino, or hydroxy; and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. For the avoidance of doubt the term "substituted amino" includes the groups alkylamino, substituted alkylamino, dialkylamino and substituted dialkylamino as defined below.

[0054] 'Alkylamino' refers to the group $–NHR^{34}$, wherein R^{34} is C_1-C_8 alkyl.

'Substituted Alkylamino' refers to the group $–NHR^{35}$, wherein R^{35} is C_1-C_8 alkyl; and the alkyl group is substituted with halo, substituted or unsubstituted amino, hydroxy, C_3-C_{10} cycloalkyl, 4-10 membered

heterocycloalkyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, aralkyl or heteroaralkyl; and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0055] 'Dialkylamino' refers to the group $-NR^{42}R^{43}$, wherein each of R^{42} and R^{43} are independently selected from C_1-C_8 alkyl.

[0056] 'Substituted Dialkylamino' refers to the group $-NR^{44}R^{45}$, wherein each of R^{44} and R^{45} are independently selected from C_1-C_8 alkyl; and the alkyl group is independently substituted with halo, hydroxy, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, aralkyl or heteroaralkyl; and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-$_4$ haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0057] "Aminosulfonyl" or "Sulfonamide" refers to the radical $-S(O_2)NH_2$.

[0058] "Substituted aminosulfonyl" or "substituted sulfonamide" refers to a radical such as $-S(O_2)N(R^{48})_2$ wherein each R^{48} is independently selected from:

- H, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy;

provided that at least one R^{48} is other than H.

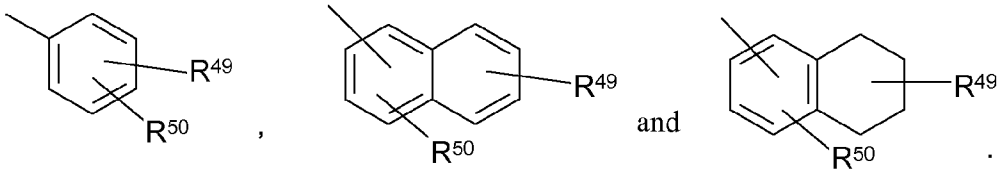
[0059] Exemplary 'substituted aminosulfonyl' or 'substituted sulfonamide' groups are $-S(O_2)N(R^{48'})$-C_1-C_8 alkyl, $-S(O_2)N(R^{48'})$-$(CH_2)_t$(C_6-C_{10} aryl), $-S(O_2)N(R^{48'})$-$(CH_2)_t$(5-10 membered heteroaryl), $-S(O_2)N(R^{48'})$-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and $-S(O_2)N(R^{48'})$-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4; each $R^{48'}$ independently represents H or C_1-C_8 alkyl; and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0060] 'Aryl' refers to a monovalent aromatic hydrocarbon group derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. In particular aryl refers to an aromatic ring structure, mono-cyclic or poly-cyclic that includes from 5 to 12 ring members, more usually 6 to 10. Where the aryl group is a monocyclic ring system it preferentially contains 6 carbon atoms. Typical aryl groups include, but are not limited to, groups derived from aceanthrylene, acenaphthylene, acephenanthrylene, anthracene, azulene, benzene, chrysene, coronene, fluoranthene, fluorene, hexacene, hexaphene, hexalene, as-indacene, s-indacene, indane, indene, naphthalene, octacene, octaphene, octalene, ovalene, penta-2,4-diene, pentacene, pentalene, pentaphene, perylene, phenalene, phenanthrene,

picene, pleiadene, pyrene, pyranthrene, rubicene, triphenylene and trinaphthalene. Particularly aryl groups include phenyl, naphthyl, indenyl, and tetrahydronaphthyl.

[0061] 'Substituted Aryl' refers to an aryl group substituted with one or more of those groups recited in the definition of 'substituted' herein, and particularly refers to an aryl group that may optionally be substituted with 1 or more substituents, for instance from 1 to 5 substituents, particularly 1 to 3 substituents, in particular 1 substituent. Particularly, 'Substituted Aryl' refers to an aryl group substituted with one or more of groups selected from halo, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 haloalkoxy, cyano, hydroxy, C_1-C_8 alkoxy, and amino.

[0062] Examples of representative substituted aryls include the following



and .

[0063] In these formulae one of R^{49} and R^{50} may be hydrogen and at least one of R^{49} and R^{50} is each independently selected from C_1-C_8 alkyl, 4-10 membered heterocycloalkyl, C_1-C_8 alkoxy, hetero-O-aryl, alkylamino, $NR^{51}COR^{52}$, $NR^{51}SOR^{52}$ $NR^{51}SO_2R^{52}$, COOalkyl, COOaryl, $CONR^{51}R^{52}$, $CONR^{51}OR^{52}$, $NR^{51}R^{52}$, $SO_2NR^{51}R^{52}$, S-alkyl, SOalkyl, SO_2alkyl, Saryl, SOaryl, SO_2aryl; or R^{49} and R^{50} may be joined to form a cyclic ring (saturated or unsaturated) from 5 to 8 atoms, optionally containing one or more heteroatoms selected from the group N, O or S. R^{51}, and R^{52} are independently hydrogen, C_1-C_8 alkyl, C_1-C_4 haloalkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, substituted aryl, 5-10 membered heteroaryl.

[0064] 'Arylalkyloxy' refers to an -O-alkylaryl radical where alkylaryl is as defined herein.

[0065] 'Substituted Arylalkyloxy' refers to an -O-alkylaryl radical where alkylaryl is as defined herein; and any aryl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, cyano, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-$_4$ haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0066] 'Azido' refers to the radical $-N_3$.

[0067] 'amido' refers to the radical $-C(O)NH_2$.

[0068] 'Substituted amido' refers to the radical $-C(O)N(R^{53})_2$ wherein each R^{53} is independently

- H, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, each of which is substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy;

provided that at least one R^{53} is other than H.

Exemplary 'Substituted Amido ' groups are $-C(O)\ NR^{53'}-C_1-C_8$ alkyl, $-C(O)NR^{53'}-(CH_2)_t(C_6-C_{10}$ aryl), $-C(O)N^{53'}-(CH_2)_t$(5-10 membered heteroaryl), $-C(O)NR^{53'}-(CH_2)_t(C_3-C_{10}$ cycloalkyl), and $-C(O)NR^{53'}-(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4, each $R^{53'}$ independently represents H or C_1-C_8 alkyl and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0069] 'Carboxy' refers to the radical -C(O)OH.

[0070] 'Cycloalkyl' refers to cyclic non-aromatic hydrocarbyl groups having from 3 to 10 carbon atoms. Such cycloalkyl groups include, by way of example, single ring structures such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl.

[0071] 'Substituted cycloalkyl' refers to a cycloalkyl group as defined above substituted with one or more of those groups recited in the definition of 'substituted' herein, and particularly refers to a cycloalkyl group having 1 or more substituents, for instance from 1 to 5 substituents, and particularly from 1 to 3 substituents, in particular 1 substituent.

[0072] 'Cyano' refers to the radical -CN.

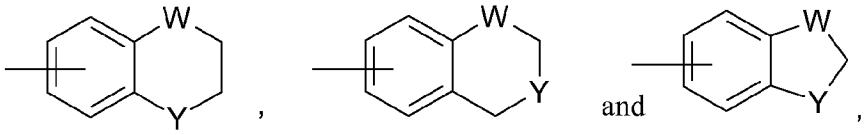
[0073] 'Halo' or 'halogen' refers to fluoro (F), chloro (Cl), bromo (Br) and iodo (I). Particular halo groups are either fluoro or chloro.

[0074] 'Hetero' when used to describe a compound or a group present on a compound means that one or more carbon atoms in the compound or group have been replaced by a nitrogen, oxygen, or sulfur heteroatom. Hetero may be applied to any of the hydrocarbyl groups described above such as alkyl, e.g. heteroalkyl, cycloalkyl, e.g. heterocycloalkyl, aryl, e.g. heteroaryl, cycloalkenyl, e.g. cycloheteroalkenyl, and the like having from 1 to 5, and particularly from 1 to 3 heteroatoms.

[0075] 'Heteroaryl' means an aromatic ring structure, mono-cyclic or polycyclic, that includes one or more heteroatoms and 5 to 12 ring members, more usually 5 to 10 ring members. The heteroaryl group can be, for example, a five membered or six membered monocyclic ring or a bicyclic structure formed from fused five and six membered rings or two fused six membered rings or, by way of a further example, two fused five membered rings. Each ring may contain up to four heteroatoms typically selected from nitrogen, sulphur and oxygen. Typically the heteroaryl ring will contain up to 4 heteroatoms, more typically up to 3 heteroatoms, more usually up to 2, for example a single heteroatom. In one embodiment, the heteroaryl ring contains at least one ring nitrogen atom. The nitrogen atoms in the heteroaryl rings can be basic, as in the case of an imidazole or pyridine, or essentially non-basic as in the case of an indole or pyrrole nitrogen. In general the number of basic nitrogen atoms present in the heteroaryl group, including any amino group substituents of the ring, will be less than five. Examples of five membered monocyclic heteroaryl groups include but are not limited to pyrrole, furan, thiophene, imidazole, furazan, oxazole, oxadiazole, oxatriazole, isoxazole, thiazole, isothiazole, pyrazole, triazole and tetrazole groups. Examples of six membered monocyclic heteroaryl groups include but are not limited to pyridine, pyrazine, pyridazine, pyrimidine and triazine. Particular examples of bicyclic heteroaryl groups containing a five membered ring fused to another five membered ring include but are not limited to imidazothiazole and

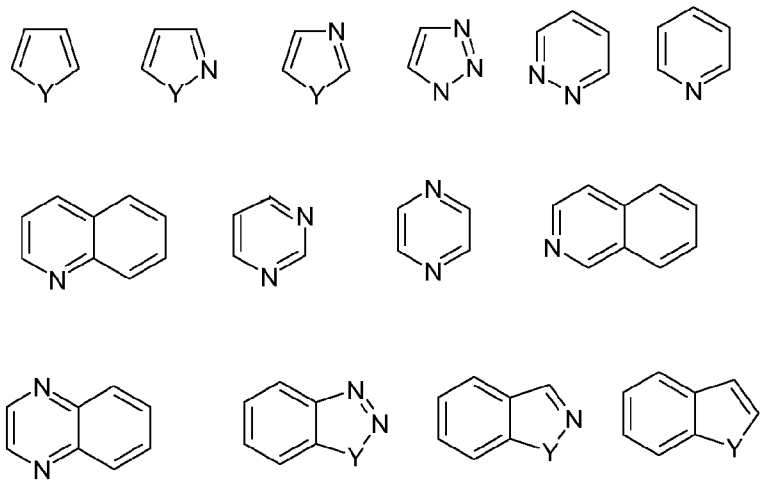
imidazoimidazole. Particular examples of bicyclic heteroaryl groups containing a six membered ring fused to a five membered ring include but are not limited to benzfuran, benzthiophene, benzimidazole, benzoxazole, isobenzoxazole, benzisoxazole, benzthiazole, benzisothiazole, isobenzofuran, indole, isoindole, isoindolone, indolizine, indoline, isoindoline, purine (e.g., adenine, guanine), indazole, pyrazolopyrimidine, triazolopyrimidine, benzodioxole and pyrazolopyridine groups. Particular examples of bicyclic heteroaryl groups containing two fused six membered rings include but are not limited to quinoline, isoquinoline, chroman, thiochroman, chromene, isochromene, chroman, isochroman, benzodioxan, quinolizine, benzoxazine, benzodiazine, pyridopyridine, quinoxaline, quinazoline, cinnoline, phthalazine, naphthyridine and pteridine groups. Particular heteroaryl groups are those derived from thiophene, pyrrole, benzothiophene, benzofuran, indole, pyridine, quinoline, imidazole, oxazole and pyrazine.

[0076] Examples of representative aryl having hetero atoms containing substitution include the following:



wherein each W is selected from $C(R^{54})_2$, NR^{54}, O and S; and each Y is selected from carbonyl, NR^{54}, O and S; and R^{54} is independently hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl.

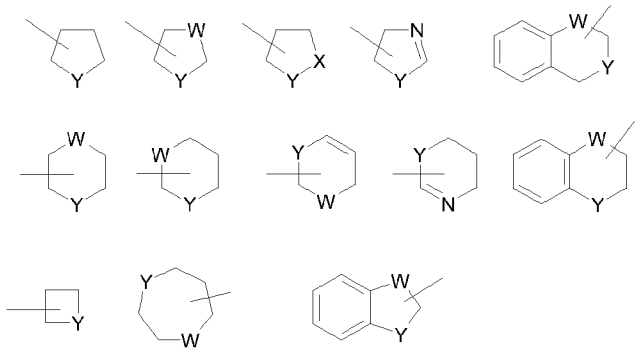
[0077] Examples of representative heteroaryls include the following:



wherein each Y is selected from carbonyl, N, NR^{55}, O and S; and R^{55} is independently hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl.

[0078] As used herein, the term 'heterocycloalkyl' refers to a 4-10 membered, stable heterocyclic non-aromatic ring and/or including rings containing one or more heteroatoms independently selected from N, O and S, fused thereto. A fused heterocyclic ring system may include carbocyclic rings and need only include one heterocyclic ring. Examples of heterocyclic rings include, but are not limited to, morpholine, piperidine (e.g. 1-piperidinyl, 2-piperidinyl, 3-piperidinyl and 4-piperidinyl), pyrrolidine (e.g. 1-pyrrolidinyl, 2-pyrrolidinyl and 3-pyrrolidinyl), pyrrolidone, pyran (2H-pyran or 4H-pyran),

dihydrothiophene, dihydropyran, dihydrofuran, dihydrothiazole, tetrahydrofuran, tetrahydrothiophene, dioxane, tetrahydropyran (e.g. 4-tetrahydro pyranyl), imidazoline, imidazolidinone, oxazoline, thiazoline, 2-pyrazoline, pyrazolidine, piperazine, and N-alkyl piperazines such as N-methyl piperazine. Further examples include thiomorpholine and its S-oxide and S,S-dioxide (particularly thiomorpholine). Still further examples include azetidine, piperidone, piperazone, and N-alkyl piperidines such as N-methyl piperidine. Particular examples of heterocycloalkyl groups are shown in the following illustrative examples:



wherein each W is selected from CR^{56}, $C(R^{56})_2$, NR^{56}, O and S; and each Y is selected from NR^{56}, O and S; and R^{56} is independently hydrogen, C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, These heterocycloalkyl rings may be optionally substituted with one or more groups selected from the group consisting of acyl, acylamino, acyloxy (-O-acyl or $-OC(O)R^{20}$), alkoxy, alkoxycarbonyl, alkoxycarbonylamino (-NR"-alkoxycarbonyl or $-NH-C(O)-OR^{27}$), amino, substituted amino, aminocarbonyl (amido or $-C(O)-NR"_2$), aminocarbonylamino ($-NR"-C(O)-NR"_2$), aminocarbonyloxy ($-O-C(O)-NR"_2$), aminosulfonyl, sulfonylamino, aryl, -O-aryl, azido, carboxyl, cyano, cycloalkyl, halogen, hydroxy, nitro, thiol, -S-alkyl, –S-aryl, -S(O)-alkyl,–S(O)-aryl, $-S(O)_2$-alkyl, and $-S(O)_2$-aryl. Substituting groups include carbonyl or thiocarbonyl which provide, for example, lactam and urea derivatives.

[0079] 'Hydroxy' refers to the radical -OH.

[0080] 'Nitro' refers to the radical $-NO_2$.

[0081] 'Substituted' refers to a group in which one or more hydrogen atoms are each independently replaced with the same or different substituent(s). Typical substituents may be selected from the group consisting of:

halogen, $-R^{57}$, $-O^-$, =O, $-OR^{57}$, $-SR^{57}$, $-S^-$, =S, $-NR^{57}R^{58}$, $=NR^{57}$, $-CCl_3$, $-CF_3$, -CN, -OCN, -SCN, -NO, $-NO_2$, $=N_2$, $-N_3$, $-S(O)_2O^-$, $-S(O)_2OH$, $-S(O)_2R^{57}$, $-OS(O_2)O^-$, $-OS(O)_2R^{57}$, $-P(O)(O^-)_2$, $-P(O)(OR^{57})(O^-)$, $-OP(O)(OR^{57})(OR^{58})$, $-C(O)R^{57}$, $-C(S)R^{57}$, $-C(O)OR^{57}$, $-C(O)NR^{57}R^{58}$, $-C(O)O^-$, $-C(S)OR^{57}$, $-NR^{59}C(O)NR^{57}R^{58}$, $-NR^{59}C(S)NR^{57}R^{58}$, $-NR^{60}C(NR^{59})NR^{57}R^{58}$ and $-C(NR^{59})NR^{57}R^{58}$;

wherein each R^{57}, R^{58}, R^{59} and R^{60} are independently:

- hydrogen, C_1-C_8 alkyl, C_6-C_{10} aryl, arylalkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, heteroarylalkyl; or

- C_1-C_8 alkyl substituted with halo or hydroxy; or
- C_6-C_{10} aryl, 5-10 membered heteroaryl, C_6-C_{10} cycloalkyl or 4-10 membered heterocycloalkyl substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

In a particular embodiment, substituted groups are substituted with one or more substituents, particularly with 1 to 3 substituents, in particular with one substituent group.

In a further particular embodiment the substituent group or groups are selected from: halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR'''SO_2R''$, $-SO_2NR''R'''$, $-C(O)R''$, $-C(O)OR''$, $-OC(O)R''$, $-NR'''C(O)R''$, $-C(O)NR''R'''$, $-NR''R'''$, $-(CR'''R''')_mOR'''$, wherein, each R'' is independently selected from H, C_1-C_8 alkyl, $-(CH_2)_t(C_6$-C_{10} aryl), $-(CH_2)_t$(5-10 membered heteroaryl), $-(CH_2)_t(C_3$-C_{10} cycloalkyl), and $-(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4; and

- any alkyl groups present, may themselves be substituted by halo or hydroxy; and
- any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. Each R'' independently represents H or C_1-C_6alkyl.

[0082] 'Substituted sulfanyl' refers to the group $-SR^{61}$, wherein R^{61} is selected from:

- C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo, substituted or unsubstituted amino, or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, each of which is substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0083] Exemplary 'substituted sulfanyl' groups are $-S$-(C_1-C_8 alkyl) and $-S$-(C_3-C_{10} cycloalkyl), $-S$-$(CH_2)_t(C_6$-C_{10} aryl), $-S$-$(CH_2)_t$(5-10 membered heteroaryl), $-S$-$(CH_2)_t(C_3$-C_{10} cycloalkyl), and $-S$-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. The term 'substituted sulfanyl' includes the groups 'alkylsulfanyl' or 'alkylthio', 'substituted alkylthio' or 'substituted alkylsulfanyl', 'cycloalkylsulfanyl' or 'cycloalkylthio', 'substituted cycloalkylsulfanyl' or 'substituted cycloalkylthio', 'arylsulfanyl' or 'arylthio' and 'heteroarylsulfanyl' or 'heteroarylthio' as defined below.

[0084] 'Substituted sulfinyl' refers to the group $-S(O)R^{68}$, wherein R^{68} is selected from:

- C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo, substituted or unsubstituted amino, or hydroxy; or

- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0085] Exemplary 'substituted sulfinyl' groups are –S(O)-(C_1-C_8 alkyl) and –S(O)-(C_3-C_{10} cycloalkyl), –S(O)-$(CH_2)_t$(C_6-C_{10} aryl), –S(O)-$(CH_2)_t$(5-10 membered heteroaryl), –S(O)-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and –S(O)-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. The term substituted sulfinyl includes the groups 'alkylsulfinyl', 'substituted alkylsulfinyl', 'cycloalkylsulfinyl', 'substituted cycloalkylsulfinyl', 'arylsulfinyl' and 'heteroarylsulfinyl' as defined herein.

[0086] 'Substituted sulfonyl' refers to the group $-S(O)_2R^{75}$, wherein R^{75} is selected from:

- C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo, substituted or unsubstituted amino, or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, each of which is substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0087] Exemplary 'substituted sulfonyl' groups are $-S(O)_2$-(C_1-C_8 alkyl) and $-S(O)_2$-(C_3-C_{10} cycloalkyl), $-S(O)_2$-$(CH_2)_t$(C_6-C_{10} aryl), $-S(O)_2$-$(CH_2)_t$(5-10 membered heteroaryl), $-S(O)_2$-$(CH_2)_t$(C_3-C_{10} cycloalkyl), and $-S(O)_2$-$(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy. The term substituted sulfonyl includes the groups alkylsulfonyl, substituted alkylsulfonyl, cycloalkylsulfonyl, substituted cycloalkylsulfonyl, arylsulfonyl and heteroarylsulfonyl.

[0088] 'Sulfo' or 'sulfonic acid' refers to a radical such as $-SO_3H$.

[0089] 'Substituted sulfo' or 'sulfonic acid ester' refers to the group $-S(O)_2OR^{82}$, wherein R^{82} is selected from:

- C_1-C_8 alkyl, C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, and heteroaralkyl; or
- C_1-C_8 alkyl substituted with halo, substituted or unsubstituted amino, or hydroxy; or
- C_3-C_{10} cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, aralkyl, 5-10 membered heteroaryl, or heteroaralkyl, each of which is substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0090] Exemplary 'Substituted sulfo' or 'sulfonic acid ester' groups are $-S(O)_2-O-(C_1-C_8$ alkyl) and $-S(O)_2-O-(C_3-C_{10}$ cycloalkyl), $-S(O)_2-O-(CH_2)_t(C_6-C_{10}$ aryl), $-S(O)_2-O-(CH_2)_t$(5-10 membered heteroaryl), $-S(O)_2-O-(CH_2)_t(C_3-C_{10}$ cycloalkyl), and $-S(O)_2-O-(CH_2)_t$(4-10 membered heterocycloalkyl), wherein t is an integer from 0 to 4 and any aryl, heteroaryl, cycloalkyl or heterocycloalkyl groups present, may themselves be substituted by unsubstituted C_1-C_4 alkyl, halo, unsubstituted C_1-C_4 alkoxy, unsubstituted C_1-C_4 haloalkyl, unsubstituted C_1-C_4 hydroxyalkyl, or unsubstituted C_1-C_4 haloalkoxy or hydroxy.

[0091] 'Thiol' refers to the group -SH.

[0092] One having ordinary skill in the art of organic synthesis will recognize that the maximum number of heteroatoms in a stable, chemically feasible heterocyclic ring, whether it is aromatic or non aromatic, is determined by the size of the ring, the degree of unsaturation and the valence of the heteroatoms. In general, a heterocyclic ring may have one to four heteroatoms so long as the heteroaromatic ring is chemically feasible and stable.

[0093] 'Pharmaceutically acceptable' means approved or approvable by a regulatory agency of the Federal or a state government or the corresponding agency in countries other than the United States, or that is listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly, in humans.

[0094] 'Pharmaceutically acceptable salt' refers to a salt of a compound of the invention that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. In particular, such salts are non-toxic may be inorganic or organic acid addition salts and base addition salts. Specifically, such salts include: (1) acid addition salts, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or formed with organic acids such as acetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, 3-(4-hydroxybenzoyl) benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethane-disulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo[2.2.2]-oct-2-ene-1-carboxylic acid, glucoheptonic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid, and the like; or (2) salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, e.g., an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, N-methylglucamine and the like. Salts further include, by way of example only, sodium, potassium, calcium, magnesium, ammonium, tetraalkylammonium, and the like; and when the compound contains a basic functionality, salts of non toxic organic or inorganic acids, such as hydrochloride, hydrobromide, tartrate, mesylate, acetate, maleate, oxalate and the like. The term "pharmaceutically acceptable cation" refers to an acceptable cationic counter-ion of an acidic

functional group. Such cations are exemplified by sodium, potassium, calcium, magnesium, ammonium, tetraalkylammonium cations, and the like.

[0095] 'Pharmaceutically acceptable vehicle' refers to a diluent, adjuvant, excipient or carrier with which a compound of the invention is administered.

[0096] 'Prodrugs' refers to compounds, including derivatives of the compounds of the invention,which have cleavable groups and become by solvolysis or under physiological conditions the compounds of the invention which are pharmaceutically active in vivo. Such examples include, but are not limited to, choline ester derivatives and the like, N-alkylmorpholine esters and the like.

[0097] 'Solvate' refers to forms of the compound that are associated with a solvent, usually by a solvolysis reaction. This physical association includes hydrogen bonding. Conventional solvents include water, ethanol, acetic acid and the like. The compounds of the invention may be prepared e.g. in crystalline form and may be solvated or hydrated. Suitable solvates include pharmaceutically acceptable solvates, such as hydrates, and further include both stoichiometric solvates and non-stoichiometric solvates. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. 'Solvate' encompasses both solution-phase and isolable solvates. Representative solvates include hydrates, ethanolates and methanolates.

[0098] 'Subject' includes humans. The terms 'human', 'patient' and 'subject' are used interchangeably herein.

[0099] 'Therapeutically effective amount' means the amount of a compound that, when administered to a subject for treating a disease, is sufficient to effect such treatment for the disease. The "therapeutically effective amount" can vary depending on the compound, the disease and its severity, and the age, weight, etc., of the subject to be treated.

[00100] 'Preventing' or 'prevention' refers to a reduction in risk of acquiring or developing a disease or disorder (i.e., causing at least one of the clinical symptoms of the disease not to develop in a subject that may be exposed to a disease-causing agent, or predisposed to the disease in advance of disease onset.

[00101] The term 'prophylaxis' is related to 'prevention', and refers to a measure or procedure the purpose of which is to prevent, rather than to treat or cure a disease. Non-limiting examples of prophylactic measures may include the administration of vaccines; the administration of low molecular weight heparin to hospital patients at risk for thrombosis due, for example, to immobilization; and the administration of an anti-malarial agent such as chloroquine, in advance of a visit to a geographical region where malaria is endemic or the risk of contracting malaria is high.

[00102] 'Treating' or 'treatment' of any disease or disorder refers, in one embodiment, to ameliorating the disease or disorder (i.e., arresting the disease or reducing the manifestation, extent or severity of at least one of the clinical symptoms thereof). In another embodiment 'treating' or 'treatment' refers to ameliorating at least one physical parameter, which may not be discernible by the subject. In yet another embodiment, 'treating' or 'treatment' refers to modulating the disease or disorder, either

physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both. In a further embodiment, "treating" or "treatment" relates to slowing the progression of the disease.

[00103] As used herein the term 'condition(s) involving inflammation' refers to the group of conditions including, rheumatoid arthritis, osteoarthritis, juvenile idiopathic arthritis, psoriasis, allergic airway disease (e.g. asthma, rhinitis), inflammatory bowel diseases (e.g. Crohn's disease, colitis), endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), and related diseases involving cartilage, such as that of the joints. Partcicularly the term refers to rheumatoid arthritis, osteoarthritis, allergic airway disease (e.g. asthma) and inflammatory bowel diseases.

[00104] As used herein the term 'condition(s) involving an immune response' or 'autoimmune diseases' are used interchangeably and refer to refers to the group of diseases including obstructive airways disease, including conditions such as COPD, asthma (e.g intrinsic asthma, extrinsic asthma, dust asthma, infantily asthma) particularly chronic or inveterate asthma (for example late asthma and airway hyperreponsiveness), bronchitis, including bronchial asthma, systemic lupus erythematosus (SLE), multiple sclerosis, type I diabetes mellitus and complications associated therewith, atopic eczema (atopic dermatitis), contact dermatitis and further eczematous dermatitis, inflammatory bowel disease (e.g. Crohn's disease and ulcerative colitis), atherosclerosis and amyotrophic lateral sclerosis. Particularly the term refers to COPD, asthma, systemic lupus erythematosis, type I diabetes mellitus and inflammatory bowel disease.

[00105] As used herein the term 'transplantation rejection' refers to the acute or chronic rejection of cells, tissue or solid organ allo- or xenografts of e.g. pancreatic islets, stem cells, bone marrow, skin, muscle, corneal tissue, neuronal tissue, heart, lung, combined heart-lung, kidney, liver, bowel, pancreas, trachea or oesophagus, or graft-versus-host diseases.

[00106] As used herein the term 'proliferative diseases' refers to conditions such as cancer (e.g. uterine leiomyosarcoma or prostate cancer), myeloproliferative disorders (e.g. polycythemia vera, essential thrombocytosis and myelofibrosis), leukemia (e.g. acute myeloid leukaemia and acute lymphoblastic leukemia), multiple myeloma, psoriasis, restenosis, sclerodermitis or fibrosis. In particular the term refers to cancer, leukemia, multiple myeloma and psoriasis.

[00107] As used herein, the term 'cancer' refers to a malignant or benign growth of cells in skin or in body organs, for example but without limitation, breast, prostate, lung, kidney, pancreas, stomach or bowel. A cancer tends to infiltrate into adjacent tissue and spread (metastasise) to distant organs, for example to bone, liver, lung or the brain. As used herein the term cancer includes both metastatic rumour cell types, such as but not limited to, melanoma, lymphoma, leukaemia, fibrosarcoma, rhabdomyosarcoma, and mastocytoma and types of tissue carcinoma, such as but not limited to, colorectal cancer, prostate cancer, small cell lung cancer and non-small cell lung cancer, breast cancer, pancreatic cancer, bladder cancer, renal cancer, gastric cancer, glioblastoma, primary liver cancer, ovarian cancer, prostate cancer and uterine leiomyosarcoma.

[00108] As used herein the term 'leukaemia' refers to neoplastic diseases of the blood and blood forming organs. Such diseases can cause bone marrow and immune system dysfunction, which renders the host highly susceptible to infection and bleeding. In particular the term leukemia refers to acute myeloid leukaemia (AML) and acute lymphoblastic leukemia (ALL).

[00109] As used herein the term 'diseases involving impairment of cartilage turnover' and specifically 'diseases involving the anabolic stimulation of chondrocytes' includes conditions such as osteoarthritis, psoriatic arthritis, juvenile rheumatoid arthritis, gouty arthritis, septic or infectious arthritis, reactive arthritis, reflex sympathetic dystrophy, algodystrophy, Tietze syndrome or costal chondritis, fibromyalgia, osteochondritis, neurogenic or neuropathic arthritis, arthropathy, endemic forms of arthritis like osteoarthritis deformans endemica, Mseleni disease and Handigodu disease; degeneration resulting from fibromyalgia, systemic lupus erythematosus, scleroderma and ankylosing spondylitis.

[00110] As used herein the term 'congenital cartilage malformation(s)' includes conditions such as hereditary chondrolysis, chondrodysplasias and pseudochondrodysplasias, in particular, but without limitation, microtia, anotia, metaphyseal chondrodysplasia, and related disorders.

[00111] As used herein the term 'disease(s) associated with hypersecretion of IL6' includes conditions such as Castleman's disease, multiple myeloma, psoriasis, Kaposi's sarcoma and/or mesangial proliferative glomerulonephritis.

[00112] 'Compound(s) of the invention', and equivalent expressions, are meant to embrace compounds of the Formula(e) as hereinbefore described, which expression includes the pharmaceutically acceptable salts, and the solvates, e.g., hydrates, and the solvates of the pharmaceutically acceptable salts where the context so permits. Similarly, reference to intermediates, whether or not they themselves are claimed, is meant to embrace their salts, and solvates, where the context so permits.

[00113] When ranges are referred to herein, for example but without limitation, C_1-C_6 alkyl, the citation of a range should be considered a representation of each member of said range.

[00114] Other derivatives of the compounds of the invention have activity in both their acid and acid derivative forms, but in the acid sensitive form often offers advantages of solubility, tissue compatibility, or delayed release in the mammalian organism (see, Bundgard, H., Design of Prodrugs, pp. 7-9, 21-24, Elsevier, Amsterdam 1985). Prodrugs include acid derivatives well know to practitioners of the art, such as, for example, esters prepared by reaction of the parent acid with a suitable alcohol, or amides prepared by reaction of the parent acid compound with a substituted or unsubstituted amine, or acid anhydrides, or mixed anhydrides. Simple aliphatic or aromatic esters, amides and anhydrides derived from acidic groups pendant on the compounds of this invention are particularly useful prodrugs. In some cases it is desirable to prepare double ester type prodrugs such as (acyloxy)alkyl esters or ((alkoxycarbonyl)oxy)alkylesters. Particular such prodrugs are the C_1 to C_8 alkyl, C_2-C_8 alkenyl, aryl, C_7-C_{12} substituted aryl, and C_7-C_{12} arylalkyl esters of the compounds of the invention.

[00115] As used herein, the term 'isotopic variant' refers to a compound that contains unnatural proportions of isotopes at one or more of the atoms that constitute such compound. For example, an 'isotopic variant' of a compound can contain one or more non-radioactive isotopes, such as for example,

deuterium (^{2}H or D), carbon-13 (^{13}C), nitrogen-15 (^{15}N), or the like. It will be understood that, in a compound where such isotopic substitution is made, the following atoms, where present, may vary, so that for example, any hydrogen may be ^{2}H/D, any carbon may be ^{13}C, or any nitrogen may be ^{15}N, and that the presence and placement of such atoms may be determined within the skill of the art. Likewise, the invention may include the preparation of isotopic variants with radioisotopes, in the instance for example, where the resulting compounds may be used for drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, i.e. ^{3}H, and carbon-14, i.e. ^{14}C, are particularly useful for this purpose in view of their ease of incorporation and ready means of detection. Further, compounds may be prepared that are substituted with positron emitting isotopes, such as ^{11}C, ^{18}F, ^{15}O and ^{13}N, and would be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy.

[00116] All isotopic variants of the compounds provided herein, radioactive or not, are intended to be encompassed within the scope of the invention.

[00117] It is also to be understood that compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are termed 'isomers'. Isomers that differ in the arrangement of their atoms in space are termed 'stereoisomers'.

[00118] Stereoisomers that are not mirror images of one another are termed 'diastereomers' and those that are non-superimposable mirror images of each other are termed 'enantiomers'. When a compound has an asymmetric center, for example, it is bonded to four different groups, a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of its asymmetric center and is described by the R- and S-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (i.e., as (+) or (-)-isomers respectively). A chiral compound can exist as either individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a 'racemic mixture'.

[00119] 'Tautomers' refer to compounds that are interchangeable forms of a particular compound structure, and that vary in the displacement of hydrogen atoms and electrons. Thus, two structures may be in equilibrium through the movement of π electrons and an atom (usually H). For example, enols and ketones are tautomers because they are rapidly interconverted by treatment with either acid or base. Another example of tautomerism is the aci- and nitro- forms of phenylnitromethane, that are likewise formed by treatment with acid or base.

[00120] Tautomeric forms may be relevant to the attainment of the optimal chemical reactivity and biological activity of a compound of interest.

[00121] The compounds of this invention may possess one or more asymmetric centers; such compounds can therefore be produced as individual (R)- or (S)- stereoisomers or as mixtures thereof.

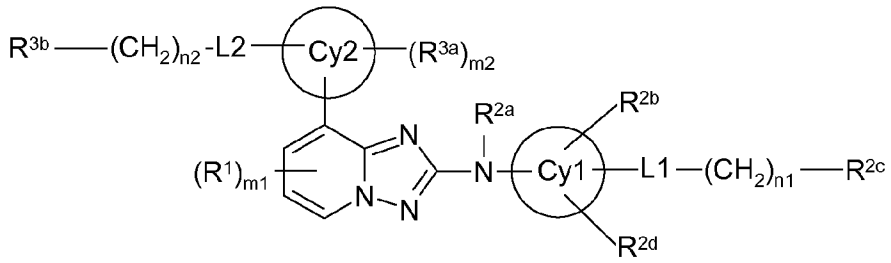
[00122] Unless indicated otherwise, the description or naming of a particular compound in the specification and claims is intended to include both individual enantiomers and mixtures, racemic or

otherwise, thereof. The methods for the determination of stereochemistry and the separation of stereoisomers are well-known in the art.

THE COMPOUNDS

[00123] The present invention is based on the discovery that inhibitors of JAK are useful for the treatment of diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g. diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). In particular diseases involving cartilage degradation, bone and/or joint degradation and/or inflammation, for example osteoarthritis. The present invention also provides methods for the production of these compounds, pharmaceutical compositions comprising these compounds and methods for treating diseases involving cartilage degradation, bone and/or joint degradation and/or inflammation by administering a compound of the invention. The present compounds may be inhibitors of one or more members of the JAK family; specifically they may inhibit the activity of one or more of JAK1, JAK2, JAK3 and/or TYK2.

[00124] Accordingly, in a first aspect of the invention, substituted bicycloheteroaryl compounds are disclosed according to Formula (I):



I

wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$-, -$N(R^{4a})$-, -$CON(R^{4a})$-, -$SO_2N(R^{4a})$-, -$N(R^{4a})CO$-, or -$N(R^{4a})SO_2$-;

each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, substituted or unsubstituted amino, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester,

carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, substituted or unsubstituted amino, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted –O-aryl, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, substituted or unsubstituted amino, substituted or unsubstituted amido, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, C_1-C_6alkyl, substituted C_1-C_6alkyl, C_3-C_7 cycloalkyl, or substituted C_3-C_7 cycloalkyl;

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts, or solvates thereof, or solvates of the pharmaceutically acceptable salts.

[00125] In a preferred embodiment, the compound is according to Formula I, wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$, -N(R^{4a})-, -CON(R^{4a})-, -SO_2N(R^{4a})-, - N(R^{4a})CO-, or - N(R^{4a})SO_2-;

each R^1 is independently selected from unsubstituted C_1-C_6 alkyl, unsubstituted acyl, unsubstituted acylamino, unsubstituted C_1-C_6 alkoxy, unsubstituted amido, unsubstituted amino, unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester, carboxy, cyano,

unsubstituted C_3-C_7 cycloalkyl, unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from unsubstituted C_1-C_6 alkyl, unsubstituted acyl, unsubstituted acylamino, unsubstituted C_1-C_6 alkoxy, unsubstituted amido, unsubstituted alkoxycarbonyl, unsubstituted arylalkyloxy, unsubstituted amino, unsubstituted aryl, unsubstituted arylalkyl, unsubstituted aminosulfonyl, unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, unsubstituted C_3-C_7 cycloalkyl, unsubstituted 4-7 membered heterocycloalkyl, halo, unsubstituted -O-(5-7-membered heteroaryl), unsubstituted 5-7-membered heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl (which C_1-C_6 alkyl may be substituted with hydroxy, unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy, cyano, halo, dialkylamino), acyl (which acyl may be substituted with unsubstituted C_1-C_4 alkyl), acylamino (which acylamino may be substituted with unsubstituted C_1-C_4 alkyl), C_1-C_6 alkoxy (which C_1-C_6 alkoxy may be substituted with halo, dialkylamido, cyano), –O-aryl (which –O-aryl may be substituted with halo, unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy), unsubstituted alkoxycarbonyl, unsubstituted arylalkyloxy, aryl (which aryl may be substituted with cyano, halo, unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy), unsubstituted arylalkyl, sulfanyl (which sulfanyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), sulfinyl (which sulfinyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), sulfonyl (which sulfonyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), aminosulfonyl (which aminosulfonyl may be substituted with unsubstituted C_1-C_4 alkyl), unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, amino (which amino may be substituted with unsubstituted C_1-C_4 alkyl), amido (which amido may be substituted with unsubstituted C_1-C_4 alkyl), cyano, C_3-C_7 cycloalkyl (which C_3-C_7 cycloalkyl may be substituted with cyano), 4-7 membered heterocycloalkyl (which heterocycloalkyl may be substituted with cyano, oxo, unsubstituted C_1-C_4 alkyl, halo, hydroxy), halo, unsubstituted -O-heteroaryl, 5-7-membered heteroaryl (which heteroaryl may be substituted with unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy, hydroxy, halo), hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, unsubstituted C_1-C_6alkyl, unsubstituted C_3-C_7 cycloalkyl

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-$_6$ alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts or solvates thereof, or the solvates of the pharmaceutically acceptable salts.

[00126] In one embodiment, with respect to compounds of Formula I, each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, and halo.

[00127] In one embodiment, with respect to compounds of Formula I, each R^1 is independently selected from H, Me, CF_3, Cl and F.

[00128] In another particular embodiment, m1 is 0.

[00129] In one embodiment, with respect to compounds of Formula I, R^{2a} is independently selected from H, C_1-C_6 alkyl, and substituted C_1-C_6 alkyl.

[00130] In one embodiment, with respect to compounds of Formula I, R^{2a} is H.

[00131] In one embodiment, with respect to compounds of Formula I, Cy1 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

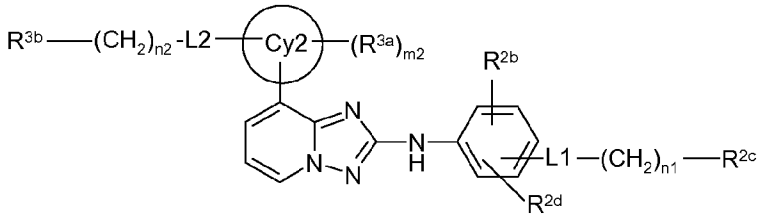
[00132] In one embodiment, with respect to compounds of Formula I, Cy1 is substituted or unsubstituted aryl.

[00133] In one embodiment, with respect to compounds of Formula I, Cy1 is substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

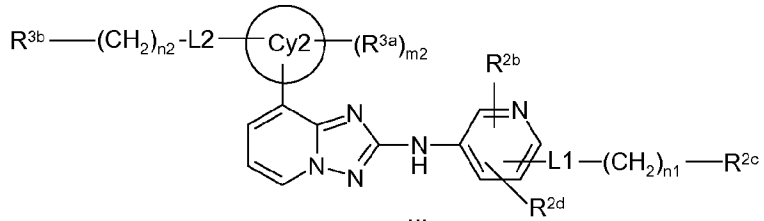
[00134] In one embodiment, with respect to compounds of Formula I, Cy1 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

[00135] In one embodiment, with respect to compounds of Formula I, Cy1 is substituted or unsubstituted phenyl.

[00136] In a more particular embodiment, with respect to compound of Formula I, the compound is according to Formula II or III:



II



III

wherein Cy2, L1, L2, R^{2b}, R^{2c}, R^{2d}, R^{3a}, R^{3b}, m2, n1, and n2 are as described above.

[00137] In one embodiment, with respect to Formulae II and III, Cy2, L1, L2, R^{2c}, R^{3a}, R^{3b}, m2, n1, and n2 are as described above and R^{2b}, and R^{2d} are independently H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy or halo.

[00138] In one embodiment, with respect to Formulae II and III, Cy2, L1, L2, R^{2c}, R^{3a}, R^{3b}, m2, n1, and n2 are as described above and R^{2b}, and R^{2d} are independently H, Me, OMe, F or Cl.

[00139] In one embodiment, with respect to Formulae II and III, L1 is a single bond, n1 is 0, and R^{2c} is H, Cl, F, Me, Et, OMe, CF_3, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

[00140] In one embodiment with respect to Formulae II and III, L1 is a single bond, n1 is 0, and R^{2c} is NHCOMe, or COOH.

[00141] In one embodiment with respect to Formulae II and III, L1 is CONH; n1 is 2 or 3; and R^{2c} is NMe_2, OMe, or NHCOMe.

[00142] In one embodiment with respect to Formulae II and III, L1 is selected from a single bond, -C(O)-, and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl and R^{2c} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 membered heterocycloalkyl.

[00143] In one embodiment with respect to Formulae II and III, L1 is selected from a single bond, -C(O)-, and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} is Me, Et, i-Pr, or 1,3-dihydroxyprop-2-yl.

[00144] In one embodiment with respect to compounds of Formulae II and III, L1 is selected from a single bond, -C(O)-, - and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.

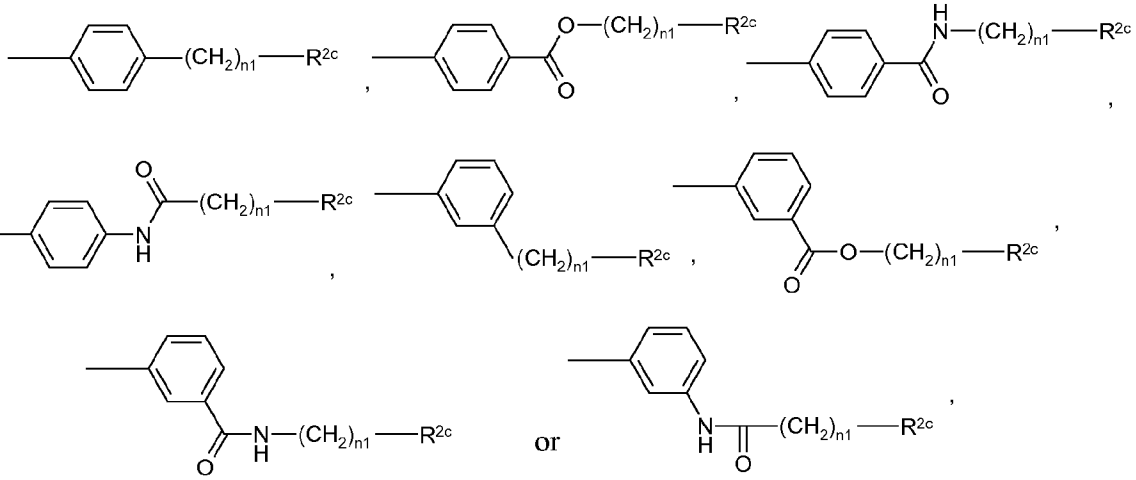
[00145] In one embodiment with respect to compounds of Formulae II and III, L1 is selected from a single bond, -C(O)-, and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted

pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

[00146] In one embodiment with respect to compounds of Formulae II and III, L1 is selected from a single bond and -C(O)-, n1 is 0, 1, 2, 3, or 4; and R^{2b} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH.

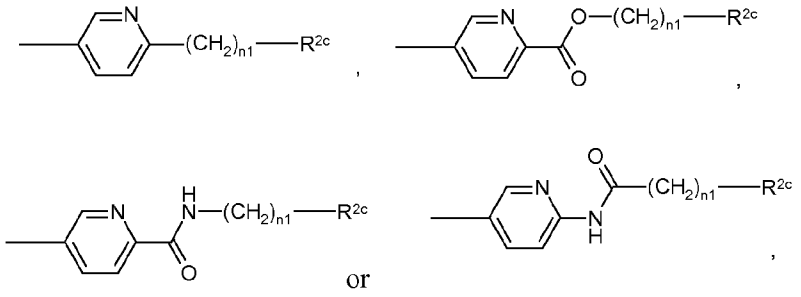
[00147] In one embodiment with respect to compounds of Formulae II and III, L1 is -CON(R^{4a})-; n1 is 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH.

[00148] In a particular embodiment,–Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:



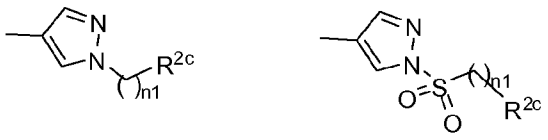
wherein n1 and R^{2c} are as described above.

[00149] In another particular embodiment, –Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:



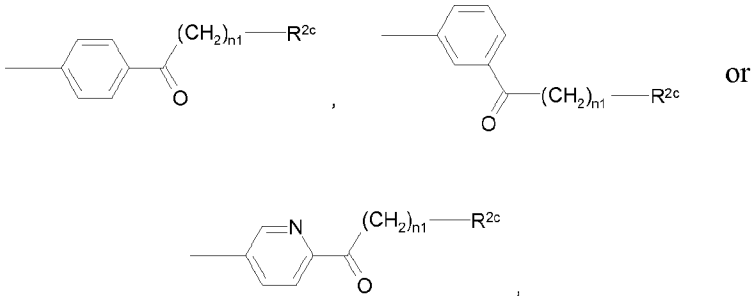
wherein n1 and R^{2c} are as described above.

[00150] In another particular embodiment, –Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:



wherein n1 and R^{2c} are as described above.

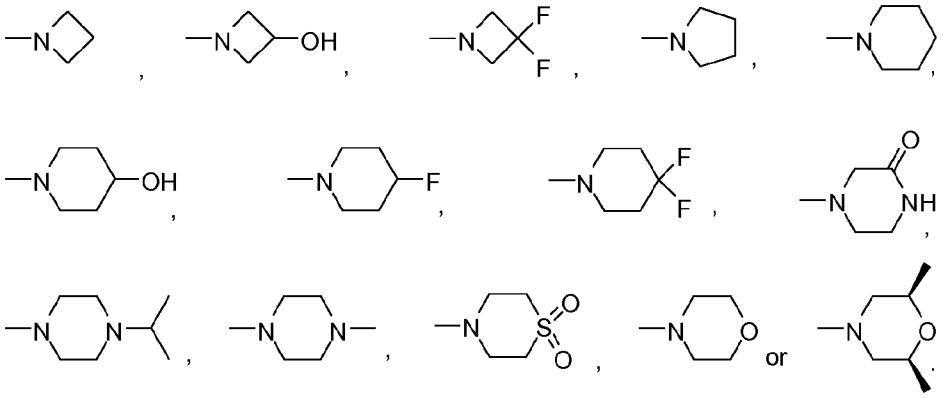
[00151] In another particular embodiment, the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



wherein n1 and R^{2c} are as described above.

[00152] In one embodiment, R^{2c} is N-containing heterocylic or heteroaryl ring.

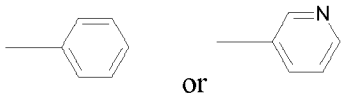
[00153] In a particular embodiment, R^{2c} is:



[00154] In another particular embodiment, R^{2c} is pyrazolyl, pyrrolyl, imidazolyl, or triazolyl.

[00155] In another particular embodiment, n1 is 0, 1 or 2.

[00156] In another embodiment, $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



[00157] In a further aspect of the invention, with respect to compounds of Formulae II and III, Cy2 is substituted or unsubstituted aryl.

[00158] In a further aspect of the invention, with respect to compounds of Formulae II and III, Cy2 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

[00159] In a further aspect of the invention, with respect to compounds of Formulae II and III, Cy2 is substituted or unsubstituted substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

[00160] In a further aspect of the invention, with respect to compounds of Formulae II and III, Cy2 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

[00161] In a further aspect of the invention, with respect to compounds of Formulae II and III, Cy2 is Ph; m2 is 1, 2 or 3; and each R^{3a} is independently C_1-C_6 alkyl, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, or halo.

[00162] In one embodiment, with respect to compounds of Formulae II and III, Cy2 is Ph; m2 is 1, 2 or 3; and each R^{3a} is independently Cl, F, Me, Et, OMe, CF_3, CONH2, CONMe2, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

[00163] In a more particular embodiment, with respect to compounds of Formulae II and III, Cy2 is Ph and each R^{3a} is H.

[00164] In one embodiment, with respect to compounds of Formulae II and III, L2 is selected from -O-, -C(O)-, $-S(O)_2N(R^{4a})-$, $-N(R^{4a})S(O)_2-$ and $-CON(R^{4a})-$; n2 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl; and R^{3b} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 memebered heterocycloalkyl.

[00165] In one embodiment, with respect to compounds of Formulae II and III, L2 is selected from -O-, -C(O)-, $S(O)_2$-, $-S(O)_2N(R^{4a})-$, $-N(R^{4a})S(O)_2-$ and $-CON(R^{4a})-$; n2 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl; and R^{3b} is Me, Et, i-Pr, 1,3-dihydroxyprop-2-yl.

[00166] In one embodiment, with respect to compounds of Formulae II and III, L2 is selected from -O-, -C(O)-, $S(O)_2$-, $-S(O)_2N(R^{4a})-$, $-N(R^{4a})S(O)_2-$ and $-CON(R^{4a})-$; n2 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl; and R^{3b} is substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.

[00167] In one embodiment, with respect to compounds of Formulae II and III, L2 is selected from -O-, -C(O)-, $S(O)_2$-, $-S(O)_2N(R^{4a})-$, $-N(R^{4a})S(O)_2-$ and $-CON(R^{4a})-$; n2 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl; and R^{3b} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

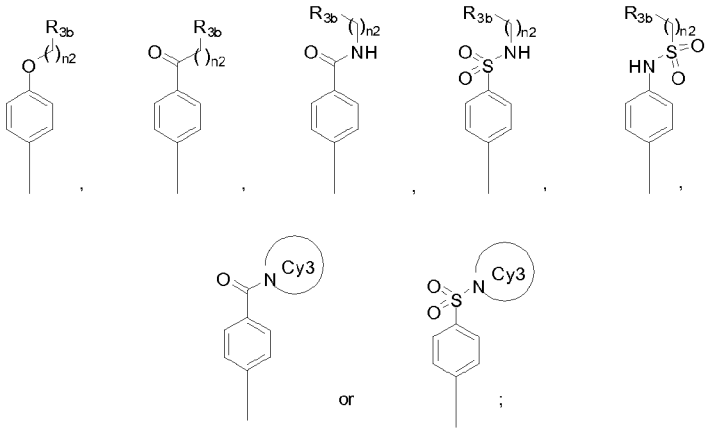
[00168] In one embodiment, with respect to compounds of Formulae II and III, L2 is selected from -O-, -C(O)-, $-S(O)_2N(R^{4a})-$, $-N(R^{4a})S(O)_2-$ and $-CON(R^{4a})-$; n2 is 0, 1, 2, 3, or 4; R^{4a} is selected from H and C_1-C_6 alkyl; and R^{3b} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH

provided that

when L2 is –O, $S(O)_2N(R^{4a})-$ and $-CON(R^{4a})-$, n2 is 1, 2, 3, or 4.

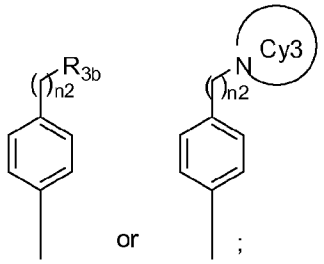
[00169] In one particular embodiment, with respect to compounds of Formulae II and III, R^{4a} is H.

[00170] In a more particular embodiment, with respect to compounds of Formulae II and III, each R^{3a} is H; and the $-Cy2-L2-(CH_2)_{n2}-R^{3b}$ is selected from:



wherein R^{3b}, and n2 are as in Formula 1; and Cy3 is substituted or unsubstituted 4-7 membered N containing 4-7 membered heterocycloalkyl.

[00171] In another more particular embodiment, with respect to compounds of Formulae II and III, each R^{3a} is H; and the $-Cy2-L2-(CH_2)_{n2}-R^{3b}$ is selected from:



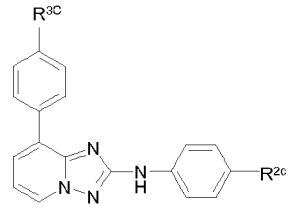
wherein R^{3b}, and n2 are as in Formula 1; and Cy3 is substituted or unsubstituted 4-7 membered N containing 4-7 membered heterocycloalkyl.

[00172] In one embodiment, with respect to compounds of Formula I, the group "$L2-(CH_2)_{n2}-R^{3b}$" is R^{3c}; and R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, OCH_2CN, $CONH_2$, CH_2CN, $(CH_2)_2CN$, $CONMe_2$, CONHMe, SO_2NH_2, SO_2NMe_2, CN, NHCOMe, COOH, OH or COOEt.

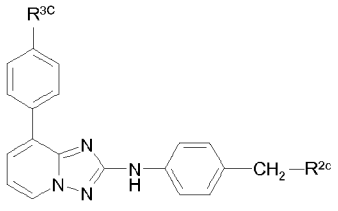
[00173] In another embodiment, with respect to compounds of Formula I, the group "$L2-(CH_2)_{n2}-R^{3b}$" is is $-O-C(CH_3)_2-C(O)NH_2$, $-CH_2-NH-(CH_2)$-cPr-OH, $-CH(CH_3)$-morpholine, $-C(CH_3)_2$-morpholine, -cPr-morpholine, -cPr-CN, or -cPr-4,4-thiomorpholine.

[00174] In another embodiment, with respect to compounds of Formula I, the group "$L2-(CH_2)_{n2}-R^{3b}$" is R^{3C}; R^{3c} is CH_2-R^{3d}, $CO-R^{3d}$, $CONH(CH_2)_{n3}-R^{3d}$, $NHCO-R^{3d}$, or $NHSO_2-R^{3d}$; and R^{3d} is substituted or unsubstituted 4-7 membered heterocycloalkyl, aryl, or heteroaryl; and n3 is 1, 2, or 3.

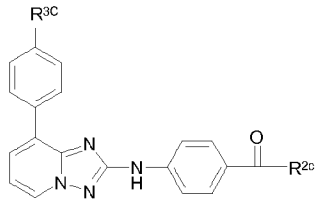
[00175] In one embodiment, with respect to compounds of Formula I, the group $L2-(CH_2)_{n2}-R^{3b}$ is R^{3c}; and the compound is according to Formula IVa, IVb, IVc, or IVd:



IVa ,

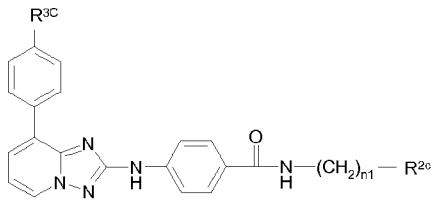


IVb ,



IVc

or



IVd ,

and wherein

n1 is 1, 2, or 3;

R^{2c} is substituted or unsubstituted dialkylamino, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted -O-aryl, or substituted or unsubstituted heteroaryl;

R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, OCH_2CN, $CONH_2$, CH_2CN, $(CH_2)_2CN$, $CONMe_2$, CONHMe, SO_2NH_2, SO_2NMe_2, CN, NHCOMe, COOH, OH or COOEt; or R^{3c} is CH_2-R^{3d}, CO-R^{3d}, $CONH(CH_2)_{n3}$-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d};

where R^{3d} is substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and

n3 is 1, 2, or 3.

[00176] In another embodiment, with respect to compounds of Formula I, the group L2-$(CH_2)_{n2}$-R^{3b} is R^{3c}; and the compound is according to Formula IVa, IVb, IVc, or IVd; and wherein

n1 is 1, 2, or 3;

R^{2c} is substituted or unsubstituted dialkylamino, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted -O-aryl, or substituted or unsubstituted heteroaryl;

R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, OCH_2CN, $CONH_2$, CH_2CN, $(CH_2)_2CN$, $CONMe_2$, CONHMe, SO_2NH_2, SO_2NMe_2, CN, NHCOMe, COOH, OH or COOEt; or R^{3c} is, R^{3d}, CH_2-R^{3d}, CO-R^{3d}, $CONH(CH_2)_{n3}$-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d};

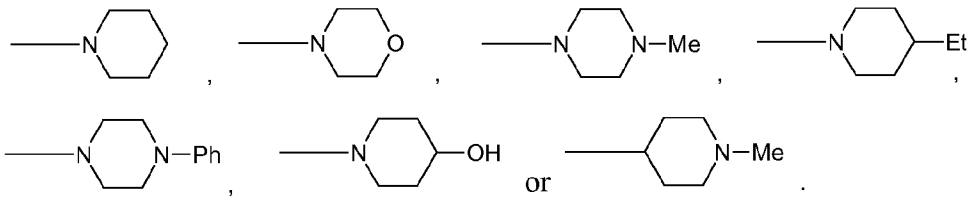
where R^{3d} is substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and

n3 is 1, 2, or 3.

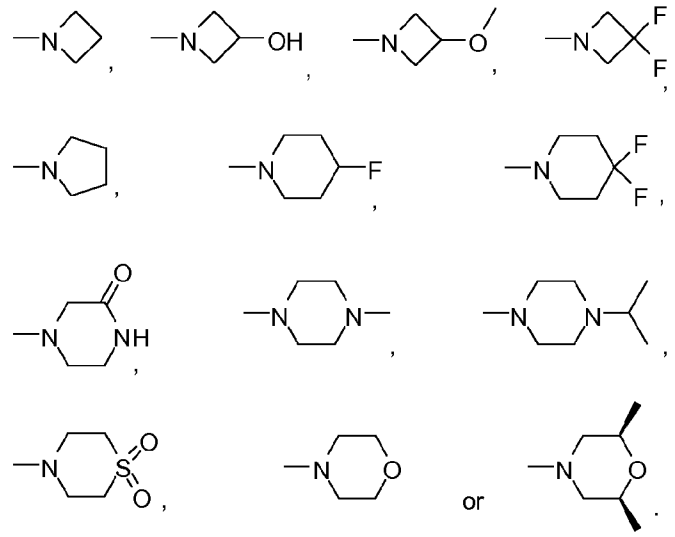
[00177] In a particular embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{2c} is NMe_2, or R^{2c} is substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted piperazinyl, or substituted or unsubstituted morpholinyl.

[00178] In another particular embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{2c} is substituted or unsubstituted azetidinyl, or substituted or unsubstituted thiomorpholinyl-4,4-dioxide.

[00179] In a more particular embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{2c} is



[00180] In another more particular embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{2c} is



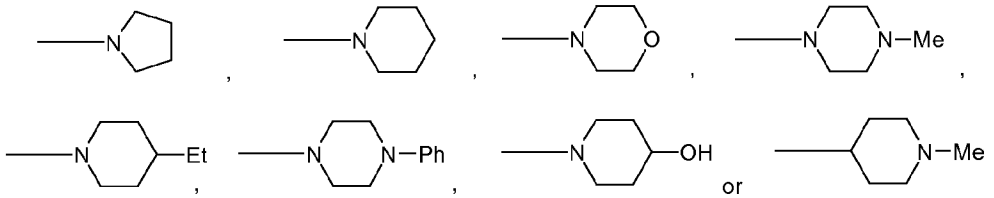
[00181] In another particular embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{2c} is substituted or unsubstituted pyrazolyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted indolyl, or substituted or unsubstituted indazolyl.

[00182] In one embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, SO_2NH_2, SO_2NMe_2, or CN.

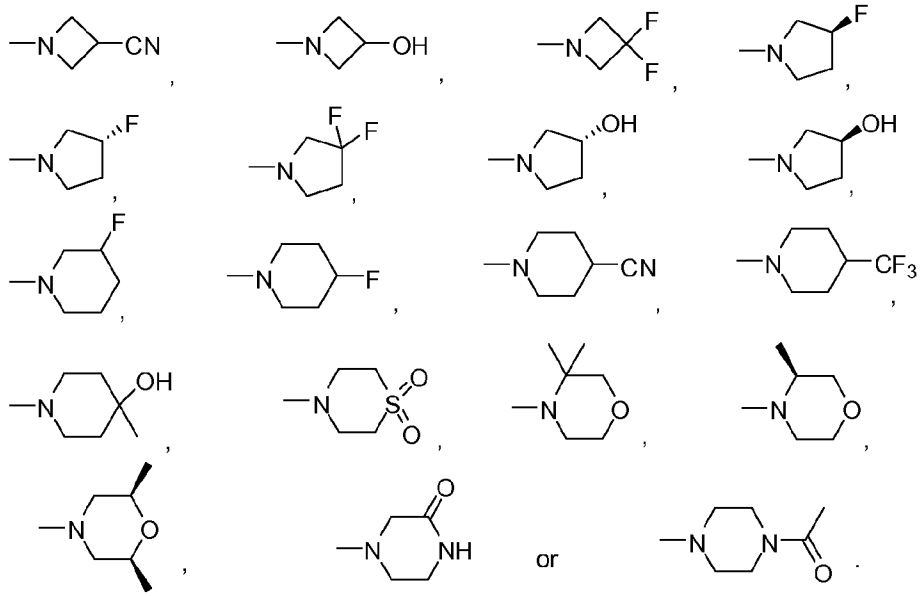
[00183] In one embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is Cl, F, Me, or OMe.

[00184] In one embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is CH_2-R^{3d}, CO-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d}; and R^{3d} is substituted or unsubstituted 4-7 membered heterocycloalkyl.

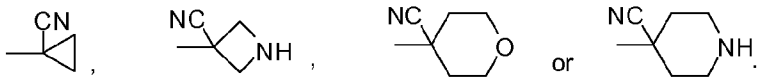
[00185] In one embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is CH_2-R^{3d}, CO-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d}; and R^{3d} is:



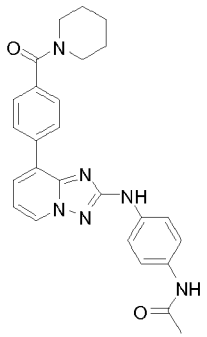
[00186] In another embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is CH_2-R^{3d}, CO-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d}; and R^{3d} is:



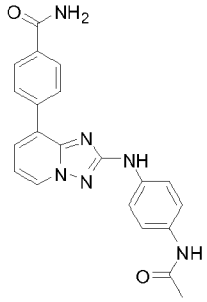
[00187] In one embodiment, with respect to compounds according to Formula IVa, IVb, IVc or IVd, R^{3c} is



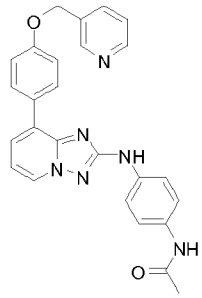
[00188] In one embodiment, with respect to compounds of Formula I, the compound is according to Formula Va, Vb, Vc, Vd, Ve, Vf, Vg, or Vh:



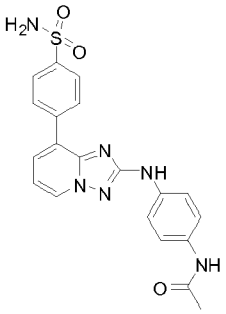
Va



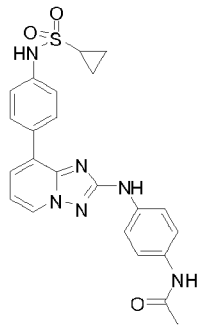
Vb



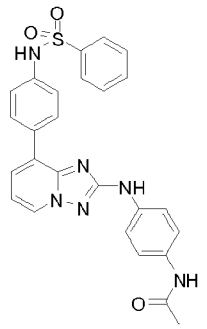
Vc



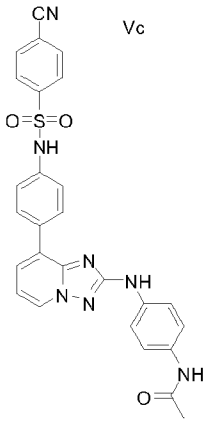
Vd



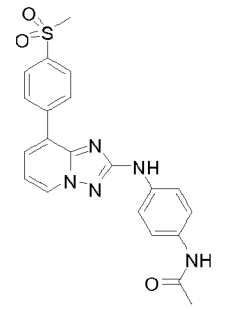
Ve



Vf

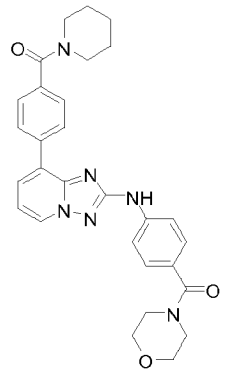


Vg

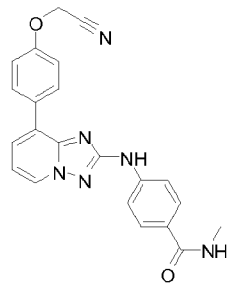


Vh

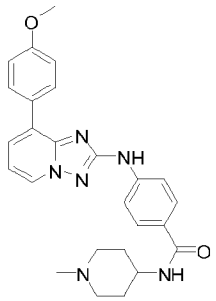
[00189] In one embodiment, with respect to compounds of Formula I, the compound is according to Formula VIa, VIb, VIc, VId, VIe or VIf:



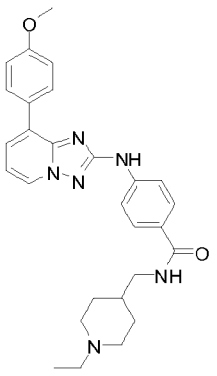
VIa



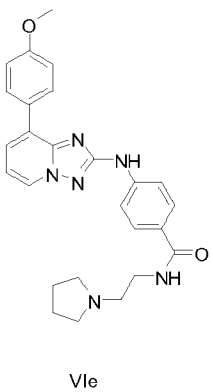
VIb



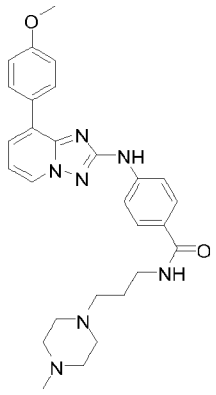
VIc



VId

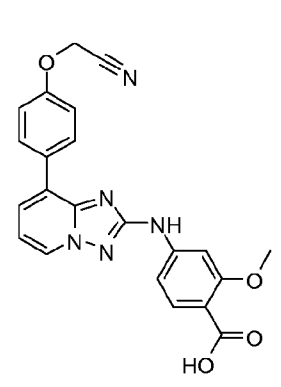


VIe

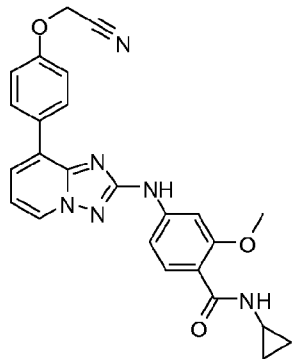


VIf

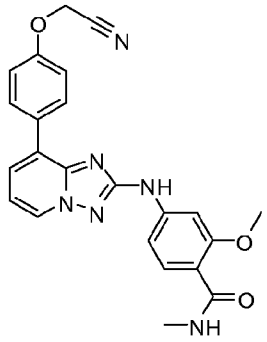
[00190] In a preferred embodiment, with respect to compounds of Formula I, the compound is according to Formula VIg, VIh, VIi, VIj, VIk, VIl, VIm or VIn:



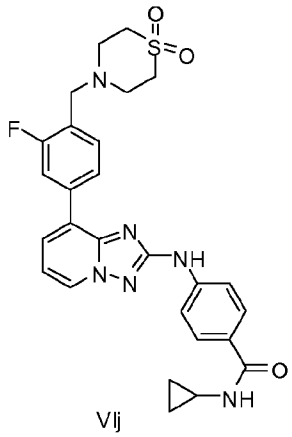
VIg



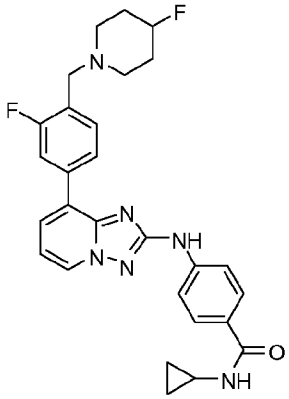
VIh



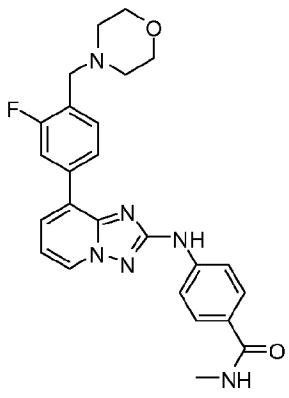
VIi



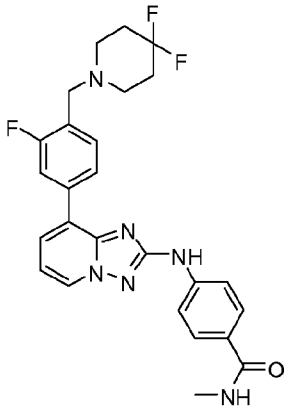
VIj



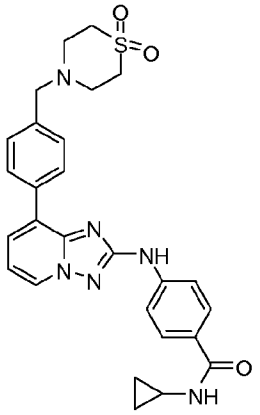
VIk



VIl



VIm



VIn

[00191] In one embodiment the compound of the invention is not an isotopic variant.

[00192] In one aspect a compound of the invention according to any one of the embodiments herein described is present as the free base.

[00193] In one aspect a compound of the invention according to any one of the embodiments herein described is a pharmaceutically acceptable salt.

[00194] In one aspect a compound of the invention according to any one of the embodiments herein described is a solvate.

[00195] In one aspect a compound of the invention according to any one of the embodiments herein described is a solvate of a pharmaceutically acceptable salt.

[00196] While specified groups for each embodiment have generally been listed above separately, a compound of the invention includes one in which several or each embodiment in the above Formula, as well as other formulae presented herein, is selected from one or more of particular members or groups designated respectively, for each variable. Therefore, this invention is intended to include all combinations of such embodiments within its scope.

[00197] In certain aspects, the present invention provides prodrugs and derivatives of the compounds according to the formulae above. Prodrugs are derivatives of the compounds of the invention, which have metabolically cleavable groups and become by solvolysis or under physiological conditions

the compounds of the invention, which are pharmaceutically active, *in vivo*. Such examples include, but are not limited to, choline ester derivatives and the like, N-alkylmorpholine esters and the like.

[00198] Other derivatives of the compounds of this invention have activity in both their acid and acid derivative forms, but the acid sensitive form often offers advantages of solubility, tissue compatibility, or delayed release in the mammalian organism (see, Bundgard, H., Design of Prodrugs, pp. 7-9, 21-24, Elsevier, Amsterdam 1985). Prodrugs include acid derivatives well know to practitioners of the art, such as, for example, esters prepared by reaction of the parent acid with a suitable alcohol, or amides prepared by reaction of the parent acid compound with a substituted or unsubstituted amine, or acid anhydrides, or mixed anhydrides. Simple aliphatic or aromatic esters, amides and anhydrides derived from acidic groups pendant on the compounds of this invention are preferred prodrugs. In some cases it is desirable to prepare double ester type prodrugs such as (acyloxy)alkyl esters or ((alkoxycarbonyl)oxy)alkylesters. Particularly useful are the C_1 to C_8 alkyl, C_2-C_8 alkenyl, aryl, C_7-C_{12} substituted aryl, and C_7-C_{12} arylalkyl esters of the compounds of the invention.

PHARMACEUTICAL COMPOSITIONS

[00199] When employed as pharmaceuticals, the compounds of this invention are typically administered in the form of a pharmaceutical composition. Such compositions can be prepared in a manner well known in the pharmaceutical art and comprise at least one active compound. Generally, the compounds of this invention are administered in a pharmaceutically effective amount. The amount of the compound actually administered will typically be determined by a physician, in the light of the relevant circumstances, including the condition to be treated, the chosen route of administration, the actual compound -administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

[00200] The pharmaceutical compositions of this invention can be administered by a variety of routes including oral, rectal, transdermal, subcutaneous, intravenous, intramuscular, and intranasal. Depending on the intended route of delivery, the compounds of this invention are preferably formulated as either injectable or oral compositions or as salves, as lotions or as patches all for transdermal administration

[00201] The compositions for oral administration can take the form of bulk liquid solutions or suspensions, or bulk powders. More commonly, however, the compositions are presented in unit dosage forms to facilitate accurate dosing. The term "unit dosage forms" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient, vehicle or carrier. Typical unit dosage forms include prefilled, premeasured ampules or syringes of the liquid compositions or pills, tablets, capsules or the like in the case of solid compositions. In such compositions, the furansulfonic acid compound is usually a minor component (from about 0.1 to about 50% by weight or preferably from about 1 to about 40% by weight)

with the remainder being various vehicles or carriers and processing aids helpful for forming the desired dosing form.

[00202] Liquid forms suitable for oral administration may include a suitable aqueous or nonaqueous vehicle with buffers, suspending and dispensing agents, colorants, flavors and the like. Solid forms may include, for example, any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[00203] Injectable compositions are typically based upon injectable sterile saline or phosphate-buffered saline or other injectable carriers known in the art. As before, the active compound in such compositions is typically a minor component, often being from about 0.05 to 10% by weight with the remainder being the injectable carrier and the like.

[00204] Transdermal compositions are typically formulated as a topical ointment or cream containing the active ingredient(s), generally in an amount ranging from about 0.01 to about 20% by weight, preferably from about 0.1 to about 20% by weight, preferably from about 0.1 to about 10% by weight, and more preferably from about 0.5 to about 15% by weight. When formulated as a ointment, the active ingredients will typically be combined with either a paraffinic or a water-miscible ointment base. Alternatively, the active ingredients may be formulated in a cream with, for example an oil-in-water cream base. Such transdermal formulations are well-known in the art and generally include additional ingredients to enhance the dermal penetration of stability of the active ingredients or the formulation. All such known transdermal formulations and ingredients are included within the scope of this invention.

[00205] The compounds of this invention can also be administered by a transdermal device. Accordingly, transdermal administration can be accomplished using a patch either of the reservoir or porous membrane type, or of a solid matrix variety.

[00206] The above-described components for orally administrable, injectable or topically administrable compositions are merely representative. Other materials as well as processing techniques and the like are set forth in Part 8 of Remington's Pharmaceutical Sciences, 17th edition, 1985, Mack Publishing Company, Easton, Pennsylvania, which is incorporated herein by reference.

[00207] The compounds of this invention can also be administered in sustained release forms or from sustained release drug delivery systems. A description of representative sustained release materials can be found in Remington's Pharmaceutical Sciences.

[00208] The following formulation examples illustrate representative pharmaceutical compositions that may be prepared in accordance with this invention. The present invention, however, is not limited to the following pharmaceutical compositions.

Formulation 1 - Tablets

[00209] A compound of the invention may be admixed as a dry powder with a dry gelatin binder in an approximate 1:2 weight ratio. A minor amount of magnesium stearate may be added as a lubricant.

The mixture may be formed into 240-270 mg tablets (80-90 mg of active amide compound per tablet) in a tablet press.

Formulation 2 - Capsules

[00210] A compound of the invention may be admixed as a dry powder with a starch diluent in an approximate 1:1 weight ratio. The mixture may be filled into 250 mg capsules (125 mg of active amide compound per capsule).

Formulation 3 - Liquid

[00211] A compound of the invention (125 mg), may be admixed with sucrose (1.75 g) and xanthan gum (4 mg) and the resultant mixture may be blended, passed through a No. 10 mesh U.S. sieve, and then mixed with a previously made solution of microcrystalline cellulose and sodium carboxymethyl cellulose (11:89, 50 mg) in water. Sodium benzoate (10 mg), flavor, and color may be diluted with water and added with stirring. Sufficient water may then be added with stirring. Sufficient water is then added to produce a total volume of 5 mL.

Formulation 4 - Tablets

[00212] A compound of the invention may be admixed as a dry powder with a dry gelatin binder in an approximate 1:2 weight ratio. A minor amount of magnesium stearate may be added as a lubricant. The mixture is formed into 450-900 mg tablets (150-300 mg of active amide compound) in a tablet press.

Formulation 5 - Injection

[00213] A compound of the invention may be dissolved or suspended in a buffered sterile saline injectable aqueous medium to a concentration of approximately 5 mg/mL.

Formulation 6 - Topical

[00214] Stearyl alcohol (250 g) and a white petrolatum (250 g) may be melted at about 75°C and then a mixture of a compound of the invention (50 g) methylparaben (0.25 g), propylparaben (0.15 g), sodium lauryl sulfate (10 g), and propylene glycol (120 g) dissolved in water (about 370 g) is added and the resulting mixture is stirred until it congeals.

METHODS OF TREATMENT

[00215] The present compounds may be used as therapeutic agents for the treatment of conditions in mammals that are causally related or attributable to aberrant activity of JAK. In particular, conditions related to aberrant activity of one or more of JAK1, JAK2, JAK3 and/or TYK2. Accordingly, a compound of the invention and pharmaceutical compositions of this invention find use as therapeutics for preventing and/or treating diseases involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g. diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6 and transplantation

rejection (e.g. organ transplant rejection). Inhibitors of JAK can also find application in the treatment of proliferative diseases. In particular the inhibitors of JAK find application in the treatment of cancers, especially leukaemias and solid tumours (e.g. uterine leiomyosarcoma, prostate cancer). In particular the conditions are selected from inflammatory conditions, conditions related to cartilage and/or joint degradation in mammals including humans. In another embodiment, the compounds and pharmaceutical compositions of this invention find use as therapeutics for preventing and/or treating proliferative disorders in mammals, including humans. In a specific embodiment the compound of the invention and pharmaceutical compositions thereof find use as therapeutics for preventing and/or treating cancer in mammals including humans.

[00216] In additional method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with condition involving an immune response or an autoimmune disease. The methods comprise administering an effective condition-treating or condition-preventing amount of one or more of the pharmaceutical compositions or a compound of the invention herein described. In a specific embodiment, the autoimmune disease is selected from COPD, asthma, systemic lupus erythematosis, type I diabetes mellitus and inflammatory bowel disease.

[00217] In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of a condition involving an autoimmune response or an autoimmune disease. In a specific embodiment, the autoimmune disease is selected from COPD, asthma, systemic lupus erythematosis, type I diabetes mellitus and inflammatory bowel disease.

[00218] In a method of treatment aspect, this invention provides a method of treatment, prevention or prophylaxis in a mammal susceptible to or afflicted with diseases involving impairment of cartilage turnover (e.g. a condition associated with, or diseases involving the anabolic stimulation of chondrocytes), for example, osteoarthritis, psoriatic arthritis, juvenile rheumatoid arthritis, gouty arthritis, septic or infectious arthritis, reactive arthritis, reflex sympathetic dystrophy, algodystrophy, Tietze syndrome or costal chondritis, fibromyalgia, osteochondritis, neurogenic or neuropathic arthritis, arthropathy, endemic forms of arthritis like osteoarthritis deformans endemica, Mseleni disease and Handigodu disease; degeneration resulting from fibromyalgia, systemic lupus erythematosus, scleroderma and ankylosing spondylitis, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described.

[00219] In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of diseases involving impairment of cartilage turnover (e.g. a condition associated with, or diseases involving the anabolic stimulation of chondrocytes), for example, osteoarthritis, psoriatic arthritis, juvenile rheumatoid arthritis, gouty arthritis, septic or infectious arthritis, reactive arthritis, reflex sympathetic dystrophy, algodystrophy, Tietze syndrome or costal chondritis, fibromyalgia, osteochondritis, neurogenic or neuropathic arthritis, arthropathy, endemic forms of arthritis like osteoarthritis deformans endemica, Mseleni disease and Handigodu disease; degeneration resulting from fibromyalgia, systemic lupus erythematosus, scleroderma and ankylosing spondylitis.

[00220] The present invention also provides a method of treatment of congenital cartilage malformations, including hereditary chondrolysis, chondrodysplasias and pseudochondrodysplasias, in particular, but without limitation, microtia, anotia, metaphyseal chondrodysplasia, and related disorders, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described.

[00221] In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of congenital cartilage malformations, including hereditary chondrolysis, chondrodysplasias and pseudochondrodysplasias, in particular, but without limitation, microtia, anotia, metaphyseal chondrodysplasia, and related disorders.

[00222] In another aspect, this invention provides a method of treating a mammal susceptible to or afflicted with a condition involving inflammation, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described. In additional method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with diseases and disorders which are mediated by or result in inflammation such as, for example rheumatoid arthritis and osteoarthritis, allergic airway disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure),, and related diseases involving cartilage, such as that of the joints, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described. In a specific embodiment, the condition involving inflammation is selected from rheumatoid arthritis, osteoarthritis, allergic airway disease (e.g. asthma) and inflammatory bowel diseases. The methods comprise administering an effective condition-treating or condition-preventing amount of one or more of the pharmaceutical compositions or compounds herein described.

[00223] In another aspect, this invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of a condition involving inflammation. In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of diseases and disorders which are mediated by or result in inflammation such as, for example rheumatoid arthritis and osteoarthritis, allergic airway disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), and related diseases involving cartilage, such as that of the joints. In a specific embodiment, the condition involving inflammation is selected from rheumatoid arthritis, osteoarthritis, allergic airway disease (e.g. asthma) and inflammatory bowel diseases.

[00224] In further method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with a proliferative disease, in particular cancer (e.g. solid tumors such as uterine leiomyosarcoma or prostate cancer), leukemia (e.g. AML or ALL), multiple myeloma and/or psoriasis, which methods comprise administering a therapeutically effective amount of a compound of the

invention, or one or more of the pharmaceutical compositions herein described. In further method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with cancer (e.g. solid tumors such as uterine leiomyosarcoma or prostate cancer) and/or leukemias, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described.

[00225] In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of a proliferative disease, in particular cancer (e.g. solid tumors such as uterine leiomyosarcoma or prostate cancer), leukemia (e.g. AML or ALL), multiple myeloma and/or psoriasis. In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of cancer (e.g solid tumors such as uterine leiomyosarcoma or prostate cancer) and/or leukemias.

[00226] In further method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with diseases associated with hypersecretion of IL6, in particular Castleman's disease or mesangial proliferative glomerulonephritis, which methods comprise administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described.

[00227] In another aspect the present invention provides a compound of the invention for use in the treatment, prevention or prophylaxis of diseases associated with hypersecretion of IL6, in particular Castleman's disease or mesangial proliferative glomerulonephritis.

[00228] In further method of treatment aspects, this invention provides methods of treating a mammal susceptible to or afflicted with transplantation rejection, which methods comprise administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described. In a specific embodiment, the invention provides methods of treating organ transplant rejection, which method comprises administering a therapeutically effective amount of a compound of the invention, or one or more of the pharmaceutical compositions herein described.

[00229] In another aspect the present invention provides the compound of the invention for use in the treatment, prevention or prophylaxis of transplantation rejection. In a specific embodiment, the invention provides methods of treating organ transplant rejection.

[00230] As a further aspect of the invention there is provided the present compounds for use as a pharmaceutical especially in the treatment or prevention of the aforementioned conditions and diseases. Also provided herein is the use of the present compounds in the manufacture of a medicament for the treatment or prevention of one of the aforementioned conditions and diseases.

[00231] A particular regimen of the present method comprises the administration to a subject in suffering from a disease involving inflammation, of an effective amount of a compound of the invention for a period of time sufficient to reduce the level of inflammation in the patient, and preferably terminate, the processes responsible for said inflammation. A special embodiment of the method comprises administering of an effective amount of a compound of the invention to a subject patient suffering from or susceptible to the development of rheumatoid arthritis, for a period of time sufficient to reduce or prevent,

respectively, inflammation in the joints of said patient, and preferably terminate, the processes responsible for said inflammation.

[00232] A further particular regimen of the present method comprises the administration to a subject in suffering from a disease condition characterized by cartilage or joint degradation (e.g. osteoarthritis) of an effective amount of a compound of the invention for a period of time sufficient to reduce, and preferably terminate, the self-perpetuating processes responsible for said degradation. A special embodiment of the method comprises administering of an effective amount of a compound of the invention to a subject patient suffering from or susceptible to the development of osteoarthritis, for a period of time sufficient to reduce or prevent, respectively, cartilage degradation in the joints of said patient, and preferably terminate, the self-perpetuating processes responsible for said degradation. In a particular embodiment said compounds exhibit cartilage anabolic and/or anti-catabolic properties.

[00233] Injection dose levels range from about 0.1 mg/kg/hour to at least 10 mg/kg/hour, all for from about 1 to about 120 hours and especially 24 to 96 hours. A preloading bolus of from about 0.1 mg/kg to about 10 mg/kg or more may also be administered to achieve adequate steady state levels. The maximum total dose is not expected to exceed about 2 g/day for a 40 to 80 kg human patient.

[00234] For the prevention and/or treatment of long-term conditions, such as degenerative conditions, the regimen for treatment usually stretches over many months or years so oral dosing is preferred for patient convenience and tolerance. With oral dosing, one to five and especially two to four and typically three oral doses per day are representative regimens. Using these dosing patterns, each dose provides from about 0.01 to about 20 mg/kg of the compound of the invention, with particular doses each providing from about 0.1 to about 10 mg/kg and especially about 1 to about 5 mg/kg.

[00235] Transdermal doses are generally selected to provide similar or lower blood levels than are achieved using injection doses.

[00236] When used to prevent the onset of an inflammatory condition, the compounds of this invention will be administered to a patient at risk for developing the condition, typically on the advice and under the supervision of a physician, at the dosage levels described above. Patients at risk for developing a particular condition generally include those that have a family history of the condition, or those who have been identified by genetic testing or screening to be particularly susceptible to developing the condition.

[00237] The compounds of the invention can be administered as the sole active agent or they can be administered in combination with other agents, including other compounds that demonstrate the same or a similar therapeutic activity, and that are determined to safe and efficacious for such combined administration. In a specific embodiment, co-administration of two (or more) agents allows for significantly lower doses of each to be used, thereby reducing the side effects seen.

[00238] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of a disease involving inflammation; particular agents include, but are not limited to, immunoregulatory agents e.g. azathioprine, corticosteroids (e.g. prednisolone or dexamethasone), cyclophosphamide, cyclosporin A, tacrolimus, Mycophenolate Mofetil,

muromonab-CD3 (OKT3, e.g. Orthocolone®), ATG, aspirin, acetaminophen, ibuprofen, naproxen, and piroxicam.

[00239] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of arthritis (e.g. rheumatoid arthritis); particular agents include but are not limited to analgesics, non-steroidal anti-inflammatory drugs (NSAIDS), steroids, synthetic DMARDS (for example but without limitation methotrexate, leflunomide, sulfasalazine, auranofin, sodium aurothiomalate, penicillamine, chloroquine, hydroxychloroquine, azathioprine, and ciclosporin), and biological DMARDS (for example but without limitation Infliximab, Etanercept, Adalimumab, Rituximab, and Abatacept).

[00240] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of proliferative disorders; particular agents include but are not limited to: methotrexate, leukovorin, adriamycin, prenisone, bleomycin, cyclophosphamide, 5-fluorouracil, paclitaxel, docetaxel, vincristine, vinblastine, vinorelbine, doxorubicin, tamoxifen, toremifene, megestrol acetate, anastrozole, goserelin, anti- HER2 monoclonal antibody (e.g. Herceptin™), capecitabine, raloxifene hydrochloride, EGFR inhibitors (e.g. Iressa®, Tarceva™, Erbitux™), VEGF inhibitors (e.g. Avastin™), proteasome inhibitors (e.g. Velcade™), Glivec® or hsp90 inhibitors (e.g. 17-AAG). Additionally, a compound of the invention may be administered in combination with other therapies including, but not limited to, radiotherapy or surgery. In a specific embodiment the proliferative disorder is selected from cancer, myeloproliferative disease or leukaemia.

[00241] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of autoimmune diseases, particular agents include but are not limited to: glucocorticoids, cytostatic agents (e.g. purine analogs), alkylating agents, (e.g nitrogen mustards (cyclophosphamide), nitrosoureas, platinum compounds, and others), antimetabolites (e.g. methotrexate, azathioprine and mercaptopurine), cytotoxic antibiotics (e.g. dactinomycin anthracyclines, mitomycin C, bleomycin, and mithramycin), antibodies(e.g., anti-CD20, anti-CD25 or anti-CD3 (OTK3) monoclonal antibodies, Atgam® and Thymoglobuline®), cyclosporin, tacrolimus, rapamycin (sirolimus), interferons (e.g. IFN-β), TNF binding proteins (e.g. infliximab (Remicade), etanercept (Enbrel), or adalimumab (Humira)), mycophenolate, Fingolimod, Myriocin.

[00242] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of transplantation rejection, particular agents include but are not limited to: calcineurin inhibitors (e.g. cyclosporin or tacrolimus (FK506)), mTOR inhibitors (e.g. sirolimus, everolimus), anti-proliferatives (e.g. azathioprine, mycophenolic acid), corticosteroids (e.g. prednisolone, hydrocortisone), Antibodies (e.g. monoclonal anti-IL-2Rα receptor antibodies, basiliximab, daclizumab), polyclonal anti-T-cell antibodies (e.g. anti-thymocyte globulin (ATG), anti-lymphocyte globulin (ALG)).

[00243] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of asthma and/or rhinitis and/or COPD, particular agents include but are not limited to: beta$_2$-adrenoceptor agonists (e.g. salbutamol, levalbuterol, terbutaline

and bitolterol.), epinephrine (inhaled or tablets), anticholinergics (e.g. ipratropium bromide), glucocorticoids (oral or inhaled) Long-acting β_2-agonists (e.g. salmeterol, formoterol, bambuterol, and sustained-release oral albuterol), combinations of inhaled steroids and long-acting bronchodilators (e.g. fluticasone/salmeterol, budesonide/formoterol), leukotriene antagonists and synthesis inhibitors (e.g. montelukast, zafirlukast and zileuton), inhibitors of mediator release (e.g. cromoglycate and ketotifen), biological regulators of IgE response (e.g. omalizumab), antihistamines (e.g. ceterizine, cinnarizine, fexofenadine), vasoconstrictors (e.g. oxymethazoline, xylomethazoline, nafazoline and tramazoline).

[00244] Additionally, a compound of the invention may be administered in combination with emergency therapies for asthma and/or COPD, such therapies include oxygen or heliox administration, nebulized salbutamol or terbutaline (optionally combined with an anticholinergic (e.g. ipratropium), systemic steroids (oral or intravenous, e.g. prednisone, prednisolone, methylprednisolone, dexamethasone, or hydrocortisone), intravenous salbutamol, nonspecific beta-agonists, injected or inhaled (e.g. epinephrine, isoetharine, isoproterenol, metaproterenol), anticholinergics (IV or nebulized, e.g. glycopyrrolate, atropine, ipratropium), methylxanthines (theophylline, aminophylline, bamiphylline), inhalation anesthetics that have a bronchodilatory effect (e.g. isoflurane, halothane, enflurane), ketamine, intravenous magnesium sulfate.

[00245] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of IBD, particular agents include but are not limited to: glucocorticoids (e.g. prednisone, budesonide) synthetis disease modifying, immunomodulatory agents (e.g. methotrexate, leflunomide, sulfasalazine, mesalazine, azathioprine, 6-mercaptopurine and ciclosporin) and biological disease modifying, immunomodulatory agents (infliximab, adalimumab, rituximab, and abatacept).

[00246] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of SLE, particular agents include but are not limited to: Disease-modifying antirheumatic drugs (DMARDs) such as antimalarials (e.g. plaquenil, hydroxychloroquine), immunosuppressants (e.g. methotrexate and azathioprine), cyclophosphamide and mycophenolic acid; immunosuppressive drugs and analgesics, such as nonsteroidal anti-inflammatory drugs, opiates (e.g. dextropropoxyphene and co-codamol), opioids (e.g. hydrocodone, oxycodone, MS Contin, or methadone) and the fentanyl duragesic transdermal patch.

[00247] In one embodiment, a compound of the invention is co-administered with another therapeutic agent for the treatment and/or prevention of psoriasis, particular agents include but are not limited to: topical treatments such as bath solutions, moisturizers, medicated creams and ointments containing coal tar, dithranol (anthralin), corticosteroids like desoximetasone (Topicort), fluocinonide, vitamin D_3 analogues (for example, calcipotriol), Argan oiland retinoids (etretinate, acitretin, tazarotene), systemic treatments such as methotrexate, cyclosporine, retinoids, tioguanine, hydroxyurea, sulfasalazine, mycophenolate mofetil, azathioprine, tacrolimus, fumaric acid esters or biologics such as Amevive, Enbrel, Humira, Remicade, Raptiva and ustekinumab (a IL-12 and IL-23 blocker). Additionally, a

compound of the invention may be administered in combination with other therapies including, but not limited to phototherapy, or photochemotherapy (e.g. psoralen and ultraviolet A phototherapy (PUVA)).

[00248] By co-administration is included any means of delivering two or more therapeutic- agents to the patient as part of the same treatment regime, as will be apparent to the skilled person. Whilst the two or more agents may be administered simultaneously in a single formulation this is not essential. The agents may be administered in different formulations and at different times.

GENERAL SYNTHETIC PROCEDURES

General

[00249] The compounds of the invention can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or particular process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[00250] Additionally, as will be apparent to those skilled in the art, conventional protecting groups may be necessary to prevent certain functional groups from undergoing undesired reactions. The choice of a suitable protecting group for a particular functional group as well as suitable conditions for protection and deprotection are well known in the art. For example, numerous protecting groups, and their introduction and removal, are described in T. W. Greene and P. G. M. Wuts, *Protecting Groups in Organic Synthesis*, Second Edition, Wiley, New York, 1991, and references cited therein.

[00251] The following methods are presented with details as to the preparation of representative bicycloheteroaryls that have been listed hereinabove. The compounds of the invention may be prepared from known or commercially available starting materials and reagents by one skilled in the art of organic synthesis.

[00252] All reagents were of commercial grade and were used as received without further purification, unless otherwise stated. Commercially available anhydrous solvents were used for reactions conducted under inert atmosphere. Reagent grade solvents were used in all other cases, unless otherwise specified. Column chromatography was performed on silica gel 60 (35-70 μm). Thin layer chromatography was carried out using pre-coated silica gel F-254 plates (thickness 0.25 mm). 1H NMR spectra were recorded on a Bruker DPX 400 NMR spectrometer (400 MHz). Chemical shifts (d) for 1H NMR spectra are reported in parts per million (ppm) relative to tetramethylsilane (d 0.00) or the appropriate residual solvent peak, i.e. CHCl3 (d 7.27), as internal reference. Multiplicities are given as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br). Coupling constants (J) are given in Hz. Electrospray MS spectra were obtained on a Micromass platform LC/MS spectrometer. Column Post-synthesis, compounds that required preparative HPLC purification were purified using reverse phase HPLC using a Waters Fractionlynx preparative HPLC system (2525 pump, 2996 UV/VIS detector, 2767 liquid handler). The Waters 2767 liquid handler acted as both auto-sampler and fraction collector.

[00253] The column used for the preparative purification of the compounds was a Waters Sunfire OBD 5 μm 19 × 100 mm unless otherwise stated.

[00254] The generic gradient used was 95% water / 5% ACN for 1 min to 5% water / 95% ACN over 5 min then held at 95% ACN for 4.0 min. The solvent mixture was then returned to the initial conditions over 0.5 min. A flow rate of 20 ml/min is used.

[00255] All compounds were screened analytically prior to the purification step. Each sample was run under both acidic and basic conditions (0.5ul injection, 5/95 gradient for 5 minutes). A decision was then made by the analyst as to what pH and which gradient to use depending on where the desired product elutes and the separation achieved.

[00256] The modifiers used under acidic/basic conditions were formic acid (0.1%) and ammonium bicarbonate (10mM) respectively.

[00257] The purification was controlled by Waters Fractionlynx software through monitoring at 210-400nm and triggered a threshold collection value at 260nm and the presence of target molecular ion as observed under APi conditions. Collected fractions were analysed by LCMS (Waters Alliance 2790 sampler with Micromass ZQ). The fractions that contained the desired product were concentrated by vacuum centrifugation and the resultant residue dried by freeze-drying. Please note a more focused gradient may have been used for the more challenging separations.

[00258] Some of the compounds may have gone through a second purification process in order to achieve the required purity due to complex mixtures.

GENERAL SYNTHETIC PROCEDURES

General

[00259] The compounds of the invention can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or particular process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[00260] Additionally, as will be apparent to those skilled in the art, conventional protecting groups may be necessary to prevent certain functional groups from undergoing undesired reactions. The choice of a suitable protecting group for a particular functional group as well as suitable conditions for protection and deprotection are well known in the art. For example, numerous protecting groups, and their introduction and removal, are described in T. W. Greene and P. G. M. Wuts, *Protecting Groups in Organic Synthesis*, Second Edition, Wiley, New York, 1991, and references cited therein.

[00261] The following methods are presented with details as to the preparation of representative bicycloheteroaryls that have been listed hereinabove. The compounds of the invention may be prepared from known or commercially available starting materials and reagents by one skilled in the art of organic synthesis.

[00262] All reagents were of commercial grade and were used as received without further purification, unless otherwise stated. Commercially available anhydrous solvents were used for reactions conducted under inert atmosphere. Reagent grade solvents were used in all other cases, unless otherwise specified. Column chromatography was performed on silica gel 60 (35-70 μm). Thin layer chromatography was carried out using pre-coated silica gel F-254 plates (thickness 0.25 mm). 1H NMR spectra were recorded on a Bruker DPX 400 NMR spectrometer (400 MHz). Chemical shifts (d) for 1H NMR spectra are reported in parts per million (ppm) relative to tetramethylsilane (d 0.00) or the appropriate residual solvent peak, i.e. CHCl3 (d 7.27), as internal reference. Multiplicities are given as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br). Coupling constants (J) are given in Hz. Electrospray MS spectra were obtained on a Micromass platform LC/MS spectrometer. Column Used for all LCMS analysis: Waters Acquity UPLC BEH C18 1.7μm, 2.1mm ID x 50mm L (Part No.186002350)). Preparative HPLC :Waters XBridge Prep C18 5μm ODB 19mm ID x 100mm L (Part No.186002978). All the methods are using MeCN/H_2O gradients. H_2O contains either 0.1% TFA or 0.1% NH_3.

[00263] List of abbreviations used in the experimental section:

DCM	Dichloromethane
DiPEA	N,N-diisopropylethylamine
MeCN	Acetonitrile
BOC	tert-Butyloxy-carbonyl
MF	N,N-dimethylformamide
Cat.	Catalytic amount
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
NMR	Nuclear Magnetic Resonnance
DMSO	Dimethylsulfoxide
LC-MS	Liquid Chromatography-Mass Spectrometry
Ppm	part-per-million
Pd/C	Palladium on Charcoal 10%
PMB	Para-methoxy-benzyl
PyBOP	benzotriazol-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluoroborate
EtOAc	ethyl acetate
APCI	atmospheric pressure chemical ionization

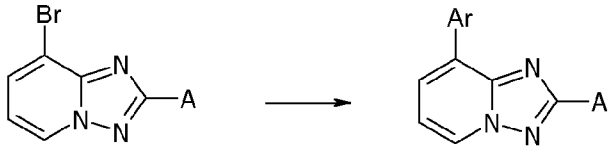
Rt	retention time
s	singlet
br s	broad singlet
m	multiplet
min	minute
mL	milliliter
μL	microliter
g	gram
mg	milligram
$PdCl_2dppf$	[1,1'-Bis(diphenylphosphino)ferrocene] dichloropalladium(II)
TEA	Triethylamine
MMP	Matrix Metallo Proteinase
NHAC	Normal Human Articular Chondrocytes
shRNA	short hairpin RNA
RNA	Ribonucleic acid
Ad-siRNA	Adenoviral encoded siRNA

PBST	Phosphate buffered saline with Tween 3.2 mM Na2HPO4, 0.5 mM KH2PO4, 1.3 mM KCl, 135 mM NaCl, 0.05% Tween 20, pH 7.4
APMA	4-aminophenylmercuric acetate
DMEM	Dulbecco's Modified Eagle Medium
FBS	Fetal bovine serum
hCAR	human cellular adenovirus receptor

3- MOI	multiplicity of infection of 3
dNTP	deoxyribonucleoside triphosphate
QPCR	quantitative polymerase chain reaction
cDNA	copy deoxyribonucleic acid
GAPDH	Glyceraldehyde phosphate dehydrogenase

General Synthetic Methods

Method A:



1 2

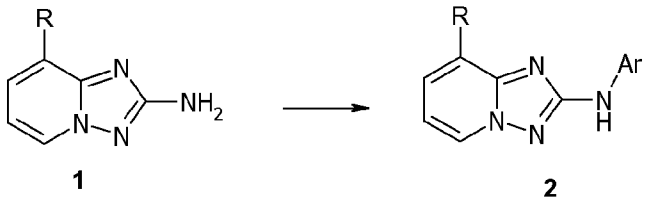
Wherein A= NH_2 or NHAr.

[00264] An appropriate aryl substituted boronic acid derivative (2eq.) is added to a solution of -8-bromo-triazolopyridine derivative in 1,4-dioxane/water (5:1) (or EtOH). K_2CO_3 (2 eq.) and $PdCl_2dppf$ (5%) (or $Pd(Ph_3)_4$) are added to the mixture. The resulting mixture is heated in a microwave oven at 110 to 140°C for 10-45 min or heated in an oil bath at 90°C for 4 to 16 h until the reaction goes to completion (monitored by LCMS). Water is added and the mixture is extracted with ethyl acetate. The organic layers are combined, dried over anhydrous $MgSO_4$ and evaporated in vacuo to yield the crude product. The crude product is then purified by flash chromatography to give the corresponding 2-amino-8-Ar-triazolopyridine derivative (2). (The compounds may be purified by preparative HPLC). If the compound is not soluble in EtOAc, after cooling to room temperature, the reaction mixture is diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer is separated and concentrated *in vacuo*. (The compounds may be further purified by preparative HPLC).

[00265] Alternatively, a mixture of 8-bromo-triazolopyridine (1 eq), the boronic ester (1.2 eq), PS-$Pd(PPh_3)_4$ (polymer supported $Pd(PPh_3)_4$, 0.03 eq) and K_2CO_3 (1 M in H_2O, 1.2 eq) in EtOH in a sealed 10 mL tube is heated at 110 °C for 10 min under microwave irradiation. Water is added and the mixture is extracted with ethyl acetate. The organic layers are combined, dried over anhydrous $MgSO_4$

and evaporated in vacuo to yield the crude product. The crude product is then purified by flash chromatography to give the corresponding 2-amino-8-Ar-triazolopyridine derivative (2). (The compounds may be purified by preparative HPLC). If the compound is not soluble in EtOAc,,after cooling to room temperature, the reaction mixture is diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer is separated and concentrated *in vacuo*. (The compounds may be further purified by preparative HPLC).

Method B:

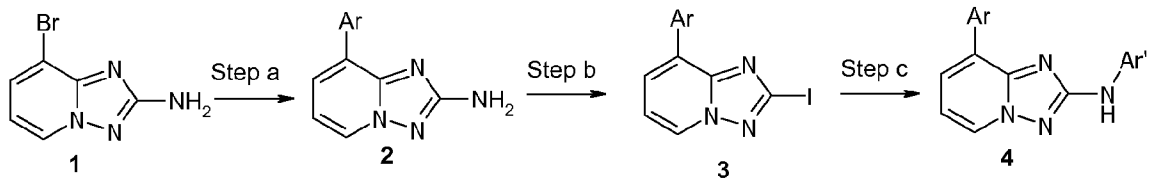


Wherein R= Aryl or Br

[00266] A mixture of the above 2-amino-8-R-triazolopyridine derivative (1) (1 eq), Cs_2CO_3 (5eq), $Pd(OAc)_2$ (0.1 eq), BINAP (0.1 eq) (or Xantphos), an appropriate aryl-halogen (wherein the halogen is selected from iodo or bromo) derivative (1.5 eq) and 1,4-dioxane is sonicated for 5 minutes under nitrogen. Afterwards, the reaction is left in a sealed tube at 120°C or in a flasked equipped with a cooling system for 16 hrs. The crude mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhydrous magnesium sulfate. The organic solvent is removed under high vacuum to yield the crude product. If the compound is not soluble in EtOAc, after cooling to room temperature, the reaction mixture is diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer is separated and concentrated *in vacuo*.The crude product is then purified by column chromatography if required to give the corresponding 2-Ar'-8-bromo-triazolopyridine derivative (2).

[00267] Alternatively, to a solution of an appropriate Aryl-halogen (wherein the halogen is selected from iodo or bromo) derivative (1.5 eq) and 2-amino-8-R-triazolopyridine derivative (1 eq) in dioxane (5 mL) are added $Pd_2(dba)_3$ (0.1 eq), Xantphos (0.1 eq) and Cs_2CO_3 (2 eq.). The reaction mixture is degassed by sonication under a stream of N_2 for 10 min and then stirred at 90 °C for 16 h. The reaction mixture is diluted with CH_2Cl_2/MeOH (1:1) filtered through Celite and the filtrate is concentrated *in vacuo*. The crude product is then purified by flash column chromatography or preparative HPLC.

Method C:



Wherein Ar', Ar = Aryl

Step a:

[00268] This compound may be prepared using Method A.

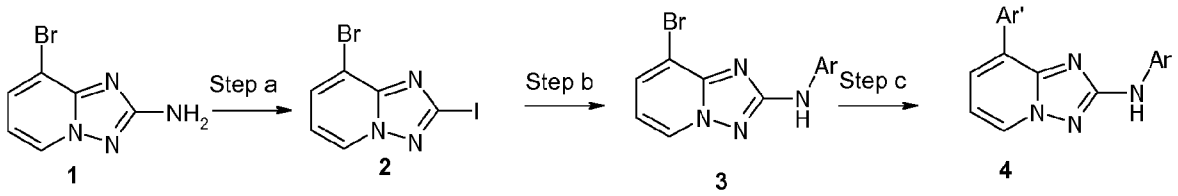
Step b. Preparation of 8-Ar-2-iodo-triazolopyridine derivatives

[00269] A mixture of the above 2-amino-8-Ar-triazolopyridine derivative (1) (1 eq.) and $NaNO_2$ in DMSO (2eq. DMSO) is treated dropwise with a solution of 57% aqueous HI (10 eq.) in DMSO at 35 °C with agitation. The mixture is stirred at 35 °C for 10 minutes or until the reaction goes to completion (monitored by LCMS), and then it is transferred to a saturated K_2CO_3 solution. The reaction mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhydrous magnesium sulfate. The organic solvent is removed under high vacuum to yield the crude product. The crude product is then purified by flash chromatography to give the corresponding 8-Ar-2-iodo-triazolopyridine derivative (**2**).

Step c. Preparation of 2-Ar'-8-Ar-triazolopyridine derivatives

[00270] A mixture of the above 8-Ar-2-iodo-triazolopyridine derivative (2) (1 eq), Cs_2CO_3 (5eq), $Pd(OAc)_2$ ($Pd_2(dba)_3$ may also equally be used) (0.1 eq), BINAP (0.1 eq) (or Xantphos), an appropriate Ar'-NH_2 derivative (1.5 eq) and toluene (or 1, 4-dioxane) is sonicated for 5 minutes under nitrogen. Afterwards, the reaction is left in a sealed tube at 120°C or in a flasked equipped with a cooling system. The crude mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhydrous magnesium sulfate. The organic solvent is removed under high vacuum to yield the crude product. If the compound is not soluble in EtOAc, after cooling to room temperature, the reaction mixture is diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer is separated and concentrated *in vacuo*. The crude product is then purified by preparative HPLC to give the corresponding 2-Ar'-8-Ar-triazolopyridine derivative (**3**).

Method C':



1 2 3 4

Step a. Preparation of 8-R-2-iodo-triazolopyridine derivatives

[00271] A mixture of the above 2-amino-8-Br-triazolopyridine derivative (**1**) (1 eq.) and $NaNO_2$ in DMSO (2eq. in DMSO) is treated dropwise with a solution of 57% aqueous HI (5 eq.) in DMSO at 35 °C with agitation. The mixture is stirred at 35 °C for 10 minutes or until the reaction goes to completion (monitored by LCMS), and then it is transferred to a saturated solution of K_2CO_3. The reaction mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhydrous magnesium sulfate. The organic solvent is removed under high vacuum to yield

the crude product. The crude product is then purified by flash chromatography to give the corresponding 8-Br-2-iodo-triazolopyridine derivative (**2**).

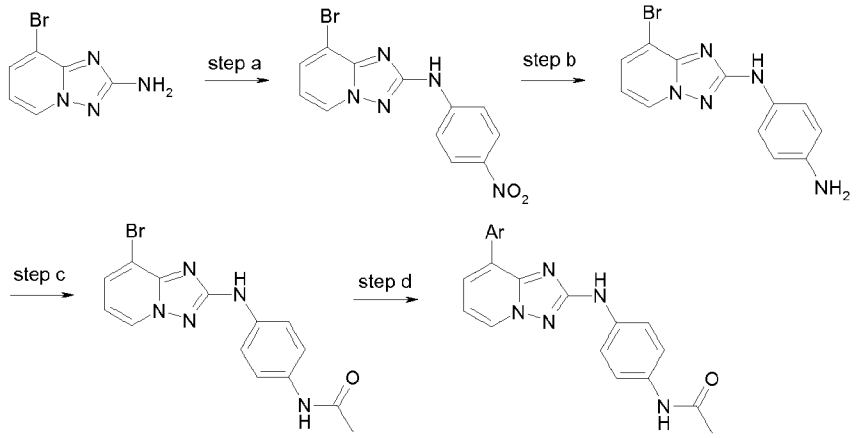
Step b. Preparation of 2-Ar-8-Br-triazolopyridine derivatives

[00272] A mixture of the above 8-bromo-2-iodo-triazolopyridine derivative (**2**) (1 eq), $CsCO_3$ (5eq), $Pd(OAc)_2$ ($Pd_2(dba)_3$ may also equally be used) (0.1 eq), BINAP (0.1 eq) (or Xantphos), an appropriate Ar'-NH_2 derivative (1.5 eq) and toluene (or 1,4-dioxan) is sonicated for 5 minutes under nitrogen. Afterwards, the reaction is left in a sealed tube at 120°C or in a flasked equipped with a cooling system. The crude mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhyd. magnesium sulfate. The organic solvent is removed under high vacuum to yield the crude product. If the compound is not soluble in EtOAc, after cooling to room temperature, the reaction mixture is diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer is separated and concentrated *in vacuo*. The crude product is then purified by preparative HPLC to give the corresponding 2-Ar-8-Bromo-triazolopyridine derivative (**3**).

Step c:

[00273] The same protocol as the one described in Method A can be used.

Method D:



Step a: (8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-nitro-phenyl)-amine

[00274] This compound may be prepared using Method B.

Step b:

[00275] (8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-nitro-phenyl)-amine (4.2 g) and $SnCl_2$ (5eq.) were mixed together in ethanol (50 mL). The reaction mixture was stirred at 80°C for 4 hours. The resulting solution was filtered and the mother liquor was basified with NaOH 1N and extracted with EtOAc. The organic layer was dried and evaporated to afford 800 mg of a first batch. The filtrated green solid was taken up in NaOH 1N and extracted with EtOAc. The organic layer was dried over $MgSO_4$

and evaporated to afford 2.8 g of the reduced compound with a total yield of 65%. The compound was used in the next step without further purification.

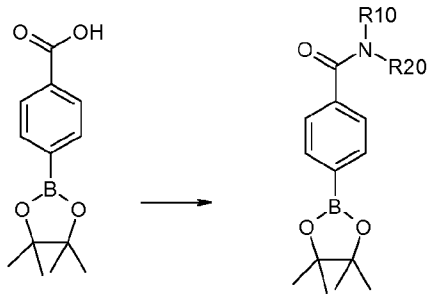
Step c: N-[4-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-acetamide

[00276] Acetic anhydride (1eq.) is added dropwise to a solution of N-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-benzene-1,4-diamine (2.8 g) in THF (20mL) at 0°C. The reaction mixture is stirred at room temperature for 2 hours. The reaction mixture is quenched with a solution of $NaHCO_3$ sat. and extracted with EtOAc. The organic layer is dried over $MgSO_4$ and concentrated to afford 1.6 g of a residue containing the expected acetamide. Water is added to the resulting solid to obtain a suspension of the title compound which is then filtered to afford 1.45 g of N-[4-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-acetamide

Step d:

[00277] [4 -[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-acetamide derivative is prepared using Method A

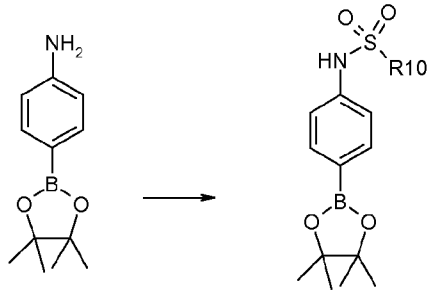
Method E:



Preparation of the para amide phenyl boronic ester derivatives

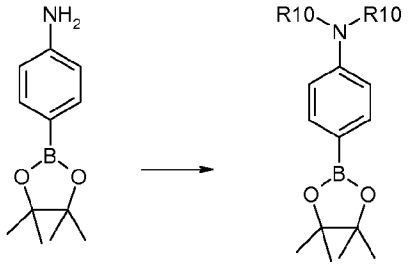
[00278] 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzoic acid (1 eq.), EDCI (1.5 eq.), HOBt (1.5eq.) and Et_3N (2eq.) are mixed together in THF at room temperature. An appropriate amine (1.1eq.) is added to the solution and the reaction mixture is stirred at room temperature for 16hrs. Water is added to the reaction. The organic phases are isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. In some cases, purification by flash chromatography may be required.

Method F:



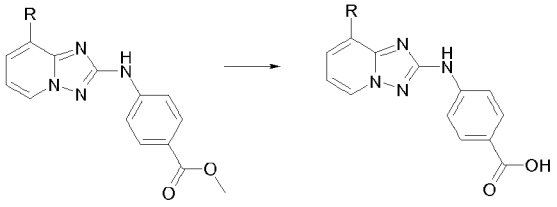
[00279] An appropriate sulfonyl chloride (1.2 eq.) is added to a solution of 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (1 eq.) and DMAP (1.2eq.) in DCM at room temperature. The resulting solution is stirred for 16hrs. Water is added. The organic phase is separated, dried over $MgSO_4$, filtered and evaporated to afford the expected product. If some cases, purification by flash chromatography is required.

Method G:



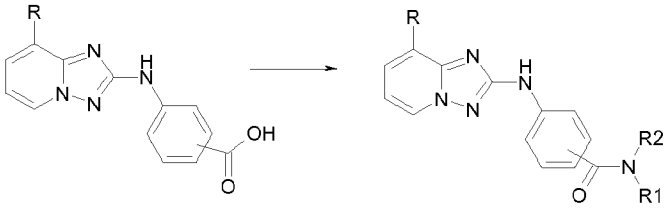
[00280] $NaCNBH_3$ (1.1 eq.) is added to a solution of 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenylamine (1eq.) and an appropriate aldehyde in methanol at room temperature. The reaction is stirred at room temperature for 16hrs. The volatiles are removed under vacuum. Water and EtOAc are added to the residue. The organic phase is separated, dried over $MgSO_4$, filtered and evaporated under vacuum. The crude product is purified by flash chromatography.

Method H



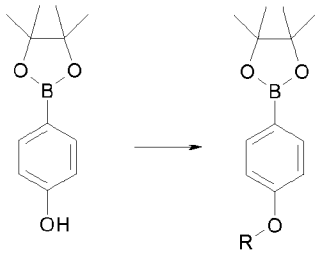
[00281] 3 or 4-[8-(R-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid methyl ester and LiOH (2eq.) are mixed together in acetone at room temperature. The reaction is heated at 70°C for 16 hrs. Acetone is evaporated. Water is added and the pH is acidified to pH=1 with HCl solution (1N). The precipitate is filtered, dried to afford the expected benzoic acid in quantative yield.

Method I:



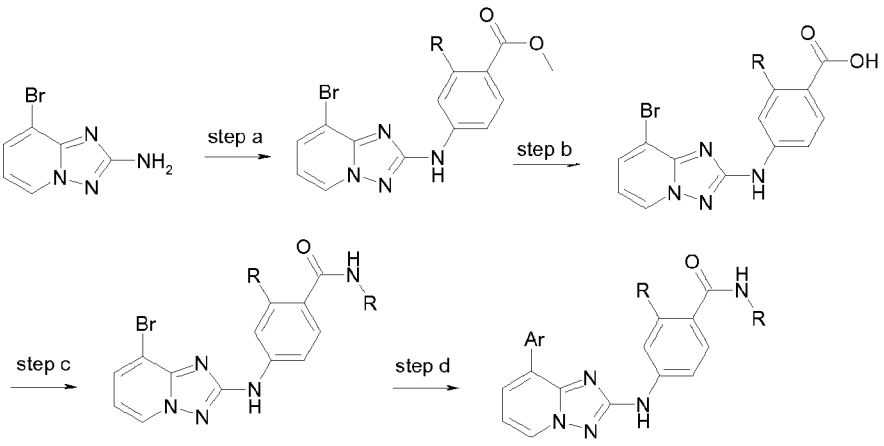
[00282] 4 or 3-[8-R-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid, EDCI (or DCI or HATU) (1.5 eq.), HOBt (1.5eq.) (not present if HATU is used) and Et_3N (2eq.) are mixed in DMF (or THF) at room temperature. An appropriate amine (1.1eq.) is added to the solution and the reaction mixture is stirred at room temperature for 16hrs. Water and EtOAc are added to the reaction. The organic phases is isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by preparative HPLC is required.

Method J:



[00283] To 4-hydroxyphenylboronic acid pinacol ester (1.0 equiv.) in acetone at room temperature are added under argon akylating derivative (1.1 eq.) and cesium carbonate (2 eq.). The reaction mixture is heated for 4 hours at reflux (when the chloro derivative is used a catalytic amount of KI is added to the reaction). The mixture is then cooled to room temperature, the acetone is evaporated. Water is added and the product is extracted with EtOAc). The organic layer is dried over magnesium sulfate, filtered and concentrated to dryness. The resulting residue is purified by chromatography over silica gel to afford the expected boronate ester derivative.

Method K:



Step a:

[00284] This compound may be prepared via Method B.

Step b:

[00285] This compound may be prepared via Method H.

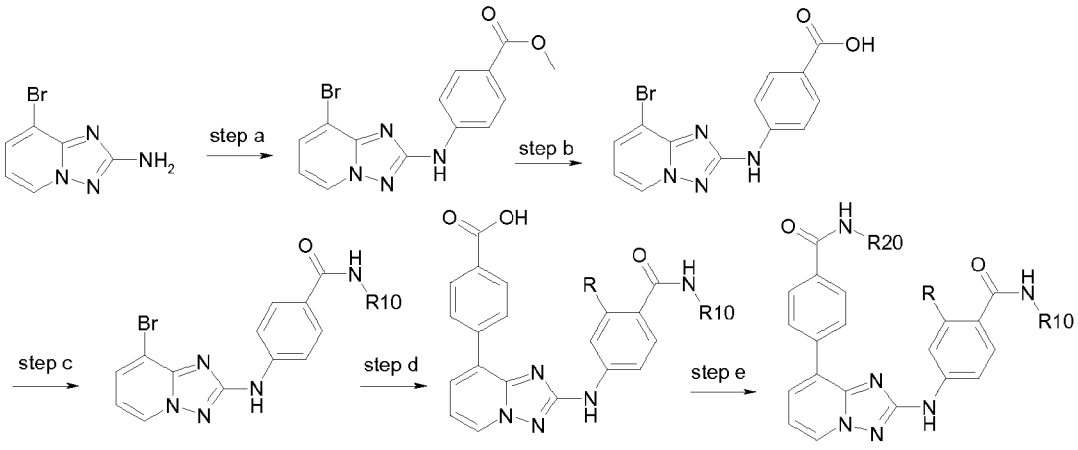
Step c:

[00286] This compound may be prepared via Method I.

Step d:

[00287] This compound may be prepared via Method A.

Method K':



Step a:

[00288] This compound may be prepared via Method B using 4-iodo-benzoic acid ethyl ester.

Step b:

[00289] This compound may be prepared via Method H.

Step c:

[00290] This compound may be prepared via Method I using an appropriate amine.

Step d:

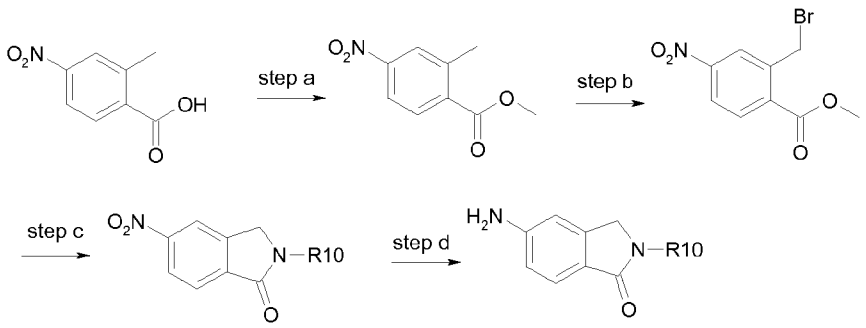
[00291] This compound may be prepared via Method A using 4-carboxyphenylboronic acid.

Step e:

[00292] Benzoic acid derivative, EDCI (or DCI or HATU) (1.5 eq.), HOBt (1.5eq.) (not used with HATU) and Et_3N (2eq.) are mixed in DMF (or THF) at room temperature. An appropriate amine (1.1eq.) is added to the solution and the reaction mixture is stirred at room temperature for 16hrs. Water

is added to the reaction. The organic phases is isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by preparative HPLC is required.

Method L:



Step a:

[00293] A mixture of 2-methyl-4-nitrobenzoic acid (1eq.) iodomethane (1.1 eq.), K_2CO_3 (1.5 eq.), and 10 mL of DMF is stirred for 2hrs at room temperature, then poured into water and extracted with AcOEt. The extract is washed with water and brine, dried over anhydrous $MgSO_4$, and evaporated to afford the expected compound in quantative yield.

Step b:

[00294] A mixture of 2-methyl-4-nitro-benzoic acid methyl ester (1eq.), NBS (1.1 eq.), benzoyl peroxide (0.01 eq.), and 20 mL of carbon tetrachloride is heated at 85°C for 8hrs. Further NBS (0.1 eq.) is added and the whole is is refluxed 1 hrs. The mixture is washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. The residue is purified by flash chromatography to afford the compound.

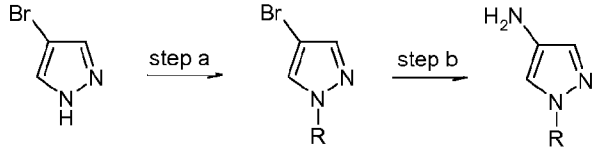
Step c:

[00295] A mixture of 2-Bromomethyl-4-nitro-benzoic acid methyl ester (1eq.) an appropriate amine (1.1 eq.), Et_3N (1.1eq), and 10 mL of methanol is refluxed for 24hrs. The mixture is diluted with EtOAc, washed with HCl (1N) and brine, dried over $MgSO_4$, and evaporated. The residue is purified by flash chromatography.to afford the expected compound.

Step d:

[00296] A mixture of 5-nitro-2,3-dihydro-isoindol-1-one derivative (1eq), 10% Pd-C (0.05 eq) and 10 mL AcOEt is hydrogenated at room temperature for 6hrs. The catalyst is removed by filtration through Celite and the filtrate is evaporated to afford the title compound.

Method M:



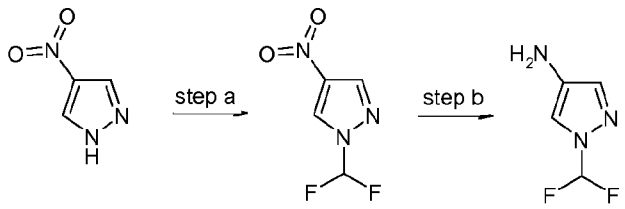
Step a:

[00297] Alkyl-bromide is added to a solution of 4-Bromo-1H-pyrazole (1eq.) and K2CO3 (2eq.) in DMA at room temperature. The solution is stirred for 20hrs. The reaction mixture is poured into water and extracted with AcOEt. The extract is washed with water and brine, dried over anhydrous $MgSO_4$, and evaporated to afford the expected compound. Purification by flash chromatography may be required in some cases.

Step b:

[00298] A mixture of the previous compound (1 eq), NaO*t*-Bu (5eq), $Pd_2(dba)_3$ (0.1 eq), Xantphos (0.1 eq), an appropriate benzophenone imine (1.5 eq) and 1,4-dioxane is sonicated for 5 minutes under nitrogen. Afterwards, the reaction is is allowed to heat at 90°C for 16 hrs. The crude mixture is extracted with ethyl acetate and the extracts are combined, washed with water and dried over anhydrous magnesium sulfate. The organic solvent is removed under vacuum to yield the crude product. The crude product is then purified by flash chromatography.

Method M':



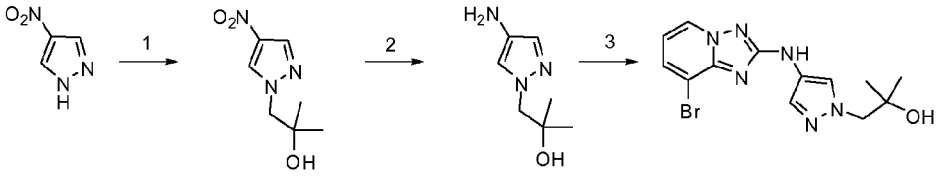
Step a:

[00299] $ClCHF_2$ is added to a solution of 4-nitro-1H-pyrazole and K_2CO_3 in DMF. The reaction is heated at 95°C for 2hrs. The reaction mixture is allowed to cool to room temperature. EtOAc and water were added to the reaction. The organic phase is separated, dried over $MgSO_4$, evaporated under reduced pressure. The crude is used without further purification.

Step b:

[00300] To a solution of 1-difluoromethyl-4-nitro-1H-pyrazole (1 eq.) in ethanol (30 mL) was added 10% Pd/C (cat.). The reaction mixture was stirred at room temperature under pressure of H_2 (40 mbarr) for 16 h. The reaction mixture was filtered through Celite and concentrated under reduced pressure. Purification by flash column chromatography (Gradient, iso-hexanes to 50% EtOAc) gave the desired product.

Method M"



Step a:

[00301] To a solution of 4-nitropyrazole (1.7 g, 15 mmol) in CH_3CN (15 mL) is added DBU (4.5 ml, 30 mmol) and 1,2-epoxy-2-methylpropane (4.3 ml, 48 mmol). The reaction mixture is stirred at 60 °C for 20 h. The solvent removed *in vacuo* and the residue dissolved in ethyl acetate and washed with 1N HCl, water and brine. The organic layer is dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the product which may be used in the next step without further purification.

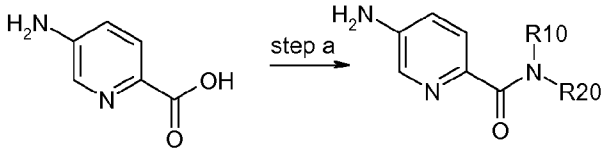
Step b:

[00302] To a solution of *2-methyl-1-(4-nitro-1H-pyrazol-1-yl)propan-2-ol* (1.7 g, 9.19 mmol) in ethanol (30 mL) is added 10% Pd/C (230 mg). The reaction mixture is stirred at room temperature under pressure of H_2 (40 mbarr) for 16 h. The reaction mixture is filtered through Celite and concentrated under reduced pressure. Purification by flash column chromatography (Gradient, iso-hexanes to 50% EtOAc) gives the desired product.

Step c:

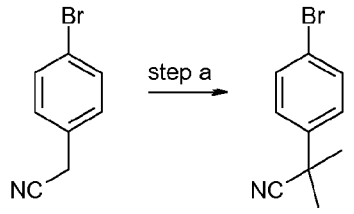
[00303] *8-Bromo-2-iodo-[1,2,4]triazolo[1,5-a]pyridine* (1.18 g, 3.6 mmol,1 eq), *1-(4-amino-1H-pyrazol-1-yl)-2-methylpropan-2-ol* (675 mg, 1.2 eq), $Pd_2(dba)_3$ (99 mg, 0.03 eq), Xantphos (125 mg, 0.06 eq) and Cs_2CO_3 (1.64 g, 1.4 eq) are suspended in degassed dioxane. The reaction mixture is further degassed by sonicating under a stream of N_2 for 5 min and then it is heated for 16 h at 100 °C. The reaction mixture is diluted with CH_2Cl_2/MeOH (1:1) filtered through Celite and the filtrate is concentrated in *vacuo*. Purification flash column chromatography (Gradient, CH_2Cl_2/ CH_2Cl_2-MeOH 15%) yields the target compound as a yellow solid (876 mg, 69%).

Method N:



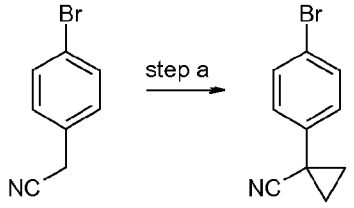
[00304] 5-Amino-pyridine-2-carboxylic acid (1eq.), EDCI (or HATU) (1.5 eq.), HOBt (1.5eq.) (not used with HATU) and Et_3N (2eq.) are mixed in DMF (or THF) at room temperature. An appropriate amine (1.1eq.) is added to the solution and the reaction mixture is stirred at room temperature for 16hrs. Water is added to the reaction. The organic phases is isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. In same cases, purification by flash chromatography is required.

Method O:



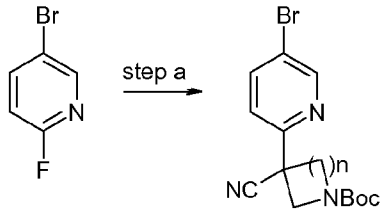
[00305] NaH (2.5 eq.) is added to (4-Bromo-phenyl)-acetonitrile (1eq) in DMF at 0°C. The reaction mixture is stirred for 20°C. MeI is added to the resulting solution at 0°C. The resulting mixture is stirred at room temperature for 19hrs. EtOAc and water are added to the reaction. The organic phases are isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by flash chromatography may be required to afford the pure product.

Method P:



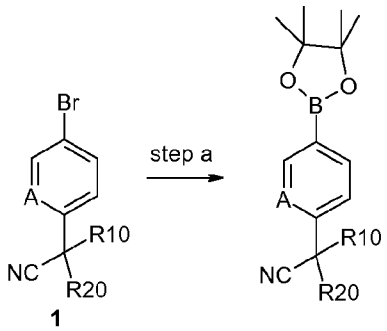
[00306] 1-bromo-2-chloroethane (1.2 eq.) is added to a solution of (4-Bromo-phenyl)-acetonitrile (1eq), NaOH (solution 1N) and $BnNEt_3Cl$ (catalytique) in H_2O at room temperature. The resulting solution is heated to 60°C for 5h. EtOAc is added to the reaction. The organic phases are isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by flash chromatography is required.

Method Q:



[00307] KHMDS (1.5 eq.) is added to a solution 1-Boc-3-cyanoazetidine (1.Eeq) (or 1-boc-4-cyanopiperidine) in toluene at 0°C. The resulting solution is stirred for 30 min at 0°C. 5-bromo-2-fluoro-pyridine (1eq) is added to the solution at 0°C. The solution is allowed to warm to room tempertaure and stirred for 16hrs. EtOAc and water are added to the reaction. The organic phases are isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by flash chromatography may be required.

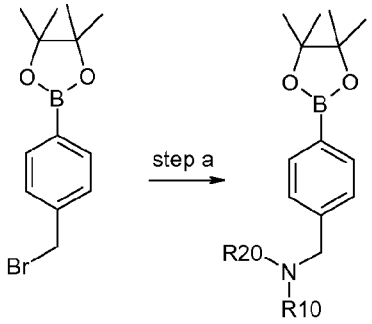
Method R:



1

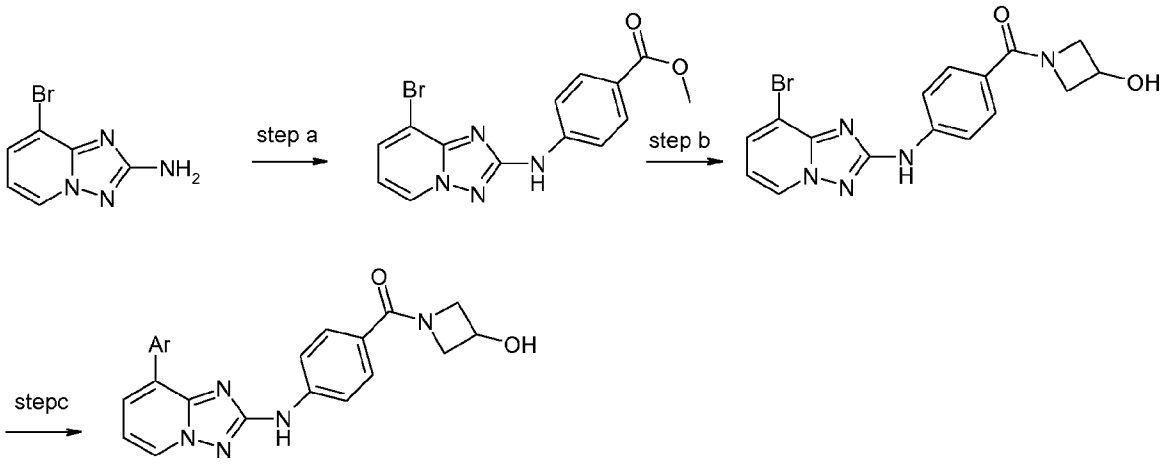
[00308] Derivative 1 (1eq.), bis(pinacolato)diboron (1.2 eq.), $Pd(dppf)Cl_2$ (5%) and KOAc (1.3 eq) are stirred in dioxane at 90°C for 4hrs to 16 hr. The resulting mixture was diluted in EtOAc and filtered through Celite and evaporated under vacuum to afford the expected product used without purification in the next step.

Method S:



[00309] 2-(4-Bromomethyl-phenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane, an appropriate amine (1eq.) and K_2CO_3 (2eq) are stirred in MeCN at room temperature for 17h. EtOAc and water are added to the reaction. The organic phases are isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by flash chromatography is required in some case.

Method T:



Step a:

[00310] This compound may be prepared via Method B using 4-Iodo-benzoic acid ethyl ester.

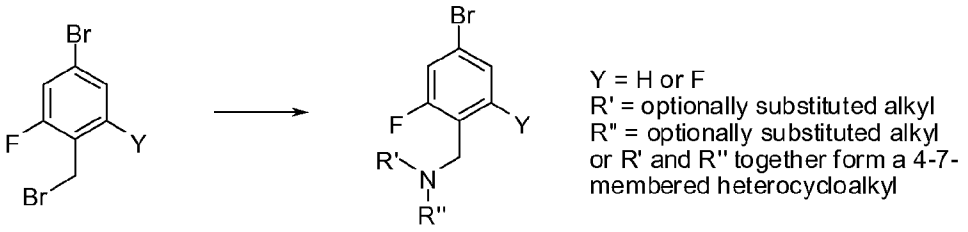
Step b:

[00311] This compound may be prepared via Method H then Method I using 3-hydroxy-azetidine.

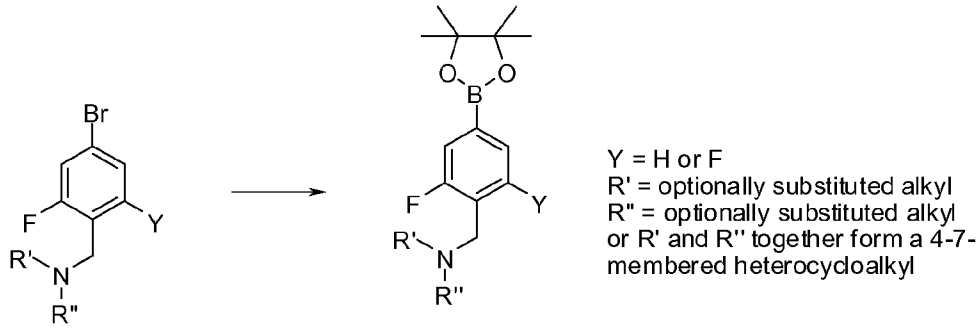
Step c:

[00312] This compound may be prepared via Method A using an appropriate boronic acid or boronate ester.

Method U



[00313] To a solution of 4-bromo-2-fluorobenzyl bromide (1 eq) in CH_3CN (3 mL) is added an appropriate amine (1.1 eq) in a sealed tube. The reaction mixture is stirred at room temp for 16 h. After cooling to room temperature, the reaction mixture is diluted in MeOH and concentrated *in vacuo*. The residue is re-dissolved in DCM/H_2O (1:1) and the organic phase is extracted over a phase separator. The solvent is removed *in vacuo* to yield the expected compound which may be used for the next step without further purification.



[00314] To a solution of amine derivative in 1,4-dioxane is added Pd(dppf)Cl_2 (0.03 eq), KOAc (1.3 eq.) and bis(pinacolato)diboron (1.3 eq.) in a sealed 25 mL tube. The reaction mixture is stirred at 90 °C for 16 h. After cooling to room temperature, the reaction mixture is filtered through Celite and concentrated under reduced pressure. Purification by flash column chromatography (Gradient, iso-hexanes to 100% EtOAc) gives the desired product.

Synthetic routes to selected compounds of the invention

Compound 1:

[00315] This compound was prepared via Method C using 4-methoxyphenyl boronic acid in step a then4-amino-phenyl)-acetamide in step c.

Compound 2:

[00316] This compound was prepared via Method C using 4-metoxyphenyl boronic acid in step a then morpholin-4-yl-pyridin-3-ylamine in step c.

Compound 3:

[00317] This compound was prepared via Method C using 4-metoxyphenyl boronic acid in step a then (4-amino-phenyl)-morpholin-4-yl-methanone in step c.

Compound 4

[00318] This compound was prepared via Method C using 4-(piperidine-1-carbonyl)phenylboronic acid in step a then N-(4-amino-phenyl)-acetamide in step c.

Compound 5

[00319] This compound was prepared via Method C using 4-(piperidine-1-carbonyl)phenylboronic acid in step a then 6-morpholin-4-yl-pyridin-3-ylamin in step c.

Compound 6

[00320] This compound was prepared via Method C using 4-(piperidine-1-carbonyl)-phenylboronic acid in step a then (4-amino-phenyl)-morpholin-4-yl-methanone in step c.

Compound 7

[00321] This compound was prepared via Method D using 4-chlorophenylboronic acid.

Compound 8

[00322] This compound was prepared via Method D using 3, 5-difluorophenylboronic acid.

Compound 9

[00323] This compound was prepared via Method D using 4-trifluoromethylphenylboronic acid.

Compound 10

[00324] This compound was prepared via Method D using 3-trifluoromethoxy-phenylboronic acid.

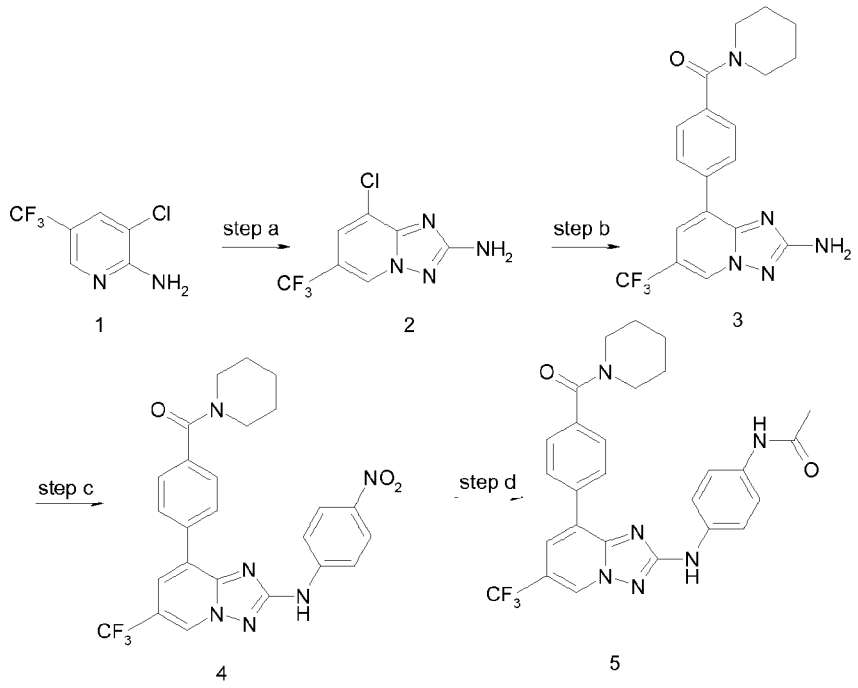
Compound 11

[00325] This compound was prepared via Method D using 4-isopropoxy-phenylboronic acid.

Compound 12

[00326] This compound was prepared via Method D using 3-fluorophenylboronic acid.

Compound 13



Step a:

[00327] To a solution of 3-chloro-5-trifluoromethyl-pyridin-2-ylamine (1 eq) in DCM cooled to 5 °C was added ethoxycarbonyl isothiocyanate (1.1 eq) dropwise over 15 min. The reaction mixture was then allowed to warm to room temp. (20 °C) and stirred for 16 h. Evaporation *in vacuo* gave a solid which was collected by filtration, thoroughly washed with petrol and air-dried to afford 2. The thiourea was used as such for the next step without any purification.

[00328] To a suspension of hydroxylamine hydrochloride (5 eq.) in EtOH/MeOH (1:1) was added N,N-diisopropylethylamine (5eq.) and the mixture was stirred at room temperature (20 °C) for 1 h. 2 (1 eq.) was then added and the mixture was slowly heated to reflux (Note: bleach scrubber is required to quench H_2S evolved). After 3 h at reflux, the mixture was allowed to cool and filtered to collect the precipitated solid. Further product was collected by evaporation in vacuo of the filtrate, addition of H_2O and filtration. The combined solids were washed successively with H_2O, EtOH/MeOH (1:1,) and Et_2O then dried in vacuo to afford 8-Chloro-6-trifluoromethyl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamine as a solid. The compound was used as such for the next step without any purification.

Step b:

[00329] This compound was prepared via Method A using 4-(Piperidine-1-carbonyl)phenylboronic acid.

Step c then d:

[00330] This compound was prepared via Method D (step b and c).

Compound 14

[00331] This compound was prepared via Method D using naphthalen-2-yl-boronic acid.

Compound 15

[00332] This compound was prepared via Method C using 4-methoxyphenyl boronic acid in step a then 6-(4-methylpiperazin-1-yl)pyridin-3-amine in step c.

Compound 16

[00333] This compound was prepared via Method C using 4- metoxyphenyl boronic acid in step a then N-(3-amino-phenyl)-acetamide in step c.

Compound 17

[00334] This compound was prepared via Method C using 4- metoxyphenyl boronic acid in step a then 4-amino-benzoic acid in step c, followed by Method H.

Compound 18

[00335] This compound was prepared via Method D using 4-methanesulfonyl-phenylboronic acid.

Compound 19

[00336] This compound was prepared via Method D using N-(2-phenoxy-ethyl)-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzamide prepared by Method E (using 2-Phenoxy-ethylamine).

Compound 20

[00337] This compound was prepared via Method D using 3-methoxy-phenylboronic acid.

Compound 21

[00338] This compound was prepared via Method D using cyclopropanesulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide prepared by Method F (using cyclopropanesulfonyl chloride).

Compound 22

[00339] This compound was prepared via Method D using phenylsulfonic acid [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amide prepared by Method F (using phenylsulfonyl chloride).

Compound 23

[00340] This compound was prepared via Method D using dipropyl-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amine prepared by Method G (using propionaldehyde).

Compound 24

[00341] This compound was prepared via Method D using 2-methoxy-phenylboronic acid.

Compound 25

[00342] This compound was prepared via Method D using benzyl-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-amine prepared by Method G (using benzaldehyde).

Compound 26

[00343] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using piperidine).

Compound 27

[00344] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-[1,2,4]triazol-1-ylmethyl-phenylamine in step c.

Compound 28

[00345] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using isopropylamine).

Compound 29

[00346] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using benzylamine).

Compound 30

[00347] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using N-methylpiperazine).

Compound 31

[00348] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 4-hydroxy-piperidine).

Compound 32

[00349] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 2,3-dihydro-1H-isoindole).

Compound 33

[00350] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-Pyridin-3-yl-methylamine).

Compound 34

[00351] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 2-Pyrrolidin-1-yl-ethylamine).

Compound 35

[00352] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-(1-ethyl-piperidin-4-yl)-methylamine).

Compound 36

[00353] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using isopropylamine).

Compound 37

[00354] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 1-methyl-piperidin-4-ylamine).

Compound 38

[00355] This compound was prepared via Method D using 3-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxymethyl]-pyridine prepared by Method J (using 3-bromomethyl-pyridine).

Compound 39

[00356] This compound was prepared via Method D using 3-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-propan-1-ol prepared by Method J (using 3-chloro-propan-1-ol).

Compound 40

[00357] This compound was prepared via Method D using N,N-dimethyl-4-benzamide boronic acid.

Compound 41

[00358] This compound was prepared via Method D using 4-(dimethylamino)phenylboronic acid.

Compound 42

[00359] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-imidazol-1-ylmethyl-phenylamine in step c.

Compound 43

[00360] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 1-methyl-piperidin-4-ylamine).

Compound 44

[00361] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H.

Compound 45

[00362] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-pyridin-2-yl-methylamine).

Compound 46

[00363] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using benzylamine).

Compound 47

[00364] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-pyridin-2-yl-methylamine).

Compound 48

[00365] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-pyridin-3-yl-methylamine).

Compound 49

[00366] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using N*1*,N*1*-dimethyl-propane-1,3-diamine).

Compound 50

[00367] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 2-pyrrolidin-1-yl-ethylamine).

Compound 51

[00368] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-(1-ethyl-piperidin-4-yl)-methylamine).

Compound 52

[00369] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then I (using 2-phenoxy-ethylamine).

Compound 53

[00370] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 2-pyridin-3-yl-ethylamine).

Compound 54

[00371] This compound was prepared via Method D using indole-5-boronic acid.

Compound 55

[00372] This compound was prepared via Method D using 1H-pyrazole-4-boronic acid.

Compound 56

[00373] This compound was prepared via Method D using 1-N-methylindole-5-boronic acid.

Compound 57

[00374] This compound was prepared via Method D using 4-(hydroxymethyl)phenylboronic acid.

Compound 58

[00375] This compound was prepared via Method D using 4-cyano-N-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzenesulfonamide prepared by Method F (using 4-cyano-benzenesulfonyl chloride).

Compound 59

[00376] This compound was prepared via Method D using N,N-dimethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzenesulfonamide.

Compound 60

[00377] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 3-(4-methyl-piperazin-1-yl)-propylamine).

Compound 61

[00378] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using C-(2,5-dimethyl-2H-pyrazol-3-yl)-methylamine).

Compound 62

[00379] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 2-pyridin-3-yl-ethylamine).

Compound 63

[00380] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 3-amino-benzoic acid methyl ester in step c followed by Method H then Method I (using 3-(4-Methyl-piperazin-1-yl)-propylamine).

Compound 64

[00381] This compound was prepared via Method D using 4-carbamoylphenylboronic acid.

Compound 65

[00382] This compound was prepared via Method D using Benzenesulfonamide-4-boronic acid pinacol ester.

Compound 66

[00383] This compound was prepared via Method D using indazole-5-boronic acid pinacol ester.

Compound 67

[00384] This compound was prepared via Method D using 4-cyano-N-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzenesulfonamide prepared by Method F (using 3,5-dichloro-benzenesulfonyl chloride).

Compound 68

[00385] This compound was prepared via Method D using 4-cyano-N-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-benzenesulfonamide prepared by Method F (using 2,4,6-trimethyl-benzenesulfonyl chloride).

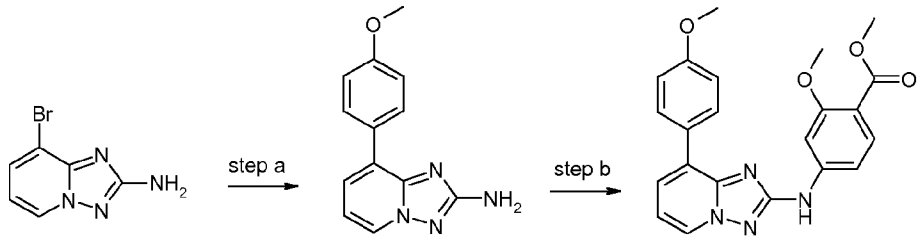
Compound 69

[00386] This compound was prepared via Method D using 4-carboxyphenylboronic acid.

Compound 70

[00387] This compound was prepared via Method K using 4-iodo-benzoic acid methyl ester and [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

Compound 71



Step a:

[00388] This compound was prepared via Method A using 4-methoxyphenylboronic acid.

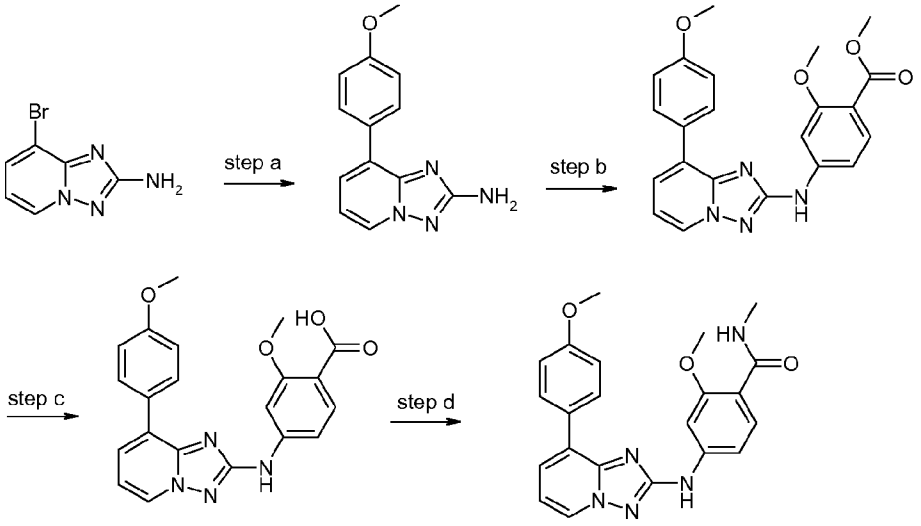
Step b:

[00389] This compound was prepared via Method B using 4-iodo-2-methoxy-benzoic acid methyl ester.

Compound 72

[00390] This compound was prepared via Method C using 4-methoxyphenylboronic acide in step a then pyrimidin-5-ylamine in step c.

Compound 73



Step a:

[00391] This compound was prepared via Method A using 4-methoxyphenylboronic acid.

Step b:

[00392] This compound was prepared via Method B using 4-iodo-2-methoxy-benzoic acid methyl ester.

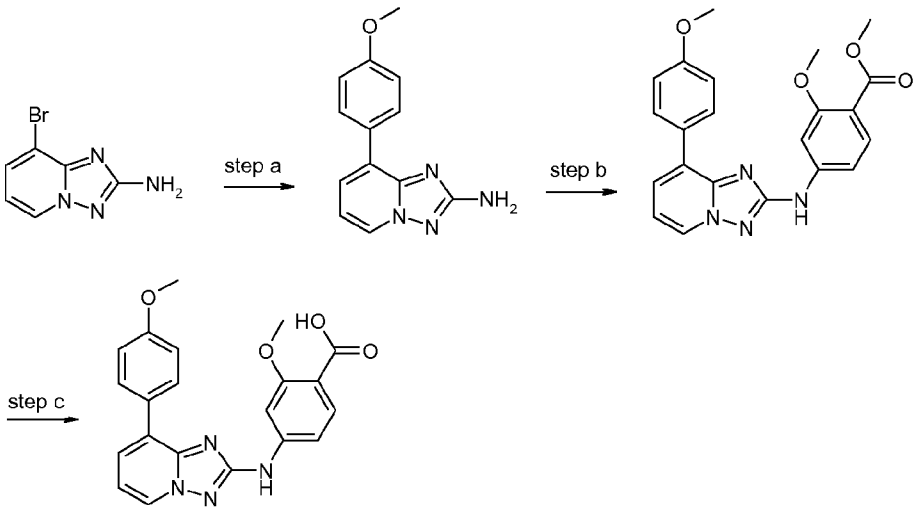
Step c:

[00393] This compound was prepared via Method H.

Step d:

[00394] This compound was prepared via Method I using methylamine.

Compound 74



Step a:

[00395] This compound was prepared via Method A using 4-methoxyphenylboronic acid.

Step b:

[00396] This compound was prepared via Method B using 4-iodo-2-methoxy-benzoic acid methyl ester.

Step c:

[00397] This compound was prepared via Method H.

Compound 75

[00398] This compound was prepared using the same procedure as described for Compound 73 using ammonia.

Compound 76

[00399] This compound was prepared via Method C using 4-methoxyphenylboronic acid in step a and 4-amino-benzonitrile in step c.

Compound 77

[00400] This compound was prepared via Method K using methyl amine and 2-chloro-5-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxymethyl]-pyridine prepared by Method J.

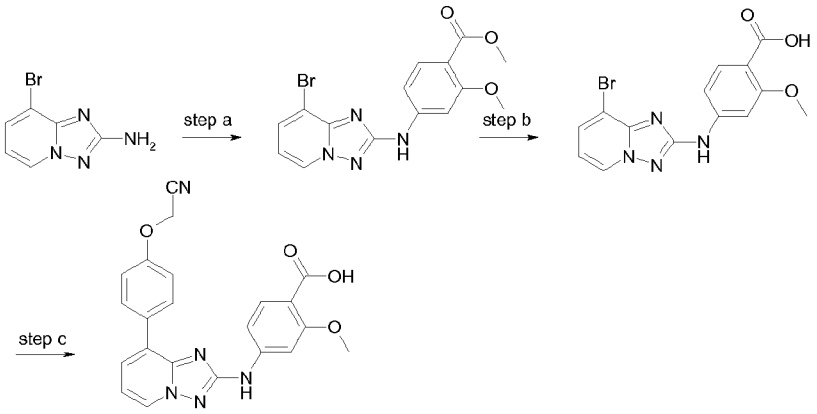
Compound 78

[00401] This compound was prepared via Method C using 5-amino-pyridine-2-carboxylic acid amide prepared by Method N using ammonia.

Compound 79

[00402] This compound was prepared using the same procedure as described for compound 73 using dimethyl amide.

Compound 80:



Step a:

[00403] This compound was prepared via Method B using 4-iodo-2-methoxy-benzoic acid methyl ester.

Step b:

[00404] This compound was prepared via Method H.

Step c:

[00405] This compound was prepared via Method A using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

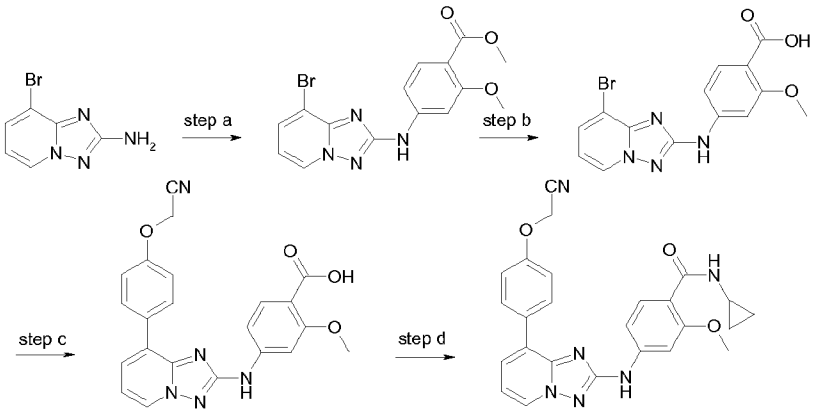
Compound 81:

[00406] This compound was prepared via Method C using 4-methoxyphenylboronic acid in step a then N-methyl-4-aminopyrazole in step c.

Compound 82:

[00407] This compound was prepared via Method C using 4-methoxyphenylboronic acid in step a then 6-amino-2,3-dihydro-isoindol-1-one in step c (prepared by Method L).

Compound 83:



Step a:

[00408] This compound was prepared via Method B using 4-iodo-2-methoxy-benzoic acid methyl ester.

Step b:

[00409] This compound was prepared via Method H.

Step c:

[00410] This compound was prepared via Method A using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

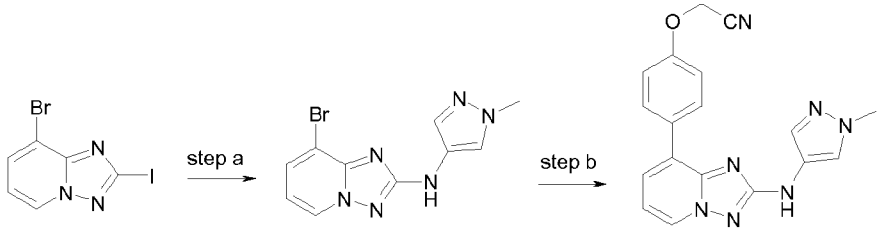
Step d:

[00411] This compound was prepared via Method I using cyclopropylamine.

Compound 84:

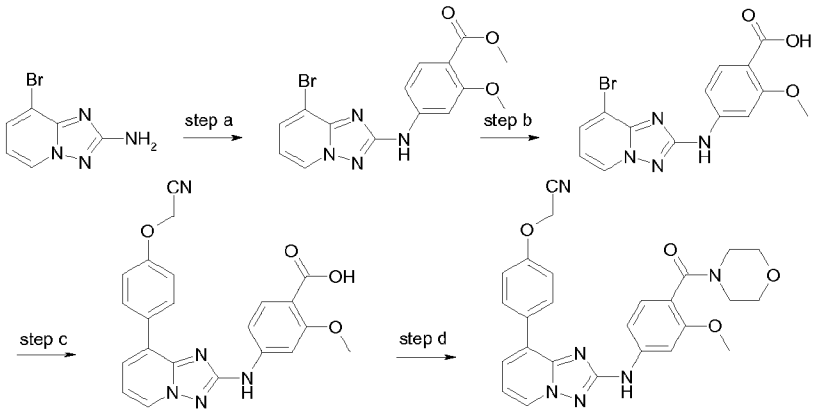
[00412] This compound was prepared following the same procedure as described for Compound 83 using methylamine.

Compound 85:



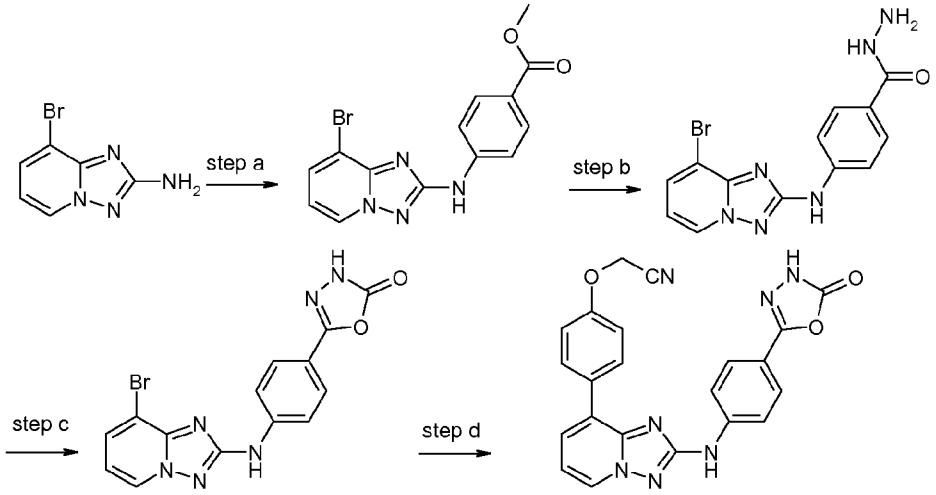
[00413] This compound was prepared via Method C' 1-methyl-1H-pyrazol-4-ylamine (prepared by Method M) and [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

Compound 86:



[00414] This compound was prepared following the same procedure as described for Compound 83 using morpholine.

Compound 87:



Step a:

[00415] This compound was prepared via Method B using 4-iodo-benzoic acid methyl ester.

Step b:

[00416] The product obtained in Step a (1eq) and $NH_2NH_2.H20$ (2eq.) were mixed in EtOH in a sealed tube. The reaction was heated at 100°C for 20 hrs. The volatiles were evaporated under vacuum. Water and EtOAc were added to the resuting mixture. The residue was triturated in EtOAc to give the expected product used in next step without further purification.

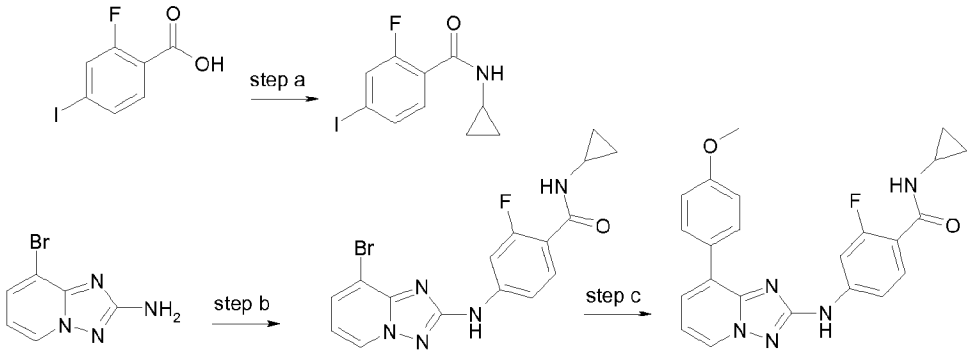
Step c:

[00417] CDI (1.2 eq) was added to a solution of the product obtained in Step b (1eq) and Et_3N (1.2 eq.) in THF at room temperature. The resulting mixture was stirred at room temperature for 20 hrs. EtOAc and water were added. The oranic phase was separated, dried over $MgSO_4$, evaporated under vacuum. The compound is used in the next step without any purification.

Step d:

[00418] This compound was prepared via Method A using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

Compound 88:



Step a:

[00419] 2-fluoro-4-iodo-benzoic acid (1 eq.), HATU (1.5 eq.), and DIPEA (2eq.) were mixed in THF at room temperature. An appropriate amine (1.1eq.) was added to the solution and the reaction mixture was stirred at room temperature for 16hrs. EtOAc and water was added to the reaction. The organic phases were isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product.

Step b:

[00420] This compound was prepared via Method B using N-cyclopropyl-2-fluoro-4-iodo-benzamide.

Step c:

[00421] This compound was prepared via Method A 4-methoxy-phenylboronic acid.

Compound 89:

[00422] This compound was prepared following the same procedure as described for Compound 88 using 4-isopropoxy-phenylboronic acid.

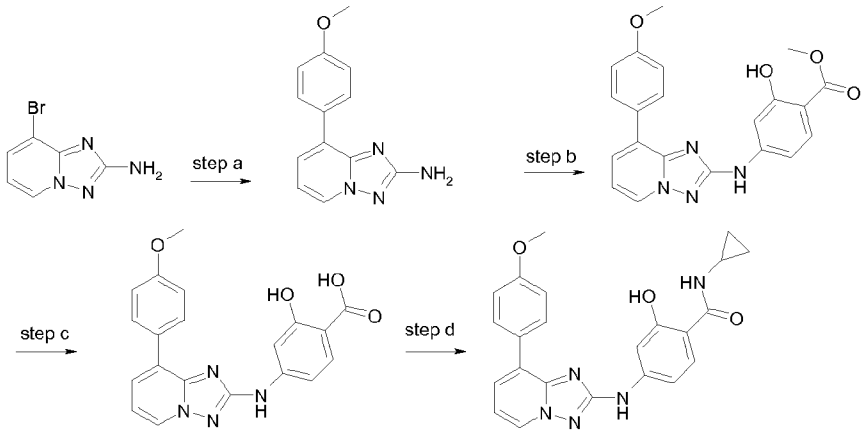
Compound 90:

[00423] This compound was prepared following the same procedure as described for Compound 88 using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile.

Compound 91:

[00424] This compound was prepared following the same procedure as described for Compound 88 using 4-trifluoromethoxy-phenylboronic acid.

Compound 92:



Step a:

[00425] This compound was prepared via Method A using 4-methoxy-phenylboronic acid.

Step b:

[00426] This compound was prepared via Method B using 2-hydroxy-4-iodo-benzoic acid methyl ester.

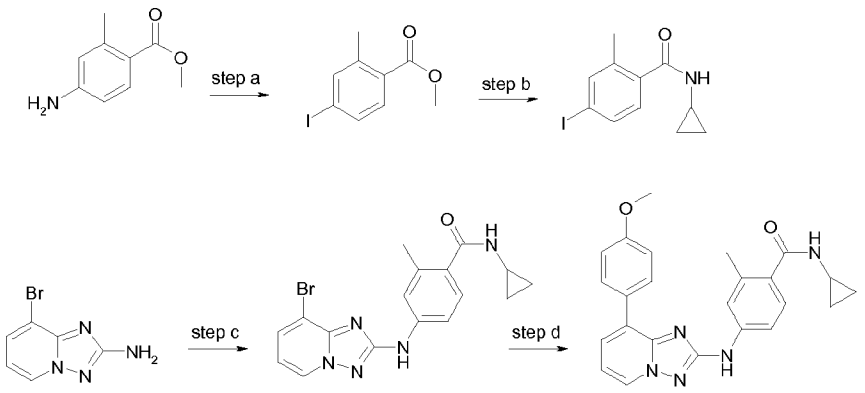
Step c:

[00427] This compound was prepared via Method H.

Step d:

[00428] This compound was prepared via Method I using cyclopropylamine.

Compound 93:



Step a:

[00429] A mixture of 4-amino-2-methyl-benzoic acid methyl ester (1 eq) and $NaNO_2$ in DMSO (2 eq .in DMSO) was treated dropwise with a solution of 57 % aqueous HI (10 eq.) in DMSO at 35 °C with stirring. The mixture was stirred at 35 °C for 10 minutes or until the reaction went to completion

(monitored by LCMS), and then it was transferred to a solution containing K_2CO_3 (500 mg) in 2 mL of water. The reaction mixture is extracted with ethyl acetate and the extracts were combined, washed with water and dried over anhyd. magnesium sulfate. The organic solvent was removed under high vacuum to yield the crude product. The crude product was then purified by flash chromatography to give the corresponding iodo derivative.

Step b:

[00430] Cyclopropylamine (1.5 eq.) was added to a solution of 4-iodo-2-methyl-benzoic acid methyl ester (1 eq.) and $AlMe_3$ (1.5 eq.) in THF. The resulting mixture was heated to 80°C for 2h. After completion of the reaction (monitored by LCMS), the reaction was allowed to cool to room temperature. Water and EtOAc were added to the residue. The organic phase was separated, dried over anhydrous $MgSO_4$, evaporated to afford the pure product, used in the next step without further purification.

Step c:

[00431] This compound was prepared via Method B using N-cyclopropyl-4-iodo-2-methyl-benzamide.

Step d:

[00432] This compound was prepared via Method A using 4-methoxy-phenylboronic acid.

Compound 94:

[00433] This compound was prepared via Method C using N,N-dimethyl-4-benzamide boronic acid in step a then 5-amino-pyridine-2-carboxylic acid methylamide (prepared by Method N) in step c.

Compound 96:

[00434] This compound was prepared via Method C using N,N-dimethyl-4-benzamide boronic acid in step a then 5-amino-pyridine-2-carboxylic acid methylamide (prepared by Method N) in step c.

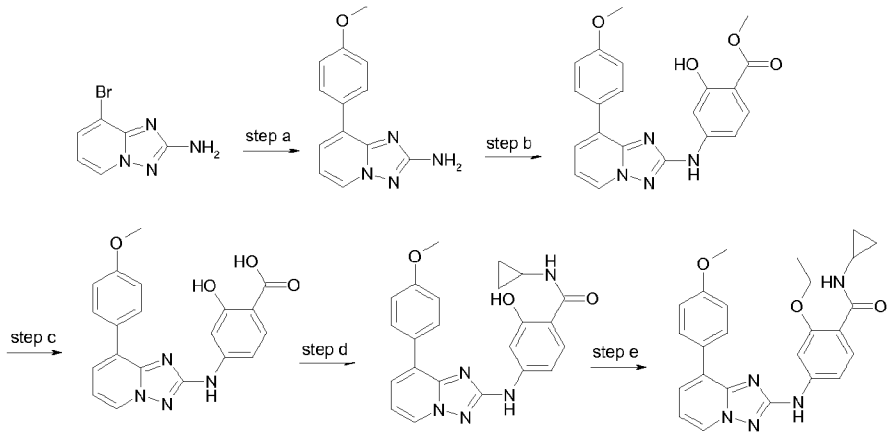
Compound 97:

[00435] This compound was prepared using the procedure as described for Compound 93 using N,N-dimethyl-4-benzamide boronic acid in step d.

Compound 98:

[00436] This compound was prepared using the procedure as described for Compound 93 using 4-trifluoromethoxy-phenylboronic acid in step d.

Compound 99:



Step a:

[00437] This compound was prepared via Method a using 4-methoxy-phenylboronic acid.

Step b:

[00438] This compound was prepared via Method b using 2-Hydroxy-4-iodo-benzoic acid methyl ester.

Step c:

[00439] This compound was prepared via Method H.

Step d:

[00440] This compound was prepared via Method I using cyclopropylamine.

Step e:

[00441] Ethyl bromide (1.2 eq) was added to a mixture of N-cyclopropyl-2-hydroxy-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide (1eq.) and K_2CO_3 (2eq.) in DMF. The reaction mixture was stirred at room temperature for 16h. Water and EtOAc were added to the residue. The organic phase was separated, dried over anhydrous $MgSO_4$, evaporated to afford the crude product purified by preparative HPLC.

Compound 100:

[00442] This compound was prepared using the procedure as described for Compound 73 above, using cyclobutylamine.

Compound 101:

[00443] This compound was prepared via Method C using N,N-dimethyl-4-benzamide boronic acid in step a then 4-(4-isopropyl-piperazin-1-yl)-phenylamine in step c.

Compound 103:

[00444] This compound was prepared via Method M to prepare 1-cyclopropylmethyl-1H-pyrazol-4-ylamine using bromomethyl-cyclopropane, or alternatively via Method C' using 1-cyclopropylmethyl-1H-pyrazol-4-ylamine in step b then 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenoxy]-acetonitrile in step c.

Compound 104:

[00445] This compound was prepared using the procedure as described for Compound 73 using 3-hydroxy-azetidine.

Compound 105:

[00446] This compound was prepared via Method K using 4-Iodo-2-methoxy-benzoic acid methyl ester, cyclopropylamine and 4-(cyanomethyl)phenylboronic acid pinacol ester.

Compound 106:

[00447] This compound was prepared via Method K using 4-Iodo-2-trifluoromethyl-benzoic acid methyl ester, cyclopropyl amine and 4-methoxy-phenylboronic acid.

Compound 107:

[00448] This compound was prepared via Method K using 4-Iodo-2-trifluoromethyl-benzoic acid methyl ester, cyclopropyl amine and 4-isopropoxy-phenylboronic acid.

Compound 108:

[00449] This compound was prepared via Method K using 4-Iodo-2-trifluoromethyl-benzoic acid methyl ester, cyclopropyl amine and 4-trifluoromethoxy-phenylboronic acid.

Compound 109:

[00450] This compound was prepared using the procedure as described for Compound 99 using 2-Chloro-N,N-dimethyl-acetamide in step c.

Compound 110:

[00451] This compound was prepared via Method C' using 1-Methyl-1H-pyrazol-4-ylamine then N,N-dimethyl-4-benzamide boronic acid.

Compound 111:

[00452] This compound was prepared via Method C' 1-cyclopropylmethyl-1H-pyrazol-4-ylamine (prepared by Method M) then N,N-dimethyl-4-benzamide boronic acid.

Compound 112:

[00453] This compound was prepared using the procedure as described for Compound 99 using 2-bromo-propane in step c.

Compound 113:

[00454] This compound was prepared via Method C using 4-methoxy-phenylboronic acid in step a then 4-(4-isopropyl-piperazin-1-yl)-phenylamine.

Compound 114:

[00455] This compound was prepared via Method C: using N,N-dimethyl-4-benzamide boronic acid then 5-amino-2-benzyl-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 115:

[00456] This compound was prepared via Method K using 2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyrazol-1-ylmethyl]-pyridine.

Compound 116:

[00457] This compound was prepared via Method K using N,N-dimethyl-4-benzamide boronic acid.

Compound 117:

[00458] This compound was prepared via Method A using 4-methoxy-phenylboronic acid followed by Method B using 4-iodo-benzoic acid methyl ester then Method H and Method I using C-cyclopropyl-methylamine.

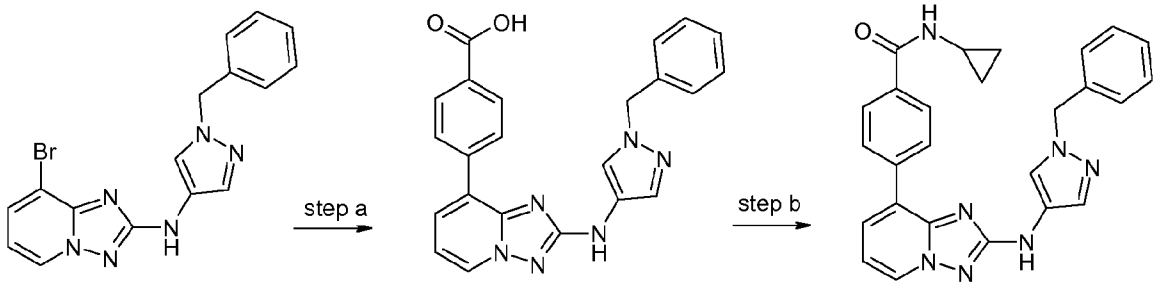
Compound 118:

[00459] This compound was prepared via Method A using 4-methoxy-phenylborinc acid followed by Method B using 4-Iodo-benzoic acid methyl ester then Method H and Method I using azetidine.

Compound 119:

[00460] This compound was prepared via Method A using 4-methoxy-phenylborinc acid followed by Method B using 4-iodo-benzoic acid methyl ester then Method H and Method I using 3-difluoro-azetidine.

Compound 120:



[00461] (1-Benzyl-1H-pyrazol-4-yl)-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine was prepared by Method C' using 1-benzyl-1H-pyrazol-4-ylamine prepared by Method M using benzyl bromide.

Step a:

[00462] This compound was prepared via Method A using 4-carboxybenzene boronic acid.

Step b:

[00463] 4-[2-(1-Benzyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzoic acid (1 eq.), HATU (1.5eq.) and DIPEA (2eq.) were mixed in DMF at room temperature. Cyclopropylamine (1.1eq.) was added to the solution and the reaction mixture was stirred at room temperature for 16hrs. EtOAc and water were added to the reaction. The organic phases were isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product purified by preparative HPLC.

Compound 121:

[00464] (1-Benzyl-1H-pyrazol-4-yl)-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine was prepared by Method C' using 1-benzyl-1H-pyrazol-4-ylamine prepared by Method M using benzyl bromide; or alternatively this compound was prepared via Method C' using N,N-dimethyl-4-benzamide boronic acid.

Compound 122:

[00465] This compound was prepared via Method C' using 5-Amino-2-cyclopropyl-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 123:

[00466] This compound was prepared via Method A using 4-methoxy-phenylboronic acid followed by Method B using 4-iodo-benzoic acid methyl ester, Method H and Method I using cyclopropyl-amine.

Compound 124:

[00467] This compound was prepared via Method T using 2-aminopyrimidine-5-boronic acid pinacol ester.

Compound 125:

[00468] This compound was prepared via Method T using 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridine.

Compound 126:

[00469] This compound was prepared via Method T using N,N-dimethyl-4-benzamide boronic acid.

Compound 127:

[00470] This compound was prepared via Method K using cyclopropylamine and 4-(cyanomethyl)-phenylboronic acid pinacol ester.

Compound 128:

[00471] This compound was prepared via Method T using 3-methanesulfonyl-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridine.

Compound 129:

[00472] This compound was prepared via Method T using 2-dimethylamino-pyrimidine-5-boronic acid pinacol ester.

Compound 130:

[00473] This compound was prepared via Method T using Dimethyl-[5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridin-2-yl]-amine.

Compound 131:

[00474] This compound was prepared via Method C' using 5-Amino-2-cyclopropyl-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 132:

[00475] This compound was prepared via Method K' using 3-hydroxy-azetidine.

Compound 133:

[00476] This compound was prepared via Method K' using 3-hydroxy-azetidine and 1-amino-2-methyl-propan-2-ol.

Compound 135:

[00477] This compound was prepared via Method K using 3-methoxy-azetidine.

Compound 136:

[00478] This compound was prepared via Method K using 1-methyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Compound 137:

[00479] This compound was prepared via Method C' using 1-pyridin-2-ylmethyl-1H-pyrazol-4-ylamine prepared by Method M.

Compound 138:

[00480] This compound was prepared via Method K using 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Compound 139:

[00481] This compound was prepared via Method K using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 140:

[00482] This compound was prepared via Method C' using 1H-pyrazol-4-ylamine.

Compound 141:

[00483] This compound was prepared via Method K using 1-methyl-5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Compound 142:

[00484] This compound was prepared via Method K using N,N-dimethyl-4-benzamide boronic acid.

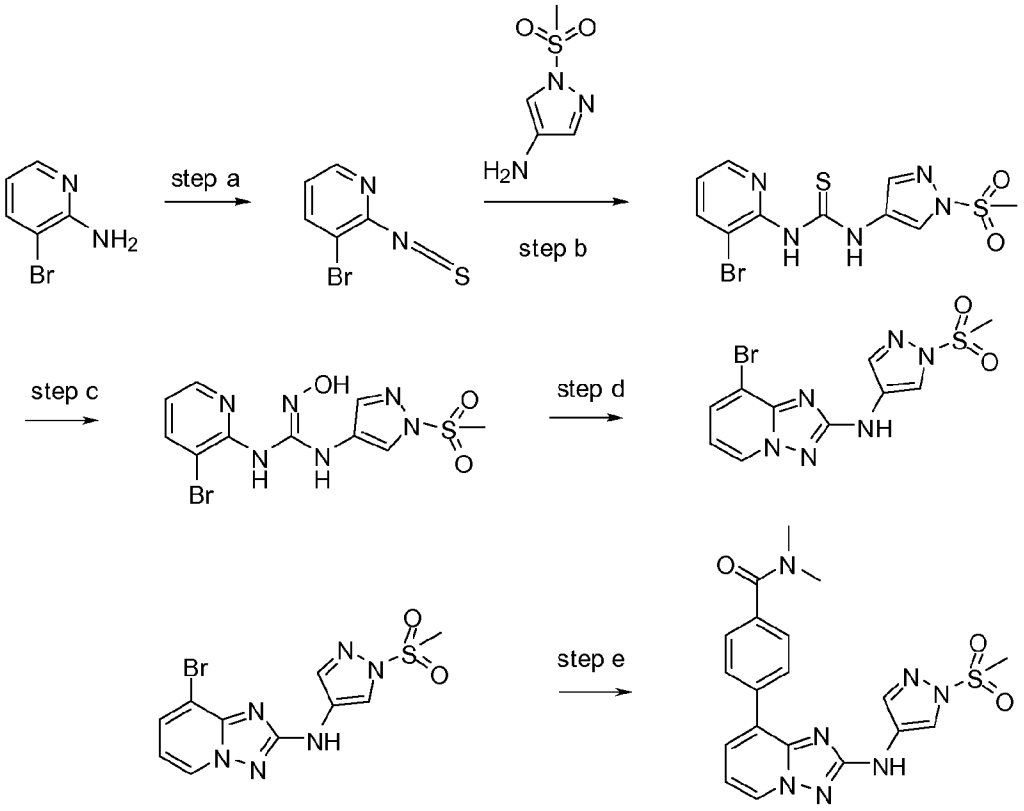
Compound 143:

[00485] This compound was prepared via Method C using (5-amino-pyridin-2-yl)-morpholin-4-yl-methanone prepared by Method N.

Compound 144:

[00486] This compound was prepared via Method C' using 5-amino-2-pyridin-2-ylmethyl-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 145:



Step a:

[00487] $CSCl_2$ (1.2 eq) was added to a solution of 3-Bromo-pyridin-2-ylamine (1eq) in CH_2Cl_2. The reactrion was allowed to stir at room temperature for 1 hr. Water and DCM were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step b:

[00488] 1-Methanesulfonyl-1H-pyrazol-4-ylamine (1eq.) was added to a solution of 3-bromo-2-isothiocyanato-pyridine (1eq.) in THF. The resulting mixture was heated at 75°C. After completion of the reaction the solvent was evaporated. The material was used without further purification.

Step c:

[00489] NaH (60%) (1.5eq.) was added to a solution of 1-(3-bromo-pyridin-2-yl)-3-(1-methanesulfonyl-1H-pyrazol-4-yl)-thiourea in THF at room temperature. The resulting mixture was stirred for 20 min. then CH_3I was added. The reaction was stirred for a further 2 hrs. The solvent was evaporated. The resulting mixture was dissolved in EtOH and iPr_2NEt was added, followed by $NH_2OH.HCl$. The reaction was heated at 75°C until completion of the reaction. EtOH was evaporated, water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step d:

[00490] Trifluoroacetic anhydride (1.2 eq.) was added to the previous compound (1eq.) in THF at room temperature. After completion of the reaction, the solvent was evaporated. MeOH was added to the crude mixture, followed by K_2CO_3, and the reaction was stirred for 15 min at room temperature. The sovent is evaporated and the finale compound was purified by flash chromatography.

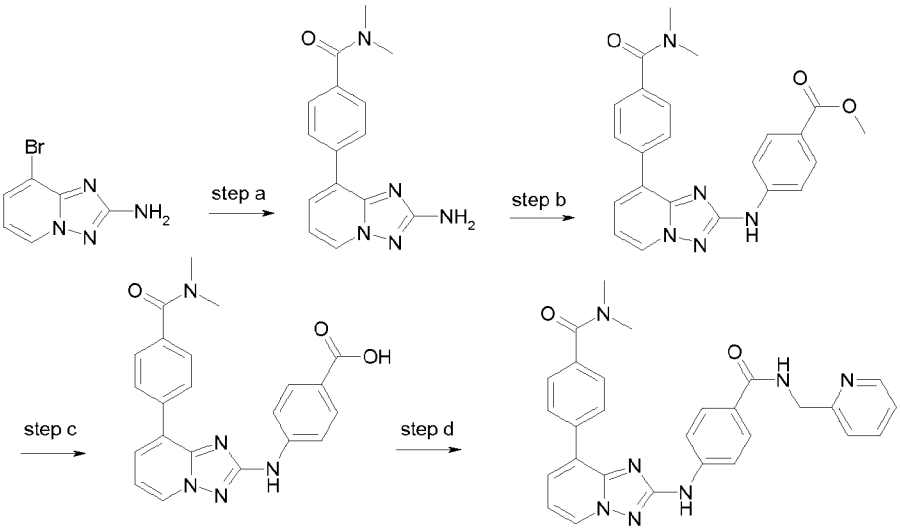
Step e:

[00491] This compound was prepared via Method A using N,N-dimethyl-4-benzamide boronic acid.

Compound 146:

[00492] This compound was prepared via Method C' using 1-isopropyl-1H-pyrazol-4-ylamine prepared by Method M.

Compound 147:



Step a:

[00493] This compound was prepared via Method A using N,N-dimethyl-4-benzamide boronic acid.

Step b:

[00494] This compound was prepared via Method B using 4-iodo-benzoic acid methyl ester.

Step c:

[00495] This compound was prepared via Method H.

Step d:

[00496] This compound was prepared via Method I using C-pyridin-2-yl-methylamine.

Compound 148:

[00497] This compound was prepared using the procedure as described for Compound 147 using piperazin-2-one in step d.

Compound 149:

[00498] This compound was prepared using the procedure as described for Compound 147 using 3,5-dimethylmorpholine in step d.

Compound 150:

[00499] This compound was prepared using the procedure as described for Compound 147 using 4-hydroxy-piperidine in step d.

Compound 151:

[00500] This compound was prepared using the procedure as described for Compound 147 using 4-fluoro-piperidine in step d.

Compound 152:

[00501] This compound was prepared using the procedure as described for Compound 147 using (R)-piperidin-3-olin step d.

Compound 153:

[00502] This compound was prepared using the procedure as described for Compound 147 using thiomorpholine 1,1-dioxide in step d.

Compound 154:

[00503] This compound was prepared using the procedure as described for Compound 147 using 1-methyl-piperazine in step d.

Compound 155:

[00504] This compound was prepared via Method C' using N,N-dimethyl-4-benzamide boronic acid then 5-amino-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 156:

[00505] This compound was prepared via Method C' using N,N-dimethyl-4-benzamide boronic acid then 5-amino-2-methyl-2,3-dihydro-isoindol-1-one prepared by Method L.

Compound 157:

[00506] This compound was prepared via Method C using 5-amino-pyridine-2-carboxylic acid dimethylamide prepared by Method N.

Compound 158:

[00507] This compound was prepared via Method K using cyclopropylamine then 2-Methyl-2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionitrile prepared by Method O followed by Method R.

Compound 160:

[00508] This compound was prepared via Method C using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetonitrile then 5-amino-pyridine-2-carboxylic acid cyclopropylamide.

Compound 161:

[00509] This compound was prepared via Method C using [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetonitrile then 5-amino-pyridine-2-carboxylic acid methylamide.

Compound 162:

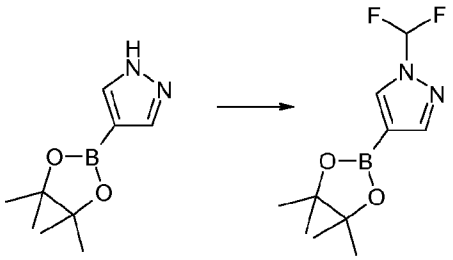
[00510] This compound was prepared via Method C using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine and 5-amino-pyridine-2-carboxylic acid methylamide.

Compound 163:

[00511] This compound was prepared via Method C using 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-isoxazole then 5-amino-pyridine-2-carboxylic acid methylamide.

Compound 164:

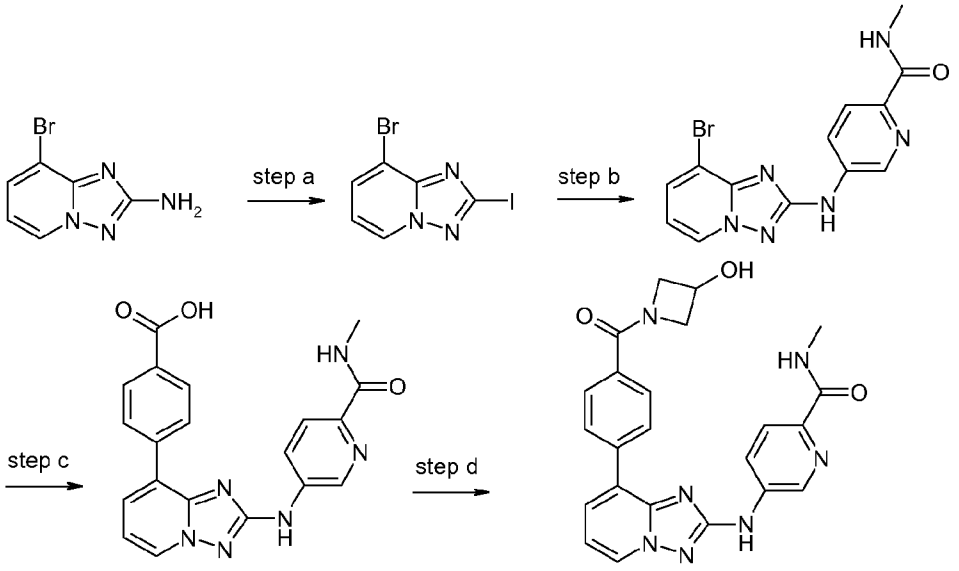
[00512] This compound was prepared via Method T using 1-Difluoromethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole prepared by the following Method:



[00513] $ClCHF_2$ was added to a solution of 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole and K_2CO_3 in DMF. The reaction was heated at 60°C for 2h. The reaction mixture was allowed to cool to room temperature. EtOAc and water were added to the reaction. The organic phase

was separated, dried over $MgSO_4$, evaporated under reduced pressure. The crude was used without further purification.

Compound 165:



Step a:

[00514] This compound was prepared using the method as described in Method C.

Step b :

[00515] This compound was prepared using the method as described in Method C, using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N.

Step c:

[00516] This compound was prepared via Method A using 4-Carboxyphenylboronic acid.

Step d:

[00517] This compound was prepared using the method as described in as step e in Method K' using azetidin-3-ol.

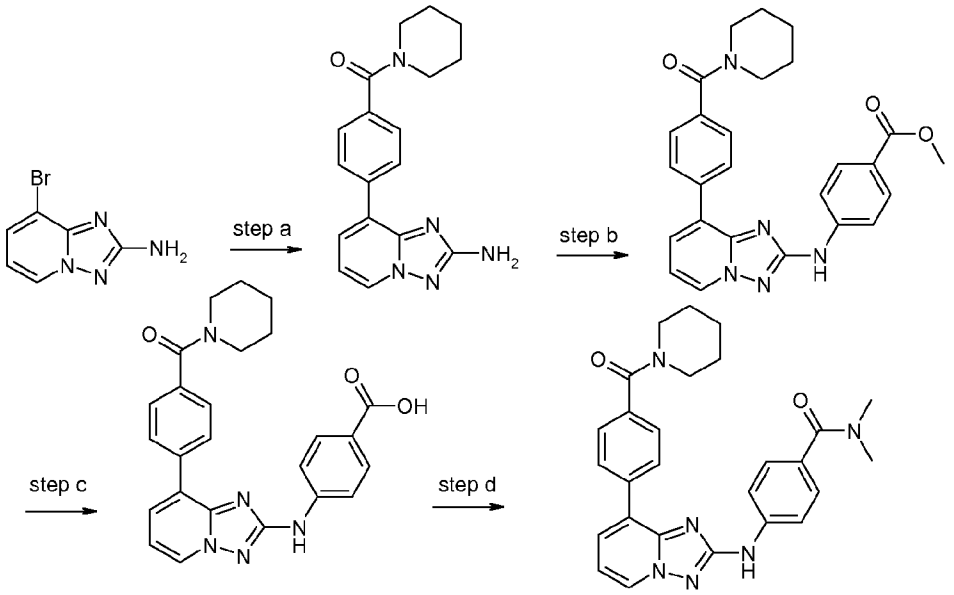
Compound 166:

[00518] This compound was prepared using the method as described for Compound 165 using 1-amino-2-methyl-propan-2-ol.

Compound 167:

[00519] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M'.

Compound 168:



Step a:

[00520] This compound was prepared via Method A using piperidin-1-yl-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-methanone.

Step b:

[00521] This compound was prepared via Method B using 4-iodo-benzoic acid methyl ester.

Step c:

[00522] This compound was prepared via Method H.

Step d:

[00523] This compound was prepared via Method I using dimethylamine.

Compound 169:

[00524] This compound was prepared using the method as described for Compound 168 using azetidine in step d.

Compound 170:

[00525] This compound was prepared using the method as described for Compound 168 using pyrolidine in step d

Compound 171:

[00526] This compound was prepared using the method as described for Compound 168 using 4-fluoro-piperidine in step d.

Compound 172:

[00527] This compound was prepared using the method as described for Compound 168 using 4-hydroxy-piperidine in step d.

Compound 173:

[00528] This compound was prepared using the method as described for Compound 168 using Piperazin-2-one in step d.

Compound 174:

[00529] This compound was prepared using the method as described for Compound 168 using cyclopropylamine in step d.

Compound 175:

[00530] This compound was prepared using the method as described for Compound 168 using 2-Amino-ethanol in step d.

Compound 176:

[00531] This compound was prepared via Method K using 3-hydroxy-azetidine 5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-2',3',5',6'-tetrahydro-1'H-[2,4']bipyridinyl-4'-carbonitrile prepared by Method Q then Method R.

Compound 177:

[00532] This compound was prepared via Method K using 3-hydroxy-azetidine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-cyclopropanecarbonitrile prepared by Method P then Method R.

Compound 178:

[00533] This compound was prepared via Method K using cyclopropylamine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-cyclopropanecarbonitrile prepared by Method P then Method R.

Compound 179:

[00534] This compound was prepared via Method K using cyclopropylamine 5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-2',3',5',6'-tetrahydro-1'H-[2,4']bipyridinyl-4'-carbonitrile prepared by Method Q then Method R.

Compound 180:

[00535] This compound was prepared via Method K using 3-hydroxyazetidine and [4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-acetonitrile.

Compound 181:

[00536] This compound was prepared via Method K using 3-hydroxy-azetidine and (R)-3-fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

Compound 182:

[00537] This compound was prepared via Method K using 3-hydroxy-azetidine and 3,3-difluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

Compound 183:

[00538] This compound was prepared via Method K using 3-hydroxy-azetidine and 4-Fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 184:

[00539] This compound was prepared via Method K using 3-hydroxy-azetidine and 4,4-difluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 185:

[00540] This compound was prepared via Method K using 3-hydroxy-azetidine and 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 186:

[00541] This compound was prepared using the method as described for Compound 165 using (R)-1-amino-propan-2-ol.

Compound 187:

[00542] This compound was prepared via Method K using cyclopropylamine 3-[5-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-pyridin-2-yl]-zetidine-3-carbonitrile prepared by Method Q and Method R.

Compound 188:

[00543] This compound was prepared via Method K' using morpholine then dimethylamine.

Compound 189:

[00544] This compound was prepared via Method K' using morpholine then 2-Methylamino-ethanol.

Compound 190:

[00545] This compound was prepared via Method K' using morpholine then pyrrolidine.

Compound 191:

[00546] This compound was prepared via Method K' using morpholine then 4-fluoro-piperidine.

Compound 192:

[00547] This compound was prepared via Method K' using morpholine then 2,6-dimethyl-morpholine.

Compound 193:

[00548] This compound was prepared via Method K' using morpholine then piperazin-2-one.

Compound 194:

[00549] This compound was prepared via Method K' using morpholine then isopropylamine.

Compound 195:

[00550] This compound was prepared via Method K' using morpholine then 2-amino-ethanol.

Compound 196:

[00551] This compound was prepared via Method K' using morpholine then C-pyridin-2-yl-methylamine.

Compound 197:

[00552] This compound was prepared via the method as described for Compound 168 using (2-methoxy-ethyl)-methyl-amine.

Compound 198:

[00553] This compound was prepared via the method as described for Compound 168 using C-Cyclopropyl-methylamine.

Compound 199:

[00554] This compound was prepared via the method as described for Compound 147 using 4,4-difluoro-piperidine.

Compound 200:

[00555] This compound was prepared via the method as described for Compound 165 using (S)-1-Amino-propan-2-ol.

Compound 201:

[00556] This compound was prepared via Method C using N,N-dimethyl-4-benzamide boronic acid then (5-Amino-pyridin-2-yl)-(3-hydroxy-azetidin-1-yl)-methanone prepared by Method N.

Compound 202:

[00557] This compound was prepared via the method as described for Compound 165 using 3-nitrile-azetidine.

Compound 203:

[00558] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' then 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 204:

[00559] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' then 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 205:

[00560] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' then (S)-3-methyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method S.

Compound 206:

[00561] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' then 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method S.

Compound 207:

[00562] This compound was prepared via Method T using 3-hydroxy-azetidine then (R)-1-Amino-propan-2-ol.

Compound 208:

[00563] This compound was prepared via Method T using 3-hydroxy-azetidine then (S)-1-Amino-propan-2-ol.

Compound 209:

[00564] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and 2-Methyl-2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propionitrile prepared by Method O followed by Method R.

Compound 210:

[00565] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and 4,4-Difluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 211:

[00566] This compound was prepared via Method C' using 5-Amino-2-cyclopropyl-2,3-dihydro-isoindol-1-one prepared by Method L and 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 212:

[00567] This compound was prepared via Method K using Cyclopropylamine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 213:

[00568] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and 2-morpholin-4-yl-2-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethanol.

Compound 214:

[00569] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and 4-methyl-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidin-4-ol prepared by Method S.

Compound 215:

[00570] This compound was prepared via Method C' using 1-Difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and (S)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidin-3-ol prepared by Method S.

Compound 216:

[00571] This compound was prepared via Method C' using 1-Difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method S.

Compound 217:

[00572] This compound was prepared via Method M'', followed by Method A using 4-Fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 218:

[00573] This compound was prepared via Method M'', followed by Method A using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 219:

[00574] This compound was prepared via Method C' using 5-Amino-pyridine-2-carboxylic acid methylamide prepared by Method N and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-cyclopropanecarbonitrile prepared by Method P followed by Method R.

Compound 220:

[00575] This compound was prepared via Method K using cyclopropyl amine and (S)-3-methyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method S.

Compound 221:

[00576] This compound was prepared via Method K using cyclopropyl amine and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method U.

Compound 222:

[00577] This compound was prepared via Method K using cyclopropyl amine and (S)-1-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidin-3-ol prepared by Method S.

Compound 223:

[00578] This compound was prepared via Method K using cyclopropyl amine and (1,1-Dioxo-tetrahydro-1lambda*6*-thiophen-3-yl)-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-amine prepared by Method S.

Compound 224:

[00579] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and (R)-3-fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

Compound 225:

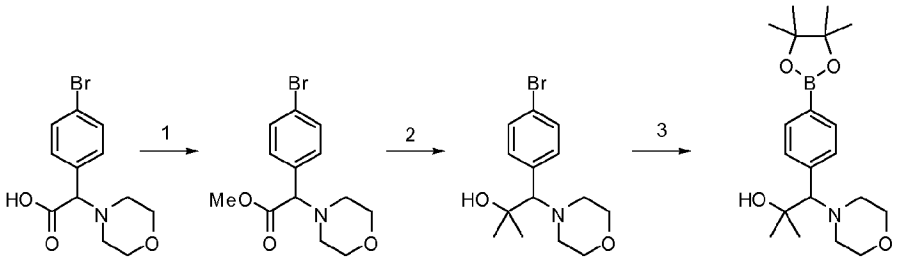
[00580] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and (S)-3-fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

Compound 226:

[00581] This compound was prepared via Method K using cyclopropyl amine and 1-methyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine prepared by Method S.

Compound 227:

[00582] This compound was prepared via Method C' using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and 2-methyl-1-morpholin-4-yl-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-propan-2-ol prepared as described below:



Step a:

[00583] To a solution of 2-(4-bromophenyl)-2-morpholinoacetic acid (500 mg, 1.66 mmol) in THF (10 mL) was added dropwise TMS-diazomethane (3.3 mL, 6.66 mmol, 2 M in hexanes). The reaction mixture was stirred at room temp for 3 h. Purification by flash column chromatography (Gradient, iso-hexanes to 25% EtOAc) gave the desired product (450 mg, 86%) as a white solid.

Step b:

[00584] To a solution of methyl 2-(4-bromophenyl)-2-morpholinoacetate (215 mg, 0.68 mmol) in THF (5 mL) was added dropwise MeMgBr (1.14 mL, 3.42 mmol, 3 M in Et_2O) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was quenched with satd. aqueous NH_4Cl (2 mL). The aqueous layer was extracted with EtOAc (2 × 5 mL), the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to afford a pale oil which was used for the next step without further purification.

Step c:

[00585] To a solution of 1-(4-bromophenyl)-2-methyl-1-morpholinopropan-2-ol (244 mg, 0.77 mmol) in dioxane (5 mL) was added $Pd(dppf)Cl_2$ (31.7 mg, 38.5 µmol), KOAc (100 mg, 1.0 mmol) and bis(pinacolato)diboron (256 mg, 1.0 mmol) in a sealed 10 mL tube. The reaction mixture was stirred at 90 °C for 16 h. After cooling to room temperature, the reaction mixture was filtered through Celite.

Purification by flash column chromatography (Gradient, iso-hexanes to 25% EtOAc) gave the desired product (242 mg, 87%) as a white solid.

Compound 228:

[00586] This compound was prepared via Method K using cyclopropyl amine and 4,4-difluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 229:

[00587] This compound was prepared via Method K using cyclopropyl amine and 4,4-difluoro-1-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidineprepared by Method U.

Compound 230:

[00588] This compound was prepared via Method K using cyclopropyl amine and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method U.

Compound 231:

[00589] This compound was prepared via Method K using cyclopropyl amine and (R)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidin-3-ol prepared by Method S.

Compound 232:

[00590] This compound was prepared via Method K using cyclopropyl amine and 2-{methyl-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-amino}-ethanol prepared by Method S.

Compound 233:

[00591] This compound was prepared via Method K using cyclopropyl amine and 1-{4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazin-1-yl}-ethanone using Method S.

Compound 234:

[00592] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and 4-fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 235:

[00593] This compound was prepared via Method K using cyclopropyl amine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-4-trifluoromethyl-piperidine prepared by Method S.

Compound 236:

[00594] This compound was prepared via Method K using cyclopropyl amine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine-4-carbonitrile prepared by Method S.

Compound 237:

[00595] This compound was prepared via Method C' using 5-amino-2-cyclopropyl-2,3-dihydro-isoindol-1-one prepared by Method L and 3-fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method S.

Compound 238:

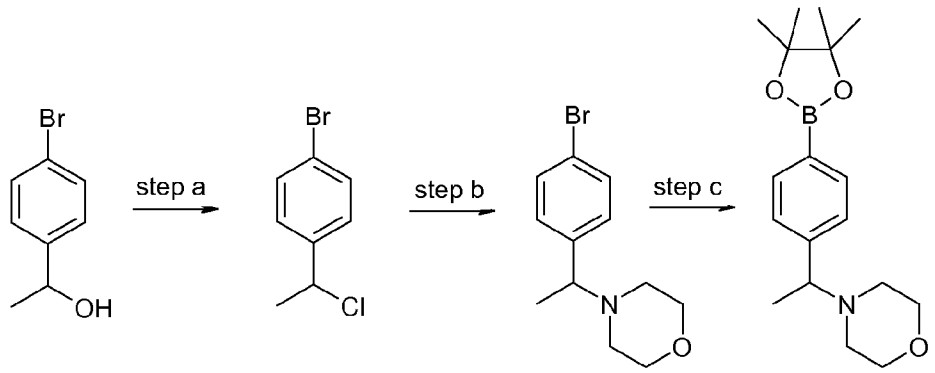
[00596] This compound was prepared via Method K using cyclopropyl amine and 4-fluoro-1-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method U.

Compound 239:

[00597] This compound was prepared via Method K using cyclopropyl amine and 1-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method U.

Compound 240:

[00598] This compound was prepared via Method K using cyclopropylamine and 4-{1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethyl}-morpholine prepared by the following method:



Step a:

[00599] 1-(4-bromo-phenyl)-ethanol was stirred in aq. HCl at room temperature for 20 h. The excess acid was evaporated under vacuum to give the expected product in quantative yield.

Step b:

[00600] Morpholine (2 eq.) was added to a solution of 1-bromo-4-(1-chloro-ethyl)-benzene (1eq) and DIPEA (2eq.) in acetonitrile. The resulting mixture was stirred at 60°C for 72 h. The solvent was evaporated under reduced pressure. Water and EtOAc were added. The organic layers were separated, dried over $MgSO_4$ and evaporated under reduced pressure to affortd the expected product in quantitative yield used in the next step without further purification.

Step c:

[00601] A mixture of 4-[1-(4-bromo-phenyl)-ethyl]-morpholine (1eq.), bis(pinacolato)diboron (1.2 eq), $PdCl_2$(dppf) (0.03 eq.) and KOAc (1.3 eq) and 1,4-dioxane in a reaction tube was purged with nitrogen gas for 10 min. The tube was sealed under nitrogen and the mixture stirred at 100 °C for 17 h. The brown mixture was filtered through Celite, washing with EtOAc. The filtrate was concentrated and the residue was used immediately without further purification.

Compound 241:

[00602] This compound was prepared via Method K using methylamine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method S.

Compound 242:

[00603] This compound was prepared via Method K using methylamine and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method U.

Compound 243:

[00604] This compound was prepared via Method K using methylamine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 244:

[00605] This compound was prepared via Method K using cyclopropyl amine and (S)-3-fluoro-1-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method U.

Compound 245:

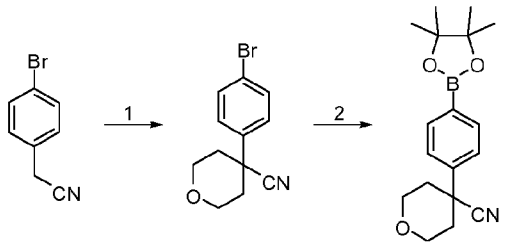
[00606] This compound was prepared via Method K using methylamine and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method U.

Compound 246:

[00607] This compound was prepared via Method K using methylamine and 4,4-difluoro-1-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine prepared by Method U.

Compound 247:

[00608] This compound was prepared via Method K using cyclopropyl amine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-tetrahydro-pyran-4-carbonitrile prepared by the following method:



Step a:

[00609] To a stirred suspension of sodium hydride (3.06 g, 76.5 mmol, 60 wt% dispersion in mineral oil) in NMP (62 mL) at −10 °C was added dropwise a solution of 4-bromophenylacetonitrile (4.99 g, 25.5 mmol) and 2-chloroethyl ether (3.00 mL, 25.6 mmol) in cyclopentyl methyl ether (13 mL), added dropwise over 25 min. The reaction mixture was allowed to warm to 20 °C over 1.75 h, then stirred at 20 °C for a further 17 h. The mixture was cooled to 0 °C and quenched with water (2 mL), before being partitioned between ether (50 mL) and water (50 mL). The aqueous layer was extracted with ether (4 x 50 mL); the combined organic layers were washed with water (3 x 50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography, (20% EtOAc-hexanes) yielded the tetrahydropyran (5.45 g, 20.5 mmol, 80%) as a colourless solid.

Step b:

[00610] A mixture of 4-(4-bromophenyl)tetrahydro-2H-pyran-4-carbonitrile (995 mg, 3.74 mmol), bis(pinacolato)diboron (1.26 g, 4.96 mmol), $PdCl_2$(dppf) (163 mg, 200 μmol) and KOAc (483 mg, 4.92 mmol) and dioxane (9 mL) in a reaction tube was purged with nitrogen gas for 10 min. The tube was sealed under nitrogen and the mixture stirred at 100 °C for 17 h. The brown mixture was filtered through Celite, washing with 30 mL EtOAc. The filtrate was concentrated and the residue was used immediately without further purification.

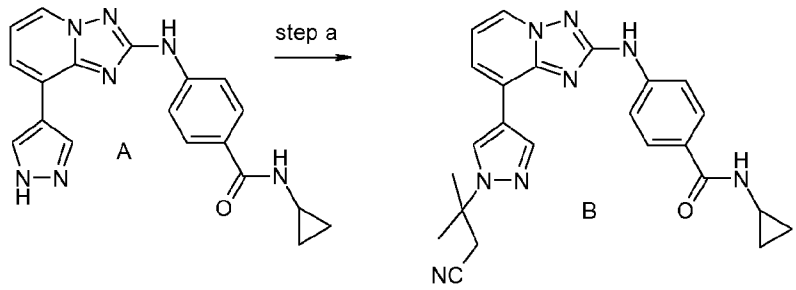
Compound 248:

[00611] This compound was prepared via Method K using cyclopropyl amine and and 1-(2-morpholinoethyl)-1h-pyrazole-4-boronic acid, pinacol ester.

Compound 249:

[00612] This compound was prepared via Method K' using azetidine-3-carbonitrile and azetidin-3-ol.

Compound 251:



[00613] Compound A was prepared via Method K using cyclopropylamine and 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Step a

[00614] Senecionitrile (1.1 eq) was added to a solution of N-cyclopropyl-4-[8-(1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide (1eq.) and DBU (1.2 eq)) in DMF at room temperature for 24 h. EtOAc and water are added to the reaction. The organic phases is isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by preparative HPLC is required.

Compound 252:

[00615] This compound was prepared via Method K using cyclopropylamine and 1,5-dimethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Compound 253:

[00616] This compound was prepared via Method K using cyclopropylamine and 3,3-Difluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine prepared by Method S.

Compound 254:

[00617] This compound was prepared via Method K using cyclopropylamine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method S.

Compound 255:

[00618] This compound was prepared via Method K using cyclopropylamine and (R)-3-Fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

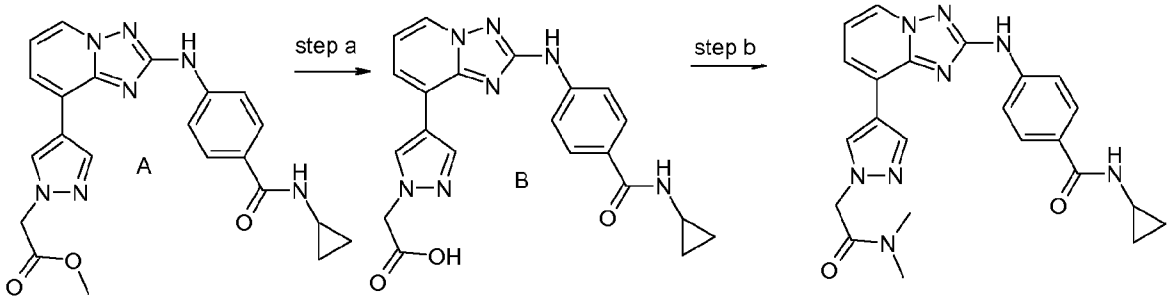
Compound 256:

[00619] This compound was prepared via Method K using cyclopropylamine and (S)-3-Fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine prepared by Method S.

Compound 257:

[00620] This compound was prepared via Method K using cyclopropylamine and 4-Fluoro-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperidine.

Compound 258:



[00621] Compound (**B**) in the scheme above was obtained by Method K using cyclopropylamine and 1-(metoxycarbonylmethyl)-1h-pyrazole-4-boronic acid, pinacol ester.

Step a:

[00622] {4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-pyrazol-1-yl}-acetic acid methyl ester and LiOH (2eq.) are mixed together in acetone at room temperature. The reaction is heated at 70°C for 16 hrs. Acetone is evaporated. Water is added and the pH is acidified to pH=1 with HCl solution (1N). The precipitate is filtered, dried to afford the expected acid in quantative yield.

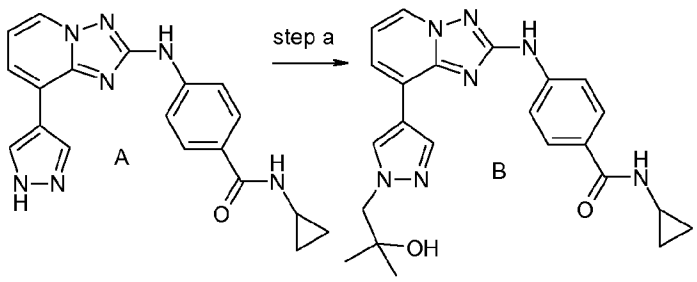
Step b:

{4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-pyrazol-1-yl}-acetic acid (1eq.), HATU (1.5 eq.), and DIPEA (2eq.) were mixed in DMF at room temperature. Dimethylamine (1.1eq.) was added to the solution and the reaction mixture was stirred at room temperature for 16hrs. EtOAc and water was added to the reaction. The organic phases were isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. The final product is purified by preparative HPLC.

Compound 259:

[00623] This compound was prepared via the method as described for Compound 258 using morpholine in the last step.

Compound 260:



[00624] Compound (**A**) in the scheme above was prepared by Method K using cyclopropylamine and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrazole.

Step a:

[00625] 1,2-Epoxy-2-methylpropane (1.1 eq) was added to a solution of N-cyclopropyl-4-[8-(1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide (1eq.), DBU (1.2 eq) and K_2CO_3 (1.2 eq) in DMF at room temperature for 24 h. EtOAc and water are added to the reaction. The organic phases is isolated, dried over $MgSO_4$, filtered and evaporated under vacuum to afford the expected product. Purification by preparative HPLC gives the product.

Compound 261:

[00626] This compound was prepared via Method C' using 5-amino-pyridine-2-carboxylic acid methylamide prepared by Method N and 1-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method S.

Compound 262:

[00627] This compound was prepared via Method C using 1-difluoromethyl-1H-pyrazol-4-ylamine prepared by Method M' and 4-{1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethyl}-morpholine prepared with the procedure described for Compound 240.

Compound 263:

[00628] This compound was prepared via Method K' using morpholine and azetidine.

Compound 264:

[00629] This compound was prepared via Method K' using morpholine and thiomorpholine 1,1-dioxide.

Compound 265:

[00630] This compound was prepared via Method K' using morpholine and cyclopropylamine.

Compound 266:

[00631] This compound was prepared via Method K using cyclopropylamine and (S)-3-methyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method S.

Compound 267:

[00632] This compound was prepared via Method K using cyclopropylamine and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method U.

Compound 268:

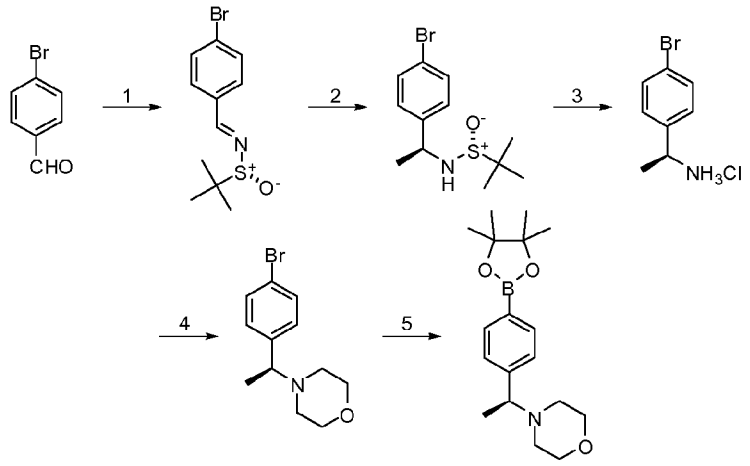
[00633] This compound was prepared via Method K using cyclopropylamine and 1-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method U.

Compound 269:

[00634] This compound was prepared via Method K using methylamine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 270:

[00635] This compound was prepared via Method K using cyclopropylamine and 4-{(S)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethyl}-morpholine prepared by the following procedure:



Step a:

[00636] A stirred solution of 4-bromobenzaldehyde (15.0 g, 81.1 mmol) in THF (240 mL) at 20 °C was treated with titanium tetraisopropoxide (48 mL, 162 mmol), followed 5 minutes later by (*R*)-*t*-butyl sulfinamide (10.0 g, 82.5 mmol). The mixture was stirred at 20 °C for 16 h, before being poured into satd. aqueous NH_4Cl (300 mL). The precipitate that formed was removed by filtration through Celite. The filtrate separated into two layers; the aqueous layer was extracted with CH_2Cl_2 (2 x 200 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to yield the sulfinimine (23.4 g, 81.1 mmol, 100%) as a colourless solid.

Step b:

[00637] A stirred solution of (*R*)-N-(4-bromobenzylidene)-2-methylpropane-2-sulfinamide from step 1 (12.0 g, 41.6 mmol) in CH_2Cl_2 (180 mL) at –78 °C was treated with MeMgBr (27.8 mL, 3 M in ether, 83.4 mmol), added dropwise over 40 min. The reaction mixture was allowed to warm to 20 °C over 5.5 h, before being quenched with satd. aqueous NH_4Cl (40 mL). The mixture was poured into 50 mL water and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL); the combined organic extracts were washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was recrystallised from 3:1:1 EtOAc:ether:hexanes to yield the sulfinamide (7.29 g, 24.0 mmol, 58%) as colourless prisms. Only one diastereomer could be detected by ^1H NMR and LCMS analysis.

Step c:

[00638] A stirred solution of *(R)-N-((S)-1-(4-bromophenyl)ethyl)-2-methylpropane-2-sulfinamide* from step 2 (7.03 g, 23.1 mmol) in MeOH (33 mL) at 20 °C was treated with HCl (11.5 mL, 4 M in dioxane, 46 mmol). NOTE: exothermic. The mixture was stirred at 20 °C for 2 h, then concentrated *in vacuo*. The colourless solid was dried under vacuum at 40 °C for 1 h, to yield the amine as its hydrochloride salt, containing some *t*-butyl methyl sulfoxide.

Step d:

[00639] A suspension of *(S)-1-(4-bromophenyl)ethanamine hydrochloride* from step 3 (2.00 g, 8.46 mmol), 2-chloroethyl ether (2.0 mL, 17.1 mmol) and K_2CO_3 (3.53 g, 25.5 mmol) in DMF (30 mL) was stirred at 100 °C for 38 h. After cooling to 20 °C, the mixture was partitioned between water (30 mL) and ether (30 mL). The aqueous layer was extracted with ether (3 x 30 mL); the combined organic extracts were washed with water (30 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by chromatography (20% EtOAc-hexanes) yielded the morpholine (270 mg, 1.00 mmol, 13% over 2 steps) as a yellow liquid.

Step 5:

[00640] A mixture of *(S)*-4-(1-(4-bromophenyl)ethyl)morpholine from step 4 (270 mg, 1.00 mmol), bis(pinacolato)diboron (330 mg, 1.30 mmol), $PdCl_2$(dppf) (41 mg, 50 µmol) and KOAc (128 mg, 1.30 mmol) and dioxane (2.6 mL) in a reaction tube was purged with nitrogen gas for 10 min. The tube was sealed under nitrogen and the mixture stirred at 90 °C for 17 h. The brown mixture was filtered through Celite, washing with 30 mL EtOAc. The filtrate was concentrated and the residue was used immediately without further purification.

Compound 271:

[00641] This compound was prepared via Method K using cyclopropylamine and 4-{(R)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethyl}-morpholine prepared by the same procedure as compound 270 but using (*S*)-*t*-butyl sulfonamide in step 1.

Compound 272:

[00642] This compound was prepared via Method C using 1-(4-amino-pyrazol-1-yl)-2-methyl-propan-2-ol prepared by Method M'' and 1-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile prepared by Method U.

Compound 273:

[00643] This compound was prepared via Method C using 1-(4-Amino-pyrazol-1-yl)-2-methyl-propan-2-ol prepared by Method M'' and 4-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared by Method U.

Compound 274:

[00644] This compound was prepared via Method C using 1-(4-amino-pyrazol-1-yl)-2-methyl-propan-2-ol prepared by Method M'' and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-cyclopropanecarbonitrile prepared by Method P.

Compound 275:

[00645] This compound was prepared via Method C using 1-(4-amino-pyrazol-1-yl)-2-methyl-propan-2-ol prepared by Method M'' and (1,1-dioxo-tetrahydro-1lambda*6*-thiophen-3-yl)-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-amine prepared by Method S.

Compound 276:

[00646] This compound was prepared via Method C using 1-(4-amino-pyrazol-1-yl)-2-methyl-propan-2-ol prepared by Method M'' and 3-fluorophenylboronic acid.

Compound 277:

[00647] This compound was prepared via Method K using methylamine and dimethyl-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-amine prepared by Method S.

Compound 278:

[00648] This compound was prepared via Method C' using aniline and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 279:

[00649] This compound was prepared via Method C' using aniline and 4-[2-fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine pepared by Method U.

Compound 280:

[00650] This compound was prepared via Method K using cyclopropylamine and 4-acetylbenzeneboronic acid followed by reaction with $NaBH_4$ in methanol to give the expected product.

Compound 281:

[00651] This compound was prepared via Method K using cyclopropylamine and 4-acetylbenzeneboronic acid.

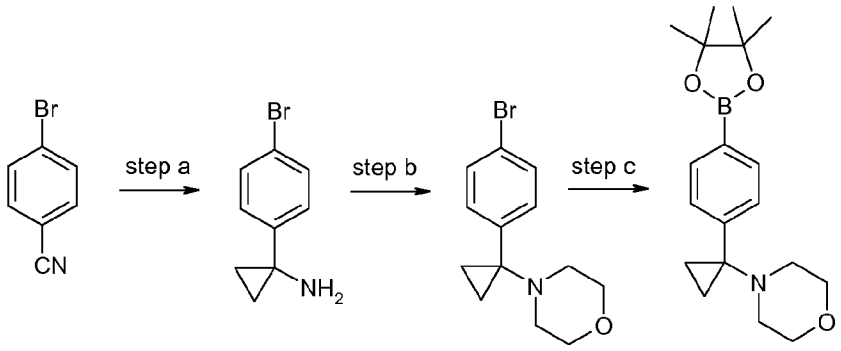
Compound 282:

[00652] This compound was prepared via Method C' using 5-amino-2-cyclopropyl-2,3-dihydro-isoindol-1-one prepared by Method L and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 283:

[00653] This compound was prepared via Method C' using aniline and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 284:



Step a

[00654] To a solution of 4-Bromo-benzonitrile (1 eq) and Ti(O*i*-Pr)$_4$ (1.1 eq.) in dry Et_2O (50 mL) was added EtMgBr (2.1 eq., 3 M in Et_2O) at -78 °C. The resulting yellow solution was stirred for 10 min at this temperature and allowed to warm to room temperature over 1 h. $BF_3.Et_2O$ (5.1 mL, 40 mmol) was added and the reaction mixture was further stirred for 1 h. The reaction mixture was quenched with HCl (1 M in H_2O) and Et_2O. NaOH (wt 10% in water) was added and the aqueous layer was extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to Et_2O) gave the desired product.

Step b

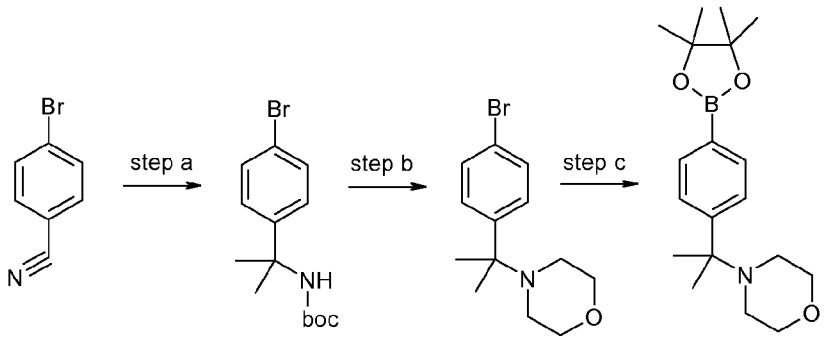
[00655] To a solution of 1-(4-bromo-phenyl)-cyclopropylamine (1 eq) in DMF in a 50 mL tube was added DIPEA (2 eq) and 1-Bromo-2-(2-bromo-ethoxy)-ethane (1.1 eq). the reaction mixture was heated at 100°C for 16 hrs.. After cooling to room temperature, EtOAc and water were added. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product.

Step c

[00656] A mixture of 4-[1-(4-Bromo-phenyl)-cyclopropyl]-morpholine (1eq.), bis(pinacolato)diboron (1.5 eq), Pd(dppf)Cl_2 (5%) and KOAc (1.5 eq.) in 1,4-dioxane in a 25 mL tube was purged with N_2 gas at room temperature for 10 min. The tube was sealed and heated to 100 °C for 20 h. After cooling to room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated *in vacuo* to give a brown solid which was used in the next step without further purification.

[00657] Compound 284 was obtained via Method A using 4-{1-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-cyclopropyl}-morpholine.

Compound 285



Step a

[00658] MeLi (2eq) was added to a solution of 4-Bromo-benzonitrile (1eq) an $CeCl_3$ (1eq) in THF at -78°C. The reaction was allowed to warm to room temperature. Boc anhydride was added to the reaction.The solution was allowed to stir for 16 hrs at room temperature. Water, followed by EtOAc were added. The combined organic layers were separated, dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product which was purified by column chromatography.

Step b

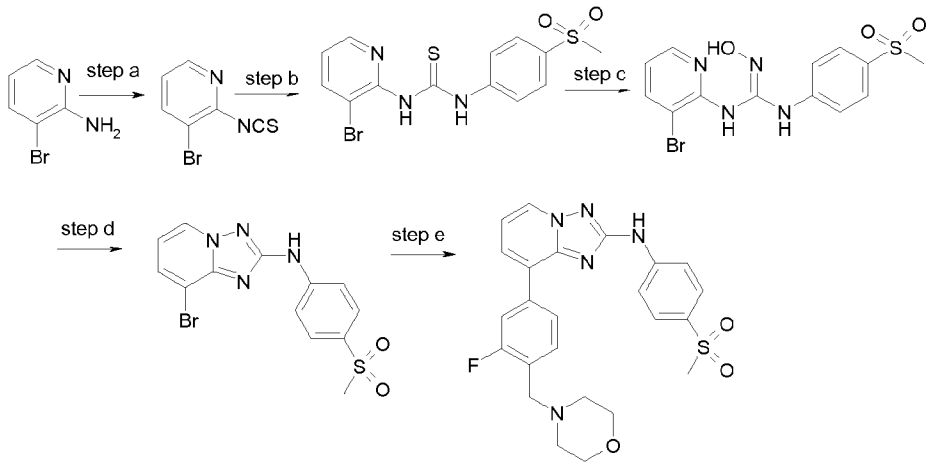
[00659] To a solution of [1-(4-Bromo-phenyl)-1-methyl-ethyl]-carbamic acid tert-butyl ester (1 eq) in DMF in a 50 mL tube was added DIPEA (2 eq) and 1-Bromo-2-(2-bromo-ethoxy)-ethane (1.1 eq). the reaction mixture was heated at 100°C for 16 hrs.. After cooling to room temperature, EtOAc and water were added. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product.

Step c

[00660] A mixture of 4-[1-(4-Bromo-phenyl)-1-methyl-ethyl]-morpholine (1eq.), bis(pinacolato)diboron (1.5 eq), $Pd(dppf)Cl_2$ (5%) and KOAc (1.5 eq.) in 1,4-dioxane in a 25 mL tube was purged with N_2 gas at room temperature for 10 min. The tube was sealed and heated to 100 °C for 20 h. After cooling to room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated *in vacuo* to give a brown solid which was used in the next step without further purification.

[00661] Compound 285 was obtained via Method A using 4-{1-Methyl-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-ethyl}-morpholine.

Compound 286



Step a

[00662] $CSCl_2$ (1.2 eq) was added to a solution of 3-Bromo-pyridin-2-ylamine (1eq) in CH_2Cl_2. The reactrion was allowed to stir at room temperature for 1 hr. Water and DCM were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step b

[00663] 4-Methanesulfonyl-phenylamine (1eq.) was added to a solution of 3-Bromo-2-isothiocyanato-pyridine (1eq) in THF at room temperature. The solution was allowed to stir for 16 hrs. The solvent was evaporated to give the crude product used in the next step without further purification.

Step c

[00664] NaH (60%) (1.5eq.) was added to a solution of 1-(3-Bromo-pyridin-2-yl)-3-(4-methanesulfonyl-phenyl)-thiourea in THF at room temperature. The resulting mixture was stirred for 20 min. then CH_3I was added. The reaction was stirred for a further 2 hrs. The solvent was evaporated. The

resulting mixture was dissolved in EtOH and iPr_2NEt was added, followed by $NH_2OH.HCl$. The reaction was heated at 75°C until completion of the reaction. EtOH was evaporated, water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step d

[00665] Trifluoroacetic anhydride (1.2 eq.) was added to the previous compound (1eq.) in THF at room temperature. After completion of the reaction, the solvent was evaporated. MeOH was added to the crude mixture, followed by K_2CO_3, and the reaction was stirred for 15 min at room temperature. The sovent is evaporated and the finale compound was purified by flash chromatography.

Step e

[00666] This compound was prepared via Method A using 4-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared via Method U.

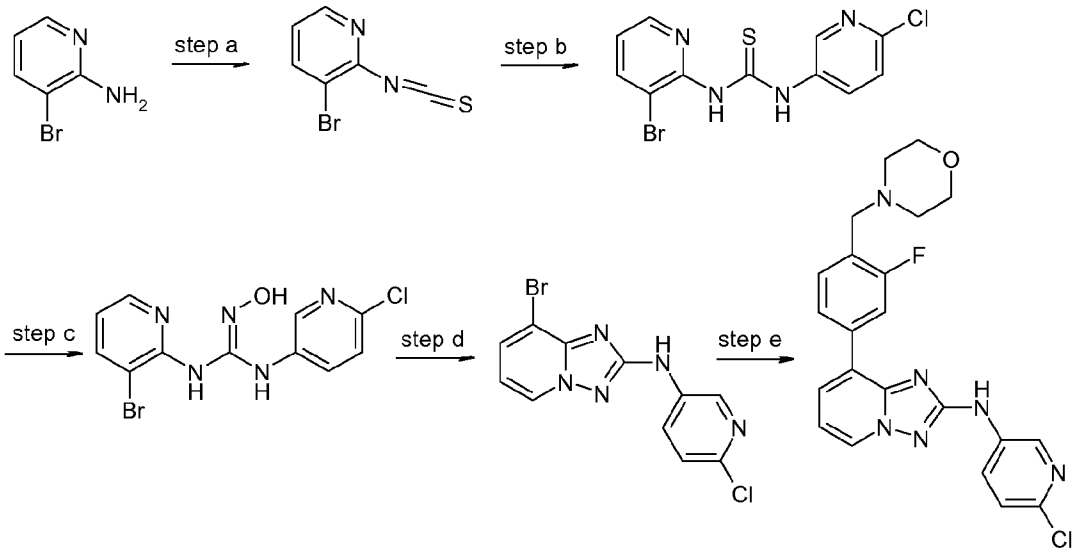
Compound 287

[00667] This compound is obtained by the same procedure as the one used for Compound 286 using 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine in Step e.

Compound 288

[00668] This compound is obtained by the same procedure as the one used for compound 286 using 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide prepared by Method S.

Compound 289



Step a

[00669] $CSCl_2$ (1.2 eq) was added to a solution of 3-Bromo-pyridin-2-ylamine (1eq) in CH_2Cl_2. The reactrion was allowed to stir at room temperature for 1 hr. Water and DCM were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step b

[00670] 6-Chloro-pyridin-3-ylamine (1eq.) was added to a solution of 3-Bromo-2-isothiocyanato-pyridine (1eq) in THF at room temperature. The solution was allowed to stir for 16 hrs. The solvent was evaporated to give the crude product used in the next step without further purification.

Step c

[00671] NaH (60%) (1.5eq.) was added to a solution of 1-(3-Bromo-pyridin-2-yl)-3-(6-chloro-pyridin-3-yl)-thiourea in THF at room temperature. The resulting mixture was stirred for 20 min. then CH_3I was added. The reaction was stirred for a further 2 hrs. The solvent was evaporated. The resulting mixture was dissolved in EtOH and iPr_2NEt was added, followed by $NH_2OH.HCl$. The reaction was heated at 75°C until completion of the reaction. EtOH was evaporated, water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

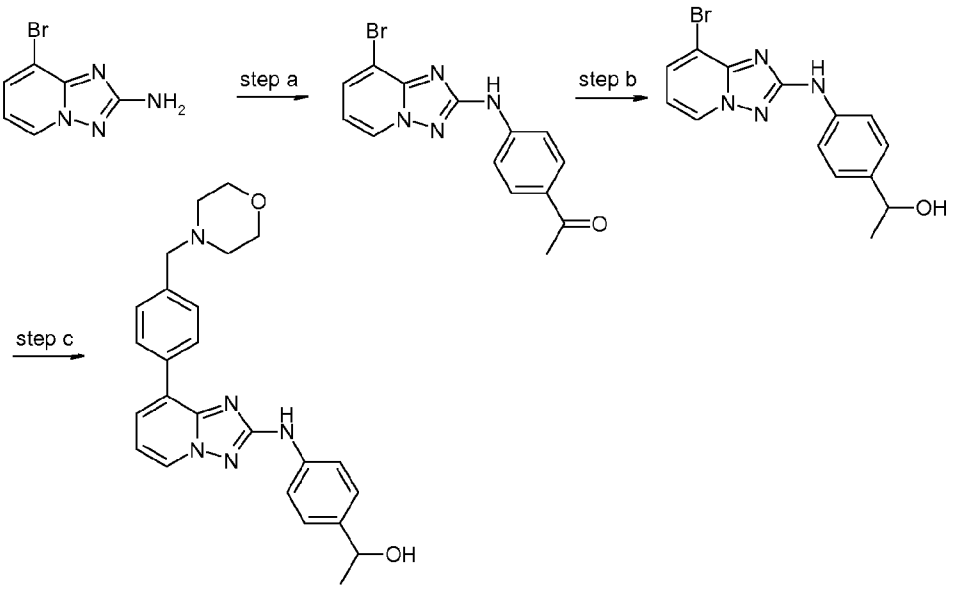
Step d

[00672] Trifluoroacetic anhydride (1.2 eq.) was added to the previous compound (1eq.) in THF at room temperature. After completion of the reaction, the solvent was evaporated. MeOH was added to the crude mixture, followed by K_2CO_3, and the reaction was stirred for 15 min at room temperature. The sovent is evaporated and the finale compound was purified by flash chromatography.

Step e

[00673] Compound 289 was prepared via Method A using 4-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine prepared via Method U.

Compound 290



Step a

[00674] To a solution of 1-(4-Iodo-phenyl)-ethanone (1.2 eq) and 8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamine (1 eq) in 1,4-dioxane were added $Pd_2(dba)_3$ (0.01 eq), Xantphos (0.01 eq) and Cs_2CO_3 (2 eq). The reaction mixture was degassed by sonication under a stream of N_2 for 10 min and then stirred at 90 °C for 16 h. The reaction mixture was diluted with CH_2Cl_2/MeOH (1:1) filtered through Celite and the filtrate was concentrated *in vacuo*. Purification by flash column chromatography yielded the target compound.

Step b

[00675] $NaBH_4$ (2eq) was added to a solution of 1-[4-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-ethanone (1eq) in MeOH. The solution was allowed to stir at room temperature for 2 days. The solvent was evaporated. Water and EtOAc were added. The organic phases was separated, dried over MgSO4 and evaporated under reduced pressure. The expected product was obtained without further purification.

Step c

[00676] Compound 290 was obtained by Method A using 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Compound 291

[00677] Compound 291 was obtained after attempted purification of Compound 307 using methanol via SCX cartridge.

Compound 292

[00678] This compound was obtained by the same method as described for Compound 290 using 4-[2-Fluoro-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine in the last step.

Compound 293

[00679] Compound 293 was obtained after attempted purification of Compound 292 using methanol via SCX cartridge.

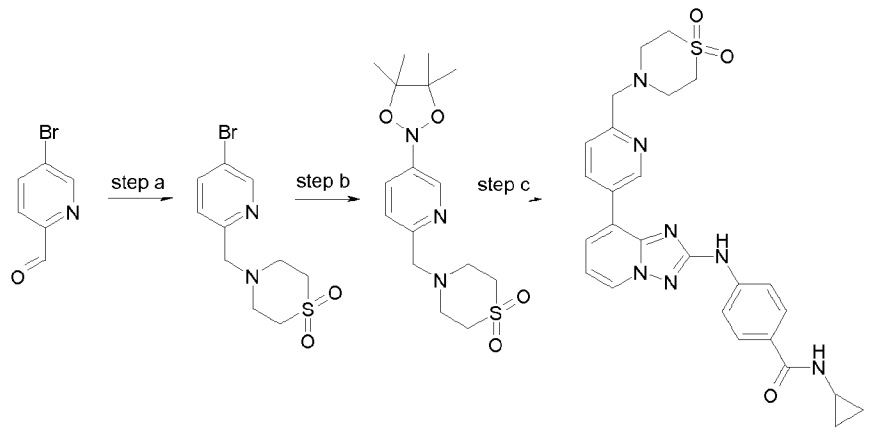
Compound 294

[00680] This compound was obtained by the same method as described for Compound 290 using 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile.

Compound 295

[00681] This compound was prepared via Method C' using aniline and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile.

Compound 296 and 297



Step a

[00682] To a solution of 5-Bromo-pyridine-2-carbaldehyde (1eq) and thiomorpholine 1,1-dioxide (1 eq) in DCM/AcOH (10:1) was added PS-NMe_3BH_3CN (polymer supported cyanoborohydride) (2 eq). The reaction mixture was shaken for 17 h at room temperature. PS-Isocyanate (0.3 eq) was added and the mixture shaken for an additional 1 h. The mixture was filtered and passed directly through an SCX cartridge to give the desired product.

Step b

[00683] To a stirred solution of 4-(5-Bromo-pyridin-2-ylmethyl)-thiomorpholine 1,1-dioxide (1 eq) in dioxane was added $Pd(dppf)Cl_2$ (5 %), KOAc (1.2 eq) and bis(pinacolato)diboron (1.2 eq) in a sealed tube. The reaction mixture was stirred at 90 °C for 17 h. After cooling to room temperature, the reaction mixture was filtered through Celite, concentrated *in vacuo*, and this crude residue was used in the next step without further purification.

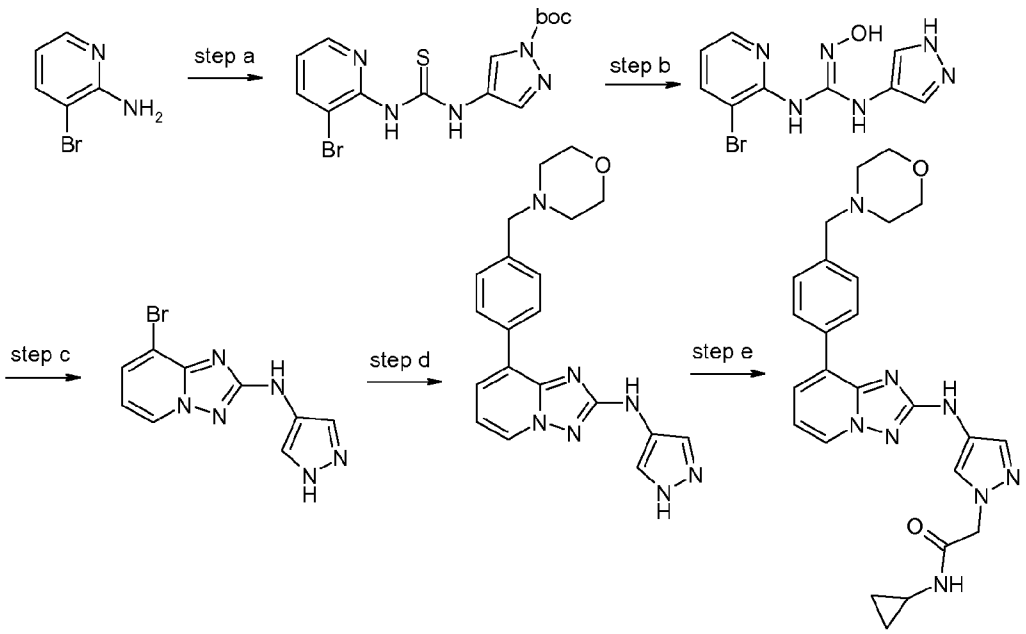
Step c

[00684] To a stirred solution of 4-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide (1 eq) prepared via method K in 1,4-dioxane/H_2O (5:1) was added 4-[5-(4,4,5,5-Tetramethyl-[1,3,2]dioxazolidin-2-yl)-pyridin-2-ylmethyl]-thiomorpholine 1,1-dioxide (1.1 eq), Pd(dppf)Cl_2 (5 %) and Na_2CO_3 (3 eq) in a sealed tube. The reaction mixture was stirred at 90 °C for 17 h. The reaction mixture was allowed to cool to room temperature and diluted with DCM/H_2O (1:1; 20 mL). The organic layer was separated, concentrated *in vacuo* and purified by flash chromatography (Gradient CH_2Cl_2 to 5% MeOH in CH_2Cl_2). The isolated solid was triturated with cold MeCN to give the desired compound and Compound 297 as a side product (due to some reduced unreacted aldehyde in step a).

Compound 298

[00685] This compound was obtained by the same procedure as the one described for Compound 286 using 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile.

Compound 299



Step a

[00686] $CSCl_2$ (1.2 eq) was added to a solution of 3-Bromo-pyridin-2-ylamine (1eq) in CH_2Cl_2. The reactrion was allowed to stir at room temperature for 1 hr. Water and DCM were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

[00687] 4-Amino-pyrazole-1-carboxylic acid tert-butyl ester (1eq.) was added to a solution of 3-Bromo-2-isothiocyanato-pyridine (1eq) in THF at room temperature. The solution was allowed to stir for 16 hrs. The solvent was evaporated to give the crude product used in the next step without further purification.

Step b

[00688] NaH (60%) (1.5eq.) was added to a solution of 4-[3-(3-Bromo-pyridin-2-yl)-thioureido]-pyrazole-1-carboxylic acid tert-butyl ester (1eq) in THF at room temperature. The resulting mixture was stirred for 20 min. then CH_3I was added. The reaction was stirred for a further 2 hrs. The solvent was evaporated. The resulting mixture was dissolved in EtOH and iPr_2NEt was added, followed by $NH_2OH.HCl$. The reaction was heated at 75°C until completion of the reaction. EtOH was evaporated, water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was obtained without further purification.

Step c

[00689] Trifluoroacetic anhydride (1.2 eq.) was added to the previous compound (1eq.) in THF at room temperature. After completion of the reaction, the solvent was evaporated. MeOH was added to the crude mixture, followed by K_2CO_3, and the reaction was stirred for 15 min at room temperature. The solvent is evaporated and the final compound was purified by flash chromatography.

Step d

[00690] This compound was prepared via Method A using 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine.

Step e

[00691] NaH (2eq) was added to a solution of [8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(1H-pyrazol-4-yl)-amine (1eq) in DMF. The solution was allowed to stir at room temperature for 30 min. Methylbromoacetate (1.2 eq) was added to the solution. The reaction mixture was allowed to stir at room temperarture for 16 hrs. Water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The expected product was purified by flash chromatography.

[00692] LiOH (2N) (2eq) was added to a solution of {4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-acetic acid methyl ester (1eq) in acetone. The resulting mixture was stirred at room temperature for 2 h. Water is added and the pH is acedified to pH=1 with HCl solution (1N). EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure.

[00693] {4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-acetic acid (1eq), HATU (1.5 eq), DIPEA (1 eq) and cyclopropylamine were stirred at room temperature in DMF for 16 hr. Water and EtOAc were added. The organic phases was separated, dried over $MgSO_4$ and evaporated under reduced pressure. The final compound was purified by preparative HPLC.

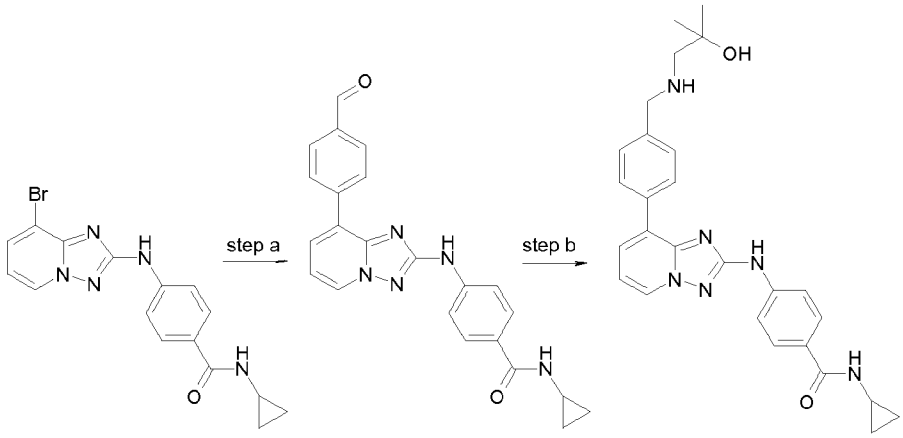
Compound 300

[00694] This compound was prepared via Method K using 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazin-2-one prepared via Method S.

Compound 301

[00695] This compound was prepared via Method K using 1-Methanesulfonyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine prepared via Method S.

Compound 302



Step a

[00696] To a solution of 4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide (1 eq) prepared by method K in EtOH and 1 N K_2CO_3 solution was added 4-formylphenylboronic acid (2 eq)) and $Pd(PPh_3)_4$ (5%) in a sealed 50 mL tube. The reaction mixture was heated at 110 °C for 10 min under microwave irradiation. After cooling to room temperature, the reaction mixture was diluted with H_2O (10 mL) and a precipitate was collected by filtration and washed with acetonitrile. The target compound was obtained.

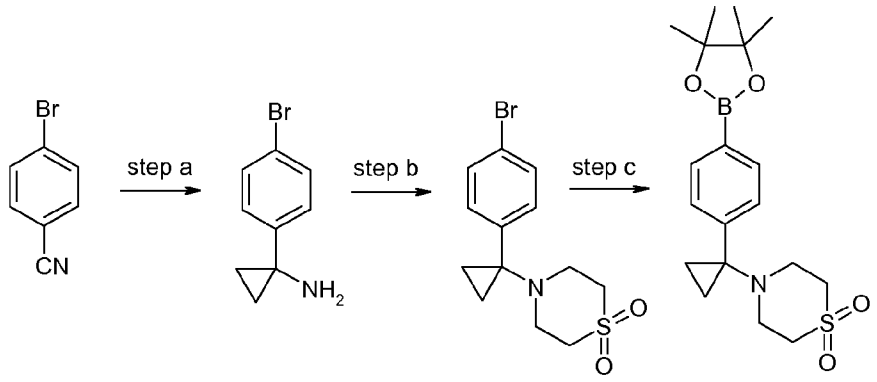
Step b

[00697] To a solution of N-cyclopropyl-4-[8-(4-formyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide (1 eq) and 1-Amino-2-methyl-propan-2-ol (1.2 eq) in a mixture of CH_2Cl_2/AcOH 10:1 was added PS-NMe_3BH_3CN (polymer supported cyanoborohydride) (2.5 eq). The reaction mixture was shaken for 14 h at room temperature then filtered. The filtrate was concentrated *in vacuo* and purified by flash column chromatography (Gradient, CH_2Cl_2 to CH_2Cl_2/MeOH [10:1]) to afford the desired product.

Compound 303

[00698] This compound was prepared via the same method as described for Compound 302 using 2-methanesulfonyl-ethylamine.

Compound 304



Step a

[00699] To a solution of 4-Bromo-benzonitrile (1 eq) and Ti(O*i*-Pr)$_4$ (1.1 eq.) in dry Et_2O (50 mL) was added EtMgBr (2.1 eq., 3 M in Et_2O) at -78 °C. The resulting yellow solution was stirred for 10 min at this temperature and allowed to warm to room temperature over 1 h. $BF_3.Et_2O$ (5.1 mL, 40 mmol) was added and the reaction mixture was further stirred for 1 h. The reaction mixture was quenched with HCl (1 M in H_2O) and Et_2O. NaOH (wt 10% in water) was added and the aqueous layer was extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to Et_2O) gave the desired product.

Step b

[00700] To a solution of **2** (1 eq) in *i*-PrOH in a 50 mL tube was added Na_2CO_3 (1.5 eq), H_2O and divinyl sulfone (1.5 eq) at room temperature. The tube was sealed and heated at 100 °C for 39 h. After cooling to room temperature a colourless precipitate formed which was collected by filtration, washed with H_2O, MeOH and Et_2O to give the desired product.

Step c

[00701] This compound was prepared via Method A using 4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methyl-benzamide prepared by Method K.

Compound 305

[00702] This compound was prepared via the same method as described for Compound 304 using 4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide prepared by Method K.

Compound 306

[00703] This compound was prepared via the same method as described for compound 289 using 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile.

Compound 307

[00704] This compound was prepared via the same method as described for Compound 302 using (S)-5-aminomethyl-pyrrolidin-2-one.

Compound 308

[00705] This compound was prepared via the samemethod as described for Compound 290 using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide.

Compound 309

[00706] This compound was prepared via Method K using cyclopropylamine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine-1-carboxylic acid amide prepared via Method S.

Compound 310

[00707] This compound was prepared via Method K using cyclopropylamine and (R)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine-3-carbonitrile prepared via Method S.

Compound 311

[00708] This compound was prepared via Method K using cyclopropylamine and (S)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidine-3-carbonitrile prepared via Method S.

Compound 312

[00709] This compound was prepared via the same procedure as described for Compound 296 using (R)-pyrrolidine-3-carbonitrile prepared via Method S.

Compound 313

[00710] This compound was prepared via the same procedure as described for Compound 296 using (S)-pyrrolidine-3-carbonitrile prepared via Method S.

Compound 314

[00711] This compound was prepared via the same procedure as described for Compound 302 using 1-aminomethyl-cyclopropanol prepared via Method S.

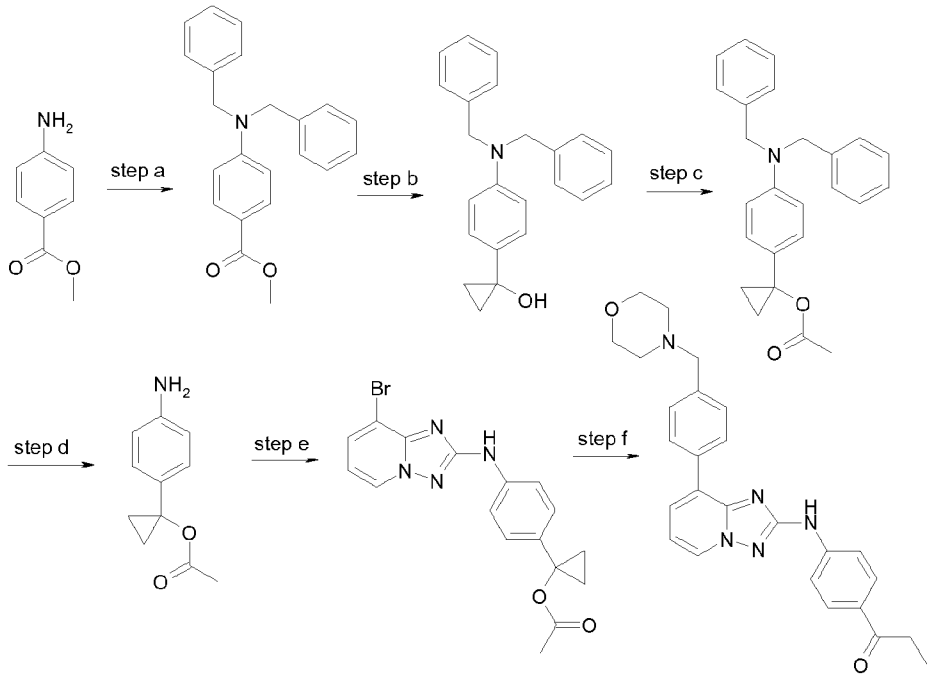
Compound 315

[00712] This compound was prepared via the same procedure as described for Compound 302 using 2-amino-ethanol.

Compound 316

[00713] This compound was prepared via the same procedure as described for Compound 302 using N-(2-amino-ethyl)-acetamide.

Compound 317



Step a

[00714] To a solution of 4-amino-benzoic acid methyl ester (3 g, 19.8 mmol) in dry DMF (50 mL) was added NaH (2.38 g, 59.5 mmol, 60% in mineral oil), followed by the addition of benzyl bromide (5.9 mL, 49.6 mmol). The reaction mixture was stirred at 40 °C for 16 h. Purification by flash column chromatography (Gradient, *iso*-hexane to 5% EtOAc) gave the desired product.

Step b

[00715] To a solution of Ti(O*i*-Pr)$_4$ (10 mL, 3 mmol) in dry Et_2O (60 mL) was added EtMgBr (14.6 mL, 44 mmol, 3 M in Et_2O) at -78 °C. The resulting red-brown mixture was stirred at -78 °C for 90 min. 4-dibenzylamino-benzoic acid methyl ester (3.31 g, 10 mmol) was then added and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was quenched with HCl (50 mL, 1 M in H_2O) and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step c

[00716] To a solution of 1-(4-dibenzylamino-phenyl)-cyclopropanol (1.1 g, 3.43 mmol) in CH_2Cl_2 (20 mL) were successively added Ac_2O (1.62 mL, 17.17 mmol), DMAP (41 mg, 0.17 mmol) and Et_3N (1.92 mL, 13.7 mmol). The reaction mixture was stirred at room temperature for 16 h. The

reaction mixture was concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step d

[00717] To a solution of acetic acid 1-(4-dibenzylamino-phenyl)-cyclopropyl ester (1.1 g, 3.43 mmol) in EtOH (20 mL) was added 10% Pd/C (126 mg) under medium pressure of H_2 (55 psi). The reaction mixture was shaken at room temperature for 16 h. The reaction mixture was filtered through Celite and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step e

[00718] To a solution of acetic acid 1-(4-amino-phenyl)-cyclopropyl ester (330 mg, 1.7 mmol) and 8-Bromo-2-iodo-[1,2,4]triazolo[1,5-a]pyridine (517 mg, 1.56 mmol) in dioxane (5 mL) were added $Pd_2(dba)_3$ (43 mg, 0.047 mmol), Xantphos (54 mg, 0.094 mmol) and Cs_2CO_3 (1 g, 3.13 mmol). The reaction mixture was degassed by sonication under a stream of N_2 for 10 min and then stirred at 90 °C for 16 h. The reaction mixture was diluted with CH_2Cl_2/MeOH (1:1) filtered through Celite and the filtrate was concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) yielded the target compound.

Step f

[00719] To a solution of acetic acid 1-[4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-cyclopropyl ester (92 mg, 0.24 mmol) in a solvent mixture of dioxane/H_2O (2.5 mL, 4:1) were added 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-morpholine (100 mg, 0.28 mmol), $Pd(dppf)Cl_2$ (5.8 mg, 7 µmol) and Na_2CO_3 (50 mg, 0.47 mmol) in a sealed tube. The reaction mixture was stirred at 90 °C for 17 h. The reaction mixture was filtered through Celite and washed with EtOAc (10 mL). The filtrate was concentrated *in vacuo* and redissolved in MeOH (3 mL). LiOH (50 mg, 2 mmol) was added and the reaction mixture was stirred at 25 °C for 16 h. Purification by preparative HPLC yielded the target compound.

Compound 318

[00720] This compound was prepared via the same procedure as described for Compound 317 using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide in the last step

Compound 319

[00721] This compound was prepared via the same method as described for Compound 302 using 2-amino-N-cyclopropyl-acetamide.

Compound 320

[00722] This compound was prepared via Method M'' followed by Method A using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide.

Compound 321

[00723] This compound was prepared via the same method as described for Compound 286 using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazin-2-one.

Compound 322

[00724] This compound was prepared via Method K using cyclopropylamine and N-{(S)-1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-pyrrolidin-3-yl}-acetamide (using (S)-3-acetamidopyrrolidine).

Compound 323

[00725] This compound was prepared via the same method as described for Compound 317 using 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-azetidine-3-carbonitrile in the last step.

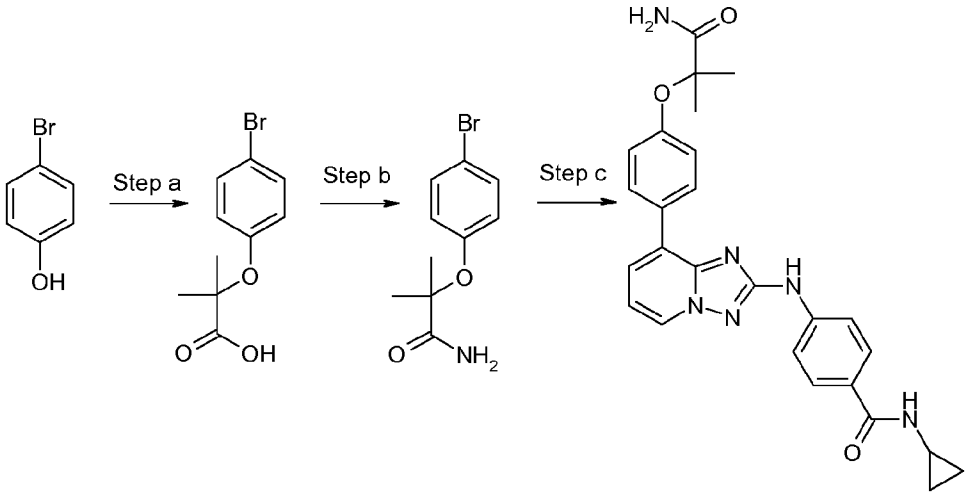
Compound 324

[00726] This compound was prepared via the same method as described for Compound 286 using 1-{4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazin-1-yl}-ethanone.

Compound 325

[00727] This compound was prepared via the same method as described for Compound 286 using 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-piperazine-1-carboxylic acid amide.

Compound 326



Step a

[00728] To a solution of 4-Bromo-phenol (50 g, 290 mmol) in $CHCl_3$ (21 mL, 260 mmol) and acetone (350 mL) was added NaOH (55 g, 1.38 mol). The reaction mixture was warmed gently resulting in a vigorous reflux and the mixture was then heated at reflux for 16 h. The mixture was diluted with water, stirred and acidified with 6 M HCl. The organic layer was separated and the solvent was removed in vacuo. The resultant oil solidified on addition of water and pet ether 40-60/Et_2O and the solid was washed with water and petroleum ether, and dried in vacuo to give the title compound.

Step b

[00729] 2-(4-Bromo-phenoxy)-2-methyl-propionic acid (15 g, 57.9 mmol) was suspended in thionyl chloride (45 mL) and the mixture heated at reflux for 2 h. The mixture was allowed to cool to room temperature and the excess thionyl chloride removed *in vacuo* to yield the crude acyl chloride which was used in the following reactions.

[00730] The crude acyl chloride (7.5 g, 27 mmol) was poured into ice cold conc. NH_3 (aq) (50 mL) resulting in the formation of an off-white precipitate. The precipitate was collected by filtration and the solid was washed with water and dried *in vacuo* yielding the product.

Step c

[00731] 2-(4-Bromo-phenoxy)-2-methyl-propionamide (1 eq), bispinacolato diboron (1.3 eq), KOAc (1.3 eq), Pd(dppf)Cl_2 (0.05 eq) and dioxane were combined, degassed and heated to 90 °C for 16 h. The reaction mixture was allowed to cool to room temperature, diluted with EtOAc and filtered through Celite. The solvent was removed *in vacuo* to yield the crude boronic ester.

[00732] A mixture of 4-(8-Bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide (1 eq), the boronic ester (1.2 eq), PS-Pd(PPh_3)$_4$ (polymer supported Pd(PPh_3)$_4$, 0.03 eq) and K_2CO_3 (1 M in H_2O, 1.2 eq) in EtOH in a sealed 10 mL tube was heated at 110 °C for 10 min under microwave irradiation. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer was separated and concentrated *in vacuo*. Purification by preparative HPLC gave the desired product.

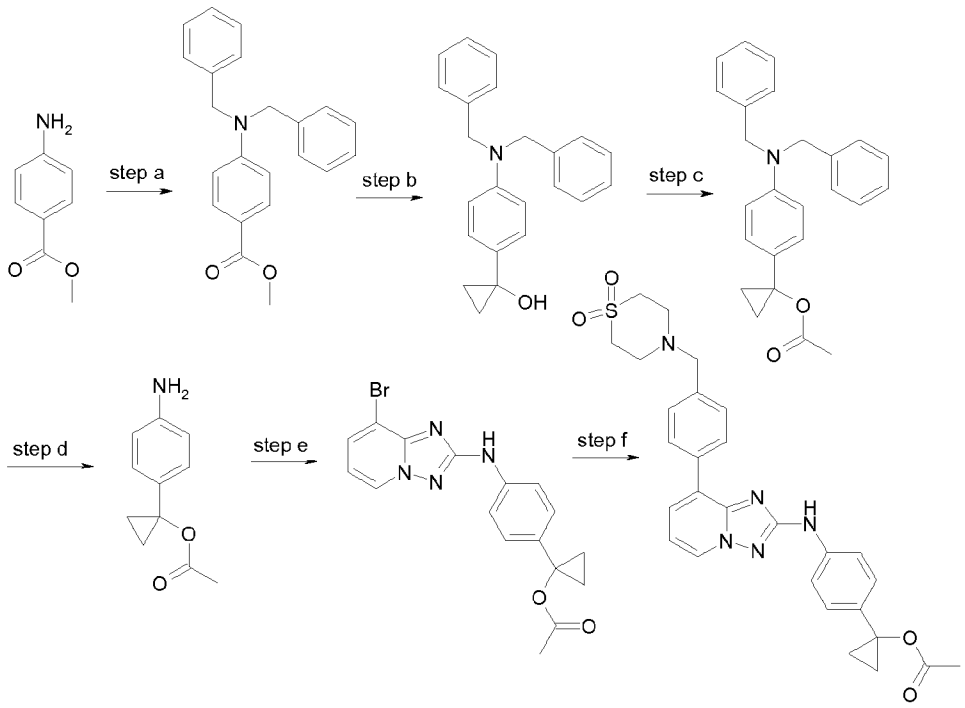
Compound 327

[00733] This compound was prepared via Method K using cyclopropylamine and 1-Methyl-4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-piperazine.

Compound 328

[00734] This compound was prepared via Method K using cyclopropylamine and 4-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-piperazine-1-carboxylic acid tert-butyl ester.

Compound 329



Step a

[00735] To a solution of 4-amino-benzoic acid methyl ester (3 g, 19.8 mmol) in dry DMF (50 mL) was added NaH (2.38 g, 59.5 mmol, 60% in mineral oil), followed by the addition of benzyl bromide (5.9 mL, 49.6 mmol). The reaction mixture was stirred at 40 °C for 16 h. Purification by flash column chromatography (Gradient, *iso*-hexane to 5% EtOAc) gave the desired product.

Step b

[00736] To a solution of Ti(O*i*-Pr)$_4$ (10 mL, 3 mmol) in dry Et_2O (60 mL) was added EtMgBr (14.6 mL, 44 mmol, 3 M in Et_2O) at -78 °C. The resulting red-brown mixture was stirred at -78 °C for 90 min. 4-Dibenzylamino-benzoic acid methyl ester (3.31 g, 10 mmol) was then added and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was quenched with HCl (50 mL, 1 M in H_2O) and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step c

[00737] To a solution of 1-(4-dibenzylamino-phenyl)-cyclopropanol (1.1 g, 3.43 mmol) in CH_2Cl_2 (20 mL) were successively added Ac_2O (1.62 mL, 17.17 mmol), DMAP (41 mg, 0.17 mmol) and Et_3N (1.92 mL, 13.7 mmol). The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step d

[00738] To a solution of acetic acid 1-(4-dibenzylamino-phenyl)-cyclopropyl ester (1.1 g, 3.43 mmol) in EtOH (20 mL) was added 10% Pd/C (126 mg) under medium pressure of H_2 (55 psi). The reaction mixture was shaken at room temperature for 16 h. The reaction mixture was filtered through Celite and concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) gave the desired product.

Step e

[00739] To a solution of acetic acid 1-(4-amino-phenyl)-cyclopropyl ester (330 mg, 1.7 mmol) and 8-Bromo-2-iodo-[1,2,4]triazolo[1,5-a]pyridine (517 mg, 1.56 mmol) in dioxane (5 mL) were added $Pd_2(dba)_3$ (43 mg, 0.047 mmol), Xantphos (54 mg, 0.094 mmol) and Cs_2CO_3 (1 g, 3.13 mmol). The reaction mixture was degassed by sonication under a stream of N_2 for 10 min and then stirred at 90 °C for 16 h. The reaction mixture was diluted with CH_2Cl_2/MeOH (1:1) filtered through Celite and the filtrate was concentrated *in vacuo*. Purification by flash column chromatography (Gradient, *iso*-hexane to EtOAc) yielded the target compound.

Step f

[00740] To a solution of acetic acid 1-[4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-cyclopropyl ester (92 mg, 0.24 mmol) in a solvent mixture of dioxane/H_2O (2.5 mL, 4:1) were added 4-[4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-thiomorpholine 1,1-dioxide (100 mg, 0.28 mmol), $Pd(dppf)Cl_2$ (5.8 mg, 7 µmol) and Na_2CO_3 (50 mg, 0.47 mmol) in a sealed tube. The reaction mixture was stirred at 90 °C for 17 h. The reaction mixture was filtered through Celite and washed with EtOAc (10 mL). The filtrate was concentrated *in vacuo* and eluted with EtOAc. Purification by preparative HPLC yielded the target compound.

Compound 330

[00741] This compound was prepared via Method K using cyclopropylamine and 1-[4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzyl]-4-(2,2,2-trifluoro-ethyl)-piperazine prepared by method S (using 1-(2,2,2-Trifluoro-ethyl)-piperazine).

Compound 331

[00742] This compound was prepared via Method K using cyclopropylamine and N,N-dimethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-benzenesulfonamide.

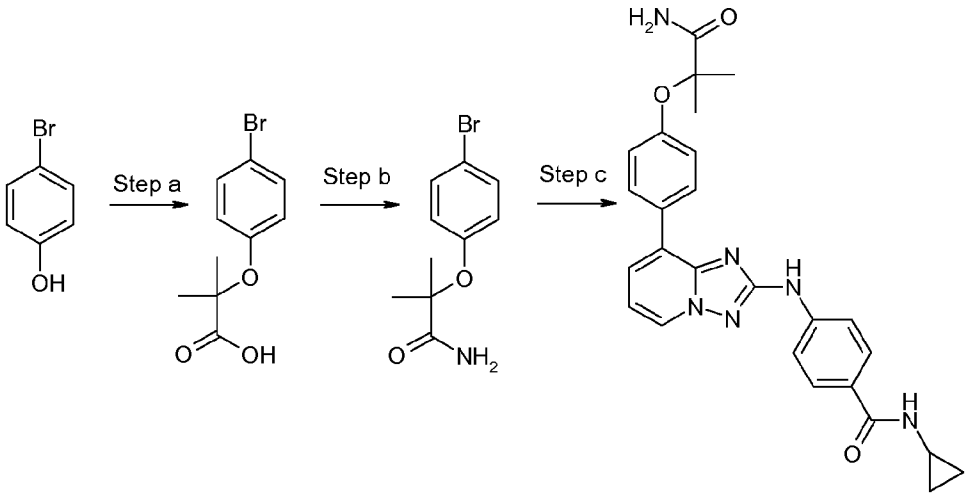
Compound 332

[00743] This compound was prepared via Method K using cyclopropylamine and benzothiophene-3-boronic acid.

Compound 333

[00744] This compound was prepared via Method K using cyclopropylamine and 2-(4-methylpiperazin-1-yl)pyridine-4-boronic acid, pinacol ester.

Compound 334



Step a

[00745] To a solution of 4-bromo-phenol (50 g, 290 mmol) in $CHCl_3$ (21 mL, 260 mmol) and acetone (350 mL) was added NaOH (55 g, 1.38 mol). The reaction mixture was warmed gently resulting in a vigorous reflux and the mixture was then heated at reflux for 16 h. The mixture was diluted with water, stirred and acidified with 6 M HCl. The organic layer was separated and the solvent was removed *in vacuo*. The resultant oil solidified on addition of water and pet ether 40-60/Et_2O and the solid was washed with water and petroleum ether, and dried *in vacuo* to give the title compound.

Step b

[00746] 2-(4-Bromo-phenoxy)-2-methyl-propionic acid (15 g, 57.9 mmol) was suspended in thionyl chloride (45 mL) and the mixture heated at reflux for 2 h. The mixture was allowed to cool to room temperature and the excess thionyl chloride removed *in vacuo* to yield the crude acyl chloride which was used in the following reactions.

[00747] A solution of methylamine was added dropwise to a solution of the crude acyl chloride in THF at 0°C. The reaction mixture was allowed to warm to room temperature and the mixture was allowed to stir for an additional 1hr. The mixture was poured into water and the aqueous axtracted with EtOAc. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo yielding the target compound.

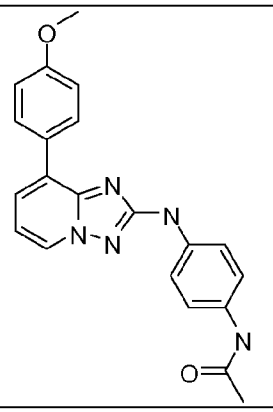
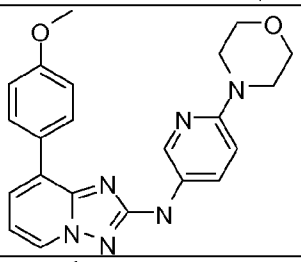
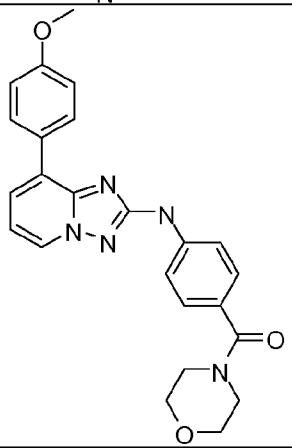
Step c

[00748] 2-(4-Bromo-phenoxy)-2,N-dimethyl-propionamide (1 eq), bispinacolato diboron (1.3 eq), KOAc (1.3 eq), Pd(dppf)Cl_2 (0.05 eq) and dioxane were combined, degassed and heated to 90 °C for 16 h. The reaction mixture was allowed to cool to room temperature, diluted with EtOAc and filtered through Celite. The solvent was removed *in vacuo* to yield the crude boronic ester.

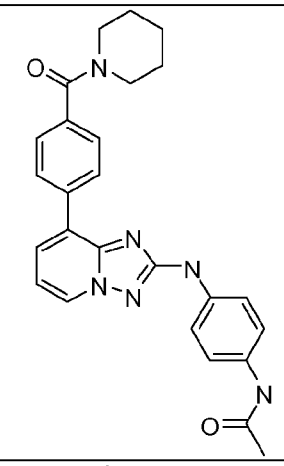
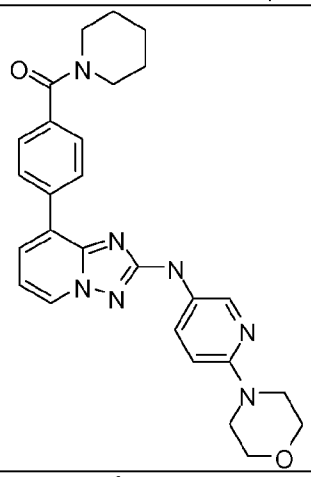
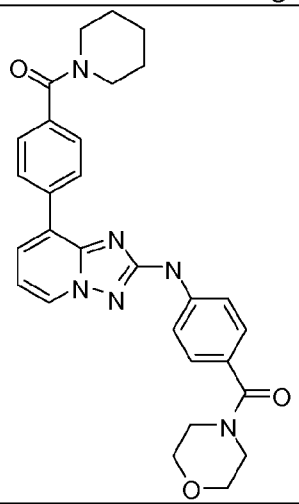
[00749] A mixture of 4-(8-bromo-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide (1 eq), the boronic ester (1.2 eq), PS-$Pd(PPh_3)_4$ (polymer supported $Pd(PPh_3)_4$, 0.03 eq) and K_2CO_3 (1 M in H_2O, 1.2 eq) in EtOH in a sealed 10 mL tube was heated at 110 °C for 10 min under microwave irradiation. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2/MeOH/H_2O and the mixture filtered through Celite. The organic layer was separated and concentrated *in vacuo*. Purification by preparative HPLC gave the desired product

[00750] The exemplary compounds have been or can be prepared according to the synthetic methods described herein are listed in Table I below. The NMR spectral data of some representative compounds of the invention is given in Table II.

[00751] **Table I: Exemplary Compounds of the Invention**

Cpd #	Structure	Name	MW	MS Mes'd
1		N-{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	373.4	374
2		[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine	402.5	403.1
3		{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-morpholin-4-yl-methanone	429.5	430

GAL-113-WO-PCT

Cpd #	Structure	Name	MW	MS Mes'd
4		N-(4-{8-[4-(Piperidine-1-carbonyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	454.5	455.1
5		{4-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-phenyl}-piperidin-1-yl-methanone	483.6	484.1
6		(4-{2-[4-(Morpholine-4-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenyl)-piperidin-1-yl-methanone	510.6	511.1

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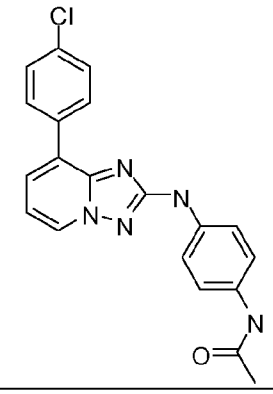
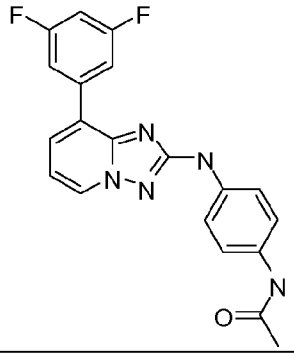
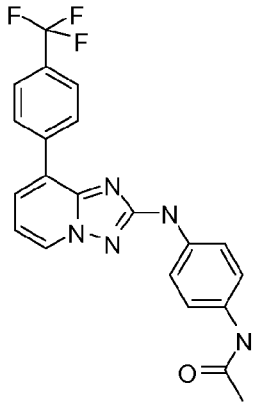
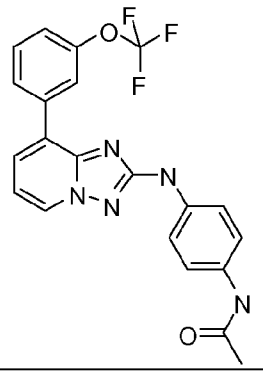
Cpd #	Structure	Name	MW	MS Mes'd
7		N-{4-[8-(4-Chloro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	378.0	378
8		N-{4-[8-(3,5-Difluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	379.0	380
9		N-{4-[8-(4-Trifluoromethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	411.0	412
10		N-{4-[8-(3-Trifluoromethoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	427.0	428

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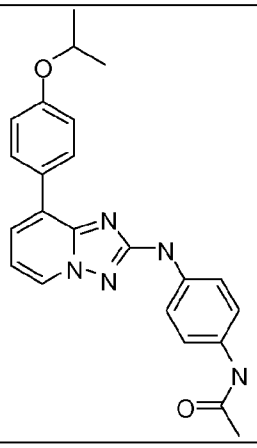
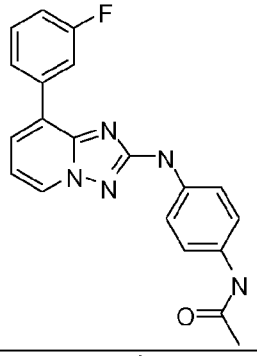
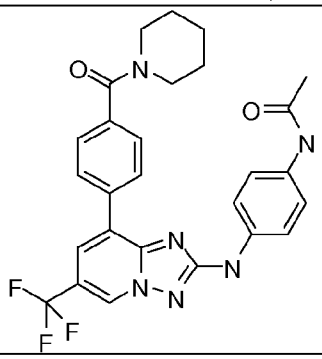
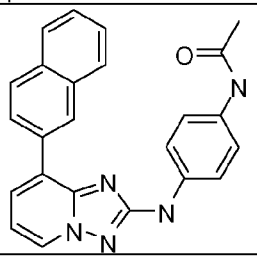
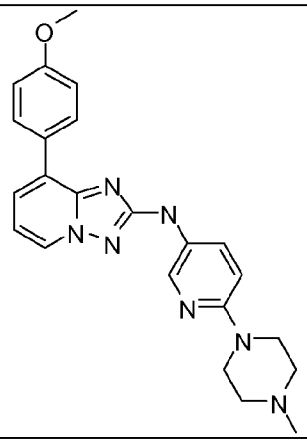
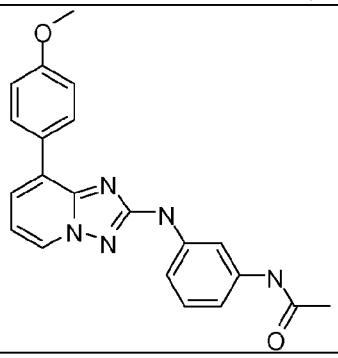
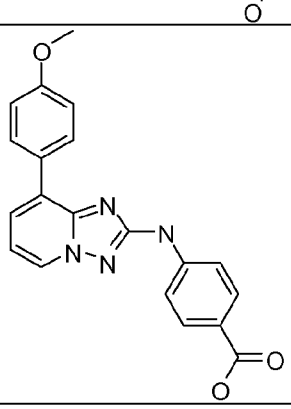
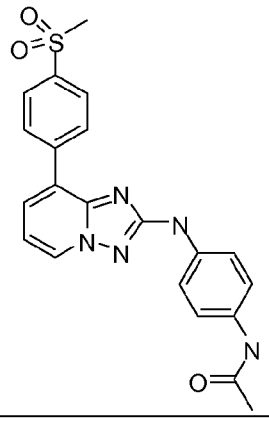
Cpd #	Structure	Name	MW	MS Mes'd
11		N-{4-[8-(4-Isopropoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	401.0	402
12		N-{4-[8-(3-Fluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	361.0	362
13		N-(4-{8-[4-(Piperidine-1-carbonyl)-phenyl]-6-trifluoromethyl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	523.0	1.31 min
14		N-[4-(8-Naphthalen-2-yl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-acetamide	393.0	394

GAL-113-WO-PCT

Cpd #	Structure	Name	MW	MS Mes'd
15		[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-amine	415.5	416.1
16		N-{3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	373.4	374
17		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid	360.4	361
18		N-{4-[8-(4-Methanesulfonyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	421.5	422

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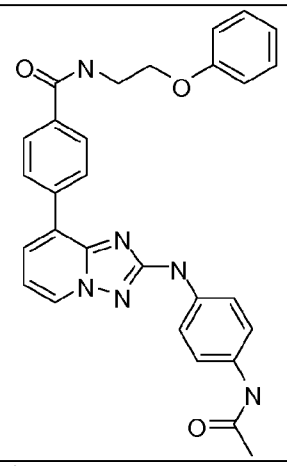
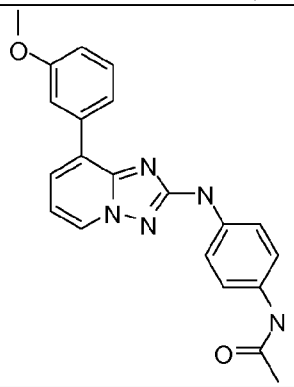
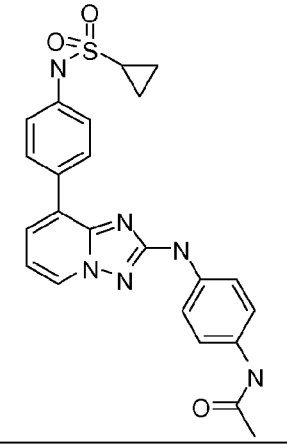
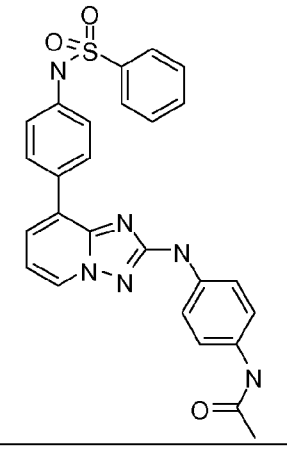
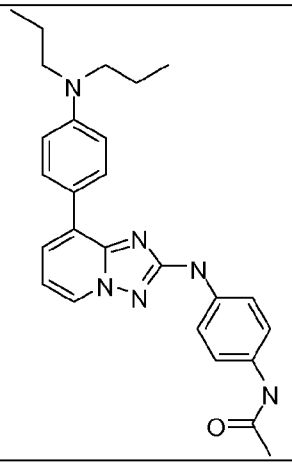
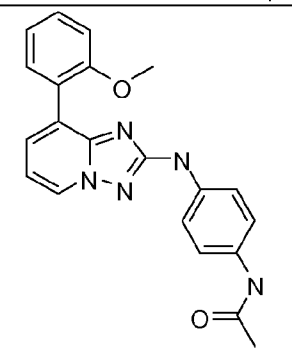
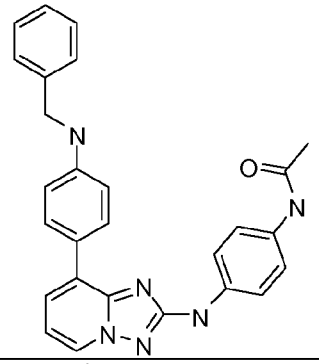
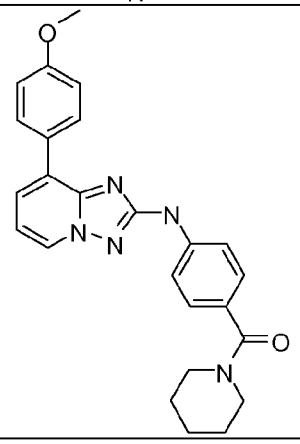
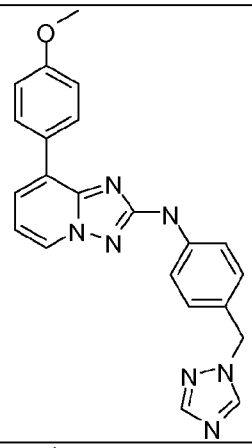
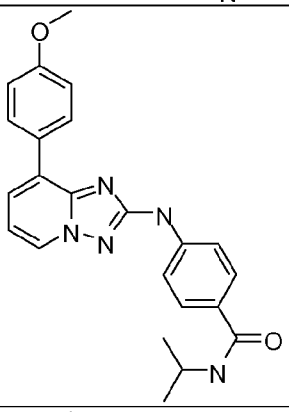
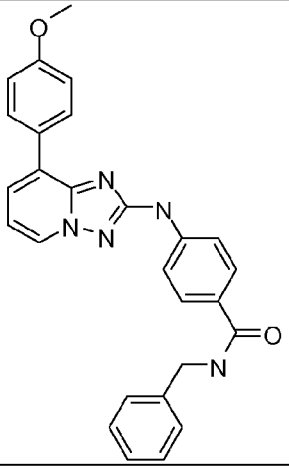
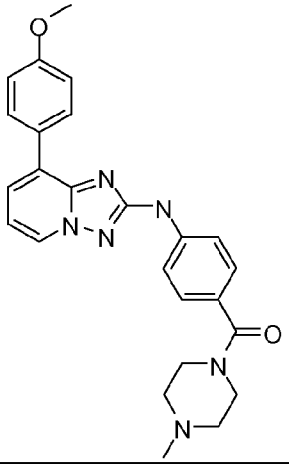
Cpd #	Structure	Name	MW	MS Mes'd
19		4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-N-(2-phenoxy-ethyl)-benzamide	506.6	507
20		N-{4-[8-(3-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	373.4	374
21		N-{4-[8-(4-Cyclopropanesulfonylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	462.5	463
22		N-{4-[8-(4-Benzenesulfonylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	498.6	499

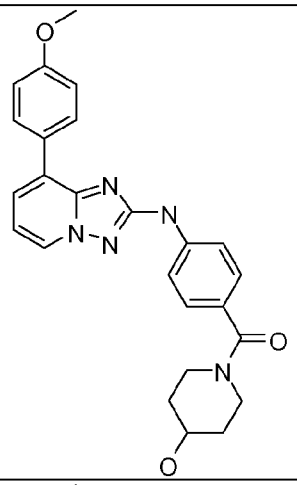
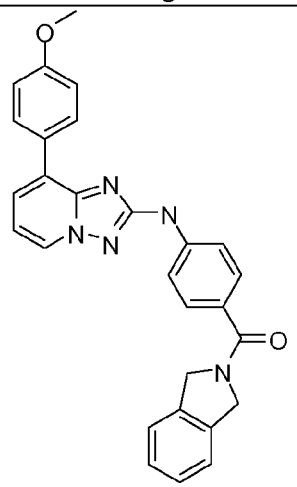
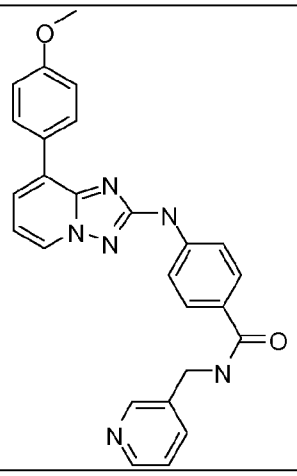
GAL-113-WO-PCT

Cpd #	Structure	Name	MW	MS Mes'd
23		N-{4-[8-(4-Dipropylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	442.6	443.1
24		N-{4-[8-(2-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	373.4	374
25		N-{4-[8-(4-Benzylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	448.5	449
26		{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-piperidin-1-yl-methanone	427.5	428.1

GAL-113-WO-PCT

Cpd #	Structure	Name	MW	MS Mes'd
27		[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-[1,2,4]triazol-1-ylmethyl-phenyl)-amine	397.4	329 (M+H-69)
28		N-Isopropyl-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	401.5	402
29		N-Benzyl-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	449.5	450
30		{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-(4-methyl-piperazin-1-yl)-methanone	442.5	443

GAL-113-WO-PCT

Cpd #	Structure	Name	MW	MS Mes'd
31		(4-Hydroxy-piperidin-1-yl)-{4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-methanone	443.5	444
32		(1,3-Dihydro-isoindol-2-yl)-{4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-methanone	461.5	462
33		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-3-ylmethyl-benzamide	450.5	451.1

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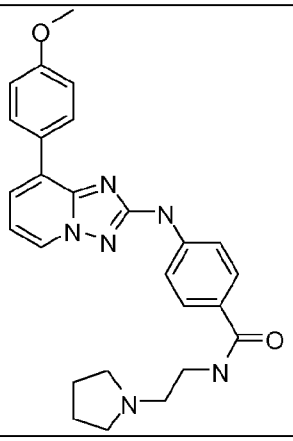
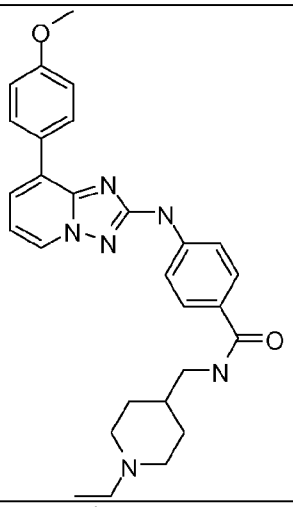
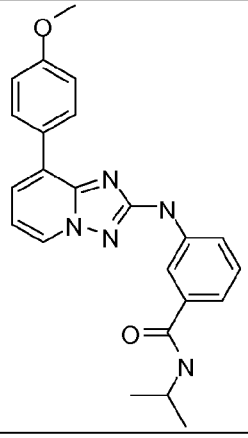
Cpd #	Structure	Name	MW	MS Mes'd
34		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	456.6	457.1
35		N-(1-Ethyl-piperidin-4-ylmethyl)-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	485.0	485.1
36		N-Isopropyl-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	401.5	402.1

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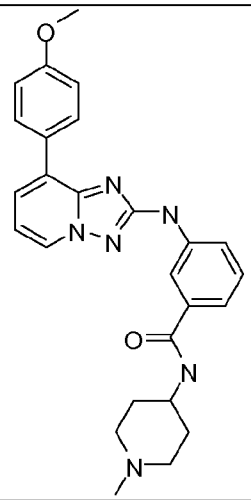
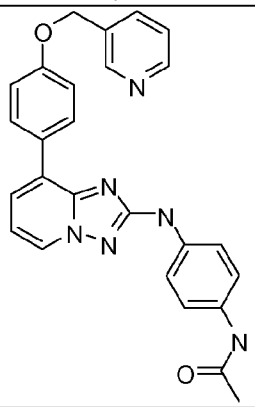
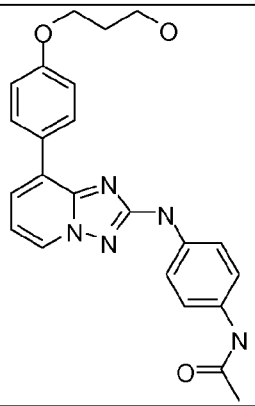
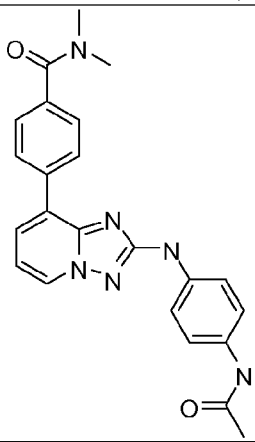
Cpd #	Structure	Name	MW	MS Mes'd
37		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(1-methyl-piperidin-4-yl)-benzamide	456.6	457.2
38		N-(4-{8-[4-(Pyridin-3-ylmethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	451.0	451
39		N-(4-{8-[4-(3-Hydroxy-propoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	417.0	418.1
40		4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-N,N-dimethyl-benzamide	414.0	415.1

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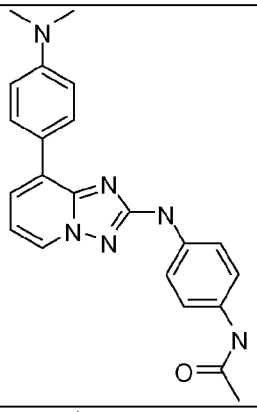
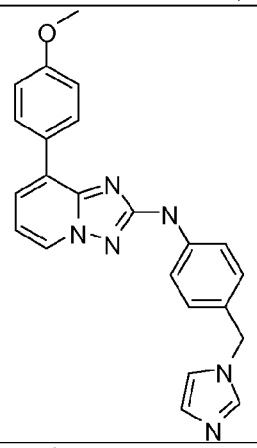
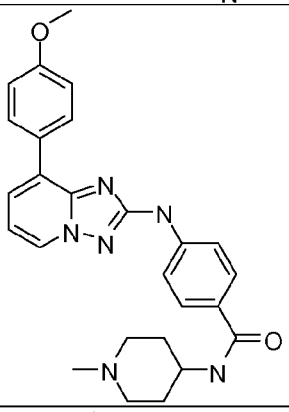
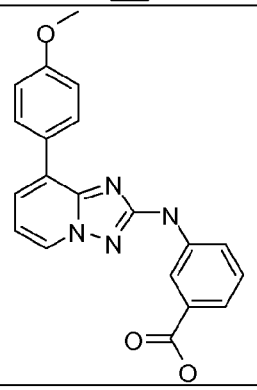
Cpd #	Structure	Name	MW	MS Mes'd
41		N-{4-[8-(4-Dimethylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	386.5	387.1
42		(4-Imidazol-1-ylmethyl-phenyl)-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine	396.5	329.0 (M+)-68
43		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(1-methyl-piperidin-4-yl)-benzamide	456.6	457.1
44		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid	360.4	361

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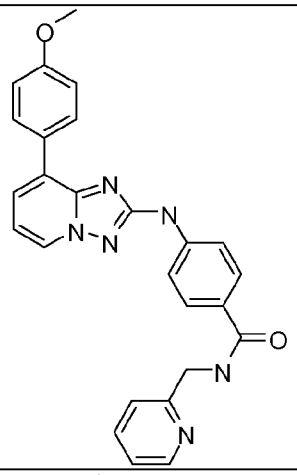
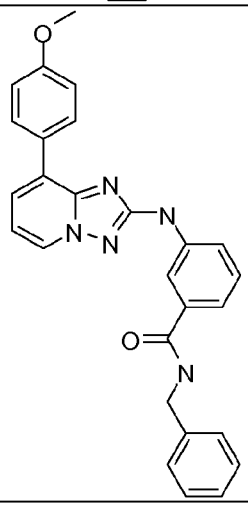
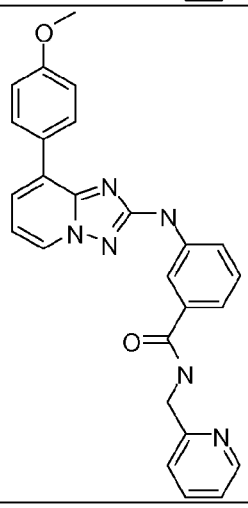
Cpd #	Structure	Name	MW	MS Mes'd
45		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-2-ylmethyl-benzamide	450.5	451.1
46		N-Benzyl-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	449.5	450
47		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-2-ylmethyl-benzamide	450.5	451.1

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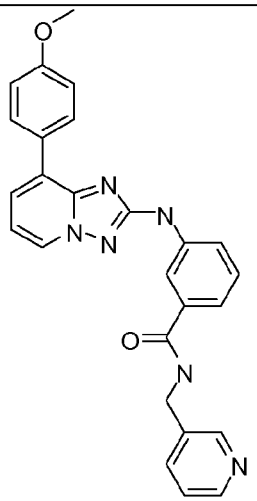
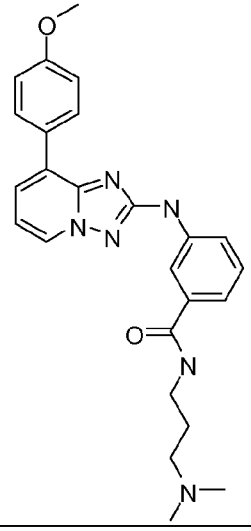
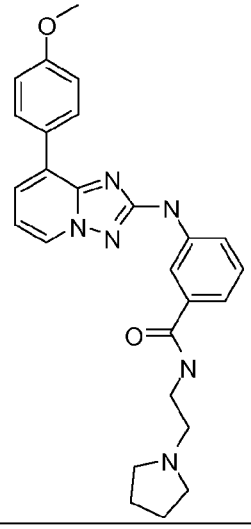
Cpd #	Structure	Name	MW	MS Mes'd
48		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-3-ylmethyl-benzamide	451.0	451.1
49		N-(3-Dimethylamino-propyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	444.5	445.1
50		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide	456.6	457.1

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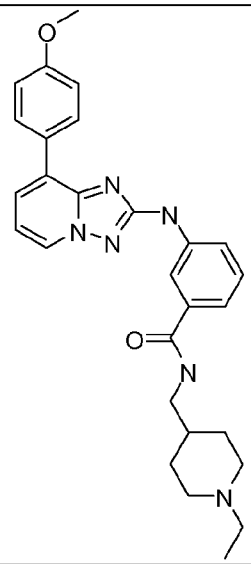
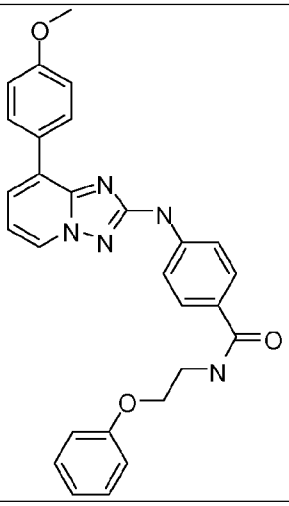
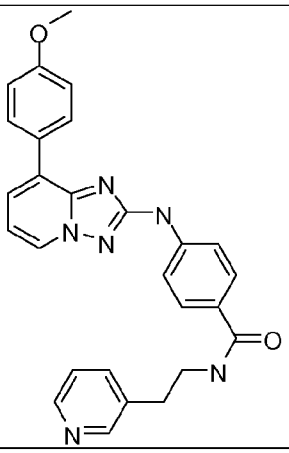
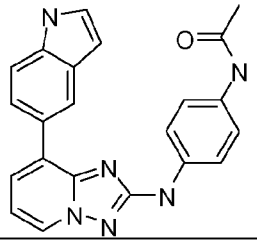
Cpd #	Structure	Name	MW	MS Mes'd
51		N-(1-Ethyl-piperidin-4-ylmethyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	484.6	485.1
52		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-phenoxy-ethyl)-benzamide	480.0	480.1
53		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyridin-3-yl-ethyl)-benzamide	464.5	465.1
54		N-{4-[8-(1H-Indol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	382.0	383

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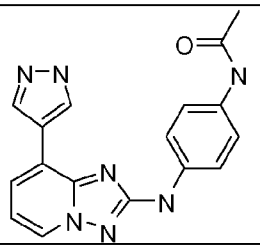
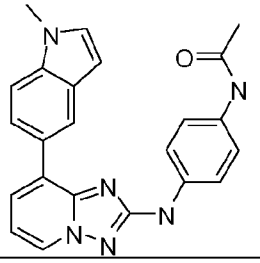
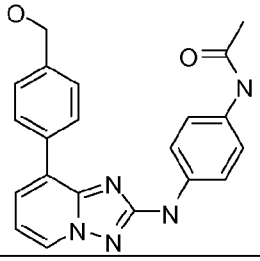
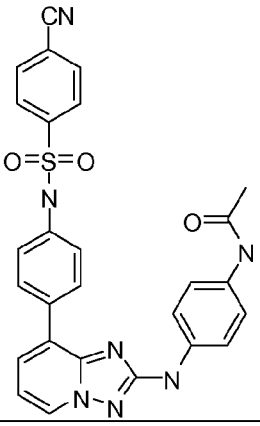
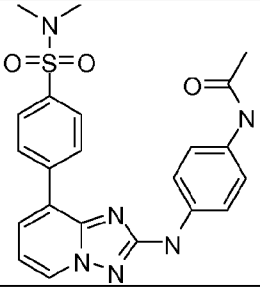
Cpd #	Structure	Name	MW	MS Mes'd
55		N-{4-[8-(1H-Pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	333.0	-
56		N-{4-[8-(1-Methyl-1H-indol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	396.0	397.1
57		N-{4-[8-(4-Hydroxymethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	373.0	374
58		N-(4-{8-[4-(4-Cyano-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	524.0	524.1
59		N-{4-[8-(4-Dimethylsulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	451.0	451.1

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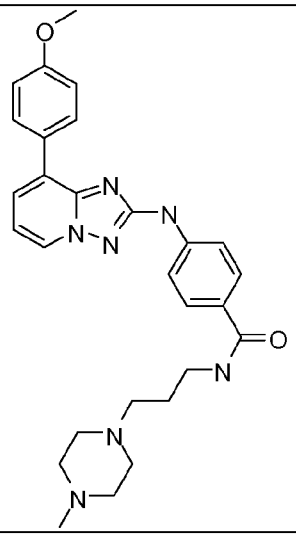
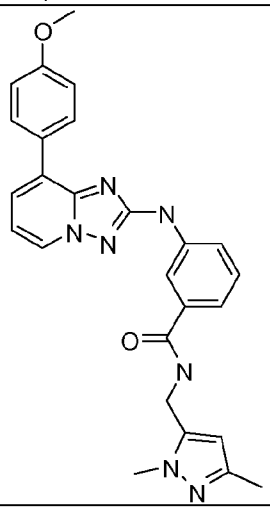
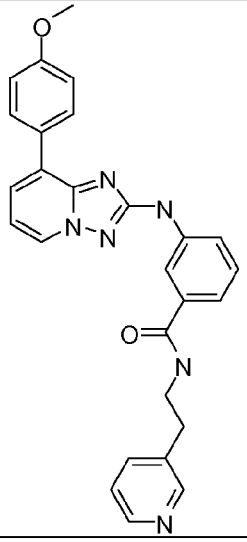
Cpd #	Structure	Name	MW	MS Mes'd
60		4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide	499.6	500.2
61		N-(2,5-Dimethyl-2H-pyrazol-3-ylmethyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	467.5	468.1
62		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyridin-3-yl-ethyl)-benzamide	464.5	465

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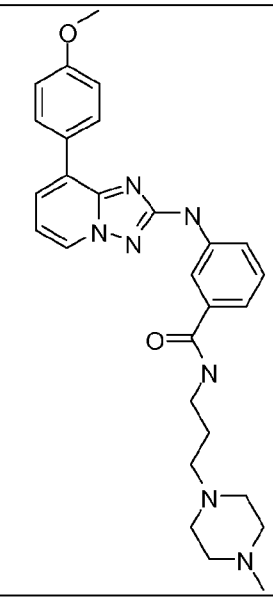
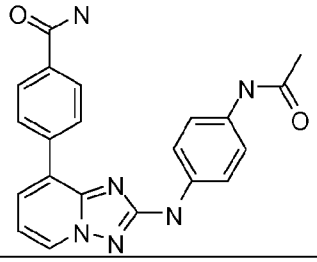
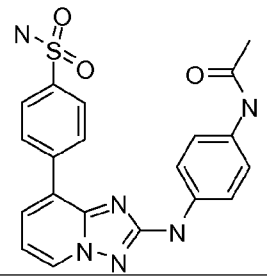
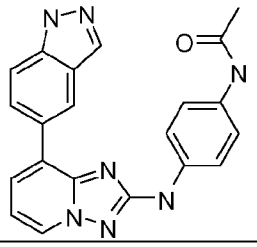
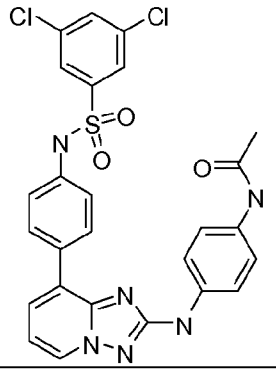
Cpd #	Structure	Name	MW	MS Mes'd
63		3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide	499.6	500.2
64		4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzamide	386.0	387.1
65		N-{4-[8-(4-Sulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	422.0	423
66		N-{4-[8-(1H-Indazol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide	383.0	384.1
67		N-(4-{8-[4-(3,5-Dichloro-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	567.0	567

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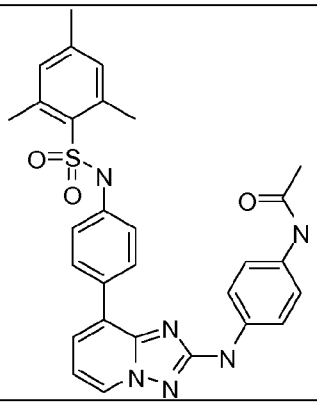
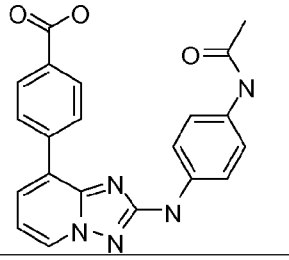
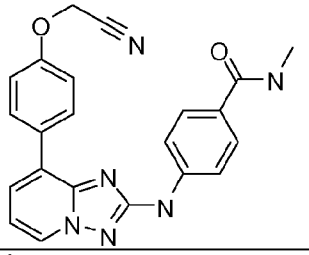
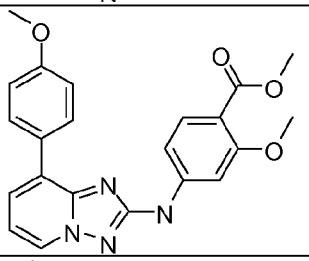
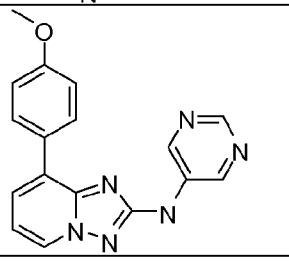
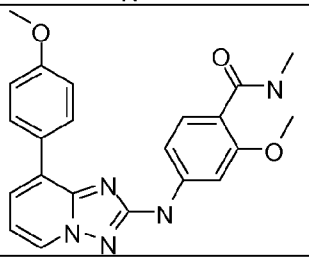
Cpd #	Structure	Name	MW	MS Mes'd
68		N-(4-{8-[4-(2,4,6-Trimethyl-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide	540.6	541.2
69		4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzoic acid	387.0	Not detected
70		4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	398.1	399
71		methyl 2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzate	404.1	405
72		8-(4-methoxyphenyl)-N-(pyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	318.1	319
73		2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	403.2	404

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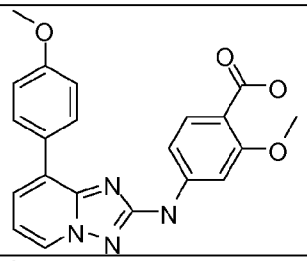
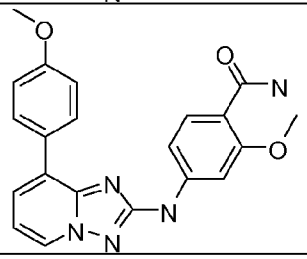
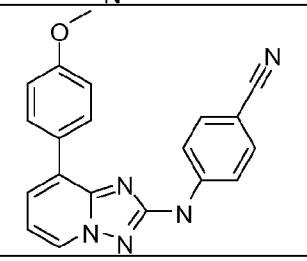
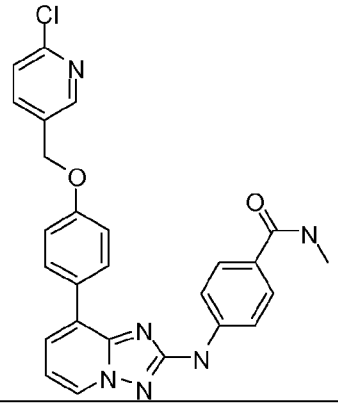
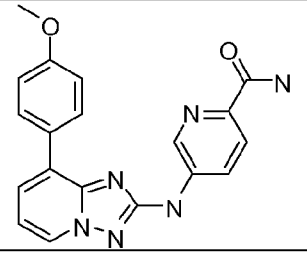
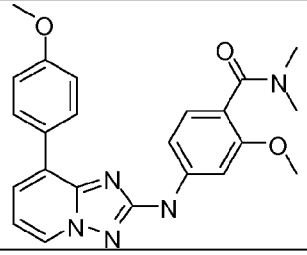
Cpd #	Structure	Name	MW	MS Mes'd
74		2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzic acid	390.1	391
75		2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	389.1	390
76		4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzonitrile	341.1	340
77		4-(8-(4-((6-chloropyridin-3-yl)methoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	484.1	485
78		5-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide	360.1	
79		2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N,N-dimethylbenzamide	417.2	418

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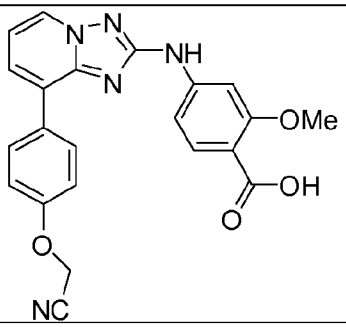
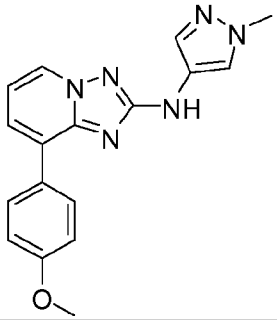
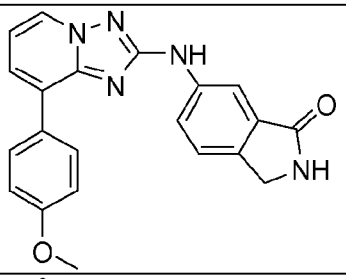
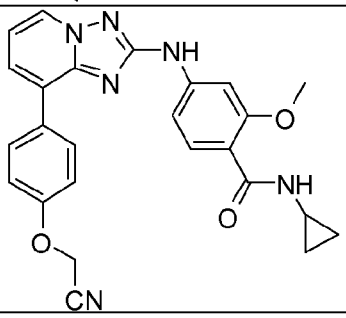
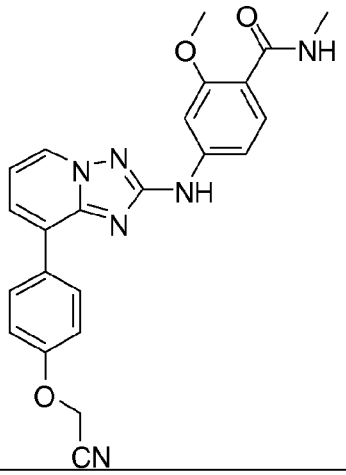
Cpd #	Structure	Name	MW	MS Mes'd
80		4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxybenzic acid	415.41	416
81		8-(4-methoxyphenyl)-N-(1-methyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	320.36	321
82		6-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one	371.40	372
83		4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methoxybenzamide	454.49	455
84		4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxy-N-methylbenzamide	428.45	429

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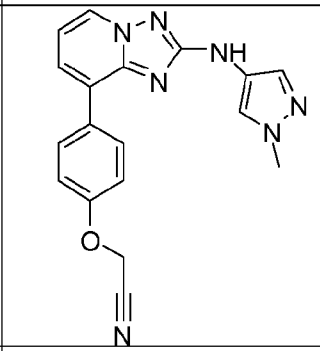
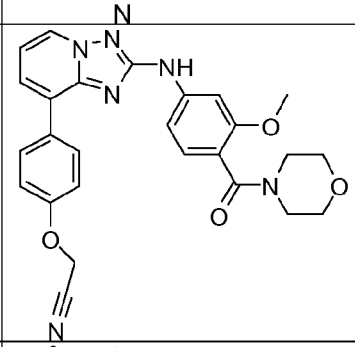
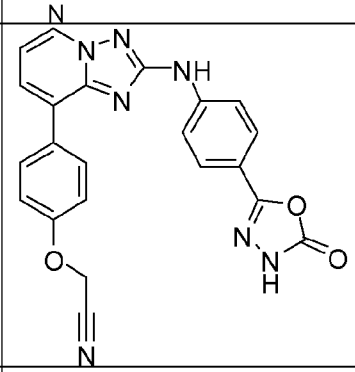
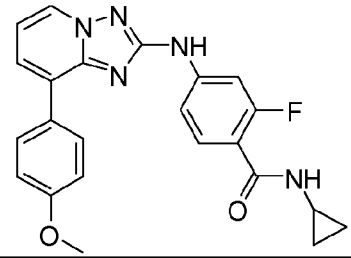
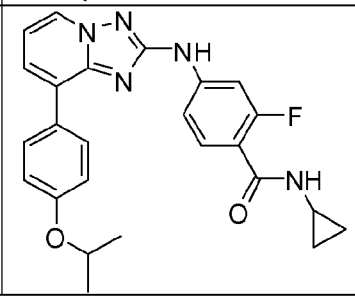
Cpd #	Structure	Name	MW	MS Mes'd
85		2-(4-(2-(1-methyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile	345.37	346
86		2-(4-(2-(3-methoxy-4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile	484.52	485
87		2-(4-(2-(4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile	425.41	426
88		N-cyclopropyl-2-fluoro-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	417.44	418
89		N-cyclopropyl-2-fluoro-4-(8-(4-isopropoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	445.50	446

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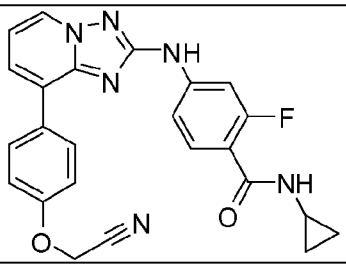
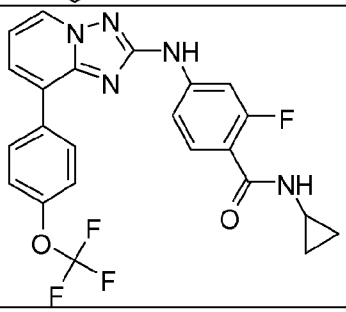
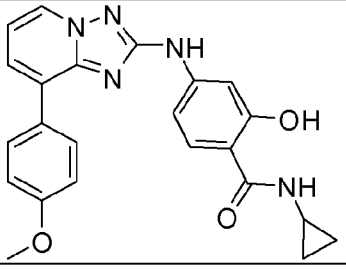
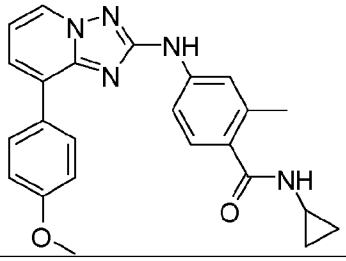
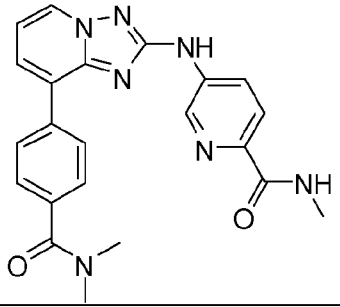
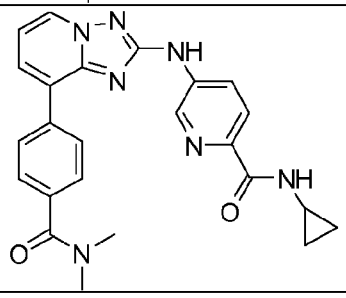
Cpd #	Structure	Name	MW	MS Mes'd
90		4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-fluorobenzamide	442.45	443
91		N-cyclopropyl-2-fluoro-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	471.41	472
92		N-cyclopropyl-2-hydroxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	415.45	416
93		N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methylbenzamide	413.48	414
94		5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	415.46	416
96		N-cyclopropyl-5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide	441.49	442

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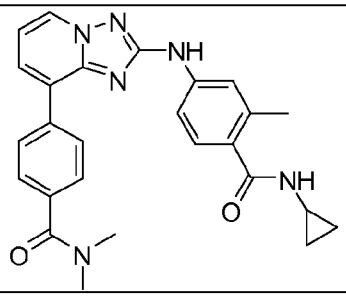
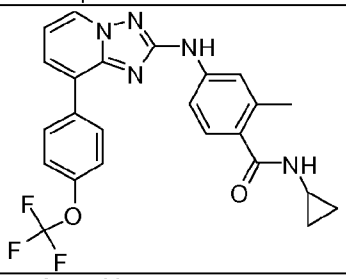
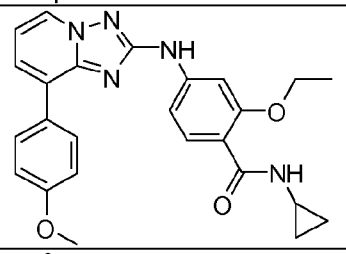
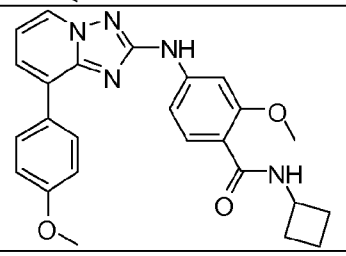
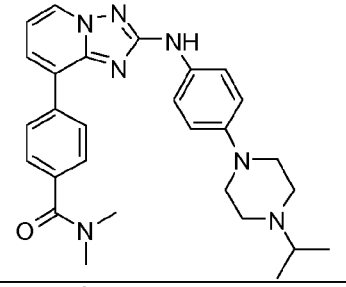
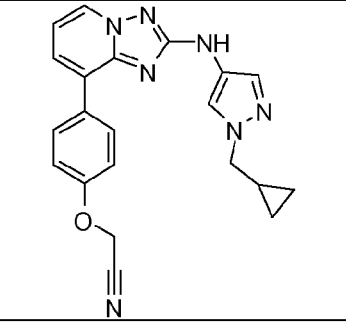
Cpd #	Structure	Name	MW	MS Mes'd
97		N-cyclopropyl-4-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methylbenzamide	454.53	455
98		N-cyclopropyl-2-methyl-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	467.45	468
99		N-cyclopropyl-2-ethoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	443.51	444
100		N-cyclobutyl-2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	443.51	444
101		4-(2-(4-(4-isopropylpiperazin-1-yl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	483.62	484
103		2-(4-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile	385.43	386

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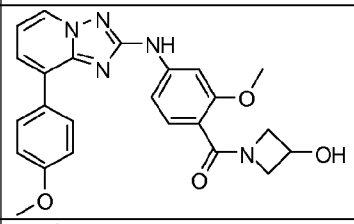
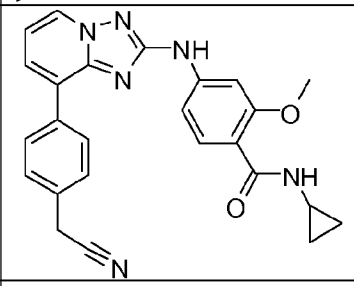
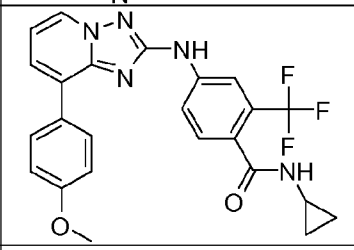
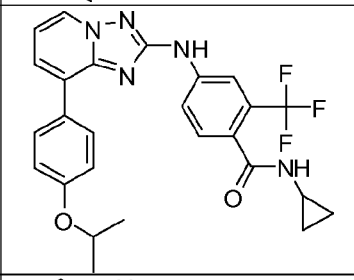
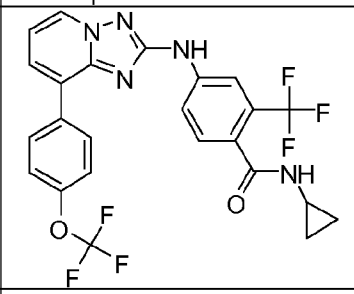
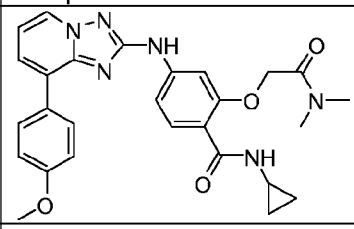
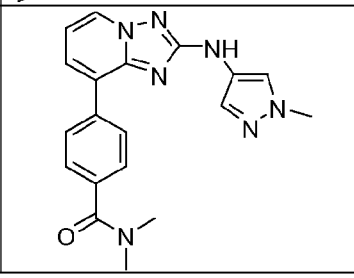
Cpd #	Structure	Name	MW	MS Mes'd
104		(3-hydroxyazetidin-1-yl)(2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	445.48	446
105		4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methoxybenzamide	438.49	439
106		N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide	467.45	468
107		N-cyclopropyl-4-(8-(4-isopropoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide	495.50	496
108		N-cyclopropyl-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide	521.42	522
109		N-cyclopropyl-2-(2-(dimethylamino)-2-oxoethoxy)-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	500.56	501
110		N,N-dimethyl-4-(2-(1-methyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	361.41	362

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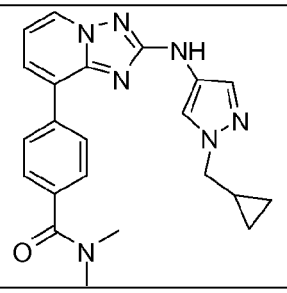
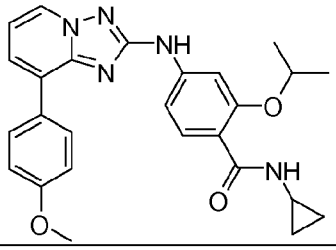
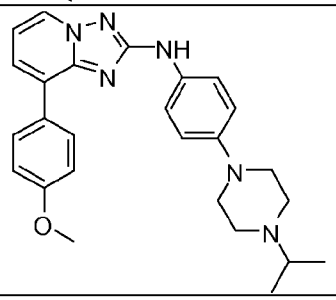
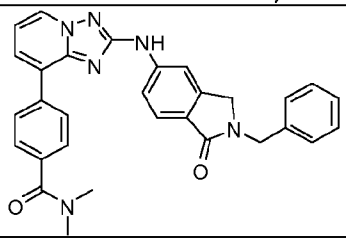
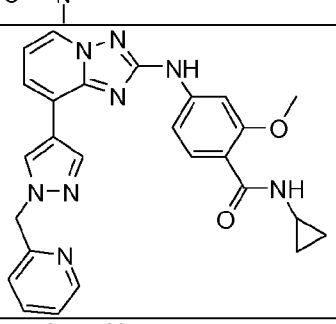
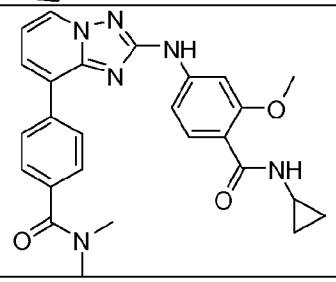
Cpd #	Structure	Name	MW	MS Mes'd
111		4-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	401.47	402
112		N-cyclopropyl-2-isopropoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	457.53	458
113		N-(4-(4-isopropylpiperazin-1-yl)phenyl)-8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	442.57	443
114		4-(2-(2-benzyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	502.58	503
115		N-cyclopropyl-2-methoxy-4-(8-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	480.53	481
116		N-cyclopropyl-4-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxybenzamide	470.53	471

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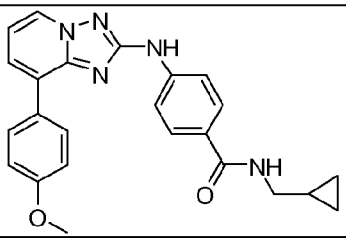
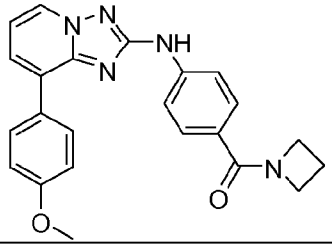
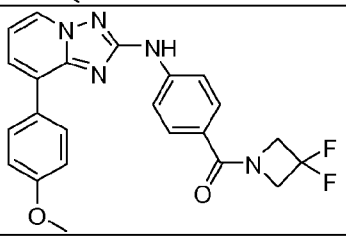
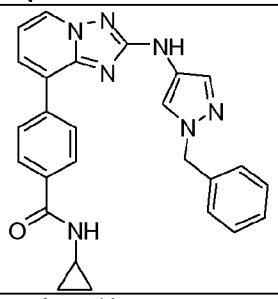
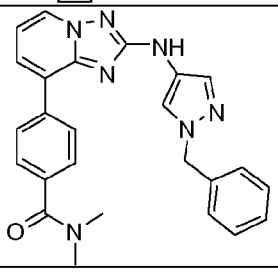
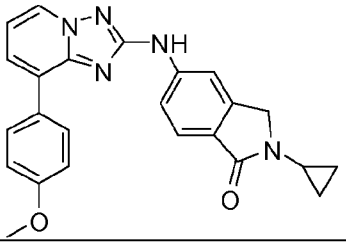
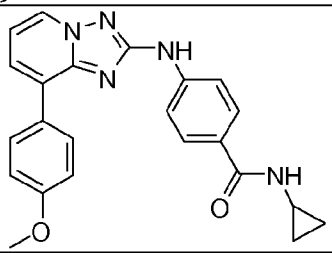
Cpd #	Structure	Name	MW	MS Mes'd
117		N-(cyclopropylmethyl)-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	413.48	414
118		azetidin-1-yl(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	399.45	400
119		(3,3-difluoroazetidin-1-yl)(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	435.43	436
120		4-(2-(1-benzyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-cyclopropylbenzamide	449.52	450
121		4-(2-(1-benzyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	437.51	438
122		2-cyclopropyl-5-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one	411.46	412
123		N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	399.45	400

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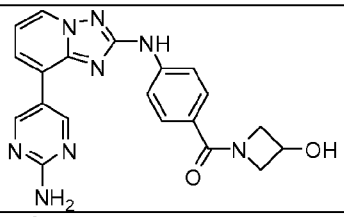
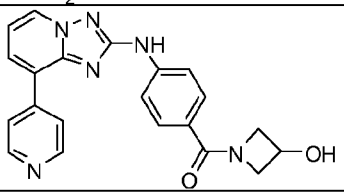
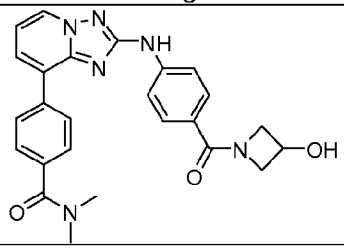
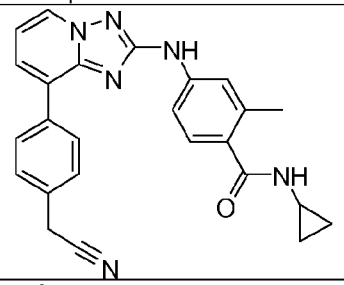
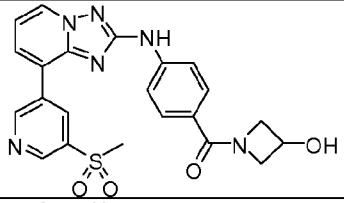
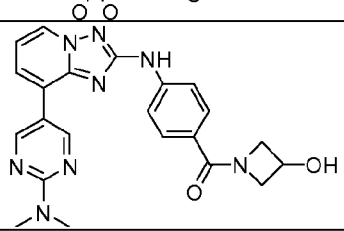
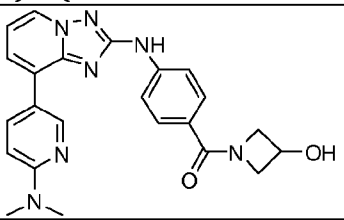
Cpd #	Structure	Name	MW	MS Mes'd
124		(4-(8-(2-aminopyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	402.42	403
125		(3-hydroxyazetidin-1-yl)(4-(8-(pyridin-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	386.41	387
126		4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	456.51	457
127		4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methylbenzamide	422.49	423
128		(3-hydroxyazetidin-1-yl)(4-(8-(5-(methylsulfonyl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	464.50	465
129		(4-(8-(2-(dimethylamino)pyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	430.47	431
130		(4-(8-(6-(dimethylamino)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	429.48	430

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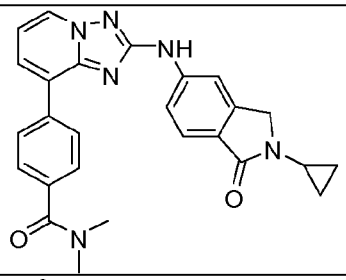
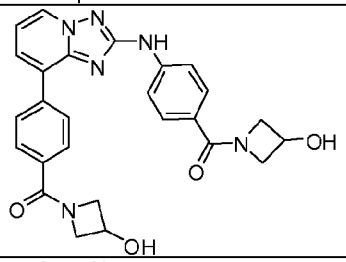
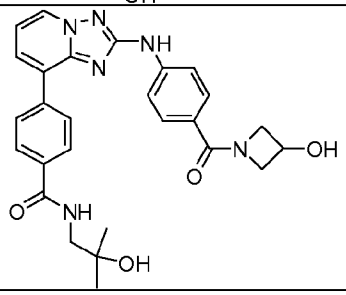
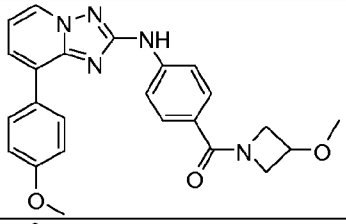
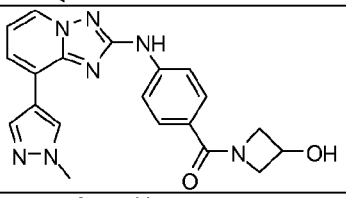
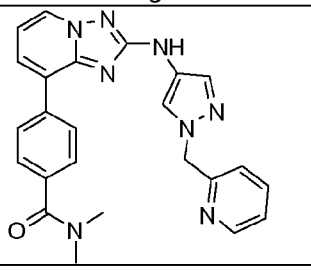
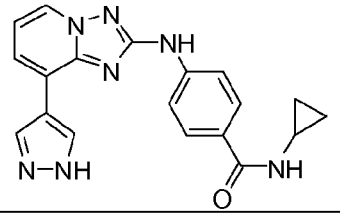
Cpd #	Structure	Name	MW	MS Mes'd
131		4-(2-(2-cyclopropyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	452.52	453
132		(3-hydroxyazetidin-1-yl)(4-(8-(4-(3-hydroxyazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	484.52	485
133		N-(2-hydroxy-2-methylpropyl)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	500.56	501
135		(3-methoxyazetidin-1-yl)(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	429.48	430
136		(3-hydroxyazetidin-1-yl)(4-(8-(1-methyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	389.42	390
137		N,N-dimethyl-4-(2-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	438.49	439
138		4-(8-(1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	359.39	360

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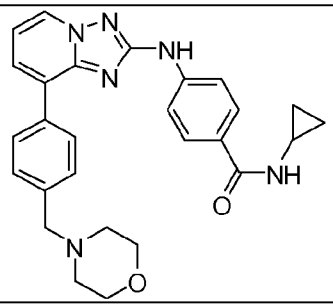
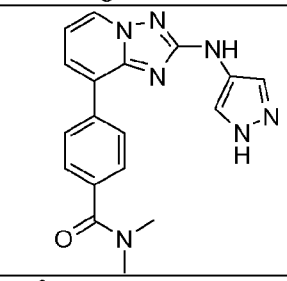
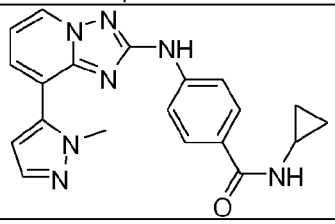
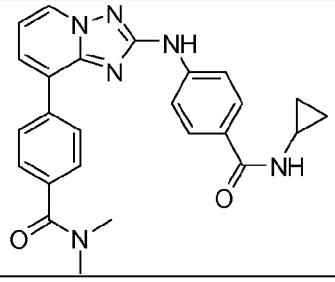
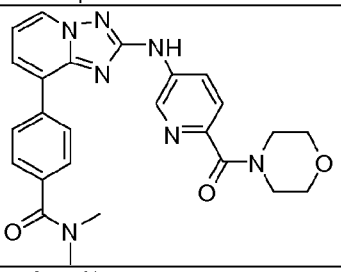
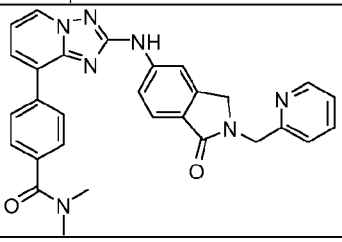
Cpd #	Structure	Name	MW	MS Mes'd
139		N-cyclopropyl-4-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	468.56	469
140		4-(2-(1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	347.38	348
141		N-cyclopropyl-4-(8-(1-methyl-1H-pyrazol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	373.42	374
142		4-(2-(4-(cyclopropylcarbamoyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	440.51	441
143		N,N-dimethyl-4-(2-(6-(morpholine-4-carbonyl)pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	471.52	472
144		N,N-dimethyl-4-(2-(1-oxo-2-(pyridin-2-ylmethyl)isoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	503.57	504

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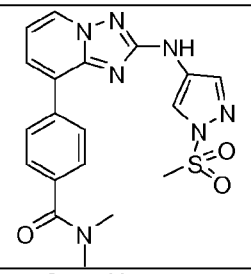
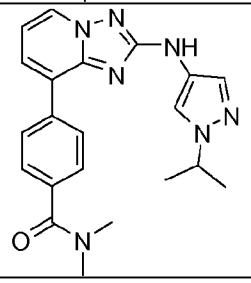
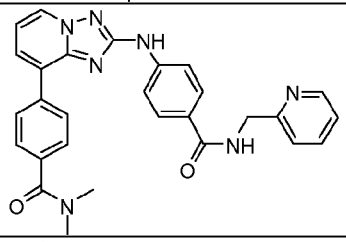
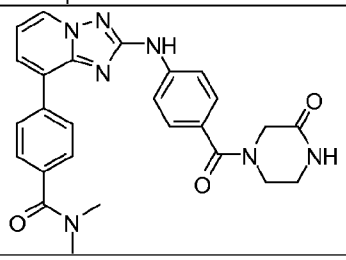
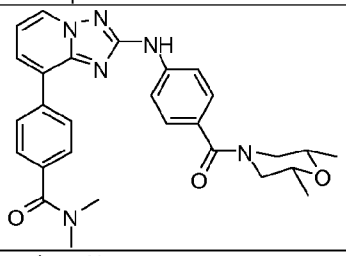
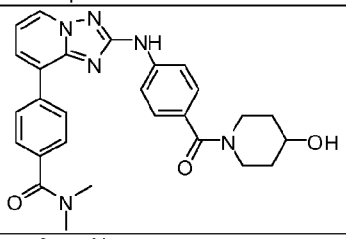
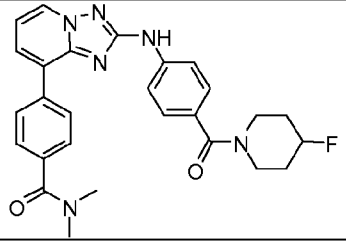
Cpd #	Structure	Name	MW	MS Mes'd
145		N,N-dimethyl-4-(2-(1-(methylsulfonyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	425.47	426
146		4-(2-(1-isopropyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	389.46	390
147		N,N-dimethyl-4-(2-(4-(pyridin-2-ylmethylcarbamoyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	491.55	492
148		N,N-dimethyl-4-(2-(4-(3-oxopiperazine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	483.53	484
149		4-(2-(4-(2,6-dimethylmorpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	498.59	499
150		4-(2-(4-(4-hydroxypiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	484.56	485
151		4-(2-(4-(4-fluoropiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	486.55	487

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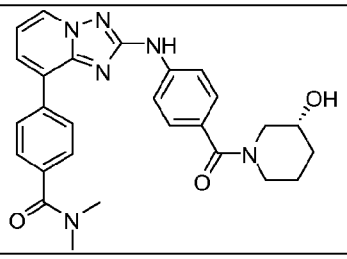
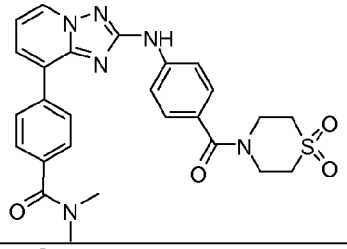
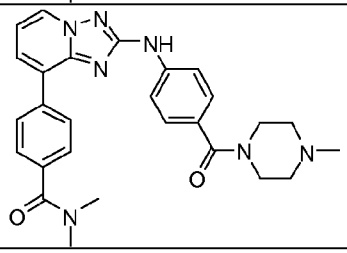
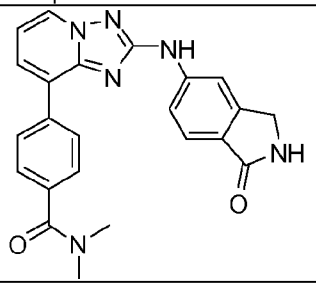
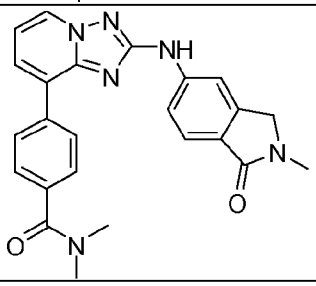
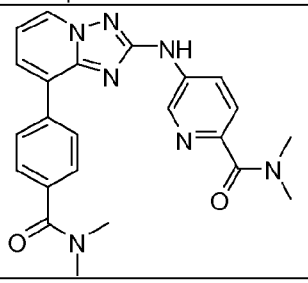
Cpd #	Structure	Name	MW	MS Mes'd
152		(R)-4-(2-(4-(3-hydroxypiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	484.56	485
153		4-{2-[4-(1,1-Dioxo-1lambda*6*-thiomorpholine-4-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-N,N-dimethyl-benzamide	518.60	519
154		N,N-dimethyl-4-(2-(4-(4-methylpiperazine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	483.58	484
155		N,N-dimethyl-4-(2-(1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	412.45	413
156		N,N-dimethyl-4-(2-(2-methyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	426.48	427
157		5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N,N-dimethylpicolinamide	429.48	430

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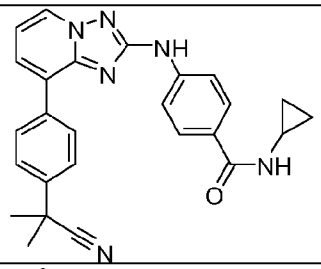
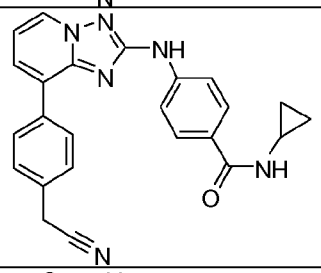
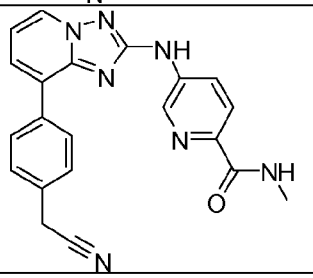
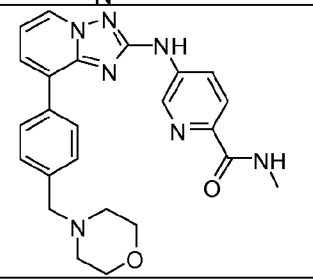
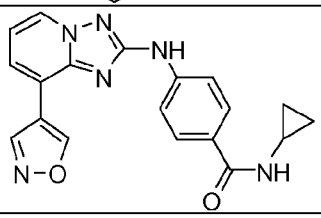
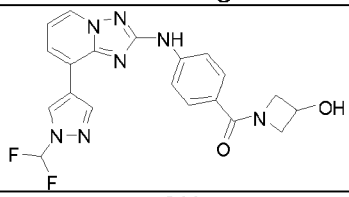
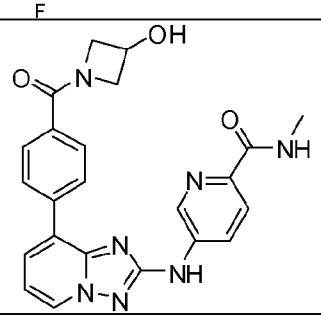
158		4-(8-(4-(2-cyanopropan-2-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	436.52	437
160		4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	408.46	409
161		5-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	383.41	384
162		N-methyl-5-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide	443.51	444
163		N-cyclopropyl-4-(8-(isoxazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	360.38	361
164		(4-(8-(1-(difluoromethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	425.40	426
165		5-(8-(4-(3-hydroxyazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	443.47	444

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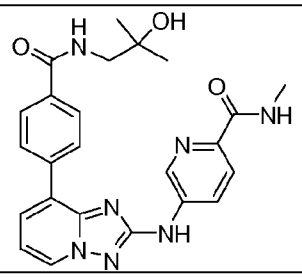
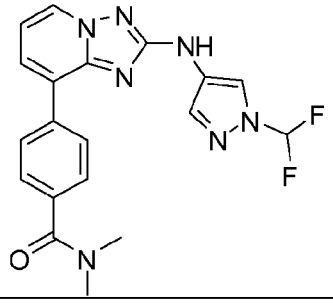
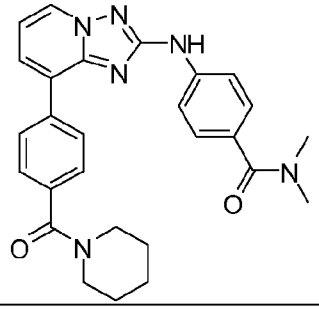
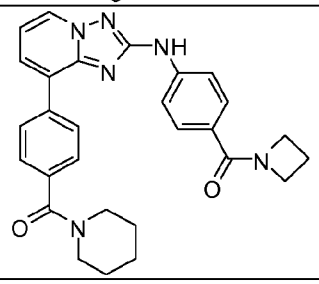
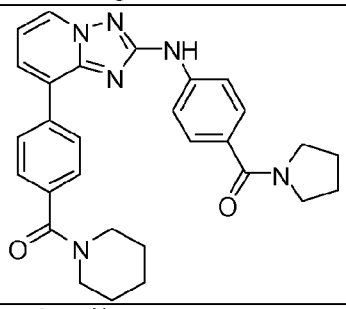
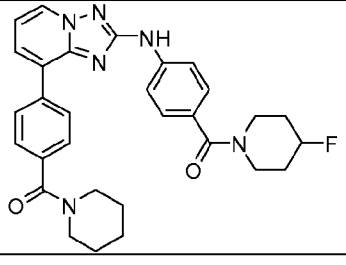
166		5-(8-(4-(2-hydroxy-2-methylpropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	459.51	460
167		4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	397.39	398
168		N,N-dimethyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	468.56	469
169		azetidin-1-yl(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	480.57	481
170		piperidin-1-yl(4-(2-(4-(pyrrolidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone	494.60	495
171		(4-fluoropiperidin-1-yl)(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	526.62	527

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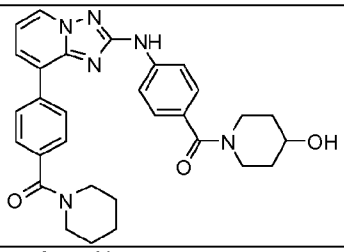
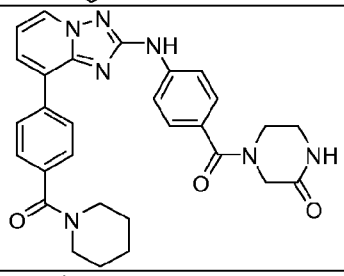
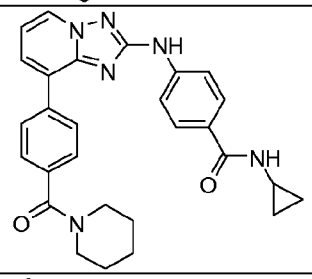
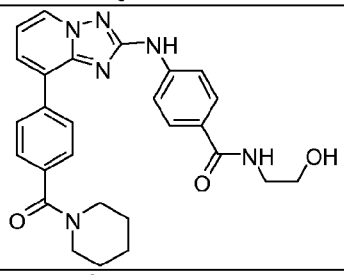
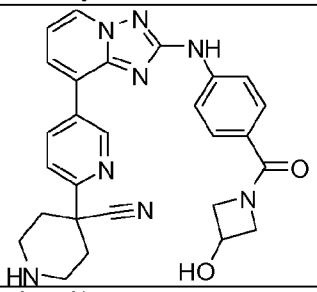
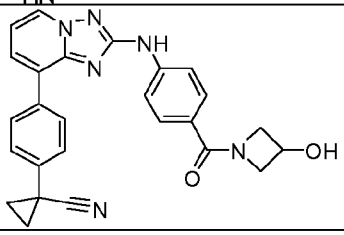
Cpd #	Structure	Name	MW	MS Mes'd
172		(4-hydroxypiperidin-1-yl)(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone	524.62	525
173		4-(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzoyl)piperazin-2-one	523.60	524
174		N-cyclopropyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	480.57	481
175		N-(2-hydroxyethyl)-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	484.56	485
176		4-(5-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)pyridin-2-yl)piperidine-4-carbonitrile	494.56	495
177		1-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)cyclopropanecarbonitrile	450.50	451

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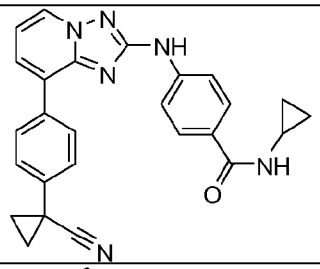
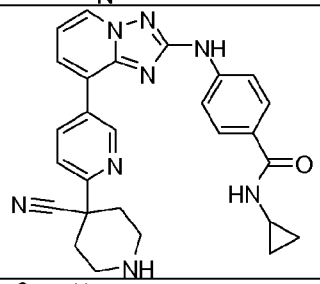
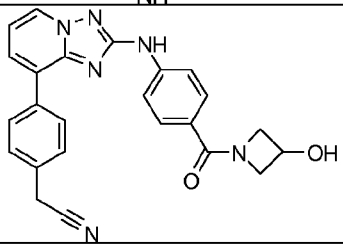
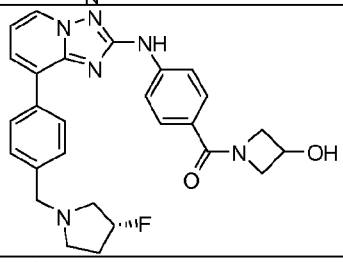
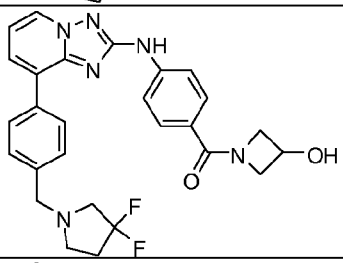
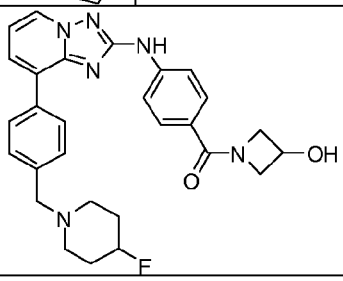
Cpd #	Structure	Name	MW	MS Mes'd
178		4-(8-(4-(1-cyanocyclopropyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	434.50	435
179		4-(8-(6-(4-cyanopiperidin-4-yl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	478.56	479
180		2-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)acetonitrile	424.46	425
181		(R)-(4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	486.55	487
182		(4-(8-(4-((3,3-difluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	504.54	505
183		(4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	500.58	501

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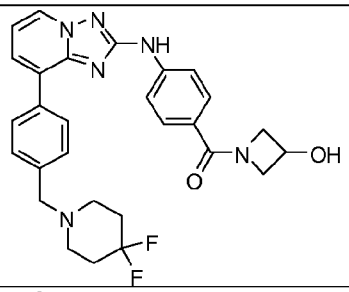
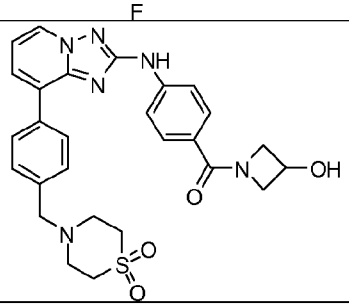
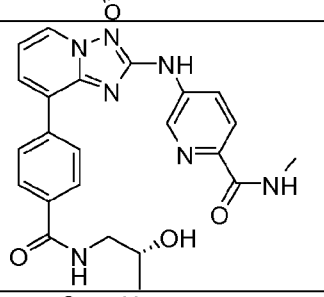
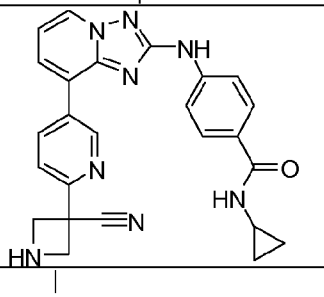
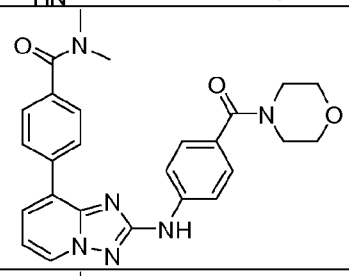
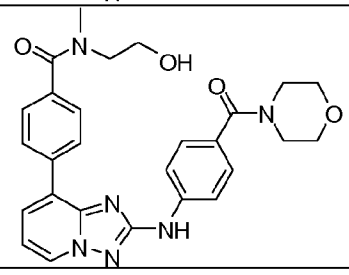
Cpd #	Structure	Name	MW	MS Mes'd
184		(4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone	518.57	519
185		(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-(3-hydroxy-azetidin-1-yl)-methanone	532.62	533
186		(R)-5-(8-(4-(2-hydroxypropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	445.48	446
187		4-(8-(6-(3-cyanoazetidin-3-yl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	450.51	451
188		N,N-dimethyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	470.53	471
189		N-(2-hydroxyethyl)-N-methyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	500.56	501

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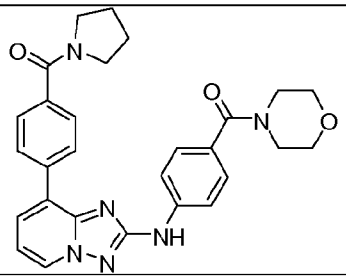
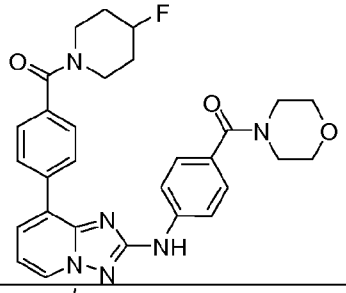
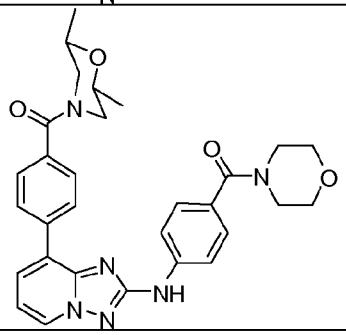
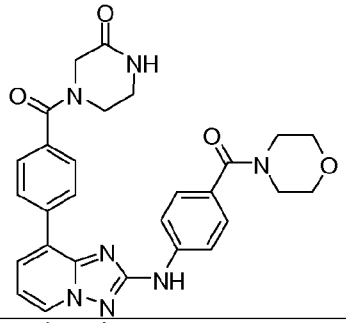
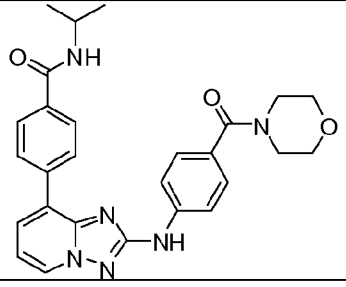
Cpd #	Structure	Name	MW	MS Mes'd
190		(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)(pyrrolidin-1-yl)methanone	496.57	497
191		(4-fluoropiperidin-1-yl)(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone	528.59	529
192		(4-(8-(4-(2,6-dimethylmorpholine-4-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(morpholino)methanone	540.62	541
193		4-(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzoyl)piperazin-2-one	525.57	526
194		N-isopropyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	484.56	485

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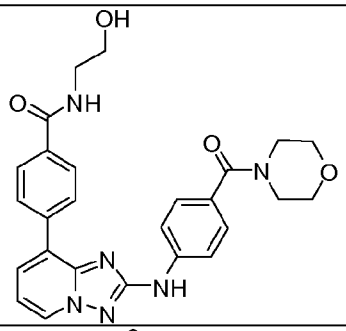
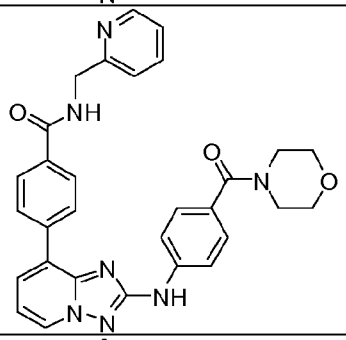
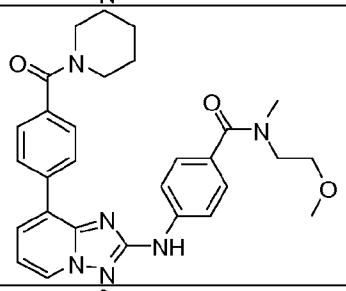
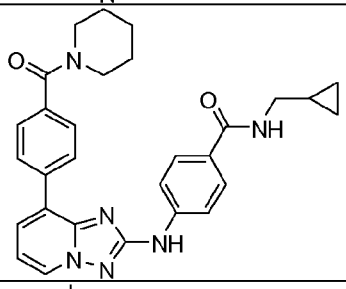
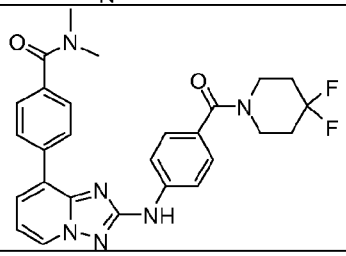
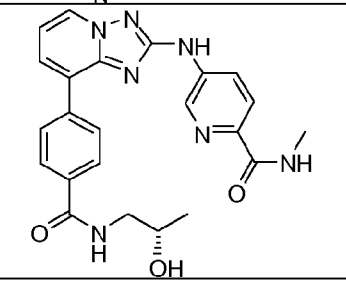
Cpd #	Structure	Name	MW	MS Mes'd
195		N-(2-hydroxyethyl)-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	486.53	487
196		4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(pyridin-2-ylmethyl)benzamide	533.59	534
197		N-(2-methoxyethyl)-N-methyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	512.61	513
198		N-(cyclopropylmethyl)-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	494.60	495
199		4-(2-(4-(4,4-difluoropiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	504.54	505
200		(S)-5-(8-(4-(2-hydroxypropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	445.48	446

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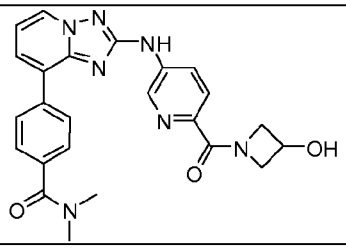
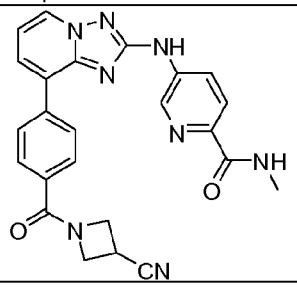
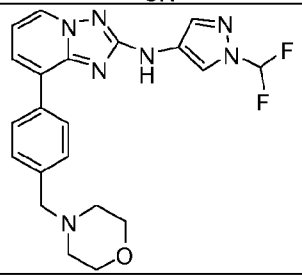
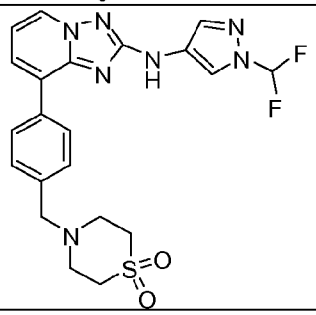
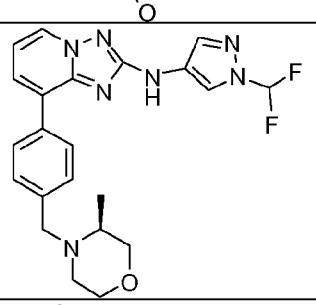
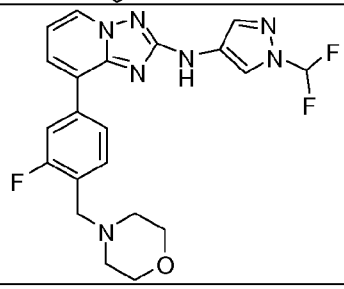
Cpd #	Structure	Name	MW	MS Mes'd
201		4-(2-(6-(3-hydroxyazetidine-1-carbonyl)pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide	457.49	458
202		5-(8-(4-(3-cyanoazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	452.48	453
203		N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	425.44	426
204		N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-((thiomorpholine-1,1-dioxide)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	473.51	474
205		(S)-N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-((3-methylmorpholino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	439.47	440
206		N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	443.43	444

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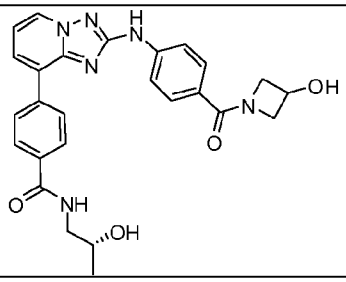
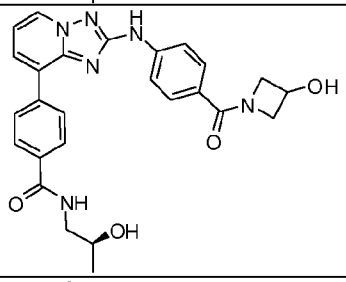
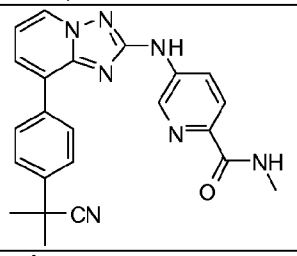
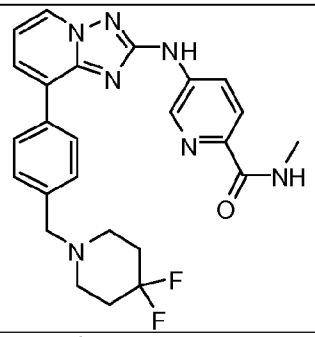
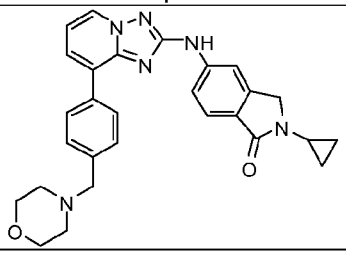
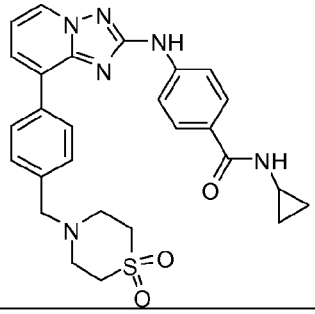
Cpd #	Structure	Name	MW	MS Mes'd
207		(R)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(2-hydroxypropyl)benzamide	486.53	487
208		(S)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(2-hydroxypropyl)benzamide	486.53	487
209		5-(8-(4-(2-cyanopropan-2-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	411.47	412
210		5-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	477.52	478
211		2-cyclopropyl-5-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one	480.57	481
212		N-Cyclopropyl-4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	516.62	517

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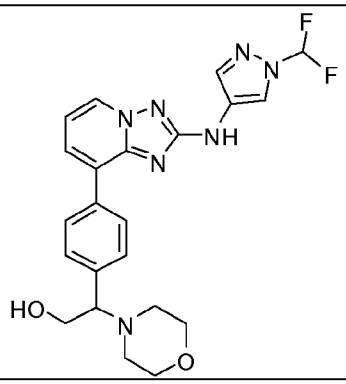
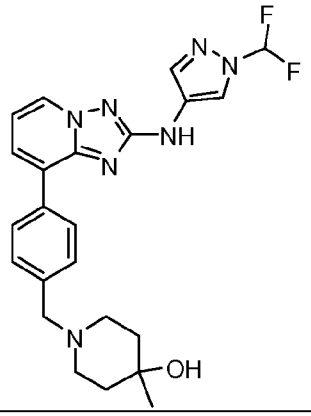
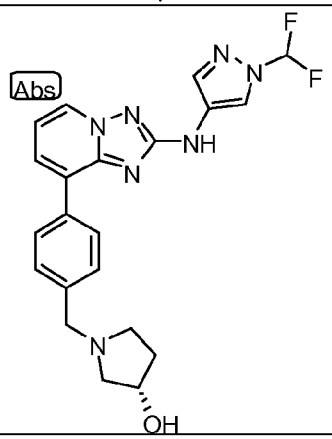
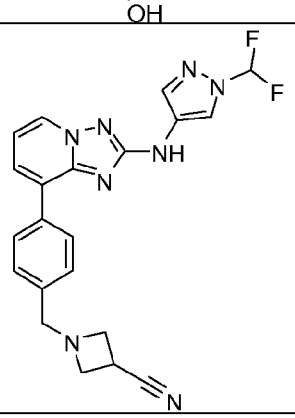
Cpd #	Structure	Name	MW	MS Mes'd
213		2-(4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)-2-morpholinoethanol	455.47	456
214		1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)-4-methylpiperidin-4-ol	453.50	454
215		(S)-1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)pyrrolidin-3-ol	425.44	426
216		1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)azetidine-3-carbonitrile	420.43	421

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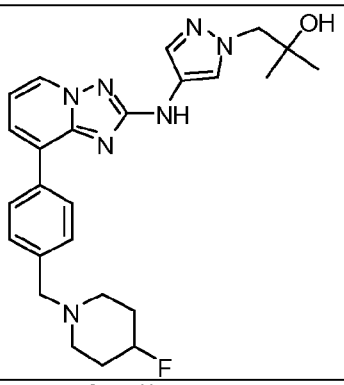
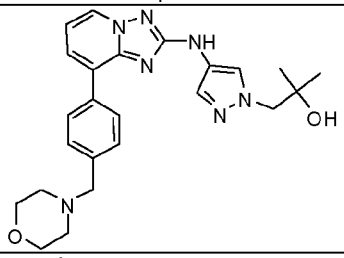
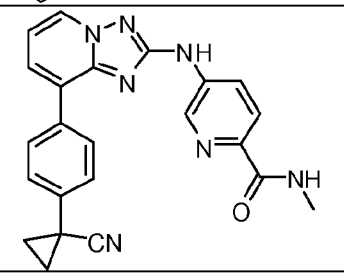
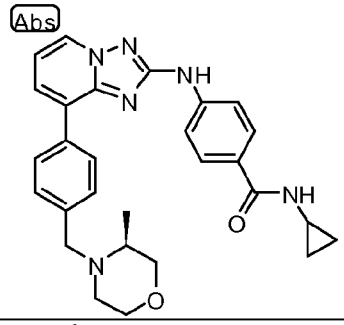
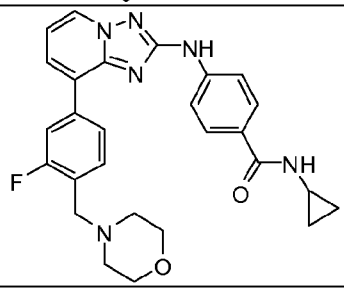
Cpd #	Structure	Name	MW	MS Mes'd
217		1-(4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol	463.56	464
218		2-methyl-1-(4-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol	447.54	448
219		5-(8-(4-(1-cyanocyclopropyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	409.45	410
220		(S)-N-cyclopropyl-4-(8-(4-((3-methylmorpholino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	482.59	483
221		N-cyclopropyl-4-(8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	486.55	487

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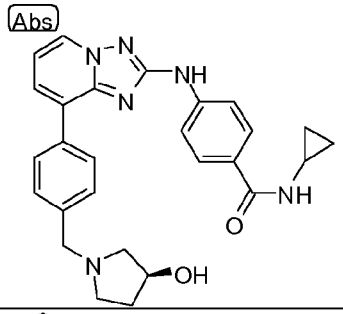
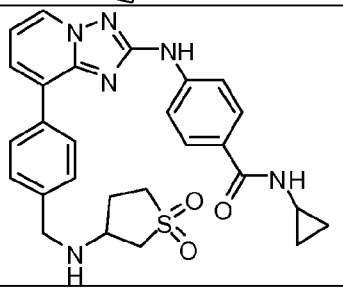
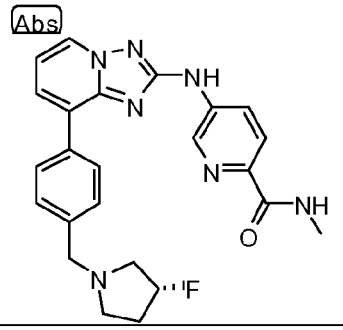
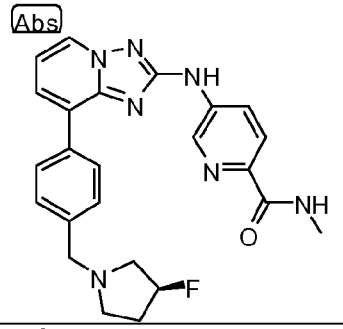
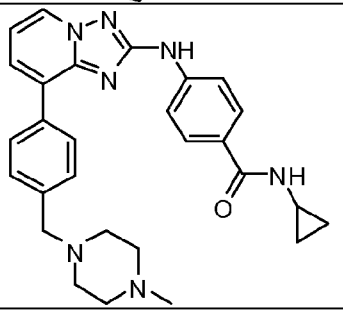
Cpd #	Structure	Name	MW	MS Mes'd
222		(S)-N-cyclopropyl-4-(8-(4-((3-hydroxypyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	468.56	469
223		N-Cyclopropyl-4-(8-{4-[(1,1-dioxo-tetrahydro-1lambda*6*-thiophen-3-ylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	516.62	517
224		(R)-5-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	445.50	446
225		(S)-5-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	445.50	446
226		N-cyclopropyl-4-(8-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	481.60	482

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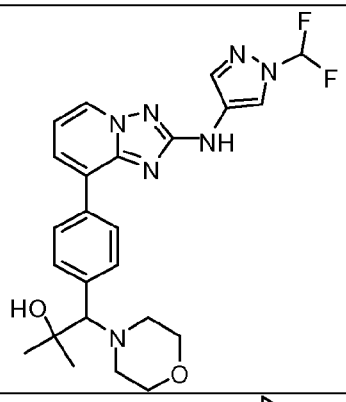
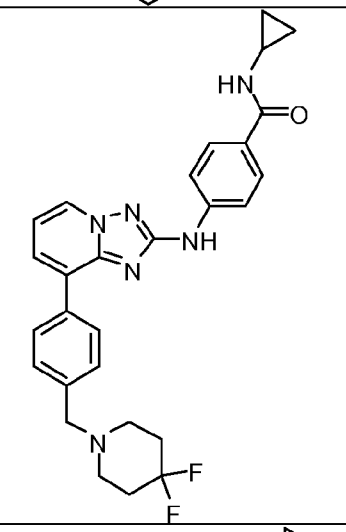
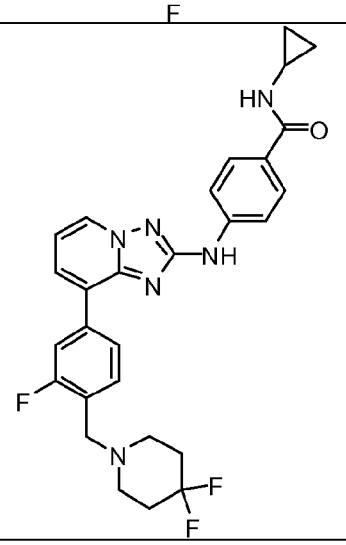
Cpd #	Structure	Name	MW	MS Mes'd
227		1-(4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)-2-methyl-1-morpholinopropan-2-ol	483.52	484
228		N-cyclopropyl-4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	502.57	503
229		N-cyclopropyl-4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	520.56	521

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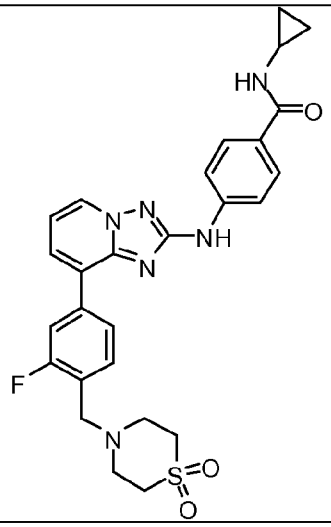
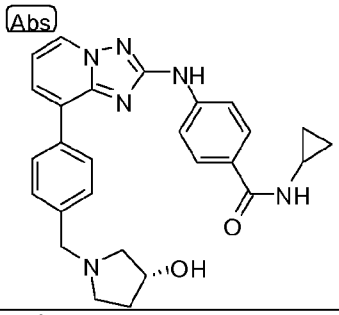
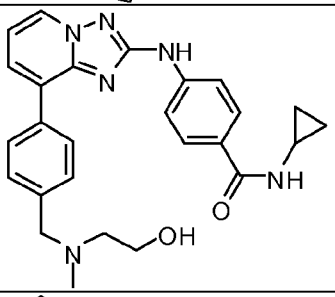
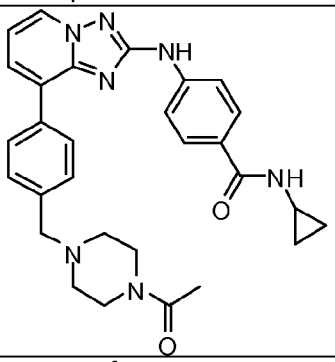
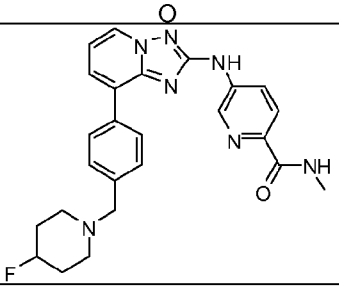
Cpd #	Structure	Name	MW	MS Mes'd
230		N-Cyclopropyl-4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	534.61	535
231		(R)-N-cyclopropyl-4-(8-(4-((3-hydroxypyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	468.56	469
232		N-cyclopropyl-4-(8-(4-(((2-hydroxyethyl)(methyl)amino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	456.55	457
233		4-(8-(4-((4-acetoylpiperazin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	509.61	510
234		5-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	459.53	460

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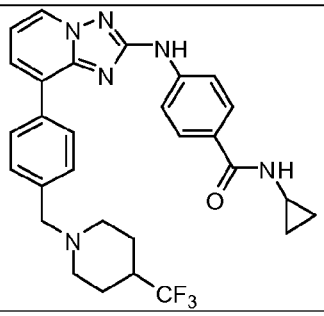
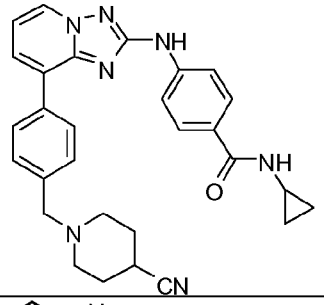
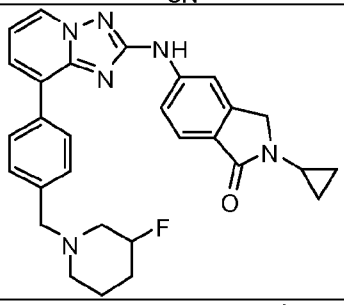
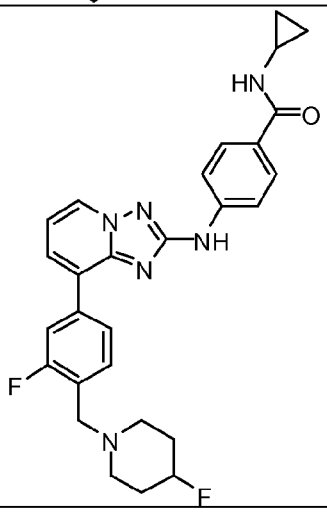
Cpd #	Structure	Name	MW	MS Mes'd
235		N-cyclopropyl-4-(8-(4-((4-(trifluoromethyl)piperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	534.59	535
236		4-(8-(4-((4-cyanopiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	491.60	492
237		2-cyclopropyl-5-(8-(4-((3-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one	496.59	497
238		N-cyclopropyl-4-(8-(3-fluoro-4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	502.57	503

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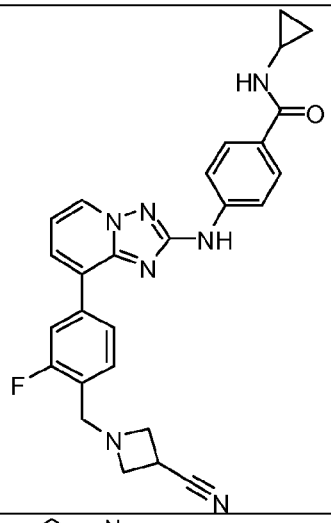
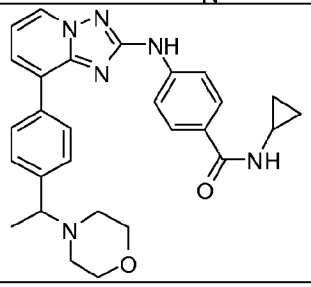
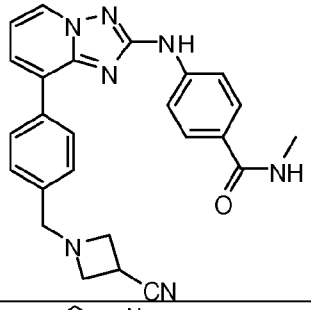
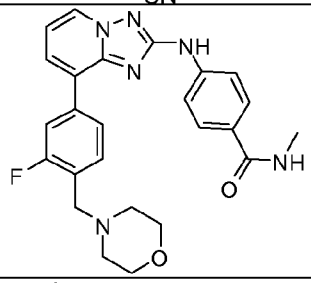
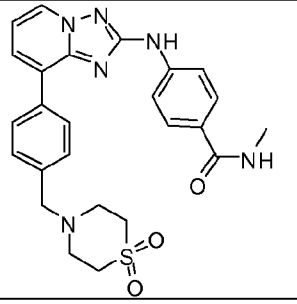
Cpd #	Structure	Name	MW	MS Mes'd
239		4-(8-(4-((3-cyanoazetidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	481.53	482
240		N-cyclopropyl-4-(8-(4-(1-morpholinoethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	482.59	483
241		4-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	437.51	438
242		4-(8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	460.51	461
243		4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide	490.59	491

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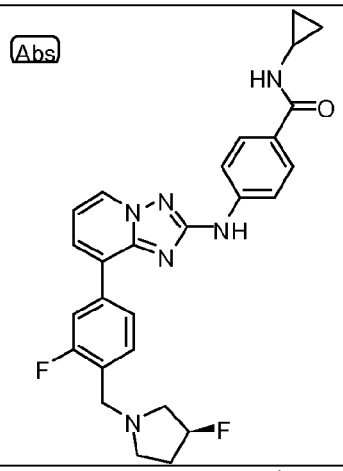
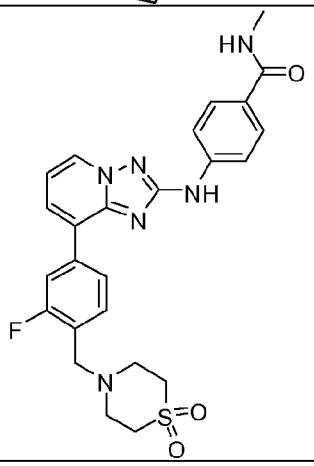
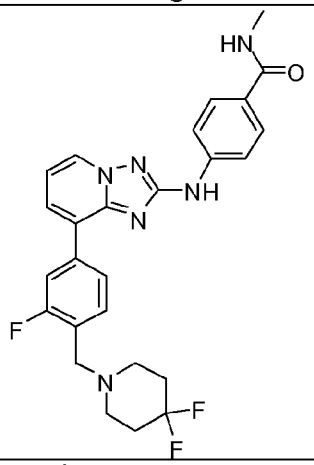
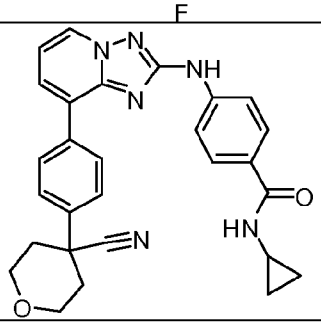
Cpd #	Structure	Name	MW	MS Mes'd
244		(S)-N-cyclopropyl-4-(8-(3-fluoro-4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	488.54	489
245		4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide	508.58	509
246		4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide	494.52	495
247		4-(8-(4-(4-cyanotetrahydro-2H-pyran-4-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	478.56	479

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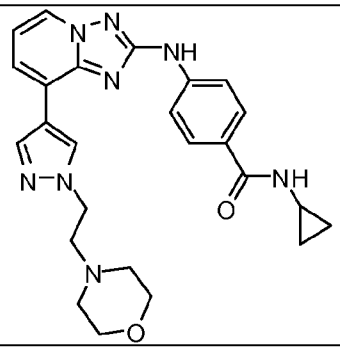
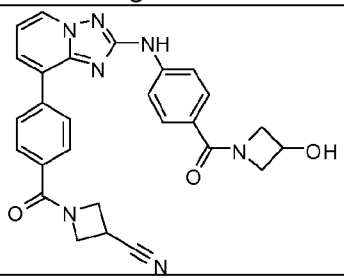
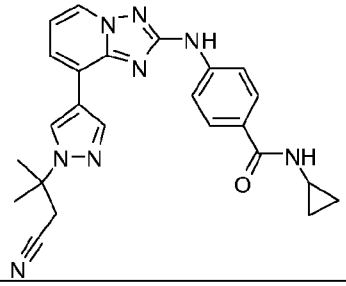
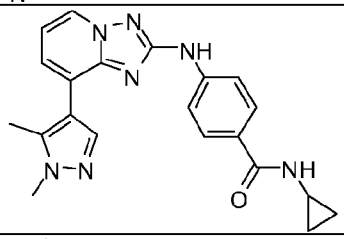
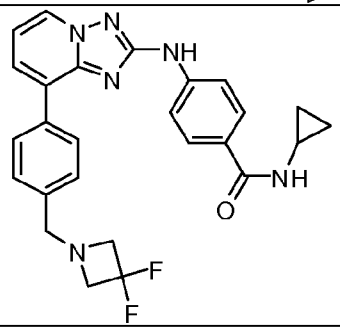
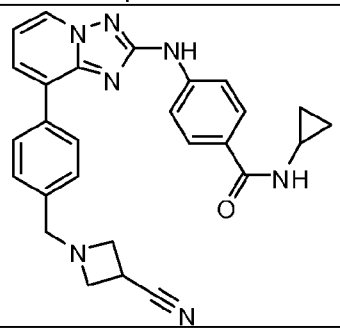
Cpd #	Structure	Name	MW	MS Mes'd
248		N-cyclopropyl-4-(8-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	472.55	473
249		1-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzoyl)azetidine-3-carbonitrile	493.53	494
251		4-(8-(1-(1-cyano-2-methylpropan-2-yl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	440.51	441
252		N-cyclopropyl-4-(8-(1,5-dimethyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	387.45	388
253		N-cyclopropyl-4-(8-(4-((3,3-difluoroazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	474.51	475
254		4-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide	463.54	464

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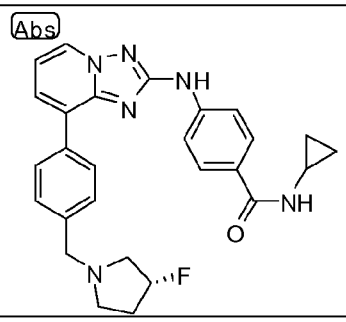
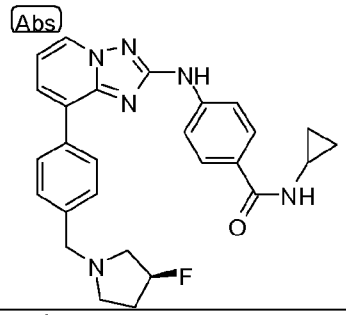
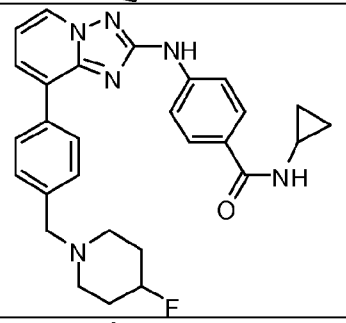
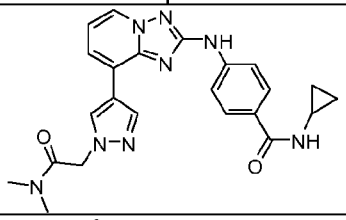
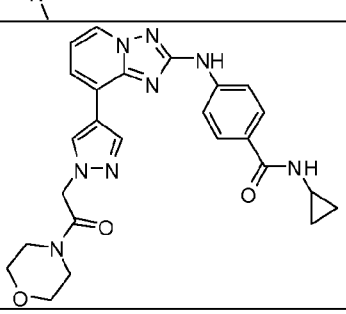
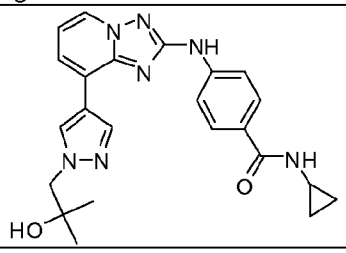
Cpd #	Structure	Name	MW	MS Mes'd
255		(R)-N-cyclopropyl-4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	470.55	471
256		(S)-N-cyclopropyl-4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	470.55	471
257		N-cyclopropyl-4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	484.58	485
258		N-cyclopropyl-4-(8-(1-(2-(dimethylamino)-2-oxoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	444.50	445
259		N-cyclopropyl-4-(8-(1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	486.54	487
260		N-cyclopropyl-4-(8-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide	431.50	432

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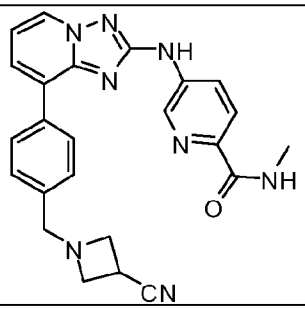
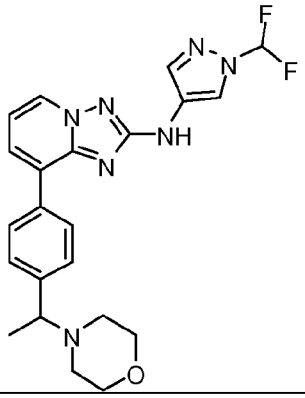
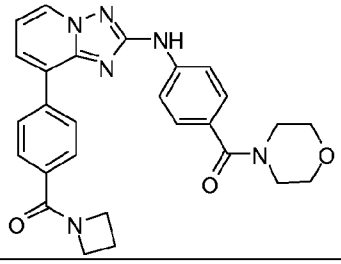
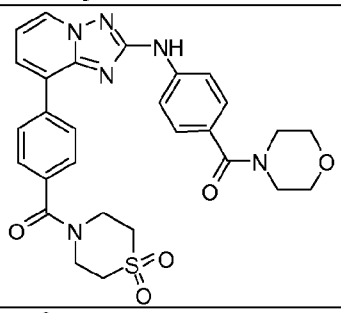
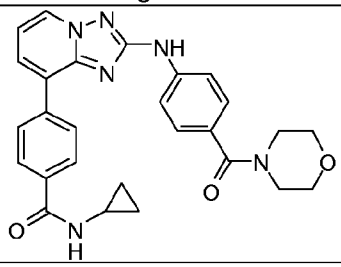
Cpd #	Structure	Name	MW	MS Mes'd
261		5-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide	438.49	439
262		N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-(1-morpholinoethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine	439.47	440
263		azetidin-1-yl(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone	482.54	483
264		(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)(thiomorpholin-1,1-dioxide)methanone	560.63	561
265		N-cyclopropyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide	482.54	483

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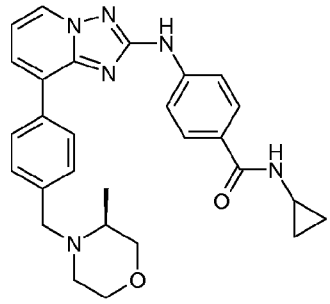
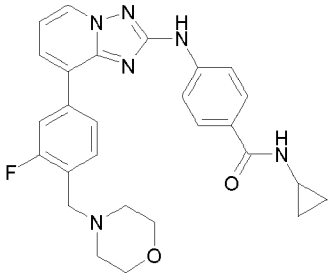
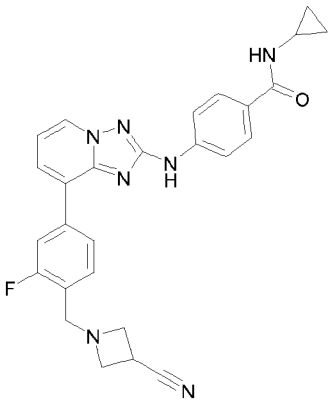
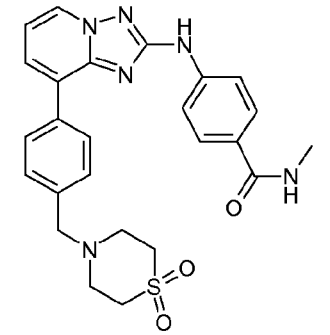
Cpd #	Structure	Name	MW	MS Mes'd
266	Chiral 	N-Cyclopropyl-4-{8-[4-((S)-3-methyl-morpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	482.588	
267		N-Cyclopropyl-4-[8-(3-fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	486.551	487
268		4-{8-[4-(3-Cyano-azetidin-1-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	481.535	482
269		4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide	490.586	491

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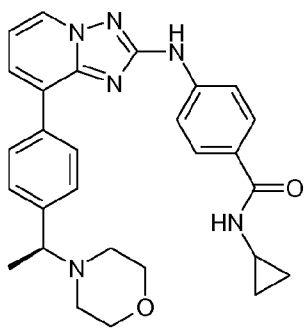
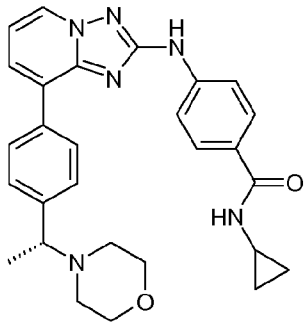
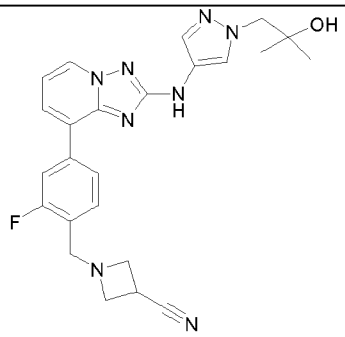
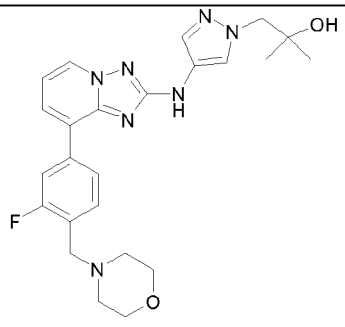
Cpd #	Structure	Name	MW	MS Mes'd
270	Chiral 	N-Cyclopropyl-4-{8-[4-((S)-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	482.588	483
271	Chiral 	N-Cyclopropyl-4-{8-[4-((R)-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	482.588	483
272		1-(2-Fluoro-4-{2-[1-(2-hydroxy-2-methyl-propyl)-1H-pyrazol-4-ylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-benzyl)-azetidine-3-carbonitrile	460.517	461
273		1-{4-[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-2-methyl-propan-2-ol	465.533	466

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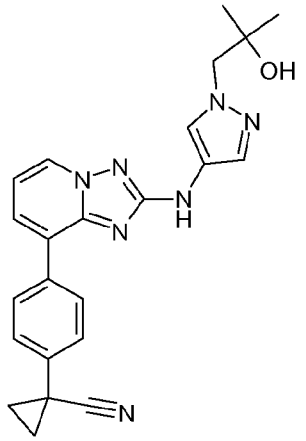
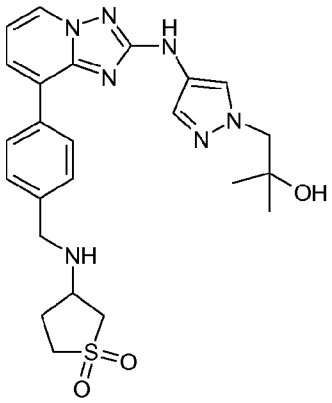
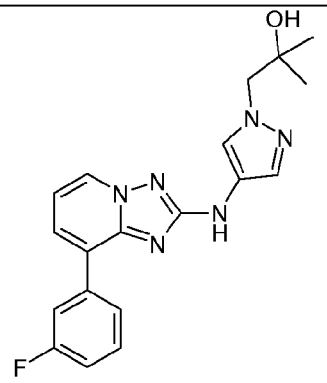
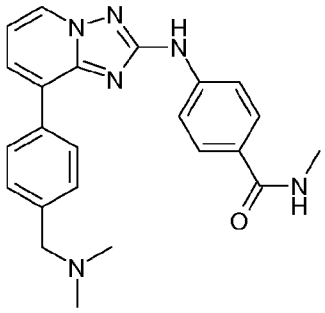
Cpd #	Structure	Name	MW	MS Mes'd
274		1-(4-{2-[1-(2-Hydroxy-2-methyl-propyl)-1H-pyrazol-4-ylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenyl)-cyclopropanecarbonitrile	413.485	414
275		1-[4-(8-{4-[(1,1-Dioxo-tetrahydro-1lambda*6*-thiophen-3-ylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol	495.606	496
276		1-{4-[8-(3-Fluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-2-methyl-propan-2-ol	366.400	367
277		4-[8-(4-Dimethylaminomethyl-phenyl) -[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-methyl-benzamide	400.486	401

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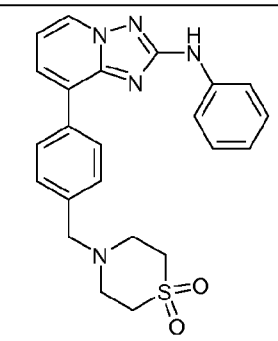
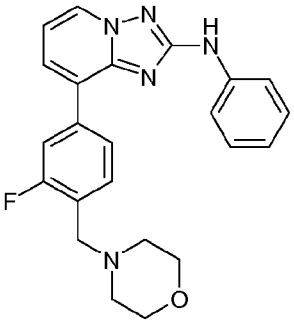
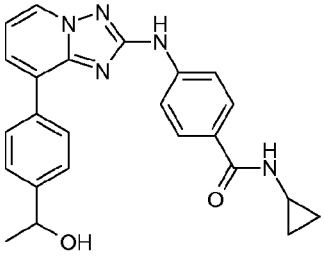
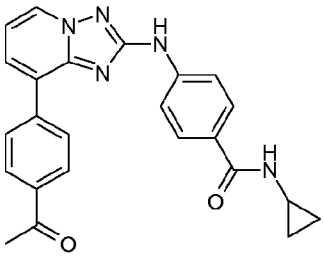
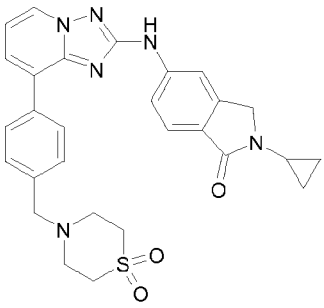
Cpd #	Structure	Name	MW	MS Mes'd
278		{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-phenyl-amine	433.534	434
279		[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-phenyl-amine	403.461	404
280		N-Cyclopropyl-4-{8-[4-(1-hydroxy-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	413.481	414
281		4-[8-(4-Acetyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-cyclopropyl-benzamide	411.465	412
282		2-Cyclopropyl-5-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-2,3-dihydro-isoindol-1-one	528.635	529

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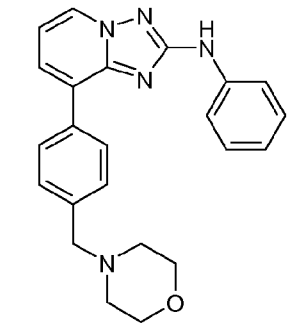
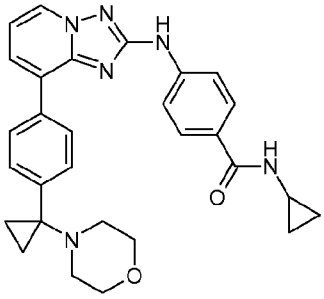
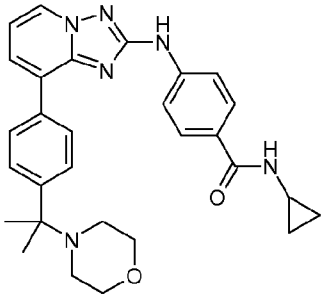
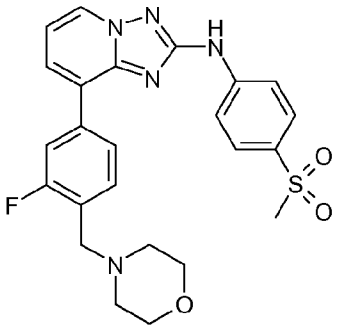
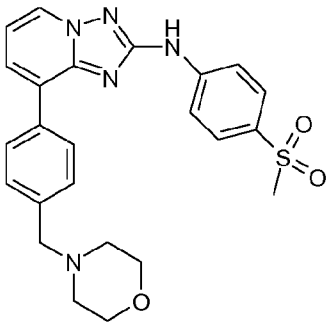
Cpd #	Structure	Name	MW	MS Mes'd
283		[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-phenyl-amine	385.471	386
284		N-Cyclopropyl-4-{8-[4-(1-morpholin-4-yl-cyclopropyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	494.60	495
285		N-Cyclopropyl-4-{8-[4-(1-methyl-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	496.61	497
286		8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-methanesulfonyl-phenyl)-amine	481.55	482
287		(4-Methanesulfonyl-phenyl)-[8-(4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine	463.56	464

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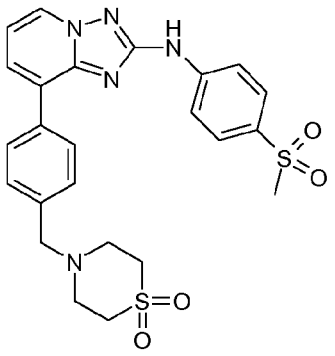
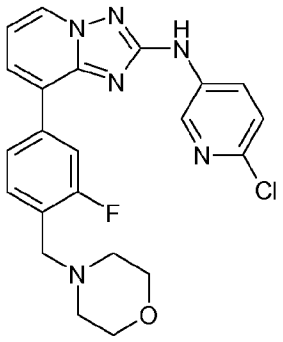
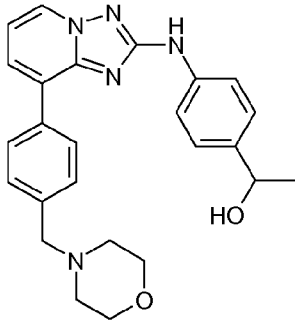
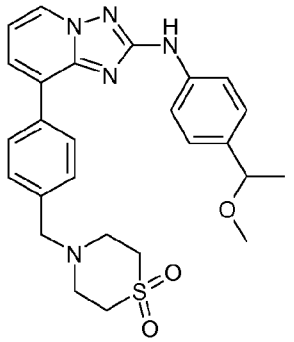
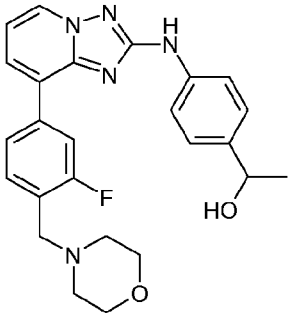
Cpd #	Structure	Name	MW	MS Mes'd
288		{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-(4-methanesulfonyl-phenyl)-amine	511.62	512
289		(6-Chloro-pyridin-3-yl)-[8-(3-fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine	438.89	439
290		1-{4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-ethanol	429.52	430
291		{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-[4-(1-methoxy-ethyl)-phenyl]-amine	491.61	492
292		1-{4-[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-ethanol	447.51	448

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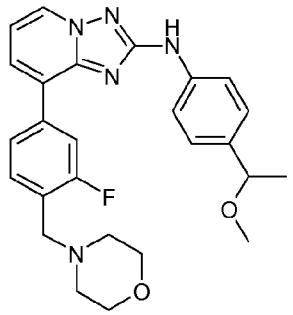
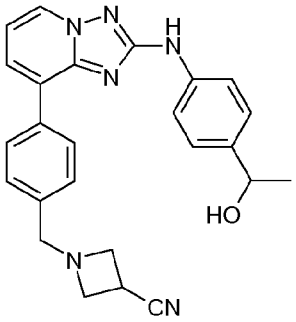
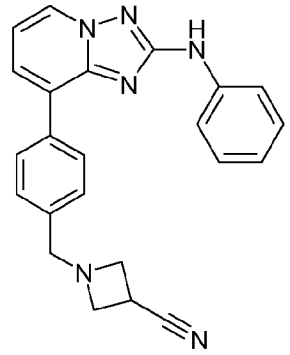
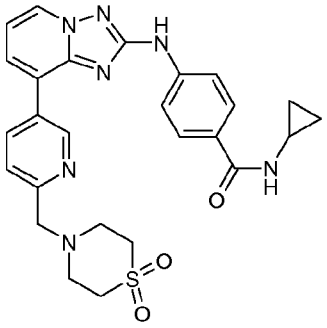
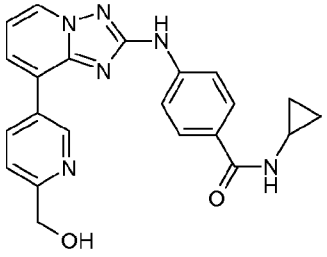
Cpd #	Structure	Name	MW	MS Mes'd
293		[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-[4-(1-methoxy-ethyl)-phenyl]-amine	461.54	462
294		1-(4-{2-[4-(1-Hydroxy-ethyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-benzyl)-azetidine-3-carbonitrile	424.51	425
295		1-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-azetidine-3-carbonitrile	380.45	381
296		N-Cyclopropyl-4-{8-[6-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	517.61	518
297		N-Cyclopropyl-4-[8-(6-hydroxymethyl-pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	400.44	401

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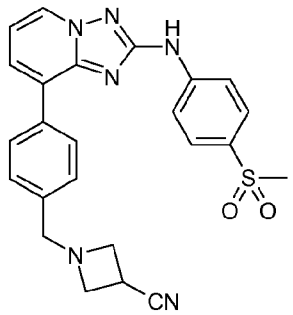
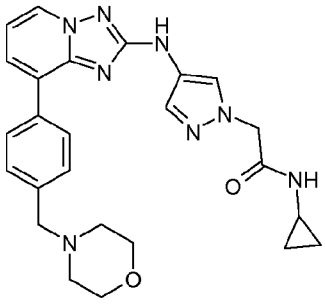
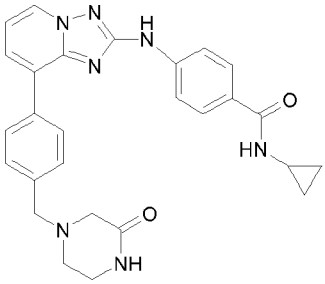
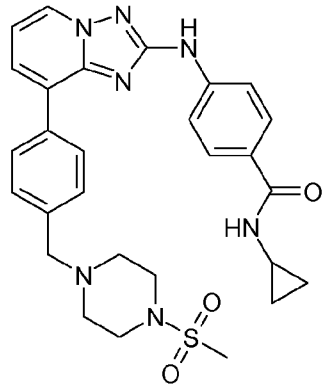
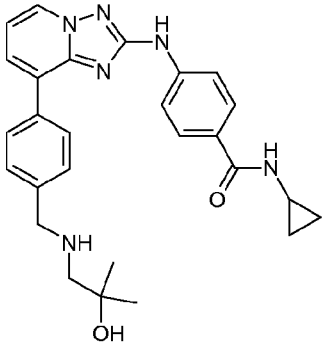
298		1-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile	458.54	459
299		N-Cyclopropyl-2-{4-[8-(4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-acetamide	472.55	473
300		N-Cyclopropyl-4-{8-[4-(3-oxo-piperazin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	481.56	482
301		N-Cyclopropyl-4-{8-[4-(4-methanesulfonyl-piperazin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	545.67	546
302		N-Cyclopropyl-4-(8-{4-[(2-hydroxy-2-methyl-propylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	570.58	571

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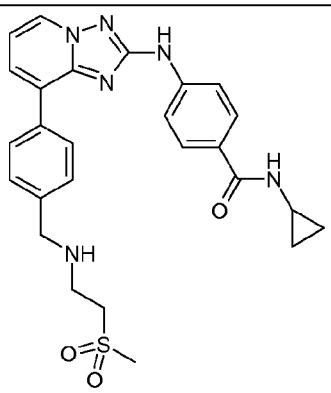
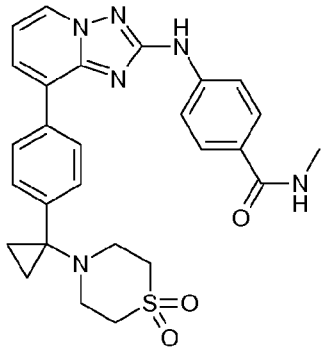
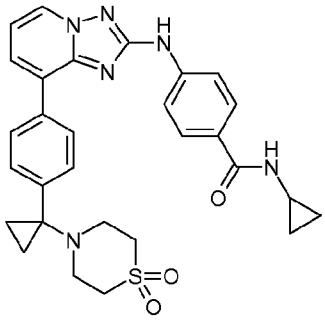
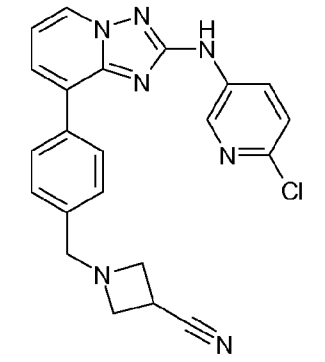
Cpd #	Structure	Name	MW	MS Mes'd
303		N-Cyclopropyl-4-(8-{4-[(2-methanesulfonyl-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	504.61	505
304		4-(8-{4-[1-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-yl)-cyclopropyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methyl-benzamide	516.62	-
305		N-Cyclopropyl-4-(8-{4-[1-(1,1-dioxo-1lambda*6*-thiomorpholin-4-yl)-cyclopropyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	542.66	-
306		1-{4-[2-(6-Chloro-pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile	415.89	416

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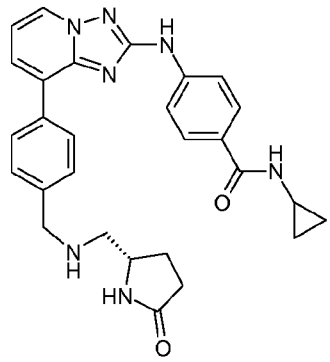
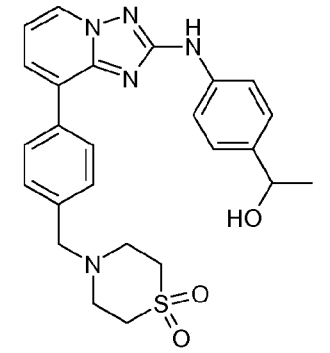
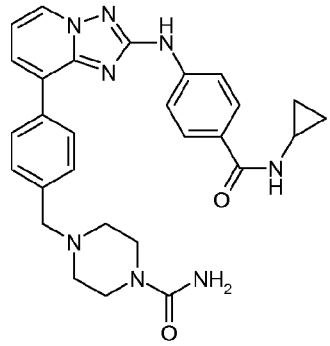
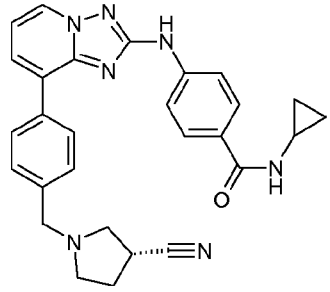
Cpd #	Structure	Name	MW	MS Mes'd
307	Chiral 	N-Cyclopropyl-4-[8-(4-{[((S)-5-oxo-pyrrolidin-2-ylmethyl)-amino]-methyl}-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	495.59	496
308		1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-ethanol	477.59	478
309		4-{4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazine-1-carboxylic acid amide	510.60	511
310		4-{8-[4-((R)-3-Cyano-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	477.57	478

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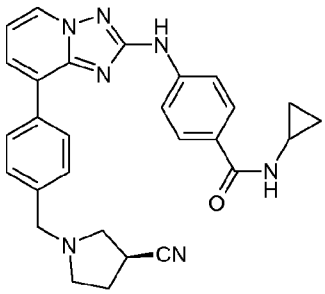
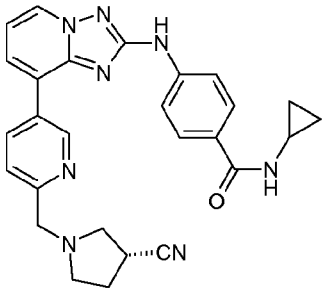
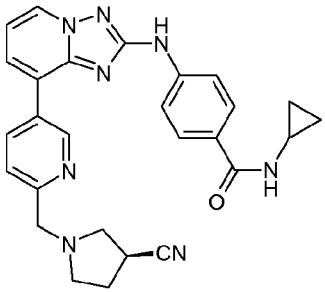
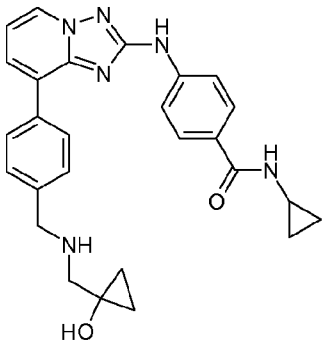
Cpd #	Structure	Name	MW	MS Mes'd
311	Chiral 	4-{8-[4-((S)-3-Cyano-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	477.57	478
312	Chiral 	4-{8-[6-((R)-3-Cyano-pyrrolidin-1-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	478.56	479
313	Chiral 	4-{8-[6-((S)-3-Cyano-pyrrolidin-1-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	478.56	479
314		N-Cyclopropyl-4-[8-(4-{[(1-hydroxy-cyclopropylmethyl)-amino]-methyl}-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	468.56	469

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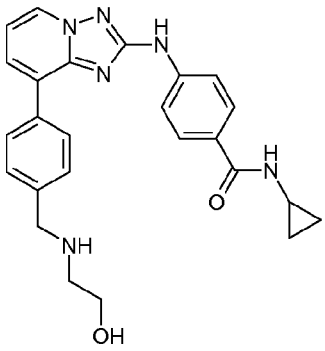
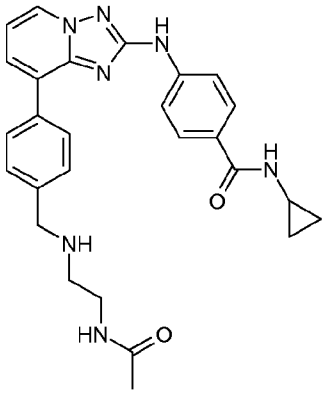
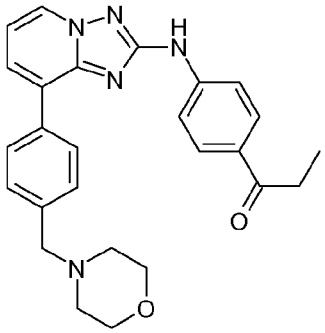
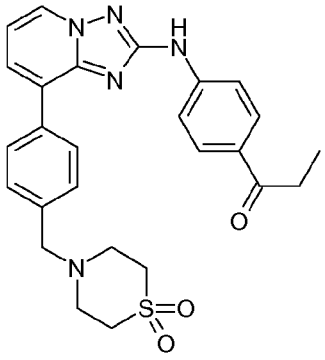
Cpd #	Structure	Name	MW	MS Mes'd
315		N-Cyclopropyl-4-(8-{4-[(2-hydroxy-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	442.53	443
316		4-(8-{4-[(2-Acetylamino-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide	483.58	484
317		1-{4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-propan-1-one	441.53	442
318		1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-propan-1-one	489.60	490

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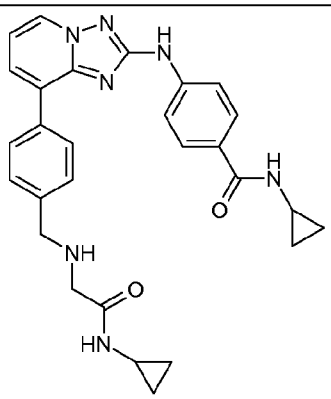
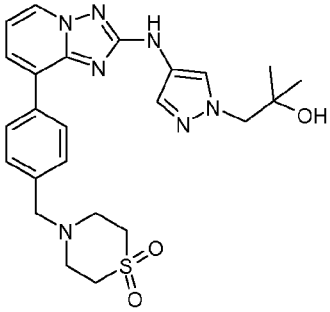
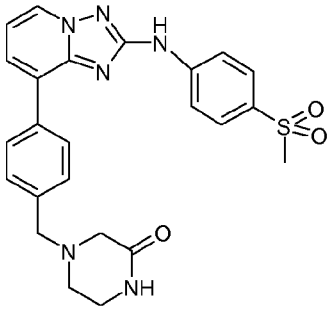
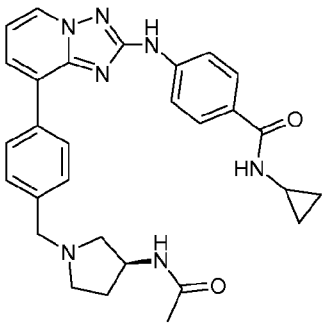
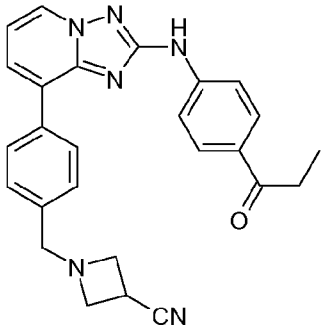
Cpd #	Structure	Name	MW	MS Mes'd
319		N-Cyclopropyl-4-(8-{4-[(cyclopropylcarbamoylmethyl-amino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	495.59	496
320		1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-pyrazol-1-yl)-2-methyl-propan-2-ol	495.61	496
321		4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazin-2-one	476.56	477
322	Chiral 	4-{8-[4-((S)-3-Acetylamino-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	509.61	510
323		1-{4-[2-(4-Propionyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile	436.52	437

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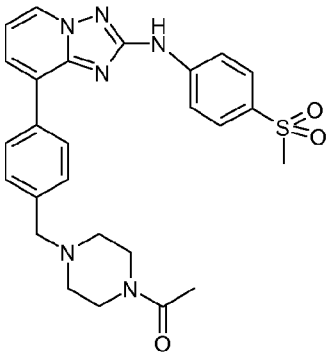
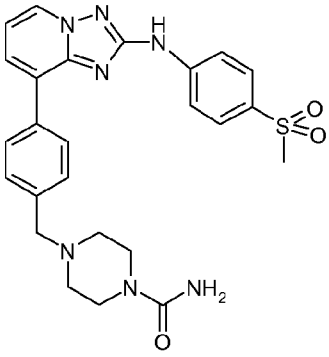
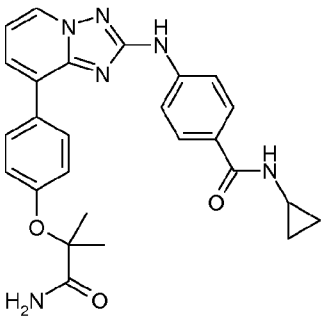
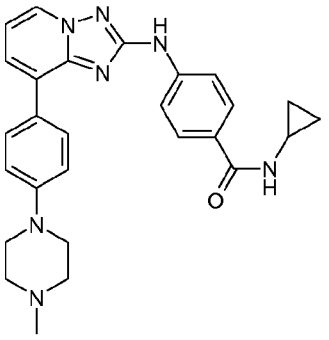
Cpd #	Structure	Name	MW	MS Mes'd
324		1-(4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazin-1-yl)-ethanone	504.61	505
325		4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazine-1-carboxylic acid amide	505.60	506
326		4-{8-[4-(1-Carbamoyl-1-methyl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide	470.53	471
327		N-Cyclopropyl-4-{8-[4-(4-methyl-piperazin-1-yl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	467.68	458

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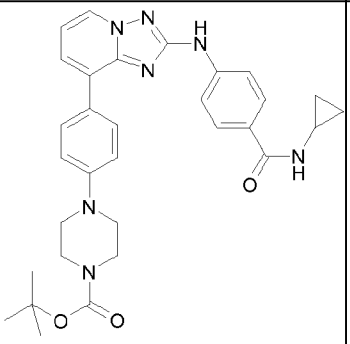
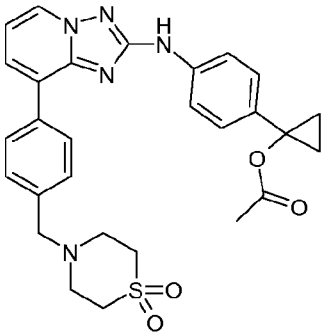
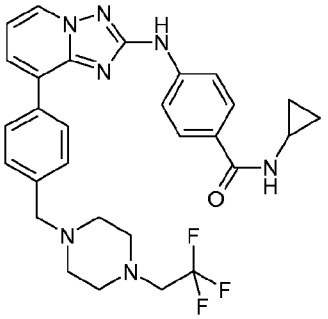
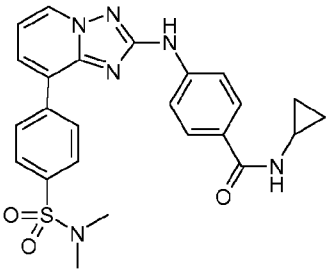
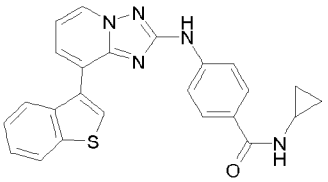
Cpd #	Structure	Name	MW	MS Mes'd
328		4-{4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-phenyl}-piperazine-1-carboxylic acid tert-butyl ester	553.67	554
329		Acetic acid 1-(4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-cyclopropyl ester	531.63	532
330		N-Cyclopropyl-4-(8-{4-[4-(2,2,2-trifluoro-ethyl)-piperazin-1-ylmethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	549.60	550
331		N-Cyclopropyl-4-[8-(4-dimethylsulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	476.56	477
332		4-(8-Benzo[b]thiophen-3-yl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide	409.45	410

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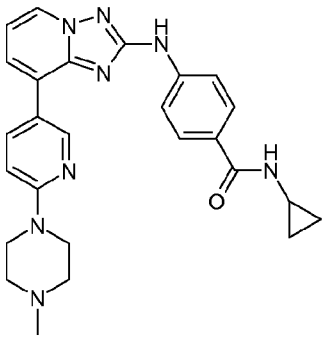
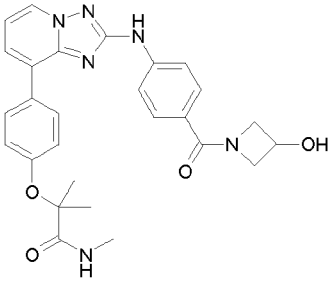
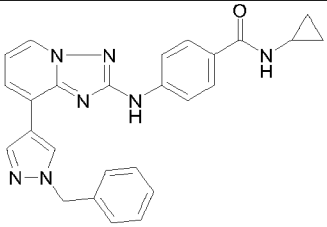
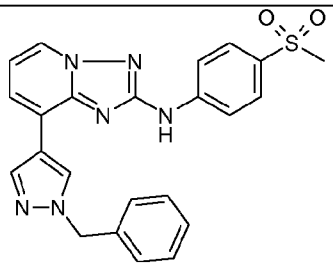
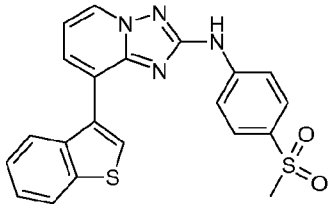
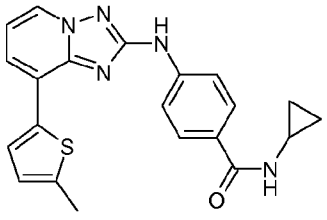
Cpd #	Structure	Name	MW	MS Mes'd
333		N-Cyclopropyl-4-{8-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	468.58	469
334		2-(4-{2-[4-(3-Hydroxy-azetidine-1-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenoxy)-2,N-dimethyl-propionamide	500.56	501
335		4-[8-(1-Benzyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-cyclopropyl-benzamide	449.52	450
336		[8-(1-Benzyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-methanesulfonyl-phenyl)-amine	444.52	445
337		(8-Benzo[b]thiophen-3-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-methanesulfonyl-phenyl)-amine	420.51	421
338		N-Cyclopropyl-4-[8-(5-methyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	389.48	390

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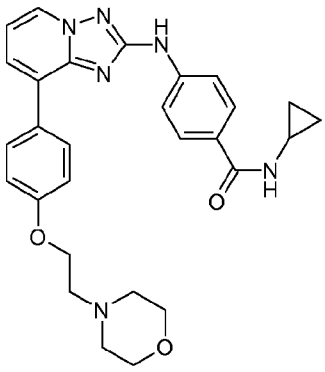
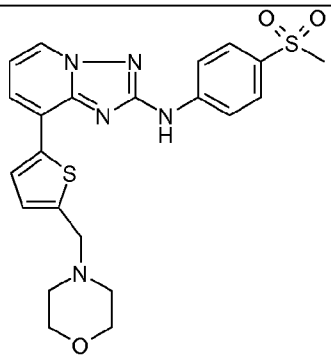
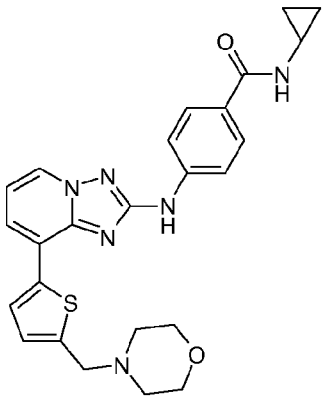
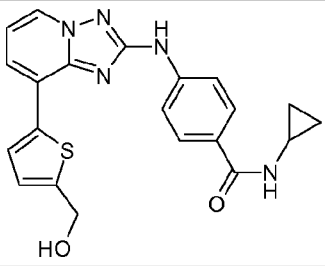
Cpd #	Structure	Name	MW	MS Mes'd
339		N-Cyclopropyl-4-{8-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	498.59	499
340		(4-Methanesulfonyl-phenyl)-[8-(5-morpholin-4-ylmethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine	469.59	470
341		N-Cyclopropyl-4-[8-(5-morpholin-4-ylmethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	474.59	475
342		N-Cyclopropyl-4-[8-(5-hydroxymethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide	405.48	406

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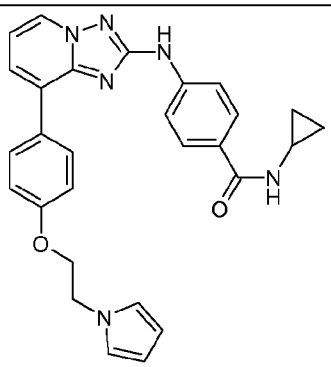
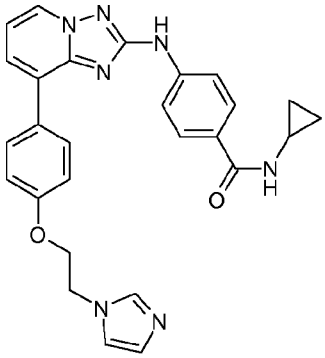
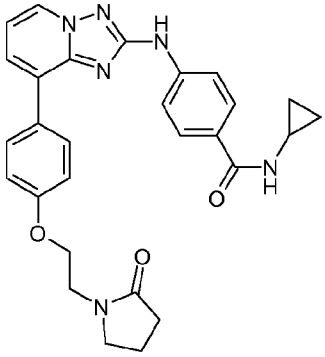
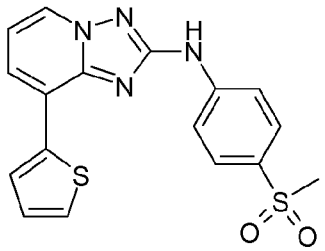
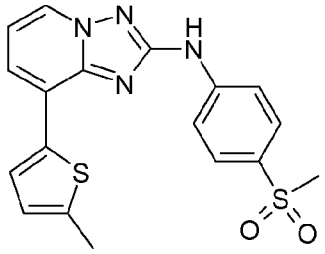
Cpd #	Structure	Name	MW	MS Mes'd
343		N-Cyclopropyl-4-{8-[4-(2-pyrrol-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	478.56	479
344		N-Cyclopropyl-4-{8-[4-(2-imidazol-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	479.54	480
345		N-Cyclopropyl-4-(8-{4-[2-(2-oxo-pyrrolidin-1-yl)-ethoxy]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	496.57	497
346		(4-Methanesulfonyl-phenyl)-(8-thiophen-2-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine	370.45	371
347		(4-Methanesulfonyl-phenyl)-[8-(5-methyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine	384.48	385

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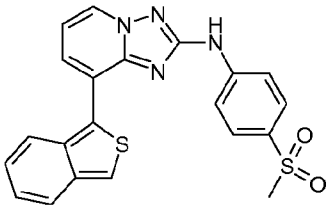
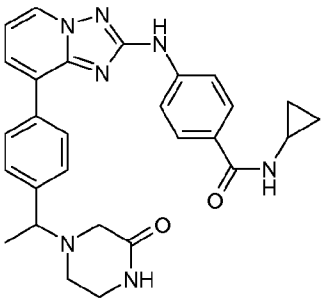
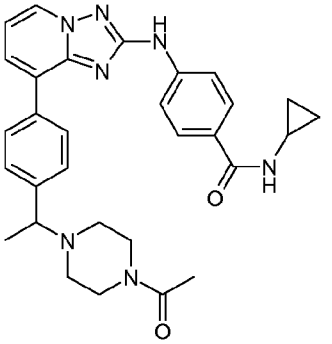
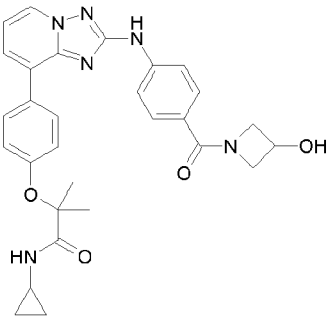
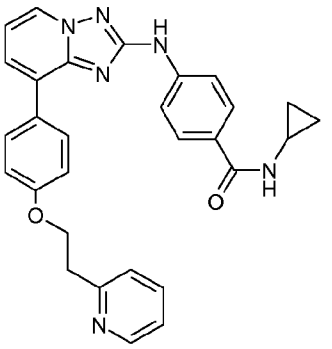
Cpd #	Structure	Name	MW	MS Mes'd
348		(8-Benzo[c]thiophen-1-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-methanesulfonyl-phenyl)-amine	420.51	421
349		N-Cyclopropyl-4-(8-{4-[1-(3-oxo-piperazin-1-yl)-ethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	495.59	496
350		4-(8-{4-[1-(4-Acetyl-piperazin-1-yl)-ethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide	523.64	524
351		N-Cyclopropyl-2-(4-{2-[4-(3-hydroxy-azetidine-1-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenoxy)-2-methyl-propionamide	526.60	527
352		N-Cyclopropyl-4-{8-[4-(2-pyridin-2-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	490.57	491

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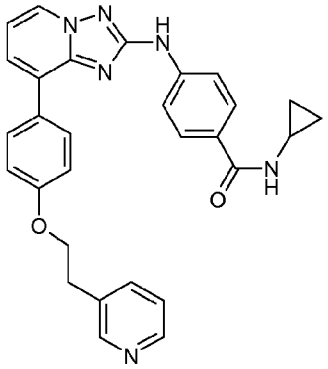
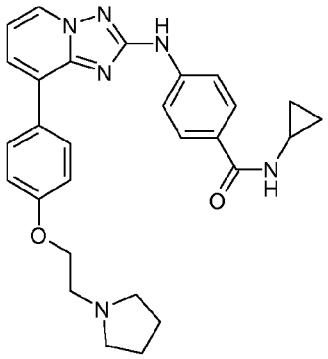
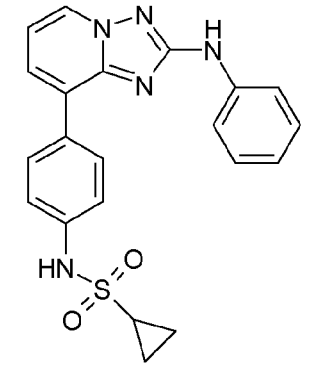
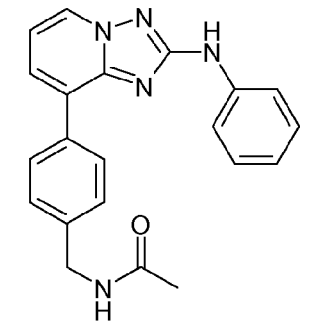
Cpd #	Structure	Name	MW	MS Mes'd
353		N-Cyclopropyl-4-{8-[4-(2-pyridin-3-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	490.57	491
354		N-Cyclopropyl-4-{8-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide	482.59	483
355		Cyclopropanesulfonic acid [4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-amide	405.48	406
356		N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-acetamide	357.42	358

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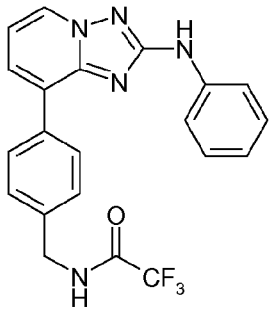
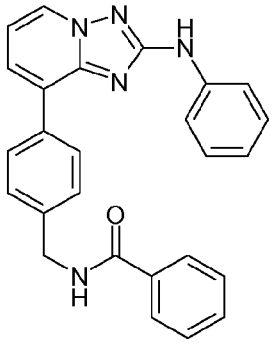
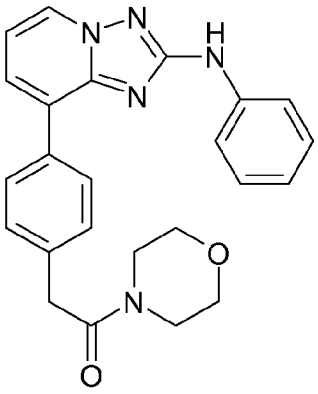
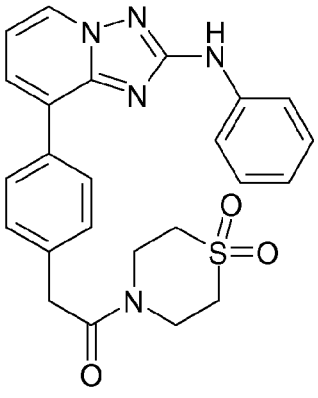
Cpd #	Structure	Name	MW	MS Mes'd
357		N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-acetamide	411.39	412
358		N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-benzamide	419.49	420
359		1-Morpholin-4-yl-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-ethanone	413.48	414
360		1-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-yl)-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-ethanone	461.54	462

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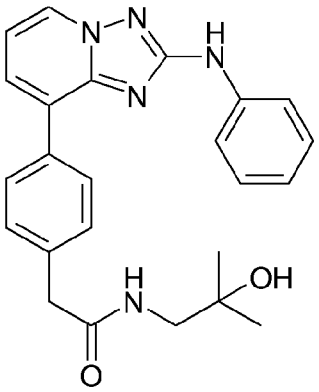
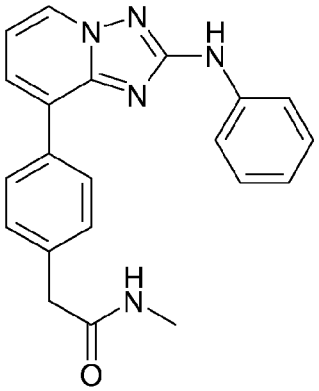
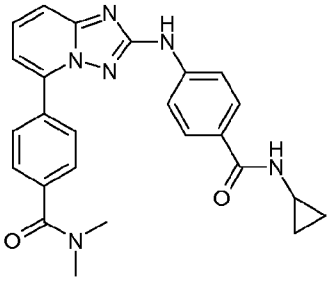
Cpd #	Structure	Name	MW	MS Mes'd
361		N-(2-Hydroxy-2-methyl-propyl)-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-acetamide	415.50	416
362		N-Methyl-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-acetamide	357.42	358
363		N-Cyclopropyl-4-(5-(4-N,N-dimethylacetamido)-phenyl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide	440.51	441

[00752] **Table II – NMR Data of Representative Compounds of the Invention**

Cpd #	(δ) NMR data
1	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.74 (1H, s, NH), 9.59 (1H, s, NH), 8.70 (1H, d, ArH), 8.13 (2H, d, ArH), 7.76 (1H, d, ArH), 7.62 (2H, d, ArH), 7.47 (2H, d, ArH), 7.09 (3H, m, ArH), 3.84 (3H, s, CH_3), 2.01 (3H, s, CH_3)
2	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.75 (1H, b, NH), 8.69 (1H, d, ArH), 8.55 (1H, d, ArH), 8.10 (2H, d, ArH), 8.03 (1H, dd, ArH), 7.78 (1H, d, ArH), 7.09 (4H, m, ArH), 3.83 (3H, s, CH_3), 3.74 (4H, m, 2xCH_2), 3.5 (4H, under water peak, 2xCH_2).
3	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.01 (1H, b, NH), 8.75 (1H, d, ArH), 8.13 (2H, d, ArH), 7.78 (3H, m, ArH), 7.39 (2H, d, ArH), 7.12 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.55 (8H, b, 4xCH_2).

Cpd #	(δ) NMR data
4	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.77 (1H, b, NH), 9.63 (1H, b, NH), 8.78 (1H, d, ArH), 8.20 (2H, d, ArH), 7.87 (1H, d, ArH), 7.62 (2H, d, ArH), 7.50 (4H, m, ArH), 7.12 (1H, m, ArH), 3.8-3.2 (4H, b, partially under water peak, 2xCH$_2$), 2.01 (3H, s, CH$_3$), 1.58 (6H, b, 3xCH$_2$).
5	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.80 (1H, b, NH), 8.78 (1H, d, ArH), 8.55 (1H, d, ArH), 8.19 (2H, d, ArH), 8.03 (1H, dd, ArH), 7.92 (1H, d, ArH), 7.51 (2H, d, ArH), 7.15 (2H, m, ArH), 3.8-3.2 (12H, b, 6xCH$_2$), 1.63 (6H, b, 3xCH$_2$).
6	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.05 (1H, s, NH), 8.83 (1H, d, ArH), 8.21 (2H, d, ArH), 7.91 (1H, d, ArH), 7.77 (2H, d, ArH), 7.52 (2H, d, ArH), 7.39 (2H, d, ArH), 7.16 (1H, m, ArH), 4-3.5 (12H, b, 6xCH$_2$), 1.5 (6H, b, 3xCH$_2$)
7	(1H, DMSO) δ 9.71 (1H, s, NH), 9.60 (1H, s, NH), 8.74 (1H, d, ArH), 8.16 (2H, d, ArH), 7.82 (1H, d, ArH), 7.57 (4H, m, ArH), 7.45 (2H, d, ArH), 7.09 (1H, m, ArH).
8	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.75 (1H, s, NH), 9.66 (1H, s, NH), 8.82 (1H, d, ArH), 8.02 (3H, m, ArH), 7.61 (2H, d, ArH), 7.47 (2h, d, arH), 7.31 (1H, m, ArH), 7.12 (1H, m, ArH).
9	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.77 (1H, s, NH), 9.66 (1H, s, NH), 8.45 (1H, d, ArH), 8.39 (2H, d, ArH), 7.94 (3H, m, ArH), 7.63 (2H, d, ArH), 7.49 (2H, d, ArH), 7.14 (1H, m, ArH).
10	(1H, DMSO) δ 9.77 (1H, s, NH), 9.63 (1H, s, NH), 8.82 (1H, d, ArH), 8.33 (1H, s, ArH), 8.18 (1H, d, ArH), 7.97 (1H, d, ArH), 7.66 (3H, m, ArH), 7.50 (3H, m, ArH), 7.15 (1H, m, ArH), 2.08 (3H, s, CH$_3$).
11	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.74 (1H, s, NH), 9.58 (1H, s, NH), 8.68 (1H, d, ArH), 8.09 (2H, d, ArH), 7.76 (1H, d, ArH), 7.61 (2H, d, ArH), 7.46 (2H, d, ArH), 7.06 (3H, m, ArH), 4.71 (1H, sept, CH), 1.98 (3H, s, CH$_3$), 1.30 (6H, d, 2xCH$_3$).
12	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.72 (1H, s, NH), 9.60 (1H, s, NH), 8.75 (1H, d, ArH), 8.08 (1H, m, ArH), 7.95 (1H, d, ArH), 7.88 (1H, d, ArH), 7.57 (3H, m, ArH), 7.44 (2H, d, ArH), 7.23 (1H, m, ArH), 7.08 (1H, m, ArH), 1.97 (3H, s, CH$_3$)
13	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.90 (1H, s, NH), 9.80 (1H, s, NH), 9.44 (1H, ArH), 8.26 (2H, d, ArH), 8.09 (1H, 1H, ArH), 7.64 (2H, d, ArH), 7.52 (4H, m, ArH), 3.63 (4H, b, 2xCH$_2$), 2.02 (3H, s, CH$_3$), 1.64 (6H, b, 3xCH$_2$).
14	^{1}H NMR δ (ppm)(CDCl$_3$): 8.55 (1H, s, NH), 8.45 (1H, d, ArH), 8.0 (4H, m, ArH), 7.71 (1H, m, ArH), 7.5 (6H, m, ArH), 7.0 (3H, m, ArH), 2.18 (3H, s, CH$_3$).

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Cpd #	(δ) NMR data
15	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.55 (1H, s, NH), 8.68 (1H, d, ArH), 8.56 (1H, d, ArH), 8.12 (2H, d, ArH), 8.00 (1H, dd, ArH), 7.77 (1H, d, ArH), 7.08 (3H, m, ArH), 6.98 (1H, s, ArH), 4.28 (2H, m, 2xCH), 3.84 (3H, s, CH_3), 3.3 (2H, under water peak, 2xCH), 3.08 (4H, m, 2xCH_2), 2.85 (3H, s, CH_3).
16	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.85 (1H, s, NH), 9.67 (1H, s, NH), 8.67 (1H, d, ArH), 8.16 (2H, d, ArH), 7.87 (1H, s, ArH), 7.78 (1H, d, ArH), 7.42 (1H, d, ArH), 7.17 (2H, m, ArH), 7.09 (3H, m, ArH), 3.84 (3H, s, CH_3), 2.05 (3H, s, CH_3).
17	(1H, DMSO) δ 10.16 (1H, s, NH), 8.77 (1H, d, ArH), 8.12 (2H, d, ArH), 7.88 (2H, d, ArH), 7.80 (3H, m, ArH), 7.09 (3H, m, ArH), 3.84 (3H, s, CH_3).
18	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.81 (1H, s, NH), 9.72 (1H, s, NH), 8.84 (1H, d, ArH), 8.41 (2H, d, ArH), 8.07 (2H, d, ArH), 7.95 (1H, d, ArH), 7.62 (2H, d, ArH), 7.49 (2H, d, ArH), 7.13 (1H, m, ArH), 3.30 (3H, s, CH_3), 2.01 (3H, s, CH_3).
20	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.66 (1H, s, NH), 8.76 (1H, d, ArH), 7.82 (2H, m, ArH), 7.62 (3H, m, ArH), 7.46 (3H, m, ArH), 7.10 (1H, m, ArH), 7.04 (1H, dd, ArH), 3.86 (3H, s, CH_3), 2.01 (3H, s, CH_3).
21	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.94 (1H, s, NH), 9.79 (1H, s, NH), 9.63 (1H, s, NH), 8.74 (1H, d, ArH), 8.13 (2H, d, ArH), 7.79 (1H, d, ArH), 7.62 (2H, d, ArH), 7.47 (2H, d, ArH), 7.37 (2H, d, ArH), 7.09 (1H, m, ArH), 2.66 (1H, m, CH), 2.01 (3H, s, CH_3), 0.97 (4H, m, 2xCH_2).
22	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.73 (1H, s, NH), 9.53 (1H, s, NH), 8.70 (1H, d, ArH), 8.02 (2H, d, ArH), 7.83 (2H, d, ArH), 7.71 (1H, d, ArH), 7.62 (5H, m, ArH), 7.46 (2H, d, ArH), 7.22 (2H, d, ArH), 7.05 (1H, m, ArH), 2.01 (3H, s, CH_3).
23	(1H, DMSO), δ 9.78 (1H, s, NH), 9.58 (1H, s, NH), 8.61 (1H, d, ArH), 8.02 (2H, d, ArH), 7.65 (3H, m, ArH), 7.47 (2H, d, ArH), 7.03 (1H, t app, ArH), 6.74 (2H, d, ArH), 3.34 (4H, m, 2xCH_2 under water peak), 2.01 (3H, s, CH_3), 1.55 (4H, m, 2xCH_2), 0.91 (6H, m, 2xCH_3).
24	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.77 (1H, b, NH), 9.59 (1H, s, NH), 8.73 (1H, d, ArH), 7.57-7.4 (7H, m, ArH), 7.18-7.01 (3H, m, ArH), 3.75 (3H, s, CH_3), 2.00 (3H, s, CH_3).
25	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.72 (1H, s, NH), 9.49 (1H, s, NH), 8.59 (1H, d, ArH), 7.93 (2H, d, ArH), 7.60 (3H, m, ArH), 7.47 (2H, d, ArH), 7.35 (4H, m, ArH), 2.21 (1H, m, ArH), 7.01 (1H, t app, ArH), 6.69 (2H, d, ArH), 6.58 (H, m, ArH), 4.35 (2H, m, CH_2), 2.01 (3H, s, CH_3).

Cpd #	(δ) NMR data
26	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.96 (1H, s, NH), 8.75 (1H, d, ArH), 8.13 (2H, d, ArH), 7.79 (1H, d, ArH), 7.75 (2H, d, ArH), 7.34 (2H, d, ArH), 7.09 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.48 (4H, b, 2xCH_2), 1.62 (2H, b, CH_2), 1.51 (4H, b, 2xCH_2).
27	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.76 (1H, s, NH), 8.71 (1H, d, ArH), 8.59 (1H, s, ArH), 8.12 (2H, d, ArH), 8.59 (1H, s, ArH), 7.77 (1H, d, ArH), 7.69 (2H, d, ArH), 7.25 (2H, d, ArH), 7.09 (4H, m, ArH), 5.32 (2H, s, CH_2), 3.84 (3H, s, CH_3).
28	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.01 (1H, s, NH), 8.77 (1H, d, ArH), 8.13 (2H, d, ArH), 7.94 (1H, d, NH), 7.81 (3H, m, ArH), 7.74 (2H, d, ArH), 7.12 (3H, m, ArH), 4.11 (1H, m, CH), 3.84 (3H, s, CH_3), 1.16 (6H, d, 2xCH_3).
29	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.06 (1H, s, NH), 8.77 (2H, m, NH, ArH), 8.13 (2H, d, ArH), 7.87 (2H, d, ArH), 7.79 (3H, m, ArH), 7.32 (4H, d, ArH), 7.24 (1H, m, ArH), 7.11 (3H, m, ArH), 4.48 (2H, d, CH_2), 3.84 (3H, s, CH_3).
30	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.06 (1H, s, NH), 8.74 (1H, d, ArH), 8.13 (2H, d, ArH), 7.80 (3H, dd, ArH), 7.44 (2H, d, ArH), 7.10 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.3 (8H, under water peak, 4xCH_2), 2.79 (3H, s, CH_3).
31	(1H, DMSO), δ 9.97, (1H, s, NH), 8.75 (1H, d, ArH), 8.13 (2H, d, Arh), 7.78 (3H, m, ArH), 7.35 (2H, d, ArH), 7.12 (4H, m, ArH), 3.84 (3H, s, CH_3), 3.74 (1H, m, CH), 3.35 (2H, under water peak, CH_2), 3.18 (2H, m, CH_2), 1.75 (2H, m, CH_2), 1.37 (2H, m, CH_2).
32	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.04 (1H, s, NH), 8.77 (1H, d, ArH), 8.14 (2H, d, ArH), 7.81 (3H, d, ArH), 7.63 (2H, d, ArH), 7.11 (7H, m, ArH), 4.88 (4H, s, 2xCH_2), 3.84 (3H, s, CH_3).
33	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.09 (1H, s, NH), 8.95 (1H, t, NH), 8.77 (1H, d, ArH), 8.70 (1H, s, ArH), 8.61 (1H, d, ArH), 8.13 (2H, d, ArH), 8.07 (1H, d, ArH), 7.86 (2H, d, ArH), 7.81 (3H, m, ArH), 7.66 (1H, m, ArH), 7.11 (3H, m, ArH), 4.56 (2H, d, CH_2), 3.84 (3H, s, CH_3).
34	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.11 (1H, s, NH), 8.76 (1H, d, ArH), 8.53 (1H, t, NH), 8.13 (2H, d, ArH), 7.82 (5H, m, ArH), 7.13 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.34 (2H, m, CH_2), 3.07 (2H, m, ArH), 2.02 (2H, m, CH_2), 1.87 (2H, m, ArH).
35	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.05 (1H, s, NH), 8.75 (1H, d, ArH), 8.35 (1H, m, NH), 8.13 (2H, d, ArH), 7.80 (5H, m, ArH), 7.11 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.19 (4H, m, partially under water peak, 2xCH_2), 3.07 (2H, m, CH_2), 2.84 (2H, m, ArH), 1.88 (3H, m, CH_2, CH), 1.42 (2H, m, CH_2), 1.21 (3H, t, CH_3).

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Cpd #	(δ) NMR data
36	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.82 (1H, s, NH), 8.73 (1H, d, ArH), 8.15 (2H, m, ArH), 8.09 (1H, d, NH), 7.86 (1H, d, ArH), 7.79 (1H, d, ArH), 7.33 (2H, m, ArH), 7.09 (3H, m, ArH).
37	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.85 (1H, s, NH), 8.72 (1H, d, NH), 8.39 (1H, d, ArH), 8.15 (3H, m, ArH), 7.89 (1H, d, ArH), 7.80 (1H, d, ArH), 7.38 (2H, m, ArH), 7.09 (3H, m, ArH), 4.01 (1H, m, CH), 3.84 (3H, s, CH_3), 3.4 (2H, under water peak, CH_2), 3.12 (2H, m, CH_2), 2.79 (3H, b, CH_3), 2.05 (2H, m, ArH), 1.77 (2H, m, ArH).
38	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, b, NH), 9.66 (1H, b, NH), 8.72 (2H, m, ArH), 8.57 (1H, m, ArH), 8.13 (2H, d, ArH), 7.91 (1H, m, ArH), 7.78 (1H, d, ArH), 7.62 (2H, m, ArH), 7.45 (3H, m, ArH), 7.18 (2H, d, ArH), 7.07 (1H, m, ArH), 5.25 (2H, s, CH_2), 2.01 (3H, s, CH_3).
39	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.66 (1H, s, NH), 8.70 (1H, d, ArH), 8.12 (2H, d, ArH), 7.77 (1H, d, ArH), 7.63 (2H, d, ArH), 7.47 (2H, d, ArH), 7.07 (3H, m, ArH), 4.60 (1H, t, OH), 4.12 (2H, t , CH2), 3.58 (2H, dd, CH2), 2.01 (3H, s, CH3), 1.89 (2H, m, CH2).
40	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.78 (1H, b, NH), 9.64 (1H, b, NH), 8.79 (1H, d, ArH), 8.23 (2H, d, ArH), 7.89 (1H, d, ArH), 7.63 (2H, d, ArH), 7.56 (2H, d, ArH), 7.48 (2H, d, ArH), 7.34 (2H, d, ArH), 7.13 (1H, m, ArH), 2.95 (6H, b, 2xCH_3), 2.02 (3H, s, CH_3).
41	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.61 (1H, s, NH), 8.64 (1H, d, ArH), 8.07 (2H, d, ArH), 7.69 (3H, m, ArH), 7.47 (2H, d, ArH), 7.04 (1H, m, ArH), 6.83 (2H, d, ArH), 2.98 (6H, s, 2xCH_3), 2.01 (3H, s, CH_3).
42	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.86 (1H, s, NH), 9.13 (1H, s, NH), 8.71 (1H, d, ArH), 8.11 (2H, d, ArH), 7.79 (1H, d, ArH), 7.74 (3H, m, ArH), 7.64 (1H, s, ArH), 7.37 (2H, d, ArH), 7.08 (4H, m, ArH), 5.33 (2H, s, CH_2), 3.83 (3H, s, CH_3).
43	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.06 (1H, s, NH), 8.75 (1H, d, ArH), 8.22 (1H, d, ArH), 8.13 (1H, d, ArH), 7.81 (5H, m, ArH), 7.11 (7H, m, ArH), 4.1 (1H, m, CH), 3.84 (3H, s, CH_3), 3.46 (2H, m, CH_2), 3.11 (2H, m, CH_2), 3.78 (3H, s, CH_3), 2.04 (2H, m, CH_2), 1.77 (2H, m, CH_2).
44	(1H, DMSO), δ 9.99 (1H, s, NH), 8.76 (1H, dd, ArH), 8.48 (1H, s, ArH), 8.18 (2H, d, ArH), 7.91 (1H, dd, ArH), 7.82 (1H, d, ArH), 7.48 (1H, d, ArH), 7.42 (1H, m, ArH), 7.10 (3H, m, ArH), 3.85 (3H, s, CH_3).

Cpd #	(δ) NMR data
45	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.15 (1H, s, NH), 9.06 (1H, t, NH), 8.79 (1H, d, ArH), 8.63 (1H, d, ArH), 8.13 (2H, d, ArH), 8.03 (1H, m, ArH), 7.90 (2H, d, ArH), 7.81 (3H, m, ArH), 7.55 (1H, d, ArH), 7.50 (1H, m, ArH), 7.12 (3H, m, ArH), 4.65 (2H, d, CH_2), 3.84 (3H, s, CH_3).
46	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.91 (1H, s, NH), 8.99 (1H, t, NH), 8.74 (1H, d, ArH), 8.23 (1H, s, ArH), 8.16 (2H, d, ArH), 7.90 (1H, m, ArH), 7.80 (1H, d, ArH), 7.40 (2H, m, ArH), 7.34 (4H, m, ArH), 7.23 (1H, m, ArH), 7.19 (3H, m, ArH), 4.49 (2H, d, CH_2), 3.82 (3H, s, CH_3).
47	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.95 (1H, s, NH), 9.17 (1H, t, NH), 8.74 (1H, d, ArH), 8.67 (1H, d, ArH), 8.26 (1H, s, ArH), 8.15 (2H, d, ArH), 8.09 (1H, m, ArH), 7.91 (1H, d, ArH), 7.81 (1H, d, ArH), 7.61 (1H, d, ArH), 7.56 (1H, m, ArH), 7.43 (2H, m, ArH), 7.09 (3H, m, ArH), 4.68 (2H, d, CH2), 3.83 (3H, s, CH3).
48	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.94 (1H, s, NH), 9.13 (1H, t, NH), 9.74 (2H, m, ArH), 8.68 (1H, m, ArH), 8.24 (1H, s, ArH), 8.15 (3H, m, ArH), 7.89 (1H, m, ArH), 7.81 (1H, d, ArH), 7.77 (1H, dd, ArH), 7.39 (2H, m, ArH), 7.09 (3H, m, ArH), 4.60 (2H, d, CH_2), 3.84 (3H, s, CH_3).
49	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.87 (1H, s, NH), 8.72 (1H, d, ArH), 8.51 (1H, t, NH), 8.16 (3H, m, ArH), 7.89 (1H, m, ArH), 7.80 (1H, d, ArH), 7.34 (2H, m, ArH), 7.09 (3H, m, ArH), 3.84 (3H, s, CH_3), 3.4 (2H, under water peak, CH_2), 3.10 (2H, m, CH_2), 2.80 (6H, s, CH_3), 2.79 (3H, s, CH_3), 1.90 (2H, m, CH_2).
50	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.95 (1H, s, NH), 9.57 (1H, b, NH), 8.74 (1H, d, ArH), 8.65 (1H, t, NH), 8.23 (1H, s, ArH), 8.16 (2H, d, ArH), 7.93 (1H, d, ArH), 7.82 (1H, d, ArH), 7.40 (2H, m, ArH), 7.10 (3H, m, ArH), 3.85 (3H, s, CH_3), 3.61 (4H, m, 2xCH_2), 3.35 (2H, m, CH_2), 3.08 (2H, m, CH_2), 2.04 (2H, m, CH_2), 1.86 (2H, m, CH_2).
51	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.92 (1H, s, NH), 9.36 (1H, b, ArH), 8.74 (1H, d, ArH), 8.52 (1H, t, NH), 8.15 (3H, d, ArH), 7.90 (1H, d, ArH), 7.81 (1H, d, ArH), 7.36 (2H, m, ArH), 7.10 (3H, m, ArH).
52	(1H, NMR) 10.13 (1H, s, NH), 8.79 (1H, d, ArH), 8.54 (1H, t, NH), 8.13 (2H, d, ArH), 7.82 (5H, m, ArH), 7.29 (1H, m, ArH), 7.11 (4H, m, ArH), 6.98 (3H, m, ArH), 4.11 (2H, m, CH_2), 3.84 (3H, s, CH_3), 3.64 (2H, m, CH_2).

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Cpd #	(δ) NMR data
54	^{1}H NMR δ (ppm)(DMSO-d$_6$): 11.25 (1H, b, NH), 9.78 (1H, s, NH), 9.64 (1H, s, NH), 8.71 (1H, d, ArH), 8.42 (1H, s, ArH), 7.79 (2H, m, ArH), 7.64 (2H, d, ArH), 7.45 (4H, m, ArH), 7.09 (1H, m, ArH), 6.53 (1H, s, ArH), 2.01 (3H, s, CH_3).
55	^{1}H NMR δ (ppm)(DMSO-d$_6$): 13.16 (1H, s, NH), 9.80 (1H, s, NH), 9.55 (1H, s, NH), 8.63 (2H, m, ArH), 8.37 (1H, s, ArH), 7.87 (1H, d, ArH), 7.65 (2H, d, ArH), 7.49 (2H, d, ArH), 7.03 (1H, m, ArH), 2.01 (3H, s, CH_3).
56	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.78 (1H, s, NH), 9.66 (1H, s, NH), 8.71 (1H, d, ArH), 8.43 (1H, s, ArH), 7.84 (2H, m, ArH), 7.66-7.39 (5H, m, ArH), 7.09 (1H, m, ArH), 6.52 (1H, d, ArH), 3.85 (3H, s, CH_3), 2.01 (3H, s, CH_3).
57	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.65 (1H, s, NH), 8.77 (1H, d, ArH), 8.12 (2H, d, ArH), 7.82 (1H, d, ArH), 7.62 (2H, d, ArH), 7.47 (3H, m, ArH), 7.10 (1H, m, ArH), 5.28 (1H, t, OH), 4.58 (2H, d, CH_2), 2.01 (3H, s, CH_3).
58	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.5 (1H, s, NH), 9.79 (1H, s, NH), 9.61 (1H, s, NH), 8.72 (1H, d, ArH), 8.02 (6H, m, ArH), 7.73 (1H, d, ArH), 7.60 (2H, d, ArH), 7.47 (2H, d, ArH), 7.22 (2H, d, ArH), 7.06 (1H, m, ArH), 2.01 (3H, s, CH_3).
59	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.80 (1H, s, NH), 9.73 (1H, s, NH), 8.85 (1H, d, ArH), 8.42 (2H, d, ArH), 7.92 (3H, m, ArH), 7.63 (2H, d, ArH), 7.48 (2H, d, ArH), 7.16 (1H, m, ArH), 2.66 (6H, s, 2xCH_3), 2.01 (3H, s, CH_3).
61	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.91 (1H, s, ArH), 8.88 (1H, t, NH), 8.74 (1H, d, ArH), 8.17 (3H, m, ArH), 7.89 (1H, dd, ArH), 7.80 (1H, d, ArH), 7.35 (2H, m, ArH), 7.11 (3H, m, ArH), 5.95 (1H, s, ArH), 4.45 (2H, d, CH_2), 3.84 (3H, s, CH_3), 3.75 (3H, s, CH_3), 2.09 (3H, s, CH_3)
62	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.86 (1H, s, NH), 8.76 (1H, d, ArH), 8.46 (3H, m, ArH), 8.16 (3H, d, ArH), 7.84 (1H, dd, ArH), 7.81 (1H, d, ArH), 7.69 (1H, d, ArH), 7.37 (2H, m, ArH), 7.33 (1H, d, ArH), 7.11 (3H, m, ArH), 3.84 (3H, s, CH_3), 3?53 (2H, m, CH_2), 2.90 (2H, m, CH_2).
64	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.70 (1H, s, NH), 8.79 (1H, d, ArH), 8.26 (2H, d, ArH), 8.01 (4H, m, ArH, NH_2), 7.62 (2H, d, ArH), 7.49 (3H, m, ArH), 7.12 (1H, m, ArH), 2.01 (3H, s, CH_3).

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Cpd #	(δ) NMR data
65	^{1}H NMR δ (ppm)(DMSO-d$_6$): 9.79 (1H, s, NH), 9.69 (1H, s, NH), 8.83 (1H, d, ArH), 8.33 (2H, d, ArH), 7.94 (3H, m, ArH), 7.62 (2H, d, ArH), 7.47 (4H, m, 2xArH, NH_2), 7.15 (1H, m, ArH), 2.01 (3H, s, CH_3).
66	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.5 (1H, too broad to be seen), 9.73 (1H, s, NH), 9.67 (1H, s, NH), 8.75 (1H, d, ArH), 8.64 (1H, s, ArH), 8.19 (1H, s, ArH), 8.05 (1H, d, ArH), 7.85 (1H, d, ArH), 7.66 (3H, m, ArH), 7.47 (2H, d, ArH), 7.11 (1H, t app, ArH), 2.01 (3H, s, CH_3).
67	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.7 (1H, b, NH), 9.79 (1H, s, NH), 9.62 (1H, s, NH), 8.74 (1H, d, ArH), 8.07 (2H, d, Ar), 7.99 (1H, m, ArH), 7.77 (3H, m, ArH), 7.60 (2H, d, ArH), 7.47 (2H, d, ArH), 7.24 (2H, d, ArH), 7.07 (1H, m, ArH), 2.01 (3H, s, CH_3).
68	^{1}H NMR δ (ppm)(DMSO-d$_6$): 10.47 (1H, b, NH), 9.78 (1H, b, NH), 9.58 (1H, b, NH), 8.69 (1H, d, ArH), 8.00 (2H, d, ArH), 7.74 (1H, d, ArH), 7.59 (2H, d, ArH), 7.50 (2H, d, ArH), 7.08 (5H, m, ArH), 3.32 (6H, d app, 2xCH_3), 2.22 (3H, s, CH_3), 2.01 (3H, s, CH_3)
69	^{1}H NMR δ (ppm)(DMSO-d$_6$): 13.08 (1H, b, NH), 9.75 (2H, d, ArH), 8.83 (1H, d, ArH), 8.29 (2H, d, ArH), 8.07 (2H, d, ArH), 7.93 (1H, d, ArH), 7.63 (2H, d, ArH), 7.47 (2H, d, ArH), 7.17 (1H, t app, ArH), 2.01 (3H, s, CH_3).
70	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.81 (3H, d, CH3), 5.31 (2H, s, CH2), 7.18 (1H, dd, ArH), 7.28 (2H, d, ArH), 7.79 (2H, d, ArH), 7.84 (2H, d, ArH), 7.88 (1H, d, ArH), 8.23 (2H, d, ArH), 8.25 (1H, m, NH), 8.85 (1H, d, ArH), 10.12 (1H, s, NH).
71	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.77 (3H, s, CH_3), 3.88 (3H, s, CH_3), 3.91 (3H, s, CH_3), 7.12 (2H, s, ArH), 7.17-7.28 (2H, m, ArH), 7.74 (1H, d, ArH), 7.85-7.87 (2H, m, ArH), 8.19 (2H, d, ArH), 8.80 (1H, d, ArH), 10.24 (1H, s, NH).
72	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.91 (3H, s, CH3), 7.19 (2H, d, ArH), 7.24 (1H, dd, ArH), 7.65 (1H, dd, ArH), 7.73 (1H, dd, ArH), 8.06 (2H, d, ArH), 8.76 (1H, s, NCHN), 9.15 (2H, s, ArH), 10.15 (1H, s, NH).
73	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.84 (3H, d, CH_3), 3.88 (3H, s, CH_3), 3.99 (3H, s, CH_3), 7.12 (2H, d, ArH), 7.18 (1H, dd, ArH), 7.27 (1H, dd, ArH), 7.83-7.87 (3H, m, ArH), 8.02 (1H, q, NH), 8.19 (2H, d, ArH), 8.79 (1H, dd, ArH), 10.11 (1H, s, NH).
74	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.81 (3H, s, CH_3), 3.87 (3H, s, CH_3), 7.07-7.16 (4H, m, ArH), 7.48 (1H, d, ArH), 7.58 (1H, s, ArH), 7.82 (1H, d, ArH), 8.19 (2H, d, ArH), 8.76 (1H, d, ArH), 9.70 (1H, s, NH) (OH too broad - not visible).

Cpd #	(δ) NMR data
75	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.88 (3H, s, CH_3), 4.00 (3H, s, CH_3), 7.12 (2H, d, ArH), 7.18 (1H, dd, ArH) 7.27 (1H, d, ArH), 7.33 (1H, s, NH), 7.54 (1H, s, NH), 7.82-7.92 (3H, m, ArH), 8.20 (2H, d, ArH), 8.79 (1H, d, ArH), 10.14 (1H, s, NH).
76	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.88 (3H, s, CH_3), 7.14 (2H, d, ArH), 7.20 (1H, dd, ArH), 7.79 (2H, d, ArH), 7.87 (1H, dd, ArH), 7.91 (2H, d, ArH), 8.16 (2H, d, ArH), 8.83 (1H, dd, ArH), 10.46 (1H, s, NH).
77	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.82 (3H, d, CH_3), 5.31 (2H, s, CH_2), 7.17 (1H, dd, ArH), 7.25 (2H, d, ArH), 7.64 (1H, d, ArH), 7.78-7.87 (5H, m, ArH), 8.03 (1H, dd, ArH), 8.19 (2H, d, ArH), 8.25 (1H, q, NH), 8.60 (1H, s, ArH), 8.83 (1H, d, ArH), 10.10 (1H, s, ArH).
79	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.83 (3H, s, CH_3), 2.99 (3H, s, CH_3), 3.87 (6H, s, 2 x CH_3), 7.08-7.13 (3H, m, ArH), 7.16 (1H, dd, ArH), 7.26 (1H, dd, ArH), 7.76 (1H, d, ArH), 7.84 (1H, dd, ArH), 8.18 (2H, m, ArH), 8.77 (1H, dd, ArH), 9.94 (1H, s, NH).
80	δH(400 MHz; DMSO-d$_6$) 3.79 (3 H, s, CH_3), 5.31 (2 H, s, CH_2), 7.09-7.18 (2 H, m, ArH), 7.26 (2 H, d, ArH), 7.38 (1 H, d, ArH), 7.53 (1 H, s, ArH), 7.86 (1 H, d, ArH), 8.25 (2 H, d, ArH), 8.78 (1 H, d, ArH), 9.68 (1 H, s, NH), (OH too broad-not visible)
82	δH(400 MHz; DMSO-d$_6$) 3.88 (3 H, s, CH_3), 4.34 (2 H, s, CH_2), 7.10-7.18 (3 H, m, ArH), 7.51 (1 H, d, ArH), 7.81-7.89 (2 H, m, ArH), 8.15-8.23 (3 H, m, ArH), 8.51 (1 H, s, NH), 8.84 (1 H, d, ArH), 10.02 (1 H, s, NH)
83	δH(400 MHz; DMSO-d$_6$) 0.54-0.61 (2 H, m, CH), 0.68-0.77 (2 H, br m, CH), 2.86 (1 H, m, CH), 3.97 (3 H, s, CH_3), 5.31 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.26 (3 H, br d, ArH), 7.75-7.96 (4 H, m, ArH), 8.25 (2 H, d, ArH), 8.82 (1 H, d, NH), 10.15 (1 H, s, NH).
84	δH(400 MHz; DMSO-d$_6$) 2.84 (3 H, d, CH_3), 3.99 (3 H, s, CH_3), 5.31 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.23-7.30 (3 H, m, ArH), 7.85 (2 H, m, ArH), 7.89 (1 H, dd, ArH), 8.02 (1 H, br q, NH), 8.25 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 10.14 (1 H, s, NH).
85	δH(400 MHz; DMSO-d$_6$) 3.85 (3 H, s, CH_3), 5.30 (2 H, s, CH_2), 7.09 (1 H, dd, ArH), 7.26 (2 H, d, ArH), 7.48 (1 H, s, ArH), 7.80-7.84 (2 H, m, ArH), 8.22 (2 H, d, ArH), 8.70 (1 H, d, ArH), 9.35 (1 H, s, NH).

Cpd #	(δ) NMR data
86	δH(400 MHz; DMSO-d6) 3.17-3.26 (2 H, m, CH), 3.51-3.58 (2 H, m, CH), 3.60-3.68 (4 H, m, CH), 3.88 (3 H, s, CH_3), 5.30 (2 H, s, CH_2), 7.12-7.21 (2 H, m, ArH), 7.26 (3 H, m, ArH), 7.76 (1 H, br d, ArH), 7.88 (1 H, d, ArH), 8.25 (2 H, d, ArH), 8.81 (1 H, d, ArH), 10.00 (1 H, s, NH).
87	^{1}H NMR δ (ppm)(DMSO-d6): 5.31 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.28 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.89 (3 H, d, ArH), 8.23 (2 H, d, ArH), 8.85 (1 H, NH), 10.29 (1 H, s, NH).
88	^{1}H NMR δ (ppm)($CHCl_3$-d): 0.60-0.65 (2 H, m, CH), 0.84-0.90 (2 H, m, CH), 2.90-2.95 (1 H, m, CH), 3.87 (3 H, s, CH_3), 6.79 (1 H, d, ArH), 6.99-7.07 (3 H, m, ArH and NH), 7.13 (1 H, dd, ArH), 7.35 (1 H, s, NH), 7.58 (1 H, dd, ArH), 7.73 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.06 (1 H, dd, ArH), 8.43 (1 H, dd, ArH).
89	^{1}H NMR δ (ppm)($CHCl_3$-d): 0.60-0.65 (2 H, m, CH), 0.84-0.90 (2 H, m, CH), 1.36 (6 H, d, CH3), 2.91-2.97 (1 H, m, CH), 4.54-4.63 (1 H, m, CH), 6.78 (1 H, d, ArH), 6.96-7.04 (3 H, m, ArH and NH), 7.08 (1 H, dd, ArH), 7.58 (1 H, dd, ArH), 7.66-7.74 (2 H, m, ArH), 7.92 (2 H, d, ArH), 8.02 (1 H, dd, ArH), 8.43 (1 H, dd, ArH).
90	^{1}H NMR δ (ppm)($CHCl_3$-d): 0.60-0.65 (2 H, m, CH), 0.84-0.90 (2 H, m, CH), 2.90-2.95 (1 H, m, CH), 3.87 (3 H, s, CH3), 6.79 (1 H, d, ArH), 6.99-7.07 (3 H, m, ArH and NH), 7.13 (1 H, dd, ArH), 7.35 (1 H, s, NH), 7.58 (1 H, dd, ArH), 7.73 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.06 (1 H, dd, ArH), 8.43 (1 H, dd, ArH).
91	^{1}H NMR δ (ppm)($CHCl_3$-d): 0.63 (2 H, s, CH), 0.85-0.91 (2 H, m, CH), 2.91-2.97 (1 H, m, CH), 6.79 (1 H, d, ArH), 7.06 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.22 (1 H, s, NH), 7.37 (2 H, d, ArH), 7.62 (1 H, d, ArH), 7.74 (1 H, dd, ArH), 8.03 (2 H, d, ArH), 8.09 (1 H, dd, ArH), 8.50 (1 H, d, ArH).
92	δH(400 MHz; DMSO-d6) 0.62-0.66 (2 H, m, CH), 0.73-0.79 (2 H, m, CH), 2.86 (1 H, m, CH), 3.87 (3 H, s, CH_3), 7.08-7.15 (3 H, m, ArH), 7.17 (1 H, dd, ArH), 7.43 (1 H, br d, ArH), 7.75 (1 H, d, ArH), 7.84 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.56 (1 H, d, NH), 8.83 (1 H, d, ArH), 10.09 (1 H, s, NH). OH missing
93	^{1}H NMR δ (ppm)(DMSO-d6): 0.52-0.57 (2 H, m, CH), 0.67-0.73 (2 H, m, CH), 2.39 (3 H, s, CH_3), 2.81-2.87 (1 H, m, CH), 3.88 (3 H, s, CH_3), 7.09-7.16 (3 H, m, ArH), 7.31 (1 H, d, ArH), 7.57 (1 H, s, NH), 7.62 (1 H, dd, ArH), 7.83 (1 H, dd, ArH), 8.12 (1 H, d, ArH), 8.17 (2 H, d, ArH), 8.79 (1 H, dd, ArH), 9.87 (1 H, s, NH).

Cpd #	(δ) NMR data
94	δH(400 MHz; DMSO-d6) 2.85 (3 H, d, CH_3), 3.04 (6 H, br d, N(CH3)2), 7.25 (1 H, dd, ArH), 7.61 (2 H, d, ArH), 7.98-8.01 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.33 (1 H, dd, ArH), 8.56 (1 H, br q, NH), 8.90-8.93 (1 H, d, ArH), 8.96 (1 H, d, ArH), 10.45 (1 H, s, NH).
96	δH(400 MHz; DMSO-d6) 0.66-0.76 (4 H, m, CH), 2.87-2.95 (1 H, m, CH), 3.04 (6 H, br d, $N(CH_3)_2$), 7.25 (1 H, dd, ArH), 7.61 (2 H, d, ArH), 7.96-8.04 (2 H, m, ArH), 8.24 (2 H, d, ArH), 8.33 (1 H, dd, ArH), 8.51 (1 H, br d, NH), 8.88-8.95 (2 H, m, ArH), 10.45 (1 H, s, NH).
97	^{1}H NMR δ (ppm)(DMSO-d6): 0.52-0.58 (2 H, m, CH), 0.66-0.73 (2 H, m, CH), 2.39 (3 H, s, CH_3), 2.80-2.87 (1 H, m, CH), 3.01 (3 H, s, CH_3), 3.05 (3 H, s, CH_3), 7.19 (1 H, dd, ArH), 7.31 (1 H, d, ArH), 7.57-7.64 (4 H, m, ArH & NH), 7.95 (1 H, dd, ArH), 8.12 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 9.92 (1 H, s, NH).
98	^{1}H NMR δ (ppm)(DMSO-d6): 0.49-0.60 (2 H, m, CH), 0.67-0.73 (2 H, m, CH), 2.38 (3 H, s, CH_3), 2.80-2.85 (1 H, m, CH), 7.19 (1 H, dd, ArH), 7.31 (1 H, d, ArH), 7.53-7.64 (4 H, m, ArH), 7.92 (1 H, d, ArH), 8.12 (1 H, d, NH), 8.31 (2 H, d, ArH), 8.88 (1 H, d, ArH), 9.92 (1 H, s, NH).
99	δH(400 MHz; DMSO-d6) 0.50-0.56 (2 H, m, CH), 0.72-0.79 (2 H, m, CH), 1.48 (3 H, t, CH_3), 2.88 (1 H, m, CH), 3.88 (3 H, s, CH_3), 4.22 (2 H, q, CH_2), 7.11 (2 H, d, ArH), 7.17 (1 H, dd, ArH), 7.24 (1 H, dd, ArH), 7.77-7.88 (3 H, m, ArH), 8.00 (1 H, d, NH), 8.18 (2 H, d, ArH), 8.78 (1 H, d, ArH), 10.11 (1 H, s, NH).
100	δH(400 MHz; DMSO-d6) 1.67-1.75 (2 H, m, CH), 2.00-2.08 (2 H, m, CH), 2.22-2.31 (2 H, m, CH), 3.88 (3 H, s, CH_3), 4.01 (3 H, s, CH_3), 4.41-4.49 (1 H, m, CH), 7.12 (2 H, d, ArH), 7.18 (1 H, dd, ArH), 7.26 (1 H, dd, ArH), 7.79 (1 H, d, ArH), 7.84-7.89 (2 H, m, ArH), 8.12 (1 H, d, NH), 8.20 (2 H, d, ArH), 8.79 (1 H, d, ArH), 10.13 (1 H, s, NH).
101	δH(400 MHz; DMSO-d6) 1.04 (6 H, d, CH3), 2.58-2.65 (4 H,m, CH), 2.66-2.74 (1 H, m, CH), 3.03 (10 H, m, CH_3 and CH), 6.94 (2 H, d, ArH), 7.09-7.16 (1 H, m, ArH), 7.56-7.64 (4 H, m, ArH), 7.91 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.81 (1 H, d, ArH), 9.48 (1 H, s, NH).
103	^{1}H NMR δ (ppm)(DMSO-d6): 0.40 (2 H, m, CH), 0.57 (2 H, m, CH), 1.26 (1 H, m, CH), 3.97 (2 H, d, CH_2), 5.30 (2 H, s, CH_2), 7.09 (1 H, dd, ArH), 7.26 (2 H, d, ArH), 7.51 (1 H, s, ArH), 7.82 (1 H, d, ArH), 7.90 (1 H, s, ArH), 8.23 (2 H, d, ArH), 8.70 (1 H, d, ArH), 9.34 (1 H, s, NH).

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Cpd #	(δ) NMR data
104	δH(400 MHz; DMSO-d6) 3.66-3.76 (2 H, m, CH), 3.84 (3 H, s, CH3), 3.87 (3 H, s, CH3), 4.00-4.10 (1 H, m, CH), 4.12-4.21 (1 H, m, CH), 4.42-4.48 (1 H, m, CH), 5.72 (1 H, d, OH), 7.08 (2 H, d, ArH), 7.14 (1 H, dd, ArH), 7.18-7.27 (2 H, m, ArH), 7.74 (1 H, s, ArH), 7.82 (1 H, d, ArH), 8.16 (2 H, d, ArH), 8.76 (1 H, d, ArH), 10.01 (1 H, s, NH).
105	^{1}H NMR δ (ppm)(DMSO-d6): 0.55-0.60 (2 H, m, CH), 0.67-0.77 (2 H, m, CH), 2.82-2.90 (1 H, m, CH), 3.96 (3 H, s, CH_3), 4.17 (2 H, s, CH_2), 7.21 (1 H, dd, ArH), 7.26 (1 H, dd, ArH), 7.54 (2 H, d, ArH), 7.80 (1 H, d, ArH), 7.84 (1 H, d, ArH), 7.91-7.94 (2 H, m, ArH & NH), 8.24 (2 H, d, ArH), 8.86 (1 H, dd, ArH), 10.13 (1 H, s, NH).
106	^{1}H NMR δ (ppm)(DMSO-d6): 0.50-0.55 (2 H, m, CH), 0.68-0.74 (2 H, m, CH), 2.78-2.84 (1 H, m, CH), 3.88 (3 H, s, CH_3), 7.12 (2 H, d, ArH), 7.18 (1 H, dd, ArH), 7.47 (1 H, d, ArH), 7.87 (1 H, d, ArH), 7.94 (1 H, dd, ArH), 8.18 (2 H, d, ArH), 8.28 (1 H, d, NH), 8.40 (1 H, d, ArH), 8.81 (1 H, d, ArH), 10.31 (1 H, s, NH).
107	^{1}H NMR δ (ppm)(DMSO-d6): 0.50-0.56 (2 H, m, CH), 0.68-0.74 (2 H, m, CH), 1.35 (6 H, d, CH_3), 2.78-2.84 (1 H, m, CH), 4.72-4.79 (1 H, m, CH), 7.09 (2 H, d, ArH), 7.18 (1 H, dd, ArH), 7.47 (1 H, d, ArH), 7.87 (1 H, dd, ArH), 7.93 (1 H, dd, ArH), 8.16 (2 H, d, ArH), 8.30 (1 H, d, ArH), 8.40 (1 H, d, NH), 8.81 (1 H, dd, ArH), 10.31 (1 H, s, NH).
108	^{1}H NMR δ (ppm)(DMSO-d6): 0.50-0.56 (2 H, m, CH), 0.67-0.74 (2 H, m, CH), 2.78-2.84 (1 H, m, CH), 7.23 (1 H, dd, ArH), 7.48 (1 H, d, ArH), 7.57 (2 H, d, ArH), 7.93 (1 H, d, ArH), 7.97 (1 H, d, ArH), 8.27 (1 H, d, NH), 8.32 (2 H, d, ArH), 8.40 (1 H, d, ArH), 8.91 (1 H, d, ArH), 10.35 (1 H, s, NH).
109	δH(400 MHz; DMSO-d6) 0.63-0.70 (2 H, m, CH), 0.70-0.78 (2 H, m, CH), 2.95 (6 H, s, CH_3), 2.94-3.01 (1 H, m, CH), 3.87 (3 H, s, CH_3), 4.99 (2 H, s, CH_2), 7.14 (2 H, d, ArH), 7.18 (1 H, dd, ArH), 7.34 (1 H, d, ArH), 7.69 (1 H, s, ArH), 7.85 (1 H, d, ArH), 7.93 (1 H, d, ArH), 8.18 (2 H, d, ArH), 8.78 (1 H, d, NH), 9.21 (1 H, d, ArH), 10.12 (1 H, s, NH).
110	^{1}H NMR δ (ppm)($CHCl_3$-d): 3.00-3.16 (3 H, br s, CH_3), 3.17 (3 H, br s, CH_3), 3.93 (3 H, s, CH_3), 6.59 (1 H, s, ArH), 6.96-7.02 (1 H, m, ArH), 7.51 (1 H, d, ArH), 7.57-7.63 (3 H, m, ArH), 7.81 (1 H, s, NH), 8.05-8.09 (2 H, m, ArH), 8.43 (1 H, dd, ArH).
111	^{1}H NMR δ (ppm)(DMSO-d6): 0.40 (2 H, d, CH), 0.57 (2 H, d, CH), 1.26 (1 H, m, CH), 3.03 (6 H, d, CH_3), 3.98 (2 H, d, CH_2), 7.12 (1 H, dd, ArH), 7.51 (1 H, s, ArH), 7.59 (2 H, d, ArH), 7.90 (2 H, m, ArH), 8.27 (2 H, d, ArH), 8.75 (1 H, d, ArH), 9.38 (1 H, s, NH).

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Cpd #	(δ) NMR data
112	δH(400 MHz; DMSO-d6) 0.47-0.55 (2 H, m, CH), 0.75-0.81 (2 H, m, CH), 1.42 (6 H, d, CH_3), 2.87-2.91 (1 H, m, CH), 3.88 (3 H, s, CH3), 4.74 (1 H, septet, CH), 7.12 (2 H, d, ArH), 7.18 (1 H, dd, ArH), 7.25 (1 H, d, ArH), 7.80-7.86 (3 H, m, Ar), 8.04 (1 H, d, NH), 8.16 (2 H, d, ArH), 8.78 (1 H, d, ArH), 10.09 (1 H, s, NH).
113	δH(400 MHz; DMSO-d6) 1.03 (6 H, d, CH_3), 2.57-2.62 (4 H, m, CH), 2.69 (1 H, m, CH), 2.99-3.10 (4 H, m, CH), 3.90 (3 H, s, CH_3), 6.91 (2 H, d, ArH), 7.14 (1 H, d, ArH), 7.18 (2 H, d, ArH), 7.51 (1 H, d, ArH), 7.54-7.66 (3 H, m, ArH), 8.08 (2 H, d, ArH), 9.31 (1 H, s, NH).
114	δH(400 MHz; DMSO-d6) 3.03 (6 H, br d, CH_3), 4.41 (2 H, s, CH_2), 4.74 (2 H, s, CH_2), 7.21 (1 H, dd, ArH), 7.29-7.34 (3 H, m, ArH), 7.36-7.42 (2 H, m, ArH), 7.60 (2 H, d, ArH), 7.69 (1 H, d, ArH), 7.80 (1 H, dd, ArH), 7.97 (1 H, d, ArH), 8.00 (1 H, s, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.28 (1 H, s, NH).
115	^{1}H NMR δ (ppm)(DMSO-d6): 0.55-0.61 (2 H, m, CH), 0.69-0.76 (2 H, m, CH), 2.85 (1 H, m, CH), 3.94 (3 H, s, CH_3), 5.58 (2 H, s, CH_2), 7.14 (1 H, dd, ArH), 7.21 (1 H, d, ArH), 7.31 (1 H, dd, ArH), 7.37 (1 H, dd, ArH), 7.75 (1 H, s, NH), 7.78-7.88 (2 H, m, ArH), 7.92 (1 H, d, ArH), 7.96 (1 H, d, ArH), 8.42 (1 H, s, ArH), 8.60 (1 H, d, ArH), 8.71 (1 H, d, ArH), 8.81 (1 H, s, ArH), 10.05 (1 H, s, NH).
116	^{1}H NMR δ (ppm)(DMSO-d6): 0.55-0.61 (2 H, m, CH), 0.69-0.76 (2 H, m, CH), 2.82-2.90 (1 H, m, CH), 3.01 (3 H, s, CH_3), 3.06 (3 H, s, CH_3), 3.96 (3 H, s, CH_3), 7.19-7.29 (2 H, m, ArH), 7.59 (2 H, d, ArH), 7.80 (1 H, d, ArH), 7.85 (1 H, s, ArH), 7.93 (1 H, d, NH), 7.97 (1 H, d, ArH), 8.28 (2 H, d, ArH), 8.88 (1 H, d, ArH), 10.16 (1 H, s, NH).
117	^{1}H NMR δ (ppm)(DMSO-d6): 0.28 (2 H, m, CH), 0.48 (2 H, m, CH), 1.08 (1 H, m, CH), 3.17 (2 H, dd, CH_2), 3.88 (3 H, s, CH_3), 7.11-7.19 (3 H, m, ArH), 7.77-7.90 (5 H, m, ArH), 8.17 (2 H, m, ArH), 8.39 (1 H, t, NH), 8.82 (1 H, dd, ArH), 10.13 (1 H, s, NH).
118	^{1}H NMR δ (ppm)(DMSO-d6): 2.29 (2 H, m, CH), 3.88 (3 H, s, CH_3), 4.06 (2 H, m, CH), 4.37 (2 H, m, CH), 7.10-7.20 (3 H, m, ArH), 7.64 (2 H, d, ArH), 7.77-7.87 (3 H, m, ArH), 8.16 (2 H, d, ArH), 8.80 (1 H, d, ArH), 10.13 (1 H, s, NH).
119	^{1}H NMR δ (ppm)(DMSO-d6): 3.85 (3 H, s, CH_3), 4.64 (4 H, m, CH), 7.07-7.16 (3 H, m, ArH), 7.68 (2 H, d, ArH), 7.79-7.84 (3 H, m, ArH), 8.14 (2 H, m, ArH), 8.79 (1 H, dd, ArH), 10.22 (1 H, s, NH).

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Cpd #	(δ) NMR data
120	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.61 (2 H, m, CH), 0.73 (2 H, m, CH), 2.89 (1 H, m, CH), 5.31 (2 H, s, CH_2), 7.09 (1 H, dd, ArH), 7.22-7.39 (5 H, m, ArH), 7.55 (1 H, m, ArH), 7.85-8.00 (4 H, m, ArH), 8.24 (2 H, d, ArH), 8.52 (1 H, m, ArH), 8.72 (1 H, d, ArH), 9.40 (1 H, s, NH).
121	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.09 (6 H, d, CH_3), 5.40 (2 H, s, CH_2), 7.17 (1 H, dd, ArH), 7.32-7.48 (4 H, m, ArH), 7.59-7.66 (2 H, m, ArH), 7.94-8.00 (2 H, m, ArH), 8.314 (2 H, d, ArH), 8.81 (1 H, d, ArH), 9.51 (1 H, s, NH).
122	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.79-0.88 (4 H, m, CH), 2.93 (1 H, m, CH), 3.88 (3 H, s, CH_3), 4.41 (2 H, s, CH_2), 7.11-7.21 (3 H, m, ArH), 7.60 (1 H, d, ArH), 7.76 (1 H, d, ArH), 7.85 (1 H, d, ArH), 7.99 (1 H, s, ArH), 8.17 (2 H, d, ArH), 8.81 (1 H, d, ArH), 10.22 (1 H, s, NH).
123	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.59 (2 H, m, CH), 0.72 (2 H, m, CH), 2.84 (1 H, m, CH), 3.84-3.90 (3 H, m, CH_3), 7.10-7.19 (3 H, s, ArH), 7.75-7.87 (5 H, m, ArH and NH), 8.17 (2 H, d, ArH), 8.24 (1 H, d, ArH), 8.81 (1 H, d, ArH), 10.09 (1 H, s, NH).
124	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.76 (1 H, m, OH), 7.01 (2 H, s, ArH and NH), 7.16 (1 H, dd, ArH), 7.64 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.79 (1 H, d, ArH), 9.09 (2 H, s, ArH), 10.10 (1 H, s, NH).
125	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.82 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.40-4.64 (2 H, m, CH), 5.75 (1 H, d, OH), 7.25 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.81 (2 H, d, ArH), 8.12 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.78 (2 H, d, ArH), 8.97 (1 H, dd, ArH), 10.23 (1 H, s, NH).
126	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, br s, CH_3), 3.06 (3 H, br s, CH_3), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, m, OH), 7.22 (1 H, dd, ArH), 7.61 (2 H, d, ArH), 7.65 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.97 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.19 (1 H, s, NH).
127	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.53-0.59 (2 H, m, CH), 0.67-0.73 (2 H, m, CH), 2.39 (3 H, s, CH_3), 2.81-2.87 (1 H, m, CH), 4.17 (2 H, s, CH_2), 7.18 (1 H, dd, ArH), 7.31 (1 H, d, ArH), 7.53-7.65 (4 H, m, ArH), 7.91 (1 H, dd, ArH), 8.12 (1 H, d, NH), 8.22 (2 H, d, ArH), 8.86 (1 H, dd, ArH), 9.88 (1 H, s, NH).

Cpd #	(δ) NMR data
128	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.47 (3 H, s, CH_3), 3.81 (1 H, m, CH), 4.09 (1 H, m, CH), 4.27 (1 H, m, CH), 4.42-4.64 (2 H, m, CH), 5.76 (1 H, d, OH), 7.29 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.85 (2 H, d, ArH), 8.21 (1 H, d, ArH), 8.98 (1 H, d, ArH), 9.18 (1 H, d, ArH), 9.21 (1 H, t, ArH), 9.69 (1 H, d, ArH), 10.21 (1 H, s, NH).
129	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.24 (6 H, s, CH_3), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.16 (1 H, dd, ArH), 7.64 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.80 (1 H, dd, ArH), 9.18 (2 H, s, ArH), 10.12 (1 H, s, NH).
130	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.16 (6 H, s, CH_3), 3.96 (2 H, s, CH), 4.40 (2 H, s, CH), 4.54 (1 H, m, CH), 5.55 (1 H, s, OH), 6.81 (1 H, d, ArH), 7.13 (1 H, dd, ArH), 7.64 (2 H, d, ArH), 7.79-7.83 (3 H, m, ArH), 8.35 (1 H, dd, ArH), 8.70 (1 H, dd, ArH), 8.99 (1 H, d, ArH), 9.86 (1 H, s, NH).
131	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.78-0.89 (4 H, m, CH), 2.93 (1 H, m, CH), 3.01 (3 H, br s, CH_3), 3.06 (3 H, br s, CH_3), 4.41 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.60 (3 H, m, ArH), 7.75 (1 H, dd, ArH), 7.94-8.01 (2 H, m, ArH), 8.26 (2 H, d, ArH), 8.91 (1 H, d, ArH), 10.28 (1 H, s, NH).
132	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.83 (2 H, m, CH), 4.13 (2 H, m, CH), 4.31 (2 H, m, CH), 4.55 (4 H, m, CH), 5.76 (1 H, d, OH), 5.82 (1 H, d, OH), 7.22 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.81 (4 H, d, ArH), 7.98 (1 H, d, ArH), 8.28 (2 H, d, ArH), 8.90 (1 H, d, ArH), 10.19 (1 H, s, NH).
133	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.17 (6 H, s, CH_3), 3.32 (2 H, d, CH_2), 3.82 (1 H, m, CH), 4.11 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 4.63 (1 H, s, OH), 5.75 (1 H, d, OH), 7.23 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.99 (1 H, d, ArH), 8.06 (2 H, d, ArH), 8.30 (2 H, d, ArH), 8.38 (1 H, t, NH), 8.90 (1 H, d, ArH), 10.17 (1 H, s, NH)
135	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.26 (3 H, s, CH_3), 3.88 (3 H, s, CH_3), 4.27 (4 H, m, CH), 4.51 (1 H, m, CH), 7.11-7.21 (3 H, m, ArH), 7.65 (2 H, d, ArH), 7.78-7.88 (3 H, m, ArH), 8.17 (2 H, d, ArH), 8.81 (1 H, d, ArH), 10.15 (1 H, s, NH).
136	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.82 (1 H, m, CH), 3.99 (3 H, s, CH_3), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, s, OH), 7.12 (1 H, dd, ArH), 7.66 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 8.34 (1 H, s, ArH), 8.61 (1 H, s, ArH), 8.70 (1 H, dd, ArH), 10.07 (1 H, s, NH).

Cpd #	(δ) NMR data
137	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, d, CH_3), 5.44 (2 H, s, CH_2), 7.06 (1 H, d, ArH), 7.14 (1 H, dd, ArH), 7.34 (1 H, m, ArH), 7.57 (4 H, m, ArH), 7.80 (1 H, m, ArH), 7.91 (1 H, d, ArH), 8.00 (1 H, s, ArH), 8.26 (2 H, d, ArH), 8.58 (1 H, m, ArH), 8.77 (1 H, d, ArH), 9.50 (1 H, s, NH).
138	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.60 (2 H, m, CH), 0.71 (2 H, m, CH), 2.86 (1 H, m, CH), 7.12 (1 H, dd, ArH), 7.77-7.86 (4 H, m, ArH), 7.95 (1 H, d, ArH), 8.26 (1 H, m, ArH), 8.43 (1 H, s, ArH), 8.63-8.72 (2 H, m, ArH, NH), 10.01 (1 H, s, NH), 13.20 (1 H, s, NH).
139	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.60 (2 H, m, CH), 0.72 (2 H, m, CH), 2.43 (4 H, m, CH), 2.85 (1 H, m, CH), 3.58 (2 H, s, CH_2), 3.63 (4 H, m, CH), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.76-7.91 (5 H, m, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, m, NH), 8.86 (1 H, d, ArH), 10.10 (1 H, s, NH).
140	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, d, CH_3), 7.12 (1 H, dd, ArH), 7.59 (3 H, d, ArH), 7.85 (1 H, br s, ArH), 7.90 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.77 (1 H, d, ArH), 9.36 (1 H, s, NH), 12.48 (1 H, s, NH).
141	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, d, CH_3), 7.12 (1 H, dd, ArH), 7.59 (3 H, d, ArH), 7.85 (1 H, br s, ArH), 7.90 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.77 (1 H, d, ArH), 9.36 (1 H, s, NH), 12.48 (1 H, s, NH).
142	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.60 (2 H, m, CH), 0.72 (2 H, m, CH), 2.85 (1 H, m, CH), 3.04 (6 H, br d, CH_3), 7.21 (1 H, dd, ArH), 7.60 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.26 (3 H, m, ArH, NH), 8.90 (1 H, dd, ArH), 10.14 (1 H, s, NH).
143	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, br s, CH_3), 3.06 (3 H, br s, CH_3), 3.62 (2 H, m, CH), 3.68 (6 H, m, CH), 7.24 (1 H, dd, ArH), 7.61 (2 H, d, ArH), 7.71 (1 H, d, ArH), 7.97-8.01 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.31 (1 H, dd, ArH), 8.89-8.92 (2 H, m, ArH), 10.40 (1 H, s, NH).
144	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, br s, CH_3), 3.05 (3 H, br s, CH_3), 4.55 (2 H, s, CH_2), 4.84 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.28-7.36 (2 H, m, ArH), 7.60 (2 H, d, ArH), 7.69 (1 H, d, ArH), 7.78-7.83 (2 H, m, ArH), 7.97 (1 H, dd, ArH), 8.03 (1 H, s, ArH), 8.26 (2 H, d, ArH), 8.56 (1 H, d, ArH), 8.90 (1 H, dd, ArH), 10.31 (1 H, s, NH).
145	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, d, CH_3), 3.52 (3 H, s, CH_3), 7.19 (1 H, dd, ArH), 7.59 (2 H, d, ArH), 7.93 (1 H, d, ArH), 8.01 (1 H, s, ArH), 8.26 (2 H, d, ArH), 8.39 (1 H, s, ArH), 8.89 (1 H, d, ArH), 10.01 (1 H, s, NH).

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Cpd #	(δ) NMR data
146	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.45 (6 H, d, CH_3), 3.03 (6 H, d, CH_3), 4.49 (1 H, m, CH), 7.11 (1 H, dd, ArH), 7.50 (1 H, s, ArH), 7.59 (2 H, d, ArH), 7.87 (1 H, s, ArH), 7.90 (1 H, d, ArH), 8.27 (2 H, d, ArH), 8.77 (1 H, d, ArH), 9.38 (1 H, s, NH).
147	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, m, CH_3), 4.61 (2 H, d, CH_2), 7.22 (1 H, dd, ArH), 7.30 (1 H, dd, ArH), 7.36 (1 H, d, ArH), 7.61 (2 H, d, ArH), 7.75-7.85 (3 H, m, ArH), 7.92-8.00 (3 H, m, ArH and NH), 8.26 (2 H, d, ArH), 8.55 (1 H, d, ArH), 8.89-8.97 (2 H, m, ArH), 10.19 (1 H, s, NH).
148	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, m, CH_3), 3.06 (3 H, br s, CH_3), 3.30 (2 H, m, CH), 3.69 (2 H, m, CH), 4.08 (2 H, s, CH_2), 7.21 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.97 (1 H, d, ArH), 8.14 (1 H, s, NH), 8.26 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.15 (1 H, s, NH).
149	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.15 (6 H, d, CH_3), 2.68 (2 H, dd, CH), 3.06 (6 H, br s, CH_3), 3.57-3.64 (2 H, m, CH), 4.03 (2 H, m, CH), 7.17 (1 H, dd, ArH), 7.40 (2 H, d, ArH), 7.59 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.74 (1 H, dd, ArH), 9.48 (1 H, s, NH).
150	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.39 (2 H, m, CH), 1.78 (2 H, m, CH), 3.01 (3 H, br s, CH_3), 3.05 (3 H, br s, CH_3), 3.21 (2 H, m, CH), 3.70-4.10 (3 H, m, CH), 4.81 (1 H, d, OH), 7.20 (1 H, dd, ArH), 7.39 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.09 (1 H, s, NH).
151	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.76 (2 H, m, CH), 1.94 (2 H, m, CH), 3.01 (3 H, br s, CH_3), 3.06 (3 H, br s, CH_3), 3.49-3.67 (4 H, m, CH), 4.96 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.43 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.96 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.11 (1 H, s, NH).
152	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.42-1.56 (2 H, m, CH), 1.76-1.84 (1 H, m, CH), 1.88-2.01 (1 H, m, CH), 2.97-3.05 (1 H, m, CH), 3.06 (6 H, br s, CH_3), 3.16-3.24 (1 H, m, CH), 3.58-3.65 (1 H, m, CH), 3.69-3.78 (1 H, m, CH), 3.86-3.93 (1 H, m, CH), 4.38 (1 H, d, OH), 7.17 (1 H, dd, ArH), 7.40 (2 H, d, ArH), 7.58 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.74 (1 H, dd, ArH), 9.44 (1 H, s, NH).
153	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (6 H, m, CH), 3.22-3.37 (4 H, m, CH), 3.93 (4 H, m, CH), 7.22 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.97 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.15 (1 H, s, NH).

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Cpd #	(δ) NMR data
154	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.23 (3 H, s, CH_3), 2.35 (4 H, m, CH), 3.01 (3 H, br s, CH_3), 3.06 (3 H, br s, CH_3), 3.54 (4 H, m, CH), 7.21 (1 H, dd, ArH), 7.41 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.96 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.88 (1 H, d, ArH), 10.10 (1 H, s, NH).
155	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.04 (6 H, d, CH_3), 4.40 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.62 (3 H, m, ArH), 7.76 (1 H, d, ArH), 7.97 (1 H, d, ArH), 8.04 (1 H, s, ArH), 8.27 (3 H, m, ArH, NH), 8.92 (1 H, d, ArH), 10.27 (1 H, s, NH).
156	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, s, CH_3), 3.07 (6 H, m, CH_3), 4.48 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.61 (3 H, m, ArH), 7.76 (1 H, dd, ArH), 7.97 (1 H, dd, ArH), 8.03 (1 H, s, ArH), 8.26 (2 H, d, ArH), 8.92 (1 H, dd, ArH), 10.27 (1 H, s, NH).
157	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.95-3.14 (12 H, m, CH_3), 7.24 (1 H, dd, ArH), 7.58-7.67 (3 H, m, ArH), 7.99 (1 H, d, ArH), 8.23-8.32 (3 H, m, ArH), 8.91 (2 H, m, ArH), 10.36 (1 H, s, NH).
158	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.59 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.79 (6 H, s, CH_3), 2.82-2.88 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.72 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.91 (1 H, d, ArH), 8.22 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.89 (1 H, d, ArH), 10.11 (1 H, s, NH).
160	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.58 (2 H, m, CH), 0.72 (2 H, m, CH), 2.85 (1 H, m, CH), 4.17 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.55 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 8.21 (2 H, d, ArH), 8.26 (1 H, d, NH), 8.88 (1 H, dd, ArH), 10.10 (1 H, s, NH).
161	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.85 (3 H, d, CH_3), 4.17 (2 H, s, CH_2), 7.24 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.22 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.57 (1 H, m, NH), 8.90 (1 H, dd, ArH), 8.95 (1 H, d, ArH), 10.42 (1 H, s, NH).
162	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.43 (4 H, m, CH), 2.85 (3 H, d, CH_3), 3.58 (2 H, s, CH_2), 3.64 (4 H, m, CH), 7.23 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 8.03 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.33 (1 H, dd, ArH), 8.57 (1 H, d, NH), 8.88 (1 H, dd, ArH), 8.95 (1 H, d, ArH), 10.41 (1 H, s, NH).

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Cpd #	(δ) NMR data
163	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.60-0.66 (2 H, m, CH), 0.71-0.72 (2 H, m, CH), 2.86-2.87 (1 H, m, CH) 7.21 (1 H, dd, ArH), 7.80 (2 H, d, ArH), 7.85 (2 H, d, ArH), 8.08 (1 H, d, ArH), 8.26 (1 H, d, NH), 8.86 (1 H, d, ArH), 9.52 (1 H, s, ArH), 9.74 (1 H, s, ArH), 10.10 (1 H, s, NH).
164	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.83 (1 H, s, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.18 (1 H, dd, ArH), 7.66 (2 H, d, ArH), 7.82 (2 H, d, ArH), 8.01 (1 H, td, CHF2), 8.09 (1 H, d, ArH), 8.72 (1 H, s, ArH), 8.81 (1 H, d, ArH), 9.12 (1 H, s, ArH), 10.13 (1 H, s, NH).
165	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.85 (3 H, br d, CH_3), 3.86 (1 H, m, CH), 4.15 (1 H, m, CH), 4.33 (1 H, m, CH), 4.56 (2 H, s, CH_2), 5.82 (1 H, br d, OH), 7.26 (1 H, dd, ArH), 7.82 (2 H, d, ArH), 7.98-8.06 (2 H, m, ArH), 8.27 (2 H, d, ArH), 8.34 (1 H, m, ArH), 8.57 (1 H, br d, NH), 8.90-8.98 (2 H, m, ArH), 10.46 (1 H, s, ArH).
166	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.17 (6 H, s, CH_3), 2.85 (3 H, d, CH_3), 3.32 (2 H, m, CH_2), 4.63 (1 H, s, OH), 7.26 (1 H, dd, ArH), 7.98-8.09 (4 H, m, ArH), 8.27-8.36 (3 H, m, ArH), 8.39 (1 H, t, NH), 8.57 (1 H, br d, NH), 8.93 (1 H, d, ArH), 8.98 (1 H, d, ArH), 10.43 (1 H, s, NH).
167	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.03 (7 H, d, CH_3), 7.18 (1 H, dd, ArH), 7.59 (2 H, d, ArH), 7.83 (1 H, t, CHF_2), 7.94 (1 H, d, ArH), 8.23-8.31 (3 H, m, ArH), 8.83 (1 H, d, ArH), 9.84 (1 H, s, NH).
168	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.46-1.73 (6 H, m, CH), 3.01 (6 H, br s, CH_3), 3.35-3.44 (2 H, m, CH), 3.65 (2 H, m, CH), 7.20 (1 H, dd, ArH), 7.43 (2 H, d, ArH), 7.56 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.09 (1 H, s, NH).
169	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.47-1.72 (6 H, m, CH), 2.29 (2 H, m, CH), 3.32-3.43 (2 H, m, CH), 3.65 (2 H, m, CH), 4.06 (2 H, m, CH), 4.38 (2 H, m, CH), 7.21 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.18 (1 H, s, NH).
170	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.47-1.72 (6 H, m, CH), 1.87 (4 H, m, CH), 3.35-3.42 (2 H, m, CH), 3.47-3.54 (4 H, m, CH), 3.65 (2 H, m, CH), 7.21 (1 H, dd, ArH), 7.53-7.58 (4 H, m, ArH), 7.79 (2 H, d, ArH), 7.95 (1 H, d, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.10 (1 H, s, NH).

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Cpd #	(δ) NMR data
171	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.48-1.82 (8 H, m, CH), 1.87-2.04 (2 H, m, CH), 3.34-3.36 (2 H, m, CH), 3.53-3.64 (6 H, m, CH), 4.97 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.43 (2 H, d, ArH), 7.56 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.10 (1 H, s, NH).
172	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.25-1.81 (8 H, m, CH), 3.20-3.29 (2 H, m, CH), 3.38-3.48 (2 H, m, CH), 3.68 (2 H, m, CH), 3.75 (3 H, m, CH), 3.95 (2 H, m, CH), 4.84 (1 H, d, OH), 7.24 (1 H, dd, ArH), 7.43 (2 H, d, ArH), 7.59 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.98 (1 H, d, ArH), 8.28 (2 H, d, ArH), 8.91 (1 H, dd, ArH), 10.12 (1 H, s, NH).
173	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.48-1.82 (8 H, m, CH), 1.87-2.04 (2 H, m, CH), 3.34-3.36 (2 H, m, CH), 3.53-3.64 (6 H, m, CH), 4.97 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.43 (2 H, d, ArH), 7.56 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.10 (1 H, s, NH).
174	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.46-1.74 (6 H, m, CH), 2.85 (1 H, m, CH), 3.36-3.42 (2 H, m, CH), 3.65 (2 H, m, CH), 7.21 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.25 (3 H, m, ArH and NH), 8.90 (1 H, dd, ArH), 10.14 (1 H, s, NH).
175	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.48-1.73 (6 H, m, CH), 3.33-3.40 (4 H, m, CH), 3.54 (2 H, m, CH_2), 3.65 (2 H, m, CH_2), 4.75 (1 H, t, OH), 7.21 (1 H, dd, ArH), 7.57 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.87 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.26 (3 H, t, ArH and NH), 8.91 (1 H, dd, ArH), 10.15 (1 H, s, NH).
176	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.02-2.19 (4 H, m, CH), 2.90 (2 H, dd, CH), 3.13 (2 H, d, CH), 3.30-3.40 (1 H, m, NH + H_2O) 3.82-3.83 (1 H, m, CH), 4.10-4.12 (1 H, m, CH), 4.25-4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.24 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.81 (1 H, d, ArH), 8.03 (1 H, dd, ArH), 8.65 (1 H, dd, ArH), 8.93 (1 H, dd, ArH), 9.36 (1 H, d, ArH), 10.20 (1 H, s, NH).
177	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.61-1.66 (2 H, m, CH), 1.83-1.88 (2 H, m, CH), 3.76-8.20 (1 H, m, CH), 4.05-4.10 (1 H, m, CH), 4.26-4.32 (1 H, m, CH), 4.48-4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.20 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 8.21 (2 H, d, ArH), 8.87 (1 H, dd, ArH), 10.16 (1 H, s, NH).

Cpd #	(δ) NMR data
178	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.61-1.66 (2 H, m, CH), 1.81-1.88 (2 H, m, CH), 2.85-2.86 (1 H, m, CH), 7.20 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 8.21 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.88 (1 H, dd, ArH), 10.11 (1 H, s, NH)
179	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.05-2.23 (4 H, m, CH), 2.80-2.91 (1 H, m, CH), 2.93 (2 H, d, CH), 3.16 (2 H, d, CH), 3.49 (1 H, m, NH+H_2O), 7.24 (1 H, dd, ArH), 7.73-7.86 (5 H, m, ArH and NH), 8.03 (1 H, d, ArH), 8.27 (1 H, dd, ArH), 8.65 (1 H, dd, ArH), 8.94 (1 H, dd, ArH), 9.38 (1 H, d, ArH), 10.16 (1 H, s, NH).
180	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.65-3.87 (1 H, m, CH), 4.02-4.07 (1 H, m, CH), 4.17 (2 H, s, CH_2), 4.21-4.30 (1 H, m, CH), 4.52-4.54 (2 H, m, CH), 5.75 (1 H, d, OH), 7.20 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 8.21 (2 H, d, ArH), 8.87 (1 H, dd, ArH), 10.15 (1 H, s, NH).
181	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.86-2.00 (1 H, m, CH), 2.13-2.27 (1 H, m, CH), 2.34-2.43 (1 H, m, CH), 2.67 (1 H, m, CH), 2.77-2.90 (2 H, m, CH), 3.72 (2 H, s, CH2), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.18-5.32 (1 H, m, CHF), 5.75 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.85 (1 H, d, ArH), 10.15 (1 H, s, NH).
182	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.23-2.38 (2 H, m, CH), 2.77 (2 H, m, CH), 2.93 (2 H, m, CH), 3.74 (2 H, s, CH_2), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.90 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.86 (1 H, d, ArH), 10.15 (1 H, s, NH).
183	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.77 (2 H, m, CH), 1.83-1.99 (2 H, m, CH), 2.37 (2 H, m, CH), 2.59 (2 H, m, CH), 3.59 (2 H, s, CH_2), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 4.74 (1 H, m, CHF), 5.75 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.13 (2 H, d, ArH), 8.85 (1 H, d, ArH), 10.15 (1 H, s, NH).
184	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.96-2.08 (4 H, m, CH), 2.56 (4 H, m, CH), 3.66 (2 H, s, CH_2), 3.81 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.85 (1 H, dd, ArH), 10.15 (1 H, s, NH).

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Cpd #	(δ) NMR data
185	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.95 (4 H, m, CH), 3.18 (4 H, m, CH), 3.79 (2 H, s, CH_2), 3.83 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (1 H, m, CH), 4.53 (2 H, m, CH), 5.75 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.85 (1 H, d, ArH), 10.16 (1 H, s, NH).
186	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.13 (3 H, d, CH_3), 2.75-2.95 (3 H, m, CH_3), 3.26-3.32 (2 H, br s, CH_2), 3.87 (1 H, m, CH), 4.82 (1 H, d, OH), 7.26 (1 H, dd, ArH), 7.99-8.09 (4 H, m, ArH), 8.26-8.36 (3 H, m, ArH and NH), 8.52-8.59 (2 H, m, ArH), 8.93 (1 H, d, NH), 8.97 (1 H, s, ArH), 10.44 (1 H, s, NH).
187	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.85 (1 H, m, CH), 4.10 (2 H, d, CH), 4.16 (2 H, d, CH), 7.25 (1 H, dd, ArH), 7.77 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.90 (1 H, d, ArH), 8.05 (1 H, d, ArH), 8.26 (1 H, d, ArH), 8.69 (1 H, dd, ArH), 8.95 (1 H, d, NH), 9.41 (1 H, d, ArH), 10.14 (1 H, s, NH).
188	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.01 (3 H, s, CH_3), 3.06 (3 H, s, CH_3), 3.55 (4 H, m, CH), 3.64 (4 H, m, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).
189	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.05 (3 H, br s, CH_3), 3.56 (6 H, m, CH), 3.64 (6 H, m, CH), 4.89 (1 H, m, OH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.96 (1 H, d, ArH), 8.24 (2 H, d, ArH), 8.88 (1 H, d, ArH), 10.13 (1 H, s, NH).
190	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.84-1.97 (4 H, m, CH), 3.47-3.58 (8 H, m, CH), 3.64 (4 H, m, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.71 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.97 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.13 (1 H, s, NH).
191	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.80 (2 H, m, CH), 1.97 (2 H, m, CH), 3.55 (6 H, m, CH), 3.64 (6 H, m, CH), 4.89-5.06 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.61 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.96 (1 H, dd, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).
192	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.05 (3 H, m, CH_3), 1.20 (3 H, m, CH_3), 2.92 (2 H, m, CH), 3.41-3.70 (10 H, m, CH), 4.44 (2 H, s, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.61 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.97 (1 H, dd, ArH), 8.28 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.12 (1 H, s, NH).

Cpd #	(δ) NMR data
193	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.31 (2 H, m, CH_2), 3.55 (4 H, m, CH), 3.64 (6 H, m, CH), 4.10 (2 H, m, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.65 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.97 (1 H, dd, ArH), 8.20 (1 H, s, NH), 8.28 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).
194	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.24 (6 H, d, CH_3), 3.48-3.61 (4 H, m, CH), 3.64 (4 H, m, CH), 4.12-4.23 (1 H, m, CH), 7.21 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.98 (1 H, dd, ArH), 8.03 (2 H, d, ArH), 8.29 (2 H, d, ArH), 8.34 (1 H, d, NH), 8.89 (1 H, dd, ArH), 10.10 (1 H, s, NH).
195	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.41 (2 H, dt, CH_2), 3.52-3.61 (6 H, m, CH and CH_2), 3.64 (4 H, m, CH), 4.80 (1 H, t, OH), 7.20 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.05 (2 H, d, ArH), 8.30 (2 H, d, ArH), 8.54-8.
196	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.55 (4 H, m, CH), 3.64 (4 H, m, CH), 4.66 (2 H, d, CH_2), 7.22 (1 H, dd, ArH), 7.32 (1 H, dd, ArH), 7.40 (1 H, d, ArH), 7.44 (2 H, d, ArH), 7.76-7.85 (3 H, m, ArH and NH), 8.01 (1 H, d, ArH), 8.12 (2 H, d, ArH), 8.33 (2 H, d, ArH), 8.57 (1 H, d, ArH), 8.90 (1 H, d, ArH), 9.21-9.28 (1 H, m, ArH), 10.12 (1 H, s, NH).
197	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.42-1.76 (6 H, m, CH), 3.02 (3 H, s, CH_3), 3.27 (2 H, s, CH), 3.35-3.40 (2 H, m, CH), 3.43-3.81 (7 H, m, CH and CH_3), 7.20 (1 H, dd, ArH), 7.41 (2 H, d, ArH), 7.56 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.25 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.08 (1 H, s, NH).
198	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.23-0.28 (2 H, m, CH), 0.40-0.49 (2 H, m, CH), 1.00-1.12 (1 H, m, CH), 1.41-1.77 (6 H, m, CH), 3.14-3.20 (2 H, m, CH), 3.34-3.36 (2 H, m, CH), 3.64 (2 H, m, CH), 7.20 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.86 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.24 (2 H, d, ArH), 8.32-8.39 (1 H, t, NH), 8.90 (1 H, dd, ArH), 10.14 (1 H, s, NH).
199	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.07 (4 H, m, CH), 3.01 (3 H, s, CH_3), 3.05 (3 H, s, CH_3), 3.64 (4 H, m, CH), 7.21 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.60 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.96 (1 H, d, ArH), 8.26 (2 H, d, ArH), 8.89 (1 H, d, ArH), 10.13 (1 H, s, NH).
200	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.12 (3 H, d, CH_3), 2.84 (3 H, m, CH_3), 3.29 (2 H, m, CH_2), 3.86 (1 H, m, CH), 7.25 (1 H, dd, ArH), 7.96-8.08 (4 H, m, ArH), 8.27 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.87 (1 H, m, ArH), 8.95 (1 H, d, ArH). NH and OH too broad-not visible.

Cpd #	(δ) NMR data
201	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.04 (6 H, d, CH_3), 3.82 (1 H, br d, CH), 4.24-4.38 (2 H, m, CH_2), 4.53 (1 H, br s, CH), 4.81 (1 H, m, CH), 5.71 (1 H, d, OH), 7.25 (1 H, dd, ArH), 7.61 (2 H, d, ArH), 7.99 (2 H, m, ArH), 8.25 (2 H, d, ArH), 8.32 (1 H, d, ArH), 8.92 (2 H, m, ArH), 10.47 (1 H, s, NH).
202	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.85 (3 H, s, CH_3), 3.92 (1 H, m, CH), 4.27 (1 H, m, CH), 4.43 (1 H, m, CH), 4.63 (1 H, m, CH), 4.69 (1 H, m, CH), 7.26 (1 H, dd, ArH), 7.84 (2 H, d, ArH), 8.02 (2 H, m, ArH), 8.29 (2 H, d, ArH), 8.34 (1 H, d, ArH), 8.57 (1 H, s, ArH), 8.94 (2 H, d, ArH, NH), 10.47 (1 H, s, NH).
203	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.43 (4 H, m, CH), 3.57 (2 H, s, CH_2), 3.63 (4 H, m, CH), 7.15 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.82 (1 H, t, CHF_2), 7.83 (1 H, s, ArH), 7.86 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.78 (1 H, s, NH).
204	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.95 (4 H, m, CH), 3.17 (4 H, m, CH), 3.79 (2 H, s, CH_2), 7.15 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.82 (1 H, s, ArH), 7.83 (1 H, t, CHF_2), 7.88 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.27 (1 H, s, ArH), 8.79 (1 H, d, ArH), 9.79 (1 H, s, NH).
205	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.07 (3 H, d, CH_3), 2.18 (1 H, m, CH), 2.45 (1 H, m, CH), 2.59 (1 H, m, CH), 3.20-3.30 (2 H, m, CH), 3.494 (1 H, m, CH), 3.68 (2 H, m, CH), 4.08 (1 H, m, CH), 7.16 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.82 (1 H, t, CHF2), 7.83 (1 H, s, ArH), 7.86 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, d, ArH), 9.77 (1 H, s, NH).
206	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.43 (4 H, m, CH), 3.54-3.62 (6 H, m, CH, and CH_2), 7.13 (1 H, dd, ArH), 7.56 (1 H, dd, ArH), 7.78 (1 H, t, CHF2), 7.80 (1 H, s, ArH), 7.96 (2 H, m, ArH), 8.13 (1 H, dd, ArH), 8.25 (1 H, s, ArH), 8.80 (1 H, dd, ArH), 9.80 (1 H, s, NH).
207	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.13 (3 H, d, CH_3), 3.24-3.32 (2 H, m, CH), 3.81-3.90 (2 H, m, CH), 4.05-4.07 (1 H, m, CH), 4.10-4.12 (1 H, m, CH), 4.53 (2 H, d, CH), 4.82 (1 H, d, OH), 5.75 (1 H, d, OH), 7.22 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.82 (2 H, d, ArH), 8.00 (1 H, dd, ArH), 8.05 (2 H, d, ArH), 8.30 (2 H, d, ArH), 8.54 (1 H, dd, NH), 8.90 (1 H, dd, ArH), 10.18 (1 H, s, NH).
208	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.13 (3 H, d, CH_3), 3.24-3.32 (2 H, m, CH), 3.81-3.92 (2 H, m, CH), 4.04-4.15 (1 H, m, CH), 4.20-4.26 (1 H, m, CH), 4.53 (2 H, d, CH), 4.81 (1 H, d, OH), 5.75 (1 H, d, OH), 7.22 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.05 (2 H, d, ArH), 8.30 (2 H, d, ArH), 8.54 (1 H, dd, NH), 8.90 (1 H, dd, ArH), 10.18 (1 H, s, NH).

Cpd #	(δ) NMR data
209	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.80 (6 H, s, CH_3), 2.85 (3 H, d, CH_3), 7.25 (1 H, dd, ArH), 7.73 (2 H, d, ArH), 7.95 (1 H, dd, ArH), 8.04 (1 H, d, ArH), 8.22 (2 H, d, ArH), 8.34 (1 H, dd, ArH), 8.56 (1 H, q, NH), 8.91 (1 H, dd, ArH), 8.94 (1 H, d, ArH), 10.43 (1 H, s, NH).
210	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.97-2.08 (4 H, m, CH), 2.52-2.62 (4 H, m, CH), 2.85 (3 H, d, CH_3), 3.67 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.33 (1 H, dd, ArH), 8.56 (1 H, q, NH), 8.88 (1 H, dd, ArH), 8.95 (1 H, d, ArH), 10.42 (1 H, s, NH).
211	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.78-0.88 (4 H, m, CH), 2.31-2.54 (4 H, m, CH), 2.90-2.96 (1 H, m, CH), 3.58 (2 H, s, CH_2), 3.58-3.70 (4 H, m, CH), 4.41 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.60 (1 H, d, ArH), 7.75 (1 H, dd, ArH), 7.89 (1 H, d, ArH), 7.99 (1 H, s, ArH), 8.13 (2 H, d, ArH), 8.86 (1 H, dd, ArH), 10.23 (1 H, s, NH).
212	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 2.85-3.04 (4 H, m, CH), 3.10-3.25 (4 H, m, CH), 3.79 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.11 (1 H, s, NH).
213	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.33-2.51 (2 H, m, CH), 3.42-3.48 (1 H, m, CH), 3.61 (4 H, m, CH), 3.73-3.77 (1 H, m, CH), 3.85-3.90 (1 H, m, CH), 4.58-4.64 (1 H, m, OH), 7.15 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.83 (2 H, m, CHF2, ArH), 7.86 (1 H, d, ArH), 8.11 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.79 (1 H, s, NH), 2 H missing under DMSO.
214	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.14 (3 H, s, CH_3), 1.52 (4 H, m, CH), 2.44 (4 H, m, CH), 3.56 (2 H, s, CH_2), 4.13 (1 H, s, OH), 7.15 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.83 (2 H, m, CHF_2 and ArH), 7.86 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.78 (1 H, s, NH).
215	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.57-1.62 (1 H, m, CH), 2.00-2.09 (1 H, m, CH), 2.34-2.42 (1 H, m, CH), 2.48-2.52 (1 H, m, CH), 2.61-2.69 (1 H, m, CH), 2.70-2.78 (1 H, m, CH), 3.67 (2 H, app q, CH), 4.20-4.30 (1 H, m, CH), 4.73 (1 H, d, OH), 7.15 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.83 (2 H, m, CHF_2 and ArH), 7.87 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.79 (1 H, s, NH).
216	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.43-3.60 (3 H, m, CH), 3.69 (2 H, s, CH_2), 7.15 (1 H, dd, ArH), 7.45 (2 H, d, ArH), 7.83 (2 H, m, CHF_2, ArH), 7.87 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.79 (1 H, s, NH), 2H missing under H_2O.

Cpd #	(δ) NMR data
217	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 1.67-1.87 (2 H, m, CH), 1.83-1.97 (2 H, m, CH), 2.28-2.45 (2 H, m, CH), 2.52-2.64 (2 H, m, CH), 3.58 (2 H, s, CH_2), 4.01 (2 H, s, CH_2), 4.64-4.81 (2 H, m, OH and CHF), 7.09 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.51 (1 H, d, ArH), 7.83 (1 H, dd, ArH), 7.87 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.71 (1 H, dd, ArH), 9.34 (1 H, s, NH).
218	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 2.35-2.51 (4 H, m, CH), 3.57 (2 H, s, CH_2), 3.60-3.65 (4 H, m, CH), 4.01 (2 H, s, CH_2), 4.71 (1 H, s, OH), 7.09 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.51 (1 H, d, ArH), 7.83 (1 H, dd, ArH), 7.87 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.71 (1 H, dd, ArH), 9.33 (1 H, s, NH).
219	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.65 (2 H, dd, CH), 1.86 (2 H, dd, CH), 2.85 (3 H, d, CH_3), 7.23 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.94 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.20 (2 H, d, ArH), 8.33 (1 H, dd, ArH), 8.56 (1 H, q, NH), 8.90 (1 H, dd, ArH), 8.94 (1 H, ArH), 10.42 (1 H, s, NH).
220	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.64 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 1.08 (3 H, d, CH_3), 2.14-2.22 (1 H, m, CH), 2.43-2.49 (1 H, m, CH), 2.53-2.62 (1 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.15-3.30 (2 H, m, CH), 3.45-3.52 (1 H, m, CH), 3.66-3.71 (2 H, m, CH), 4.08 (1 H, d, CH), 7.18 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.09 (1 H, s, NH).
221	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.74 (2 H, m, CH), 2.39-2.53 (4 H, m, CH), 2.83-2.87 (1 H, m, CH), 3.60-3.66 (6 H, m, CH and CH_2), 7.20 (1 H, dd, ArH), 7.60 (1 H, dd, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.97-8.02 (2 H, m, ArH), 8.15 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).
222	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.58-0.62 (2 H, m, CH), 0.68-0.73 (2 H, m, CH), 1.59-1.61 (1 H, m, CH), 2.03-2.09 (1 H, m, CH), 2.35-2.40 (1 H, m, CH), 2.44-2.52 (1 H, m, CH), 2.64-2.74 (2 H, m, CH), 2.84-2.86 (1 H, m, CH), 3.59-3.74 (2 H, m, CH), 4.22-4.27 (1 H, m, CH), 4.73 (1 H, d, OH), 7.19 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
223	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.06-2.12 (1 H, m, CH), 2.30-2.36 (1 H, m, CH), 2.82-2.88 (1 H, m, CH), 2.97-3.01 (1 H, m, CH), 3.07-3.13 (1 H, m, CH), 3.50-3.54 (1 H, m, CH), 3.79-3.91 (2 H, m, CH_2), 7.19 (1 H, dd, ArH), 7.55 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.78-7.86 (2 H, m, ArH), 7.90 (1 H, dd, ArH), 8.16 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.09 (1 H, s, NH), 2 H missing under H_2O, NH not visible.
224	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.87-1.98 (1 H, m, CH), 2.15-2.26 (1 H, m, CH), 2.35-2.42 (1 H, m, CH), 2.62-2.74 (1 H, m, CH), 2.79-2.91 (5 H, m, CH), 3.73 (2 H, s, CH_2), 5.26 (1 H, m, CHF), 7.23 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.57 (1 H, q, NH), 8.88 (1 H, dd, ArH), 8.96 (1 H, d, ArH), 10.41 (1 H, s, NH).
225	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.84-2.01 (1 H, m, CH), 2.11-2.29 (1 H, m, CH), 2.39 (1 H, app q, CH), 2.67 (1 H, ddd, CH), 2.77-2.91 (5 H, m, CH and CH_3), 3.72 (2 H, s, CH_2), 5.14-5.34 (1 H, m, CHF), 7.22 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.57 (1 H, q, NH), 8.87 (1 H, dd, ArH), 8.96 (1 H, d, ArH), 10.41 (1 H, s, NH).
226	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.21 (3 H, s, CH_3), 2.23-2.61 (8 H, m, CH), 2.82-2.87 (1 H, m, CH), 3.57 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.24 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.09 (1 H, s, NH).
227	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.07 (3 H, s, CH_3), 1.36 (3 H, s, CH_3), 2.30-2.46 (2 H, m, CH), 2.64-2.82 (2 H, m, CH), 3.28 (1 H, s, OH), 3.53-3.67 (4 H, m, CH), 4.52 (1 H, s, CH), 7.15 (1 H, dd, ArH), 7.58 (2 H, d, ArH), 7.82 (2 H, m, CHF2 and ArH), 7.87 (1 H, dd, ArH), 8.10 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.79 (1 H, dd, ArH), 9.80 (1 H, s, NH).
228	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.61 (2 H, m, CH), 0.68-0.73 (2 H, m, CH), 1.95-2.08 (4 H, m, CH), 2.84-2.87 (1 H, m, CH), 3.67 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH), 4 H missing under DMSO.
229	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.76 (2 H, m, CH), 1.95-2.07 (4 H, m, CH), 2.51-2.67 (4 H, m, CH), 2.81-2.90 (1 H, m, CH), 3.71 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.59 (1 H, dd, ArH), 7.79 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.96-8.01 (2 H, m, ArH), 8.15 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).

Cpd #	(δ) NMR data
230	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.58-0.61 (2 H, m, CH), 0.69-0.73 (2 H, m, CH), 2.84-2.86 (1 H, m, CH), 2.91-3.04 (4 H, m, CH), 3.14-3.23 (4 H, m, CH), 3.86 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.61-7.66 (1 H, m, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 8.01 (2 H, app td, ArH), 8.16 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).
231	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.54-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.58-1.66 (1 H, m, CH), 2.02-2.08 (1 H, m, CH), 2.34-2.45 (1 H, m, CH), 2.65-2.79 (2 H, m, CH), 2.82-2.87 (1 H, m, CH), 3.64-3.75 (2 H, m, CH), 4.22-4.29 (1 H, m, CH), 4.73-4.79 (1 H, m, OH), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.74-7.85 (4 H, m, ArH), 7.89 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, d, ArH), 10.10 (1 H, s, NH), 1 H missing under DMSO.
232	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.61 (2 H, m, CH), 0.69-0.73 (2 H, m, CH), 2.25 (2 H, m, CH), 2.81-2.86 (1 H, m, CH), 3.54-3.68 (2 H, m, CH_2), 7.19 (1 H, dd, ArH), 7.52 (2 H, s, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.90 (1 H, d, ArH), 8.15 (2 H, s, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH), 3 H missing under DMSO, 2 H missing under H_2O, OH not visible.
233	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.74 (2 H, m, CH), 2.02 (3 H, s, CH_3), 2.32-2.43 (2 H, m, CH), 2.39-2.51 (2 H, m, CH), 2.83-2.87 (1 H, m, CH), 3.41-3.55 (4 H, m, CH), 3.61 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
234	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.64-1.90 (2 H, m, CH), 1.84-1.95 (2 H, m, CH), 2.26-2.47 (2 H, m, CH), 2.49-2.66 (2 H, m, CH), 2.85 (3 H, d, CH_3), 3.59 (2 H, s, CH_2), 4.65-4.82 (1 H, m, CHF), 7.22 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 8.03 (1 H, d, ArH), 8.13 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.56 (1 H, q, NH), 8.87 (1 H, dd, ArH), 8.95 (1 H, d, ArH), 10.41 (1 H, s, NH).
235	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.58-0.62 (2 H, m, CH), 0.68-0.73 (2 H, m, CH), 1.51 (2 H, m, CH), 1.83 (2 H, m, CH), 2.04 (2 H, m, CH), 2.31-2.37 (1 H, m, CH), 2.83-2.87 (1 H, m, CH), 2.96 (2 H, m, CH), 3.60 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).

GAL-113-WO-PCT

Cpd #	(δ) NMR data
236	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.63-0.75 (2 H, m, CH), 1.71-1.81 (2 H, m, CH), 1.83-1.99 (2 H, m, CH), 2.21-2.47 (2 H, m, CH), 2.51-2.68 (2 H, m, CH), 2.77-2.93 (1 H, m, CH), 2.90-2.96 (1 H, m, CH), 3.58 (2 H, s, CH2), 7.18 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).
237	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.78-0.88 (4 H, m, CH), 1.47-1.63 (2 H, m, CH), 1.69-1.93 (2 H, m, CH), 2.27-2.37 (1 H, m, CH), 2.39-2.50 (2 H, m, CH), 2.73 (1 H, dd, CH), 2.89-2.97 (1 H, m, CH), 3.62 (2 H, s, CH_2), 4.41 (2 H, s, CH_2), 4.58-4.82 (1 H, m, CHF), 7.19 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.60 (1 H, d, ArH), 7.75 (1 H, dd, ArH), 7.89 (1 H, dd, ArH), 7.99 (1 H, s, ArH), 8.12 (2 H, d, ArH), 8.86 (1 H, d, ArH), 10.23 (1 H, s, NH).
238	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.66-1.88 (2 H, m, CH), 1.81-2.00 (2 H, m, CH), 2.27-2.52 (2 H, m, CH), 2.51-2.71 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.65 (2 H, s, CH_2), 4.62-4.84 (1 H, m, CHF), 7.20 (1 H, dd, ArH), 7.59 (1 H, dd, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.97-8.03 (2 H, m, ArH), 8.14 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).
239	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.65 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 2.85 (1 H, m, CH), 3.40 (2 H, m, CH), 3.50-3.59 (3 H, m, CH), 3.73 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.51-7.60 (1 H, m, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 8.00 (2 H, app td, ArH), 8.15 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).
240	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.65 (2 H, m, CH), 0.68-0.76 (2 H, m, CH), 1.37 (3 H, d, CH_3), 2.20-2.50 (2 H, m, CH), 2.34-2.60 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.35-3.54 (1 H, m, CH), 3.49-3.74 (4 H, m, CH), 7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, d, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, d, ArH), 10.10 (1 H, s, NH).
241	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.81 (3 H, d, CH_3), 3.48-3.57 (3 H, m, CH), 3.69 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.46 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, q, NH), 8.86 (1 H, ArH), 10.10 (1 H, s, NH), 2 H missing under H_2O.
242	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.39-2.52 (4 H, m, CH), 2.81 (3 H, d, CH_3), 3.60-3.66 (6 H, m, CH and CH_2), 7.20 (1 H, dd, ArH), 7.60 (1 H, dd, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.97-8.02 (2 H, m, ArH), 8.16 (1 H, dd, ArH), 8.25 (1 H, q, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).

Cpd #	(δ) NMR data
243	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.81 (3 H, d, CH_3), 2.87-3.05 (4 H, m, CH), 3.10-3.26 (4 H, m, CH), 3.79 (2 H, s, CH2), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.24 (1 H, s, NH), 8.87 (1 H, d, ArH), 10.11 (1 H, s, NH).
244	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.88-2.00 (1 H, m, CH), 2.15-2.25 (1 H, m, CH), 2.43 (1 H, app q, CH), 2.64-2.77 (1 H, m, CH), 2.81-2.93 (3 H, m, CH), 3.78 (2 H, s, CH_2), 5.25 (1 H, m, CHF), 7.20 (1 H, dd, ArH), 7.61 (1 H, dd, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.98-8.04 (2 H, m, ArH), 8.16 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).
245	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.81 (3 H, d, CH_3), 2.91-3.05 (4 H, m, CH), 3.13-3.25 (4 H, m, CH), 3.86 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.64 (1 H, dd, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 8.01 (2 H, app td, ArH), 8.16 (1 H, dd, ArH), 8.26 (1 H, q, NH), 8.91 (1 H, dd, ArH), 10.14 (1 H, s, NH).
246	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.94-2.09 (4 H, m, CH), 2.50-2.67 (4 H, m, CH), 2.81 (3 H, d, CH_3), 3.72 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.60 (1 H, dd, ArH), 7.80 (2 H, d, ArH), 7.84 (2 H, d, ArH), 8.00 (2 H, dd, ArH, 8.15 (1 H, dd, ArH), 8.26 (1 H, q, NH), 8.90 (1 H, d, ArH), 10.13 (1 H, s, NH).
247	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.64 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 2.12-2.25 (4 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.69-3.78 (2 H, m, CH), 4.03-4.14 (2 H, m, CH), 7.21 (1 H, dd, ArH), 7.71-7.80 (4 H, m, ArH), 7.83 (2 H, d, ArH), 7.93 (1 H, dd, ArH), 8.21-8.28 (3 H, m, ArH and NH), 8.89 (1 H, dd, ArH), 10.13 (1 H, s, NH).
248	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.47 (4 H, m, CH), 2.78-2.89 (3 H, m, CH and CH_2), 3.58 (4 H, m, CH), 4.37 (2 H, m, CH_2), 7.12 (1 H, dd, ArH), 7.77-7.87 (4 H, m, ArH), 7.90 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.38 (1 H, s, ArH), 8.64 (1 H, s, ArH), 8.70 (1 H, dd, ArH), 10.00 (1 H, s, NH).
249	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.82 (1 H, m, CH), 3.86-3.98 (1 H, m, CH), 4.10 (1 H, m, CH), 4.27 (2 H, m, CH), 4.43 (1 H, m, CH), 4.53 (2 H, m, CH), 4.62 (1 H, m, CH), 4.68 (1 H, m, CH), 5.75 (1 H, d, OH), 7.22 (1 H, dd, ArH), 7.65 (2 H, d, ArH), 7.76-7.86 (4 H, m, ArH), 7.98 (1 H, dd, ArH), 8.29 (2 H, d, ArH), 8.91 (1 H, d, ArH), 10.21 (1 H, s, NH).
251	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.78 (6 H, s, CH_3), 2.86 (1 H, m, CH), 3.32 (2 H, s, CH_2), 7.14 (1 H, dd, ArH), 7.83 (4 H, s, ArH), 7.98 (1 H, d, ArH), 8.26 (1 H, d, NH), 8.51 (1 H, s, ArH), 8.72 (1 H, dd, ArH), 8.85 (1 H, s, ArH), 10.01 (1 H, s, NH).

Cpd #	(δ) NMR data
252	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.63-0.74 (2 H, m, CH), 2.48 (3 H, s, CH_3), 2.80-2.89 (1 H, m, CH), 3.88 (3 H, s, CH_3), 7.12 (1 H, dd, ArH), 7.56 (1 H, dd, ArH), 7.72-7.85 (4 H, m, ArH), 8.02 (1 H, s, ArH), 8.23 (1 H, d, NH), 8.74 (1 H, dd, ArH), 9.99 (1 H, s, NH).
253	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.68 (4 H, m, CH), 3.84 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
254	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.67 (2 H, m, CH), 0.66-0.75 (2 H, m, CH), 2.81-2.90 (1 H, m, CH), 3.47-3.58 (5 H, m, CH), 3.68 (2 H, s, CH_2), 7.17 (1 H, dd, ArH), 7.45 (2 H, d, ArH), 7.77-7.90 (5 H, m, ArH), 8.12 (2 H, d, ArH), 8.26 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).
255	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.66 (2 H, m, CH), 0.66-0.75 (2 H, m, CH), 1.84-2.02 (1 H, m, CH), 2.11-2.28 (1 H, m, CH), 2.39 (1 H, m, CH), 2.58-2.74 (1 H, m, CH), 2.77-2.91 (3 H, m, CH), 3.65-3.75 (2 H, m, CH_2), 5.25 (1 H, ddd, CH), 7.18 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.24 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).
256	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 1.84-2.02 (1 H, m, CH), 2.11-2.28 (1 H, m, CH), 2.34-2.44 (1 H, m, CH), 2.67 (1 H, m, CH), 2.79-2.91 (3 H, m, CH), 3.66-3.74 (2 H, m, CH_2), 5.25 (1 H, ddd, CH), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
257	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.77 (2 H, m, CH), 1.87 (1 H, m, CH), 1.93 (1 H, m, CH), 2.37 (2 H, m, CH), 2.58 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.59 (2 H, s, CH_2), 4.74 (1 H, br d, CH), 7.19 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.74-7.86 (4 H, m, ArH), 7.89 (1 H, d, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, d, ArH), 10.09 (1 H, s, NH).
258	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.66 (2 H, m, CH), 0.66-0.75 (2 H, m, CH), 2.86 (1 H, m, CH), 2.92 (3 H, s, CH_3), 3.11 (3 H, s, CH_3), 5.28 (2 H, s, CH_2), 7.12 (1 H, dd, ArH), 7.76-7.88 (4 H, m, ArH), 7.93 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.36 (1 H, s, ArH), 8.61 (1 H, s, ArH), 8.71 (1 H, dd, ArH), 10.07 (1 H, s, NH).

Cpd #	(δ) NMR data
259	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.82-2.90 (1 H, m, CH), 3.52 (2 H, m, CH), 3.59 (2 H, m, CH), 3.61-3.65 (2 H, m, CH), 3.63-3.72 (2 H, m, CH), 5.32 (2 H, s, CH_2), 7.08-7.15 (1 H, dd, ArH), 7.76-7.87 (4 H, m, ArH), 7.93 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.28 (1 H, s, ArH), 8.62 (1 H, s, ArH), 8.72 (1 H, dd, ArH), 10.03 (1 H, s, NH).
260	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.11-1.21 (6 H, s, CH_3), 2.86 (1 H, m, CH), 4.15 (2 H, s, CH_2), 4.84 (1 H, s, OH), 7.12 (1 H, dd, ArH), 7.79-7.86 (4 H, m, ArH), 7.93 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.35 (1 H, s, ArH), 8.65 (1 H, s, ArH), 8.70 (1 H, dd, ArH), 10.02 (1 H, s, NH).
261	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.84 (3 H, d, CH_3), 3.34 (2 H, m, CH), 3.51 (2 H, m, CH), 3.68 (2 H, s, CH_2), 5.74 (1 H, s, CH), 7.22 (1 H, dd, ArH), 7.46 (2 H, d, ArH), 7.90 (1 H, d, ArH), 8.01 (1 H, d, ArH), 8.11 (2 H, d, ArH), 8.32 (1 H, dd, ArH), 8.59 (1 H, d, NH), 8.83 (1 H, d, ArH), 8.93 (1 H, d, ArH), 10.41 (1 H, s, NH).
262	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.37 (3 H, d, CH_3), 2.36 (2 H, m, CH), 2.47 (2 H, m, CH), 3.45 (1 H, m, CH), 3.61 (4 H, m, CH), 7.11-7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.82 (2 H, m, CHF_2 and ArH), 7.85-7.90 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.28 (1 H, s, ArH), 8.76-8.79 (1 H, dd, ArH), 9.78 (1 H, s, NH).
263	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.27-2.38 (2 H, m, CH), 3.55 (4 H, m, CH), 3.64 (4 H, m, CH), 4.07-4.16 (2 H, m, CH), 4.36-4.45 (2 H, m, CH), 7.18-7.23 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.78-7.84 (4 H, m, ArH), 7.97 (1 H, dd, ArH), 8.27 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.12 (1 H, s, NH)
264	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.33 (4 H, m, CH, under H_2O), 3.55 (4 H, m, CH), 3.64 (4 H, m, CH), 3.83 (2 H, m, CH), 4.05 (2 H, m, CH), 7.18-7.23 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.69 (2 H, d, ArH), 7.81 (2 H, d, ArH), 7.97 (1 H, dd, ArH), 8.29 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.12 (1 H, s, NH).
265	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.62-0.67 (2 H, m, CH), 0.73-0.79 (2 H, m, CH), 2.89-2.95 (1 H, m, CH), 3.55 (4 H, m, CH), 3.64 (4 H, m, CH), 7.18-7.23 (1 H, dd, ArH), 7.44 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.95-8.02 (3 H, m, ArH), 8.28 (2 H, d, ArH), 8.55 (1 H, d, NH), 8.89 (1 H, dd, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
266	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.64-0.68 (2 H, m, CH), 0.74-0.81 (2 H, m, CH), 1.15 (3 H, d, CH_3), 2.20-2.29 (1 H, m, CH), 2.43-2.62 (1 H, m, CH), 2.60-2.70 (1 H, m, CH), 2.89-2.95 (1 H, m, CH), 3.23-3.36 (2 H, m, CH), 3.50-3.61 (1 H, m, CH), 3.72-3.78 (2 H, m, CH), 4.14 (1 H, d, CH), 7.25 (1 H, dd, ArH), 7.56 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.89 (2 H, d, ArH), 7.94 (1 H, d, ArH), 8.19 (2 H, d, ArH), 8.31 (1 H, d, NH), 8.92 (1 H, dd, ArH), 10.16 (1 H, s, NH).
267	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.37-2.54 (4 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.56-3.67 (6 H, m, CH and CH_2), 7.20 (1 H, dd, ArH), 7.60 (1 H, m, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.97-8.02 (2 H, m, ArH), 8.15 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.12 (1 H, s, NH).
268	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.39 (2 H, s, CH), 3.53-3.58 (3 H, m, CH), 3.73 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.53-7.59 (1 H, m, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.96-8.03 (2 H, m, ArH), 8.15 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.90 (1 H, dd, ArH), 10.13 (1 H, s, NH).
269	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.81 (3 H, d, CH_3), 2.96 (4 H, m, CH), 3.18 (4 H, m, CH), 3.79 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, m, NH), 8.87 (1 H, d, ArH), 10.11 (1 H, s, NH).
270	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.37 (3 H, d, CH_3), 2.31-2.38 (2 H, m, CH), 2.38-2.57 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.46 (1 H, q, CH), 3.59-3.64 (4 H, m, CH), 7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
271	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.37 (3 H, d, CH_3), 2.31-2.38 (2 H, m, CH), 2.42-2.53 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.46 (1 H, q, CH), 3.59-3.64 (4 H, m, CH), 7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
272	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 3.33-3.44 (2 H, m, CH), 3.49-3.59 (3 H, m, CH), 3.72 (2 H, s, CH_2), 4.01 (2 H, s, CH_2), 4.71 (1 H, s, OH), 7.10 (1 H, dd, ArH), 7.49-7.57 (2 H, m, ArH), 7.86 (1 H, s, ArH), 7.94 (1 H, d, ArH), 8.02 (1 H, dd, ArH), 8.16 (1 H, dd, ArH), 8.75 (1 H, dd, ArH), 9.40 (1 H, s, NH).

Cpd #	(δ) NMR data
273	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 2.34-2.58 (4 H, m, CH), 3.56-3.68 (6 H, m, CH and CH_2), 4.01 (2 H, s, CH_2), 4.72 (1 H, s, OH), 7.10 (1 H, dd, ArH), 7.53 (1 H, d, ArH), 7.58 (1 H, m, ArH), 7.86 (1 H, d, ArH), 7.94 (1 H, dd, ArH), 8.01 (1 H, dd, ArH), 8.16 (1 H, dd, ArH), 8.75 (1 H, dd, ArH), 9.39 (1 H, s, NH).
274	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 1.60-1.65 (2 H, m, CH), 1.83-1.87 (2 H, m, CH), 4.01 (2 H, s, CH_2), 4.72 (1 H, s, OH), 7.10 (1 H, dd, ArH), 7.49-7.53 (3 H, m, ArH), 7.83-7.86 (2 H, m, ArH), 8.22 (2 H, d, ArH), 8.73 (1 H, dd, ArH), 9.35 (1 H, s, NH).
275	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 2.03-2.10 (1 H, m, CH), 2.27-2.32 (1 H, m, CH), 2.97 (1 H, dd, CH), 3.09 (1 H, dt, CH), 3.27-3.31 (1 H, m, CH), 3.37-3.43 (1 H, m, CH), 3.49 (1 H, m, CH), 3.79-3.84 (2 H, m, CH2), 4.00 (2 H, s, CH_2), 4.71 (1 H, s, OH), 7.09 (1 H, dd, ArH), 7.49-7.54 (3 H, m, ArH), 7.83 (1 H, dd, ArH), 7.86 (1 H, s, ArH), 8.15 (2 H, d, ArH), 8.71 (1 H, dd, ArH), 9.33 (1 H, s, NH), 1 NH not visible.
276	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 4.01 (2 H, s, CH_2), 7.11 (1 H, dd, ArH), 7.31 (1 H, app td, ArH), 7.52 (1 H, s, ArH), 7.55-7.65 (1 H, m, ArH), 7.87 (1 H, s, ArH), 7.94 (1 H, dd, ArH), 8.05 (1 H, d, ArH), 8.16 (1 H, dt, ArH), 8.77 (1 H, dd, ArH), 9.41 (1 H, s, NH), 1 OH not visible.
277	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.23 (6 H, s, CH_3), 2.81 (3 H, d, CH_3), 3.52 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, q, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
278	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.89-3.01 (4 H, m, CH), 3.14-3.21 (4 H, m, CH), 3.79 (2 H, s, CH_2), 6.92 (1 H, tt, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.52 (2 H, d, ArH), 7.76 (2 H, dd, ArH), 7.87 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 9.76 (1 H, s, NH).
279	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.39-2.53 (4 H, m, CH), 3.59-3.64 (6 H, m, CH and CH_2), 6.90-6.96 (1 H, m, ArH), 7.16 (1 H, dd, ArH), 7.30-7.37 (2 H, m, ArH), 7.56-7.62 (1 H, m, ArH), 7.76 (2 H, d, ArH), 7.97 (1 H, dd, ArH), 8.00 (1 H, dd, ArH), 8.16 (1 H, dd, ArH), 8.86 (1 H, dd, ArH), 9.79 (1 H, s, NH).
280	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 1.42 (3 H, d, CH_3), 2.81-2.89 (1 H, m, CH), 4.80-4.88 (1 H, m, CH), 5.27 (1 H, d, OH), 7.18 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.76-7.79 (2 H, m, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.09 (1 H, s, NH).

Cpd #	(δ) NMR data
281	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.69 (3 H, s, CH_3), 2.82-2.88 (1 H, m, CH), 7.23 (1 H, dd, ArH), 7.77-7.81 (2 H, m, ArH), 7.79-7.87 (2 H, m, ArH), 8.02 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.26 (1 H, d, NH), 8.36 (2 H, d, ArH), 8.94 (1 H, dd, ArH), 10.16 (1 H, s, NH).
282	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.77-0.86 (4 H, m, CH), 2.91-2.97 (5 H, m, CH), 3.13-3.23 (4 H, m, CH), 3.80 (2 H, s, CH_2), 4.41 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.60 (1 H, d, ArH), 7.75 (1 H, dd, ArH), 7.90 (1 H, dd, ArH), 7.99 (1 H, d, ArH), 8.15 (2 H, d, ArH), 8.87 (1 H, dd, ArH), 10.24 (1 H, s, NH).
283	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.36-2.50 (4 H, m, CH), 3.58 (2 H, s, CH_2), 3.61-3.65 (4 H, m, CH), 6.88-6.95 (1 H, m, ArH), 7.15 (1 H, dd, ArH), 7.29-7.36 (2 H, m, ArH), 7.49 (2 H, d, ArH), 7.76 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 9.75 (1 H, s, NH).
284	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 0.83-0.88 (2 H, m, CH), 0.96-1.00 (2 H, m, CH), 2.46-2.56 (4 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.53-3.57 (4 H, m, CH), 7.19 (1 H, dd, ArH), 7.45 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.87 (1 H, d, ArH), 10.11 (1 H, s, NH).
285	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.64 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 1.39 (6 H, s, CH3), 2.36-2.54 (4 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.60-3.64 (4 H, m, CH), 7.18 (1 H, dd, ArH), 7.68 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.87 (1 H, dd, ArH), 8.10 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).
286	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.41-2.51 (4 H, m, CH), 3.19 (3 H, s, CH_3), 3.60-3.66 (6 H, m, CH and CH_2), 7.24 (1 H, dd, ArH), 7.61 (1 H, dd, ArH), 7.88 (2 H, d, ArH), 7.96 (2 H, d, ArH), 8.00-8.04 (2 H, m, ArH), 8.14 (1 H, dd, ArH), 8.92 (1 H, dd, ArH), 10.47 (1 H, s, NH).
287	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.38-2.48 (4 H, m, CH), 3.18 (3 H, s, CH_3), 3.58 (2 H, s, CH_2), 3.61-3.66 (4 H, m, CH), 7.22 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.88 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.14 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.45 (1 H, s, NH).

Cpd #	(δ) NMR data
288	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.90-3.02 (4 H, m, CH), 3.12-3.23 (7 H, m, CH and CH_3), 3.80 (2 H, s, CH_2), 7.23 (1 H, dd, ArH), 7.54 (2 H, d, ArH), 7.88 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.15 (2 H, d, ArH), 8.89 (1 H, dd, ArH), 10.46 (1 H, s, NH).
289	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.39-2.52 (4 H, m, CH), 3.60-3.66 (6 H, m, CH and CH_2), 7.22 (1 H, dd, ArH), 7.50 (1 H, d, ArH), 7.60 (1 H, dd, ArH), 7.98-8.02 (2 H, m, ArH), 8.13 (1 H, dd, ArH), 8.21 (1 H, dd, ArH), 8.79 (1 H, d, ArH), 8.89 (1 H, dd, ArH), 10.24 (1 H, s, NH).
290	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.35 (3 H, d, CH_3), 2.35-2.50 (4 H, m, CH), 3.57 (2 H, s, CH_2), 3.61-3.65 (4 H, m, CH), 4.67-4.73 (1 H, m, CH), 5.02 (1 H, d, OH), 7.14 (1 H, dd, ArH), 7.29 (2 H, d, ArH), 7.49 (2 H, d, ArH), 7.68 (2 H, d, ArH), 7.85 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.67 (1 H, s, NH).
291	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.37 (3 H, d, CH_3), 2.87-3.02 (4 H, m, CH), 3.13 (3 H, s, CH_3), 3.15-3.20 (4 H, m, CH), 3.79 (2 H, s, CH_2), 4.27 (1 H, q, CH), 7.15 (1 H, dd, ArH), 7.26 (2 H, d, ArH), 7.52 (2 H, d, ArH), 7.72 (2 H, d, ArH), 7.87 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 9.76 (1 H, s, NH).
292	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.35 (3 H, d, CH3), 2.40-2.51 (4 H, m, CH), 3.60-3.65 (6 H, m, CH and CH_2), 4.67-4.72 (1 H, m, CH), 5.03 (1 H, d, OH), 7.15 (1 H, dd, ArH), 7.30 (2 H, d, ArH), 7.59 (1 H, dd, ArH), 7.69 (2 H, d, ArH), 7.96 (1 H, d, ArH), 8.00 (1 H, dd, ArH), 8.16 (1 H, dd, ArH), 8.85 (1 H, dd, ArH), 9.71 (1 H, s, NH).
293	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.27 (3 H, d, CH_3), 2.30-2.42 (4 H, m, CH), 3.03 (3 H, s, CH_3), 3.50-3.56 (6 H, m, CH and CH_2), 4.15-4.21 (1 H, m, CH), 7.06 (1 H, dd, ArH), 7.16 (2 H, d, ArH), 7.49 (1 H, dd, ArH), 7.63 (2 H, d, ArH), 7.87 (1 H, dd, ArH), 7.90 (1 H, dd, ArH), 8.06 (1 H, dd, ArH), 8.75 (1 H, dd, ArH), 9.68 (1 H, s, NH).
294	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.35 (3 H, d, CH_3), 3.49-3.57 (3 H, m, CH), 3.69 (2 H, s, CH_2), 4.67-4.72 (1 H, m, CH), 5.02 (1 H, d, OH), 7.14 (1 H, dd, ArH), 7.29 (2 H, d, ArH), 7.45 (2 H, d, ArH), 7.68 (2 H, d, ArH), 7.85 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.68 (1 H, s, NH), 2 H under H_2O.
295	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.49-3.59 (3 H, m, CH), 3.68 (2 H, s, CH_2), 6.92 (1 H, tt, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.45 (2 H, d, ArH), 7.75 (2 H, dd, ArH), 7.86 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 9.77 (1 H, s, NH), 2 H under H_2O.

Cpd #	(δ) NMR data
296	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 2.95-3.10 (4 H, m, CH), 3.17-3.22 (4 H, m, CH), 3.93 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.68 (1 H, d, ArH), 7.77 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.55 (1 H, dd, ArH), 8.91 (1 H, dd, ArH), 9.30 (1 H, d, ArH), 10.13 (1 H, s, NH).
297	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.82-2.87 (1 H, m, CH), 4.69 (2 H, d, CH_2), 5.54 (1 H, t, OH), 7.22 (1 H, dd, ArH), 7.67 (1 H, d, ArH), 7.78 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.57 (1 H, dd, ArH), 8.90 (1 H, dd, ArH), 9.27 (1 H, d, ArH), 10.11 (1 H, s, NH).
298	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.18 (3 H, s, CH_3), 3.40-3.66 (3 H, m, CH), 3.70 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.87 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.14 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.46 (1 H, s, NH), 2 H under H_2O.
299	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.30-0.35 (2 H, m, CH), 0.51-0.57 (2 H, m, CH), 2.22-2.38 (4 H, m, CH), 2.52-2.58 (1 H, m, CH), 3.44 (2 H, s, CH_2), 3.48-3.52 (4 H, m, CH), 4.57 (2 H, s, CH_2), 6.96 (1 H, dd, ArH), 7.35 (2 H, d, ArH), 7.38 (1 H, s, ArH), 7.70 (1 H, dd, ArH), 7.72 (1 H, s, ArH), 8.01 (2 H, d, ArH), 8.11 (1 H, d, NH), 8.59 (1 H, dd, ArH), 9.25 (1 H, s, NH).
300	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.60-2.66 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 2.98 (2 H, s, CH_2), 3.15-3.27 (2 H, m, CH), 3.66 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.74-7.86 (5 H, m, ArH and NH), 7.89 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
301	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 2.92 (3 H, s, CH_3), 3.08-3.26 (4 H, m, CH), 3.64 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH), 4 H under H_2O.
302	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.16 (6 H, s, CH_3), 2.46 (2 H, s, CH_2), 2.82-2.87 (1 H, m, CH), 3.20 (1 H, s, OH), 3.87 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 NH not visible.

Cpd #	(δ) NMR data
303	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.83-2.87 (1 H, m, CH), 2.96-3.02 (2 H, m, CH), 3.08 (3 H, s, CH_3), 3.28-3.35 (2 H, m, CH), 3.84 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.11 (1 H, s, NH), 1 NH not visible.
304	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.91-0.97 (2 H, m, CH), 1.03-1.09 (2 H, m, CH), 2.81 (3 H, d, CH_3), 2.84-3.12 (4 H, m, CH), 3.04-3.15 (4 H, m, CH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.84 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, q, NH), 8.88 (1 H, dd, ArH), 10.12 (1 H, s, NH).
305	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 0.91-0.96 (2 H, m, CH), 1.03-1.08 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 2.88-3.08 (4 H, m, CH), 3.05-3.15 (4 H, m, CH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.87 (1 H, dd, ArH), 10.11 (1 H, s, NH).
305	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.30-3.37 (2 H, m, CH), 3.48-3.57 (3 H, m, CH), 3.69 (2 H, s, CH_2), 7.20 (1 H, dd, ArH), 7.46 (2 H, d, ArH), 7.50 (1 H, d, ArH), 7.90 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.22 (1 H, dd, ArH), 8.78 (1 H, d, ArH), 8.85 (1 H, dd, ArH), 10.23 (1 H, s, NH).
306	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.68-1.75 (1 H, m, CH), 2.09-2.19 (3 H, m, CH), 2.82-2.87 (1 H, m, CH), 3.62-3.68 (2 H, m, CH), 3.81-3.85 (2 H, m, CH), 7.19 (1 H, dd, ArH), 7.53 (2 H, d, ArH), 7.73 (1 H, s, NH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.27 (1 H, s, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 H under DMSO.
307	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.35 (3 H, d, CH_3), 2.87-3.02 (4 H, m, CH), 3.15-3.22 (4 H, m, CH), 3.79 (2 H, s, CH_2), 4.66-4.73 (1 H, m, CH), 5.02 (1 H, d, OH), 7.14 (1 H, dd, ArH), 7.29 (2 H, d, ArH), 7.52 (2 H, d, ArH), 7.68 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.69 (1 H, s, NH).
308	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.74 (2 H, m, CH), 2.31-2.42 (4 H, m, CH), 2.83-2.86 (1 H, m, CH), 3.60 (2 H, s, CH_2), 5.97 (2 H, s, NH_2), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.89 (1 H, d, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, d, ArH), 10.10 (1 H, s, NH), 4 H under H_2O.

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Cpd #	(δ) NMR data
309	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.97-2.05 (1 H, m, CH), 2.20-2.27 (1 H, m, CH), 2.45-2.55 (1 H, m, CH), 2.70-2.79 (3 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.30-3.33 (1 H, m), 3.71-3.75 (2 H, m, CH), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
310	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.97-2.05 (1 H, m, CH), 2.20-2.28 (1 H, m, CH), 2.47-2.52 (1 H, m, CH), 2.70-2.79 (3 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.29-3.35 (1 H, m, CH), 3.72-3.74 (2 H, m, CH), 7.19 (1 H, dd, ArH), 7.50 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
311	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.96-2.07 (1 H, m, CH), 2.20-2.31 (1 H, m, CH), 2.57-2.62 (1 H, m, CH), 2.78-2.87 (4 H, m, CH), 3.29-3.34 (1 H, m, CH), 3.85-3.89 (2 H, m, CH), 7.22 (1 H, dd, ArH), 7.62 (1 H, d, ArH), 7.77 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.56 (1 H, dd, ArH), 8.91 (1 H, dd, ArH), 9.28 (1 H, d, ArH), 10.12 (1 H, s, NH).
312	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.96-2.07 (1 H, m, CH), 2.20-2.31 (1 H, m, CH), 2.57-2.62 (1 H, m, CH), 2.79-2.88 (4 H, m, CH), 3.31-3.35 (1 H, m, CH), 3.85-3.89 (2 H, m, CH), 7.22 (1 H, dd, ArH), 7.62 (1 H, d, ArH), 7.77 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.99 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.56 (1 H, dd, ArH), 8.91 (1 H, dd, ArH), 9.28 (1 H, d, ArH), 10.12 (1 H, s, NH).
313	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.45-0.49 (2 H, m, CH), 0.56-0.62 (4 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.67 (2 H, s, CH_2), 2.82-2.88 (1 H, m, CH), 3.89 (2 H, s, CH_2), 5.21 (1 H, s, OH), 7.18 (1 H, dd, ArH), 7.54 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.78-7.86 (2 H, m, ArH), 7.89 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 NH not visible.
314	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.63 (2 H, t, CH_2), 2.82-2.87 (1 H, m, CH), 3.53 (2 H, q, CH_2), 3.82 (2 H, s, CH_2), 4.52 (1 H, t, OH), 7.18 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 NH not visible.

GAL-113-WO-PCT

Cpd #	(δ) NMR data
315	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.83 (3 H, s, CH_3), 2.57-2.63 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.16-3.23 (2 H, m, CH), 3.81 (2 H, s, CH_2), 7.18 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.80-7.86 (3 H, m, ArH and NH), 7.89 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 NH not visible.
316	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.12 (3 H, t, CH_3), 2.29-2.57 (4 H, m, CH), 3.01 (2 H, q, CH_2), 3.58 (2 H, s, CH_2), 3.61-3.65 (4 H, m, CH), 7.21 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.85 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 7.98 (2 H, d, ArH), 8.14 (2 H, d, ArH), 8.87 (1 H, dd, ArH), 10.31 (1 H, s, NH).
317	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.12 (3 H, t, CH_3), 2.93-2.98 (4 H, m, CH), 3.01 (2 H, q, CH_2), 3.15-3.20 (4 H, m, CH), 3.80 (2 H, s, CH_2), 7.21 (1 H, dd, ArH), 7.54 (2 H, d, ArH), 7.85 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 7.99 (2 H, d, ArH), 8.15 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.32 (1 H, s, NH).
318	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.42-0.47 (2 H, m, CH), 0.56-0.62 (2 H, m, CH), 0.62-0.68 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.64-2.73 (1 H, m, CH), 2.81-2.89 (1 H, m, CH), 3.09 (2 H, s, CH_2), 3.77 (2 H, s, CH_2), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.83-7.92 (2 H, m, ArH and NH), 8.14 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH), 1 NH not visible.
319	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.11 (6 H, s, CH_3), 2.90-2.99 (4 H, m, CH), 3.14-3.19 (4 H, m, CH), 3.78 (2 H, s, CH_2), 4.01 (2 H, s, CH_2), 4.72 (1 H, s, OH), 7.09 (1 H, dd, ArH), 7.49-7.53 (3 H, m, ArH), 7.84 (1 H, dd, ArH), 7.86 (1 H, s, ArH), 8.16 (2 H, d, ArH), 8.72 (1 H, dd, ArH), 9.35 (1 H, s, NH).
320	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.58-2.66 (2 H, m, CH), 2.98 (2 H, s, CH_2), 3.18 (3 H, s, CH_3), 3.15-3.26 (2 H, m, CH), 3.66 (2 H, s, CH_2), 7.23 (1 H, dd, ArH), 7.52 (2 H, d, ArH), 7.80 (1 H, s, ArH), 7.88 (2 H, d, ArH), 7.89-7.97 (3 H, m, ArH and NH), 8.15 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.45 (1 H, s, NH).
321	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.56-1.64 (1 H, m, CH), 1.81 (3 H, s, CH_3), 2.08-2.17 (1 H, m, CH), 2.30-2.37 (1 H, m, CH), 2.44-2.51 (1 H, m, CH), 2.62-2.75 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.65.3.69 (2 H, m, CH), 4.12-4.23 (1 H, m, CH), 7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, d, ArH), 8.03 (1 H, d, NH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, d, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
322	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.12 (3 H, t, CH_3), 3.01 (2 H, q, CH_2), 3.49-3.54 (3 H, m, CH), 3.69 (2 H, s, CH_2), 7.21 (1 H, dd, ArH), 7.47 (2 H, d, ArH), 7.85 (2 H, d, ArH), 7.90 (1 H, dd, ArH), 7.99 (2 H, d, ArH), 8.14 (2 H, d, ArH), 8.87 (1 H, dd, ArH), 10.32 (1 H, s, NH), 2 H under H_2O.
323	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.02 (3 H, s, CH_3), 2.29-2.47 (2 H, m, CH), 2.41-2.47 (2 H, m, CH), 3.18 (3 H, s, CH_3), 3.45-3.50 (4 H, m, CH), 3.61 (2 H, s, CH_2), 7.22 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.88 (2 H, d, ArH), 7.92 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.14 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.45 (1 H, s, NH).
324	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.35-2.40 (4 H, m, CH), 3.18 (3 H, s, CH_3), 3.31-3.35 (4 H, m, CH), 3.60 (2 H, s, CH_2), 5.97 (2 H, s, NH_2), 7.22 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.88 (2 H, d, ArH), 7.91 (1 H, dd, ArH), 7.95 (2 H, d, ArH), 8.13 (2 H, d, ArH), 8.88 (1 H, dd, ArH), 10.45 (1 H, s, NH).
325	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.60 (2 H, m, CH), 0.69-0.72 (2 H, m, CH), 1.53 (6 H, s, CH_3), 2.84-2.86 (1 H, m, CH), 7.06 (2 H, d, ArH), 7.16 (1 H, dd, ArH), 7.36 (1 H, s, NH), 7.62 (1 H, s, NH), 7.74-7.85 (5 H, m, ArH), 8.12 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.82 (1 H, dd, ArH), 10.10 (1 H, s, NH).
326	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.28 (3 H, s, CH_3), 2.49-2.53 (4 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.26-3.32 (4 H, m, CH), 7.08-7.18 (3 H, m, ArH), 7.77-7.85 (5 H, m, ArH), 8.11 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.76 (1 H, dd, ArH), 10.08 (1 H, s, NH).
327	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 1.47 (9 H, s, CH_3), 2.81-2.89 (1 H, m, CH), 3.25-3.29 (4 H, m, CH), 3.50-3.55 (4 H, m, CH), 7.09-7.17 (3 H, m, ArH), 7.74-7.85 (5 H, m, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.77 (1 H, dd, ArH), 10.08 (1 H, s, NH).
328	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.16-1.22 (2 H, m, CH), 1.21-1.27 (2 H, m, CH), 2.05 (3 H, s, CH_3), 2.89-3.00 (4 H, m, CH), 3.13-3.23 (4 H, m, CH), 3.79 (2 H, s, CH_2), 7.15 (1 H, dd, ArH), 7.23 (2 H, d, ArH), 7.52 (2 H, d, ArH), 7.68 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.14 (2 H, d, ArH), 8.80 (1 H, dd, ArH), 9.77 (1 H, s, NH).
329	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.55-0.64 (2 H, m, CH), 0.64-0.75 (2 H, m, CH), 2.32-2.58 (4 H, m, CH), 2.54-2.80 (4 H, m, CH), 2.81-2.89 (1 H, m, CH), 3.19 (2 H, q, CH_2), 3.57 (2 H, s, CH_2), 7.18 (1 H, dd, ArH), 7.48 (2 H, d, ArH), 7.78 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.26 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
330	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.64 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 2.71 (6 H, s, CH_3), 2.81-2.89 (1 H, m, CH), 7.24 (1 H, dd, ArH), 7.79 (2 H, d, ArH), 7.83 (2 H, d, ArH), 7.94 (2 H, d, ArH), 8.03 (1 H, dd, ArH), 8.26 (1 H, d, NH), 8.45 (2 H, d, ArH), 8.95 (1 H, dd, ArH), 10.17 (1 H, s, NH).
331	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.55-0.63 (2 H, m, CH), 0.67-0.75 (2 H, m, CH), 2.80-2.87 (1 H, m, CH), 7.23 (1 H, dd, ArH), 7.45-7.53 (2 H, m, ArH), 7.72 (2 H, d, ArH), 7.79 (2 H, d, ArH), 7.85 (1 H, dd, ArH), 7.87-7.93 (1 H, m, ArH), 8.12-8.17 (1 H, m, ArH), 8.23-8.27 (2 H, m, ArH and NH), 8.94 (1 H, dd, ArH), 10.08 (1 H, s, NH).
332	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.27 (3 H, s, CH_3), 2.43-2.49 (4 H, m, CH), 2.82-2.87 (1 H, m, CH), 3.60-3.66 (4 H, m, CH), 7.02 (1 H, d, ArH), 7.15 (1 H, dd, ArH), 7.77 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.25 (1 H, d, NH), 8.39 (1 H, dd, ArH), 8.78 (1 H, dd, ArH), 8.99 (1 H, d, ArH), 10.08 (1 H, s, NH).
333	^{1}H NMR δ (ppm)(DMSO-d$_6$): 1.52 (6 H, s, CH_3), 2.69 (3 H, d, CH_3), 3.75-3.88 (1 H, m, CH), 4.02-4.18 (1 H, m, CH), 4.21-4.32 (1 H, m, CH), 4.42-4.62 (2 H, m, CH), 5.75 (1 H, s, OH), 7.04 (2 H, d, ArH), 7.17 (1 H, dd, ArH), 7.64 (2 H, d, ArH), 7.80 (2 H, d, ArH), 7.85 (1 H, dd, ArH), 8.09-8.16 (3 H, m, ArH and NH), 8.82 (1 H, dd, ArH), 10.13 (1 H, s, NH).
335	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.33-0.39 (2 H, m, CH), 0.45-0.51 (2 H, m, CH), 2.59-2.65 (1 H, m, CH), 5.26 (2 H, s, CH_2), 6.88 (1 H, t, ArH), 7.06-7.21 (5 H, m, ArH), 7.52-7.62 (4 H, m, ArH), 7.69 (1 H, d, ArH), 8.01 (1 H, d, NH), 8.18 (1 H, s, ArH), 8.47 (2 H, m, ArH), 9.76 (1 H, s, NH).
336	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.19 (3 H, s, CH_3), 5.51 (2 H, s, CH_2), 7.15 (1 H, t, ArH), 7.33-7.45 (5 H, m, ArH), 7.88 (2 H, d, ArH), 7.85-7.98 (3 H, m, ArH), 8.41 (1 H, s, ArH), 8.71-8.75 (2 H, m, ArH), 10.35 (1 H, s, NH).
337	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.17 (3 H, s, CH_3), 7.26 (1 H, m, ArH), 7.49 (2 H, d, ArH), 7.77-7.92 (6 H, m, ArH), 8.15 (1 H, d, ArH), 8.26 (1 H, s, ArH), 8.95 (1 H, d, ArH), 10.43 (1 H, s, NH).
338	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.58 (3 H, s, CH_3), 2.82-2.89 (1 H, m, CH), 6.99 (1 H, d, ArH), 7.13 (1 H, dd, ArH), 7.83 (4 H, m, ArH), 7.89 (1 H, d, ArH), 8.03 (1 H, d, ArH), 8.27 (1 H, d, NH), 8.76 (1 H, d, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
339	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.55-0.64 (2 H, m, CH), 0.64-0.75 (2 H, m, CH), 2.71-2.79 (2 H, t, CH_2), 2.85 (1 H, m, CH), 3.63 (4 H, m, CH_2), 4.21 (2 H, t, CH_2), 7.11-7.19 (3 H, m, ArH), 7.76-7.87 (5 H, m, ArH), 8.13-8.19 (2 H, m, ArH), 8.25 (1 H, d, NH), 8.81 (1 H, dd, ArH), 10.10 (1 H, s, NH).(4 H under DMSO)
340	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.68-2.78 (4 H, m, CH), 3.40 (3 H, s, CH_3), 3.86 (4 H, m, CH), 4.01 (2 H, s, CH_2), 7.33-7.40 (2 H, m, ArH), 8.10 (2 H, d, ArH), 8.17-8.28 (4 H, m, ArH), 9.01 (1 H, d, ArH), 10.66 (1 H, s, NH).
341	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.63 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.47-2.56 (4 H, m, CH), 2.82-2.89 (1 H, m, CH), 3.62-3.67 (4 H, m, CH), 3.79 (2 H, s, CH_2), 7.10-7.16 (2 H, m, ArH), 7.77-7.85 (4 H, m, ArH), 7.95 (1 H, d, ArH), 8.06 (1 H, d, ArH, 8.26 (1 H, d, NH), 8.78 (1 H, d, ArH), 10.11 (1 H, s, NH).
342	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.66 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.81-2.90 (1 H, m, CH), 4.75 (2 H, d, CH_2), 5.65 (1 H, t, OH), 7.11 (1 H, d, ArH), 7.14 (1 H, dd, ArH), 7.83 (4 H, s, ArH), 7.94 (1 H, dd, ArH), 8.06 (1 H, d, ArH), 8.27 (1 H, d, NH), 8.78 (1 H, dd, ArH), 10.11 (1 H, s, NH).
343	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.58-0.64 (2 H, m, CH), 0.70-0.75 (2 H, m, CH), 2.86 (1 H, m, CH), 4.35 (4 H, s, CH_2), 6.05 (2 H, m, ArH), 6.89 (2 H, m, ArH), 7.11-7.20 (3 H, m, ArH), 7.79-7.88 (5 H, m, ArH), 8.16 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.81 (1 H, dd, ArH), 10.10 (1 H, s, NH).
344	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 4.35-4.46 (4 H, m, CH_2), 6.95 (1 H, s, ArH), 7.11-7.19 (3 H, m, ArH), 7.31 (1 H, s, ArH), 7.74-7.87 (6 H, m, ArH), 8.16 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.81 (1 H, dd, ArH), 10.09 (1 H, s, NH).
345	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.55-0.64 (2 H, m, CH), 0.65-0.76 (2 H, m, CH), 1.91-2.04 (2 H, m, CH_2), 2.27 (2 H, t, CH_2), 2.80-2.89 (1 H, m, CH), 3.52 (2 H, t, CH_2), 3.62 (2 H, t, CH_2), 4.21 (2 H, t, CH_2), 7.11-7.18 (3 H, m, ArH), 7.74-7.87 (5 H, m, ArH), 8.16 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.81 (1 H, dd, ArH), 10.10 (1 H, s, NH).
346	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.19 (3 H, s, CH_3), 7.20 (1 H, dd, ArH), 7.31 (1 H, dd, ArH), 7.79 (1 H, dd, ArH), 7.90 (2 H, d, ArH), 7.99-8.09 (3 H, m, ArH), 8.21 (1 H, dd, ArH), 8.83 (1 H, dd, ArH), 10.46 (1 H, s, NH).

GAL-113-WO-PCT

Cpd #	(δ) NMR data
347	^{1}H NMR δ (ppm)(DMSO-d$_6$): 2.59 (3 H, s, CH_3), 3.19 (3 H, s, CH_3), 7.00 (1 H, d, ArH), 7.17 (1 H, ArH), 7.86-7.96 (3 H, m, ArH), 7.98-8.06 (3 H, m, ArH), 8.78 (1 H, d, ArH), 10.44 (1 H, s, NH).
348	^{1}H NMR δ (ppm)(DMSO-d$_6$): 3.20 (3 H, s, CH_3), 7.26 (1 H, dd, ArH), 7.45-7.51 (2 H, m, ArH), 7.93 (2 H, d, ArH), 7.97-8.13 (5 H, m, ArH), 8.66 (1 H, s, ArH), 8.92 (1 H, d, ArH), 10.55 (1 H, s, NH).
349	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.57-0.62 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 1.41 (3 H, d, CH_3), 2.59 (2 H, m, CH), 2.81-2.89 (1 H, m, CH), 2.92 (1 H, d, CH), 3.06 (1 H, d, CH), 3.17 (2 H, m, CH), 3.60 (1 H, q, CH), 7.19 (1 H, dd, ArH), 7.51 (2 H, d, ArH), 7.74-7.86 (5 H, m, ArH and NH), 7.89 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.86 (1 H, dd, ArH), 10.10 (1 H, s, NH).
350	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.40 (3 H, d, CH_3), 1.99 (3 H, s, CH_3), 2.29-2.49 (4 H, m, CH), 2.85 (1 H, m, ArH), 3.41-3.48 (4 H, m, CH), 3.57 (1 H, q, CH), 7.18 (1 H, dd, ArH), 7.49 (2 H, d, ArH), 7.77 (2 H, d, ArH), 7.82 (2 H, d, ArH), 7.88 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.26 (1 H, d, NH), 8.85 (1 H, dd, ArH), 10.10 (1 H, s, NH).
351	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.48-0.54 (2 H, m, CH), 0.60-0.68 (2 H, m, CH), 1.51 (6 H, s, CH_3), 2.69-2.76 (1 H, m, CH), 3.76-3.92 (1 H, m, CH), 4.00-4.17 (1 H, m, CH), 4.21-4.35 (1 H, m, CH), 4.53 (2 H, m CH), 5.75 (1 H, d, OH), 7.01 (2 H, d, ArH), 7.13-7.20 (1 H, m, ArH), 7.64 (2 H, d, ArH), 7.76-7.88 (3 H, m, ArH), 8.10-8.21 (3 H, m, ArH and NH), 8.81 (1 H, d, ArH), 10.13 (1 H, s, NH).
352	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.61 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 2.82-2.88 (1 H, m, CH), 3.27 (2 H, t, CH_2), 4.45-4.53 (2 H, m, CH_2), 7.11-7.19 (3 H, m, ArH), 7.30 (1 H, ddd, ArH), 7.44 (1 H, d, ArH), 7.75-7.86 (6 H, m, ArH), 8.15 (2 H, d, ArH), 8.24 (1 H, d, NH), 8.55-8.58 (1 H, m, ArH), 8.80 (1 H, dd, ArH), 10.09 (1 H, s, NH).
353	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.47-0.72 (2 H, m, CH), 0.69-0.75 (2 H, m, CH), 2.76-2.94 (1 H, m, CH), 3.14 (2 H, t, CH_2), 4.35 (2 H, t, CH_2), 7.10-7.18 (3 H, m, ArH), 7.39 (1 H, dd, ArH), 7.75-7.85 (6 H, m, ArH), 8.15 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.49 (1 H, d, ArH), 8.61 (1 H, s, ArH), 8.80 (1 H, d, ArH), 10.09 (1 H, s, NH).
354	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.66 (2 H, m, CH), 0.68-0.75 (2 H, m, CH), 1.70-1.77 (4 H, m, CH), 2.52-2.55 (4 H, m, CH), 2.81-2.88 (3 H, m, CH and CH_2), 4.18 (2 H, t, CH_2), 7.10-7.20 (3 H, m, ArH), 7.75-7.86 (5 H, m, ArH), 8.16 (2 H, d, ArH), 8.25 (1 H, d, NH), 8.80 (1 H, dd, ArH), 10.10 (1 H, s, NH).

Cpd #	(δ) NMR data
355	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.98-1.03 (4 H, m, CH), 2.70-2.76 (1 H, m, CH), 6.92 (1 H, t, ArH), 7.14 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.40 (2 H, d, ArH), 7.75 (2 H, d, ArH), 7.84 (1 H, dd, ArH), 8.16 (2 H, d, ArH), 8.80 (1 H, dd, ArH), 9.73 (1 H, s, NH), 10.00 (1 H, br s, NH).
356	δH(400 MHz; DMSO-d$_6$): 1.94 (3 H, s, CH_3), 4.36 (2 H, d, CH_2), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.43 (2 H, d, ArH), 7.73-7.76 (2 H, m, ArH), 7.85 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.45 (1 H, br t, NH), 8.82 (1 H, dd, ArH), 9.75 (1 H, s, NH)
357	δH(400 MHz; DMSO-d$_6$): 4.48 (2 H, s, CH_2), 6.92 (1 H, dd, ArH), 7.16 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.47 (2 H, d, ArH), 7.72-7.77 (2 H, m, ArH), 7.86 (1 H, dd, ArH), 8.12-8.19 (2 H, d, ArH), 8.83 (1 H, dd, ArH), 9.76 (1 H, s, NH), 10.12 (1 H, s, NH)
358	δH(400 MHz; DMSO-d$_6$): 4.60 (2 H, d, CH_2), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.32 (2 H, dd, ArH), 7.49-7.62 (5 H, m, ArH), 7.74 (2 H, d, ArH), 7.84 (1 H, dd, ArH), 7.96 (2 H, d, ArH), 8.13 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.15 (1 H, t, NH), 9.73 (1 H, s, NH)
359	δH(400 MHz; DMSO-d$_6$): 3.50-3.54 (2 H, m, CH), 3.51-3.67 (6 H, m, CH), 3.84 (2 H, s, CH_2), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.41 (2 H, d, ArH), 7.75 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.12 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.75 (1 H, s, NH)
360	δH(400 MHz; DMSO-d$_6$): 3.08-3.26 (2 H, m, CH), 3.15-3.35 (2 H, m, CH), 3.90-4.02 (6 H, m, CH), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.42 (2 H, d, ArH), 7.75 (2 H, d, ArH), 7.86 (1 H, dd, ArH), 8.13 (2 H, d, ArH), 8.82 (1 H, dd, ArH), 9.76 (1 H, s, NH)
361	δH(400 MHz; DMSO-d$_6$): 1.08 (6 H, s, CH_3), 3.08 (2 H, d, CH_2), 3.59 (2 H, s, CH_2), 4.50 (1 H, s, OH), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.46 (2 H, d, ArH), 7.75 (2 H, d, ArH), 7.85 (1 H, dd, ArH), 7.99 (1 H, br t, NH), 8.11 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.76 (1 H, s, NH)
362	δH(400 MHz; DMSO-d$_6$): 2.63 (3 H, d, CH_3), 3.51 (2 H, s, CH_2), 6.92 (1 H, dd, ArH), 7.15 (1 H, dd, ArH), 7.33 (2 H, dd, ArH), 7.43 (2 H, d, ArH), 7.75 (2 H, dd, ArH), 7.84 (1 H, dd, ArH), 8.00-8.07 (1 H, m, NH), 8.10 (2 H, d, ArH), 8.81 (1 H, dd, ArH), 9.75 (1 H, s, NH)

Cpd #	(δ) NMR data
363	^{1}H NMR δ (ppm)(DMSO-d$_6$): 0.56-0.62 (2 H, m, CH), 0.67-0.74 (2 H, m, CH), 2.81-2.88 (1 H, m, CH), 3.03 (3 H, s, CH_3), 3.08 (3 H, s, CH_3), 7.32 (1 H, dd, ArH), 7.63-7.83 (8 H, m, ArH), 8.16 (2 H, d, ArH), 8.23 (1 H, d, NH), 10.03 (1 H, s, NH).

Biological Examples

Example 1 – *in vitro* assays

Example 1.1 JAK1 inhibition assay

1.1.1 Assay 1

[00753] Recombinant human JAK1 (catalytic domain, amino acids 850-1154; catalog number 08-144) was purchased from Carna Biosciences. 10 ng of JAK1 was incubated with 12.5 µg polyGT substrate (Sigma catalog number P0275) in kinase reaction buffer (15 mM Tris-HCl pH 7.5, 1 mM DTT, 0.01% Tween-20, 10 mM $MgCl_2$, 2 µM non-radioactive ATP, 0.25 µCi 33P-gamma-ATP (GE Healthcare, catalog number AH9968) final concentrations) with or without 5µL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 25 µL, in a polypropylene 96-well plate (Greiner, V-bottom). After 45 min at 30 °C, reactions were stopped by adding of 25 µL/well of 150 mM phosphoric acid. All of the terminated kinase reaction was transferred to prewashed (75 mM phosphoric acid) 96 well filter plates (Perkin Elmer catalog number 6005177) using a cell harvester (Perkin Elmer). Plates were washed 6 times with 300 µL per well of a 75 mM phosphoric acid solution and the bottom of the plates was sealed. 40 µL/well of Microscint-20 was added, the top of the plates was sealed and readout was performed using the Topcount (Perkin Elmer). Kinase activity was calculated by subtracting counts per minute (cpm) obtained in the presence of a positive control inhibitor (10 µM staurosporine) from cpm obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00754] Percentage inhibition = ((cpm determined for sample with test compound present – cpm determined for sample with positive control inhibitor) divided by (cpm determined in the presence of vehicle – cpm determined for sample with positive control inhibitor)) * 100%.

[00755] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the JAK1 assay and the calculation of the IC_{50} for each compound. Each compound was routinely tested at concentration of 20µM followed by a 1/3 serial dilution, 8 points (20µM - 6.67µM - 2.22µM - 740nM - 247nM - 82nM - 27nM - 9nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration were lowered (e.g. 5 µM, 1 µM).

[00756] Semi-quantitative score:

* > 1001 nM

** 501-1000 nM

*** 101-500 nM

**** 0.01-100 nM

[00757] **TABLE IIIa: JAK1 IC_{50} Values of Compounds determined using Assay 1.1.1**

Cpd #	JAK1
1	****
2	****
3	****
4	****
5	****
6	****
7	****
8	****
9	****
10	***
11	****
12	****
13	*
14	**
15	****
16	****
17	****
18	****
19	****
20	***
21	****
22	****
23	**
24	****
25	****
26	****
27	****
28	****
29	***
30	****
31	****
32	***
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47	****
48	***
49	****
50	****
51	***
52	***
53	****
54	****
55	****
56	****
57	****
58	****
59	****
60	****
61	***
62	***
63	***
64	****
65	****
66	****

Cpd #	JAK1
67	****
68	***
69	****
70	****
71	****
72	***
73	****
74	****
75	****
76	**
77	****
78	****
79	****
80	****
81	****
82	***
83	****
84	****
85	****
86	****
87	****
88	****
89	****
90	****
91	***
92	***
93	****
94	****
96	****
97	****
98	***
99	****
100	****
101	****
103	****
104	****

Cpd #	JAK1
105	****
106	***
107	***
108	*
109	****
110	****
111	****
112	****
113	****
114	****
115	****
116	****
117	****
118	****
119	****
120	****
121	****
122	****
123	****
124	***
125	****
126	****
127	****
128	***
129	***
130	****
131	****
132	****
133	****
135	****
136	****
137	***
138	****
139	****
140	****
141	***

Cpd #	JAK1
142	****
143	***
144	****
145	****
146	****
147	****
148	****
149	****
150	****
151	****
152	****
153	****
154	****
155	****
156	****
157	***
158	****
160	****
161	****
162	****
163	***
164	****
165	****
166	****
167	****
168	****
169	****
170	****
171	****
172	****
173	****
174	****
175	****
176	****
177	****
178	****

Cpd #	JAK1
179	****
180	****
181	****
182	****
183	****
184	****
185	****
186	****
187	****
188	****
189	****
190	****
191	****
192	****
193	****
194	****
195	****
196	****
197	****
198	****
199	****
200	****
201	***
202	****
203	****
204	****
205	****
206	****
207	****
208	****
209	****
210	****
211	****
212	****
213	****
214	****

Cpd #	JAK1
215	****
216	****
217	****
218	***
219	****
220	****
221	****
222	****
223	****
224	****
225	****
226	****
227	****
228	****
229	****
230	****
231	****
232	****
233	****
234	****
235	****
236	****
237	****
238	****
239	****
240	****
241	****
242	****
243	****
244	****
245	****
246	****
247	****
248	****
249	****
251	****

Cpd #	JAK1
252	****
253	****
254	****
255	****
256	****
257	****
258	*
259	*
260	****
261	****
262	****
263	****
264	****
265	****
270	****
271	****
272	****
273	****
274	****
275	****
276	****
277	****
278	****
279	****
280	****
281	****
282	****
283	****
284	****
285	****
286	****
287	****
288	****
289	****
290	****
291	****

Cpd #	JAK1
292	****
293	****
294	****
295	****
296	****
297	****
298	****
299	****
300	****
301	****
302	****
303	****
304	****
305	*
306	**
308	****
309	****

Cpd #	JAK1
310	****
311	****
312	****
313	****
314	****
315	****
316	****
317	***
318	****
319	****
320	****
321	****
322	****
323	****
324	****
325	****
326	****

1.1.2 Assay 2

[00758] Recombinant human JAK1 (catalytic domain, amino acids 866-1154; catalog number PV4774) was purchased from Invitrogen. 1 ng of JAK1 was incubated with 20 nM Ulight-JAK1(tyr1023) peptide (Perkin Elmer catalog number TRF0121) in kinase reaction buffer (25mM MOPS pH6.8, 0.016% Brij-35, 8.33mM MgCl2, 3.33mM DTT, 7μM ATP) with or without 4μL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 20 μL, in a white 384 Luminotrac 200 plate (Greiner, catalog number 781075). After 60 min at room temperature, reactions were stopped by adding of 20 μL/well of detection mixture (1xdetection buffer (Perkin Elmer, catalog number CR97-100C), 0.5nM Europium-anti-phosphotyrosine (PT66) (Perkin Elmer, catalog number AD0068), 10 mM EDTA). Readout was performed using the Envision with excitation at 320nm and measuring emission at 615 nm (Perkin Elmer). Kinase activity was calculated by subtracting relative fluorescence units (RFU) obtained in the presence of a positive control inhibitor (10 μM staurosporine) from RFU obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00759] Percentage inhibition = 1- ((RFU determined for sample with test compound present – RFU determined for sample with positive control inhibitor) divided by (RFU determined in the presence of vehicle – RFU determined for sample with positive control inhibitor)) * 100.

[00760] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the JAK1 assay and the calculation of the IC50 for each compound. Each compound

was routinely tested at concentration of 20μM followed by a 1/5 serial dilution, 8 points (20μM - 4μM – 800nM – 160nM – 32nM – 6.4nM – 1.28nM – 0.26nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration were lowered (e.g. 5 μM, 1 μM).

[00761] Semi-quantitative score:

* > 1001 nM

** 501-1000 nM

*** 101-500 nM

**** 0.01-100 nM

[00762] **TABLE IIIb: JAK1 IC_{50} Values of Compounds determined using Assay 1.1.2**

Cpd #	JAK1
327	****
328	***
329	****
330	****
331	****
332	***
333	***
334	****
352	****
353	****
354	****
355	****
356	****
357	****
358	***
359	****
360	****
361	****

Example 1.2 JAK2 inhibition assay

1.2.1 Assay 1

[00763] Recombinant human JAK2 (catalytic domain, amino acids 808-1132; catalog number PV4210) was purchased from Invitrogen. 0.025mU of JAK2 was incubated with 2.5 μg polyGT substrate (Sigma catalog number P0275) in kinase reaction buffer (5 mM MOPS pH 7.5, 9 mM MgAc, 0.3mM EDTA, 0.06% Brij and 0.6 mM DTT, 1 μM non-radioactive ATP, 0.25 μCi 33P-gamma-ATP

(GE Healthcare, catalog number AH9968) final concentrations) with or without 5μL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 25 μL, in a polypropylene 96-well plate (Greiner, V-bottom). After 90 min at 30 °C, reactions were stopped by adding of 25 μL/well of 150 mM phosphoric acid. All of the terminated kinase reaction was transferred to prewashed (75 mM phosphoric acid) 96 well filter plates (Perkin Elmer catalog number 6005177) using a cell harvester (Perkin Elmer). Plates were washed 6 times with 300 μL per well of a 75 mM phosphoric acid solution and the bottom of the plates was sealed. 40 μL/well of Microscint-20 was added, the top of the plates was sealed and readout was performed using the Topcount (Perkin Elmer). Kinase activity was calculated by subtracting counts per minute (cpm) obtained in the presence of a positive control inhibitor (10 μM staurosporine) from cpm obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00764] Percentage inhibition = ((cpm determined for sample with test compound present – cpm determined for sample with positive control inhibitor) divided by (cpm determined in the presence of vehicle – cpm determined for sample with positive control inhibitor)) * 100%.

[00765] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the JAK2 assay and the calculation of the IC_{50} for each compound. Each compound was routinely tested at concentration of 20μM followed by a 1/3 serial dilution, 8 points (20μM - 6.67μM - 2.22μM - 740nM - 247nM - 82nM - 27nM - 9nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration was lowered (e.g. 5 μM, 1 μM).

[00766] Semi-quantitative score:

\# > 1001 nM
501-1000 nM
101-500 nM
0.01-100 nM

[00767] **TABLE IVa: JAK2 IC_{50} Values of Compounds**

Cpd #	JAK2
1	####
2	####
3	####
4	####
5	####
6	####
7	####
8	####
9	####
10	####

Cpd #	JAK2
11	####
12	####
13	#
14	###
15	####
16	####
17	####
18	####
19	####
20	####

Cpd #	JAK2
21	####
22	####
23	##
24	###
25	####
26	####
27	####
28	####
29	####
30	####
31	####
32	###
33	####
34	###
35	####
36	####
37	####
38	####
39	####
40	####
41	####
42	####
43	####
44	###
45	####
46	###
47	####
48	####
49	####
50	####
51	####
52	###
53	####
54	####
55	####
56	####

Cpd #	JAK2
57	####
58	####
59	####
60	####
61	####
62	####
63	####
64	####
65	####
66	####
67	####
68	###
69	####
70	####
71	####
72	####
73	####
74	####
75	####
76	####
77	####
78	####
79	####
80	####
81	####
82	####
83	####
84	####
85	####
86	####
87	####
88	####
89	####
90	####
91	###
92	####

Cpd #	JAK2
93	####
94	####
96	####
97	####
98	####
99	####
100	####
101	####
103	####
104	####
105	####
106	####
107	####
108	###
109	####
110	####
111	####
112	####
113	####
114	####
115	####
116	####
117	####
118	####
119	####
120	####
121	####
122	####
123	####
124	####
125	####
126	####
127	####
128	####
129	####
130	####

Cpd #	JAK2
131	####
132	####
133	####
135	####
136	####
137	####
138	####
139	####
140	####
141	###
142	####
143	####
144	####
145	####
146	####
147	####
148	####
149	####
150	####
151	####
152	####
153	####
154	####
155	####
156	####
157	####
158	####
160	####
161	####
162	####
163	####
164	####
165	####
166	####
167	####
168	####

Cpd #	JAK2
169	####
170	####
171	####
172	####
173	####
174	####
175	####
176	####
177	####
178	####
179	####
180	####
181	####
182	####
183	####
184	####
185	####
186	####
187	####
188	####
189	####
190	####
191	####
192	####
193	####
194	####
195	####
196	####
197	####
198	####
199	####
200	####
201	####
202	####
203	####
204	####

Cpd #	JAK2
205	####
206	####
207	####
208	####
209	####
210	####
211	####
212	####
213	####
214	####
215	####
216	####
217	####
218	####
219	####
220	####
221	####
222	####
223	####
224	####
225	####
226	####
227	####
228	####
229	####
230	####
231	####
232	####
233	####
234	####
235	####
236	####
237	####
238	####
239	####
240	####

Cpd #	JAK2
241	####
242	####
243	####
244	####
245	####
246	####
247	####
248	####
249	####
251	####
252	####
253	####
254	####
255	####
256	####
257	####
258	###
259	###
260	####
261	####
262	####
263	####
264	####
265	####
270	####
271	####
272	####
273	####
274	####
275	####
276	####
277	####
278	####
279	####
280	####
281	####

Cpd #	JAK2
282	####
283	####
284	####
285	####
286	####
287	####
288	####
289	####
290	####
291	####
292	####
293	####
294	####
295	####
296	####
297	####
298	####
299	####
300	####
301	####
302	####
303	####
304	####
305	####
306	####
308	####
309	####
310	####
311	####
312	####
313	####
314	####
315	####
316	####
317	####
318	####

Cpd #	JAK2
319	####
320	####
321	####
322	####

Cpd #	JAK2
323	####
324	####
325	####
326	####

1.2.2 Assay 2

[00768] Recombinant human JAK2 (catalytic domain, amino acids 866-1154; catalog number PV4210) was purchased from Invitrogen. 0.0125mU of JAK2 was incubated with 25 nM Ulight-JAK1(tyr1023) peptide (Perkin Elmer catalog number TRF0121) in kinase reaction buffer (41.66mM HEPES pH7.0, 0.016% Triton X-100, 12.5mM MgCl2 , 3.33mM DTT, 7.5μM ATP) with or without 4μL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 20 μL, in a white 384 Luminotrac 200 plate (Greiner, catalog number 781075). After 60 min at room temperature, reactions were stopped by adding of 20 μL/well of detection mixture (1xdetection buffer (Perkin Elmer, catalog number CR97-100C), 0.5nM Europium-anti-phosphotyrosine (PT66) (Perkin Elmer, catalog number AD0068), 10 mM EDTA). Readout was performed using the Envision with excitation at 320nm and measuring emission at 615 nm (Perkin Elmer). Kinase activity was calculated by subtracting relative fluorescence units (RFU) obtained in the presence of a positive control inhibitor (10 μM staurosporine) from RFU obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00769] Percentage inhibition = 1- ((RFU determined for sample with test compound present – RFU determined for sample with positive control inhibitor) divided by (RFU determined in the presence of vehicle – RFU determined for sample with positive control inhibitor)) * 100.

[00770] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the JAK1 assay and the calculation of the IC50 for each compound. Each compound was routinely tested at concentration of 20μM followed by a 1/5 serial dilution, 8 points (20μM - 4μM – 800nM – 160nM – 32nM – 6.4nM – 1.28nM – 0.26nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration were lowered (e.g. 5 μM, 1 μM).

[00771] Semi-quantitative score:

* > 1001 nM

** 501-1000 nM

*** 101-500 nM

**** 0.01-100 nM

[00772] **TABLE IIIb: JAK1 IC_{50} Values of Compounds determined using Assay 1.2.2**

Cpd #	JAK1

Cpd #	JAK1
327	####
328	####
329	####
330	####
331	####
332	####
333	####
334	####
335	####
336	####
338	####
339	####
340	####
341	####
342	####
343	####
344	####
346	####
347	####
348	####
349	####
350	####
351	####
352	####
353	####
354	####
355	####
356	####
357	####
358	####
359	####
360	####
361	####
362	####

Example 1.3 JAK3 inhibition assay

[00773] Recombinant human JAK3 (catalytic domain, amino acids 781-1124; catalog number PV3855) was purchased from Invitrogen. 0.025mU of JAK3 was incubated with 2.5 µg polyGT substrate (Sigma catalog number P0275) in kinase reaction buffer (25 mM Tris pH 7.5, 0.5 mM EGTA, 0.5 mM Na3VO4, 5 mM b-glycerolphosphate, 0.01% Triton X-100, 1 µM non-radioactive ATP, 0.25 µCi 33P-gamma-ATP (GE Healthcare, catalog number AH9968) final concentrations) with or without 5µL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 25 µL, in a polypropylene 96-well plate (Greiner, V-bottom). After 105 min at 30 °C, reactions were stopped by adding of 25 µL/well of 150 mM phosphoric acid. All of the terminated kinase reaction was transferred to prewashed (75 mM phosphoric acid) 96 well filter plates (Perkin Elmer catalog number 6005177) using a cell harvester (Perkin Elmer). Plates were washed 6 times with 300 µL per well of a 75 mM phosphoric acid solution and the bottom of the plates was sealed. 40 µL/well of Microscint-20 was added, the top of the plates was sealed and readout was performed using the Topcount (Perkin Elmer). Kinase activity was calculated by subtracting counts per minute (cpm) obtained in the presence of a positive control inhibitor (10 µM staurosporine) from cpm obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00774] Percentage inhibition = ((cpm determined for sample with test compound present – cpm determined for sample with positive control inhibitor) divided by (cpm determined in the presence of vehicle – cpm determined for sample with positive control inhibitor)) * 100%.

[00775] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the JAK3 assay and the calculation of the IC_{50} for each compound. Each compound was routinely tested at concentration of 20µM followed by a 1/3 serial dilution, 8 points (20µM - 6.67µM - 2.22µM - 740nM - 247nM - 82nM - 27nM - 9nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration was lowered (e.g. 5 µM, 1 µM).

[00776] Semi-quantitative score:

+> 1001 nM
++ 501-1000 nM
+++ 101-500 nM
++++ 0.01-100 nM
N/A – not available

[00777] **TABLE V: JAK3 IC_{50} Values of Compounds**

Cpd #	JAK3
1	++
2	++
3	++++
4	++
5	+++

Cpd #	JAK3
6	++++
7	+++
11	++++
12	+++
18	++++

Cpd #	JAK3
19	++++
21	++++
22	++++
25	++++
33	+++
35	++++
38	++++
39	++++
40	++++
43	++++
57	++++
58	++++
64	++++
65	++++
83	++++
85	++++
86	++++
101	++++
104	++++
113	++++
142	++++
162	++++
183	++++
184	++++
203	++++
204	++++
206	++++
211	++++
218	++++
220	++++
221	++++

Cpd #	JAK3
230	++++
235	++++
236	++++
237	++++
238	++++
239	++++
240	++++
241	++++
242	++++
243	++++
244	++++
245	++++
246	++++
247	++++
251	++++
252	++++
270	++++
271	++++
272	++++
273	++++
274	++++
275	++++
276	++++
277	++++
278	++++
279	++++
280	++++
281	++++
282	++++
283	++++

Example 1.4 TYK2 inhibition assay

[00778] Recombinant human TYK2 (catalytic domain, amino acids 871-1187; catalog number 08-147) was purchased from Carna biosciences. 5 ng of TYK2 was incubated with 12.5 µg polyGT substrate (Sigma catalog number P0275) in kinase reaction buffer (25 mM Hepes pH 7.5, 100 mM

NaCl, 0.2 mM Na3VO4, 0.1% NP-40, 0.1 µM non-radioactive ATP, 0.125 µCi 33P-gamma-ATP (GE Healthcare, catalog number AH9968) final concentrations) with or without 5µL containing test compound or vehicle (DMSO, 1% final concentration), in a total volume of 25 µL, in a polypropylene 96-well plate (Greiner, V-bottom). After 90 min at 30 °C, reactions were stopped by adding of 25 µL/well of 150 mM phosphoric acid. All of the terminated kinase reaction was transferred to prewashed (75 mM phosphoric acid) 96 well filter plates (Perkin Elmer catalog number 6005177) using a cell harvester (Perkin Elmer). Plates were washed 6 times with 300 µL per well of a 75 mM phosphoric acid solution and the bottom of the plates was sealed. 40 µL/well of Microscint-20 was added, the top of the plates was sealed and readout was performed using the Topcount (Perkin Elmer). Kinase activity was calculated by subtracting counts per minute (cpm) obtained in the presence of a positive control inhibitor (10 µM staurosporine) from cpm obtained in the presence of vehicle. The ability of a test compound to inhibit this activity was determined as:

[00779] Percentage inhibition = ((cpm determined for sample with test compound present – cpm determined for sample with positive control inhibitor) divided by (cpm determined in the presence of vehicle – cpm determined for sample with positive control inhibitor)) * 100%.

[00780] Dose dilution series were prepared for the compounds enabling the testing of dose-response effects in the TYK2 assay and the calculation of the IC_{50} for each compound. Each compound was routinely tested at concentration of 20µM followed by a 1/3 serial dilution, 8 points (20µM - 6.67µM - 2.22µM - 740nM - 247nM - 82nM - 27nM - 9nM) in a final concentration of 1% DMSO. When potency of compound series increased, more dilutions were prepared and/or the top concentration was lowered (e.g. 5 µM, 1 µM).

[00781] Semi-quantitative score:

- > 1001 nM
--501-1000 nM
--- 101-500 nM
---- 0.01-100 nM
N/A – not available

[00782] **TABLE VI: TYK2 IC_{50} Values of Compounds**

Cpd #	TYK2
1	-
2	-
3	--
4	--
5	--
6	---
11	-
12	-

Cpd #	TYK2
18	--
19	-
21	----
22	-
25	-
33	-
35	---
38	-

Cpd #	TYK2
39	--
40	---
43	--
57	---
58	---
64	---
65	---
83	----
85	----
86	----
94	---
101	----
104	---
113	---
123	---
125	---
126	----
127	----
131	---
132	----
133	---
136	---
142	---
162	----
184	----
203	---
204	----
206	----
235	----
236	----
237	----
238	----
239	----
240	----
241	----
242	----

Cpd #	TYK2
243	----
244	----
245	----
246	----
247	----
251	----
252	----
270	----
271	----
272	----
273	----
274	----
275	----
276	----
277	----
278	----
279	----
280	----
281	----
282	----
283	----
83	----
85	----
86	----
94	---
101	----
104	---
113	---
123	---
125	---
126	----
127	----
131	---
132	----
133	---
136	---

Cpd #	TYK2
142	---
162	----
184	----
203	---
204	----
206	----
235	----
236	----
237	----
238	----
239	----
240	----
241	----
242	----
243	----
244	----
245	----
246	----

Cpd #	TYK2
247	----
251	----
252	----
270	----
271	----
272	----
273	----
274	----
275	----
276	----
277	----
278	----
279	----
280	----
281	----
282	----
283	----

Example 2. Cellular assays

Example 2.1 JAK-STAT signalling assay:

[00783] HeLa cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM) containing 10% heat inactivated fetal calf serum, 100 U/mL penicillin and 100 µg/mL streptomycin. HeLa cells were used at 70 % confluence for transfection. 20,000 cells in 87 µL cell culture medium were transiently transfected with 40 ng pSTAT1(2)-luciferase reporter (Panomics), 8 ng of LacZ reporter as internal control reporter and 52 ng of pBSK using 0.32 µL Jet-PEI (Polyplus) as transfection reagent per well in 96-well plate format. After overnight incubation at 37°C, 10% CO_2, transfection medium was removed. 75 µL of DMEM + 1.5% heat inactivated fetal calf serum was added. 15 µL of compound at 6.7x concentration was added for 60 min and then 10 µL of human OSM (Peprotech) at 33 ng/mL final concentration.

[00784] All compounds were tested in duplicate starting from 20 µM followed by a 1/3 serial dilution, 8 doses in total (20 µM – 6.6 µM – 2.2 µM – 740 nM – 250 nM – 82 nM – 27 nM – 9 nM) in a final concentration of 0.2% DMSO.

[00785] After overnight incubation at 37°C, 10% CO_2 cells were lysed in 100 µL lysis buffer/well (PBS, 0.9 mM $CaCl_2$, 0.5 mM MgCl2, 5% Trehalose, 0.025% Tergitol NP9, 0.15% BSA).

[00786] 40 µL of cell lysate was used to read □-galactosidase activity by adding 180 µL βGal solution (30µl ONPG 4mg/mL + 150 µL □-Galactosidase buffer (0.06 M Na_2HPO_4, 0.04 M NaH_2PO_4, 1

mM $MgCl_2$)) for 20 min. The reaction was stopped by addition of 50 µL Na_2CO_3 1 M. Absorbance was read at 405 nm.

[00787] Luciferase activity was measured using 40 µL cell lysate plus 40 µl of Steadylite® as described by the manufacturer (Perkin Elmer), on the Envision (Perkin Elmer).

[00788] 10 µM of a pan-JAK inhibitor was used as a positive control (100% inhibition). As negative control 0.5% DMSO (0% inhibition) was used. The positive and negative controls were used to calculate z' and 'percent inhibition' (PIN) values.

[00789] Percentage inhibition = ((fluorescence determined in the presence of vehicle - fluorescence determined for sample with test compound present) divided by (fluorescence determined in the presence of vehicle – fluorescence determined for sample without trigger)) * 100 %.

[00790] PIN values were plotted for compounds tested in dose-response and EC_{50} values were derived.

[00791] **TABLE VII: STAT signalling EC_{50} Values of Compounds**

* > 1001 nM

**501-1000 nM

*** 101-500 nM

**** 1- 100 nM

Cpd #	EC_{50} (nM)
1	**
2	*
3	**
4	***
5	**
6	***
7	**
8	***
9	*
11	**
12	**
15	*
16	**
17	*
18	***
19	***

Cpd #	EC_{50} (nM)
21	***
22	***
24	*
25	***
26	*
27	**
28	**
30	*
31	*
33	***
35	***
37	*
38	***
39	***
40	**
41	**

Cpd #	EC_{50} (nM)
42	*
43	**
45	**
47	*
49	*
50	*
53	*
54	**
55	*
56	**
57	***
58	***
59	***
60	**
64	*
65	*
66	***
67	**
70	***
71	**
73	***
74	*
75	***
77	****
78	***
79	***
80	**
81	**
83	****
84	****
85	****
86	****

Cpd #	EC_{50} (nM)
87	***
88	*
89	*
90	****
93	***
94	*
96	*
97	*
99	**
100	**
101	***
103	****
104	***
105	****
109	***
110	**
111	**
112	***
113	***
114	**
115	***
116	***
117	***
118	***
119	***
120	*
121	**
122	***
123	***
125	*
126	*
127	****

Cpd #	EC_{50} (nM)
130	**
131	***
132	*
133	*
135	***
136	*
138	*
139	****
140	*
142	*
144	***
145	*
146	***
147	***
148	*
149	**
150	*
151	***
152	*
153	*
154	**
155	*
156	***
158	***
160	****
161	****
162	***
164	***
165	*
166	*
167	***
168	***

Cpd #	EC_{50} (nM)
169	***
170	***
171	***
172	***
173	*
174	****
175	**
176	*
177	****
178	****
179	*
180	****
181	***
182	***
183	****
184	****
185	***
186	*
187	*
188	**
189	*
190	***
191	***
192	***
193	*
194	*
195	*
196	*
197	***
198	***
199	**
200	*

Cpd #	EC_{50} (nM)
202	***
203	***
204	***
205	**
206	***
207	*
209	**
210	***
211	***
212	***
213	***
214	**
215	**
216	***
217	***
218	**
219	***
220	***
221	****
222	**
223	***
224	***
225	***
226	*
227	***
228	****
229	****
230	****
231	**
232	***
233	**
234	***

Cpd #	EC_{50} (nM)
235	**
236	***
237	***
238	****
239	****
240	***
241	****
242	****
243	***
244	***
245	****
246	****
247	***
248	**
249	*
251	****
252	**
253	****
254	***
255	***
256	***
257	****
260	***
261	***
262	***
263	***
265	**
270	****
271	****
272	***
273	***
274	***

Cpd #	EC_{50} (nM)
275	*
276	**
277	***
278	***
279	***
280	***
281	***
282	****
283	***
284	***
285	***
286	***
287	***
288	***
289	**
290	***
291	****
292	****
293	**
294	***
295	***
296	*
297	*
298	***

Cpd #	EC_{50} (nM)
299	***
300	*
301	***
302	***
303	*
304	****
308	****
309	*
310	***
311	***
312	**
314	*
315	*
318	****
319	*
320	*
321	**
322	*
323	***
324	**
325	*
326	***

Example 2.2 OSM/IL-1β signaling Assay

[00792] OSM and IL-1β were shown to synergistically upregulate MMP13 levels in the human chondrosarcoma cell line SW1353. The cells were seeded in 96 well plates at 15,000 cells/well in a volume of 120 µL DMEM (Invitrogen) containing 10% (v/v) FBS and 1% penicillin/streptomycin (InVitrogen) incubated at 37°C 5% CO_2. Cells were preincubated with 15 µL compound in M199 medium with 2% DMSO 1 hr before triggering with 15 µL OSM and IL-1β to reach 25 ng/mL OSM and 1 ng/mL IL-1β, and MMP13 levels were measured in conditioned medium 48 hours after triggering.

MMP13 activity was measured using an antibody capture activity assay. For this purpose, 384 well plates (NUNC, 460518, MaxiSorb black) were coated with 35 µL of a 1.5 µg/mL anti-human MMP13 antibody (R&D Systems, MAB511) solution for 24 hours at 4°C. After washing the wells 2 times with PBS + 0.05% Tween, the remaining binding sites were blocked with 100 µL 5% non-fat dry milk (Santa Cruz, sc-2325, Blotto) in PBS for 24 hours at 4°C. Next, the wells were washed 2 times with PBS + 0.05% Tween and 35 µL of 1/10 dilution of culture supernatant containing MMP13 in 100-fold diluted blocking buffer was added and incubated for 4 hours at room temperature. Next the wells were washed twice with PBS + 0.05% Tween followed by MMP13 activation by addition of 35 µL of a 1.5 mM 4-Aminophenylmercuric acetate (APMA) (Sigma, A9563) solution and incubation at 37 °C for 1 hour. The wells were washed again with PBS + 0.05% Tween and 35 µL MMP13 substrate (Biomol, P-126, OmniMMP fluorogenic substrate) was added. After incubation for 24 hours at 37°C fluorescence of the converted substrate was measured in a Perkin Elmer Wallac EnVision 2102 Multilabel Reader (wavelength excitation: 320 nm, wavelength emission: 405 nm).

[00793] Percentage inhibition = ((fluorescence determined in the presence of vehicle - fluorescence determined for sample with test compound present) divided by (fluorescence determined in the presence of vehicle – fluorescence determined for sample without trigger)) * 100 %.

[00794]

* > 1001 nM

**501-1000 nM

*** 1-500 nM

[00795] **TABLE VIII: MMP13 EC_{50} Values of Compounds**

Cpd #	EC_{50} (nM)
1	*
2	*
3	**
4	***
5	**
6	***
7	*
8	*
9	*
11	*
12	*
16	*
18	*

Cpd #	EC_{50} (nM)
19	*
21	***
22	**
24	*
26	*
27	*
28	*
30	*
31	*
33	***
34	*
35	*
38	***

Cpd #	EC_{50} (nM)
39	**
40	*
41	**
43	*
45	*
47	*
52	*
53	**
54	*
55	*
56	*
57	*
58	***
59	***
60	*
65	*
66	*
67	*
70	***
73	***
74	*
75	***
77	***
78	*
80	*
81	*
83	***
84	***
85	***
86	***
87	*
90	***
94	*
96	*
97	*

Cpd #	EC_{50} (nM)
100	*
101	*
103	***
104	**
105	***
110	*
114	*
115	*
116	***
117	*
118	***
119	*
122	*
123	***
125	*
126	*
127	***
130	***
131	***
132	*
133	*
135	***
136	**
137	***
138	***
139	***
140	***
142	***
144	***
146	*
147	*
148	*
149	*
150	*
151	*

Cpd #	EC_{50} (nM)
154	*
155	***
156	***
158	***
160	***
161	***
162	***
164	***
165	*
166	*
167	**
168	***
169	***
170	***
171	***
172	***
173	***
174	***
175	*
176	*
177	***
178	***
179	*
180	***
181	***
182	***
183	***
184	***
185	***
186	*
187	*
188	**
189	*
190	***
191	***

Cpd #	EC_{50} (nM)
192	***
193	*
194	*
195	*
196	**
197	***
198	***
199	***
200	*
202	***
203	***
204	***
205	**
206	***
207	*
208	*
209	***
210	***
211	***
212	***
213	***
215	***
216	***
217	***
218	***
219	**
220	**
221	***
222	***
223	**
224	***
225	***
226	**
227	*
228	**

Cpd #	EC_{50} (nM)
229	**
230	***
231	***
232	***
233	*
234	*
235	*
236	**
237	**
238	**
239	***
240	***
241	***
242	***
243	***
244	***
245	***
246	***
247	***
248	**
249	*
251	***
253	***
254	***
255	***
256	***

Cpd #	EC_{50} (nM)
257	***
261	***
262	***
263	***
264	***
270	*
271	**
272	***
273	***
274	**
275	*
278	***
279	*
280	*
281	*
282	*
283	**
284	***
285	***
286	***
288	***
289	***
290	***
294	***
295	***

Example 2.3 PBL Proliferation assay

[00796] Human peripheral blood lymphocytes (PBL) are stimulated with IL-2 and proliferation measured using a BrdU incorporation assay. The PBL are first stimulated for 72 hrs with PHA to induce IL-2 receptor, fasted for 24 hrs to stop cell proliferation followed by IL-2 stimulation for another 72 hrs (including 24hr BrdU labeling). Cells are preincubated with test compounds 1 hr before IL-2 addition. Cells are cultured in RPMI 1640 containing 10% (v/v) FBS.

Example 3. *In vivo* models

Example 3.1 CIA model

3.1.1 Materials

[00797] Completed Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) were purchased from Difco. Bovine collagen type II (CII), lipopolysaccharide (LPS), and Enbrel were obtained from Chondrex (Isle d'Abeau, France); Sigma (P4252, L'Isle d'Abeau, France), Whyett (25mg injectable syringe, France) Acros Organics (Palo Alto, CA), respectively. All other reagents used were of reagent grade and all solvents were of analytical grade.

3.1.2 Animals

[00798] Dark Agouti rats (male, 7-8 weeks old) were obtained from Harlan Laboratories (Maison-Alfort, France). DBA/1J mice (male, 7 weeks old) were obtained from Centre d'Elevage et de Reproduction JANVIER (CERJ) (Laval, France). Rats and mice were kept on a 12 hours light/dark cycle (0700 - 1900). The temperature was maintained at 22°C, and food and water were provided *ad libitum*.

3.1.3 Collagen induced arthritis (CIA)

[00799] One day before the experiment, CII solution (2 mg/mL) was prepared with 0.05 M acetic acid and stored at 4°C. Just before the immunization, equal volumes of adjuvant (IFA) and CII were mixed by a homogenizer in a pre-cooled glass bottle in an ice water bath. Extra adjuvant and prolonged homogenization might be required if an emulsion is not formed.

[00800] Mice: 0.1 mL of the emulsion was injected intradermally at the base of the tail of each mouse on day 1, a second booster intradermal injection (CII solution at 1 mg/mL in CFA 0.1 mL saline) was performed on day 21. This immunization method was modified from published methods (David D Brand Kary A Latham, & Edward F Rosloniec. Collagen-induced arthritis. Nature Methods 2 (5): 1269-1275, 2007).

[00801] Rat: 0.2 mL of the emulsion was injected intradermally at the base of the tail of each rat on day 1, a second booster intradermal injection (CII solution at 2 mg/mL in CFA 0.1 mL saline) was performed on day 9. This immunization method was modified from published methods (Sims NA *et al.*, (2004) Targeting osteoclasts with zoledronic acid prevents bone destruction in collagen-induced arthritis, Arthritis Rheum. 50 2338-2346; Jou *et al.*, 2005).

3.1.4 Study design

[00802] The therapeutic effects of the test compounds were tested in the rat or mouse CIA model. Animals were randomly divided into equal groups and each group contained 10 animals. All rats were immunized on day 1 and boosted on day 9. All mice were immunized on day 1 and boosted on day 21. Therapeutic dosing lasted from day 16 to day 30. The negative control group was treated with vehicle (MC 0,5%) and the positive control group with Enbrel (10 mg/kg, 3x week., s.c.). A compound of interest was typically tested at 3 doses, e.g. 3, 10, 30 mg/kg, p.o.

3.1.5 Clinical assessment of arthritis

[00803] Arthritis was scored according the method of Khachigian 2006, Lin *et al* 2007 and Nishida *et al.* 2004). The swelling of each of the four paws was ranked with the arthritic score as follows: 0-no symptoms; 1-mild, but definite redness and swelling of one type of joint such as the ankle

or wrist, or apparent redness and swelling limited to individual digits, regardless of the number of affected digits; 2-moderate redness and swelling of two or more types of joints; 3-severe redness and swelling of the entire paw including digits; 4-maximally inflamed limb with involvement of multiple joints (maximum cumulative clinical arthritis score 16 per animal) (Nishida *et al.*, 2004).

3.1.6 Change in body weight (%) after onset of arthritis

[00804] Clinically, body weight loss is associated with arthritis (Shelton *et al.*, 2005; Argiles *et al.*, 1998; Rall, 2004; Walsmith *et a*l., 2004) Hence, changes in body weight after onset of arthritis could be used as a non-specific endpoint to evaluate the effect of therapeutics in the rat model. The change in body weight (%) after onset of arthritis was calculated as follows:

[00805] Mice: $\frac{\text{Body Weight}_{(week6)} - \text{Body Weight}_{(week5)}}{\text{Body Weight}_{(week5)}} \times 100\%$

[00806] Rats: $\frac{\text{Body Weight}_{(week4)} - \text{Body Weight}_{(week3)}}{\text{Body Weight}_{(week3)}} \times 100\%$

3.1.7 Radiology

[00807] X-ray photos were taken of the hind paws of each individual animal. A random blind identity number was assigned to each of the photos, and the severity of bone erosion was ranked by two independent scorers with the radiological Larsen's score system as follows: 0- normal with intact bony outlines and normal joint space; 1- slight abnormality with any one or two of the exterior metatarsal bones showing slight bone erosion; 2-definite early abnormality with any three to five of the exterior metatarsal bones showing bone erosion; 3-medium destructive abnormality with all the exterior metatarsal bones as well as any one or two of the interior metatarsal bones showing definite bone erosions; 4-severe destructive abnormality with all the metatarsal bones showing definite bone erosion and at least one of the inner metatarsal joints completely eroded leaving some bony joint outlines partly preserved; 5-mutilating abnormality without bony outlines. This scoring system is a modification from Salvemini *et al.*, 2001; Bush *et al.*, 2002; Sims *et a*l., 2004; Jou *et al.*, 2005.

3.1.8 Histology

[00808] After radiological analysis, the hind paws of mice were fixed in 10% phosphate-buffered formalin (pH 7.4), decalcified with rapid bone decalcifiant for fine histology (Laboratories Eurobio) and embedded in paraffin. To ensure extensive evaluation of the arthritic joints, at least four serial sections (5 µm thick) were cut and each series of sections were 100 µm in between. The sections were stained with hematoxylin and eosin (H&E). Histologic examinations for synovial inflammation and bone and cartilage damage were performed double blind. In each paw, four parameters were assessed using a four-point scale. The parameters were cell infiltration, pannus severity, cartilage erosion and bone erosion. Scoring was performed as follows: 1-normal, 2-mild, 3-moderate, 4-marked. These four scores were summed together and represented as an additional score, namely the 'RA total score'.

3.1.9 Micro-computed tomography (µCT) analysis of calcaneus (heel bone):

[00809] Bone degradation observed in RA occurs especially at the cortical bone and can be revealed by μCT analysis (Sims NA *et al.*, 2004; Oste L *et al.*, ECTC Montreal 2007). After scanning and 3D volume reconstruction of the calcaneus bone, bone degradation was measured as the number of discrete objects present per slide, isolated *in silico* perpendicular to the longitudinal axis of the bone. The more the bone that was degraded, the more discrete objects that were measured. 1000 slices, evenly distributed along the calcaneus (spaced by about 10.8 μm), are analyzed.

3.1.10 Results

[00810] The following compounds were efficacious in all readouts performed in the rat CIA study at 30 mg/kg: 6, 101, 162, 221

[00811] Compound 139 was efficacious in all readouts performed in the mouse CIA study at 30 mg/kg.

Example 3.2 Septic shock model

[00812] Injection of lipopolysaccharide (LPS) induces a rapid release of soluble tumour necrosis factor (TNF-alpha) into the periphery. This model is used to analyse prospective blockers of TNF release *in vivo*.

[00813] Six BALB/cJ female mice (20 g) per group were treated at the intended dosing once, po. Thirty minutes later, LPS (15 μg/kg; *E. Coli* serotype 0111:B4) was injected ip. Ninety minutes later, mice were euthanized and blood was collected. Circulating TNF alpha levels were determined using commercially available ELISA kits. Dexamethasone (5 μg/kg) was used as a reference anti-inflammatory compound. Selected compounds are tested at one or multiple doses, e.g. 3 and/or 10 and/or 30 mg/kg, po.

[00814] The following compounds exhibited a statistically significant reduction in the TNF release (>50%) at 30mg/kg po.: 1, 6, 57, 77, 94, 115, 125, 131, 132, 139, 142, 144, 155, 164, 203, or 204

Example 3.3 MAB model

[00815] The MAB model allows a rapid assessment of the modulation of an RA-like inflammatory response by therapeutics (Kachigian LM. Nature Protocols (2006) 2512-2516: Collagen antibody-induced arthritis). DBA/J mice are injected i.v. with a cocktail of mAbs directed against collagen II. One day later, compound treatment is initiated (vehicle: 10% (v/v) HPβCD). Three days later, mice receive an i.p. LPS injection (50 μg/mouse), resulting in a fast onset of inflammation. Compound treatment is continued until 10 days after the mAb injection. Inflammation is read by measuring paw swelling and recording the clinical score of each paw. The cumulative clinical arthritis score of four limbs is presented to show the severity of inflammation. A scoring system is applied to each limb using a scale of 0–4, with 4 being the most severe inflammation.

0 Symptom free

1 Mild, but definite redness and swelling of one type of joint such as the ankle or wrist, or apparent redness and swelling limited to individual digits, regardless of the number of affected digits

2 Moderate redness and swelling of two or more types of joints

3 Severe redness and swelling of the entire paw including digits

4 Maximally inflamed limb with involvement of multiple joints

Example 3.4 Oncology models

[00816] *In vitro* and *in vivo* models to validate efficacy of small molecules towards JAK2-driven myleoproliferative diseases are described by Wernig *et al.* Cancer Cell 13, 311, 2008 and Geron *et al.* Cancer Cell 13, 321, 2008.

Example 3.5 Mouse IBD model

[00817] *In vivo* models to validate efficacy of small molecules towards IBD are described by Wirtz *et al.* 2007.

Example 3.6 Mouse Asthma model

[00818] *In vitro* and *in vivo* models to validate efficacy of small molecules towards asthma are described by Nials *et al.*, 2008; Ip *et al.* 2006; Pernis *et al.*, 2002; Kudlacz *et al.*, 2008)

Example 4: Toxicity, DMPK and Safety Models

Example 4.1 Thermodynamic solubility

[00819] A solution of 1 mg/mL of the test compound is prepared in a 0.2M phosphate buffer pH7.4 or a 0.1M citrate buffer pH3.0 at room temperature in a glass vial.

[00820] The samples are rotated in a Rotator drive STR 4 (Stuart Scientific, Bibby) at speed 3.0 at room temperature for 24 hours.

[00821] After 24 hours, 800µL of the sample is transferred to an eppendorf tube and centrifuged 5 min at 14000rpm. 200 µL of the supernatant of the sample is then transferred to a MultiscreenR Solubility Plate (Millipore, MSSLBPC50) and the supernatant is filtered (10-12" Hg) with the aid of a vacuum manifold into a clean Greiner polypropylene V-bottom 96well plate (Cat no.651201). 5 µL of the filtrate is diluted into 95 µL (F20) of the same buffer used to incubate in the plate containing the standard curve (Greiner,Cat no.651201).

[00822] The standard curve for the compound is prepared freshly in DMSO starting from a 10mM DMSO stock solution diluted factor 2 in DMSO (5000µM) and then further diluted in DMSO up to 19.5µM. 3µL of the dilution series as from 5000µM is then transferred to a 97µL acetonitrile-buffer mixture (50/50). The final concentration range is 2.5 to 150 µM.

[00823] The plate is sealed with sealing mats (MA96RD-04S, www.kinesis.co.uk) and samples are measured at room temperature on LCMS (ZQ 1525 from Waters) under optimized conditions using Quanoptimize to determine the appropriate mass of the molecule.

[00824] The samples are analyzed on LCMS with a flow rate of 1mL/min. Solvent A is 15mM ammonia and solvent B is acetonitrile. The sample is run under positive ion spray on an XBridge C18 3.5µM (2.1 x 30mm) column, from Waters. The solvent gradient has a total run time of 2 minutes and ranges from 5% B to 95% B.

[00825] Peak areas are analyzed with the aid of Masslynx software package and peak areas of the samples are plotted against the standard curve to obtain the solubility of the compound.

[00826] Solubility values are reported in µM or µg/mL.

Example 4.2 Aqueous Solubility

[00827] Starting from a 10mM stock in DMSO, a serial dilution of the compound is prepared in DMSO. The dilution series is transferred to a 96 NUNC Maxisorb plate F-bottom (Cat no. 442404) and 0.2M phosphate buffer pH7.4 or 0.1M citrate buffer pH3.0 at room temperature is added.

[00828] The final concentration ranged from 200µM to 2.5µM in 5 equal dilution steps. The final DMSO concentration did not exceed 2%. 200µM Pyrene is added to the corner points of each 96 well plate and serves as a reference point for calibration of Z-axis on the microscope.

[00829] The assay plates are sealed and incubated for 1 hour at 37°C while shaking at 230rpm. The plates are then scanned under a white light microscope, yielding individual pictures of the precipitate per concentration. The precipitate is analyzed and converted into a number which is plotted onto a graph. The first concentration at which the compound appears completely dissolved is the concentration reported, however the true concentration lies somewhere between this concentration and one dilution step higher.

[00830] Solubility values are reported in µg/mL

Example 4.3 Plasma Protein Binding (Equilibrium Dialysis)

[00831] A 10mM stock solution of the compound in DMSO is diluted with a factor 5 in DMSO. This solution is further diluted in freshly thawed human, rat, mouse or dog plasma (BioReclamation INC) with a final concentration of 10µM and final DMSO concentration of 0.5% (5.5µl in 1094.5µl plasma in a PP-Masterblock 96well (Greiner, Cat no. 780285))

[00832] A Pierce Red Device plate with inserts (ThermoScientific, Cat no. 89809) is prepared and filled with 750µL PBS in the buffer chamber and 500µL of the spiked plasma in the plasma chamber. The plate is incubated for 4 hours at 37°C while shaking at 230rpm. After incubation, 120µL of both chambers is transferred to 360µL acetonitrile in a 96-well round bottom, PP deep-well plates (Nunc, Cat no. 278743) and sealed with an aluminum foil lid. The samples are mixed and placed on ice for 30min. This plate is then centrifuged 30 min at 1200rcf at 4°C and the supernatant is transferred to a 96 v-bottom PP plate (Greiner, 651201) for analysis on LCMS.

[00833] The plate is sealed with sealing mats (MA96RD-04S) of www.kinesis.co.uk and samples are measured at room temperature on LCMS (ZQ 1525 from Waters) under optimized conditions using Quanoptimize to determine the appropriate mass of the molecule.

[00834] The samples are analyzed on LCMS with a flow rate of 1mL/min. Solvent A was 15mM ammonia and solvent B was acetonitrile. The sample was run under positive ion spray on an XBridge C18 3.5µM (2.1 x 30mm) column, from Waters. The solvent gradient has a total run time of 2 minutes and ranges from 5% B to 95% B.

[00835] Peak area from the compound in the buffer chamber and the plasma chamber are considered to be 100% compound. The percentage bound to plasma is derived from these results and was reported to the LIMS as percentage bound to plasma.

[00836] The solubility of the compound in the final test concentration in PBS is inspected by microscope to indicate whether precipitation is observed or not.

Example 4.4 Liability for QT prolongation

[00837] Potential for QT prolongation is assessed in the hERG patch clamp assay.

4.4.1 Conventional whole-cell patch-clamp

[00838] Whole-cell patch-clamp recordings are performed using an EPC10 amplifier controlled by Pulse v8.77 software (HEKA). Series resistance is typically less than 10 MΩ and compensated by greater than 60%, recordings are not leak subtracted. Electrodes are manufactured from GC150TF pipette glass (Harvard).

[00839] The external bathing solution contains: 135 mM NaCl, 5 mM KCl, 1.8 mM $CaCl_2$, 5 mM Glucose, 10 mM HEPES, pH 7.4.

[00840] The internal patch pipette solution contains: 100mM Kgluconate, 20 mM KCl, 1mM $CaCl_2$, 1 mM $MgCl_2$, 5mM Na_2ATP, 2mM Glutathione, 11 mM EGTA, 10 mM HEPES, pH 7.2.

[00841] Drugs are perfused using a Biologic MEV-9/EVH-9 rapid perfusion system.

[00842] All recordings are performed on HEK293 cells stably expressing hERG channels. Cells are cultured on 12 mm round coverslips (German glass, Bellco) anchored in the recording chamber using two platinum rods (Goodfellow). hERG currents are evoked using an activating pulse to +40 mV for 1000 ms followed by a tail current pulse to –50 mV for 2000 ms, holding potential was -80 mV. Pulses are applied every 20s and all experiments are performed at room temperature.

4.4.2 Data Analysis

[00843] IC_{50} and IC_{20} values are calculated for each compound tested. The fold difference between the IC_{20} and the unbound C_{max} concentrations of the test compound obtained at relevant therapeutic doses as determined by results obtained from the rat CIA model is calculated.

[00844] For the concentration response curves, peak tail current amplitude is measured during the voltage step to -50 mV. Curve-fitting of concentration-response data is performed using the equation:

$$y = a + [(b - a)/ (1 + 10^{\wedge} ((\log c - x) d)]$$

[00845] where a is minimum response, b is maximum response and d is Hill slope, this equation can be used to calculate both IC_{50} (where y = 50 and c is the IC_{50} value) and IC_{20} (where y = 20 and c is the IC_{20} value). GraphPad® Prism® (Graphpad® Software Inc.) software was used for all curve fitting.

[00846] A difference of 100 fold or greater indicates a low potential for QT prolongation.

Example 4.5 Microsomal stability

[00847] A 10mM stock solution of compound in DMSO was diluted 1000 fold in a 182 mM phosphate buffer pH7.4 in a 96 deep well plate (Greiner, Cat no.780285) and pre-incubated at 37°C.

[00848] 40µL of deionised water was added to a well of a polypropylene Matrix 2D barcode labelled storage tube (Thermo Scientific) and pre-incubated at 37°C.

[00849] A Glucose-6-phophate-dehydrogenase (G6PDH) working stock solution was prepared in 182mM phosphate buffer pH7.4 and placed on ice before use. A co-factor containing MgCl2, glucose-6-phosphate and NADP+ was prepared in deionised water and placed on ice before use.

[00850] A final working solution containing liver microsomes (Xenotech) of a species of interest (human, mouse, rat, dog), previously described G6PDH and co-factors was prepared and this mix was incubated for no longer than 20 minutes at room temperature.

[00851] 30µL of the pre-heated compound dilution was added to 40µL of pre-heated water in the Matrix tubes and 30µL of the microsomal mix was added. Final reaction concentrations were 3µM compound, 1mg microsomes, 0.4U/mL GDPDH, 3.3mM $MgCl_2$, 3.3mM glucose-6-phosphate and 1.3mM NADP+.

[00852] To measure percentage remaining of compound at time zero MeOH or ACN was added (1:1) to the well before adding the microsomal mix. The plates were sealed with Matrix Sepra sealsTM (Matrix, Cat. No.4464) and shaken for a few seconds ensure complete mixing of all components.

[00853] The samples which were not stopped are incubated at 37°C, 300rpm and after 1 hour of incubation the reaction was stopped with MeOH or ACN (1:1).

[00854] After stopping the reaction the samples were mixed and placed on ice for 30min to precipitate the proteins. The plates were then centrifuged 30 min at 1200rcf at 4°C and the supernatant was transferred to a 96 v-bottom PP plate (Greiner, 651201) for analysis on LCMS.

[00855] These plates were sealed with sealing mats (MA96RD-04S) of www.kinesis.co.uk and samples were measured at room temperature on LCMS (ZQ 1525 from Waters) under optimized conditions using Quanoptimize to determine the appropriate mass of the parent molecule.

[00856] The samples were analyzed on LCMS with a flow rate of 1mL/min. Solvent A was 15mM ammonia and solvent B was methanol or acetonitrile, depending on the stop solution used. The samples were run under positive ion spray on an XBridge C18 3.5µM (2.1 x 30mm) column, from Waters. The solvent gradient had a total run time of 2 minutes and ranges from 5% B to 95% B.

Peak area from the parent compound at time 0 was considered to be 100% remaining. The percentage remaining after 1 hour incubation was calculated from time 0 and was calculated as the percentage

remaining.The solubility of the compound in the final test concentration in buffer is inspected by microscope and results are reported.

[00857] The data on microsomal stability are expressed as a percentage of the total amount of compound remaining after 60 minutes.

TABLE IX – Microsomal stability

* 0-25

** 26-50

*** 51-75

**** 76-100

Compound #	Human (%)	Rat (%)
1	*	*
2	*	*
3	***	*
4	***	*
5	*	*
6	*	*
7	**	*
8	*	*
9	****	**
11	***	***
12	*	*
15	*	*
16	*	*
17	**	****
18	**	****
19	*	*
21	**	***
22	***	****
24	**	*
25	**	**
26	*	*
28	**	*
30	*	*
31	****	*
33	*	*

Compound #	Human (%)	Rat (%)
34	***	**
35	****	****
37	***	**
38	*	*
39	*	**
40	***	***
41	*	*
42	**	**
43	**	**
45	**	*
47	*	*
50	***	**
52	**	**
54	**	*
55	*	*
56	*	*
57	**	****
58	**	****
59	*	*
60	***	*
64	***	*
65	**	*
66	***	**
67	**	***
70	*	***
71	*	*
73	*	*
74	****	****
75	*	*
77	*	*
78	*	*
79	*	*
80	****	***
81	*	*
82	****	***
83	**	**

Compound #	Human (%)	Rat (%)
84	*	**
85	**	*
86	*	*
87	****	****
88	****	**
89	****	****
93	****	***
94	****	***
96	***	**
97	****	***
99	****	***
100	**	**
101	****	***
103	*	*
104	***	*
105	*	*
110	****	**
111	*	*
112	****	****
114	**	***
115	*	*
116	*	*
118	**	*
119	***	**
120	****	**
121	*	*
122	****	***
123	****	***
125	***	***
126	****	****
127	**	*
129	****	****
130	*	*
131	**	***
132	****	****
133	****	****

Compound #	Human (%)	Rat (%)
135	**	*
136	****	***
137	***	*
139	**	*
143	****	****
144	*	*
146	*	*
147	*	**
148	****	****
151	*	**
152	***	***
153	****	****
154	**	**
155	****	****
156	***	***
158	****	****
160	*	**
161	*	*
162	***	***
164	**	***
165	****	****
166	****	****
167	***	**
168	****	****
169	*	****
170	*	****
171	*	****
172	***	****
173	**	****
174	**	****
175	***	***
176	****	****
177	****	****
178	****	****
179	****	****
180	***	**

Compound #	Human (%)	Rat (%)
181	***	*
182	**	*
183	**	**
184	*	*
185	***	***
187	****	***
190	**	**
191	*	**
192	***	**
197	*	*
198	*	***
202	****	****
203	***	*
204	**	*
205	*	*
206	*	*
208	*	****
209	**	**
210	*	*
211	*	*
212	*	**
213	**	*
216	*	*
217	***	*
218	***	*
219	***	***
220	*	*
221	**	*
222	**	**
223	***	**
224	*	*
225	*	*
226	****	***
227	*	*
228	**	*
229	*	*

Compound #	Human (%)	Rat (%)
230	**	**
231	****	**
232	****	*
233	**	***
234	*	*
235	*	***
236	*	*
237	*	*
238	*	*
239	*	*
240	*	*
241	*	*
242	*	*
243	*	**
244	*	*
245	*	**
246	*	*
247	**	**
248	*	*
249	****	****
251	*	****
252	****	**
253	*	*
254	**	*
255	**	*
256	**	*
257	**	*
260	****	***
261	*	*
262	*	*
263	***	***
264	****	****
265	***	***
270	N/A	*
271	N/A	*
272	N/A	*

Compound #	Human (%)	Rat (%)
275	N/A	**
278	N/A	**
279	N/A	*
282	N/A	**
283	N/A	*
284	N/A	****
285	N/A	***
286	N/A	*
287	N/A	*
288	N/A	**
289	N/A	*
290	N/A	*
291	N/A	*
292	N/A	*
293	N/A	*
294	N/A	*
295	N/A	*
296	N/A	****
299	N/A	*
300	N/A	*
301	N/A	****
302	N/A	****
303	N/A	****
304	N/A	***
305	N/A	**
308	N/A	*
309	N/A	****
310	N/A	*
311	N/A	*
312	N/A	*
313	N/A	*
314	N/A	****
315	N/A	**
316	N/A	***
317	N/A	*
318	N/A	*

Compound #	Human (%)	Rat (%)
319	N/A	***
320	N/A	**
321	N/A	*
322	N/A	***
324	N/A	***
325	N/A	****
326	N/A	****

Example 4.6 Caco2 Permeability

[00858] Bi-directional Caco-2 assays were performed as described below. Caco-2 cells were obtained from European Collection of Cell Cultures (ECACC, cat 86010202) and used after a 21 day cell culture in 24-well Transwell plates (Fisher TKT-545-020B).

[00859] $2x10^5$ cells/well were seeded in plating medium consisting of DMEM + GlutaMAXI + 1% NEAA + 10% FBS (FetalClone II) + 1% Pen/Strep. The medium was changed every 2 – 3 days.

[00860] Test and reference compounds (propranolol and rhodamine123 or vinblastine, all purchased from Sigma) were prepared in Hanks' Balanced Salt Solution containing 25 mM HEPES (pH7.4) and added to either the apical (125µL) or basolateral (600µL) chambers of the Transwell plate assembly at a concentration of 10 µM with a final DMSO concentration of 0.25%.

[00861] 50µM Lucifer Yellow (Sigma) was added to the donor buffer in all wells to assess integrity of the cell layers by monitoring Lucifer Yellow permeation. As Lucifer Yellow (LY) cannot freely permeate lipophilic barriers, a high degree of LY transport indicates poor integrity of the cell layer.

[00862] After a 1 hour incubation at 37°C while shaking at an orbital shaker at 150rpm, 70µL aliquots were taken from both apical (A) and basal (B) chambers and added to 100µLl 50:50 acetonitrile:water solution containing analytical internal standard (0.5µM carbamazepine) in a 96 well plate.

[00863] Lucifer yellow was measured with a Spectramax Gemini XS (Ex 426nm and Em 538nm) in a clean 96 well plate containing 150µL of liquid from basolateral and apical side.

[00864] Concentrations of compound in the samples were measured by high performance liquid-chromatography/mass spectroscopy (LC-MS/MS).

[00865] Apparent permeability (P_{app}) values were calculated from the relationship:

$$P_{app} = [compound]_{acceptor\ final} \times V_{acceptor} / ([compound]_{donor\ initial} \times V_{donor}) / T_{inc} \times V_{donor} / \text{surface area} \times 60 \times 10^{-6}\ cm/s$$

V = chamber volume

T_{inc} = incubation time.

Surface area = $0.33cm^2$

[00866] The Efflux ratios, as an indication of active efflux from the apical cell surface, were calculated using the ratio of P_{app} B>A/ P_{app} A>B.

[00867] The following assay acceptance criteria were used:

Propranolol: P_{app} (A>B) value ≥ 20($\times 10^{-6}$ cm/s)

Rhodamine 123 or Vinblastine: P_{app} (A>B) value < 5 ($\times 10^{-6}$ cm/s) with Efflux ratio ≥5.

Lucifer yellow permeability: ≤100 nm/s

Table X – Caco2 Efflux rate

Cpd #	Papp (A2B) cmx10^{-6}sec^{-1}	Efflux ratio
1	15.73	1
2	29.35	0.65
3	13.86	0.62
4	4.3	8.71
5	31.75	0.85
6	7.49	3.37
7	6	0.55
8	18.4	1
9	12.1	1
11	14.09	0.55
12	23.05	1
16	32.65	0.7
17	24.95	1
19	13.15	5.5
21	2.6	23.35
22	3.6	8.85
33	6	7.5
35	2.9	12
38	6.2	0.9
40	4	17.5
43	13.4	2
58	1.45	29.5
64	1.1	49.65
69	0.3	36.5
74	13.5	2
77	5.79	0.1
79	11.5	0.7

Cpd #	Papp (A2B) cmx10^{-6}sec^{-1}	Efflux ratio
83	1.75	1
85	33.5	1.5
94	2	34.4
97	2	37.75
101	15.8	2.05
110	12.15	3.8
126	0.1	399.7
131	2.55	31.3
132	1.65	11.6
133	0.8	27.5
136	0.4	160.1
139	11.85	3.75
146	12.05	3.25
147	0.05	46.41
162	14.5	1.8
184	1.3	25
185	0.1	780
192	2.5	22.5
203	20	1.15
204	13.5	3
205	10.9	0.96
206	9.8	1.03
209	17.31	1.42
210	5.6	1.13
211	9.15	1.8
212	0.4	111.46
216	23.75	1

Cpd #	Papp (A2B) $cmx10^{-6}sec^{-1}$	Efflux ratio
219	22.75	0.57
220	21.75	1.22
221	13.65	2.07
222	0.1	434.4
224	13.3	1.21
226	1.78	30.5
228	7.64	2.65
230	0.73	120.25
232	0.22	283.5
234	15.24	1.05
235	5.58	2.33
236	5.78	3.3
237	4.79	1.4
238	7.62	1.26
239	3.09	7.47
240	10.65	1.79
241	5.2	6.73
242	17.1	1.44
243	0.79	49.95
244	9.43	2.32
245	1.02	40.37
246	5.41	1.99

Cpd #	Papp (A2B) $cmx10^{-6}sec^{-1}$	Efflux ratio
247	11.95	3.43
248	0.6	46.38
249	0.95	336.64
251	2.6	14.14
252	2.55	20.7
254	3.25	11.18
257	8.8	1.25
260	0.59	80.62
261	11.29	2.14
262	15.25	0.93
263	1.78	21.5
264	1.3	10.18
265	1.15	84.69
270	14.05	1.76
271	16.75	1.66
272	3.9	9.9
275	0.74	38.2
282	0.43	71.05
284	4.6	2.4
285	0.25	2.2
296	0.05	447.72

Example 4.7 Pharmacokinetic study in rodents

4.7.1 Pharmacokinetic study

[00868] Compounds are formulated in PEG200/physiological saline or PEG400/DMSO/physiological saline mixtures for the intravenous route and in 0.5% methylcellulose or 10-30% hydroxylpropyl-β-cyclodextrine pH3 or pH7.4 for the oral route. Test compounds are orally dosed as a single esophageal gavage at 5-10 mg/kg and intravenously dosed as a bolus via the caudal vein at 1 mg/kg. Each group consists of 3 rats. Blood samples are collected either via the jugular vein using cannulated rats or at the retro-orbital sinus with lithium heparin as anti-coagulant at the time points in the following range: 0.05 to 8 hours (intravenous route), and 0.25 to 6 or 24 hours (oral route). Whole blood samples are centrifuged at 5000 rpm for 10 min and the resulting plasma samples are stored at -20°C pending analysis.

4.7.2 Quantification of compound levels in plasma

[00869] Plasma concentrations of each test compound are determined by an LC-MS/MS method in which the mass spectrometer was operated in positive electrospray mode.

4.7.3 Determination of pharmacokinetic parameters

[00870] Pharmacokinetic parameters are calculated using Winnonlin® (Pharsight®, United States).

Example 4.8 7-Day rat toxicity study

[00871] A 7-day oral toxicity study with test compounds is performed in Sprague-Dawley male rats to assess their toxic potential and toxicokinetics, at daily doses of 100, 300 and 500 mg/kg/day, by gavage, at the constant dosage-volume of 5 mL/kg/day.

[00872] The test compounds are formulated in 30% (v/v) HPβCD in purified water. Each group included 5 principal male rats as well as 3 satellite animals for toxicokinetics. A fourth group is given 30% (v/v) HPβCD in water only, at the same frequency, dosage volume and by the same route of administration, and acted as the vehicle control group. The goal of the study is to determine the lowest dose that resulted in no adverse events being identified (no observable adverse effect level - NOAEL).

[00873] It will be appreciated by those skilled in the art that the foregoing descriptions are exemplary and explanatory in nature, an as indiced intended to illustrate the invention and its preferred embodiments. Through routine experimentation, an artisan will recognise apparent modifications and variations that may be made without departing from the spirit of the invention. Thus, the invention is intended to be defined not by the above description, but by the following claims and their equivalents.

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[00875] All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

[00876] From the foregoing description, various modifications and changes in the compositions and methods of this invention will occur to those skilled in the art. All such modifications coming within the scope of the appended claims are intended to be included therein.

[00877] It should be understood that factors such as the differential cell penetration capacity of the various compounds can contribute to discrepancies between the activity of the compounds in the *in vitro* biochemical and cellular assays.

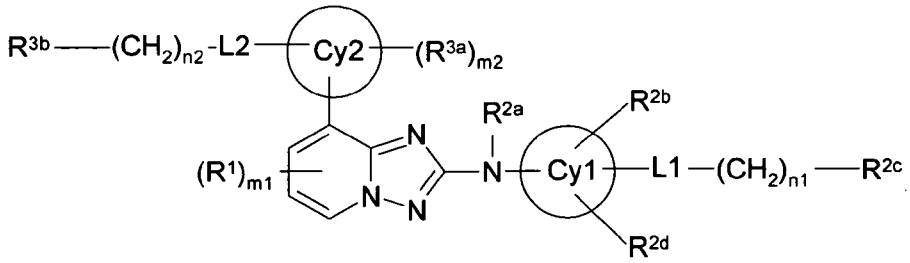
[00878] At least some of the chemical names of compounds of the invention as given and set forth in this application, may have been generated on an automated basis by use of a commercially available chemical naming software program, and have not been independently verified. Representative programs performing this function include the Lexichem naming tool sold by Open Eye Software, Inc. and the Autonom Software tool sold by MDL, Inc. In the instance where the indicated chemical name and the depicted structure differ, the depicted structure will control.

[00879] Chemical structures shown herein were prepared using either ChemDraw® or ISIS® /DRAW. Any open valency appearing on a carbon, oxygen or nitrogen atom in the structures herein indicates the presence of a hydrogen atom. Where a chiral center exists in a structure but no specific stereochemistry is shown for the chiral center, both enantiomers associated with the chiral structure are encompassed by the structure.

GAL-113-WO-PCT

WHAT IS CLAIMED IS:

1. A compound according to Formula I:



I

wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$-, -$N(R^{4a})$-, -$CON(R^{4a})$-, -$SO_2N(R^{4a})$-, -$N(R^{4a})CO$-, or -$N(R^{4a})SO_2$-;

each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, substituted or unsubstituted amino, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, substituted or unsubstituted amino, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted –O-aryl, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, substituted or unsubstituted amino, substituted or unsubstituted amido, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or

unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, C_1-C_6alkyl, substituted C_1-C_6alkyl, C_3-C_7 cycloalkyl, or substituted C_3-C_7 cycloalkyl;

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$-, -N(R^{4a})-, -CON(R^{4a})-, -SO_2N(R^{4a})-, - N(R^{4a})CO-, or - N(R^{4a})SO_2-;

each R^1 is independently selected from unsubstituted C_1-C_6 alkyl, unsubstituted acyl, unsubstituted acylamino, unsubstituted C_1-C_6 alkoxy, unsubstituted amido, unsubstituted amino, unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester, carboxy, cyano, unsubstituted C_3-C_7 cycloalkyl, unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from unsubstituted C_1-C_6 alkyl, unsubstituted acyl, unsubstituted acylamino, unsubstituted C_1-C_6 alkoxy, unsubstituted amido, unsubstituted alkoxycarbonyl, unsubstituted arylalkyloxy, unsubstituted amino, unsubstituted aryl, unsubstituted arylalkyl, unsubstituted aminosulfonyl, unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, unsubstituted C_3-C_7 cycloalkyl, unsubstituted 4-7 membered heterocycloalkyl, halo, unsubstituted -O-(5-7-membered heteroaryl), unsubstituted 5-7-membered heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl (which C_1-C_6 alkyl may be substituted with hydroxy, unsubstituted C_1-C_4 alkoxy, cyano, halo, dialkylamino, 5-7-membered heterocycloalkyl, acyl) 5-7-membered heterocycloalkyl (optionally substituted with C_1-C_6 alkyl (optionally substituted with halo), halo, hydroxy, oxo, cyano, acyl (optionally substituted with C_1-C_6 alkyl), amido (optionally substituted with C_1-C_6 alkyl, C_3-C_7 cycloalkyl), C_3-C_7 cycloalkyl), sulfonyl (substituted C_1-C_6 alkyl), acyl (which acyl may be substituted with unsubstituted C_1-C_4 alkyl), acylamino (which acylamino may be substituted with unsubstituted C_1-C_4 alkyl), C_1-C_6 alkoxy (which C_1-C_6 alkoxy may be substituted with halo, dialkylamido, cyano), –O-aryl (which –O-aryl may be substituted with halo, unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy), unsubstituted alkoxycarbonyl, unsubstituted arylalkyloxy, aryl (which aryl may be substituted with cyano,

halo, unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy), unsubstituted arylalkyl, sulfanyl (which sulfanyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), sulfinyl (which sulfinyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), sulfonyl (which sulfonyl may be substituted with unsubstituted aryl, unsubstituted C_1-C_4 alkyl), aminosulfonyl (which aminosulfonyl may be substituted with unsubstituted C_1-C_4 alkyl), unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, amino (which amino may be substituted with C_1-C_4 alkyl (optionally substituted with OH, C_3-C_7 cycloalkyl (optionally substituted with OH)), unsubstituted 5-7-membered heterocycloalkyl), sulfonyl (substituted C_1-C_6 alkyl), amido (which amido may be substituted with unsubstituted C_1-C_4 alkyl, or the nitrogen and its two substituent may form together an unsubstituted 4-7 membered heterocycloalkyl), C_3-C_7 cycloalkyl (which C_3-C_7 cycloalkyl may be substituted with cyano, amido (optionally substituted with C_1-C_4 alkyl), 4-7 membered heterocycloalkyl (which heterocycloalkyl may be substituted with cyano, oxo, C_1-C_4 alkyl (optionally substituted with halo), halo, hydroxy, acyl, amino (optionally substituted with acyl), sulfonyl (substituted with C_1-C_4 alkyl)), halo, unsubstituted -O-heteroaryl, 5-7-membered heteroaryl (which heteroaryl may be substituted with unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkoxy, hydroxy, halo), cyano, hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, unsubstituted C_1-C_6 alkyl, unsubstituted C_3-C_7 cycloalkyl;

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts thereof.

3. The compound according to claim 1 or 2 wherein m1 is 1 or 2; each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, and halo.

4. The compound according to claim 3 wherein each R^1 is independently selected from Me, CF_3, Cl and F.

5. The compound according to claim 1 or 2 wherein R^{2a} is independently selected from H, C_1-C_6 alkyl, and substituted C_1-C_6 alkyl.

6. The compound according to claim 5 wherein R^{2a} is H.

7. The compound according to claim 1 or 2 wherein Cy1 is substituted or unsubstituted aryl.

8. The compound according to claim 7 wherein Cy1 is substituted or unsubstituted phenyl.

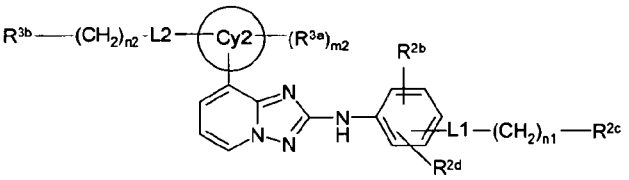
9. The compound according to claim 1 or 2 wherein Cy1 is substituted or unsubstituted heteroaryl.

GAL-113-WO-PCT

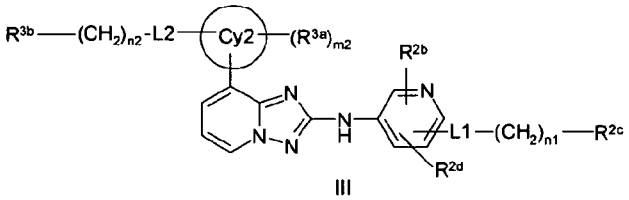
10. The compound according to claim 9 wherein Cy1 is substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

11. The compound according to claim 9 wherein Cy1 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

12. The compound according to claim 1 or 2 wherein the compound is according to Formula II or III:



II



III

wherein Cy2, L1, L2, R^{2b}, R^{2c}, R^{2d}, R^{3a}, R^{3b}, m2, n1, and n2 are as in claim 1 or 2.

13. The compound according to claim 12 wherein R^{2b}, and R^{2d} are independently H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy or halo.

14. The compound according to claim 13 wherein R^{2b}, and R^{2d} are independently H, Me, OMe, F or Cl.

15. The compound according to any one of claims 1-14 wherein L1 is a single bond, n1 is 0, and R^{2c} is H, Cl, F, Me, Et, OMe, CF_3, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

16. The compound according to any one of claims 1-14 wherein L1 is a single bond, n1 is 0, and R^{2c} is NHCOMe, or COOH.

17. The compound according to any one of claims 1-14, wherein L1 is CONH; n1 is 2 or 3; and R^{2c} is NMe_2, OMe, or NHCOMe.

18. The compound according to any one of claims 1-14 wherein L1 is selected from a single bond, -C(O)-, and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl,

substituted or unsubstituted heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 membered heterocycloalkyl.

19. The compound according to claim 18, wherein R^{2c} is C_1-C_6 alkyl.

20. The compound according to claim 18, wherein R^{2c} is Me, Et, i-Pr, 1,3-dihydroxyprop-2-yl.

21. The compound according to claim 18, wherein R^{2c} is substituted or unsubstituted C_3-C_7 cycloalkyl.

22. The compound according to claim 21, wherein R^{2c} is substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.

23. The compound according to claim 18, wherein R^{2c} is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

24. The compound according to claim 23, wherein R^{2c} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

25. The compound according to claim 18, wherein R^{2c} is substituted or unsubstituted 4-7 membered heterocycloalkyl.

26. The compound according to claim 25, wherein R^{2c} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH.

27. The compound according to any one of claims 18-26, wherein R^{4a} is H.

28. The compound according to any one of claims 18-26, wherein L1 is CONH; and n1 is 0, 1, 2 or 3.

29. The compound according to claim 28 wherein L1 is CONH; and n1 is 0, or 1.

30. The compound according to any one of claims 18-26, wherein L1 is CO; and n1 is 0, 1, 2 or 3.

31. The compound according to claim 30, wherein L1 is CO; and n1 is 0, or 1.

32. The compound according to any one of claims 1-8 or 12-14 wherein the –Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:

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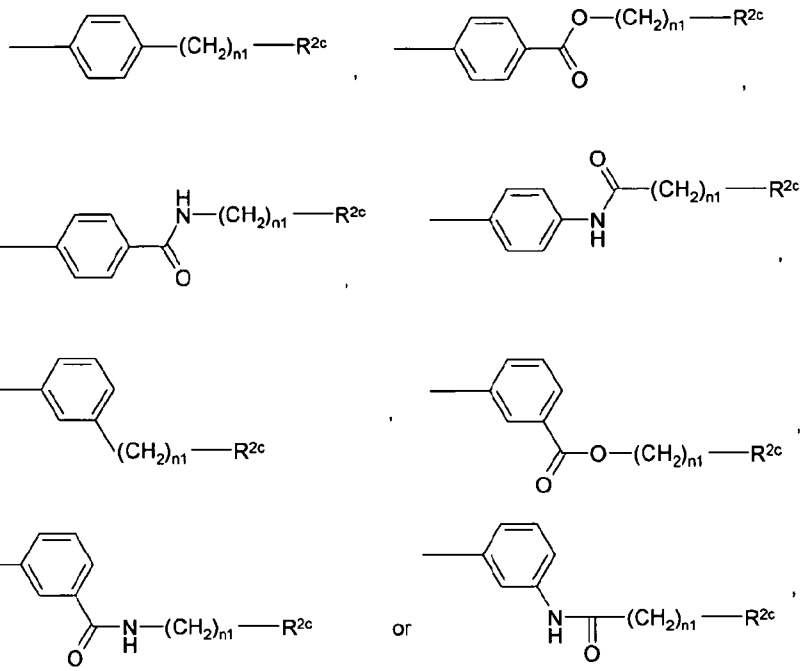
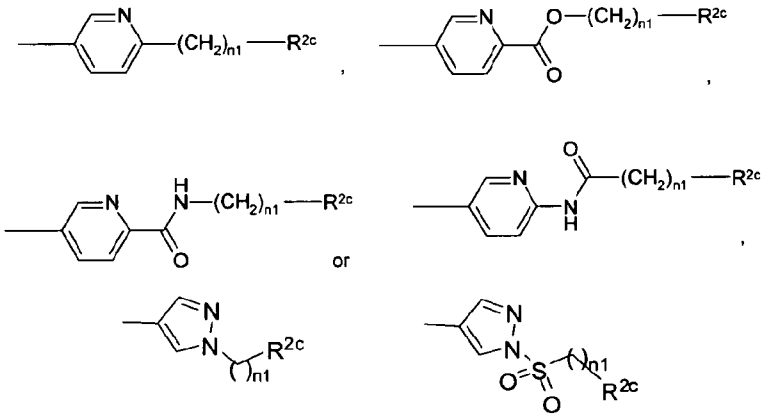


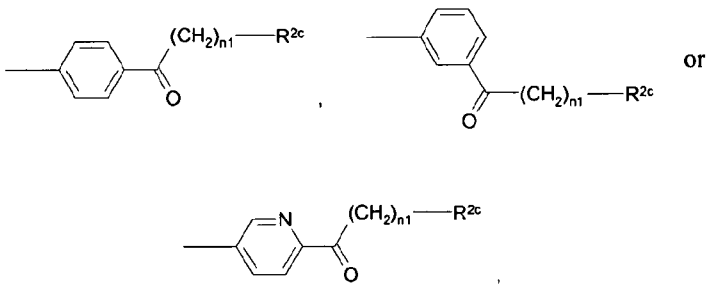
and wherein n1 and R^{2c} are as decribed in the previous claims.

33. The compound according to any one of claims 1-6, or 9-14 wherein the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



and wherein n1 and R^{2c} are as described in the previous claims.

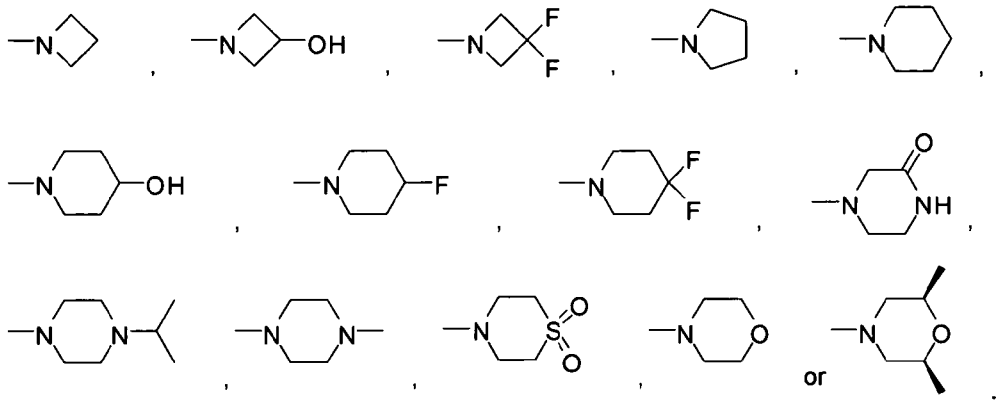
34. The compound according to any one of claims 1-10 or 12-14 wherein the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



and wherein n1 and R^{2c} are as described in the previous claims.

35. The compound according to any one of claims 32-34, wherein R^{2c} is 4-7 membered N-containing heterocycloalkyl or heteroaryl.

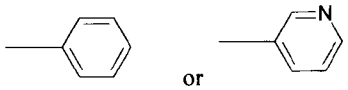
36. The compound according to claim 35, wherein R^{2c} is:



37. The compound according to claim 35, wherein R^{2c} is pyrazolyl, pyrrolyl, imidazolyl, or triazolyl.

38. The compound according to any one of claims 32-37, wherein n1 is 0, 1 or 2.

39. The compound according to any one of claims 1-6, and 9-10 wherein the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



40. The compound according to any one of claims 1-39, wherein Cy2 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

41. The compound according to claim 40, wherein Cy2 is substituted or unsubstituted aryl.

42. The compound according to claim 41, wherein Cy2 is Ph; and m2 is 0.

43. The compound according to claim 40, wherein Cy2 is Ph; m2 is 1, 2 or 3; and each R^{3a} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, halo, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

44. The compound according to claim 43, wherein each R^{3a} is independently Cl, F, Me, Et, OMe, CF_3, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

45. The compound according to claim 43 or 44, wherein m2 is 1.

46. The compound according to claim 40, wherein Cy2 is substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

47. The compound according to claim 41, wherein Cy2 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

48. The compound according to any one of claims 1-47 wherein L2 is selected from -O-, -C(O)-, $S(O)_2$-, $-S(O)_2N(R^{4a})$-, $-N(R^{4a})S(O)_2$- and $-CON(R^{4a})$-; n2 is 0, 1, 2, 3, or 4; and R^{3b} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 membered heterocycloalkyl.

49. The compound according to claim 48, wherein R^{3b} is C_1-C_6 alkyl.

50. The compound according to claim 49, wherein R^{3b} is Me, Et, i-Pr.

51. The compound according to claim 48, wherein R^{3b} is 1,3-dihydroxyprop-2-yl.

52. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted C_3-C_7 cycloalkyl.

53. The compound according to claim 52, wherein R^{3b} is substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.

54. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

55. The compound according to claim 54, wherein R^{3b} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

56. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted 4-7 membered heterocycloalkyl;

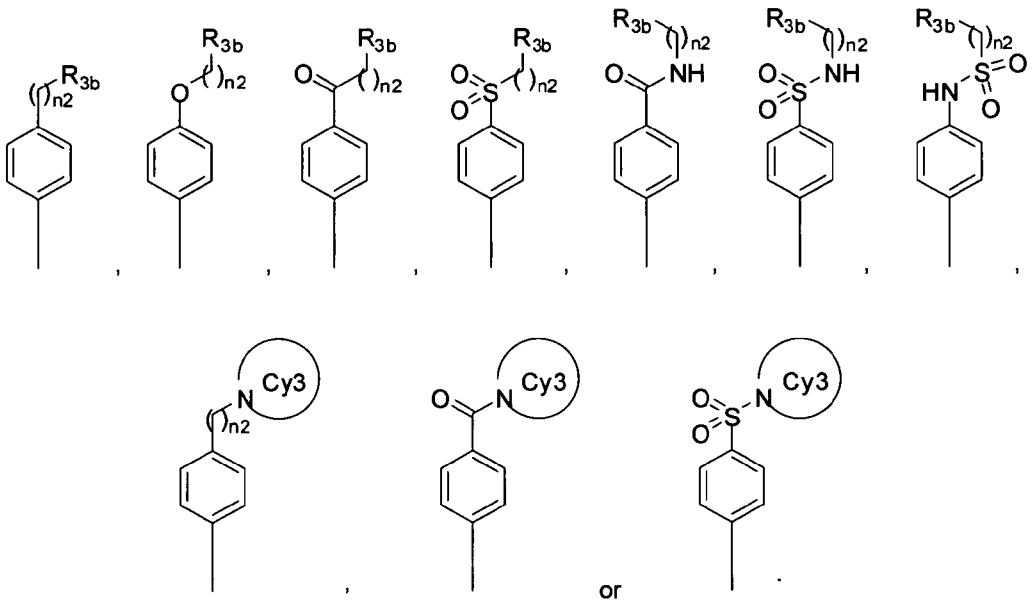
provided that

when L2 is –O-, $S(O)_2N(R^{4a})$- and $-CON(R^{4a})$-, n2 is 1, 2, 3, or 4.

57. The compound according to claim 56, wherein R^{3b} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH;

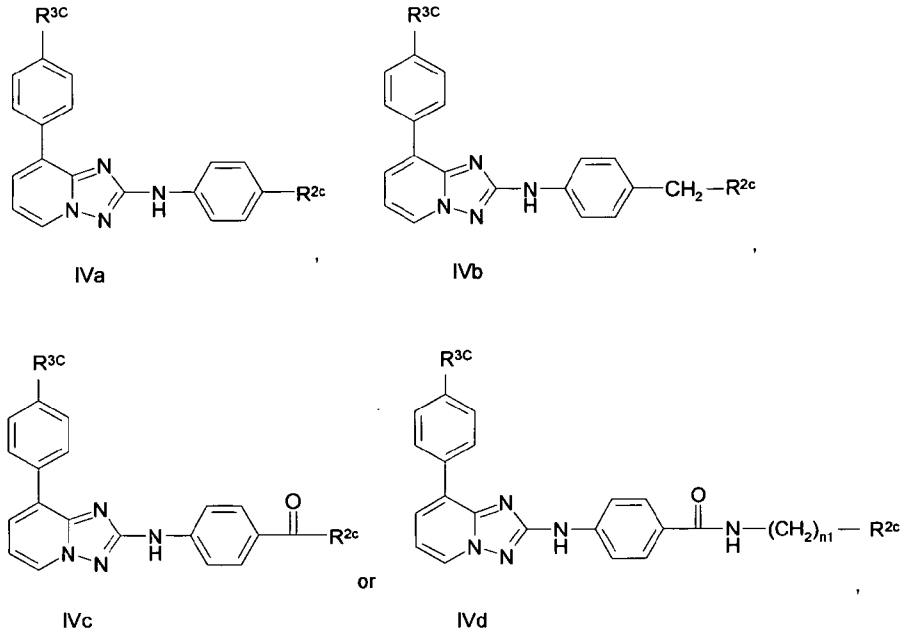
58. The compound according to any one of claims 48-57, wherein R^{4a} is H.

59. The compound according to any one of claims 1-45 wherein each R^{3a} is H; and the –Cy2-L2-$(CH_2)_{n2}$-R^{3b} is selected from:



wherein R^{3b}, and n2 are as described in the preceeding claims; and Cy3 is 4-7 membered N containing heterocycloalkyl.

60. The compound according to claim 1 or 2 wherein the group L2-(CH_2)n2-R^{3b} is R^{3c}; and the compound is according to Formula IVa, IVb, IVc, or IVd:



wherein n1 is 1, 2, or 3; R^{2c} is substituted or unsubstituted dialkylamino, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted -O-aryl, or substituted or unsubstituted heteroaryl;

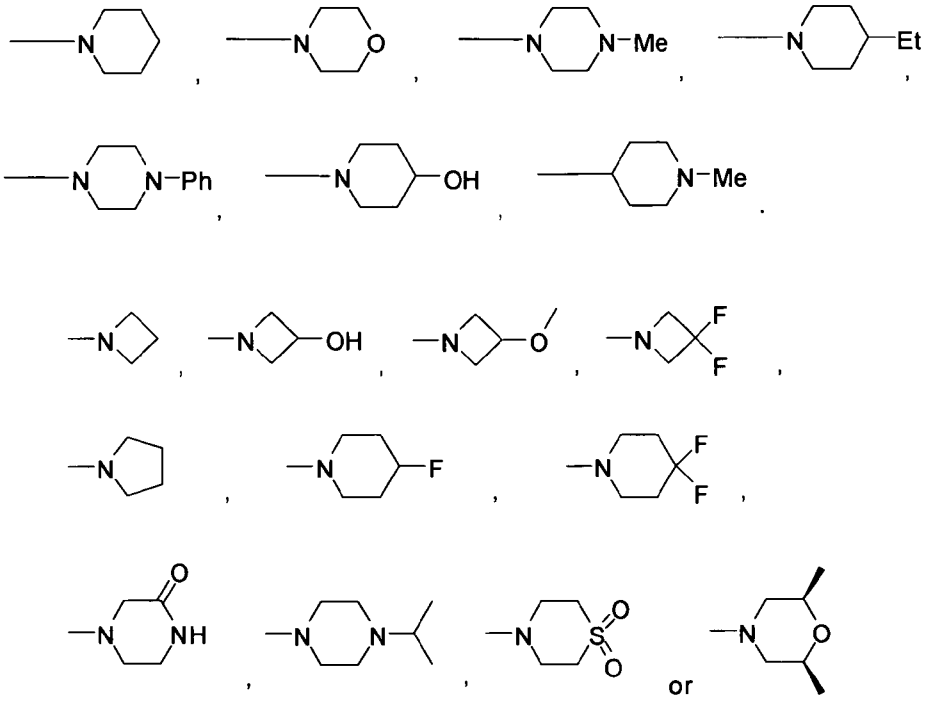
R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, OCH_2CN, CH_2CN, $(CH_2)_2CN$, $CONH_2$, $CONMe_2$, CONHMe, SO_2NH_2, SO2NMe2, CN, NHCOMe, COOH, OH or COOEt; or

R^{3c} is R^{3d}, CH_2-R^{3d}, CO-R^{3d}, $CONH(CH_2)_{n3}$-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d};

R^{3d} is substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and n3 is 1, 2, or 3.

61. The compound according to claim 60, wherein R^{2c} is NMe_2; or R^{2c} is substituted or unsubstituted azetidinyl, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted piperazinyl, substituted or unsubstituted thiomorpholinyl-4,4-dioxide, or substituted or unsubstituted morpholinyl.

62. The compound according to claim 60 wherein R^{2c} is



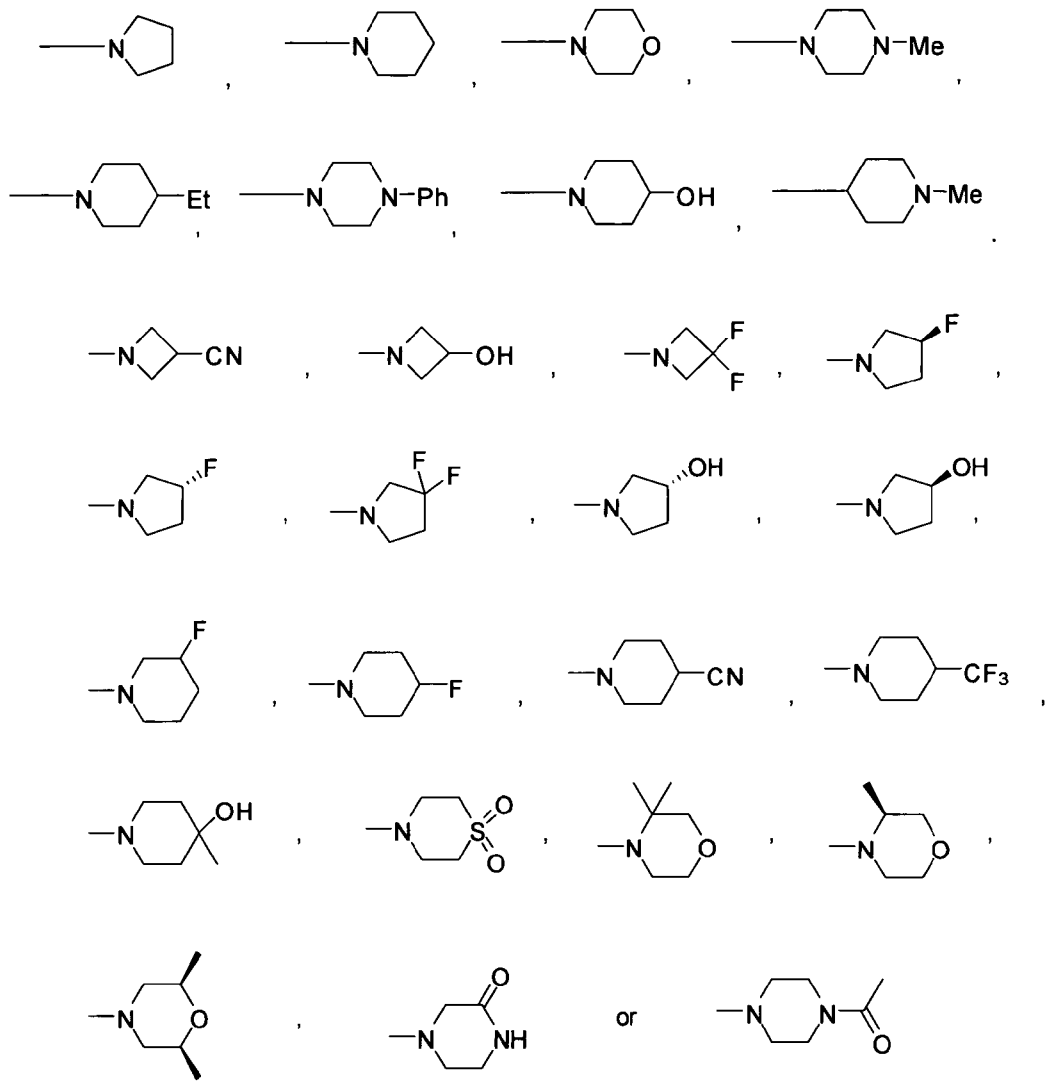
63. The compound according to claim 60 wherein R^{2c} is substituted or unsubstituted pyrazolyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted indolyl, or substituted or unsubstituted indazolyl.

64. The compound according to any one of claims 60-63, wherein R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, SO_2NH_2, SO_2NMe_2, or CN.

65. The compound according to claim 64, wherein R^{3c} is Cl, F, Me, or OMe.

66. The compound according to any one of claims 60-63, wherein R^{3c} is CH_2-R^{3d}, CO-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d}; and R^{3d} is substituted or unsubstituted 4-7 membered heterocycloalkyl.

67. The compound according to claim 66 wherein R^{3d} is



68. The compound according to claim 1 or 2, wherein the compound is according to Formula Va, Vb, Vc, Vd, Ve, Vf, Vg, or Vh:

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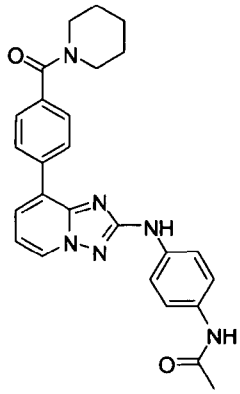
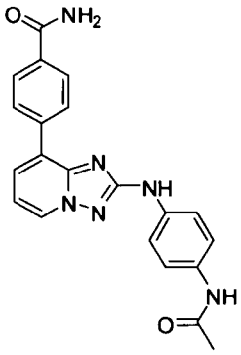
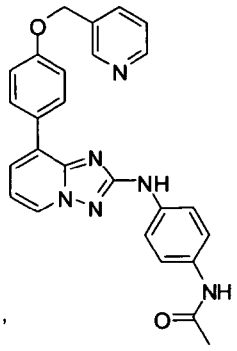


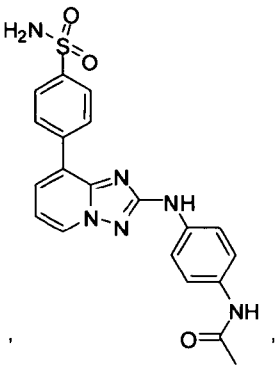
Va



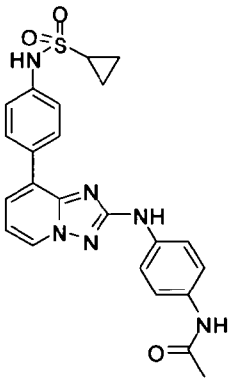
Vb



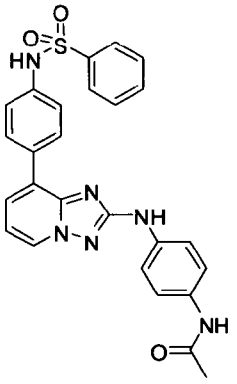
Vc



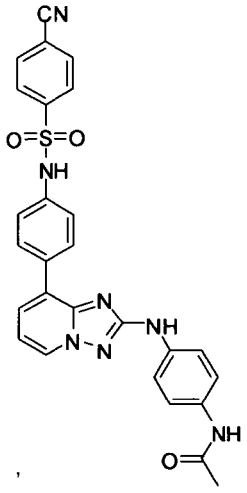
Vd



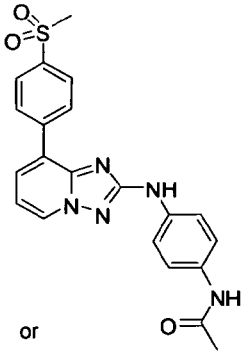
Ve



Vf



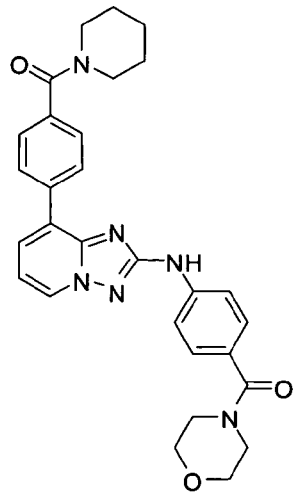
Vg



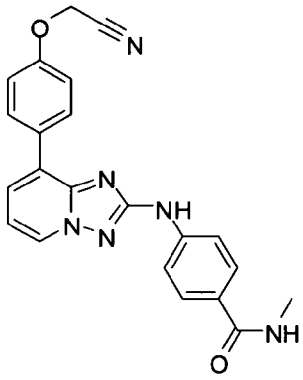
or Vh

69. The compound according to claim 1 or 2, wherein the compound is according to Formula VIa, VIb, VIc, VId, VIe, VIf, VIg, VIh, VIi, VIj, VIk, VIl, VIm or VIn:

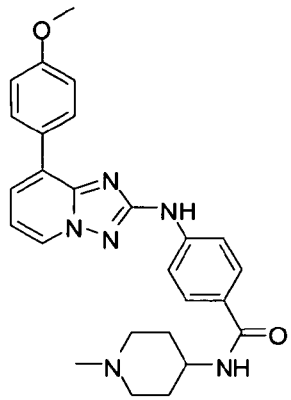
GAL-113-WO-PCT



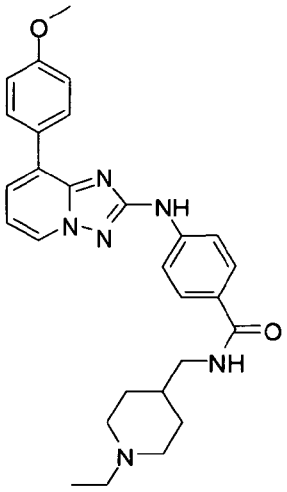
VIa ,



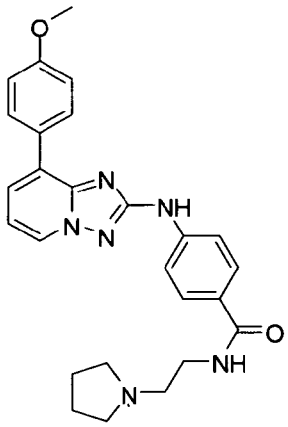
VIb ,



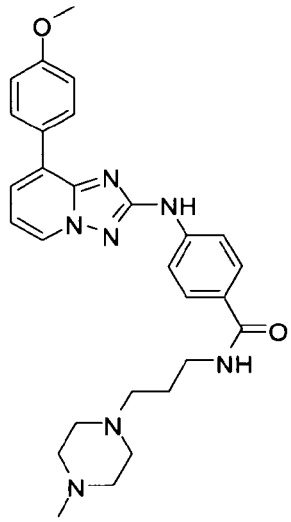
VIc ,



VId ,

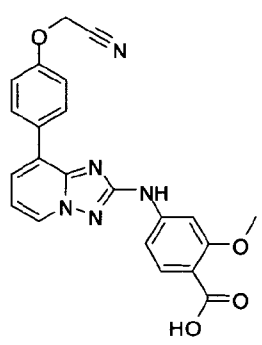


VIe ,

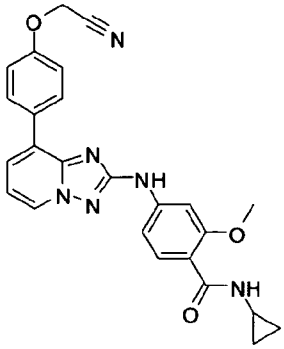


VIf ,

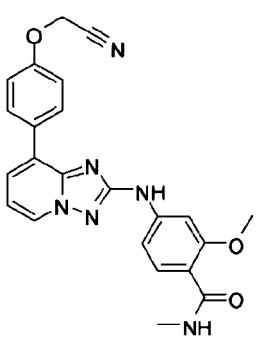
GAL-113-WO-PCT



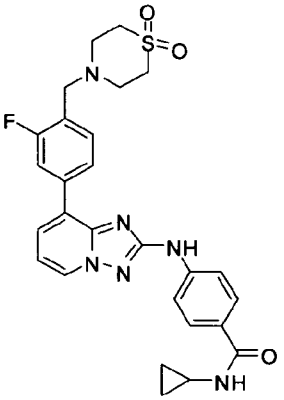
VIg ,



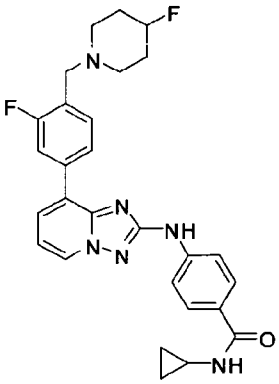
VIh ,



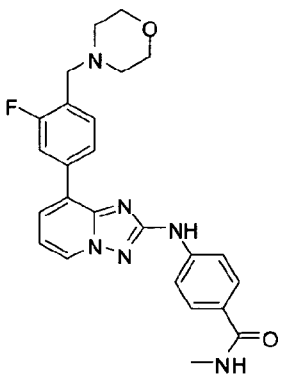
VIi ,



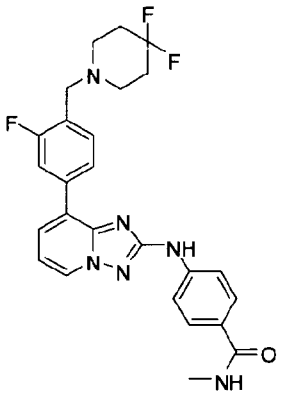
VIj ,



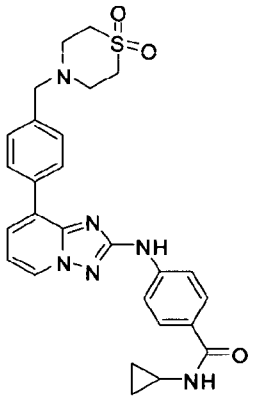
VIk ,



VII ,

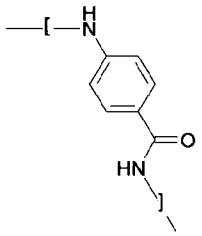


VIm or



VIn

70. The compound according to claim 1 or 2, wherein the compound is according to Formula IVa, IVb, IVc, IVd, Va, Vb, Vc, Vd, Ve, Vf, Vg, Vh VIa, VIb, VIc, VId, VIe or VIf; and the phenyl ring of the group:



is replaced with pyrrolyl, furanyl, thiophenyl, pyrazolyl, oxazolyl, thiazolyl, isoxazolyl, or isothiazolyl group.

71. The compound according to any one of claims 1 to 70, wherein the compound is selected from the compounds listed in Table 1.

72. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound according to any one of claims 1 to 71.

73. The pharmaceutical composition of claim 71, wherein the carrier is a parenteral carrier.

74. The pharmaceutical composition of claim 72, wherein the carrier is an oral carrier.

75. The pharmaceutical composition of claim 72, wherein the carrier is a topical carrier.

76. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 75 for use in medicine.

77. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 75 for use in the treatment or prophylaxis of a disease involving cartilage degradation, bone and/or joint degradation, for example osteoarthritis; and/or conditions involving inflammation or immune responses, such as Crohn's disease, rheumatoid arthritis, psoriasis, allergic airways disease (e.g. asthma, rhinitis), juvenile idiopathic arthritis, colitis, inflammatory bowel diseases, endotoxin-driven disease states (e.g. complications after bypass surgery or chronic endotoxin states contributing to e.g. chronic cardiac failure), diseases involving impairment of cartilage turnover (e.g. diseases involving the anabolic stimulation of chondrocytes), congenital cartilage malformations, diseases associated with hypersecretion of IL6, transplantation rejection (e.g. organ transplant rejection) or proliferative diseases..

78. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 75 for use in the treatment or prophylaxis of rheumatoid arthritis.

79. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 75, for use in the treatment or prophylaxis of a condition or a disease involving inflammation.

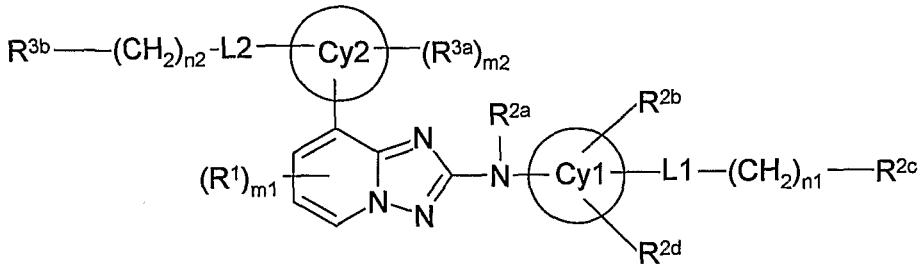
80. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 75, for use in the treatment or prophylaxis of a condition or a disease characterized by abnormal JAK1 activity.

AMENDED CLAIMS

received by the International Bureau on 30 Nomvember 2009 (30.11.2009)

WHAT IS CLAIMED IS:

1. A compound according to Formula I:



I

wherein

each Cy1 and Cy2 is independently selected from aryl and heteroaryl;

each L1 and L2 is independently selected from a single bond, -O-, -C(O)-, -$S(O)_2$-, -$N(R^{4a})$-, -$CON(R^{4a})$-, -$SO_2N(R^{4a})$-, -$N(R^{4a})CO$-, or -$N(R^{4a})SO_2$-;

each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, substituted or unsubstituted amino, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, sulfonic acid, sulfonic acid ester, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, and hydroxyl;

each R^{3a} is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted amido, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, substituted or unsubstituted amino, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2b}, R^{2c}, R^{2d}, and R^{3b} is independently selected from H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, acyl, substituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted –O-aryl, alkoxycarbonyl, substituted alkoxycarbonyl, arylalkyloxy, substituted arylalkyloxy, aryl, substituted aryl, arylalkyl, substituted sulfanyl, substituted sulfinyl, substituted sulfonyl, substituted or unsubstituted

aminosulfonyl, substituted or unsubstituted arylsulfonyl, sulfonic acid, sulfonic acid ester, azido, carboxy, substituted or unsubstituted amino, substituted or unsubstituted amido, cyano, substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, halo, -O-heteroaryl, substituted or unsubstituted heteroaryl, hydroxy, nitro, and thiol;

each R^{2a} and R^{4a} is independently selected from H, C_1-C_6alkyl, substituted C_1-C_6alkyl, C_3-C_7 cycloalkyl, or substituted C_3-C_7 cycloalkyl;

m1 is 0, 1, or 2; m2 is 0, 1, 2, 3, or 4; and each n1 and n2 is independently 0, 1, 2, 3, or 4;

provided that

when L1 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{2c} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n1 is 1, 2, 3, or 4; and

when L2 is -N(R^{4a})-, -CON(R^{4a})-, or -SO_2N(R^{4a})-, and R^{3b} is other than H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, aryl or heteroaryl, then n2 is 1, 2, 3, or 4;

or pharmaceutically acceptable salts thereof.

2. The compound according to claim 1 wherein m1 is 1 or 2; each R^1 is independently selected from C_1-C_6 alkyl, substituted C_1-C_6 alkyl, and halo.

3. The compound according to claim 2 wherein each R^1 is independently selected from Me, CF_3, Cl and F.

4. The compound according to claim 1 wherein R^{2a} is independently selected from H, C_1-C_6 alkyl, and substituted C_1-C_6 alkyl.

5. The compound according to claim 4 wherein R^{2a} is H.

6. The compound according to claim 1 wherein Cy1 is substituted or unsubstituted aryl.

7. The compound according to claim 6 wherein Cy1 is substituted or unsubstituted phenyl.

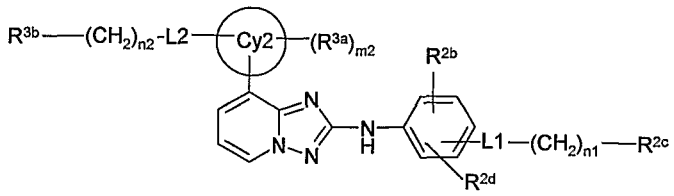
8. The compound according to claim 1 wherein Cy1 is substituted or unsubstituted heteroaryl.

9. The compound according to claim 8 wherein Cy1 is substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

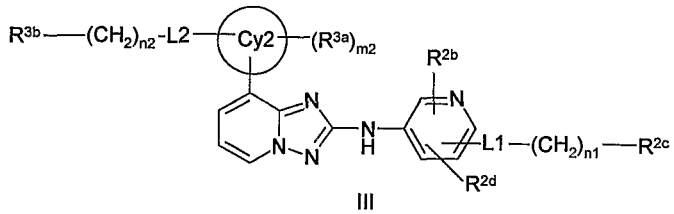
10. The compound according to claim 8 wherein Cy1 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or

unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

11. The compound according to claim 1 wherein the compound is according to Formula II or III:



II



III

wherein Cy2, L1, L2, R^{2b}, R^{2c}, R^{2d}, R^{3a}, R^{3b}, m2, n1, and n2 are as in claim 1.

12. The compound according to claim 11 wherein R^{2b}, and R^{2d} are independently H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_1-C_6 alkoxy or halo.

13. The compound according to claim 12 wherein R^{2b}, and R^{2d} are independently H, Me, OMe, F or Cl.

14. The compound according to any one of claims 1-13 wherein L1 is a single bond, n1 is 0, and R^{2c} is H, Cl, F, Me, Et, OMe, CF_3, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

15. The compound according to any one of claims 1-13 wherein L1 is a single bond, n1 is 0, and R^{2c} is NHCOMe, or COOH.

16. The compound according to any one of claims 1-13 , wherein L1 is CONH; n1 is 2 or 3; and R^{2c} is NMe_2, OMe, or NHCOMe.

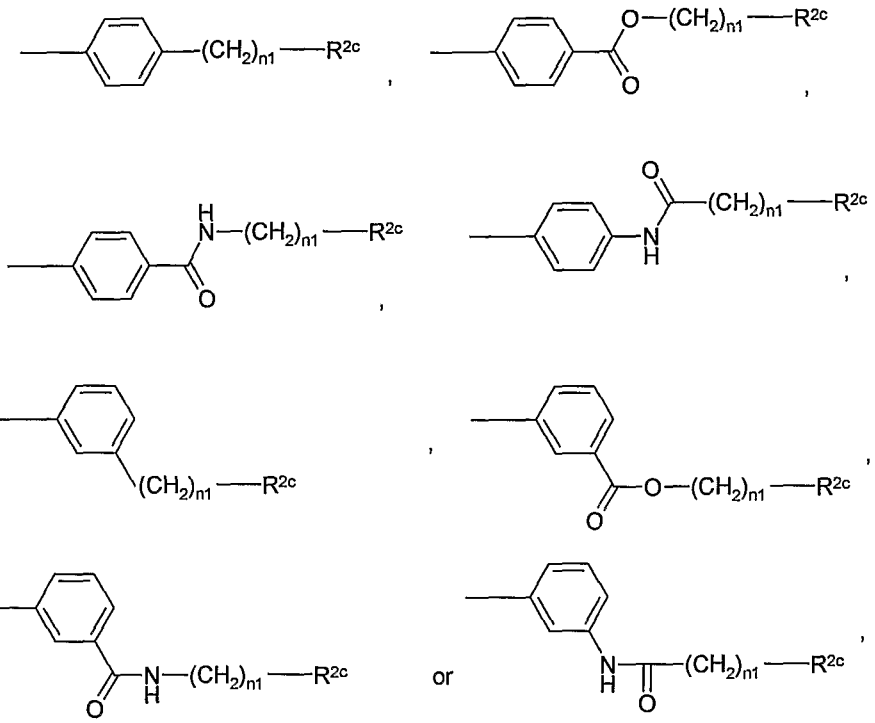
17. The compound according to any one of claims 1-13 wherein L1 is selected from a single bond, -C(O)-, and -CON(R^{4a})-; n1 is 0, 1, 2, 3, or 4; R^{4a} is selected from selected from H and C_1-C_6 alkyl and R^{2c} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 membered heterocycloalkyl.

18. The compound according to claim 17, wherein R^{2c} is C_1-C_6 alkyl.

19. The compound according to claim 17, wherein R^{2c} is Me, Et, i-Pr, 1,3-dihydroxyprop-2-yl.

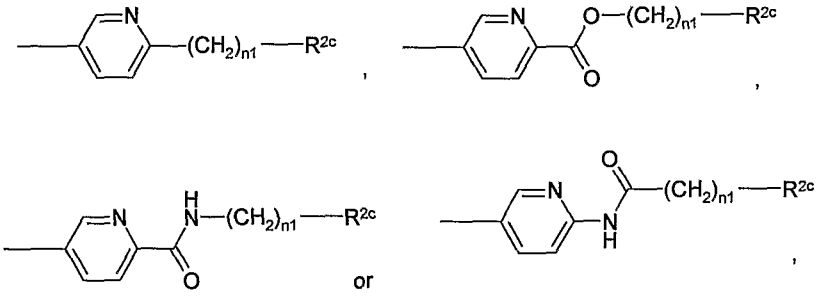
20. The compound according to claim 17, wherein R^{2c} is substituted or unsubstituted C_3-C_7 cycloalkyl.

21. The compound according to claim 20, wherein R^{2c} is substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.
22. The compound according to claim 17, wherein R^{2c} is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.
23. The compound according to claim 22, wherein R^{2c} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.
24. The compound according to claim 17, wherein R^{2c} is substituted or unsubstituted 4-7 membered heterocycloalkyl.
25. The compound according to claim 24, wherein R^{2c} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH.
26. The compound according to any one of claims 17-25, wherein R^{4a} is H.
27. The compound according to any one of claims 17-25, wherein L1 is CONH; and n1 is 0, 1, 2 or 3.
28. The compound according to claim 27 wherein L1 is CONH; and n1 is 0, or 1.
29. The compound according to any one of claims 17-25, wherein L1 is CO; and n1 is 0, 1, 2 or 3.
30. The compound according to claim 29, wherein L1 is CO; and n1 is 0, or 1.
31. The compound according to any one of claims 1-7 or 11-13 wherein the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



and wherein n1 and R^{2c} are as described in the previous claims.

32. The compound according to any one of claims 1-5, or 8-13 wherein the -Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:

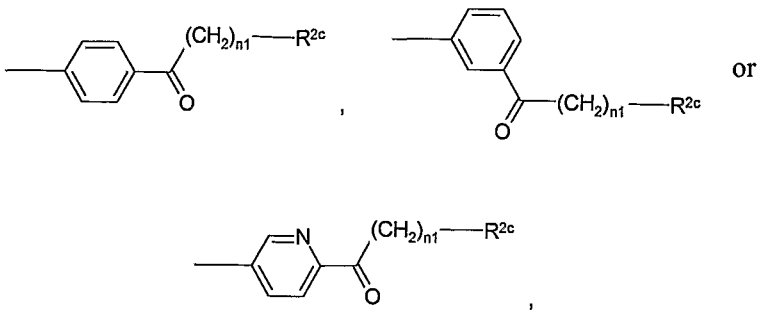


and wherein n1 and R^{2c} are as described in the previous claims.

33. The compound according to any one of claims 1-5, or 8-13 wherein the -Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:

and wherein n1 and R^{2c} are as described in the previous claims.

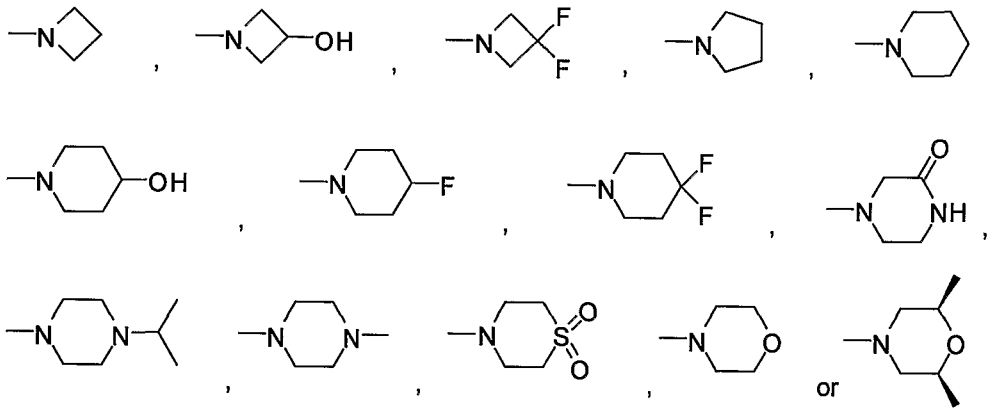
34. The compound according to any one of claims 1-9 or 11-13 wherein the -Cy1-L1-$(CH_2)_{n1}$-R^{2c} is selected from:



and wherein n1 and R^{2c} are as described in the previous claims.

35. The compound according to any one of claims 32-34, wherein R^{2c} is 4-7 membered N-containing heterocycloalkyl or heteroaryl.

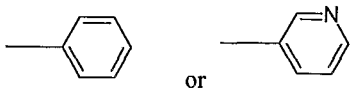
36. The compound according to claim 35, wherein R^{2c} is:



37. The compound according to claim 35, wherein R^{2c} is pyrazolyl, pyrrolyl, imidazolyl, or triazolyl.

38. The compound according to any one of claims 32-37, wherein n1 is 0, 1 or 2.

39. The compound according to any one of claims 1-5, and 8-9 wherein the $-Cy1-L1-(CH_2)_{n1}-R^{2c}$ is selected from:



40. The compound according to any one of claims 1-39, wherein Cy2 is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

41. The compound according to claim 40, wherein Cy2 is substituted or unsubstituted aryl.

42. The compound according to claim 41, wherein Cy2 is Ph; and m2 is 0.

43. The compound according to claim 40, wherein Cy2 is Ph; m2 is 1, 2 or 3; and each R^{3a} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, halo, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

44. The compound according to claim 43, wherein each R^{3a} is independently Cl, F, Me, Et, OMe, CF_3, $CONH_2$, $CONMe_2$, CONHMe, CN, NHCOMe, COOH, OH or COOEt.

45. The compound according to claim 43 or 44, wherein m2 is 1.

46. The compound according to claim 40, wherein Cy2 is substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

47. The compound according to claim 41, wherein Cy2 is substituted or unsubstituted pyrrolyl, substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or unsubstituted isoxazolyl, or substituted or unsubstituted isothiazolyl.

48. The compound according to any one of claims 1-47 wherein L2 is selected from -O-, -C(O)-, $S(O)_2$-, $-S(O)_2N(R^{4a})$-, $-N(R^{4a})S(O)_2$- and $-CON(R^{4a})$-; n2 is 0, 1, 2, 3, or 4; and R^{3b} is substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted 4-7 membered heterocycloalkyl.

49. The compound according to claim 48, wherein R^{3b} is C_1-C_6 alkyl.

50. The compound according to claim 49, wherein R^{3b} is Me, Et, i-Pr.

51. The compound according to claim 48, wherein R^{3b} is 1,3-dihydroxyprop-2-yl.

52. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted C_3-C_7 cycloalkyl.

53. The compound according to claim 52, wherein R^{3b} is substituted or unsubstituted cyclopropyl, substituted or unsubstituted cyclobutyl, substituted or unsubstituted cyclohexyl, or substituted or unsubstituted cyclopentyl.

54. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

55. The compound according to claim 54, wherein R^{3b} is substituted or unsubstituted Ph, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted thiazolyl, substituted or

unsubstituted indolyl, substituted or unsubstituted indazolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted benzodioxanyl, substituted or unsubstituted benzoxazolyl, substituted or unsubstituted quinolinyl, or substituted or unsubstituted isoquinolinyl.

56. The compound according to claim 48, wherein R^{3b} is substituted or unsubstituted 4-7 membered heterocycloalkyl;

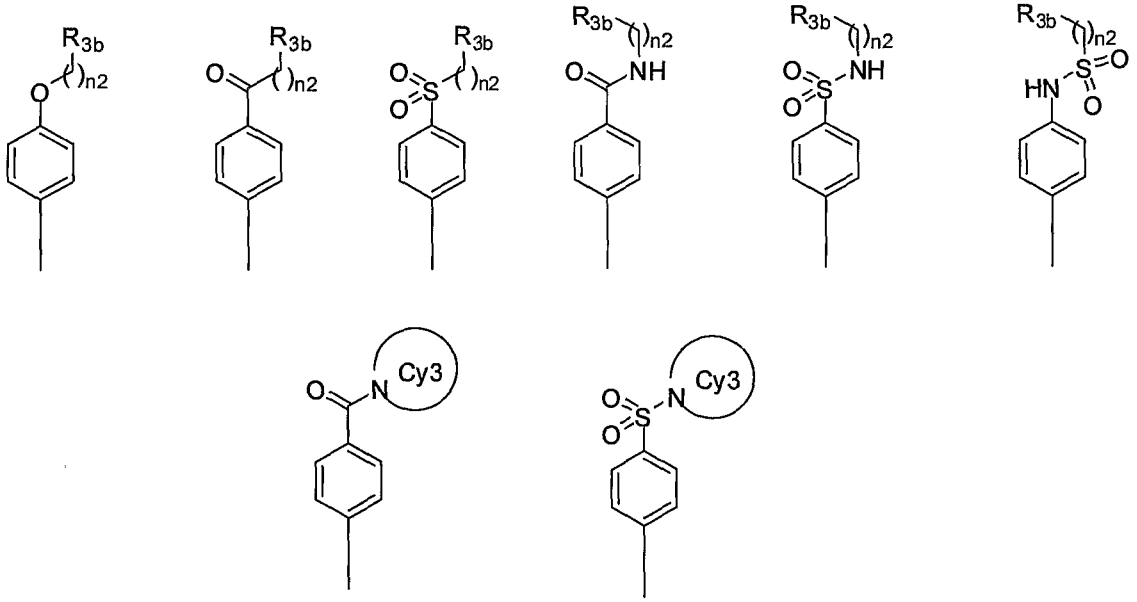
provided that

when L2 is –O-, $S(O)_2N(R^{4a})$- and -$CON(R^{4a})$-, n2 is 1, 2, 3, or 4.

57. The compound according to claim 56, wherein R^{3b} is piperidinyl, morpholinyl, piperazinyl, or pyrrolidinyl, each of which may be unsubstituted or substituted with C_1-C_6 alkyl, acyl, phenyl, or OH;

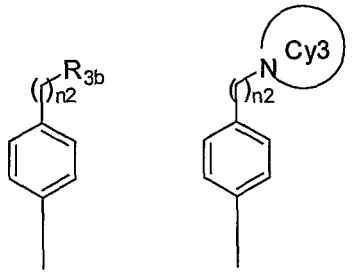
58. The compound according to any one of claims 48-57, wherein R^{4a} is H.

59. The compound according to any one of claims 1-45 wherein each R^{3a} is H; and the –Cy2-L2-$(CH_2)_{n2}$-R^{3b} is selected from:



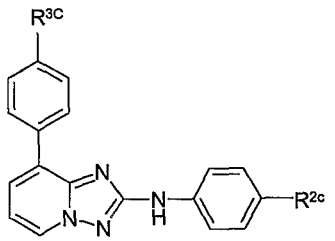
wherein R^{3b}, and n2 are as described in the preceeding claims; and Cy3 is 4-7 membered N containing heterocycloalkyl.

60. The compound according to any one of claims 1-45 wherein each R^{3a} is H; and the –Cy2-L2-$(CH_2)_{n2}$-R^{3b} is selected from:

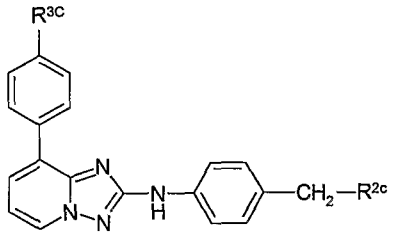


wherein R^{3b}, and n2 are as described in the preceeding claims; and Cy3 is 4-7 membered N containing heterocycloalkyl.

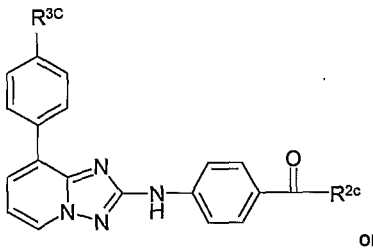
61. The compound according to claim 1 wherein the group L2-(CH_2)n2-R^{3b} is R^{3c}; and the compound is according to Formula IVa, IVb, IVc, or IVd:



IVa ,

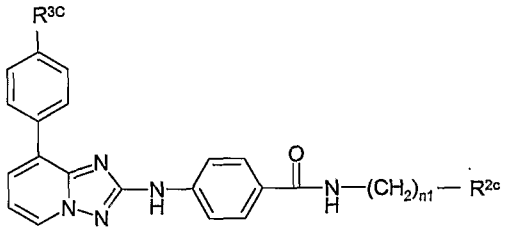


IVb ,



IVc

or



IVd ,

wherein n1 is 1, 2, or 3; R^{2c} is substituted or unsubstituted dialkylamino, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted -O-aryl, or substituted or unsubstituted heteroaryl;

R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, OCH_2CN, CH_2CN, $(CH_2)_2CN$, $CONH_2$, $CONMe_2$, CONHMe, SO_2NH_2, SO2NMe2, CN, NHCOMe, COOH, OH or COOEt; or

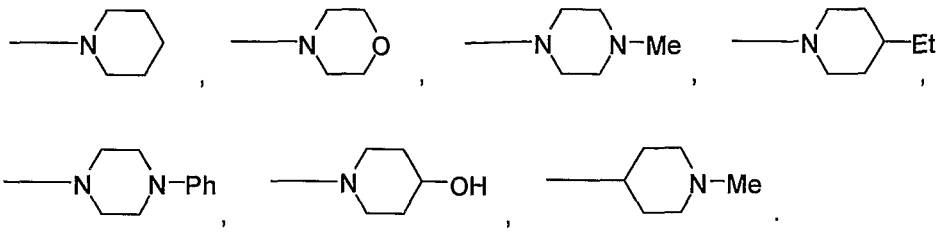
R^{3c} is R^{3d}, CH_2-R^{3d}, CO-R^{3d}, $CONH(CH_2)_{n3}$-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d};

R^{3d} is substituted or unsubstituted C_3-C_7 cycloalkyl, substituted or unsubstituted 4-7 membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and n3 is 1, 2, or 3.

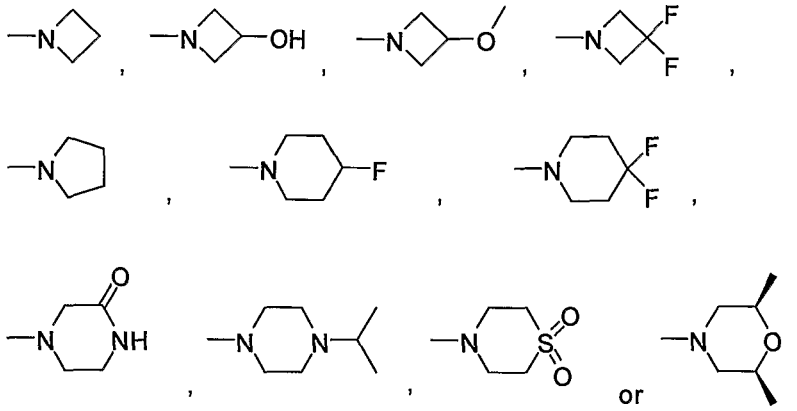
62. The compound according to claim 61, wherein R^{2c} is NMe_2; or R^{2c} is substituted or unsubstituted azetidinyl, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted piperidinyl,

substituted or unsubstituted piperazinyl, substituted or unsubstituted thiomorpholinyl-4,4-dioxide, or substituted or unsubstituted morpholinyl.

63. The compound according to claim 61 wherein R^{2c} is



64. The compound according to claim 61 wherein R^{2c} is



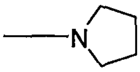
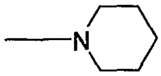
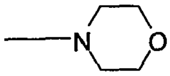
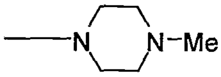
65. The compound according to claim 61 wherein R^{2c} is substituted or unsubstituted pyrazolyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted triazolyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted pyridyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted indolyl, or substituted or unsubstituted indazolyl.

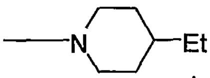
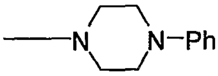
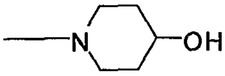
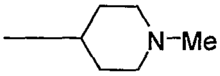
66. The compound according to any one of claims 61-65, wherein R^{3c} is Cl, F, Me, Et, OMe, OEt, O-i-Pr, CF_3, OCF_3, SO_2NH_2, SO_2NMe_2, or CN.

67. The compound according to claim 66, wherein R^{3c} is Cl, F, Me, or OMe.

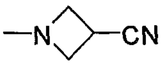
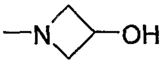
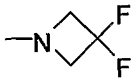
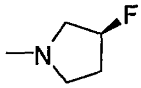
68. The compound according to any one of claims 61-65, wherein R^{3c} is CH_2-R^{3d}, CO-R^{3d}, NHCO-R^{3d}, or $NHSO_2$-R^{3d}; and R^{3d} is substituted or unsubstituted 4-7 membered heterocycloalkyl.

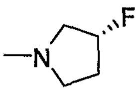
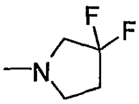
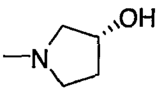
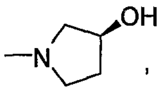
69. The compound according to claim 68 wherein R^{3d} is

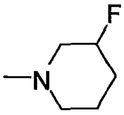
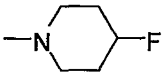
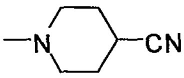
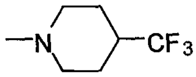
 ,  ,  ,  ,

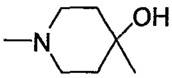
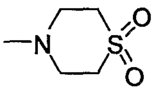
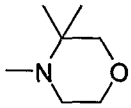
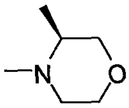
 ,  ,  ,  .

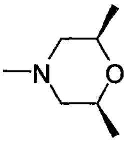
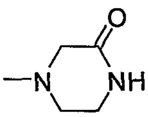
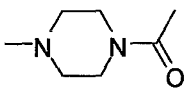
70. The compound according to claim 68 wherein R^{3d} is

 ,  ,  ,  ,

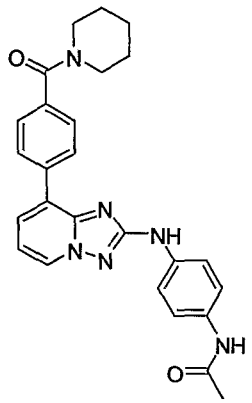
 ,  ,  ,  ,

 ,  ,  ,  ,

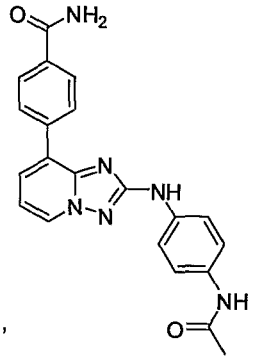
 ,  ,  ,  ,

 ,  or 

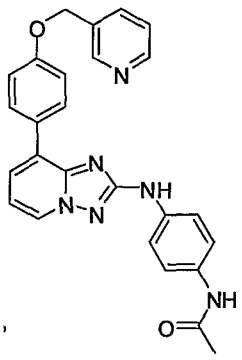
71. The compound according to claim 1, wherein the compound is according to Formula Va, Vb, Vc, Vd, Ve, Vf, Vg, or Vh:



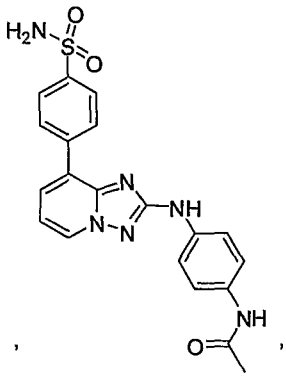
Va



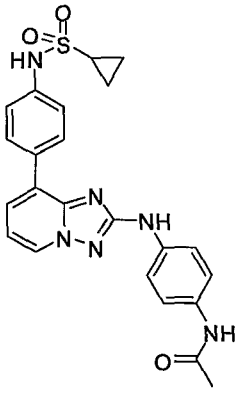
Vb



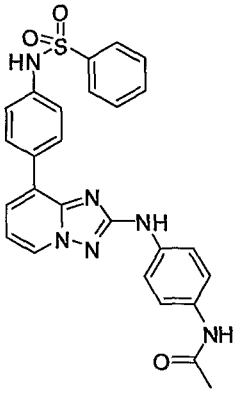
Vc



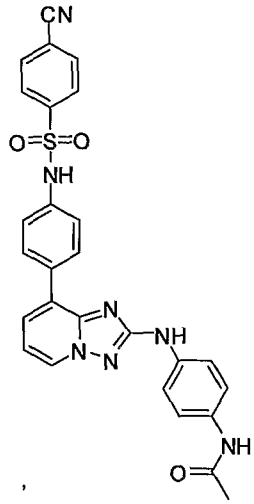
Vd



Ve

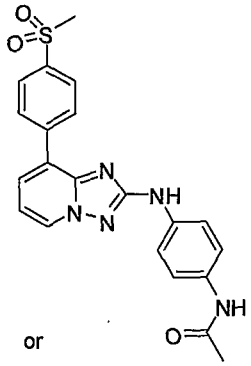


Vf



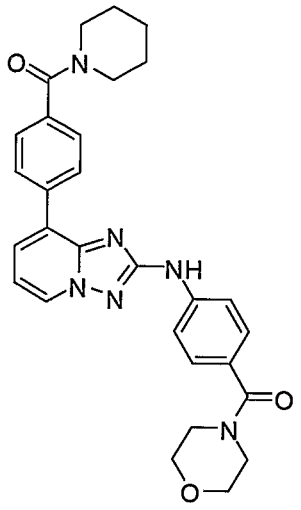
Vg

or

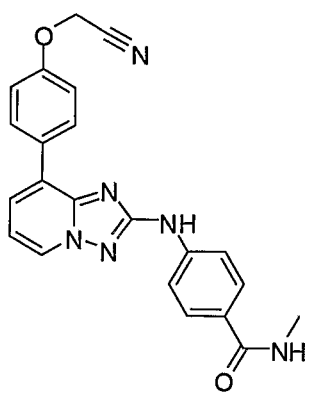


Vh

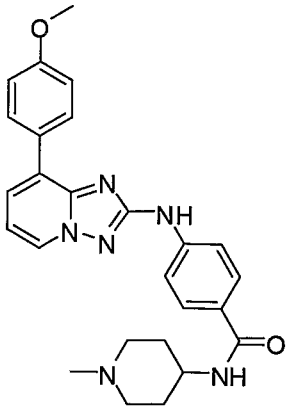
72. The compound according to claim 1 or 2, wherein the compound is according to Formula VIa, VIb, VIc, VId, VIe, or VIf:



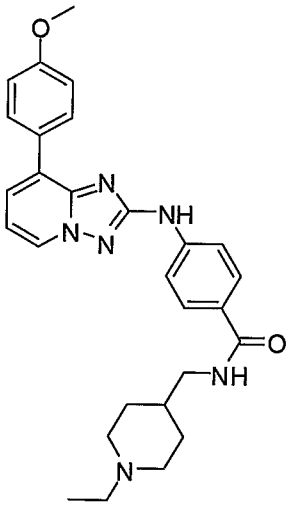
VIa ,



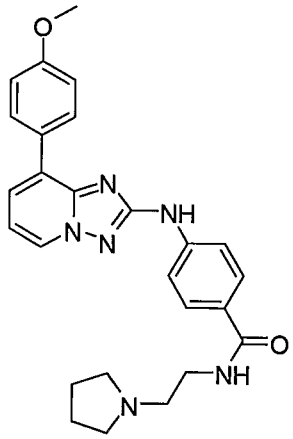
VIb ,



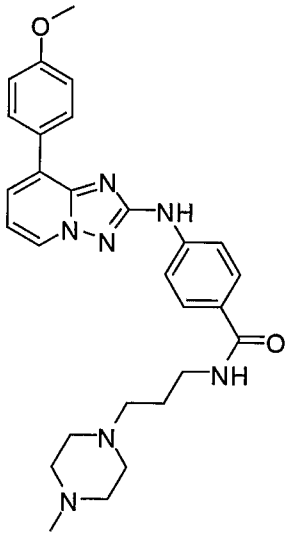
VIc ,



VId ,

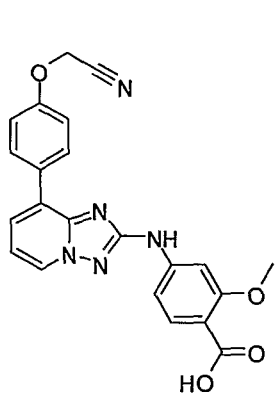


VIe ,

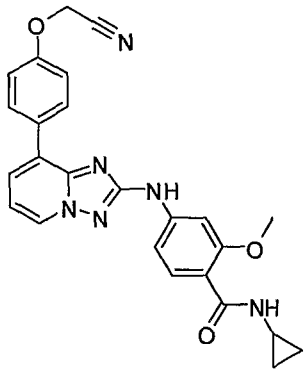


VIf ,

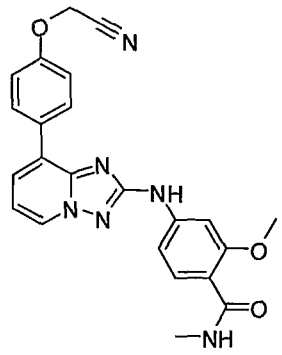
73. The compound according to claim 1, wherein the compound is according to Formula VIg, VIh, VIi, VIj, VIk, VIl, VIm or VIn:



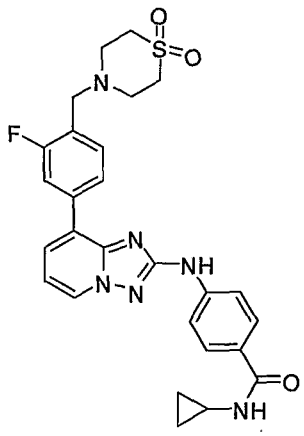
VIg ,



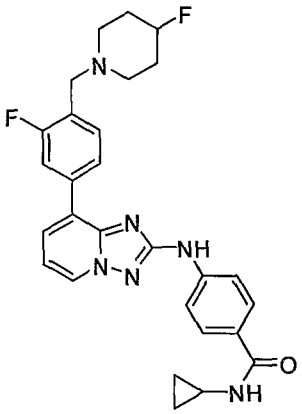
VIh ,



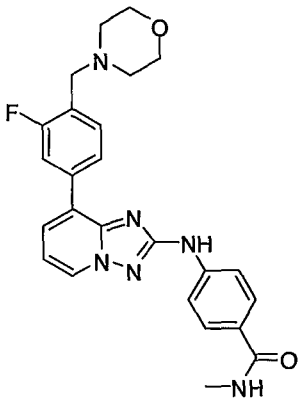
VIi ,



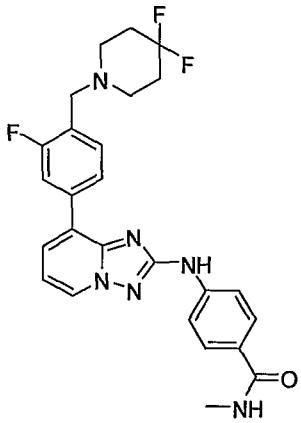
VIj ,



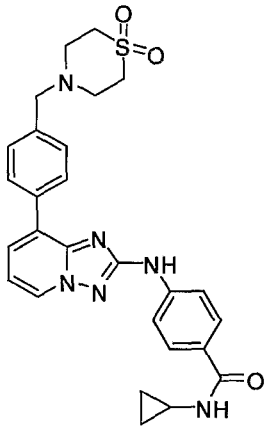
VIk ,



VII ,

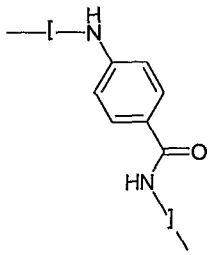


VIm or



VIn

74. The compound according to claim 1 or 2, wherein the compound is according to Formula IVa, IVb, IVc, IVd, Va, Vb, Vc, Vd, Ve, Vf, Vg, Vh VIa, VIb, VIc, VId, VIe or VIf; and the phenyl ring of the group:



is replaced with pyrrolyl, furanyl, thiophenyl, pyrazolyl, oxazolyl, thiazolyl, isoxazolyl, or isothiazolyl group. 75. The compound according to any one of claims 1-74, wherein the compound is selected from:

N-{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine

{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-morpholin-4-yl-methanone

N-(4-{8-[4-(Piperidine-1-carbonyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

{4-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-phenyl}-piperidin-1-yl-methanone

(4-{2-[4-(Morpholine-4-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenyl)-piperidin-1-yl-methanone

N-{4-[8-(4-Chloro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(3,5-Difluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Trifluoromethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(3-Trifluoromethoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Isopropoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(3-Fluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-(4-{8-[4-(Piperidine-1-carbonyl)-phenyl]-6-trifluoromethyl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

N-[4-(8-Naphthalen-2-yl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-phenyl]-acetamide

[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-amine

N-{3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid

N-{4-[8-(4-Methanesulfonyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-N-(2-phenoxy-ethyl)-benzamide

N-{4-[8-(3-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Cyclopropanesulfonylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Benzenesulfonylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Dipropylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(2-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Benzylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-piperidin-1-yl-methanone

[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-[1,2,4]triazol-1-ylmethyl-phenyl)-amine

N-Isopropyl-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Benzyl-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

{4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-(4-methyl-piperazin-1-yl)-methanone

(4-Hydroxy-piperidin-1-yl)-{4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-methanone

(1,3-Dihydro-isoindol-2-yl)-{4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-methanone

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-3-ylmethyl-benzamide

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide

N-(1-Ethyl-piperidin-4-ylmethyl)-4-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Isopropyl-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(1-methyl-piperidin-4-yl)-benzamide

N-(4-{8-[4-(Pyridin-3-ylmethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

N-(4-{8-[4-(3-Hydroxy-propoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-N,N-dimethyl-benzamide

N-{4-[8-(4-Dimethylamino-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

(4-Imidazol-1-ylmethyl-phenyl)-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(1-methyl-piperidin-4-yl)-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzoic acid

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-2-ylmethyl-benzamide

N-Benzyl-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-2-ylmethyl-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-pyridin-3-ylmethyl-benzamide

N-(3-Dimethylamino-propyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyrrolidin-1-yl-ethyl)-benzamide

N-(1-Ethyl-piperidin-4-ylmethyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-phenoxy-ethyl)-benzamide

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyridin-3-yl-ethyl)-benzamide

N-{4-[8-(1H-Indol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(1H-Pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(1-Methyl-1H-indol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(4-Hydroxymethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-(4-{8-[4-(4-Cyano-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

N-{4-[8-(4-Dimethylsulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

4-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide

N-(2,5-Dimethyl-2H-pyrazol-3-ylmethyl)-3-[8-(4-methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-(2-pyridin-3-yl-ethyl)-benzamide

3-[8-(4-Methoxy-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-[3-(4-methyl-piperazin-1-yl)-propyl]-benzamide

4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzamide

N-{4-[8-(4-Sulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-{4-[8-(1H-Indazol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-acetamide

N-(4-{8-[4-(3,5-Dichloro-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

N-(4-{8-[4-(2,4,6-Trimethyl-benzenesulfonylamino)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-acetamide

4-[2-(4-Acetylamino-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzoic acid

4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

Methyl 2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzate

8-(4-methoxyphenyl)-N-(pyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzic acid

2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzonitrile

4-(8-(4-((6-chloropyridin-3-yl)methoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

5-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide, and

2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N,N-dimethylbenzamide

76. The compound according to any one of claims 1-74, wherein the compound is selected from:

4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxybenzic acid

8-(4-methoxyphenyl)-N-(1-methyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

6-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one

4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methoxybenzamide

4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxy-N-methylbenzamide

2-(4-(2-(1-methyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile

2-(4-(2-(3-methoxy-4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile

2-(4-(2-(4-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile

N-cyclopropyl-2-fluoro-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-2-fluoro-4-(8-(4-isopropoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-(cyanomethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-fluorobenzamide

N-cyclopropyl-2-fluoro-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-2-hydroxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methylbenzamide

5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-cyclopropyl-5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide

N-cyclopropyl-4-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methylbenzamide

N-cyclopropyl-2-methyl-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-2-ethoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclobutyl-2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(2-(4-(4-isopropylpiperazin-1-yl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

2-(4-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenoxy)acetonitrile

(3-hydroxyazetidin-1-yl)(2-methoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methoxybenzamide

N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide

N-cyclopropyl-4-(8-(4-isopropoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide

N-cyclopropyl-4-(8-(4-(trifluoromethoxy)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-(trifluoromethyl)benzamide

N-cyclopropyl-2-(2-(dimethylamino)-2-oxoethoxy)-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N,N-dimethyl-4-(2-(1-methyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

4-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N-cyclopropyl-2-isopropoxy-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-(4-(4-isopropylpiperazin-1-yl)phenyl)-8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

4-(2-(2-benzyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N-cyclopropyl-2-methoxy-4-(8-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-2-methoxybenzamide

N-(cyclopropylmethyl)-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

azetidin-1-yl(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

(3,3-difluoroazetidin-1-yl)(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

4-(2-(1-benzyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-cyclopropylbenzamide

4-(2-(1-benzyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

2-cyclopropyl-5-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one

N-cyclopropyl-4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

(4-(8-(2-aminopyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(3-hydroxyazetidin-1-yl)(4-(8-(pyridin-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-2-methylbenzamide

(3-hydroxyazetidin-1-yl)(4-(8-(5-(methylsulfonyl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

(4-(8-(2-(dimethylamino)pyrimidin-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(4-(8-(6-(dimethylamino)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

4-(2-(2-cyclopropyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

(3-hydroxyazetidin-1-yl)(4-(8-(4-(3-hydroxyazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

N-(2-hydroxy-2-methylpropyl)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

(3-methoxyazetidin-1-yl)(4-(8-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

(3-hydroxyazetidin-1-yl)(4-(8-(1-methyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

N,N-dimethyl-4-(2-(1-(pyridin-2-ylmethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

4-(8-(1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

N-cyclopropyl-4-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(2-(1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N-cyclopropyl-4-(8-(1-methyl-1H-pyrazol-5-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(2-(4-(cyclopropylcarbamoyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N,N-dimethyl-4-(2-(6-(morpholine-4-carbonyl)pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N,N-dimethyl-4-(2-(1-oxo-2-(pyridin-2-ylmethyl)isoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N,N-dimethyl-4-(2-(1-(methylsulfonyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

4-(2-(1-isopropyl-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N,N-dimethyl-4-(2-(4-(pyridin-2-ylmethylcarbamoyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N,N-dimethyl-4-(2-(4-(3-oxopiperazine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

4-(2-(4-(2,6-dimethylmorpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

4-(2-(4-(4-hydroxypiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

4-(2-(4-(4-fluoropiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

(R)-4-(2-(4-(3-hydroxypiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

4-{2-[4-(1,1-Dioxo-1lambda*6*-thiomorpholine-4-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-N,N-dimethyl-benzamide

N,N-dimethyl-4-(2-(4-(4-methylpiperazine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N,N-dimethyl-4-(2-(1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N,N-dimethyl-4-(2-(2-methyl-1-oxoisoindolin-5-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

5-(8-(4-(dimethylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N,N-dimethylpicolinamide

4-(8-(4-(2-cyanopropan-2-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

4-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

5-(8-(4-(cyanomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-methyl-5-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)picolinamide

N-cyclopropyl-4-(8-(isoxazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

(4-(8-(1-(difluoromethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

5-(8-(4-(3-hydroxyazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

5-(8-(4-(2-hydroxy-2-methylpropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

N,N-dimethyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

azetidin-1-yl(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

piperidin-1-yl(4-(2-(4-(pyrrolidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone

(4-fluoropiperidin-1-yl)(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

(4-hydroxypiperidin-1-yl)(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)methanone

4-(4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzoyl)piperazin-2-one

N-cyclopropyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-(2-hydroxyethyl)-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(5-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)pyridin-2-yl)piperidine-4-carbonitrile

1-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)cyclopropanecarbonitrile

4-(8-(4-(1-cyanocyclopropyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

4-(8-(6-(4-cyanopiperidin-4-yl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

2-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)acetonitrile

(R)-(4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(4-(8-(4-((3,3-difluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(3-hydroxyazetidin-1-yl)methanone

(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-(3-hydroxy-azetidin-1-yl)-methanone

(R)-5-(8-(4-(2-hydroxypropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

4-(8-(6-(3-cyanoazetidin-3-yl)pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

N,N-dimethyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N-(2-hydroxyethyl)-N-methyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)(pyrrolidin-1-yl)methanone

(4-fluoropiperidin-1-yl)(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone

(4-(8-(4-(2,6-dimethylmorpholine-4-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)phenyl)(morpholino)methanone

4-(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzoyl)piperazin-2-one

N-isopropyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N-(2-hydroxyethyl)-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(pyridin-2-ylmethyl)benzamide

N-(2-methoxyethyl)-N-methyl-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-(cyclopropylmethyl)-4-(8-(4-(piperidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(2-(4-(4,4-difluoropiperidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

(S)-5-(8-(4-(2-hydroxypropylcarbamoyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

4-(2-(6-(3-hydroxyazetidine-1-carbonyl)pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N,N-dimethylbenzamide

5-(8-(4-(3-cyanoazetidine-1-carbonyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-((thiomorpholine-1,1-dioxide)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

(S)-N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-((3-methylmorpholino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

(R)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(2-hydroxypropyl)benzamide

(S)-4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-(2-hydroxypropyl)benzamide

5-(8-(4-(2-cyanopropan-2-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

5-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

2-cyclopropyl-5-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one

N-Cyclopropyl-4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

2-(4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)-2-morpholinoethanol

1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)-4-methylpiperidin-4-ol

(S)-1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)pyrrolidin-3-ol

1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzyl)azetidine-3-carbonitrile

1-(4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol

2-methyl-1-(4-(8-(4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol

5-(8-(4-(1-cyanocyclopropyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

(S)-N-cyclopropyl-4-(8-(4-((3-methylmorpholino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

(S)-N-cyclopropyl-4-(8-(4-((3-hydroxypyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-Cyclopropyl-4-(8-{4-[(1,1-dioxo-tetrahydro-1lambda*6*-thiophen-3-ylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

(R)-5-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

(S)-5-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-cyclopropyl-4-(8-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

1-(4-(2-(1-(difluoromethyl)-1H-pyrazol-4-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)-2-methyl-1-morpholinopropan-2-ol

N-cyclopropyl-4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-Cyclopropyl-4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

(R)-N-cyclopropyl-4-(8-(4-((3-hydroxypyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-(((2-hydroxyethyl)(methyl)amino)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-((4-acetoylpiperazin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

5-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-cyclopropyl-4-(8-(4-((4-(trifluoromethyl)piperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-((4-cyanopiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

2-cyclopropyl-5-(8-(4-((3-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)isoindolin-1-one

N-cyclopropyl-4-(8-(3-fluoro-4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-((3-cyanoazetidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

N-cyclopropyl-4-(8-(4-(1-morpholinoethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

4-(8-(3-fluoro-4-(morpholinomethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide

(S)-N-cyclopropyl-4-(8-(3-fluoro-4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide

4-(8-(4-((4,4-difluoropiperidin-1-yl)methyl)-3-fluorophenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylbenzamide

4-(8-(4-(4-cyanotetrahydro-2H-pyran-4-yl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

N-cyclopropyl-4-(8-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

1-(4-(2-(4-(3-hydroxyazetidine-1-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzoyl)azetidine-3-carbonitrile

4-(8-(1-(1-cyano-2-methylpropan-2-yl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

N-cyclopropyl-4-(8-(1,5-dimethyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-((3,3-difluoroazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

4-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropylbenzamide

(R)-N-cyclopropyl-4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

(S)-N-cyclopropyl-4-(8-(4-((3-fluoropyrrolidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(4-((4-fluoropiperidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(1-(2-(dimethylamino)-2-oxoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

N-cyclopropyl-4-(8-(1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)benzamide

5-(8-(4-((3-cyanoazetidin-1-yl)methyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methylpicolinamide

N-(1-(difluoromethyl)-1H-pyrazol-4-yl)-8-(4-(1-morpholinoethyl)phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine

azetidin-1-yl(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)methanone

(4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)phenyl)(thiomorpholin-1,1-dioxide)methanone

N-cyclopropyl-4-(2-(4-(morpholine-4-carbonyl)phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)benzamide

N-Cyclopropyl-4-{8-[4-((S)-3-methyl-morpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-[8-(3-fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

4-{8-[4-(3-Cyano-azetidin-1-ylmethyl)-3-fluoro-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4

]triazolo[1,5-a]pyridin-2-ylamino}-N-methyl-benzamide

N-Cyclopropyl-4-{8-[4-((S)-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-((R)-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

1-(2-Fluoro-4-{2-[1-(2-hydroxy-2-methyl-propyl)-1H-pyrazol-4-ylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-benzyl)-azetidine-3-carbonitrile

1-{4-[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-2-methyl-propan-2-ol

1-(4-{2-[1-(2-Hydroxy-2-methyl-propyl)-1H-pyrazol-4-ylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenyl)-cyclopropanecarbonitrile

1-[4-(8-{4-[(1,1-Dioxo-tetrahydro-1lambda*6*-thiophen-3-ylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol

1-{4-[8-(3-Fluoro-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-2-methyl-propan-2-ol

4-[8-(4-Dimethylaminomethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-methyl-benzamide

{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-phenyl-amine

[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-phenyl-amine

N-Cyclopropyl-4-{8-[4-(1-hydroxy-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]

pyridin-2-ylamino}-benzamide

4-[8-(4-Acetyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-cyclopropyl-benzamide

2-Cyclopropyl-5-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-2,3-dihydro-isoindol-1-one

[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-phenyl-amine

N-Cyclopropyl-4-{8-[4-(1-morpholin-4-yl-cyclopropyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-(1-methyl-1-morpholin-4-yl-ethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-methanesulfonyl-phenyl)-amine

(4-Methanesulfonyl-phenyl)-[8-(4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine

{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-(4-methanesulfonyl-phenyl)-amine

(6-Chloro-pyridin-3-yl)-[8-(3-fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine

1-{4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-ethanol

{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl}-[4-(1-methoxy-ethyl)-phenyl]-amine

1-{4-[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-ethanol

[8-(3-Fluoro-4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-[4-(1-methoxy-ethyl)-phenyl]-amine

1-(4-{2-[4-(1-Hydroxy-ethyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-benzyl)-azetidine-3-carbonitrile

1-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-azetidine-3-carbonitrile

N-Cyclopropyl-4-{8-[6-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-[8-(6-hydroxymethyl-pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

1-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile

N-Cyclopropyl-2-{4-[8-(4-morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-pyrazol-1-yl}-acetamide

N-Cyclopropyl-4-{8-[4-(3-oxo-piperazin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-(4-methanesulfonyl-piperazin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-(8-{4-[(2-hydroxy-2-methyl-propylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

N-Cyclopropyl-4-(8-{4-[(2-methanesulfonyl-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

4-(8-{4-[1-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-yl)-cyclopropyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-methyl-benzamide

N-Cyclopropyl-4-(8-{4-[1-(1,1-dioxo-1lambda*6*-thiomorpholin-4-yl)-cyclopropyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

1-{4-[2-(6-Chloro-pyridin-3-ylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile

N-Cyclopropyl-4-[8-(4-{[((S)-5-oxo-pyrrolidin-2-ylmethyl)-amino]-methyl}-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-ethanol

4-{4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazine-1-carboxylic acid amide

4-{8-[4-((R)-3-Cyano-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

4-{8-[4-((S)-3-Cyano-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

4-{8-[6-((R)-3-Cyano-pyrrolidin-1-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

4-{8-[6-((S)-3-Cyano-pyrrolidin-1-ylmethyl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

N-Cyclopropyl-4-[8-(4-{[(1-hydroxy-cyclopropylmethyl)-amino]-methyl}-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Cyclopropyl-4-(8-{4-[(2-hydroxy-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

4-(8-{4-[(2-Acetylamino-ethylamino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide

1-{4-[8-(4-Morpholin-4-ylmethyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-phenyl}-propan-1-one

1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-propan-1-one

N-Cyclopropyl-4-(8-{4-[(cyclopropylcarbamoylmethyl-amino)-methyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

1-(4-{8-[4-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-pyrazol-1-yl)-2-methyl-propan-2-ol

4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazin-2-one

4-{8-[4-((S)-3-Acetylamino-pyrrolidin-1-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

1-{4-[2-(4-Propionyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-azetidine-3-carbonitrile

1-(4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazin-1-yl)-ethanone

4-{4-[2-(4-Methanesulfonyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-benzyl}-piperazine-1-carboxylic acid amide

4-{8-[4-(1-Carbamoyl-1-methyl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-N-cyclopropyl-benzamide

N-Cyclopropyl-4-{8-[4-(4-methyl-piperazin-1-yl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

4-{4-[2-(4-Cyclopropylcarbamoyl-phenylamino)-[1,2,4]triazolo[1,5-a]pyridin-8-yl]-phenyl}-piperazine-1-carboxylic acid tert-butyl ester

Acetic acid 1-(4-{8-[4-(1,1-dioxo-1lambda*6*-thiomorpholin-4-ylmethyl)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-phenyl)-cyclopropyl ester

N-Cyclopropyl-4-(8-{4-[4-(2,2,2-trifluoro-ethyl)-piperazin-1-ylmethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

N-Cyclopropyl-4-[8-(4-dimethylsulfamoyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

4-(8-Benzo[b]thiophen-3-yl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide

N-Cyclopropyl-4-{8-[6-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

2-(4-{2-[4-(3-Hydroxy-azetidine-1-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenoxy)-2,N-dimethyl-propionamide

4-[8-(1-Benzyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-N-cyclopropyl-benzamide

[8-(1-Benzyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-(4-methanesulfonyl-phenyl)-amine

(8-Benzo[b]thiophen-3-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-methanesulfonyl-phenyl)-amine

N-Cyclopropyl-4-[8-(5-methyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Cyclopropyl-4-{8-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

(4-Methanesulfonyl-phenyl)-[8-(5-morpholin-4-ylmethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine

N-Cyclopropyl-4-[8-(5-morpholin-4-ylmethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Cyclopropyl-4-[8-(5-hydroxymethyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino]-benzamide

N-Cyclopropyl-4-{8-[4-(2-pyrrol-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-(2-imidazol-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-(8-{4-[2-(2-oxo-pyrrolidin-1-yl)-ethoxy]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

(4-Methanesulfonyl-phenyl)-(8-thiophen-2-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

(4-Methanesulfonyl-phenyl)-[8-(5-methyl-thiophen-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]-amine

(8-Benzo[c]thiophen-1-yl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-(4-methanesulfonyl-phenyl)-amine

N-Cyclopropyl-4-(8-{4-[1-(3-oxo-piperazin-1-yl)-ethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

4-(8-{4-[1-(4-Acetyl-piperazin-1-yl)-ethyl]-phenyl}-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-N-cyclopropyl-benzamide

N-Cyclopropyl-2-(4-{2-[4-(3-hydroxy-azetidine-1-carbonyl)-phenylamino]-[1,2,4]triazolo[1,5-a]pyridin-8-yl}-phenoxy)-2-methyl-propionamide

N-Cyclopropyl-4-{8-[4-(2-pyridin-2-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-(2-pyridin-3-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

N-Cyclopropyl-4-{8-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino}-benzamide

Cyclopropanesulfonic acid [4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-amide

N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-acetamide

N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-acetamide

N-[4-(2-Phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-benzyl]-benzamide

1-Morpholin-4-yl-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-ethanone

1-(1,1-Dioxo-1lambda*6*-thiomorpholin-4-yl)-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-ethanone

N-(2-Hydroxy-2-methyl-propyl)-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-acetamide

N-Methyl-2-[4-(2-phenylamino-[1,2,4]triazolo[1,5-a]pyridin-8-yl)-phenyl]-acetamide, and

N-Cyclopropyl-4-(5-(4-N,N-dimethylacetamido)-phenyl-[1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-benzamide

77. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound according to any one of claims 1 to 76

78. The pharmaceutical composition of claim 77, wherein the carrier is a parenteral carrier.

79. The pharmaceutical composition of claim 77, wherein the carrier is an oral carrier.

80. The pharmaceutical composition of claim 77, wherein the carrier is a topical carrier.

81. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 76 for use in medicine.

82. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 76 for use in the treatment or prophylaxis of a disease involving cartilage degradation, bone and/or joint degradation.

83. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 76 for use in the treatment or prophylaxis of rheumatoid arthritis.

84. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 76, for use in the treatment or prophylaxis of a condition or a disease involving inflammation.

85. A compound or pharmaceutically acceptable salt according to any one of claims 1 to 76, for use in the treatment or prophylaxis of a condition or a disease characterized by abnormal JAK1 activity.

86. A method of treatment or prophylaxis of a disease involving degradation of cartilage, comprising administering to a subject a therapeutically effective amount of a compound according to any one of claims 1-76, or a pharmaceutical composition according to claims 77-81.

87. A method of treatment or prevention of osteoarthritis, comprising administering to a subject, a therapeutically effective amount of a compound according to any one of claims 1-76, or a pharmaceutical composition according to claims 77-81.

88. A method of treatment or prevention of a condition or a disease involving inflammation, comprising administering to a subject a therapeutically effective amount of a compound according to any one of claims 1-76, or a pharmaceutical composition according to claims 77-81.

89. Use of a compound according to any one of claim 1-76 in the manufacture of a medicament for the treatment or prevention of a disease involving degradation of cartilage.

90. Use of a compound according to any one of claim 1-76 in the manufacture of a medicament for the treatment or prevention of osteoarthritis.

91. Use of a compound according to any one of claim 1-76 in the manufacture of a medicament for the treatment or prevention of a condition or a disease involving inflammation.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/059595

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D471/04 A61K31/437 A61P19/02 A61P29/00

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)
C07D

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 practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	WO 2008/025821 A (CELLZOME (UK), LTD.) 6 March 2008 (2008-03-06) claims 1-37	1-80
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Y	WO 2006/018735 A (FARMACIA & UPJOHN COMPANY LLC) 23 February 2006 (2006-02-23) claims 1-28	1-80

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[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

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"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
7 October 2009	19/10/2009

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	Herz, Claus

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/059595

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Information on patent family members

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