Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3073333 A1 2019/02/28

(21) 3 073 333

(12) **DEMANDE DE BREVET CANADIEN**
CANADIAN PATENT APPLICATION

(13) **A1**

(86) Date de dépôt PCT/PCT Filing Date: 2018/08/20
(87) Date publication PCT/PCT Publication Date: 2019/02/28
(85) Entrée phase nationale/National Entry: 2020/02/19
(86) N° demande PCT/PCT Application No.: EP 2018/072398
(87) N° publication PCT/PCT Publication No.: 2019/038215
(30) Priorité/Priority: 2017/08/21 (EP17187101.5)

(51) Cl.Int./Int.Cl. *C07D 403/12* (2006.01), *A61K 31/4184* (2006.01), *A61P 31/00* (2006.01), *A61P 35/00* (2006.01), *C07D 235/30* (2006.01), *C07D 235/32* (2006.01), *C07D 401/12* (2006.01), *C07D 401/14* (2006.01), *C07D 403/14* (2006.01), *C07D 405/14* (2006.01), *C07D 413/14* (2006.01), *C07D 487/10* (2006.01), *C07D 498/10* (2006.01)

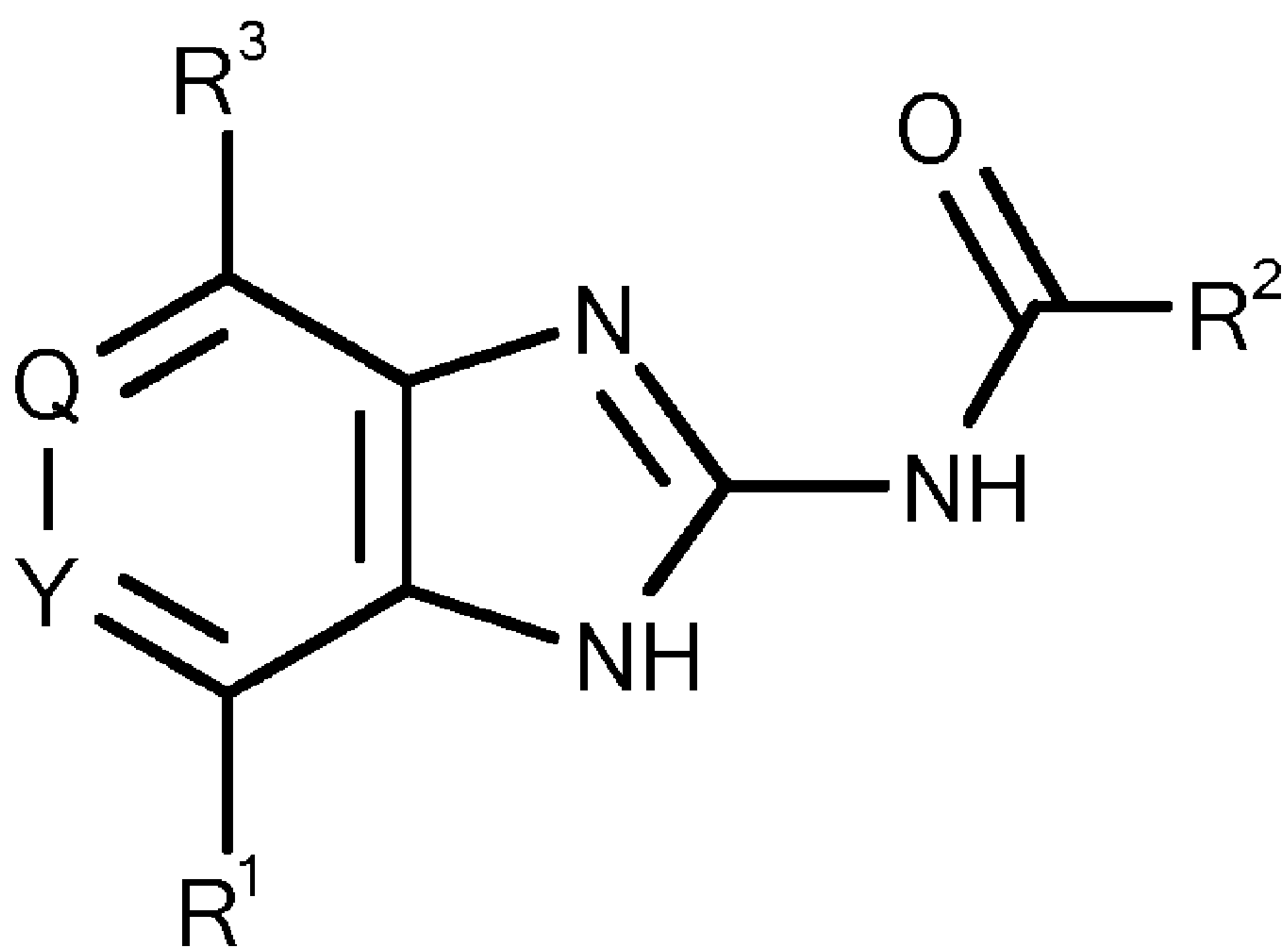
(71) Demandeur/Applicant:
MERCK PATENT GMBH, DE

(72) Inventeurs/Inventors:
TANZER, EVA-MARIA, DE;
SCHIEMANN, KAI, DE;
KLEIN, MARKUS, DE

(74) Agent: SMART & BIGGAR IP AGENCY CO.

(54) Titre : DERIVES DE BENZIMIDAZOLE UTILISES EN TANT QU'ANTAGONISTES DU RECEPTEUR DE L'ADENOSINE
(54) Title: BEZIMIDAZOLE DERIVATIVES AS ADENOSINE RECEPTOR ANTAGONISTS

(I)



(57) Abrégé/Abstract:
The invention relates to benzimidazole derivatives of the general formula (I), and the use of the compounds of the present invention for the treatment and/or prevention of hyperproliferative or infectious diseases and disorders in mammals, especially humans, and pharmaceutical compositions containing such compound.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 February 2019 (28.02.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/038215 A1

(51) International Patent Classification:
C07D 403/12 (2006.01) *C07D 403/14* (2006.01)
C07D 401/14 (2006.01) *C07D 487/10* (2006.01)
C07D 405/14 (2006.01) *C07D 498/10* (2006.01)
C07D 413/14 (2006.01) *A61P 31/00* (2006.01)
C07D 401/12 (2006.01) *A61P 35/00* (2006.01)
C07D 235/30 (2006.01) *A61K 31/4184* (2006.01)
C07D 235/32 (2006.01)

(21) International Application Number:
PCT/EP2018/072398

(22) International Filing Date:
20 August 2018 (20.08.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
17187101.5 21 August 2017 (21.08.2017) EP

(71) Applicant: **MERCK PATENT GMBH** [DE/DE]; Frankfurter Strasse 250, 64293 Darmstadt (DE).

(72) Inventors: **TANZER, Eva-Maria**; Bluetenallee 2, 64291 DARMSTADT (DE). **SCHIEMANN, Kai**; Am Roedergraben 8, 64342 SEEHEIM-JUGENHEIM (DE). **KLEIN, Markus**; Lindenweg 35, 64291 DARMSTADT (DE).

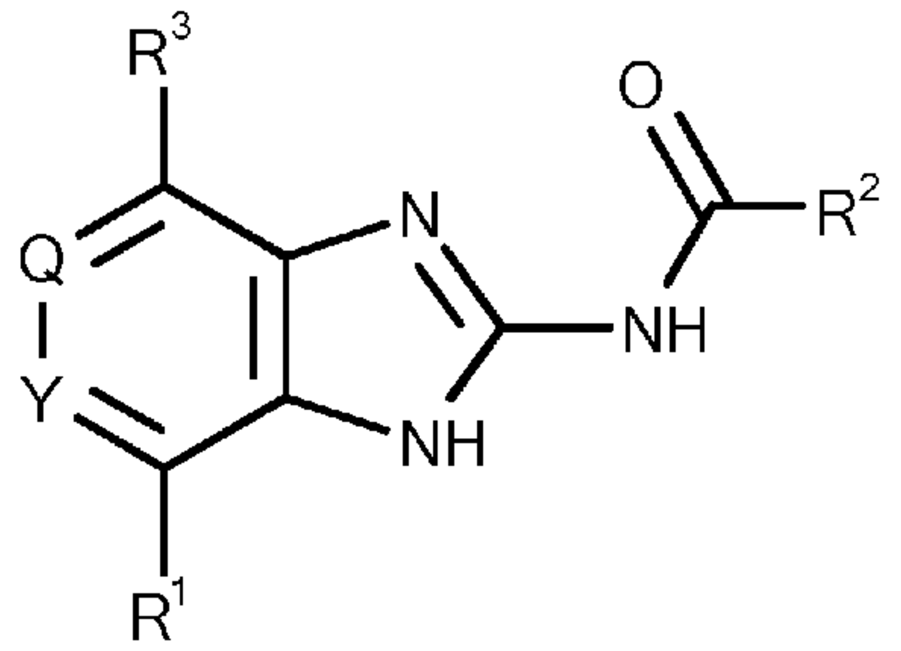
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*

(54) Title: BEZIMIDAZOLE DERIVATIVES AS ADENOSINE RECEPTOR ANTAGONISTS

(I)

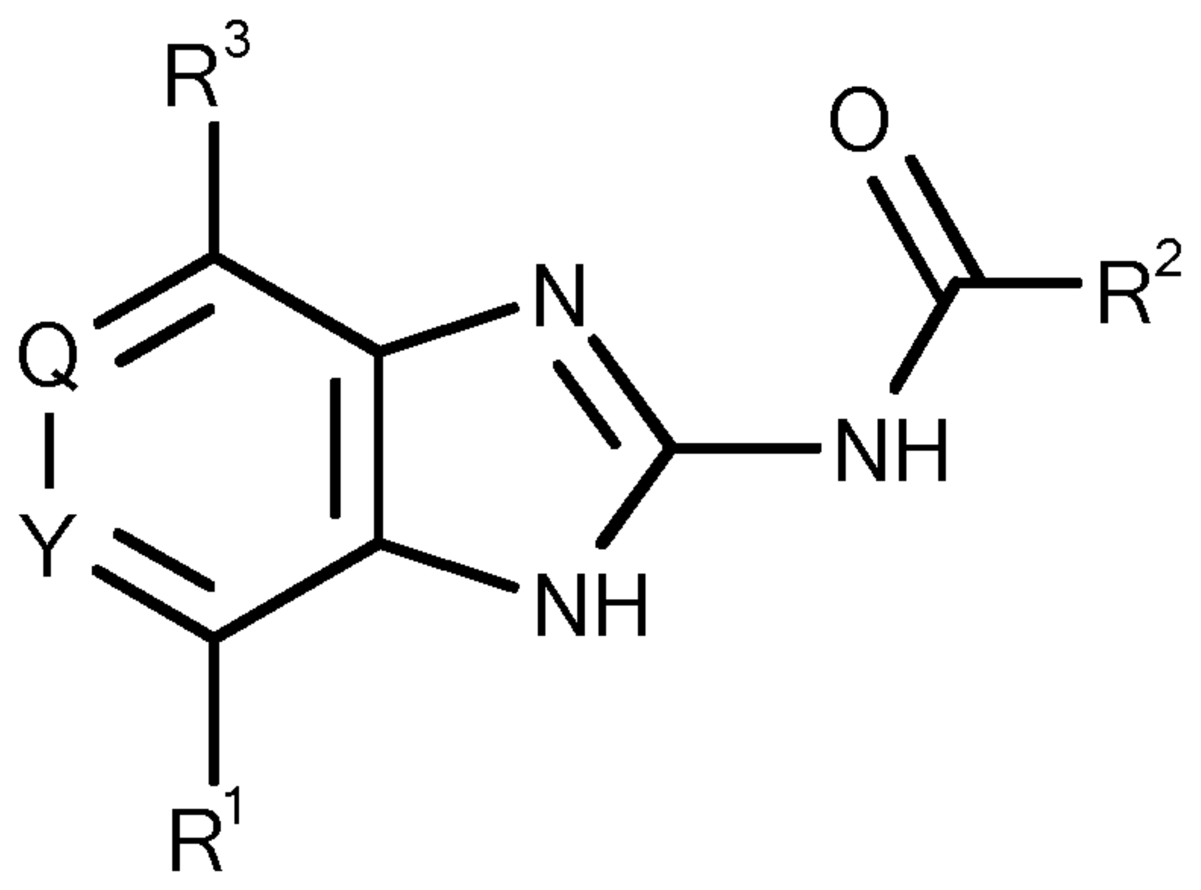


(57) Abstract: The invention relates to benzimidazole derivatives of the general formula (I), and the use of the compounds of the present invention for the treatment and/or prevention of hyperproliferative or infectious diseases and disorders in mammals, especially humans, and pharmaceutical compositions containing such compound.

WO 2019/038215 A1

Bezimidazole derivatives as adenosine receptor antagonists

The invention relates to benzimidazole derivatives of the general formula I,



I

and the use of the compounds of the present invention for the treatment and/or prevention of hyperproliferative or infectious diseases and disorders in mammals, especially humans, and pharmaceutical compositions containing such compounds.

Background of the invention

Adenosine is an ubiguitous modulator of numerous physiological activities, particularly within the cardiovascular, nervous and immune systems. Adenosine is related both structurally and metabolically to the bioactive nucleotides adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP) and cyclic adenosine monophosphate (cAMP), to the biochemical methylating agent S-adenosyl-L-methione (SAM) and structurally to the coenzymes NAD, FAD and coenzym A and to RNA.

Via cell surface receptors, adenosine modulates diverse physiological functions including induction of sedation, vasodilatation, suppression of cardiac rate and contractility, inhibition of platelet aggregability, stimulation of gluconeogenesis and inhibition of lipolysis. Studies show that adenosine is able to activate adenylate cyclases, open potassium channels, reduce flux through calcium channels, and inhibit or stimulate phosphoinositide turnover through receptor-mediated mechanisms (Muller C. E. and Stein B., Current Pharmaceutical Design, 2: 501, 1996; Muller C. E., Exp. Opin. Ther. Patents, 7(5): 419, 1997).

Adenosine receptors belong to the superfamily of G-protein-coupled receptors (GPCRs). Four major subtypes of adenosine receptors have been pharmacologically, structurally and functionally characterized (Fredholm et al., Pharm. Rev., 46: 143-156, 1994) and referred to as A_1, A_{2A}, A_{2B} and A_3. Though the same adenosine receptor can couple to different G-proteins, adenosine A_1 and A_3 receptors usually couple to inhibitory G-proteins referred to as G_i and G_0 which inhibit adenylate cyclase and down-regulate cellular cAMP levels. In contrast, the adenosine A_{2A} and A_{2B} receptors couple to stimulatory G-proteins referred to as G_S that activate adenylate cyclase and increase intracellular levels of cAMP (Linden J., Annu. Rev. Pharmacol. Toxicol., 41: 775-87 2001).

According to the invention, "adenosine-receptor-selective ligands" are substances which bind selectively to one or more subtypes of the adenosine receptors, thus either mimicking the action of adenosine (adenosine agonists) or blocking its action (adenosine antagonists). According to their receptor selectivity, adenosine-receptor-selective ligands can be divided into different categories, for example ligands which bind selectively to the A_1 or A_2 receptors and in the case of the latter also, for example, those which bind selectively to the A_{2A} or the A_{2B} receptors. Also possible are adenosine receptor ligands which bind selectively to a plurality of subtypes of the adenosine receptors, for example ligands which bind selectively to the A_1 and the A_2, but not to the A_3 receptors. The abovementioned receptor selectivity can be determined by the effect of the substances on cell lines which, after stable transfection with the corresponding cDNA, express the receptor subtypes in question (Olah, M. E. et al., J. Biol. Chem., 267: 10764-10770, 1992). The effect of the substances on such cell lines can be monitored by biochemical measurement of the intracellular messenger cAMP (Klotz, K. N. et al., Naunyn Schmiedebergs Arch. Pharmacol. 357: 1-9, 1998).

It is known that the A_1 receptor system include the activation of phospholipase C and modulation of both potassium and calcium ion channels. The A_3 subtype, in addition to its association with adenylate cyclase, also stimulates phospholipase C and so activates calcium ion channels.

The A_1 receptor (326-328 amino acids) was cloned from various species (canine, human, rat, dog, chick, bovine, guinea-pig) with 90-95 % sequence identify among the mammalian species. The A_{2A} receptor (409-412 amino acids) was cloned from canine, rat, human, guinea pig and mouse. The A_{2B} receptor (332 amino acids) was cloned from human and mouse with 45 % homology of human A_{2B} with human A_1 and A_{2A} receptors. The A_3 receptor (317-320 amino acids) was cloned from human, rat, dog, rabbit and sheep.

The A_1 and A_{2A} receptor subtypes are proposed to play complementary roles in adenosine's regulation of the energy supply. Adenosine, which is a metabolic product of ATP, diffuses from the cell and acts locally to activate adenosine receptors to decrease the oxygen demand (A_1 and A_3) or increase the oxygen supply (A_{2A}) and so reinstate the balance of energy supply / demand within the tissue. The actions of both subtype is to increase the amount of available oxygen to tissue and to protect cells against damage caused by a short term imbalance of oxygen. One of the important functions of endogenous adenosine is preventing damage during traumas such as hypoxia, ischaemia, hypotension and seizure activity. Furthermore, it is known that the binding of the adenosine receptor agonist to mast cells expressing the rat A_3 receptor resulted in increased inositol triphosphate and intracellular calcium concentrations, which potentiated antigen induced secretion of inflammatory mediators. Therefore, the A_3 receptor plays a role in mediating asthmatic attacks and other allergic responses.

These adenosine receptors are encoded by distinct genes and are classified according to their affinities for adenosine analogues and methylxanthine antagonists (Klinger et al., Cell Signal., 14 (2): 99-108, 2002).

Concerning the role of adenosine on the nervous system, the first observations were made on the effects of the most widely used of all psychoactive drugs being caffeine. Actually, caffeine is a well-known adenosine receptor antagonist that is able to enhance the awareness and learning abilities of mammals. The adenosine A_{2A} receptor pathway is responsible for these effects (Fredholm et al., Pharmacol.

Rev., 51 (1): 83-133, 1999; Huang et al., Nat Neurosci., 8 (7): 858-9, 2005), and the effects of caffeine on the adenosine A_{2A} receptor signaling pathway encouraged the research of highly specific and potent adenosine A_{2A} antagonists.

In mammals, adenosine A_{2A} receptors have a limited distribution in the brain and are found in the striatum, olfactory tubercle and nucleus acumbens (Dixon et al., Br. J. Pharmacol., 118 (6): 1461-8, 1996). High and intermediate levels of expression can be observed in immune cells, heart, lung and blood vessels. In the peripheral system, G_3 seems to be the major G-protein associated with adenosine A_{2A} receptor but in the striatum, it has been shown that striatal adenosine A_{2A} receptors mediate their effects through activation of a G-protein referred to as $G_o$if (Kull et al., Mol. Pharmacol., 58 (4): 772-7, 2000), which is similar to G_3 and also couples to adenylate cyclase.

To date, studies on genetically modified mice and pharmacological analysis suggest that A_{2A} receptor is a promising therapeutic target for the treatment of central nervous system (CNS) disorders and diseases such as Parkinson's disease, Huntington's disease, attention deficit hyperactivity disorders (ADHD), stroke (ischemic brain injury), and Alzheimer's disease (Fredholm et al., Annu. Rev. Pharmacol. Toxicol., 45: 385-412, 2005; Higgins et al.; Behav. Brain Res. 185: 32-42, 2007; Dall' Igna et al., Exp. Neurol., 203 (1): 241-5, 2007; Arendash et al., Neuroscience, 142 (4): 941-52, 2006; Trends in Neurosci., 29 (11), 647-654, 2006; Expert Opinion Ther. Patents, 17, 979-991, 2007; Exp. Neurol., 184 (1), 285-284, 2003; Prog. Brain Res, 183, 183-208, 2010; J. Alzheimer Dis., Suppl 1, 1 17-126, 2010; J. Neurosci., 29 (47), 14741-14751, 2009; Neuroscience, 166 (2), 590-603, 2010; J. Pharmacol. Exp. Ther., 330 (1), 294-303, 2009; Frontiers Biosci., 13, 2614-2632, 2008) but also for various psychoses of organic origin (Weiss et al., Neurology, 61 (11 Suppl 6): 88-93, 2003).

The use of adenosine A_{2A} receptor knockout mice has shown that adenosine A_{2A} receptor inactivation protects against neuronal cell death induced by ischemia (Chen et al., J. Neurosci., 19 (21): 9192-200, 1999 and Monopoli et al., Neuroreport, 9 (17): 3955-9, 1998) and the mitochondrial toxin 3-NP (Blum et al., J. Neurosci., 23 (12): 5361-9, 2003). Those results provided a basis for treating ischasmia and Huntington's disease with adenosine A_{2A} antagonists. The blockade of adenosine A_{2A} receptors has also an antidepressant effect (El Yacoubi et al., Neuropharmacology, 40 (3): 424-32, 2001). Finally, this blockade prevents memory dysfunction (Cunha et al., Exp. Neurol., 210 (2): 776-81, 2008; Takahashi et al., Front. Biosci., 13: 2614-32, 2008) and this could be a promising therapeutic route for the treatment and/or prevention of Alzheimer's disease.

For reviews concerning A_{2A} adenosine receptors see e.g. Moreau et al. (Brain Res. Reviews 31: 65-82, 1999) and Svenningsson et al. (Progress in Neurobiology 59: 355-396, 1999).

To date, several adenosine A_{2A} receptor antagonists have shown promising potential for treatment of Parkinson's disease. As an example, KW-6002 (Istradefylline) completed a phase III clinical trial in the USA after studies demonstrated its efficacy in alleviation of symptoms of the disease (Bara-Himenez et al., Neurology, 61 (3): 293-6, 2003 and Hauser et al., Neurology, 61 (3): 297-303, 2003). SCH420814 (Preladenant), which is now in phase II clinical trial in the USA and produces an improvement in motor function in animal models of Parkinson's disease (Neustadt et al., Bioorg. Med. Chem. Lett., 17 (5): 1376-80, 2001) and also in human patients (Hunter J. C, poster Boston 2006 - http://www.a2apd.org/Speaker abstracts/Hunter.pdf).

Besides the welcome utility of A_{2A} receptor antagonists to treat neurodegenerative diseases, those compounds have been considered for complementary symptomatic indications. These are based on the evidence that A_{2A} receptor activation may contribute to the pathophysiology of a range of neuropsychiatric disorders and dysfunctions such as depression, excessive daytime sleepiness, restless legs syndrome, attention deficit hyperactivity disorder, and cognitive fatigue (Neurology, 61 (Suppl 6), 82-87, 2003; Behav. Pharmacol., 20 (2), 134-145, 2009; CNS Drug Discov., 2 (1), 1-21, 2007).

Some authors suggest the application of A_{2A} antagonists for the treatment of diabetes (WO1999035147; WO2001002400). Other studies suggest the involvement of A_{2A} adenosine receptors in wound healing or atrial fibrillation (Am. J. Path., 6, 1774- 1778, 2007; Arthritis & Rheumatism, 54 (8), 2632-2642, 2006).

Some of the potent adenosine A_{2A} antagonists discovered in the past by the pharmaceutical companies, have advanced into clinical trials showing positive results and demonstrating the potential of this compound class for the treatment of neurodegenerative disorders like Parkinson's, Huntington's or Alzheimer's disease, but also in other CNS related diseases like depression, restless syndrome, sleep and anxiety disorders (Clin. Neuropharmacol., 33, 55-60, 2010; J. Neurosci., 30 (48), 2010), 16284-16292; Parkinson Relat. Disord., 16 (6), 423-426, 2010; Expert Opinion Ther. Patents, 20(8), 987-1005, 2010; Current Opinion in Drug Discovery & Development, 13 (4), 466-480 ,2010 and references therein; Mov. Disorders, 25 (2), S305, 2010).

Known A_{2A} inhibitors are Istradefylline (KW-6002), Preladenant (SCH420814), SCH58261, CGS15943, Tozadenant, Vipadenant (V-2006), V-81444 (CPI-444, HTL-1071, PBF-509, Medi-9447, PNQ-370, ZM-241385, ASO-5854, ST-1535, ST-4206, DT1133 and DT-0926, which are in most cases developed for Parkinson's disease.

Adenosine A_{2B} receptors were cloned from rat hypothalamus (Rivkees and Reppert, 1992), human hippocampus (Pierce et al., 1992), and mouse mast cells (Marquardt et al., 1994), employing standard polymerase chain reaction techniques with degenerate oligonucleotide primers designed to recognize conserved regions of most G protein-coupled receptors. The human A_{2B} receptor shares 86 to 87% amino acid sequence homology with the rat and mouse A_{2B} receptors (Rivkees and Reppert, 1992; Pierce et al., 1992; Marquardt et al., 1994) and 45% amino acid sequence homology with human A_1 and A_{2A} receptors. As expected for closely related species, the rat and mouse A_{2B} receptors share 96% amino acid sequence homology. By comparison, the overall amino acid identity between A_1 receptors from various species is 87% (Palmer and Stiles, 1995). A_{2A} receptors share 90% of homology between species (Ongini and Fredholm, 1996), with most differences occurring in the 2^{nd} extracellular loop and the long C-terminal domain (Palmer and Stiles, 1995). The lowest (72%) degree of identity between species is observed for A_3 receptor sequences (Palmer and Stiles, 1995).

The adenosine analog NECA remains the most potent A_{2B} agonist (Bruns, 1981; Feoktistov and Biaggioni, 1993, 1997; Brackett and Daly, 1994), with a concentration producing a half-maximal effect (EC_{50}) for stimulation of adenyl cyclase of approximately 2 μM. It is, however, nonselective and activates other adenosine receptors with even greater affinity, with an EC_{50} in the low nanomolar (A_1 and A_{2A}) or high nanomolar (A_3) range. The characterization of A_{2B} receptors, therefore, often relies on the lack of effectiveness of compounds that are potent and selective agonists of other receptor types. A_{2B} receptors have been characterized by a method of exclusion, i.e., by the lack of efficacy of agonists that are specific for other receptors. The A_{2A} selective agonist CGS-21680 (Webb et al., 1992), for example, has been useful in differentiating between A_{2A} and A_{2B} adenosine receptors (Hide et al., 1992; Chern et al., 1993; Feoktistov and Biaggioni, 1995; van der Ploeg et al., 1996). Both receptors are positively coupled to adenyl cyclase and are activated by the nonselective agonist NECA. CGS-21680 is virtually ineffective on A_{2B} receptors but is as potent as NECA in activating A_{2A} receptors, with an EC_{50} in the low nanomolar range for both agonists (Jarvis et al., 1989; Nakane and Chiba, 1990; Webb et al., 1992; Hide et al., 1992; Feoktistov and Biaggioni, 1993; Alexander et al., 1996). A_{2B} receptors have also a very low affinity for the A_1selective agonist R-PIA (Feoktistov and Biaggioni, 1993; Brackett and Daly, 1994) as well as for the A_3 selective agonist N^6-(3-iodobenzyl)-N-methyl-5′-carbamoyladenosine (IB-MECA) (Feoktistov and Biaggioni, 1997). The agonist profile NECA > R-PIA = IB-MECA > CGS-21680 was determined in human erythroleukemia (HEL) cells for A_{2B}-mediated cAMP accumulation. The difference between EC_{50} for NECA and the rest of the agonists is approximately 2 orders of magnitude. Therefore, responses elicited by NECA at concentrations in the low micromolar range (1–10 μM), but not by R-PIA, IB-MECA or CGS-21680, are characteristic of A_{2B} receptors.

Whereas A_{2B} receptors have, in general, a lower affinity for agonists compared to other receptor subtypes, this is not true for antagonists. The structure activity relationship of adenosine antagonists on A_{2B} receptors has not been fully characterized, but at least some xanthines are as or more potent antagonists of A_{2B} receptor subtypes than of other subtypes. In particular, DPSPX (1,3-dipropyl-8-sulphophenylxanthine), DPCPX (1,3-diproyl-8c-yclopentylxanthine), DPX (1,3 diethylphenylxanthine), the antiasthmatic drug enprofylline (3-n-propylxanthine) and the non-xanthine compound 2,4-dioxobenzopteridine (alloxazine) have affinities in the mid to high nM range.

Other known A_{2B} inhibitors are ATL801, PSB-605, PSB-1115, ISAM-140, GS6201, MRS1706 and MRS1754.

It is disclosed herein that adenosine receptors play a non-redundant role in down-regulation of inflammation in vivo by acting as a physiological "STOP" (a termination mechanism) that can limit the immune response and thereby protect normal tissues form excessive immune damage during pathogenesis of different diseases.

A_{2A} receptor antagonists provide long term enhancement of immune responses by reducing T-cell mediated tolerance to antigenic stimuli, enhancing the induction of memory T cells and enhancing the efficacy of passive antibody administration for the treatment of cancer and infectious diseases while A_{2A} receptor agonists provide long term reduction of immune responses by enhancing T-cell mediated tolerance to antigenic stimuli, in particular to reduce use of immunosuppressive agents in certain conditions.

Immune modulation is a critical aspect of the treatment of a number of diseases and disorders. T cells in particularly play a vital role in fighting infections and have the capability to recognize and destroy cancer cells. Enhancing T cell mediated responses is a key component to enhancing responses to therapeutic agents. However, it is critical in immune modulation that any enhancement of an immune response is balanced against the need to prevent autoimmunity as well as chronic inflammation. Chronic inflammation and self-recognition by T cells is a major cause for the pathogenesis of systemic disorders such as rheumatoid arthritis, multiple sclerosis and systemic lupus erythematosus. Furthermore, long term immunosuppression is required in preventing rejection of transplanted organs or grafts.

Tumor-induced immunosuppression is a major hurdle to the efficacy of current cancer therapies. Because of their remarkable clinical efficacy against a broader range of cancers, recent successes with immune checkpoint blockade inhibitors such as anti-CTLA-4 and anti-PD-1/PDL1 are revolutionizing cancer treatment.

Adenosine is one of the new promising immunosuppressive targets revealed in preclinical studies. This metabolite is produced by the ectoenzyme - CD73 expressed on host suppressor cells and tumor cells. Increased expression of CD73 correlates with poor prognosis in patients with a number of cancers, including colorectal cancer (Liu et al, J. Surgical Oncol, 2012), gastric cancer (Lu et al., World J. Gastroenterol., 2013), gallbladder cancer (Xiong et al., Cell and Tissue Res., 2014). Preclinical studies demonstrated that protumor effects of CD73 can be driven (at least in part) by adenosine-mediated immunosuppression. As disclosed above, adenosine binds to four known receptors A_1, A_{2A}, A_{2B}, and A_3, with the activation of A_{2A} and A_{2B} receptors known to suppress the effector functions of many immune cells, i.e. A_{2A} and A_{2B} receptors induce adenylate-cyclase-dependent accumulation of cAMP leading to immunosuppression. Since antagonizing A_1 and A_3 would counteract the desired effect and A_1 and A_3 agonists serve as potential cardioprotective agents, selectivity towards A_1 and A_3 needs to be achieved (Antonioli et al., Nat. rev. Cancer, 2013, Thiel et al., Microbes and Infection, 2003). In the microenvironment of the tumor, both A_{2A} and A_{2B} receptor activation has been demonstrated to suppress antitumor immunity and increase the spread of CD73 tumors. In addition, either A_{2A} or A_{2B} blockade with small molecule antagonists can reduce tumor metastasis. It has been found that blocking of A_{2A} receptor can overcome tumor escape mechanisms including both anergy and regulatory T cell induction caused by tumor cells and cause long-term tumor susceptibility to treatment. Ohta et al. demonstrated rejection of approximately 60% of established CL8-1 melanoma tumors in A_{2A} receptor-deficient mice compared to no rejection in normal mice (Ohta, et al.; PNAS 103 (35): 13132-7, 2006). In agreement, the investigators also showed improved inhibition of tumor growth, destruction of metastases and prevention of neovascularization by anti-tumor T cells after treatment with an A_{2A} receptor antagonist.

Tumors have been shown to evade immune destruction by impeding T cell activation through inhibition of co-stimulatory factors in the B7-CD28 and TNF families, as well as by attracting regulatory T cells, which inhibit anti-tumor T cell responses (Wang, Cancer. Semin. Cancer. Biol. 16: 73-79, 2006; Greenwald, et al., Ann. Rev. Immunol. 23: 515-48, 2005; Watts, Ann. Rev. Immunol. 23: 23-68, 2005; Sadum et al., Clin. Canc. Res. 13 (13): 4016-4025, 2007). Because A_{2A} receptor expression is increased in lymphocytes following activation, therapies that liberate lymphocyte effector responses, such as anti-CTLA-4 and anti-PD-1, may also increase the effects of A_{2A}-mediated immunosuppression. Immune checkpoint blockade in combination with A_{2A} or dual $A_{2A/2B}$ antagonists increase the magnitude of immune responses to tumors and metastasis. Accordingly, combination of A_{2A} inhibition with anti-PD-1 therapy enhances IFN-γ production by T-cells in a co-culture with MC38 tumor cells, improves mouse survival in 4T1 mammary tumor model and decreases tumor growth in AT-3ova^{dim} CD73^{+} tumors (Beavis et al., Cancer Immunol. Res., 2015; Mittal et al., Cancer Res., 2014).

Furthermore, preclinical studies demonstrated that A_{2B} inhibition leads to decreased tumor growth and extended survival of mice in Lewis lung carcinoma, MB49 bladder carcinoma, ortho 4T1 mammary carcinoma models (Ryzhov et al., 2009, Cekic et al., 2012) and the combination of A_{2B} inhibition with anti-PD-1 therapy reduces lung metastases of B16-F10 melanoma tumors and improves mouse survival in the 4T1 mammary tumor model.

WO 03/050241 describes the methods to increase an immune response to an antigen, increasing vaccine efficacy or increasing an immune response to a tumor antigen or immune cell-mediated tumor destruction by administering an agent that inhibits extracellular adenosine or inhibits adenosine receptors.

WO 2004/089942, WO 2005/000842 and WO 2006/008041 disclose benzothiazole derivatives, including Tozadenant, as A_{2A} inhibitors for the treatment of Parkinson's disease. WO 2004/092171 and WO 2005/028484 disclose similar thiazolopyridine and pyrazolopyrimidine derivatives also as A_{2A} inhibitors for the treatment of Parkinson's disease. However, these compounds do not show significant A_{2B} inhibitory activity and do only show good pharmacokinetic properties in the rat, the Parkison's disease animal model but not in the mouse, the cancer animal model. Furthermore, the compounds do not show that they are able to prevent immunosuppression and thus are able to support anti-tumor T cell induced inhibition of tumor growth, reduction or destruction of metastases and prevention of neovascularization.

Thus, there remains a need for therapies that provide long term enhancement of immune responses to specific antigens, particularly for the treatment and prevention of hyperproliferative and infectious diseases and disorders and thus the object of the present invention was to provide methods of treatment that allow simplified treatment protocols and enhance immune responses against certain antigens. It was a specific object of the invention to provide improved methods of preventing or treating hyperproliferative and infectious diseases and disorders in a host, especially to provide effective A_{2A} or dual $A_{2A/2B}$ antagonists for the treatment and prevention of such diseases.

Summary of the invention

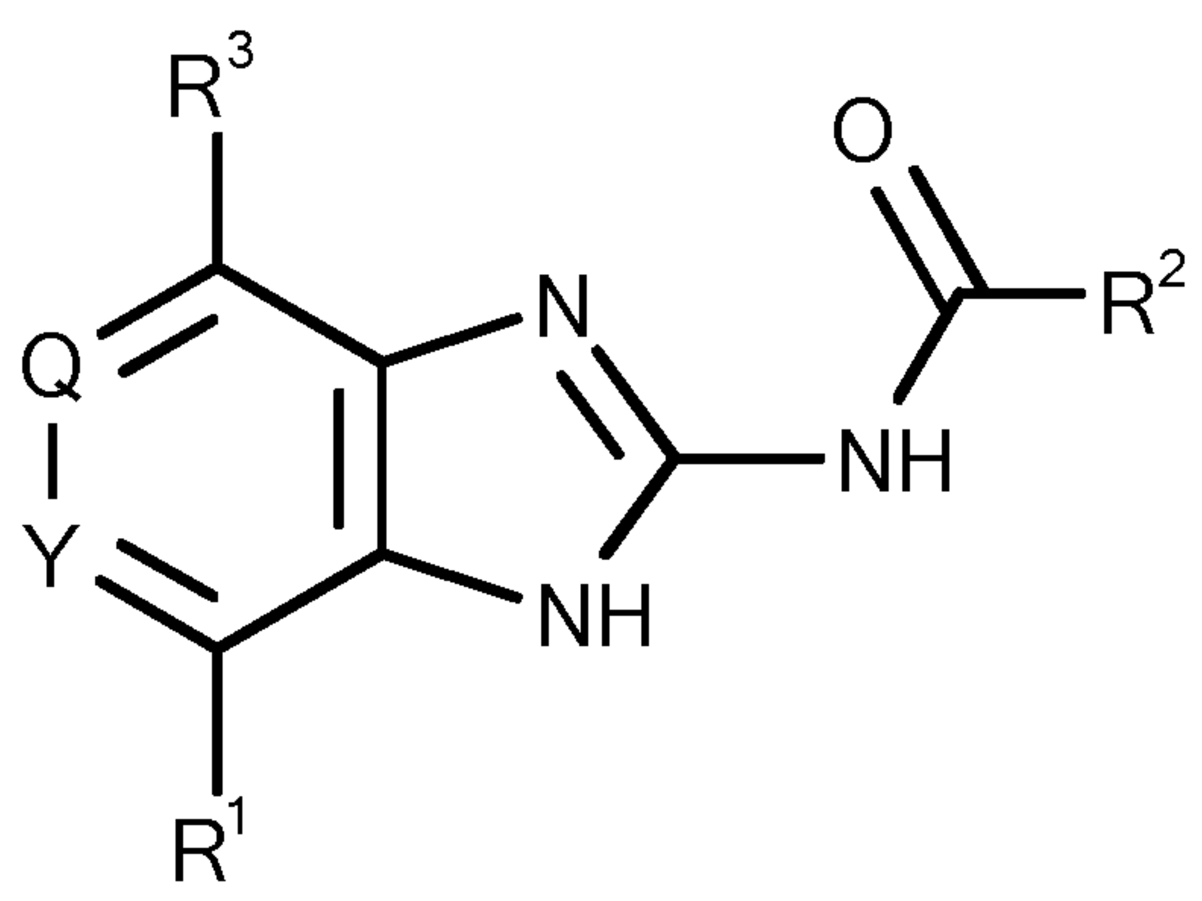
Surprisingly, it has been found that the benzimidazole derivatives according to the invention are highly effective inhibitors of the A_{2A} adenosine receptor or both the A_{2A} and A_{2B} adenosine receptors and at the same time have high selectivity over the A_1 and A_3 adenosine receptors, and thus the compounds of the present invention can be used for the treament of hyperproliferative diseases and disorders such as cancer and infectious diseases and disorders.

Particularly, in contrast to the known adenosine A_{2A} receptor antagonist Tozadenant and similar benzothiazole derivatives, the compounds of the present invention surprisingly show an A_{2A}/A_{2B} dual activity which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above or the compounds of the present invention show at least a high A_{2A} inhibitory activity together with the other surprising advantages disclosed herein leading to a high efficacy in the treatment and/or prevention of hyperproliferative and infectious diseases and disorders.

Additionally, in comparison with the known adenosine A_{2A} receptor antagonist Tozadenant and similar benzothiazole derivatives, the compounds of the present invention surprisingly show better pharmacokinetic properties in mouse as the animal model relevant for cancer, which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above.

Furthermore, as discussed above, adenosine in tumor microenvironment can inhibit T cell activity by signaling through A_{2A} receptors and suppress cytokine secretion by T cells. A_{2A} specific agonists like CGS-21680, similar to adenosine, inhibit T cell cytokine secretion in vitro and in vivo. In contrast, potential A_{2A} antagonists or A_{2A}/A_{2B} dual antagonists can rescue T cells from this inhibition. In contrast to the known adenosine A_{2A} receptor antagonist Tozadenant, the compounds of the present invention show that they are able to rescue T cells from inhibition and are able to prevent the suppression of cyctokine secretion as induced by adenosine or A_{2A} specific agonists like CGS-2168, which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above. Therefore, the compounds of the present invention surprisingly are able to prevent immunosuppression and thus are able to support anti-tumor T cell induced inhibition of tumor growth, reduction or destruction of metastases and prevention of neovascularization.

The invention relates to benzimidazole derivatives of the general formula I,



I

wherein

Q, Y are independently of one another CH or N,

R^1 is Hal or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^4,

R^2 is linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-11 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^4,

R^3 is linear or branched alkyl or O-alkyl having 1-6 C atoms or cyclic alkyl having 3-6 C atoms, which is unsubstituted or mono-, di- or trisubstituted by H, =S, =NH, =O, OH, cyclic alkyl having 3-6 C atoms, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$ or NO_2,

R^4 is H, R^5, =S, $=NR^5$, =O, OH, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$, NO_2, or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^5 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by by R^5 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, –$NRSO_2R^4$–, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^5,

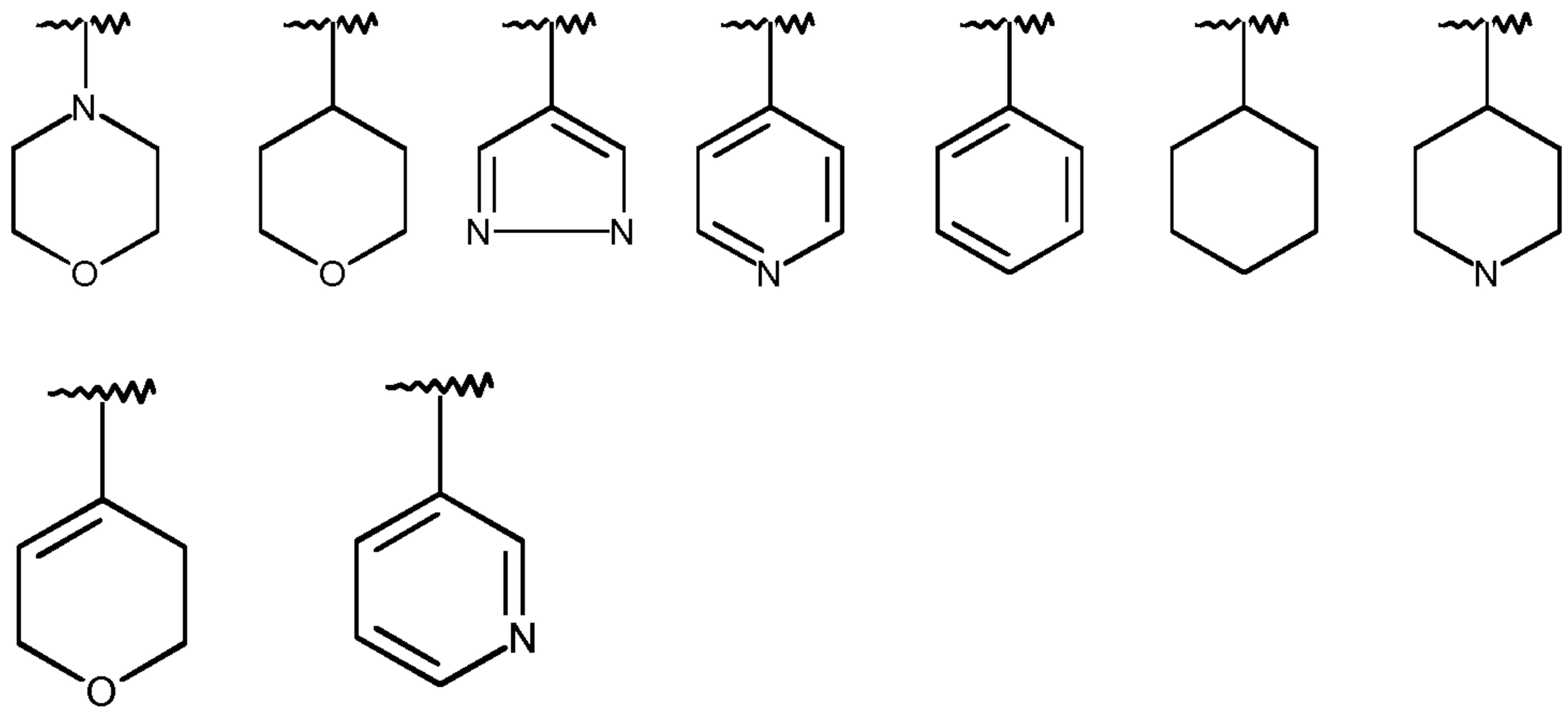
R^5, R^6 are independently of one another selected from the group consisting of H, =S, =NH, =O, OH, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$, NO_2 and linear or branched alkyl having 1-10 C atoms in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–,–COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl,

Hal is F, C, Br, or I,

and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

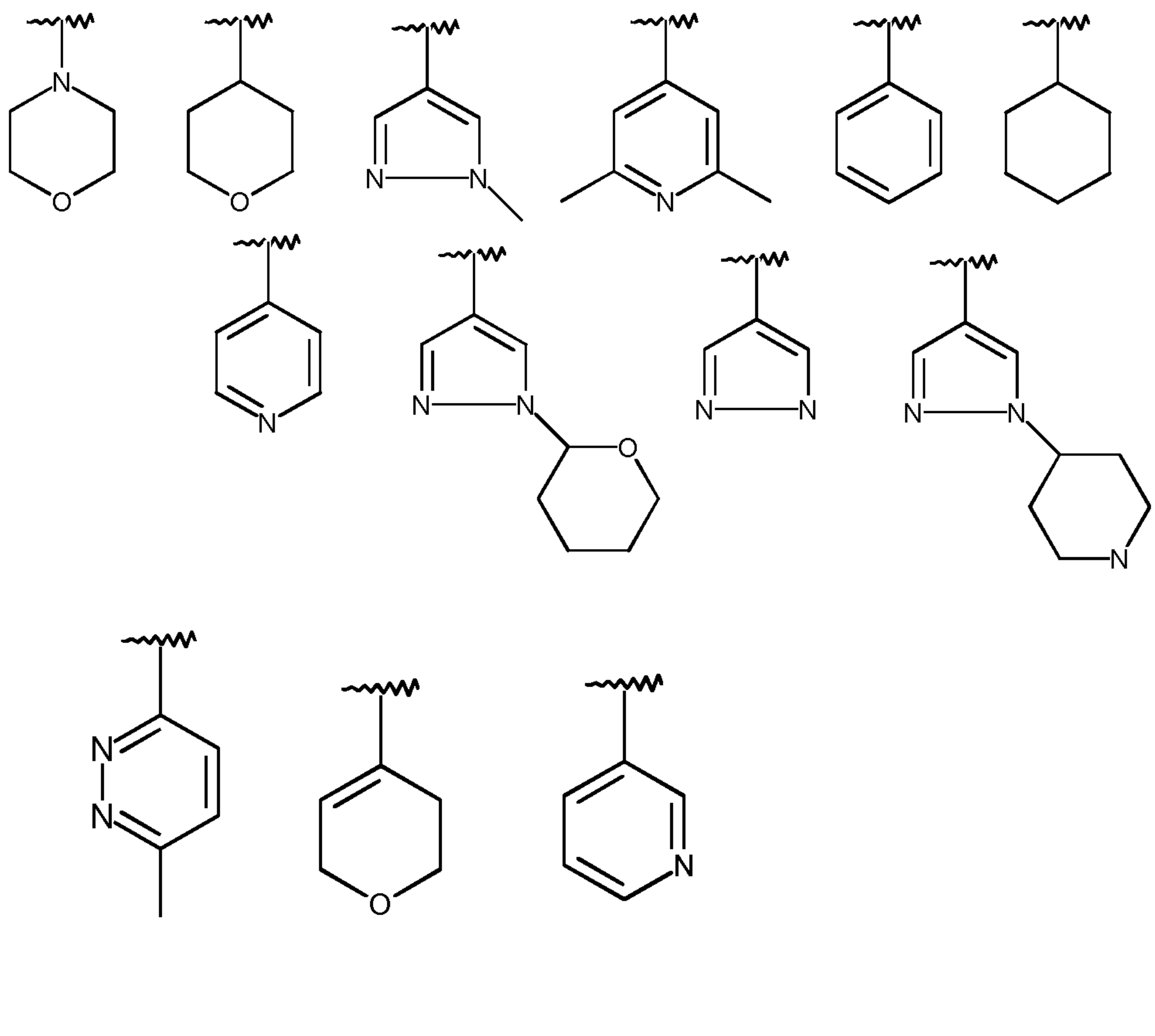
The invention preferably relates to a compound of formula I, wherein

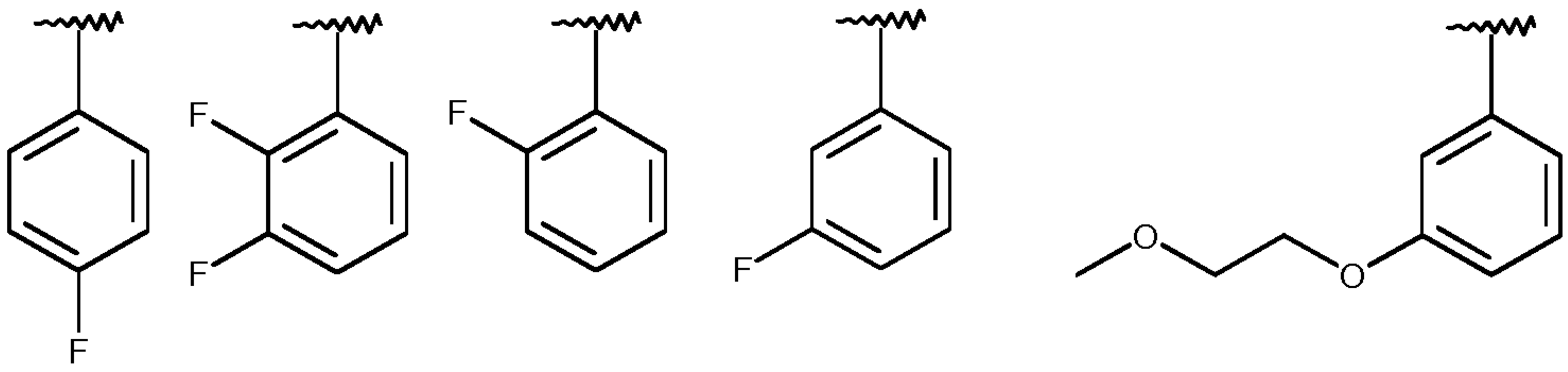
R^1 is Hal or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, –$NR^5SO_2R^6$–, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or one of the following structures:



which is unsubstituted or mono-, di- or trisubstituted with R^4 and wherein Q, Y, R^2, R^3, R^4, R^5 and R^6 have the meanings as disclosed above.

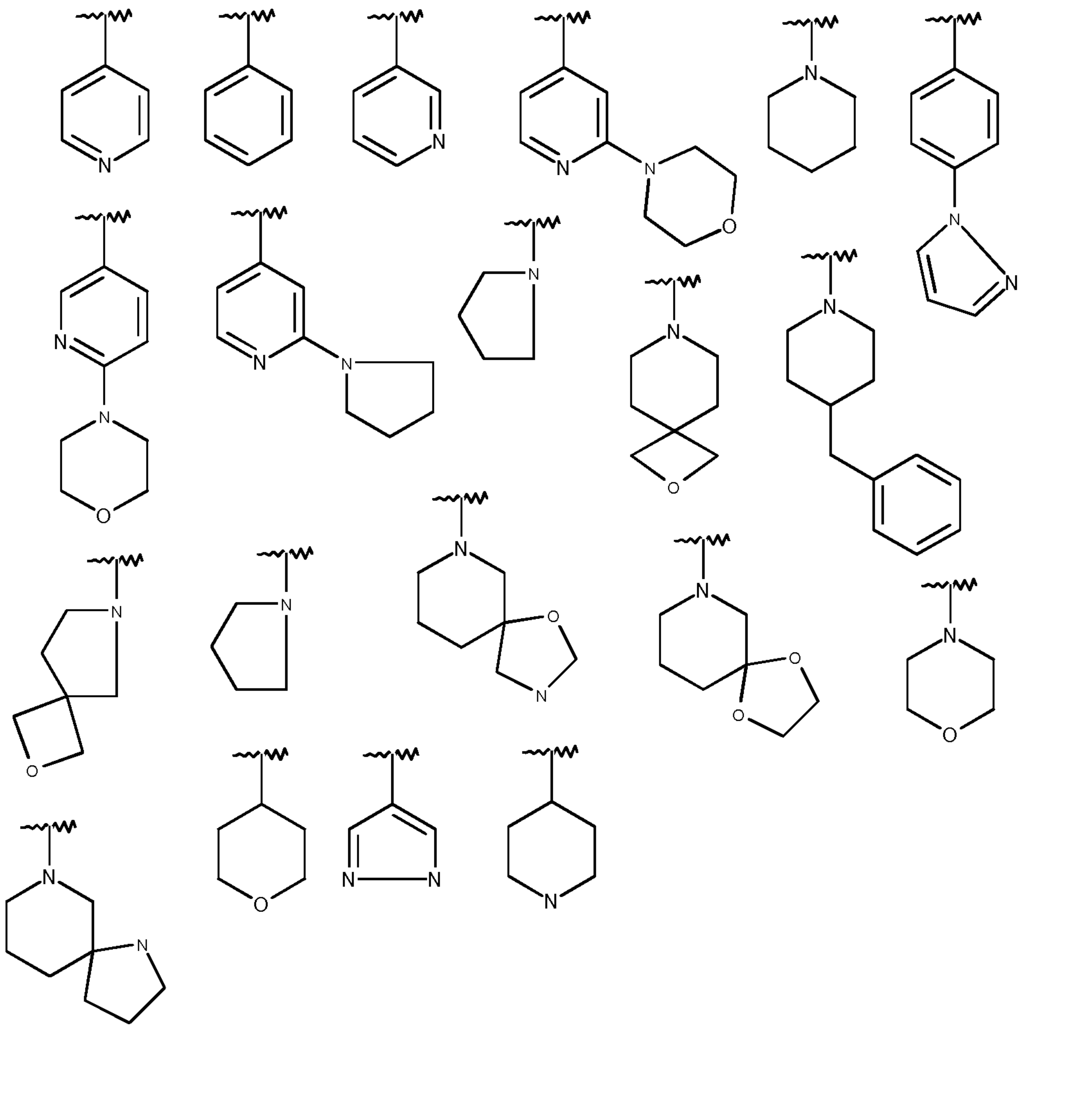
The invention particularly preferably relates to a compound of formula I, wherein R^1 is Br or one of the following structures:

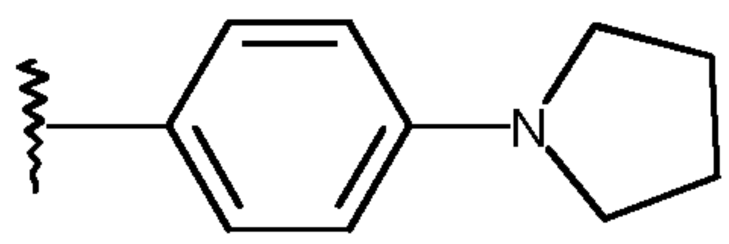
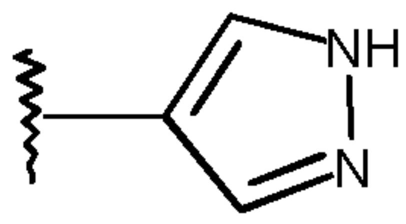
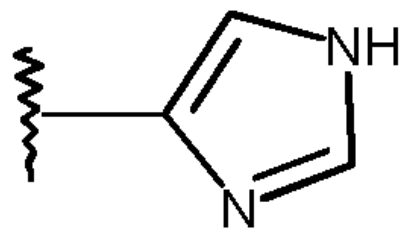
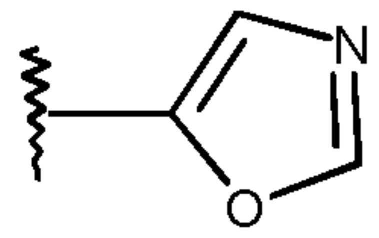


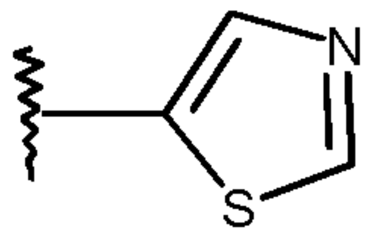
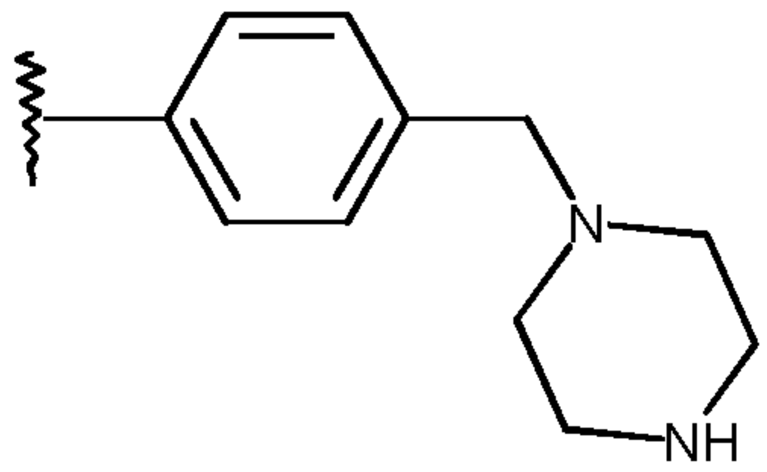


which is unsubstituted or mono-, di- or trisubstituted with R^5
and wherein Q, Y, R^2, R^3, R^4, R^5 and R^6 have the meanings as disclosed above.

The invention particularly preferably relates to a compound of formula I, wherein R^2 is one of the following structures:

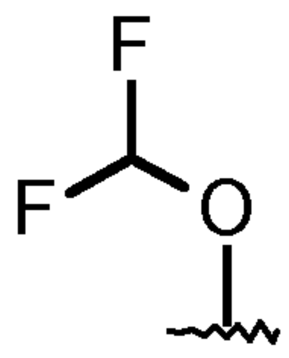
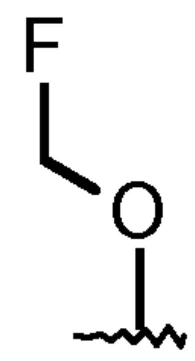
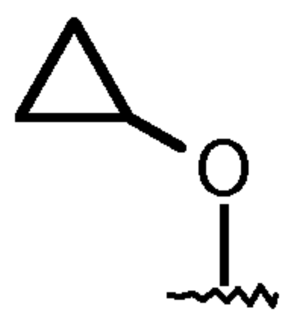
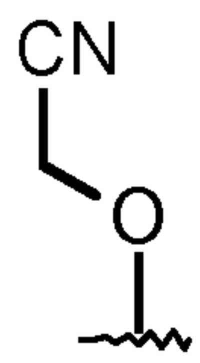
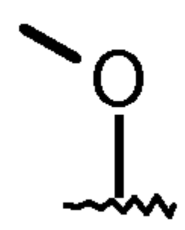


which is unsubstituted or mono-, di- or trisubstituted with R^5
and wherein Q, Y, R^1, R^3, R^4, R^5 and R^6 have the meanings as disclosed above.

The invention preferably relates to a compound of formula I, wherein

R^3 one of the following structures     

and Q, Y, R^1, R^2, R^4, R^5 and R^6 have the meanings as disclosed above.

The invention preferably relates to a compound of formula I, wherein
R^3 is O-alkyl having 1-6 C atoms, which is unsubstituted or mono-, di- or trisubstituted with F
and Q, Y, R^1, R^2, R^4, R^5 and R^6 have the meanings as disclosed above.

The invention preferably relates to a compound of formula I, wherein
R^3 is OMe
and Q, Y, R^1, R^2, R^4, R^5 and R^6 have the meanings as disclosed above.

The invention particularly preferably relates to a compound selected from the group consisting of:

No.	IUPAC-Name
1	7-Methoxy-4-phenyl-1H-benzoimidazol-2-ylamine
2	4-Fluoro-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide

3	2-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-isonicotinamide
4	2-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-isonicotinamide
5	6-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-nicotinamide
6	6-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-nicotinamide
7	N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
8	N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-6-morpholin-4-yl-nicotinamide
9	N'-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-N,N-dimethyl-formamidine
10	4-Chloromethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
11	4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
12	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide
13	4-Aminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
14	4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-ylamine
15	4-Imidazol-1-ylmethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
16	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (4-cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-amide
17	N-(4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
18	7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-ylamine
19	7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-ylamine
20	7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-ylamine
21	4-hydroxy-N-(7-methoxy-4-morpholino-1H-benzimidazol-2-yl)-4-methyl-piperidine-1-carboxamide
22	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

23	N-(7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
24	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
25	4-Methoxy-7-phenyl-3H-imidazo[4,5-c]pyridin-2-ylamine
26	N-[7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-2-morpholin-4-yl-isonicotinamide
27	4-Methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-ylamine
28	4-Methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide
29	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-6-morpholin-4-yl-nicotinamide
30	2-(3-Hydroxy-3-methyl-pyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-isonicotinamide
31	3-Hydroxy-3-methyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
32	4-Hydroxy-4-trifluoromethyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
33	2-Oxa-7-aza-spiro[3.5]nonane-7-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
34	4-Difluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
35	4-Hydroxymethyl-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
36	4-Fluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
37	4-Methoxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
38	3-Oxa-9-aza-spiro[5.5]undecane-9-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

39	4-Methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
40	4-Hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
41	4-Benzyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
42	N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide
43	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
44	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1-oxa-3,8-diazaspiro[4.5]decane-8-carboxamide
45	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,4-dioxa-8-azaspiro[4.5]decane-8-carboxamide
46	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]morpholine-4-carboxamide
47	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
48	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
49	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(methoxymethyl)benzamide
50	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,4-dioxo-1,3,8-triazaspiro[4.5]decane-8-carboxamide
51	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1,8-diazaspiro[4.5]decane-8-carboxamide
52	4-(2-hydroxyethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2,3,6-tetrahydropyridine-1-carboxamide
53	3-butyl-4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide

54	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-phenoxypiperidine-1-carboxamide
55	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(pyridin-3-yl)piperidine-1-carboxamide
56	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methylpropyl)piperidine-1-carboxamide
57	N-[4-(2,6-dimethylpyridin-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide
58	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-oxopiperidine-1-carboxamide
59	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
60	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
61	3,3-diethyl-1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
62	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-5-oxo-1,4,9-triazaspiro[5.5]undecane-9-carboxamide
63	4-fluoro-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
64	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-oxaspiro[2.5]octane-1-carboxamide
65	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-{3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy}pyrazine-2-carboxamide
66	(chloromethyl)({2-[(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}-4-methylpiperidin-4-yl)oxy]ethyl})dimethylazanium hydrochloride
67	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
68	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
69	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide

70	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxabicyclo[3.1.0]hexane-6-carboxamide
71	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
72	(1S,2S)-2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
73	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyrazine-2-carboxamide
74	4-hydroxy-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
75	4-benzyl-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
76	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
77	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
78	4-hydroxy-N-{7-methoxy-4-[1-(oxan-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
79	4-hydroxy-N-[7-methoxy-4-(1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
80	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
81	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyrazine-2-carboxamide
82	4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-4-methylpiperidine-1-carboxamide
83	4-benzyl-4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]piperidine-1-carboxamide
84	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2-oxazole-3-carboxamide

85	N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
86	1-(1-chloro-3-hydroxypropan-2-yl)-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-pyrazole-4-carboxamide
87	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
88	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
89	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
90	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
91	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
92	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
93	N4-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
94	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(trifluoromethoxy)benzamide
95	2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
96	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-4-carboxamide
97	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
98	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-benzoxazole-5-carboxamide
99	3-amino-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
100	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide

101	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide
102	4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
103	4-benzyl-4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
104	2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
105	2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
106	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
107	2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
108	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide
109	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
110	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
111	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
112	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
113	(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
114	(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
115	(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide

116	(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
117	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
118	2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
119	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
120	2-(4-fluorophenoxy)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methylpropanamide
121	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
122	2-(3-hydroxy-3-methylpyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
123	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
124	1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidine-4-carboxylic acid
125	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
126	N1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1,4-dicarboxamide
127	4-(diethylamino)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
128	4-hydroxy-N-{7-methoxy-4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
129	N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
130	2-(1-{[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid

131	4-hydroxy-N-[7-methoxy-4-(2-methylphenyl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
132	2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid
133	N4-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
134	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
135	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide
136	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
137	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
138	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
139	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide
140	(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
141	(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
142	2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
143	2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
144	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
145	tert-butyl 4-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)piperidine-1-carboxylate

146	4-{[2-amino-7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-1-yl]methyl}benzoic acid
147	(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
148	(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
149	(5S)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
150	(5R)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
151	4-hydroxy-N-{7-methoxy-4-[1-(3-methylbutyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
152	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(morpholin-4-yl)methyl]benzamide
153	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5R)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide
154	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5S)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide
155	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
156	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
157	4-hydroxy-N-{4-methoxy-7-[1-(piperidin-4-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
158	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyridine-2-carboxamide
159	2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-3-yl)acetic acid
160	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

161	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
162	N5-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
163	4-hydroxy-N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
164	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
165	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide
166	3-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]propanamide
167	1-(2-Hydroxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
168	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide
169	1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
170	5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
171	5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
172	1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
173	Thiazole-5-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
174	5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
175	4-(4-Methyl-piperazin-1-yl)-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
176	4-Hydroxy-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

177	4-Acetylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
178	4-Dimethylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
179	(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
180	(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
181	(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
182	(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
183	5-Methyl-isoxazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide
184	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
185	1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide
186	Pyridine-2,5-dicarboxylic acid 2-dimethylamide 5-{[7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide}
187	1-(2-Methoxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
188	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-morpholin-4-ylmethyl-benzamide
189	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-(4-methyl-piperazin-1-ylmethyl)-benzamide
190	1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
191	5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

192	5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
193	1-(2-Methoxy-ethyl)-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
194	1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
195	1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
196	Thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
197	2-Methyl-oxazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
198	2-Methyl-thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
199	Imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
200	5-Amino-2H-[1,2,4]triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
201	(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
202	(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
203	(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
204	(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
205	Pyrazolo[1,5-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
206	1H-[1,2,4]Triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

207	5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
208	2,3-Dimethyl-3H-imidazole-4-sulfonic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
209	1-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-3-thiazol-2-ylmethyl-urea
210	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
211	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
212	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
213	1-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
214	N5-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
215	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
216	N-[4-(azepan-1-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
217	N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
218	N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
219	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-thiazole-5-carboxamide
220	(3R)-3-methanesulfonyl-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
221	(3S)-3-fluoro-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
222	4-hydroxy-N-[7-methoxy-4-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide

223	(3S)-3-(aminomethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
224	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
225	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
226	1-cyano-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
227	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide
228	3-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea
229	N-{7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-hydroxy-4-methylpiperidine-1-carboxamide
230	4-hydroxy-N-(4-methoxy-7-{1-[2-(2-methoxyethoxy)ethyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
231	4-hydroxy-N-{4-methoxy-7-[1-(pyridin-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
232	N-[7-methoxy-4-(1-propylcyclopropyl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
233	N-[4-(hexan-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
234	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
235	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide
236	4-hydroxy-N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
237	4-hydroxy-N-(4-methoxy-7-{1-[(pyridin-3-yl)methyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
238	4-hydroxy-N-{7-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide

239	N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
240	N4-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
241	4-hydroxy-N-{4-methoxy-7-[1-(oxolan-3-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
242	N4-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
243	N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
244	N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
245	tert-butyl 3-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)azetidine-1-carboxylate
246	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-oxopyrrolidine-3-carboxamide
247	3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea
248	4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
249	1-[(3R,4S)-4-fluoropyrrolidin-3-yl]-3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
250	4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
251	tert-butyl (3S,4R)-3-fluoro-4-({[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}amino)pyrrolidine-1-carboxylate
252	N4-[7-methoxy-4-(1,2,3,6-tetrahydropyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
253	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1H-imidazole-4-carboxamide
254	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-imidazole-5-carboxamide

255	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1H-imidazole-4-carboxamide
256	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide
257	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-thiazole-5-carboxamide
258	2-amino-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide
259	N4-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
260	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
261	N4-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
262	N4-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
263	3-{[dimethyl(oxo)-lambda6-sulfanylidene]amino}-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
264	N-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
265	N-[7-(3-fluorophenyl)-4-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
266	N-[4-methoxy-7-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
267	N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-1H-imidazole-4-carboxamide
268	N-[4-methoxy-7-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
269	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-dimethyl-1H-pyrazole-4-carboxamide
270	4-hydroxy-N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
271	4-hydroxy-N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
272	4-hydroxy-N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide

273	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
274	4-hydroxy-N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
275	4-hydroxy-N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
276	(2Z)-2-cyano-3-hydroxy-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)but-2-enamide
277	N4-[5-fluoro-7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
278	N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
279	N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
280	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
281	N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
282	N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
283	N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
284	N2-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N5,N5-dimethylpyridine-2,5-dicarboxamide
285	4-(2,5-dioxopyrrolidin-1-yl)-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)benzamide
286	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyridine-3-carboxamide
287	4,4-difluoro-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)piperidine-1-carboxamide
288	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-b]pyridazine-3-carboxamide
289	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyrimidine-3-carboxamide
290	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-(pyridin-4-yl)-1H-imidazole-4-carboxamide

291	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-5H,6H,7H,8H-imidazo[1,2-a]pyridine-3-carboxamide
292	N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
293	N1-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N4-propylbenzene-1,4-dicarboxamide
294	N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(4-methylpiperazine-1-carbonyl)benzamide
295	N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-(2-methoxyethyl)-N1-methylbenzene-1,4-dicarboxamide
296	N1-[2-(dimethylamino)ethyl]-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methylbenzene-1,4-dicarboxamide
297	N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methyl-N1-propylbenzene-1,4-dicarboxamide
298	N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(morpholine-4-carbonyl)benzamide
299	N-[4-methoxy-7-(2-methylpyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
300	N-(5-cyano-7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
301	N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
302	N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
303	4-hydroxy-N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
304	N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
305	4-hydroxy-N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
306	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
307	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide

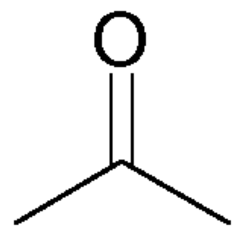
308	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-oxazole-5-carboxamide
309	N4-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N1,N1-dimethylbenzene-1,4-dicarboxamide
310	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
311	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
312	N1-(2-hydroxyethyl)-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)benzene-1,4-dicarboxamide
313	N4-[7-methoxy-4-(1,4-oxazepan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
314	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
315	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
316	N4-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
317	4-(2,5-dioxopyrrolidin-1-yl)-N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]benzamide
318	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
319	N4-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
320	N-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
321	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
322	N-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
323	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
324	N4-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
325	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

326	(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}morpholin-2-yl)methyl carbamate
327	(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl cyanate
328	(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl carbamate
329	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-oxa-8-azaspiro[4.5]decane-8-carboxamide
330	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
331	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
332	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
333	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
334	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
335	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
336	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide

and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

All above-mentioned preferred, particularly preferred and very particularly preferred meanings of the above radicals of the compounds of the formula I should be understood in such a way that these preferred particularly preferred and very particularly preferred meanings or embodiments can be combined with one another in any possible combination to give compounds of the formula I and preferred, particularly preferred and very particularly preferred compounds of the formula I of this type are likewise explicitly disclosed hereby.

Hal denotes fluorine, chlorine, bromine or iodine, in particular fluorine, bromine or chlorine.

−(C=O)− or =O denotes carbonyl oxygen and stands for  or oxygen atom bonded to a carbon atom by means of a double bond.

Alkyl is a saturated unbranched (linear) or branched hydrocarbon chain and has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 C atoms. Alkyl preferably denotes alkenyl methyl, furthermore ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl or tert-butyl, furthermore also pentyl, 1-, 2- or 3-methylbutyl, 1,1- , 1,2- or 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1- , 2- , 3- or 4-methylpentyl, 1,1- , 1,2- , 1,3- , 2,2- , 2,3- or 3,3-dimethylbutyl, 1- or 2-ethylbutyl, 1-ethyl-1-methylpropyl, 1-ethyl-2-methylpropyl, 1,1,2- or 1,2,2-trimethylpropyl, linear or branched heptyl, octyl, nonyl or decyl, further preferably, for example, trifluoromethyl.

Cyclic alkyl or cycloalkyl is a saturated cyclic hydrocarbon chain and has 3-10, preferably 3-7 C atoms and preferably denotes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl. Cycloalkyl also denotes a partially unsaturated cyclic akyl, such as, for example, cyclohexenyl or cyclohexynyl.

Alkenyl denotes an unsaturated unbranched (linear) or branched hydrocarbon chain and has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 C atoms.

O-alkyl or OA denotes linear or branched alkoxyl having 1-6 C atoms, and is preferably methoxyl, furthermore also e.g. ethoxyl, n-propoxyl, isopropoxyl, n-butoxyl, isobutoxyl, sec-butoxyl or tert-butoxyl.

Alkyloxycarbonyl refers to straight or branched chain esters of a carboxylic acid derivative of the present invention, i.e. methyloxycarbonyl (MeOCO-), ethyloxycarbonyl, or butyloxycarbonyl.

Alkylcarbonyl refers to straight or branched chain alkyl and a carboxylic acid group.

Aryl, Ar or aromatic ring denotes a mono- or polycyclic aromatic or fully unsaturated cyclic hydrocarbon chain, for example unsubstituted phenyl, naphthyl or biphenyl, furthermore preferably phenyl, naphthyl or biphenyl, each of which is mono-, di- or trisubstituted, for example, by A, fluorine, chlorine, bromine, iodine, hydroxyl, methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, nitro, cyano, formyl, acetyl, propionyl, trifluoromethyl, amino, methylamino, ethylamino, dimethylamino, diethylamino, benzyloxy, sulfonamido, methylsulfonamido, ethylsulfonamido, propylsulfonamido, butylsulfonamido, dimethylsulfonamido, phenylsulfonamido, carboxyl, methoxycarbonyl, ethoxycarbonyl, aminocarbonyl.

Heterocycle and heterocyclyl refer to saturated or unsaturated non-aromatic rings or ring systems containing at least one heteroatom selected from O. S and N. further including the oxidized forms of sulfur, namely SO and SO_2. Examples of heterocycles include tetrahydrofuran (THF), dihydrofuran, 1,4-dioxane, morpholine, 1,4-dithiane, piperazine, piperidine, 1,3-dioxolane, imidazolidine, imidazoline, pyrroline, pyrrolidine, tetrahydropyran, dihydropyran, oxathiolane, dithiolane, 1,3-dioxane, 1,3-dithiane, oxathiane, thiomorpholine, and the like.

Heteroaryl means an aromatic or partially aromatic heterocycle that contains at least one ring heteroatom selected from O. S and N. Heteroaryls thus includes heteroaryls fused to other kinds of rings, such as aryls, cycloalkyls and heterocycles that are not aromatic. Examples of heteroaryl groups include: pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, pyridyl, oxazolyl, oxadiazolyl, thiadiazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, furanyl, triazinyl, thienyl, pyrimidyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzothiadiazolyl, dihydrobenzofuranyl, indolinyl, pyridazinyl, indazolyl, isoxazolyl, isoindolyl, dihydrobenzothienyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, carbazolyl, benzdioxinyl, benzodioxolyl, quinoxalinyl, purinyl, furazanyl, thiophenyl, isobenzylfuranyl, benzimidazolyl, benzofuranyl, benzothienyl, quinolyl, indolyl, isoquinolyl, dibenzofuranyl, and the like. For heterocyclyl and heteroaryl groups, rings and ring systems containing from 3-15 atoms are included, forming 1-3 rings.

Mono- or bicyclic saturated, unsaturated or aromatic heterocycle preferably denotes unsubstituted or mono-, di- or trisubstituted 2- or 3-furyl, 2- or 3-thienyl, 1-, 2- or 3-pyrrolyl, 1-, 2, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, furthermore preferably 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-

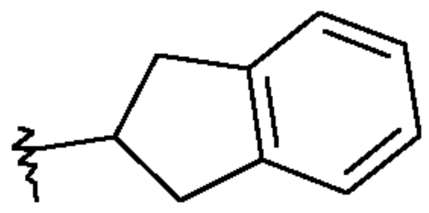
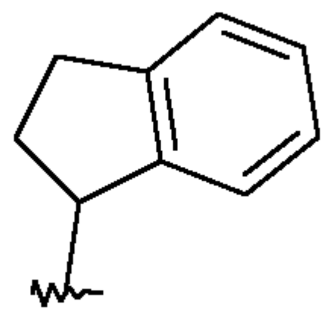
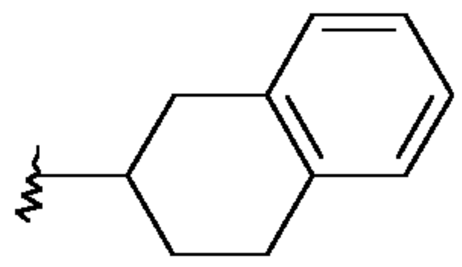
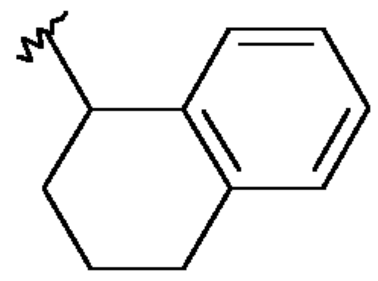
1-, -3- or 5-yl, 1- or 5-tetrazolyl, 1,2,3-oxadiazol-4- or -5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 3- or 4-pyridazinyl, pyrazinyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 4- or 5-isoindolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-benzopyrazolyl, 2-, 4-, 5-, 6- or 7-benzoxazolyl, 3-, 4-, 5-, 6- or 7- benzisoxazolyl, 2-, 4-, 5-, 6- or 7-benzothiazolyl, 2-, 4-, 5-, 6- or 7-benzisothiazolyl, 4-, 5-, 6- or 7-benz-2,1,3-oxadiazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 5- or 6-quinoxalinyl, 2-, 3-, 5-, 6-, 7- or 8-2H-benzo-1,4-oxazinyl, further preferably 1,3-benzodioxol-5-yl, 1,4-benzodioxan-6-yl, 2,1,3-benzothiadiazol-4- or -5-yl or 2,1,3-benzoxadiazol-5-yl.

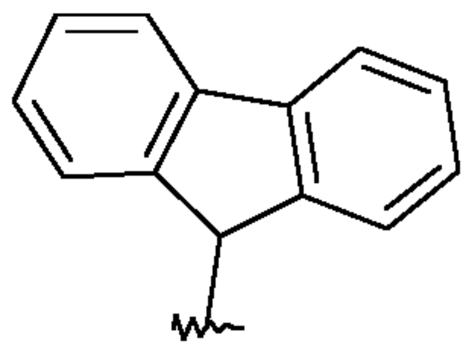
The heterocyclic radicals may also be partially or fully hydrogenated and also denote, for example, 2,3-dihydro-2-, -3-, -4- or -5-furyl, 2,5-dihydro-2-, -3-, -4- or 5-furyl, tetrahydro-2- or -3-furyl, 1,3-dioxolan-4-yl, tetrahydro-2- or -3-thienyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 2,5-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 1-, 2- or 3-pyrrolidinyl, tetrahydro-1-, -2- or -4-imidazolyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrazolyl, tetrahydro-1-, -3- or -4-pyrazolyl, 1,4-dihydro-1-, -2-, -3- or -4-pyridyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5- or -6-pyridyl, 1-, 2-, 3- or 4-piperidinyl, 2-, 3- or 4-morpholinyl, tetrahydro-2-, -3- or -4-pyranyl, 1,4-dioxanyl, 1,3-dioxan-2-, -4- or -5-yl, hexahydro-1-, -3- or -4-pyridazinyl, hexahydro-1-, -2-, -4- or -5-pyrimidinyl, 1-, 2- or 3-piperazinyl, 1,2,3,4-tetrahydro-1-,-2-,-3-, -4-, -5-, -6-, -7- or -8-quinolyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-isoquinolyl, 2-, 3-, 5-, 6-, 7- or 8- 3,4-dihydro-2H-benzo-1,4-oxazinyl, further preferably 2,3-methylenedioxyphenyl, 3,4-methylenedioxyphenyl, 2,3-ethylenedioxyphenyl, 3,4-ethylenedioxyphenyl, 3,4-(difluoromethylenedioxy)phenyl, 2,3-dihydrobenzofuran-5- or 6-yl, 2,3-(2-oxomethylenedioxy)phenyl or also 3,4-dihydro-2H-1,5-benzodioxepin-6- or -7-yl, furthermore preferably 2,3-dihydrobenzofuranyl or 2,3-dihydro-2-oxofuranyl.

Heterocycle furthermore denotes, for example, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, 2-oxo-1*H*-pyridin-1-yl, 3-oxomorpholin-4-yl, 4-oxo-1*H*-pyridin-1-yl, 2,6-dioxopiperidin1-yl, 2-oxopiperazin-1-yl, 2,6-dioxopiperazin-1-yl, 2,5-dioxopyrrolidin-1-yl, 2-oxo-1,3-oxazolidin-3-yl, 3-oxo-2*H*-pyridazin-2-yl, 2-caprolactam-1-yl (= 2-oxoazepan-1-yl), 2-hydroxy-6-oxopiperazin-1-yl, 2-methoxy-6-oxopiperazin-1-yl or 2-azabicyclo[2.2.2]octan-3-on-2-yl.

Heterocycloalkyl here denotes a fully hydrogenated or saturated heterocycle, heterocycloalkenyl (one or more double bonds) or heterocycloalkynyl (one or more triple bonds) denotes a partially or incompletely hydrogenated or unsaturated heterocycle, heteroaryl denotes an aromatic or fully unsaturated heterocycle.

A cyclic alkylaryl group in connection with the present invention means that and one or two aromatic rings Ar are condensed onto an unsubstituted or a mono- or disubstituted cyclic alkyl, in which one or two CH_2 groups and/or, in addition, 1-11 H atoms may be replaced, such as, for example, in the radicals depicted below:


,

,

,

and



Furthermore, the abbreviations below have the following meanings:

Boc ter-butoxycarbonyl
CBZ benzyloxycarbonyl
DNP 2,4-dinitrophenyl
FMOC 9-fluorenylmethoxycarbonyl
imi-DNP 2,4-dinitrophenyl in the 1-position of the imidazole ring
OMe methyl ester
POA phenoxyacetyl
DCCIdicyclohexylcarbodiimide
HOBt1-hydroxybenzotriazole

The invention therefore relates to a pharmaceutical preparation comprising the compound accoirding to the present invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios.

The invention also relates to a pharmaceutical preparation according to the invention of this type, comprising further excipients and/or adjuvants.

In addition, the invention relates to an above pharmaceutical preparation according to the invention, comprising at least one further medicament active compound.

Pharmaceutically or physiologically acceptable derivatives are taken to mean, for example, salts ofthe compound of the present invention, and also so-called prodrug compounds. Prodrug compounds are taken to mean derivatives the compound of the present invention which have been modified by means of, for example, alkyl or acyl groups (see also amino- and hydroxyl-protecting groups below), sugars or oligopeptides and which are rapidly cleaved or liberated in the organism to form the effective molecules. These also include biodegradable polymer derivatives of the compound of the present invention, as described, for example, in Int. J. Pharm. 115 (1995), 61-67.

The compound of the present invention can be used in its final non-salt form. On the other hand, the present invention also encompasses the use of pepstatin in the form of its pharmaceutically acceptable salts, which can be derived from various organic and inorganic bases by procedures known in the art. Pharmaceutically acceptable salt forms of pepstatin are for the most part prepared by conventional methods. If the compound of the present invention contains a carboxyl group, one of its suitable salts can be formed by reacting the compound of the present invention ith a suitable base to give the corresponding base-addition salt. Such bases are, for example, alkali metal hydroxides, including potassium hydroxide, sodium hydroxide and lithium hydroxide; alkaline-earth metal hydroxides, such as barium hydroxide and calcium hydroxide; alkali metal alkoxides, for example potassium ethoxide and sodium propoxide; and various organic bases, such as piperidine, diethanolamine and N-methylglutamine. The aluminium salts of pepstatin are likewise included.

Furthermore, the base salts of the compound of the present invention include aluminium, ammonium, calcium, copper, iron(III), iron(II), lithium, magnesium, manganese(III), manganese(II), potassium, sodium and zinc salts, but this is not intended to represent a restriction.

Of the above-mentioned salts, preference is given to ammonium; the alkali metal salts sodium and potassium, and the alkaline-earth metal salts calcium and magnesium. Salts of cthe ompound of the present invention which are derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary and tertiary amines, substituted amines, also including naturally occurring substituted amines, cyclic amines, and basic ion exchanger resins, for example arginine, betaine, caffeine, chloroprocaine, choline, N,N'-dibenzylethylenediamine (benzathine), dicyclohexylamine, diethanolamine, diethylamine, 2-diethylamino-ethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lidocaine, lysine, meglumine, N-methyl-D-glucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethanolamine, triethylamine, trimethylamine, tripropylamine and tris-(hydroxymethyl)methylamine (tromethamine), but this is not intended to represent a restriction.

As mentioned, the pharmaceutically acceptable base-addition salts of pepstatin are formed with metals or amines, such as alkali metals and alkaline-earth metals or organic amines. Preferred metals are sodium, potassium, magnesium and calcium. Preferred organic amines are N,N’-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, N-methyl-D-glucamine and procaine.

The base-addition salts of the compound of the present invention are prepared by bringing the free acid form into contact with a sufficient amount of the desired base, causing the formation of the salt in a conventional manner. The free acid can be regenerated by bringing the salt form into contact with an acid and isolating the free acid in a conventional manner. The free acid forms differ in a certain respect from the corresponding salt forms thereof with respect to certain physical properties, such as solubility in polar solvents; for the purposes of the invention, however, the salts otherwise correspond to the respective free acid forms thereof.

In view of that stated above, it can be seen that the term “pharmaceutically acceptable salt” in the present connection is taken to mean an active compound which comprises the compound of the present invention in the form of one of its salts, in particular if this salt form imparts improved pharmacokinetic properties on the active compound compared with the free form of the active compound or any other salt form of the active compound used earlier. The pharmaceutically acceptable salt form of the active compound can also provide this active compound for the first time with a desired pharmacokinetic property which it did not have earlier and can even have a positive influence on the pharmacodynamics of this active compound with respect to its therapeutic efficacy in the body.

Solvates of the compound of the present invention are taken to mean adductions of inert solvent molecules pepstatin which form owing to their mutual attractive force. Solvates are, for example, hydrates, such as monohydrates or dihydrates, or alcoholates, i.e. addition compounds with alcohols, such as, for example, with methanol or ethanol.

All physiologically acceptable salts, derivatives, solvates and stereoisomers of these compounds, including mixtures thereof in all ratios, are also in accordance with the invention.

Compounds of the general formula I may contain one or more centres of chirality, so that all stereoisomers, enentiomers, diastereomers, etc., of the compounds of the general formula I are also claimed in the present invention.

The invention also relates to the optically active forms (stereoisomers), the enantiomers, the racemates, the diastereomers and hydrates and solvates of these compounds.

Compounds of the formula I according to the invention may be chiral owing to their molecular structure and may accordingly occur in various enantiomeric forms. They may therefore be in racemic or optically active form. Since the pharmaceutical efficacy of the racemates or stereoisomers of the compounds according to the invention may differ, it may be desirable to use the enantiomers. In these cases, the end product, but also even the intermediates, may be separated into enantiomeric compounds by chemical or physical measures known to the person skilled in the art or already employed as such in the synthesis.

Pharmaceutically or physiologically acceptable derivatives are taken to mean, for example, salts of the compounds according to the invention and also so-called prodrug compounds. Prodrug compounds are taken to mean compounds of the formula I which have been modified with, for example, alkyl or acyl groups (see also amino- and hydroxyl-protecting groups below), sugars or oligopeptides and which are rapidly cleaved or liberated in the organism to form the effective compounds according to the invention. These also include biodegradable polymer derivatives of the compounds according to the invention, as described, for example, in Int. J. Pharm. 115 (1995), 61-67.

Suitable acid-addition salts are inorganic or organic salts of all physiologically or pharmacologically acceptable acids, for example halides, in particular hydrochlorides or hydrobromides, lactates, sulfates, citrates, tartrates, maleates, fumarates, oxalates, acetates, phosphates, methylsulfonates or p-toluenesulfonates.

Very particular preference is given to the hydrochlorides, the trifluoroacetates or the bistrifluoroacetates of the compounds according to the invention.

Solvates of the compounds of the formula I are taken to mean adductions of inert solvent molecules onto the compounds of the formula I which form owing to their mutual attractive force. Solvates are, for example, hydrates, such as monohydrates or dihydrates, or alcoholates, i.e. addition compounds with alcohols, such as, for example, with methanol or ethanol.

It is furthermore intended that a compound of the formula I includes isotope-labelled forms thereof. An isotope-labelled form of a compound of the formula I is identical to this compound apart from the fact that one or more atoms of the compound have been replaced by an atom or atoms having an atomic mass or mass number which differs from the atomic mass or mass number of the atom which usually occurs naturally. Examples of isotopes which are readily commercially available and which can be incorporated into a compound of the formula I by well-known methods include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and chlorine, for example ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F and ^{36}Cl, respectively. A compound of the formula I, a prodrug thereof or a pharmaceutically acceptable salt of either which contains one or more of the above-mentioned isotopes and/or other isotopes of other atoms is intended to be part of the present invention. An isotope-labelled compound of the formula I can be used in a number of beneficial ways. For example, an isotope-labelled compound of the formula I into which, for example, a radioisotope, such as ^{3}H or ^{14}C, has been incorporated is suitable for medicament and/or substrate tissue distribution assays. These radioisotopes, i.e. tritium (^{3}H) and carbon-14 (^{14}C), are particularly preferred owing to their simple preparation and excellent detectability. Incorporation of heavier isotopes, for example deuterium (^{2}H), into a compound of the formula I has therapeutic advantages owing to the higher metabolic stability of this isotope-labelled compound. Higher metabolic stability translates directly into an increased in-vivo half-life or lower dosages, which under most circumstances would represent a preferred embodiment of the present invention. An isotope-labelled compound of the formula I can usually be prepared by carrying out the procedures disclosed in the synthesis schemes and the related description, in the example part and in the preparation part in the present text, replacing a non-isotope-labelled reactant with a readily available isotope-labelled reactant.

In order to manipulate the oxidative metabolism of the compound by way of the primary kinetic isotope effect, deuterium (^{2}H) can also be incorporated into a compound of the formula I. The primary kinetic isotope effect is a change in the rate of a chemical reaction that results from exchange of isotopic nuclei, which in turn is caused by the change in ground state energies necessary for covalent bond formation after this isotopic exchange. Exchange of a heavier isotope usually results in a lowering of the ground state energy for a chemical bond and thus causes a reduction in the rate in rate-limiting bond breakage. If the bond breakage occurs in or in the vicinity of a saddle-point region along the coordinate of a multi-product reaction, the product distribution ratios can be altered substantially. For explanation: if deuterium is bonded to a carbon atom in a non-exchangeable position, rate differences of k_M/k_D = 2-7 are typical. If this rate difference is successfully applied to a compound of the formula I that is susceptible to oxidation, the profile of this compound in vivo can thereby be drastically modified and result in improved pharmacokinetic properties.

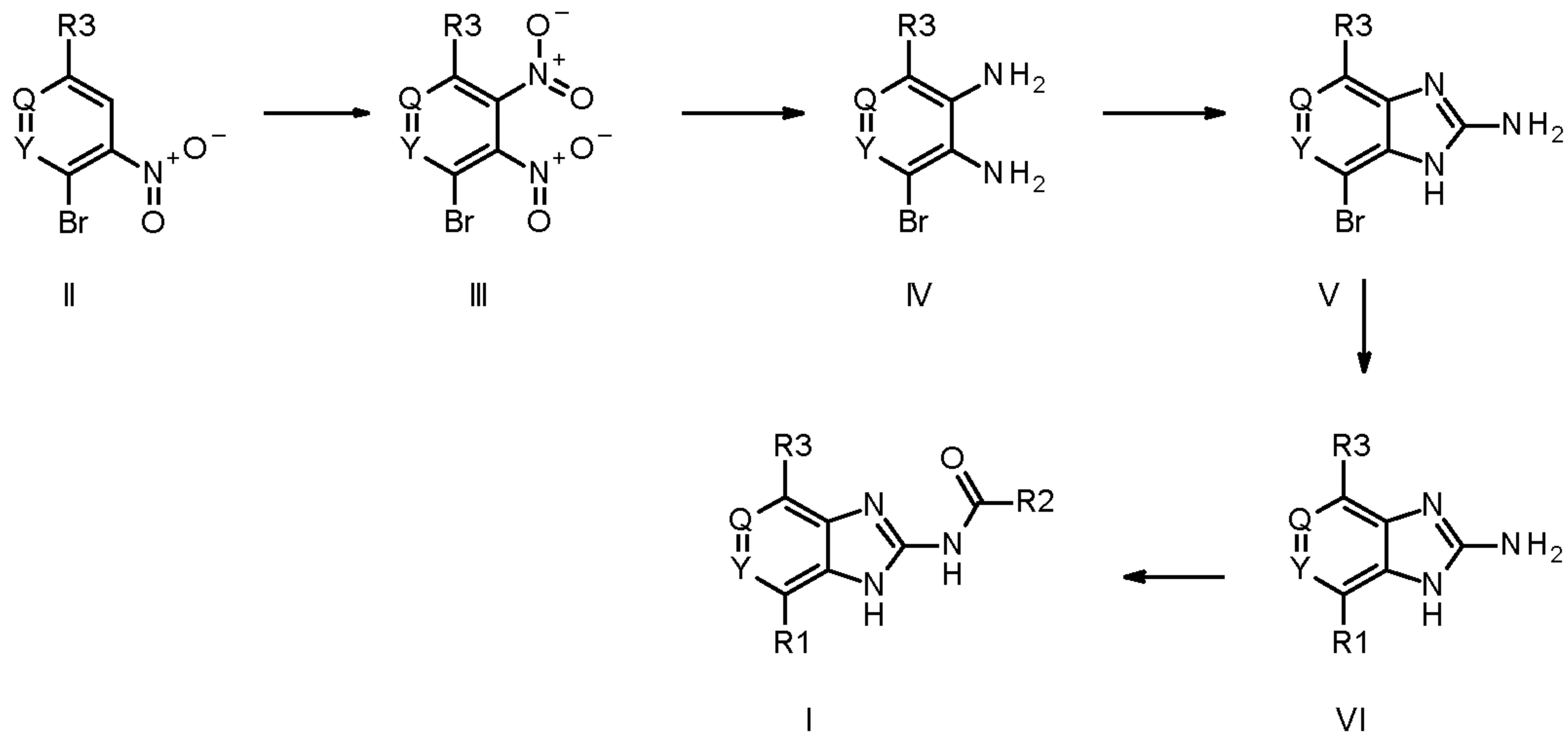
When discovering and developing therapeutic agents, the person skilled in the art attempts to optimise pharmacokinetic parameters while retaining desirable in-vitro properties. It is reasonable to assume that many compounds with poor pharmacokinetic profiles are susceptible to oxidative metabolism. In-vitro liver microsomal assays currently available provide valuable information on the course of oxidative metabolism of this type, which in turn permits the rational design of deuterated compounds of the formula I with improved stability through resistance to such oxidative metabolism. Significant improvements in the pharmacokinetic profiles of the compounds of the formula I are thereby obtained and can be expressed quantitatively in terms of increases in the in-vivo half-life (T/2), concentration at maximum therapeutic effect (C_{max}), area under the dose response curve (AUC), and F; and in terms of reduced clearance, dose and costs of materials.

The following is intended to illustrate the above: a compound of the formula I which has multiple potential sites of attack for oxidative metabolism, for example benzylic hydrogen atoms and hydrogen atoms bonded to a nitrogen atom, is prepared as a series of analogues in which various combinations of hydrogen atoms are replaced by deuterium atoms, so that some, most or all of these hydrogen atoms have been replaced by deuterium atoms. Half-life determinations enable favourable and accurate determination of the extent to which the improvement in resistance to oxidative metabolism has improved. In this way, it is determined that the half-life of the parent compound can be extended by up to 100% as the result of deuterium-hydrogen exchange of this type.

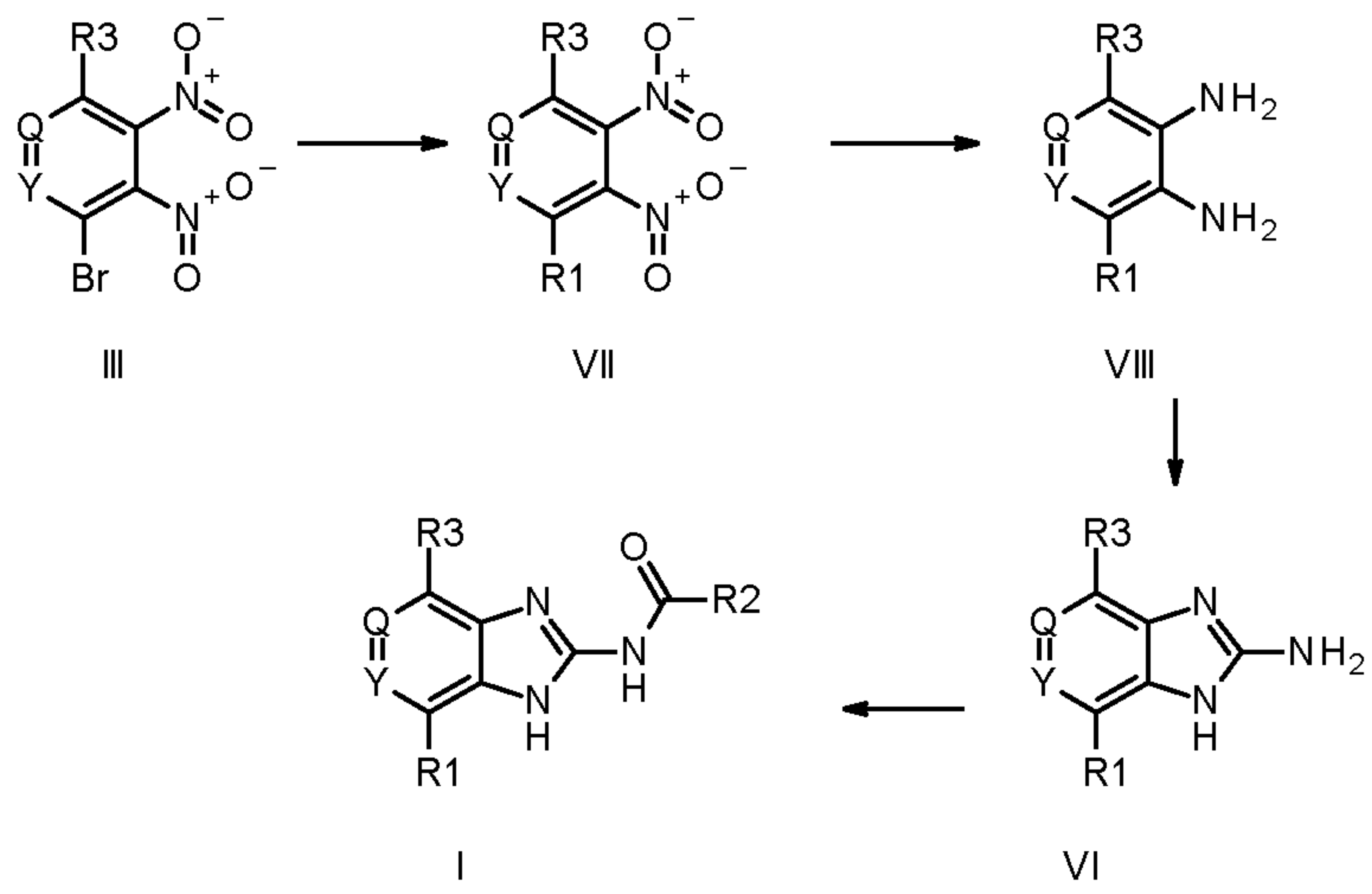
The replacement of hydrogen by deuterium in a compound of the formula I can also be used to achieve a favourable modification of the metabolite spectrum of the starting compound in order to diminish or eliminate undesired toxic metabolites. For example, if a toxic metabolite arises through oxidative carbon-hydrogen (C-H) bond cleavage, it can reasonably be assumed that the deuterated analogue will greatly diminish or eliminate production of the undesired metabolite, even if the particular oxidation is not a rate-determining step. Further information on the state of the art with respect to deuterium-hydrogen exchange is given, for example in Hanzlik et al., J. Org. Chem. 55, 3992-3997, 1990, Reider et al., J. Org. Chem. 52, 3326-3334, 1987, Foster, Adv. Drug Res. 14, 1-40, 1985, Gillette et al., Biochemistry 33(10), 2927-2937, 1994, and Jarman et al., Carcinogenesis 16(4), 683-688, 1993.

The invention also relates to mixtures of the compounds of the formula I according to the invention, for example mixtures of two diastereomers, for example in the ratio 1:1, 1:2, 1:3, 1:4, 1:5, 1:10, 1:100 or 1:1000. These are particularly preferably mixtures of two stereoisomeric compounds. However, preference is also given to mixtures of two or more compounds of the formula I.

In addition, the invention relates to a process for the preparation of the compounds of the formula I, characterized in that



a) a compound of the formula II undergoes a nitration reaction, followed by a reduction to give a compound of formula IV, a compound of formula IVI is cyclized to give a compound of formula V, a compound of formula V is reacted in a Suzuki type reaction toformula VI employing the use of catalyst and base, a compound of formula VI is converted to a compound of the formula VII by standard amidation or carbamide formation conditions to give a compound of the formula I and wherein Q, Y, R^1, R^2 and R^3 have the meanings as disclosed above,



b) a compound of the formula III is reacted with a boronic ester or acid under Suzuki-type reaction conditions to give a compound of the formula VII or reacted with an amine in a nuclophilic substitution reaction under increased temperature to form a compound of the formula VII , a compound of formula VII is reduced to a compound of the formula VIIand cyclized to a compound of the formula VI and finally reacted with to compound of the formula I under standard amidation or carbamide formation conditions and wherein Q, Y, R^1, R^2 and R^3 have the meanings as disclosed above,

c) the base of a compound of the formula I is converted into one of its salts by treatment with an acid, or

d) an acid of a compound of the formula I is converted into one of its salts by treatment with a base.

It is also possible to carry out the reactions stepwise in each case and to modify the sequence of the linking reactions of the building blocks with adaptation of the protecting-group concept.

The starting materials or starting compounds are generally known. If they are novel, they can be prepared by methods known per se.

If desired, the starting materials can also be formed in situ by not isolating them from the reaction mixture, but instead immediately converting them further into the compounds of the formula I.

The compounds of the formula I are preferably obtained by liberating them from their functional derivatives by solvolysis, in particular by hydrolysis, or by hydrogenolysis. Preferred starting materials for the solvolysis or hydrogenolysis are those which contain correspondingly protected amino, carboxyl and/or hydroxyl groups instead of one or more free amino, carboxyl and/or hydroxyl groups, preferably those which carry an amino-protecting group instead of an H atom which is connected to an N atom. Preference is furthermore given to starting materials which carry a hydroxyl-protecting group instead of the H atom of a hydroxyl group. Preference is also given to starting materials which carry a protected carboxyl group instead of a free carboxyl group. It is also possible for a plurality of identical or different protected amino, carboxyl and/or hydroxyl groups to be present in the molecule of the starting material. If the protecting groups present are different from one another, they can in many cases be cleaved off selectively.

The term “amino-protecting group” is generally known and relates to groups which are suitable for protecting (blocking) an amino group against chemical reactions, but which can easily be removed after the desired chemical reaction has been carried out elsewhere in the molecule. Typical of such groups are, in particular, unsubstituted or substituted acyl groups, furthermore unsubstituted or substituted aryl (for example 2,4-dinitophenyl) or aralkyl groups (for example benzyl, 4-nitrobenzyl, triphenylmethyl). Since the amino-protecting groups are removed after the desired reaction or reaction sequence, their type and size is, in addition, not crucial, but preference is given to those having 1-20, in particular 1-8, C atoms. The term “acyl group” is to be understood in the broadest sense in connection with the present process. It encompasses acyl groups derived from aliphatic, araliphatic, aromatic or heterocyclic carboxylic acids or sulfonic acids and, in particular, alkoxy-carbonyl, aryloxycarbonyl and especially aralkoxycarbonyl groups. Examples of such acyl groups are alkanoyl, such as acteyl, propionyl, buturyl, aralkanoyl, such as phenylacetyl, aroyl, such as benzoyl or toluyl, aryoxyaklkanoyl, such as phenoxyacetyl, alkyoxycarbonyyl, such as methoxycarbonyl, ethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, BOC, 2-iodoethoxycaronyl, aralkoxycarbonyl. such as CBZ, 4-methoxybenzyloxycarbonyl or FMOC. Preferred acyl groups are CBZ, FMOC, benzyl and acetyl.

The term “acid-protecting group” or “carboxyl-protecting group” is likewise generally known and relates to groups which are suitable for protecting a −COOH group against chemical reactions, but which can easily be removed after the desired chemical reaction has been carried out elsewhere in the molecule. The use of esters instead of the free acids, for example of substituted and unsubstituted alkyl esters (such as methyl, ethyl, tert-butyl and substituted derivatives thereof), of substituted and unsubstituted benzyl esters or silyl esters, is typical. The type and size of the acid-protecting groups is not crucial, but preference is given to those having 1-20, in particular 1-10, C atoms.

The term “hydroxyl-protecting group” is likewise generally known and relates to groups which are suitable for protecting a hydroxyl group against chemical reactions, but which can easily be removed after the desired chemical reaction has been carried out elsewhere in the molecule. Typical of such groups are the above-mentioned unsubstituted or substituted aryl, aralkyl or acyl groups, furthermore also alkyl groups. Their type and size of the hydroxyl-protecting groups is not crucial, but preference is given to those having 1-20, in particular 1-10, C atoms. Examples of hyrdoxyl-protecting groups are, inter alia, benzyl, p-nitrobenzoyl, p-toluenesulfonyl and acetyl, where benzyl and acetyl are preferred.

Further typical examples of amino-, acid- and hydroxyl-protecting groups are found, for example, in “Greene’s Protective Groups in Organic Synthesis”, fourth edition, Wiley-Interscience, 2007.

The functional derivatives of the compounds of the formula I to be used as starting materials can be prepared by known methods of amino-acid and peptide synthesis, as described, for example, in the said standard works and patent applications.

The compounds of the formula I are liberated from their functional derivatives, depending on the protecting group used, for example, with the aid of strong acids, advantageously using trifluoroacetic acid or perchloric acid, but also using other strong inorganic acids, such as hydrochloric acid or sulfuric acid, strong organic acids, such as trichloroacetic acid, or sulfonic acids, such as benzoyl- or p- toluenesulfonic acid. The presence of an additional inert solvent and/or a catalyst is possible, but is not always necessary.

Depending on the respective synthetic route, the starting materials can optionally be reacted in the presence of an inert solvent.

Suitable inert solvents are, for example, heptane, hexane, petroleum ether, DMSO, benzene, toluene, xylene, trichloroethylene-, 1,2-dichloroethanecarbon tetrachloride, chloroform or dichloromethane; alcohols, such as methanol, ethanol, isopropanol, n-propanol, n-butanol or tert-butanol; ethers, such as diethyl ether, diisopropyl ether (preferably for substitution on the indole nitrogen), tetrahydrofuran (THF) or dioxane; glycol ethers, such as ethylene glycol monomethyl or monoethyl ether, ethylene glycol dimethy-l ether (diglyme); ketones, such as acetone or butanone; amides, such as acetamide, dimethylacetamide, N-methylpyrrolidone (NMP) or dimethylformamide (DMF); nitriles, such as acetonitrile; esters, such as ethyl acetate, carboxylic acids or acid anhydrides, such as, for example, such as acetic acid or acetic anhydride, nitro compounds, such as nitromethane or nitro-benzene, optionally also mixtures of the said solvents with one another or mixtures with water.

The amount of solvent is not crucial; 10 g to 500 g of solvent can preferably be added per g of the compound of the formula I to be reacted.

It may be advantageous to add an acid-binding agent, for example an alkali metal or alkaline-earth metal hydroxide, carbonate or bicarbonate or other alkali or alkaline-earth metal salts of weak acids, preferably a potassium, sodium or calcium salt, or to add an organic base, such as, for example, on triethylamine, dimethylamine, pyridine or quinoline, or an excess of the amine component.

The resultant compounds according to the invention can be separated from the corresponding solution in which they are prepared (for example by centrifugation and washing) and can be stored in another composition after separation, or they can remain directly in the preparation solution. The resultant compounds according to the invention can also be taken up in desired solvents for the particular use.

The reaction duration depends on the reaction conditions selected. In general, the reaction duration is 0.5 hour to 10 days, preferably 1 to 24 hours. On use of a microwave, the reaction time can be reduced to values of 1 to 60 minutes.

The compounds of the formula I and also the starting materials for their preparation are, in addition, prepared by known methods, as described in the literature (for example in standard works, such as Houben-Weyl, Methoden der organischen Chemie [Methods of Organic Chemistry], Georg-Thieme-Verlag, Stuttgart), for example under reaction conditions which are known and suitable for the said reactions. Use can also be made here of variants known per se, which are not described here in greater detail.

Conventional work-up steps, such as, for example, addition of water to the reaction mixture and extraction, enable the compounds to be obtained after removal of the solvent. It may be advantageous, for further purification of the product, to follow this with a distillation or crystallisation or to carry out a chromatographic purification.

An acid of the formula I can be converted into the associated addition salt using a base, for example by reaction of equivalent amounts of the acid and base in an inert solvent, such as ethanol, and inclusive evaporation. Suitable bases for this reaction are, in particular, those which give physiologically acceptable salts. Thus, the acid of the formula I can be converted into the corresponding metal salt, in particular alkali or alkaline-earth metal salt, using a base (for example sodium hydroxide, potassium hydroxide, sodium carbonate or potassium carbonate) or into the corresponding ammonium salt. Organic bases which give physiologically acceptable salts, such as, for example, ethanolamine, are also suitable for this reaction.

On the other hand, a base of the formula I can be converted into the associated acid-addition salt using an acid, for example by reaction of equivalent amounts of the base and acid in an inert solvent, such as ethanol, with subsequent evaporation. Suitable acids for this reaction are, in particular, those which give physiologically acceptable salts. Thus, it is possible to use inorganic acids, for example sulfuric acid, nitric acid, hydrohalic acids, such as hydrochloric acid or hydrobromic acid, phosphoric acids, such as orthophosphoric acid, sulfamic acid, furthermore organic acids, in particular aliphatic, alicyclic, araliphatic, aromatic or heterocyclic, mono- or polybasic carboxylic, sulfonic or sulfuric acids, for example formic acid, acetic acid, propionic acid, pivalic acid, diethylacetic acid, malonic acid, succinic acid, pimelic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, malic acid, citric acid, gluconic acid, ascorbic acid, nicotinic acid, isonicotinic acid, methane- or ethanesulfonic acid, ethanedisulfonic acid, 2-hydroxysulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, naphthalenemom- and disulfonic acids or laurylsulfuric acid. Salts with physiologically unacceptable acids, for example picrates, can be used for the isolation and/or purification of the compounds of the formula I.

It has been found that the compounds of the formula I are well tolerated and have valuable pharmacological properties.

Since adenosine receptors, such as A_{2A} and A_{2B}, are shown to down-regulate the immune response during inflammation and protect tissues from immune damage, inhibition of signaling through adenosine receptors can be used to intensify and prolong the immune response.

Methods are provided herein to increase an immune response. In one example, the method increases desirable and targeted tissue damage, such as damage of a tumor, for example cancer. Disclosed herein are methods of inhibiting one or more processes conducive to the production of extracellular adenosine and adenosine-triggered signaling through adenosine receptors. For example, enhancement of an immune response, local tissue inflammation, and targeted tissue destruction is accomplished by: inhibiting or reducing the adenosine-producing local tissue hypoxia; by degrading (or rendering inactive) accumulated extracellular adenosine; by preventing or decreasing expression of adenosine receptors on immune cells; and or by inhibiting/antagonizing signaling by adenosine ligands through adenosine receptors. The results disclosed herein demonstrate that by in vivo administration of agents that disrupt the "hypoxia -> adenosine accumulation -> immunosuppressive adenosine receptor signaling to immune cells" pathway in subjects suffering from various diseases (e.g. cancer and sepsis) can result in in vivo treatment of tumors or improved immunization.

In one example, the method includes administering one or more inhibitors of extracellular adenosine and or adenosine receptor inhibitors, such as an adenosine receptor antagonist. To increase the efficacy of a vaccine, one or more adenosine receptor inhibitors and/or inhibitors of extracellular adenosine can be administered in conjunction with the vaccine. In one example, one or more adenosine receptor inhibitors or inhibitors of extracellular adenosine are administered to increase an immune response/inflammation. In another example, a method is provided to achieve targeted tissue damage, such as for tumor destruction.

The invention therefore furthermore relates to the use of compounds according to the invention for the preparation of a medicament for the treatment and/or prophylaxis of diseases which are caused, promoted and/or propagated by adenosine or other A_{2A} and/or A_{2B} receptor agonists.

The invention thus also relates, in particular, to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states.

Particular preference is given, in particular, to physiological and/or pathophysiological states which are connected to adenosine A_{2A} and/or A_{2B} receptors.

Physiological and/or pathophysiological states are taken to mean physiological and/or pathophysiological states which are medically relevant, such as, for example, diseases or illnesses and medical disorders, complaints, symptoms or complications and the like, in particular diseases.

The invention furthermore relates to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states selected from the group consisting of hyperproliferative and infectious diseases and disorders.

The invention further relates to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states selected from the group consisting of hyperproliferative and infectious diseases and disorders, wherein the hyperproliferative disease or disorder is cancer.

The invention thus particularly preferably relates to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, wherein the cancer is selected from the group consisting of acute and chronic lymphocytic leukemia, acute granulocytic leukemia, adrenal cortex cancer, bladder cancer, brain cancer, breast cancer, cervical cancer, cervical hyperplasia, cervical cancer, chorio cancer, chronic granulocytic leukemia, chronic lymphocytic leukemia, colon cancer, endometrial ccancer, esophageal cancer, essential thrombocytosis, genitourinary carcinoma, glioma, glioblastoma, hairy cell leukemia, head and neck carcinoma, Hodgkin's disease, Kaposi's sarcoma, lung carcinoma, lymphoma, malignant carcinoid carcinoma, malignant hypercalcemia, malignant melanoma, malignant pancreatic insulinoma, medullary thyroid carcinoma, melanoma, multiple myeloma, mycosis fungoides, myeloid and lymphocytic leukemia, neuroblastoma, non-Hodgkin's lymphoma, non-small cell lung cancer, osteogenic sarcoma, ovarian carcinoma, pancreatic carcinoma, polycythemia vera, primary brain carcinoma, primary macroglobulinemia, prostatic cancer, renal cell cancer, rhabdomyosarcoma, skin cancer, small-cell lung cancer, soft-tissue sarcoma, squamous cell cancer, stomach cancer, testicular cancer, thyroid cancer and Wilms' tumor.

The invention further preferably relates to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states selected from the group consisting of hyperproliferative and infectious diseases and disorders, wherein the hyperproliferative disease or disorder is selected from the group consisting of age-related macular degeneration, Crohn's disease, cirrhosis, chronic inflammatory-related disorders, proliferative diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, granulomatosis, immune hyperproliferation associated with organ or tissue transplantation and an immunoproliferative disease or disorder selected from the group comnsisting of inflammatory bowel disease, psoriasis, rheumatoid arthritis, systemic lupus erythematosus (SLE), vascular hyperproliferation secondary to retinal hypoxia and vasculitis.

The invention further preferably relates to a medicament comprising at least one compound according to the invention and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states selected from the group consisting of hyperproliferative and infectious diseases and disorders, wherein the infectious disease or disorder is selected from the group consisting of

a) virally induced infectious diseases which are caused by retroviruses, hepadnaviruses, herpesviruses, flaviviridae and/or adenoviruses wherein the retroviruses are selected from lentiviruses or oncoretroviruses, wherein the lentivirus is selected from the group consisting of HIV-1, HIV-2, FIV, BIV, SIVs, SHIV, CAEV, VMV and EIAV and the oncoretrovirus is selected from the group consisting of HTLV-I, HTLV-II and BLV, the hepadnavirus is selected from the group consisting of HBV, GSHV and WHV, the herpesivirus is selected from the group from the group consisting of HSV I, HSV II, EBV, VZV, HCMV or HHV 8 and the flaviviridae is selected from the group consisting of HCV, West nile and Yellow Fever,
b) bacterial infectious diseases which are caused by Gram-positive bacteria wherein the Gram-positive bacteria are selected from the group consisting of methicillin-susceptible and methicillin-resistant staphylococci (including Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus saprophyticus, and coagulase-negative staphylococci), glycopeptides-intermediate susceptible Staphylococcus aureus (GISA), penicillin-susceptible and penicillin-resistant streptococci (including Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus avium, Streptococcus bovis, Streptococcus lactis, Streptococcus sanguis and Streptococci Group C (GCS),

Streptococci Group G (GGS) and viridans streptococci), enterococci (including vancomycinsusceptible and vancomycin-resistant strains such as Enterococcus faecalis and Enterococcus faecium), Clostridium difficile, listeria monocytogenes, Corynebacterium jeikeium, Chlamydia spp (including C. pneumoniae) and Mycobacterium tuberculosis,

c) bacterial infectious diseases which are caused by Gram-negative bacteria wherein the Gram-negative bacteria are selected from the group consisting of the Genus Enterobacteriacae, including Escherichia spp. (including Escherichia coli), Klebsiella spp., Enterobacter spp., Citrobacter spp., Serratia spp., Proteus spp., Providencia spp., Salmonella spp., Shigella spp., the genus Pseudomonas (including P. aeruginosa), Moraxella spp. (including M. catarrhalis), Haemophilus spp. and Neisseria spp.,

d) infectious diseases induced by intracellular active parasites selected from the group consisting of phylum Apicomplexa, or Sarcomastigophora (including Trypanosoma, Plasmodia, Leishmania, Babesia or Theileria), Cryptosporidia, Sacrocystida, Amoebia, Coccidia and Trichomonadia.

It is intended that the medicaments disclosed above include a corresponding use of the compounds according to the invention for the preparation of a medicament for the treatment and/or prophylaxis of the above physiological and/or pathophysiological states.

It is additionally intended that the medicaments disclosed above include a corresponding method for the treatment and/or prophylaxis of the above physiological and/or pathophysiological states in which at least one compound according to the invention is administered to a patient in need of such a treatment.

The compounds according to the invention preferably exhibit an advantageous biological activity which can easily be demonstrated in enzyme assays and animal experiments, as described in the examples. In such enzyme-based assays, the compounds according to the invention preferably exhibit and cause an inhibiting effect, which is usually documented by IC_{50} values in a suitable range, preferably in the micromolar range and more preferably in the nanomolar range.

The compounds according to the invention can be administered to humans or animals, in particular mammals, such as apes, dogs, cats, rats or mice, and can be used in the therapeutic treatment of the human or animal body and in the combating of the above-mentioned diseases. They can furthermore be used as diagnostic agents or as reagents.

Furthermore, compounds according to the invention can be used for the isolation and investigation of the activity or expression of adenosine A_{2A} and/or A_{2B} receptors. In addition, they are particularly suitable for use in diagnostic methods for diseases in connection with disturbed adenosine A_{2A} and/or A_{2B} receptor activity. The invention therefore furthermore relates to the use of the compounds according to the invention for the isolation and investigation of the activity or expression of adenosine A_{2A} and/or A_{2B} receptors or as binders and inhibitors of adenosine A_{2A} and/or A_{2B} receptors.

For diagnostic purposes, the compounds according to the invention can, for example, be radioactively labelled. Examples of radioactive labels are ^{3}H, ^{14}C, ^{231}I and ^{125}I. A preferred labelling method is the iodogen method (Fraker et al., 1978). In addition, the compounds according to the invention can be labelled by enzymes, fluorophores and chemophores. Examples of enzymes are alkaline phosphatase, β-galactosidase and glucose oxidase, an example of a fluorophore is fluorescein, an example of a chemophore is luminol, and automated detection systems, for example for fluorescent colorations, are described, for example, in US 4,125,828 and US 4,207,554.

The present invention further relates to pharmaceutical compositions containing the compounds of the present invention and their use for the treatment and/or prophylaxis of diseases and disorders where the partial or total inactivation of adenosine A_{2A} and/or A_{2B} receptors could be beneficial.

The compounds of the formula I can be used for the preparation of pharmaceutical preparations, in particular by non-chemical methods. In this case, they are brought into a suitable dosage form together with at least one solid, liquid and/or semi-liquid excipient or adjuvant and optionally in combination with one or more further active compound(s).

The invention therefore furthermore relates to pharmaceutical preparations comprising at least one compound of the formula I and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios. In particular, the invention also relates to pharmaceutical preparations which comprise further excipients and/or adjuvants, and also to pharmaceutical preparations which comprise at least one further medicament active compound.

In particular, the invention also relates to a process for the preparation of a pharmaceutical preparation, characterised in that a compound of the formula I and/or one of its physiologically acceptable salts, derivatives, solvates and stereoisomers, including mixtures thereof in all ratios, is brought into a suitable dosage form together with a solid, liquid or semi-liquid excipient or adjuvant and optionally with a further medicament active compound.

The pharmaceutical preparations according to the invention can be used as medicaments in human or veterinary medicine. The patient or host can belong to any mammal species, for example a primate species, particularly humans; rodents, including mice, rats and hamsters; rabbits; horses, cattle, dogs, cats, etc. Animal models are of interest for experimental investigations, where they provide a model for the treatment of a human disease.

Suitable carrier substances are organic or inorganic substances which are suitable for enteral (for example oral), parenteral or topical administration and do not react with the novel compounds, for example water, vegetable oils (such as sunflower oil or cod-liver oil), benzyl alcohols, polyethylene glycols, gelatine, carbohydrates, such as lactose or starch, magnesium stearate, talc, lanolin or Vaseline. Owing to his expert knowledge, the person skilled in the art is familiar with which adjuvants are suitable for the desired medicament formulation. Besides solvents, for example water, physiological saline solution or alcohols, such as, for example, ethanol, propanol or glycerol, sugar solutions, such as glucose or mannitol solutions, or a mixture of the said solvents, gel formers, tablet assistants and other active-ingredient carriers, it is also possible to use, for example, lubricants, stabilisers and/or wetting agents, emulsifiers, salts for influencing the osmotic pressure, anti-oxidants, dispersants, antifoams, buffer substances, flavours and/or aromas or flavour correctants, preservatives, solubilisers or dyes. If desired, preparations or medicaments according to the invention may comprise one or more further active compounds, for example one or more vitamins.

If desired, preparations or medicaments according to the invention may comprise one or more further active compounds and/or one or more action enhancers (adjuvants).

The terms “pharmaceutical formulation” and “pharmaceutical preparation” are used as synonyms for the purposes of the present invention.

As used here, “pharmaceutically tolerated” relates to medicaments, precipitation reagents, excipients, adjuvants, stabilisers, solvents and other agents which facilitate the administration of the pharmaceutical preparations obtained therefrom to a mammal without undesired physiological side effects, such as, for example, nausea, dizziness, digestion problems or the like.

In pharmaceutical preparations for parenteral administration, there is a requirement for isotonicity, euhydration and tolerability and safety of the formulation (low toxicity), of the adjuvants employed and of the primary packaging. Surprisingly, the compounds according to the invention preferably have the advantage that direct use is possible and further purification steps for the removal of toxicologically unacceptable agents, such as, for example, high concentrations of organic solvents or other toxicologically unacceptable adjuvants, are thus unnecessary before use of the compounds according to the invention in pharmaceutical formulations.

The invention particularly preferably also relates to pharmaceutical preparations comprising at least one compound according to the invention in precipitated non-crystalline, precipitated crystalline or in dissolved or suspended form, and optionally excipients and/or adjuvants and/or further pharmaceutical active compounds.

The compounds according to the invention preferably enable the preparation of highly concentrated formulations without unfavourable, undesired aggregation of the compounds according to the invention occurring. Thus, ready-to-use solutions having a high active-ingredient content can be prepared with the aid of compounds according to the invention with aqueous solvents or in aqueous media.

The compounds and/or physiologically acceptable salts and solvates thereof can also be lyophilised and the resultant lyophilisates used, for example, for the preparation of injection preparations.

Aqueous preparations can be prepared by dissolving or suspending compounds according to the invention in an aqueous solution and optionally adding adjuvants. To this end, defined volumes of stock solutions comprising the said further adjuvants in defined concentration are advantageously added to a solution or suspension having a defined concentration of compounds according to the invention, and the mixture is optionally diluted with water to the pre-calculated concentration. Alternatively, the adjuvants can be added in solid form. The amounts of stock solutions and/or water which are necessary in each case can subsequently be added to the aqueous solution or suspension obtained. Compounds according to the invention can also advantageously be dissolved or suspended directly in a solution comprising all further adjuvants.

The solutions or suspensions comprising compounds according to the invention and having a pH of 4 to 10, preferably having a pH of 5 to 9, and an osmolality of 250 to 350 mOsmol/kg can advantageously be prepared. The pharmaceutical preparation can thus be administered directly substantially without pain intravenously, intra-arterially, intra-articularly, subcutaneously or percutaneously. In addition, the preparation may also be added to infusion solutions, such as, for example, glucose solution, isotonic saline solution or Ringer‘s solution, which may also contain further active compounds, thus also enabling relatively large amounts of active compound to be administered.

Pharmaceutical preparations according to the invention may also comprise mixtures of a plurality of compounds according to the invention.

The preparations according to the invention are physiologically well tolerated, easy to prepare, can be dispensed precisely and are preferably stable with respect to assay, decomposition products and aggregates throughout storage and transport and during multiple freezing and thawing processes. They can preferably be stored in a stable manner over a period of at least three months to two years at refrigerator temperature (2-8°C) and at room temperature (23-27°C) and 60% relative atmospheric humidity (R.H.).

For example, the compounds according to the invention can be stored in a stable manner by drying and when necessary converted into a ready-to-use pharmaceutical preparation by dissolution or suspension. Possible drying methods are, for example, without being restricted to these examples, nitrogen-gas drying, vacuum-oven drying, lyophilisation, washing with organic solvents and subsequent air drying, liquid-bed drying, fluidised-bed drying, spray drying, roller drying, layer drying, air drying at room temperature and further methods.

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

In addition, the term “therapeutically effective amount” denotes an amount which, compared with a corresponding subject who has not received this amount, has the following consequence: improved treatment, healing, prevention or elimination of a disease, syndrome, disease state, complaint, disorder or prevention of side effects or also a reduction in the progress of a disease, complaint or disorder. The term “therapeutically effective amount” also encompasses the amounts which are effective for increasing normal physiological function.

On use of preparations or medicaments according to the invention, the compounds according to the invention and/or physiologically acceptable salts and solvates thereof are generally used analogously to known, commercially available preparations or preparations, preferably in dosages of between 0.1 and 500 mg, in particular 5 and 300 mg, per use unit. The daily dose is preferably between 0.001 and 250 mg/kg, in particular 0.01 and 100 mg/kg, of body weight. The preparation can be administered one or more times per day, for example two, three or four times per day. However, the individual dose for a patient depends on a large number of individual factors, such as, for example, on the efficacy of the particular compound used, on the age, body weight, general state of health, sex, nutrition, on the time and method of administration, on the excretion rate, on the combination with other medicaments and on the severity and duration of the particular disease.

A measure of the uptake of a medicament active compound in an organism is its bioavailability. If the medicament active compound is delivered to the organism intravenously in the form of an injection solution, its absolute bioavailability, i.e. the proportion of the pharmaceutical which reaches the systemic blood, i.e. the major circulation, in unchanged form, is 100%. In the case of oral administration of a therapeutic active compound, the active compound is generally in the form of a solid in the formulation and must therefore first be dissolved in order that it is able to overcome the entry barriers, for example the gastrointestinal tract, the oral mucous membrane, nasal membranes or the skin, in particular the stratum corneum, or can be absorbed by the body. Data on the pharmacokinetics, i.e. on the bioavailability, can be obtained analogously to the method of J. Shaffer et al., J. Pharm. Sciences, 88 (1999), 313-318.

Furthermore, medicaments of this type can be prepared by means of one of the processes generally known in the pharmaceutical art.

Medicaments can be adapted for administration via any desired suitable route, for example by the oral (including buccal or sublingual), rectal, pulmonary, nasal, topical (including buccal, sublingual or transdermal), vaginal or parenteral (including subcutaneous, intramuscular, intravenous, intradermal and in particular intra-articular) routes. Medicaments of this type can be prepared by means of all processes known in the pharmaceutical art by, for example, combining the active compound with the excipient(s) or adjuvant(s).

Parenteral administration is preferably suitable for administration of the medicaments according to the invention. In the case of parenteral administration, intra-articular administration is particularly preferred.

The invention thus preferably also relates to the use of a pharmaceutical preparation according to the invention for intra-articular administration in the treatment and/or prophylaxis of physiological and/or pathophysiological states selected from the group consisting of osteoarthritis, traumatic cartilage injuries, arthritis, pain, allodynia or hyperalgesia.

Intra-articular administration has the advantage that the compound according to the invention can be administered directly into the synovial fluid in the vicinity of the joint cartilage and is also able to diffuse from there into the cartilage tissue. Pharmaceutical preparations according to the invention can thus also be injected directly into the joint gap and thus develop their action directly at the site of action as intended. The compounds according to the invention are also suitable for the preparation of medicaments to be administered parenterally having slow, sustained and/or controlled release of active compound. They are thus also suitable for the preparation of delayed-release formulations, which are advantageous for the patient since administration is only necessary at relatively large time intervals.

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

The compounds according to the invention can also be administered in the form of liposome delivery systems, such as, for example, small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from various phospholipids, such as, for example, cholesterol, stearylamine or phosphatidylcholines.

The compounds according to the invention can also be coupled to soluble polymers as targeted medicament excipients. Such polymers can encompass polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidophenol, polyhydroxyethylaspartamidophenol or polyethylene oxide polylysine, substituted by palmitoyl radicals. The compounds according to the invention can furthermore be coupled to a class of biodegradable polymers which are suitable for achieving slow release of a medicament, for example polylactic acid, poly-epsilon-caprolactone, polyhydroxybutyric acid, polyorthoesters, polyacetals, polydihydroxypyrans, poly-cyanoacrylates, polylactic-co-glycolic acid, polymers, such as conjugates between dextran and methacrylates, polyphosphoesters, various polysaccharides and poly-amines and poly-ε-caprolactone, albumin, chitosan, collagen or modified gelatine and crosslinked or amphipathic block copolymers of hydrogels.

Suitable for enteral administration (oral or rectal) are, in particular, tablets, dragees, capsules, syrups, juices, drops or suppositories, and suitable for topical use are ointments, creams, pastes, lotions, gels, sprays, foams, aerosols, solutions (for example solutions in alcohols, such as ethanol or isopropanol, acetonitrile, DMF, dimethylacetamide, 1,2-propanediol or mixtures thereof with one another and/or with water) or powders. Also particularly suitable for topical uses are liposomal preparations.

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

Medicaments adapted to transdermal administration can be delivered as independent plasters for extended, close contact with the epidermis of the recipient. Thus, for example, the active compound can be supplied from the plaster by means of iontophoresis, as described in general terms in Pharmaceutical Research, 3 (6), 318 (1986).

It goes without saying that, besides the constituents particularly mentioned above, the medicaments according to the invention may also comprise other agents usual in the art with respect to the particular type of pharmaceutical formulation.

The invention also relates to a set (kit) consisting of separate packs of

a) an effective amount of a compound of the formula I and/or physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios, and
b) an effective amount of a further medicament active compound.

The set comprises suitable containers, such as boxes or cartons, individual bottles, bags or ampoules. The set may, for example, comprise separate ampoules each containing an effective amount of a compound of the formula I and/or pharmaceutically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios, and an effective amount of a further medicament active compound in dissolved or lyophilised form.

Furthermore, the medicaments according to the invention can be used in order to provide additive or synergistic effects in certain known therapies and/or can be used in order to restore the efficacy of certain existing therapies.

Besides the compounds according to the invention, the pharmaceutical preparations according to the invention may also comprise further medicament active compounds, for example for use in the treatment of cancer, other anti-tumor medicaments. For the treatment of the other diseases mentioned, the pharmaceutical preparations according to the invention may also, besides the compounds according to the invention, comprise further medicament active compounds which are known to the person skilled in the art in the treatment thereof.

In one principal embodiment, methods are provided for enhancing an immune response in a host in need thereof. The immune response can be enhanced by reducing T cell tolerance, including by increasing IFN-γ release, by decreasing regulatory T cell production or activation, or by increasing antigen-specific memory T cell production in a host. In one embodiment, the method comprises administering a compound of the present invention to a host in combination or alternation with an antibody. In particular subembodiments, the antibody is a therapeutic antibody. In one particular embodiment, a method of enhancing efficacy of passive antibody therapy is provided comprising administering a compound of the present invention in combination or alternation with one or more passive antibodies. This method can enhance the efficacy of antibody therapy for treatment of abnormal cell proliferative disorders such as cancer, or can enhance the efficacy of therapy in the treatment or prevention of infectious diseases. The compound of the present invention can be administered in combination or alternation with antibodies such as rituximab, herceptin or erbitux, for example.

In another principal embodiment, a method of treating or preventing abnormal cell proliferation is provided comprising administering a compound of the present invention to a host in need thereof substantially in the absence of another anti-cancer agent.

In another principal embodiment, a method of treating or preventing abnormal cell proliferation in a host in need thereof is provided, comprising administering a first a compound of the present invention substantially in combination with a first anti-cancer agent to the host and subsequently administering a second A_{2A} and/or A_{2B} receptor antagonist. In one subembodiment, the second antagonist is administered substantially in the absence of another anti-cancer agent. In another principal embodiment, a method of treating or preventing abnormal cell proliferation in a host in need thereof is provided, comprising administering a compound of the present invention substantially in combination with a first anti-cancer agent to the host and subsequently administering a second anti-cancer agent in the absence of the antagonist.

Thus, the cancer treatment disclosed here can be carried out as therapy with a compound of the present invention or in combination with an operation, irradiation or chemotherapy. Chemotherapy of this type can include the use of one or more active compounds of the following categories of antitumour active compounds:

(i) antiproliferative/antineoplastic/DNA-damaging active compounds and combinations thereof, as used in medical oncology, such as alkylating active compounds (for example cis-platin, parboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulphan and nitrosoureas); antimetabolites (for example antifolates such as fluoropyrimidines such as 5-fluorouracil and tegafur, raltitrexed, methotrexate, cytosine arabinoside, hydroxyurea and gemcitabine); antitumour antibiotics (for example anthracyclines, such as adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin and mithramycin) ; antimitotic active compounds (for example vinca alkaloids, such as vincristine, vinblastine, vindesine and vinorelbine, and taxoids, such as taxol and taxotere) ; topoisomerase inhibitors (for example epipodophyllotoxins, such as etoposide and teniposide, amsacrine, topotecan, irinotecan and camptothecin) and cell-differentiating active compounds (for example all-trans-retinoic acid, 13-cis-retinoic acid and fenretinide);

(ii) cytostatic active compounds, such as anti-oestrogens (for example tamoxifen, toremifene, raloxifene, droloxifene and iodoxyfene), oestrogen receptor regulators (for example fulvestrant), anti-androgens (for example bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (for example goserelin, leuprorelin and buserelin), progesterones (for example megestrol acetate), aromatase inhibitors (for example anastrozole, letrozole, vorazole and exemestane) and inhibitors of 5α-reductase, such as finasteride;

(iii) active compounds which inhibit cancer invasion including for example metallo-proteinase inhibitors, like marimastat, and inhibitors of urokinase plasminogen activator receptor function;

(iv) inhibitors of growth factor function, for example growth factor antibodies, growth factor receptor antibodies, for example the anti-erbb2 antibody trastuzumab [Herceptin™] and the anti-erbbl antibody cetuximab [C225]), farnesyl transferase inhibitors, tyrosine kinase inhibitors and serine/threonine kinase inhibitors, for example inhibitors of the epidermal growth factor family (for example EGFR family tyrosine kinase inhibitors, such as N-(3-chloro-4-fluorophenyl)-7-methoxy-6- (3-morpholinopropoxy) quinazolin-4-amine (gefitinib, AZD1839), N-(3-ethynylphenyl)-6,7-bis (2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774) and 6-acrylamido-N-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (CI 1033), for example inhibitors of the platelet-derived growth factor family and, for example, inhibitors of the hepatocyte growth factor family;

(v) anti-angiogenic active compounds, such as bevacizumab, angiostatin, endostatin, linomide, batimastat, captopril, cartilage derived inhibitor, genistein, interleukin 12, lavendustin, medroxypregesterone acetate, recombinant human platelet factor 4, tecogalan, thrombospondin, TNP-470, anti-VEGF monoclonal antibody, soluble VEGF-receptor chimaeric protein, anti-VEGF receptor antibodies, anti-PDGF receptors, inhibitors of integrins, tyrosine kinase inhibitors, serine/threonine kinase inhibitors, antisense oligonucleotides, antisense oligodexoynucleotides, siRNAs, anti-VEGF aptamers, pigment epithelium derived

factor and compounds which have been published in the international patent applications WO 97/22596, WO 97/30035, WO 97/32856 and WO 98/13354);
(vi) vessel-destroying agents, such as combretastatin A4 and compounds which have been published in the international patent applications WO 99/02166, WO 00/40529, WO 00/41669, WO 01/92224, WO 02/04434 and WO 02/08213;
(vii) antisense therapies, for example those directed to the targets mentioned above, such as ISIS 2503, an anti-Ras antisense;
(viii) gene therapy approaches, including, for example, approaches for replacement of abnormal, modified genes, such as abnormal p53 or abnormal BRCA1 or BRCA2, GDEPT approaches (gene-directed enzyme pro-drug therapy), such as those which use cytosine deaminase, thymidine kinase or a bacterial nitroreductase enzyme, and approaches which increase the tolerance of a patient to chemotherapy or radiotherapy, such as multi-drug resistance therapy; and
(ix) immunotherapy approaches, including, for example, ex-vivo and in-vivo approaches for increasing the immunogenicity of tumour cells of a patient, such as transfection with cytokines, such as interleukin 2, interleukin 4 or granulocyte macrophage colony stimulating factor, approaches for decreasing T-cell anergy, approaches using transfected immune cells, such as cytokine-transfected dendritic cells, approaches for use of cytokine-transfected tumour cells and approaches for use of anti-idiotypic antibodies
(x) chemotherapeutic agents including foor example abarelix, aldesleukin, alemtuzumab, alitretinoin, allopurinol, altretamine, amifostine, anastrozole, arsenic trioxide, asparaginase, BCG live, bevaceizumab, bexarotene, bleomycin, bortezomib, busulfan, calusterone, camptothecin, capecitabine, carboplatin, carmustine, celecoxib, cetuximab, chlorambucil, cinacalcet, cisplatin, cladribine, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, darbepoetin alfa, daunorubicin, denileukin diftitox, dexrazoxane, docetaxel, doxorubicin, dromostanolone, epirubicin, epoetin alfa, estramustine, etoposide, exemestane, filgrastim, floxuridine, fludarabine, fluorouracil, fulvestrant and gemcitabine.

The medicaments from table 1 can preferably, but not exclusively, be combined with the compounds of the formula I.

Table 1		
Alkylating active compounds	Cyclophosphamide Busulfan Ifosfamide Melphalan Hexamethylmelamine Thiotepa chloroambucil Dacarbazine Carmustine	Lomustine Procarbazine Altretamine Estramustine phosphate Mechloroethamine Streptozocin Temozolomide Semustine
Platinum active compounds	Cisplatin Oxaliplatin Spiroplatin Carboxyphthalatoplatinum Tetraplatin Ormiplatin Iproplatin	Carboplatin ZD-0473 (AnorMED) Lobaplatin (Aetema) Satraplatin (Johnson Matthey) BBR-3464 (Hoffrnann-La Roche) SM-11355 (Sumitomo) AP-5280 (Access)
Antimetabolites	Azacytidine Gemcitabine Capecitabine 5-Fluorouracil Floxuridine 2-Chlorodesoxyadenosine 6-Mercaptopurine 6-Thioguanine Cytarabine 2-Fluorodesoxycytidine Methotrexate Idatrexate	Tomudex Trimetrexate Deoxycoformycin Fludarabine Pentostatin Raltitrexed Hydroxyurea Decitabine (SuperGen) Clofarabine (Bioenvision) Irofulven (MGI Pharrna) DMDC (Hoffmann-La Roche) Ethynylcytidine (Taiho)
Topoisomerase inhibitors	Amsacrine Epirubicin Etoposide Teniposide or mitoxantrone Irinotecan (CPT-11) 7-ethyl-10-hydroxycamptothecin Topotecan Dexrazoxanet (TopoTarget) Pixantrone (Novuspharrna) Rebeccamycin analogue (Exelixis) BBR-3576 (Novuspharrna)	Rubitecan (SuperGen) Exatecan mesylate (Daiichi) Quinamed (ChemGenex) Gimatecan (Sigma- Tau) Diflomotecan (Beaufour-Ipsen) TAS-103 (Taiho) Elsamitrucin (Spectrum) J-107088 (Merck & Co) BNP-1350 (BioNumerik) CKD-602 (Chong Kun Dang) KW-2170 (Kyowa Hakko)
Antitumour antibiotics	Dactinomycin (Actinomycin D) Doxorubicin (Adriamycin) Deoxyrubicin	Amonafide Azonafide Anthrapyrazole Oxantrazole

	Valrubicin Daunorubicin (Daunomycin) Epirubicin Therarubicin Idarubicin Rubidazon Plicamycinp Porfiromycin Cyanomorpholinodoxorubicin Mitoxantron (Novantron)	Losoxantrone Bleomycin sulfate (Blenoxan) Bleomycinic acid Bleomycin A Bleomycin B Mitomycin C MEN-10755 (Menarini) GPX-100 (Gem Pharmaceuticals)
Antimitotic active compounds	Paclitaxel Docetaxel Colchicine Vinblastine Vincristine Vinorelbine Vindesine Dolastatin 10 (NCI) Rhizoxin (Fujisawa) Mivobulin (Warner-Lambert) Cemadotin (BASF) RPR 109881A (Aventis) TXD 258 (Aventis) Epothilone B (Novartis) T 900607 (Tularik) T 138067 (Tularik) Cryptophycin 52 (Eli Lilly) Vinflunine (Fabre) Auristatin PE (Teikoku Hormone) BMS 247550 (BMS) BMS 184476 (BMS) BMS 188797 (BMS) Taxoprexin (Protarga)	SB 408075 (GlaxoSmithKline) E7010 (Abbott) PG-TXL (Cell Therapeutics) IDN 5109 (Bayer) A 105972 (Abbott) A 204197 (Abbott) LU 223651 (BASF) D 24851 (ASTA Medica) ER-86526 (Eisai) Combretastatin A4 (BMS) Isohomohalichondrin-B (PharmaMar) ZD 6126 (AstraZeneca) PEG-Paclitaxel (Enzon) AZ10992 (Asahi) !DN-5109 (Indena) AVLB (Prescient NeuroPharma) Azaepothilon B (BMS) BNP- 7787 (BioNumerik) CA-4-prodrug (OXiGENE) Dolastatin-10 (NrH) CA-4 (OXiGENE)
Aromatase inhibitors	Aminoglutethimide Letrozole Anastrazole Formestan	Exemestan Atamestan (BioMedicines) YM-511 (Yamanouchi)
Thymidylate Synthase inhibitors	Pemetrexed (Eli Lilly) ZD-9331 (BTG)	Nolatrexed (Eximias) CoFactor™ (BioKeys)
DNA antagonists	Trabectedin (PharmaMar) Glufosfamide (Baxter International) Albumin + 32P (isotope solutions) Thymectacin (NewBiotics) Edotreotid (Novartis)	Mafosfamide (Baxter International) Apaziquone (Spectrum Pharmaceuticals) O6-benzylguanine (Paligent)

Farnesyl transferase inhibitors	Arglabin (NuOncology Labs) Lonafarnib (Schering-Plough) BAY-43-9006 (Bayer)	Tipifarnib (Johnson & Johnson) Perillyl alcohol (DOR BioPharma)
Pump inhibitors	CBT-1 (CBA Pharma) Tariquidar (Xenova) MS-209 (Schering AG)	Zosuquidar trihydrochloride (Eli Lilly) Biricodar dicitrate (Vertex)
Histone acetyl trans-ferase inhibitors	Tacedinaline (Pfizer) SAHA (Aton Pharma) MS-275 (Schering AG)	Pivaloyloxymethyl butyrate (Titan) Depsipeptide (Fujisawa)
Metalloproteinase inhibitors Ribonucleoside reductase inhibitors	Neovastat (Aeterna Laboratories) Marimastat (British Biotech) Gallium maltolate (Titan) Triapin (Vion)	CMT -3 (CollaGenex) BMS-275291 (Celltech) Tezacitabine (Aventis) Didox (Molecules for Health)
TNF-alpha agonists / antagonists	Virulizin (Lorus Therapeutics) CDC-394 (Celgene)	Revimid (Celgene)
Endothelin-A re-ceptor antagonists	Atrasentan (Abbot) ZD-4054 (AstraZeneca)	YM-598 (Yamanouchi)
Retinoic acid receptor agonists	Fenretinide (Johnson & Johnson) LGD-1550 (ligand)	Alitretinoin (Ligand)
Immunomodulators	Interferon Oncophage (Antigenics) GMK (Progenics) Adenocarcinoma vaccine (Biomira) CTP-37 (AVI BioPharma) JRX-2 (Immuno-Rx) PEP-005 (Peplin Biotech) Synchrovax vaccines (CTL Immuno) Melanoma vaccines (CTL Immuno) p21-RAS vaccine (GemVax)	Dexosome therapy (Anosys) Pentrix (Australian Cancer Technology) JSF-154 (Tragen) Cancer vaccine (Intercell) Norelin (Biostar) BLP-25 (Biomira) MGV (Progenics) !3-Alethin (Dovetail) CLL-Thera (Vasogen)
Hormonal and antihormonal active compounds	Oestrogens Conjugated oestrogens Ethynyloestradiol Chlorotrianisene Idenestrol Hydroxyprogesterone	Prednisone Methylprednisolone Prednisolone Aminoglutethimide Leuprolide Goserelin

	caproate Medroxyprogesterone Testosterone Testosterone propionate Fluoxymesterone Methyltestosterone Diethylstilbestrol Megestrol Tamoxifen Toremofin Dexamethasone	Leuporelin Bicalutamide Flutamide Octreotide Nilutamide Mitotan P-04 (Novogen) 2-Methoxyoestradiol (En_-treMed) Arzoxifen (Eli Lilly)
Photodynamic active compounds	Talaporfin (Light Sciences) Theralux (Theratechnologies) Motexafin-Gadolinium (Pharmacyclics)	Pd bacteriopheophorbide (Yeda) Lutetium texaphyrin (Pharmacyclics) Hypericin
Tyrosine kinase inhibitors	Imatinib (Novartis) Leflunomide(Sugen/Pharmacia) ZDl839 (AstraZeneca) Erlotinib (Oncogene Science) Canertjnib (Pfizer) Squalamine (Genaera) SU5416 (Pharmacia) SU6668 (Pharmacia) ZD4190 (AstraZeneca) ZD6474 (AstraZeneca) Vatalanib (Novartis) PKI166 (Novartis) GW2016 (GlaxoSmithKline) EKB-509 (Wyeth) EKB-569 (Wyeth)	Kahalide F (PharmaMar) CEP- 701 (Cephalon) CEP-751 (Cephalon) MLN518 (Millenium) PKC412 (Novartis) Phenoxodiol O Trastuzumab (Genentech) C225 (ImClone) rhu-Mab (Genentech) MDX-H210 (Medarex) 2C4 (Genentech) MDX-447 (Medarex) ABX-EGF (Abgenix) IMC-1C11 (ImClone)
Various other active compounds	SR-27897 (CCK-A inhibitor, Sanofi-Synthelabo) Tocladesine (cyclic AMP agonist, Ribapharm) Alvocidib (CDK inhibitor, Aventis) CV-247 (COX-2 inhibitor, Ivy Medical) P54 (COX-2 inhibitor, Phytopharm) CapCell™ (CYP450 stimulant, Bavarian Nordic) GCS-IOO (gal3 antagonist, GlycoGenesys) G17DT immunogen (gastrin inhibitor, Aphton) Efaproxiral (oxygenator, Allos Therapeutics) PI-88 (heparanase inhibitor,	BCX-1777 (PNP inhibitor, BioCryst) Ranpirnase (ribonuclease stimulant, Alfacell) Galarubicin (RNA synthesis inhibitor, Dong-A) Tirapazamine (reducing agent, SRI International) N-Acetylcysteine (reducing agent, Zambon) R-Flurbiprofen (NF-kappaB inhibitor, Encore) 3CPA (NF-kappaB inhibitor, Active Biotech) Seocalcitol (vitamin D receptor agonist, Leo) 131-I-TM-601 (DNA antagonist, TransMolecular)

	Progen)	Eflornithin (ODC inhibitor, ILEX Oncology)
	Tesmilifen (histamine antagonist, YM BioSciences)	Minodronic acid (osteoclast inhibitor, Yamanouchi)
	Histamine (histamine H2 receptor agonist, Maxim)	
	Tiazofurin (IMPDH inhibitor, Ribapharm)	Indisulam (p53 stimulant, Eisai)
	Cilengitide (integrin antagonist, Merck KGaA)	Aplidin (PPT inhibitor, PharmaMar)
	SR-31747 (IL-1 antagonist, Sanofi-Synthelabo)	Rituximab (CD20 antibody, Genentech)
	CCI-779 (mTOR kinase inhibitor, Wyeth)	Gemtuzumab (CD33 antibody, Wyeth Ayerst)
	Exisulind (PDE-V inhibitor, Cell Pathways)	PG2 (haematopoiesis promoter, Pharmagenesis)
	CP-461 (PDE-V inhibitor, Cell Pathways)	Immunol™ (triclosan mouthwash, Endo)
	AG-2037 (GART inhibitor, Pfizer)	Triacetyluridine (uridine prodrug, Wellstat)
	WX-UK1 (plasminogen activator inhibitor, Wilex)	SN-4071 (sarcoma agent, Signature BioScience)
	PBI-1402 (PMN stimulant, ProMetic LifeSciences)	TransMID-107™ (immunotoxin, KS Biomedix)
	Bortezomib (proteasome inhibitor, Millennium)	PCK-3145 (apoptosis promoter, Procyon)
	SRL-172 (T-cell stimulant, SR Pharma)	Doranidazole (apoptosis promoter, Pola)
	TLK-286 (glutathione-S transferase inhibitor, Telik)	CHS-828 (cytotoxic agent, Leo)
	PT-100 (growth factor agonist, Point Therapeutics)	trans-Retinoic acid (differentiator, NIH)
	Midostaurin (PKC inhibitor, Novartis)	MX6 (apoptosis promoter, MAXIA)
	Bryostatin-1 (PKC stimulant, GPC Biotech)	Apomine (apoptosis promoter, ILEX Oncology)
	CDA-II (apoptosis promoter, Everlife)	Urocidin (apoptosis promoter, Bioniche)
	SDX-101 (apoptosis promoter, Salmedix)	Ro-31-7453 (apoptosis promoter, La Roche)
	Ceflatonin (apoptosis promoter, ChemGenex)	Brostallicin (apoptosis promoter, Pharmacia)

Even without further embodiments, it is assumed that a person skilled in the art will be able to use the above description in the broadest scope. The preferred embodiments should therefore merely be regarded as descriptive disclosure which is absolutely not limiting in any way.

The following examples are thus intended to explain the invention without limiting it. Unless indicated otherwise, per cent data denote per cent by weight. All temperatures are indicated in degrees Celsius. “Conventional work-up”: water is added if necessary, the pH is adjusted, if necessary, to values between 2 and 10, depending on the constitution of the end product, the mixture is extracted with ethyl acetate or dichloromethane, the phases are separated, the organic phase is dried over sodium sulfate, filtered and evaporated, and the product is purified by chromatography on silica gel and/or by crystallisation.
Rf values on silica gel; mass spectrometry: EI (electron impact ionisation): M^+, FAB (fast atom bombardment): $(M+H)^+$, THF (tetrahydrofuran), NMP (N-methlpyrrolidone), DMSO (dimethyl sulfoxide), EA (ethyl acetate), MeOH (methanol), TLC (thin-layer chromatography)

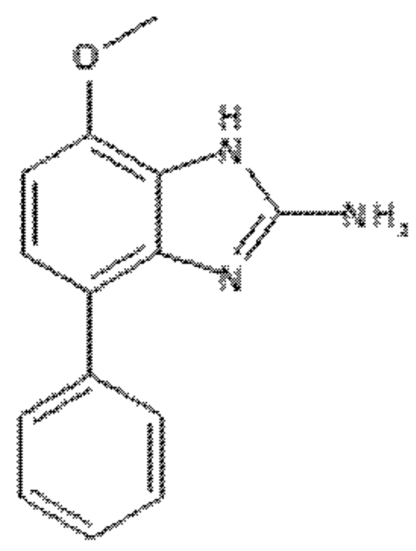
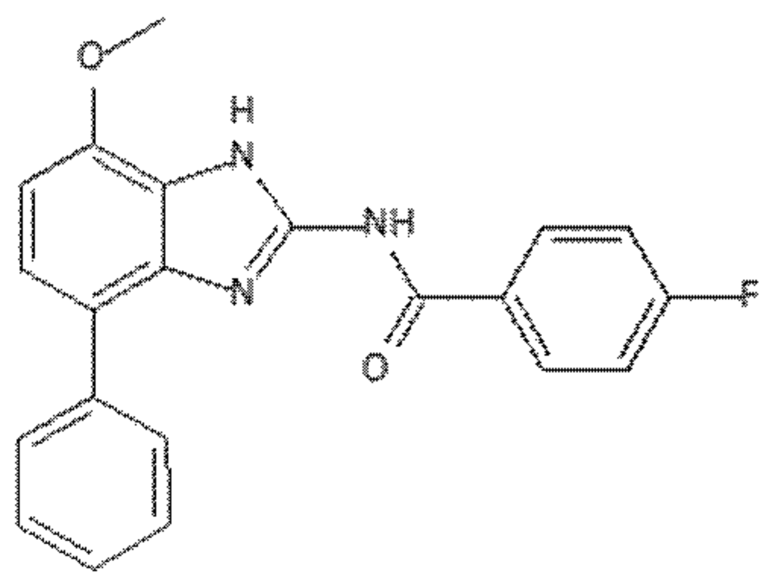
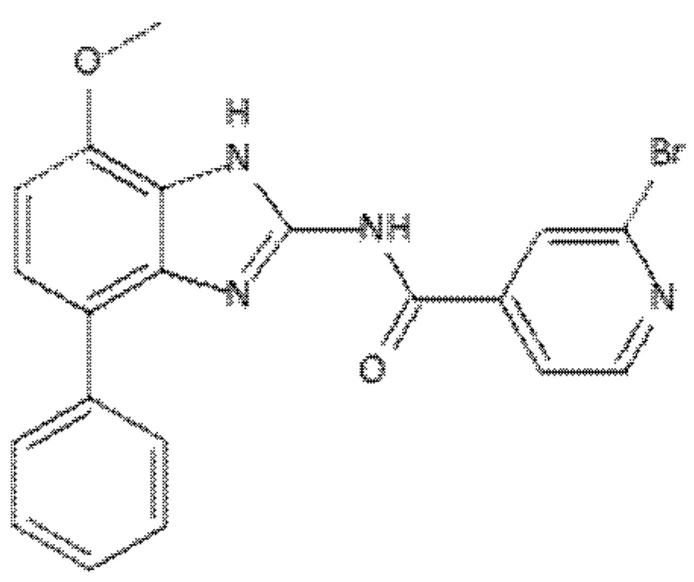
List of Abbreviations

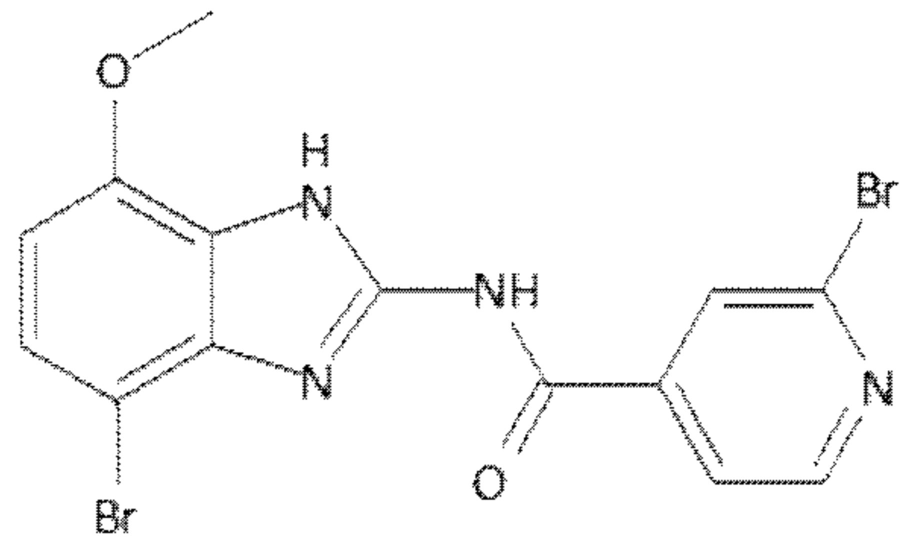
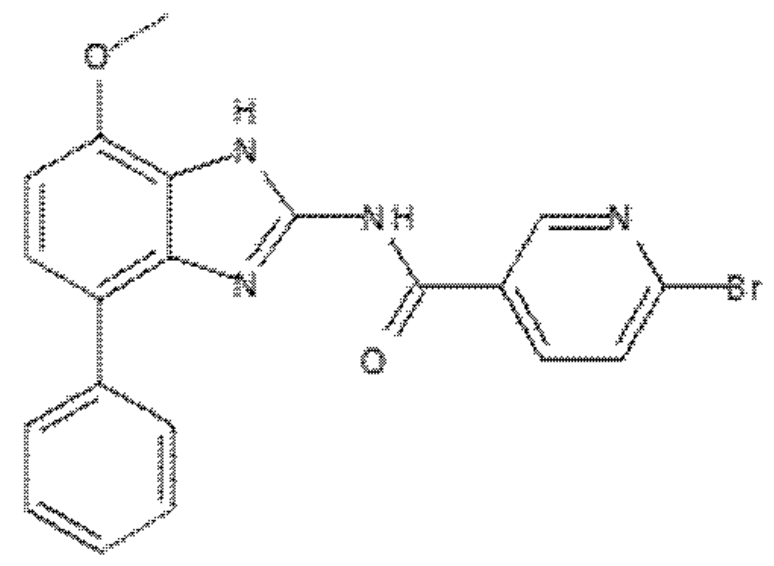
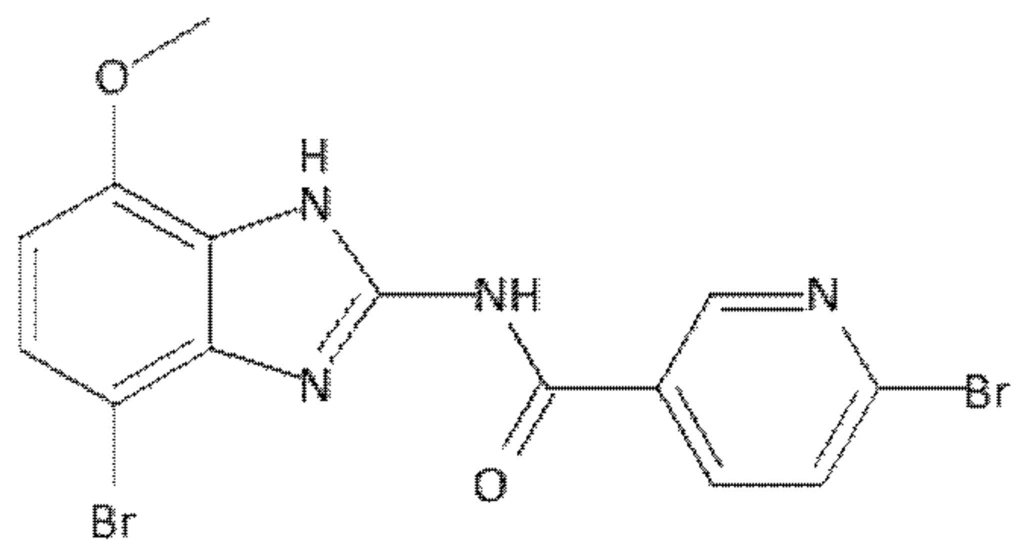
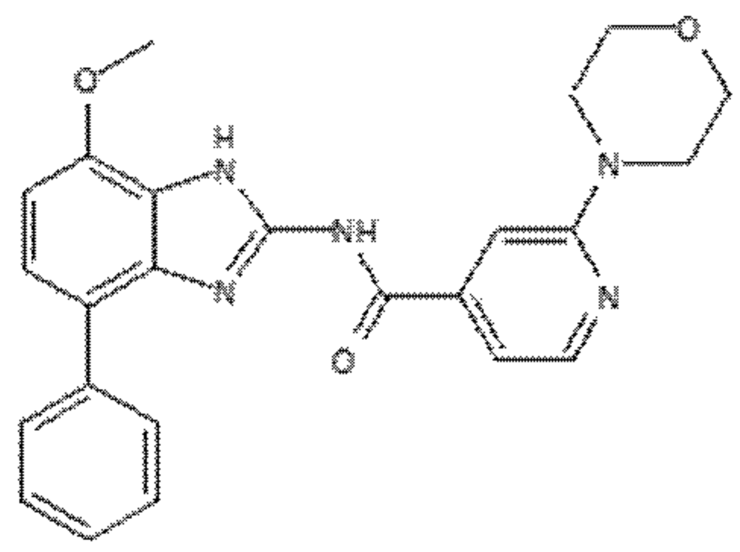
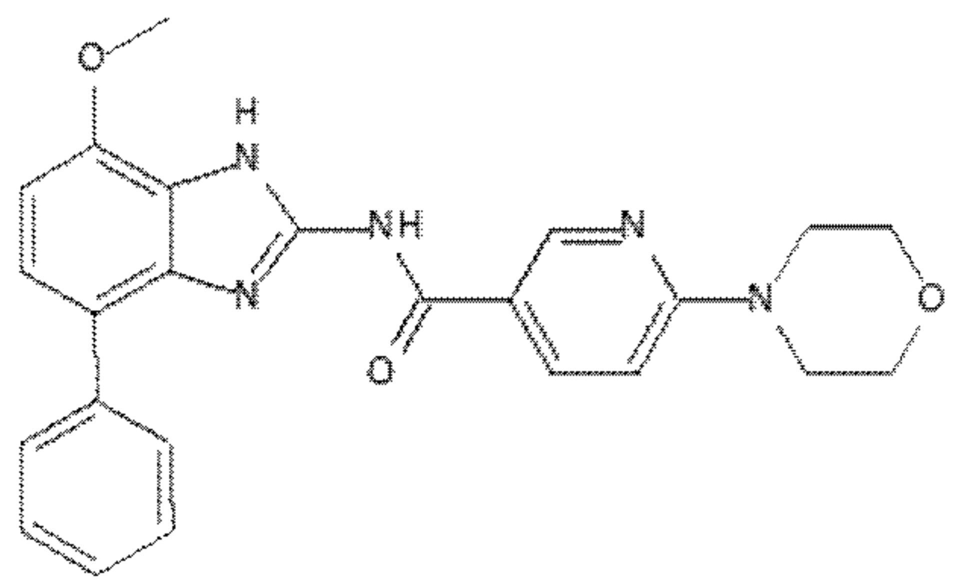
AUC	Area under the plasma drug concentration-time curve
C_{max}	Maximum plasma concentration
CL	Clearance
CV	Coefficient of variation
CYP	Cytochrome P450
DMSO	Dimethyl sulfoxide
F	Bioavailability
f_a	Fraction absorbed
iv	Intravenous
LC-MS/MS	Liquid chromatography tandem mass spectrometry
LLOQ	Lower limit of quantification
NC	Not calculated
ND	Not determined
PEG	Polyethylene glycol
Pgp	Permeability glycoprotein
PK	Pharmacokinetic(s)
po	Per os (oral)
$t_{1/2}$	Half-life
t_{max}	Time at which maximum plasma concentration of drug is reached
UPLC	Ultra performance liquid chromatography
V_{ss}	Volume of distribution (at steady state)
v/v	Volume to volume

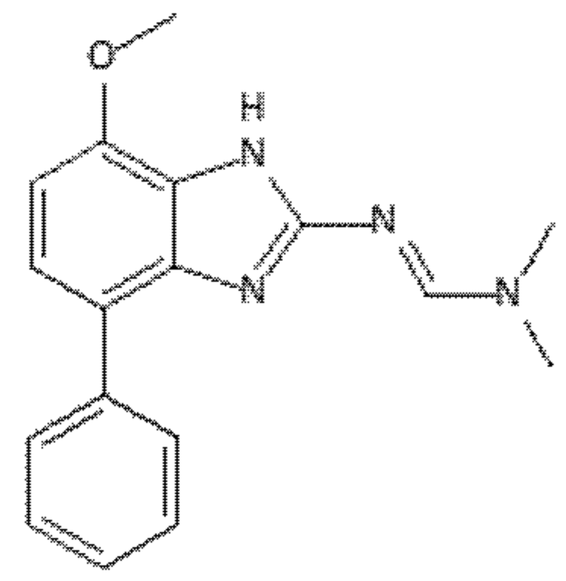
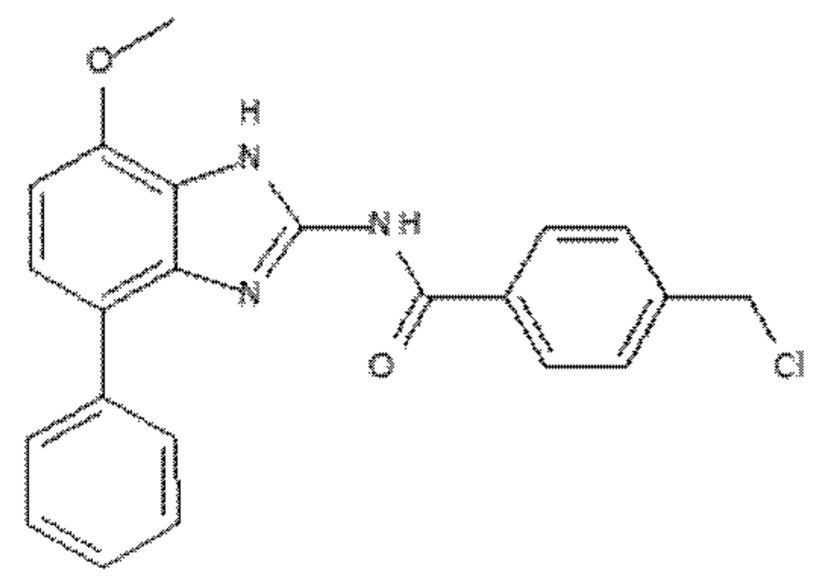
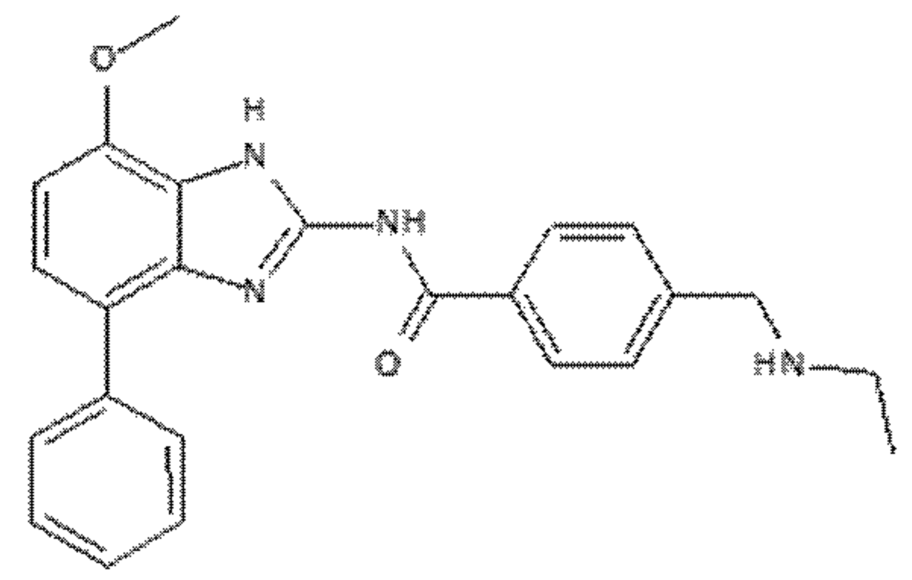
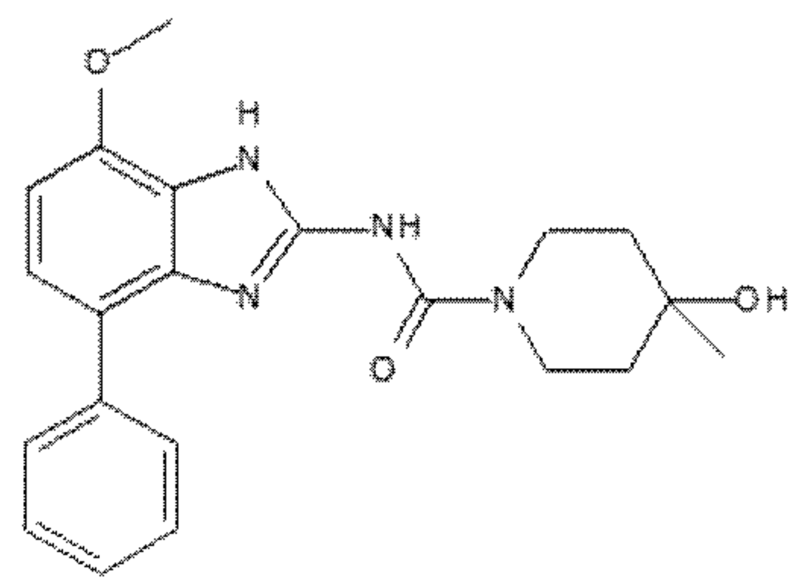
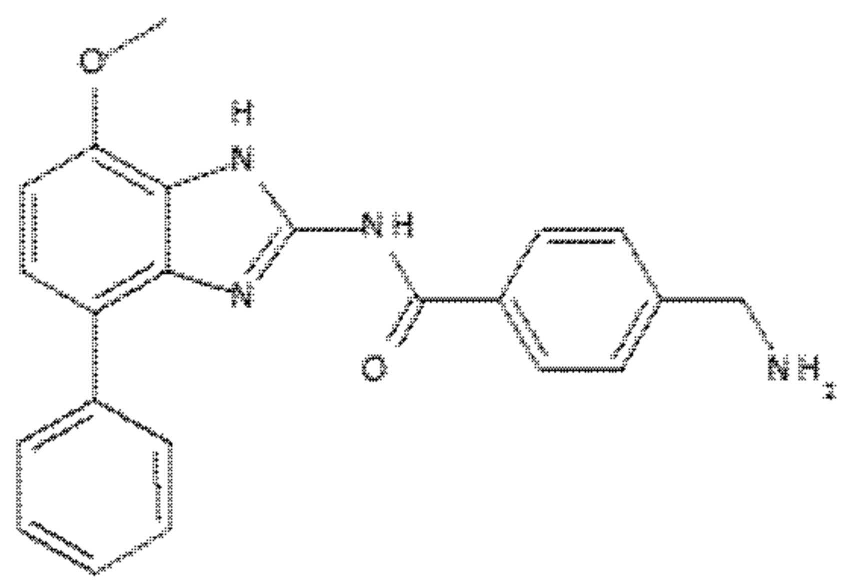
Example 1: Examples of compounds of the present invention

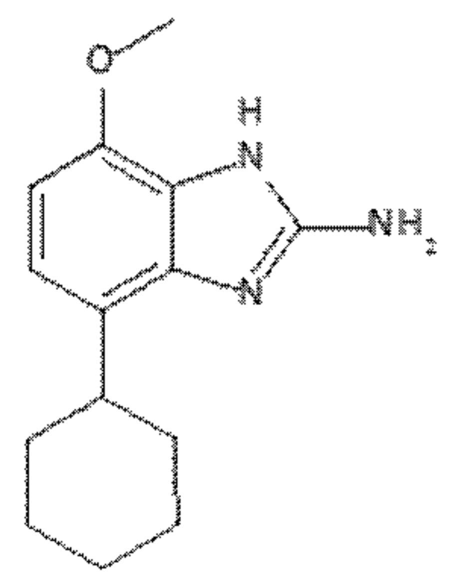
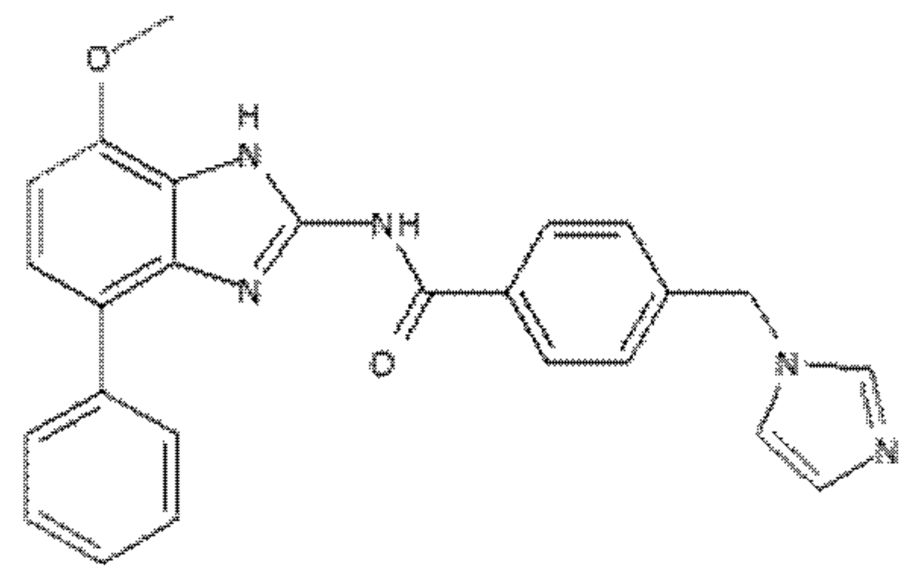
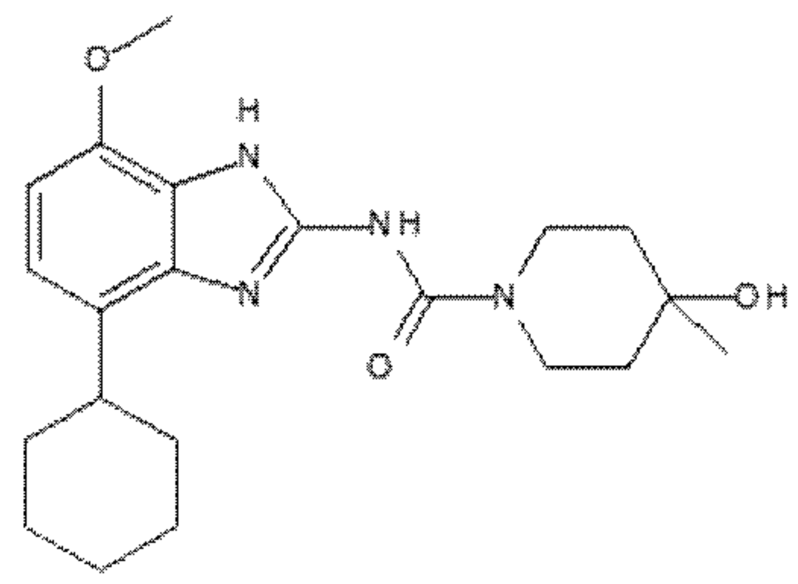
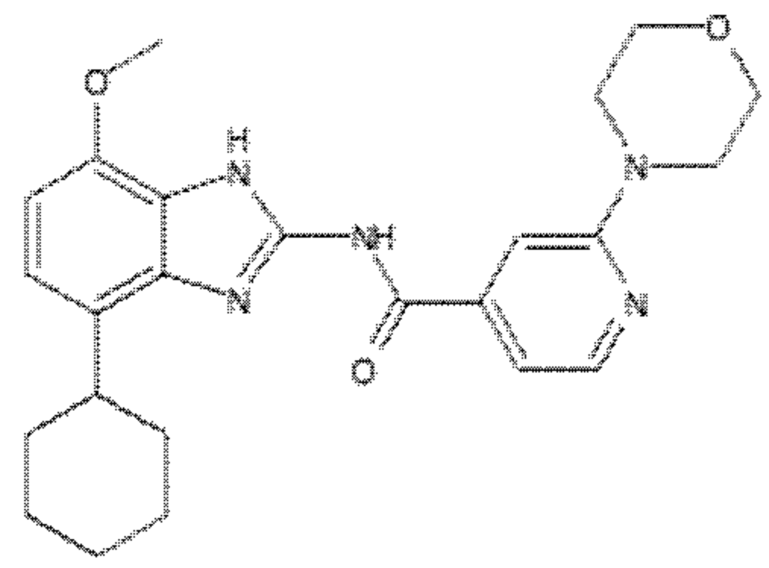
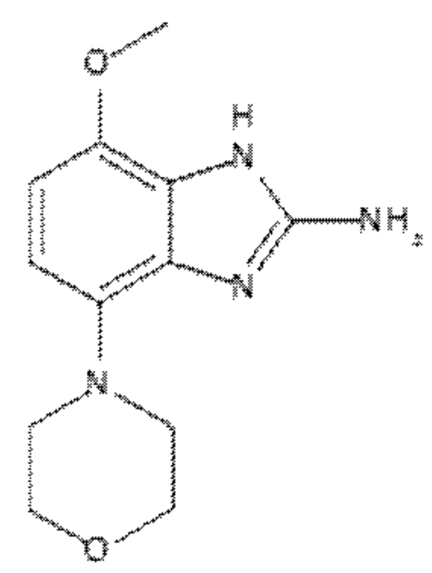
The invention especially relates to the compounds of table 2 and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

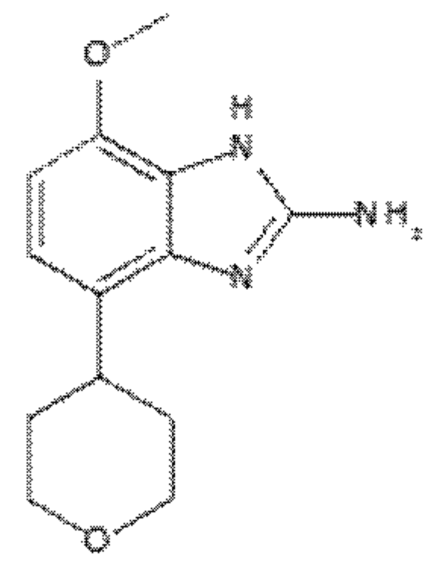
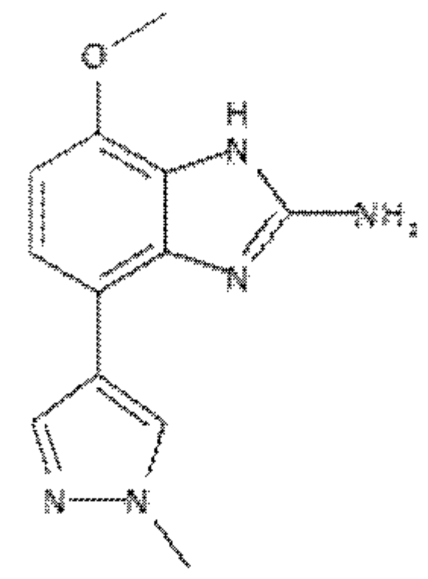
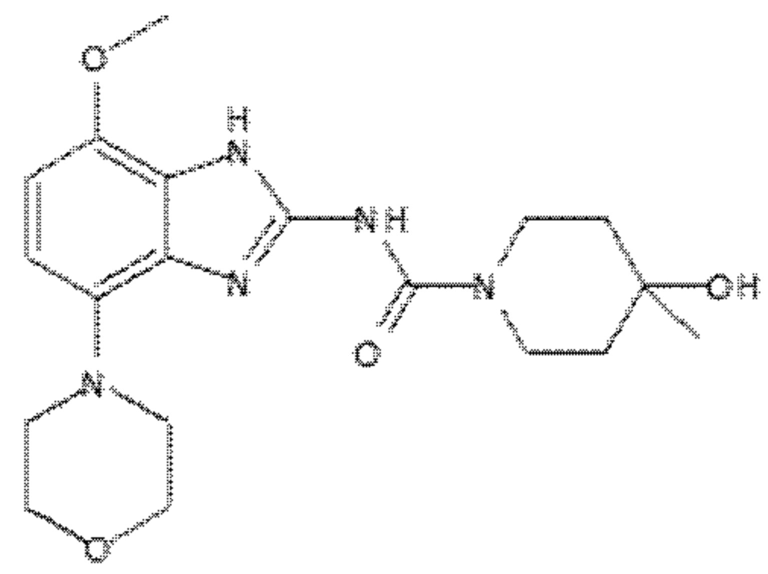
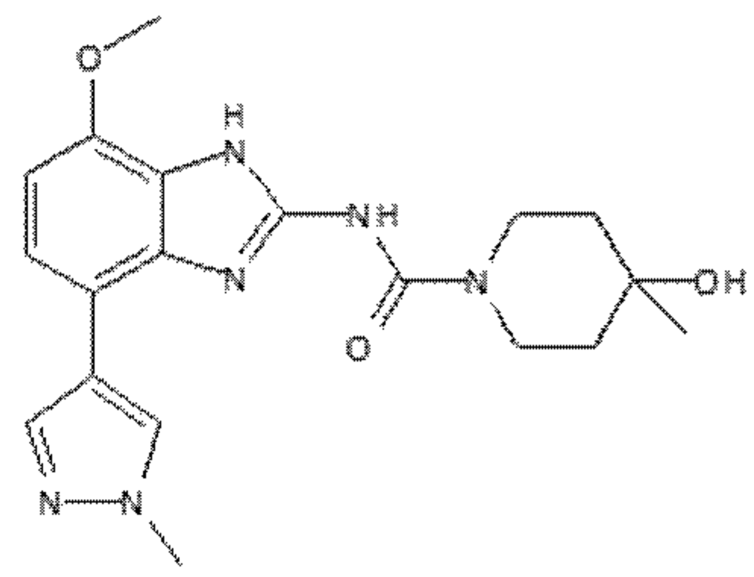
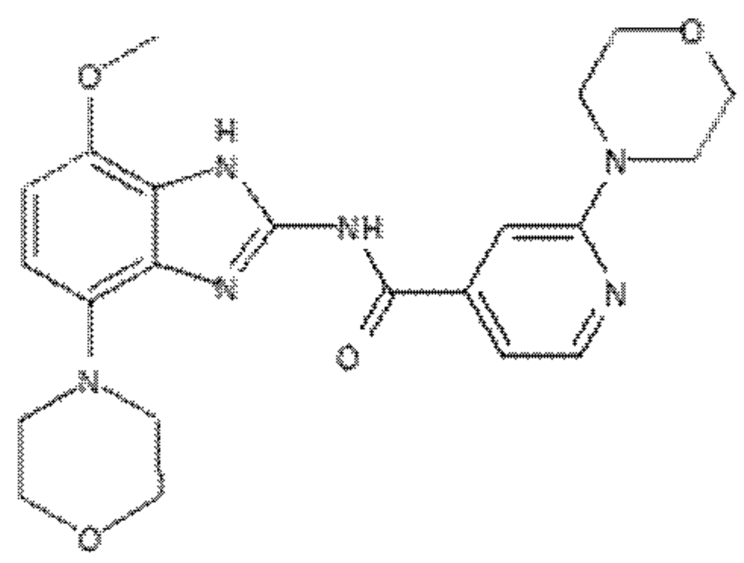
Table 2 – examples of compounds of the present invention

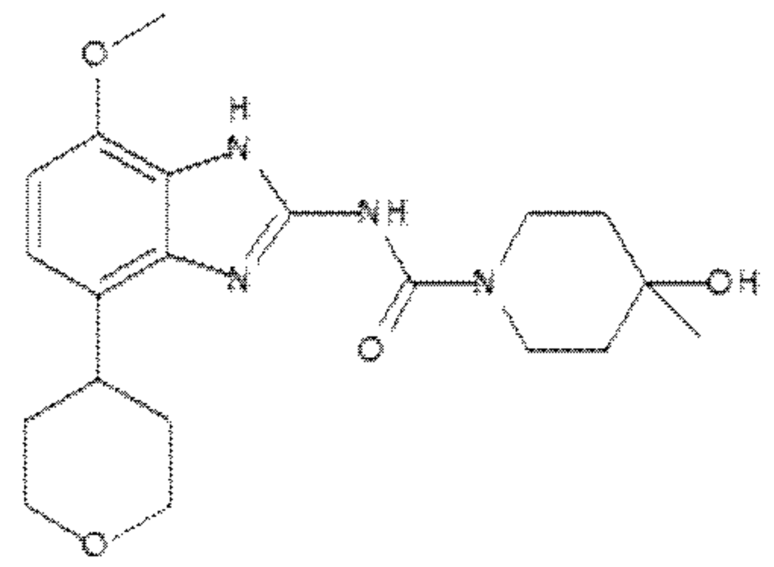
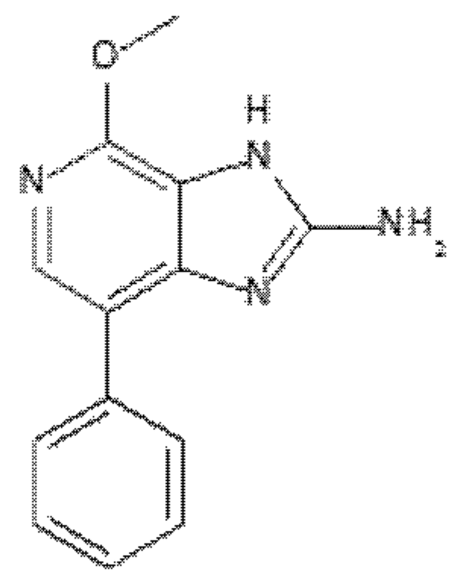
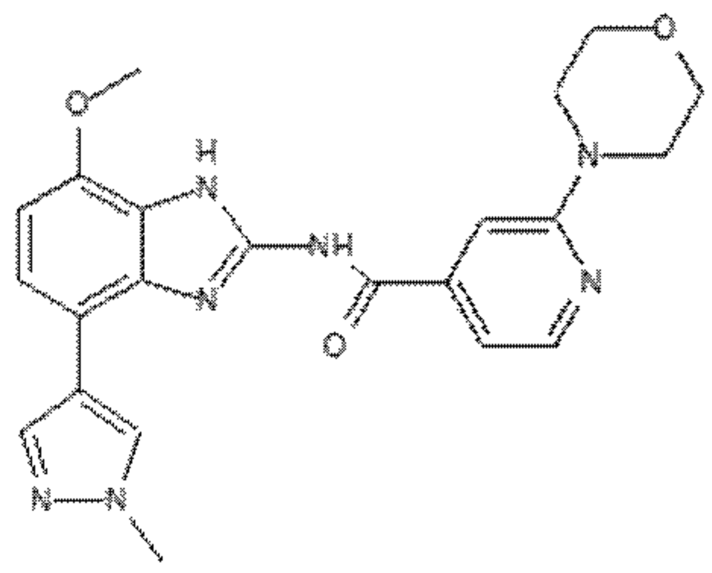
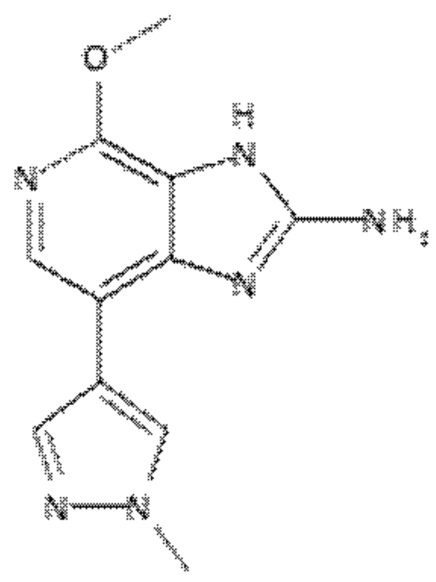
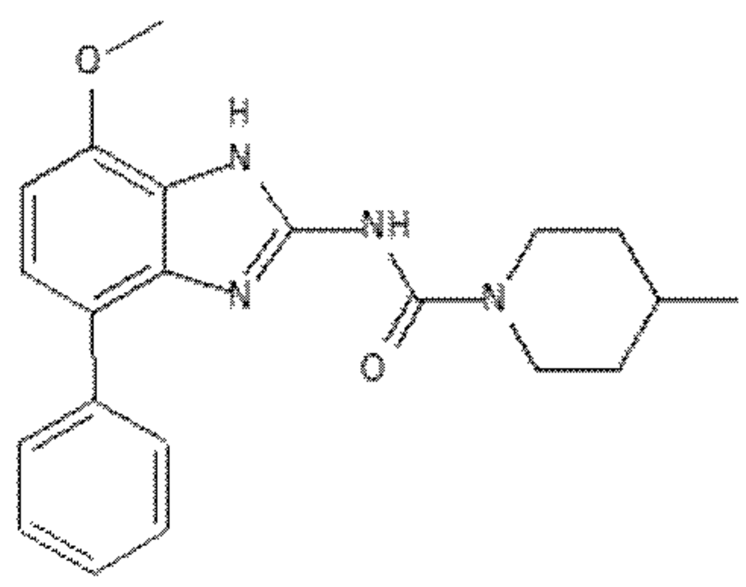
No.	Structure	IUPAC-Name
1		7-Methoxy-4-phenyl-1H-benzoimidazol-2-ylamine
2		4-Fluoro-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
3		2-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-isonicotinamide

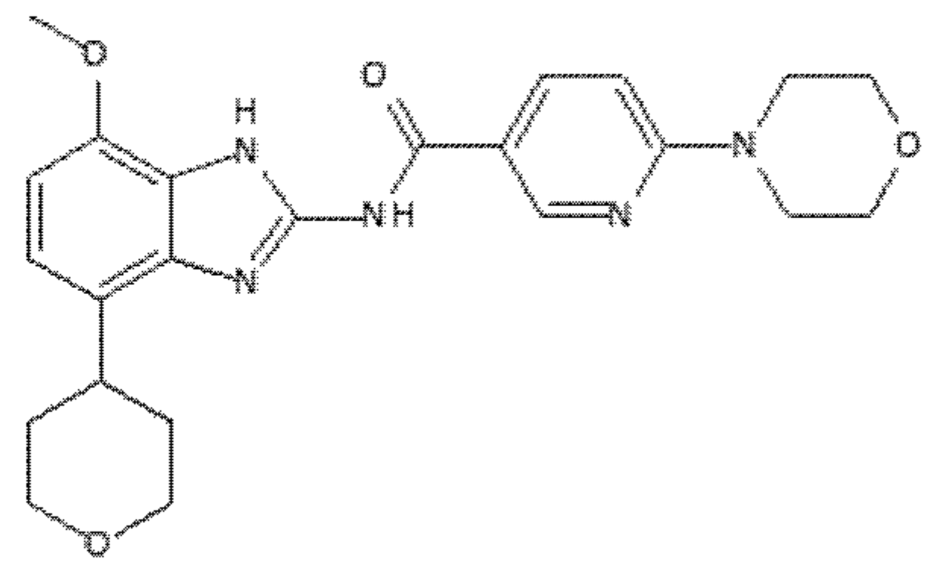
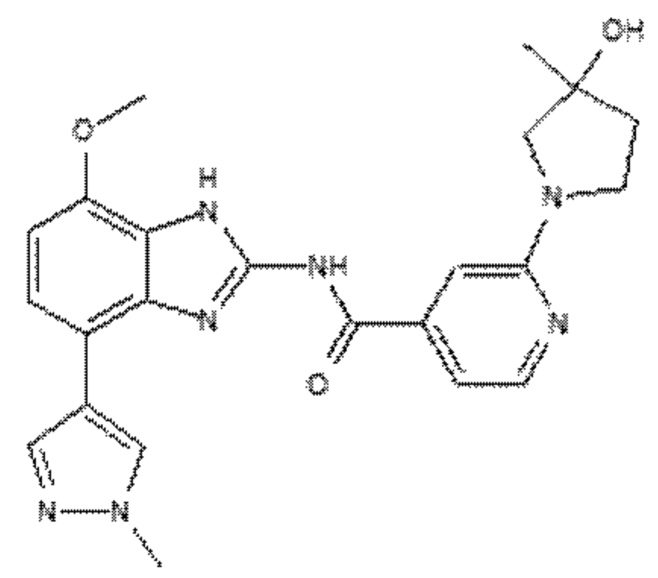
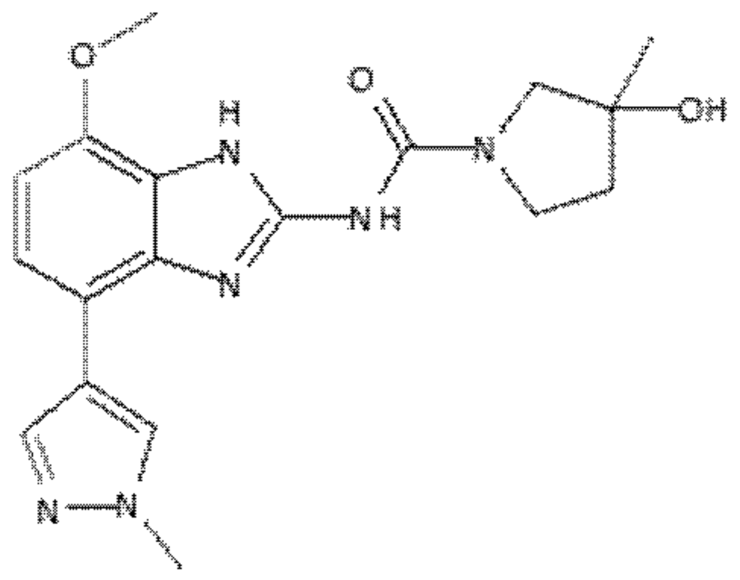
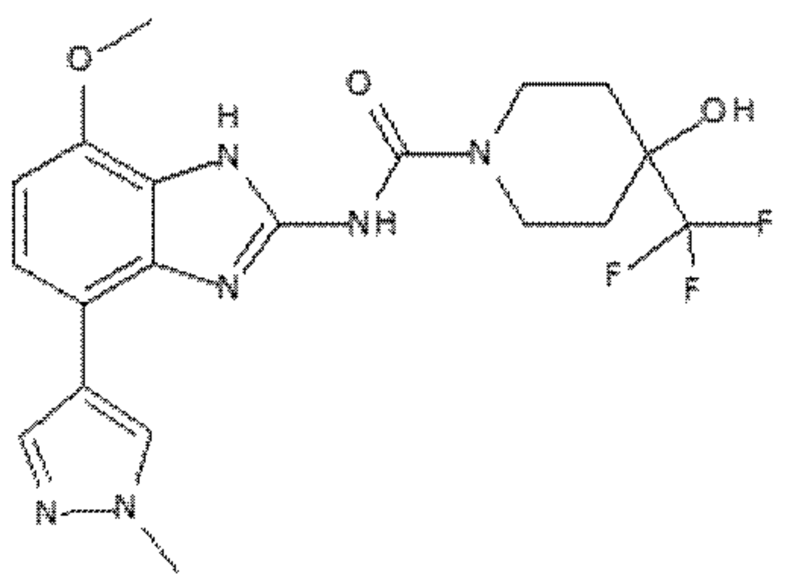
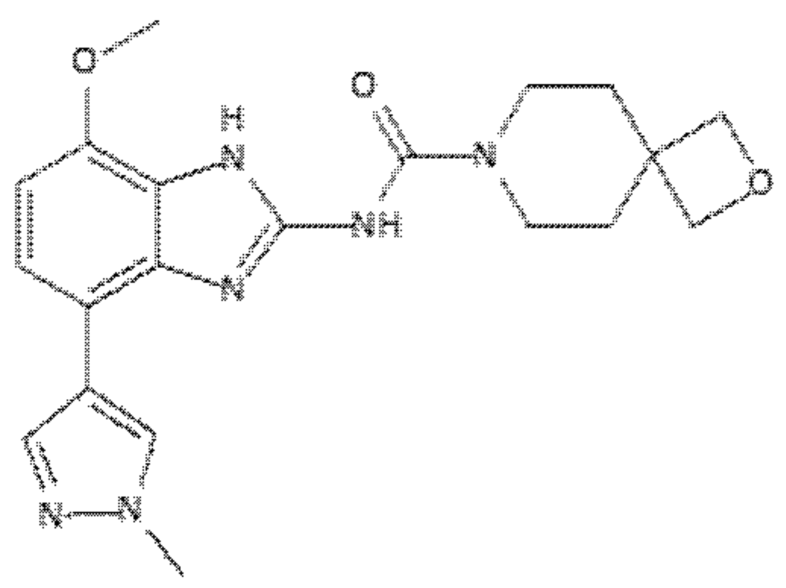
4		2-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-isonicotinamide
5		6-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-nicotinamide
6		6-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-nicotinamide
7		N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
8		N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-6-morpholin-4-yl-nicotinamide

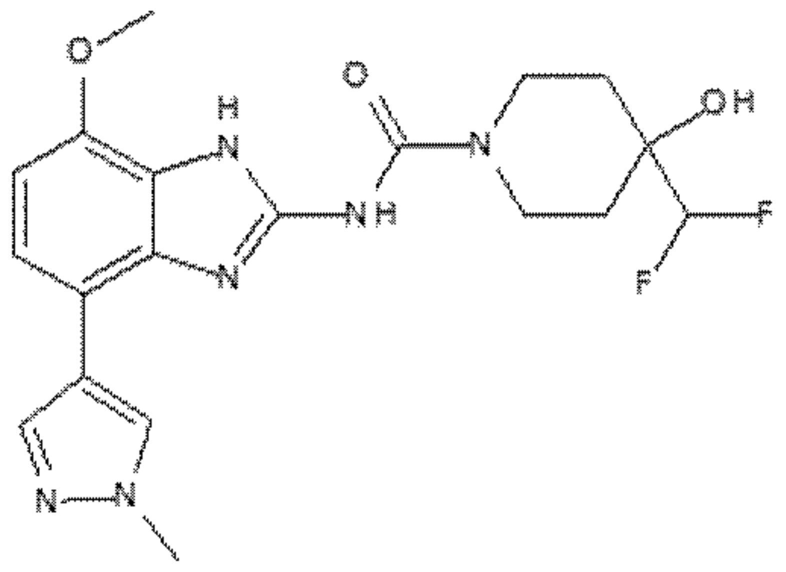
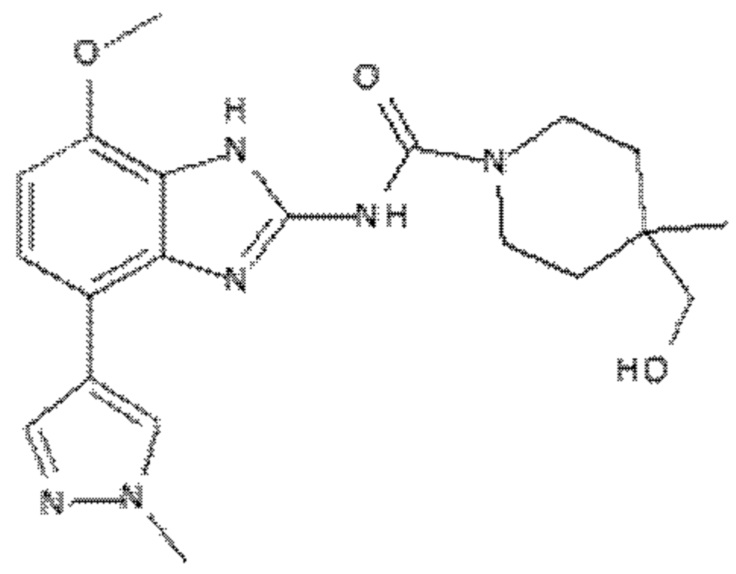
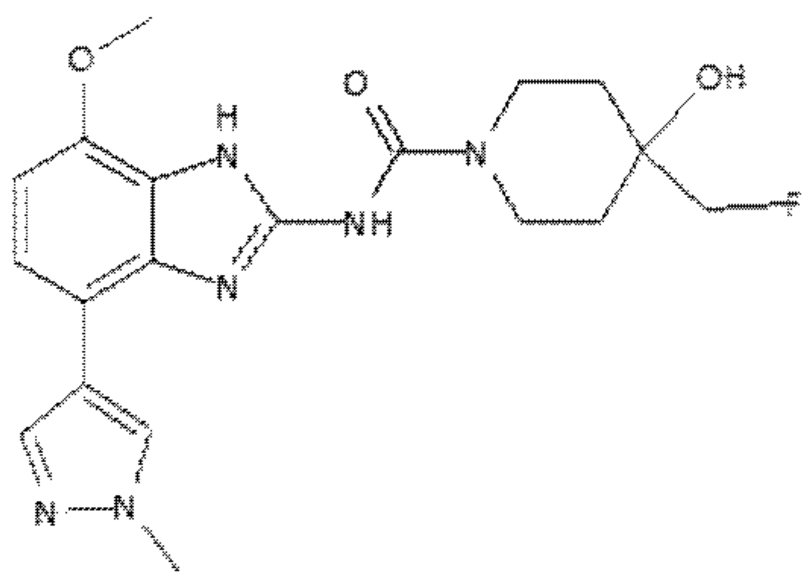
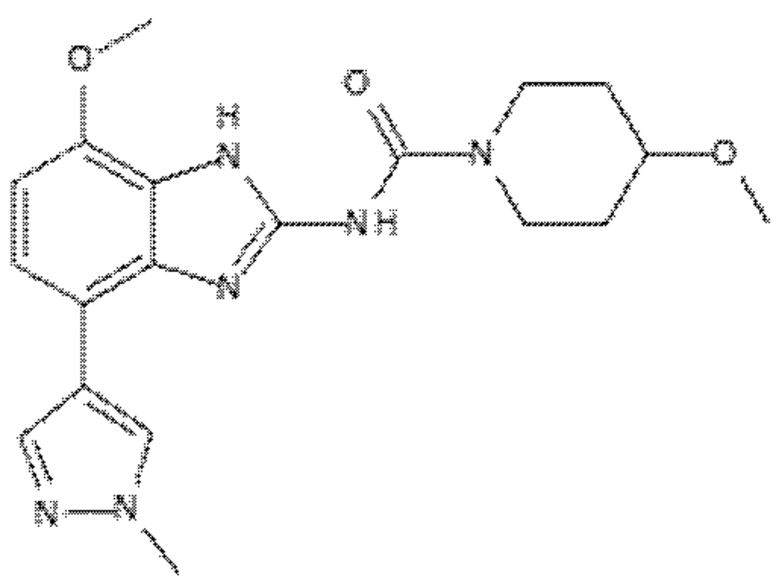
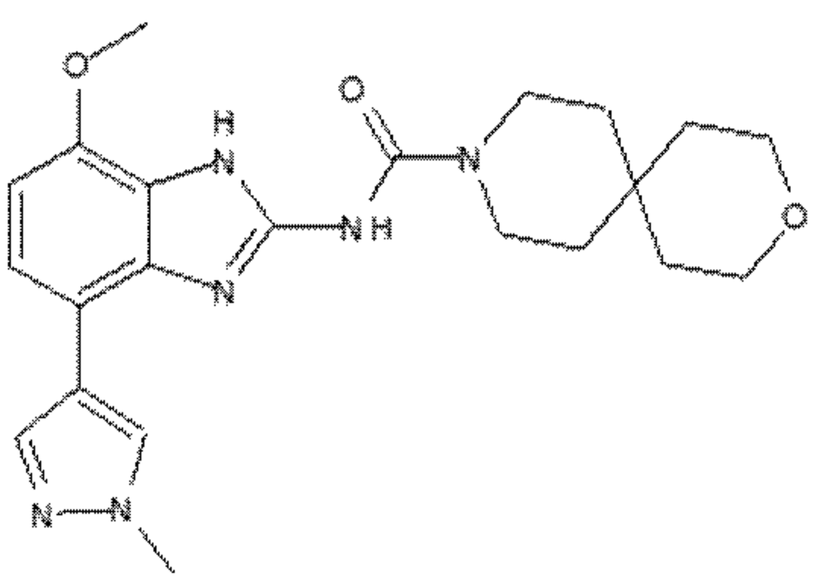
9		N'-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-N,N-dimethyl-formamidine
10		4-Chloromethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
11		4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
12		4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide
13		4-Aminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide

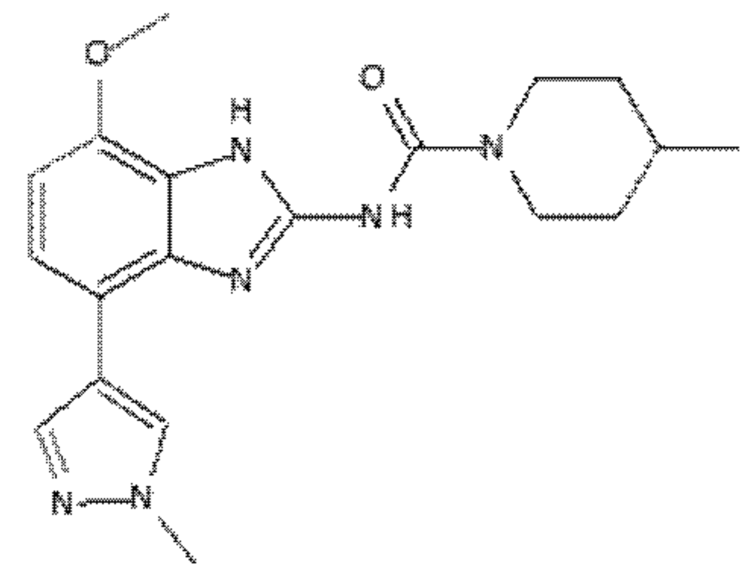
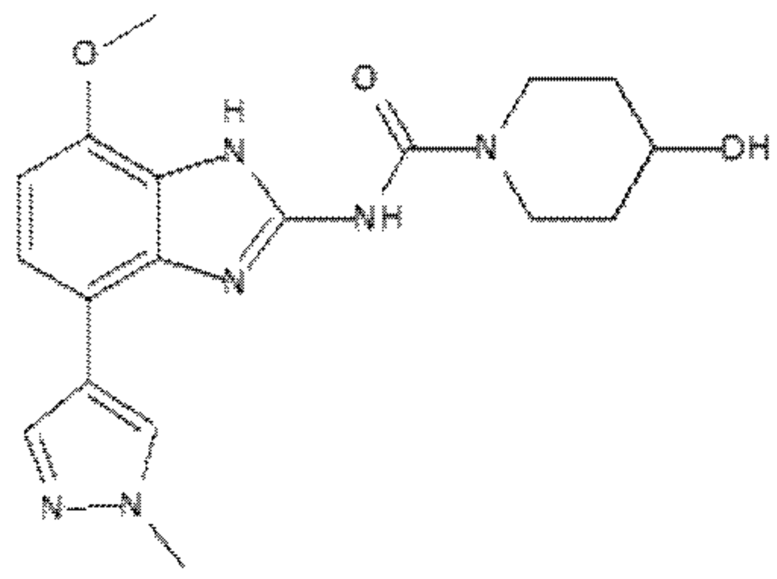
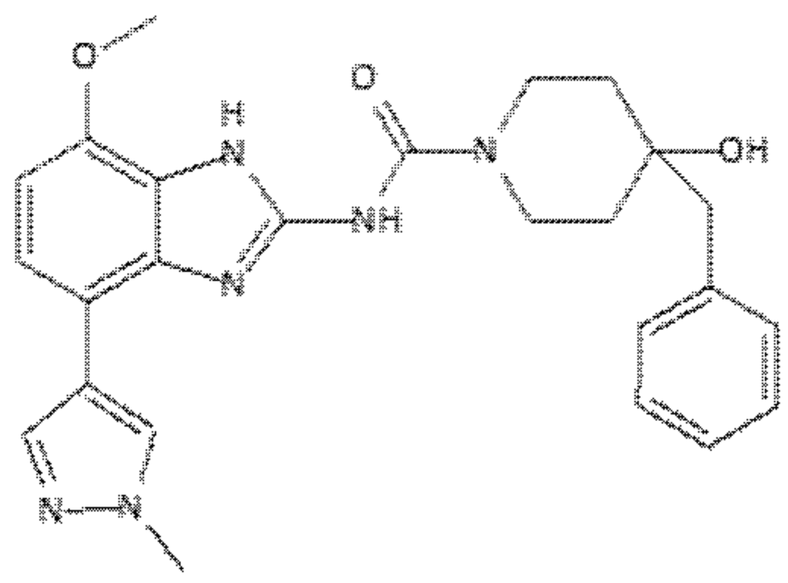
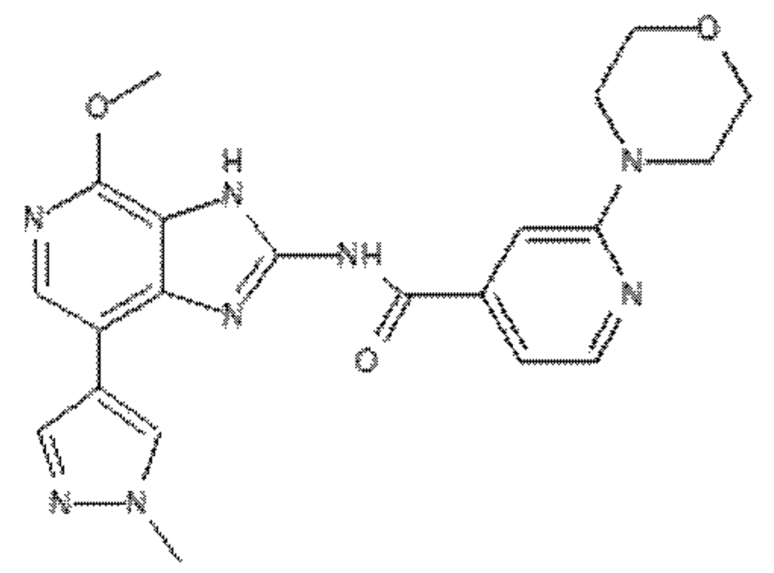
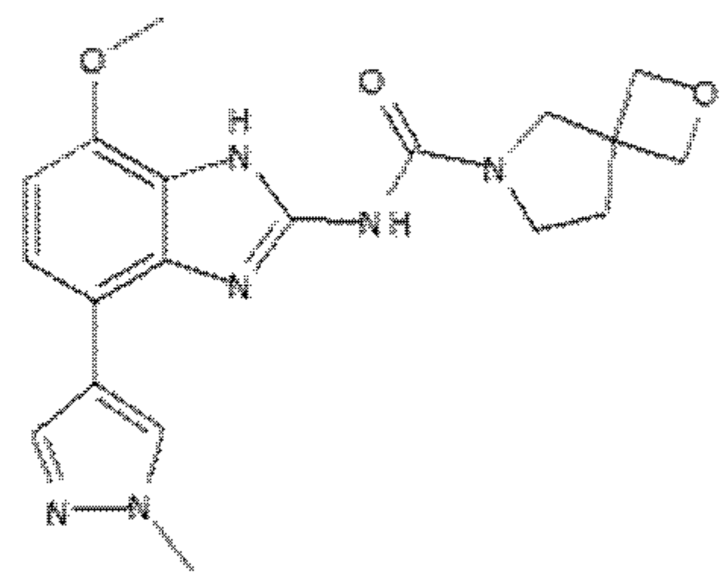
14		4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-ylamine
15		4-Imidazol-1-ylmethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
16		4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (4-cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-amide
17		N-(4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
18		7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-ylamine

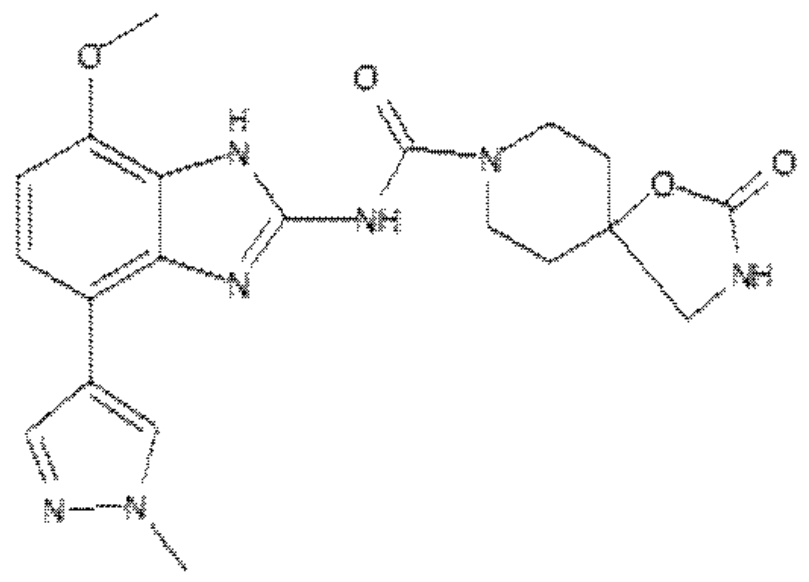
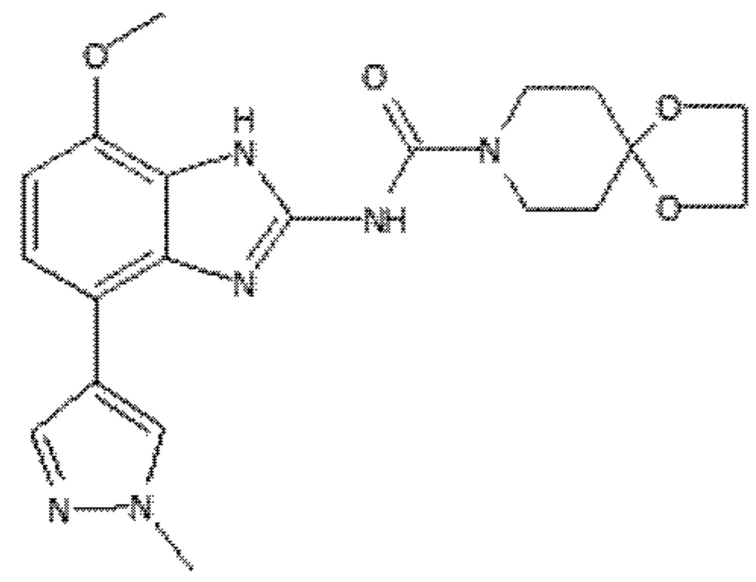
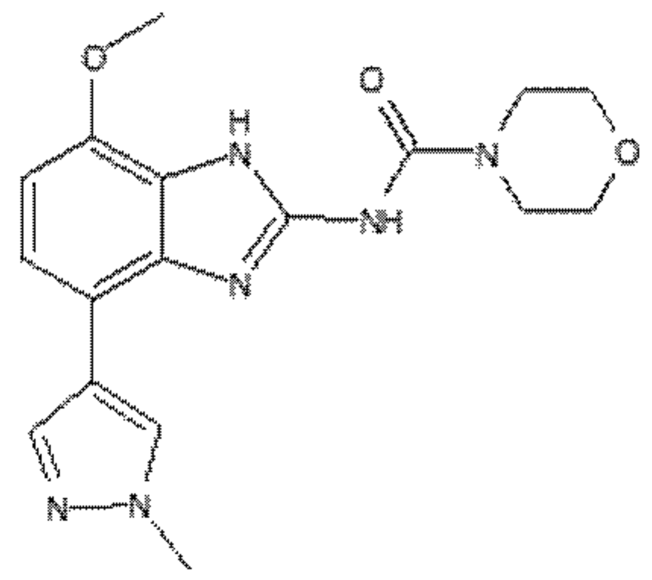
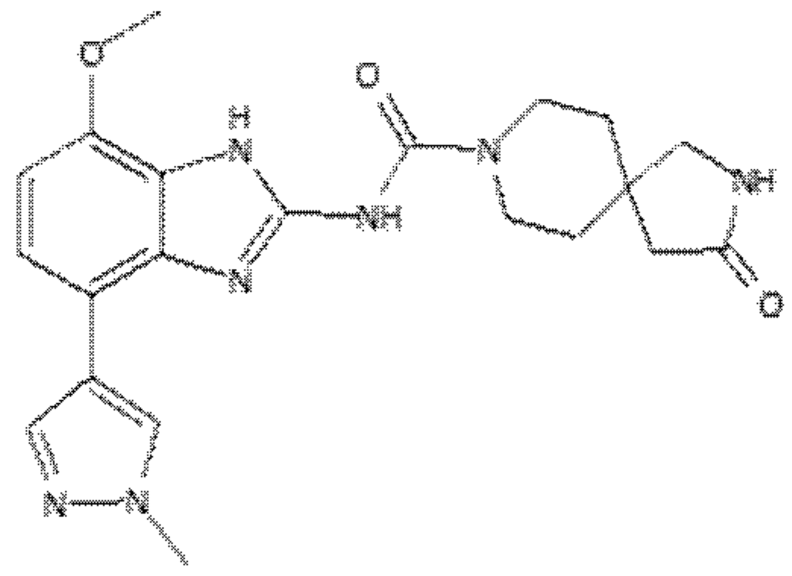
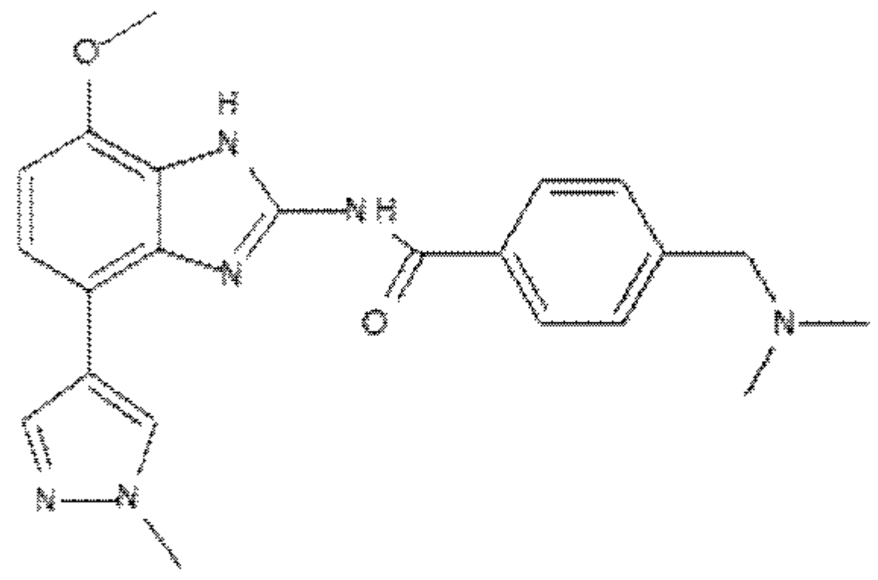
19		7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-ylamine
20		7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-ylamine
21		4-hydroxy-N-(7-methoxy-4-morpholino-1H-benzimidazol-2-yl)-4-methyl-piperidine-1-carboxamide
22		4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
23		N-(7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide

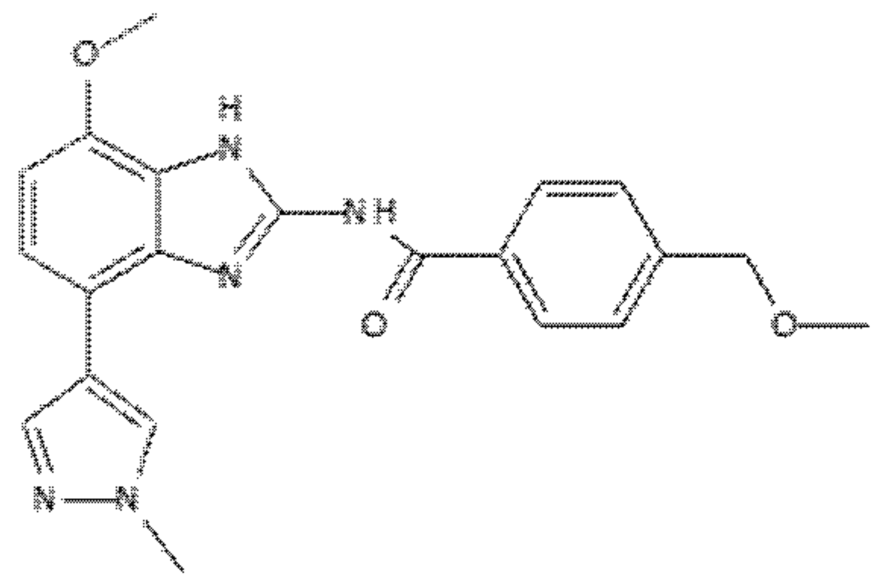
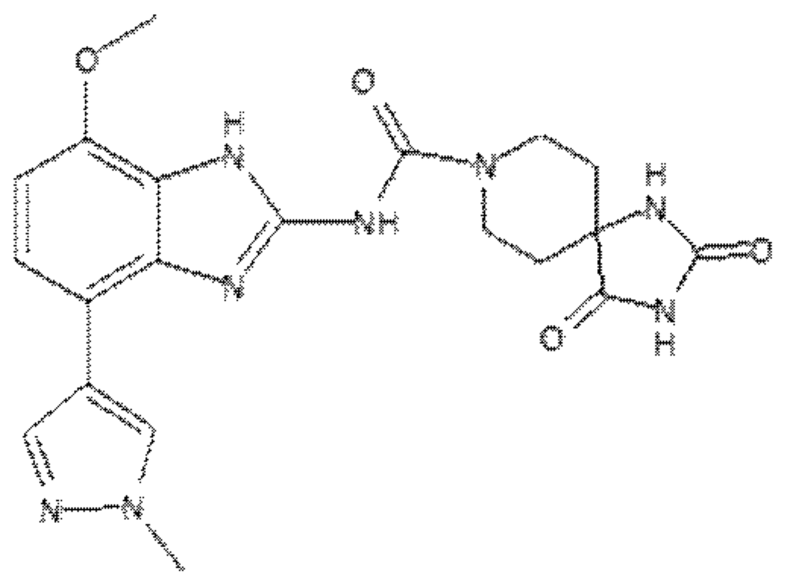
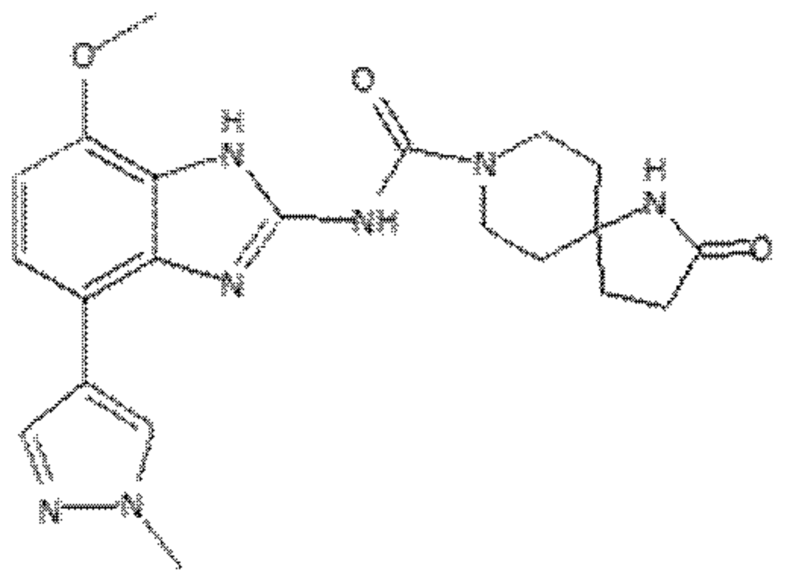
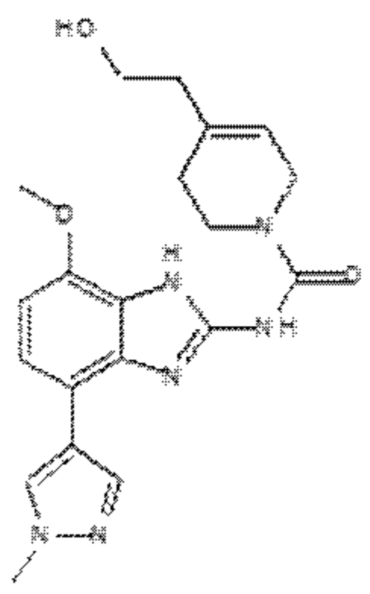
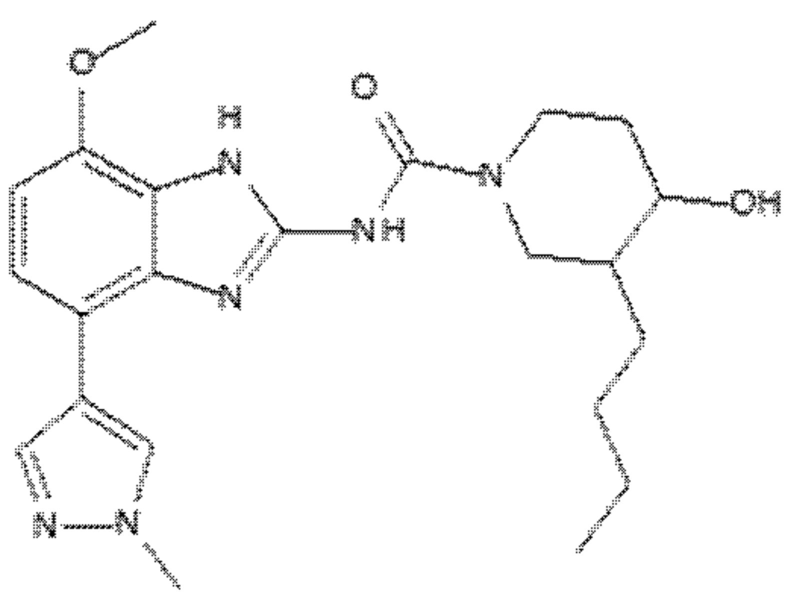
24		4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
25		4-Methoxy-7-phenyl-3H-imidazo[4,5-c]pyridin-2-ylamine
26		N-[7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-2-morpholin-4-yl-isonicotinamide
27		4-Methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-ylamine
28		4-Methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide

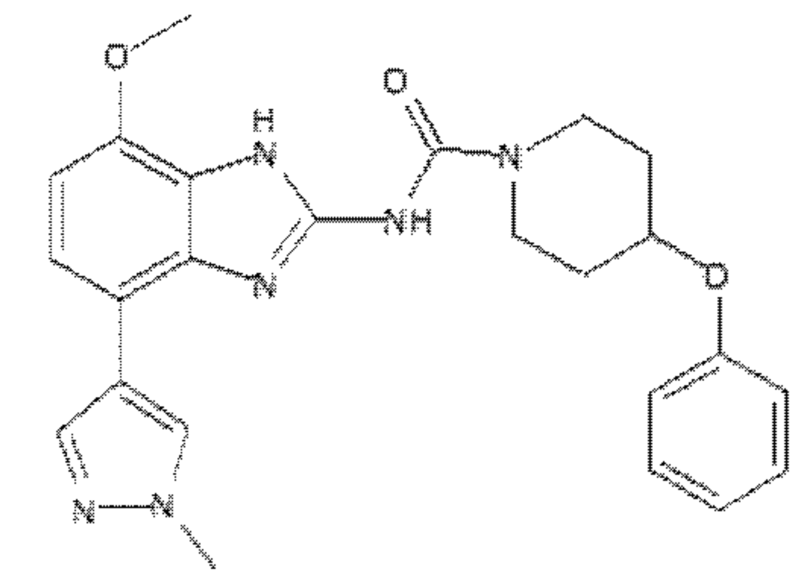
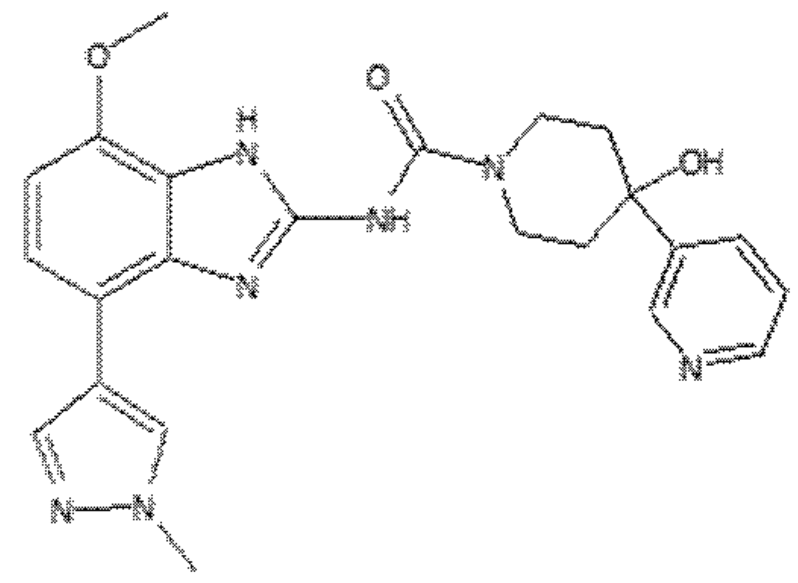
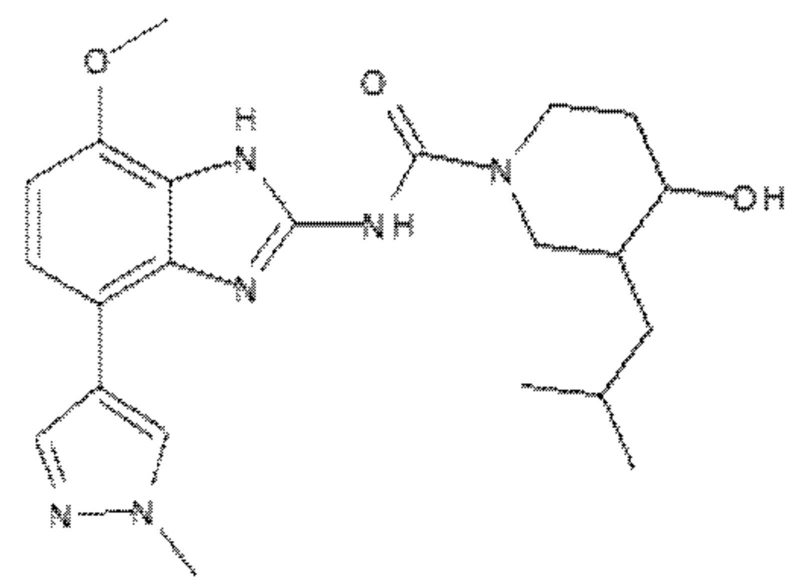
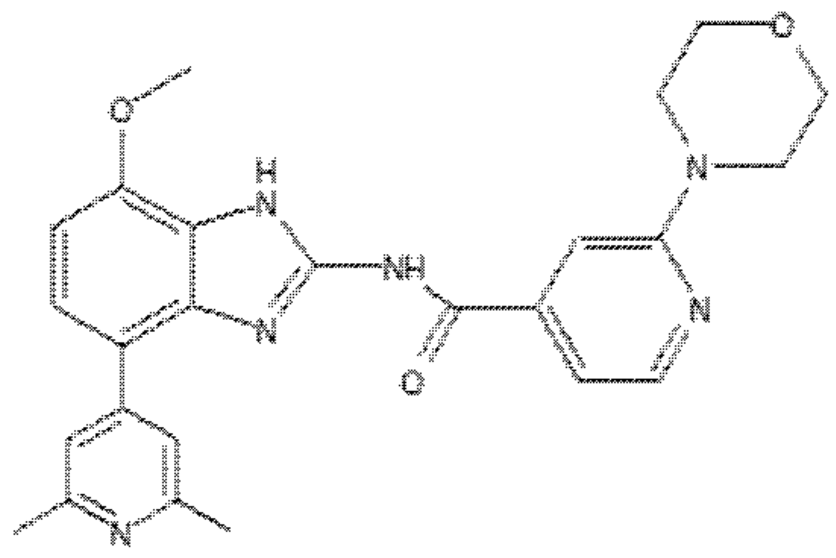
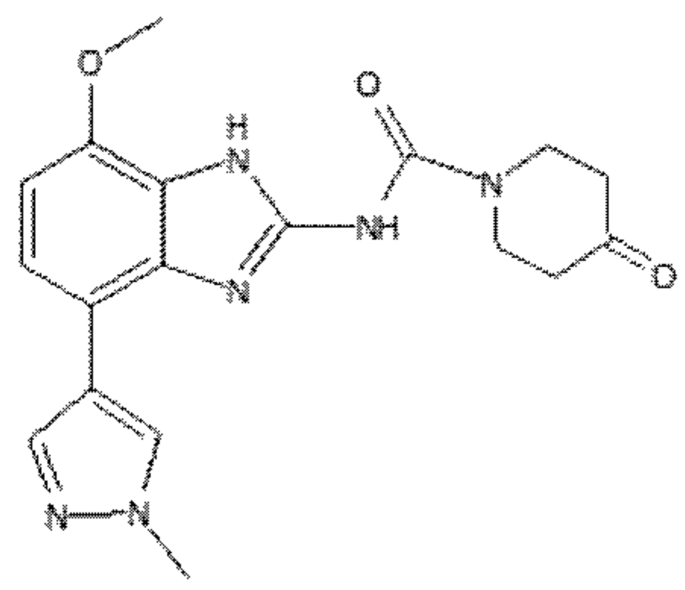
29		N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-6-morpholin-4-yl-nicotinamide
30		2-(3-Hydroxy-3-methyl-pyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-isonicotinamide
31		3-Hydroxy-3-methyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
32		4-Hydroxy-4-trifluoromethyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
33		2-Oxa-7-aza-spiro[3.5]nonane-7-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

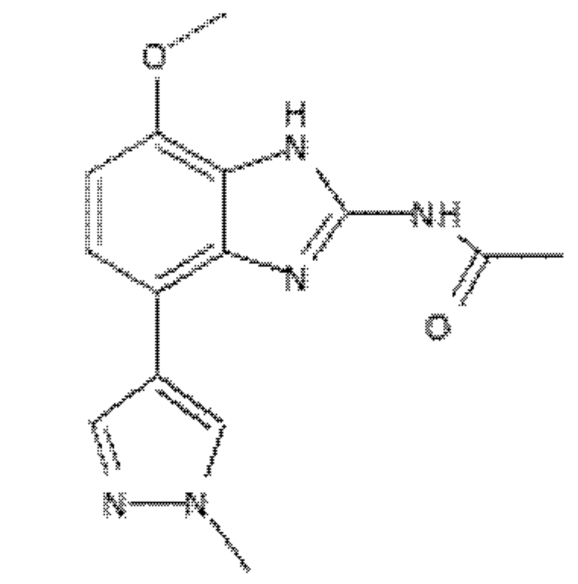
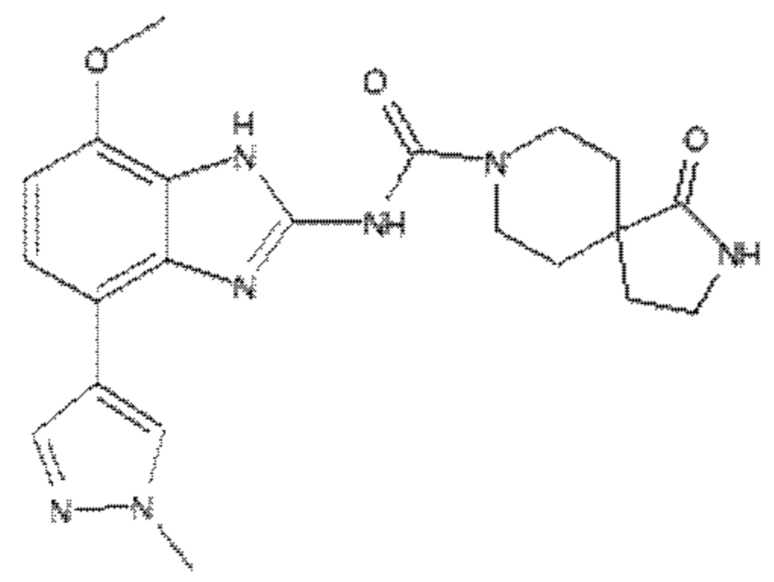
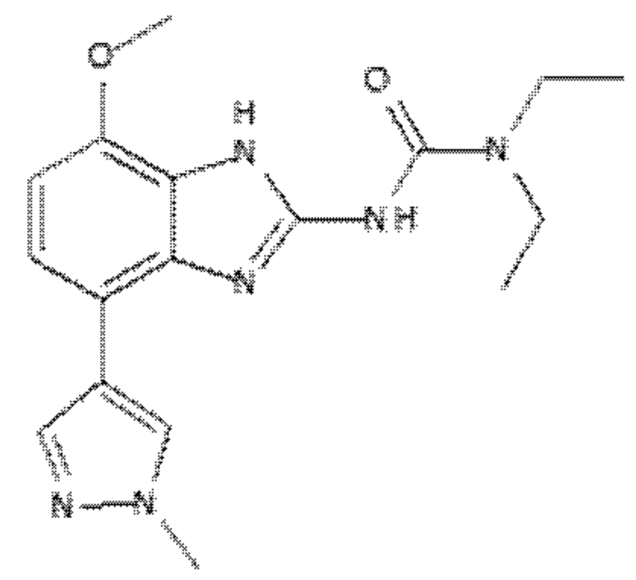
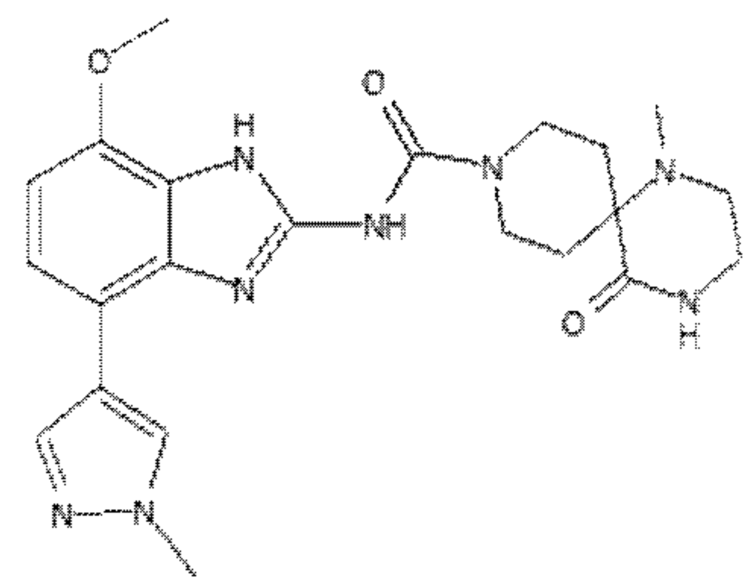
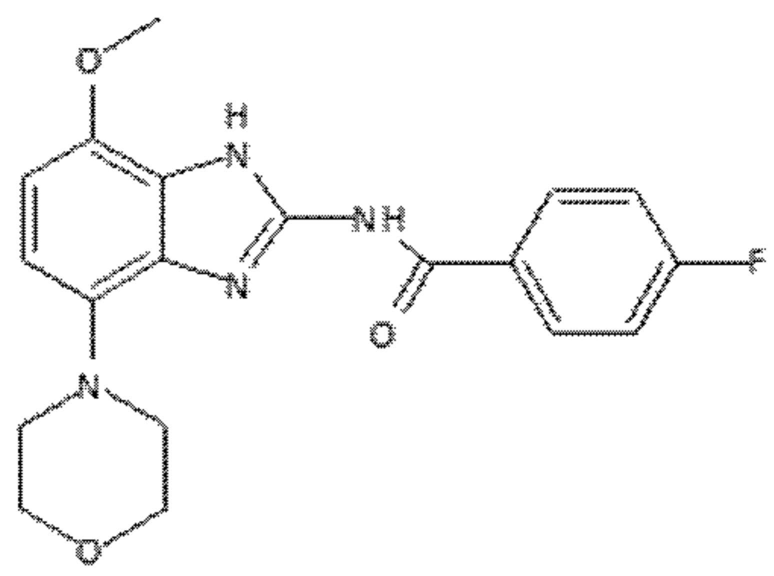
34		4-Difluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
35		4-Hydroxymethyl-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
36		4-Fluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
37		4-Methoxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
38		3-Oxa-9-aza-spiro[5.5]undecane-9-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

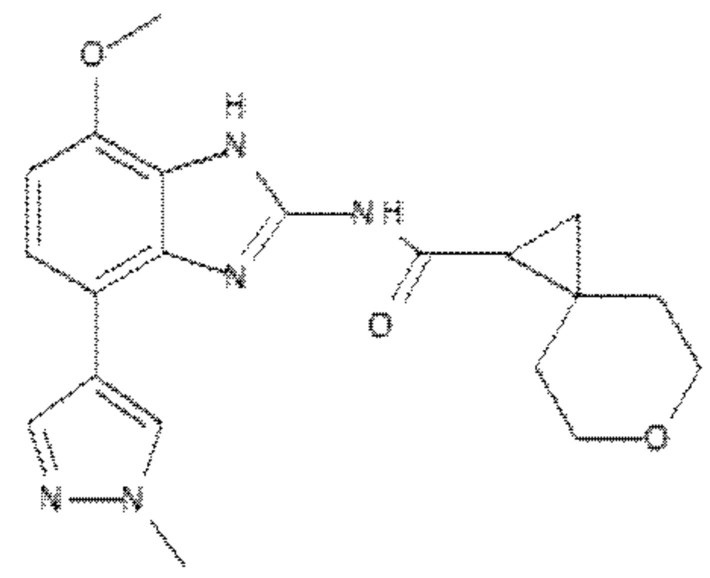
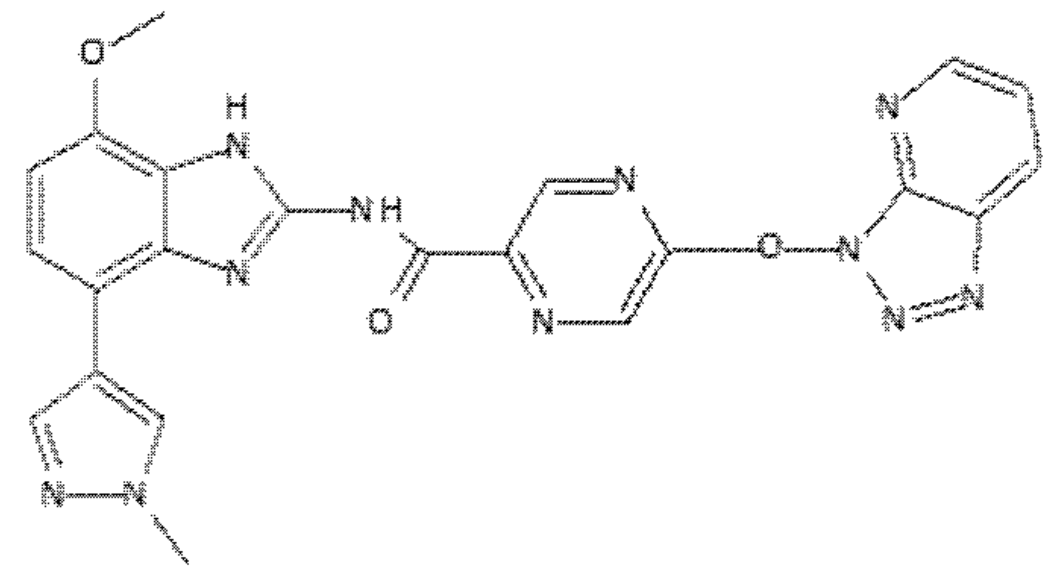
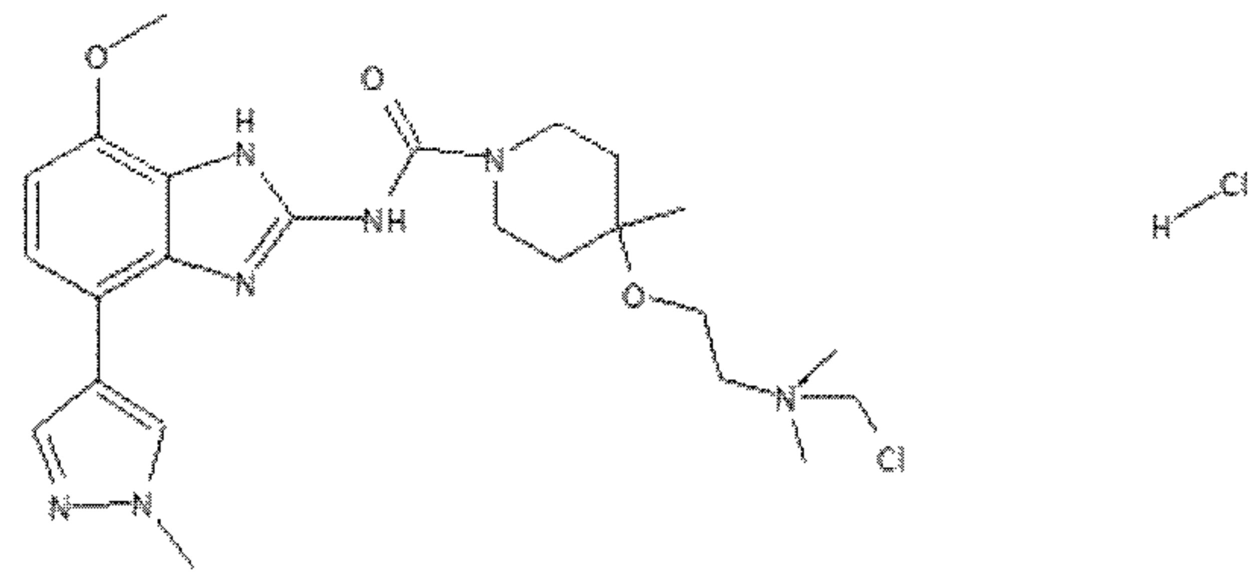
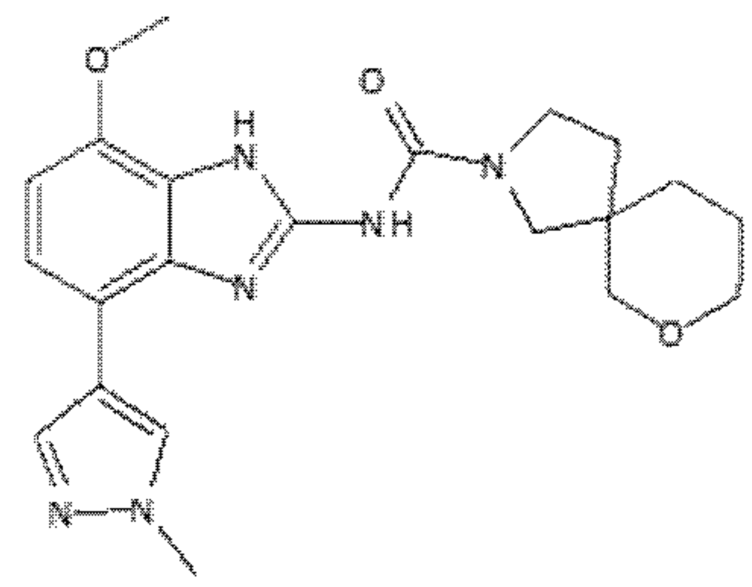
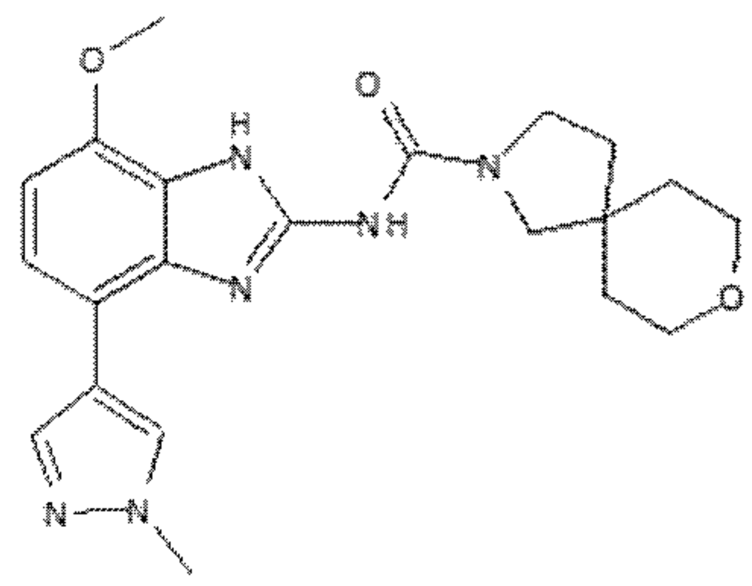
39		4-Methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
40		4-Hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
41		4-Benzyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
42		N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide
43		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide

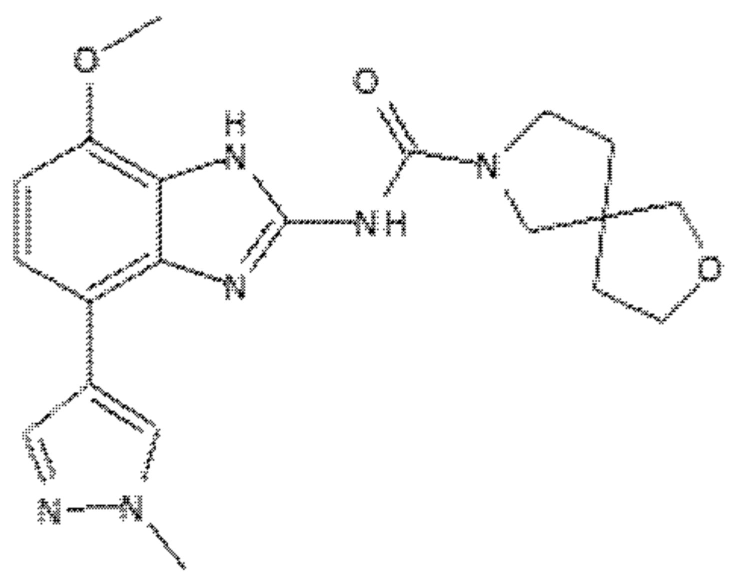
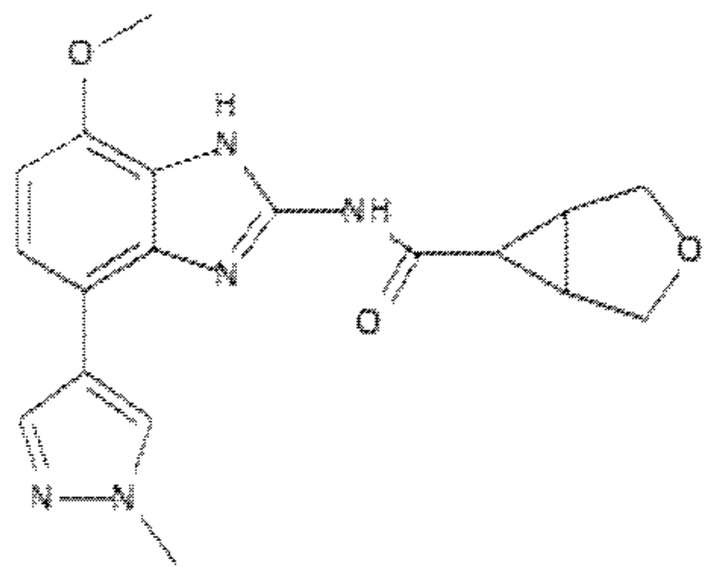
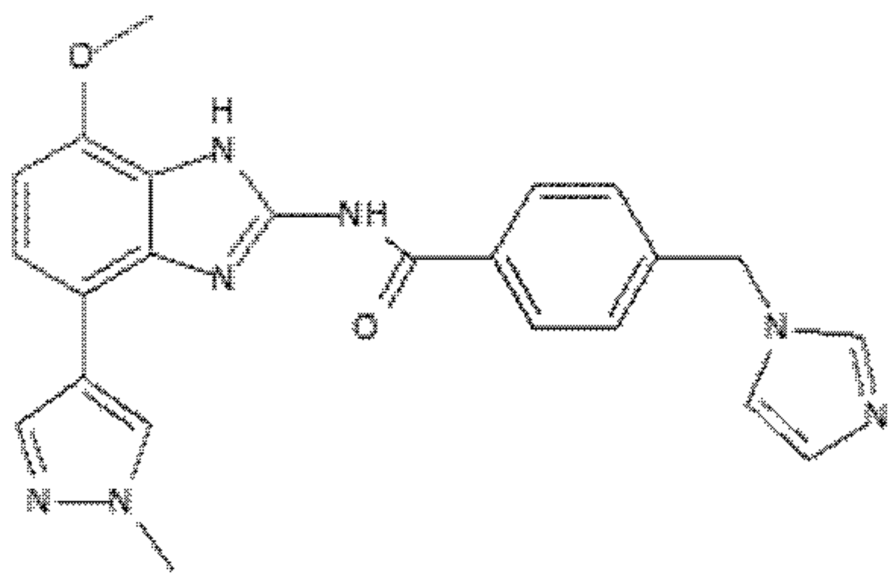
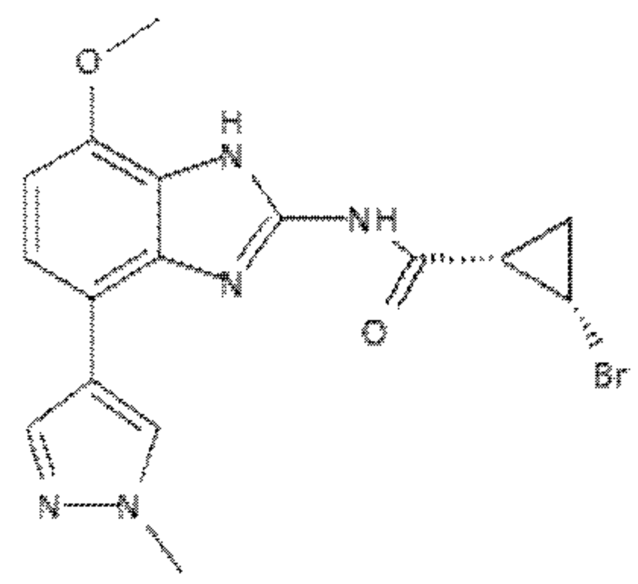
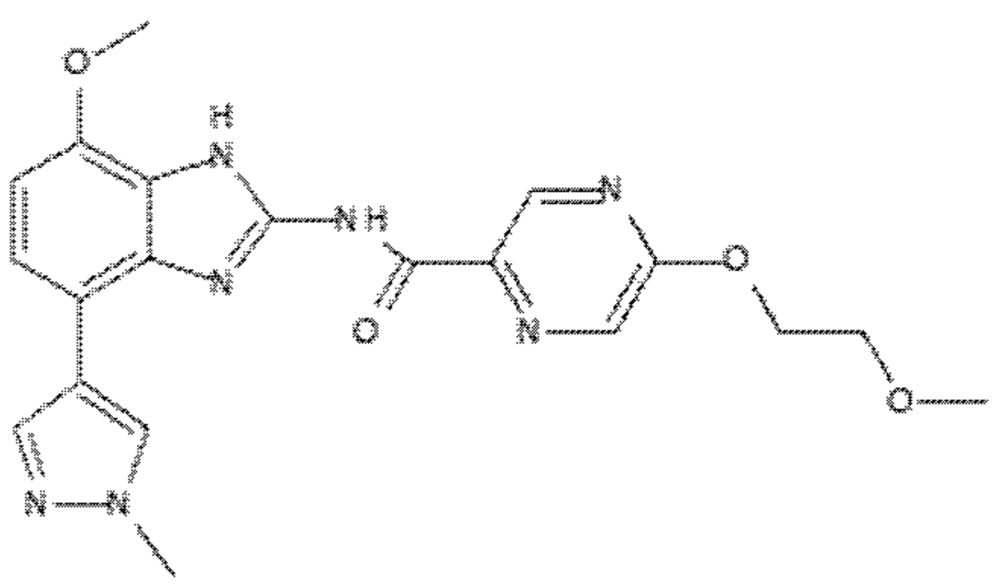
44		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1-oxa-3,8-diazaspiro[4.5]decane-8-carboxamide
45		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,4-dioxa-8-azaspiro[4.5]decane-8-carboxamide
46		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]morpholine-4-carboxamide
47		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
48		4-[(dimethylamino)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

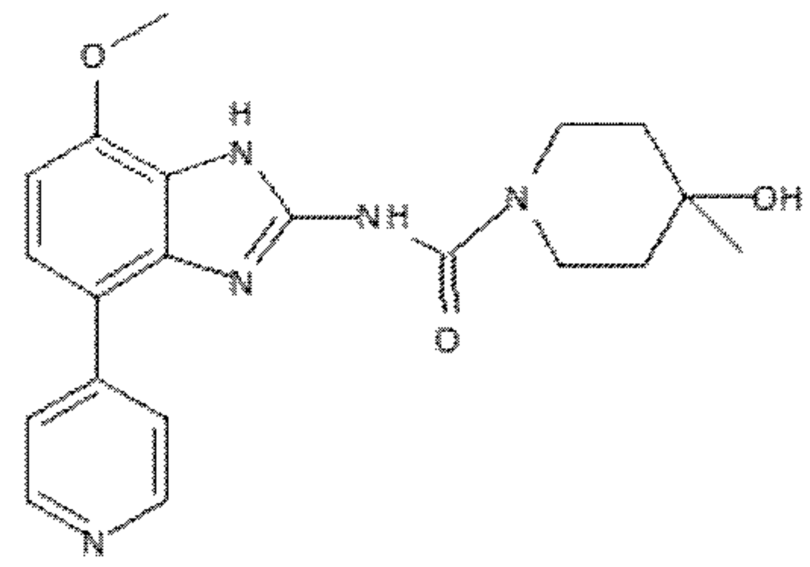
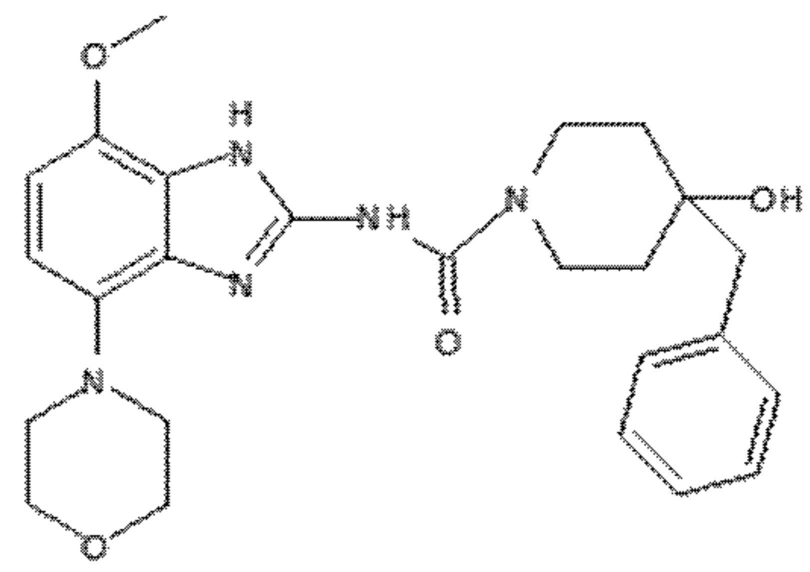
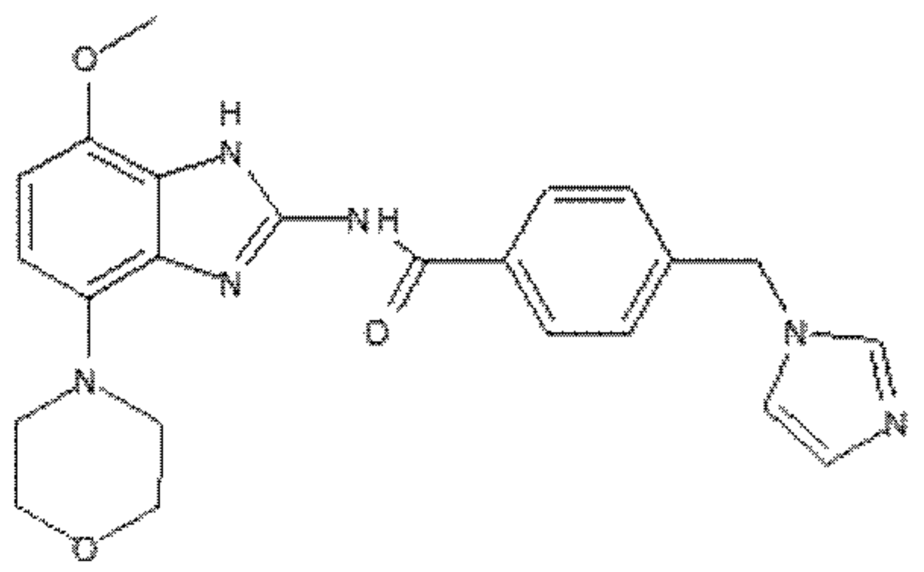
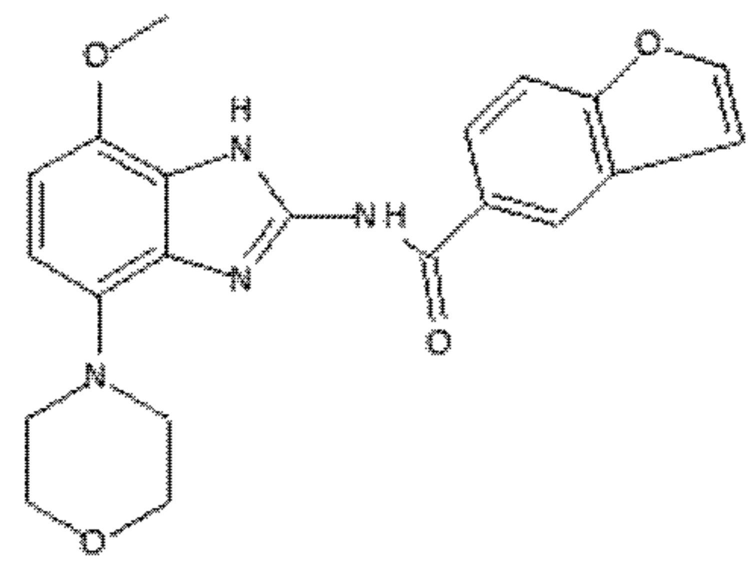
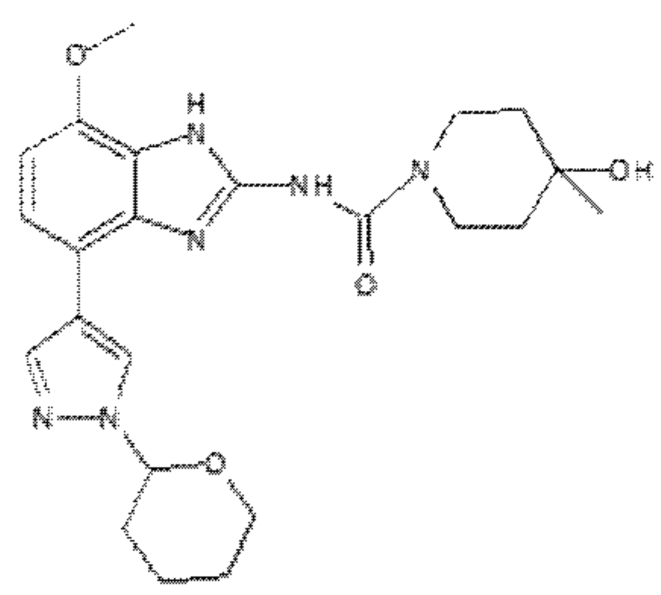
49		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(methoxymethyl)benzamide
50		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,4-dioxo-1,3,8-triazaspiro[4.5]decane-8-carboxamide
51		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1,8-diazaspiro[4.5]decane-8-carboxamide
52		4-(2-hydroxyethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2,3,6-tetrahydropyridine-1-carboxamide
53		3-butyl-4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide

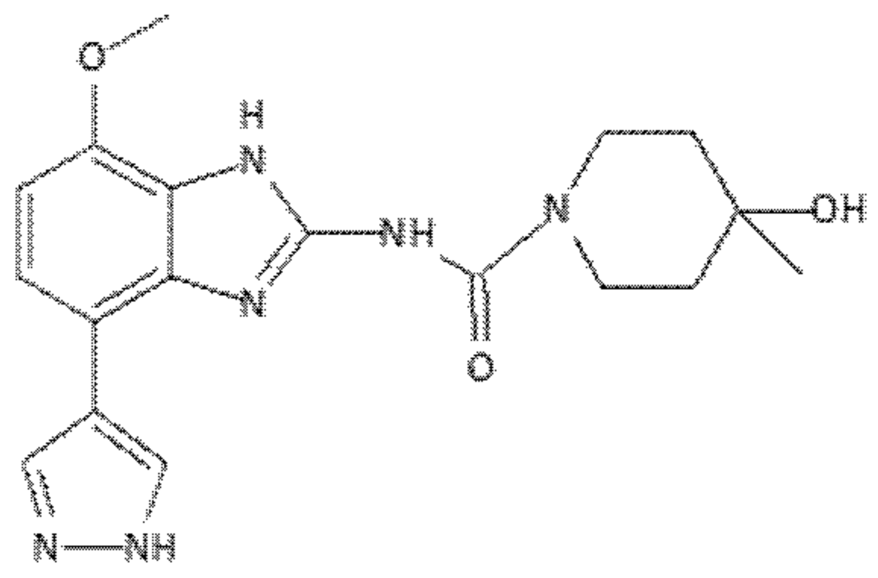
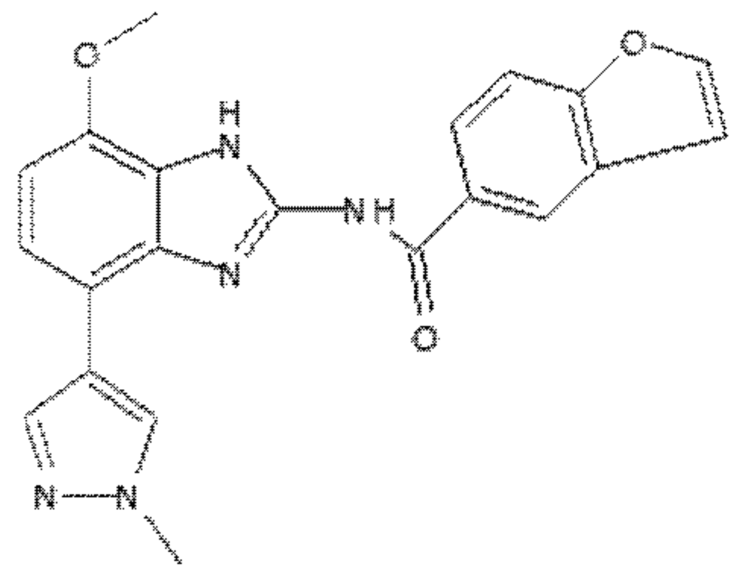
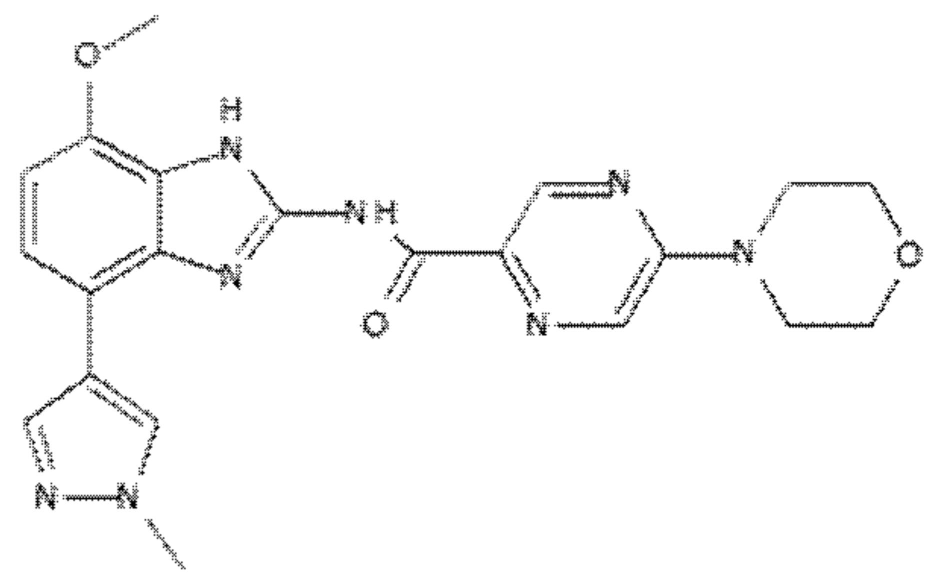
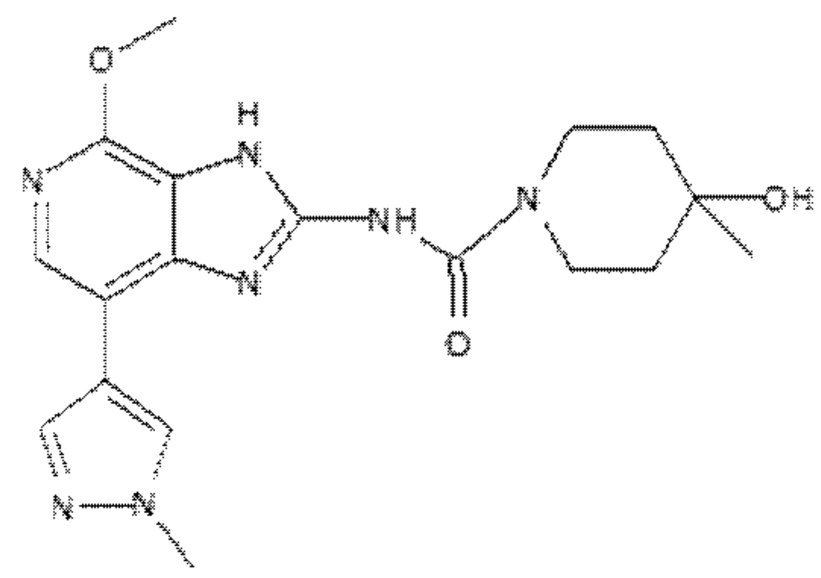
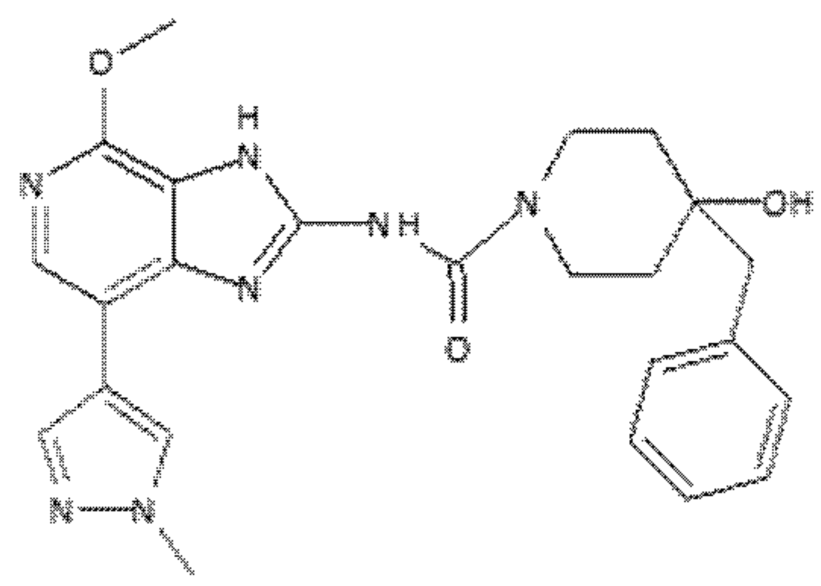
54		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-phenoxypiperidine-1-carboxamide
55		4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(pyridin-3-yl)piperidine-1-carboxamide
56		4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methylpropyl)piperidine-1-carboxamide
57		N-[4-(2,6-dimethylpyridin-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide
58		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-oxopiperidine-1-carboxamide

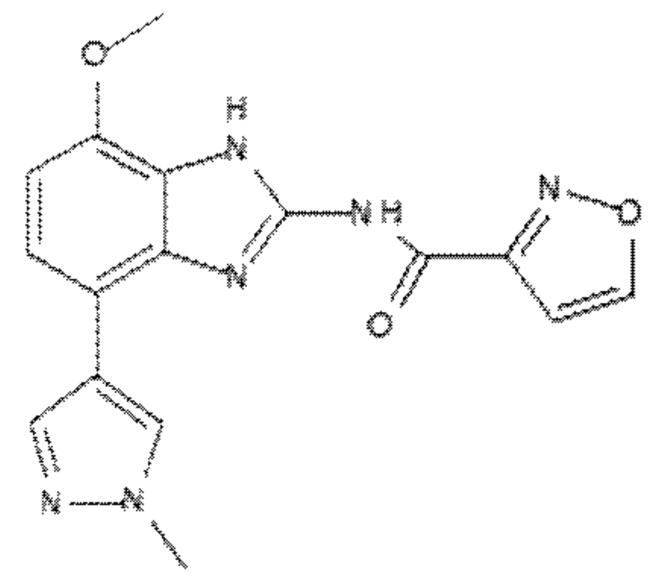
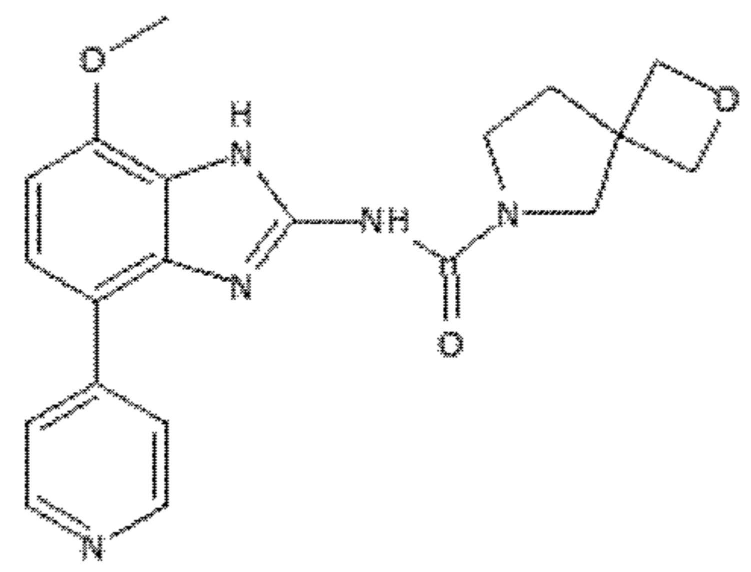
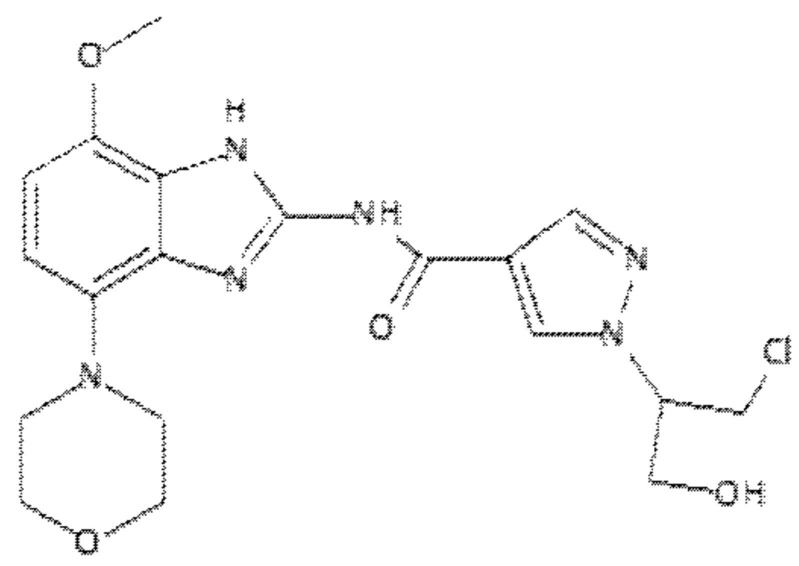
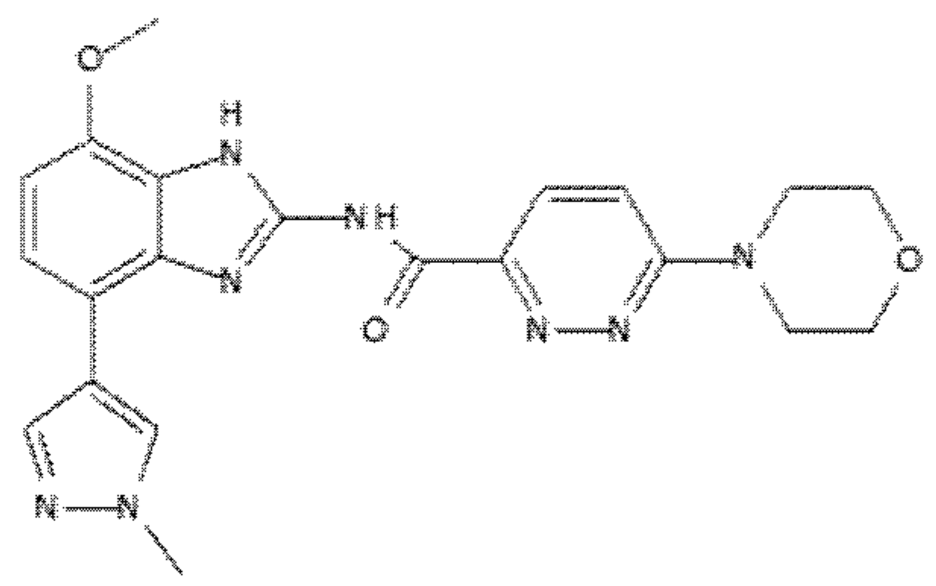
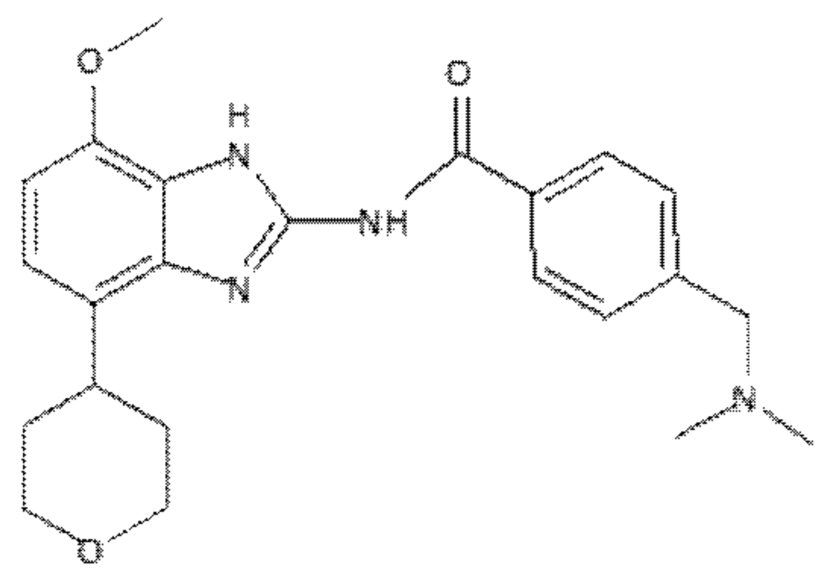
59		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
60		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
61		3,3-diethyl-1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
62		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-5-oxo-1,4,9-triazaspiro[5.5]undecane-9-carboxamide
63		4-fluoro-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

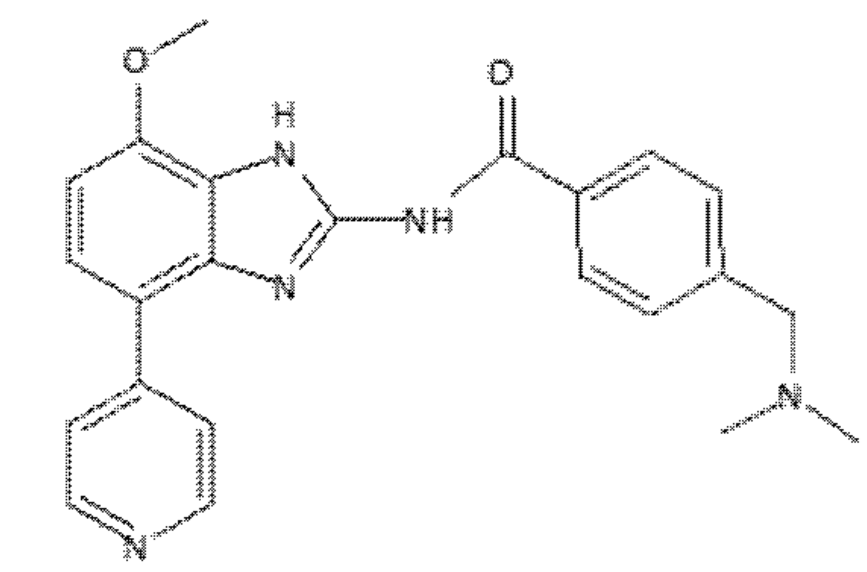
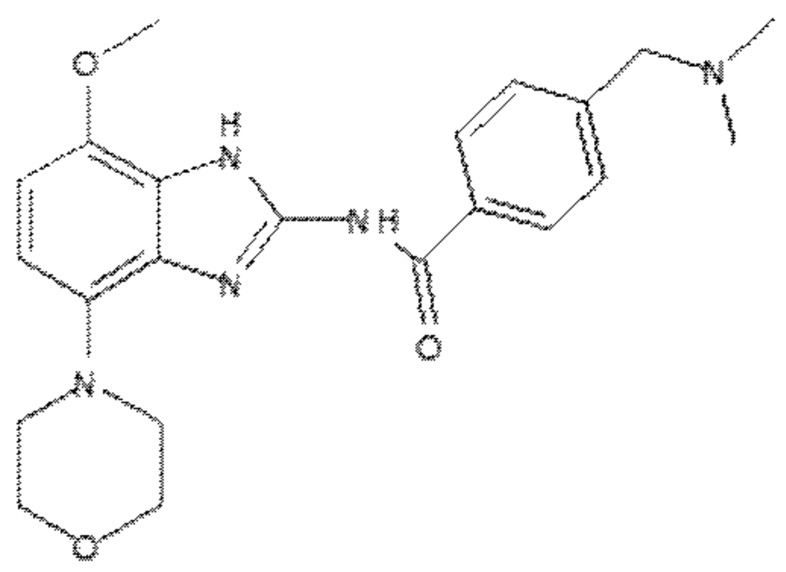
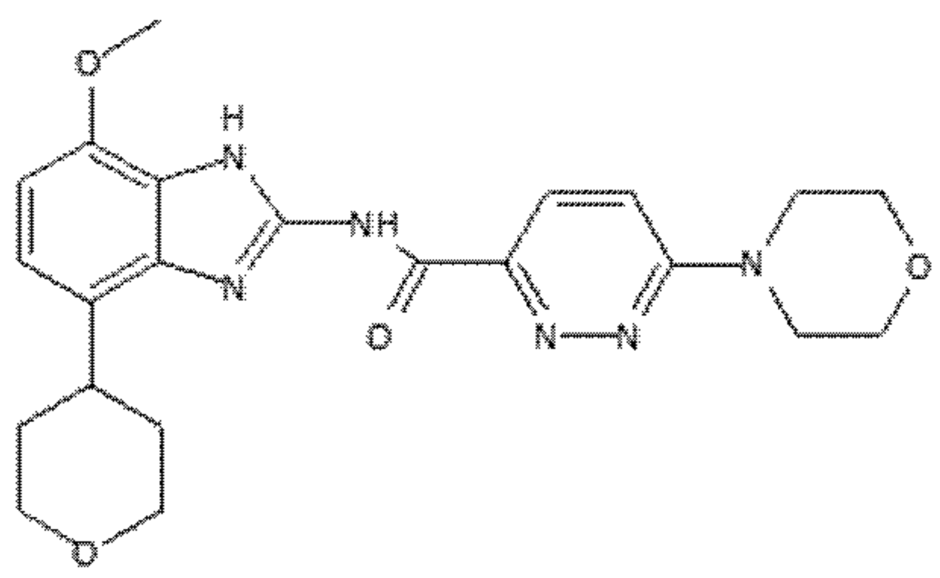
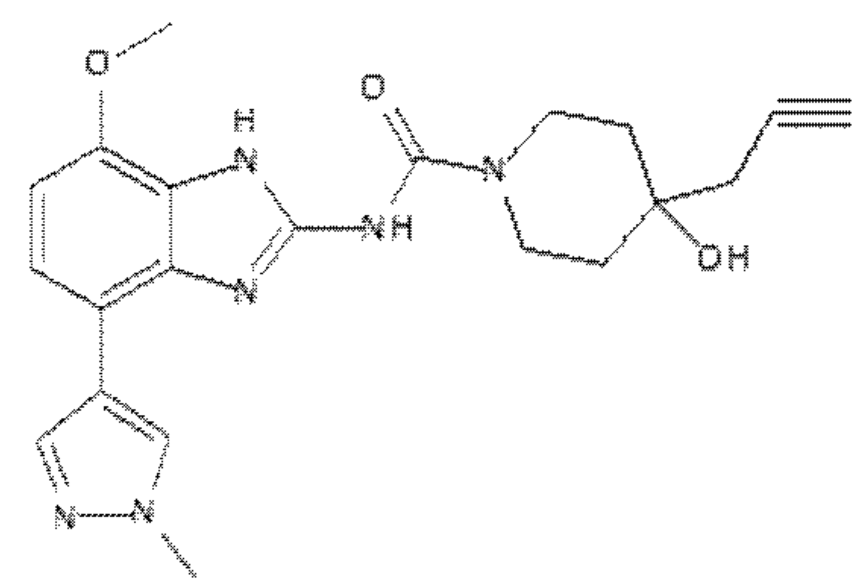
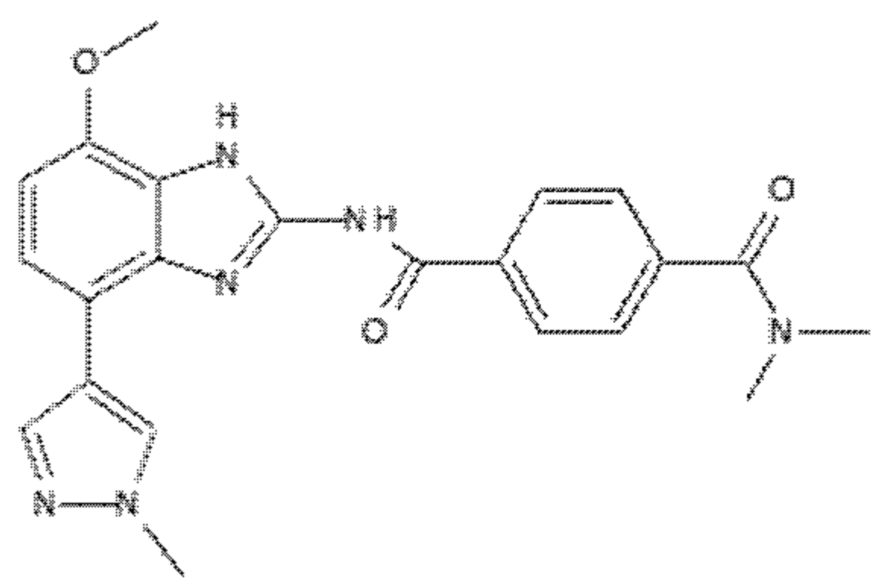
64		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-oxaspiro[2.5]octane-1-carboxamide
65		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-{3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy}pyrazine-2-carboxamide
66		(chloromethyl)({2-[(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}-4-methylpiperidin-4-yl)oxy]ethyl})dimethylazanium hydrochloride
67		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
68		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide

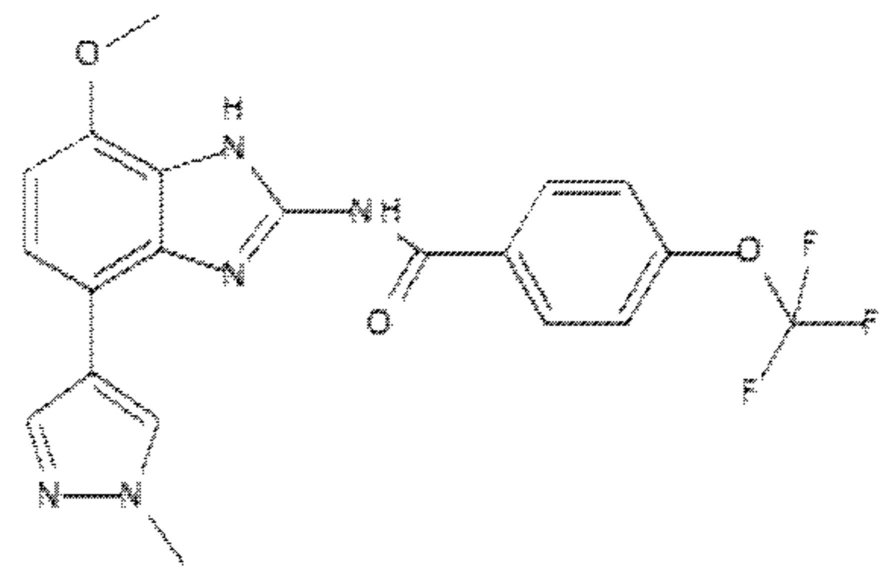
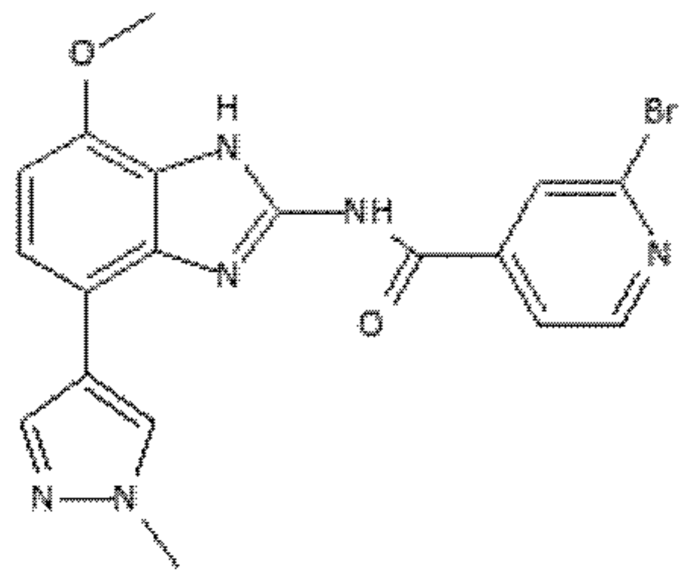
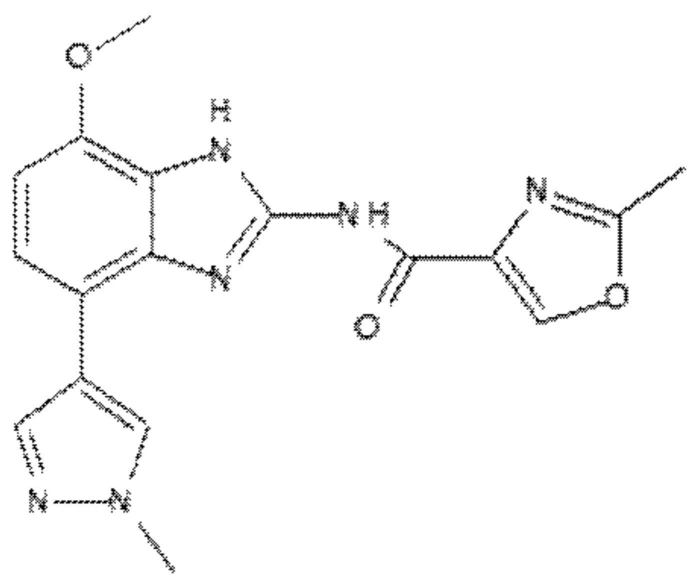
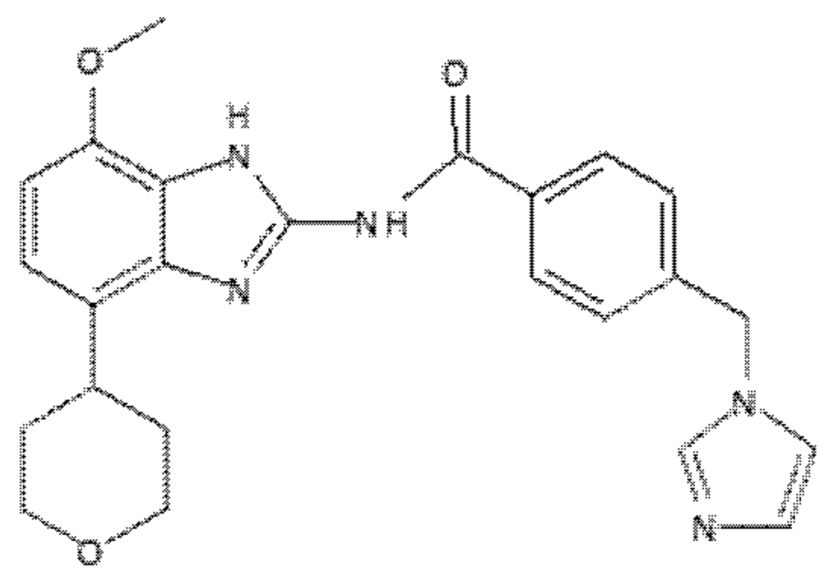
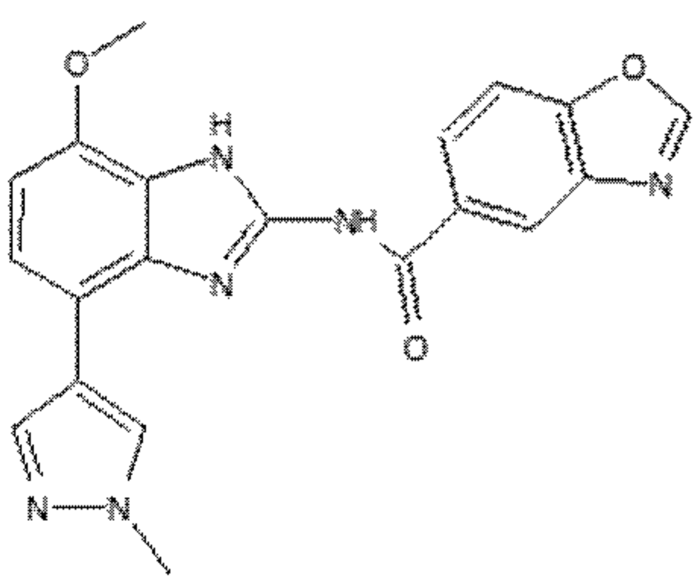
69		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
70		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxabicyclo[3.1.0]hexane-6-carboxamide
71		4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
72		(1S,2S)-2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
73		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyrazine-2-carboxamide

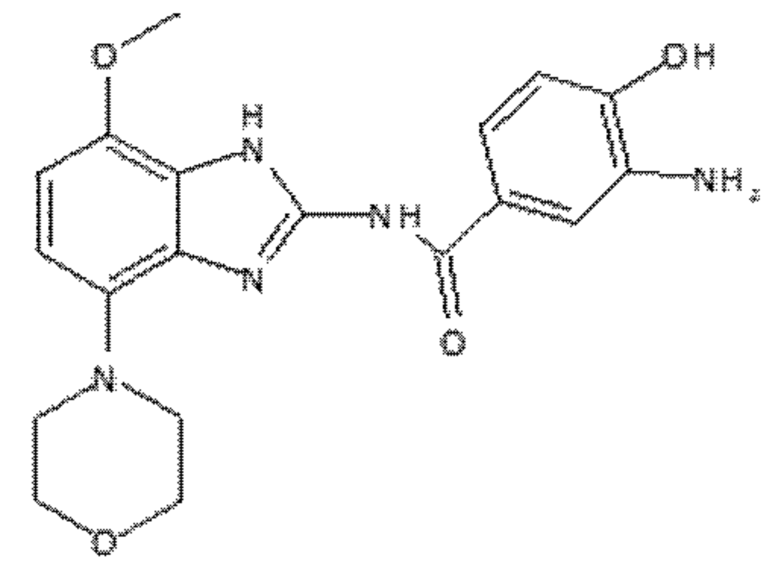
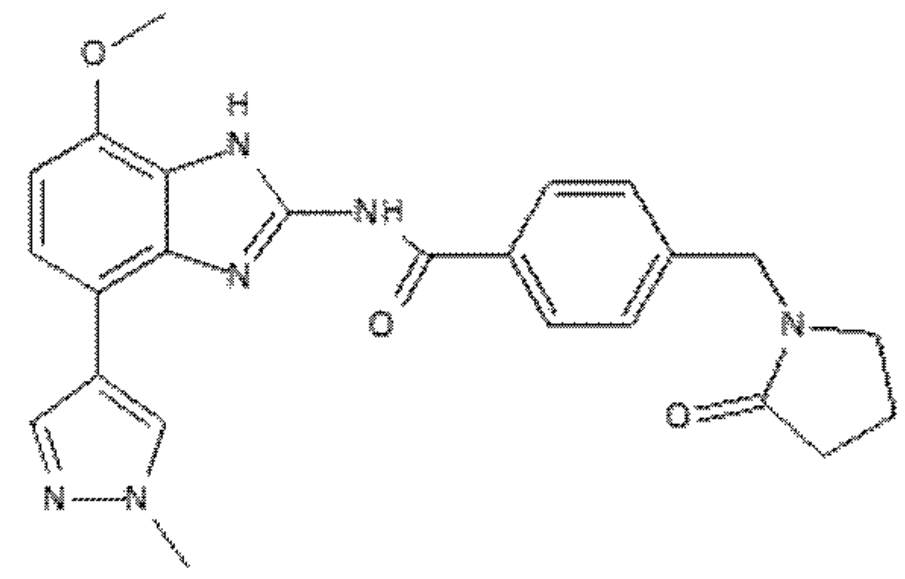
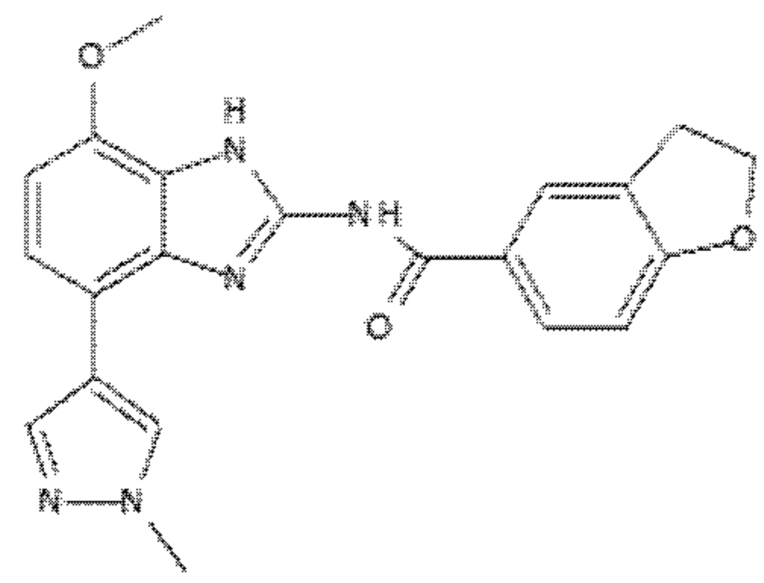
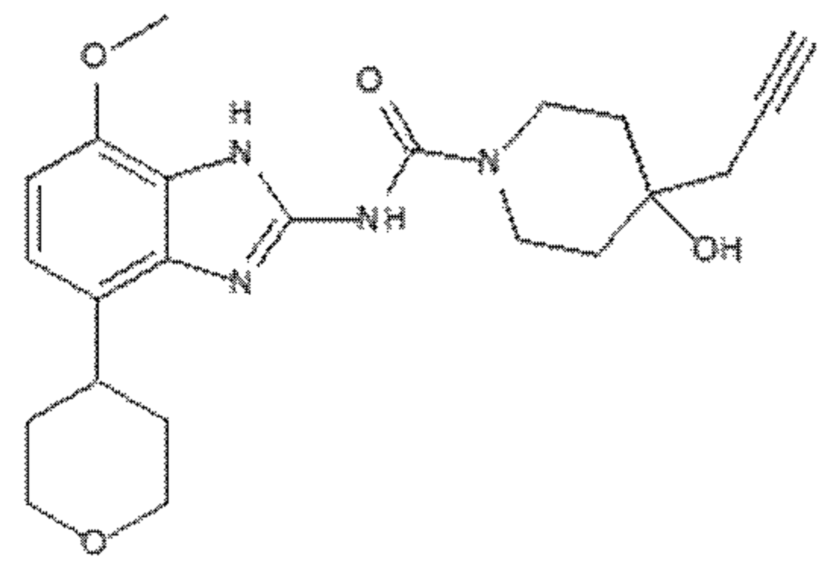
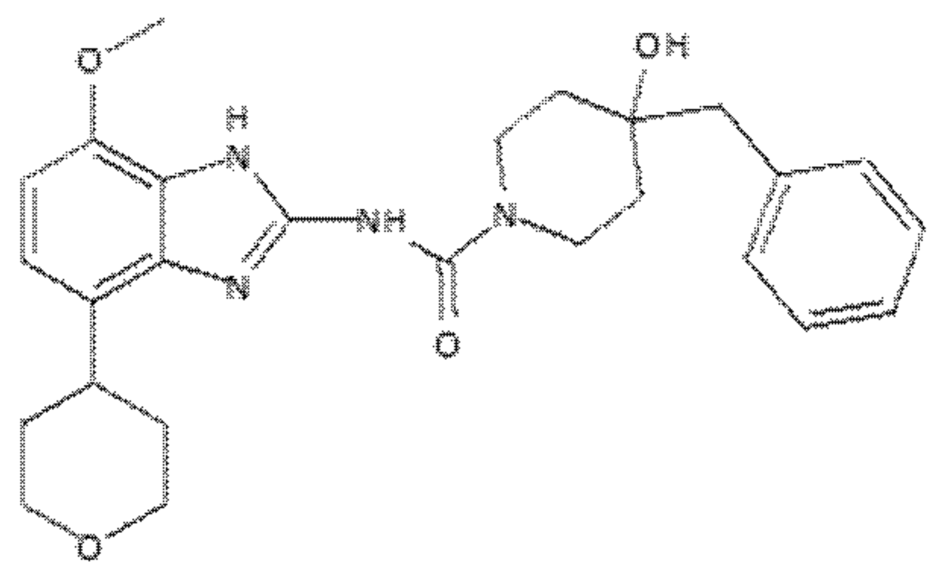
74		4-hydroxy-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
75		4-benzyl-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
76		4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
77		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
78		4-hydroxy-N-{7-methoxy-4-[1-(oxan-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide

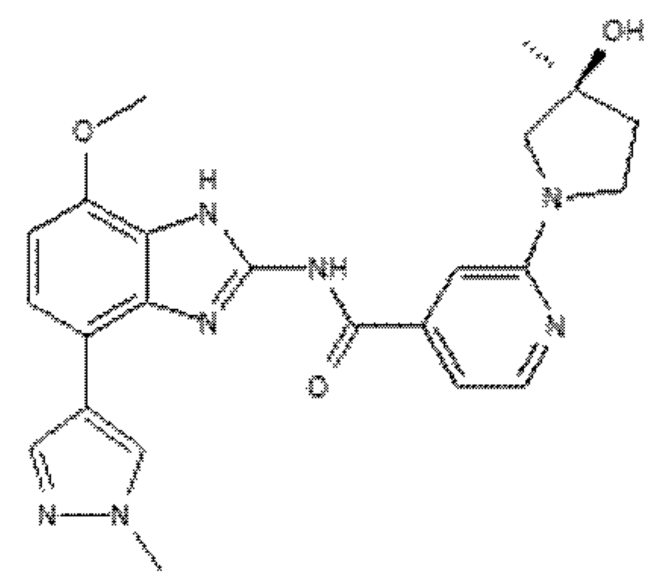
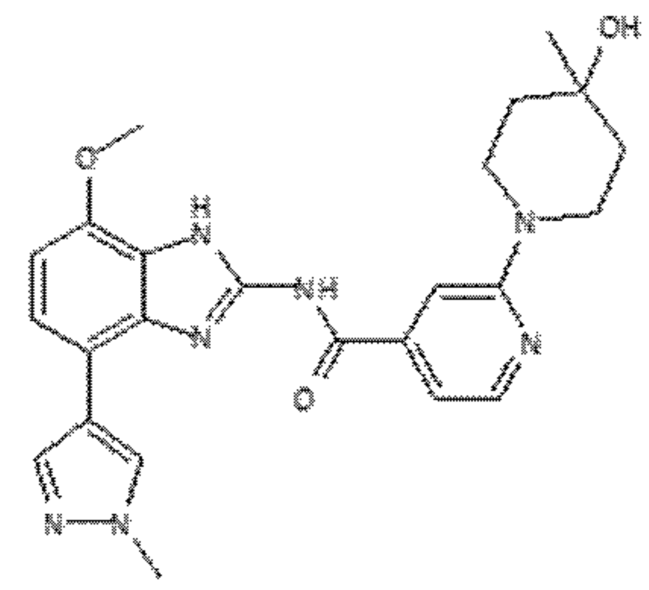
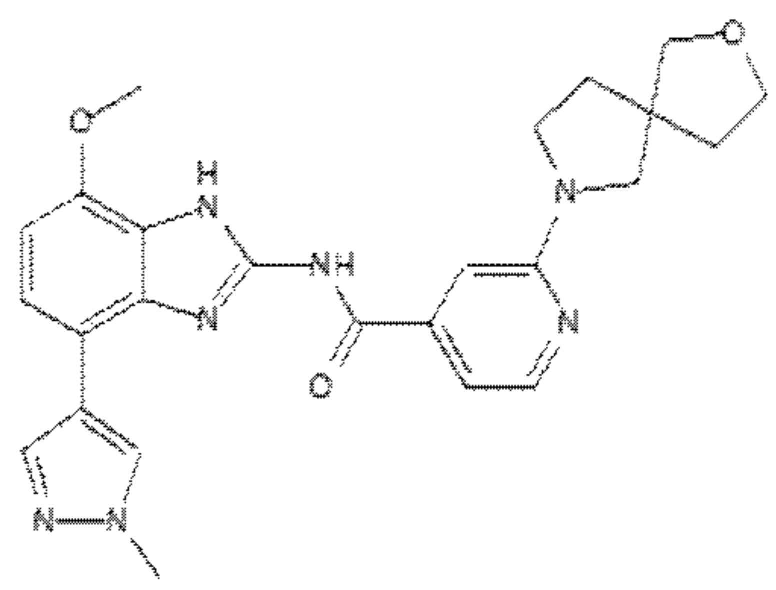
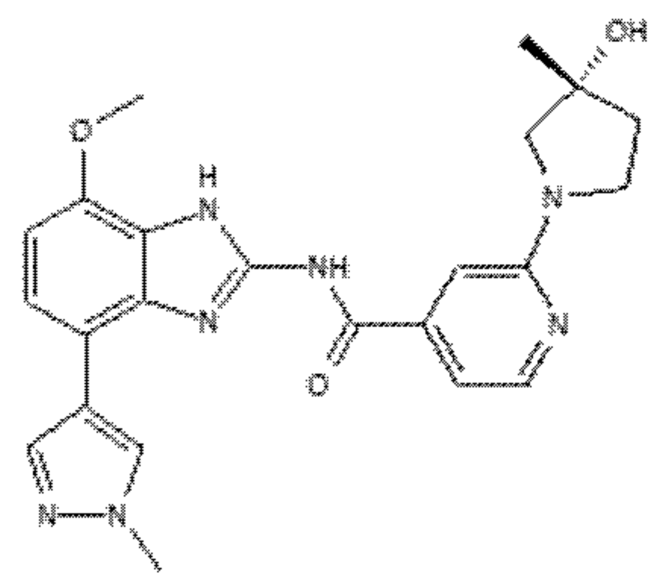
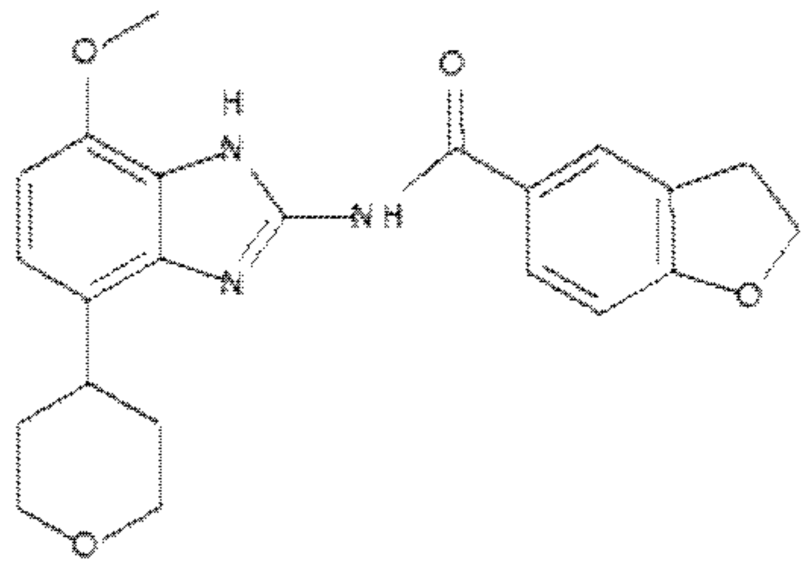
79		4-hydroxy-N-[7-methoxy-4-(1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
80		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
81		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyrazine-2-carboxamide
82		4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-4-methylpiperidine-1-carboxamide
83		4-benzyl-4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]piperidine-1-carboxamide

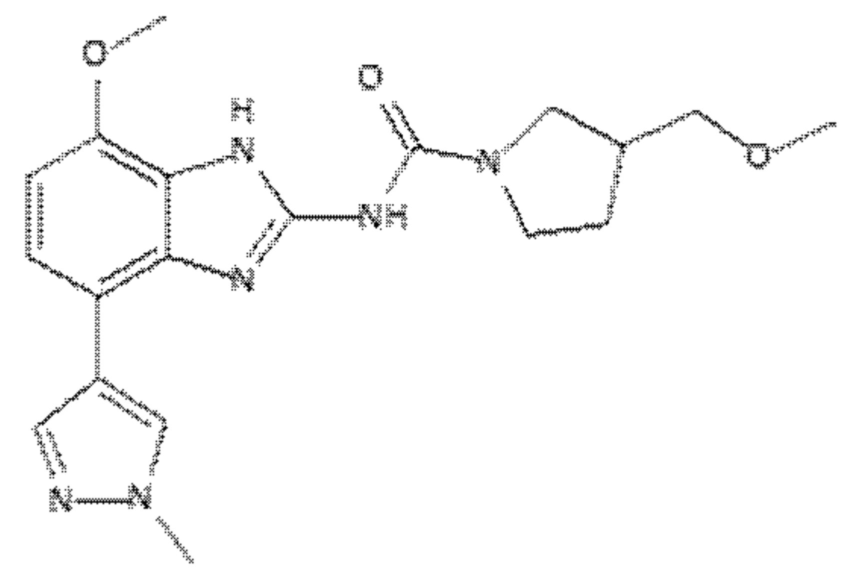
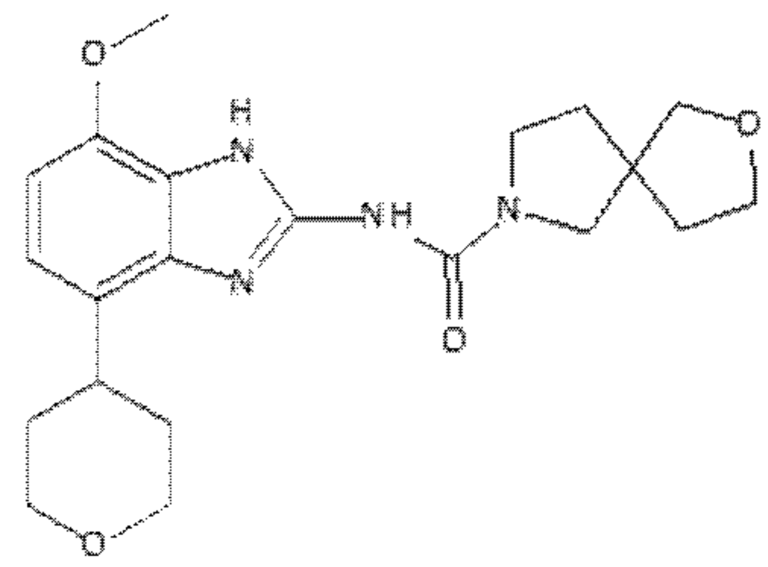
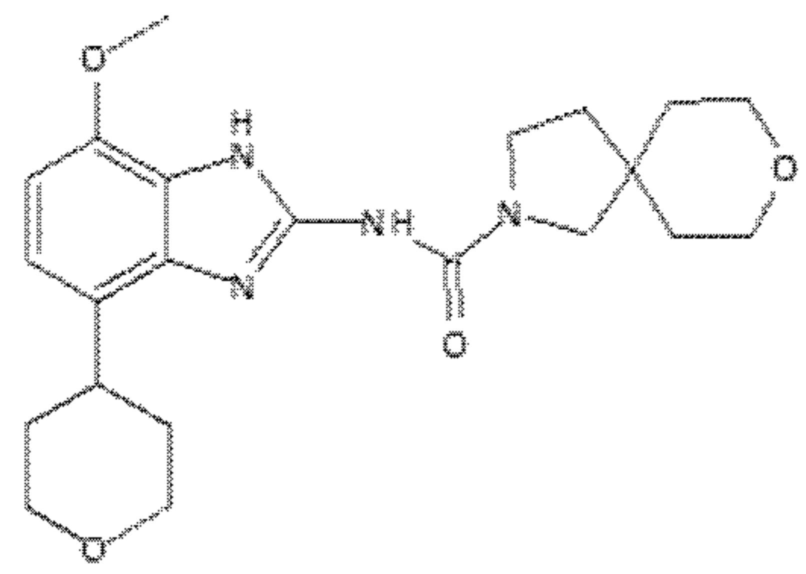
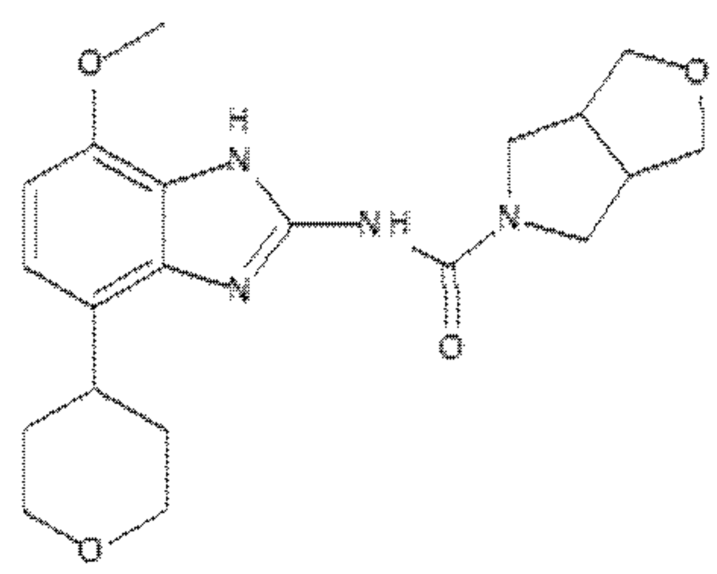
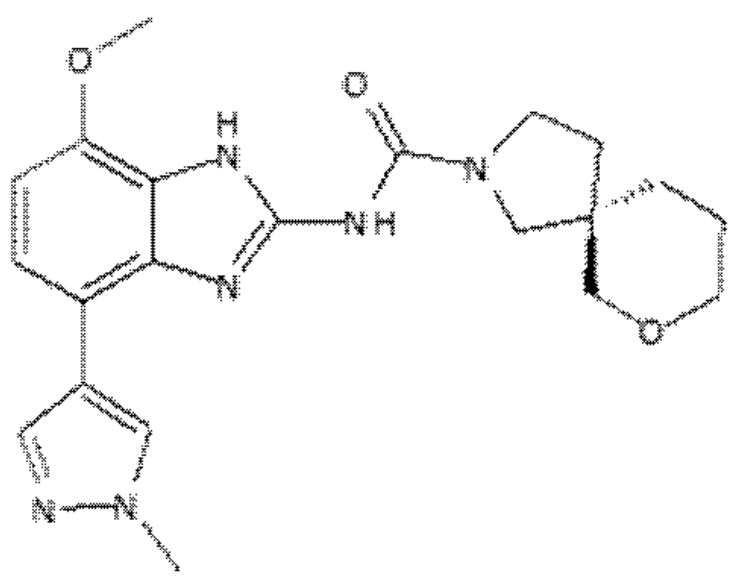
84		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2-oxazole-3-carboxamide
85		N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
86		1-(1-chloro-3-hydroxypropan-2-yl)-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-pyrazole-4-carboxamide
87		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
88		4-[(dimethylamino)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

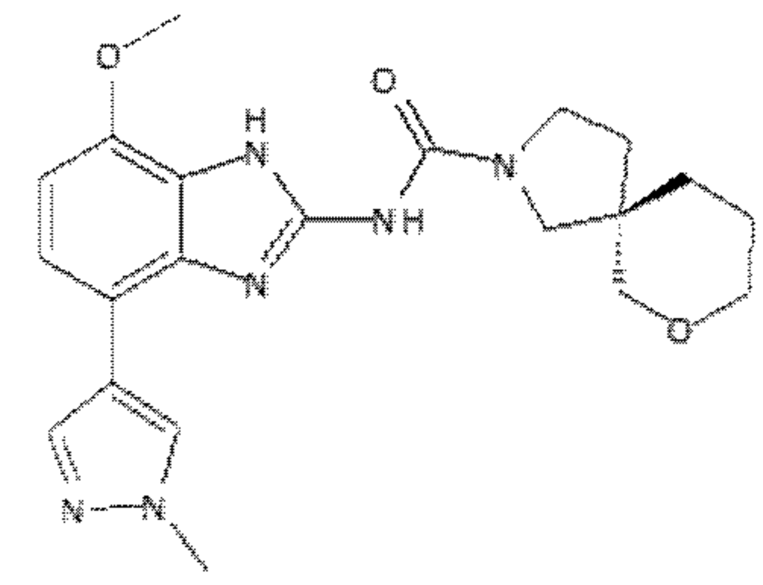
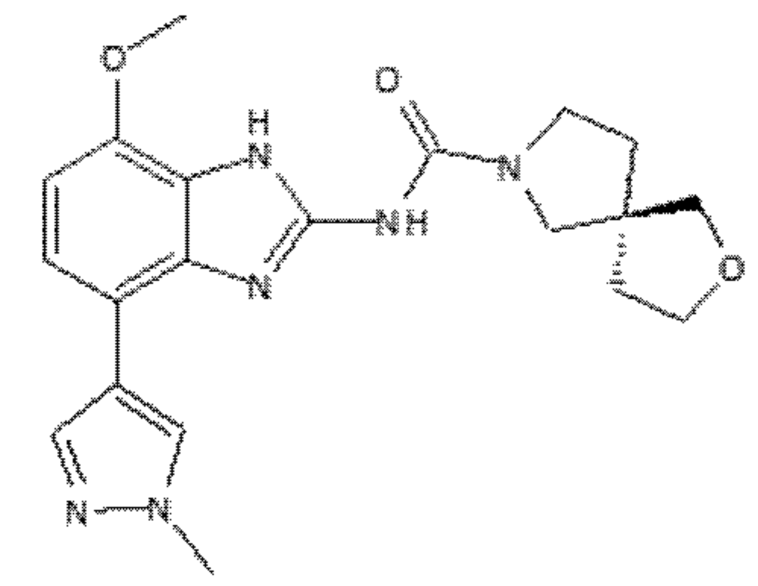
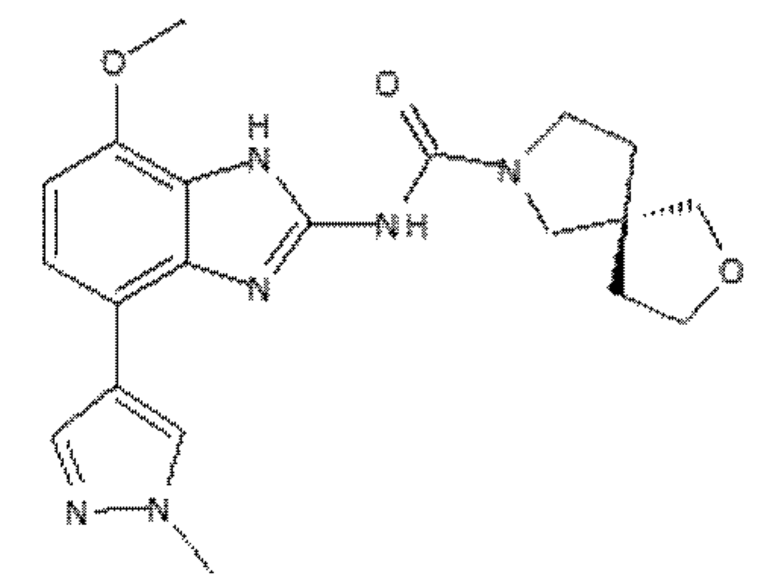
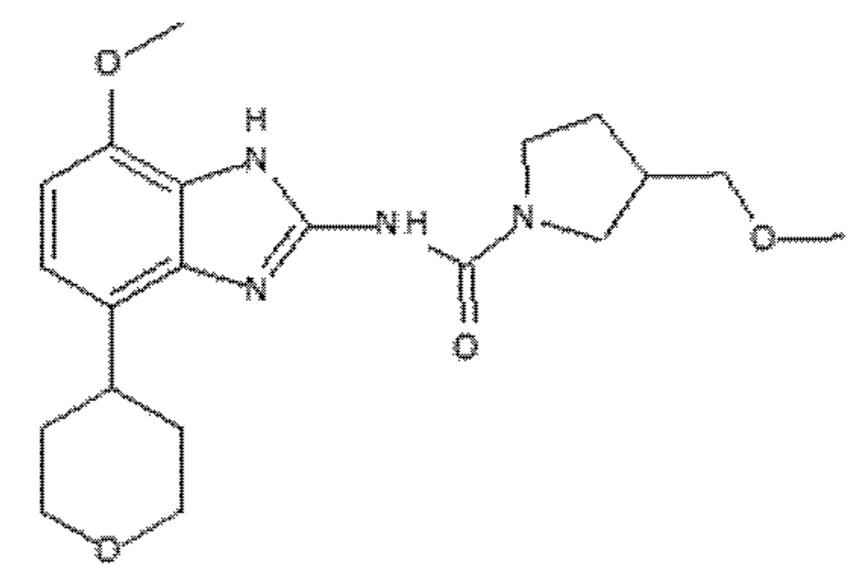
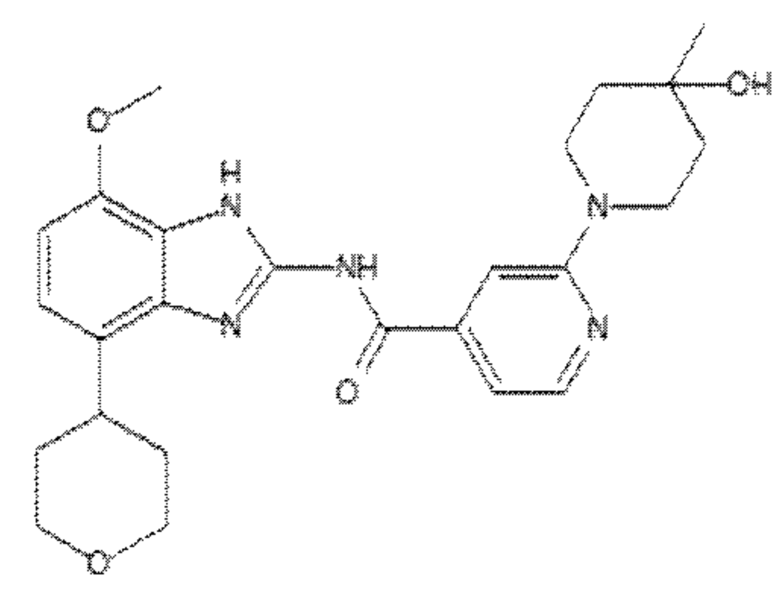
89		4-[(dimethylamino)methyl]-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
90		4-[(dimethylamino)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
91		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
92		4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
93		N4-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide

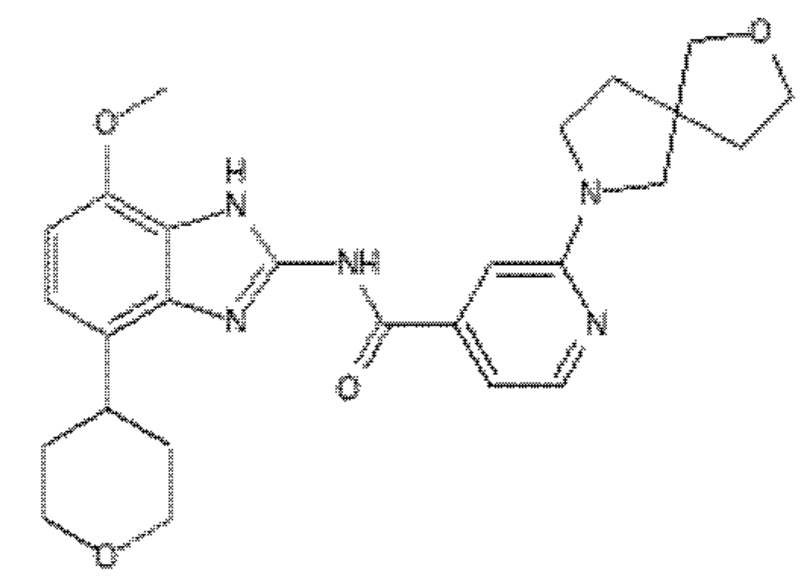
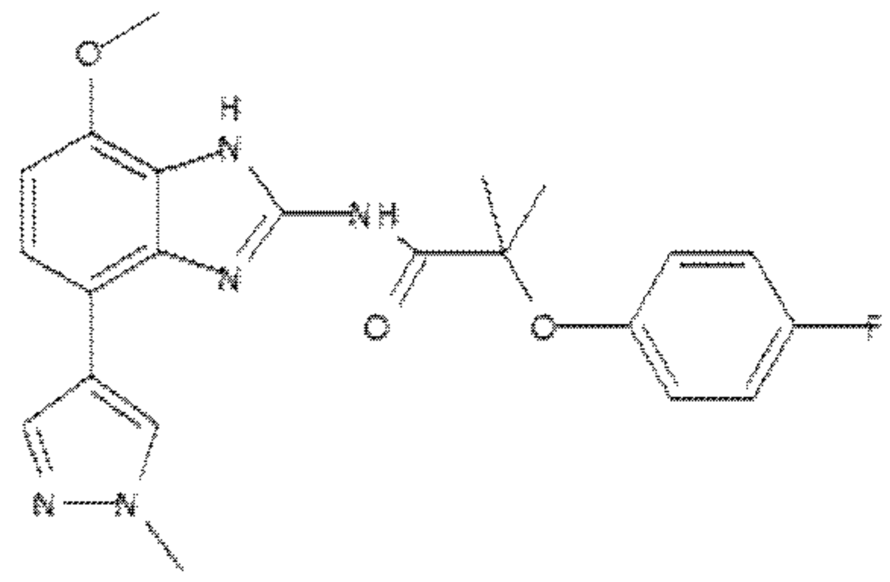
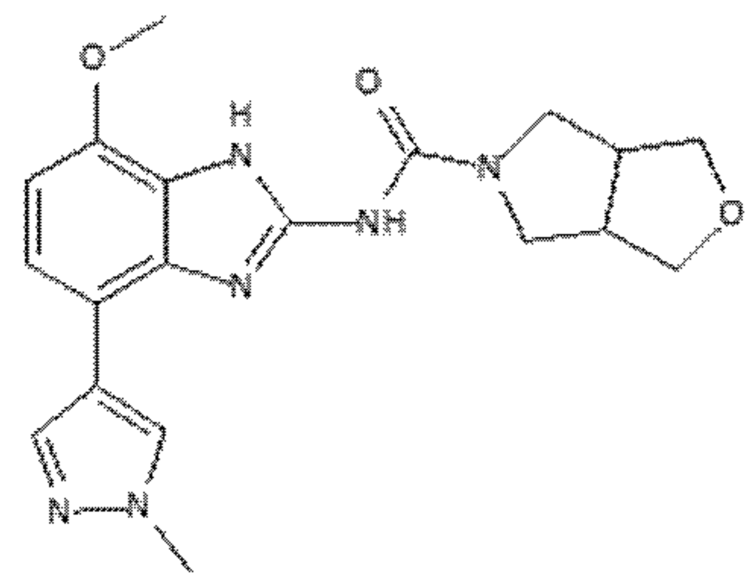
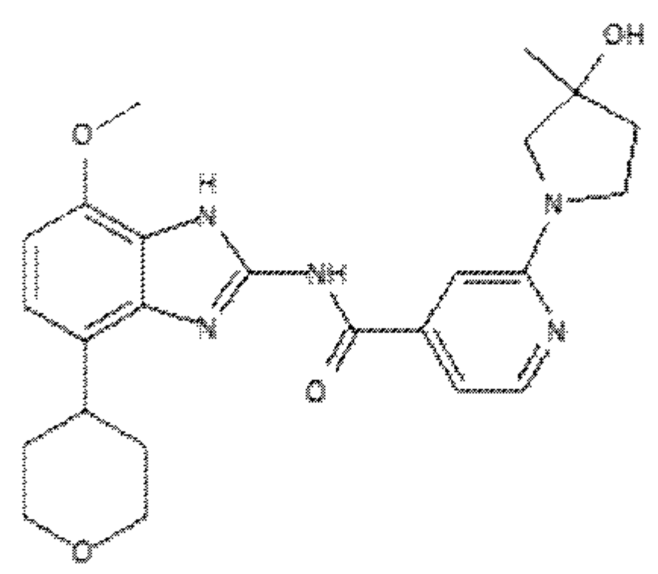
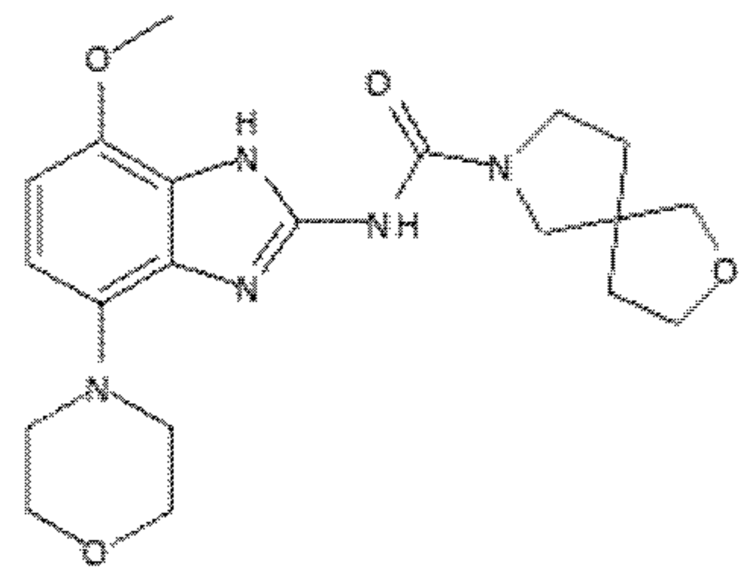
94		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(trifluoromethoxy)benzamide
95		2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
96		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-4-carboxamide
97		4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
98		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-benzoxazole-5-carboxamide

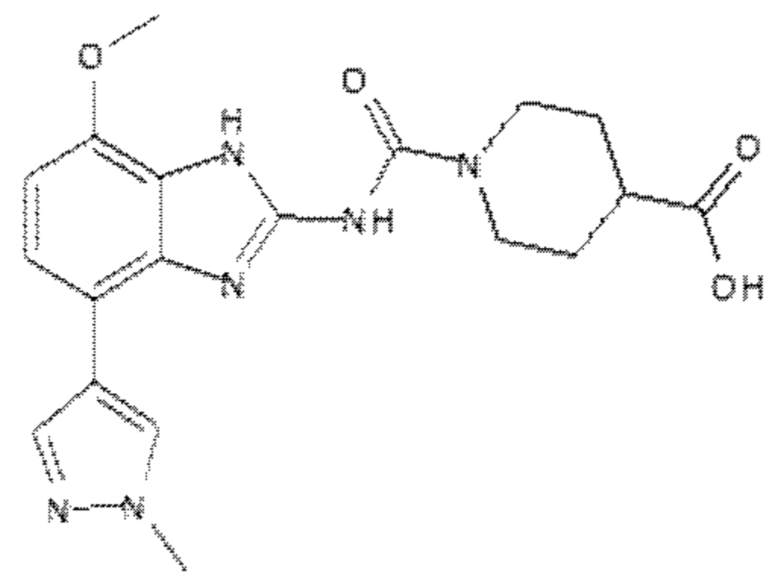
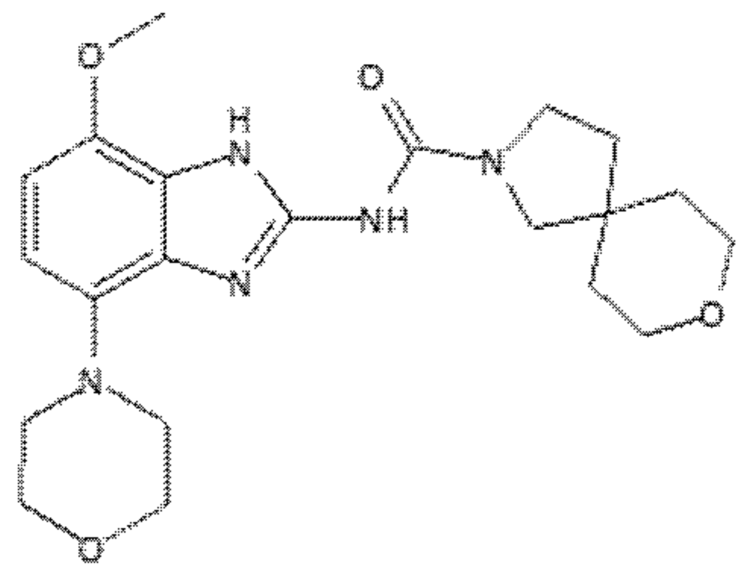
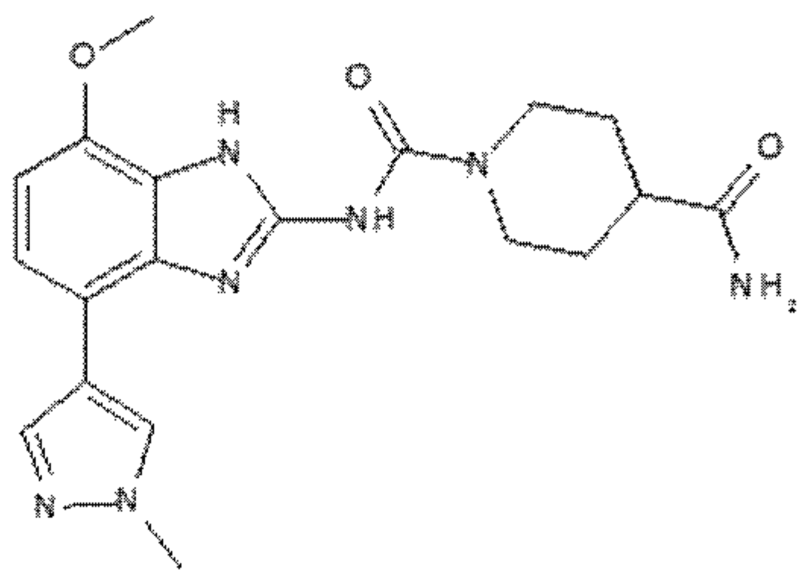
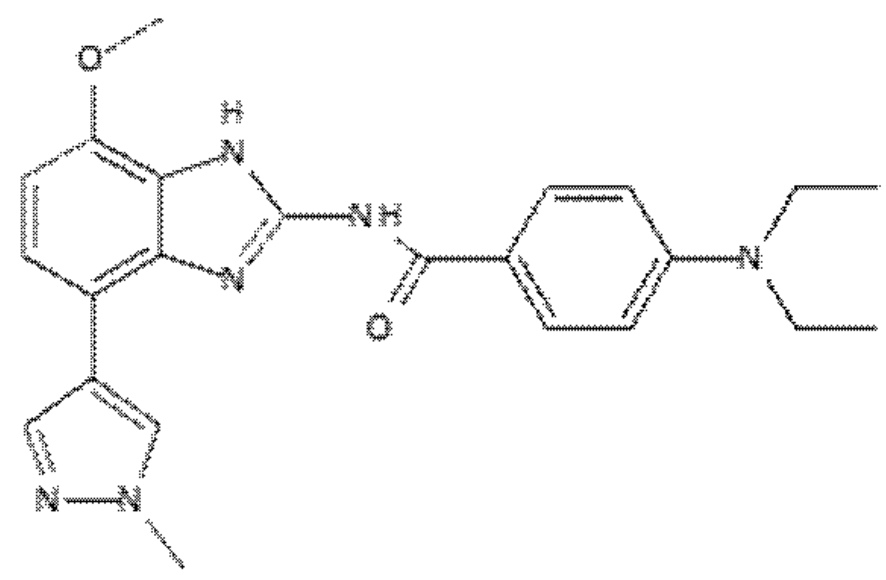
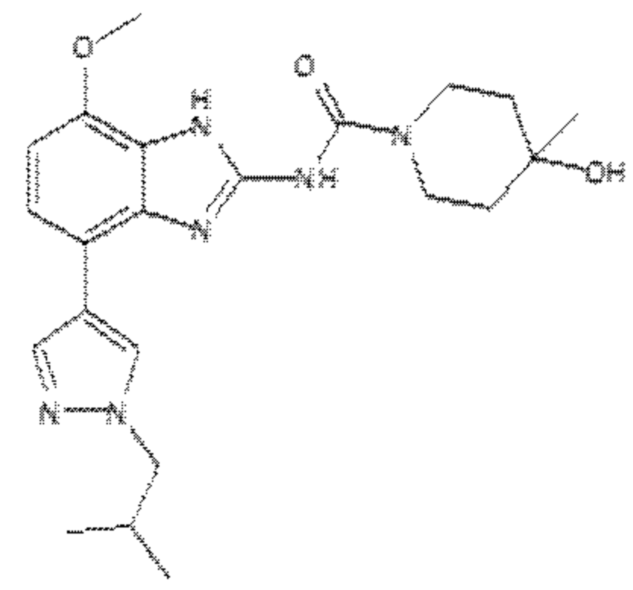
99		3-amino-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
100		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
101		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide
102		4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
103		4-benzyl-4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide

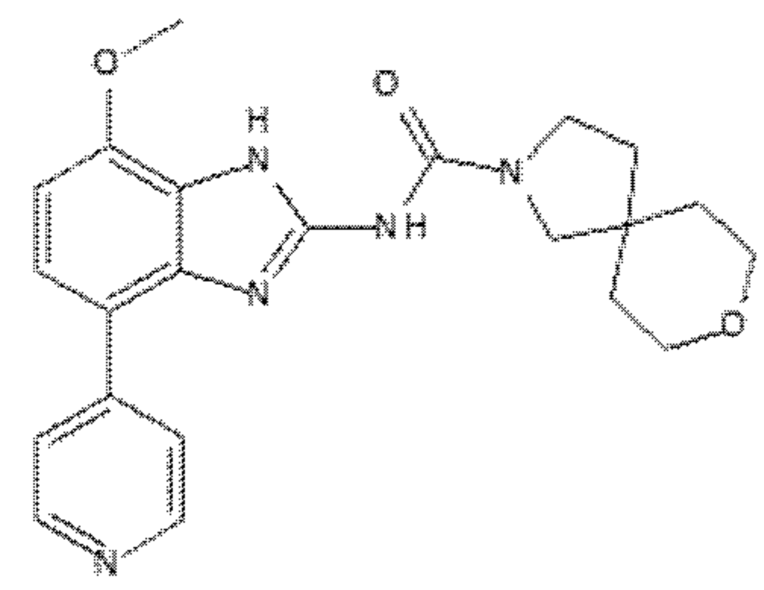
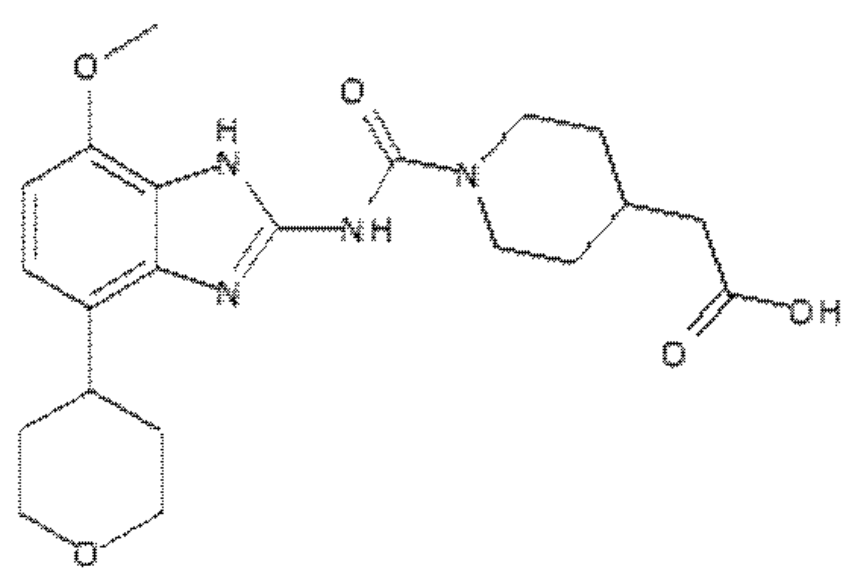
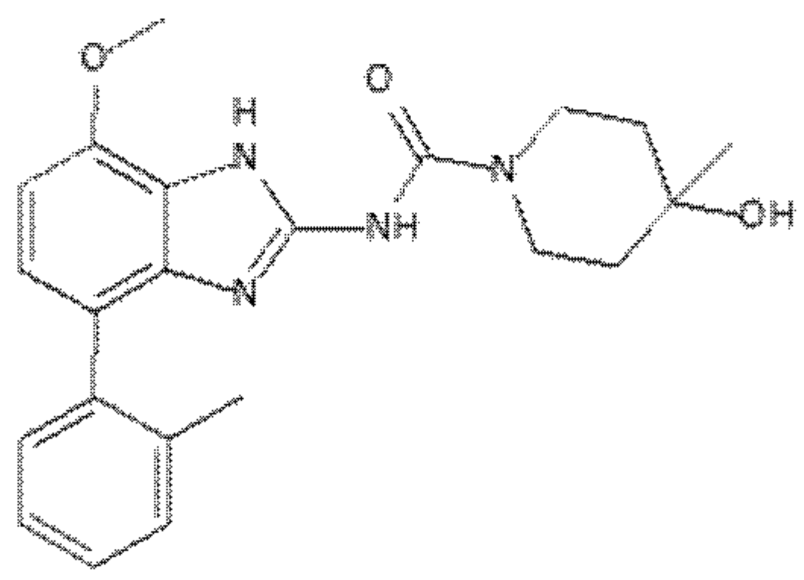
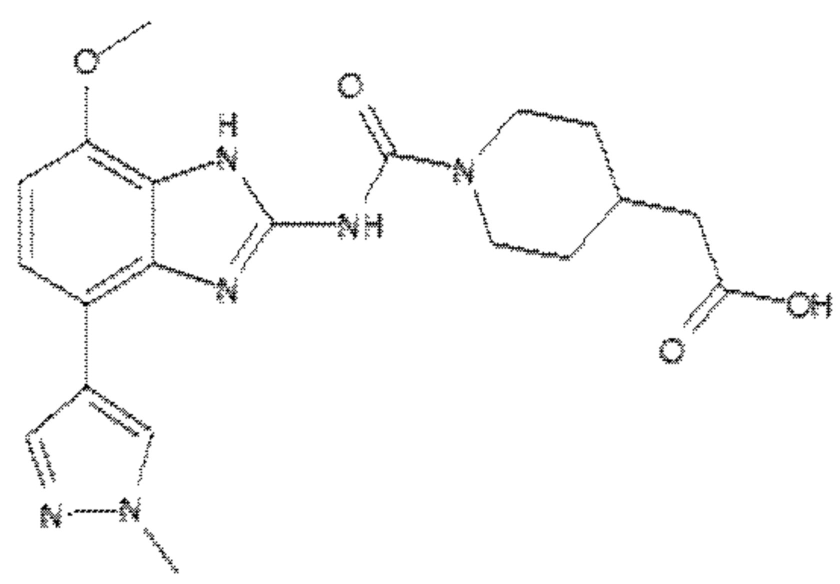
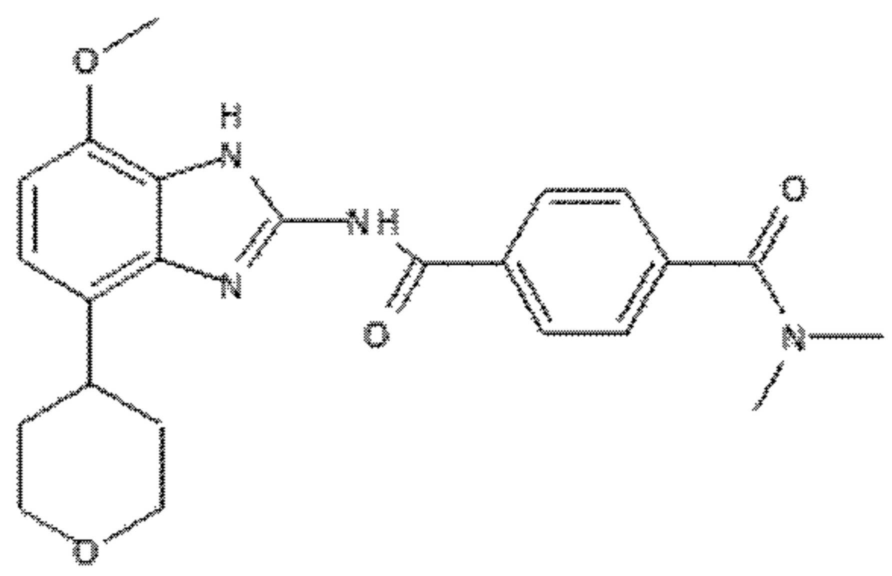
104		2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
105		2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
106		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
107		2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
108		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide

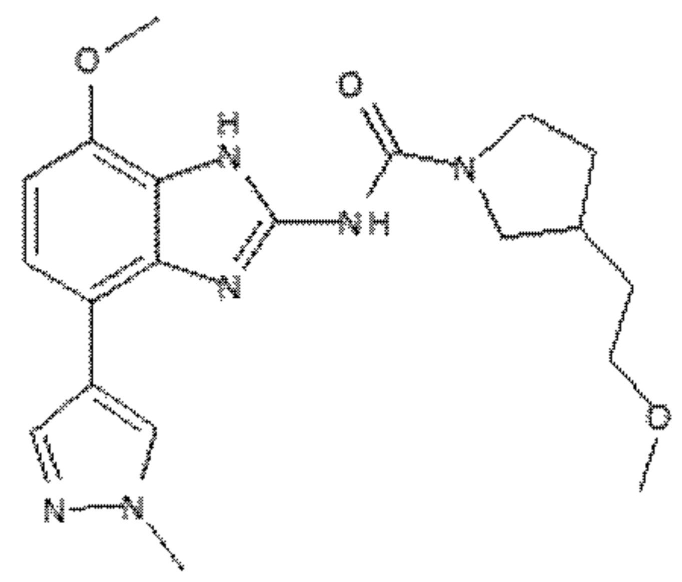
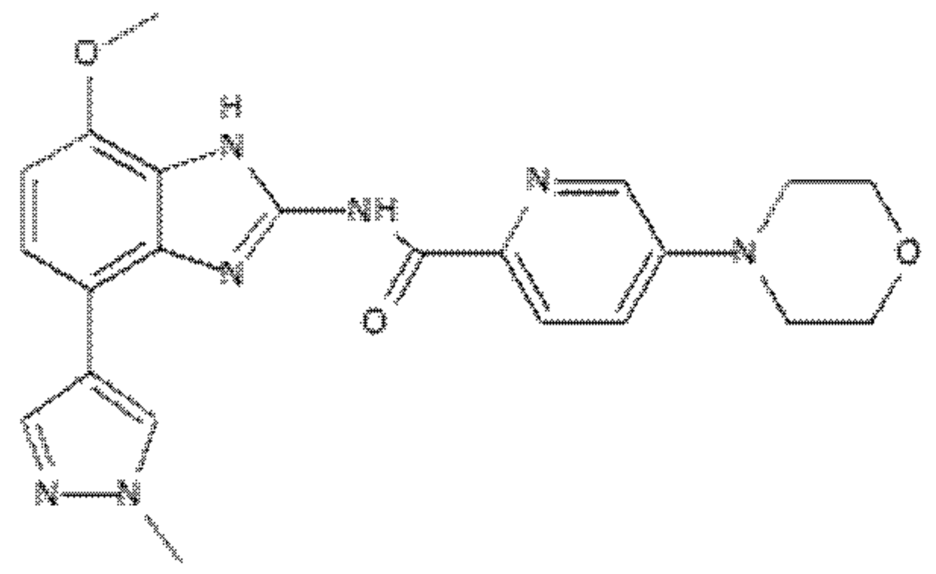
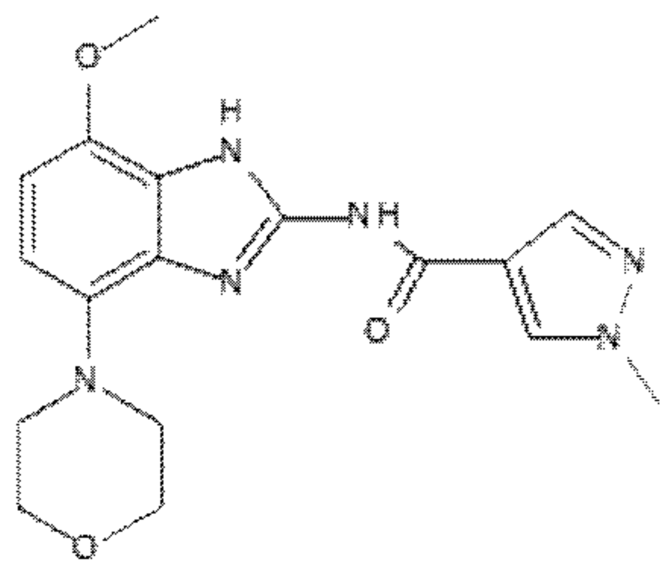
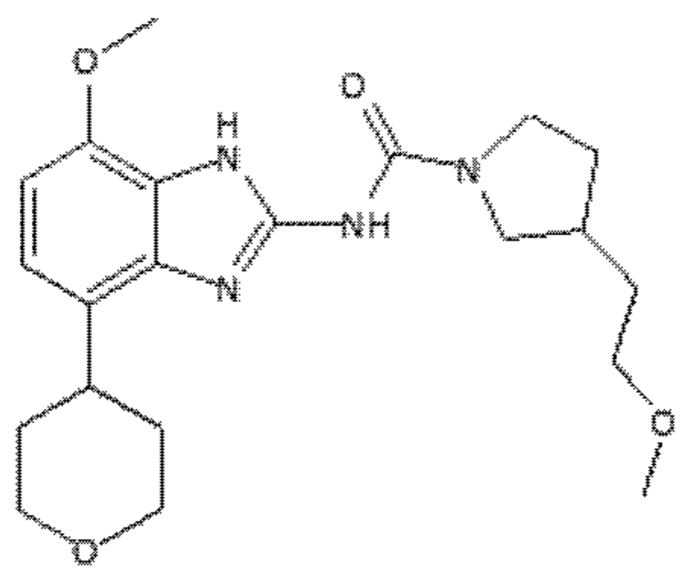
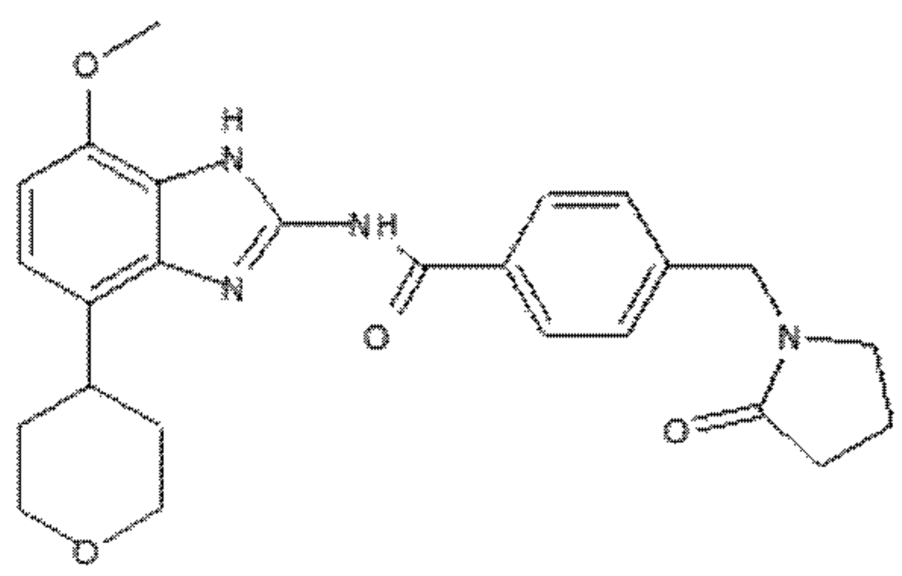
109		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
110		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
111		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
112		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
113		(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide

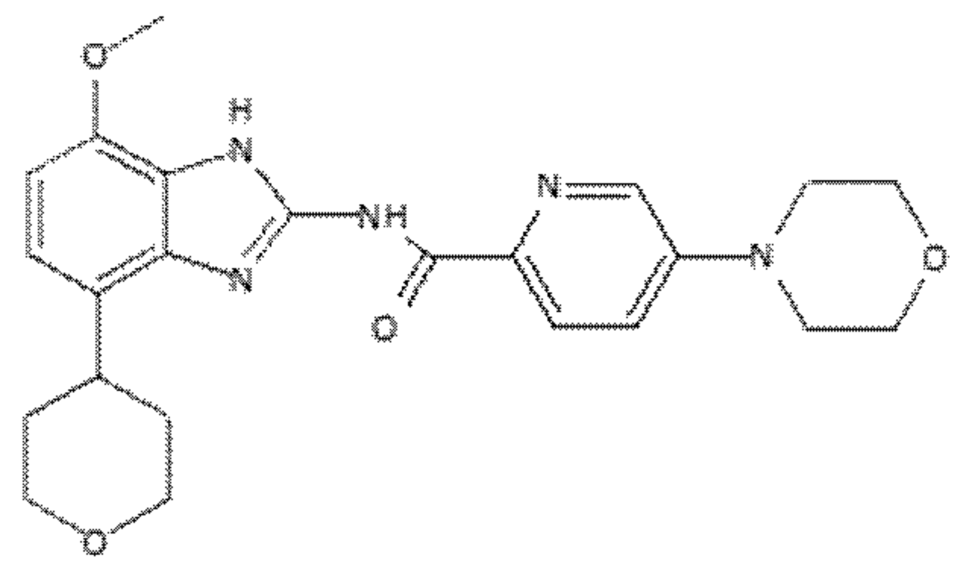
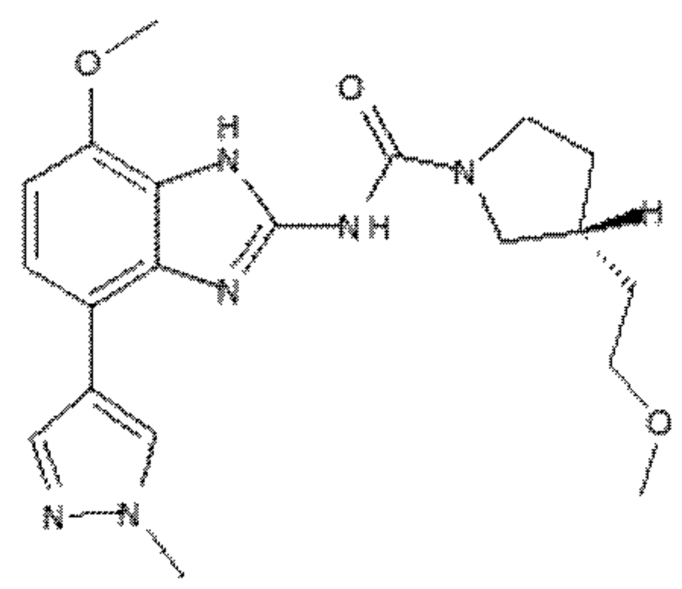
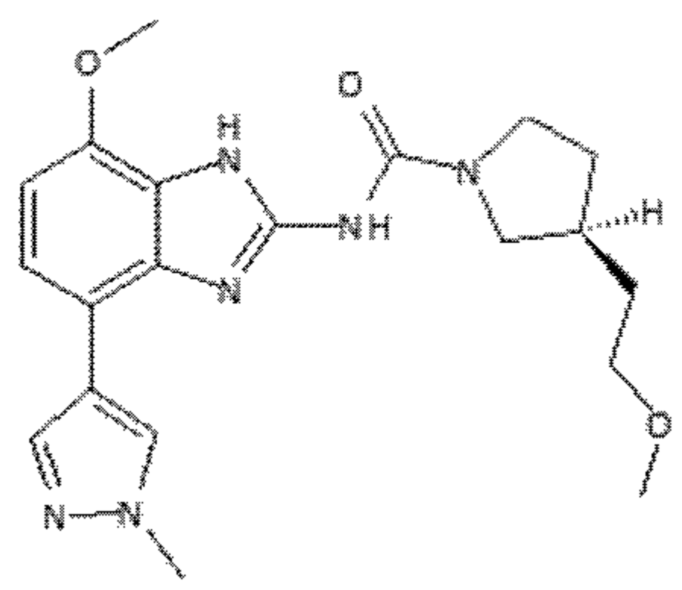
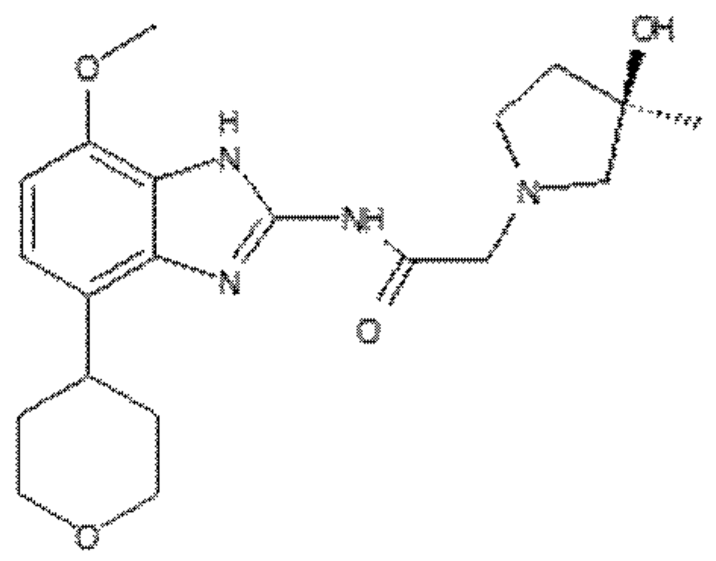
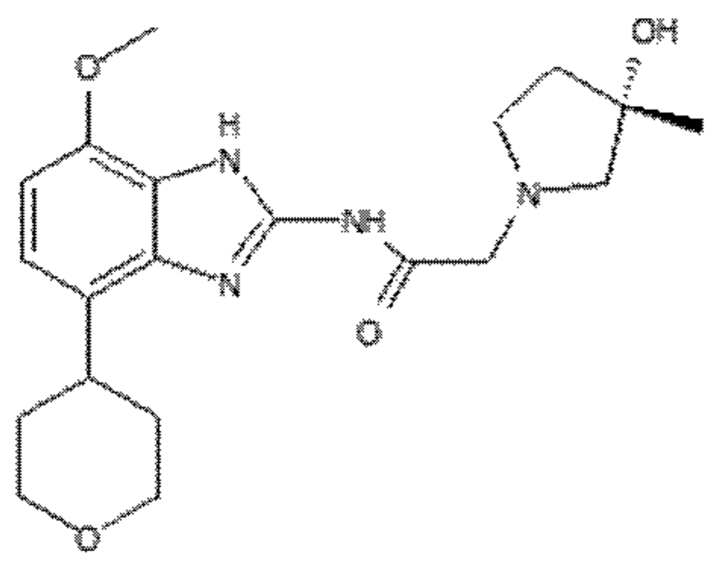
114		(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
115		(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
116		(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
117		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
118		2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide

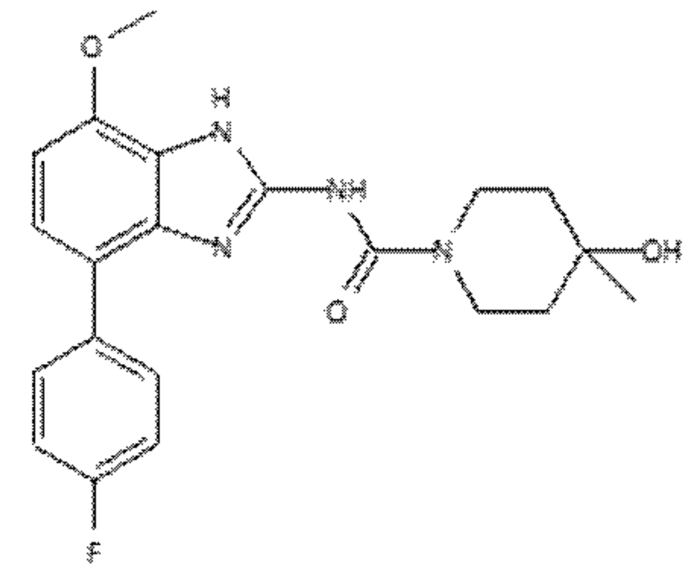
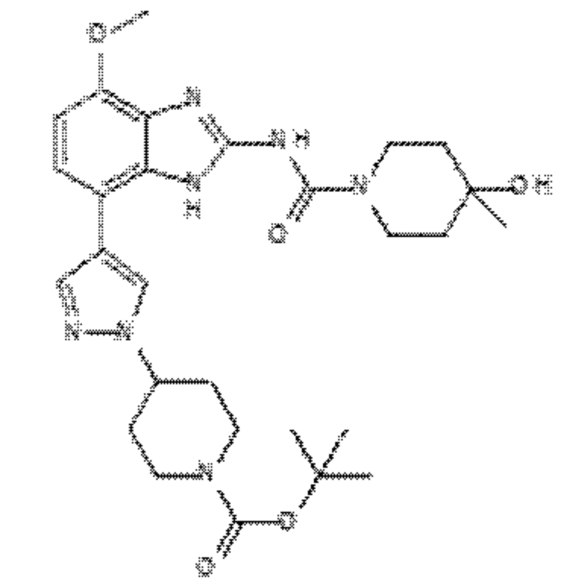
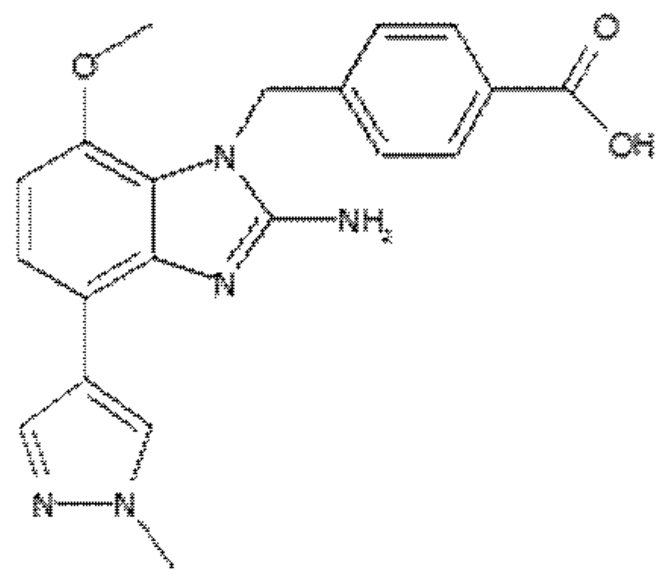
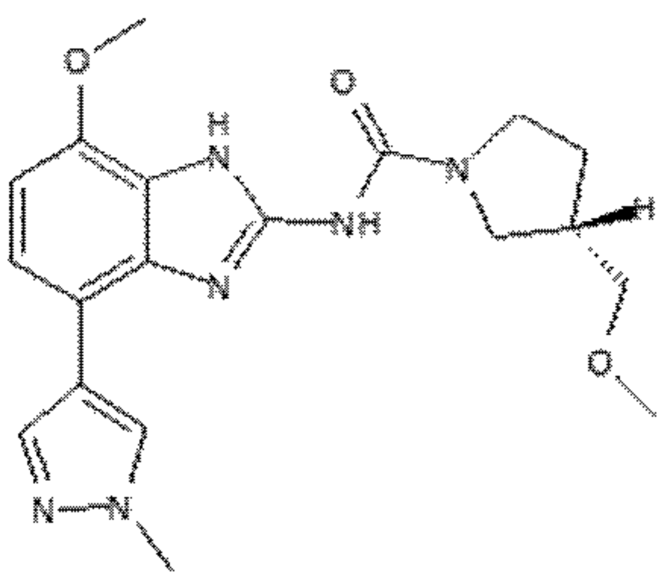
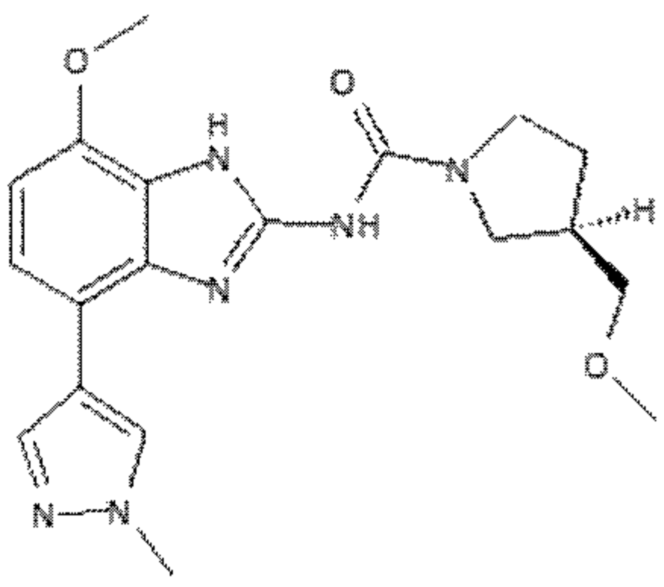
119		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
120		2-(4-fluorophenoxy)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methylpropanamide
121		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
122		2-(3-hydroxy-3-methylpyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
123		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide

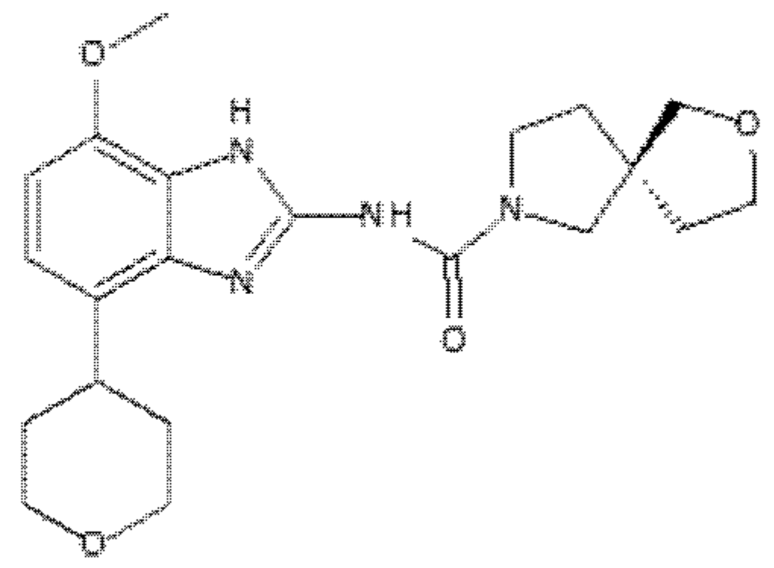
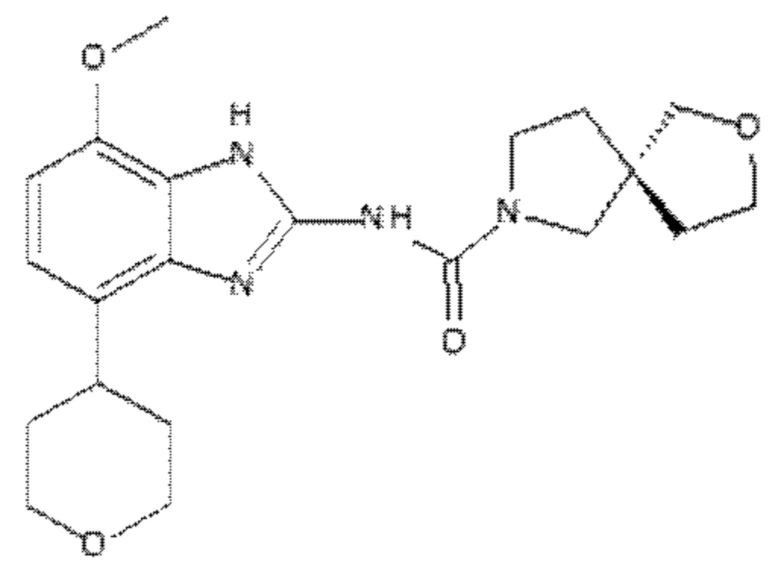
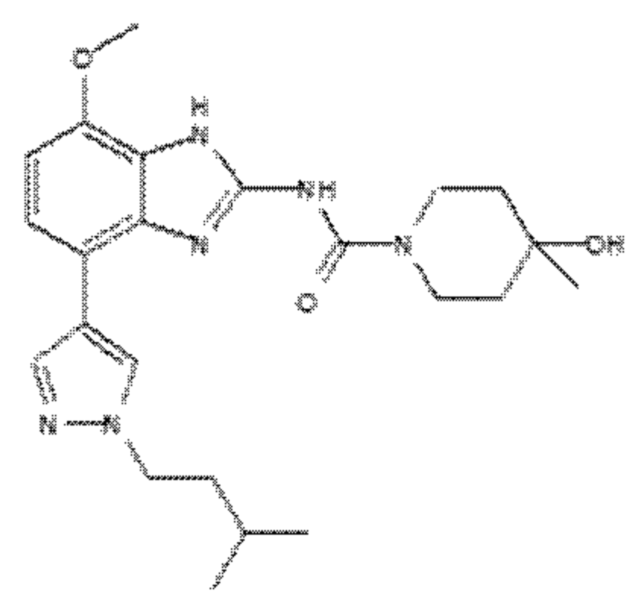
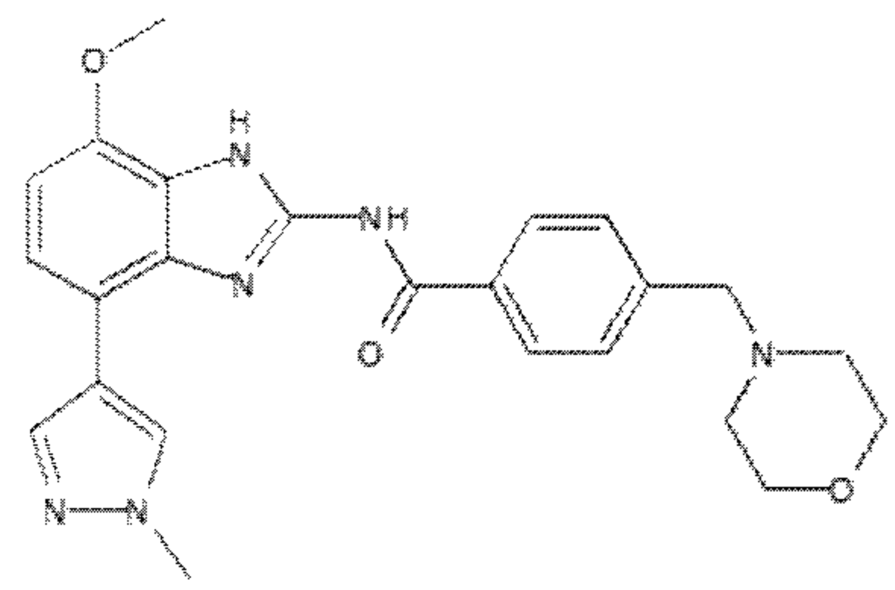
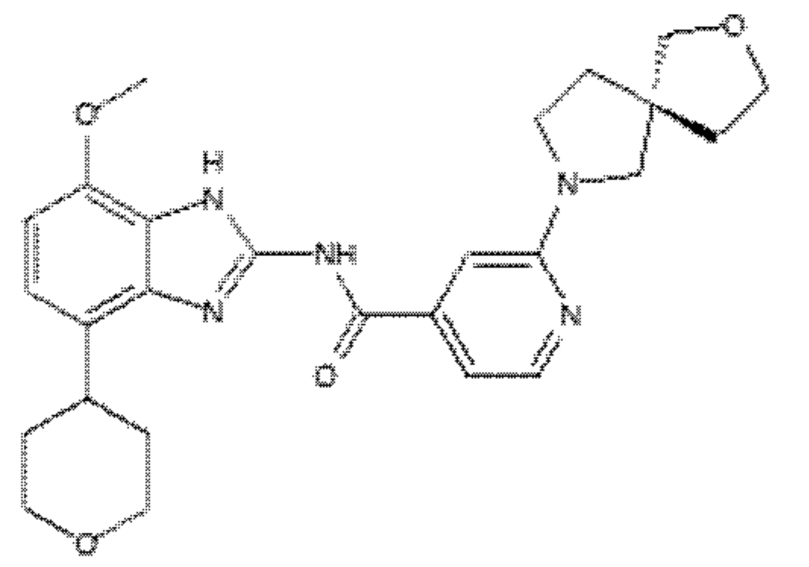
124		1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidine-4-carboxylic acid
125		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
126		N1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1,4-dicarboxamide
127		4-(diethylamino)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
128		4-hydroxy-N-{7-methoxy-4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide

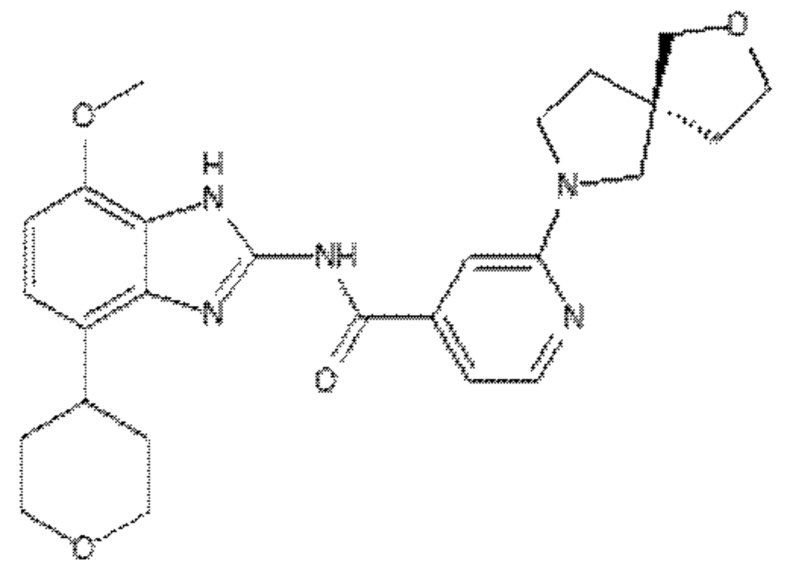
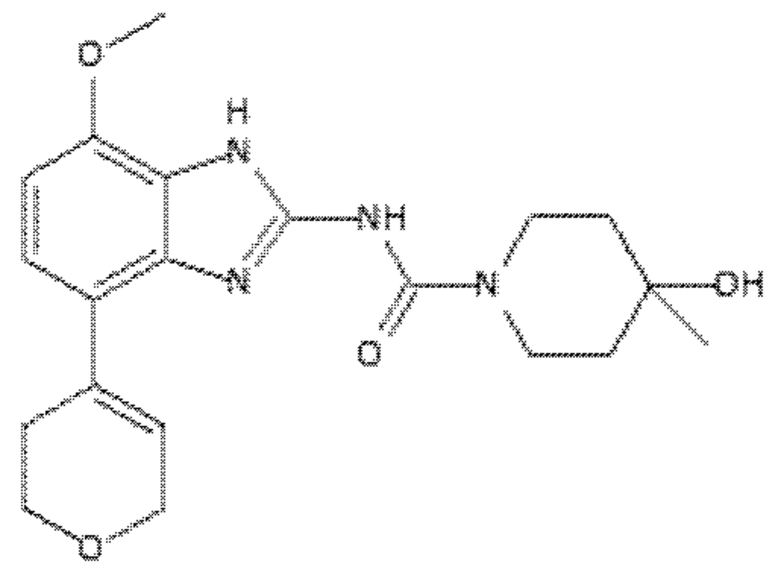
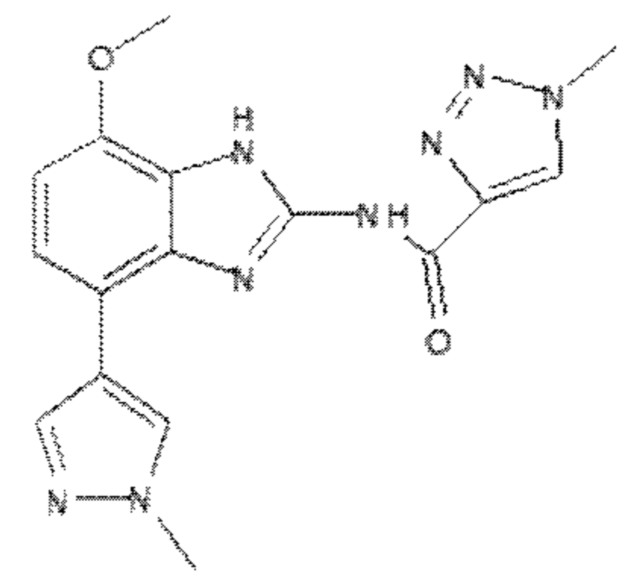
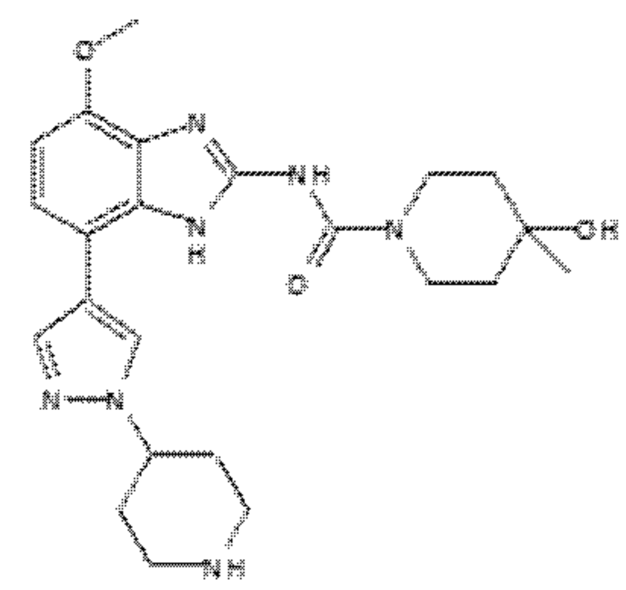
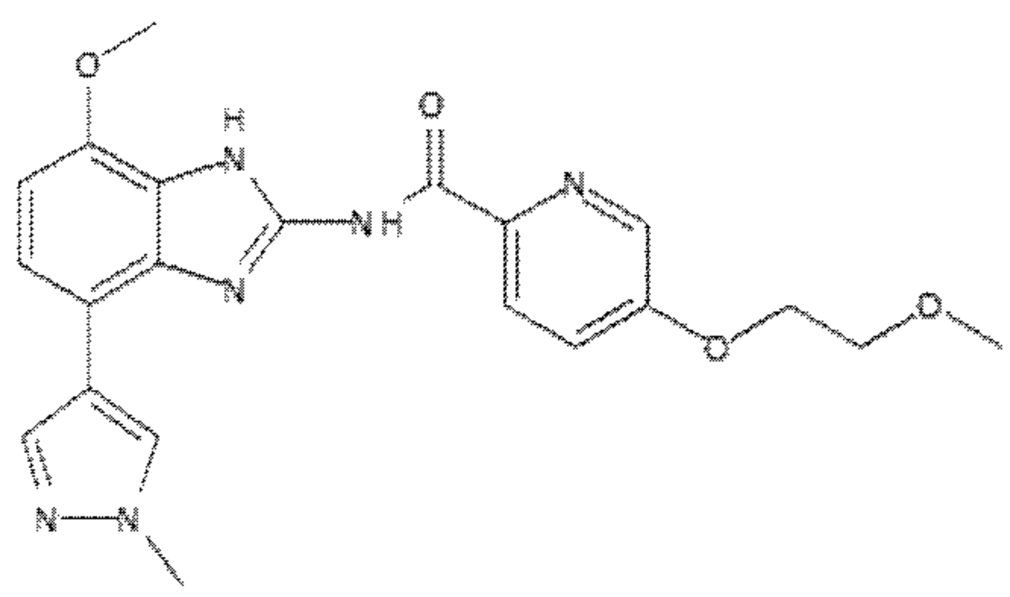
129		N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
130		2-(1-{[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid
131		4-hydroxy-N-[7-methoxy-4-(2-methylphenyl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
132		2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid
133		N4-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide

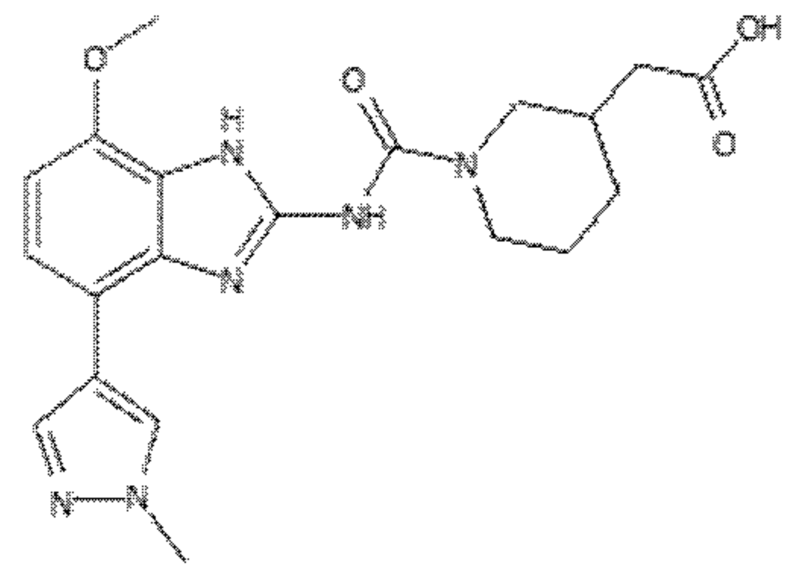
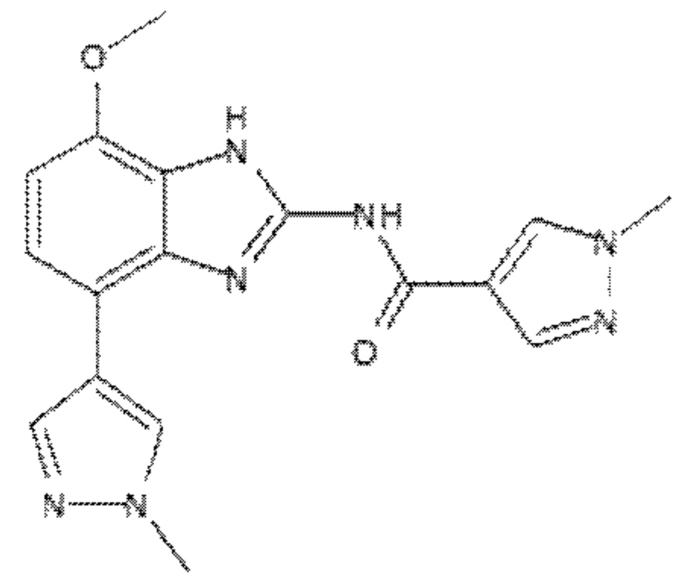
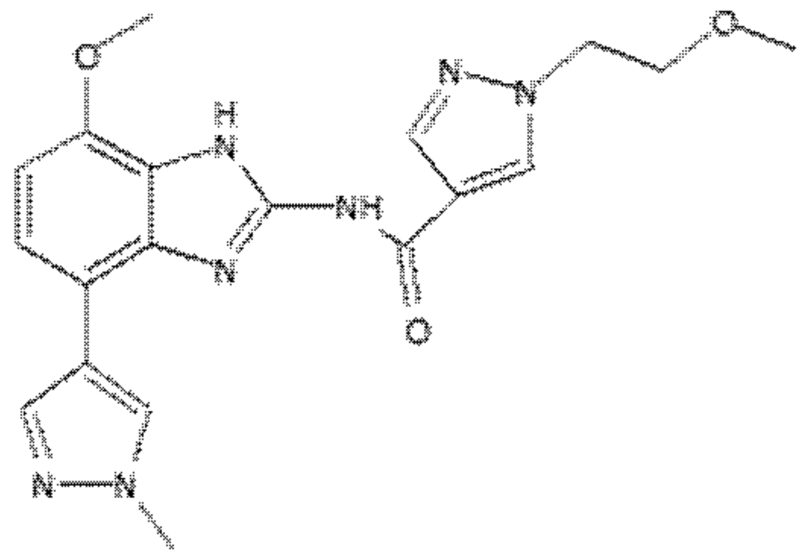
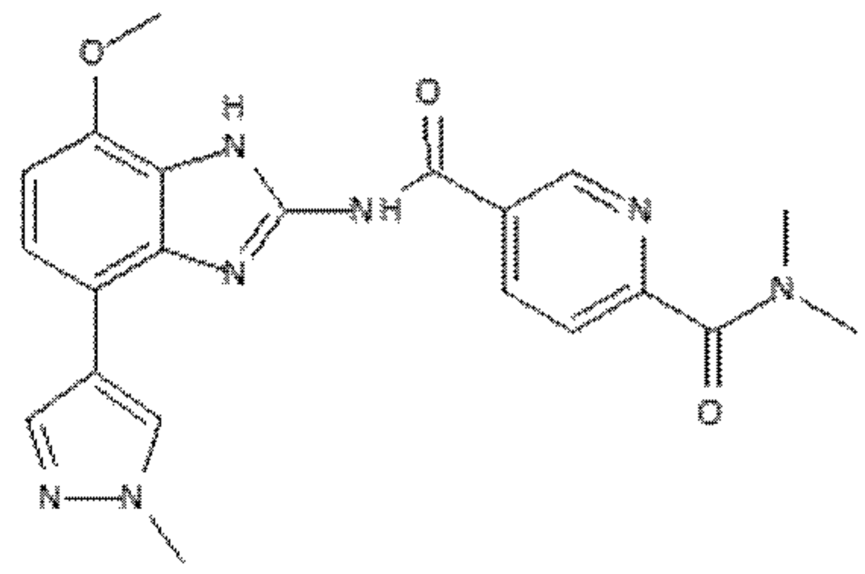
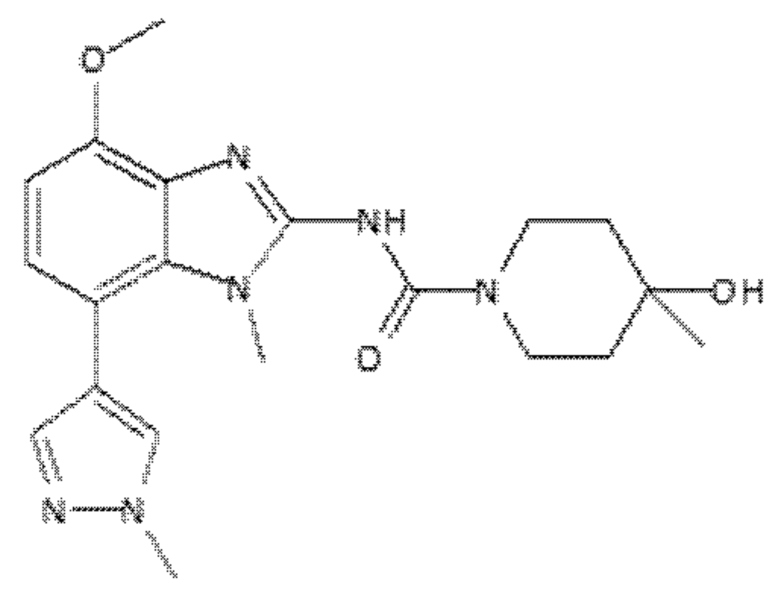
134		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
135		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide
136		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
137		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
138		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide

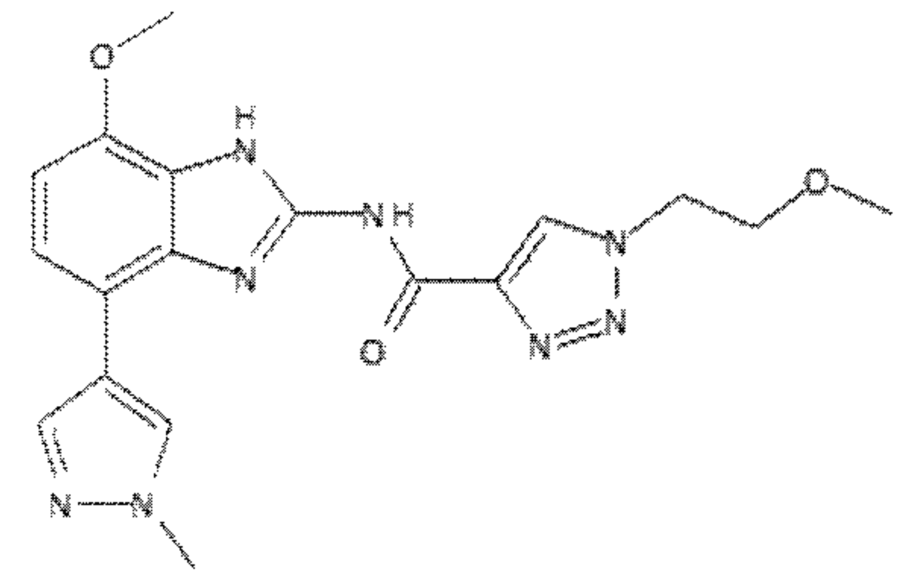
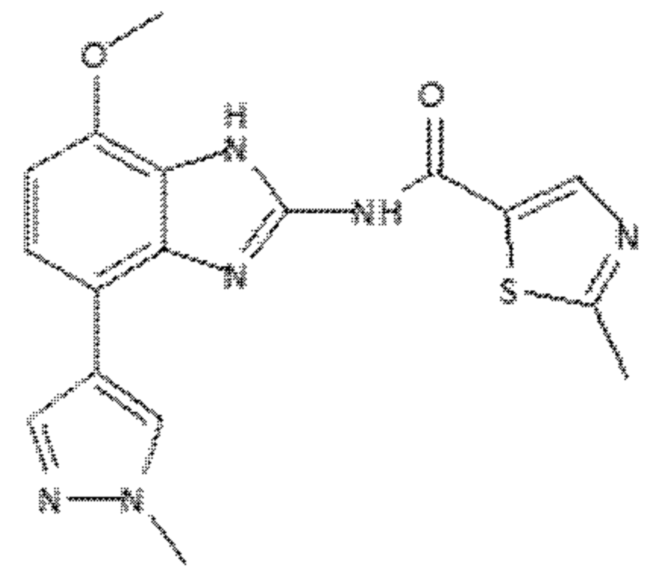
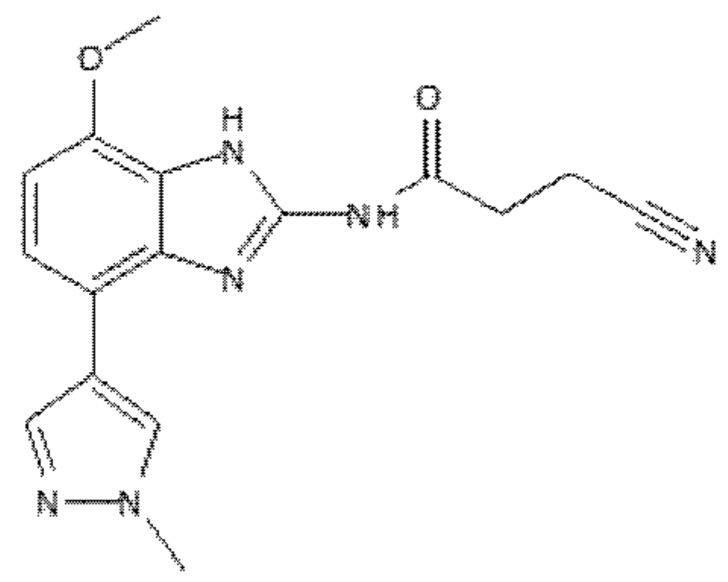
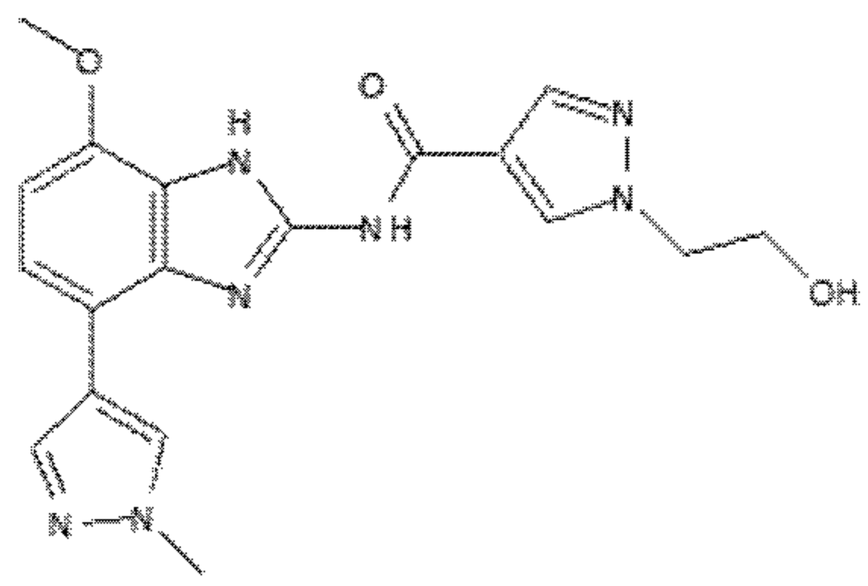
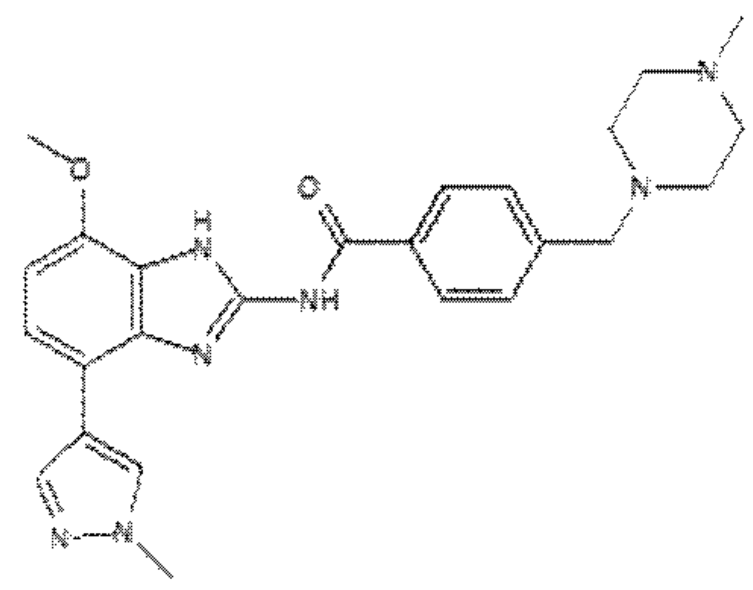
139		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide
140		(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
141		(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
142		2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
143		2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide

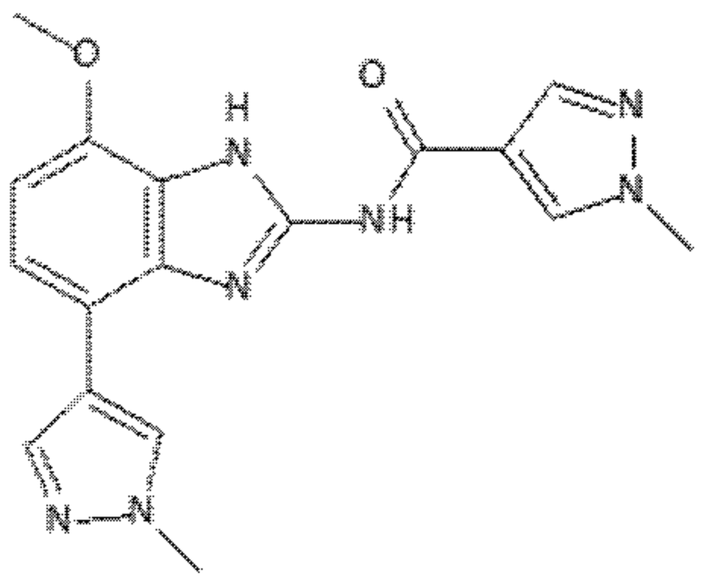
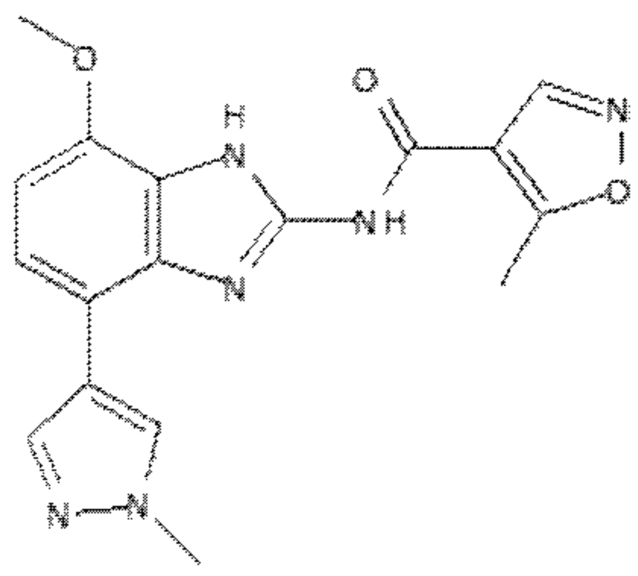
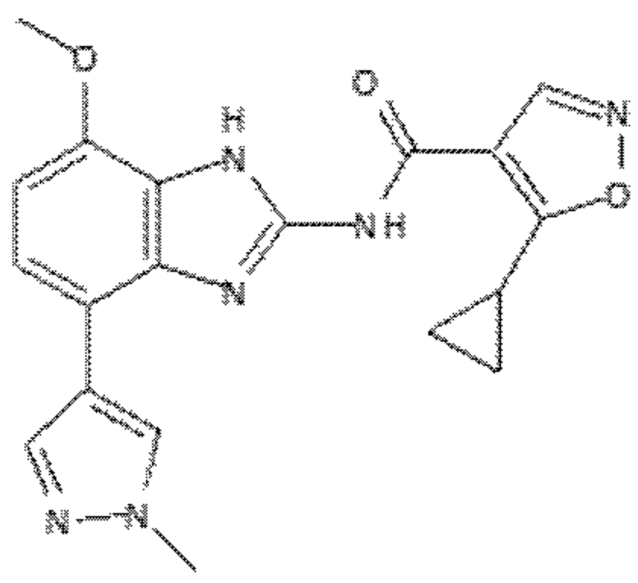
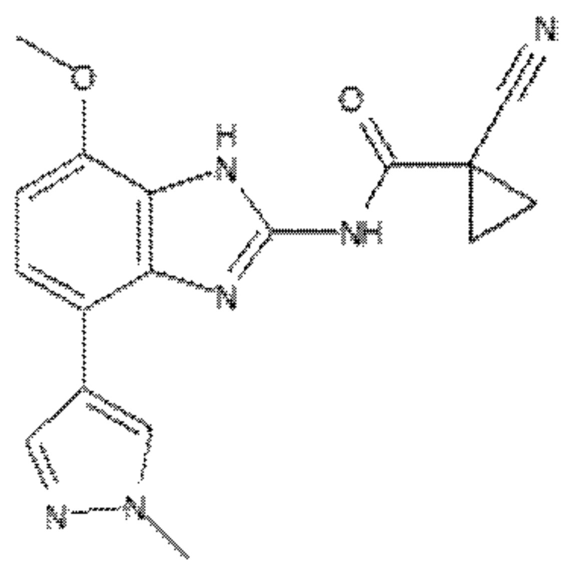
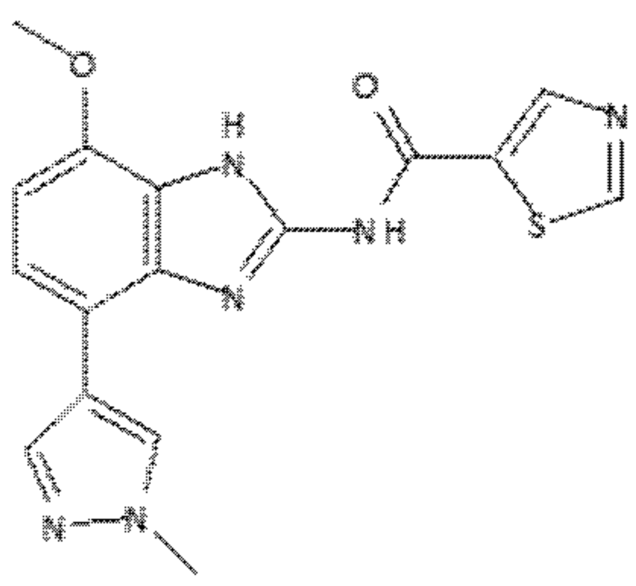
144		N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
145		tert-butyl 4-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)piperidine-1-carboxylate
146		4-{[2-amino-7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-1-yl]methyl}benzoic acid
147		(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
148		(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide

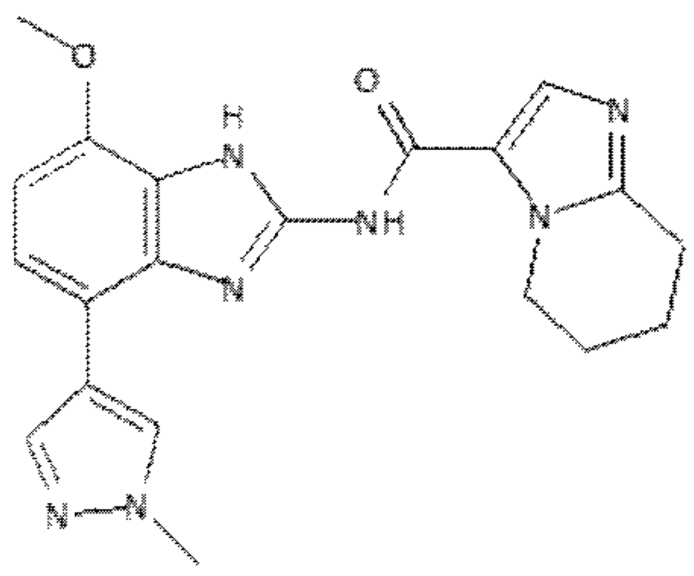
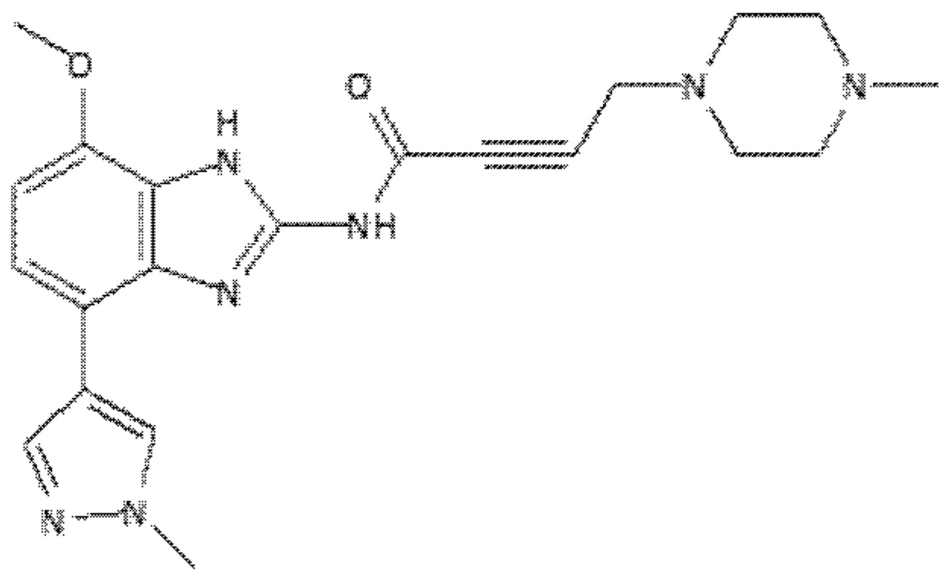
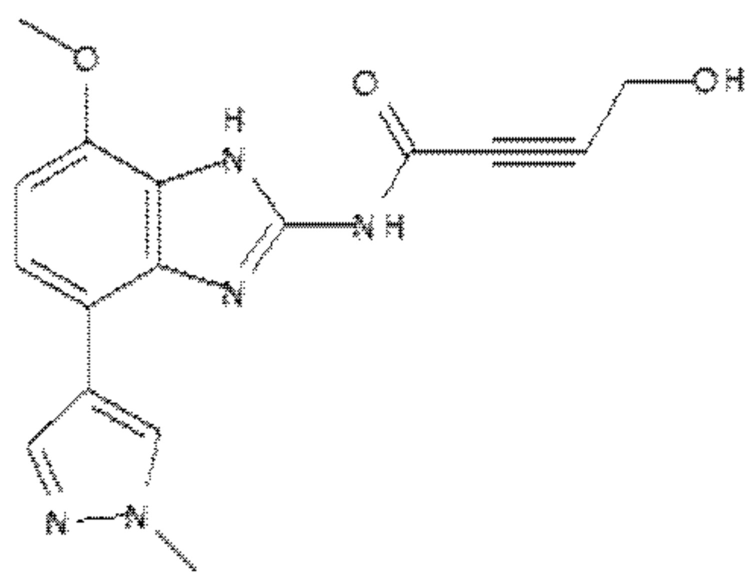
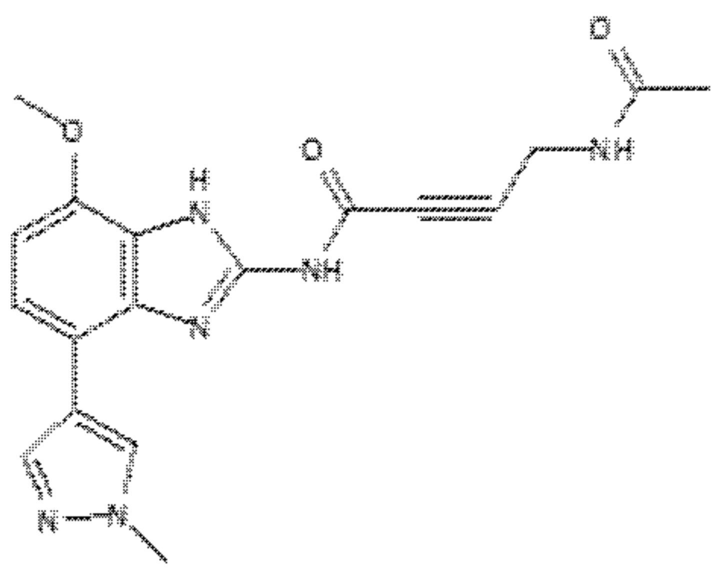
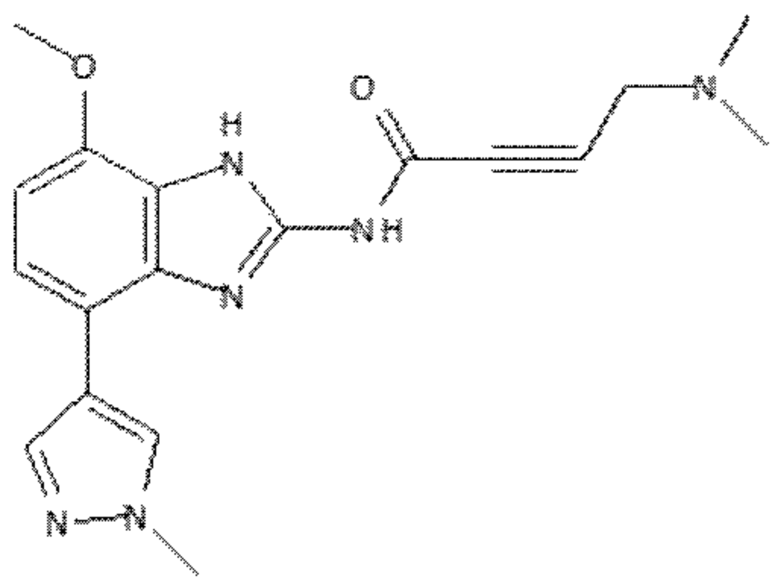
149		(5S)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
150		(5R)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
151		4-hydroxy-N-{7-methoxy-4-[1-(3-methylbutyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
152		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(morpholin-4-yl)methyl]benzamide
153		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5R)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide

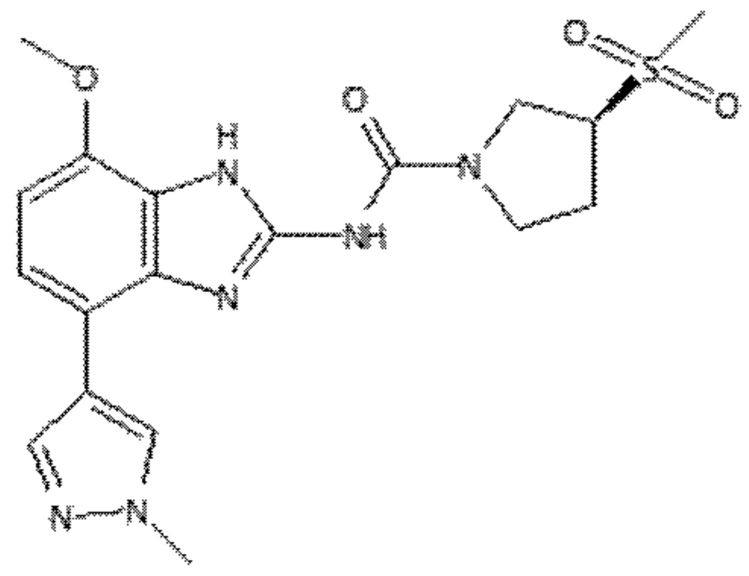
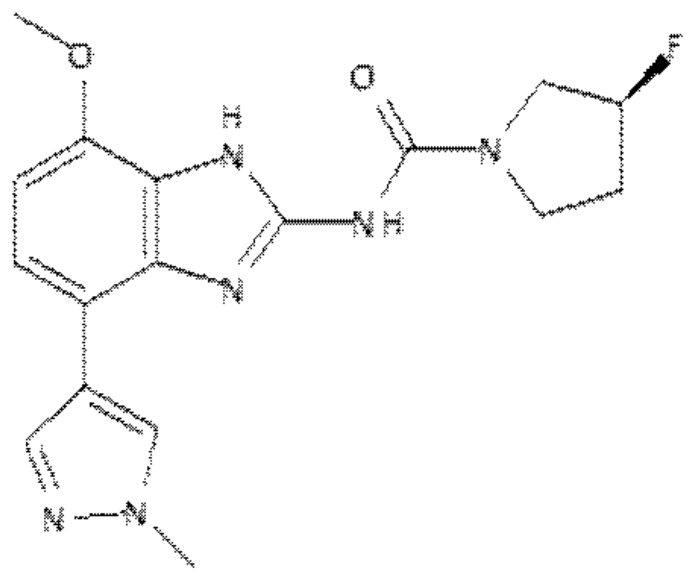
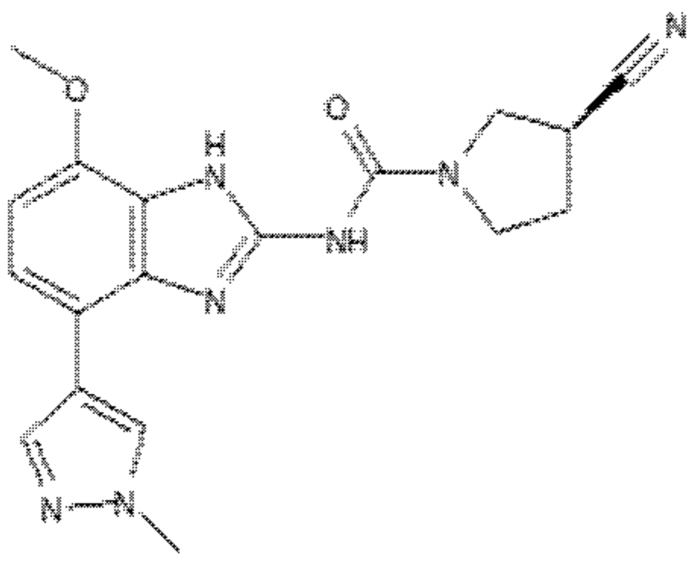
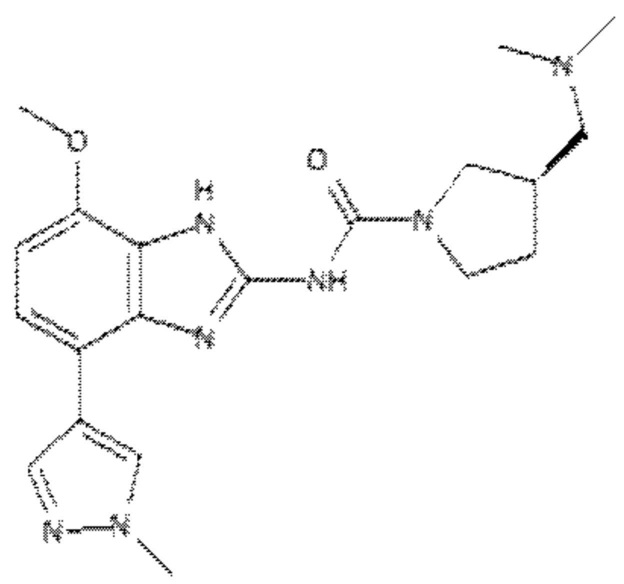
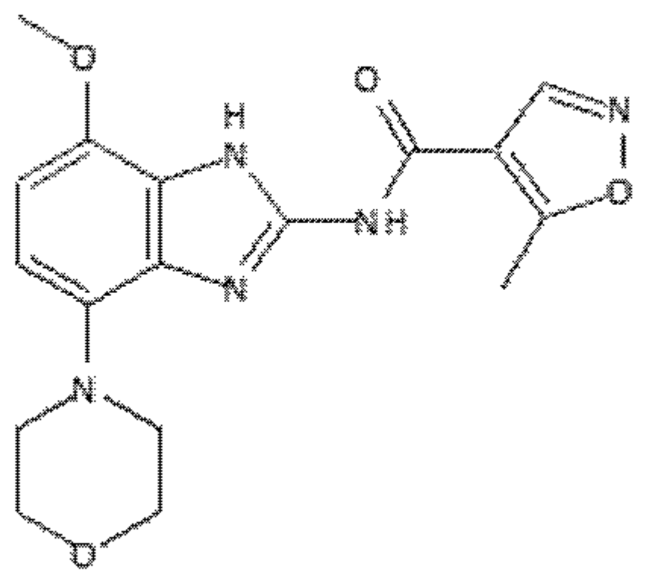
154		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5S)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide
155		N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
156		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
157		4-hydroxy-N-{4-methoxy-7-[1-(piperidin-4-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
158		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyridine-2-carboxamide

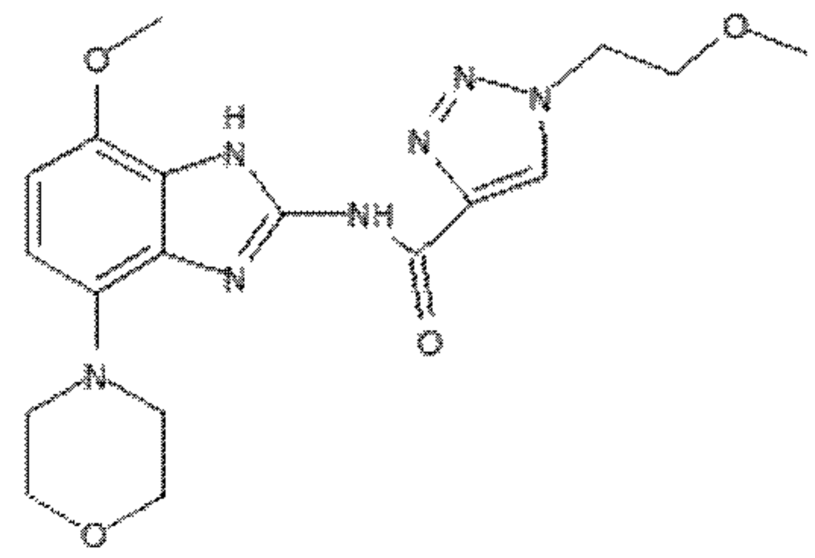
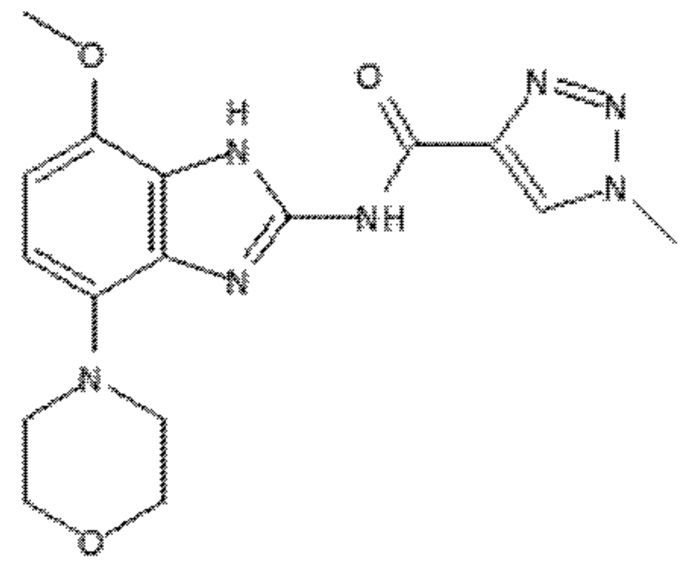
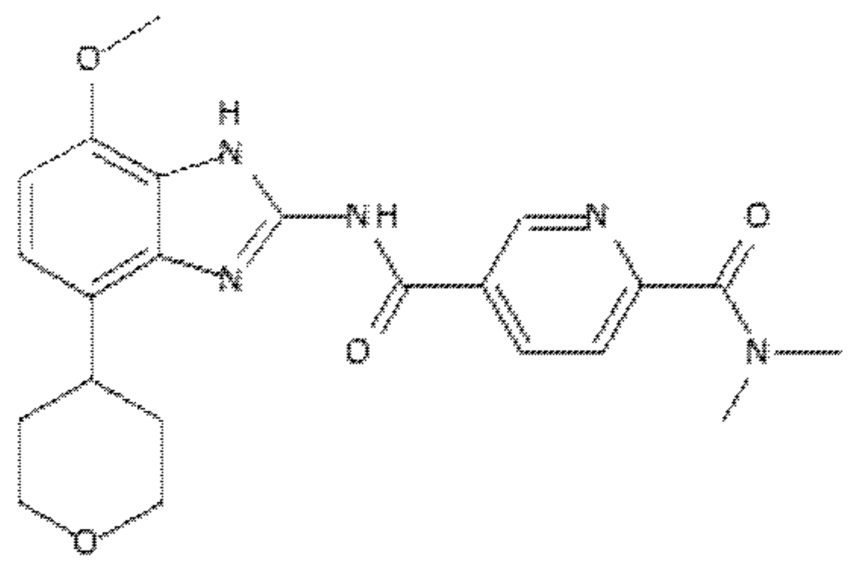
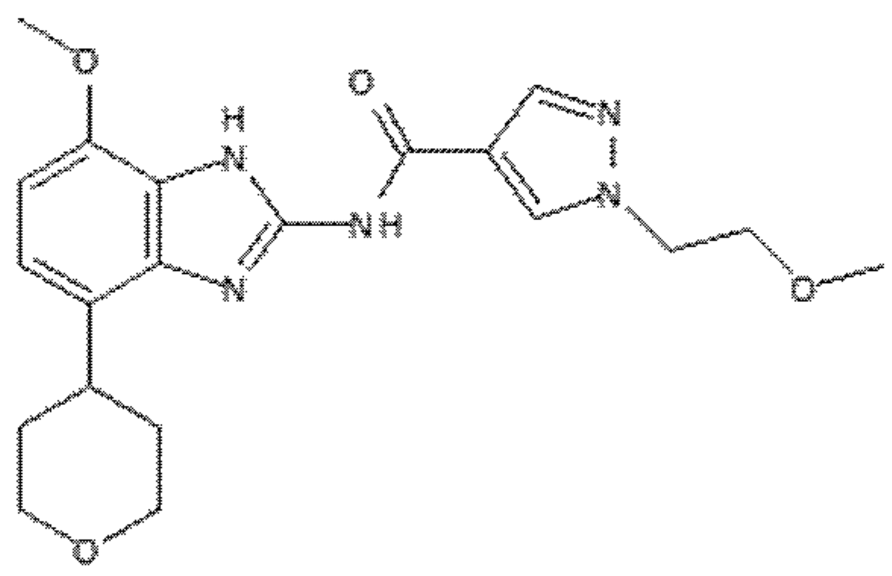
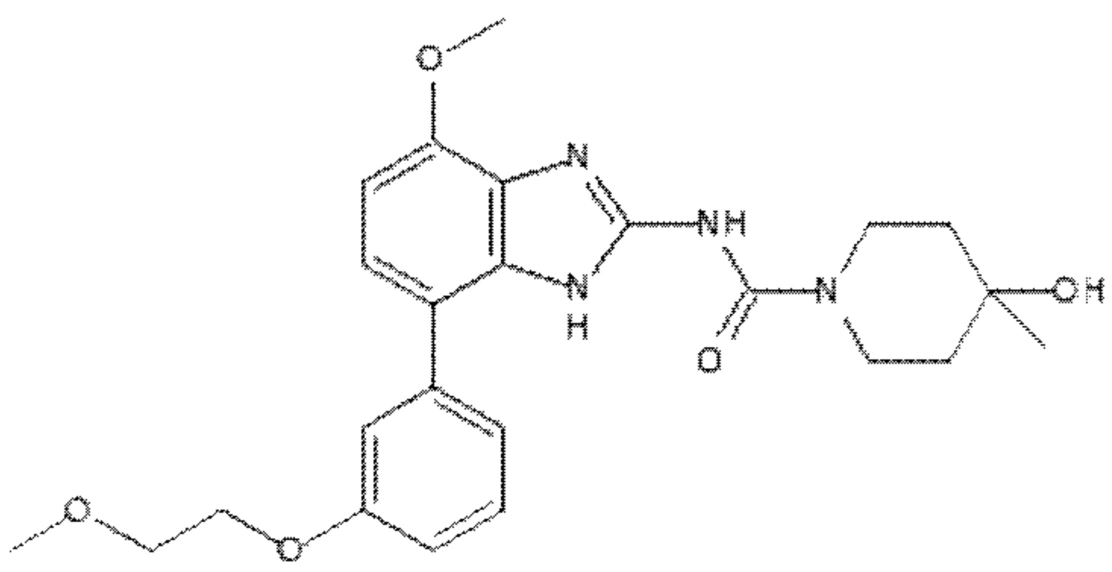
159		2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-3-yl)acetic acid
160		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
161		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
162		N5-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
163		4-hydroxy-N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide

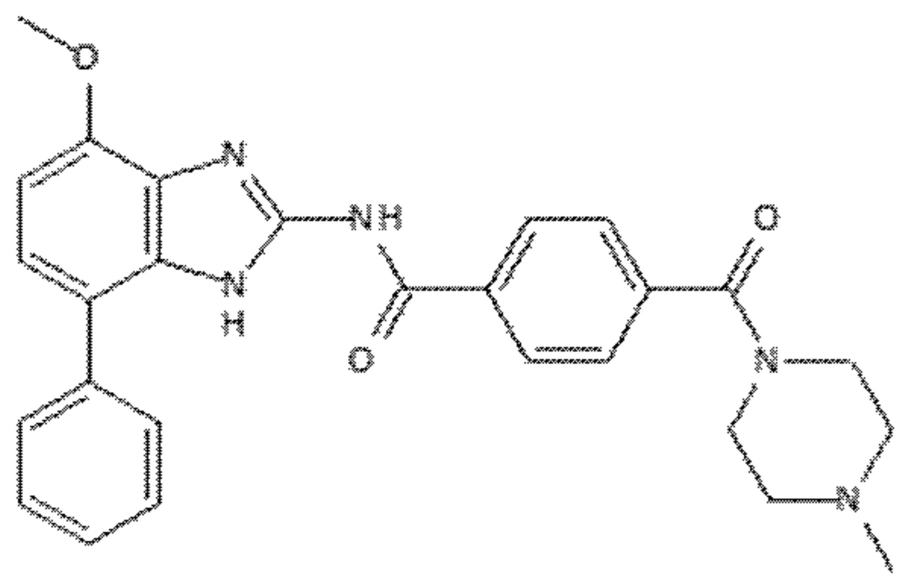
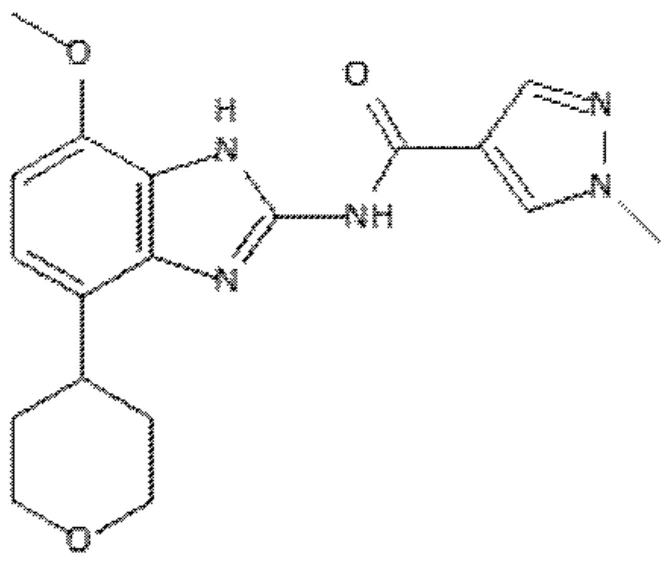
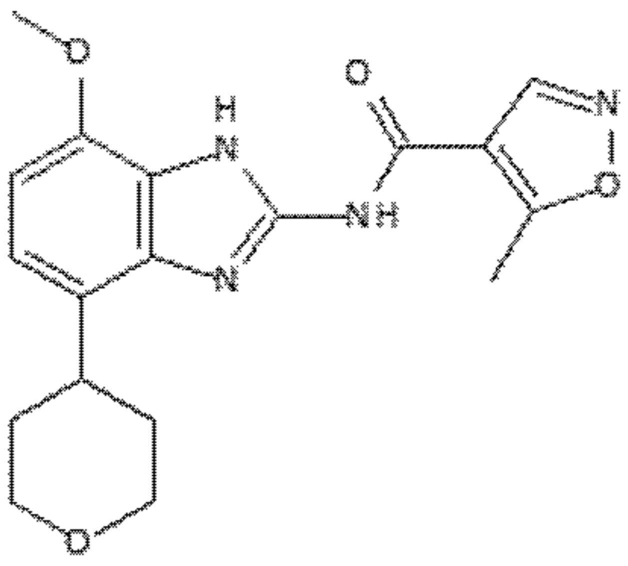
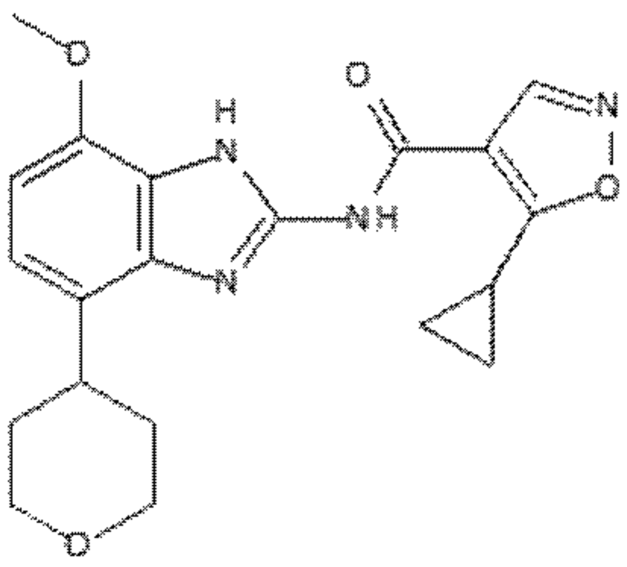
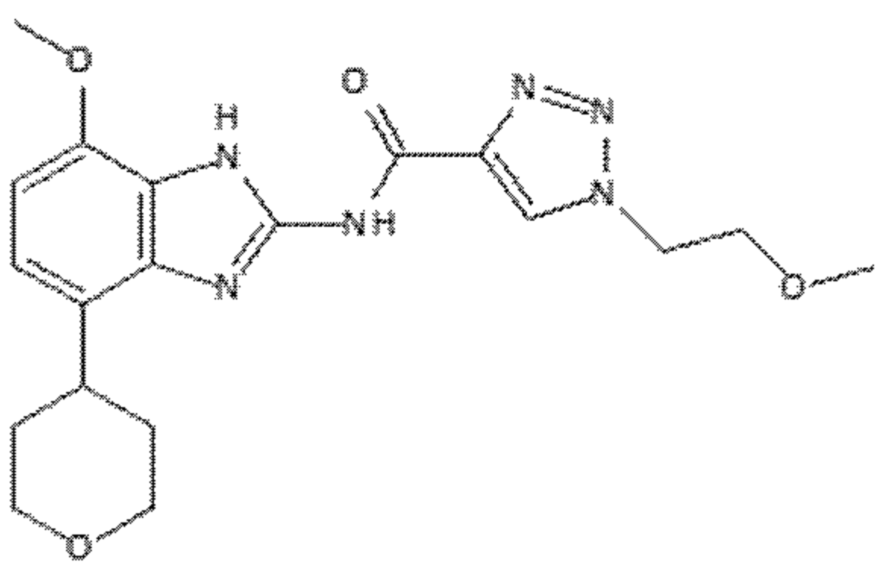
164		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
165		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide
166		3-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]propanamide
167		1-(2-Hydroxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
168		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide

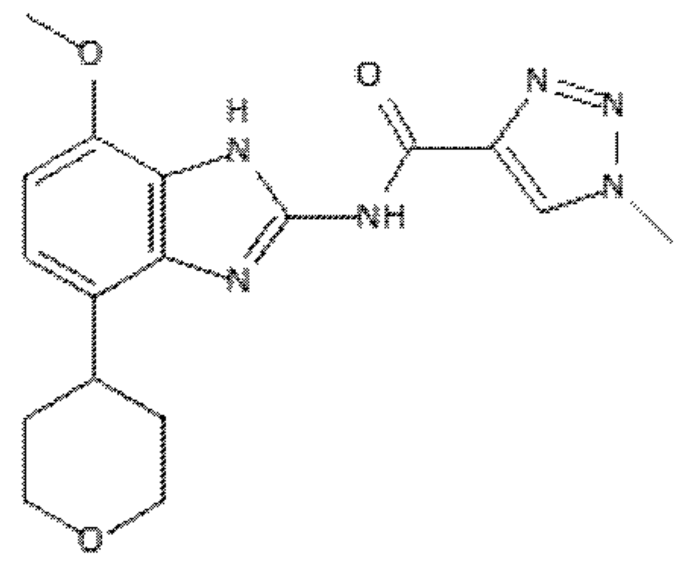
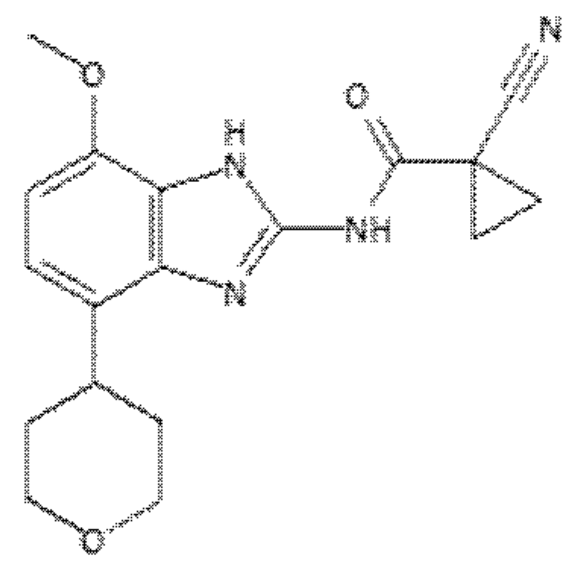
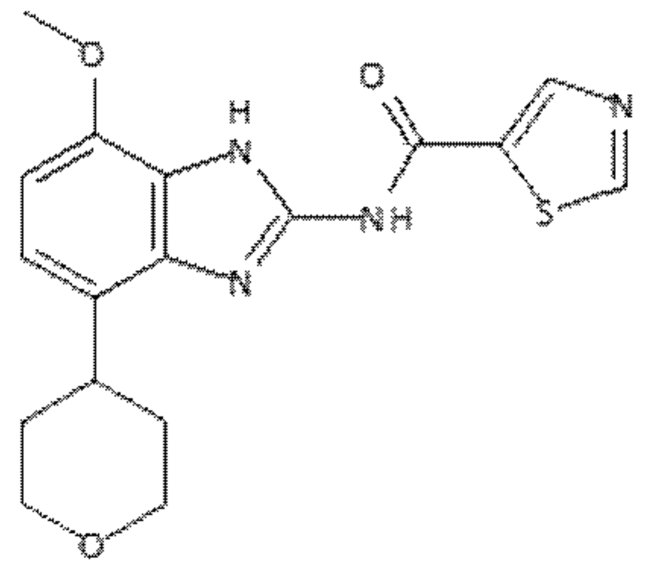
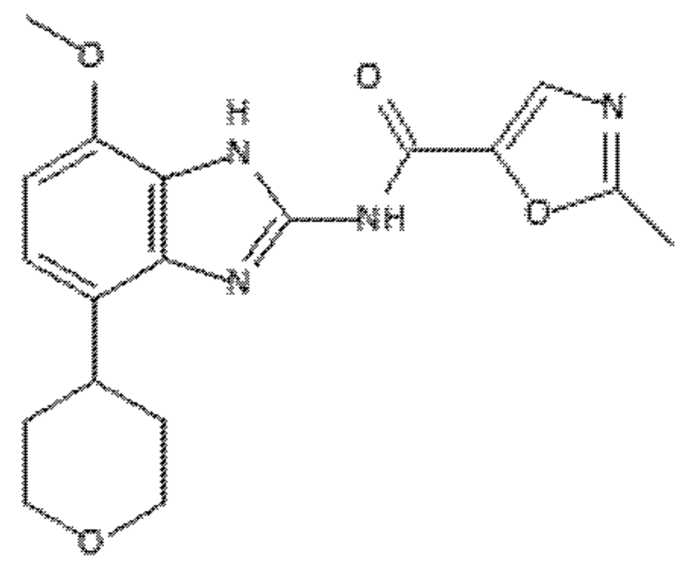
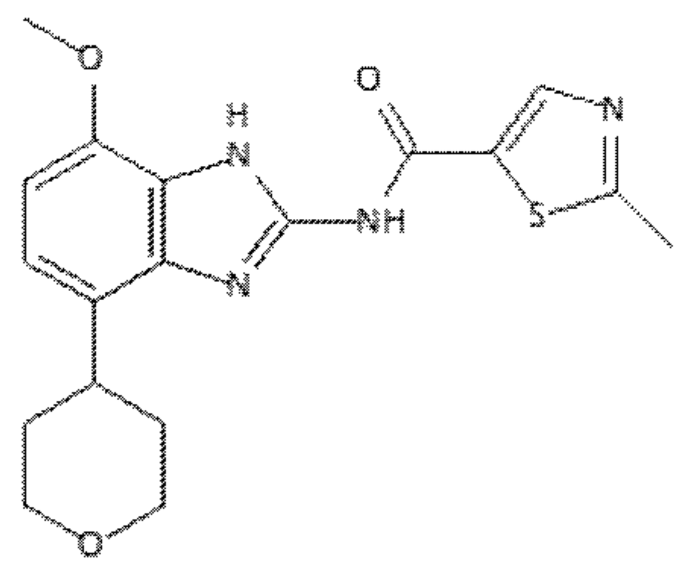
169		1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
170		5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
171		5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
172		1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
173		Thiazole-5-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

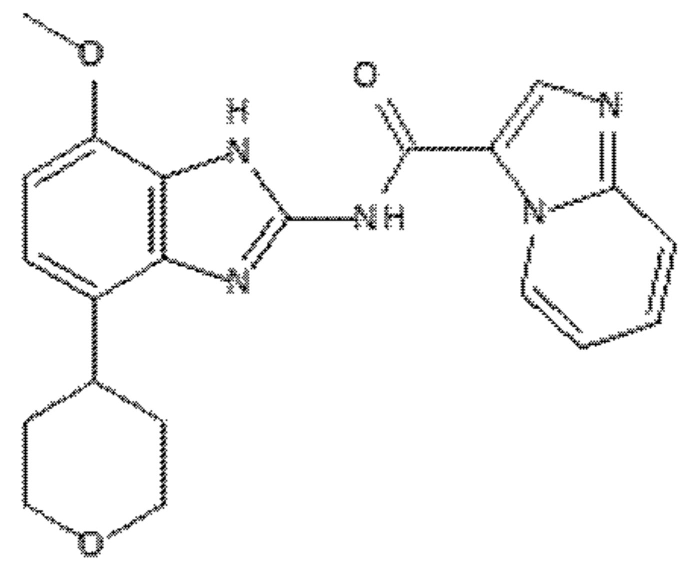
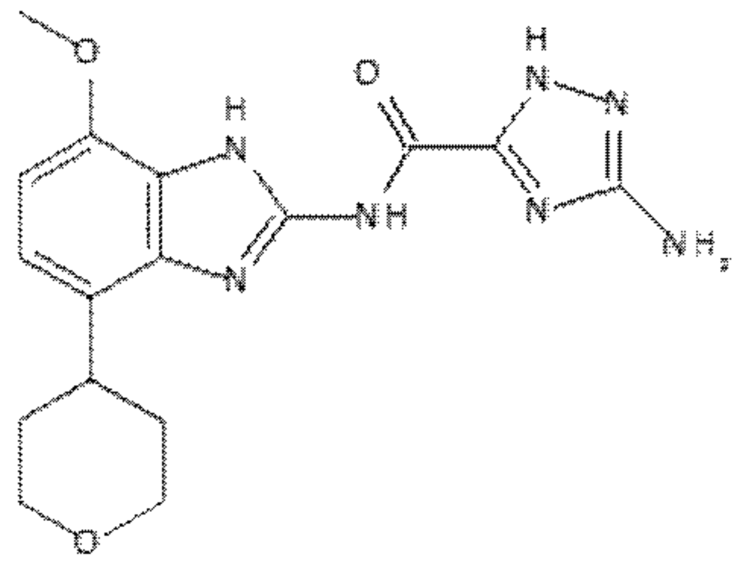
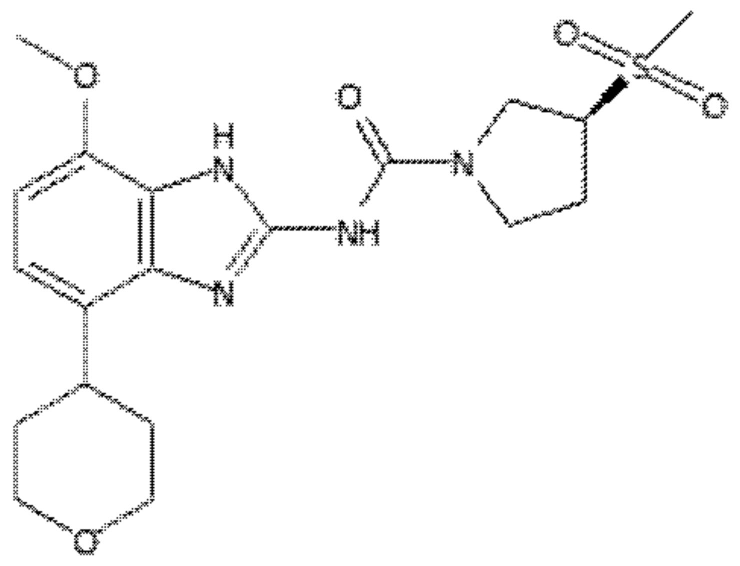
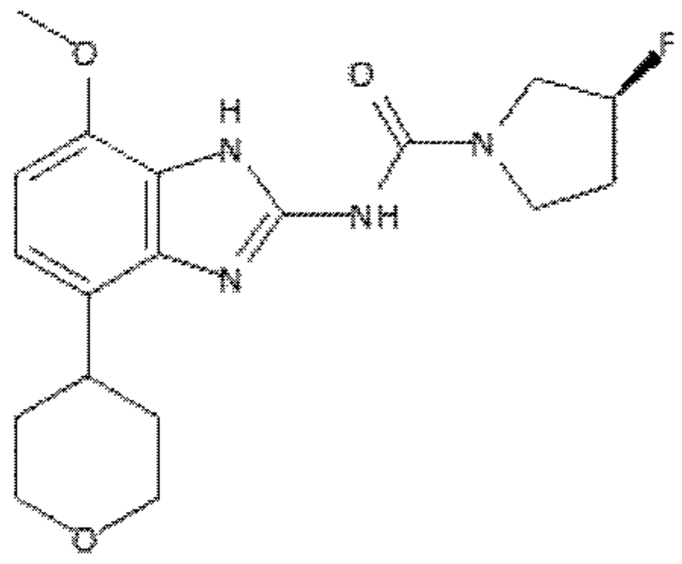
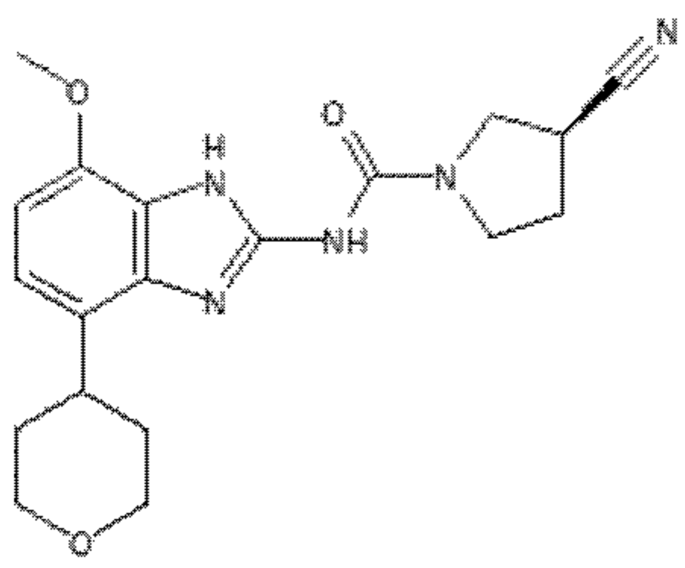
174		5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
175		4-(4-Methyl-piperazin-1-yl)-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
176		4-Hydroxy-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
177		4-Acetylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
178		4-Dimethylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

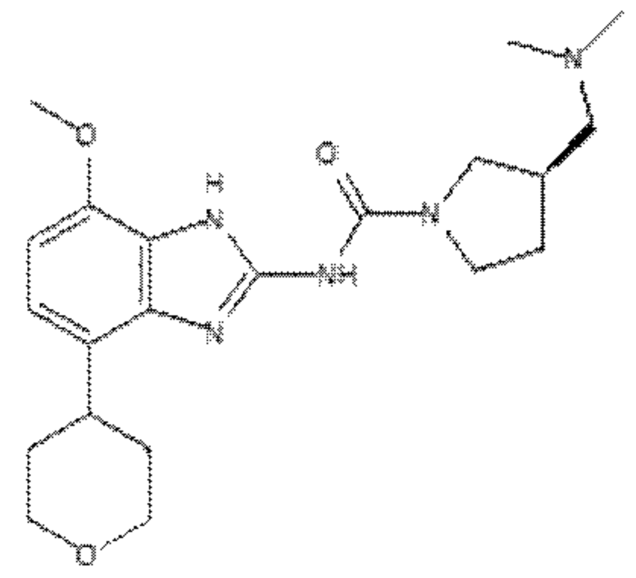
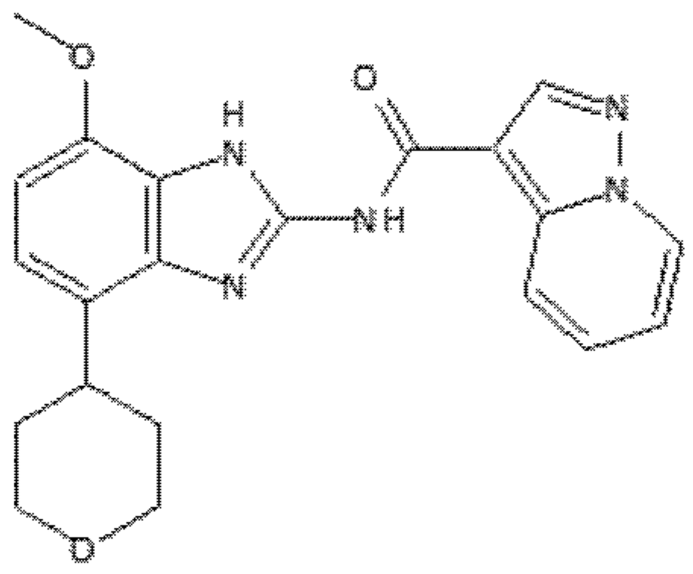
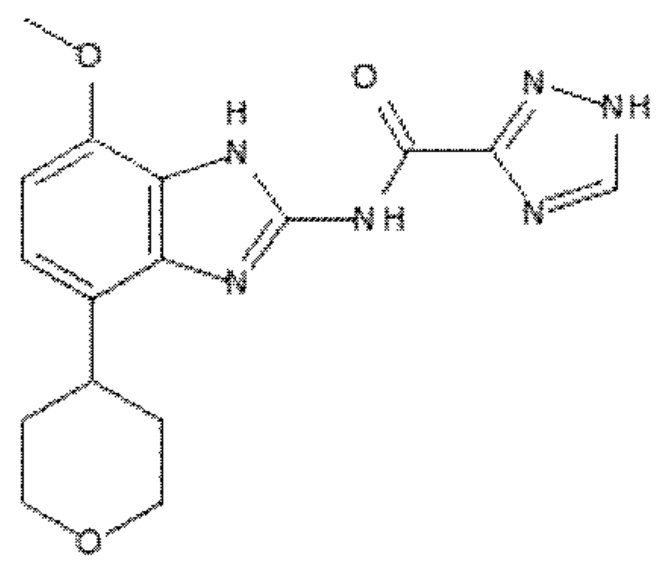
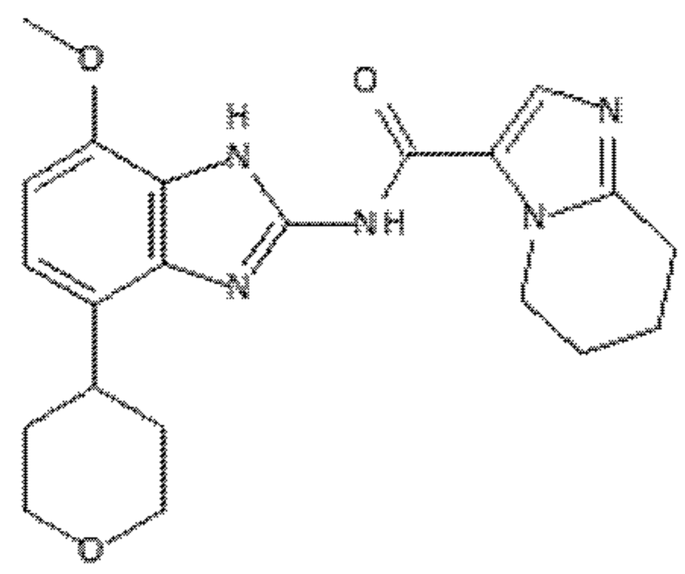
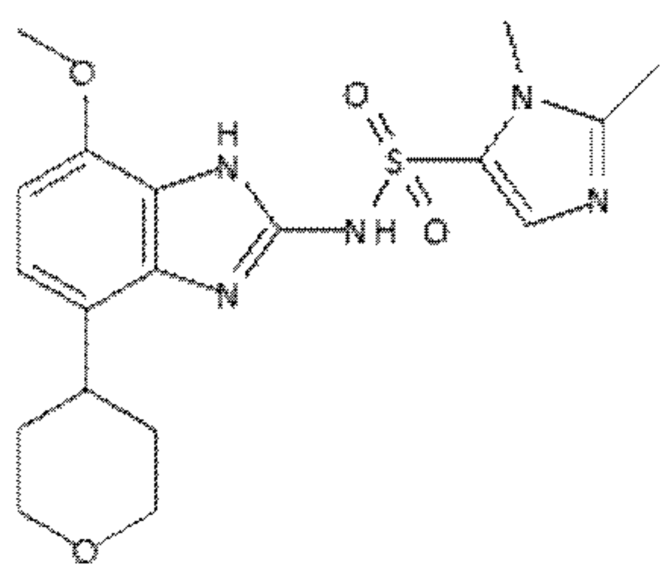
179		(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
180		(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
181		(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
182		(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
183		5-Methyl-isoxazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide

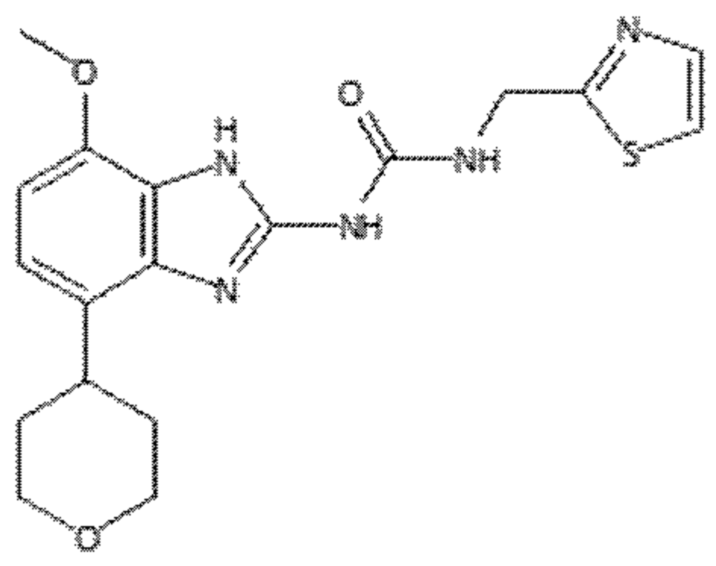
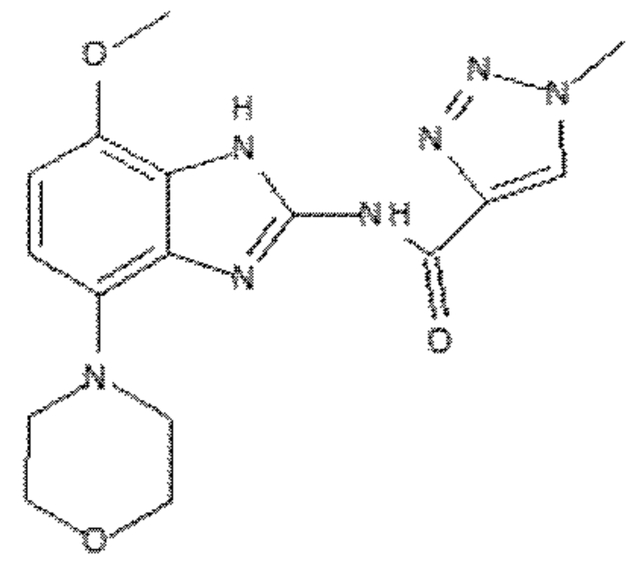
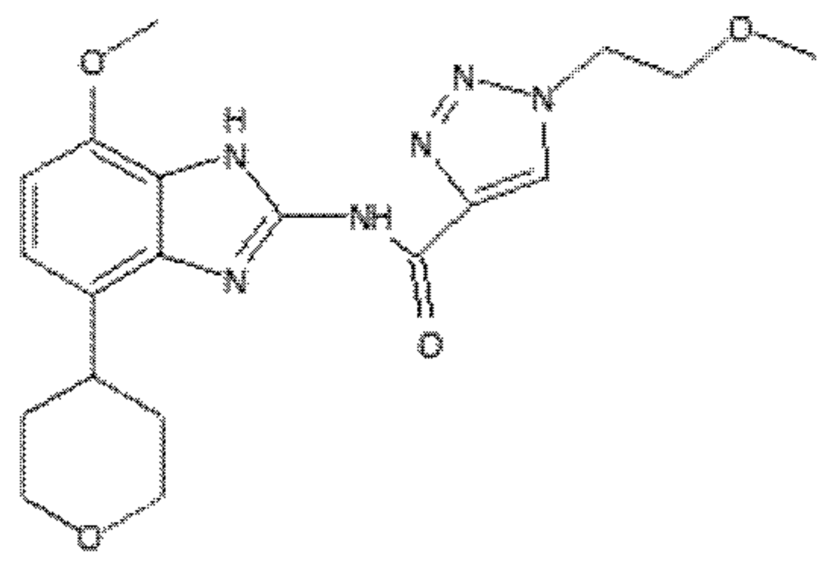
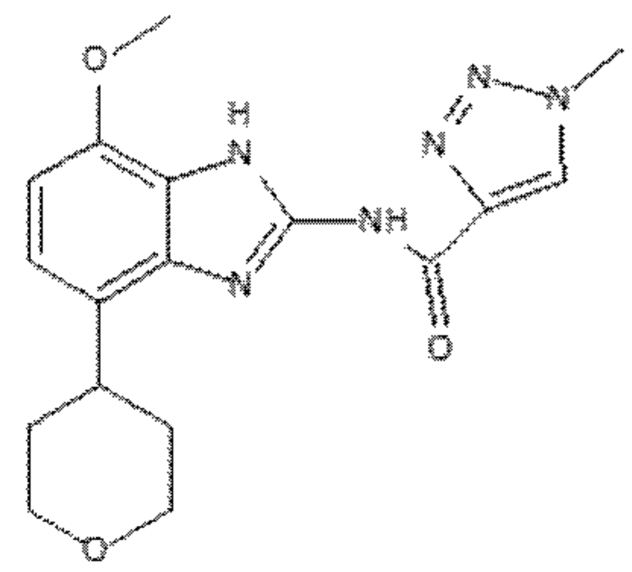
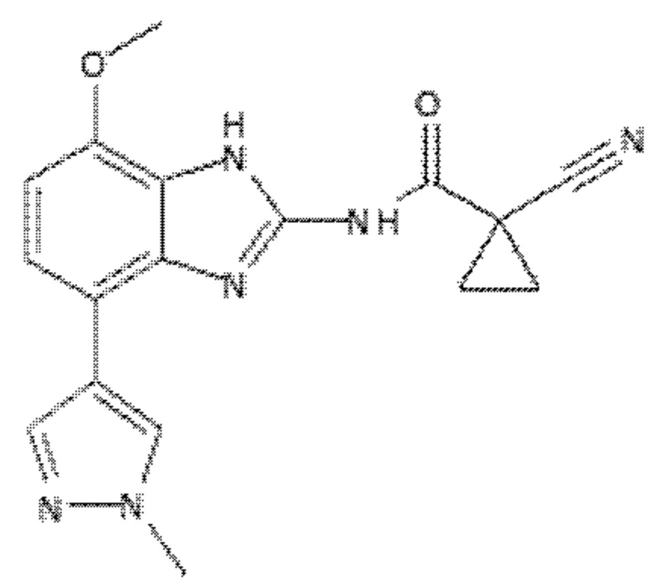
184		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
185		1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide
186		Pyridine-2,5-dicarboxylic acid 2-dimethylamide 5-{[7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide}
187		1-(2-Methoxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
188		N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-morpholin-4-ylmethyl-benzamide

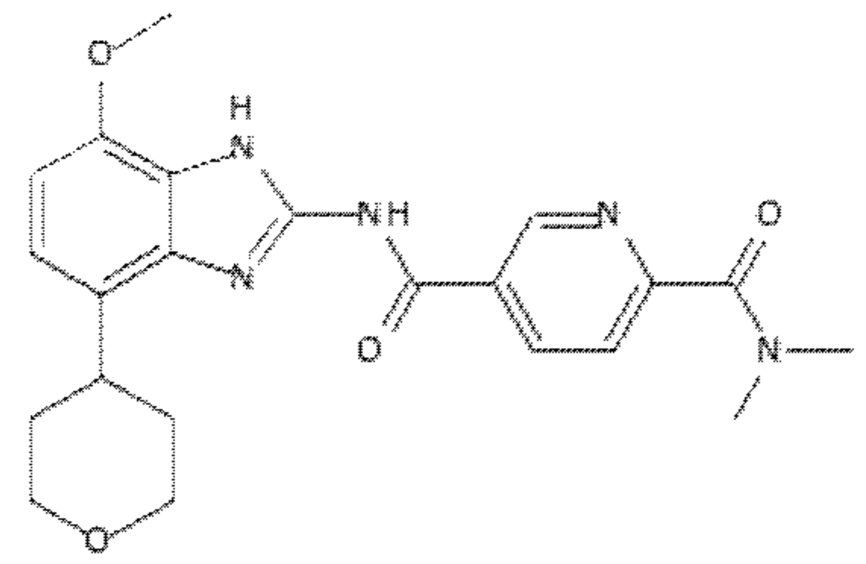
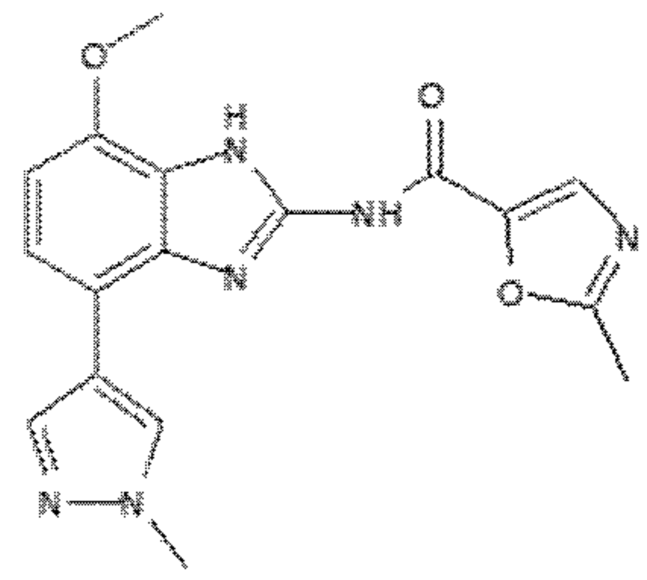
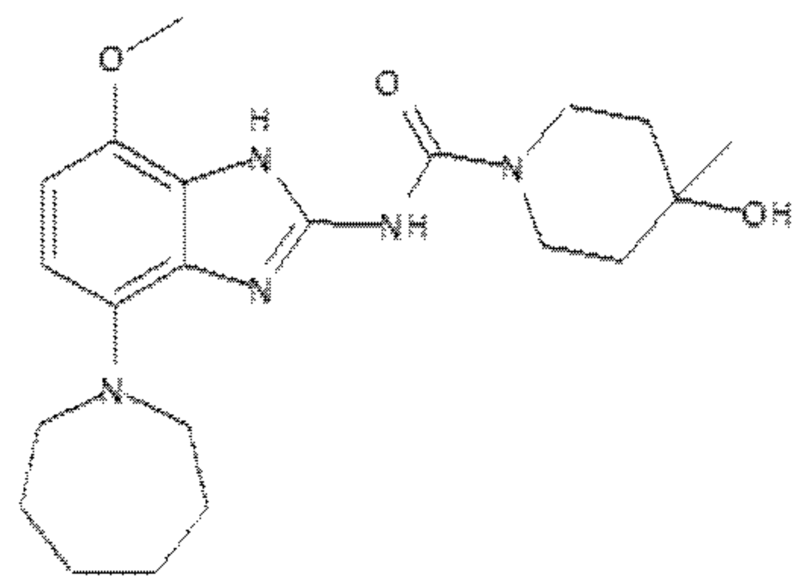
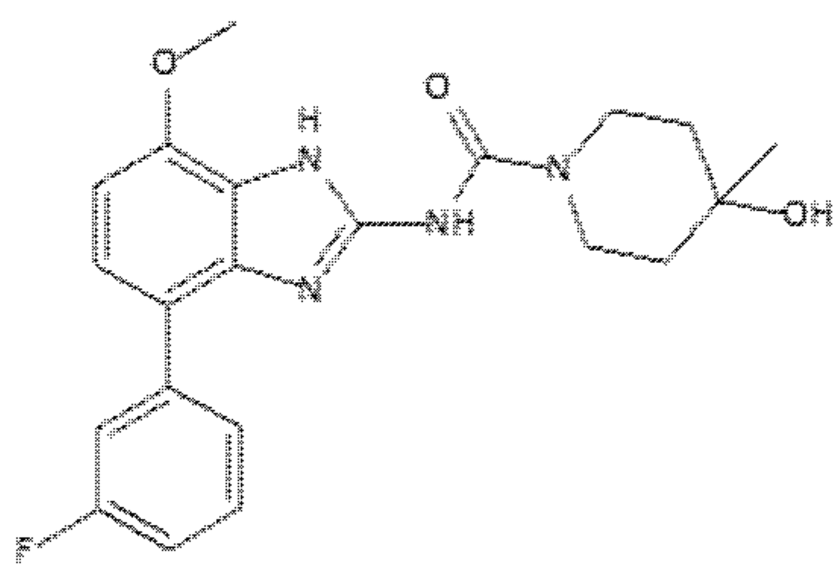
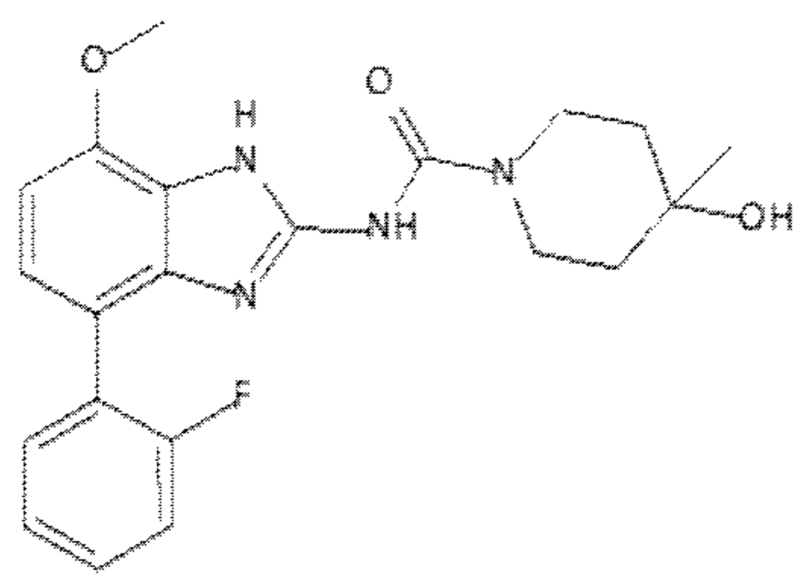
189		N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-(4-methyl-piperazin-1-ylmethyl)-benzamide
190		1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
191		5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
192		5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
193		1-(2-Methoxy-ethyl)-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

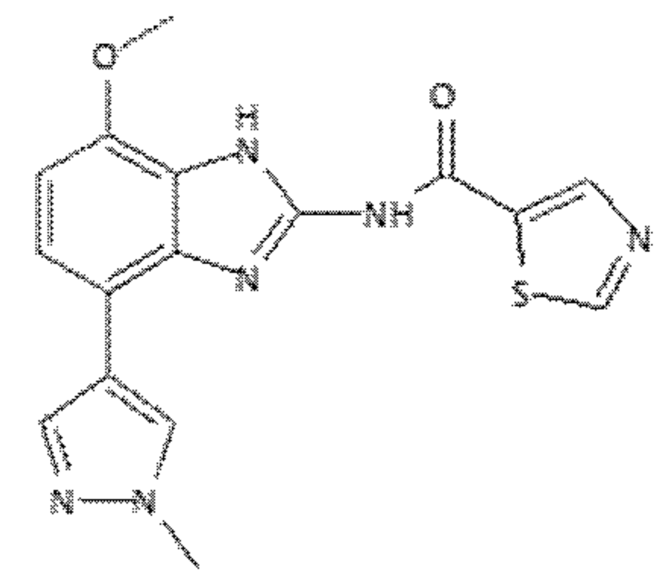
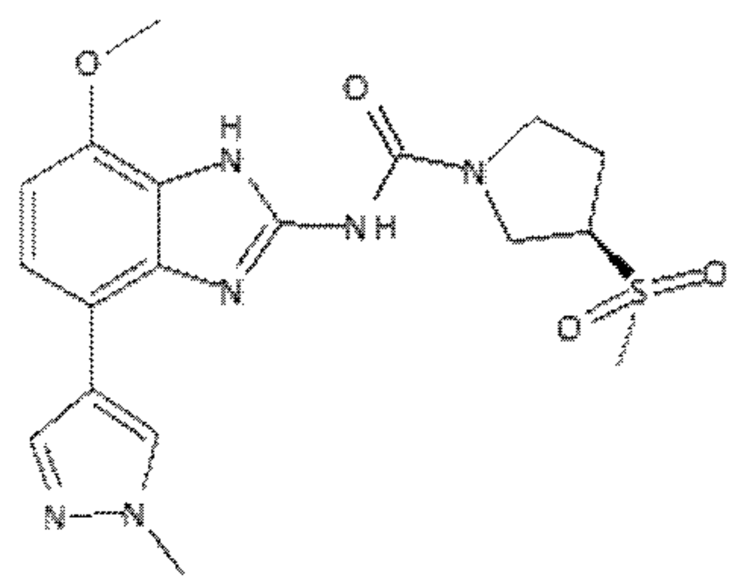
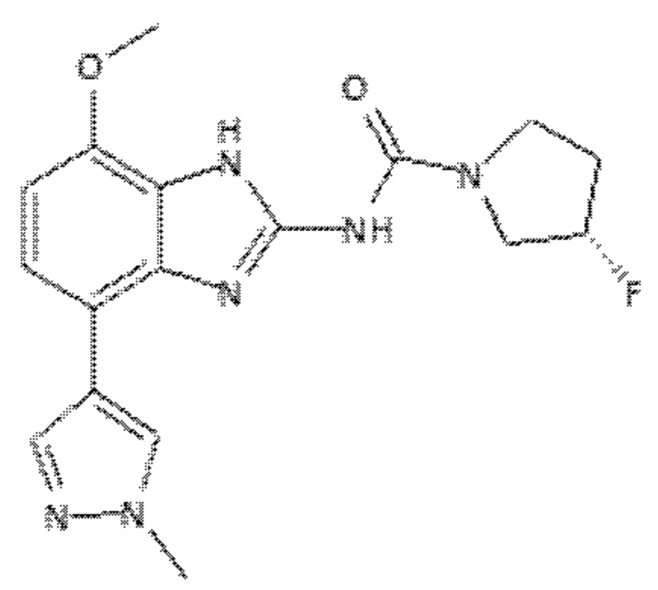
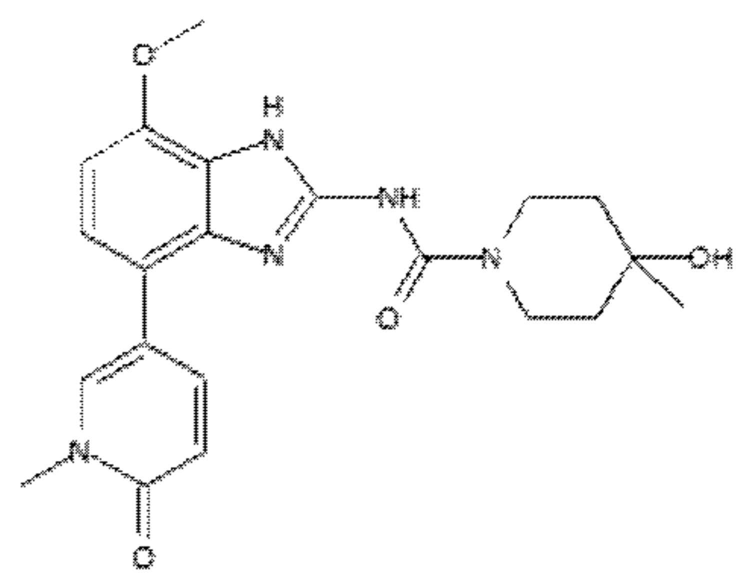
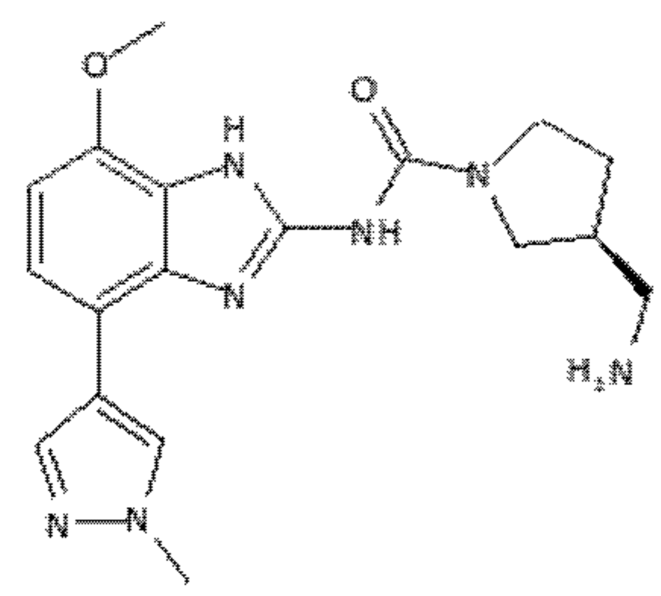
194		1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
195		1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
196		Thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
197		2-Methyl-oxazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
198		2-Methyl-thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

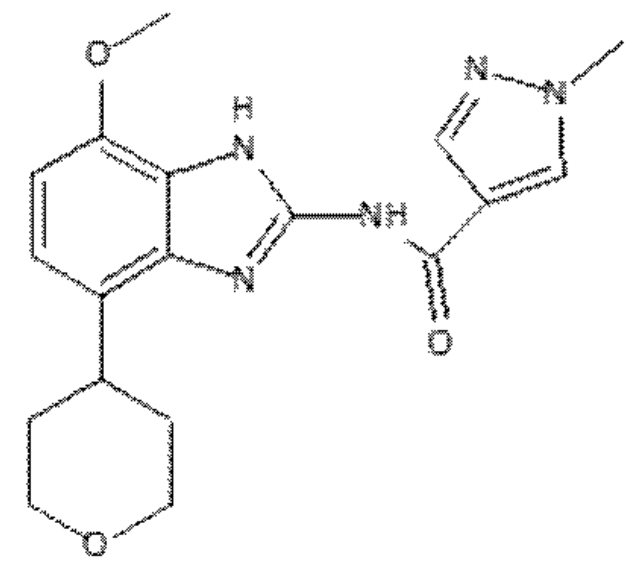
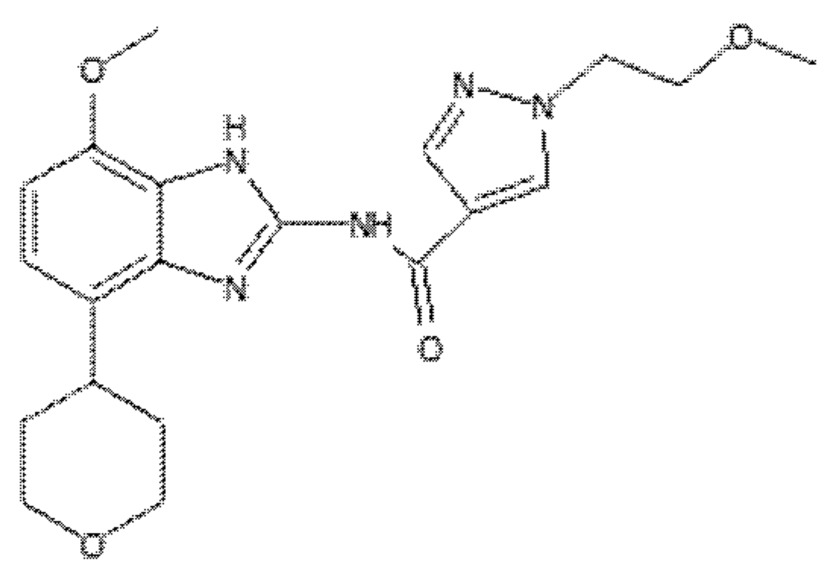
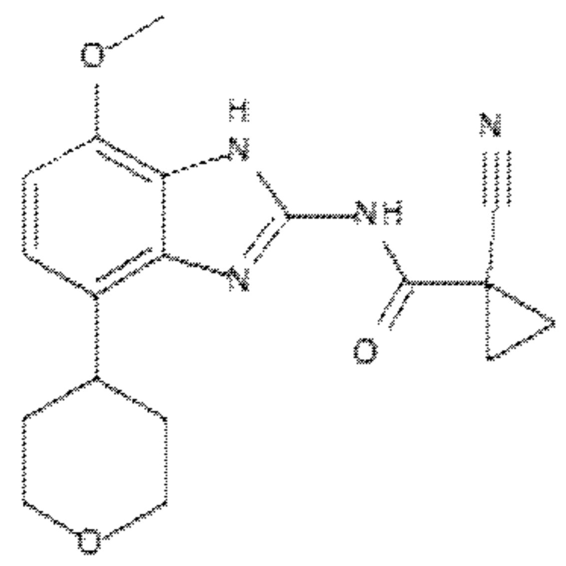
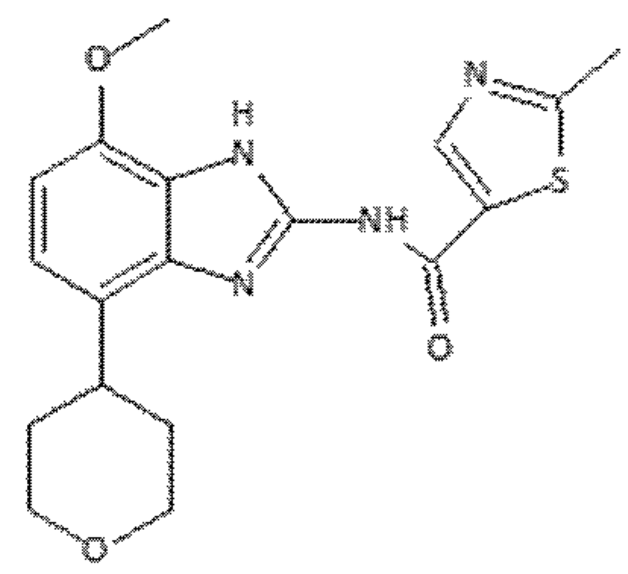
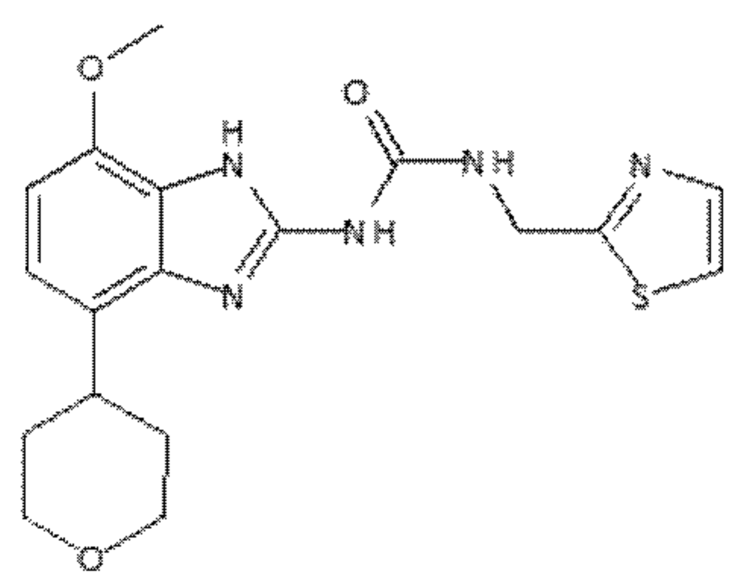
199		Imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
200		5-Amino-2H-[1,2,4]triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
201		(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
202		(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
203		(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

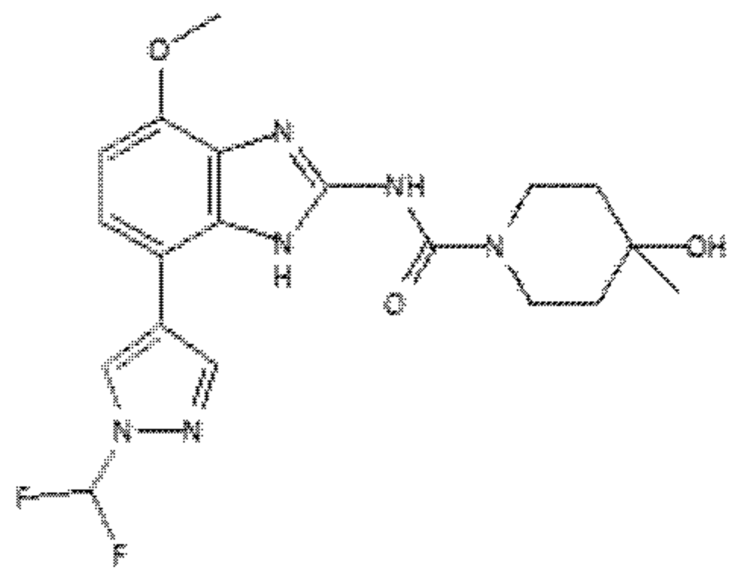
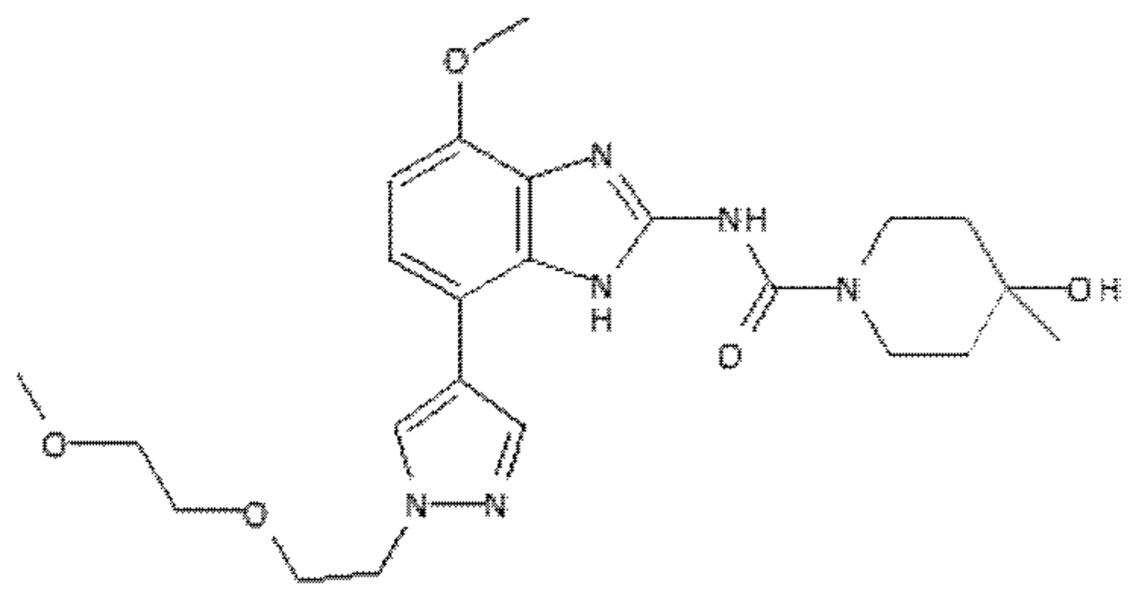
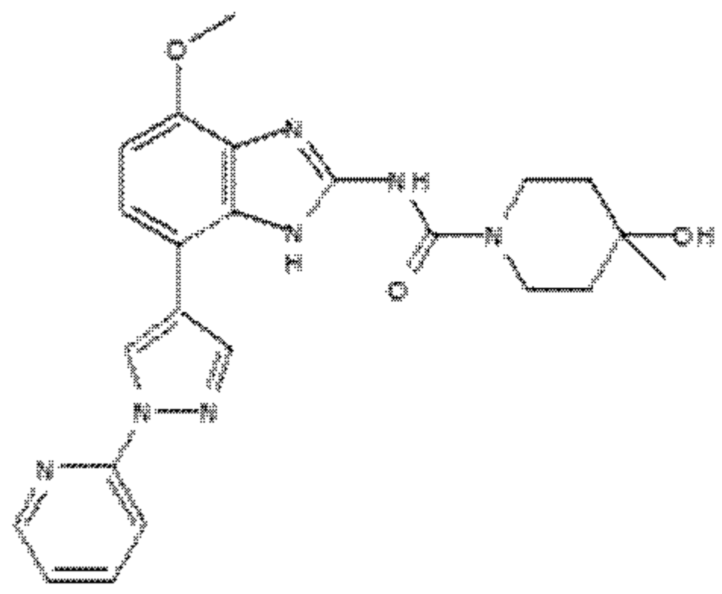
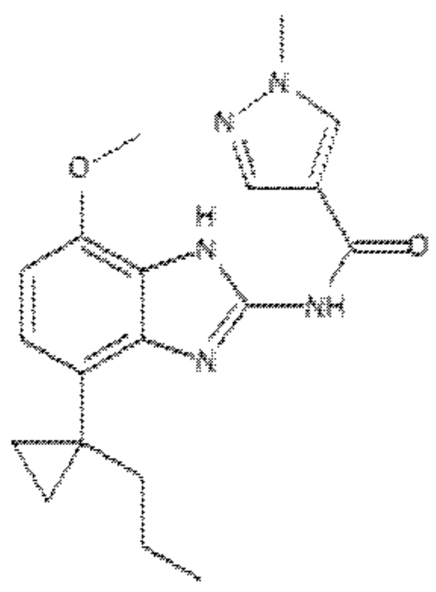
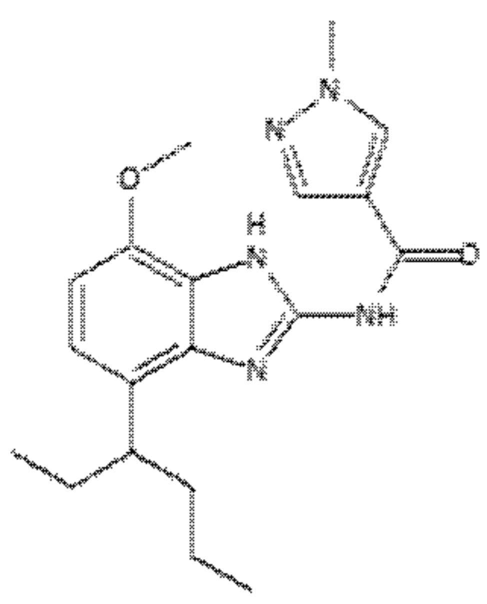
204		(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
205		Pyrazolo[1,5-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
206		1H-[1,2,4]Triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
207		5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
208		2,3-Dimethyl-3H-imidazole-4-sulfonic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

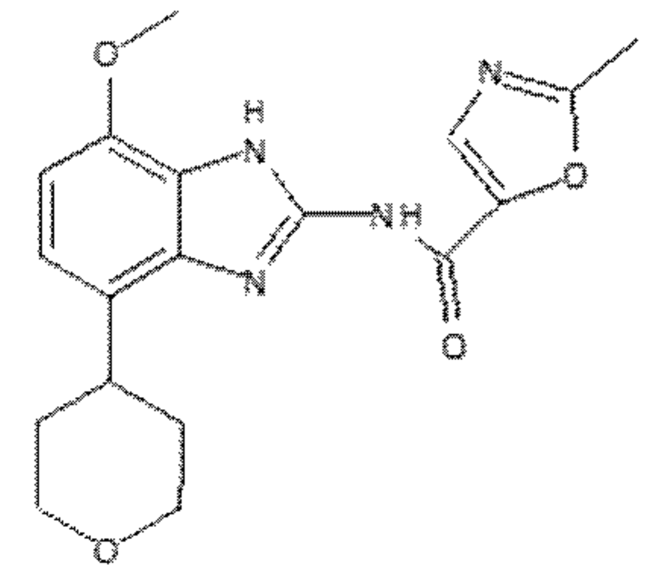
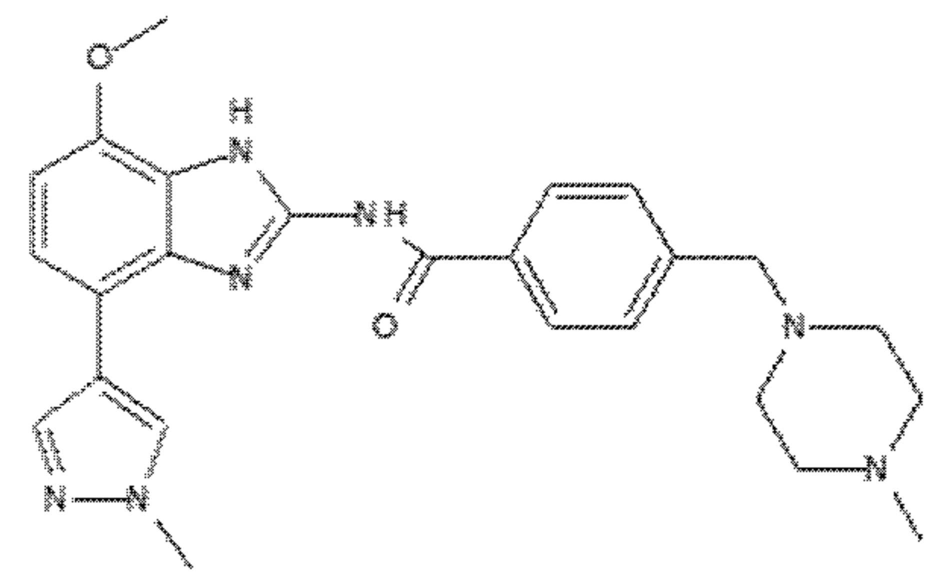
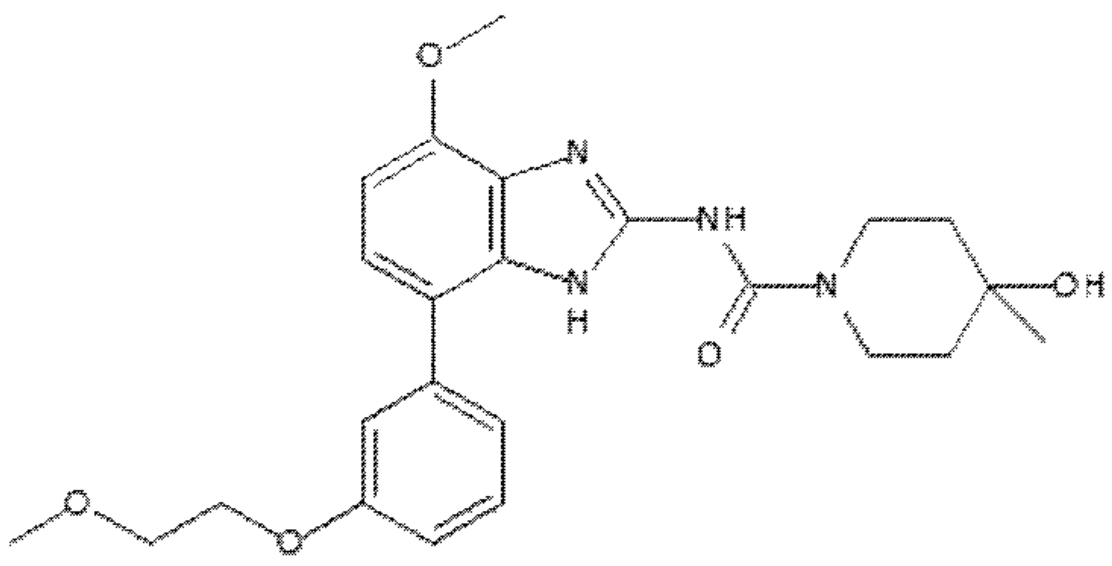
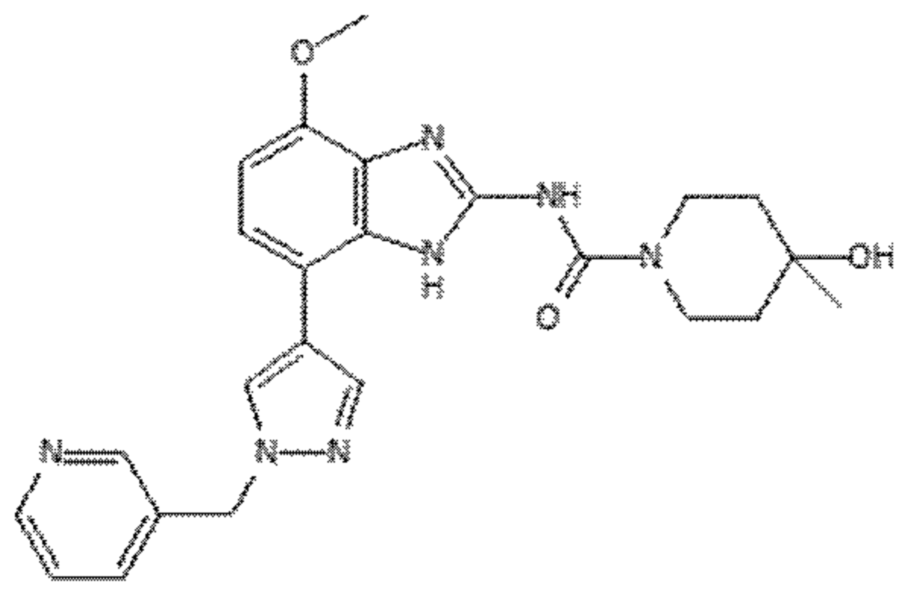
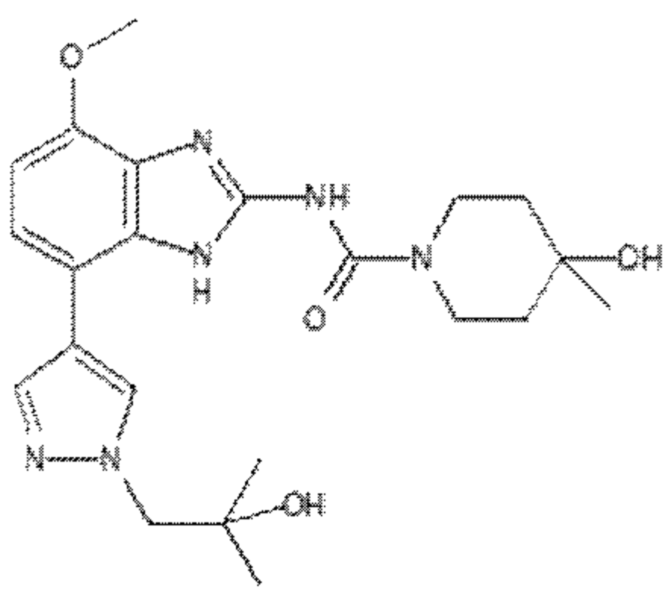
209		1-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-3-thiazol-2-ylmethyl-urea
210		N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
211		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
212		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
213		1-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide

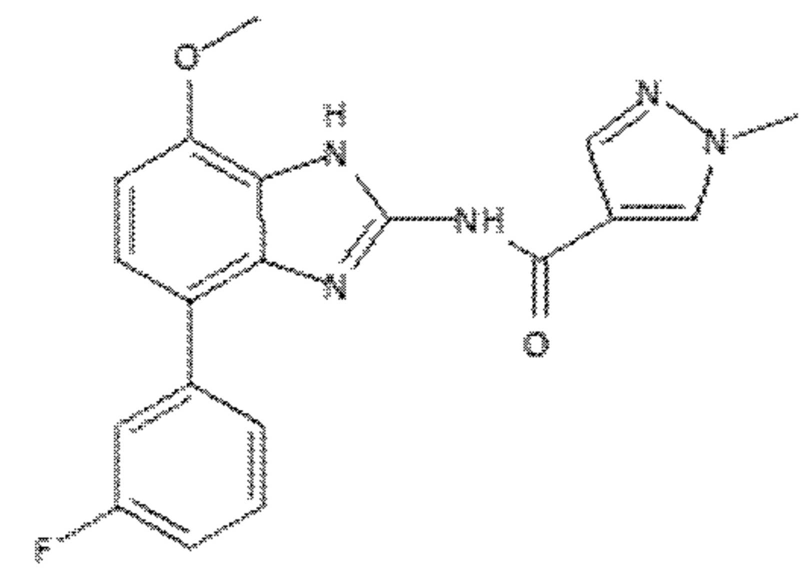
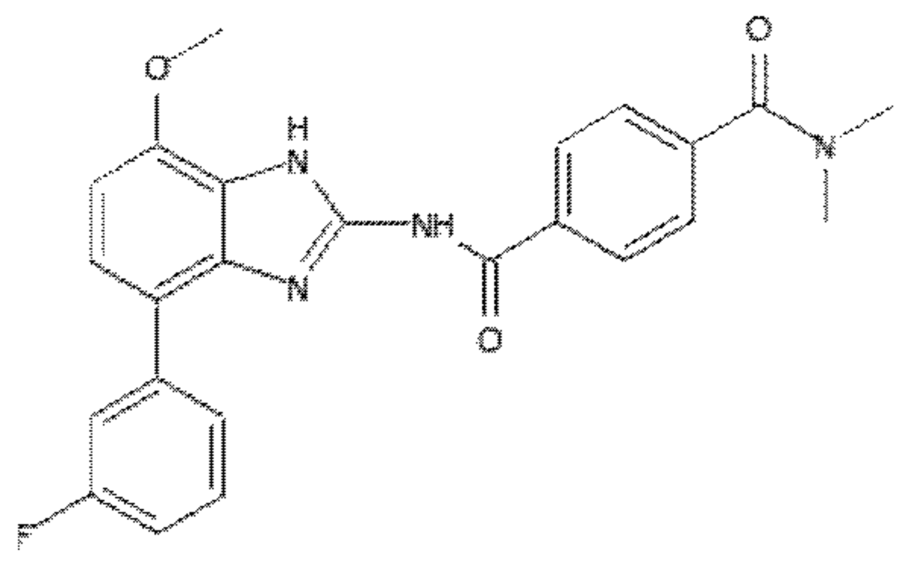
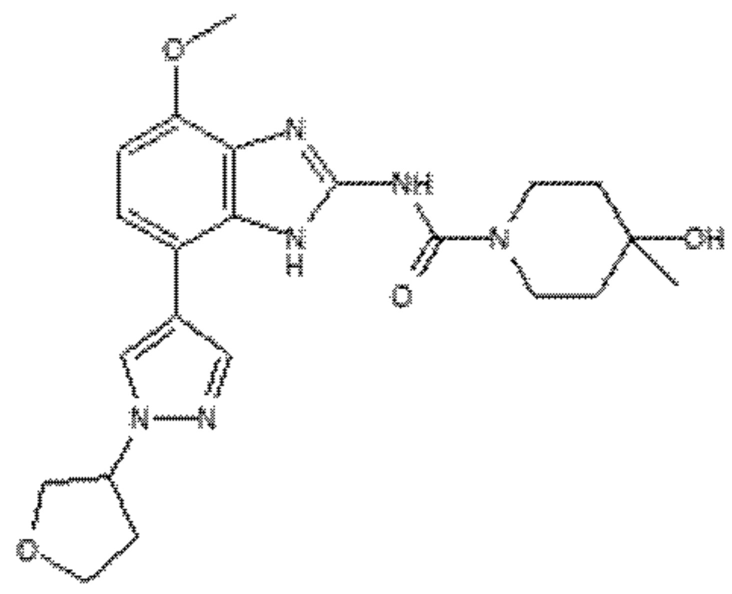
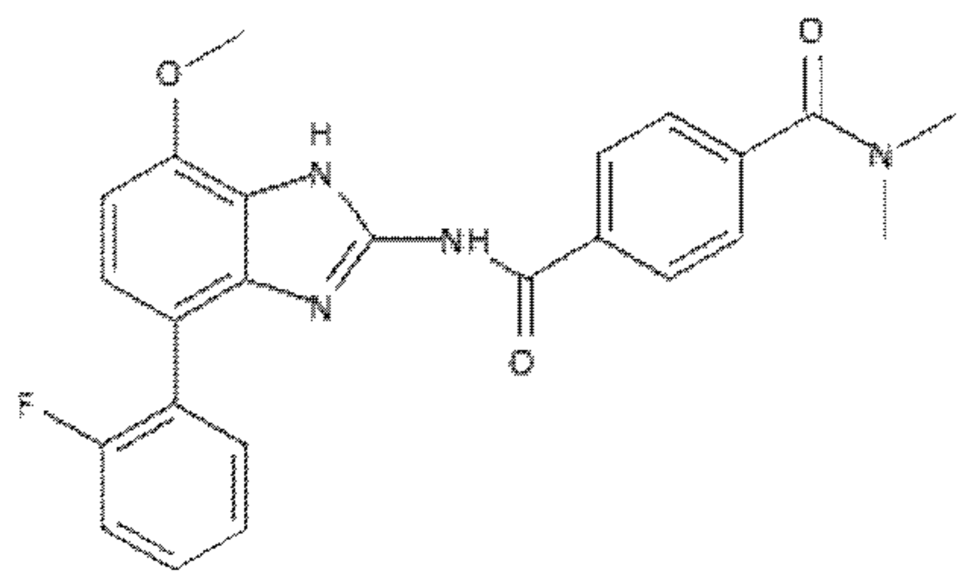
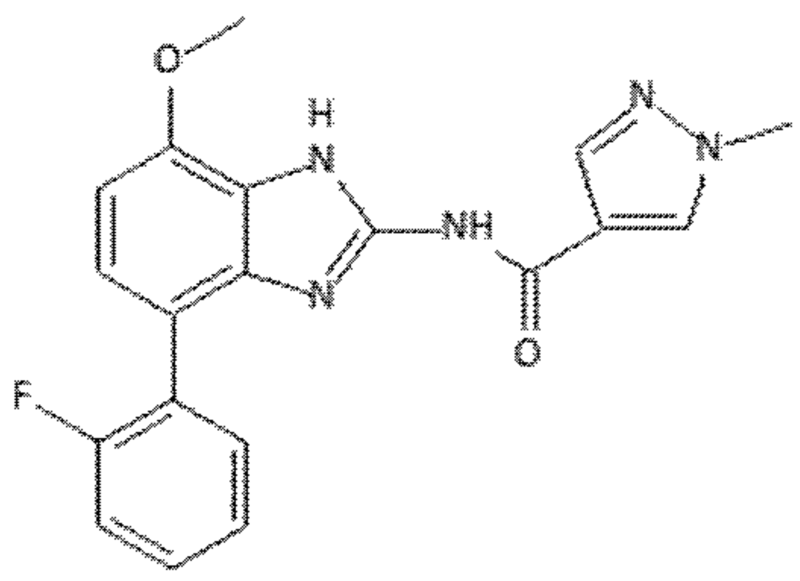
214		N5-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
215		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
216		N-[4-(azepan-1-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
217		N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
218		N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide

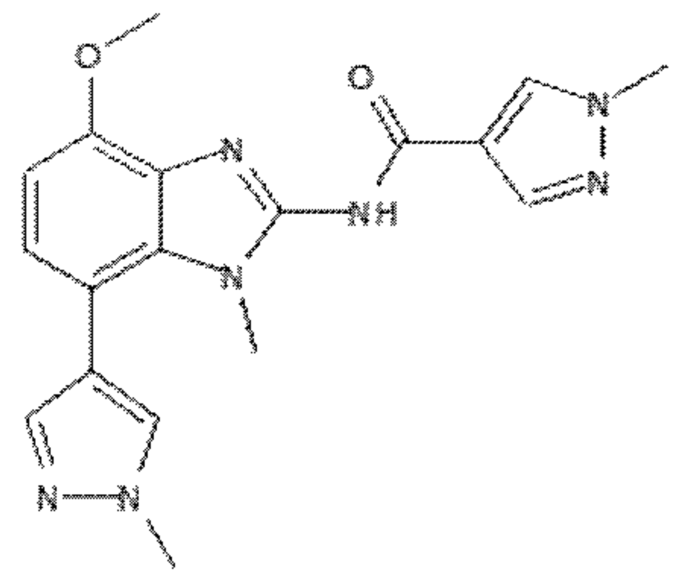
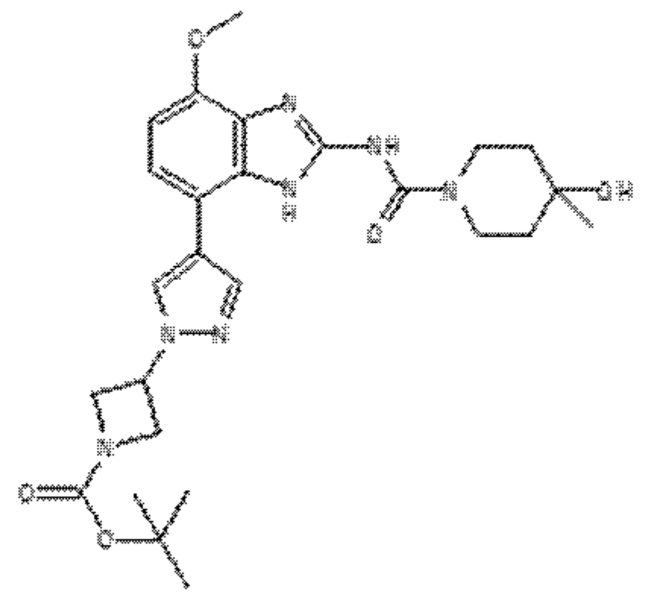
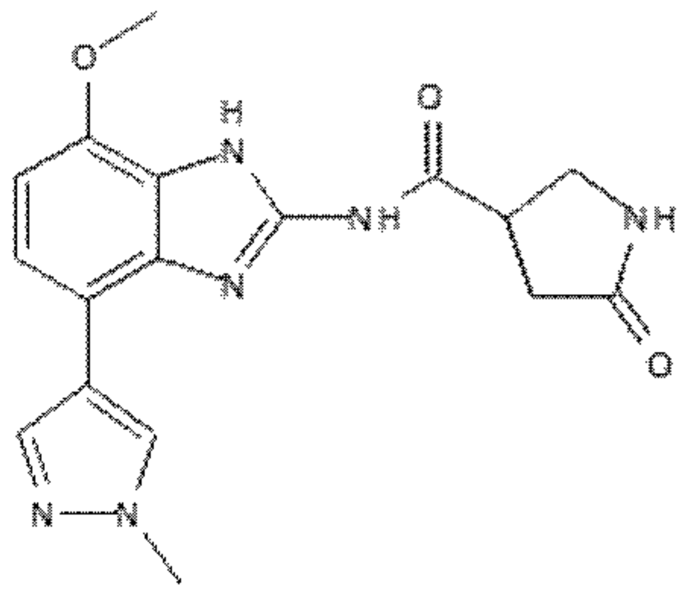
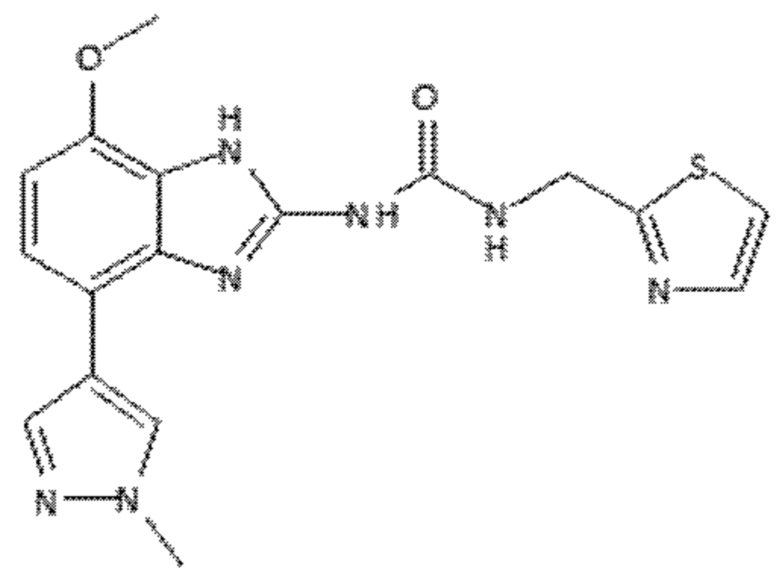
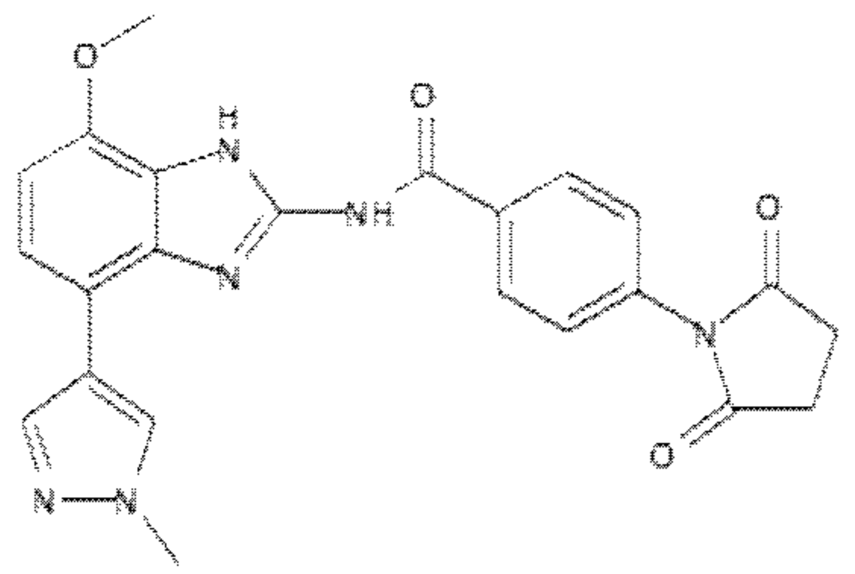
219		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-thiazole-5-carboxamide
220		(3R)-3-methanesulfonyl-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
221		(3S)-3-fluoro-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
222		4-hydroxy-N-[7-methoxy-4-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
223		(3S)-3-(aminomethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide

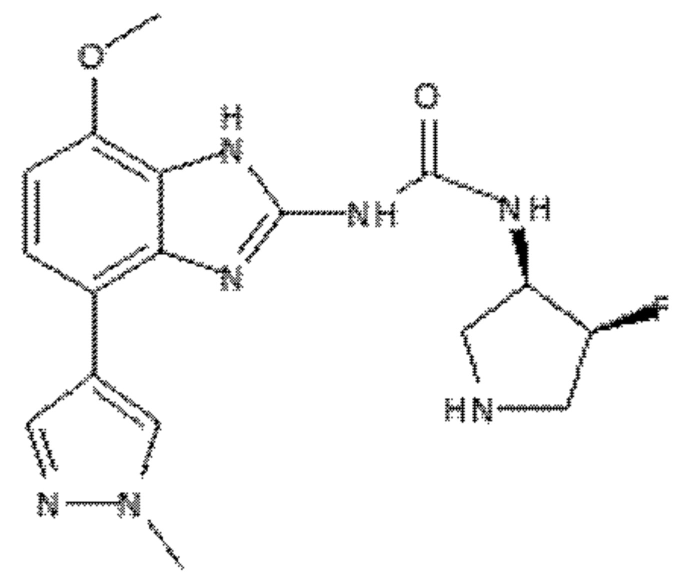
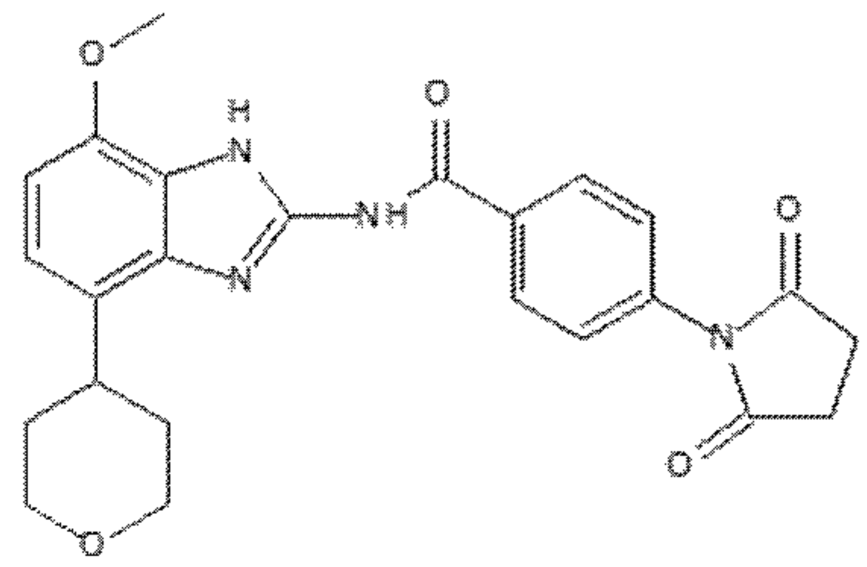
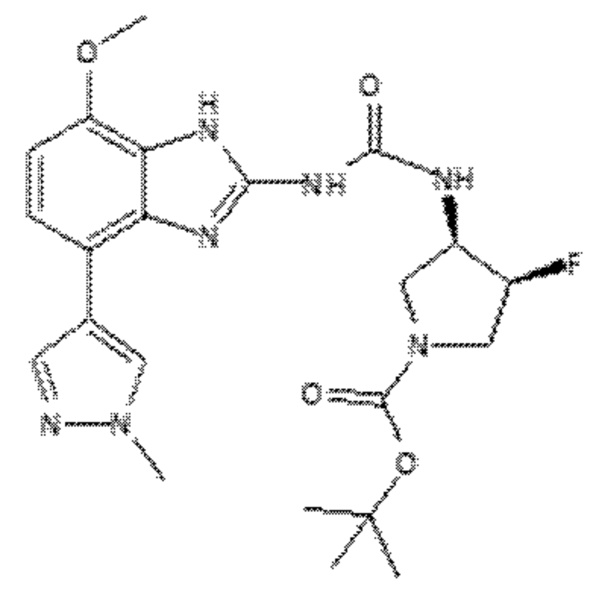
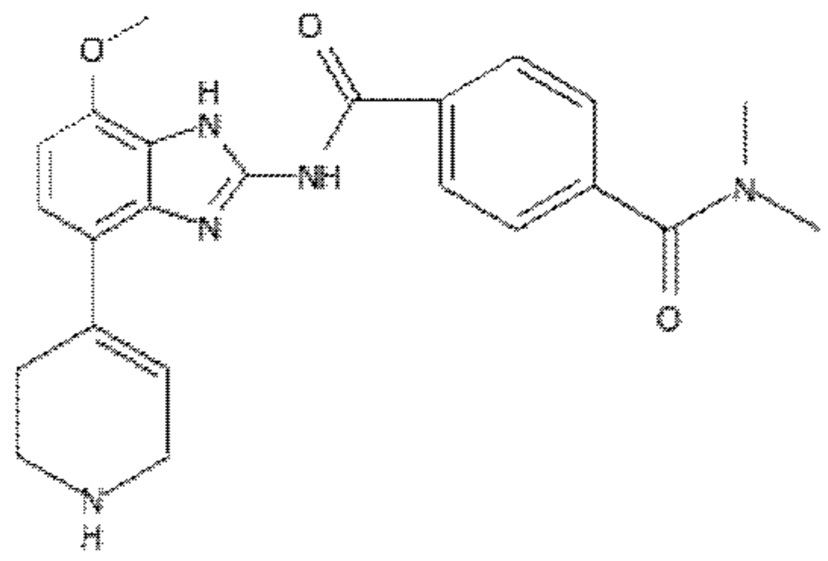
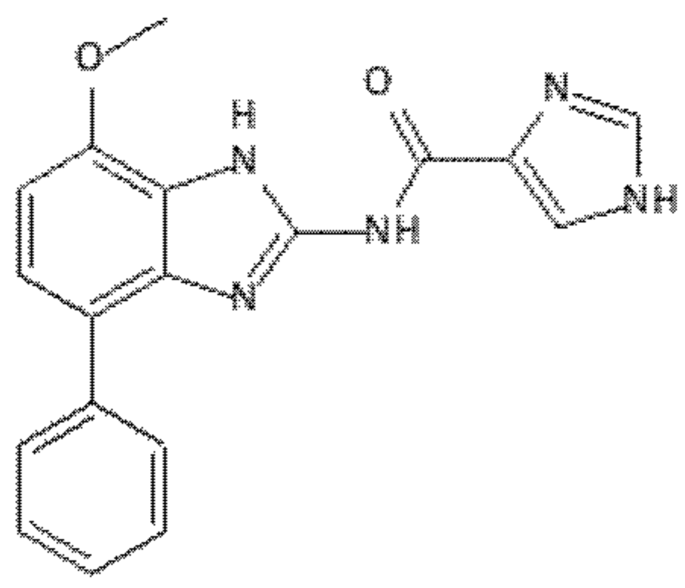
224		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
225		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
226		1-cyano-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
227		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide
228		3-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea

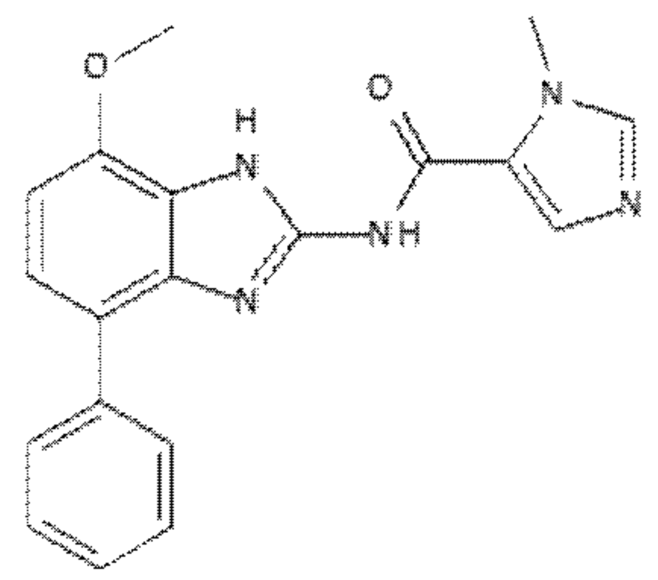
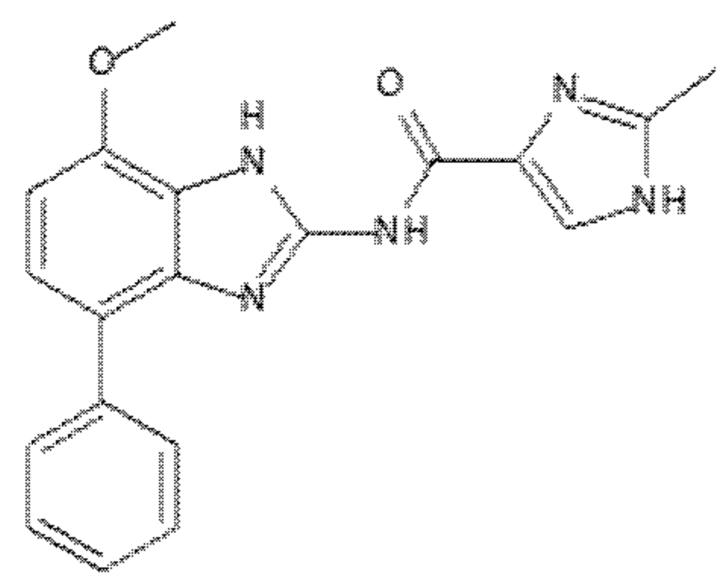
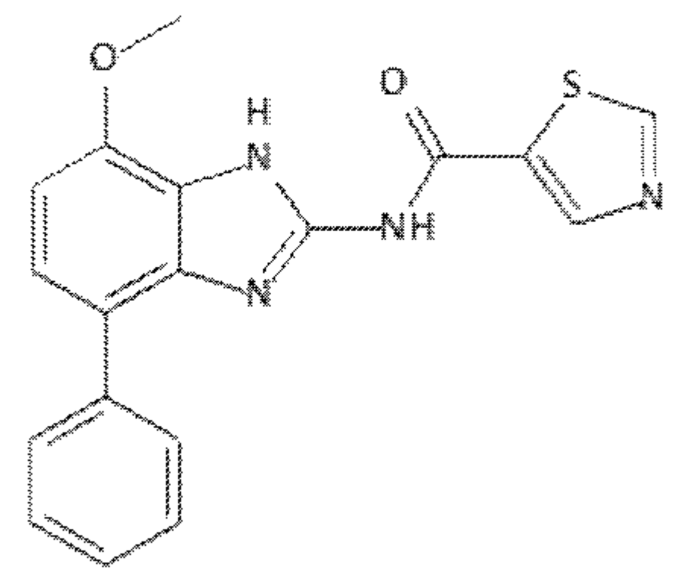
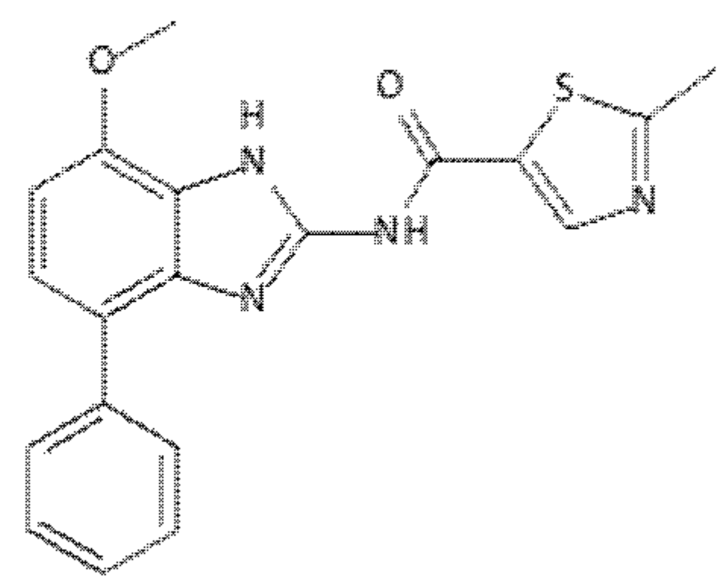
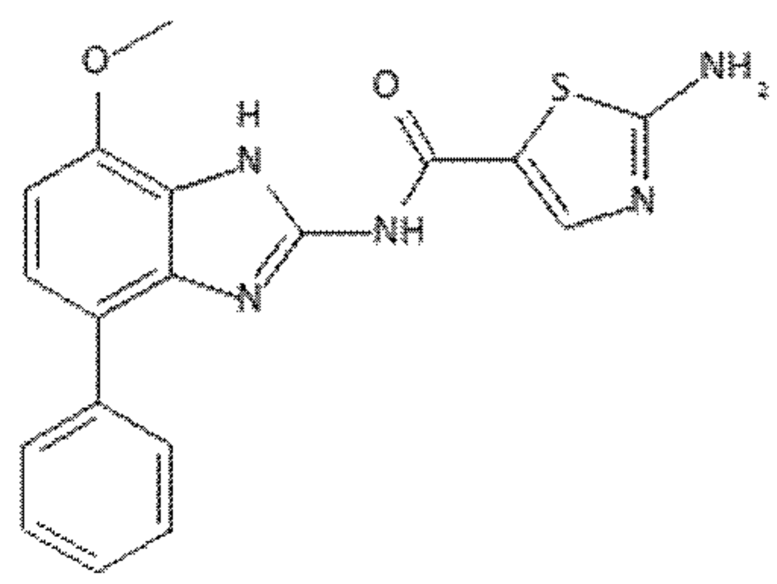
229		N-{7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-hydroxy-4-methylpiperidine-1-carboxamide
230		4-hydroxy-N-(4-methoxy-7-{1-[2-(2-methoxyethoxy)ethyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
231		4-hydroxy-N-{4-methoxy-7-[1-(pyridin-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
232		N-[7-methoxy-4-(1-propylcyclopropyl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
233		N-[4-(hexan-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

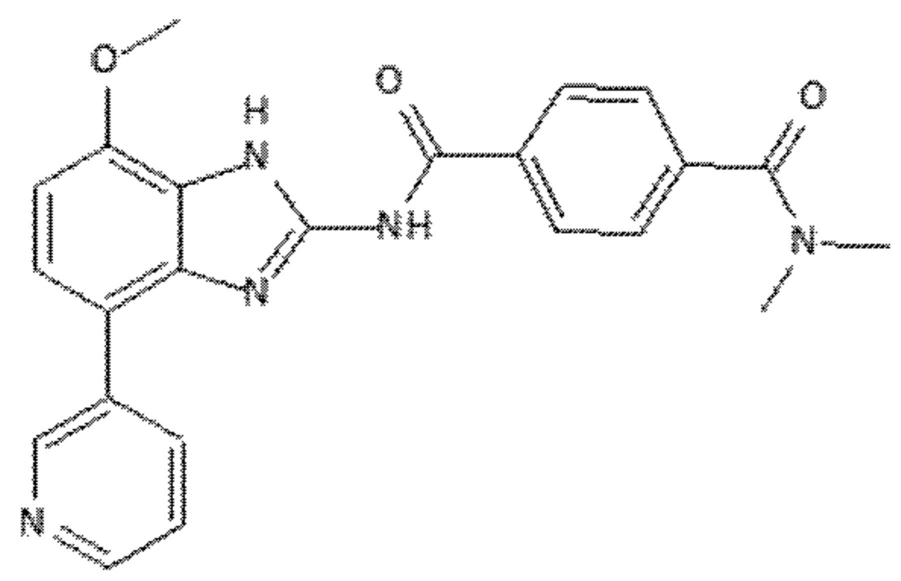
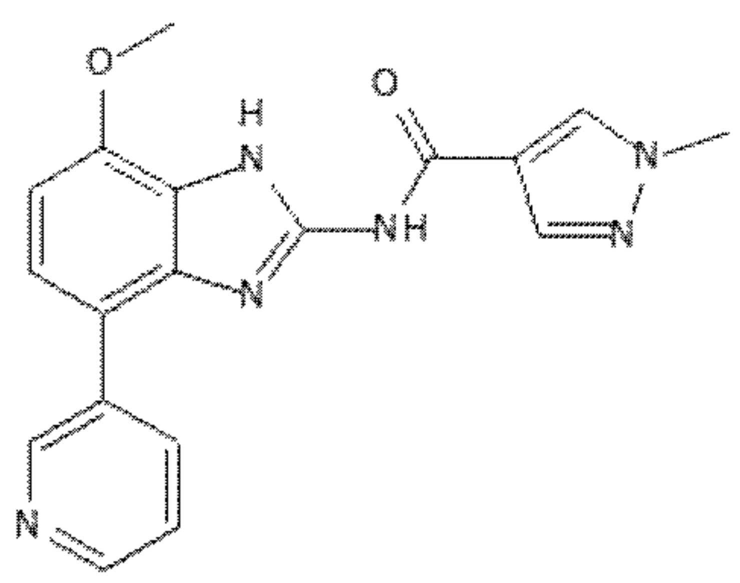
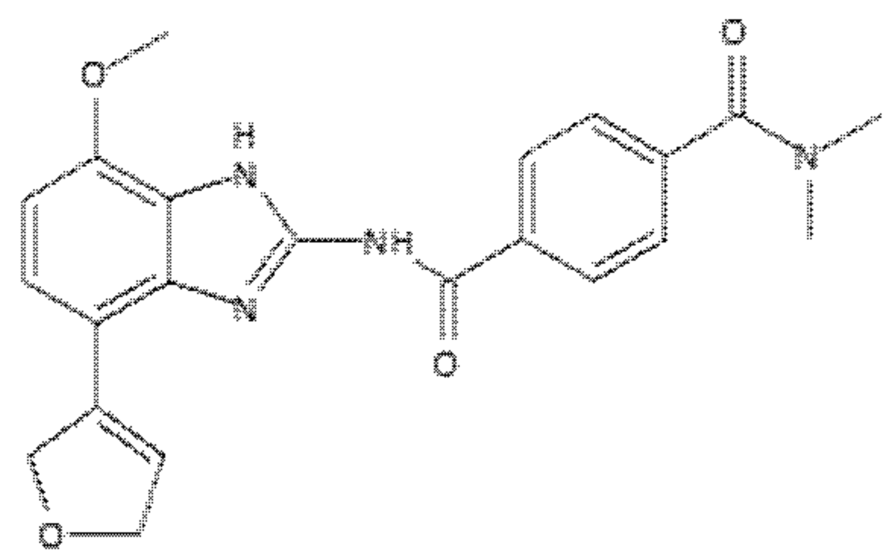
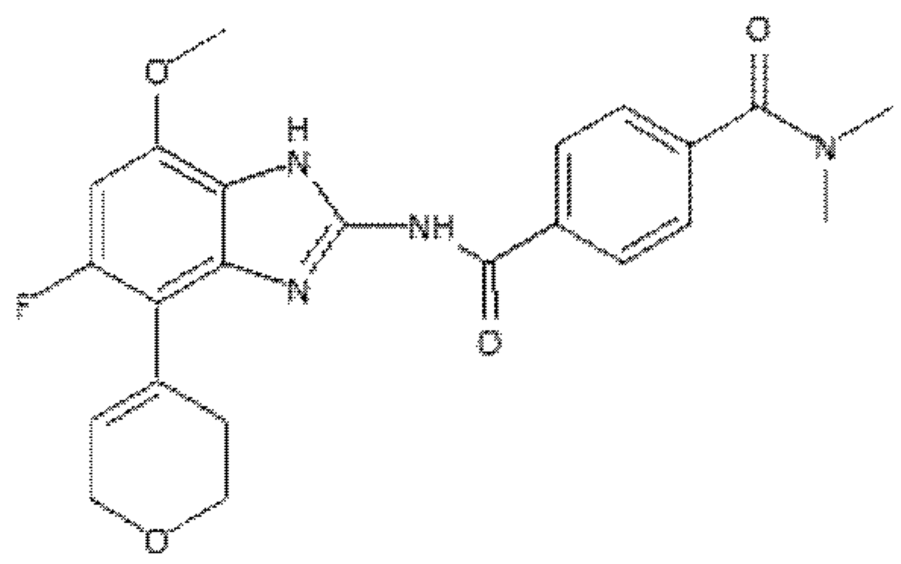
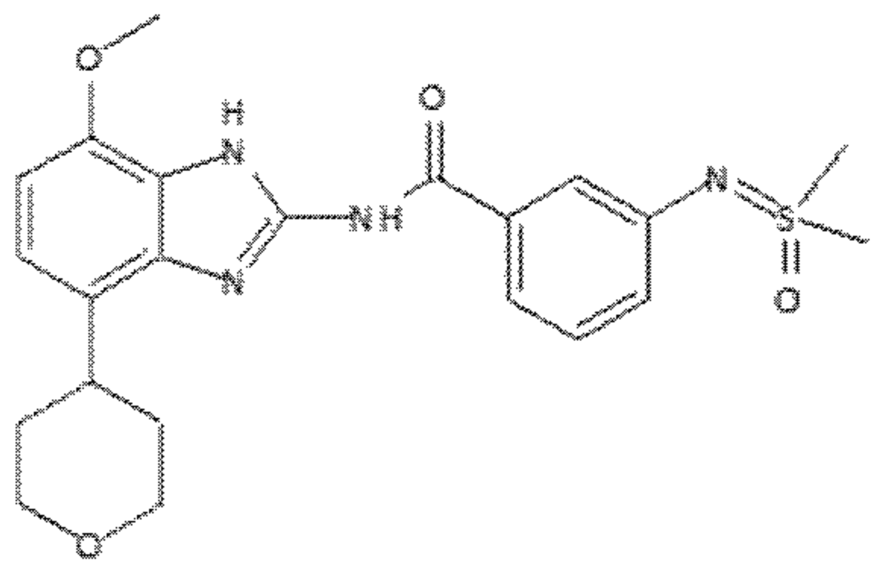
234		N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
235		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide
236		4-hydroxy-N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
237		4-hydroxy-N-(4-methoxy-7-{1-[(pyridin-3-yl)methyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
238		4-hydroxy-N-{7-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide

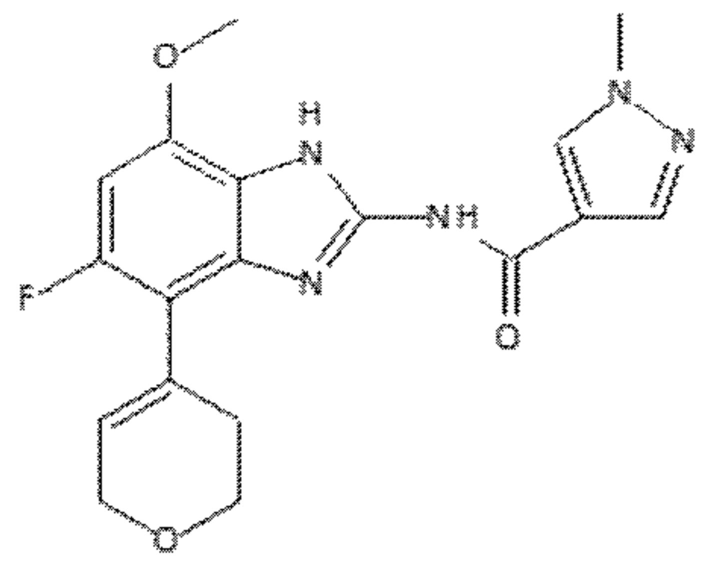
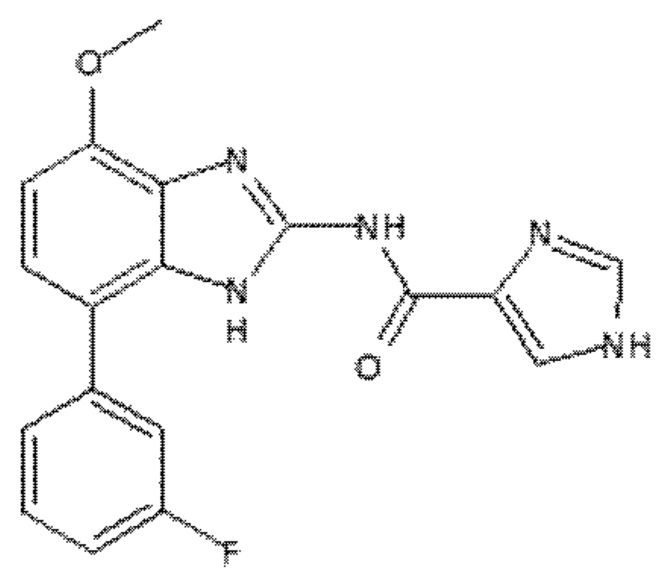
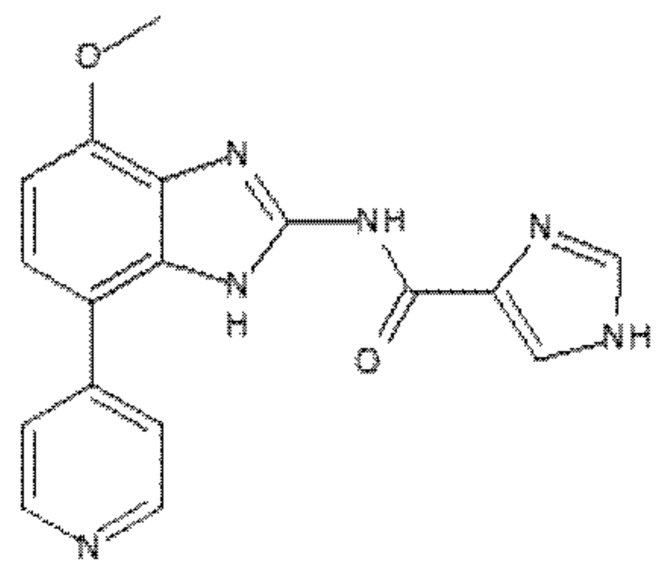
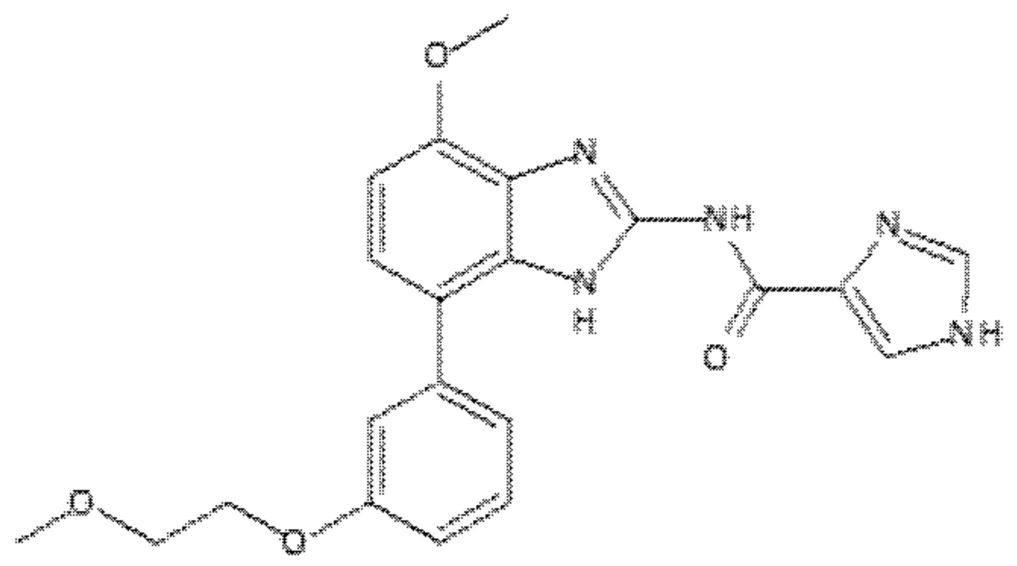
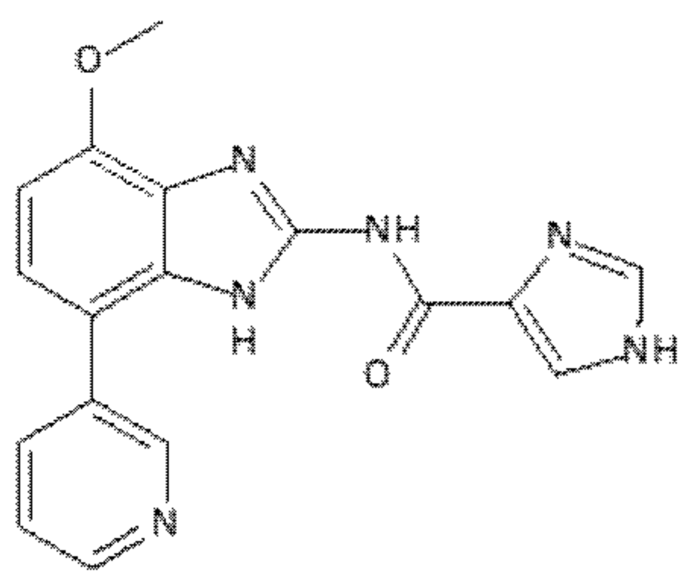
239		N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
240		N4-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
241		4-hydroxy-N-{4-methoxy-7-[1-(oxolan-3-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
242		N4-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
243		N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

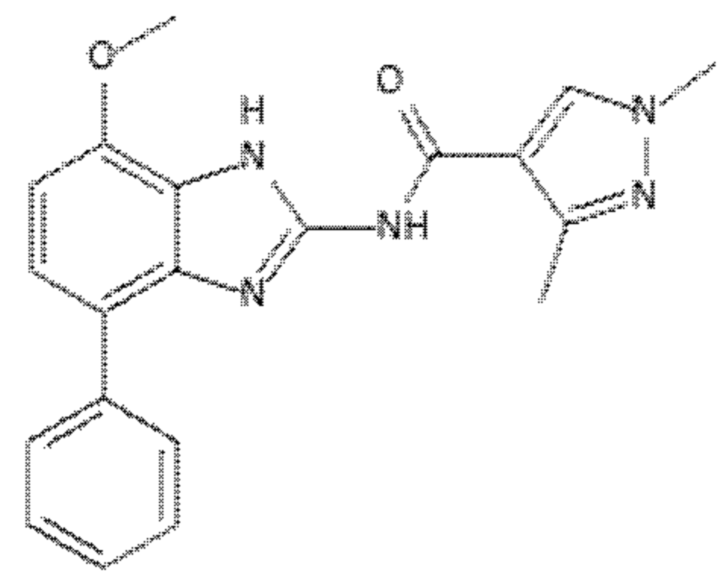
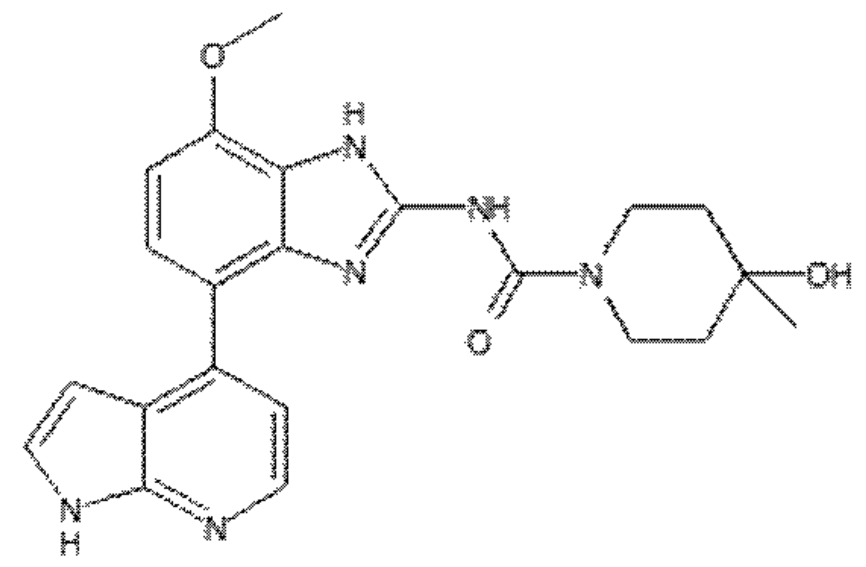
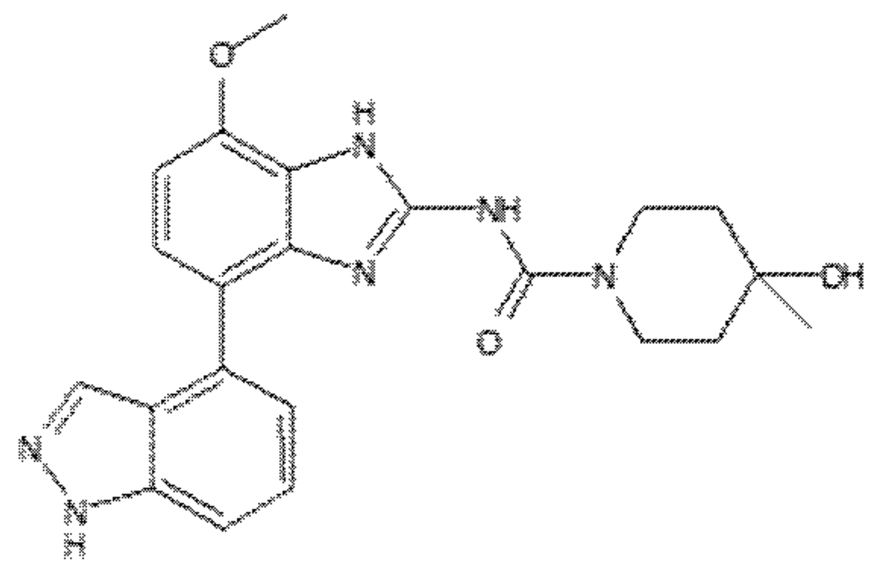
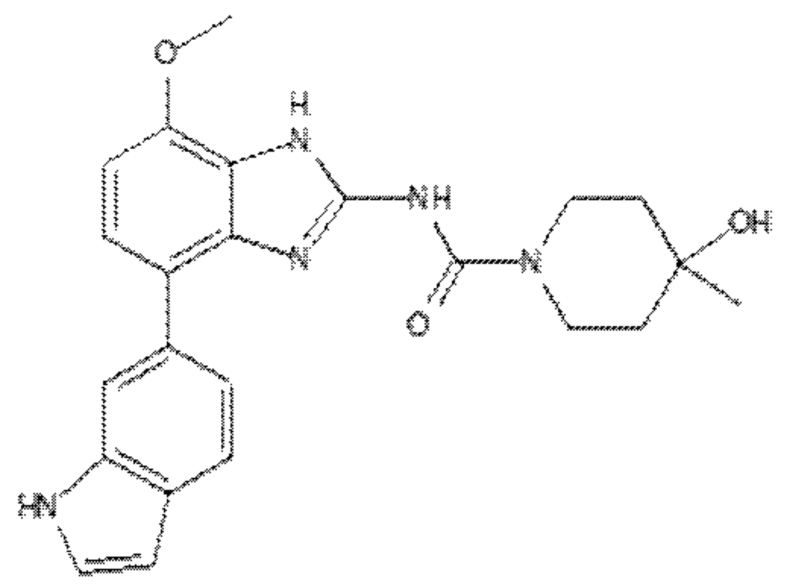
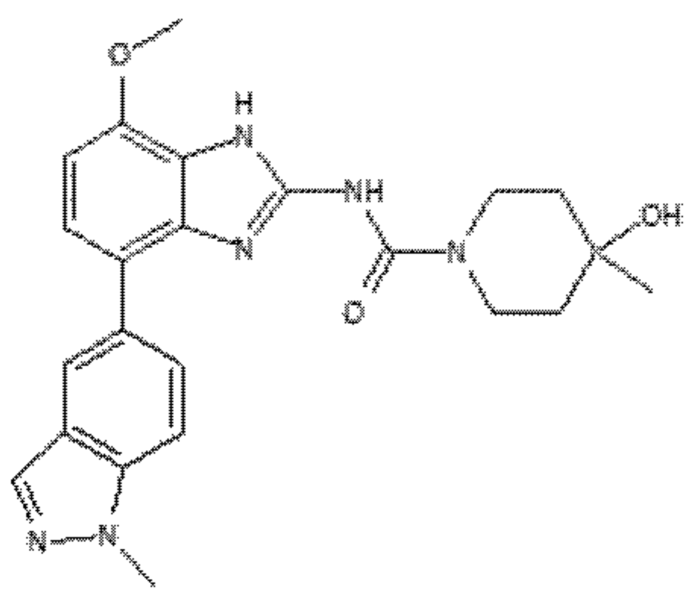
244		N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
245		tert-butyl 3-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)azetidine-1-carboxylate
246		N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-oxopyrrolidine-3-carboxamide
247		3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea
248		4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

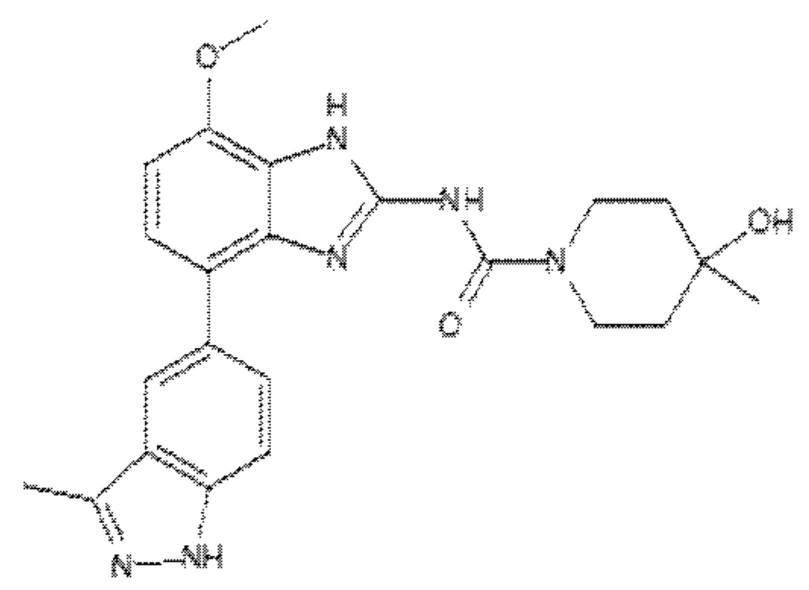
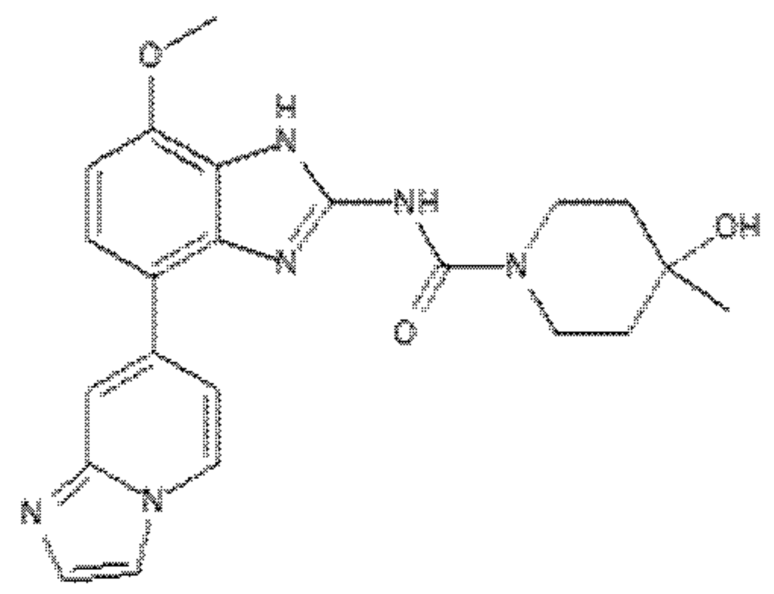
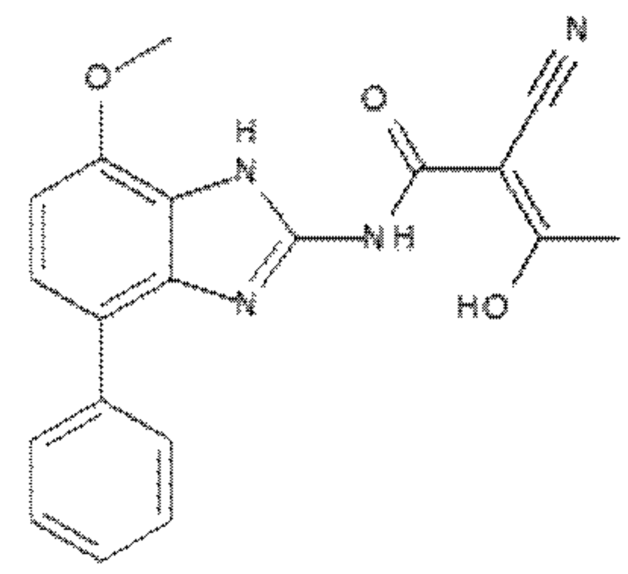
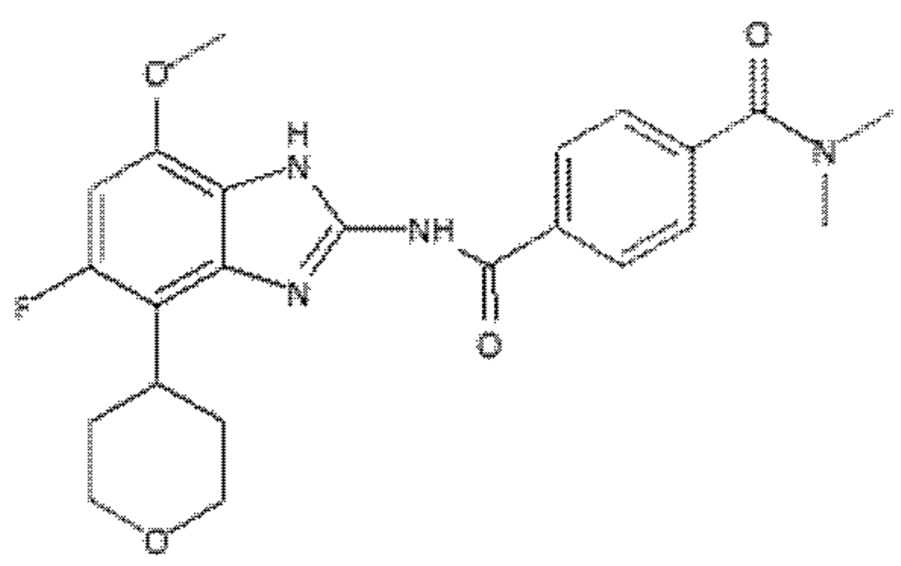
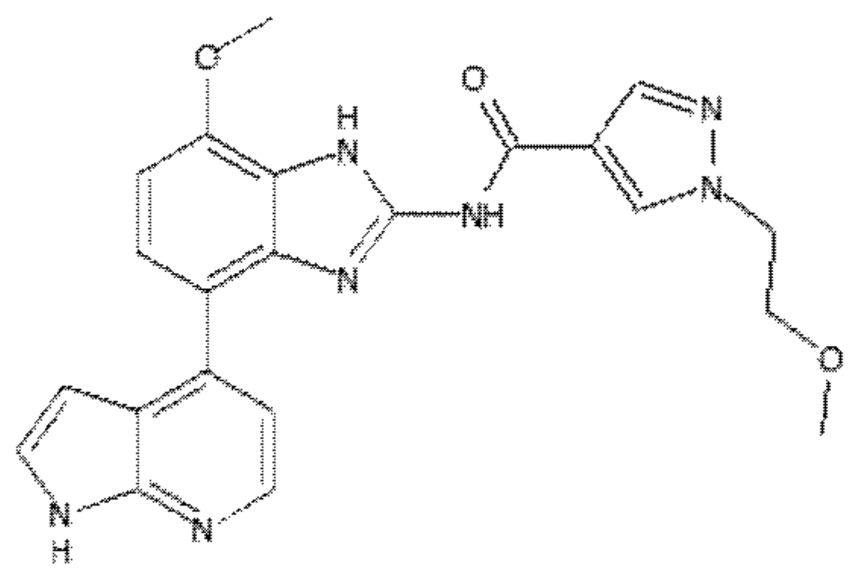
249		1-[(3R,4S)-4-fluoropyrrolidin-3-yl]-3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
250		4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
251		tert-butyl (3S,4R)-3-fluoro-4-({[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}amino)pyrrolidine-1-carboxylate
252		N4-[7-methoxy-4-(1,2,3,6-tetrahydropyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
253		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1H-imidazole-4-carboxamide

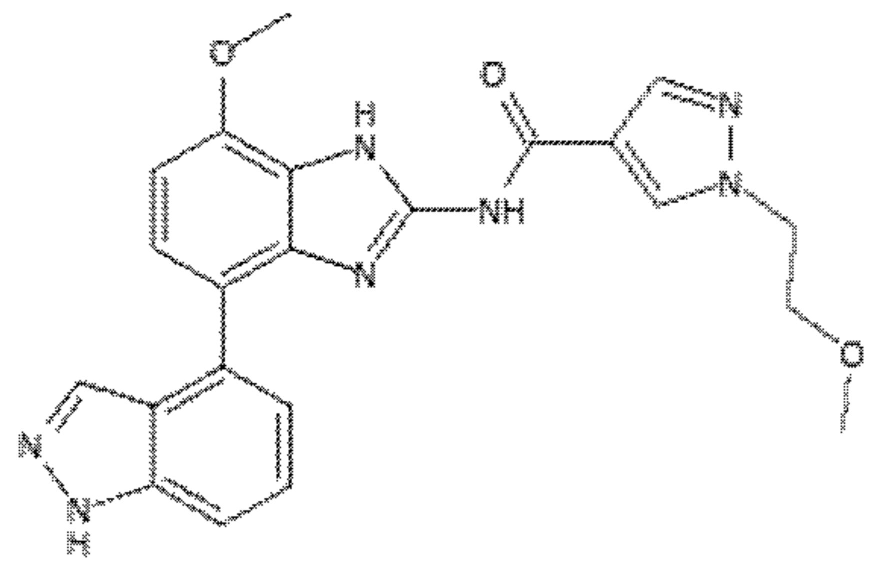
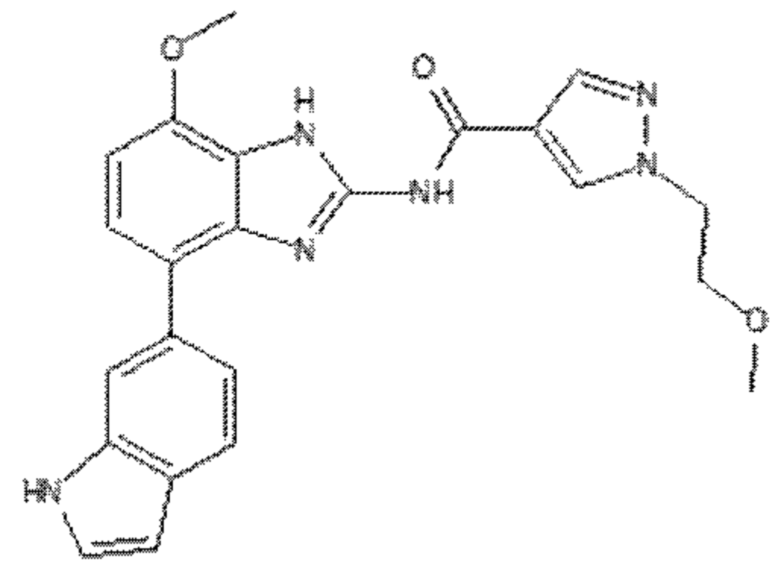
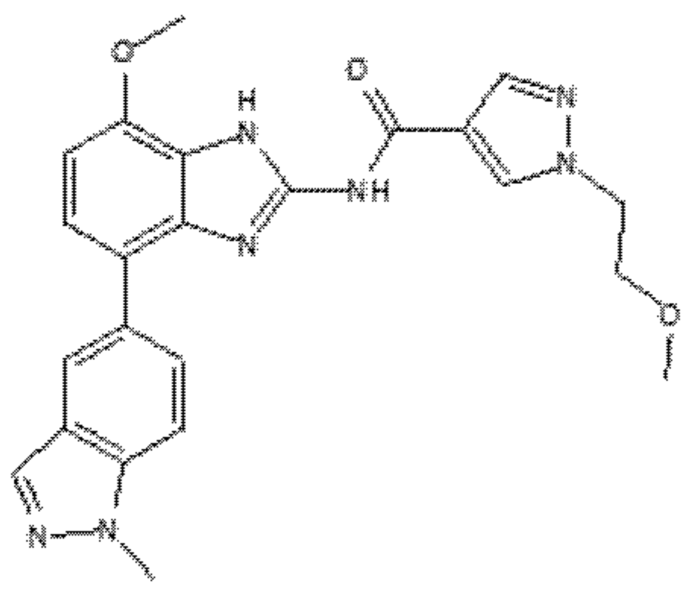
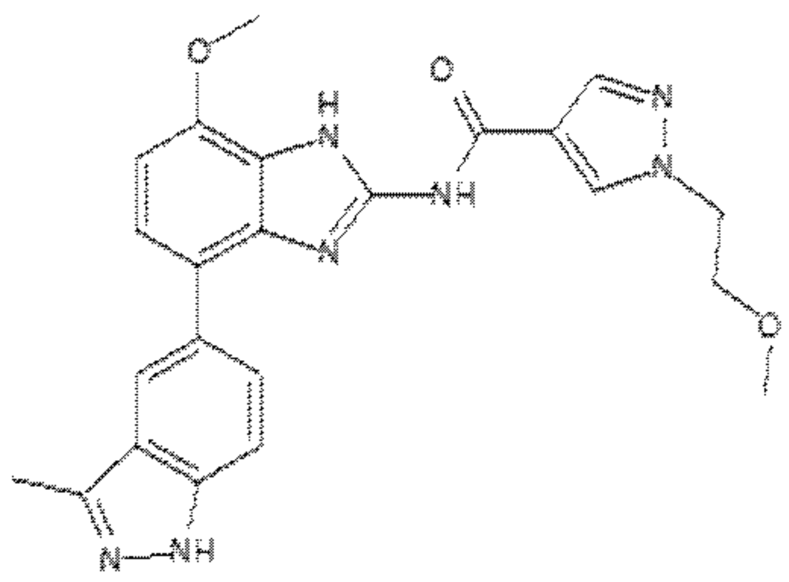
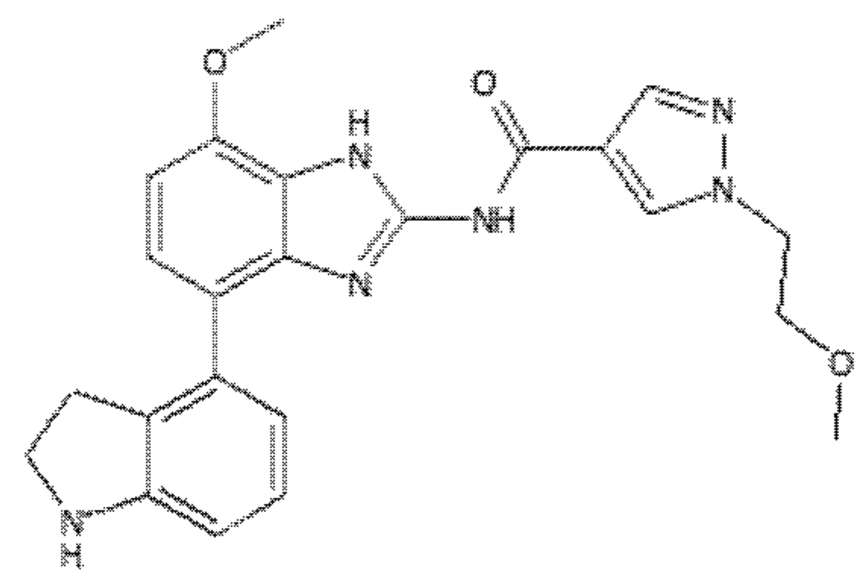
254		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-imidazole-5-carboxamide
255		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1H-imidazole-4-carboxamide
256		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide
257		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-thiazole-5-carboxamide
258		2-amino-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide

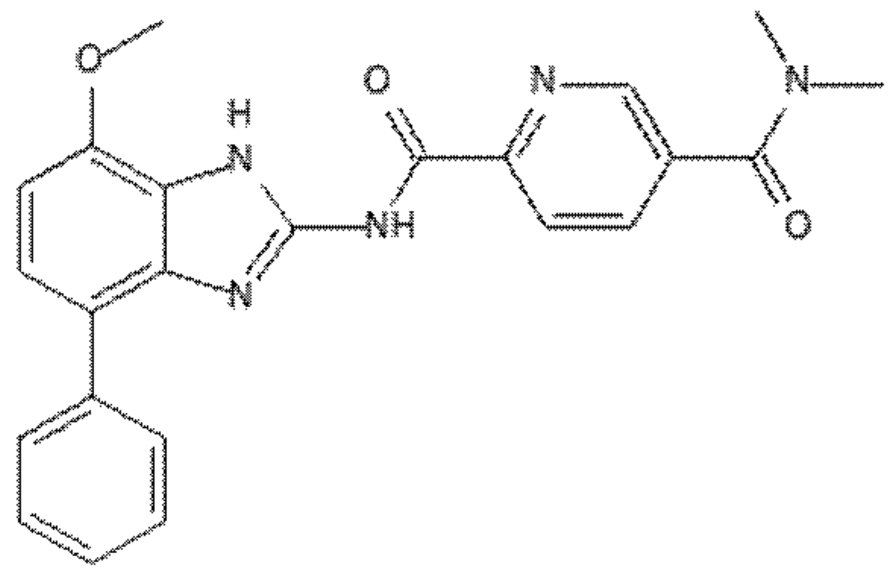
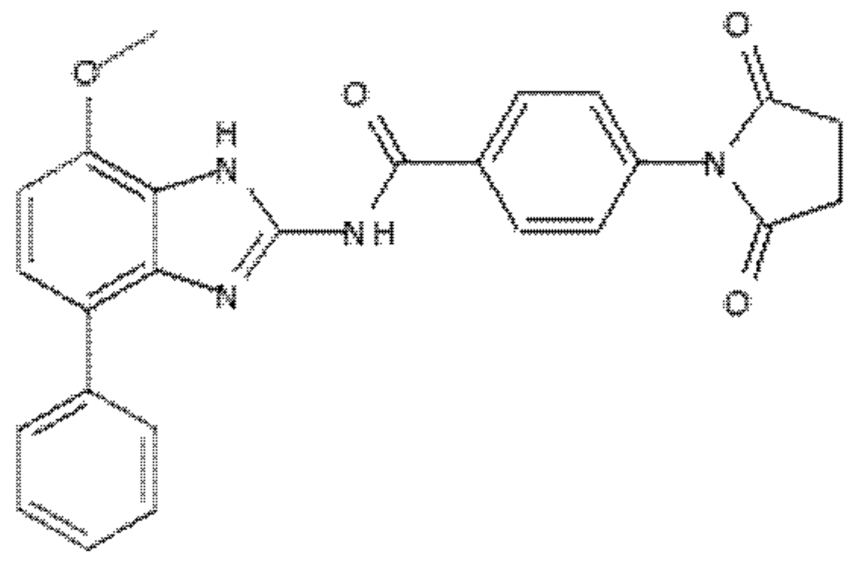
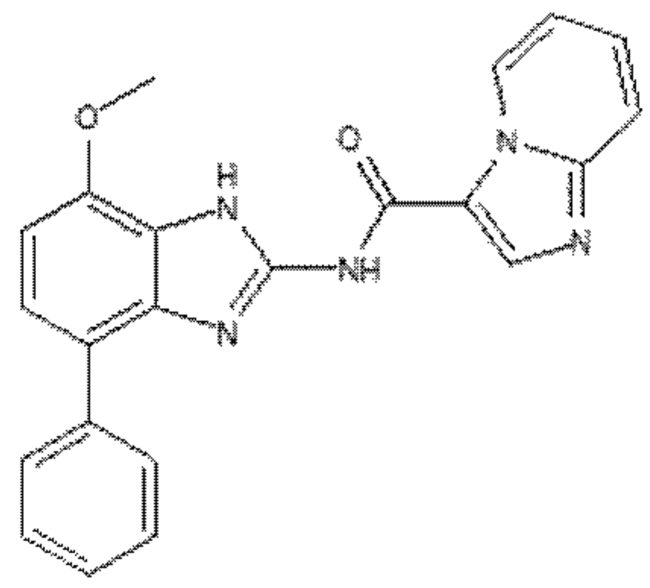
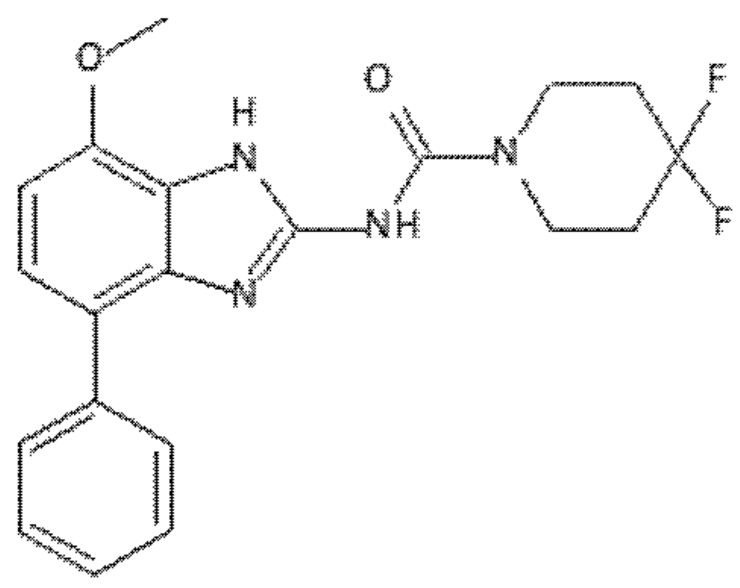
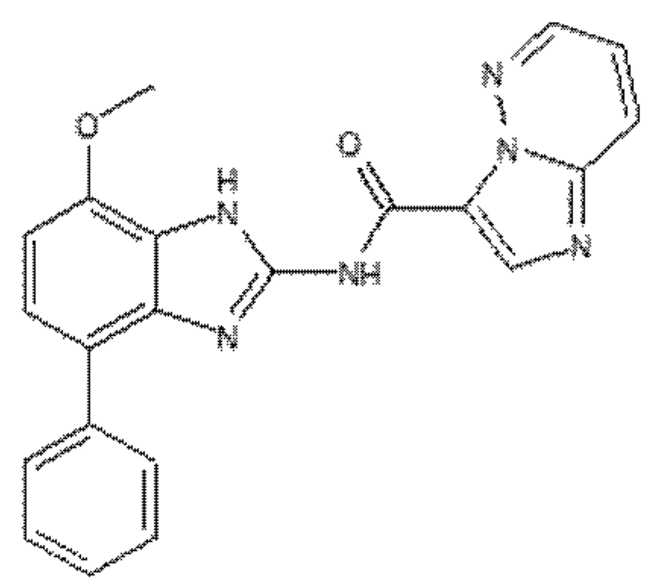
259		N4-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
260		N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
261		N4-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
262		N4-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
263		3-{[dimethyl(oxo)-lambda6-sulfanylidene]amino}-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

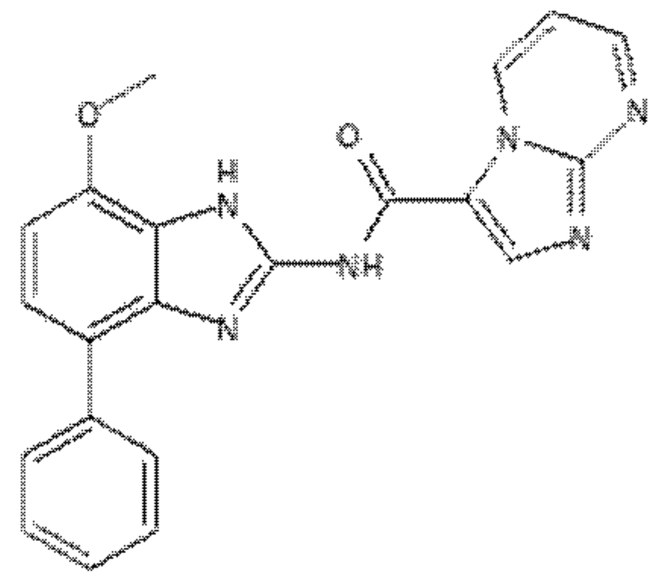
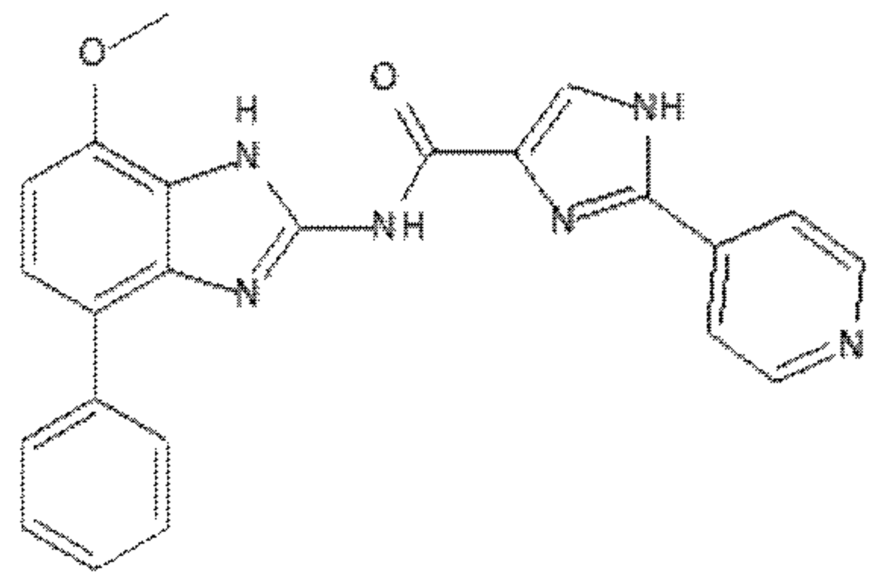
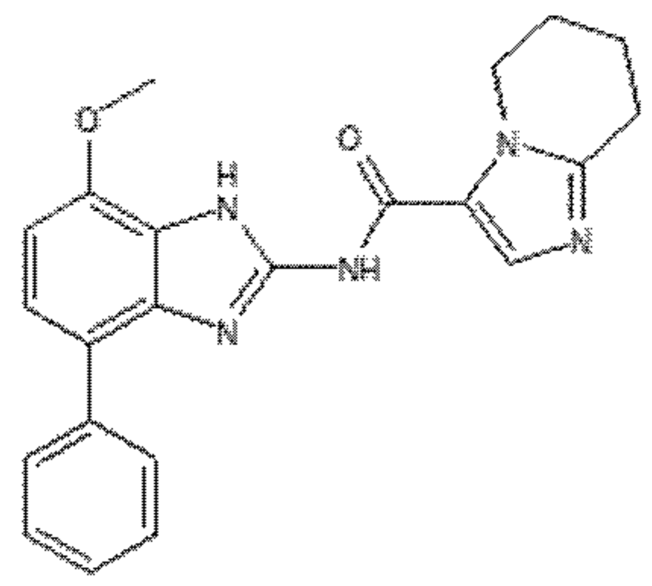
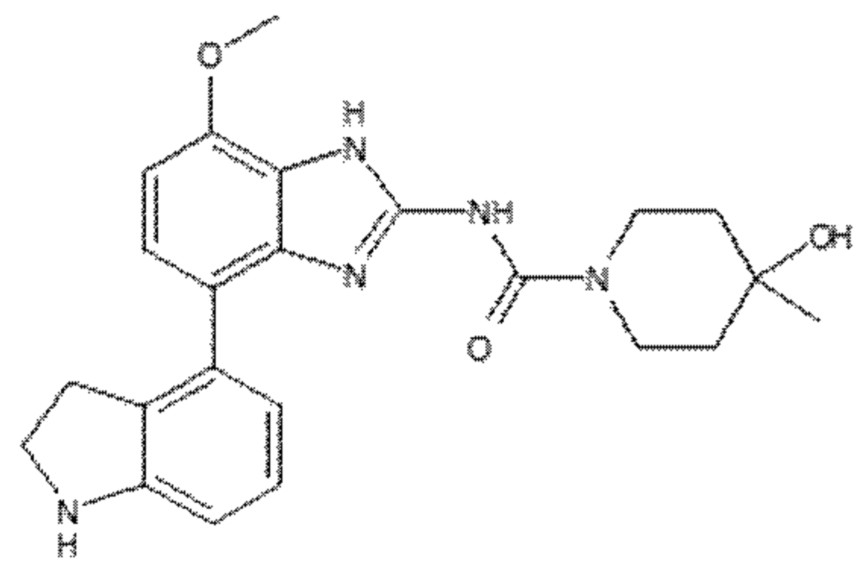
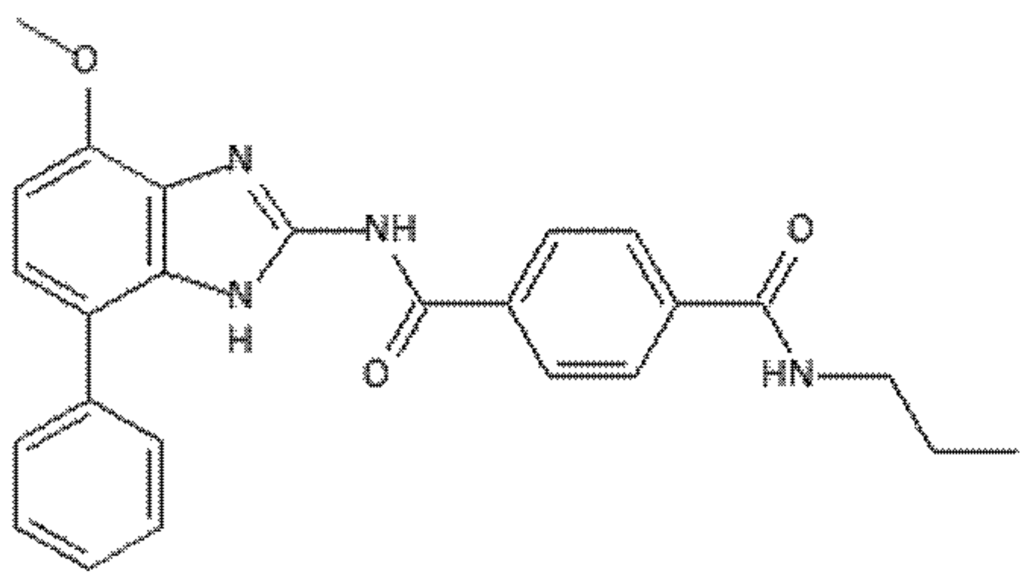
264		N-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
265		N-[7-(3-fluorophenyl)-4-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
266		N-[4-methoxy-7-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
267		N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-1H-imidazole-4-carboxamide
268		N-[4-methoxy-7-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide

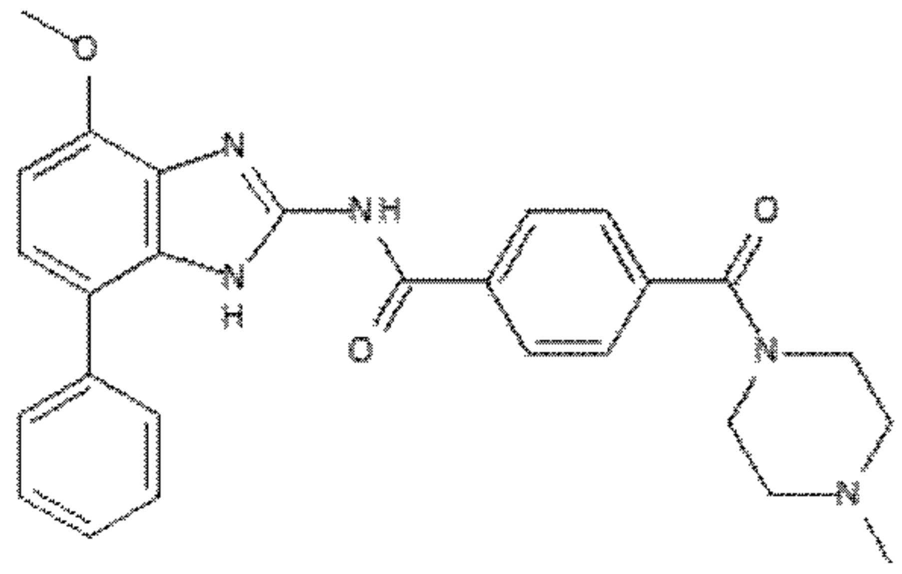
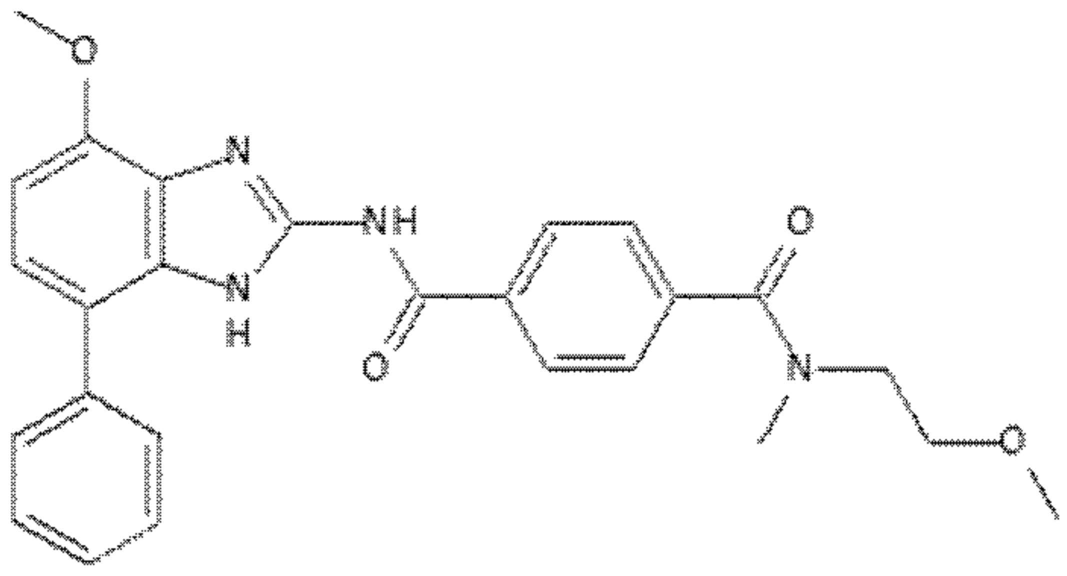
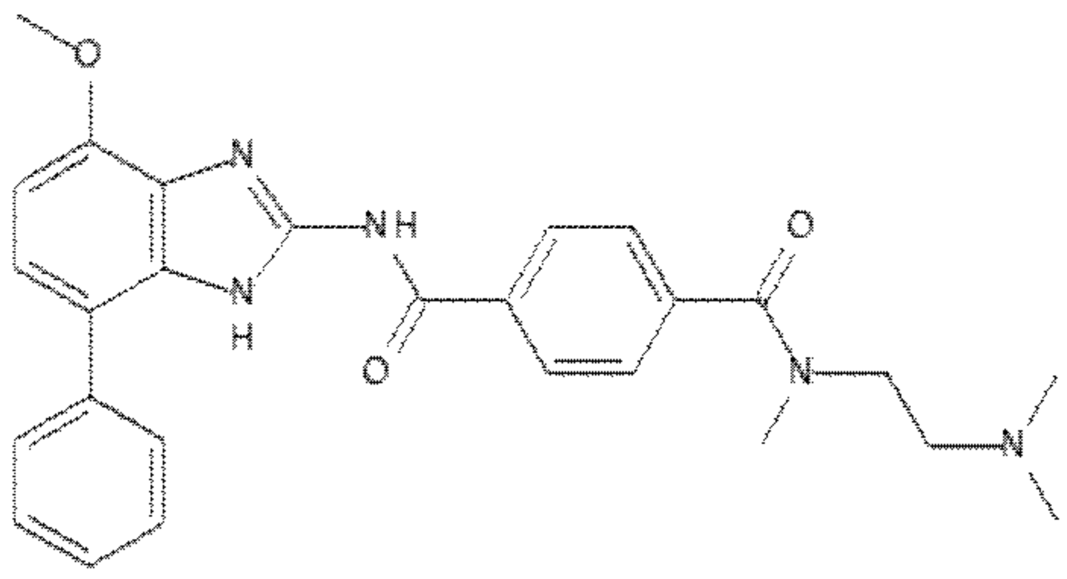
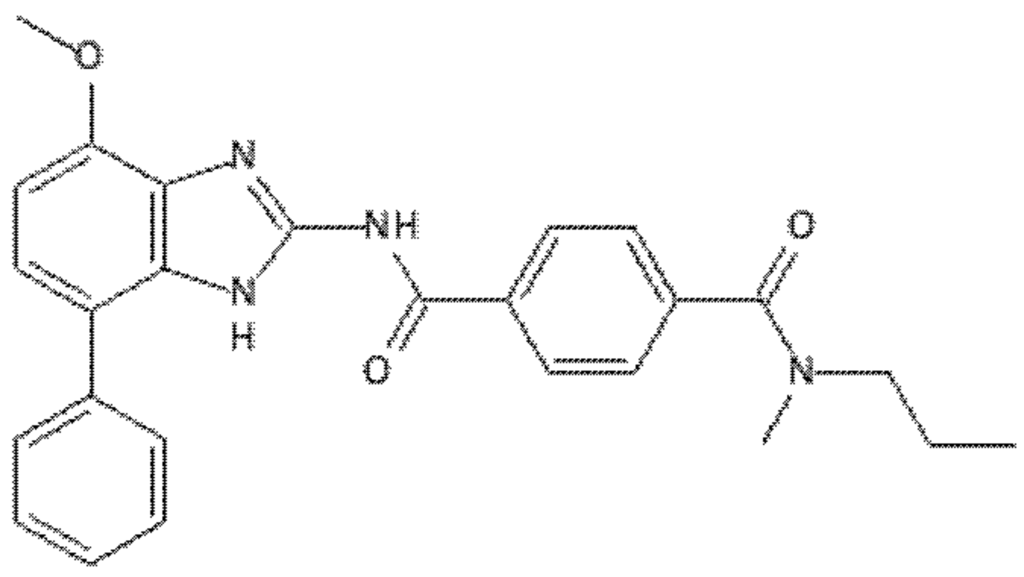
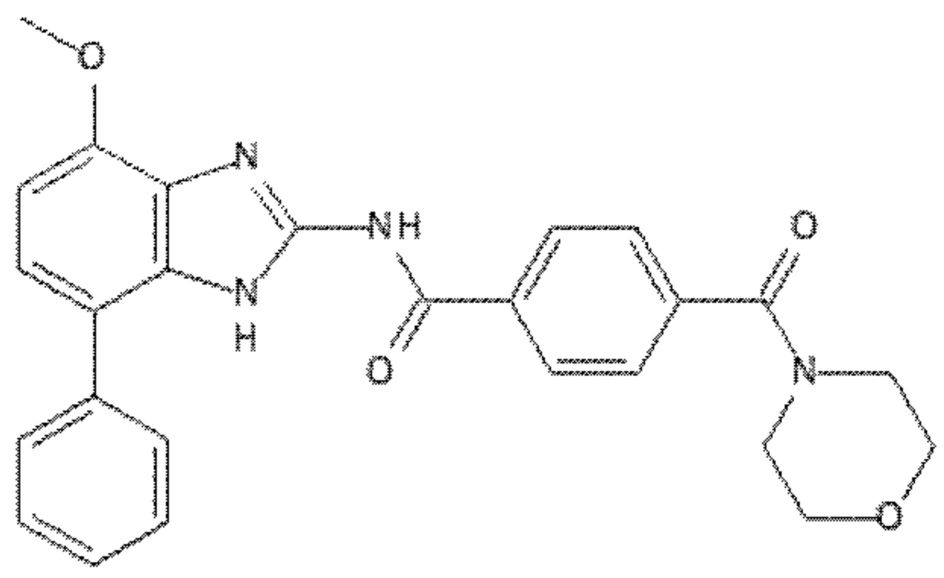
269		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-dimethyl-1H-pyrazole-4-carboxamide
270		4-hydroxy-N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
271		4-hydroxy-N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
272		4-hydroxy-N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
273		4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide

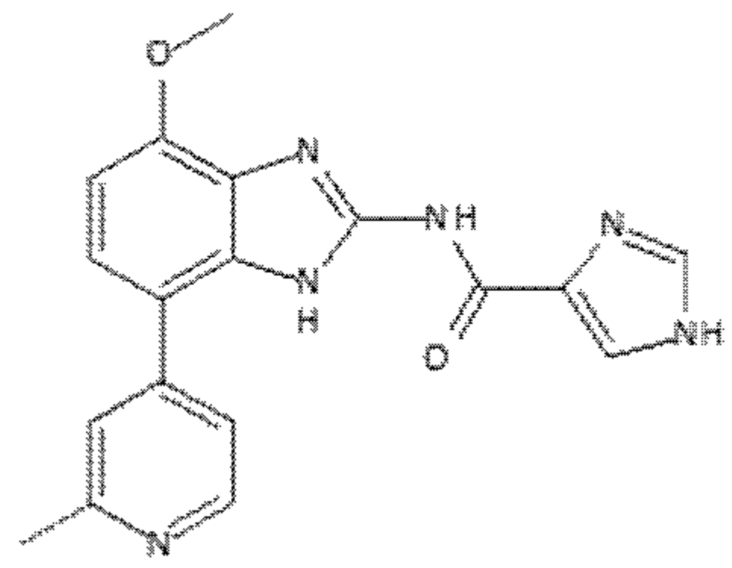
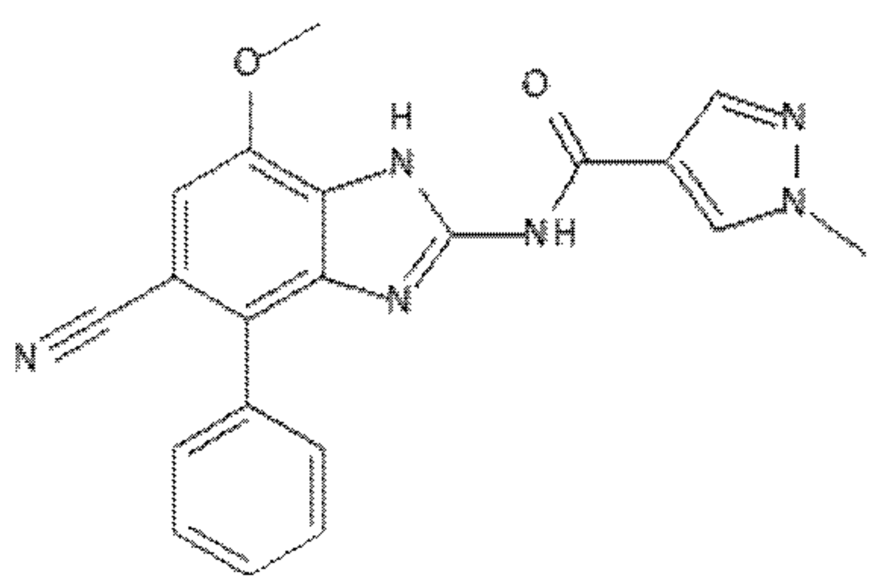
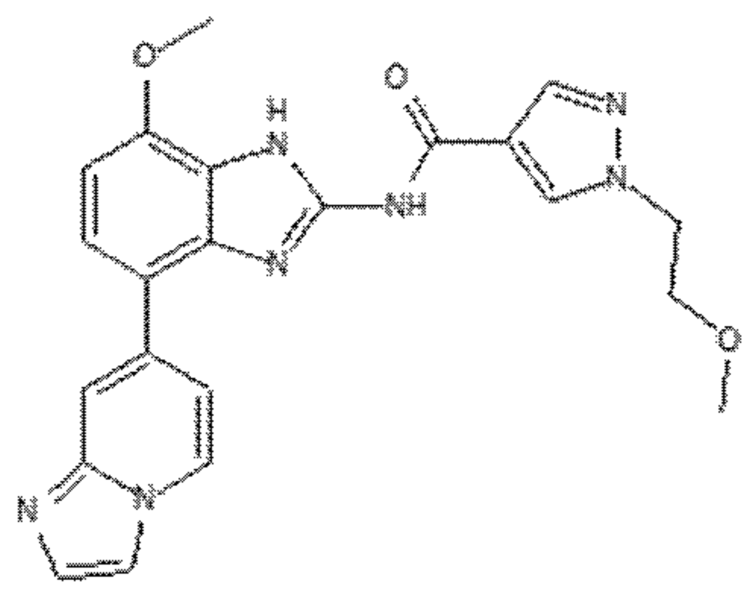
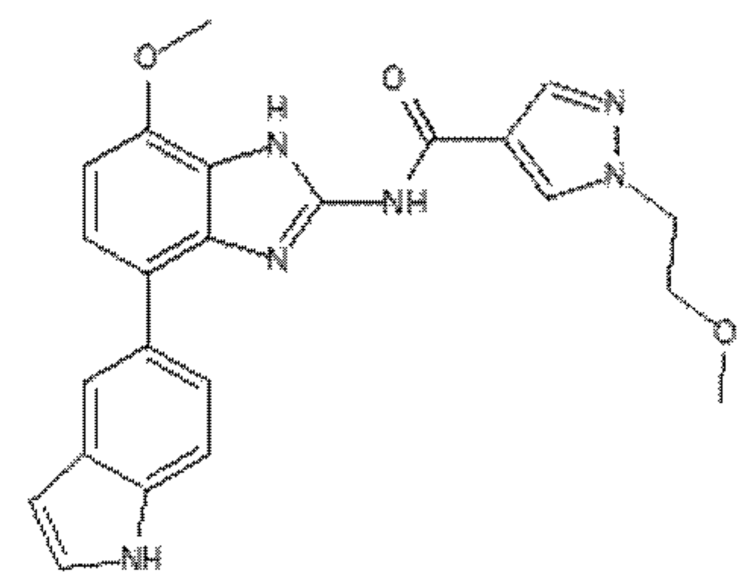
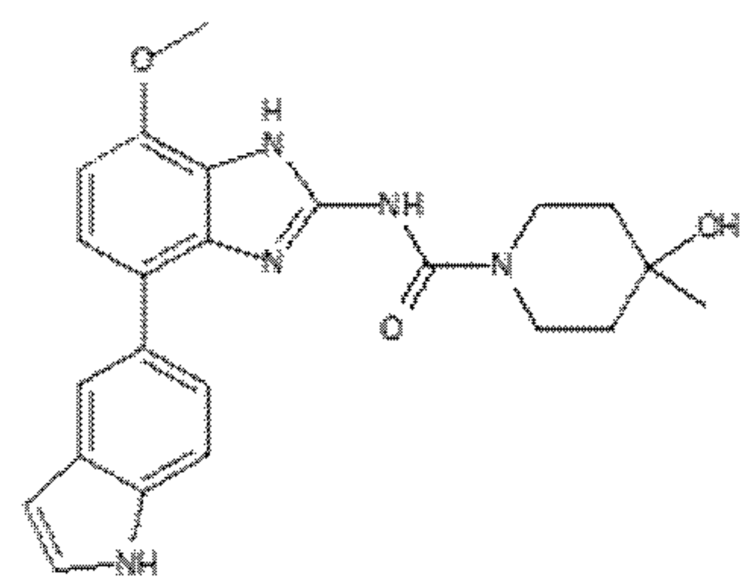
274		4-hydroxy-N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
275		4-hydroxy-N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
276		(2Z)-2-cyano-3-hydroxy-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)but-2-enamide
277		N4-[5-fluoro-7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
278		N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide

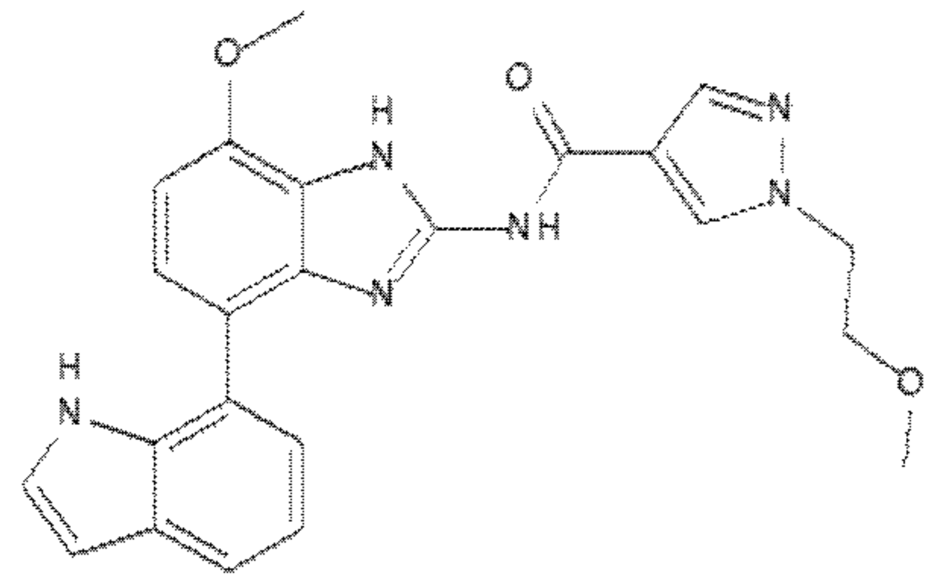
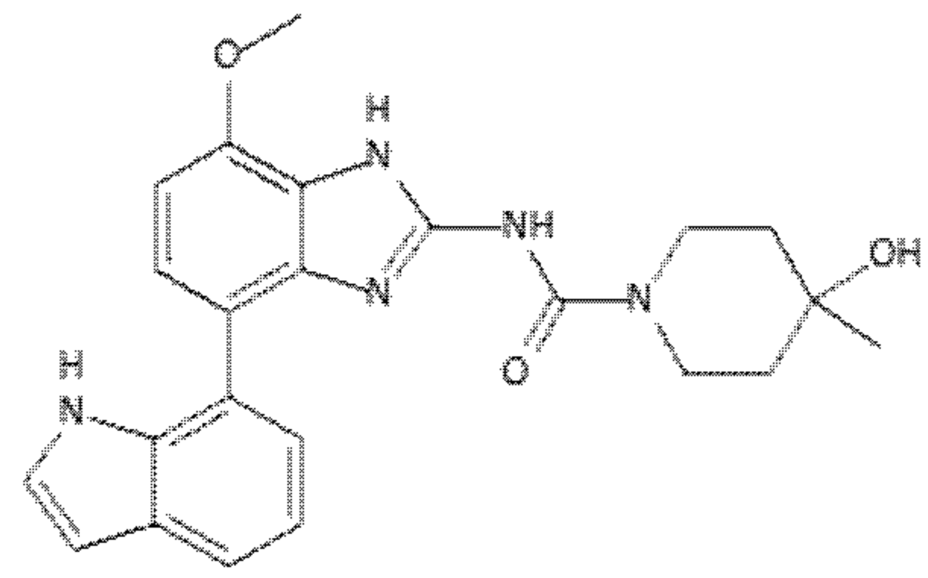
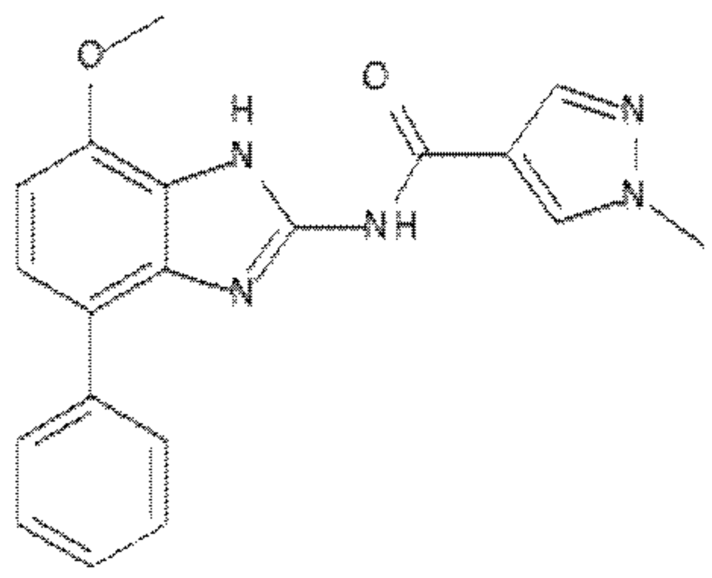
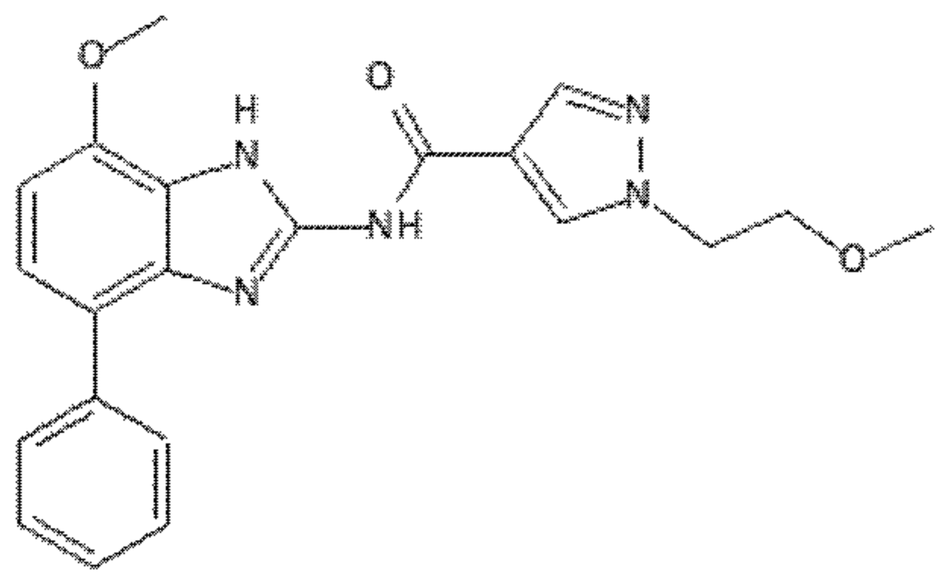
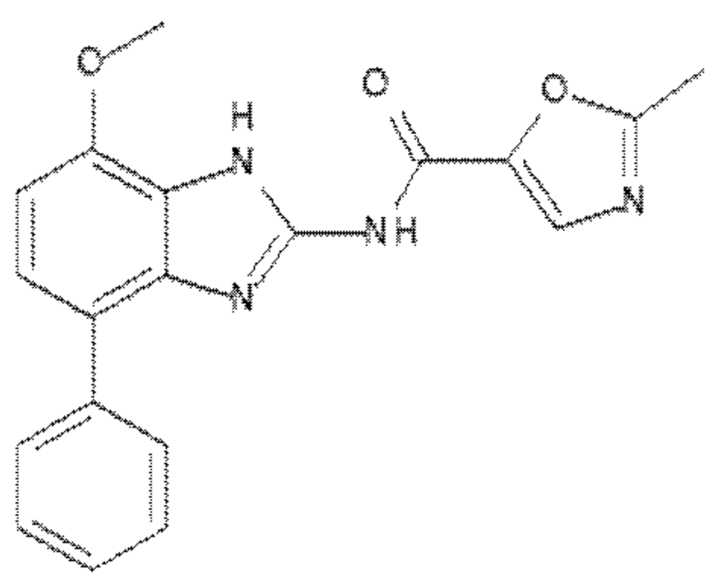
279		N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
280		N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
281		N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
282		N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
283		N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide

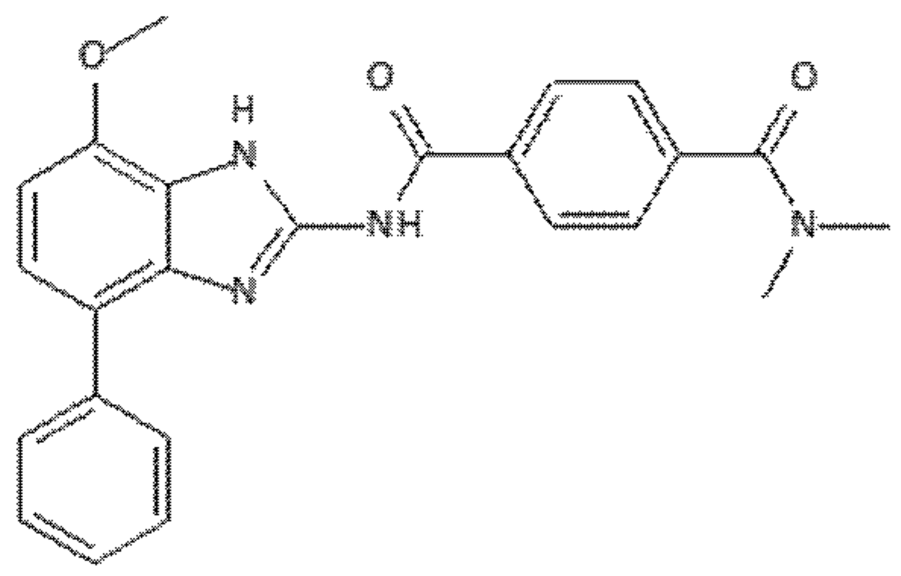
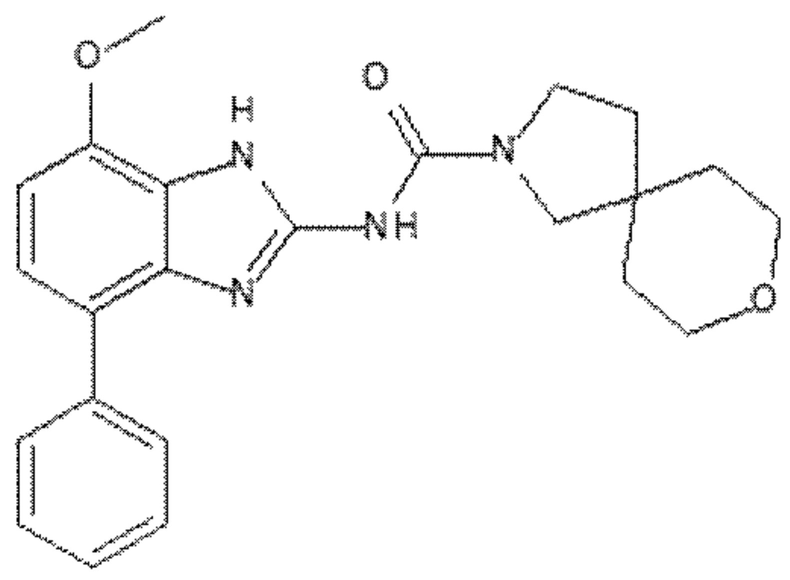
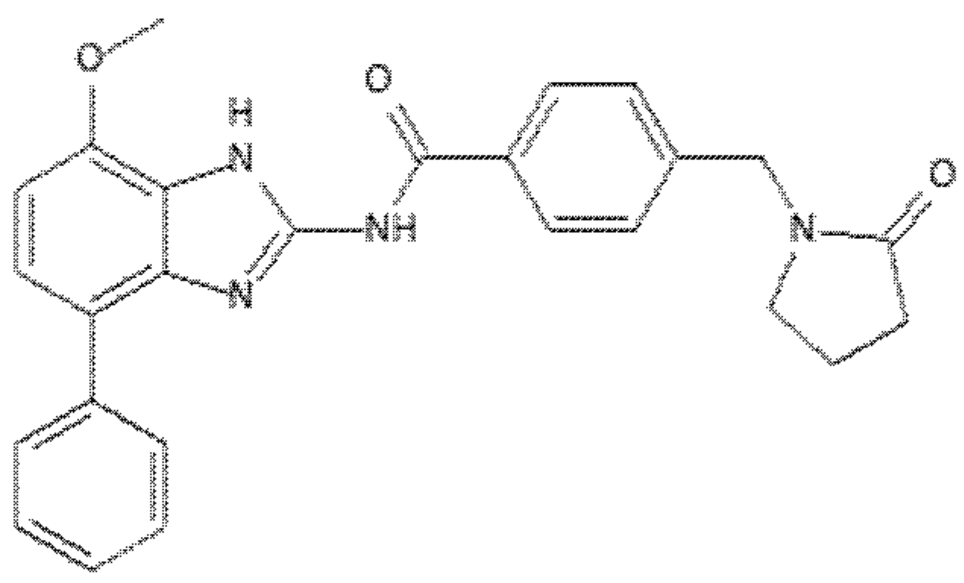
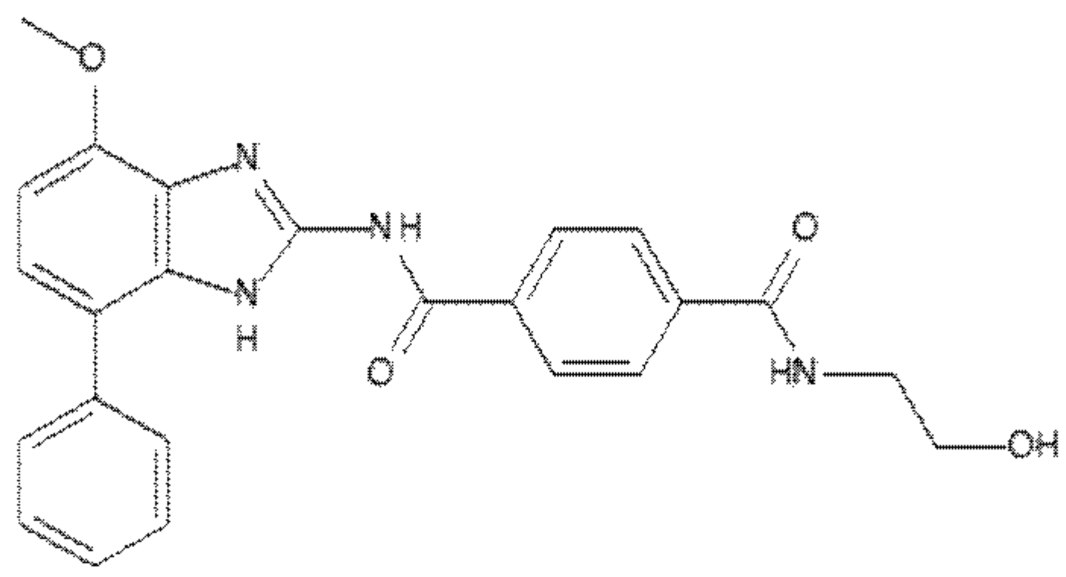
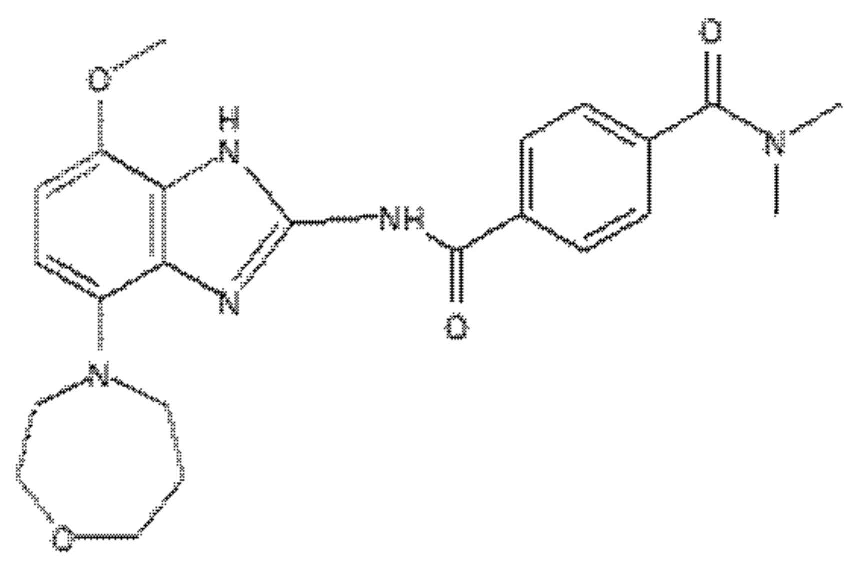
284		N2-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N5,N5-dimethylpyridine-2,5-dicarboxamide
285		4-(2,5-dioxopyrrolidin-1-yl)-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)benzamide
286		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyridine-3-carboxamide
287		4,4-difluoro-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)piperidine-1-carboxamide
288		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-b]pyridazine-3-carboxamide

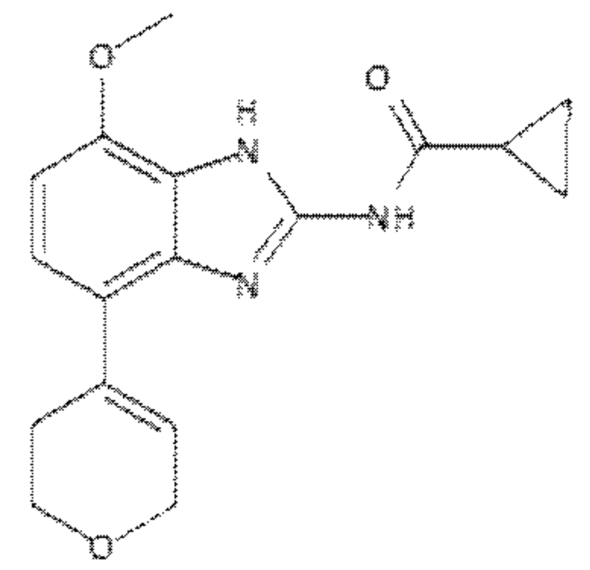
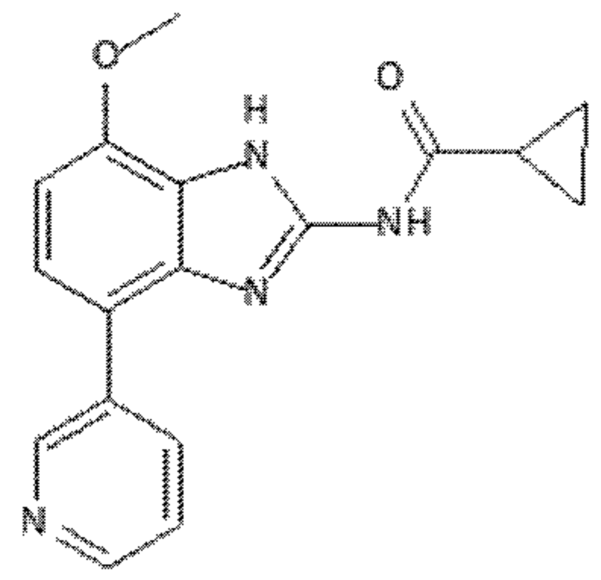
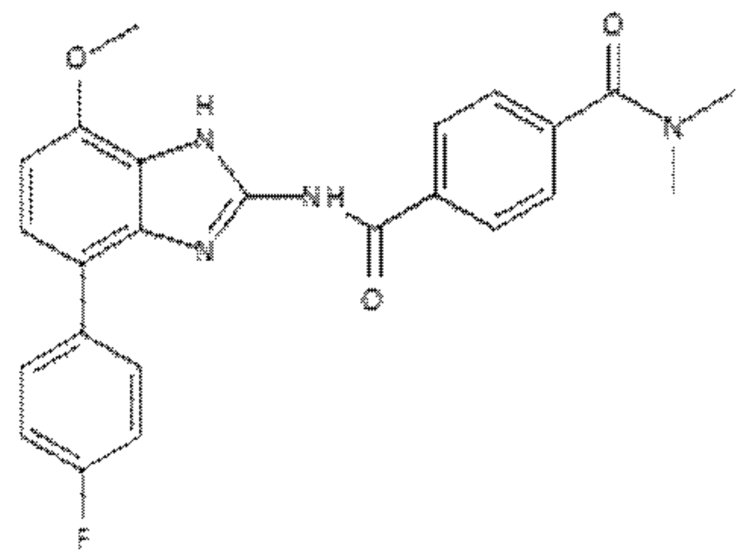
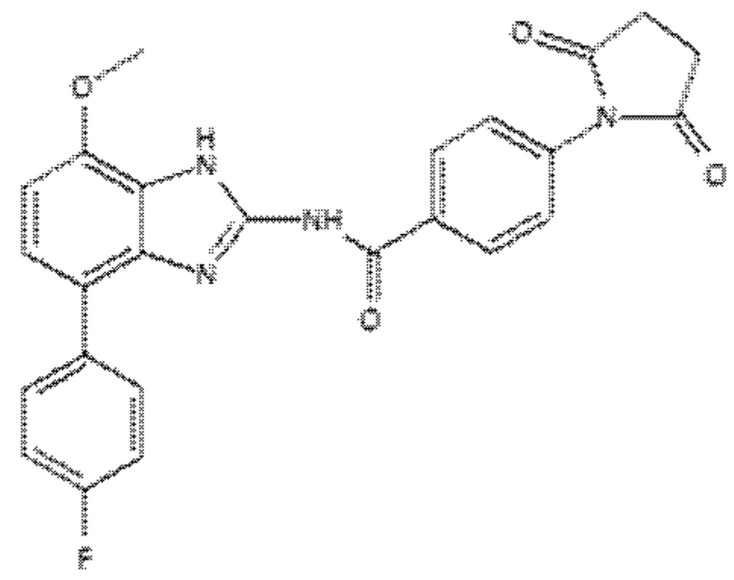
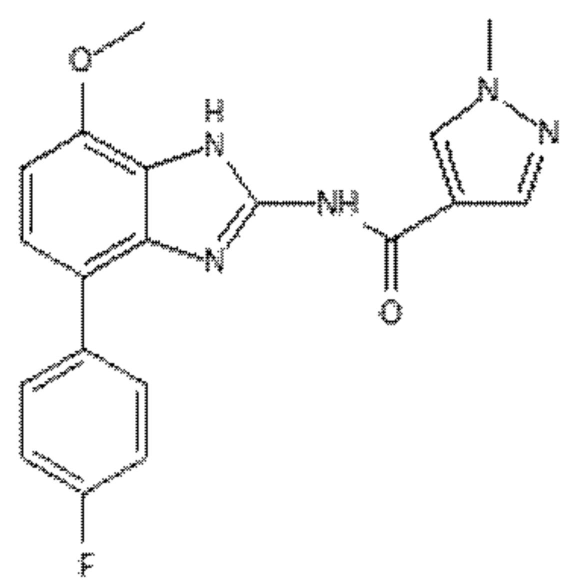
289		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyrimidine-3-carboxamide
290		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-(pyridin-4-yl)-1H-imidazole-4-carboxamide
291		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-5H,6H,7H,8H-imidazo[1,2-a]pyridine-3-carboxamide
292		N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
293		N1-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N4-propylbenzene-1,4-dicarboxamide

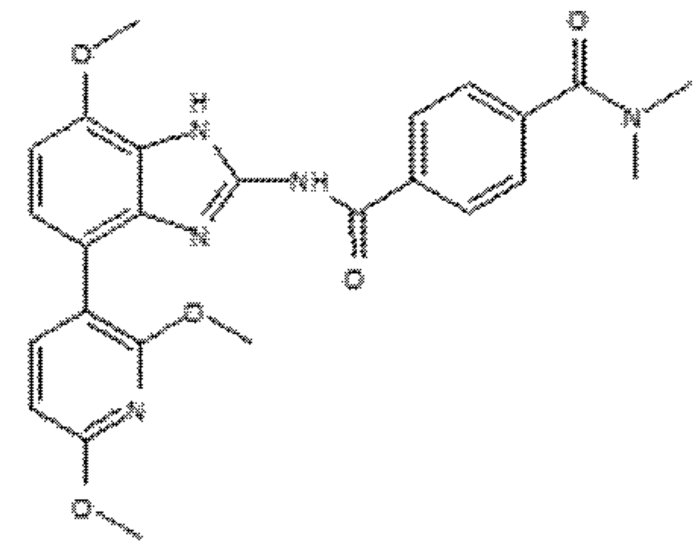
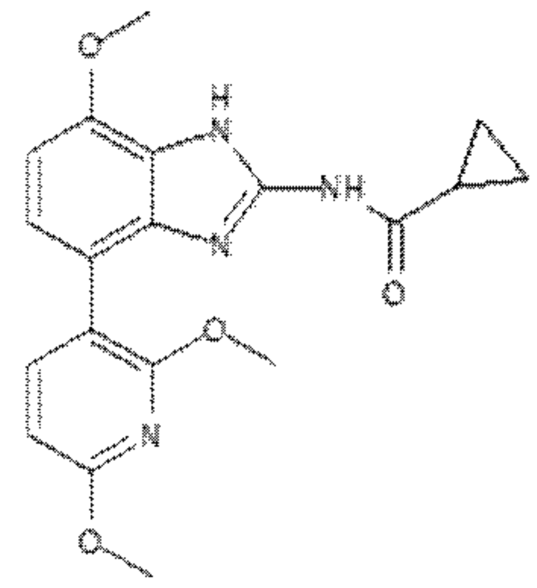
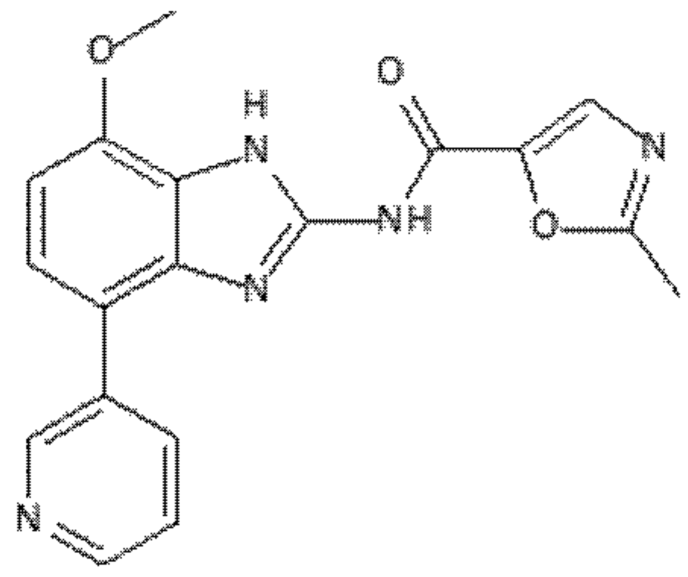
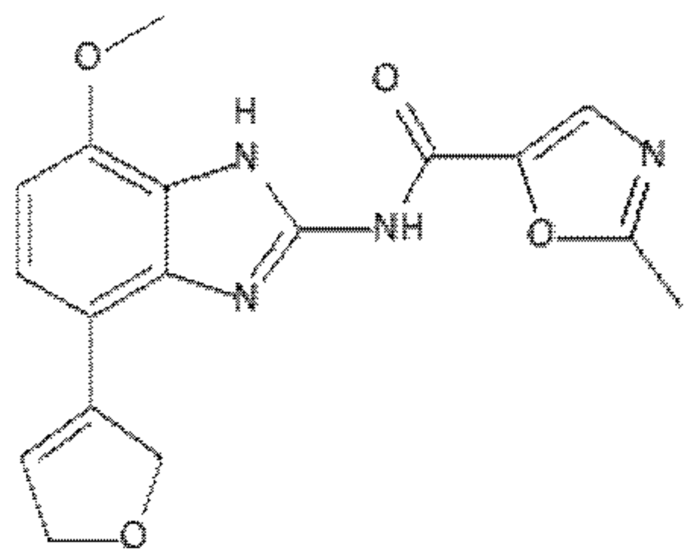
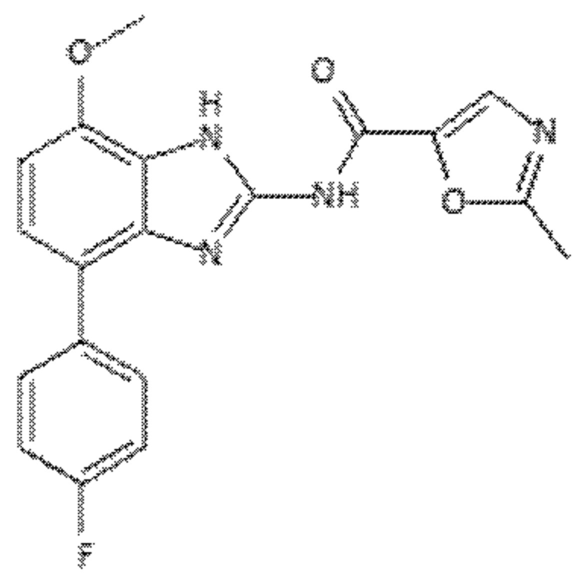
294		N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(4-methylpiperazine-1-carbonyl)benzamide
295		N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-(2-methoxyethyl)-N1-methylbenzene-1,4-dicarboxamide
296		N1-[2-(dimethylamino)ethyl]-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methylbenzene-1,4-dicarboxamide
297		N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methyl-N1-propylbenzene-1,4-dicarboxamide
298		N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(morpholine-4-carbonyl)benzamide

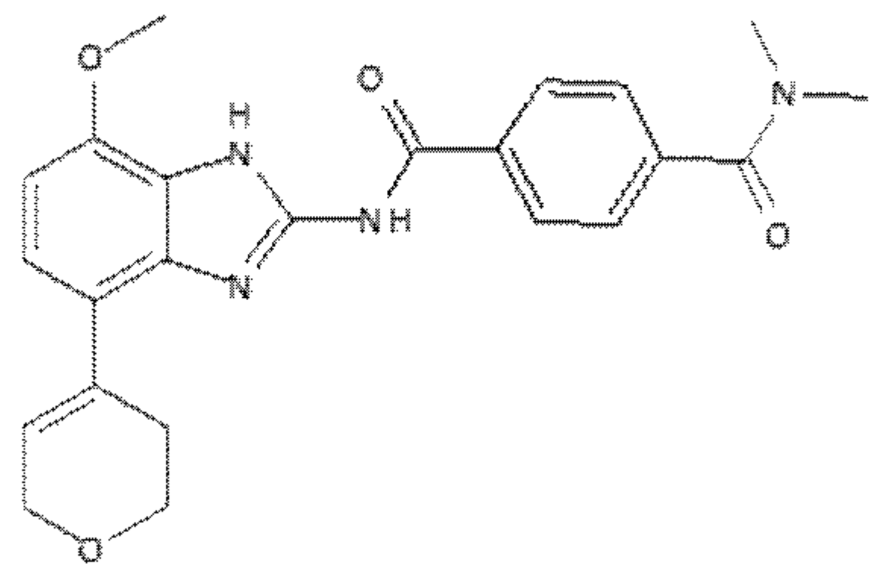
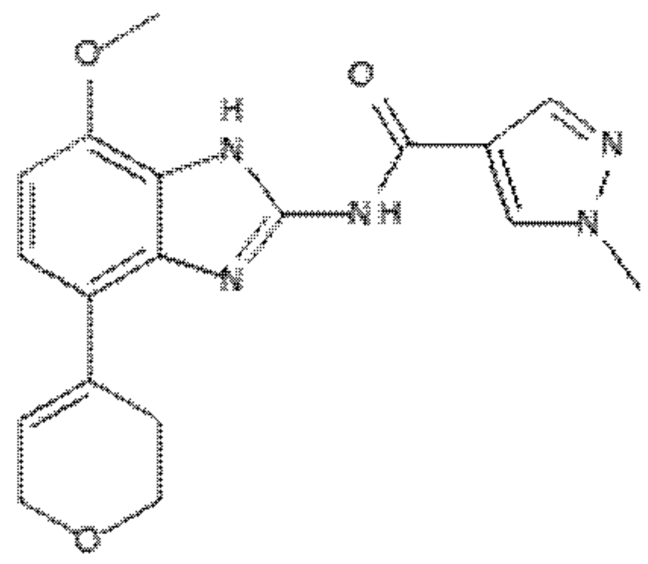
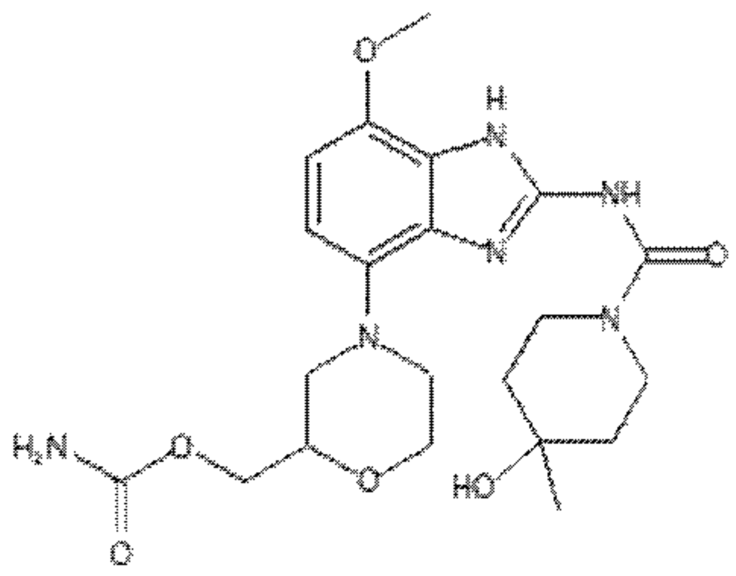
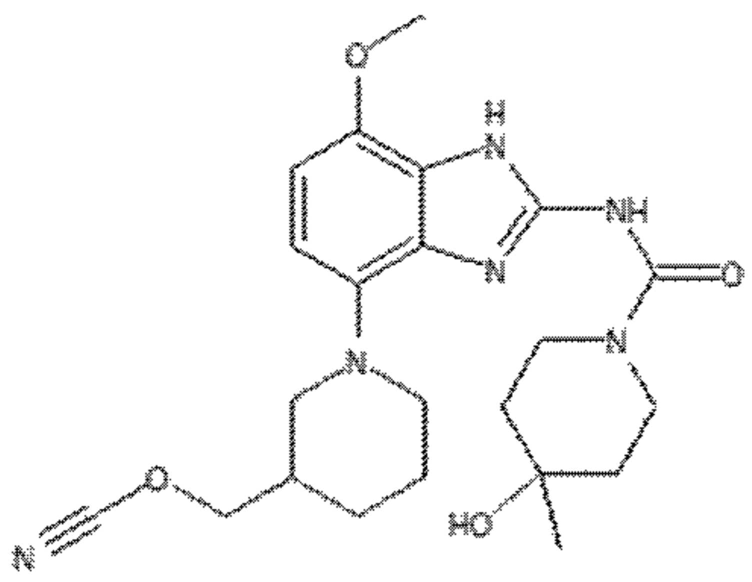
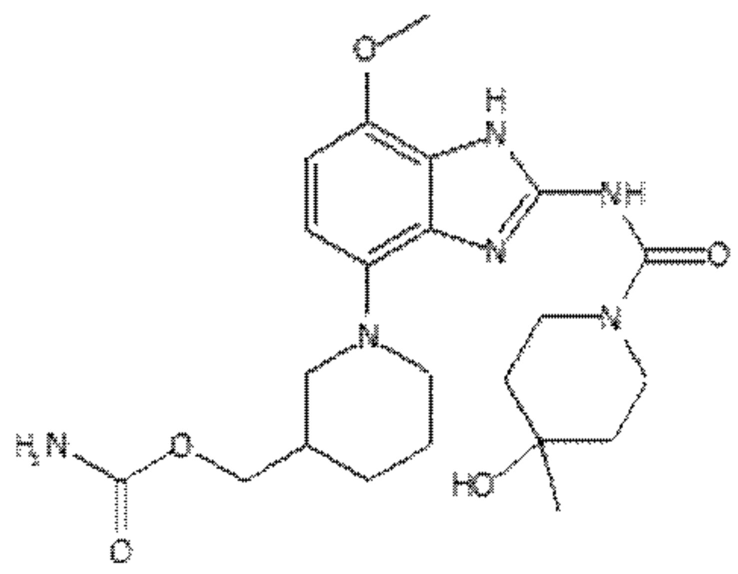
299		N-[4-methoxy-7-(2-methylpyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
300		N-(5-cyano-7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
301		N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
302		N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
303		4-hydroxy-N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide

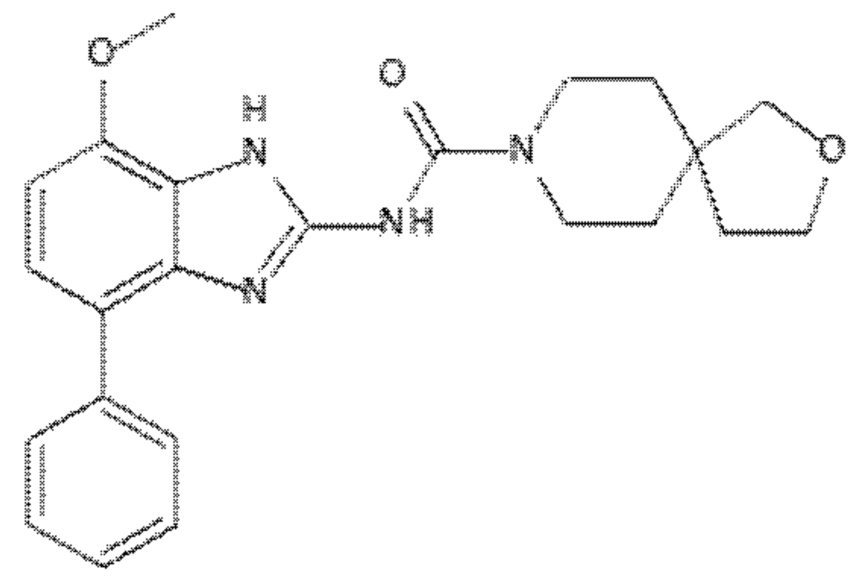
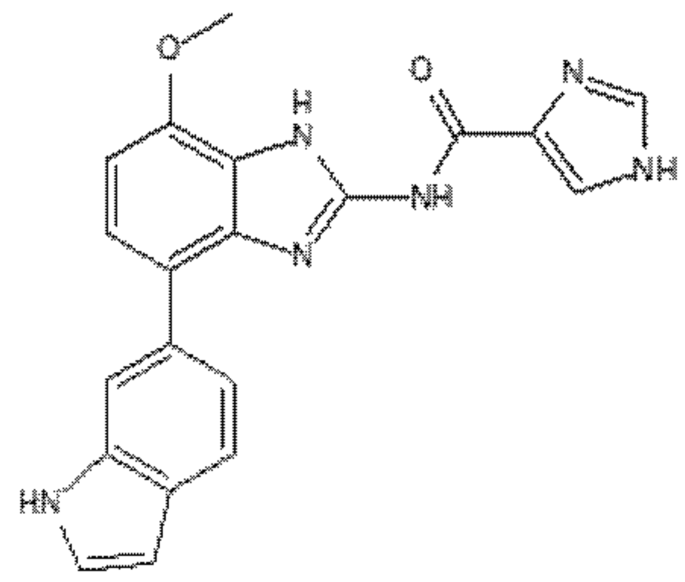
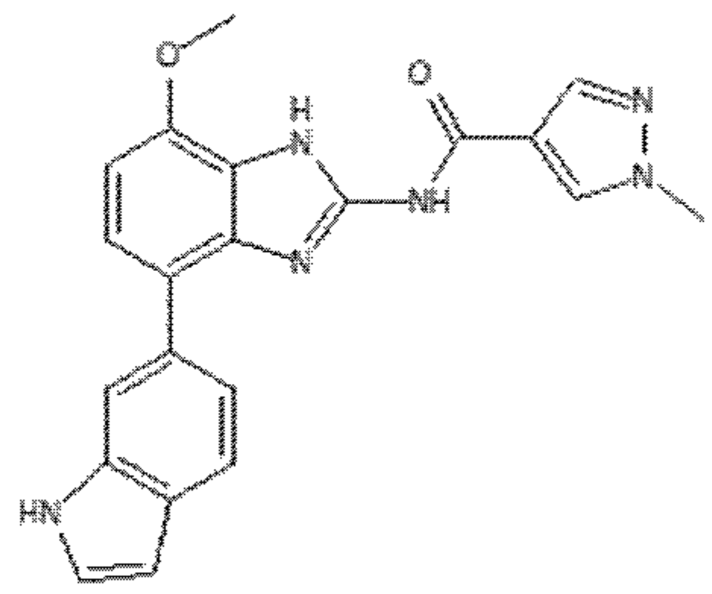
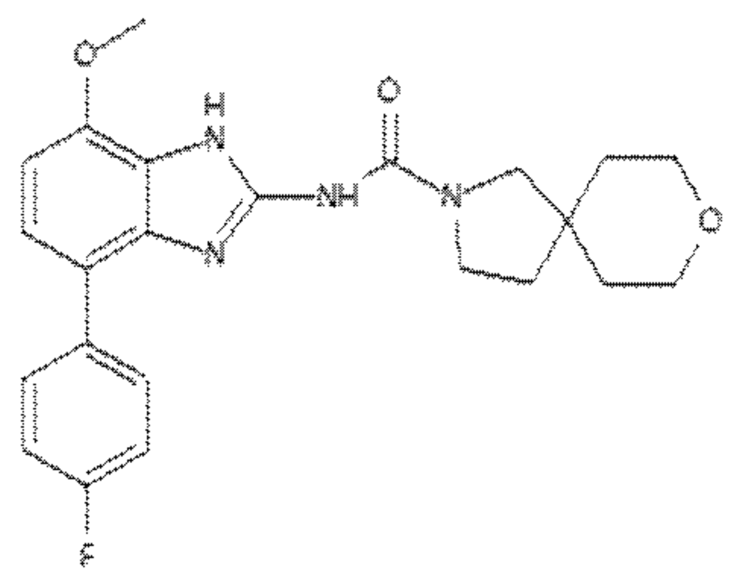
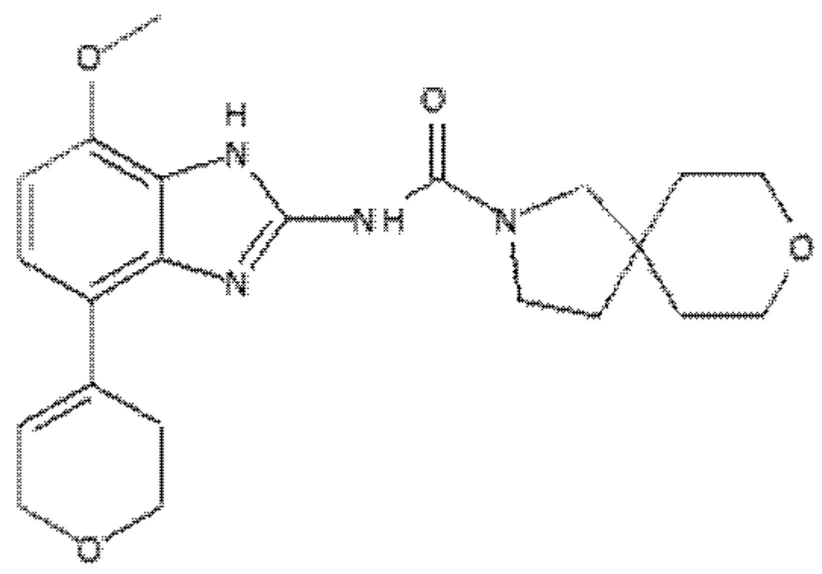
304		N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
305		4-hydroxy-N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
306		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
307		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
308		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-oxazole-5-carboxamide

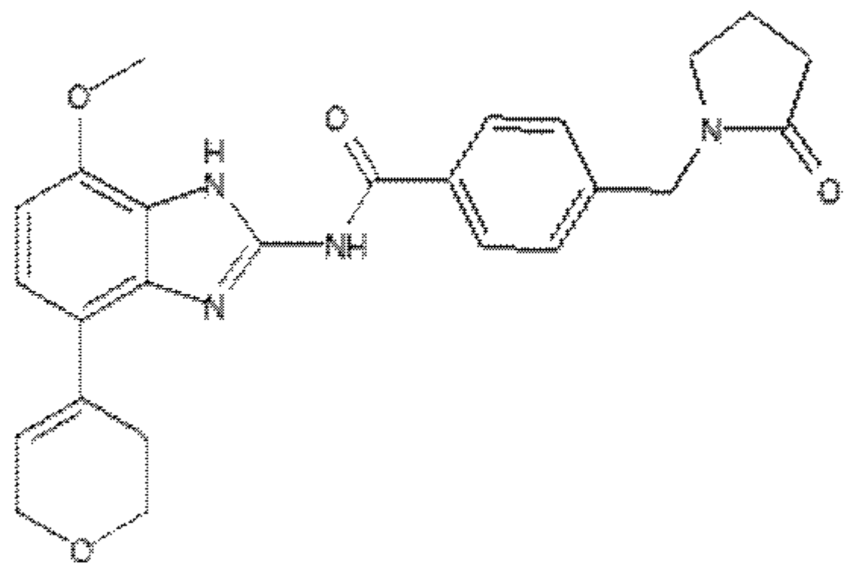
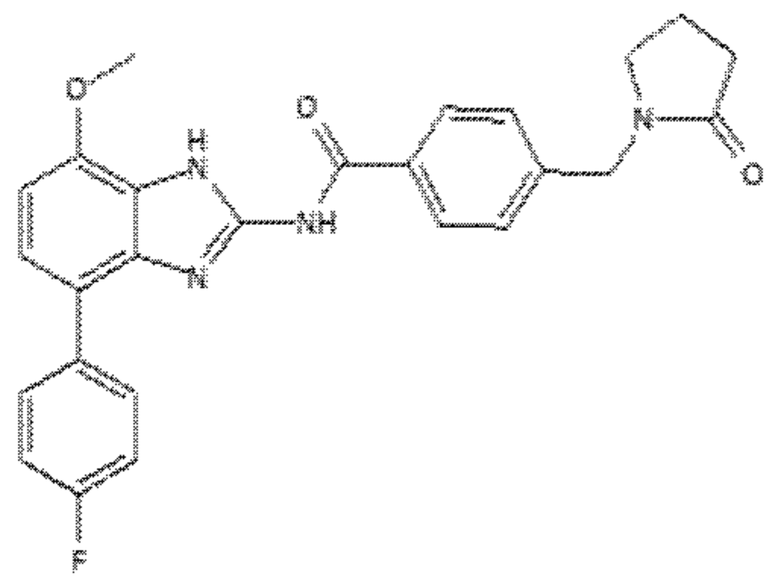
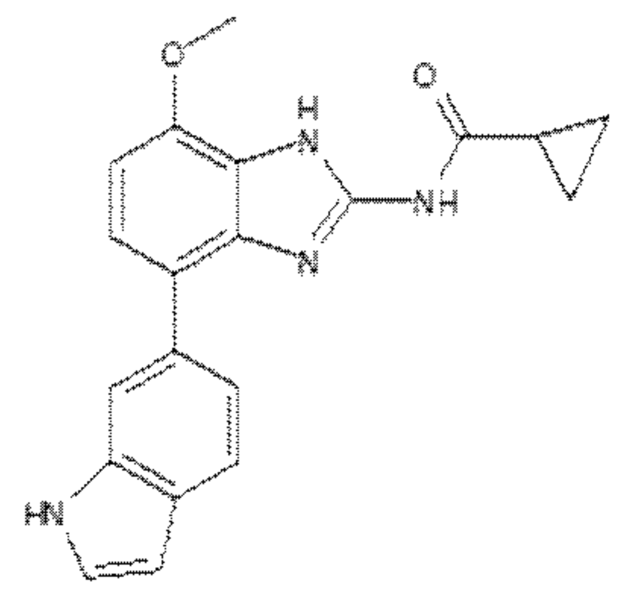
309		N4-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N1,N1-dimethylbenzene-1,4-dicarboxamide
310		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
311		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
312		N1-(2-hydroxyethyl)-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)benzene-1,4-dicarboxamide
313		N4-[7-methoxy-4-(1,4-oxazepan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide

314		N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
315		N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
316		N4-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
317		4-(2,5-dioxopyrrolidin-1-yl)-N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]benzamide
318		N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

319		N4-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
320		N-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
321		N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
322		N-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
323		N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide

324		N4-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
325		N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
326		(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}morpholin-2-yl)methyl carbamate
327		(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl cyanate
328		(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl carbamate

329		N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-oxa-8-azaspiro[4.5]decane-8-carboxamide
330		N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
331		N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
332		N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
333		N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide

334		N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
335		N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
336		N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide

No.	MW	[M+H]+1
1	239,28	240
2	361,37	362
3	423,27	424
4	426,07	427
5	423,27	424
6	426,07	427
7	429,48	430
8	429,48	430
9	294,36	295
10	391,86	393
11	400,48	401
12	380,45	381
13	372,43	373
14	245,32	246
15	423,47	424
16	386,49	387
17	435,53	437

18	248,28	249
19	247,30	248
20	243,27	244
21	389,45	390
22	384,44	385
23	438,49	439
24	388,47	389
25	240,26	241
26	433,47	434
27	244,26	245
28	364,45	365
29	437,50	438
30	447,50	448
31	370,41	371
32	438,41	439
33	396,45	397
34	420,42	421
35	398,46	399
36	402,43	403
37	384,44	385
38	424,50	426
39	368,44	369
40	370,41	371
41	460,54	462
42	434,46	435
43	382,42	383
44	425,45	426
45	412,45	413
46	356,38	357
47	423,47	424
48	404,47	405
49	391,43	392
50	438,45	439
51	423,47	424
52	396,45	397
53	426,52	428
54	446,51	448
55	447,50	448
56	426,52	428
57	458,52	460
58	368,40	369
59	285,31	286

60	423,47	424
61	342,40	343
62	452,52	454
63	370,38	371
64	381,43	382
65	483,45	484
66	541,50	543
67	410,48	411
68	410,48	411
69	396,45	397
70	353,38	354
71	427,47	428
72	390,24	391
73	423,43	424
74	381,43	382
75	465,55	467
76	432,48	433
77	392,41	393
78	454,53	456
79	370,41	371
80	387,40	388
81	434,46	435
82	385,43	386
83	461,52	463
84	338,33	339
85	379,42	380
86	434,88	436
87	434,46	435
88	408,50	409
89	401,47	402
90	409,49	410
91	438,49	439
92	408,46	409
93	418,45	419
94	431,37	432
95	427,26	428
96	352,35	353
97	431,49	432
98	388,39	389
99	383,41	384
100	444,49	445
101	389,41	390

102	412,49	413
103	464,56	466
104	447,50	448
105	461,52	463
106	473,53	475
107	447,50	448
108	393,44	394
109	384,44	385
110	400,48	401
111	414,50	416
112	386,45	387
113	410,48	411
114	410,48	411
115	396,45	397
116	396,45	397
117	388,47	389
118	465,55	467
119	477,56	479
120	423,45	424
121	382,42	383
122	451,52	453
123	401,46	402
124	398,42	399
125	415,49	416
126	397,44	398
127	418,50	419
128	426,52	428
129	407,47	408
130	416,48	417
131	394,47	395
132	412,45	413
133	422,48	423
134	398,46	399
135	433,47	434
136	356,38	357
137	402,49	403
138	448,52	450
139	437,50	438
140	398,46	399
141	398,46	399
142	388,47	389
143	388,47	389

144	398,44	399
145	553,66	555
146	377,40	378
147	384,44	385
148	384,44	385
149	400,48	401
150	400,48	401
151	440,54	442
152	446,51	448
153	477,56	479
154	477,56	479
155	386,45	387
156	352,36	353
157	453,54	455
158	422,44	423
159	412,45	413
160	351,37	352
161	395,42	396
162	419,44	420
163	398,46	399
164	396,41	397
165	368,42	369
166	324,34	325
167	381,40	382
168	459,55	461
169	351,37	352
170	352,35	353
171	378,39	379
172	336,35	337
173	354,39	355
174	391,43	392
175	407,48	408
176	325,33	326
177	366,38	367
178	352,40	353
179	418,48	419
180	358,38	359
181	365,40	366
182	397,48	398
183	357,37	358
184	401,42	402
185	357,37	358

186	423,47	424
187	399,45	400
188	450,54	452
189	463,58	465
190	355,40	356
191	356,38	357
192	382,42	383
193	400,44	401
194	356,39	357
195	340,38	341
196	358,42	359
197	356,38	357
198	372,45	373
199	391,43	392
200	357,37	358
201	422,50	424
202	362,40	363
203	369,42	370
204	401,51	403
205	391,43	392
206	342,36	343
207	395,46	396
208	405,48	406
209	387,46	388
210	357,37	358
211	400,44	401
212	356,38	357
213	336,35	337
214	423,47	424
215	352,35	353
216	401,51	403
217	398,44	399
218	398,44	399
219	354,39	355
220	418,48	419
221	358,38	359
222	411,46	412
223	369,43	370
224	355,40	356
225	399,45	400
226	340,38	341
227	372,45	373

228	387,46	388
229	420,42	421
230	472,54	474
231	447,50	448
232	353,42	354
233	355,44	356
234	356,38	357
235	459,55	461
236	454,52	456
237	461,52	463
238	442,52	444
239	365,37	366
240	432,45	433
241	440,50	442
242	432,45	433
243	365,37	366
244	365,40	366
245	525,61	527
246	354,37	355
247	383,43	384
248	444,45	445
249	373,39	374
250	448,48	449
251	473,51	475
252	419,48	420
253	333,35	334
254	347,38	348
255	347,38	348
256	350,40	351
257	364,43	365
258	365,42	366
259	415,45	416
260	348,36	349
261	406,44	407
262	438,46	439
263	442,54	444
264	371,37	372
265	351,34	352
266	334,34	335
267	407,43	408
268	334,34	335
269	361,40	362

270	420,47	421
271	420,47	421
272	419,48	420
273	434,50	435
274	434,50	435
275	420,47	421
276	348,36	349
277	440,47	441
278	431,45	432
279	431,45	432
280	430,47	431
281	445,48	446
282	445,48	446
283	432,48	433
284	415,45	416
285	440,46	441
286	383,41	384
287	386,40	387
288	384,40	385
289	384,40	385
290	410,44	411
291	387,44	388
292	421,50	422
293	428,49	429
294	469,54	471
295	458,52	460
296	471,56	473
297	442,52	444
298	456,50	457
299	348,36	349
300	372,39	373
301	431,45	432
302	430,47	431
303	419,48	420
304	430,47	431
305	419,48	420
306	347,38	348
307	391,43	392
308	348,36	349
309	414,46	415
310	406,48	407
311	440,50	442

312	430,46	431
313	437,50	438
314	313,36	314
315	308,34	309
316	432,45	433
317	458,45	459
318	365,37	366
319	475,50	477
320	368,39	369
321	349,35	350
322	340,34	341
323	366,35	367
324	420,47	421
325	353,38	354
326	462,50	464
327	442,52	444
328	460,53	462
329	406,48	407
330	372,39	373
331	386,41	387
332	424,47	425
333	412,49	413
334	446,50	448
335	458,49	459
336	346,39	347

Table 3 – NMR profiles of the compounds of the present invention

The Nos. recited herein corresponds to the numbering of the compounds disclosed in table 2

No.	NMR
1	NMR, but no peak listing available
2	1H NMR (400 MHz, DMSO-d6) ppm = 8.22 - 8.17 (m, 2H), 7.85 (d, J = 7.6 Hz, 2H), 7.51 - 7.46 (m, 2H), 7.42 - 7.33 (m, 3H), 7.31 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H).

3	1H NMR (400 MHz, DMSO-d6) ppm = 12.57 - 12.34 (m, 1H), 8.58 (d, J = 5.0 Hz, 1H), 8.22 - 8.20 (m, 1H), 8.00 (dd, J = 5.1, 1.4 Hz, 1H), 7.87 - 7.64 (m, 2H), 7.56 - 7.47 (m, 2H), 7.42 - 7.35 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.97 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H).
4	1H NMR (400 MHz, DMSO-d6) ppm = 12.57 - 12.34 (m, 1H), 8.58 (d, J = 5.0 Hz, 1H), 8.22 - 8.20 (m, 1H), 8.00 (dd, J = 5.1, 1.4 Hz, 1H), 7.87 - 7.64 (m, 2H), 7.56 - 7.47 (m, 2H), 7.42 - 7.35 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.97 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H).
5	1H NMR (400 MHz, DMSO-d6) ppm = 9.04 - 9.03 (m, 1H), 8.34 (dd, J = 8.3, 2.6 Hz, 1H), 7.86 - 7.78 (m, 3H), 7.53 - 7.48 (m, 2H), 7.39 - 7.34 (m, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H).
6	1H NMR (400 MHz, DMSO-d6) ppm = 9.04 - 9.03 (m, 1H), 8.34 (dd, J = 8.3, 2.6 Hz, 1H), 7.86 - 7.78 (m, 3H), 7.53 - 7.48 (m, 2H), 7.39 - 7.34 (m, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H).
7	1H NMR (400 MHz, DMSO-d6) ppm = 8.29 (d, J = 5.1 Hz, 1H), 7.89 - 7.82 (m, 2H), 7.54 - 7.52 (m, 1H), 7.51 - 7.46 (m, 2H), 7.38 - 7.30 (m, 2H), 7.26 - 7.23 (m, 1H), 6.92 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H), 3.76 - 3.72 (m, 4H), 3.59 - 3.55 (m, 4H).
8	1H NMR (400 MHz, DMSO-d6) ppm = 8.87 (d, J = 2.5 Hz, 1H), 8.23 (dd, J = 9.1, 2.5 Hz, 1H), 7.88 - 7.82 (m, 2H), 7.51 - 7.46 (m, 2H), 7.37 - 7.32 (m, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 9.1 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H), 3.72 - 3.68 (m, 4H), 3.66 - 3.62 (m, 4H).
9	NMR available, but no peak listing
10	1H NMR (500 MHz, DMSO-d6) ppm = 12.82 - 11.31 (m, 1H), 8.14 - 8.11 (m, 2H), 7.87 - 7.82 (m, 2H), 7.64 - 7.60 (m, 2H), 7.52 - 7.47 (m, 2H), 7.38 - 7.34 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 4.86 (s, 2H), 4.00 (s, 3H).

11	1H NMR (400 MHz, DMSO-d6) ppm = 8.91 - 8.82 (m, 2H), 8.16 - 8.12 (m, 2H), 7.86 - 7.81 (m, 2H), 7.66 - 7.62 (m, 2H), 7.51 - 7.45 (m, 2H), 7.37 - 7.32 (m, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.24 - 4.19 (m, 2H), 3.97 (s, 3H), 3.06 - 2.96 (m, 2H), 1.22 (t, J = 7.3 Hz, 3H).
12	1H NMR (400 MHz, DMSO-d6) ppm = 7.73 - 7.68 (m, 2H), 7.53 - 7.48 (m, 2H), 7.41 - 7.36 (m, 1H), 7.31 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 3.98 (s, 3H), 3.87 - 3.79 (m, 2H), 3.35 - 3.26 (m, 2H), 1.54 - 1.41 (m, 4H), 1.15 (s, 3H).
13	#NV
14	1H NMR (400 MHz, DMSO-d6) ppm = 10.72 (s, 1H), 6.62 (d, J = 8.2 Hz, 1H), 6.42 (d, J = 8.2 Hz, 1H), 5.79 - 5.69 (m, 2H), 3.81 (s, 3H), 2.93 - 2.71 (m, 1H), 1.85 - 1.67 (m, 5H), 1.54 - 1.18 (m, 5H).
15	1H NMR (400 MHz, DMSO-d6) ppm = 9.33 - 9.31 (m, 1H), 8.18 - 8.14 (m, 2H), 7.88 - 7.84 (m, 1H), 7.85 - 7.83 (m, 2H), 7.75 - 7.73 (m, 1H), 7.57 - 7.54 (m, 2H), 7.51 - 7.46 (m, 2H), 7.38 - 7.33 (m, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 5.56 (s, 2H), 3.99 (s, 3H).
16	1H NMR (400 MHz, DMSO-d6) ppm = 7.06 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 3.91 (s, 3H), 3.87 - 3.79 (m, 2H), 3.37 - 3.27 (m, 2H), 3.05 - 2.94 (m, 1H), 1.86 - 1.70 (m, 5H), 1.56 - 1.20 (m, 9H), 1.16 (s, 3H).
17	1H NMR (400 MHz, DMSO-d6) ppm = 8.29 (d, J = 5.3 Hz, 1H), 7.55 (s, 1H), 7.28 (d, J = 5.3 Hz, 1H), 6.98 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 3.91 (s, 3H), 3.77 - 3.73 (m, 4H), 3.60 - 3.55 (m, 4H), 3.09 - 2.99 (m, 1H), 1.91 - 1.70 (m, 5H), 1.56 - 1.22 (m, 5H).
18	NMR available, but no peak listing
19	NMR available, but no peak listing
20	1H NMR (400 MHz, DMSO-d6) ppm = 12.76 - 12.40 (m, 1H), 8.12 - 8.09 (m, 1H), 7.83 - 7.80 (m, 1H), 7.67 - 7.54 (m, 2H), 7.28 - 7.20 (m, 2H), 6.92 (d, J = 8.6 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H).
21	1H NMR (400 MHz, DMSO-d6) ppm = 7.10 - 7.04 (m, 1H), 6.86 (d, J = 8.7 Hz, 1H), 3.92 (s, 3H), 3.90 - 3.81 (m, 6H), 3.37 - 3.21 (m, 6H), 1.57 - 1.42 (m, 4H), 1.16 (s, 3H).

22	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.93 (s, 1H), 7.38 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.89 - 3.82 (m, 2H), 3.39 - 3.29 (m, 2H), 1.57 - 1.44 (m, 4H), 1.17 (s, 3H).
23	1H NMR (400 MHz, DMSO-d6) ppm = 8.28 (d, J = 5.6 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.31 – 7.27 (m, 1H), 7.27 – 7.18 (m, 1H), 6.84 (d, J = 8.6 Hz, 1H), 4.00 – 3.95 (m, 4H), 3.94 (s, 3H), 3.79 – 3.73 (m, 4H), 3.67 – 3.62 (m, 4H), 3.61 – 3.46 (m, 4H).
24	1H NMR (400 MHz, DMSO-d6) ppm = 7.13 (d, J = 8.5 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 4.00 – 3.91 (m, 5H), 3.89 – 3.82 (m, 2H), 3.53 – 3.28 (m, 5H), 1.77 – 1.69 (m, 4H), 1.57 – 1.43 (m, 4H), 1.17 (s, 3H).
25	1H NMR (400 MHz, DMSO-d6) ppm = 8.03 (s, 1H), 7.77 – 7.73 (m, 2H), 7.68 – 7.59 (m, 2H), 7.52 – 7.47 (m, 2H), 7.42 – 7.37 (m, 1H), 3.97 (s, 3H).
26	1H NMR (400 MHz, DMSO-d6) ppm = 8.30 (s, 1H), 8.26 (d, J = 5.8 Hz, 1H), 8.01 (s, 1H), 7.73 – 7.71 (m, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.35 – 7.33 (m, 1H), 6.89 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.79 – 3.74 (m, 4H), 3.71 – 3.66 (m, 4H).
27	NMR available, but no peak listing
28	1H NMR (400 MHz, DMSO-d6) ppm = 7.77 – 7.70 (m, 2H), 7.52 – 7.46 (m, 2H), 7.39 – 7.34 (m, 1H), 7.27 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.22 – 4.13 (m, 2H), 3.97 (s, 3H), 2.91 – 2.80 (m, 2H), 1.69 – 1.54 (m, 3H), 1.12 – 1.00 (m, 2H), 0.92 (d, J = 6.3 Hz, 3H).
29	1H NMR (500 MHz, DMSO-d6) ppm = 13.34 – 11.32 (m, 1H), 8.90 (d, J = 2.4 Hz, 1H), 8.27 (dd, J = 9.1, 2.5 Hz, 1H), 7.12 (d, J = 8.3 Hz, 1H), 7.02 (d, J = 9.2 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 4.01 – 3.96 (m, 2H), 3.95 (s, 3H), 3.75 – 3.64 (m, 8H), 3.55 – 3.47 (m, 2H), 3.40 – 3.33 (m, 1H), 1.83 – 1.72 (m, 4H).
30	1H NMR (400 MHz, DMSO-d6) ppm = 8.29 – 8.26 (m, 1H), 8.11 (d, J = 6.5 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.64 – 7.60 (m, 1H), 7.37 – 7.33 (m, 2H), 6.89 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.79 – 3.73 (m, 2H), 3.63 – 3.49 (m, 2H), 2.12 – 1.97 (m, 2H), 1.42 (s, 3H).

31	1H NMR (400 MHz, DMSO-d6) ppm = 11.61 – 10.67 (m, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 3.73 – 3.19 (m, 4H), 2.00 – 1.80 (m, 2H), 1.34 (s, 3H).
32	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 (s, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H), 4.25 – 4.18 (m, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 3.19 – 3.10 (m, 2H), 1.77 – 1.64 (m, 4H).
33	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 – 7.92 (m, 1H), 7.39 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.71 (s, 2H), 3.66 – 3.49 (m, 4H), 3.40 (s, 2H), 1.60 – 1.46 (m, 4H).
34	1H NMR (400 MHz, DMSO-d6) ppm = 8.24 (s, 1H), 7.94 (s, 1H), 7.34 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 5.75 (t, J = 56.0 Hz, 1H), 4.19 – 4.12 (m, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 3.23 – 3.12 (m, 2H), 1.61 – 1.56 (m, 4H).
35	1H NMR (500 MHz, DMSO-d6) ppm = 11.96 – 10.14 (m, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.83 – 3.76 (m, 2H), 3.38 – 3.29 (m, 2H), 3.19 (s, 2H), 1.54 – 1.45 (m, 2H), 1.29 – 1.22 (m, 2H), 0.93 (s, 3H).
36	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 – 7.92 (m, 1H), 7.38 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 8.5 Hz, 1H), 4.19 (d, J = 47.8 Hz, 2H), 4.07 – 4.00 (m, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.33 – 3.22 (m, 2H), 1.64 – 1.50 (m, 4H).
37	1H NMR (500 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.93 (s, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.87 – 3.81 (m, 2H), 3.46 – 3.40 (m, 1H), 3.31 – 3.24 (m, 5H), 1.91 – 1.84 (m, 2H), 1.48 – 1.41 (m, 2H).
38	1H NMR (500 MHz, DMSO-d6) ppm = 12.48 – 10.34 (m, 1H), 8.23 (s, 1H), 7.94 – 7.92 (m, 1H), 7.40 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.5 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.60 – 3.55 (m, 8H), 1.57 – 1.51 (m, 4H), 1.50 – 1.45 (m, 4H).

39	1H NMR (400 MHz, DMSO-d6) ppm = 8.24 (s, 1H), 7.95 (s, 1H), 7.29 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 4.24 – 4.16 (m, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 2.93 – 2.83 (m, 2H), 1.71 – 1.56 (m, 3H), 1.14 – 1.02 (m, 2H), 0.93 (d, J = 6.3 Hz, 3H).
40	1H NMR (500 MHz, DMSO-d6) ppm = 14.03 – 10.78 (m, 2H), 8.24 (s, 1H), 7.95 – 7.93 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 3.97 (s, 3H), 3.93 – 3.87 (m, 5H), 3.79 – 3.73 (m, 1H), 3.35 – 3.25 (m, 2H), 1.84 – 1.77 (m, 2H), 1.45 – 1.36 (m, 2H).
41	1H NMR (500 MHz, DMSO-d6) ppm = 13.52 – 9.93 (m, 2H), 8.23 (s, 1H), 7.94 (s, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.25 – 7.18 (m, 3H), 6.90 (d, J = 8.4 Hz, 1H), 3.98 – 3.93 (m, 5H), 3.90 (s, 3H), 3.27 – 3.17 (m, 2H), 2.72 (s, 2H), 1.53 – 1.41 (m, 4H).
42	NMR available, but no peak listing
43	1H NMR (400 MHz, DMSO-d6) ppm = 11.44 – 10.20 (m, 1H), 8.26 – 8.23 (m, 1H), 7.97 – 7.93 (m, 1H), 7.40 – 7.36 (m, 1H), 6.96 – 6.91 (m, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.76 (s, 2H), 3.67 – 3.56 (m, 2H), 3.45 (s, 2H), 3.43 – 3.36 (m, 2H), 2.27 – 1.78 (m, 2H).
44	1H NMR (700 MHz, DMSO-d6) ppm = 13.26 – 11.37 (m, 1H), 11.36 – 9.74 (m, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.56 (s, 1H), 7.29 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.84 – 3.80 (m, 2H), 3.48 – 3.41 (m, 2H), 3.29 (s, 2H), 1.86 – 1.81 (m, 2H), 1.81 – 1.74 (m, 2H).
45	1H NMR (500 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 8.6 Hz, 1H), 3.94 - 3.93 (m, 3H), 3.93 - 3.92 (m, 4H), 3.90 - 3.89 (m, 3H), 3.64 - 3.60 (m, 4H), 1.69 - 1.65 (m, 4H).
46	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.67 - 3.62 (m, 4H), 3.60 - 3.55 (m, 4H).

47	1H NMR (500 MHz, DMSO-d6) ppm = 12.23 - 10.69 (m, 1H), 8.25 - 8.23 (m, 1H), 7.94 - 7.93 (m, 1H), 7.60 - 7.57 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.72 - 3.64 (m, 2H), 3.55 - 3.46 (m, 2H), 3.10 (s, 2H), 2.15 - 2.13 (m, 2H), 1.63 - 1.58 (m, 4H).
48	1H NMR (400 MHz, DMSO-d6) ppm = 10.91 - 10.81 (m, 1H), 8.33 - 8.31 (m, 1H), 8.24 - 8.20 (m, 2H), 8.05 - 8.04 (m, 1H), 7.81 - 7.76 (m, 2H), 7.38 (d, J = 8.3 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 4.40 - 4.37 (m, 2H), 3.97 (s, 3H), 3.91 (s, 3H), 2.75 - 2.71 (m, 6H).
49	1H NMR (400 MHz, DMSO-d6) ppm = 12.17 - 11.61 (m, 1H), 8.36 - 8.32 (m, 1H), 8.13 - 8.10 (m, 2H), 8.07 - 8.03 (m, 1H), 7.51 - 7.47 (m, 2H), 7.32 (d, J = 8.2 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 4.52 (s, 2H), 3.95 (s, 3H), 3.90 (s, 3H), 3.40 - 3.34 (m, 3H).
50	1H NMR (500 MHz, DMSO-d6) ppm = 12.11 - 10.86 (m, 1H), 10.78 - 10.75 (m, 1H), 8.66 - 8.63 (m, 1H), 8.23 (s, 1H), 7.93 (s, 1H), 7.40 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 4.15 - 4.08 (m, 2H), 3.96 (s, 3H), 3.91 (s, 3H), 3.42 - 3.30 (m, 2H), 1.90 - 1.81 (m, 2H), 1.70 - 1.62 (m, 2H).
51	1H NMR (500 MHz, DMSO-d6) ppm = 12.32 - 10.92 (m, 1H), 8.25 - 8.23 (m, 1H), 8.16 - 8.13 (m, 1H), 7.94 - 7.93 (m, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.74 - 3.66 (m, 2H), 3.65 - 3.57 (m, 2H), 2.26 - 2.21 (m, 2H), 1.90 (t, J = 8.0 Hz, 2H), 1.69 - 1.59 (m, 4H).
52	NMR available, but no peak listing
53	1H NMR (700 MHz, DMSO-d6) ppm = 13.49 – 10.13 (m, 2H), 8.24 (s, 1H), 7.95 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 4.13 – 4.08 (m, 1H), 4.08 – 4.03 (m, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.30 (td, J = 9.1, 4.3 Hz, 1H), 3.11 – 3.03 (m, 1H), 2.79 – 2.70 (m, 1H), 1.87 – 1.82 (m, 1H), 1.72 – 1.66 (m, 1H), 1.48 – 1.21 (m, 6H), 1.12 – 1.05 (m, 1H), 0.89 (t, J = 7.1 Hz, 3H).

54	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.94 (s, 1H), 7.33 - 7.27 (m, 3H), 7.02 - 6.98 (m, 2H), 6.96 - 6.91 (m, 1H), 6.83 (d, J = 8.4 Hz, 1H), 4.67 - 4.60 (m, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.47 - 3.38 (m, 4H), 2.04 - 1.96 (m, 2H), 1.69 - 1.59 (m, 2H).
55	1H NMR (700 MHz, DMSO-d6) ppm = 12.42 - 10.52 (m, 1H), 8.99 (d, J = 2.0 Hz, 1H), 8.83 - 8.81 (m, 1H), 8.70 - 8.68 (m, 1H), 8.26 (s, 1H), 8.03 (dd, J = 8.2, 5.6 Hz, 1H), 7.97 (s, 1H), 7.37 (d, J = 8.5 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.09 - 5.67 (m, 1H), 4.27 - 4.23 (m, 2H), 3.95 (s, 3H), 3.90 (s, 3H), 3.40 - 3.30 (m, 2H), 2.11 - 2.06 (m, 2H), 1.77 - 1.74 (m, 2H).
56	1H NMR (700 MHz, DMSO-d6) ppm = 13.51 – 11.54 (m, 1H), 11.52 – 10.37 (m, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 4.10 – 4.06 (m, 1H), 4.05 – 4.00 (m, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.27 (td, J = 8.8, 4.1 Hz, 1H), 3.14 – 3.06 (m, 1H), 2.77 – 2.68 (m, 1H), 1.87 – 1.82 (m, 1H), 1.79 – 1.71 (m, 1H), 1.52 – 1.47 (m, 1H), 1.41 – 1.34 (m, 2H), 1.02 – 0.97 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H).
57	NMR available, but no peak listing
58	1H NMR (500 MHz, DMSO-d6) ppm = 12.18 - 10.47 (m, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.90 - 3.85 (m, 4H), 2.49 - 2.45 (m, 4H).
59	1H NMR (400 MHz, DMSO-d6) ppm = 11.82 - 11.70 (m, 1H), 8.26 (s, 1H), 8.00 (s, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.20 (s, 3H).
60	1H NMR (700 MHz, DMSO-d6) ppm = 12.74 - 9.93 (m, 2H), 8.25 (s, 1H), 7.95 (s, 1H), 7.62 (s, 1H), 7.28 (d, J = 8.3 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 4.14 - 4.09 (m, 2H), 3.92 (s, 3H), 3.90 (s, 3H), 3.20 (t, J = 6.8 Hz, 2H), 3.14 - 3.08 (m, 2H), 2.02 (t, J = 6.8 Hz, 2H), 1.67 - 1.61 (m, 2H), 1.44 - 1.40 (m, 2H).

61	1H NMR (500 MHz, DMSO-d6) ppm = 11.86 – 10.17 (m, 1H), 8.26 – 8.25 (m, 1H), 7.95 – 7.94 (m, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.50 – 3.42 (m, 4H), 1.17 (t, J = 7.1 Hz, 6H).
62	1H NMR (500 MHz, DMSO-d6) ppm = 12.04 - 11.88 (m, 1H), 8.32 - 8.27 (m, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.37 (d, J = 8.4 Hz, 1H), 6.93 (d, J = 8.5 Hz, 1H), 4.29 - 4.02 (m, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.83 - 3.65 (m, 2H), 3.59 - 3.31 (m, 4H), 2.85 (s, 3H), 2.42 - 2.21 (m, 3H), 2.02 - 1.87 (m, 1H).
63	1H NMR (400 MHz, DMSO-d6) ppm = 8.22 - 8.16 (m, 2H), 7.44 - 7.37 (m, 2H), 7.16 - 7.09 (m, 1H), 6.82 (d, J = 8.7 Hz, 1H), 3.97 - 3.91 (m, 7H), 3.70 - 3.50 (m, 4H).
64	1H NMR (400 MHz, DMSO-d6) ppm = 12.12 - 12.02 (m, 1H), 8.28 - 8.26 (m, 1H), 8.02 - 7.99 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.75 - 3.55 (m, 3H), 3.48 - 3.40 (m, 1H), 2.01 - 1.95 (m, 1H), 1.77 - 1.54 (m, 3H), 1.43 - 1.35 (m, 1H), 1.19 (t, J = 4.7 Hz, 1H), 1.07 (dd, J = 7.8, 4.2 Hz, 1H).
65	NMR available, but no peak listing
66	NMR available, but no peak listing
67	1H NMR (400 MHz, DMSO-d6) ppm = 11.10 - 9.59 (m, 2H), 8.24 - 8.22 (m, 1H), 7.95 - 7.92 (m, 1H), 7.34 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.69 - 3.16 (m, 8H), 1.92 - 1.49 (m, 6H).
68	1H NMR (400 MHz, DMSO-d6) ppm = 11.04 - 9.94 (m, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.69 - 3.33 (m, 8H), 1.94 - 1.78 (m, 2H), 1.57 - 1.50 (m, 4H).
69	1H NMR (400 MHz, DMSO-d6) ppm = 8.25 - 8.22 (m, 1H), 7.95 - 7.92 (m, 1H), 7.40 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.84 - 3.77 (m, 2H), 3.72 - 3.35 (m, 6H), 2.04 - 1.84 (m, 4H).

70	1H NMR (500 MHz, DMSO-d6) ppm = 11.98 - 11.84 (m, 1H), 8.27 - 8.25 (m, 1H), 8.02 - 7.99 (m, 1H), 7.29 (d, J = 8.2 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.86 (d, J = 8.8 Hz, 2H), 3.71 - 3.67 (m, 2H), 2.23 - 2.20 (m, 2H), 1.95 - 1.88 (m, 1H).
71	1H NMR (500 MHz, DMSO-d6) ppm = 15.05 - 14.13 (m, 1H), 12.69 - 11.24 (m, 1H), 9.35 - 9.33 (m, 1H), 8.33 - 8.30 (m, 1H), 8.19 - 8.16 (m, 2H), 8.06 - 8.03 (m, 1H), 7.84 (t, J = 1.7 Hz, 1H), 7.74 (t, J = 1.7 Hz, 1H), 7.59 - 7.56 (m, 2H), 7.34 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 5.57 (s, 2H), 3.95 (s, 3H), 3.90 (s, 3H).
72	1H NMR (400 MHz, DMSO-d6) ppm = 12.43 - 11.91 (m, 1H), 8.27 (s, 1H), 8.01 (s, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.46 - 3.41 (m, 1H), 2.54 - 2.50 (m, 1H), 1.68 - 1.54 (m, 2H).
73	1H NMR (400 MHz, DMSO-d6) ppm = 12.11 - 11.00 (m, 1H), 8.99 (d, J = 1.3 Hz, 1H), 8.52 (d, J = 1.3 Hz, 1H), 8.34 - 8.31 (m, 1H), 8.02 - 8.00 (m, 1H), 7.41 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.60 - 4.55 (m, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.76 - 3.72 (m, 2H), 3.33 (s, 3H).
74	1H NMR (500 MHz, DMSO-d6) ppm = 10.62 - 10.51 (m, 1H), 8.95 - 8.91 (m, 2H), 8.86 - 8.83 (m, 2H), 7.91 (d, J = 8.7 Hz, 1H), 6.99 (d, J = 8.7 Hz, 1H), 4.03 (s, 3H), 3.88 - 3.82 (m, 2H), 3.33 - 3.26 (m, 2H), 1.54 - 1.43 (m, 4H), 1.16 (s, 3H).
75	1H NMR (500 MHz, DMSO-d6) ppm = 11.22 - 10.61 (m, 1H), 7.29 - 7.25 (m, 2H), 7.24 - 7.18 (m, 3H), 7.07 - 6.98 (m, 1H), 6.85 (d, J = 8.6 Hz, 1H), 3.97 - 3.89 (m, 5H), 3.89 - 3.83 (m, 4H), 3.23 (d, J = 11.3 Hz, 6H), 2.72 (s, 2H), 1.54 - 1.41 (m, 4H).
76	1H NMR (400 MHz, DMSO-d6) ppm = 15.23 - 14.03 (m, 1H), 12.89 - 11.51 (m, 1H), 9.37 - 9.35 (m, 1H), 8.19 - 8.14 (m, 2H), 7.84 (t, J = 1.7 Hz, 1H), 7.74 (t, J = 1.7 Hz, 1H), 7.60 - 7.55 (m, 2H), 7.17 - 7.05 (m, 1H), 6.80 (d, J = 8.6 Hz, 1H), 5.57 (s, 2H), 3.98 - 3.90 (m, 7H), 3.55 - 3.40 (m, 4H).

77	1H NMR (400 MHz, DMSO-d6) ppm = 8.52 - 8.49 (m, 1H), 8.15 (d, J = 2.2 Hz, 1H), 8.10 (dd, J = 8.7, 1.9 Hz, 1H), 7.80 - 7.75 (m, 1H), 7.13 (dd, J = 2.3, 0.9 Hz, 1H), 7.11 - 7.01 (m, 1H), 6.81 (d, J = 8.6 Hz, 1H), 4.00 - 3.89 (m, 7H), 3.56 - 3.41 (m, 4H).
78	1H NMR (500 MHz, DMSO-d6) ppm = 12.37 – 10.91 (m, 1H), 10.91 – 9.79 (m, 1H), 8.47 (s, 1H), 8.05 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 5.43 (dd, J = 10.0, 2.1 Hz, 1H), 3.98 – 3.94 (m, 1H), 3.92 (s, 3H), 3.88 – 3.81 (m, 2H), 3.70 – 3.63 (m, 1H), 3.34 – 3.25 (m, 2H), 2.16 – 2.07 (m, 1H), 2.01 – 1.94 (m, 2H), 1.76 – 1.66 (m, 1H), 1.59 – 1.53 (m, 2H), 1.53 – 1.43 (m, 4H), 1.16 (s, 3H).
79	1H NMR (500 MHz, DMSO-d6) ppm = 12.37 – 10.91 (m, 1H), 10.91 – 9.79 (m, 1H), 8.47 (s, 1H), 8.05 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 5.43 (dd, J = 10.0, 2.1 Hz, 1H), 3.98 – 3.94 (m, 1H), 3.92 (s, 3H), 3.88 – 3.81 (m, 2H), 3.70 – 3.63 (m, 1H), 3.34 – 3.25 (m, 2H), 2.16 – 2.07 (m, 1H), 2.01 – 1.94 (m, 2H), 1.76 – 1.66 (m, 1H), 1.59 – 1.53 (m, 2H), 1.53 – 1.43 (m, 4H), 1.16 (s, 3H).
80	1H NMR (700 MHz, DMSO-d6) ppm = 12.55 - 11.83 (m, 1H), 8.53 (d, J = 1.5 Hz, 1H), 8.35 - 8.33 (m, 1H), 8.16 - 8.15 (m, 1H), 8.12 (dd, J = 8.7, 1.9 Hz, 1H), 8.06 - 8.04 (m, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.16 - 7.14 (m, 1H), 6.88 (d, J = 8.4 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H).
81	1H NMR (500 MHz, DMSO-d6) ppm = 11.73 - 11.31 (m, 1H), 8.85 (d, J = 1.2 Hz, 1H), 8.42 (d, J = 1.2 Hz, 1H), 8.32 - 8.30 (m, 1H), 7.99 - 7.98 (m, 1H), 7.44 (d, J = 8.3 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H), 3.93 (s, 3H), 3.81 - 3.78 (m, 4H), 3.76 - 3.73 (m, 4H).
82	1H NMR (400 MHz, DMSO-d6) ppm = 11.19 - 10.06 (m, 1H), 8.34 - 8.32 (m, 1H), 8.08 (s, 1H), 8.07 - 8.06 (m, 1H), 4.08 (s, 3H), 3.91 (s, 3H), 3.89 - 3.82 (m, 2H), 3.35 - 3.26 (m, 2H), 1.55 - 1.42 (m, 4H), 1.16 (s, 3H).

83	1H NMR (400 MHz, DMSO-d6) ppm = 10.83 – 10.18 (m, 1H), 8.31 (s, 1H), 8.08 – 8.04 (m, 2H), 7.30 – 7.17 (m, 5H), 4.04 (s, 3H), 3.99 – 3.92 (m, 2H), 3.90 (s, 3H), 3.24 – 3.14 (m, 2H), 2.72 (s, 2H), 1.53 – 1.39 (m, 4H).
84	1H NMR (500 MHz, DMSO-d6) ppm = 9.18 (d, J = 1.7 Hz, 1H), 8.30 (s, 1H), 8.01 (s, 1H), 7.36 (d, J = 8.3 Hz, 1H), 7.14 – 7.11 (m, 1H), 6.86 (d, J = 8.3 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H).
85	1H NMR (700 MHz, DMSO-d6) ppm = 12.10 – 11.31 (m, 1H), 10.51 – 10.44 (m, 1H), 8.97 – 8.92 (m, 2H), 8.86 – 8.84 (m, 2H), 7.92 (d, J = 8.6 Hz, 1H), 6.99 (d, J = 8.6 Hz, 1H), 4.03 (s, 3H), 3.75 – 3.74 (m, 2H), 3.66 – 3.40 (m, 6H), 1.96 – 1.79 (m, 2H).
86	1H NMR (700 MHz, DMSO-d6) ppm = 11.94 – 11.85 (m, 1H), 8.65 (s, 1H), 8.29 (s, 1H), 7.17 – 6.83 (m, 1H), 6.79 – 6.75 (m, 1H), 4.63 – 4.58 (m, 1H), 4.11 – 4.00 (m, 2H), 3.95 – 3.88 (m, 9H), 3.82 – 3.76 (m, 4H).
87	1H NMR (500 MHz, DMSO-d6) ppm = 12.87 – 11.27 (m, 1H), 8.31 – 8.30 (m, 1H), 8.07 (d, J = 9.6 Hz, 1H), 7.99 – 7.98 (m, 1H), 7.49 – 7.45 (m, 2H), 7.01 (d, J = 8.5 Hz, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 3.81 – 3.75 (m, 8H).
88	1H NMR (500 MHz, DMSO-d6) ppm = 10.58 – 10.48 (m, 1H), 8.23 – 8.20 (m, 2H), 7.75 – 7.71 (m, 2H), 7.01 (d, J = 8.3 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 4.37 (d, J = 5.1 Hz, 2H), 4.00 – 3.96 (m, 2H), 3.93 (s, 3H), 3.51 (td, J = 11.3, 2.8 Hz, 2H), 3.36 – 3.29 (m, 1H), 2.74 (d, J = 4.6 Hz, 6H), 1.86 – 1.74 (m, 4H).
89	1H NMR (500 MHz, DMSO-d6) ppm = 12.34 – 12.13 (m, 1H), 10.97 – 10.88 (m, 1H), 8.98 – 8.94 (m, 2H), 8.91 – 8.87 (m, 2H), 8.22 – 8.18 (m, 2H), 7.99 (d, J = 8.6 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.07 (d, J = 8.7 Hz, 1H), 4.38 (d, J = 5.0 Hz, 2H), 4.08 (s, 3H), 2.73 (d, J = 4.4 Hz, 6H).

90	1H NMR (500 MHz, DMSO-d6) ppm = 12.58 – 11.92 (m, 1H), 10.99 – 10.86 (m, 1H), 8.21 – 8.18 (m, 2H), 7.79 – 7.76 (m, 2H), 7.28 – 7.13 (m, 1H), 6.83 (d, J = 8.6 Hz, 1H), 4.38 (d, J = 5.4 Hz, 2H), 3.99 – 3.95 (m, 4H), 3.95 (s, 3H), 3.62 – 3.46 (m, 4H), 2.72 (d, J = 4.8 Hz, 6H).
91	1H NMR (500 MHz, DMSO-d6) ppm = 13.15 – 11.08 (m, 1H), 8.07 (d, J = 9.6 Hz, 1H), 7.47 (d, J = 9.6 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 3.99 (dt, J = 10.9, 3.1 Hz, 2H), 3.97 (s, 3H), 3.82 – 3.75 (m, 8H), 3.56 – 3.50 (m, 2H), 3.42 – 3.34 (m, 1H), 1.83 – 1.74 (m, 4H).
92	1H NMR (400 MHz, DMSO-d6) ppm = 8.24 – 8.22 (m, 1H), 7.93 – 7.92 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 4.05 – 3.99 (m, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.36 – 3.19 (m, 2H), 2.83 (t, J = 2.6 Hz, 1H), 2.34 (d, J = 2.7 Hz, 2H), 1.73 – 1.56 (m, 4H).
93	1H NMR (400 MHz, DMSO-d6) ppm = 8.32 (s, 1H), 8.22 – 8.17 (m, 2H), 8.04 – 8.02 (m, 1H), 8.50 – 7.02 (m, 2H), 7.62 – 7.57 (m, 2H), 7.39 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 3.06 – 2.89 (m, 6H).
94	1H NMR (500 MHz, DMSO-d6) ppm = 13.28 – 10.50 (m, 1H), 8.31 (s, 1H), 8.28 – 8.23 (m, 2H), 8.03 (s, 1H), 7.58 – 7.53 (m, 2H), 7.33 (d, J = 8.2 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H).
95	1H NMR (400 MHz, DMSO-d6) ppm = 12.69 - 12.13 (m, 1H), 8.62 - 8.58 (m, 1H), 8.30 - 8.25 (m, 1H), 8.25 - 8.23 (m, 1H), 8.01 (dd, J = 5.0, 1.4 Hz, 1H), 8.00 - 7.97 (m, 1H), 7.33 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H).
96	1H NMR (400 MHz, DMSO-d6) ppm = 8.90 (s, 1H), 8.30 - 8.28 (m, 1H), 7.99 - 7.98 (m, 1H), 7.39 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 2.55 (s, 3H).

97	1H NMR (500 MHz, DMSO-d6) ppm = 15.08 – 14.12 (m, 1H), 12.94 – 11.51 (m, 1H), 9.33 – 9.31 (m, 1H), 8.19 – 8.15 (m, 2H), 7.83 (t, J = 1.7 Hz, 1H), 7.73 (t, J = 1.7 Hz, 1H), 7.58 – 7.53 (m, 2H), 6.99 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 5.55 (s, 2H), 4.00 – 3.96 (m, 2H), 3.92 (s, 3H), 3.50 (td, J = 11.4, 2.7 Hz, 2H), 3.35 – 3.28 (m, 1H), 1.86 – 1.73 (m, 4H).
98	1H NMR (400 MHz, DMSO-d6) ppm = 12.23 – 11.42 (m, 1H), 11.03 – 10.94 (m, 1H), 9.72 (s, 1H), 8.82 (d, J = 2.2 Hz, 1H), 8.35 (d, J = 1.8 Hz, 1H), 8.33 (s, 1H), 8.03 (s, 1H), 7.82 (dd, J = 8.4, 2.3 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H).
99	1H NMR (500 MHz, DMSO-d6/TFA) ppm = 8.21 – 8.15 (m, 2H), 7.42 – 7.39 (m, 1H), 7.23 (d, J = 8.5 Hz, 1H), 6.96 – 6.93 (m, 1H), 4.08 – 4.03 (m, 4H), 4.01 (s, 3H), 3.78 – 3.71 (m, 4H).
100	1H NMR (500 MHz, DMSO-d6) ppm = 12.66 - 11.05 (m, 1H), 8.32 (s, 1H), 8.13 - 8.10 (m, 2H), 8.03 (s, 1H), 7.42 - 7.39 (m, 2H), 7.34 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 4.47 (s, 2H), 3.96 (s, 3H), 3.91 (s, 3H), 3.29 (t, J = 7.0 Hz, 2H), 2.33 (t, J = 8.1 Hz, 2H), 2.01 - 1.93 (m, 2H).
101	1H NMR (400 MHz, DMSO-d6) ppm = 12.40 - 11.15 (m, 1H), 8.32 (s, 1H), 8.06 - 8.05 (m, 1H), 8.04 (s, 1H), 7.98 (dd, J = 8.4, 2.0 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.67 (t, J = 8.8 Hz, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.28 (t, J = 8.7 Hz, 2H).
102	1H NMR (400 MHz, DMSO-d6) ppm = 7.04 (d, J = 8.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 4.04 – 3.93 (m, 4H), 3.91 (s, 3H), 3.54 – 3.45 (m, 2H), 3.34 – 3.17 (m, 3H), 2.82 (t, J = 2.6 Hz, 1H), 2.33 (d, J = 2.7 Hz, 2H), 1.81 – 1.52 (m, 8H).
103	1H NMR (400 MHz, DMSO-d6) ppm = 7.30 – 7.17 (m, 5H), 7.07 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.00 – 3.91 (m, 4H), 3.91 (s, 3H), 3.53 – 3.45 (m, 2H), 3.33 – 3.16 (m, 3H), 2.72 (s, 2H), 1.80 – 1.68 (m, 4H), 1.53 – 1.41 (m, 4H).

104	1H NMR (700 MHz, DMSO-d6) ppm = 12.00 (s, 1H), 11.87 (s, 1H), 8.40 (s, 1H), 8.24 - 8.20 (m, 1H), 8.11 (s, 1H), 7.38 - 7.33 (m, 1H), 7.13 - 7.06 (m, 2H), 6.82 - 6.78 (m, 1H), 4.84 (s, 1H), 3.95 (s, 3H), 3.92 - 3.88 (m, 3H), 3.62 - 3.54 (m, 2H), 3.50 - 3.45 (m, 1H), 3.36 - 3.33 (m, 1H), 2.00 - 1.90 (m, 2H), 1.38 (s, 3H).
105	1H NMR (500 MHz, DMSO-d6) ppm = 12.62 - 11.71 (m, 1H), 8.32 (s, 1H), 8.18 (d, J = 5.9 Hz, 1H), 8.06 - 8.00 (m, 1H), 7.78 - 7.73 (m, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.27 - 7.21 (m, 1H), 6.87 - 6.83 (m, 1H), 4.03 - 3.97 (m, 2H), 3.95 (s, 3H), 3.90 (s, 3H), 3.53 - 3.46 (m, 2H), 1.63 - 1.54 (m, 4H), 1.18 (s, 3H).
106	1H NMR (500 MHz, DMSO-d6) ppm = 8.30 (s, 1H), 8.13 (d, J = 6.5 Hz, 1H), 8.00 (s, 1H), 7.66 (s, 1H), 7.38 – 7.34 (m, 2H), 6.90 (d, J = 8.4 Hz, 1H), 3.98 – 3.94 (m, 3H), 3.92 (s, 3H), 3.87 – 3.82 (m, 2H), 3.77 – 3.69 (m, 2H), 3.69 (d, J = 8.6 Hz, 1H), 3.66 – 3.62 (m, 2H), 3.60 (d, J = 8.6 Hz, 1H), 2.14 – 2.09 (m, 2H), 2.04 – 1.92 (m, 2H).
107	1H NMR (700 MHz, DMSO-d6) ppm = 12.00 (s, 1H), 11.87 (s, 1H), 8.40 (s, 1H), 8.24 - 8.20 (m, 1H), 8.11 (s, 1H), 7.38 - 7.33 (m, 1H), 7.13 - 7.06 (m, 2H), 6.82 - 6.78 (m, 1H), 4.84 (s, 1H), 3.95 (s, 3H), 3.92 - 3.88 (m, 3H), 3.62 - 3.54 (m, 2H), 3.50 - 3.45 (m, 1H), 3.36 - 3.33 (m, 1H), 2.00 - 1.90 (m, 2H), 1.38 (s, 3H).
108	1H NMR (500 MHz, DMSO-d6) ppm = 12.30 – 11.36 (m, 1H), 8.04 – 8.02 (m, 1H), 7.96 (dd, J = 8.4, 2.0 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 4.66 (t, J = 8.8 Hz, 2H), 4.00 – 3.95 (m, 2H), 3.92 (s, 3H), 3.51 (td, J = 11.4, 2.8 Hz, 2H), 3.36 – 3.29 (m, 1H), 3.27 (t, J = 8.8 Hz, 2H), 1.86 – 1.73 (m, 4H).
109	1H NMR (500 MHz, DMSO-d6) ppm = 10.77 – 10.36 (m, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.34 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.70 – 3.40 (m, 3H), 3.39 – 3.18 (m, 3H), 3.28 (s, 3H), 2.58 – 2.49 (m, 1H), 2.07 – 1.96 (m, 1H), 1.76 – 1.63 (m, 1H).

110	1H NMR (500 MHz, DMSO-d6) ppm = 11.25 – 9.80 (m, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.99 – 3.94 (m, 2H), 3.91 (s, 3H), 3.84 – 3.76 (m, 2H), 3.59 (d, J = 8.4 Hz, 1H), 3.55 (d, J = 8.5 Hz, 1H), 3.59 – 3.38 (m, 6H), 3.33 – 3.25 (m, 1H), 2.01 – 1.83 (m, 4H), 1.81 – 1.70 (m, 4H).
111	1H NMR (500 MHz, DMSO-d6) ppm = 11.21 – 9.86 (m, 1H), 7.02 (d, J = 8.3 Hz, 1H), 6.81 (d, J = 8.3 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.91 (s, 3H), 3.68 – 3.60 (m, 2H), 3.57 – 3.46 (m, 6H), 3.45 – 3.32 (m, 2H), 3.31 – 3.24 (m, 1H), 1.92 – 1.69 (m, 6H), 1.56 – 1.48 (m, 4H).
112	1H NMR (400 MHz, DMSO-d6) ppm = 7.17 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 4.00 - 3.94 (m, 2H), 3.94 (s, 3H), 3.84 - 3.79 (m, 2H), 3.77 - 3.69 (m, 2H), 3.61 - 3.55 (m, 2H), 3.55 - 3.43 (m, 4H), 3.41 - 3.31 (m, 1H), 3.06 - 2.96 (m, 2H), 1.80 - 1.69 (m, 4H).
113	1H NMR (500 MHz, DMSO-d6) ppm = 12.72 - 10.62 (m, 1H), 10.49 - 10.05 (m, 1H), 8.29 - 8.25 (m, 1H), 8.00 - 7.96 (m, 1H), 7.27 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.81 - 3.46 (m, 5H), 3.43 (d, J = 11.2 Hz, 1H), 3.33 (d, J = 11.2 Hz, 1H), 3.26 - 3.15 (m, 1H), 1.89 - 1.50 (m, 6H).
114	1H NMR (500 MHz, DMSO-d6) ppm = 12.72 - 10.62 (m, 1H), 10.49 - 10.05 (m, 1H), 8.29 - 8.25 (m, 1H), 8.00 - 7.96 (m, 1H), 7.27 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.81 - 3.46 (m, 5H), 3.43 (d, J = 11.2 Hz, 1H), 3.33 (d, J = 11.2 Hz, 1H), 3.26 - 3.15 (m, 1H), 1.89 - 1.50 (m, 6H).
115	1H NMR (500 MHz, DMSO-d6) ppm = 11.90 - 10.97 (m, 1H), 10.25 - 10.06 (m, 1H), 8.30 - 8.24 (m, 1H), 8.02 - 7.95 (m, 1H), 7.25 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.3 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.84 - 3.76 (m, 2H), 3.62 - 3.50 (m, 4H), 3.49 - 3.39 (m, 2H), 1.98 - 1.82 (m, 4H).

116	1H NMR (500 MHz, DMSO-d6) ppm = 11.90 - 10.97 (m, 1H), 10.25 - 10.06 (m, 1H), 8.30 - 8.24 (m, 1H), 8.02 - 7.95 (m, 1H), 7.25 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.3 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.84 - 3.76 (m, 2H), 3.62 - 3.50 (m, 4H), 3.49 - 3.39 (m, 2H), 1.98 - 1.82 (m, 4H).
117	1H NMR (500 MHz, DMSO-d6) ppm = 3.66 – 3.41 (m, 4H), 3.40 – 3.34 (m, 1H), 3.34 – 3.29 (m, 2H), 3.28 (s, 3H), 3.28 – 3.16 (m, 2H), 7.07 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 3.99 – 3.94 (m, 2H), 3.92 (s, 3H), 2.08 – 1.94 (m, 1H), 1.81 – 1.60 (m, 6H).
118	1H NMR (700 MHz, DMSO-d6) ppm = 13.05 - 11.77 (m, 1H), 8.19 - 8.13 (m, 1H), 7.80 - 7.68 (m, 1H), 7.32 - 7.22 (m, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.85 - 6.79 (m, 1H), 4.00 - 3.95 (m, 4H), 3.92 (s, 3H), 3.54 - 3.47 (m, 4H), 3.33 - 3.27 (m, 1H), 1.82 - 1.73 (m, 4H), 1.64 - 1.55 (m, 4H), 1.18 (s, 3H).
119	1H NMR (700 MHz, DMSO-d6) ppm = 14.36 - 11.93 (m, 2H), 8.11 (d, J = 6.4 Hz, 1H), 7.62 - 7.57 (m, 1H), 7.41 - 7.35 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 3.98 (dt, J = 11.0, 3.1 Hz, 2H), 3.93 (s, 3H), 3.87 - 3.81 (m, 2H), 3.77 - 3.67 (m, 3H), 3.65 - 3.61 (m, 2H), 3.60 (d, J = 8.6 Hz, 1H), 3.54 - 3.48 (m, 2H), 3.32 - 3.26 (m, 1H), 2.15 - 2.07 (m, 2H), 2.03 - 1.92 (m, 2H), 1.80 - 1.72 (m, 4H).
120	1H NMR (700 MHz, DMSO-d6) ppm = 11.66 - 11.54 (m, 1H), 8.30 (s, 1H), 8.00 (s, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.17 - 7.13 (m, 2H), 7.10 - 7.07 (m, 2H), 6.88 (d, J = 8.3 Hz, 1H), 3.95 (s, 3H), 3.89 (s, 3H), 1.56 (s, 6H).
121	1H NMR (700 MHz, DMSO-d6) ppm = 11.04 - 10.74 (m, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.39 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.81 (dd, J = 8.8, 6.7 Hz, 2H), 3.76 - 3.70 (m, 2H), 3.58 (dd, J = 8.9, 3.4 Hz, 2H), 3.49 - 3.43 (m, 2H), 3.04 - 2.97 (m, 2H).

122	1H NMR (700 MHz, DMSO-d6) ppm = 14.22 – 12.03 (m, 2H), 8.09 (d, J = 6.4 Hz, 1H), 7.60 (s, 1H), 7.40 – 7.35 (m, 1H), 7.07 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 4.00 – 3.96 (m, 2H), 3.93 (s, 3H), 3.80 – 3.70 (m, 2H), 3.61 – 3.48 (m, 4H), 3.33 – 3.26 (m, 1H), 2.09 – 1.99 (m, 2H), 1.80 – 1.71 (m, 4H), 1.42 (s, 3H).
123	1H NMR (700 MHz, DMSO-d6) ppm = 11.31 – 10.27 (m, 1H), 7.07 – 6.96 (m, 1H), 6.83 (d, J = 8.6 Hz, 1H), 3.91 (s, 3H), 3.90 – 3.84 (m, 4H), 3.83 – 3.76 (m, 2H), 3.64 – 3.37 (m, 6H), 3.35 – 3.19 (m, 4H), 2.04 – 1.83 (m, 4H).
124	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.93 (s, 1H), 7.37 (d, J = 8.4 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.15 – 4.07 (m, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.13 – 3.04 (m, 2H), 2.60 – 2.50 (m, 1H), 1.93 – 1.85 (m, 2H), 1.60 – 1.48 (m, 2H).
125	1H NMR (700 MHz, DMSO-d6) ppm = 10.61 – 10.17 (m, 1H), 6.78 – 6.65 (m, 2H), 3.88 (s, 3H), 3.84 – 3.80 (m, 4H), 3.68 – 3.60 (m, 2H), 3.55 – 3.49 (m, 2H), 3.49 – 3.28 (m, 4H), 3.28 – 3.18 (m, 4H), 1.91 – 1.74 (m, 2H), 1.54 – 1.49 (m, 4H).
126	1H NMR (400 MHz, DMSO-d6) ppm = 8.23 (s, 1H), 7.93 (s, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.34 – 7.27 (m, 1H), 6.98 (d, J = 8.5 Hz, 1H), 6.84 – 6.76 (m, 1H), 4.23 – 4.17 (m, 2H), 3.96 (s, 3H), 3.91 (s, 3H), 3.06 – 2.96 (m, 2H), 2.44 – 2.35 (m, 1H), 1.83 – 1.76 (m, 2H), 1.59 – 1.48 (m, 2H).
127	1H NMR (400 MHz, DMSO-d6) ppm = 12.20 – 11.42 (m, 1H), 8.31 (s, 1H), 8.04 – 7.99 (m, 3H), 7.37 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.81 – 6.76 (m, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.45 (q, J = 7.0 Hz, 4H), 1.14 (t, J = 7.0 Hz, 6H).
128	1H NMR (400 MHz, DMSO-d6) ppm = 8.27 (s, 1H), 7.97 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 3.96 (d, J = 7.2 Hz, 2H), 3.94 (s, 3H), 3.89 – 3.81 (m, 2H), 3.37 – 3.27 (m, 2H), 2.17 (hept, J = 6.8 Hz, 1H), 1.56 – 1.43 (m, 4H), 1.16 (s, 3H), 0.88 (d, J = 6.6 Hz, 6H).

129	1H NMR (700 MHz, DMSO-d6) ppm = 15.75 – 15.03 (m, 1H), 12.09 – 11.45 (m, 1H), 10.43 (s, 1H), 8.98 – 8.92 (m, 2H), 8.86 – 8.84 (m, 2H), 7.92 (d, J = 8.7 Hz, 1H), 6.98 (d, J = 8.7 Hz, 1H), 4.03 (s, 3H), 3.71 – 3.25 (m, 8H), 1.91 – 1.75 (m, 2H), 1.56 – 1.49 (m, 4H).
130	1H NMR (700 MHz, DMSO-d6) ppm = 12.90 – 11.39 (m, 1H), 7.09 (d, J = 8.2 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 4.22 – 4.15 (m, 2H), 3.99 – 3.95 (m, 2H), 3.92 (s, 3H), 3.52 – 3.47 (m, 2H), 3.33 – 3.26 (m, 1H), 2.99 – 2.88 (m, 2H), 2.20 (d, J = 7.0 Hz, 2H), 1.97 – 1.90 (m, 1H), 1.77 – 1.69 (m, 6H), 1.20 – 1.12 (m, 2H).
131	1H NMR (700 MHz, DMSO-d6) ppm = 13.55 – 11.72 (m, 1H), 11.55 – 10.37 (m, 1H), 7.37 – 7.33 (m, 2H), 7.31 – 7.28 (m, 1H), 7.26 – 7.23 (m, 1H), 7.13 – 7.09 (m, 1H), 7.03 – 6.98 (m, 1H), 4.00 (s, 3H), 3.81 – 3.76 (m, 2H), 3.32 – 3.24 (m, 2H), 2.14 (s, 3H), 1.51 – 1.47 (m, 2H), 1.46 – 1.41 (m, 2H), 1.14 (s, 3H).
132	1H NMR (700 MHz, DMSO-d6) ppm = 13.31 – 10.06 (m, 2H), 8.23 (s, 1H), 7.92 (s, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.24 – 4.16 (m, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 2.99 – 2.89 (m, 2H), 2.19 (d, J = 7.0 Hz, 2H), 1.98 – 1.90 (m, 1H), 1.77 – 1.72 (m, 2H), 1.21 – 1.13 (m, 2H).
133	1H NMR (400 MHz, DMSO-d6) ppm = 8.19 – 8.14 (m, 2H), 7.58 – 7.53 (m, 2H), 6.98 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.92 (s, 3H), 3.55 – 3.47 (m, 2H), 3.36 – 3.26 (m, 1H), 3.01 (s, 3H), 2.92 (s, 3H), 1.88 – 1.73 (m, 4H).
134	1H NMR (400 MHz, DMSO-d6) ppm = 8.19 (s, 1H), 7.91 (s, 1H), 7.33 - 7.29 (m, 1H), 6.88 - 6.84 (m, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.73 (dd, J = 10.6, 7.3 Hz, 1H), 3.67 - 3.60 (m, 1H), 3.48 - 3.39 (m, 3H), 3.28 (s, 3H), 3.27 - 3.24 (m, 1H), 3.15 - 3.08 (m, 1H), 2.35 - 2.25 (m, 1H), 2.14 - 2.04 (m, 1H), 1.70 - 1.63 (m, 2H).
135	1H NMR (700 MHz, DMSO-d6) ppm = 11.90 - 11.57 (m, 1H), 8.45 (d, J = 2.9 Hz, 1H), 8.29 (s, 1H), 8.10 (d, J = 8.9 Hz, 1H), 7.96 (s, 1H), 7.54 (dd, J = 8.9, 2.9 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 3.99 (s, 3H), 3.94 (s, 3H), 3.80 - 3.77 (m, 4H), 3.46 - 3.44 (m, 4H).

136	1H NMR (400 MHz, DMSO-d6) ppm = 11.80 - 11.70 (m, 1H), 8.47 (s, 1H), 8.18 (s, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.65 - 6.59 (m, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 3.84 - 3.80 (m, 4H), 3.34 - 3.25 (m, 4H).
137	1H NMR (400 MHz, DMSO-d6) ppm = 7.02 (d, J = 8.3 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 4.00 – 3.94 (m, 2H), 3.91 (s, 3H), 3.73 – 3.43 (m, 5H), 3.39 – 3.27 (m, 3H), 3.25 (s, 3H), 3.18 – 2.97 (m, 1H), 2.30 – 1.99 (m, 2H), 1.83 – 1.69 (m, 4H), 1.67 – 1.51 (m, 3H).
138	1H NMR (700 MHz, DMSO-d6) ppm = 12.28 - 11.76 (m, 1H), 8.11 - 8.09 (m, 2H), 7.40 - 7.38 (m, 2H), 6.99 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.2 Hz, 1H), 4.47 (s, 2H), 4.00 - 3.96 (m, 2H), 3.92 (s, 3H), 3.53 - 3.48 (m, 2H), 3.35 - 3.30 (m, 1H), 3.28 (t, J = 7.0 Hz, 2H), 2.33 (t, J = 8.1 Hz, 2H), 1.99 - 1.94 (m, 2H), 1.84 - 1.75 (m, 4H).
139	NMR available, but no peak listing
144	1H NMR (400 MHz, DMSO-d6, 90°C) d 11.36 - 9.96 (m, 2H), 7.90 - 7.79 (m, 2H), 7.26 - 7.19 (m, 2H), 7.18 - 7.12 (m, 1H), 6.78 (d, J = 8.3 Hz, 1H), 4.05 (s, 1H), 3.95 (s, 3H), 3.83 - 3.74 (m, 2H), 3.38 - 3.29 (m, 2H), 1.57 - 1.41 (m, 4H), 1.15 (s, 3H).
151	1H NMR (500 MHz, DMSO-d6) ppm = 11.47 - 11.27 (m, 1H), 10.35 - 10.02 (m, 1H), 8.40 - 8.24 (m, 1H), 8.13 - 7.96 (m, 1H), 7.29 - 7.16 (m, 1H), 6.71 (d, J = 8.3 Hz, 1H), 4.36 (s, 1H), 4.18 - 4.12 (m, 2H), 3.90 (s, 3H), 3.88 - 3.82 (m, 2H), 3.29 - 3.24 (m, 2H), 1.75 - 1.69 (m, 2H), 1.59 - 1.41 (m, 5H), 1.15 (s, 3H), 0.93 (d, J = 6.6 Hz, 6H).
152	1H NMR (700 MHz, DMSO-d6) d 11.46 – 11.36 (m, 1H), 8.33 (s, 1H), 8.24 – 8.21 (m, 2H), 8.05 (s, 1H), 7.85 – 7.82 (m, 2H), 7.39 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 4.45 (s, 2H), 3.97 (s, 3H), 3.97 – 3.93 (m, 2H), 3.92 (s, 3H), 3.85 – 3.79 (m, 2H), 3.28 – 3.22 (m, 2H), 3.17 – 3.10 (m, 2H).
155	1H NMR (500 MHz, DMSO-d6) ppm = 11.68 - 11.12 (m, 1H), 10.71 - 10.03 (m, 1H), 6.97 (d, J = 8.3 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 7.38 - 5.74 (m, 1H), 4.35 (s, 1H), 4.25 (q, J = 2.7 Hz, 2H), 3.89 (s, 3H), 3.87 - 3.81 (m, 4H), 3.30 - 3.22 (m, 2H), 2.58 - 2.50 (m, 2H), 1.50 - 1.39 (m, 4H), 1.14 (s, 3H).

156	1H NMR (400 MHz, DMSO-d6) d 8.89 (s, 1H), 8.32 – 8.30 (m, 1H), 8.02 – 8.01 (m, 1H), 7.38 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 4.17 (s, 3H), 3.97 (s, 3H), 3.92 (s, 3H).
157	1H NMR (400 MHz, DMSO-d6) ppm = 8.35 - 8.32 (m, 1H), 8.00 - 7.97 (m, 1H), 7.24 (d, J = 8.4 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 4.36 (s, 1H), 4.25 - 4.16 (m, 1H), 3.90 (s, 3H), 3.89 - 3.81 (m, 4H), 3.09 - 3.02 (m, 2H), 2.64 - 2.56 (m, 2H), 2.02 - 1.95 (m, 2H), 1.87 - 1.75 (m, 2H), 1.53 - 1.40 (m, 4H), 1.15 (s, 3H).
158	1H NMR (400 MHz, DMSO-d6) d 11.98 - 11.04 (m, 1H), 8.50 (d, J = 2.8 Hz, 1H), 8.33 - 8.31 (m, 1H), 8.24 - 8.20 (m, 1H), 8.01 - 8.00 (m, 1H), 7.70 (dd, J = 8.8, 2.9 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.37 - 4.33 (m, 2H), 3.97 (s, 3H), 3.93 (s, 3H), 3.75 - 3.72 (m, 2H), 3.34 (s, 3H).
159	1H NMR (400 MHz, DMSO-d6) d 12.58 - 10.47 (m, 1H), 8.24 - 8.23 (m, 1H), 7.94 - 7.93 (m, 1H), 7.41 (d, J = 8.4 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 4.15 - 4.01 (m, 2H), 3.96 (s, 3H), 3.91 (s, 3H), 3.09 - 3.00 (m, 1H), 2.85 - 2.76 (m, 1H), 2.27 (dd, J = 15.6, 6.5 Hz, 1H), 2.16 (dd, J = 15.7, 7.2 Hz, 1H), 1.95 - 1.81 (m, 2H), 1.75 - 1.67 (m, 1H), 1.54 - 1.41 (m, 1H), 1.32 - 1.21 (m, 1H).
160	1H NMR (500 MHz, DMSO-d6) d 12.69 – 11.26 (m, 1H), 8.33 (s, 1H), 8.04 (s, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.34 – 7.31 (m, 1H), 6.84 (d, J = 8.3 Hz, 1H), 4.17 (s, 3H), 3.95 (s, 3H), 3.90 (s, 3H).
161	1H NMR (500 MHz, DMSO-d6) d 11.78 - 11.67 (m, 1H), 8.53 - 8.52 (m, 1H), 8.34 - 8.32 (m, 1H), 8.22 - 8.21 (m, 1H), 8.07 - 8.04 (m, 1H), 7.31 (d, J = 8.2 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 4.34 (t, J = 5.1 Hz, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 3.72 (t, J = 5.2 Hz, 2H), 3.26 (s, 3H).
162	1H NMR (500 MHz, DMSO-d6) d 9.24 - 9.22 (m, 1H), 8.53 (dd, J = 8.1, 2.3 Hz, 1H), 8.33 - 8.30 (m, 1H), 8.05 - 8.01 (m, 1H), 7.73 - 7.70 (m, 1H), 7.34 (d, J = 8.3 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.04 (s, 3H), 2.94 (s, 3H).

163	1H NMR (500 MHz, DMSO-d6) d 10.77 - 9.85 (m, 1H), 7.87 - 7.86 (m, 1H), 7.56 - 7.55 (m, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H), 4.29 (s, 1H), 3.92 (s, 3H), 4.10 - 3.80 (m, 2H), 3.89 (s, 3H), 3.38 - 3.13 (m, 2H), 3.23 (s, 3H), 1.48 - 1.33 (m, 4H), 1.13 (s, 3H).
164	1H NMR (400 MHz, DMSO-d6) d 12.27 - 11.35 (m, 1H), 8.90 (s, 1H), 8.34 - 8.31 (m, 1H), 8.04 - 8.02 (m, 1H), 7.36 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.67 (t, J = 5.1 Hz, 2H), 3.96 (s, 3H), 3.91 (s, 3H), 3.80 (t, J = 5.2 Hz, 2H), 3.28 (s, 3H).
165	1H NMR (400 MHz, DMSO-d6) d 8.54 – 8.49 (m, 1H), 8.28 (s, 1H), 7.99 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.71 (s, 3H).
166	1H NMR (400 MHz, DMSO-d6) d 12.00 – 11.55 (m, 1H), 8.27 (s, 1H), 8.03 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 2.89 – 2.84 (m, 2H), 2.81 – 2.76 (m, 2H).
168	1H NMR (400 MHz, DMSO-d6,90°C) d 8.26 – 8.24 (m, 1H), 8.20 – 8.16 (m, 2H), 8.00 – 7.99 (m, 1H), 7.69 – 7.65 (m, 2H), 7.32 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.05 – 4.02 (m, 2H), 3.99 (s, 3H), 3.92 (s, 3H), 3.42 – 3.31 (m, 4H), 3.14 – 3.02 (m, 4H), 2.78 (s, 3H).
184	1H NMR (500 MHz, DMSO-d6) d 12.79 - 10.98 (m, 1H), 8.91 (s, 1H), 7.13 - 7.06 (m, 1H), 6.85 (d, J = 8.6 Hz, 1H), 4.67 (t, J = 5.1 Hz, 2H), 3.94 (s, 3H), 3.94 - 3.91 (m, 4H), 3.80 (t, J = 5.1 Hz, 2H), 3.48 - 3.42 (m, 4H), 3.27 (s, 3H).
210	1H NMR (400 MHz, DMSO-d6) d 12.37 - 11.35 (m, 1H), 8.89 (s, 1H), 7.29 (d, J = 8.6 Hz, 1H), 6.89 (d, J = 8.6 Hz, 1H), 4.17 (s, 3H), 4.00 - 3.96 (m, 4H), 3.95 (s, 3H), 3.55 - 3.49 (m, 4H).
211	1H NMR (500 MHz, DMSO-d6) d 12.54 – 11.12 (m, 1H), 8.87 (s, 1H), 7.03 (d, J = 8.3 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 4.68 – 4.65 (m, 2H), 4.00 – 3.96 (m, 2H), 3.92 (s, 3H), 3.81 – 3.78 (m, 2H), 3.50 (td, J = 11.4, 2.8 Hz, 2H), 3.34 – 3.27 (m, 1H), 3.28 (s, 3H), 1.85 – 1.73 (m, 4H).

212	1H NMR (500 MHz, DMSO-d6) d 13.05 – 10.88 (m, 1H), 8.88 (s, 1H), 7.09 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 8.3 Hz, 1H), 4.17 (s, 3H), 4.01 – 3.96 (m, 2H), 3.94 (s, 3H), 3.51 (td, J = 11.2, 3.1 Hz, 2H), 3.36 – 3.29 (m, 1H), 1.84 – 1.73 (m, 4H).
213	1H NMR (500 MHz, DMSO-d6) d 14.13 – 10.81 (m, 1H), 8.18 (s, 1H), 7.85 (s, 1H), 7.29 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 1.66 – 1.60 (m, 4H).
214	1H NMR (400 MHz, DMSO-d6) d 9.26 (d, J = 2.1 Hz, 1H), 8.55 (dd, J = 8.1, 2.2 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.01 – 3.95 (m, 2H), 3.94 (s, 3H), 3.57 – 3.47 (m, 2H), 3.38 – 3.29 (m, 1H), 3.04 (s, 3H), 2.95 (s, 3H), 1.84 – 1.73 (m, 4H).
215	1H NMR (400 MHz, DMSO-d6) d 8.30 (s, 1H), 8.05 – 8.02 (m, 1H), 8.01 (s, 1H), 7.33 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.54 (s, 3H).
216	1H NMR (400 MHz, DMSO-d6) d 7.47 (d, J = 8.7 Hz, 1H), 6.80 (d, J = 8.7 Hz, 1H), 3.93 (s, 3H), 3.87 - 3.84 (m, 2H), 3.84 - 3.81 (m, 2H), 3.80 - 3.75 (m, 2H), 3.34 - 3.25 (m, 2H), 2.09 - 2.00 (m, 4H), 1.78 - 1.72 (m, 4H), 1.55 - 1.42 (m, 4H), 1.16 (s, 3H).
217	1H NMR (400 MHz, DMSO-d6) d 7.71 - 7.65 (m, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.55 - 7.48 (m, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.18 (td, J = 8.7, 2.6 Hz, 1H), 6.94 (d, J = 8.5 Hz, 1H), 3.98 (s, 3H), 3.88 - 3.80 (m, 2H), 3.35 - 3.26 (m, 2H), 1.54 - 1.41 (m, 4H), 1.15 (s, 3H).
218	1H NMR (500 MHz, DMSO-d6) d 11.73 - 10.00 (m, 1H), 7.57 (td, J = 7.7, 1.8 Hz, 1H), 7.49 - 7.44 (m, 1H), 7.37 - 7.31 (m, 2H), 7.23 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H), 3.84 - 3.77 (m, 2H), 3.32 - 3.24 (m, 2H), 1.52 - 1.40 (m, 4H), 1.14 (s, 3H).
219	1H NMR (500 MHz, DMSO-d6) d 9.34 (s, 1H), 8.82 - 8.75 (m, 1H), 8.30 (s, 1H), 8.00 (s, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H).

220	1H NMR (700 MHz, DMSO-d6) d 11.30 - 10.03 (m, 1H), 8.25 (s, 1H), 7.95 (s, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 4.08 - 4.02 (m, 1H), 3.93 (s, 3H), 3.95 - 3.89 (m, 1H), 3.90 (s, 3H), 3.86 - 3.81 (m, 1H), 3.70 - 3.65 (m, 1H), 3.61 - 3.54 (m, 1H), 3.08 (s, 3H), 2.40 - 2.32 (m, 2H).
221	1H NMR (400 MHz, DMSO-d6) d 8.25 (s, 1H), 7.96 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 5.49 - 5.30 (m, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.85 - 3.68 (m, 4H), 2.29 - 2.02 (m, 2H).
222	1H NMR (400 MHz, DMSO-d6, 90 Â°C) d 11.21 - 9.99 (m, 1H), 8.37 - 8.29 (m, 1H), 8.05 - 7.98 (m, 1H), 7.04 (d, J = 8.3 Hz, 1H), 6.65 (d, J = 8.3 Hz, 1H), 6.45 (d, J = 9.4 Hz, 1H), 5.75 - 5.67 (m, 1H), 3.93 (s, 3H), 3.83 - 3.75 (m, 2H), 3.53 (s, 3H), 3.42 - 3.33 (m, 2H), 1.50 - 1.43 (m, 4H), 1.17 (s, 3H).
223	1H NMR (500 MHz, DMSO-d6) d 11.51 - 10.37 (m, 1H), 8.26 (s, 1H), 8.07 - 7.99 (m, 3H), 7.97 (s, 1H), 7.40 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.75 - 3.45 (m, 4H), 3.31 - 3.17 (m, 1H), 2.94 - 2.85 (m, 2H), 2.20 - 2.08 (m, 1H), 1.86 - 1.75 (m, 1H).
224	1H NMR (400 MHz, DMSO-d6) d 12.17 – 11.45 (m, 1H), 8.48 (s, 1H), 8.18 (s, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.92 (s, 3H), 3.91 (s, 3H), 3.54 – 3.46 (m, 2H), 3.36 – 3.25 (m, 1H), 1.88 – 1.72 (m, 4H).
225	1H NMR (500 MHz, DMSO-d6) d 12.14 – 11.62 (m, 1H), 8.52 (s, 1H), 8.20 (s, 1H), 7.00 (d, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 4.35 (t, J = 5.1 Hz, 2H), 4.00 – 3.95 (m, 2H), 3.92 (s, 3H), 3.73 – 3.70 (m, 2H), 3.50 (td, J = 11.4, 2.6 Hz, 2H), 3.34 – 3.27 (m, 1H), 3.25 (s, 3H), 1.86 – 1.73 (m, 4H).
226	1H NMR (400 MHz, DMSO-d6) d 13.40 – 11.58 (m, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.5 Hz, 1H), 3.98 – 3.93 (m, 2H), 3.89 (s, 3H), 3.53 – 3.45 (m, 2H), 3.27 – 3.18 (m, 1H), 1.73 – 1.66 (m, 4H), 1.59 – 1.55 (m, 4H).

227	1H NMR (500 MHz, DMSO-d6) d 8.52 – 8.41 (m, 1H), 7.04 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 8.3 Hz, 1H), 3.99 – 3.95 (m, 2H), 3.91 (s, 3H), 3.53 – 3.46 (m, 2H), 3.32 – 3.25 (m, 1H), 2.71 (s, 3H), 1.81 – 1.71 (m, 4H).
228	1H NMR (500 MHz, Methanol-d4) delta 7.98 - 7.96 (m, 1H), 7.81 - 7.80 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 4.94 (s, 2H), 4.10 - 4.06 (m, 2H), 4.01 (s, 3H), 3.65 (td, J = 11.6, 2.5 Hz, 2H), 3.30 - 3.23 (m, 1H), 1.92 - 1.79 (m, 4H).
229	1H NMR (700 MHz, DMSO-d6) d 11.45 – 9.57 (m, 2H), 8.86 (s, 1H), 8.44 (s, 1H), 7.86 (t, J = 59.5 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 4.38 (s, 1H), 3.92 (s, 3H), 3.87 – 3.82 (m, 2H), 3.34 – 3.25 (m, 2H), 1.52 – 1.43 (m, 4H), 1.15 (s, 3H).
230	1H NMR (500 MHz, DMSO-d6) d 11.66 – 9.66 (m, 2H), 8.34 – 8.28 (m, 1H), 8.06 – 7.99 (m, 1H), 7.23 (d, J = 8.2 Hz, 1H), 6.71 (d, J = 8.3 Hz, 1H), 4.37 (s, 1H), 4.28 (t, J = 5.4 Hz, 2H), 3.90 (s, 3H), 3.89 – 3.83 (m, 2H), 3.82 – 3.79 (m, 2H), 3.53 – 3.50 (m, 2H), 3.43 – 3.39 (m, 2H), 3.33 – 3.25 (m, 2H), 3.20 (s, 3H), 1.52 – 1.41 (m, 4H), 1.15 (s, 3H).
231	1H NMR (500 MHz, DMSO-d6) d 11.77 – 10.96 (m, 1H), 10.87 – 10.05 (m, 1H), 9.45 – 9.32 (m, 1H), 8.52 – 8.49 (m, 1H), 8.49 – 8.43 (m, 1H), 8.03 – 7.96 (m, 2H), 7.47 (d, J = 8.2 Hz, 1H), 7.38 – 7.34 (m, 1H), 6.76 (d, J = 8.4 Hz, 1H), 4.39 (s, 1H), 3.93 (s, 3H), 3.90 – 3.83 (m, 2H), 3.34 – 3.25 (m, 2H), 1.54 – 1.43 (m, 4H), 1.16 (s, 3H).
232	1H NMR (400 MHz, DMSO-d6) d 8.49 (s, 1H), 8.18 (s, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.73 (d, J = 8.1 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 1.60 - 1.54 (m, 2H), 1.24 - 1.14 (m, 2H), 0.77 (t, J = 7.3 Hz, 3H), 0.75 - 0.73 (m, 4H).
233	1H NMR (400 MHz, DMSO-d6) d 12.19 - 11.46 (m, 1H), 8.48 (s, 1H), 8.17 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 3.92 (s, 3H), 3.92 (s, 3H), 3.08 - 2.99 (m, 1H), 1.76 - 1.62 (m, 4H), 1.25 - 1.03 (m, 2H), 0.81 (t, J = 7.3 Hz, 3H), 0.73 (t, J = 7.3 Hz, 3H).

234	1H NMR (500 MHz, DMSO-d6) d 12.76 - 11.68 (m, 1H), 8.00 - 7.76 (m, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 3.99 - 3.95 (m, 2H), 3.91 (s, 3H), 3.52 - 3.46 (m, 2H), 3.29 - 3.21 (m, 1H), 2.52 (s, 3H), 1.83 - 1.68 (m, 4H).
235	1H NMR (400 MHz, DMSO-d6,90°C) d 8.26 – 8.24 (m, 1H), 8.20 – 8.16 (m, 2H), 8.00 – 7.99 (m, 1H), 7.69 – 7.65 (m, 2H), 7.32 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.05 – 4.02 (m, 2H), 3.99 (s, 3H), 3.92 (s, 3H), 3.42 – 3.31 (m, 4H), 3.14 – 3.02 (m, 4H), 2.78 (s, 3H).
236	1H NMR (500 MHz, DMSO-d6) d 11.89 – 11.21 (m, 1H), 10.85 – 10.21 (m, 1H), 7.61 – 7.10 (m, 4H), 6.95 – 6.86 (m, 1H), 6.79 (d, J = 8.3 Hz, 1H), 4.36 (s, 1H), 4.19 – 4.12 (m, 2H), 3.94 (s, 3H), 3.90 – 3.78 (m, 2H), 3.71 – 3.66 (m, 2H), 3.33 (s, 3H), 3.31 – 3.22 (m, 2H), 1.50 – 1.39 (m, 4H), 1.16 – 1.10 (m, 3H).
238	1H NMR (500 MHz, DMSO-d6) d 11.65 – 11.00 (m, 1H), 10.90 – 9.85 (m, 1H), 8.40 – 8.19 (m, 1H), 8.10 – 7.91 (m, 1H), 7.27 – 7.21 (m, 1H), 6.71 (d, J = 8.4 Hz, 1H), 4.75 (s, 1H), 4.40 (s, 1H), 4.04 (s, 2H), 3.90 (s, 3H), 3.88 – 3.81 (m, 2H), 3.34 – 3.25 (m, 2H), 1.52 – 1.41 (m, 4H), 1.15 (s, 3H), 1.10 (s, 6H).
239	1H NMR (700 MHz, DMSO-d6) d 11.96 – 11.80 (m, 1H), 8.51 (s, 1H), 8.20 (s, 1H), 7.88 – 7.81 (m, 1H), 7.78 – 7.74 (m, 1H), 7.52 – 7.48 (m, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.17 – 7.13 (m, 1H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.91 (s, 3H).
240	1H NMR (700 MHz, DMSO-d6) d 12.74 – 11.46 (m, 1H), 8.18 – 8.14 (m, 2H), 7.89 – 7.82 (m, 1H), 7.79 – 7.74 (m, 1H), 7.58 – 7.55 (m, 2H), 7.53 – 7.49 (m, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.16 (td, J = 8.5, 2.7 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.00 (s, 3H), 3.02 (s, 3H), 2.91 (s, 3H).
241	1H NMR (500 MHz, DMSO-d6) d 11.54 - 11.26 (m, 1H), 10.37 - 10.07 (m, 1H), 8.48 - 8.30 (m, 1H), 8.20 - 7.99 (m, 1H), 7.27 (s, 1H), 6.71 (d, J = 8.3 Hz, 1H), 5.09 - 5.02 (m, 1H), 4.37 (s, 1H), 4.05 - 3.99 (m, 2H), 3.95 (dd, J = 9.3, 3.9 Hz, 1H), 3.90 (s, 3H), 3.88 - 3.81 (m, 3H), 2.47 - 2.25 (m, 4H), 1.52 - 1.41 (m, 4H), 1.15 (s, 3H).

242	1H NMR (500 MHz, DMSO-d6) d 8.15 - 8.12 (m, 2H), 7.63 (td, J = 7.7, 1.9 Hz, 1H), 7.56 - 7.53 (m, 2H), 7.48 - 7.43 (m, 1H), 7.37 - 7.31 (m, 2H), 7.23 - 7.20 (m, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.00 (s, 3H), 3.01 (s, 3H), 2.90 (s, 3H).
243	1H NMR (400 MHz, DMSO-d6) d 12.12 – 11.68 (m, 1H), 10.60 – 10.33 (m, 1H), 8.48 – 8.46 (m, 1H), 8.17 – 8.16 (m, 1H), 7.62 (td, J = 7.6, 1.7 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.36 – 7.29 (m, 2H), 7.21 – 7.18 (m, 1H), 6.91 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.90 (s, 3H).
246	1H NMR (400 MHz, DMSO-d6) d 12.07 – 11.65 (m, 1H), 8.27 (s, 1H), 8.01 (s, 1H), 7.70 – 7.67 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 8.3 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.59 – 3.51 (m, 2H), 3.44 – 3.40 (m, 1H), 2.48 – 2.44 (m, 2H).
247	1H NMR (400 MHz, DMSO-d6) delta 8.70 - 8.64 (m, 1H), 8.20 - 8.18 (m, 1H), 7.91 - 7.90 (m, 1H), 7.78 (d, J = 3.3 Hz, 1H), 7.67 (d, J = 3.2 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.75 (d, J = 5.8 Hz, 2H), 3.94 (s, 3H), 3.89 (s, 3H).
248	1H NMR (400 MHz, DMSO-d6) delta 8.34 - 8.32 (m, 1H), 8.25 - 8.21 (m, 2H), 8.06 - 8.04 (m, 1H), 7.51 - 7.47 (m, 2H), 7.35 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 2.83 (s, 4H).
250	1H NMR (500 MHz, DMSO-d6) delta 8.23 - 8.20 (m, 2H), 7.49 - 7.46 (m, 2H), 7.01 (d, J = 8.2 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 4.00 - 3.96 (m, 2H), 3.93 (s, 3H), 3.54 - 3.48 (m, 2H), 3.36 - 3.29 (m, 1H), 2.82 (s, 4H), 1.85 - 1.75 (m, 4H).
252	1H NMR (400 MHz, DMSO-d6) delta 11.04 - 10.82 (m, 1H), 9.32 - 9.20 (m, 2H), 8.18 - 8.14 (m, 2H), 7.59 - 7.55 (m, 2H), 7.16 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.5 Hz, 1H), 6.75 - 6.67 (m, 1H), 3.96 (s, 3H), 3.83 - 3.77 (m, 2H), 3.39 - 3.32 (m, 2H), 3.04 - 2.89 (m, 6H), 2.87 - 2.81 (m, 2H).
253	1H NMR (400 MHz, DMSO-d6) d 12.83 – 12.68 (m, 1H), 11.76 – 11.57 (m, 1H), 10.99 – 10.69 (m, 1H), 8.11 – 7.94 (m, 2H), 7.87 (s, 1H), 7.70 – 7.14 (m, 5H), 6.86 (d, J = 8.1 Hz, 1H), 3.97 (s, 3H).

254	1H NMR (400 MHz, DMSO-d6) d 12.07 – 11.85 (m, 1H), 11.73 – 11.42 (m, 1H), 8.14 – 7.94 (m, 2H), 7.91 (s, 1H), 7.73 – 7.13 (m, 5H), 6.88 (d, J = 8.3 Hz, 1H), 3.98 (s, 3H), 3.91 (s, 3H).
255	1H NMR (400 MHz, DMSO-d6) d 12.75 – 12.40 (m, 1H), 11.86 – 11.56 (m, 1H), 10.96 – 10.35 (m, 1H), 8.05 – 7.98 (m, 1H), 7.96 – 7.86 (m, 1H), 7.67 – 7.14 (m, 5H), 6.89 – 6.81 (m, 1H), 3.97 (s, 3H), 2.38 – 2.31 (m, 3H).
256	1H NMR (400 MHz, DMSO-d6) d 12.68 – 11.66 (m, 2H), 9.35 – 9.25 (m, 1H), 8.97 – 8.48 (m, 1H), 8.08 – 7.60 (m, 2H), 7.56 – 7.45 (m, 2H), 7.42 – 7.33 (m, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H).
257	1H NMR (500 MHz, DMSO-d6) d 12.47 – 11.62 (m, 2H), 8.72 – 8.28 (m, 1H), 8.07 – 7.59 (m, 2H), 7.56 – 7.43 (m, 2H), 7.41 – 7.24 (m, 2H), 6.92 (d, J = 8.4 Hz, 1H), 3.97 (s, 3H), 2.71 (s, 3H).
258	1H NMR (400 MHz, DMSO-d6) d 12.02 – 11.78 (m, 1H), 11.60 – 11.37 (m, 1H), 8.22 – 7.79 (m, 4H), 7.67 – 7.14 (m, 5H), 6.86 (d, J = 8.3 Hz, 1H), 3.97 (s, 3H).
259	1H NMR (400 MHz, DMSO-d6) delta 12.36 - 12.11 (m, 1H), 9.67 - 9.59 (m, 1H), 9.23 - 9.16 (m, 1H), 8.85 - 8.79 (m, 1H), 8.19 - 8.10 (m, 3H), 7.71 (d, J = 8.4 Hz, 1H), 7.60 - 7.55 (m, 2H), 7.02 (d, J = 8.5 Hz, 1H), 4.04 (s, 3H), 3.02 (s, 3H), 2.91 (s, 3H).
260	1H NMR (500 MHz, DMSO-d6) d 11.98 – 11.87 (m, 1H), 9.62 – 9.58 (m, 1H), 9.20 – 9.15 (m, 1H), 8.81 – 8.79 (m, 1H), 8.51 – 8.50 (m, 1H), 8.21 – 8.20 (m, 1H), 8.14 – 8.09 (m, 1H), 7.68 (d, J = 8.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 4.02 (s, 3H), 3.92 (s, 3H).
261	1H NMR (400 MHz, DMSO-d6) d 12.55 – 11.32 (m, 1H), 8.19 – 8.15 (m, 2H), 7.60 – 7.55 (m, 2H), 6.99 (d, J = 8.3 Hz, 1H), 6.93 – 6.84 (m, 1H), 6.80 (d, J = 8.4 Hz, 1H), 5.06 – 5.01 (m, 2H), 4.83 – 4.78 (m, 2H), 3.96 (s, 3H), 3.02 (s, 3H), 2.92 (s, 3H).
262	1H NMR (400 MHz, DMSO-d6) d 8.17 – 8.12 (m, 2H), 7.58 – 7.54 (m, 2H), 6.77 (d, J = 13.4 Hz, 1H), 6.07 – 6.04 (m, 1H), 4.26 (q, J = 2.6 Hz, 2H), 3.95 (s, 3H), 3.86 (t, J = 5.4 Hz, 2H), 3.04 – 2.98 (m, 3H), 2.94 – 2.88 (m, 3H), 2.52 – 2.47 (m, 2H).

263	1H NMR (400 MHz, DMSO-d6) d 7.63 – 7.60 (m, 2H), 7.40 (t, J = 8.1 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.14 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.00 – 3.95 (m, 2H), 3.94 (s, 3H), 3.55 – 3.32 (m, 3H), 3.27 (s, 6H), 1.83 – 1.73 (m, 4H).
264	1H NMR (400 MHz, DMSO-d6) d 11.97 – 11.71 (m, 1H), 8.47 (s, 1H), 8.17 – 8.16 (m, 1H), 6.71 (d, J = 13.3 Hz, 1H), 6.07 – 6.04 (m, 1H), 4.25 (q, J = 2.8 Hz, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 3.85 (t, J = 5.4 Hz, 2H), 2.54 – 2.48 (m, 2H).
265	1H NMR (400 MHz, DMSO-d6) d 13.10 – 12.37 (m, 1H), 11.96 – 11.53 (m, 1H), 11.26 – 10.59 (m, 1H), 8.07 (s, 1H), 8.06 – 7.95 (m, 1H), 7.91 – 7.82 (m, 2H), 7.57 – 7.36 (m, 2H), 7.28 – 7.07 (m, 1H), 6.87 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H).
266	1H NMR (500 MHz, DMSO-d6) d 11.53 – 11.19 (m, 1H), 8.91 – 8.85 (m, 2H), 8.86 – 8.83 (m, 2H), 8.21 (s, 1H), 8.18 – 8.17 (m, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.05 (d, J = 8.7 Hz, 1H), 4.06 (s, 3H).
267	1H NMR (400 MHz, DMSO-d6) d 13.30 – 12.36 (m, 1H), 11.81 – 11.52 (m, 1H), 8.10 – 8.00 (m, 1H), 7.88 (s, 1H), 7.69 – 7.51 (m, 1H), 7.48 – 7.29 (m, 2H), 7.26 – 7.12 (m, 1H), 7.01 – 6.80 (m, 2H), 4.21 – 4.14 (m, 2H), 3.97 (s, 3H), 3.73 – 3.68 (m, 2H), 3.36 – 3.30 (m, 3H).
268	1H NMR (500 MHz, DMSO-d6) d 9.42 (s, 1H), 8.85 – 8.81 (m, 1H), 8.71 (dd, J = 5.3, 1.5 Hz, 1H), 8.37 (s, 1H), 8.21 – 8.18 (m, 1H), 7.87 (dd, J = 8.1, 5.2 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 4.02 (s, 3H).
269	1H NMR (700 MHz, DMSO-d6) delta 11.76 - 11.46 (m, 2H), 8.58 - 8.49 (m, 1H), 8.02 - 7.97 (m, 1H), 7.69 - 7.12 (m, 5H), 6.86 (d, J = 8.3 Hz, 1H), 3.97 (s, 3H), 3.82 (s, 3H), 2.43 - 2.37 (m, 3H).
270	1H NMR (700 MHz, DMSO-d6) delta 11.89 - 11.76 (m, 1H), 11.67 - 11.38 (m, 1H), 10.61 - 10.31 (m, 1H), 8.35 - 8.20 (m, 1H), 7.67 - 7.37 (m, 2H), 7.34 - 7.12 (m, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.58 - 6.34 (m, 1H), 4.34 (s, 1H), 3.98 (s, 3H), 3.89 - 3.74 (m, 2H), 3.30 - 3.17 (m, 2H), 1.51 - 1.34 (m, 4H), 1.13 (s, 3H).

271	1H NMR (700 MHz, DMSO-d6) d 13.36 – 13.11 (m, 1H), 12.52 – 9.90 (m, 1H), 7.99 (s, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.34 – 7.30 (m, 1H), 6.98 (d, J = 8.3 Hz, 1H), 4.00 (s, 3H), 3.82 – 3.75 (m, 2H), 3.30 – 3.22 (m, 2H), 1.50 – 1.39 (m, 4H), 1.13 (s, 3H).
272	
273	1H NMR (700 MHz, DMSO-d6) delta 13.53 - 9.83 (m, 2H), 8.16 - 8.08 (m, 1H), 8.09 (s, 1H), 7.80 - 7.72 (m, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 4.09 (s, 3H), 3.97 (s, 3H), 3.84 - 3.79 (m, 2H), 3.31 - 3.24 (m, 2H), 1.51 - 1.41 (m, 4H), 1.15 (s, 3H).
274	1H NMR (700 MHz, DMSO-d6) d 12.90 – 12.52 (m, 1H), 11.27 – 10.02 (m, 1H), 7.98 – 7.93 (m, 1H), 7.73 – 7.62 (m, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 3.97 (s, 3H), 3.84 – 3.78 (m, 2H), 3.33 – 3.24 (m, 2H), 2.53 (s, 3H), 1.52 – 1.41 (m, 4H), 1.15 (s, 3H).
275	1H NMR (700 MHz, DMSO-d6) d 14.34 – 13.99 (m, 1H), 12.14 – 11.43 (m, 1H), 10.54 – 10.33 (m, 1H), 8.91 – 8.89 (m, 1H), 8.84 – 8.68 (m, 1H), 8.30 – 8.28 (m, 1H), 8.32 – 8.23 (m, 1H), 8.15 (d, J = 2.1 Hz, 1H), 7.69 – 7.64 (m, 1H), 6.94 (d, J = 8.5 Hz, 1H), 4.00 (s, 3H), 3.87 – 3.82 (m, 2H), 3.32 – 3.26 (m, 2H), 1.53 – 1.43 (m, 4H), 1.16 (s, 3H).
277	1H NMR (500 MHz, DMSO-d6) d 12.54 – 11.55 (m, 1H), 8.18 – 8.13 (m, 2H), 7.59 – 7.54 (m, 2H), 6.69 (d, J = 13.6 Hz, 1H), 3.99 – 3.95 (m, 2H), 3.92 (s, 3H), 3.50 – 3.40 (m, 3H), 3.04 – 2.89 (m, 6H), 2.32 – 2.22 (m, 2H), 1.62 – 1.55 (m, 2H).
278	1H NMR (500 MHz, DMSO-d6) d 12.11 – 12.06 (m, 1H), 12.04 – 11.82 (m, 1H), 8.51 (s, 1H), 8.38 (d, J = 5.3 Hz, 1H), 8.20 – 8.18 (m, 1H), 7.70 – 7.60 (m, 1H), 7.63 – 7.61 (m, 1H), 7.52 (d, J = 8.3 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.65 – 6.60 (m, 1H), 4.33 (t, J = 5.2 Hz, 2H), 4.03 (s, 3H), 3.73 – 3.69 (m, 2H), 3.25 (s, 3H).

279	1H NMR (500 MHz, DMSO-d6) d 13.32 – 13.01 (m, 1H), 12.00 – 11.78 (m, 1H), 8.49 (s, 1H), 8.17 (s, 1H), 8.01 (d, J = 1.0 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.48 – 7.44 (m, 1H), 7.46 – 7.40 (m, 1H), 7.38 (d, J = 8.2 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.32 (t, J = 5.2 Hz, 2H), 4.02 (s, 3H), 3.72 – 3.68 (m, 2H), 3.24 (s, 3H).
280	1H NMR (500 MHz, DMSO-d6) d 12.05 – 11.75 (m, 1H), 11.17 – 11.09 (m, 1H), 8.51 (s, 1H), 8.19 (s, 1H), 7.84 – 7.74 (m, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.47 – 7.38 (m, 1H), 7.38 (t, J = 2.7 Hz, 1H), 7.26 (d, J = 8.3 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 6.48 – 6.45 (m, 1H), 4.34 (t, J = 5.2 Hz, 2H), 3.99 (s, 3H), 3.73 – 3.70 (m, 2H), 3.25 (s, 3H).
281	1H NMR (500 MHz, DMSO-d6) d 12.01 – 11.76 (m, 1H), 8.52 (s, 1H), 8.28 – 8.23 (m, 1H), 8.21 – 8.20 (m, 1H), 8.10 – 8.09 (m, 1H), 7.93 – 7.87 (m, 1H), 7.72 (d, J = 8.7 Hz, 1H), 7.32 (d, J = 8.3 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 4.34 (t, J = 5.2 Hz, 2H), 4.09 (s, 3H), 3.99 (s, 3H), 3.73 – 3.70 (m, 2H), 3.25 (s, 3H).
282	1H NMR (500 MHz, DMSO-d6) d 12.88 – 12.40 (m, 1H), 12.11 – 11.66 (m, 1H), 8.51 (s, 1H), 8.21 – 8.18 (m, 1H), 8.07 – 8.03 (m, 1H), 7.87 – 7.79 (m, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 4.33 (t, J = 5.2 Hz, 2H), 3.99 (s, 3H), 3.73 – 3.69 (m, 2H), 3.25 (s, 3H), 2.54 (s, 3H).
283	1H NMR (500 MHz, DMSO-d6) d 12.10 – 11.52 (m, 1H), 8.49 – 8.48 (m, 1H), 8.18 – 8.16 (m, 1H), 7.40 – 7.33 (m, 2H), 7.24 – 7.18 (m, 1H), 7.13 (d, J = 8.2 Hz, 1H), 6.87 (d, J = 8.3 Hz, 1H), 4.33 (t, J = 5.2 Hz, 2H), 3.99 (s, 3H), 3.72 – 3.69 (m, 2H), 3.64 (t, J = 7.9 Hz, 2H), 3.24 (s, 3H), 3.13 (t, J = 7.9 Hz, 2H).
284	1H NMR (500 MHz, DMSO-d6) d 11.89 – 11.21 (m, 1H), 8.81 (dd, J = 2.1, 0.8 Hz, 1H), 8.25 (dd, J = 8.0, 0.8 Hz, 1H), 8.15 (dd, J = 8.0, 2.1 Hz, 1H), 7.89 – 7.85 (m, 2H), 7.52 – 7.48 (m, 2H), 7.38 – 7.34 (m, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.00 (s, 3H), 3.05 (s, 3H), 2.95 (s, 3H).

285	1H NMR (500 MHz, DMSO-d6) d 12.30 – 11.76 (m, 2H), 8.23 – 8.19 (m, 2H), 8.11 – 7.60 (m, 2H), 7.57 – 7.42 (m, 4H), 7.40 – 7.24 (m, 2H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 2.82 (s, 4H).
286	1H NMR (500 MHz, DMSO-d6) d 12.41 – 11.59 (m, 2H), 9.66 – 9.48 (m, 1H), 8.90 – 8.55 (m, 1H), 8.08 – 7.90 (m, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.74 – 7.16 (m, 7H), 6.90 (d, J = 8.3 Hz, 1H), 4.00 (s, 3H).
287	1H NMR (500 MHz, DMSO-d6) d 11.83 – 10.34 (m, 2H), 7.95 – 7.57 (m, 2H), 7.51 – 7.44 (m, 2H), 7.37 – 7.31 (m, 1H), 7.23 – 7.17 (m, 1H), 6.84 (d, J = 8.3 Hz, 1H), 3.94 (s, 3H), 3.70 – 3.63 (m, 4H), 2.04 – 1.93 (m, 4H).
288	1H NMR (500 MHz, DMSO-d6) d 11.95 – 11.63 (m, 1H), 11.63 – 11.48 (m, 1H), 8.95 – 8.91 (m, 1H), 8.63 (s, 1H), 8.44 – 8.41 (m, 1H), 8.06 – 7.62 (m, 2H), 7.58 (dd, J = 9.2, 4.5 Hz, 1H), 7.55 – 7.44 (m, 2H), 7.41 – 7.26 (m, 2H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H).
289	1H NMR (500 MHz, DMSO-d6/TFA) d 10.35 (dd, J = 6.9, 1.9 Hz, 1H), 9.07 (dd, J = 4.4, 1.9 Hz, 1H), 8.91 (s, 1H), 7.75 (dd, J = 6.9, 4.4 Hz, 1H), 7.66 – 7.63 (m, 2H), 7.56 – 7.51 (m, 2H), 7.44 – 7.39 (m, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.5 Hz, 1H), 4.01 (s, 3H).
290	1H NMR (500 MHz, DMSO-d6/TFA) d 9.09 – 9.05 (m, 2H), 8.62 (s, 1H), 8.61 – 8.58 (m, 2H), 7.67 – 7.63 (m, 2H), 7.59 – 7.54 (m, 2H), 7.49 (d, J = 8.4 Hz, 1H), 7.48 – 7.44 (m, 1H), 7.18 (d, J = 8.5 Hz, 1H), 4.04 (s, 3H).
291	1H NMR (500 MHz, DMSO-d6) d 12.15 – 11.48 (m, 2H), 8.08 (s, 1H), 8.01 – 7.58 (m, 2H), 7.53 – 7.43 (m, 2H), 7.38 – 7.25 (m, 2H), 6.89 (d, J = 8.3 Hz, 1H), 4.38 – 4.30 (m, 2H), 4.00 – 3.94 (m, 3H), 2.89 – 2.84 (m, 2H), 1.99 – 1.92 (m, 2H), 1.88 – 1.82 (m, 2H).
292	1H NMR (400 MHz, DMSO-d6) d 7.50 – 7.38 (m, 3H), 7.25 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 4.00 (s, 3H), 3.87 – 3.79 (m, 2H), 3.71 (t, J = 7.8 Hz, 2H), 3.37 – 3.26 (m, 2H), 3.13 (t, J = 7.8 Hz, 2H), 1.55 – 1.41 (m, 4H), 1.15 (s, 3H).

293	1H NMR (500 MHz, DMSO-d6) d 12.28 – 12.04 (m, 1H), 11.98 – 11.76 (m, 1H), 8.64 – 8.57 (m, 1H), 8.20 – 8.16 (m, 2H), 8.06 – 7.93 (m, 3H), 7.79 – 7.18 (m, 5H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.27 – 3.22 (m, 2H), 1.60 – 1.52 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).
294	1H NMR (500 MHz, DMSO-d6) d 12.17 – 11.97 (m, 2H), 8.19 – 8.15 (m, 2H), 7.97 – 7.77 (m, 2H), 7.56 – 7.52 (m, 2H), 7.52 – 7.45 (m, 2H), 7.37 – 7.28 (m, 2H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.70 – 3.58 (m, 2H), 3.36 – 3.27 (m, 2H), 2.43 – 2.24 (m, 4H), 2.20 (s, 3H).
295	1H NMR (500 MHz, DMSO-d6) d 12.26 – 12.04 (m, 1H), 12.02 – 11.76 (m, 1H), 8.20 – 8.11 (m, 2H), 8.11 – 7.56 (m, 2H), 7.54 – 7.50 (m, 2H), 7.57 – 7.22 (m, 4H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.68 – 3.54 (m, 2H), 3.45 – 3.34 (m, 2H), 3.34 – 3.16 (m, 3H), 3.04 – 2.90 (m, 3H).
296	1H NMR (500 MHz, DMSO-d6) d 12.14 – 11.97 (m, 2H), 8.15 (d, J = 7.8 Hz, 2H), 7.93 – 7.81 (m, 2H), 7.54 – 7.51 (m, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.61 – 3.52 (m, 1H), 3.32 – 3.22 (m, 1H), 3.03 – 2.87 (m, 3H), 2.55 – 2.32 (m, 2H), 2.24 (s, 3H), 1.98 (s, 3H).
297	1H NMR (500 MHz, DMSO-d6) d 12.25 – 12.04 (m, 1H), 12.03 – 11.75 (m, 1H), 8.19 – 8.13 (m, 2H), 8.09 – 7.58 (m, 2H), 7.57 – 7.20 (m, 6H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.46 – 3.40 (m, 1H), 3.17 – 3.10 (m, 1H), 3.00 – 2.85 (m, 3H), 1.67 – 1.47 (m, 2H), 0.96 – 0.66 (m, 3H).
298	1H NMR (500 MHz, DMSO-d6) d 12.26 – 12.05 (m, 1H), 12.00 – 11.78 (m, 1H), 8.20 – 8.16 (m, 2H), 8.09 – 7.60 (m, 2H), 7.60 – 7.54 (m, 2H), 7.55 – 7.24 (m, 4H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.72 – 3.27 (m, 8H).
299	1H NMR (500 MHz, DMSO-d6) d 13.03 – 12.47 (m, 1H), 12.01 – 11.64 (m, 1H), 11.18 – 10.68 (m, 1H), 8.51 – 8.42 (m, 1H), 8.10 – 8.05 (m, 1H), 7.90 – 7.87 (m, 1H), 8.02 – 7.27 (m, 3H), 6.90 (d, J = 8.4 Hz, 1H), 3.99 (s, 3H), 2.54 (s, 3H).
300	

301	1H NMR (700 MHz, DMSO-d6) d 14.56 – 14.02 (m, 1H), 12.33 – 11.85 (m, 1H), 11.85 – 11.82 (m, 1H), 8.94 – 8.92 (m, 1H), 8.79 – 8.73 (m, 1H), 8.54 (s, 1H), 8.31 – 8.30 (m, 1H), 8.32 – 8.27 (m, 1H), 8.23 (s, 1H), 8.17 (d, J = 2.1 Hz, 1H), 7.73 (d, J = 8.3 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 4.35 (t, J = 5.2 Hz, 2H), 4.04 (s, 3H), 3.73 (t, J = 5.2 Hz, 2H), 3.26 (s, 3H).
302	1H NMR (700 MHz, DMSO-d6) d 12.53 – 11.05 (m, 2H), 11.16 – 11.13 (m, 1H), 8.51 (s, 1H), 8.19 (s, 1H), 8.01 – 7.91 (m, 1H), 7.52 – 7.46 (m, 2H), 7.40 – 7.38 (m, 1H), 7.26 (d, J = 8.2 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.50 – 6.48 (m, 1H), 4.34 (t, J = 5.2 Hz, 2H), 3.98 (s, 3H), 3.71 (t, J = 5.2 Hz, 2H), 3.25 (s, 3H).
303	1H NMR (700 MHz, DMSO-d6) d 11.86 – 11.14 (m, 1H), 11.19 – 11.05 (m, 1H), 10.74 – 10.10 (m, 1H), 8.20 – 7.23 (m, 2H), 7.53 – 7.45 (m, 1H), 7.38 (s, 1H), 7.19 – 7.07 (m, 1H), 6.80 (d, J = 8.3 Hz, 1H), 6.47 (s, 1H), 4.39 – 4.36 (m, 1H), 3.93 (s, 3H), 3.87 – 3.80 (m, 2H), 3.29 – 3.23 (m, 2H), 1.48 – 1.38 (m, 4H), 1.13 (s, 3H).
304	1H NMR (700 MHz, DMSO-d6) d 12.01 – 11.81 (m, 1H), 12.08 – 10.92 (m, 1H), 10.80 – 10.69 (m, 1H), 8.48 (s, 1H), 8.17 (s, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 7.14 – 7.10 (m, 1H), 6.94 (d, J = 8.1 Hz, 1H), 6.52 (s, 1H), 4.32 (t, J = 5.2 Hz, 2H), 4.02 (s, 3H), 3.69 (t, J = 5.2 Hz, 2H), 3.23 (s, 3H).
305	1H NMR (700 MHz, DMSO-d6) d 12.25 – 11.21 (m, 1H), 10.80 (s, 1H), 10.93 – 10.19 (m, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.30 (t, J = 2.8 Hz, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.18 (d, J = 7.1 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.00 – 6.96 (m, 1H), 6.54 – 6.52 (m, 1H), 4.00 (s, 3H), 3.80 – 3.75 (m, 2H), 3.28 – 3.22 (m, 2H), 1.49 – 1.38 (m, 4H), 1.13 (s, 3H).
306	1H NMR (700 MHz, DMSO-d6) d 11.99 – 11.80 (m, 1H), 11.66 – 11.55 (m, 1H), 8.52 – 8.46 (m, 1H), 8.21 – 8.16 (m, 1H), 8.02 – 7.98 (m, 1H), 7.65 – 7.17 (m, 5H), 6.88 – 6.84 (m, 1H), 3.97 (s, 3H), 3.91 (s, 3H).

307	1H NMR (700 MHz, DMSO-d6) d 11.99 – 11.81 (m, 1H), 11.65 – 11.56 (m, 1H), 8.55 – 8.49 (m, 1H), 8.24 – 8.18 (m, 1H), 8.01 – 7.99 (m, 1H), 7.66 – 7.17 (m, 5H), 6.88 – 6.84 (m, 1H), 4.33 (t, J = 5.2 Hz, 2H), 3.97 (s, 3H), 3.72 – 3.70 (m, 2H), 3.26 – 3.24 (m, 3H).
308	1H NMR (700 MHz, DMSO-d6) delta 12.46 - 11.63 (m, 2H), 8.16 - 7.23 (m, 7H), 6.95 - 6.89 (m, 1H), 3.98 (s, 3H), 2.52 (s, 3H).
309	1H NMR (700 MHz, DMSO-d6) delta 12.25 - 12.04 (m, 1H), 12.03 - 11.74 (m, 1H), 8.17 - 8.14 (m, 2H), 8.04 - 7.95 (m, 1H), 7.56 - 7.54 (m, 2H), 7.77 - 7.21 (m, 5H), 6.90 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.02 - 2.90 (m, 6H).
310	1H NMR (700 MHz, DMSO-d6) delta 11.63 - 11.30 (m, 1H), 10.39 - 10.10 (m, 1H), 8.02 - 7.92 (m, 1H), 7.69 - 7.07 (m, 5H), 6.80 (d, J = 8.3 Hz, 1H), 3.94 (s, 3H), 3.66 - 3.37 (m, 8H), 1.88 - 1.71 (m, 2H), 1.52 - 1.47 (m, 4H).
311	1H NMR (700 MHz, DMSO-d6) delta 12.25 - 11.94 (m, 1H), 11.94 - 11.63 (m, 1H), 8.11 - 8.08 (m, 2H), 8.03 - 7.96 (m, 1H), 7.68 - 7.19 (m, 5H), 7.38 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.3 Hz, 1H), 4.46 (s, 2H), 3.98 (s, 3H), 3.27 (t, J = 7.0 Hz, 2H), 2.32 (t, J = 8.1 Hz, 2H), 1.98 - 1.93 (m, 2H).
314	1H NMR (400 MHz, DMSO-d6) d 12.33 – 11.98 (m, 1H), 7.10 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 6.64 – 6.58 (m, 1H), 4.27 (q, J = 2.4 Hz, 2H), 3.93 (s, 3H), 3.86 (t, J = 5.4 Hz, 2H), 2.58 – 2.52 (m, 2H), 2.03 – 1.96 (m, 1H), 0.98 – 0.92 (m, 4H).
315	1H NMR (400 MHz, DMSO-d6) d 12.14 (s, 1H), 9.60 – 9.58 (m, 1H), 9.18 – 9.13 (m, 1H), 8.82 – 8.79 (m, 1H), 8.11 (dd, J = 8.3, 5.6 Hz, 1H), 7.68 (d, J = 8.5 Hz, 1H), 6.97 (d, J = 8.5 Hz, 1H), 4.00 (s, 3H), 2.04 – 1.97 (m, 1H), 0.98 – 0.92 (m, 4H).
316	1H NMR (700 MHz, DMSO-d6) delta 12.62 - 11.53 (m, 1H), 8.16 - 8.14 (m, 2H), 7.96 - 7.91 (m, 2H), 7.57 - 7.55 (m, 2H), 7.33 - 7.29 (m, 3H), 6.92 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 3.03 - 2.90 (m, 6H).

317	1H NMR (700 MHz, DMSO-d6) delta 12.34 - 12.04 (m, 1H), 8.22 - 8.19 (m, 2H), 7.98 - 7.91 (m, 2H), 7.48 - 7.46 (m, 2H), 7.33 - 7.29 (m, 3H), 6.91 (d, J = 8.3 Hz, 1H), 3.99 (s, 3H), 2.82 (s, 4H).
318	1H NMR (500 MHz, DMSO-d6) delta 12.10 - 11.65 (m, 1H), 8.50 - 8.48 (m, 1H), 8.19 - 8.18 (m, 1H), 7.96 - 7.90 (m, 2H), 7.32 - 7.27 (m, 3H), 6.89 (d, J = 8.3 Hz, 1H), 3.98 (s, 3H), 3.91 (s, 3H).
319	1H NMR (500 MHz, DMSO-d6) d 12.37 – 12.03 (m, 1H), 11.92 – 11.38 (m, 1H), 8.17 – 8.13 (m, 2H), 7.80 – 7.73 (m, 1H), 7.55 – 7.51 (m, 2H), 7.16 – 7.08 (m, 1H), 6.89 – 6.83 (m, 1H), 6.56 – 6.50 (m, 1H), 3.97 (s, 3H), 4.02 – 3.92 (m, 6H), 3.04 – 2.88 (m, 6H).
320	1H NMR (500 MHz, DMSO-d6) d 12.04 – 11.90 (m, 1H), 11.29 – 11.07 (m, 1H), 7.97 – 7.69 (m, 1H), 7.24 – 7.00 (m, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.55 – 6.43 (m, 1H), 3.97 – 3.84 (m, 9H), 1.99 – 1.90 (m, 1H), 0.94 – 0.89 (m, 4H).
321	1H NMR (400 MHz, DMSO-d6, 90°C) d 9.29 – 9.26 (m, 1H), 8.63 (dd, J = 5.1, 1.5 Hz, 1H), 8.63 – 8.58 (m, 1H), 8.01 (s, 1H), 7.74 – 7.69 (m, 1H), 7.48 (d, J = 8.2 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 4.04 (s, 3H), 2.54 (s, 3H).
322	1H NMR (500 MHz, DMSO-d6) d 8.07 – 8.04 (m, 1H), 6.98 (d, J = 8.3 Hz, 1H), 6.88 – 6.83 (m, 1H), 6.79 (d, J = 8.4 Hz, 1H), 5.03 – 5.00 (m, 2H), 4.81 – 4.77 (m, 2H), 3.95 (s, 3H), 2.54 (s, 3H).
323	1H NMR (400 MHz, DMSO-d6, 90°C) d 7.95 (s, 1H), 7.91 – 7.84 (m, 2H), 7.30 – 7.23 (m, 3H), 7.75 – 6.19 (m, 2H), 6.91 (d, J = 8.4 Hz, 1H), 4.04 – 3.99 (m, 3H), 2.52 (s, 3H).

324	1H NMR (400 MHz, DMSO-d6) d 8.20 – 8.14 (m, 2H), 7.61 – 7.56 (m, 2H), 7.15 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.67 – 6.56 (m, 1H), 4.31 – 4.26 (m, 2H), 3.96 (s, 3H), 3.88 (t, J = 5.4 Hz, 2H), 3.04 – 2.89 (m, 6H), 2.60 – 2.54 (m, 2H).
325	1H NMR (400 MHz, DMSO-d6) d 12.18 – 11.88 (m, 1H), 8.52 (s, 1H), 8.21 (s, 1H), 7.15 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 6.63 – 6.54 (m, 1H), 4.28 (q, J = 2.7 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.87 (t, J = 5.4 Hz, 2H), 2.58 – 2.53 (m, 2H).
329	1H NMR (700 MHz, DMSO-d6) d 12.06 – 11.36 (m, 1H), 10.63 – 10.34 (m, 1H), 8.02 – 7.93 (m, 1H), 7.65 – 7.07 (m, 5H), 6.84 – 6.79 (m, 1H), 3.94 (s, 3H), 3.75 (t, J = 7.1 Hz, 2H), 3.64 – 3.57 (m, 2H), 3.49 – 3.42 (m, 4H), 1.74 (t, J = 7.1 Hz, 2H), 1.54 – 1.46 (m, 4H).

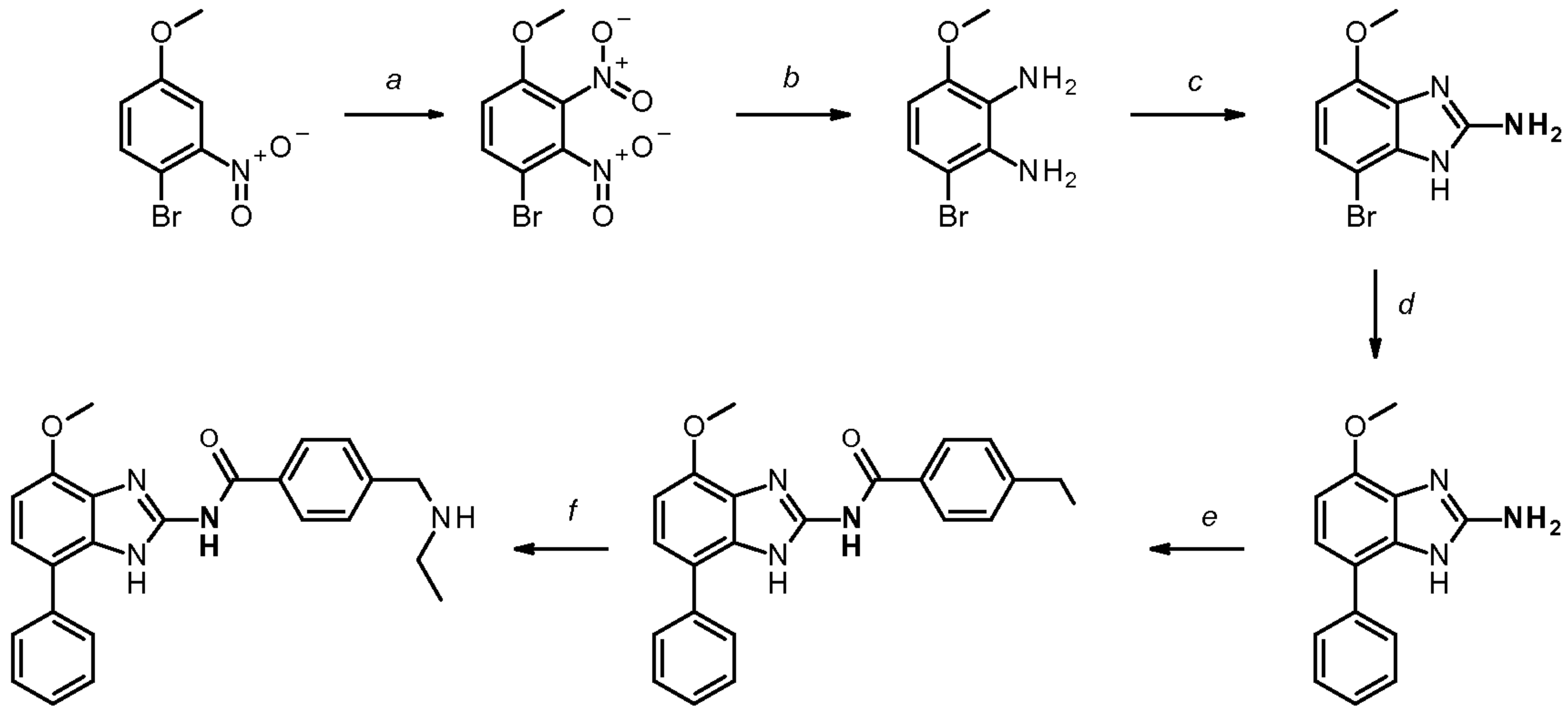
Example 2: Preparation of the compounds of the present invention and analytical methods

All solvents used were commercially available and were used without further purification. Reactions were typically run using anhydrous solvents under an inert atmosphere of nitrogen. Flash column chromatography was generally carried out using Silica gel 60 (0.035-0.070 mm particle size).

All NMR experiments were recorded either on Bruker Mercury Plus 400 NMR Spectrometer equipped with a Bruker 400 BBFO probe at 400 MHz for proton NMR or on Bruker Mercury Plus 300 NMR Spectrometer equipped with a Bruker 300 BBFO probe at 300 MHz for proton NMR. All deuterated solvents contained typically 0.03% to 0.05% v/v tetramethylsilane, which was used as the reference signal (set at ppm = 0.00 for both 1H and 13C).

LC-MS analyses were performed on an Agilent Technologies LC-MS 1200 series consisting of a LCMS 6110 Quadrupole MS detector. The column used and the conditions are described in the HPLC methods. The column temperature was at 40°C with the flow rate stated. The Diode Array detector was scanned from 200-400 nm. The mass spectrometer was equipped with an electro spray ion source (ES) operated in a positive or negative mode. The mass spectrometer was scanned between m/z 90-900 with a scan time of 0.6 s.

1. 4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide, **11**



General procedure for nitration of the aromatic ring

a. 1-Bromo-4-methoxy-2,3-dinitro-benzene

4-Bromo-3-nitroanisole, 97% (10.0 g, 43.1 mmol) was nitrated by dropwise addition of 10 ml of a mixture of nitric acid, fuming 100% (40 ml) and sulfuric acid, 95-98% (6 ml). The mixture was stirred for 1 h at RT. The reaction mixture was poured onto ice water and extracted three times with ethyl acetate. The combined organic layers are washed with water and brine, dried over Na_2SO_4, filtered and concentrated to dryness. The crude material was purified by flash chromatography (ethyl acetate/cyclohexane) to yield in 5.30 g (44%) of the title compound as a yellow solid. HPLC/MS (purity) 100%. Rt 2.65 min (method A). [M+H]+ 276.8, 278.9.

General procedure to reduce the nitro group

b. 3-Bromo-6-methoxy-benzene-1,2-diamine

Into a 250-ml round-bottom flask was placed sponge-Nickel-catalyst, THF wet (2.00 g), THF (60 ml) and 1-bromo-4-methoxy-2,3-dinitro-benzene (5.30 g, 19.1 mmol). The mixture was stirred for 6 h at RT under a hydrogen atmosphere. The solids were filtered off and discarded. The filtrate was evaporated to dryness to yield in 3.90 g (94%) of 3-bromo-6-methoxy-benzene-1,2-diamine as a yellow solid, which was used without further purification. HPLC/MS (purity) 100%. Rt 1.42 min (method A). [M+H]+ 217.0, 218.9.

General procedure to form the benzimidazole ring

c. 4-Bromo-7-methoxy-1H-benzoimidazol-2-ylamine

To 3-bromo-6-methoxy-benzene-1,2-diamine (3.90 g, 18.0 mmol), dissolved in methanol (50 ml) and water (25 ml), was added cyanogen bromide (2.86 g, 27.0 mmol) at RT and the resulting mixture was stirred at RT for 20 h. The reaction mixture was evaporated to remove the methanol. Under cooling the aqueous solution basified with ammonia. The precipitate was filtered off and crystallized from dichloromethane to yield in 3.90 g (89%) of the title compound as a yellow solid. HPLC/MS (purity) 99%. Rt 1.72 min (method A). [M+H]+ 242.0, 243.9.

General procedure for Suzuki reactions:

d. 7-Methoxy-4-phenyl-1H-benzoimidazol-2-ylamine

Into pressure tank reactor purged and maintained with an inert atmosphere of argon was placed 4-bromo-7-methoxy-1H-benzoimidazol-2-ylamine, 99% (1.68 g, 7.02 mmol), benzeneboronic acid, 98% (1.05 g, 8.43 mmol), potassium carbonate, 2 M (5 ml, 49,1 mmol), Pd(dppf)Cl_2 dichloromethane complex, 95% (449 mg, 0.562 mmol), ethanol (2.5 ml) and toluene (25 ml) The mixture was stirred for 20 h at 90°C, cooled to room temperature and concentrated to dryness under vacuum. The residue was purified by column chromatography (dichloromethane/ethanol, gradient) to yield in 1.22 g (70%) of the title compound as a yellow solid. HPLC/MS (purity) 97%. Rt 2.09 min (method A). [M+H]+ 240.1.

General procedure to form the amide bond formation

e. 4-Chloromethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide

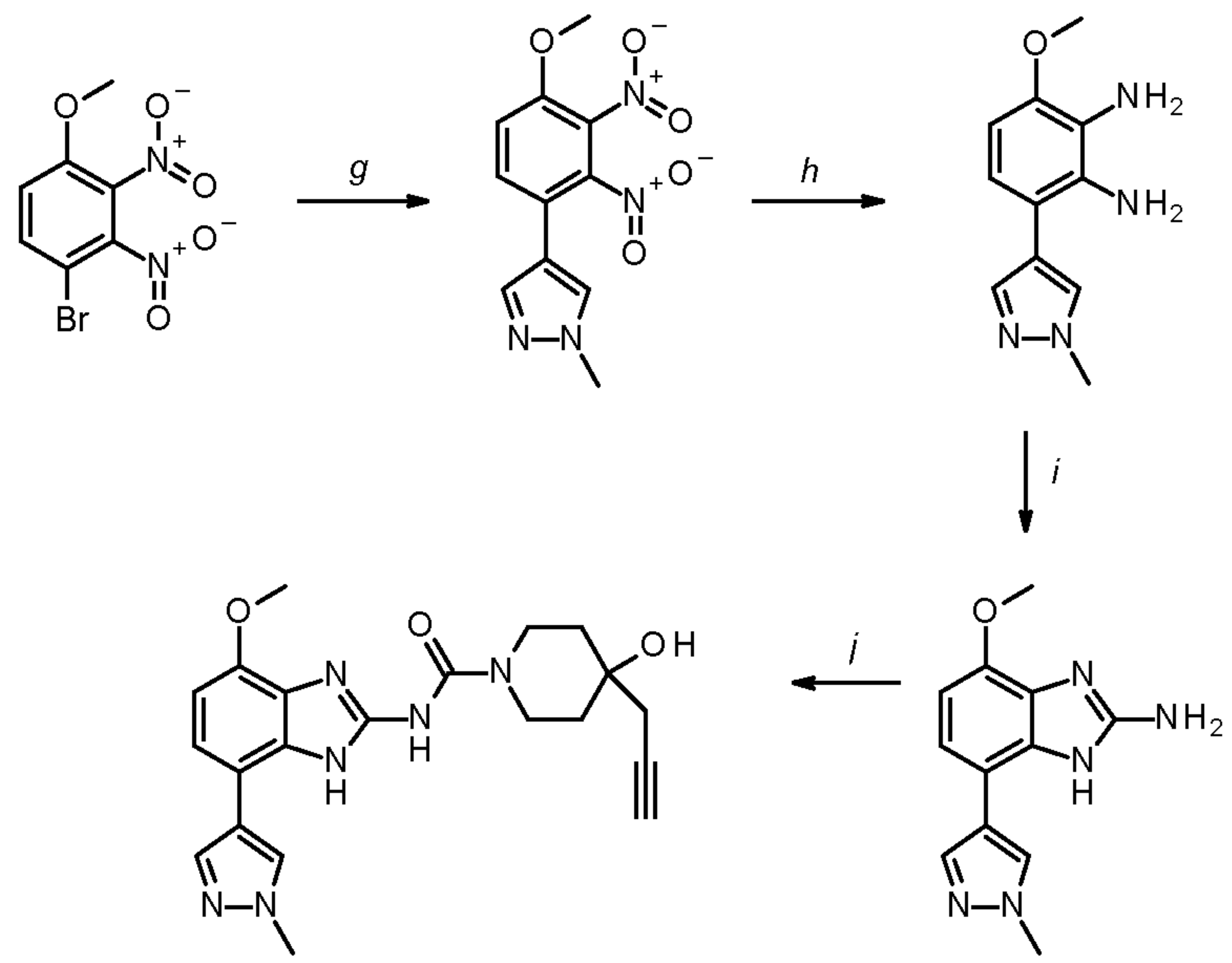
To a stirred solution of 7-methoxy-4-phenyl-1H-benzoimidazol-2-ylamine (300 mg, 1.22 mmol) and N-ethyldiisopropylamin (1.24 ml, 7.30 mmol) in tetrahydrofuran (6 mL) at RT was added dropwise a solution of 4-(chloromethyl)benzoyl chloride, 97% (276 mg, 1.46 mmol) in dichloromethane (3 ml) and stirred for 60 h at RT. The residue was purified by column chromatography (ethyl acetate/cyclohexane, gradient). Three drops of 1 N HCl solution were added to the dissolved pure fraction and evaporated to dryness to yield in 50.0 mg (10%) of the HCl salt of the title compound as a colorless solid. 1H NMR (500 MHz, DMSO-d6) ppm = 12.82 - 11.31

(m, 1H), 8.14 - 8.11 (m, 2H), 7.87 - 7.82 (m, 2H), 7.64 - 7.60 (m, 2H), 7.52 - 7.47 (m, 2H), 7.38 - 7.34 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 4.86 (s, 2H), 4.00 (s, 3H). HPLC/MS (purity) 100%. Rt 2.92 min (method A). [M+H]+ 392.0.

f. 4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide

To a stirred solution of 4-chloromethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide, hydrochloride (44.0 mg, 0.103 mmol) in tetrahydrofuran (2 ml), ethylamine, 2 M in THF (1 ml) was added and stirred for 20 h at RT and then for additional 20 h at 50°C. The mixture was evaporated to dryness and the residue was purified by preparative HPLC (acetonitrile/water, gradient). Five drops of 1 N HCl solution were added to the dissolved pure fraction and evaporated to dryness to yield in 10.0 mg (21%) of the dihydrochloride salt of the title compound as a colorless solid. 1H NMR (400 MHz, DMSO-d6) ppm = 8.91 - 8.82 (m, 2H), 8.16 - 8.12 (m, 2H), 7.86 - 7.81 (m, 2H), 7.66 - 7.62 (m, 2H), 7.51 - 7.45 (m, 2H), 7.37 - 7.32 (m, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.24 - 4.19 (m, 2H), 3.97 (s, 3H), 3.06 - 2.96 (m, 2H), 1.22 (t, J = 7.3 Hz, 3H). HPLC/MS (purity) 100%. Rt 2.42 min (method A). [M+H]+ 401.1.

2. 4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide



g. 4-(4-Methoxy-2,3-dinitro-phenyl)-1-methyl-1H-pyrazole

Into pressure tank reactor purged and maintained with an inert atmosphere of argon was placed 1-bromo-4-methoxy-2,3-dinitro-benzene, 88% (4.00 g, 12.7 mmol), 1-methyl-1H-pyrazol-4-boronic acid, pinacol ester (3.17 g, 15.2 mmol), potassium carbonate, 2 M (16 ml, 157 mmol), Pd(dppf)Cl_2 dichloromethane complex, (1.01 g, 1.27 mmol), ethanol (8 ml) and toluene (80 ml) The mixture was stirred for 2 h at 90°C, cooled to room temperature and concentrated to dryness under vacuum. The residue was purified by column chromatography (ethyl acetate/cyclohexane, gradient) to yield in 2.70 g (76%) of the title compound as a yellow solid. HPLC/MS (purity) 100%. Rt 2.38 min (method A). [M+H]+ 279.0.

h. 3-Methoxy-6-(1-methyl-1H-pyrazol-4-yl)-benzene-1,2-diamine

Into flask was placed Palladium/carbon, E101 R Noblyst, 5% (1.50 g, 14.1 mmol), tetrahydrofuran (30 ml) and 4-(4-methoxy-2,3-dinitro-phenyl)-1-methyl-1H-pyrazole, (2.70 g, 9.71 mmol). The mixture was stirred for 18 h at RT under a hydrogen atmosphere. The solids were filtered off and discarded. The filtrate was evaporated to dryness and the residue was used without further purification to yield in 2.10 g (91%) of title compound as a brownish solid. HPLC/MS (purity) 92%. Rt 1.44 min (method A). [M+H]+ 219.1.

i. 7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-ylamine

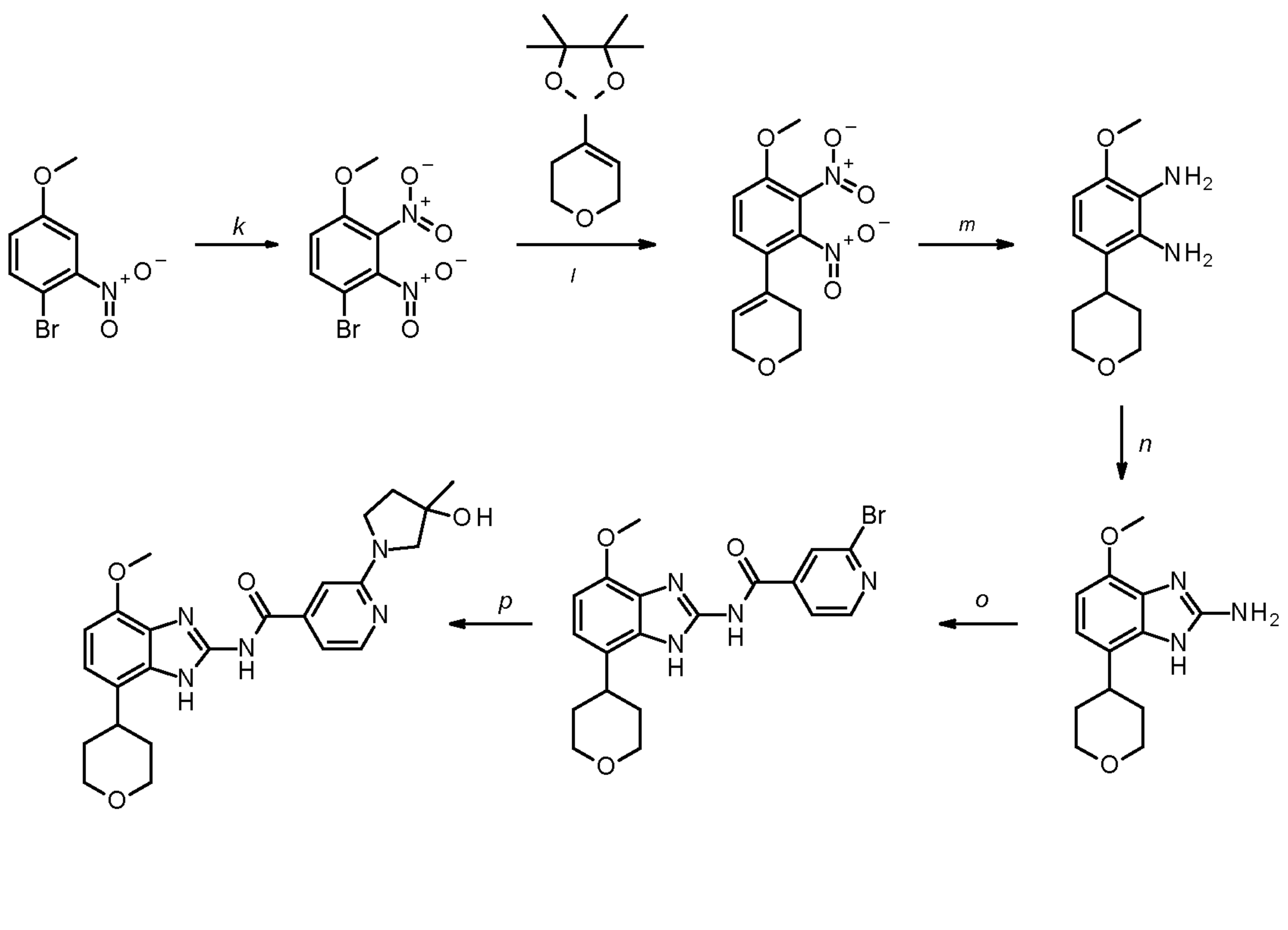
3-Methoxy-6-(1-methyl-1H-pyrazol-4-yl)-benzene-1,2-diamine, 92% (2.10 g, 8.85 mmol) was dissolved in methanol (100 ml) and water (20 ml). Cyanogen bromide (1.44 g, 13.3 mmol) was added and the reaction stirred at RT for 2 h. The mixture was evaporated to dryness and purified by column chromatography (dichloromethane/ethanol, gradient) to yield in 2.20 g (100%) of the title compound as a yellow solid. HPLC/MS (purity) 98%. Rt 1.74 min (method A). [M+H]+ 244.1.

General procedure to form ureas

j. 4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide

To a stirred solution of 1,1'-carbonyldiimidazole (84.9 mg, 0.524 mmol) in dichloromethane (5 ml) was slowly added 7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-ylamine, 98% (100 mg, 0.403 mmol) suspended in dichloromethane (1 ml) at 60°C. After 20 h at 70°C, 4-prop-2-ynyl-piperidin-4-ol, hydrochloride (92.0 mg, 0.524 mmol) and triethylamine (0.168 ml, 1.21 mmol) were added and the mixture was stirred for additional 2 h at 60°C. The mixture was evaporated to dryness and the residue was purified by preparative HPLC (acetonitrile/water, gradient). Five drops of 1 N HCl solution were added to the dissolved pure fraction and evaporated to dryness to yield in 30.0 mg (17%) of the hydrochloride salt of the title compound as a light beige solid. 1H NMR (400 MHz, DMSO-d6) d 8.24 – 8.22 (m, 1H), 7.93 – 7.92 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 4.05 – 3.99 (m, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.36 – 3.19 (m, 2H), 2.83 (t, J = 2.6 Hz, 1H), 2.34 (d, J = 2.7 Hz, 2H), 1.73 – 1.56 (m, 4H). HPLC/MS (purity) 100%. Rt 2.00 min (method A). [M+H]+ 409.2.

3. 2-(3-hydroxy-3-methylpyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide



k. 1-Bromo-4-methoxy-2,3-dinitro-benzene

Into 3-necked round-bottom flask was placed 1-bromo-4-methoxy-2-nitrobenzene (50.0 g, 205 mmol) in sulfuric acid (100 ml). Nitric acid (24 ml, 530 mmol) was added dropwise with stirring at 0°C. The solution was stirred for 1 h at room temperature and quenched with 1000 ml of ice water. The solution was extracted twice with 1000 ml of ethyl acetate, the combined organic layers were dried over anhydrous sodium sulfate and concentrated to dryness. The crude material was recrystallized from ethyl acetate/hexane (2:3) to result in 20.0 g (32%) of 1-bromo-4-methoxy-2,3-dinitrobenzene as a yellow solid. Melting point: 150-153°C. 1H NMR (400 MHz, DMSO-d6) ppm = 8.19 (d, J = 9.3 Hz, 1H), 7.70 (d, J = 9.3 Hz, 1H), 4.02 (s, 3H). HPLC/MS (purity) 91%. [M+H]+ 276.8, 278.9.

l. 4-(4-Methoxy-2,3-dinitro-phenyl)-3,6-dihydro-2H-pyran

Into pressure tank reactor purged and maintained with an inert atmosphere of argon, was placed 1-bromo-4-methoxy-2,3-dinitrobenzene, 91% (15.7 g, 51.4 mmol), 2-(3,6-dihydro-2H-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 95% (13.7 g, 61.7 mmol), Pd(dppf)Cl_2 dichloromethane complex, 95% (4.42 g, 5.14 mmol), potassium carbonate (8.53 g, 61.7 mmol, dissolved in water (12 ml), ethanol (31.6 ml) and toluene (316 ml). The mixture was stirred for 1 h at 100°C, cooled to room temperature and concentrated to dryness under vacuum. The residue was purified by column chromatography (ethyl acetate/petrol ether: 1/1) to yield in 13.0 g (86%) of 4-(4-methoxy-2,3-dinitrophenyl)-3,6-dihydro-2H-pyran as an orange solid. HPLC/MS (purity) 95%. [M+H]+ 281.2.

m. 3-Methoxy-6-(tetrahydro-pyran-4-yl)-benzene-1,2-diamine

Into a 250-ml round-bottom flask was placed Palladium/carbon, 10% (4.00 g, 3.76 mmol), methanol (100 ml) and 4-(4-methoxy-2,3-dinitrophenyl)-3,6-dihydro-2H-pyran, 95% (10.5 g, 33.9 mmol). The mixture was stirred for 15 h at 35°C under a hydrogen atmosphere. The solids were filtered off and discarded. The filtrate was evaporated to dryness and the residue was purified by column chromatography (ethyl acetate/hexane, 70/30) to yield in 4.51 g (58%) of 3-methoxy-6-(oxan-4-yl)benzene-1,2-diamine as a yellow solid. Melting point: 116-117°C. 1H NMR (400 MHz, Chloroform-d) 6.67 (d, J = 8.5 Hz, 1H), 6.45 (d, J = 8.5 Hz, 1H), 4.18 -4.09 (m, 2H), 3.86 (s, 3H), 3.65 -3.53 (m, 2H), 3.46(s, 4H), 2.82 -2.64 (m, 1H), 1.93 -1.73 (m, 4H). HPLC/MS (purity) 97%. [M+H]+ 223.1.

n. 7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-ylamine

To 3-bromo-6-methoxy-benzene-1,2-diamine, 97% (1.86 g, 8.10 mmol) dissolved in methanol (40 ml) and water (10 ml) was added cyanogen bromide, 98% (1.31 g, 12.2 mmol) at RT and the resulting mixture was stirred at RT for 20 h. The reaction mixture was evaporated to remove the methanol. Under cooling the aqueous solution was basified with ammonia and evaporated to dryness. The residue was taken up in water and extracted 3 times with dichloromethane. The combined organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. The residue was purified by column chromatography (dichloromethane/ethanol, gradient) to yield in 2.11 g (100%) of the title compound as a beige solid. HPLC/MS (purity) 95%. Rt 1.74 min (method A). [M+H]+ 248.1.

o. 2-Bromo-N-[7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-isonicotinamide

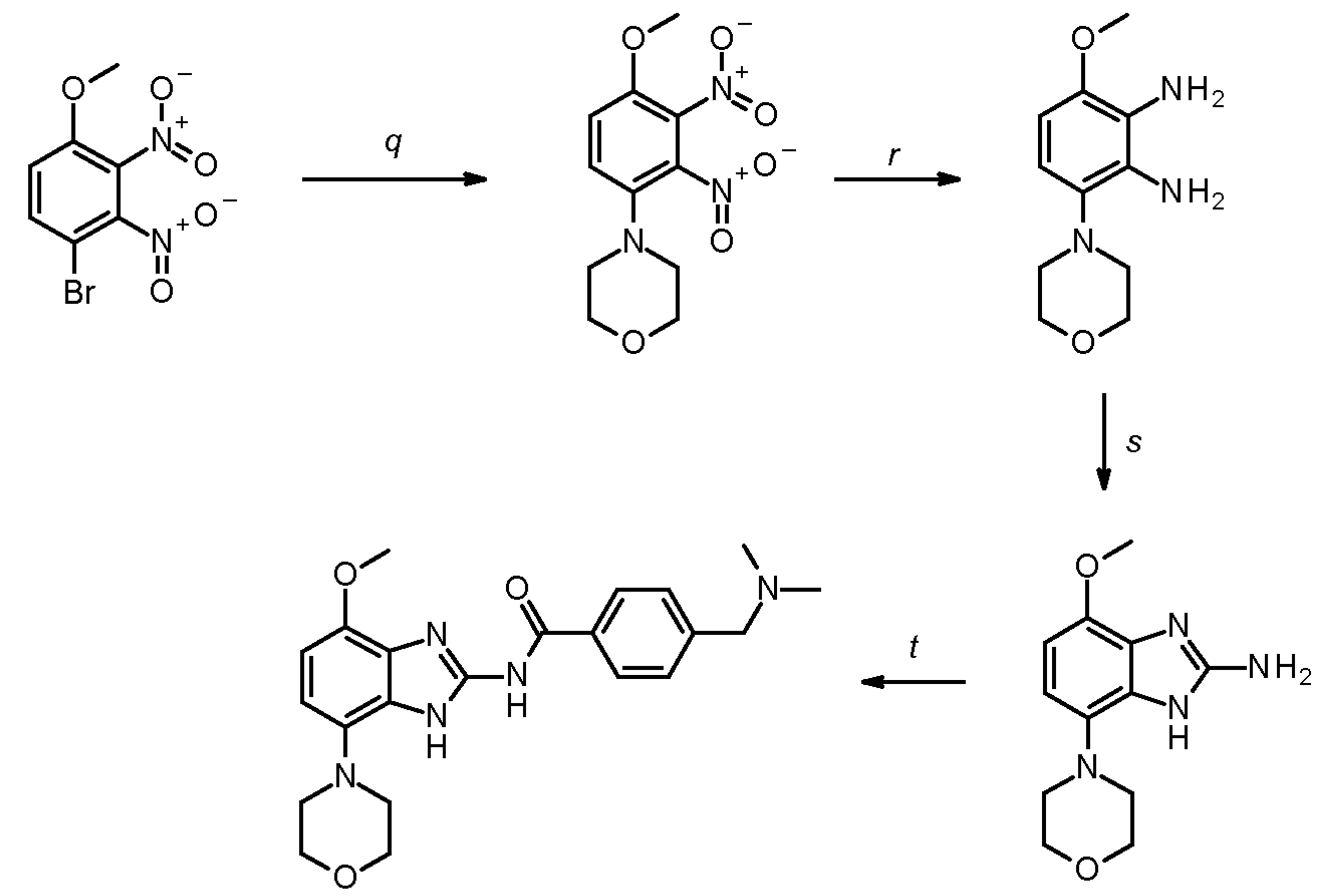
7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-ylamine, 95% (1.00 g, 3.84 mmol), 2-bromopyridine-4-carboxylic acid, 97% (1.01 g, 4.99 mmol) 1-hydroxybenzotriazole hydrate (156 mg, 1.15 mmol) and [dimethylamino-([1,2,3]triazolo[4,5-b]pyridin-3-yloxy)-methylene]-dimethyl-ammonium, hexafluoro phosphate (HATU, 1.90 g, 4.99 mmol) were dissolved in N,N-dimethylformamide (30 ml). Then 4-methylmorpholine (1.27 ml, 11.5 mmol) was added at RT and the mixture stirred at RT for 3 days. The reaction mixture was evaporated to dryness, taken up in dichloromethane and stirred for 1 h. The precipitate formed was filtered off and discarded. The filtrate was evaporated to dryness and the residue was purified by column chromatography (dichloromethane/ethanol, gradient) to yield in 2.67 g (100%) of the title compound as a light yellow fine powder. HPLC/MS (purity) 62%. Rt 2.34 min (method A). [M+H]+ 201.9, 203.9.

p. 2-(3-hydroxy-3-methylpyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide

2-Bromo-N-[7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-isonicotinamide, 62% (300 mg, 0.431 mmol), 3-methylpyrrolidin-3-ol (77.2 mg, 0.561 mmol), cesium carbonate (281 mg, 0.863 mmol) and 2,6-di-tert-butyl-4-methylphenol (0.009 ml, 0.043 mmol) were dissolved in 1-methyl-2-pyrrolidone for synthesis (10 ml) and the mixture was stirred at 140°C for 3 days. The reaction mixture was evaporated to dryness and the residue was purified by preparative HPLC (acetonitrile/water, gradient). Three drops of 1 N HCl solution were added to the dissolved pure fraction and evaporated to dryness to yield in 13.0 mg (6%) of the hydrochloride salt of the title compound as a light beige solid. 1H NMR (700 MHz, DMSO-d6) ppm = 14.22 – 12.03 (m, 2H), 8.09 (d, J = 6.4 Hz, 1H), 7.60 (s, 1H), 7.40 – 7.35 (m, 1H), 7.07 (d, J = 8.3 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 4.00 –

3.96 (m, 2H), 3.93 (s, 3H), 3.80 – 3.70 (m, 2H), 3.61 – 3.48 (m, 4H), 3.33 – 3.26 (m, 1H), 2.09 – 1.99 (m, 2H), 1.80 – 1.71 (m, 4H), 1.42 (s, 3H). HPLC/MS (purity) 100%. Rt 2.02 min (method A). [M+H]+ 452.2.

4. 4-[(dimethylamino)methyl]-N-(4-methoxy-7-morpholino-1H-benzimidazol-2-yl)benzamide



q. 4-(4-methoxy-2,3-dinitro-phenyl)morpholine

Into a pressure tank reactor was placed 1-bromo-4-methoxy-2,3-dinitrobenzene, 90% (25.0 g, 81.2 mmol), dioxane (300 ml) and morpholine, 95% (29.8 g, 325 mmol). The mixture was stirred for 15 h at 100°C. The solids were filtered off and discarded. The filtrate was concentrated under vacuum and the residue was purified by column chromatography (ethyl acetate/hexane, 60/40) to yield in 13.0 g (51%) of 4-(4-methoxy-2,3-dinitrophenyl)morpholine as a dark red solid. HPLC/MS (purity) 90%. [M+H]+ 284.0.

r. 3-methoxy-6-morpholino-benzene-1,2-diamine

Into a 250-ml round-bottom flask was placed Palladium/carbon, 10 % (3.00 g, 2.82 mmol), methanol (100 ml) and 4-(4-methoxy-2,3-dinitrophenyl)morpholine, 90% (12.7 g, 40.3 mmol). The mixture was stirred for 4 h at RT under hydrogen atmosphere. The solids were filtered off and discarded. The filtrate was evaporated to dryness and the residue was purified by column chromatography (ethyl acetate/hexane/NEt_3, 69.5/29.5/1%) to yield in 7.30 g (77%) of 3-methoxy-6-

(morpholin-4-yl)benzene-1,2-diamine as a pink solid. 1H NMR (500 MHz, DMSO-d6) ppm = 1H NMR (400 MHz, DMSO-d6) 6.34 (d, J = 8.6 Hz, 1H), 6.22 (d, J = 8.6 Hz, 1H), 4.22 (s, 4H), 3.75 -3.71 (m, 4H), 3.70 (s, 3H), 2.73 -2.68 (m, 4H). Melting point: 113-115°C, HPLC/MS (purity) 95%. [M+H]+ 224.1

s. 4-methoxy-7-morpholino-1H-benzimidazol-2-amine

To 3-methoxy-6-morpholin-4-yl-benzene-1,2-diamine, 95% (4.90 g, 20.8 mmol) dissolved in methanol (40 ml) and water (10 ml) was added cyanogen bromide, 98% (3.38 g, 31.3 mmol) at RT and the resulting mixture was stirred at RT for 20 h. Under cooling the aqueous solution was basified with ammonia and evaporated to dryness. The residue purified directly by column chromatography (dichloromethane/ethanol, gradient) to yield in 5.28 g (100%) of the title compound as a yellow solid. HPLC/MS (purity) 98%. Rt 1.64 min (method A). [M+H]+ 249.1.

t. 4-[(dimethylamino)methyl]-N-(4-methoxy-7-morpholino-1H-benzimidazol-2-yl)benzamide

7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-ylamine, 98% (100 mg, 0.395 mmol), 4-[(dimethylamino)methyl]benzoic acid, hydrochloride (111 mg, 0.513 mmol), [dimethylamino-([1,2,3]triazolo[4,5-b]pyridin-3-yloxy)-methylene]-dimethyl-ammonium, hexafluoro phosphate (HATU, 195 mg, 0.513 mmol), 4-(dimethylamino)pyridine (48.2 mg, 0.395 mmol) and 1-hydroxybenzotriazole hydrate (16.0 mg, 0.118 mmol) were dissolved in N,N-dimethylformamide (5 mL). To this mixture 4-methylmorpholine (0.13 ml, 1.18 mmol) was added and the mixture stirred at RT for 3 days. The reaction mixture was evaporated to dryness and the residue was purified by preparative HPLC (acetonitrile/water, gradient). Three drops of 1 N HCl solution were added to the dissolved pure fraction and evaporated to dryness to yield in 90.0 mg (51%) of the hydrochloride of the title compound as a colorless solid. 1H NMR (500 MHz, DMSO-d6) ppm = 12.58 – 11.92 (m, 1H), 10.99 – 10.86 (m, 1H), 8.21 – 8.18 (m, 2H), 7.79 – 7.76 (m, 2H), 7.28 – 7.13 (m, 1H), 6.83 (d, J = 8.6 Hz, 1H), 4.38 (d, J = 5.4 Hz, 2H), 3.99 – 3.95 (m, 4H), 3.95 (s, 3H), 3.62 – 3.46 (m, 4H), 2.72 (d, J = 4.8 Hz, 6H). HPLC/MS (purity) 100%. Rt 1.74 min (method A). [M+H]+ 410.1.

Method A

Agilent Technologies 1200 series; column: Chromolith Performance RP18e; 100 x 3 mm; mobile phase A: water/0.1% TFA, mobile phase B: acetonitrile/0.1% TFA; Gradient:1%B for 0.2 min, 1%B to 100%B in 3.8 min, hold 0.4 min; flow rate: 2 mL/min, wave length: 220 nm

$Pd(dppf)Cl_2$ = 1,1′-bis(diphenylphosphino)ferrocene]palladium(II)dihydrochloride

Example 3: Testing compounds of the present invention for inhibitory activities against human adenosine receptors in recombinant cells.

The functional activities of human A_{2A}, A_{2B}, A_1 and A_3 receptors were determined by quantification of cAMP, being the second messenger for adenosine receptors. For this purpose recombinant HEK293 cells, expressing either human A_{2A} or A_{2B} receptors (both Gs coupled were seeded into 394-well microtiter plates, test compounds and agonist (NECA) were added. After a 15 min incubation, HTRF reagents (cAMP dynamic 2, Cis Bio) were added and the cellular cAMP levels were determined using the ENVISION (Perkin Elmer) plate reader.

For human A_1 and A_3 receptors, recombinant CHO cells, expressing either A_1 or A3-receptor, were used. As both receptors couple to Gi proteins, the assay protocol was adapted:
Cells were seeded into 384-well plates, forskolin, test compounds and agonists (CPA for A_1- and IB-MECA for A_3-receptor) were added. After 30 min incubation, HTRF reagents (cAMP dynamic 2, Cis Bio) were added and the cellular cAMP levels were determined using the ENVISION (Perkin Elmer) plate reader.
Obtained raw data were normalized against the inhibitor control and the neural control (DMSO) and the normalized data were fitted using GeneData software.

The compounds of the present invention show a high selectivity for adenosine A_{2A} and A_{2B} receptors over adenosine A_1 and A_3 receptors (see e.g. the data of some examples of the compounds of the present invention in table 4)

Particularly, in contrast to the known adenosine A_{2A} receptor antagonist Tozadenant and similar benzothiazole derivatives, the compounds of the present invention surprisingly show an A_{2A}/A_{2B} dual activity (see table 4) which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above or the compounds of the present invention show at least a high A_{2A} inhibitory activity together with the other surprising advantages disclosed herein leading to a high efficacy in the treatment and/or prevention of hyperproliferative and infectious diseases and disorders.

Table 4

No.	Functional A2A receptor activity, HEK293, cAMP, IC50 [µM]	Functional A2B receptor activity, HEK293, cAMP, IC50 [µM]	Functional A1 receptor activity, CHO, cAMP, IC50 [µM]	Functional A3 receptor activity, CHO, cAMP, IC50 [µM]
2	A	B		A
3	A	B		A
5	A	B		A
7	A	C	D	B
8	A	D	D	C
10	A	B	D	
11	A	B	D	D
12	A	C	C	C
13	A	C	D	C
15	A	A	C	B
16	A	D	D	C
17	A	D		C
26	A	D	D	C
28	A	C		C
30	A	D		C
48	A	D	D	D
49	A	C	D	B
54	B	C	C	D
63	A	C	D	B
71	A	B	D	C
76	A	C	D	D
79	B	C	D	D
80	B	C	D	C
84	B	C	C	C
85	B	C	D	D
86	A	D	D	D

88	A	D	D	D
89	B	C		D
92	A	C	D	D
93	A	B	D	D
94	A	C	D	C
95	A	C	C	A
97	A	B	D	D
98	B	C	D	C
99	A	D	D	D
100	A	C	D	D
101	A	C	C	C
102	A	D	D	D
103	A	C	C	D
104	A	D	D	C
105	A	C	D	C
106	A	D	D	C
107	A	C	D	C
108	A	C	D	C
114	A	D	D	D
118	A	D	D	
119	A	D	D	D
122	A	D	D	D
133	A	C	D	D
134	B	C	D	D
136	A	D	D	D
138	A	C	D	D
144	A	C	C	D
145	A	D	D	D
150	A	D	D	D
151	A	D	C	D
152	B	C	D	C
153	A	D	D	D
154	A	D	D	C
160	A	B	D	B
161	A	C	D	C
162	B	C	D	D
165	A	C	C	A
168	A	D	D	C
215	A	B		
216	B		D	D
217	A	B	C	D
218	A	B	C	D

219	A	A	C	
221	A	B	D	D
224	A	B	D	C
225	A	B	D	D
226	B		D	D
227	A	B	D	
228	B		D	
229	B		D	D
230	B		D	D
231	B		C	C
232	B		D	C
233	B		D	A
234	A		D	C
235	A			C
236	A	B	C	C
237	B	B	C	C
238	B			D
239	A	A		
240	A	A	C	C
241	B		D	D
242	A	A	C	C
243	A	A	C	
245	B		D	D
246	B			D
247	B			D
248	A	B	D	D
249	B			
250	A	B		D
253	A	A	C	C
254	A	A	C	
255	A	A	C	C
256	A	A	C	
257	A	A	C	
258	A	A	C	
259	A	A	C	D
260	A	A	C	
261	A	A	D	C
262	A	A	D	C
263	B			D
264	A	B	D	C
265	A	B	C	C
266	B	B	D	

267	A	A	C	
268	A	B	D	D
269	B	B	D	C
270	B		D	D
271	B	B	D	D
272	B	B	D	
273	B		D	D
277	B	B		D
278	B	B	D	C
279	B	B	C	C
280	B	B		
282	B	B	C	C
283	B	B	D	C
284	B	B	D	D
285	B	A	C	C
286	B	B		
287	B	B	C	D
288	B	B		C
289	B	A		
290	B	B		
291	B	B	C	
292	B		A	D
293	B	B		C
294	B	A		C
295	B	B		C
296	B	A		C
297	B	B		C
298	B	A		C
299	B	B		
300	B	B		
301	B			C
302	B	B		
303	B			D
304	B	B		C
305	B	B		D
306	B	A		
307	B	A		
308	B	B		
309	B	A		
310	B	B		D
311	B	A		C
312	A	A	C	C

313	A	D		D
314	B	C	D	C
315	B	B	D	C
316	A	A	C	C
317	A	A	C	C
318	A	A	B	B

A means IC_{50} value is < 10 nM, B means IC_{50} value is < 100 nM, C means IC_{50} value is < 1 µM, D means IC_{50} value is > 1 µM.

Example 4: Testing the effects of the compounds of the present invention against endogenous human A_{2A} receptor

The endogenous functional activity of the Gs-coupled human A_{2A} receptor was measured in T cells, where this receptor is highly expressed. Determination of receptor activity was done by quantification of cAMP, which is a second messenger for adenosine receptors.

In short, human pan T cells were isolated from human PBMC (MACS Pan T Cell Isolation Kit, Miltenyi Biotec) that have been derived from fresh whole blood. The T cells were seeded in 384-well microtiter plates and treated with test compounds. After 10min incubation at room temperature, the A_{2A} adenosine receptor agonist CGS-21680 was added, and the plates were incubated for another 45min. Finally, HTRF reagents (cAMP Femto Kit, CisBio) were added to the wells, and after 1h cellular cAMP levels were determined using the ENVISION (Perkin Elmer) plate reader.

The obtained raw data were normalized against the inhibitor control and the neutral control (DMSO) and the normalized data were fitted using Genedata Screener software.

The compounds of the present invention show that they are able to inhibit the A_{2A} receptor expressed in human T cells which incubated with the A_{2A} adenosine receptor agonist CGS-21680 (as measured by quantification of cAMP), which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above. Therefore, the compounds of the present invention surprisingly are able to prevent immunosuppression and thus are able to support anti-tumor T cell induced inhibition of tumor growth, reduction or destruction of metastases and prevention of neovascularization.

Example 5: Testing the pharmacokinetic properties of the compounds of the present invention in rat and mouse

The objective of the study was to obtain information on the pharmacokinetic properties of the compounds of the present invention in female Wistar rats/mice following single intravenous and oral administration.

Material and Methods:
Animal Experiments (In-Life Phase)
Female Wistar rats/mice (n=6) received either a single intravenous (bolus) injection or an oral administration (by gavage) of the tested compound. Doses of 0,2 and 10 mg/kg (per compound) were given intravenously and per os, respectively, as a solution in DMSO (0,2%)/PEG 200 (40%)/water for iv administration and as a suspension in Methocel (0,5%)/Tween 20 (0,25%) in water for oral dosing. Consecutive blood samples were taken sub-lingually under isoflurane inhalation from 3 animals per route of administration after 0.1 (only iv), 0.25 (only po), 0.5, 1, 2, 4, 6 and 24 h and were further processed to obtain plasma. Also, urine and feces samples of 3 rats per route of administration were collected over the time interval from 0-24 h and were pooled for analysis.

Bioanalytics:
The concentrations of the compounds in plasma, feces were quantified using an UPLC method with tandem mass spectrometric detection (LC-MS/MS) previously developed at the ‘Institute of Drug Metabolism and Pharmacokinetics’. The LC-MS/MS system consisted of a Waters Acquity UPLC coupled to an AB Sciex mass spectrometer API 5500 Q-trap. The UPLC separation was carried out on a reversed phase column (HSS T3, 1.8 µM, 2.1 × 50 mm) using a mobile phase gradient with 0.1% formic acid and acetonitrile as eluents. The detection of the compounds was performed using multiple reaction monitoring in the positive ionization mode. Plasma samples were spiked with internal standard (20 µl) and the analyte was

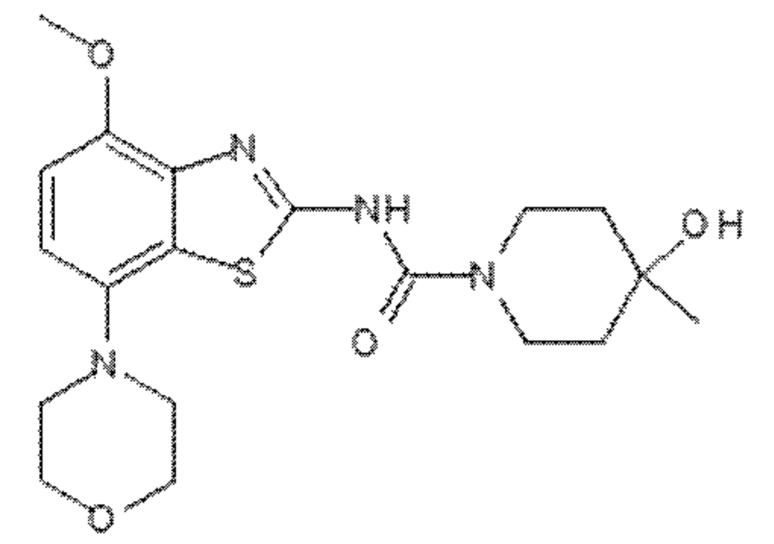
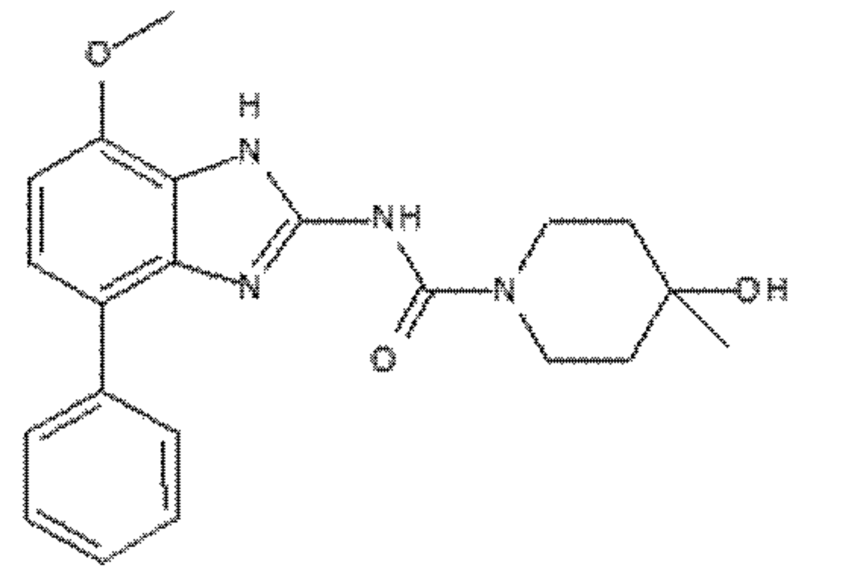
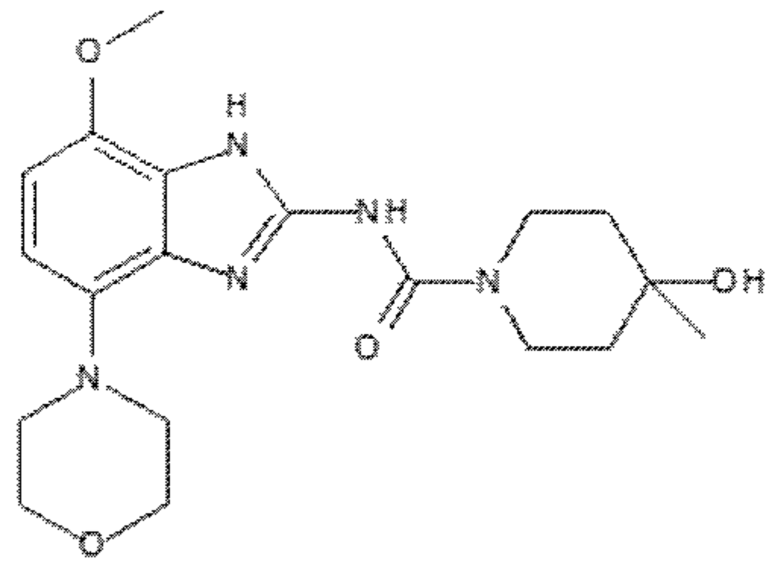
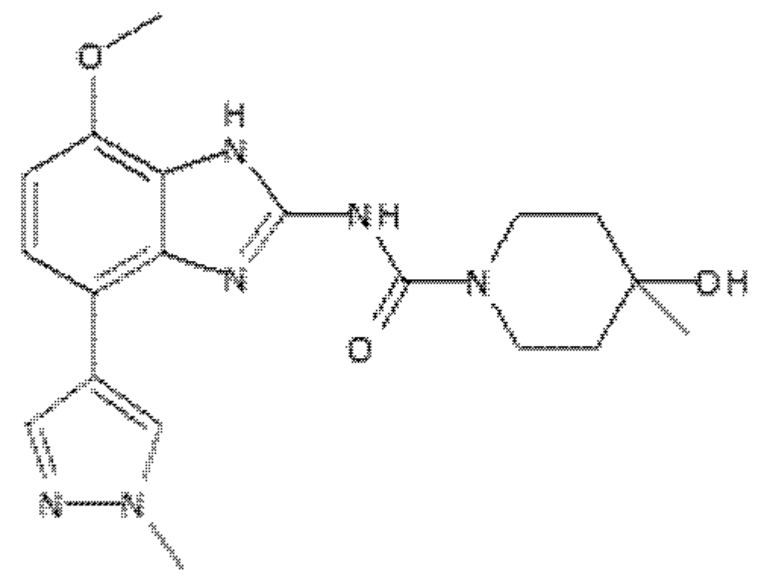
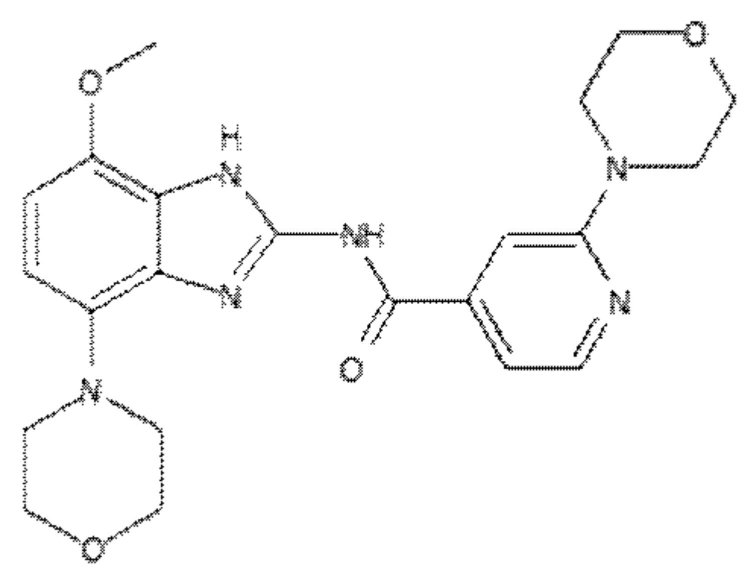
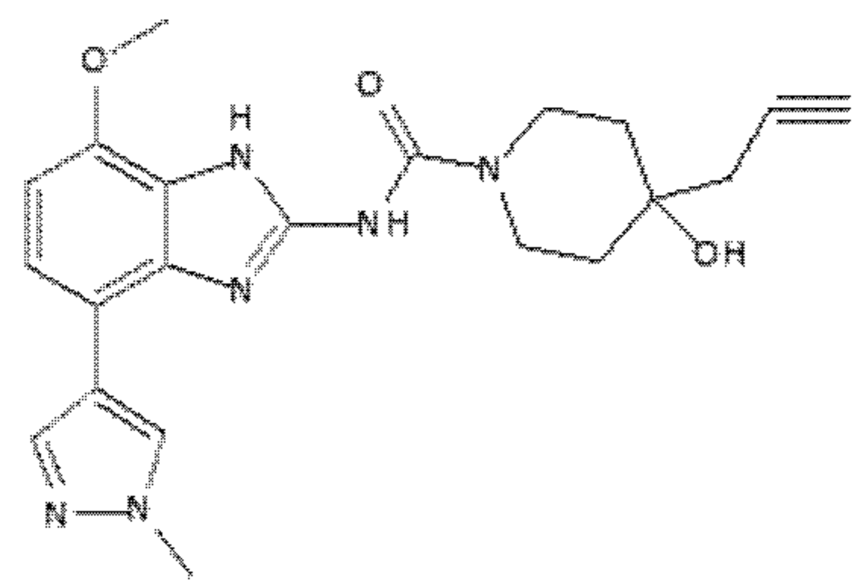
extracted from the matrix using tertiary-butyl methyl ether (tBME). The organic phase was evaporated to dryness under a stream of nitrogen. The residue was dissolved in acetonitrile/0.1% formic acid for LC-MS/MS analysis. Feces samples were homogenized with 4-times their volume of an ethanol/water mixture (4:1, v/v). Aliquots of the aqueous-ethanolic extracts were spiked with internal standard, diluted with acetonitrile/water (1:1, v/v) and directly injected into the LC-MS/MS system.

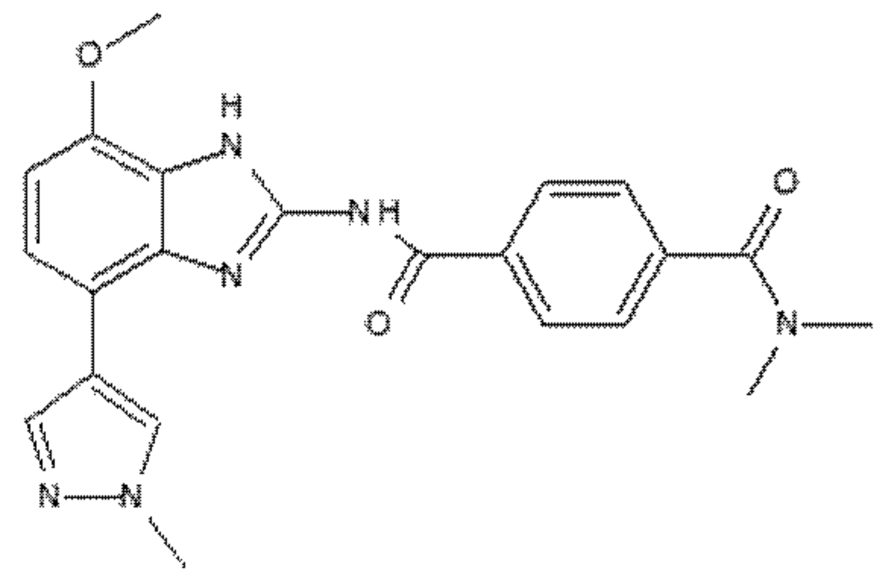
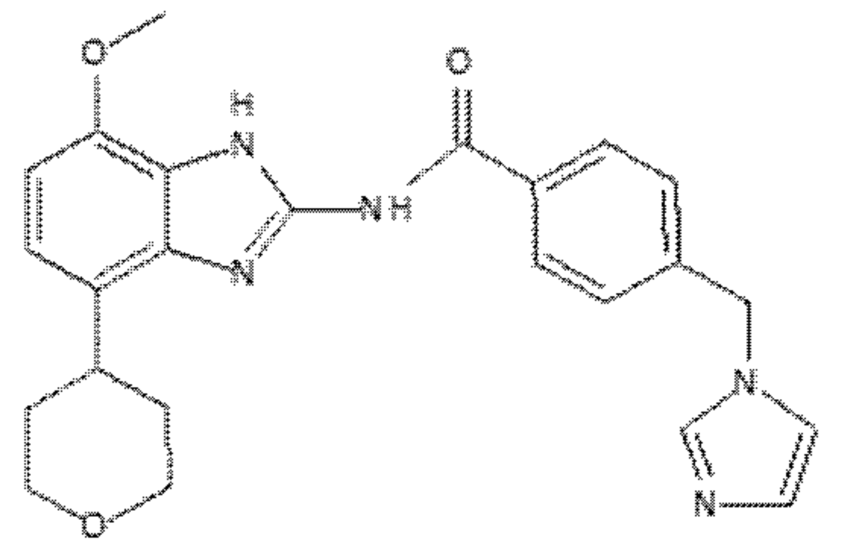
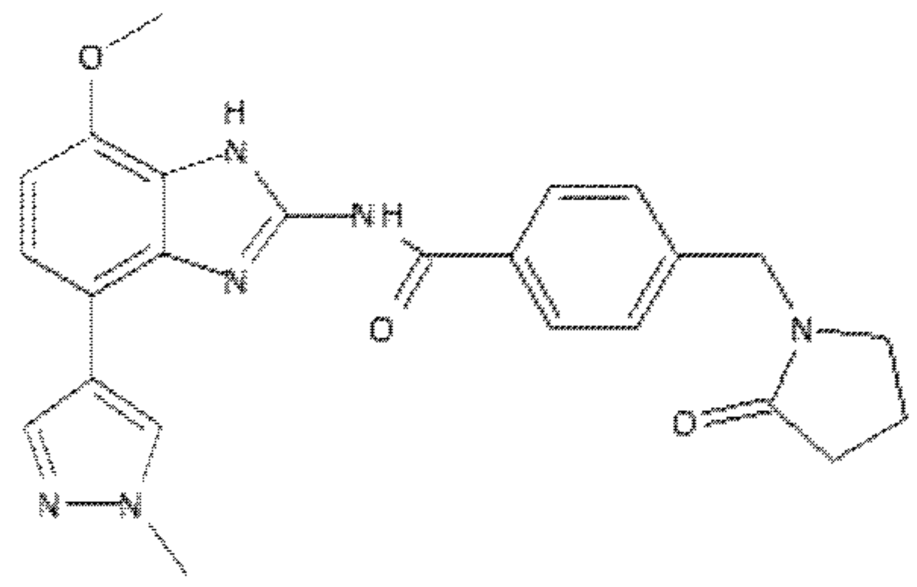
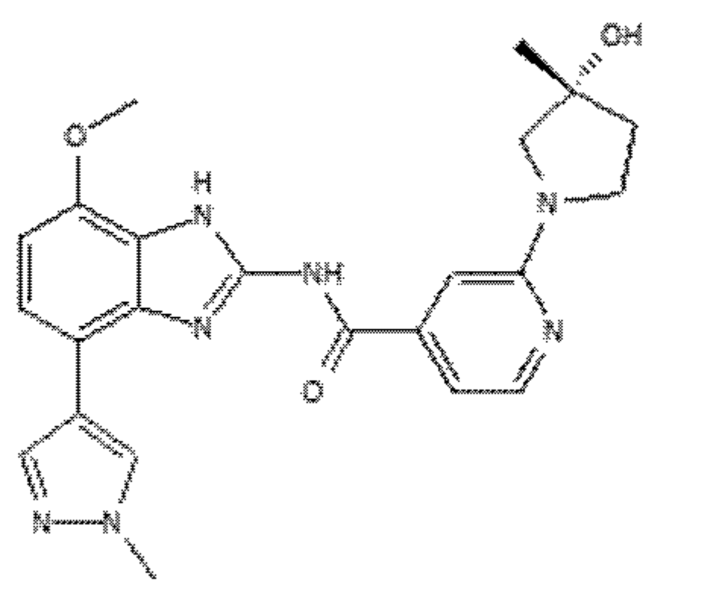
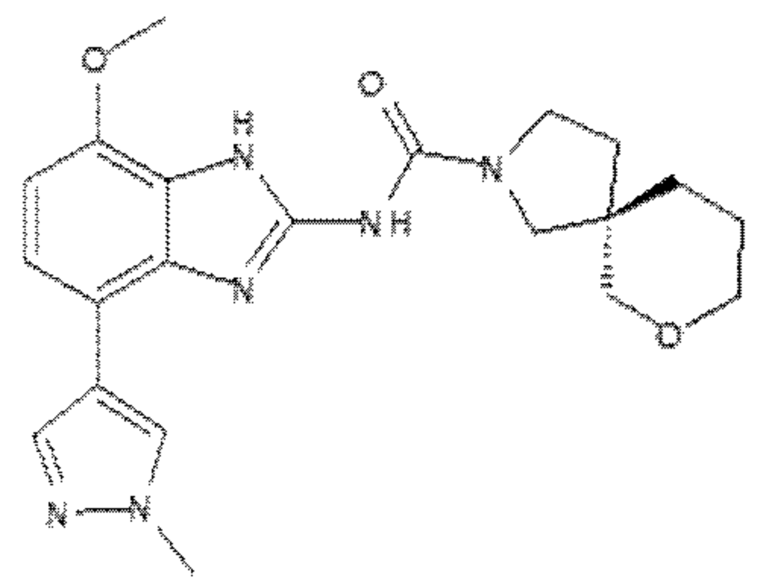
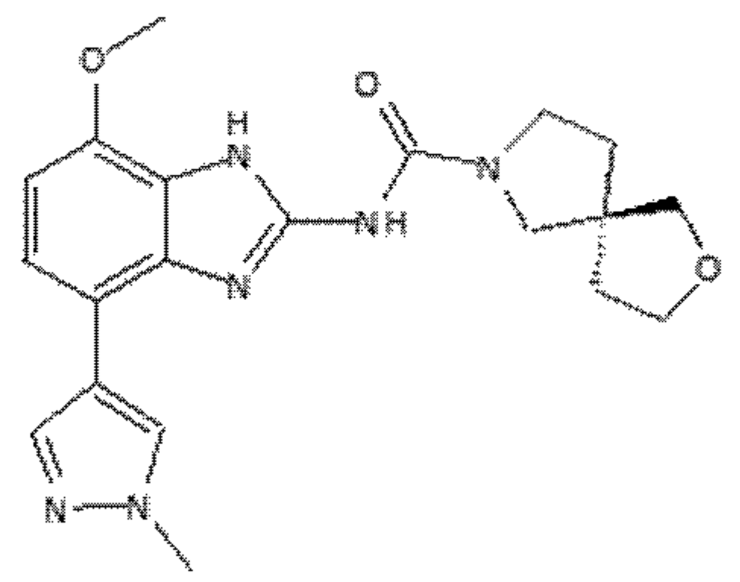
Pharmacokinetic Evaluation:
Pharmacokinetic parameters C_{max} and t_{max} were taken from the observed data. Area under the curve (AUC), clearance (CL), volume (V), half-life ($t_{1/2}$), F and all dose-normalized values were calculated using the custom-made software ‘DDS-TOX’. ‘DDS-TOX’ values were evaluated for several compounds and shown comparable to the values given by the validated software WinNonLin. AUC values were calculated by non-compartmental analysis using the linear up/log down method. Numerical data for mean plasma concentrations and derived pharmacokinetic parameters were rounded to 3 significant digits for presentation. Oral bioavailability and excretion data – expressed as % of dose – are displayed using 2 significant digits.

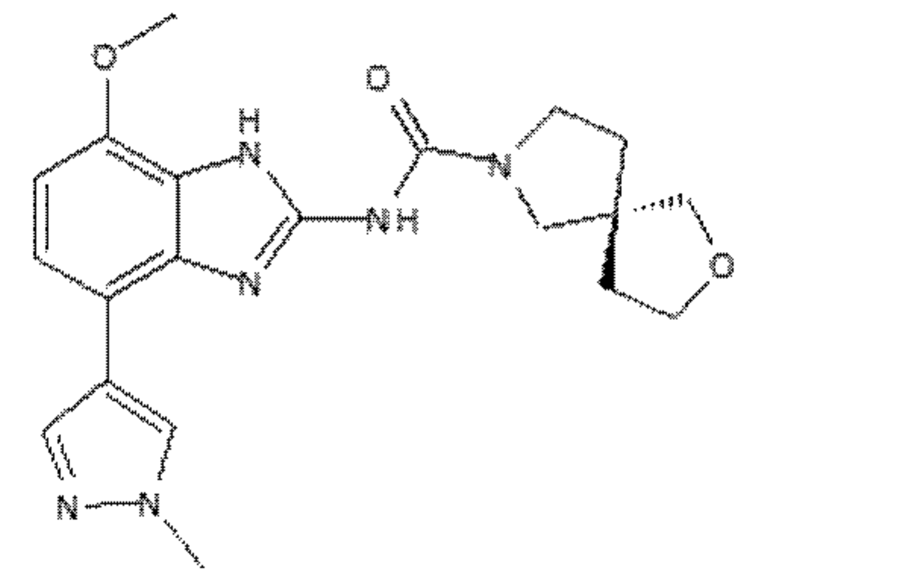
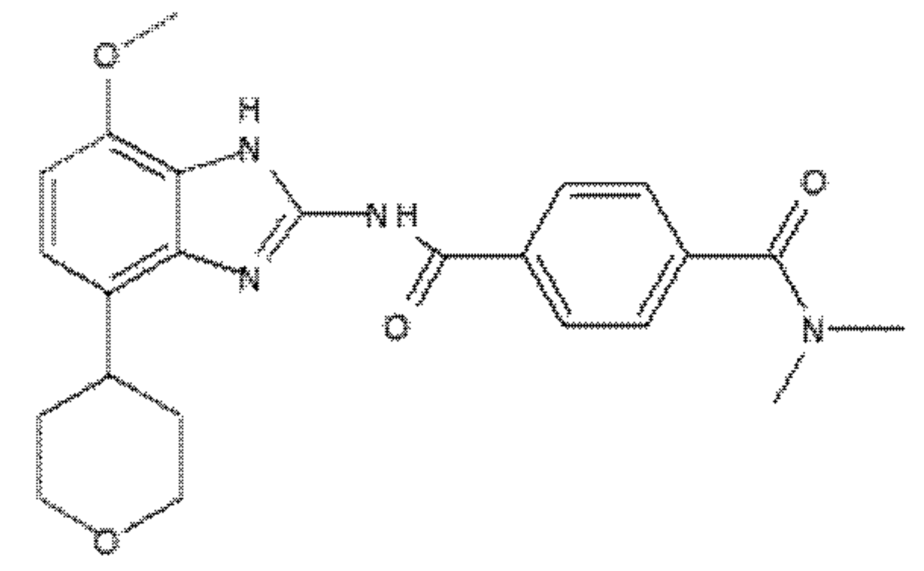
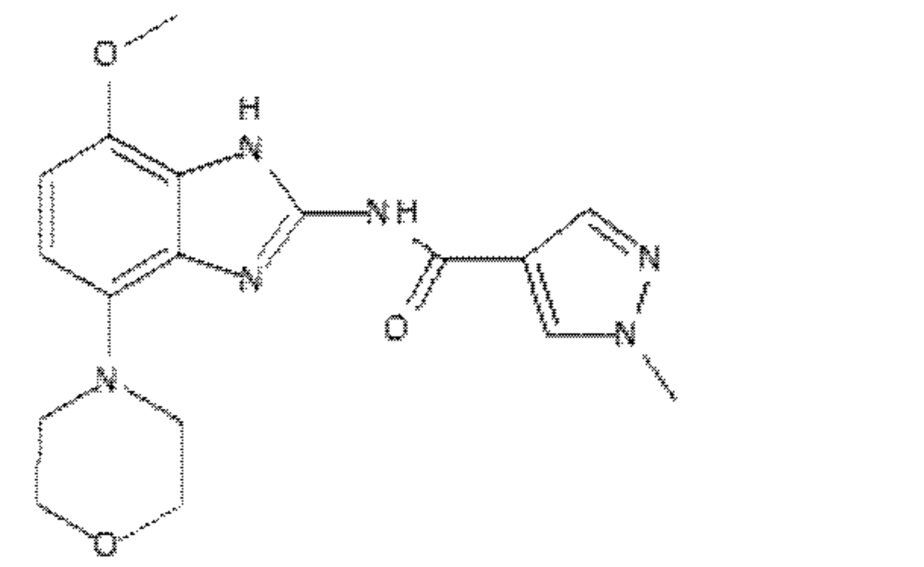
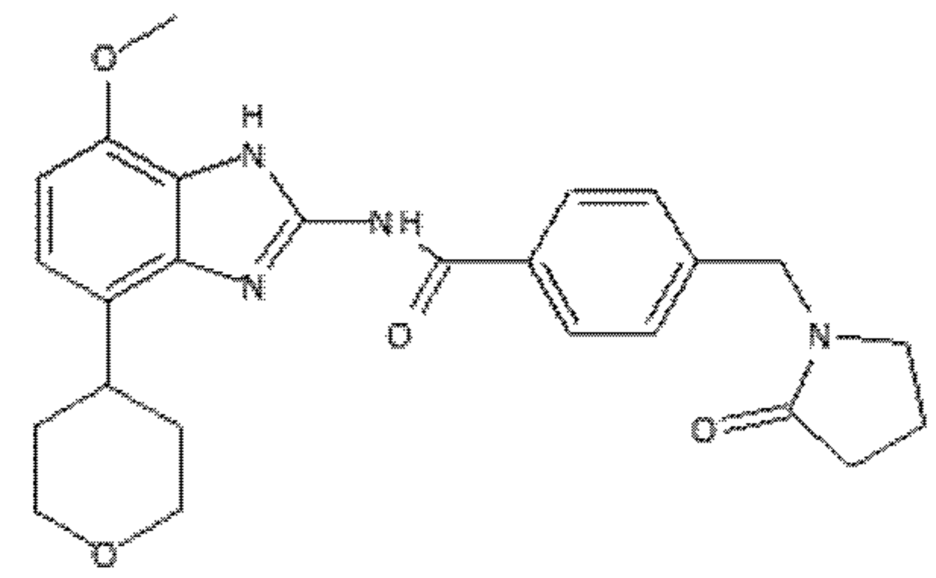
in comparison with the known adenosine A_{2A} receptor antagonist Tozadenant and similar benzothiazole derivatives, the compounds of the present invention surprisingly show better pharmacokinetic properties in mouse as the animal model relevant for cancer (see table 6), which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above.

Table 6 – PK data in mouse

Name, No.	**Structure**	**CL [L/h/kg]**	**t1/2 [h]**	**Vss [L/kg]**	**Feces iv [%]**	**CMax (iv) @ 1 mg/kg [ng/ml]**

Tozadenant		8,68	0,184	2,03	23@0.2	337
12		0,681	0,71	0,568	27@0.2	1820
21		0,763	0,839	0,508	38@0.08	2650
22		1,17	0,867	1,02	46@0.2	1320
23		0,619	1,72	1,54	11@0.2	733
92		1,9	0,556	1,17	26@0.2	892

93		0,406	0,768	0,357	42@0.2	3160
97		0,749	0,966	1,01	29@0.2	1050
100		1,35	0,549	1,05	12.5@0.2	888
107		1,9	0,622	1,54	34@0.2	718
114		0,566	1,11	0,842	9@0.2	1440
115		0,324	0,989	0,425	8.6@0.2	2450

116		0,739	0,967	0,917	16.9@0.2	1130
133		0,76	0,669	0,402	2.5@0.2	2640
136		0,333	1,15	0,522	5.6@0.2	2100
138		1,71	0,539	1,06		1,9

Example 6: Testing the effect of the compounds of the present invention on mouse T cells

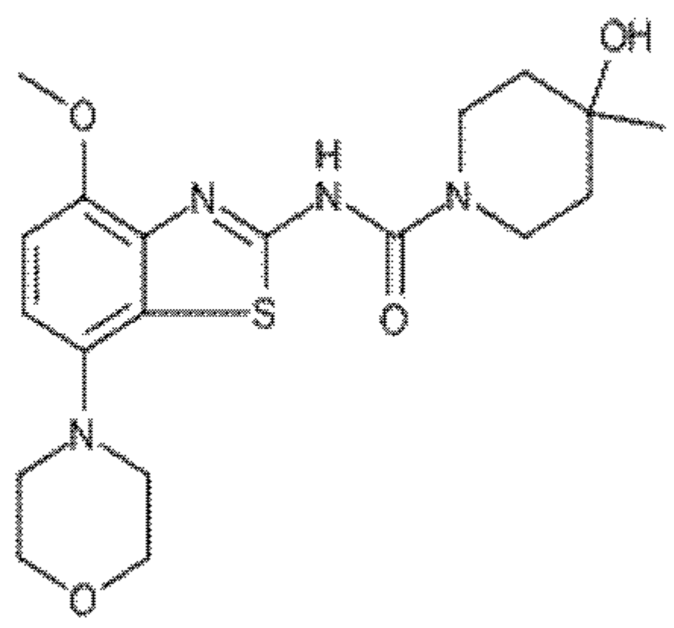
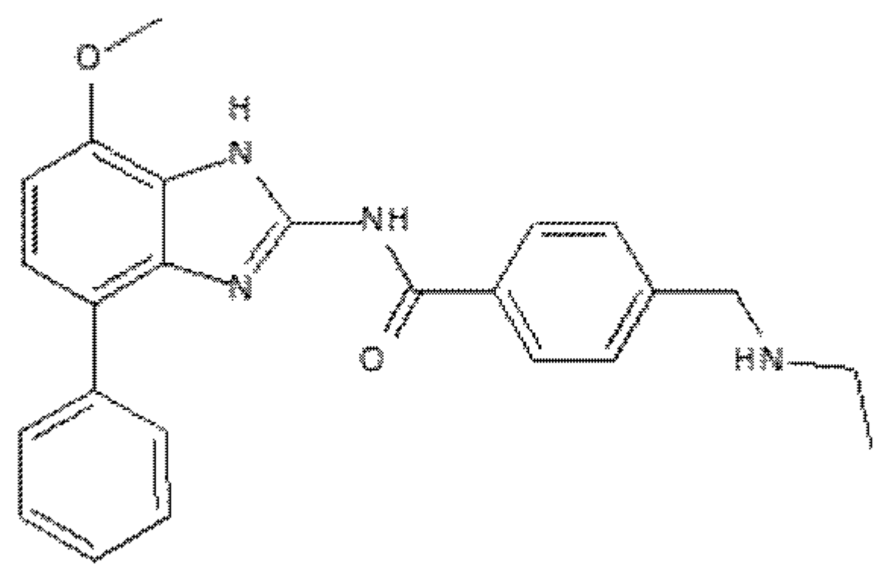
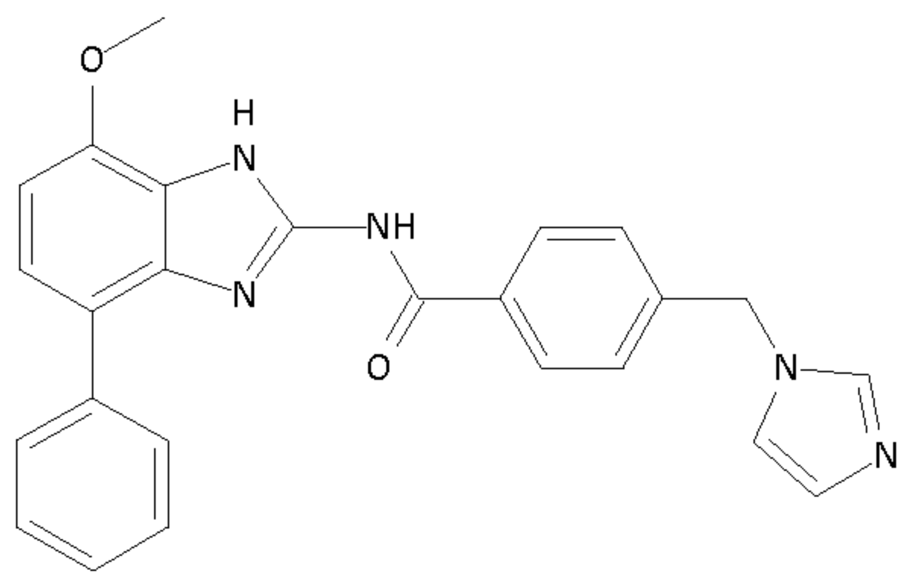
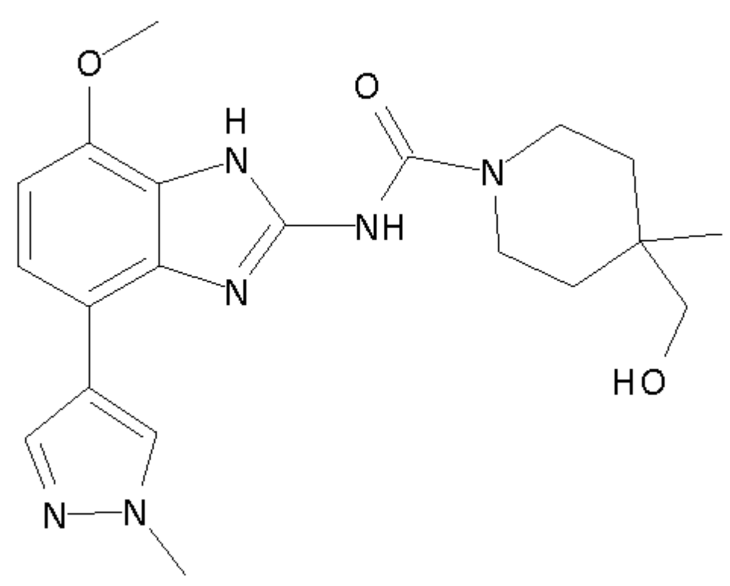
Background:

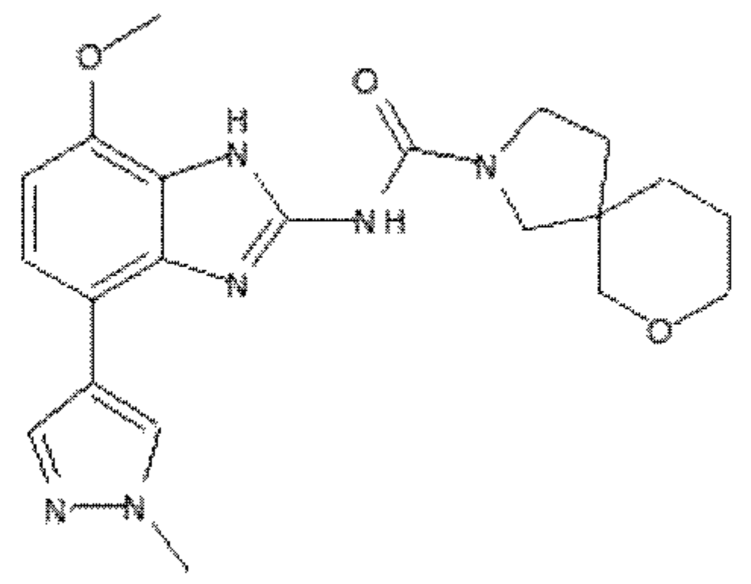
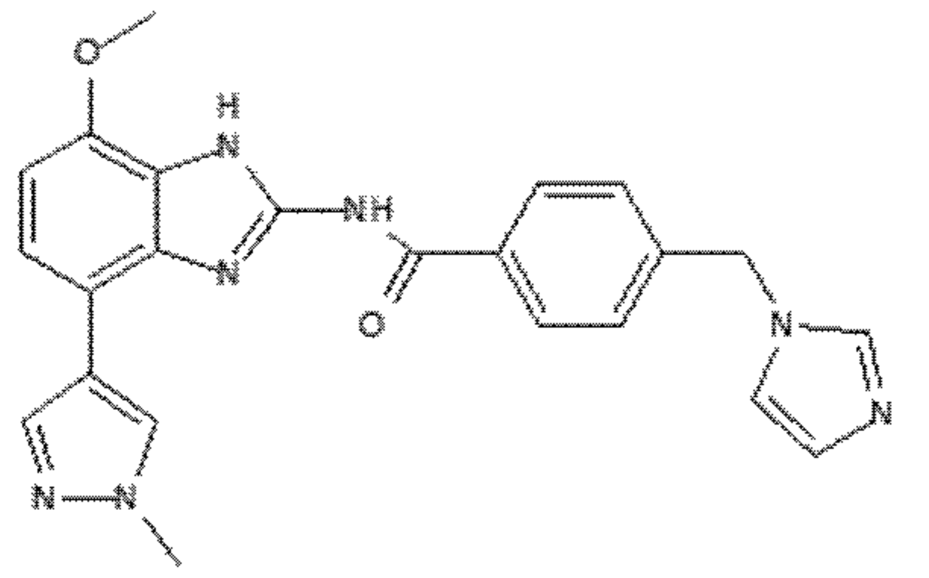
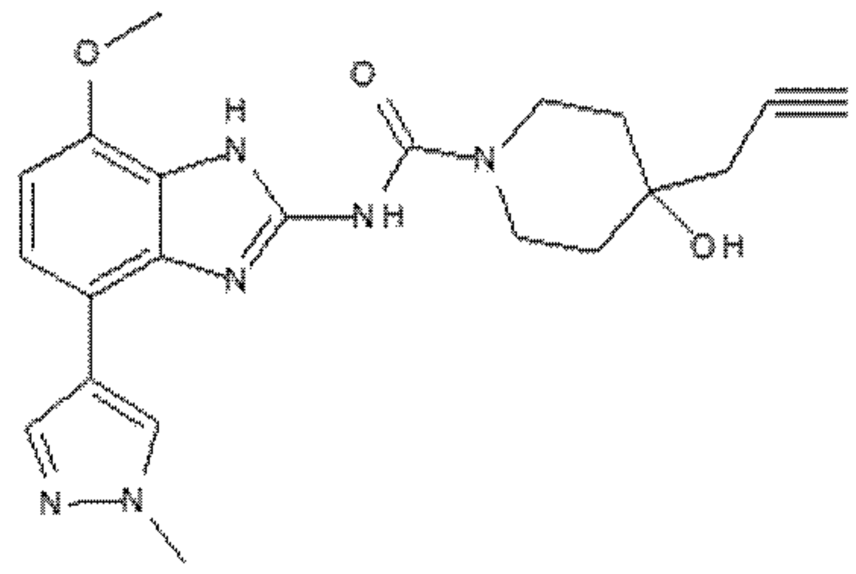
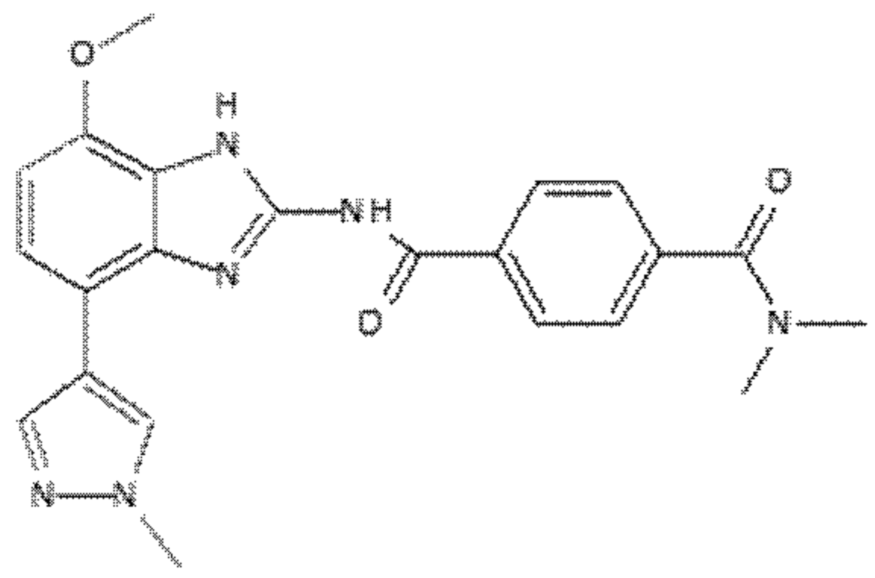
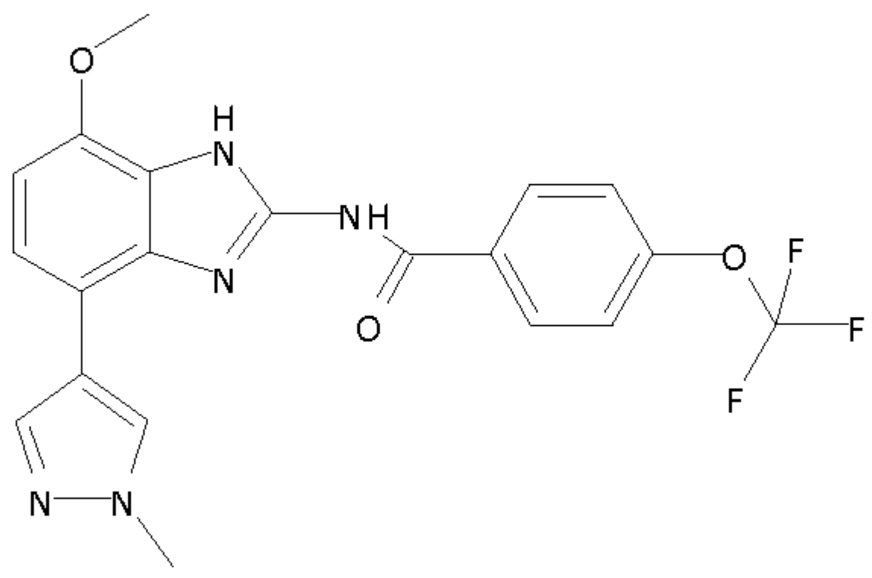
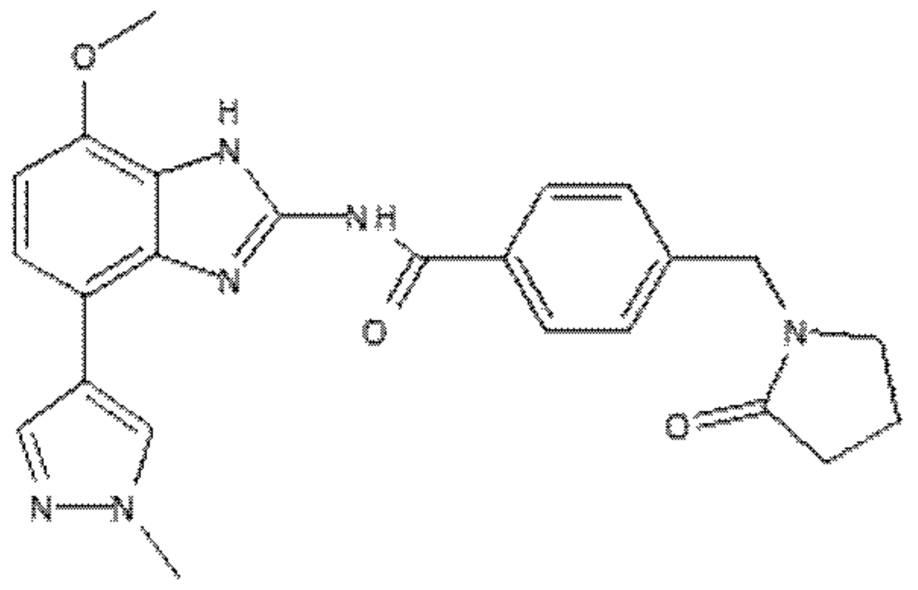
Adenosine (Ado) in tumor microenvironment can inhibit T cell activity by signaling through A_{2A} receptors and suppress cytokine secretion by T cells. A_{2A} specific agonists like CGS-21680 does similar job of inhibition of T cell cytokine secretion in vitro and in vivo. Potential A_{2A} antagonists or A_{2A}/A_{2B} dual antagonists can rescue T cells from this inhibition. Herein, we describe the in vitro system we established using Pan T cells from mouse spleens to screen potential A_{2A} antagonists or A_{2A}/A_{2B} dual antagonists for their activity. The method described involves the use of CD3/CD28 pre-coated beads to stimulate Pan T cells purified from mouse splenocytes, combined with the addition of A_{2A} agonist along with potential A_{2A} or A_{2A}/A_{2B} dual antagonists to evaluate potentiation of T cell cytokine production.

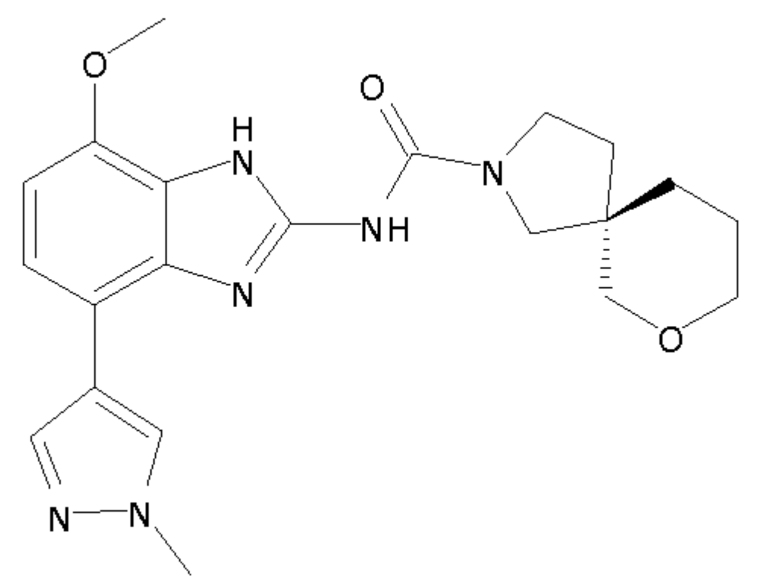
Assay description:
Briefly, mouse Pan T cells are purified from spleens of BALB/c mice using Pan T cell isolation kit Mouse II (MACS Miltenyi biotech Cat# Order no. 130-095-130) according to manufacturer's protocol. The purified T cells are seeded in Nunc™ 96-Well Polystyrene Round Bottom Microwell Plates in RPMI medium with 10% heat inactivated fetal bovine serum. The cells are rested at 37°C for 1 h before activating with CD3/CD28 pre-coated beads (Dynabeads™ Mouse T-Activator CD3/CD28; Cat# 11456D). After 30 min the cells are treated with varying doses of test antagonist(s). The cells are incubated for additional 30 min at 37°C before treating with A_{2A} agonist CGS-21680 (1 μM) or neutral control (DMSO). After 24 h incubation IL-2 levels in the supernatants and after 48 h incubation IFN-γ levels in the supernatants are measured by ELISAs according to manufacturer's protocol (R&D systems Cat# DY402 (IL-2); DY485 (IFN-γ)). Once the concentrations are calculated, the difference of cytokine concentration of DMSO control and agonist alone control is calculated (called Δ) and the percentage of rescue by each concentration of antagonist is calculated by using Microsoft Excel. These percentages of cytokine rescue in a dose dependent manner of antagonist is plotted in GraphPad Prism software and IC_{50} is calculated.

In contrast to the known adenosine A_{2A} receptor antagonist Tozadenant, the compounds of the present invention show that they are able to rescue T cells from inhibition and are able to prevent the suppression of cyctokine secretion as induced by adenosine or A_{2A} specific agonists like CGS-2168 (see table 7), which is preferred for the treatment and/or prevention of hyperproliferative and infectious diseases and disorders as it is disclosed above. Therefore, the compounds of the present invention surprisingly are able to prevent immunosuppression and thus are able to support anti-tumor T cell induced inhibition of tumor growth, reduction or destruction of metastases and prevention of neovascularization.

Table 7

No.	Name	Structure	Mouse T-Cell IL-2 [nM]	Mouse IFN-γ [nM]
	Tozadenant		NA (< 50% rescue)	NA (< 50% rescue)
11	4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide		44	75
15	4-Imidazol-1-ylmethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide		1111	
35	4-Hydroxymethyl-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide		120	220

67	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide			800
71	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide		40	40
92	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide		1000	500
93	N4-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide		111	350
94	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(trifluoromethoxy)benzamide			1000
100	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide		100	80

114	(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide		900	900

Example 7: Injection vials

A solution of 100 g of a compound of the present invention and 5 g of disodium hydrogenphosphate in 3 l of bidistilled water is adjusted to pH 6.5 using 2 N hydrochloric acid, filtered under sterile conditions, transferred into injection vials, lyophilised under sterile conditions and sealed under sterile conditions. Each injection vial contains 5 mg of a compound of the present invention.

Example 8: Solution

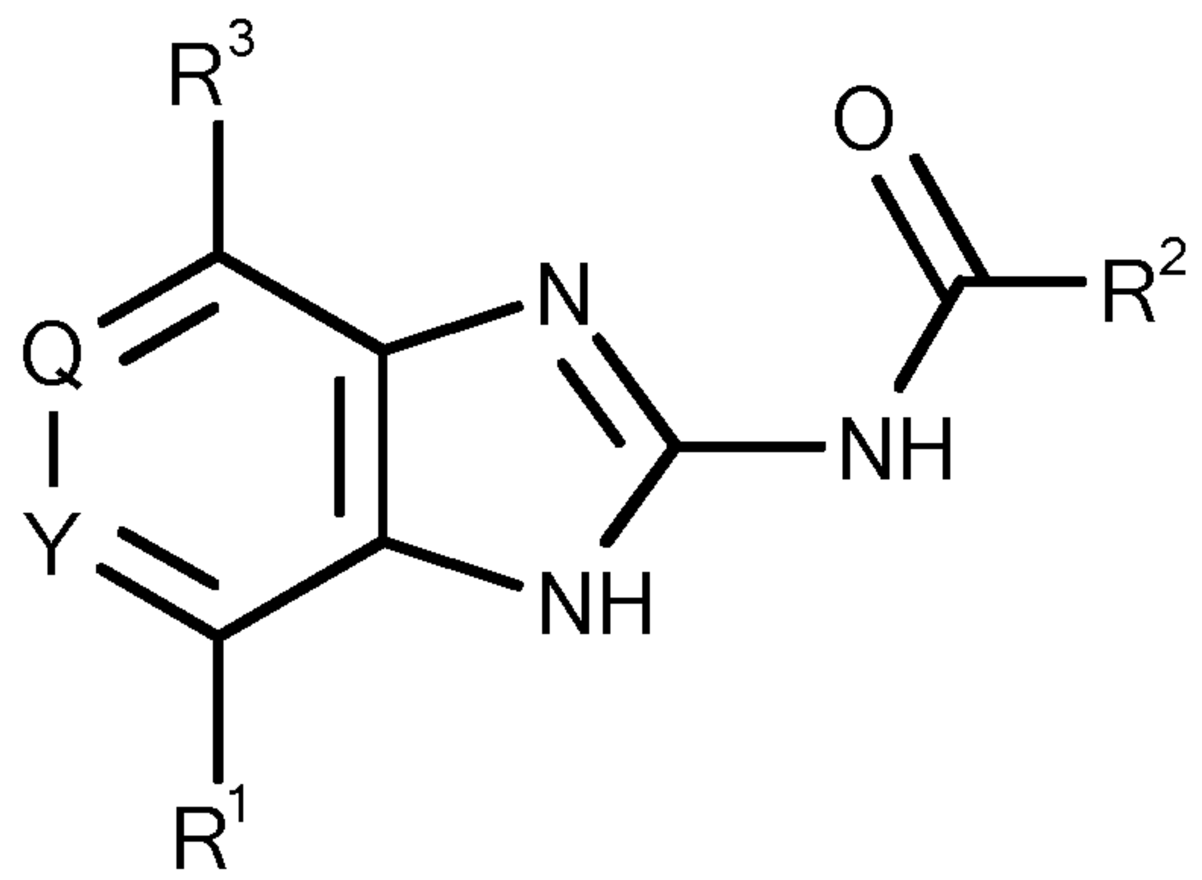
A solution is prepared from 1 g of a compound of the present invention, 9.38 g of NaH_2PO_4 2 H_2O, 28.48 g of $Na_2HPO_4 \cdot$ 12 H_2O and 0.1 g of benzalkonium chloride in 940 ml of bidistilled water. The pH is adjusted to 6.8, and the solution is made up to 1 l and sterilised by irradiation.

Example 9: Ampoules

A solution of 1 kg of a compound of the present invention in 60 l of bidistilled water is filtered under sterile conditions, transferred into ampoules, lyophilised under sterile conditions and sealed under sterile conditions. Each ampoule contains 10 mg of a compound of the present invention.

Claims

1. Compound of the formula I,



I

wherein

Q, Y are independently of one another CH or N,

R^1 is Hal or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, –$NR^5SO_2R^6$–, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, –$NR^5SO_2R^6$–, –COO–, –CONH–, –NCH_3CO–, –$CONCH_3$–, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^4,

R^2 is linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO,

SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or cyclic alkyl having 3-7 C atoms which is un-substituted or mono-, di- or trisubstituted by by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-11 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^4,

R^3 is linear or branched alkyl or O-alkyl having 1-6 C atoms or cyclic alkyl having 3-6 C atoms, which is unsubstituted or mono-, di- or trisubstituted by H, =S, =NH, =O, OH, cyclic alkyl having 3-6 C atoms, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$ or NO_2,

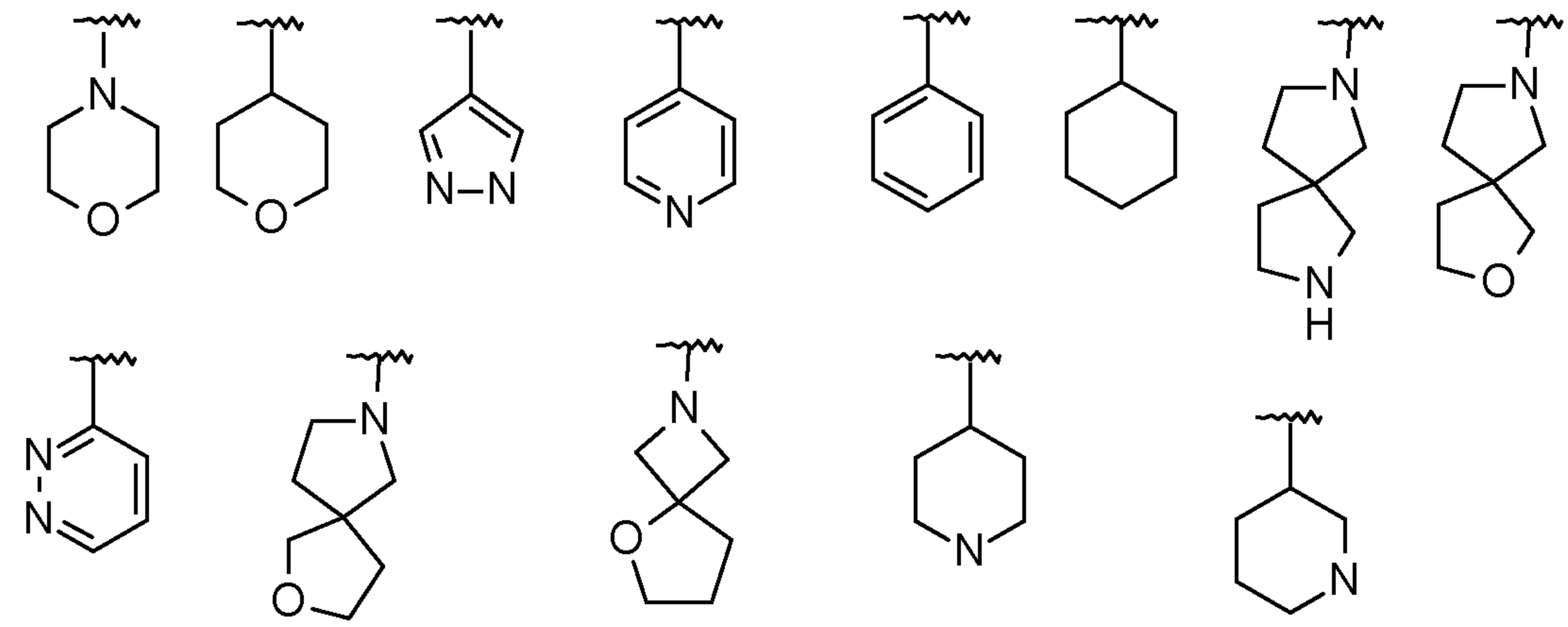
R^4 is H, R^5, =S, $=NR^5$, =O, OH, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$, NO_2, or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^5 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic cyclic alkyl having 3-7 C atoms which is un-substituted or mono-, di- or trisubstituted by by R^5 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NRSO_2R^4–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or by –CH=CH– groups and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or mono- or bicyclic heteroaryl, heterocyclyl, aryl or cyclic alkylaryl, containing 3 to 14 carbon atoms and 0-4 heteroatoms, independently selected from N, O and S, which is unsubstituted or mono-, di- or trisubstituted by R^5,

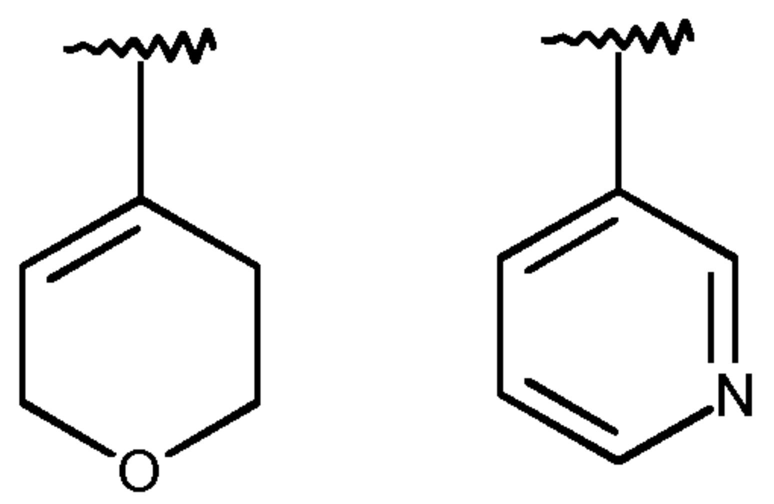
R^5, R^6 are independently of one another selected from the group consisting of H, =S, =NH, =O, OH, COOH, Hal, NH_2, SO_2CH_3, SO_2NH_2, CN, $CONH_2$, $NHCOCH_3$, $NHCONH_2$, NO_2 and linear or branched alkyl having 1-10 C atoms in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–,–COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl,

Hal is F, C, Br, or I,

and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compound according to claim 1, wherein R^1 is Hal or linear or branched alkyl having 1-10 C atoms which is unsubstituted or mono-, di- or trisubstituted by R^4 and in which 1-4 C atoms may be replaced, independently of one another, by O, S, SO, SO_2, NH, NCH_3, –OCO–, –NHCONH–, –NHCO–, $–NR^5SO_2R^6–$, –COO–, –CONH–, $–NCH_3CO–$, $–CONCH_3–$, –C≡C– groups and/or –CH=CH– groups, and/or, in addition, 1-10 H atoms may be replaced by F and/or Cl, or one of the following structures:

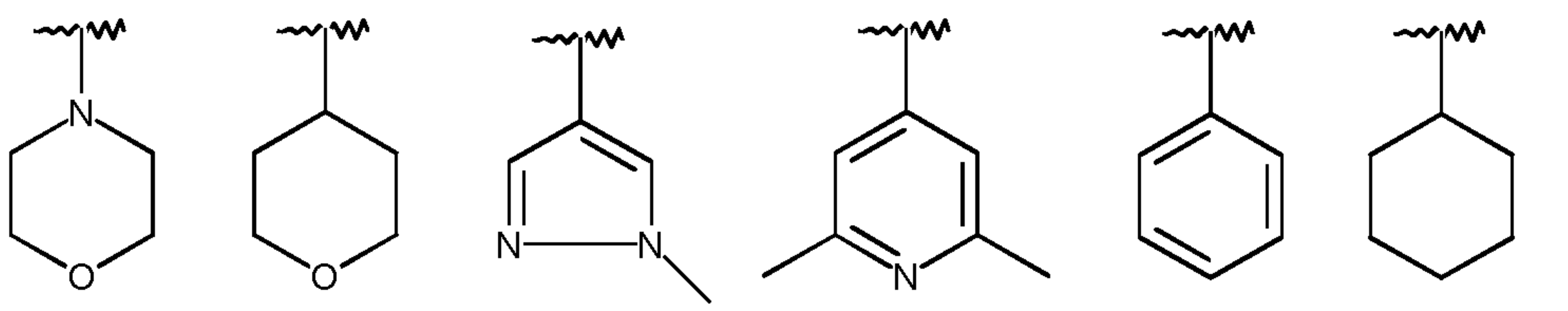


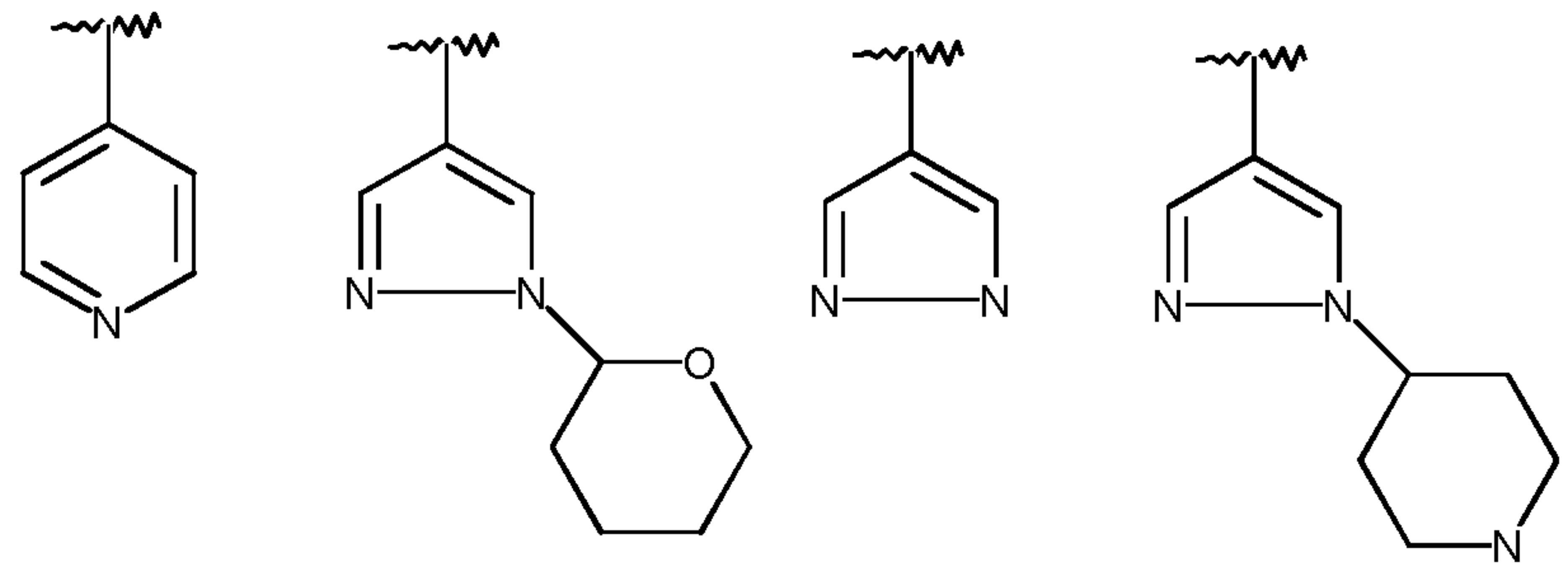


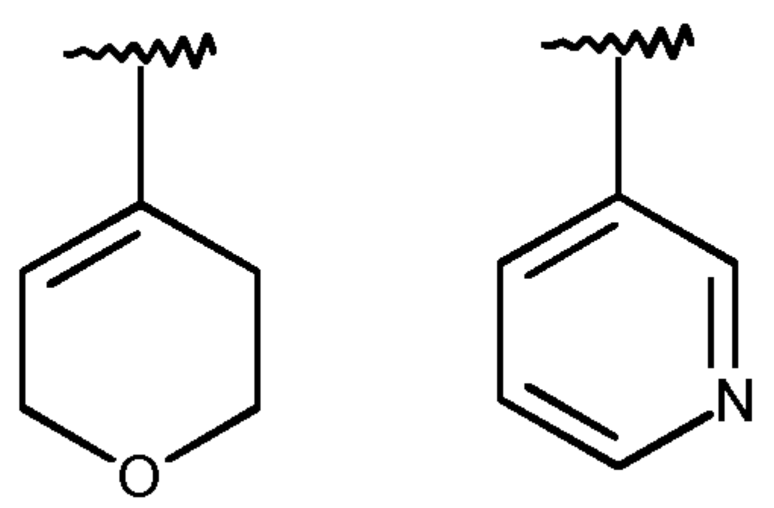
which is unsubstituted or mono-, di- or trisubstituted with R^4

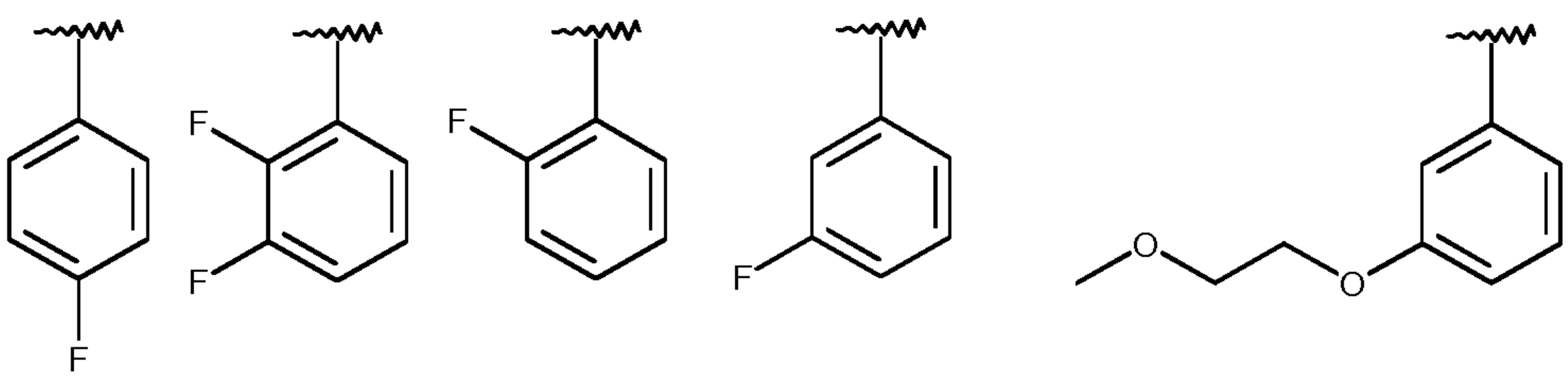
and wherein Q, Y, R^2, R^3, R^4, R^5 and R^6 have the meanings as disclosed in Claim 1, and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compound according to claim 1 or 2, wherein R^1 is Br or one of the following structures:





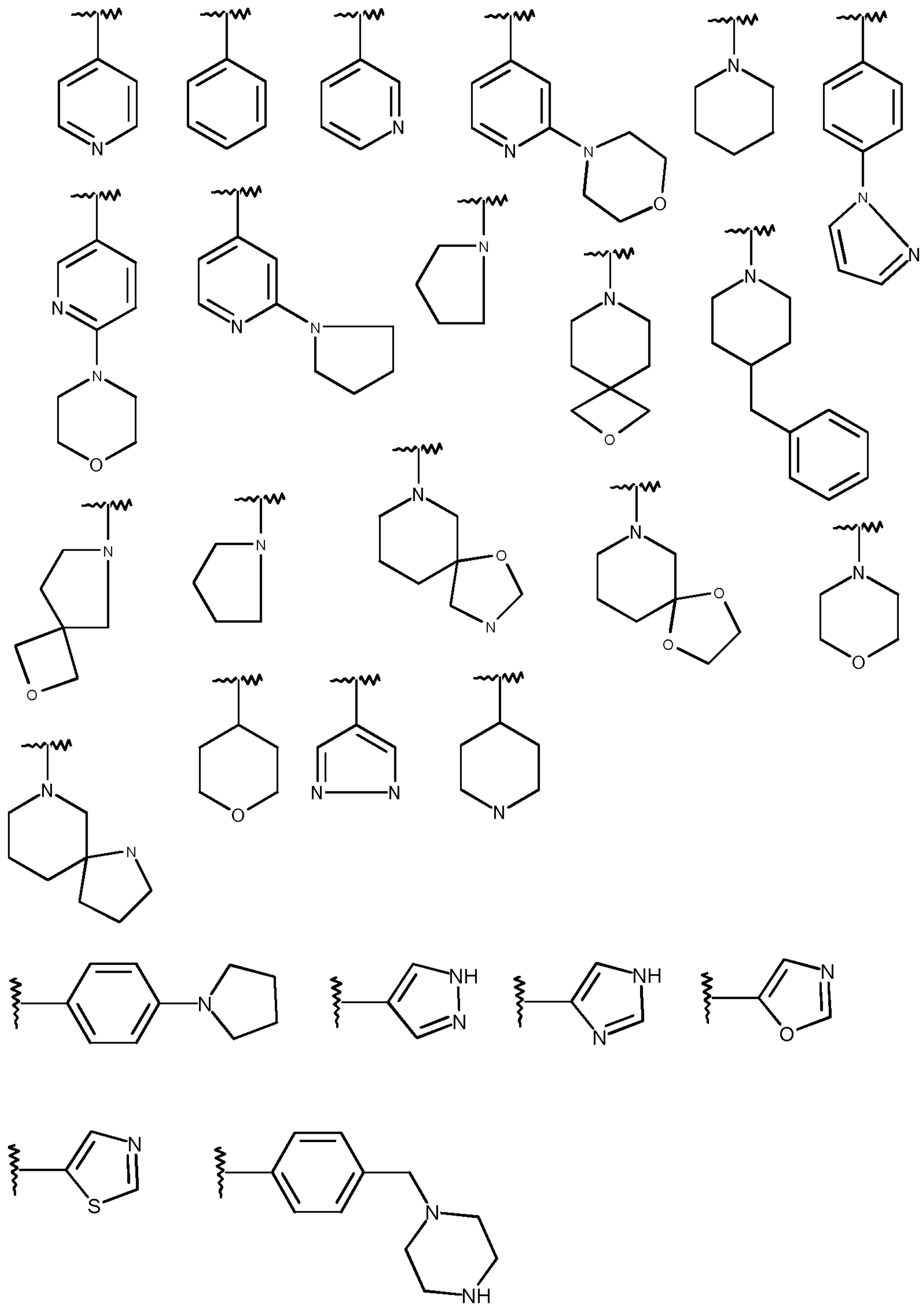




which is unsubstituted or mono-, di- or trisubstituted with R^5

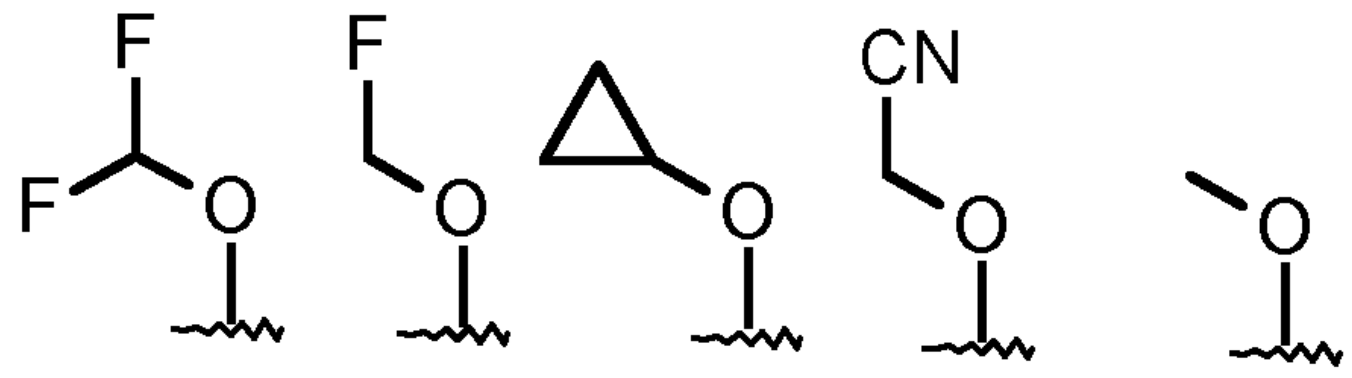
and wherein Q, Y, R^2, R^3, R^4, R^5 and R^6 have the meanings as disclosed in Claim 1, and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compound according to one or more of the preceding claims, wherein R^2 is one of the following structures:



which is unsubstituted or mono-, di- or trisubstituted with R^5
and wherein Q, Y, R^1, R^3, R^4, R^5 and R^6 have the meanings as disclosed in Claim 1, and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compound according to one or more of the preceding claims, wherein R^3 one of the following structures



and Q, Y, R^1, R^2, R^4, R^5 and R^6 have the meanings as disclosed in Claim 1, and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compound according to one or more of the preceding claims, wherein R^3 is OMe
and Q, Y, R^1, R^2, R^4, R^5 and R^6 have the meanings as disclosed in Claim 1, and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compound selected from the group consisting of:

No.	IUPAC-Name
1	7-Methoxy-4-phenyl-1H-benzoimidazol-2-ylamine
2	4-Fluoro-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
3	2-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-isonicotinamide
4	2-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-isonicotinamide
5	6-Bromo-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-nicotinamide
6	6-Bromo-N-(4-bromo-7-methoxy-1H-benzoimidazol-2-yl)-nicotinamide
7	N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
8	N-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-6-morpholin-4-yl-nicotinamide

9	N'-(7-Methoxy-4-phenyl-1H-benzoimidazol-2-yl)-N,N-dimethyl-formamidine
10	4-Chloromethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
11	4-Ethylaminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
12	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide
13	4-Aminomethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
14	4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-ylamine
15	4-Imidazol-1-ylmethyl-N-(7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-benzamide
16	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid (4-cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-amide
17	N-(4-Cyclohexyl-7-methoxy-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
18	7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-ylamine
19	7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-ylamine
20	7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-ylamine
21	4-hydroxy-N-(7-methoxy-4-morpholino-1H-benzimidazol-2-yl)-4-methyl-piperidine-1-carboxamide
22	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
23	N-(7-Methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-2-morpholin-4-yl-isonicotinamide
24	4-Hydroxy-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
25	4-Methoxy-7-phenyl-3H-imidazo[4,5-c]pyridin-2-ylamine
26	N-[7-Methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-2-morpholin-4-yl-isonicotinamide
27	4-Methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-ylamine

28	4-Methyl-piperidine-1-carboxylic acid (7-methoxy-4-phenyl-1H-benzoimidazol-2-yl)-amide
29	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-6-morpholin-4-yl-nicotinamide
30	2-(3-Hydroxy-3-methyl-pyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-isonicotinamide
31	3-Hydroxy-3-methyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
32	4-Hydroxy-4-trifluoromethyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
33	2-Oxa-7-aza-spiro[3.5]nonane-7-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
34	4-Difluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
35	4-Hydroxymethyl-4-methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
36	4-Fluoromethyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
37	4-Methoxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
38	3-Oxa-9-aza-spiro[5.5]undecane-9-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
39	4-Methyl-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
40	4-Hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
41	4-Benzyl-4-hydroxy-piperidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
42	N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide

43	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
44	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1-oxa-3,8-diazaspiro[4.5]decane-8-carboxamide
45	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,4-dioxa-8-azaspiro[4.5]decane-8-carboxamide
46	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]morpholine-4-carboxamide
47	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
48	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
49	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(methoxymethyl)benzamide
50	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,4-dioxo-1,3,8-triazaspiro[4.5]decane-8-carboxamide
51	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxo-1,8-diazaspiro[4.5]decane-8-carboxamide
52	4-(2-hydroxyethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2,3,6-tetrahydropyridine-1-carboxamide
53	3-butyl-4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
54	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-phenoxypiperidine-1-carboxamide
55	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(pyridin-3-yl)piperidine-1-carboxamide
56	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methylpropyl)piperidine-1-carboxamide
57	N-[4-(2,6-dimethylpyridin-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-(morpholin-4-yl)pyridine-4-carboxamide

58	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-oxopiperidine-1-carboxamide
59	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
60	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-oxo-2,8-diazaspiro[4.5]decane-8-carboxamide
61	3,3-diethyl-1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
62	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-5-oxo-1,4,9-triazaspiro[5.5]undecane-9-carboxamide
63	4-fluoro-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
64	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-oxaspiro[2.5]octane-1-carboxamide
65	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-{3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy}pyrazine-2-carboxamide
66	(chloromethyl)({2-[(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}-4-methylpiperidin-4-yl)oxy]ethyl})dimethylazanium hydrochloride
67	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
68	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
69	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
70	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-oxabicyclo[3.1.0]hexane-6-carboxamide
71	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
72	(1S,2S)-2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
73	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyrazine-2-carboxamide

74	4-hydroxy-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
75	4-benzyl-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
76	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
77	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
78	4-hydroxy-N-{7-methoxy-4-[1-(oxan-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
79	4-hydroxy-N-[7-methoxy-4-(1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
80	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-benzofuran-5-carboxamide
81	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyrazine-2-carboxamide
82	4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]-4-methylpiperidine-1-carboxamide
83	4-benzyl-4-hydroxy-N-[4-methoxy-7-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl]piperidine-1-carboxamide
84	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,2-oxazole-3-carboxamide
85	N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-6-azaspiro[3.4]octane-6-carboxamide
86	1-(1-chloro-3-hydroxypropan-2-yl)-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-pyrazole-4-carboxamide
87	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
88	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
89	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide

90	4-[(dimethylamino)methyl]-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
91	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-6-(morpholin-4-yl)pyridazine-3-carboxamide
92	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
93	N4-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
94	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(trifluoromethoxy)benzamide
95	2-bromo-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
96	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-4-carboxamide
97	4-[(1H-imidazol-1-yl)methyl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
98	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-benzoxazole-5-carboxamide
99	3-amino-4-hydroxy-N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
100	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
101	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide
102	4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-(prop-2-yn-1-yl)piperidine-1-carboxamide
103	4-benzyl-4-hydroxy-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1-carboxamide
104	2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
105	2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide

106	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
107	2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
108	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2,3-dihydro-1-benzofuran-5-carboxamide
109	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
110	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
111	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
112	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
113	(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
114	(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-7-oxa-2-azaspiro[4.5]decane-2-carboxamide
115	(5S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
116	(5R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
117	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
118	2-(4-hydroxy-4-methylpiperidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
119	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-{2-oxa-7-azaspiro[4.4]nonan-7-yl}pyridine-4-carboxamide
120	2-(4-fluorophenoxy)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methylpropanamide

121	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-hexahydro-1H-furo[3,4-c]pyrrole-5-carboxamide
122	2-(3-hydroxy-3-methylpyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]pyridine-4-carboxamide
123	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
124	1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidine-4-carboxylic acid
125	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
126	N1-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]piperidine-1,4-dicarboxamide
127	4-(diethylamino)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
128	4-hydroxy-N-{7-methoxy-4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
129	N-[7-methoxy-4-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
130	2-(1-{[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid
131	4-hydroxy-N-[7-methoxy-4-(2-methylphenyl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
132	2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-4-yl)acetic acid
133	N4-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
134	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
135	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide

136	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
137	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
138	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
139	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(morpholin-4-yl)pyridine-2-carboxamide
140	(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
141	(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(2-methoxyethyl)pyrrolidine-1-carboxamide
142	2-[(3R)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
143	2-[(3S)-3-hydroxy-3-methylpyrrolidin-1-yl]-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]acetamide
144	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
145	tert-butyl 4-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)piperidine-1-carboxylate
146	4-{[2-amino-7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-1-yl]methyl}benzoic acid
147	(3S)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
148	(3R)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-3-(methoxymethyl)pyrrolidine-1-carboxamide
149	(5S)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide
150	(5R)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-oxa-7-azaspiro[4.4]nonane-7-carboxamide

151	4-hydroxy-N-{7-methoxy-4-[1-(3-methylbutyl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
152	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(morpholin-4-yl)methyl]benzamide
153	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5R)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide
154	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-[(5S)-2-oxa-7-azaspiro[4.4]nonan-7-yl]pyridine-4-carboxamide
155	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
156	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
157	4-hydroxy-N-{4-methoxy-7-[1-(piperidin-4-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
158	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-(2-methoxyethoxy)pyridine-2-carboxamide
159	2-(1-{[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}piperidin-3-yl)acetic acid
160	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
161	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
162	N5-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
163	4-hydroxy-N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
164	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
165	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide

166	3-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]propanamide
167	1-(2-Hydroxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
168	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide
169	1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
170	5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
171	5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
172	1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
173	Thiazole-5-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
174	5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
175	4-(4-Methyl-piperazin-1-yl)-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
176	4-Hydroxy-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
177	4-Acetylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
178	4-Dimethylamino-but-2-ynoic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
179	(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
180	(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
181	(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide

182	(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-benzoimidazol-2-yl]-amide
183	5-Methyl-isoxazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide
184	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
185	1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid (7-methoxy-4-morpholin-4-yl-1H-benzoimidazol-2-yl)-amide
186	Pyridine-2,5-dicarboxylic acid 2-dimethylamide 5-{[7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide}
187	1-(2-Methoxy-ethyl)-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
188	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-morpholin-4-ylmethyl-benzamide
189	N-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-4-(4-methyl-piperazin-1-ylmethyl)-benzamide
190	1-Methyl-1H-pyrazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
191	5-Methyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
192	5-Cyclopropyl-isoxazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
193	1-(2-Methoxy-ethyl)-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
194	1-Methyl-1H-[1,2,3]triazole-4-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
195	1-Cyano-cyclopropanecarboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
196	Thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide

197	2-Methyl-oxazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
198	2-Methyl-thiazole-5-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
199	Imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
200	5-Amino-2H-[1,2,4]triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
201	(S)-3-Methanesulfonyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
202	(S)-3-Fluoro-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
203	(S)-3-Cyano-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
204	(R)-3-Dimethylaminomethyl-pyrrolidine-1-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
205	Pyrazolo[1,5-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
206	1H-[1,2,4]Triazole-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
207	5,6,7,8-Tetrahydro-imidazo[1,2-a]pyridine-3-carboxylic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
208	2,3-Dimethyl-3H-imidazole-4-sulfonic acid [7-methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-amide
209	1-[7-Methoxy-4-(tetrahydro-pyran-4-yl)-1H-benzoimidazol-2-yl]-3-thiazol-2-ylmethyl-urea
210	N-[7-methoxy-4-(morpholin-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide
211	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-1,2,3-triazole-4-carboxamide
212	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-1,2,3-triazole-4-carboxamide

213	1-cyano-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
214	N5-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N2,N2-dimethylpyridine-2,5-dicarboxamide
215	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
216	N-[4-(azepan-1-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
217	N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
218	N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
219	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1,3-thiazole-5-carboxamide
220	(3R)-3-methanesulfonyl-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
221	(3S)-3-fluoro-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
222	4-hydroxy-N-[7-methoxy-4-(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
223	(3S)-3-(aminomethyl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]pyrrolidine-1-carboxamide
224	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
225	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
226	1-cyano-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]cyclopropane-1-carboxamide
227	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-thiazole-5-carboxamide
228	3-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea

229	N-{7-[1-(difluoromethyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-hydroxy-4-methylpiperidine-1-carboxamide
230	4-hydroxy-N-(4-methoxy-7-{1-[2-(2-methoxyethoxy)ethyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
231	4-hydroxy-N-{4-methoxy-7-[1-(pyridin-2-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
232	N-[7-methoxy-4-(1-propylcyclopropyl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
233	N-[4-(hexan-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
234	N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
235	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-4-[(4-methylpiperazin-1-yl)methyl]benzamide
236	4-hydroxy-N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
237	4-hydroxy-N-(4-methoxy-7-{1-[(pyridin-3-yl)methyl]-1H-pyrazol-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
238	4-hydroxy-N-{7-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]-4-methoxy-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
239	N-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
240	N4-[4-(3-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
241	4-hydroxy-N-{4-methoxy-7-[1-(oxolan-3-yl)-1H-pyrazol-4-yl]-1H-1,3-benzodiazol-2-yl}-4-methylpiperidine-1-carboxamide
242	N4-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
243	N-[4-(2-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

244	N-[4-methoxy-1-methyl-7-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
245	tert-butyl 3-(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-4-methoxy-1H-1,3-benzodiazol-7-yl}-1H-pyrazol-1-yl)azetidine-1-carboxylate
246	N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-5-oxopyrrolidine-3-carboxamide
247	3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]-1-[(1,3-thiazol-2-yl)methyl]urea
248	4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
249	1-[(3R,4S)-4-fluoropyrrolidin-3-yl]-3-[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]urea
250	4-(2,5-dioxopyrrolidin-1-yl)-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
251	tert-butyl (3S,4R)-3-fluoro-4-({[7-methoxy-4-(1-methyl-1H-pyrazol-4-yl)-1H-1,3-benzodiazol-2-yl]carbamoyl}amino)pyrrolidine-1-carboxylate
252	N4-[7-methoxy-4-(1,2,3,6-tetrahydropyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
253	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1H-imidazole-4-carboxamide
254	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-imidazole-5-carboxamide
255	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1H-imidazole-4-carboxamide
256	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide
257	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-thiazole-5-carboxamide
258	2-amino-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-thiazole-5-carboxamide
259	N4-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
260	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide

261	N4-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
262	N4-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
263	3-{[dimethyl(oxo)-lambda6-sulfanylidene]amino}-N-[7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]benzamide
264	N-[4-(3,6-dihydro-2H-pyran-4-yl)-5-fluoro-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
265	N-[7-(3-fluorophenyl)-4-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
266	N-[4-methoxy-7-(pyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
267	N-{4-methoxy-7-[3-(2-methoxyethoxy)phenyl]-1H-1,3-benzodiazol-2-yl}-1H-imidazole-4-carboxamide
268	N-[4-methoxy-7-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
269	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1,3-dimethyl-1H-pyrazole-4-carboxamide
270	4-hydroxy-N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
271	4-hydroxy-N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
272	4-hydroxy-N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
273	4-hydroxy-N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
274	4-hydroxy-N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
275	4-hydroxy-N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-4-methylpiperidine-1-carboxamide
276	(2Z)-2-cyano-3-hydroxy-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)but-2-enamide
277	N4-[5-fluoro-7-methoxy-4-(oxan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide

278	N-(7-methoxy-4-{1H-pyrrolo[2,3-b]pyridin-4-yl}-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
279	N-[4-(1H-indazol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
280	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
281	N-[7-methoxy-4-(1-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
282	N-[7-methoxy-4-(3-methyl-1H-indazol-5-yl)-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
283	N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
284	N2-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N5,N5-dimethylpyridine-2,5-dicarboxamide
285	4-(2,5-dioxopyrrolidin-1-yl)-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)benzamide
286	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyridine-3-carboxamide
287	4,4-difluoro-N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)piperidine-1-carboxamide
288	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-b]pyridazine-3-carboxamide
289	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)imidazo[1,2-a]pyrimidine-3-carboxamide
290	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-(pyridin-4-yl)-1H-imidazole-4-carboxamide
291	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-5H,6H,7H,8H-imidazo[1,2-a]pyridine-3-carboxamide
292	N-[4-(2,3-dihydro-1H-indol-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-hydroxy-4-methylpiperidine-1-carboxamide
293	N1-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N4-propylbenzene-1,4-dicarboxamide
294	N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(4-methylpiperazine-1-carbonyl)benzamide
295	N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-(2-methoxyethyl)-N1-methylbenzene-1,4-dicarboxamide

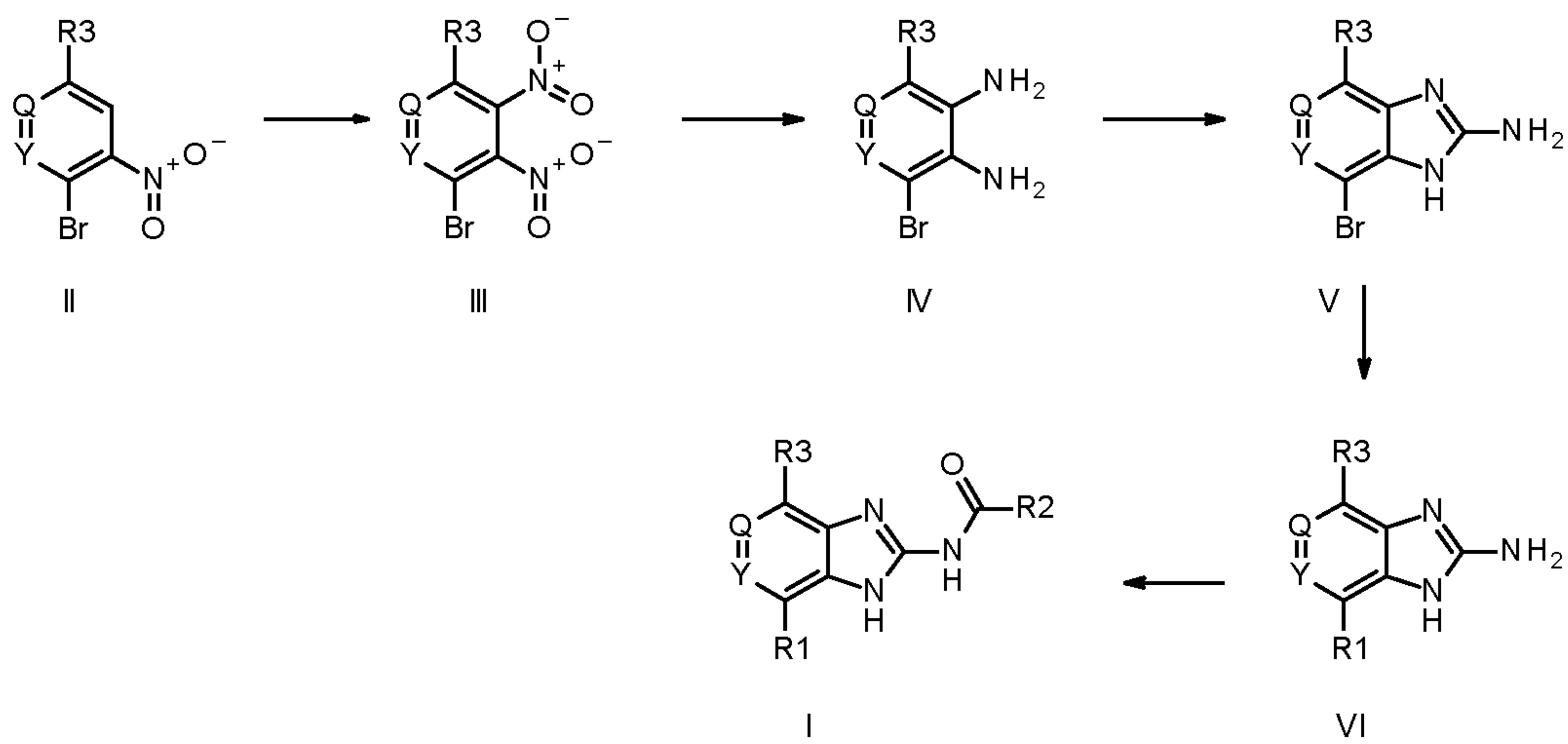
296	N1-[2-(dimethylamino)ethyl]-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methylbenzene-1,4-dicarboxamide
297	N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-N1-methyl-N1-propylbenzene-1,4-dicarboxamide
298	N-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)-4-(morpholine-4-carbonyl)benzamide
299	N-[4-methoxy-7-(2-methylpyridin-4-yl)-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
300	N-(5-cyano-7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
301	N-(4-{imidazo[1,2-a]pyridin-7-yl}-7-methoxy-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
302	N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
303	4-hydroxy-N-[4-(1H-indol-5-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
304	N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
305	4-hydroxy-N-[4-(1H-indol-7-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-methylpiperidine-1-carboxamide
306	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-methyl-1H-pyrazole-4-carboxamide
307	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-1-(2-methoxyethyl)-1H-pyrazole-4-carboxamide
308	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-methyl-1,3-oxazole-5-carboxamide
309	N4-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-N1,N1-dimethylbenzene-1,4-dicarboxamide
310	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
311	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
312	N1-(2-hydroxyethyl)-N4-(4-methoxy-7-phenyl-1H-1,3-benzodiazol-2-yl)benzene-1,4-dicarboxamide

313	N4-[7-methoxy-4-(1,4-oxazepan-4-yl)-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
314	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
315	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
316	N4-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
317	4-(2,5-dioxopyrrolidin-1-yl)-N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]benzamide
318	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
319	N4-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
320	N-[4-(2,6-dimethoxypyridin-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide
321	N-[7-methoxy-4-(pyridin-3-yl)-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
322	N-[4-(2,5-dihydrofuran-3-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
323	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-2-methyl-1,3-oxazole-5-carboxamide
324	N4-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-N1,N1-dimethylbenzene-1,4-dicarboxamide
325	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
326	(4-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}morpholin-2-yl)methyl carbamate
327	(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl cyanate
328	(1-{2-[(4-hydroxy-4-methylpiperidine-1-carbonyl)amino]-7-methoxy-1H-1,3-benzodiazol-4-yl}piperidin-3-yl)methyl carbamate
329	N-(7-methoxy-4-phenyl-1H-1,3-benzodiazol-2-yl)-2-oxa-8-azaspiro[4.5]decane-8-carboxamide

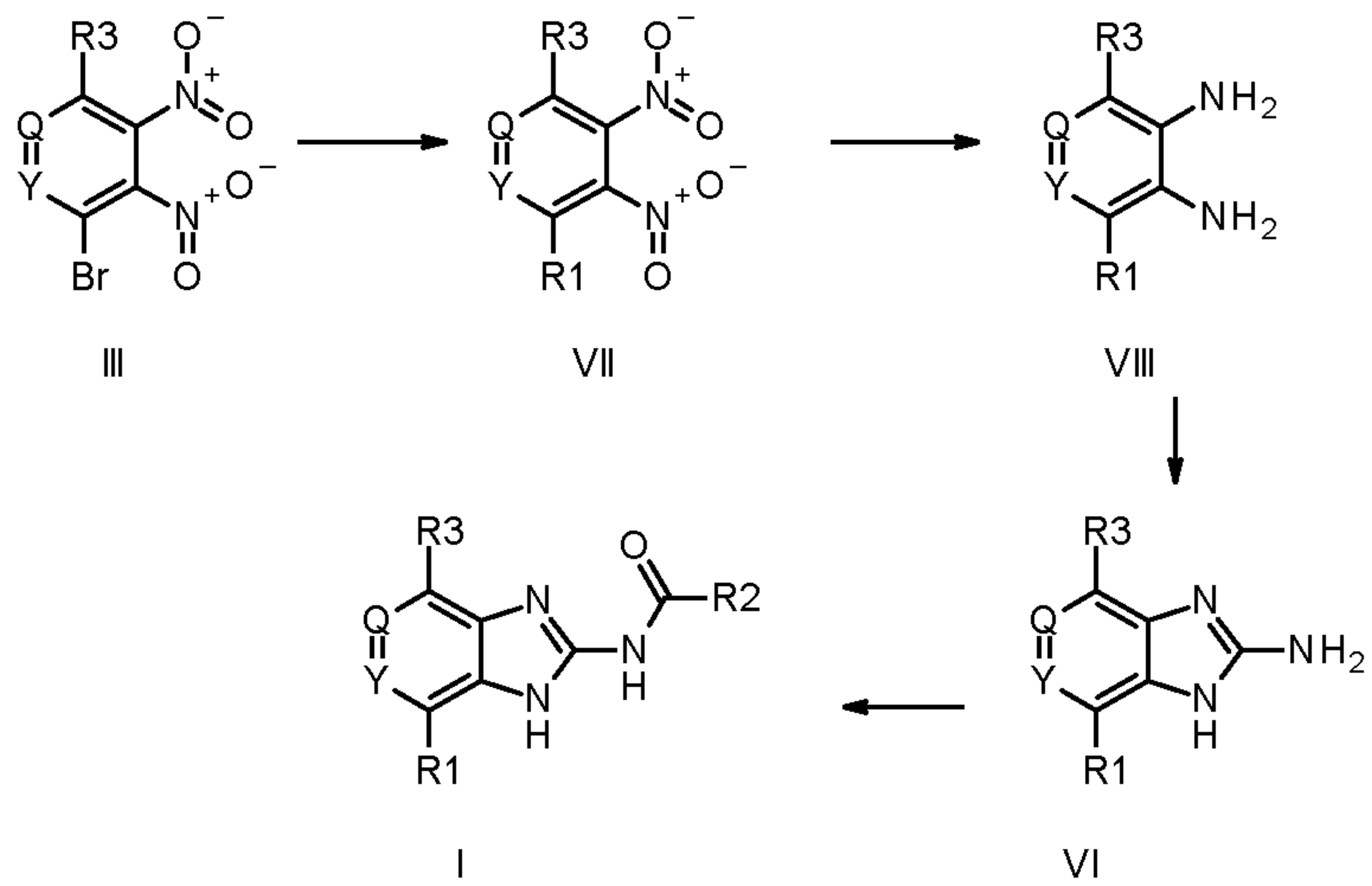
330	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1H-imidazole-4-carboxamide
331	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-1-methyl-1H-pyrazole-4-carboxamide
332	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
333	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-8-oxa-2-azaspiro[4.5]decane-2-carboxamide
334	N-[4-(3,6-dihydro-2H-pyran-4-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
335	N-[4-(4-fluorophenyl)-7-methoxy-1H-1,3-benzodiazol-2-yl]-4-[(2-oxopyrrolidin-1-yl)methyl]benzamide
336	N-[4-(1H-indol-6-yl)-7-methoxy-1H-1,3-benzodiazol-2-yl]cyclopropanecarboxamide

and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

8. Process for the preparation of a compound of the formula I, characterized in that



a) a compound of the formula II undergoes a nitration reaction, followed by a reduction to give a compound of formula IV, a compound of formula IVI is cyclized to give a compound of formula V, a compound of formula V is reacted in a Suzuki type reaction toformula VI employing the use of catalyst and base, a compound of formula VI is converted to a compound of the formula VII by standard amidation or carbamide formation conditions to give a compound of the formula I and wherein Q, Y, R^1, R^2 and R^3 have the meanings as disclosed above,



b) a compound of the formula III is reacted with a boronic ester or acid under Suzuki-type reaction conditions to give a compound of the formula VII or reacted with an amine in a nuclophilic substitution reaction under increased temperature to form a compound of the formula VII , a compound of formula VII is reduced to a compound of the formula VIIand cyclized to a compound of the formula VI and finally reacted with to compound of the formula I under standard amidation or carbamide formation conditions and wherein Q, Y, R^1, R^2 and R^3 have the meanings as disclosed above,

c) the base of a compound of the formula I is converted into one of its salts by treatment with an acid, or

d) an acid of a compound of the formula I is converted into one of its salts by treatment with a base.

9. Compound according to one or more of Claims 1 to 7 and physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios, as adenosine A_{2A} and/or A_{2B} receptor inhibitor.

10. Pharmaceutical preparation comprising at least one compound according to one or more of Claims 1 to 7 and/or physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios.

11. Pharmaceutical preparation according to Claim 10 comprising further excipients and/or adjuvants.

12. Pharmaceutical preparation comprising at least one compound according to one or more of Claims 1 to 7 and/or physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active compound.

13. Process for the preparation of a pharmaceutical preparation, characterised in that a compound according to one or more of Claims 1 to 7 and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, is brought into a suitable dosage form together with a solid, liquid or semi-liquid excipient or adjuvant.

14. Medicament comprising at least one compound according to one or more of Claims 1 to 7 and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states.

15. Medicament comprising at least one compound according to one or more of Claims 1 to 7 and/or one of its physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers, including mixtures thereof in all ratios, for use in the treatment and/or prophylaxis of physiological and/or pathophysiological states, selected from the group consisting of hyperproliferative and infectious diseases and disorders.

16. Medicament according to Claim 15, wherein the hyperproliferative disease or disorder is cancer.

17. Medicament according to Claim 16, wherein the cancer is selected from the group consisting of acute and chronic lymphocytic leukemia, acute granulocytic leukemia, adrenal cortex cancer, bladder cancer, brain cancer, breast cancer, cervical cancer, cervical hyperplasia, cervical cancer, chorio cancer, chronic granulocytic leukemia, chronic lymphocytic leukemia, colon cancer, endometrial ccancer, esophageal cancer, essential thrombocytosis, genitourinary carcinoma, glioma, glioblastoma, hairy cell leukemia, head and neck carcinoma, Hodgkin's disease, Kaposi's sarcoma, lung carcinoma, lymphoma, malignant carcinoid carcinoma, malignant hypercalcemia, malignant melanoma, malignant pancreatic insulinoma, medullary thyroid carcinoma, melanoma, multiple myeloma, mycosis fungoides, myeloid and lymphocytic leukemia, neuroblastoma, non-Hodgkin's lymphoma, non-small cell lung cancer, osteogenic sarcoma, ovarian carcinoma, pancreatic carcinoma, polycythemia vera, primary brain carcinoma, primary macroglobulinemia, prostatic cancer, renal cell cancer, rhabdomyosarcoma, skin cancer, small-cell lung cancer, soft-tissue sarcoma, squamous cell cancer, stomach cancer, testicular cancer, thyroid cancer and Wilms' tumor.

18. Medicament according to Claim 15, wherein the hyperproliferative disease or disorder is selected from the group consisting of age-related macular degeneration, Crohn's disease, cirrhosis, chronic inflammatory-related disorders, proliferative diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, granulomatosis, immune hyperproliferation associated with organ or tissue transplantation and an immunoproliferative disease or disorder selected from the group comnsisting of inflammatory bowel disease, psoriasis, rheumatoid arthritis, systemic lupus erythematosus (SLE), vascular hyperproliferation secondary to retinal hypoxia and vasculitis.

19. Medicament according to Claim 15, wherein the infectious disease or disorder is selected from the group consisting of
    a) virally induced infectious diseases which are caused by retroviruses, hepadnaviruses, herpesviruses, flaviviridae and/or adenoviruses wherein the retroviruses are selected from lentiviruses or oncoretroviruses, wherein the lentivirus is selected from the group consisting of HIV-1, HIV-2, FIV, BIV, SIVs, SHIV, CAEV, VMV and EIAV and the oncoretrovirus is

selected from the group consisting of HTLV-I, HTLV-II and BLV, the hepadnavirus is selected from the group consisting of HBV, GSHV and WHV, the herpesivirus is selected from the group from the group consisting of HSV I, HSV II, EBV, VZV, HCMV or HHV 8 and the flaviviridae is selected from the group consisting of HCV, West nile and Yellow Fever,

b) bacterial infectious diseases which are caused by Gram-positive bacteria wherein the Gram-positive bacteria are selected from the group consisting of methicillin-susceptible and methicillin-resistant staphylococci (including Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus saprophyticus, and coagulase-negative staphylococci), glycopeptides-intermediate susceptible Staphylococcus aureus (GISA), penicillin-susceptible and penicillin-resistant streptococci (including Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus avium, Streptococcus bovis, Streptococcus lactis, Streptococcus sanguis and Streptococci Group C (GCS), Streptococci Group G (GGS) and viridans streptococci), enterococci (including vancomycinsusceptible and vancomycin-resistant strains such as Enterococcus faecalis and Enterococcus faecium), Clostridium difficile, listeria monocytogenes, Corynebacterium jeikeium, Chlamydia spp (including C. pneumoniae) and Mycobacterium tuberculosis,

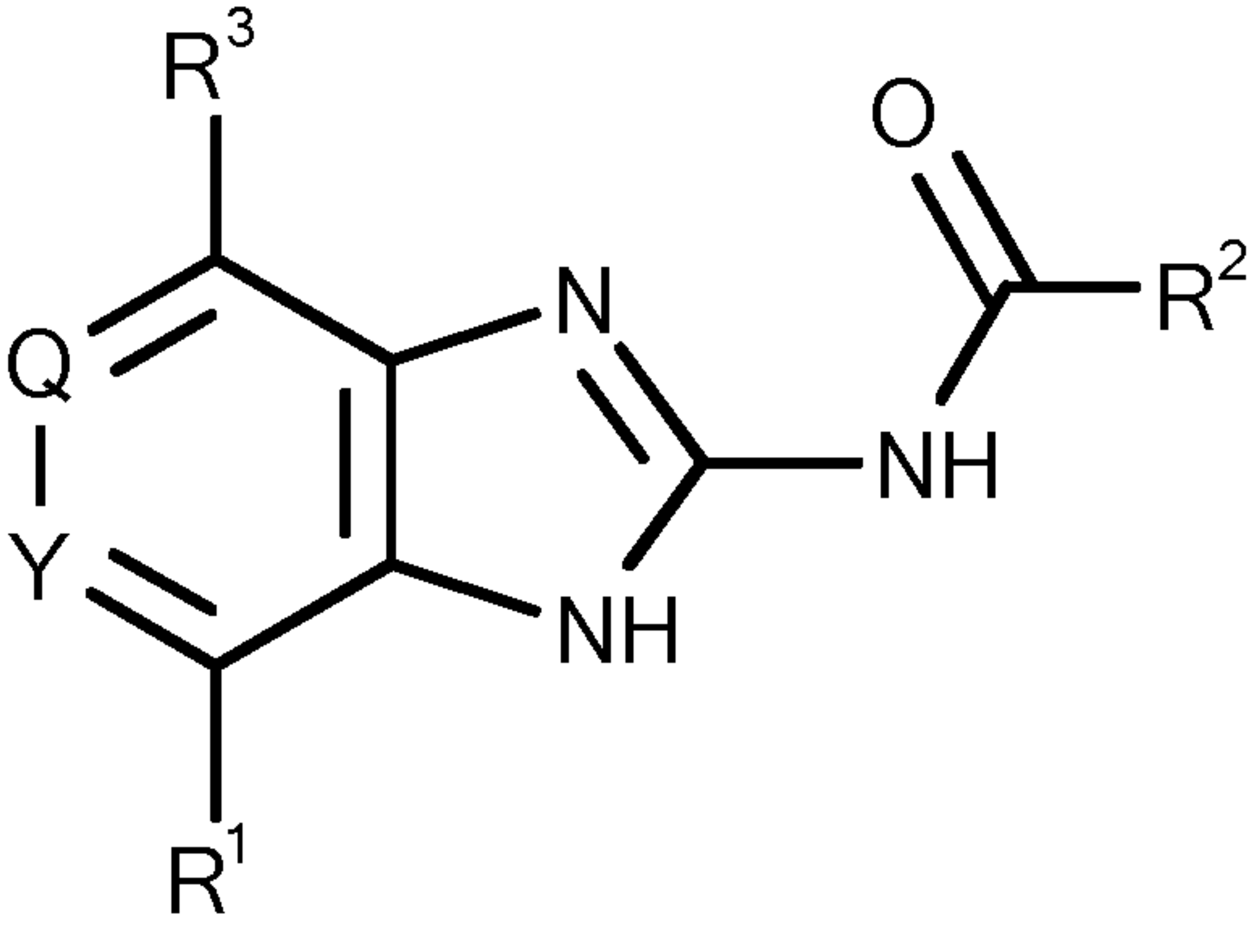
c) bacterial infectious diseases which are caused by Gram-negative bacteria wherein the Gram-negative bacteria are selected from the group consisting of the Genus Enterobacteriacae, including Escherichia spp. (including Escherichia coli), Klebsiella spp., Enterobacter spp., Citrobacter spp., Serratia spp., Proteus spp., Providencia spp., Salmonella spp., Shigella spp., the genus Pseudomonas (including P. aeruginosa), Moraxella spp. (including M. catarrhalis), Haemophilus spp. and Neisseria spp.,

d) infectious diseases induced by intracellular active parasites selected from the group consisting of phylum Apicomplexa, or Sarcomastigophora (including Trypanosoma, Plasmodia, Leishmania, Babesia or Theileria), Cryptosporidia, Sacrocystida, Amoebia, Coccidia and Trichomonadia.

20. Set (kit) consisting of separate packs of

a) an effective amount of a compound according to one or more of Claims 1 to 7 and/or physiologically acceptable salts, derivatives, solvates, prodrugs and stereoisomers thereof, including mixtures thereof in all ratios, and

b) an effective amount of a further medicament active compound.



(I)