COMPOUNDS FOR TREATING SPINAL MUSCULAR ATROPHY

[0001] The technology described herein has not been made with U.S. Government support.

CROSS-REFERENCE

[0002] This application claims the benefit of priority to United States Provisional Application Serial No. 61/597,523, filed February 10, 2012, which is incorporated herein by reference in its entirety and for all purposes.

STATEMENT ON JOINT RESEARCH AGREEMENT

[0003] The subject matter disclosed was developed and the claimed invention was made by, or on behalf of, one or more parties to a joint research agreement that was in effect on or before the effective filing date of the claimed invention;

[0004] the claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and

[0005] the application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement.

INTRODUCTION

[0006] Provided herein are compounds, compositions thereof and uses therewith for treating Spinal Muscular Atrophy.

BACKGROUND

[0007] Spinal muscular atrophy (SMA), in its broadest sense, describes a collection of inherited and acquired central nervous system (CNS) diseases characterized by progressive motor neuron loss in the spinal cord and brainstem causing muscle weakness and muscle atrophy. The most common form of SMA is caused by mutations in the Survival Motor Neuron (SMN) gene and manifests over a wide range of severity affecting infants through adults (Crawford and Pardo, Neurobiol. Dis., 1996, 3:97).

[0008] Infantile SMA is the most severe form of this neurodegenerative disorder. Symptoms include muscle weakness, poor muscle tone, weak cry, limpness or a tendency to flop, difficulty sucking or swallowing, accumulation of secretions in the lungs or throat, feeding difficulties, and increased susceptibility to respiratory tract infections. The legs tend to be weaker than the arms and developmental milestones, such as lifting the head or sitting up, cannot be reached. In general, the earlier the symptoms appear, the shorter the lifespan. As the motor neuron cells deteriorate, symptoms appear shortly afterward. The severe forms of the disease are fatal and all forms have no known cure. The course of SMA is directly related to the rate of motor neuron cell deterioration and the resulting severity of weakness. Infants with a severe form of SMA frequently succumb to respiratory disease due to weakness in the muscles that support breathing. Children with milder forms of SMA live much longer, although they may need extensive medical support, especially those at the more severe end of the spectrum. The clinical spectrum of SMA disorders has been divided into the following five groups.

[0009] (a) Type 0 SMA (In Utero SMA) is the most severe form of the disease and begins before birth. Usually, the first symptom of Type 0 SMA is reduced movement of the fetus that can first be observed between 30 and 36 weeks of pregnancy. After birth, these newborns have little movement and have difficulties with swallowing and breathing.

[0010] (b) Type 1 SMA (Infantile SMA or Werdnig-Hoffmann disease) typically presents symptoms between 0 and 6 months. This form of SMA is also very severe. Patients never achieve the ability to sit, and death usually occurs within the first 2 years without ventilatory support.

[0011] (c) Type 2 SMA (Intermediate SMA) has an age of onset at 7-18 months. Patients achieve the ability to sit unsupported, but never stand or walk unaided. Prognosis in this group is largely dependent on the degree of respiratory involvement.

[0012] (d) Type 3 SMA (Juvenile SMA or Kugelberg-Welander disease) is generally diagnosed after 18 months. Type 3 SMA individuals are able to walk independently at some point during their disease course but often become wheelchair-bound during youth or adulthood.

[0013] (e) Type 4 SMA (Adult onset SMA). Weakness usually begins in late adolescence in the tongue, hands, or feet, then progresses to other areas of the body. The course of adult SMA is much slower and has little or no impact on life expectancy.

[0014] The SMN gene has been mapped by linkage analysis to a complex region in chromosome 5q. In humans, this region contains an approximately 500 thousand base pairs (kb) inverted duplication resulting in two nearly identical copies of the SMN gene. SMA is caused by an inactivating mutation or deletion of the telomeric copy of the gene (SMN1) in both chromosomes, resulting in the loss of SMN1 gene function. However, all patients retain the centromeric copy of the gene (SMN2), and the copy number of the SMN2 gene in SMA patients generally correlates inversely with the disease severity; *i.e.*, patients with less severe SMA have more copies of SMN2. Nevertheless, SMN2 is unable to compensate completely for the loss of SMN1 function due to alternative splicing of exon 7 caused by a translationally silent C to T mutation in exon 7. As a result, the majority of transcripts produced from SMN2 lack exon 7 (SMN2 Δ7), and encode a truncated Smn protein that has an impaired function and is rapidly degraded.

[0015] The Smn protein is thought to play a role in RNA processing and metabolism, having a well characterized function of mediating the assembly of a specific class of RNA-protein complexes termed snRNPs. Smn may have other functions in motor neurons, however its role in preventing the selective degeneration of motor neurons is not well established.

[0016] In most cases, SMA is diagnosed based on clinical symptoms and by the absence of all copies of exon 7 in the SMN1 gene, as determined by genetic testing. However, in approximately 5% of cases, SMA is caused by mutations other than a deletion of the entire SMN1 gene or other than a deletion of the entire exon 7 in the SMN1 gene, some known and others not yet defined. In such cases, when the SMN1 gene test is not feasible or the SMN1 gene sequence does not show any abnormality, other tests such as an electromyography (EMG) or muscle biopsy may be indicated.

[0017] Medical care for SMA patients at present is limited to supportive therapy including respiratory, nutritional and rehabilitation care; there is no drug known to address the underlying cause of the disease. Current treatment for SMA consists of prevention and management of the secondary effects of chronic motor unit loss. The major management issue in Type 1 SMA is the prevention and early treatment of pulmonary problems, which are the primary cause of death in the majority of the cases. While some infants afflicted with SMA grow to be adults, those with Type 1 SMA have a life expectancy of less than two years.

[0018] Several mouse models of SMA have been developed. In particular, the SMNΔ7 model (Le et al., Hum. Mol. Genet., 2005, 14:845) carries both the SMN2 gene and several copies of the SMN2Δ7 cDNA and recapitulates many of the phenotypic features of Type 1 SMA. The SMNΔ7 model can be used for both SMN2 expression studies as well as the evaluation of motor function and survival. The C/C-allele mouse model (Jackson Laboratory strain No.: 008714) provides a less severe SMA disease model, with mice having reduced levels of both SMN2 full length (SMN2 FL) mRNA and Smn protein. The C/C-allele mouse phenotype has the SMN2 gene and a hybrid mSmn1-SMN2 gene that undergoes alternative splicing, but does not have overt muscle weakness. The C/C-allele mouse model is used for SMN2 expression studies.

[0019] As a result of improved understanding of the genetic basis and pathophysiology of SMA, several strategies for treatment have been explored, but none have yet demonstrated success in the clinic.

[0020] Gene replacement of SMN1, using viral delivery vectors, and cell replacement, using differentiated $SMN1^{+/+}$ stem cells, have demonstrated efficacy in animal models of SMA. More research is needed to determine the safety and immune response and to address the requirement for the initiation of treatment at the neonatal stage before these approaches can be applied to humans.

[0021] Correction of alternative splicing of SMN2 in cultured cells has also been achieved using synthetic nucleic acids as therapeutic agents: (i) antisense oligonucleotides that target sequence elements in SMN2 pre-mRNA and shift the outcome of the splicing reaction toward the generation of full length SMN2 mRNA (Passini et al., Sci. Transl. Med., 2011, 3:72ra18; and, Hua et al., Nature, 2011, 478:123) and (ii) trans-splicing RNA molecules that provide a fully functional RNA sequence that replace the mutant fragment during splicing and generate a full length SMN1 mRNA (Coady and Lorson, J Neurosci., 2010, 30:126).

[0022] Other approaches under exploration include searching for drugs that increase Smn levels, enhance residual Smn function, or compensate for loss of Smn. Aminoglycosides have been shown to enhance expression of stabilized Smn protein produced from SMN2 Δ7 mRNA by promoting the translational read-through of the aberrant stop codon, but have poor central nervous system penetration and are toxic after repeated dosing. Chemotherapeutic agents, such as aclarubicin, have been shown to increase Smn protein in cell culture; however, the toxicity

profile of these drugs prohibits long-term use in SMA patients. Some drugs under clinical investigation for the treatment of SMA include transcription activators such as histone deacetylase ("HDAC") inhibitors (*e.g.*, butyrates, valproic acid, and hydroxyurea), and mRNA stabilizers (mRNA decapping inhibitor RG3039 from Repligen), intended to increase the amount of total RNA transcribed from the SMN2 gene. However, the use of HDAC inhibitors or mRNA stabilizers does not address the underlying cause of SMA and may result in a global increase in transcription and gene expression with potential safety problems in humans.

[0023] In an alternative approach, neuroprotective agents such as olesoxime have been chosen for investigation. Such strategies are not aimed at increasing the production of functional Smn for the treatment of SMA, but instead are being explored to protect the Smn-deficient motor neurons from neurodegeneration.

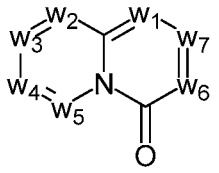
[0024] A system designed to identify compounds that increase the inclusion of exon 7 of SMN into RNA transcribed from the SMN2 gene and certain benzooxazole and benzoisoxazole compounds identified thereby have been described in International Application PCT/US2009/003238 filed May 27, 2009 (published as International Publication Number WO2009/151546 and United States Publication Number US2011/0086833). A system designed to identify compounds that produce a stabilized Smn protein from SMN2 Δ7 mRNA and certain isoindolinone compounds identified thereby have been described in International Application PCT/US2009/004625 filed August 13, 2009 (published as International Publication Number WO2010/019236 and United States Publication Number US2011/0172284). Each of the foregoing documents is herein incorporated in their entirety and for all purposes.

[0025] All other documents referred to herein are incorporated by reference into the present application as though fully set forth herein.

[0026] Despite the progress made in understanding the genetic basis and pathophysiology of SMA, there remains a need to identify compounds that alter the course of spinal muscular atrophy, one of the most devastating childhood neurological diseases.

SUMMARY

[0027] In one aspect, provided herein are compounds of Formula (I):



(I)

[0028] or a form thereof, wherein w_1, w_2, w_3, w_4, w_5, w_6 and w_7 are as defined herein. In one embodiment, provided herein is a pharmaceutical composition comprising a compound of Formula (I) or a form thereof, and a pharmaceutically acceptable carrier, excipient or diluent. In a specific embodiment, provided herein is a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof for treating spinal muscular atrophy (SMA).

[0029] SMA is caused by deletion or mutation of the SMN1 gene, resulting in selective degeneration of Smn-deficient motor neurons. Although human subjects retain several copies of the SMN2 gene, the small amount of functional Smn protein expressed from SMN2 does not fully compensate for the loss of Smn that would have been expressed from the SMN1 gene. The compounds, compositions thereof and uses therewith described herein are based, in part, on the Applicants discovery that a compound of Formula (I) increases the inclusion of exon 7 of SMN2 into mRNA that is transcribed from an SMN2 minigene. The minigene reproduces the alternative splicing reaction of exon 7 of SMN2 which results in exon 7 skipping in the majority of SMN2 transcripts. Thus, compounds of Formula (I) or a form thereof may be used to modulate inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. Applicants have also discovered that a compound of Formula (I) increases the inclusion of exon 7 of SMN1 into mRNA that is transcribed from an SMN1 minigene. Thus, compounds of Formula (I) or a form thereof may be used to modulate inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene.

[0030] In a specific embodiment, provided herein are compounds of Formula (I) or a form thereof that may be used to modulate the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. In another specific embodiment, provided herein are compounds of Formula (I) or a form thereof that may be used to modulate the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene. In yet another embodiment, provided herein are compounds of Formula (I) or a form thereof that may be used to modulate the inclusion of exon 7 of SMN1 and SMN2 into mRNA that is transcribed from the SMN1 and SMN2 genes, respectively.

[0031] In another aspect, provided herein is the use of a compound of Formula (I) or a form thereof for treating SMA. In a specific embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject an effective amount of a compound of Formula (I) or a form thereof. The compound of Formula (I) or a form thereof is preferably administered to a human subject in a pharmaceutical composition. In another specific embodiment, provided herein is the use of a compound of Formula (I) for treating SMA, wherein the compound enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. Without being limited by theory, compounds of Formula (I) enhance inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene and increase levels of Smn protein produced from the SMN2 gene, and thus can be used to treat SMA in a human subject in need thereof.

[0032] In another aspect, provided herein are primers and/or probes described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13, and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) and the use of those primers and/or probes. In a specific embodiment, provided herein is an isolated nucleotide sequence comprising SEQ ID NO. 1, 2, 3, 7, 8, 9, 10, 11, 12 or 13. In another specific embodiment, provided herein is an isolated nucleotide sequence consisting essentially of SEQ ID NO. 1, 2, 3, 7, 8, 9, 10, 11, 12 or 13. In another specific embodiment, provided herein is an isolated nucleotide sequence consisting of SEQ ID NO. 1, 2, 3, 7, 8, 9, 10, 11, 12 or 13.

[0033] In certain embodiments, the amount of mRNA that is transcribed from the SMN1 gene and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 may be used as a biomarker for SMA, such as disclosed herein. In other embodiments, the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 may be used as a biomarker for treating a patient with a compound, such as disclosed herein. In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0034] In certain embodiments, the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 as well as the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 may be used as biomarkers for treating a patient with a compound, such as

disclosed herein. In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0035] In accordance with these embodiments, an SMN primer(s) and/or an SMN probe described below may be used in assays, such as PCR (*e.g.*, qPCR), rolling circle amplification, and RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR) to assess and/or quantify the amount of mRNA that is transcribed from the SMN1 gene and/or SMN2 gene and does or does not include exon 7 of SMN1 and/or SMN2.

[0036] In a specific embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to determine whether a compound (*e.g.*, a compound of Formula (I) or a form thereof) enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from an SMN2 gene.

[0037] In a specific embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to determine whether a compound (*e.g.*, a compound of Formula (I) or a form thereof) enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from an SMN1 gene.

[0038] In a specific embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to determine whether a compound (*e.g.*, a compound of Formula (I) or a form thereof) enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from an SMN1 and/or SMN2 gene.

[0039] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 7, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-

qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor the amount of mRNA that is transcribed from the SMN2 gene and includes exon 7 of SMN2 in a patient sample. In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0040] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 7, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor the amount of mRNA that is transcribed from the SMN1 gene and includes exon 7 of SMN1 in a patient sample. In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0041] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 7, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in a patient sample. In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0042] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 7, 8, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor a patient's response to a compound (*e.g.*, a compound of Formula (I) or a form thereof). In a specific embodiment, the patient is an SMA patient. In another specific embodiment, the patient is not an SMA patient.

[0043] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7

of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising (a) contacting mRNA that is transcribed from an SMN2 minigene described herein or in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a compound (*e.g.*, a compound of Formula (I) disclosed herein) with a primer(s) described herein (*e.g.*, SEQ ID NO. 1 and/or 2) along with applicable components for, *e.g.*, RT-PCR, RT-qPCR, PCR, endpoint RT-PCR, qPCR or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene.

[0044] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene, comprising (a) contacting mRNA that is transcribed from an SMN1 minigene described in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a compound (*e.g.*, a compound of Formula (I) disclosed herein) with a primer(s) described herein (*e.g.*, SEQ ID NO. 1 and/or 2) along with applicable components for, *e.g.*, RT-PCR, RT-qPCR, PCR, endpoint RT-PCR, qPCR or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN1, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1

gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene.

[0045] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising (a) contacting mRNA that is transcribed from an SMN2 minigene described herein or in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a compound (*e.g.*, a compound of Formula (I) disclosed herein) with a probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g.*, RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene.

[0046] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene, comprising (a) contacting mRNA that is transcribed from an SMN1 minigene described in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a

compound (*e.g.*, a compound of Formula (I) disclosed herein) with a probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g.*, RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN1, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene.

[0047] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising (a) contacting mRNA that is transcribed from an SMN2 minigene described herein or in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a compound (*e.g.*, a compound of Formula (I) disclosed herein) with a primer(s) (*e.g.*, SEQ ID NO. 1 or 2) and/or a probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g*, RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the presence of the compound relative to the

amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN2 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene.

[0048] In another embodiment, provided herein is a method for determining whether a compound (*e.g.*, a compound of Formula (I) disclosed herein) enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene, comprising (a) contacting mRNA that is transcribed from an SMN1 minigene described in International Application PCT/US2009/004625, filed August 13, 2009 (published as International Publication Number WO2010/019236) or United States Publication Number US2011/0172284 in the presence of a compound (*e.g.*, a compound of Formula (I) disclosed herein) with a primer(s) (*e.g.*, SEQ ID NO. 1 or 2) and/or a probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g*, RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the minigene and includes exon 7 of the SMN1, wherein (1) an increase in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound enhances inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the presence of the compound relative to the amount of mRNA that is transcribed from the minigene and includes exon 7 of SMN1 in the absence of the compound indicates that the compound does not enhance the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene.

[0049] In another aspect, provided herein are kits comprising a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) and the use thereof.

BRIEF DESCRIPTION OF THE FIGURES

[0050] Figure 1, referenced in Biological Example 1, is a schematic drawing of the SMN2-A minigene construct, which produces two alternatively spliced mRNA transcripts: a full length

mRNA that contains exon 7 and a Δ7 mRNA that lacks exon 7. The adenine nucleotide inserted in exon 7 of SMN2-A after nucleic residue 48 is represented by the letter "A." Alternatively, the nucleotide may also be selected from cytosine or thymine. Due to the insertion of one nucleotide (A, C, or T) after nucleic residue 48, the full length mRNA does not contain a stop codon in the SMN open reading frame, whereas the Δ7 mRNA has a stop codon in Exon 8 that is indicated by the word "Stop."

[0051] Figure 2, referenced in Biological Example 1, provides the DNA sequence of the minigene from the SMN2-A minigene construct **SEQ ID NO. 21** (Figure 2a). As shown in Figure 2b, the following sub-sequences can be found:

1-70: 5'UTR (deg);

71-79: exon 6: start codon and BamHI site (atgggatcc);

80-190: exon 6;

191-5959: intron 6;

5960-6014: exon 7 with the adenine nucleotide "A" insert (position 6008);

6015-6458: intron 7;

6459-6481: part of exon 8;

6482-8146: BamHI site (sequence at the 5' end), luciferase coding sequence starting with codon 2 (without initiation codon), NotI site (sequence at the 3' end), TAA stop codon; and

8147-8266: 3'UTR (deg).

[0052] To generate the SMN1 version of the minigene, the sixth nucleotide of exon 7 (a thymine residue) of the SMN2-A minigene construct is changed to cytosine using site directed mutagenesis. Thus, similar to the SMN2-A minigene construct, the SMN1 minigene construct has a single adenine residue inserted after nucleic residue 48 of exon 7. The SMN1 minigene construct is referred to as SMN1-A. Similarly, the nucleotide inserted in the SMN1 minigene construct after nucleic residue 48 of exon 7 may also be selected alternatively from cytosine or thymine.

[0053] Figure 3, referenced in Biological Example 2, shows the correction of SMN2 minigene alternative splicing in cells treated with rising concentrations of Compound **6** (Figure 3a) and Compound **170** (Figure 3b) over a 24 hr period. The levels of full length SMN2 minigene mRNA were quantified using reverse transcription-quantitative PCR (RT-qPCR). The

level of full length SMN2 minigene mRNA in compound-treated samples was normalized to that in vehicle-treated samples and plotted as a function of the compound concentration.

[0054] Figure 4, referenced in Biological Example 3, shows the correction of SMN2 alternative splicing in Type 1 SMA patient fibroblasts treated with rising concentrations of Compound **6** (Figure 4a) and Compound **170** (Figure 4b) over a 24 hr period. The levels of full length and Δ7 SMN2 mRNA were quantified using RT-qPCR. The levels of full length and Δ7 SMN2 mRNA in compound-treated samples were normalized to those in vehicle-treated samples and plotted as a function of the compound concentration.

[0055] Figure 5, referenced in Biological Example 4, shows the correction of SMN2 alternative splicing in Type 1 SMA patient fibroblasts treated with rising concentrations of Compound **6** (Figure 5a) and Compound **170** (Figure 5b) over a 24 hr period. The full length and Δ7 SMN2 mRNA were amplified using reverse transcription-end point PCR (RT-PCR) and PCR products were separated using agarose gel electrophoresis. The top and bottom bands correspond to the full length and Δ7 SMN2 mRNA respectively. The intensity of each band is proportional to the amount of RNA present in the sample.

[0056] Figure 6, referenced in Biological Example 5, shows the correction of SMN2 alternative splicing (in both the SMN2 gene and the hybrid mouse Smn1-SMN2 gene) in brain and muscle tissues in a C/C-allele SMA mouse model resulting from treatment for 10 days twice per day (BID) with 10 mg/kg of Compound **6** (Figure 6a) and Compound **170** (Figure 6b). The levels of full length and Δ7 SMN2 mRNA were quantified using RT-qPCR, the combined full length and Δ7 SMN2 mRNA quantity was set to 1, and fractional quantities of full length and Δ7 SMN2 were calculated.

[0057] Figure 7, referenced in Biological Example 6, shows the correction of SMN2 alternative splicing (in both the SMN2 gene and the hybrid mouse Smn1-SMN2 gene) in brain and muscle tissues in a C/C-allele SMA mouse model resulting from treatment for 10 days BID with 10 mg/kg of Compound **6** (Figure 7a) and Compound **170** (Figure 7b). The full length and Δ7 SMN2 mRNA were amplified using RT-PCR. The PCR products were separated using agarose gel electrophoresis. The top and bottom bands correspond to the full length and Δ7 SMN2 mRNA, respectively. The intensity of each band is proportional to the amount of RNA present in the sample.

[0058] Figure 8, referenced in Biological Example 7, shows a dose dependent increase in Smn protein expression in SMA Type 1 human fibroblast cells treated over a 48 hour period with Compound **6** (Figure 8a) and Compound **170** (Figure 8b).

[0059] Figure 9, referenced in Biological Example 8, shows an increase in nuclear speckle counts (gems) in Type 1 SMA patient fibroblasts treated with Compound **6** (Figure 9a) and Compound **170** (Figure 9b) over a 48 hour period. Speckles were counted using fluorescence microscopy. The number of speckles in compound-treated samples was normalized to that in vehicle-treated samples and plotted as a function of the compound concentration.

[0060] Figure 10, referenced in Biological Example 9, shows an increase in Smn protein expression (black circles) in motor neurons generated from iPS cells generated from Type 1 SMA patient fibroblasts treated with Compound **6** (Figure 10). The level of Smn protein was quantified using Smn immunostaining and confocal fluorescence microscopy. The level of Smn protein in compound-treated samples was normalized to that in vehicle-treated samples and plotted as a function of the compound concentration.

[0061] Figure 11, referenced in Biological Example 11, shows increased Smn protein expression in brain, spinal cord, and muscle tissues in a C/C-allele SMA mouse model resulting from treatment for 10 days BID with 100 mg/kg of Compound **6** (Figure 11a, for $n = 10$) and 10 mg/kg of Compound **170** (Figure 11b, for $n = 5$). The p value by ANOVA in each Figure is indicated with three stars (***) for $p < 0.001$.

[0062] Figure 12, referenced in Biological Example 12, shows a dose dependent increase in Smn protein expression in tissues in a neonatal Δ7 SMA mouse model resulting from treatment for 7 days once per day (QD) with Compound **6** (brain, Figure 12a; spinal cord, Figure 12b; muscle, Figure 12c; and skin, Figure 12d, for $n = 6$ to 9) and Compound **170** (brain, Figure 12e; spinal cord, Figure 12f; muscle, Figure 12g, for $n = 7$). The p value by ANOVA in each Figure is indicated with one star (*) for $p < 0.05$, two stars (**) for $p < 0.01$ and three stars (***) for $p < 0.001$.

[0063] Figure 13, referenced in Biological Example 13, shows differences in body weight in a neonatal Δ7 SMA mouse model resulting from treatment up to Postnatal Day (PND) 59 with Compound **6** (Figure 13a) and until PND 92 with Compound **170** (Figure 13b).

[0064] Figure 14, referenced in Biological Example 14, shows an improved righting reflex in a neonatal Δ7 SMA mouse model resulting from treatment with Compound **6** (Figure 14a) and Compound **170** (Figure 14b).

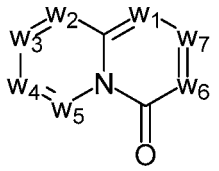
[0065] Figure 15, referenced in Biological Example 15, shows improved survival in a neonatal Δ7 SMA mouse model resulting from treatment with Compound **6** (Figure 15a) and Compound **170** (Figure 15b).

[0066] Figure 16, referenced in Biological Example 15, shows increased Smn protein expression in brain, spinal cord, and muscle tissues in a Δ7 SMA mouse model resulting from treatment with Compound **6** until PND 156 (Figure 16a) and with Compound **170** until PND 185 (Figure 16b) relative to vehicle treated and age-matched heterozygous mice, respectively.

[0067] Figure 17, referenced in Biological Example 16, shows a dose dependent increase in SMN1 minigene FL mRNA and a dose dependent decrease in SMN1 minigene Δ7 mRNA in HEK293H human cells treated over a 7 hour period with Compound **6** (Figure 17a) and Compound **170** (Figure 17b). The full length and Δ7 SMN1 minigene mRNA were each amplified using RT-PCR and the resulting PCR products were separated using agarose gel electrophoresis. The top and bottom bands correspond to the full length and Δ7 SMN1 minigene mRNA, respectively. The intensity of each band is proportional to the amount of RNA present in the sample.

DETAILED DESCRIPTION

[0068] Provided herein are compounds of Formula (I):



(I)

[0069] or a form thereof, wherein:

[0070] w_1 and w_5 are independently C-R_a or N;

[0071] w_2 is C-R_b or N;

[0072] w_3, w_4 and w_7 are independently C-R_1, C-R_2, C-R_a or N;

[0073] w_6 is C-R_1, C-R_2, C-R_c or N;

[0074] wherein one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[0075] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[0076] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[0077] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[0078] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N; and,

[0079] wherein any one, two or three of w_1, w_2, w_3, w_4, w_5, w_6 and w_7 may optionally be N;

[0080] R_1 is C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy, C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino,

(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino,
(hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino,
(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino,
[(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino,
[(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino, (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl;

[0081] wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or,

[0082] wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

[0083] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[0084] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent;

[0085] R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

[0086] R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

[0087] R_c is hydrogen, halogen or C_{1-8}alkyl;

[0088] R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkyl-carbonyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl-amino, $[(C_{1-8}alkyl)_2\text{-}amino\text{-}C_{1-8}alkyl]_2$-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, $[(C_{1-8}alkyl)_2\text{-}amino\text{-}C_{1-8}alkyl](C_{1-8}alkyl)$amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, C_{1-8}alkyl-carbonyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino or $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino;

[0089] R_4 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-C_{1-8}alkyl, C_{3-14}cycloalkyl-amino, aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl, aryl-sulfonyloxy-C_{1-8}alkyl, heterocyclyl or heterocyclyl-C_{1-8}alkyl; wherein, each instance of C_{3-14}cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R_5 substituents;

[0090] R_5 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio;

[0091] R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, C_{2-8}alkenyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio; and,

[0092] R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

EMBODIMENTS

[0093] In one embodiment of a compound of Formula (I), w_1 is C-R_a.

[0094] In another embodiment of a compound of Formula (I), w_1 is N.

[0095] In one embodiment of a compound of Formula (I), w_2 is C-R_b.

[0096] In another embodiment of a compound of Formula (I), w_2 is N.

[0097] In one embodiment of a compound of Formula (I), w_3 is C-R_a.

[0098] In another embodiment of a compound of Formula (I), w_3 is N.

[0099] In one embodiment of a compound of Formula (I), w_4 is C-R_a.

[00100] In another embodiment of a compound of Formula (I), w_4 is N.

[00101] In one embodiment of a compound of Formula (I), w_5 is C-R_a.

[00102] In another embodiment of a compound of Formula (I), w_5 is N.

[00103] In one embodiment of a compound of Formula (I), w_6 is C-R_c.

[00104] In another embodiment of a compound of Formula (I), w_6 is N.

[00105] In one embodiment of a compound of Formula (I), w_7 is C-R_a.

[00106] In another embodiment of a compound of Formula (I), w_7 is N.

[00107] In one embodiment of a compound of Formula (I), w_3 is C-R_1 and w_6 is C-R_2.

[00108] In another embodiment of a compound of Formula (I), w_3 is C-R_2 and w_6 is C-R_1.

[00109] In one embodiment of a compound of Formula (I), w_4 is C-R_1 and w_7 is C-R_2.

[00110] In another embodiment of a compound of Formula (I), w_4 is C-R_2 and w_7 is C-R_1.

[00111] In one embodiment of a compound of Formula (I), w_3 is C-R_1, w_6 is C-R_2 and w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00112] In another embodiment of a compound of Formula (I), w_3 is C-R_2, w_6 is C-R_1 and w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00113] In one embodiment of a compound of Formula (I), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00114] In another embodiment of a compound of Formula (I), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00115] In one embodiment of a compound of Formula (I), w_1 and w_2 are N.

[00116] In one embodiment of a compound of Formula (I), w_1 and w_3 are N.

[00117] In one embodiment of a compound of Formula (I), w_1 and w_4 are N.

[00118] In one embodiment of a compound of Formula (I), w_1 and w_5 are N.

[00119] In one embodiment of a compound of Formula (I), w_1 and w_6 are N.

[00120] In one embodiment of a compound of Formula (I), w_1 and w_7 are N.

[00121] In one embodiment of a compound of Formula (I),

[00122] R_1 is C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy, C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino,

(heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00123] In another embodiment of a compound of Formula (I),

[00124] R_1 is amino, (C_{1-8}alkyl)$_2$-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy, C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino,

hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino, (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00125] In another embodiment of a compound of Formula (I),

[00126] R_1 is C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy, C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino or [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino.

[00127] In another embodiment of a compound of Formula (I),

[00128] R_1 is heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00129] In another embodiment of a compound of Formula (I),

[00130] R_1 is heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl or heterocyclyl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00131] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl optionally substituted with R_3 and R_4 substituents.

[00132] In another embodiment of a compound of Formula (I), R_1 is C_{3-14}cycloalkyl optionally substituted with R_3 and R_4 substituents.

[00133] In another embodiment of a compound of Formula (I),

[00134] R_1 is aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of aryl is optionally substituted with R_3 and R_4 substituents.

[00135] In another embodiment of a compound of Formula (I), R_1 is aryl-C_{1-8}alkyl-amino optionally substituted with R_3 and R_4 substituents.

[00136] In another embodiment of a compound of Formula (I),

[00137] R_1 is heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00138] In another embodiment of a compound of Formula (I), R_1 is heteroaryl optionally substituted with R_3 and R_4 substituents.

[00139] In one embodiment of a compound of Formula (I),

[00140] R_1 is heterocyclyl selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one,

hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
octahydro-2H-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl,
(1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl,
(1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl,
(1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl,
(1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl,
(1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl,
3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl,
1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl or 6,9-diazaspiro[4.5]decyl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00141] In another embodiment of a compound of Formula (I),

[00142] R_1 is heterocyclyl selected from azetidin-1-yl, tetrahydrofuran-3-yl, pyrrolidin-1-yl, piperidin-1-yl, piperidin-4-yl, piperazin-1-yl, 1,4-diazepan-1-yl,
1,2,5,6-tetrahydropyridin-5-yl, 1,2,3,6-tetrahydropyridin-4-yl,
hexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl,
(3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl,
(3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,
(3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,
hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,
(3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
hexahydropyrrolo[1,2-*a*]pyrazin-6(2*H*)-one,

hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
octahydro-2H-pyrido[1,2-*a*]pyrazin-2-yl, 3-azabicyclo[3.1.0]hex-3-yl,
8-azabicyclo[3.2.1]oct-3-yl, (1R,5S)-8-azabicyclo[3.2.1]oct-3-yl,
8-azabicyclo[3.2.1]oct-2-en-3-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-3-yl,
9-azabicyclo[3.3.1]non-3-yl, (1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl,
2,5-diazabicyclo[2.2.1]hept-2-yl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]hept-2-yl,
2,5-diazabicyclo[2.2.2]oct-2-yl, 3,8-diazabicyclo[3.2.1]oct-3-yl,
(1*R*,5*S*)-3,8-diazabicyclo[3.2.1]oct-3-yl, 1,4-diazabicyclo[3.2.2]non-4-yl,
azaspiro[3.3]hept-2-yl, 2,6-diazaspiro[3.3]hept-2-yl, 2,7-diazaspiro[3.5]non-7-yl,
5,8-diazaspiro[3.5]non-8-yl, 2,7-diazaspiro[4.4]non-2-yl or
6,9-diazaspiro[4.5]dec-9-yl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00143] In another embodiment of a compound of Formula (I),

[00144] R_1 is substituted heterocyclyl selected from 4-methyl-1,4-diazepan-1-yl,
(3a*S*,6a*S*)-1-methylhexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,
(3a*S*,6a*S*)-5-methylhexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl,
(3a*R*,6a*R*)-1-methylhexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,
(3a*R*,6a*S*)-5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,
(3a*R*,6a*S*)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,
(3a*R*,6a*S*)-5-(propan-2-yl)hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,
(3a*R*,6a*S*)-5-ethylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,
(4a*R*,7a*R*)-1-methyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*R*,7a*R*)-1-ethyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*R*,7a*R*)-1-(2-hydroxyethyl)octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*S*,7a*S*)-1-methyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,
(4a*S*,7a*S*)-1-(2-hydroxyethyl)octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(7*R*,8a*S*)-7-hydroxyhexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*S*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(1*R*,5*S*,6s)-6-(dimethylamino)-3-azabicyclo[3.1.0]hex-3-yl,
(1*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl,
9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(3-exo)-9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(1*R*,5*S*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(1*S*,4*S*)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl or
(1*S*,4*S*)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl.

[00145] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkyl, wherein heterocyclyl is selected from morpholinyl, piperidinyl, piperazinyl, imidazolyl or pyrrolidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00146] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkyl selected from morpholin-4-yl-methyl, morpholin-4-yl-ethyl, morpholin-4-yl-propyl, piperidin-1-yl-methyl, piperazin-1-yl-methyl, piperazin-1-yl-ethyl, piperazin-1-yl-propyl, piperazin-1-yl-butyl, imidazol-1-yl-methyl, imidazol-1-yl-ethyl, imidazol-1-yl-propyl, imidazol-1-yl-butyl, pyrrolidin-1-yl-methyl, pyrrolidin-1-yl-ethyl, pyrrolidin-1-yl-propyl or pyrrolidin-1-yl-butyl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00147] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkoxy, wherein heterocyclyl is selected from pyrrolidinyl, piperidinyl or morpholinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00148] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkoxy selected from pyrrolidin-2-yl-methoxy, pyrrolidin-2-yl-ethoxy, pyrrolidin-1-yl-methoxy, pyrrolidin-1-yl-ethoxy, piperidin-1-yl-methoxy, piperidin-1-yl-ethoxy, morpholin-4-yl-methoxy or morpholin-4-yl-ethoxy; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00149] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-amino, wherein heterocyclyl is selected from azetidinyl, pyrrolidinyl, piperidinyl, 9-azabicyclo[3.3.1]nonyl or

(1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00150] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-amino selected from azetidin-3-yl-amino, pyrrolidin-3-yl-amino, piperidin-4-yl-amino, 9-azabicyclo[3.3.1]non-3-yl-amino, (1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl-amino, 9-methyl-9-azabicyclo[3.3.1]non-3-yl-amino, (3-exo)-9-methyl-9-azabicyclo[3.3.1]non-3-yl-amino or (1*R*,5*S*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl-amino; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00151] In one embodiment of a compound of Formula (I), R_1 is (heterocyclyl)(C_{1-8}alkyl)amino, wherein heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00152] In another embodiment of a compound of Formula (I), R_1 is (heterocyclyl)(C_{1-8}alkyl)amino selected from (pyrrolidin-3-yl)(methyl)amino or (piperidin-4-yl)(methyl)amino; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00153] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-amino-C_{1-8}alkyl, wherein heterocyclyl is selected from tetrahydrofuranyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00154] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-amino-C_{1-8}alkyl, selected from 3-(tetrahydrofuran-3-yl-amino)propyl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00155] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, wherein heterocyclyl is selected from tetrahydrofuranyl, thienyl or pyridinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00156] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, selected from 3-[(tetrahydrofuran-2-ylmethyl)amino]propyl, 3-[(thienyl-3-ylmethyl)amino]propyl, 3-[(pyridin-2-ylmethyl)amino]propyl or 3-[(pyridin-4-ylmethyl)amino]propyl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00157] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-oxy, wherein heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00158] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-oxy selected from pyrrolidin-3-yl-oxy or piperidin-4-yl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00159] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-carbonyl, wherein heterocyclyl is selected from piperazinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00160] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-carbonyl selected from piperazin-1-yl-carbonyl; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00161] In one embodiment of a compound of Formula (I), R_1 is heterocyclyl-carbonyl-oxy, wherein heterocyclyl is selected from piperazinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00162] In another embodiment of a compound of Formula (I), R_1 is heterocyclyl-carbonyl-oxy selected from piperazin-1-yl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents.

[00163] In one embodiment of a compound of Formula (I), R_1 is C_{3-14}cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl or cycloheptyl; wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with R_3 and R_4 substituents.

[00164] In another embodiment of a compound of Formula (I), R_1 is C_{3-8}cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl or cycloheptyl; wherein, each instance of C_{3-8}cycloalkyl is optionally substituted with R_3 and R_4 substituents.

[00165] In one embodiment of a compound of Formula (I), R_1 is aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R_3 and R_4 substituents.

[00166] In another embodiment of a compound of Formula (I), R_1 is aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl selected from 3-(benzylamino)propyl; wherein, each instance of aryl is optionally substituted with R_3 and R_4 substituents.

[00167] In one embodiment of a compound of Formula (I), R_1 is heteroaryl, wherein heteroaryl is selected from pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00168] In another embodiment of a compound of Formula (I), R_1 is heteroaryl selected from pyridin-4-yl; wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00169] In one embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl, wherein heteroaryl is selected from 1*H*-imidazolyl; and, wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00170] In another embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl selected from 1*H*-imidazol-1-yl-methyl; wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00171] In one embodiment of a compound of Formula (I), R_1 is (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, wherein heteroaryl is selected from pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00172] In another embodiment of a compound of Formula (I), R_1 is (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino selected from (pyridin-3-ylmethyl)(methyl)amino; wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00173] In one embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, wherein heteroaryl is selected from thienyl or pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00174] In another embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl selected from thien-3-yl-methyl-amino-propyl, pyridin-2-yl-methyl-amino-propyl, pyridin-3-yl-methyl-amino-propyl or pyridin-4-yl-methyl-amino-propyl; wherein, each instance of heteroaryl is optionally substituted with R_3 and R_4 substituents.

[00175] In one embodiment of a compound of Formula (I), R_3 is selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkyl-carbonyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino,

C_{1-8}alkoxy-C_{1-8}alkyl-amino, C_{1-8}alkyl-carbonyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino or (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino.

[00176] In another embodiment of a compound of Formula (I), R_3 is selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino or (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino.

[00177] In one embodiment of a compound of Formula (I), R_3 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

[00178] In another embodiment of a compound of Formula (I), R_3 is C_{1-8}alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00179] In one embodiment of a compound of Formula (I), R_3 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, halo-ethyl, trihalo-propyl, dihalo-propyl or halo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00180] In another embodiment of a compound of Formula (I), R_3 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, trihalo-propyl or dihalo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00181] In one embodiment of a compound of Formula (I), R_3 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00182] In another embodiment of a compound of Formula (I), R_3 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00183] In one embodiment of a compound of Formula (I), R_3 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00184] In one embodiment of a compound of Formula (I), R_3 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00185] In one embodiment of a compound of Formula (I), R_3 is C_{1-8}alkoxy-carbonyl-amino selected from methoxy-carbonyl-amino, ethoxy-carbonyl-amino, propoxy-carbonyl-amino, isopropoxy-carbonyl-amino, tert-butoxy-carbonyl-amino.

[00186] In one embodiment of a compound of Formula (I), R_4 is C_{3-14}cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with R_5 substituents.

[00187] In another embodiment of a compound of Formula (I), R_4 is C_{3-8}cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; wherein, each instance of C_{3-8}cycloalkyl is optionally substituted with R_5 substituents.

[00188] In one embodiment of a compound of Formula (I), R_4 is C_{3-14}cycloalkyl-C_{1-8}alkyl, wherein C_{3-14}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with R_5 substituents.

[00189] In another embodiment of a compound of Formula (I), R_4 is C_{3-8}cycloalkyl-C_{1-8}alkyl, wherein C_{3-8}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C_{3-8}cycloalkyl is optionally substituted with R_5 substituents.

[00190] In one embodiment of a compound of Formula (I), R_4 is C_{3-14}cycloalkyl-amino, wherein C_{3-14}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with R_5 substituents.

[00191] In another embodiment of a compound of Formula (I), R_4 is C_{3-8}cycloalkyl-amino, wherein C_{3-8}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C_{3-8}cycloalkyl is optionally substituted with R_5 substituents.

[00192] In one embodiment of a compound of Formula (I), R_4 is aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl or aryl-sulfonyloxy-C_{1-8}alkyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R_5 substituents.

[00193] In another embodiment of a compound of Formula (I), R_4 is aryl-C_{1-8}alkyl or aryl-C_{1-8}alkoxy-carbonyl, wherein each instance of aryl is optionally substituted with R_5 substituents.

[00194] In one embodiment of a compound of Formula (I), R_4 is heterocyclyl selected from oxetanyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,3-dioxanyl or morpholinyl, wherein each instance of heterocyclyl is optionally substituted with R_5 substituents.

[00195] In another embodiment of a compound of Formula (I), R_4 is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1,3-dioxan-5-yl or morpholin-4-yl, wherein each instance of heterocyclyl is optionally substituted with R_5 substituents.

[00196] In one embodiment of a compound of Formula (I), R_4 is heterocyclyl-C_{1-8}alkyl, wherein each instance of heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R_5 substituents.

[00197] In another embodiment of a compound of Formula (I), R_4 is heterocyclyl-C_{1-8}alkyl selected from pyrrolidin-1-yl-C_{1-8}alkyl or piperidin-1-yl-C_{1-8}alkyl, wherein each instance of heterocyclyl is optionally substituted with R_5 substituents.

[00198] In one embodiment of a compound of Formula (I), R_5 is selected from halogen, hydroxy, cyano, nitro, halo-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio; wherein, halogen and halo is selected from fluoro, chloro, bromo or iodo.

[00199] In one embodiment of a compound of Formula (I), R_5 is hydroxy.

[00200] In one embodiment of a compound of Formula (I), R_5 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl, n-butyl or tert-butyl.

[00201] In another embodiment of a compound of Formula (I), R_5 is C_{1-8}alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00202] In one embodiment of a compound of Formula (I), R_5 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, halo-ethyl, trihalo-propyl, dihalo-propyl or halo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00203] In one embodiment of a compound of Formula (I), R_5 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00204] In one embodiment of a compound of Formula (I), R_5 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00205] In one embodiment of a compound of Formula (I), R_2 is aryl selected from phenyl optionally substituted with R_6 and R_7 substituents.

[00206] In one embodiment of a compound of Formula (I), R_2 is aryl-amino, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R_6 and R_7 substituents.

[00207] In another embodiment of a compound of Formula (I), R_2 is aryl-amino selected from phenyl-amino; wherein, each instance of aryl is optionally substituted with R_6 and R_7 substituents.

[00208] In one embodiment of a compound of Formula (I), R_2 is aryl-amino-carbonyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R_6 and R_7 substituents.

[00209] In another embodiment of a compound of Formula (I), R_2 is aryl-amino-carbonyl selected from phenyl-amino-carbonyl; wherein, each instance of aryl is optionally substituted with R_6 and R_7 substituents.

[00210] In one embodiment of a compound of Formula (I),

[00211] R_2 is heterocyclyl selected from 1,2,3,6-tetrahydropyridinyl, 1,3-benzodioxolyl or 2,3-dihydro-1,4-benzodioxinyl; wherein, each instance of heterocyclyl is optionally substituted with R_6 and R_7 substituents.

[00212] In another embodiment of a compound of Formula (I),

[00213] R_2 is heterocyclyl selected from 1,2,3,6-tetrahydropyridin-4-yl, 1,3-benzodioxol-5-yl or 2,3-dihydro-1,4-benzodioxin-6-yl; wherein, each instance of heterocyclyl is optionally substituted with R_6 and R_7 substituents.

[00214] In one embodiment of a compound of Formula (I),

[00215] R_2 is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl,

imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00216] In another embodiment of a compound of Formula (I),

[00217] R_2 is heteroaryl selected from thien-2-yl, thien-3-yl, 1*H*-pyrazol-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1,3-thiazol-2-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-4-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl, 1*H*-indol-5-yl, 1*H*-indol-6-yl, 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, indolizin-2-yl, benzofuran-2-yl, benzofuran-5-yl, benzothien-2-yl, benzothien-3-yl, 1*H*-benzimidazol-2-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-2-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-yl, 1,3-benzothiazol-2-yl, 1,3-benzothiazol-5-yl, 1,3-benzothiazol-6-yl, 9*H*-purin-8-yl, furo[3,2-*b*]pyridin-2-yl, furo[3,2-*c*]pyridin-2-yl, furo[2,3-*c*]pyridin-2-yl, thieno[3,2-*c*]pyridin-2-yl, thieno[2,3-*d*]pyrimidin-6-yl, 1*H*-pyrrolo[2,3-*b*]pyridin-5-yl, 1*H*-pyrrolo[2,3-*c*]pyridin-4-yl, pyrrolo[1,2-*a*]pyrimidin-7-yl, pyrrolo[1,2-*a*]pyrazin-7-yl, pyrrolo[1,2-*b*]pyridazin-2-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*a*]pyrazin-2-yl, imidazo[1,2-*a*]pyridin-2-yl, imidazo[1,2-*a*]pyridin-6-yl, imidazo[1,2-*a*]pyrimidin-2-yl, imidazo[1,2-*a*]pyrimidin-6-yl, imidazo[1,2-*c*]pyrimidin-2-yl, imidazo[1,2-*b*]pyridazin-2-yl, imidazo[1,2-*a*]pyrazin-2-yl, imidazo[2,1-*b*][1,3]thiazol-6-yl, imidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, [1,3]oxazolo[4,5-*b*]pyridin-2-yl or quinoxalin-2-yl; wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00218] In another embodiment of a compound of Formula (I),

[00219] R_2 is substituted heteroaryl selected from 4-methylthien-2-yl, 1-methyl-1*H*-pyrazol-3-yl, 4-methyl-1*H*-pyrazol-3-yl, 1-phenyl-1*H*-pyrazol-3-yl, 1-phenyl-1*H*-imidazol-4-yl, 2-methyl-1-(pyridin-2-yl)-1*H*-imidazol-4-yl,

4-methyl-1,3-thiazol-2-yl, 4-(trifluoromethyl)-1,3-thiazol-2-yl, 4-phenyl-1,3-thiazol-2-yl, 5-phenyl-1,2,4-oxadiazol-3-yl, 3-fluoropyridin-4-yl, 6-fluoropyridin-2-yl, 2-chloropyridin-4-yl, 4-chloropyridin-3-yl, 5-chloropyridin-2-yl, 6-methylpyridin-3-yl, 2-(trifluoromethyl)pyridin-3-yl, 4-(trifluoromethyl)pyridin-2-yl, 6-(trifluoromethyl)pyridin-2-yl, 2-methoxypyridin-4-yl, 4-methoxypyridin-3-yl, 6-methoxypyridin-2-yl, 2-ethoxypyridin-3-yl, 6-ethoxypyridin-2-yl, 6-(propan-2-yloxy)pyridin-2-yl, 6-(dimethylamino)pyridin-3-yl, 6-(methylsulfanyl)pyridin-2-yl, 6-(cyclobutyloxy)pyridin-2-yl, 6-(pyrrolidin-1-yl)pyridin-2-yl, 2-methylpyrimidin-4-yl, 2-(propan-2-yl)pyrimidin-4-yl, 2-cyclopropylpyrimidin-4-yl, 1-methyl-1H-indol-3-yl, 2-methyl-2*H*-indazol-5-yl, 2-methyl-1-benzofuran-5-yl, 1-methyl-1*H*-benzimidazol-2-yl, 4-methyl-1*H*-benzimidazol-2-yl 5-fluoro-1*H*-benzimidazol-2-yl, 4-fluoro-1,3-benzoxazol-2-yl, 5-fluoro-1,3-benzoxazol-2-yl, 4-chloro-1,3-benzoxazol-2-yl, 4-iodo-1,3-benzoxazol-2-yl, 2-methyl-1,3-benzoxazol-6-yl, 4-methyl-1,3-benzoxazol-2-yl, 4-(trifluoromethyl)-1,3-benzoxazol-2-yl, 7-(trifluoromethyl)-1,3-benzoxazol-2-yl, 2-methyl-1,3-benzothiazol-2-yl, 2-methyl-1,3-benzothiazol-5-yl, 2-methyl-1,3-benzothiazol-6-yl, 4-chloro-1,3-benzothiazol-2-yl, 7-chloro-1,3-benzothiazol-2-yl, 4-(trifluoromethyl)-1,3-benzothiazol-2-yl, 5-methylfuro[3,2-*b*]pyridin-2-yl, 4,6-dimethylfuro[3,2-*c*]pyridin-2-yl, 5,7-dimethylfuro[2,3-*c*]pyridin-2-yl, 4,6-dimethylthieno[3,2-*c*]pyridin-2-yl, 2,4-dimethylthieno[2,3-*d*]pyrimidin-6-yl, 1-methylpyrrolo[1,2-*a*]pyrazin-7-yl, 3-methylpyrrolo[1,2-*a*]pyrazin-7-yl, 1,3-dimethylpyrrolo[1,2-*a*]pyrazin-7-yl, 2-methylpyrrolo[1,2-*b*]pyridazin-2-yl, 4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl, 5-methylpyrazolo[1,5-*a*]pyridin-2-yl, 4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl, 2-chloroimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-methylimidazo[2,1-*b*][1,3]thiazol-6-yl, 3-methylimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-ethylimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-methylimidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, 6-cyanoimidazo[1,2-*a*]pyridin-2-yl (also referred to as 2-imidazo[1,2-*a*]pyridine-6-carbonitrile), 6-fluoroimidazo[1,2-*a*]pyridin-2-yl, 8-fluoroimidazo[1,2-*a*]pyridin-2-yl,

6,8-difluoroimidazo[1,2-*a*]pyridin-2-yl,
7-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl,
8-(trifluoromethyl)imidazo[1,2-*a*]pyridin-2-yl,
6-chloroimidazo[1,2-*a*]pyridin-2-yl, 7-chloroimidazo[1,2-*a*]pyridin-2-yl,
8-chloroimidazo[1,2-*a*]pyridin-2-yl, 8-bromoimidazo[1,2-*a*]pyridin-2-yl,
2-methylimidazo[1,2-*a*]pyridin-2-yl, 5-methylimidazo[1,2-*a*]pyridin-2-yl,
6-methylimidazo[1,2-*a*]pyridin-2-yl, 7-methylimidazo[1,2-*a*]pyridin-2-yl,
8-methylimidazo[1,2-*a*]pyridin-2-yl, 7-ethylimidazo[1,2-*a*]pyridin-2-yl,
8-ethylimidazo[1,2-*a*]pyridin-2-yl, 6,8-dimethylimidazo[1,2-*a*]pyridin-2-yl,
8-ethyl-6-methylimidazo[1,2-*a*]pyridin-2-yl,
7-methoxyimidazo[1,2-*a*]pyridin-2-yl, 8-methoxyimidazo[1,2-*a*]pyridin-2-yl,
6-fluoro-8-methylimidazo[1,2-*a*]pyridin-2-yl,
8-fluoro-6-methylimidazo[1,2-*a*]pyridin-2-yl,
8-chloro-6-methylimidazo[1,2-*a*]pyridin-2-yl,
6-methyl-8-nitroimidazo[1,2-*a*]pyridin-2-yl,
8-cyclopropylimidazo[1,2-*a*]pyridin-2-yl, 2-methylimidazo[1,2-*a*]pyridin-6-yl,
2-ethylimidazo[1,2-*a*]pyridin-6-yl, 2,3-dimethylimidazo[1,2-*a*]pyridin-6-yl,
2,8-dimethylimidazo[1,2-*a*]pyridin-6-yl,
2-(trifluoromethyl)imidazo[1,2-*a*]pyridin-6-yl, 8-chloro-2-
methylimidazo[1,2-*a*]pyridin-6-yl, 8-fluoro-2-methylimidazo[1,2-*a*]pyridin-6-yl,
6-fluoroimidazo[1,2-*a*]pyrimidin-2-yl, 6-chloroimidazo[1,2-*a*]pyrimidin-2-yl,
6-methylimidazo[1,2-*a*]pyrimidin-2-yl, 7-methylimidazo[1,2-*a*]pyrimidin-2-yl,
2-methylimidazo[1,2-*a*]pyrimidin-6-yl, 6-methylimidazo[1,2-*b*]pyridazin-2-yl,
2-methyl-3-(1,2,3,6-tetrahydropyridin-4-yl)imidazo[1,2-*b*]pyridazin-6-yl,
6-methylimidazo[1,2-*a*]pyrazin-2-yl, 8-methylimidazo[1,2-*a*]pyrazin-2-yl,
6,8-dimethylimidazo[1,2-*a*]pyrazin-2-yl, 6-
chloro-8-methylimidazo[1,2-*a*]pyrazin-2-yl,
6-methyl-8-(trifluoromethyl)imidazo[1,2-*a*]pyrazin-2-yl,
8-(methylsulfanyl)imidazo[1,2-*a*]pyrazin-2-yl,
2-methylimidazo[2,1-*b*][1,3]thiazol-6-yl, 3-methylimidazo[2,1-*b*][1,3]thiazol-6-yl
or 2-methylimidazo[2,1-*b*][1,3,4]thiadiazol-6-yl.

[00220] In another embodiment of a compound of Formula (I),

[00221] R_2 is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl; wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00222] In another embodiment of a compound of Formula (I),

[00223] R_2 is heteroaryl selected from furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00224] In one embodiment of a compound of Formula (I), R_2 is heteroaryl-amino, wherein heteroaryl is selected from pyridinyl or pyrimidinyl; and, wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00225] In another embodiment of a compound of Formula (I), R_2 is heteroaryl-amino selected from pyridin-2-yl-amino, pyridin-3-yl-amino or pyrimidin-2-yl-amino; wherein, each instance of heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00226] In one embodiment of a compound of Formula (I), R_6 is selected from halogen, hydroxy, cyano, nitro, $C_{1\text{-}8}$alkyl, halo-$C_{1\text{-}8}$alkyl, hydroxy-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkoxy, halo-$C_{1\text{-}8}$alkoxy, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl, $(C_{1\text{-}8}alkyl)_2$-amino or $C_{1\text{-}8}$alkyl-thio; wherein, halogen and halo is selected from fluoro, chloro, bromo or iodo.

[00227] In one embodiment of a compound of Formula (I), R_6 is $C_{1\text{-}8}$alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

[00228] In another embodiment of a compound of Formula (I), R_6 is $C_{1\text{-}8}$alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00229] In one embodiment of a compound of Formula (I), R_6 is C_{2-8}alkenyl selected from ethenyl, allyl or buta-1,3-dienyl.

[00230] In another embodiment of a compound of Formula (I), R_6 is C_{2-8}alkenyl selected from ethenyl or allyl.

[00231] In one embodiment of a compound of Formula (I), R_6 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, halo-ethyl, trihalo-propyl, dihalo-propyl or halo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00232] In one embodiment of a compound of Formula (I), R_6 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00233] In another embodiment of a compound of Formula (I), R_6 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00234] In one embodiment of a compound of Formula (I), R_6 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00235] In one embodiment of a compound of Formula (I), R_6 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00236] In one embodiment of a compound of Formula (I), R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl; wherein C_{3-14}cycloalkyl is selected from cyclopropyl or cyclobutoxy; wherein aryl is selected from phenyl; wherein heterocyclyl is selected from oxetanyl, pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl; and, wherein heteroaryl is selected from thienyl or pyridinyl.

[00237] In another embodiment of a compound of Formula (I), R_7 is C_{3-14}cycloalkyl or C_{3-14}cycloalkyl-oxy, wherein each instance of C_{3-14}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

[00238] In another embodiment of a compound of Formula (I), R_7 is C_{3-8}cycloalkyl or C_{3-8}cycloalkyl-oxy, wherein each instance of C_{3-8}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

[00239] In one embodiment of a compound of Formula (I), R_7 is aryl selected from phenyl.

[00240] In one embodiment of a compound of Formula (I), R_7 is heterocyclyl selected from oxetanyl, pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl.

[00241] In another embodiment of a compound of Formula (I), R_7 is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl or 1,2,3,6-tetrahydropyridin-4-yl.

[00242] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from thienyl or pyridinyl.

[00243] In another embodiment of a compound of Formula (I), R_7 is heteroaryl selected from pyridinyl.

[00244] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from thien-2-yl or pyridin-2-yl.

[00245] In another embodiment of a compound of Formula (I), R_7 is heteroaryl selected from pyridin-2-yl.

[00246] In one embodiment of a compound of Formula (I), R_c is hydrogen or C_{1-8}alkyl.

[00247] In another embodiment of a compound of Formula (I),

[00248] R_1 is heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents; and,

[00249] wherein, heterocyclyl is selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, octahydro-2H-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl or 6,9-diazaspiro[4.5]decyl.

[00250] In another embodiment of a compound of Formula (I),

[00251] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00252] wherein, aryl is phenyl;

[00253] wherein, heterocyclyl is selected from 1,2,3,6-tetrahydropyridinyl, 1,3-benzodioxolyl or 2,3-dihydro-1,4-benzodioxinyl;

[00254] wherein, heteroaryl is selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; and, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00255] In another embodiment of a compound of Formula (I),

[00256] R_1 is heterocyclyl, heterocyclyl-$C_{1\text{-}8}$alkyl, heterocyclyl-$C_{1\text{-}8}$alkoxy, heterocyclyl-amino, (heterocyclyl)($C_{1\text{-}8}$alkyl)amino, heterocyclyl-amino-$C_{1\text{-}8}$alkyl, heterocyclyl-$C_{1\text{-}8}$alkyl-amino, (heterocyclyl-$C_{1\text{-}8}$alkyl)$_2$-amino, (heterocyclyl-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino, heterocyclyl-$C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl, (heterocyclyl-$C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl, (heterocyclyl-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino-$C_{1\text{-}8}$alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, $C_{3\text{-}14}$cycloalkyl, aryl-$C_{1\text{-}8}$alkyl-amino, (aryl-$C_{1\text{-}8}$alkyl)$_2$-amino, (aryl-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino, aryl-$C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl, (aryl-$C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl, (aryl-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino-$C_{1\text{-}8}$alkyl, heteroaryl, heteroaryl-$C_{1\text{-}8}$alkyl, heteroaryl-$C_{1\text{-}8}$alkoxy, heteroaryl-amino, heteroaryl-$C_{1\text{-}8}$alkyl-amino,

(heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl;

[00257] wherein, heterocyclyl is selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, octahydro-2H-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl or

6,9-diazaspiro[4.5]decyl; and, wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents; and

[00258] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00259] wherein, heterocyclyl is selected from 1,2,3,6-tetrahydropyridin-4-yl, 1,3-benzodioxol-5-yl or 2,3-dihydro-1,4-benzodioxin-6-yl;

[00260] wherein, heteroaryl is selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; and, wherein, each instance of heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00261] In another embodiment of a compound of Formula (I),

[00262] R_1 is C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy,

C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino or [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino; and

[00263] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00264] In another embodiment of a compound of Formula (I),

[00265] R_1 is heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino,

aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents; and

[00266] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00267] In another embodiment of a compound of Formula (I),

[00268] R_1 is heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl or heterocyclyl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R_3 and R_4 substituents; and

[00269] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00270] In another embodiment of a compound of Formula (I),

[00271] R_1 is heterocyclyl optionally substituted with R_3 and R_4 substituents; and

[00272] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00273] In another embodiment of a compound of Formula (I),

[00274] R_1 is C_{3-14}cycloalkyl optionally substituted with R_3 and R_4 substituents; and

[00275] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00276] In another embodiment of a compound of Formula (I),

[00277] R_1 is aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of aryl is optionally substituted with R_3 and R_4 substituents; and

[00278] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00279] In another embodiment of a compound of Formula (I),

[00280] R_1 is aryl-C_{1-8}alkyl-amino optionally substituted with R_3 and R_4 substituents; and

[00281] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00282] In another embodiment of a compound of Formula (I),

[00283] R_1 is heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino,(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl; wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with R_3 and R_4 substituents; and

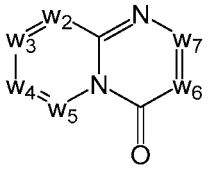
[00284] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00285] In another embodiment of a compound of Formula (I),

[00286] R_1 is heteroaryl optionally substituted with R_3 and R_4 substituents; and

[00287] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R_6 and R_7 substituents.

[00288] An embodiment of the compound of Formula (I) is a compound selected from Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV):



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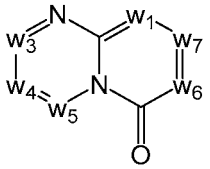

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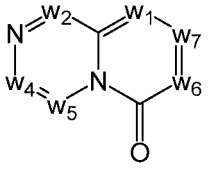

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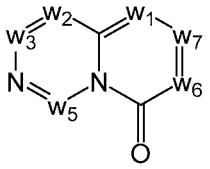

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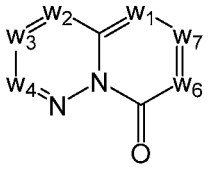

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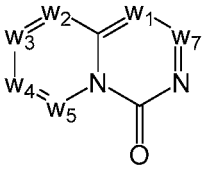

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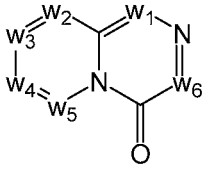

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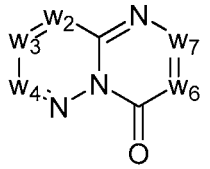

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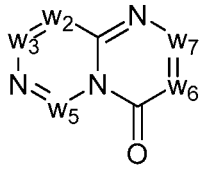

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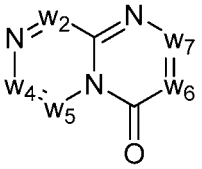

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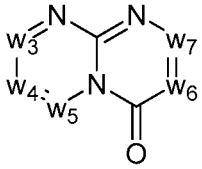

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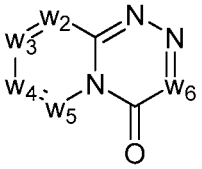
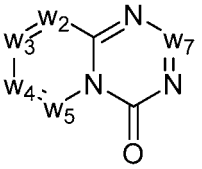


(XIII), or



(XIV)

[00289] or a form thereof.

[00290] In an embodiment of the compound of Formula (I), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00291] In another embodiment of the compound of Formula (I), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00292] In another embodiment of the compound of Formula (I), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00293] In another embodiment of the compound of Formula (I), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00294] In an embodiment of the compound of Formula (II), w_3 is C-R_1, w_6 is C-R_2, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00295] In another embodiment of the compound of Formula (II), w_3 is C-R_2, w_6 is C-R_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00296] In another embodiment of the compound of Formula (II), w_4 is C-R_1, w_7 is C-R_2, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00297] In another embodiment of the compound of Formula (II), w_4 is C-R_2, w_7 is C-R_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00298] In an embodiment of the compound of Formula (III), w_3 is C-R_1, w_6 is C-R_2 and w_1, w_4, w_5 and w_7 are independently C-R_a or N.

[00299] In another embodiment of the compound of Formula (III), w_3 is C-R_2, w_6 is C-R_1 and w_1, w_4, w_5 and w_7 are independently C-R_a or N.

[00300] In another embodiment of the compound of Formula (III), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00301] In another embodiment of the compound of Formula (III), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00302] In an embodiment of the compound of Formula (IV), w_4 is C-R_1, w_7 is C-R_2, w_1 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00303] In another embodiment of the compound of Formula (IV), w_4 is C-R_2, w_7 is C-R_1, w_1 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00304] In an embodiment of the compound of Formula (V), w_3 is C-R_1, w_6 is C-R_2, w_1, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00305] In another embodiment of the compound of Formula (V), w_3 is C-R_2, w_6 is C-R_1, w_1, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00306] In an embodiment of the compound of Formula (VI), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00307] In another embodiment of the compound of Formula (VI), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00308] In another embodiment of the compound of Formula (VI), w_4 is C-R_1, w_7 is C-R_2, w_1 and w_3 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00309] In another embodiment of the compound of Formula (VI), w_4 is C-R_2, w_7 is C-R_1, w_1 and w_3 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00310] In another embodiment of the compound of Formula (VII), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00311] In another embodiment of the compound of Formula (VII), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00312] In another embodiment of the compound of Formula (VIII), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00313] In another embodiment of the compound of Formula (VIII), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00314] In an embodiment of the compound of Formula (IX), w_3 is C-R_1, w_6 is C-R_2, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00315] In another embodiment of the compound of Formula (IX), w_3 is C-R_2, w_6 is C-R_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00316] In another embodiment of the compound of Formula (IX), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00317] In another embodiment of the compound of Formula (IX), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00318] In an embodiment of the compound of Formula (X), w_3 is C-R_1, w_6 is C-R_2, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00319] In another embodiment of the compound of Formula (X), w_3 is C-R_2, w_6 is C-R_1, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00320] In an embodiment of the compound of Formula (XI), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00321] In another embodiment of the compound of Formula (XI), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00322] In an embodiment of the compound of Formula (XII), w_3 is C-R_1, w_6 is C-R_2 and w_4, w_5 and w_7 are independently C-R_a or N.

[00323] In another embodiment of the compound of Formula (XII), w_3 is C-R_2, w_6 is C-R_1 and w_4, w_5 and w_7 are independently C-R_a or N.

[00324] In another embodiment of the compound of Formula (XII), w_4 is C-R_1, w_7 is C-R_2, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00325] In another embodiment of the compound of Formula (XII), w_4 is C-R_2, w_7 is C-R_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

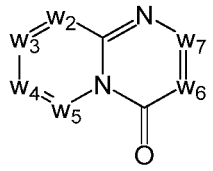
[00326] In an embodiment of the compound of Formula (XIII), w_3 is C-R_1, w_6 is C-R_2, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

[00327] In another embodiment of the compound of Formula (XIII), w_3 is C-R_2, w_6 is C-R_1, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

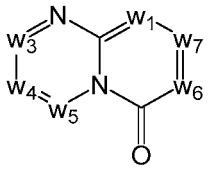
[00328] In an embodiment of the compound of Formula (XIV), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

[00329] In another embodiment of the compound of Formula (XIV), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

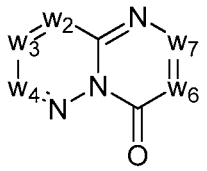
[00330] Another embodiment of the compound of Formula (I) is a compound selected from Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII):



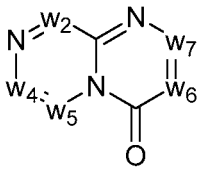
(II),



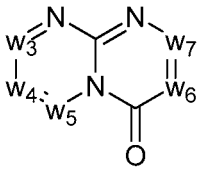
(III),



(IX),



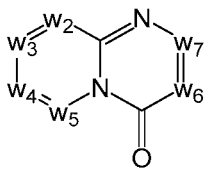
(XI), or



(XII)

[00331] or a form thereof.

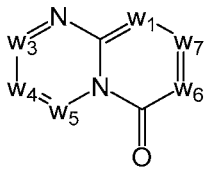
[00332] Another embodiment of the compound of Formula (I) is a compound of Formula (II):



(II)

[00333] or a form thereof.

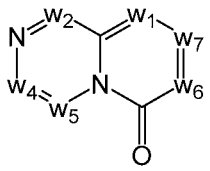
[00334] Another embodiment of the compound of Formula (I) is a compound of Formula (III):



(III)

[00335] or a form thereof.

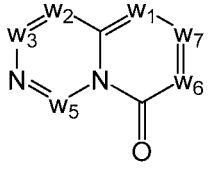
[00336] Another embodiment of the compound of Formula (I) is a compound of Formula (IV):



(IV)

[00337] or a form thereof.

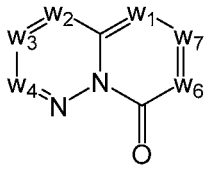
[00338] Another embodiment of the compound of Formula (I) is a compound of Formula (V):



(V)

[00339] or a form thereof.

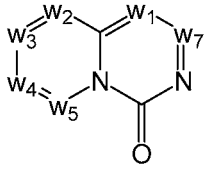
[00340] Another embodiment of the compound of Formula (I) is a compound of Formula (VI):



(VI)

[00341] or a form thereof.

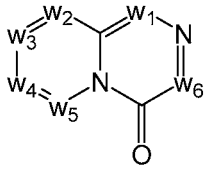
[00342] Another embodiment of the compound of Formula (I) is a compound of Formula (VII):



(VII)

[00343] or a form thereof.

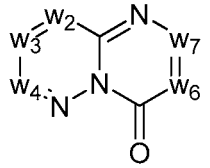
[00344] Another embodiment of the compound of Formula (I) is a compound of Formula (VIII):



(VIII)

[00345] or a form thereof.

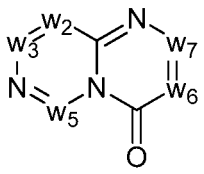
[00346] Another embodiment of the compound of Formula (I) is a compound of Formula (IX):



(IX)

[00347] or a form thereof.

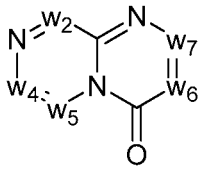
[00348] Another embodiment of the compound of Formula (I) is a compound of Formula (X):



(X)

[00349] or a form thereof.

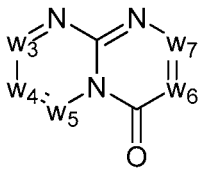
[00350] Another embodiment of the compound of Formula (I) is a compound of Formula (XI):



(XI)

[00351] or a form thereof.

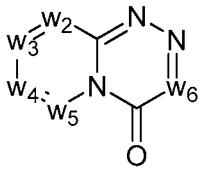
[00352] Another embodiment of the compound of Formula (I) is a compound of Formula (XII):



(XII)

[00353] or a form thereof.

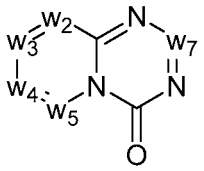
[00354] Another embodiment of the compound of Formula (I) is a compound of Formula (XIII):



(XIII)

[00355] or a form thereof.

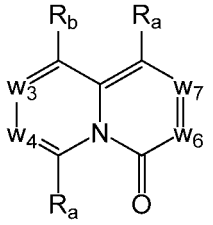
[00356] Another embodiment of the compound of Formula (I) is a compound of Formula (XIV):



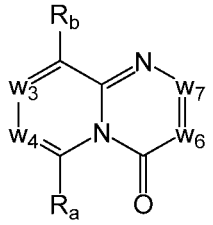
(XIV)

[00357] or a form thereof.

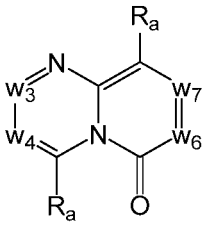
[00358] An embodiment of the compound of Formula (I), Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV) is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IVa), Formula (Va), Formula (VIa), Formula (VIIa), Formula (VIIIa), Formula (IXa), Formula (Xa), Formula (XIa), Formula (XIIa), Formula (XIIIa) or Formula (XIVa), respectively:



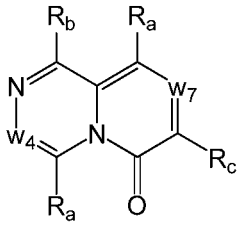
(Ia),



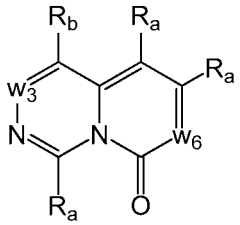
(IIa),



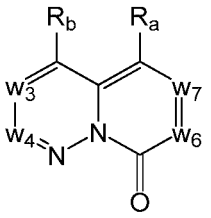
(IIIa),



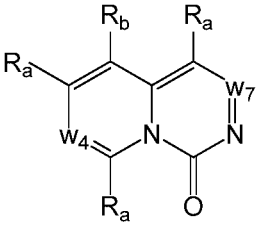
(IVa),



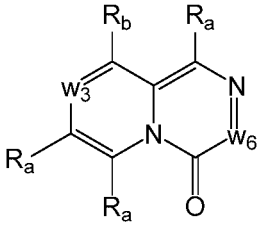
(Va),



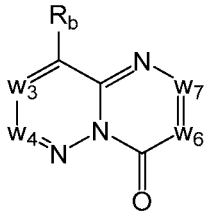
(VIa),



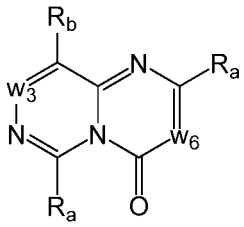
(VIIa),



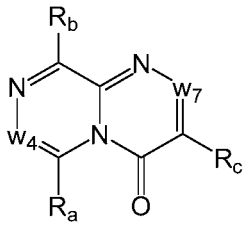
(VIIIa),



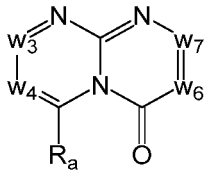
(IXa),



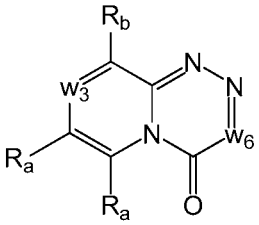
(Xa),



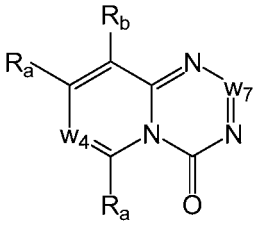
(XIa),



(XIIa),



(XIIIa), or



(XIVa)

[00359] or a form thereof.

[00360] In an embodiment of the compound of Formula (Ia), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00361] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00362] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00363] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00364] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00365] In an embodiment of the compound of Formula (IIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00366] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00367] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00368] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00369] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00370] In an embodiment of the compound of Formula (IIIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00371] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00372] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00373] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00374] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00375] In an embodiment of the compound of Formula (IVa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00376] In an embodiment of the compound of Formula (Va), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00377] In an embodiment of the compound of Formula (VIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00378] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00379] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00380] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00381] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00382] In an embodiment of the compound of Formula (VIIa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00383] In an embodiment of the compound of Formula (VIIIa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00384] In an embodiment of the compound of Formula (IXa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00385] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00386] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00387] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00388] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00389] In an embodiment of the compound of Formula (Xa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00390] In an embodiment of the compound of Formula (XIa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00391] In an embodiment of the compound of Formula (XIIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00392] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00393] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

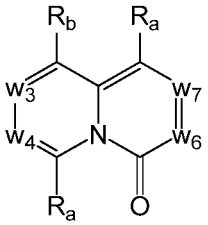
[00394] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00395] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

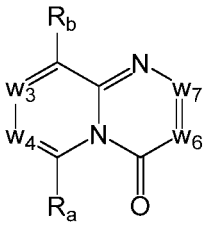
[00396] In an embodiment of the compound of Formula (XIIIa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00397] In an embodiment of the compound of Formula (XIVa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

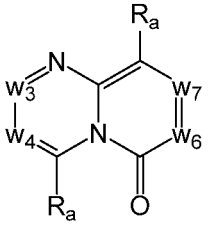
[00398] An embodiment of the compound of Formula (I), Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII) is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IXa), Formula (XIa) or Formula (XIIa), respectively:



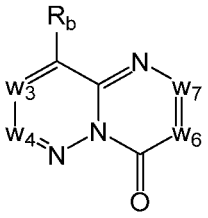
(Ia),



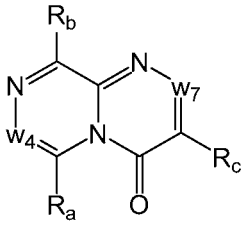
(IIa),



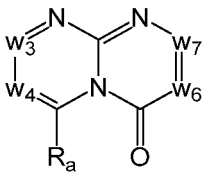
(IIIa),



(IXa),



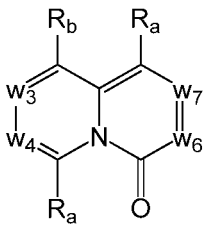
(XIa), or



(XIIa)

[00399] or a form thereof.

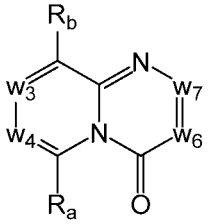
[00400] Another embodiment of the compound of Formula (I) is a compound of Formula (Ia):



(Ia)

[00401] or a form thereof.

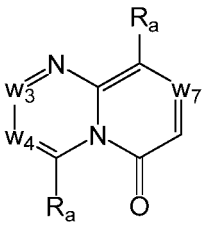
[00402] Another embodiment of the compound of Formula (II) is a compound of Formula (IIa):



(IIa)

[00403] or a form thereof.

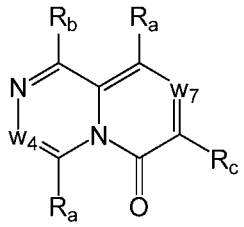
[00404] Another embodiment of the compound of Formula (III) is a compound of Formula (IIIa):



(IIIa)

[00405] or a form thereof.

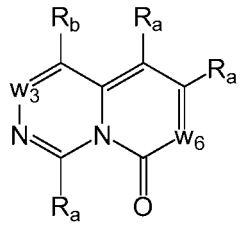
[00406] Another embodiment of the compound of Formula (IV) is a compound of Formula (IVa):



(IVa)

[00407] or a form thereof.

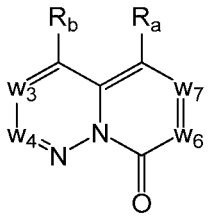
[00408] Another embodiment of the compound of Formula (V) is a compound of Formula (Va):



(Va)

[00409] or a form thereof.

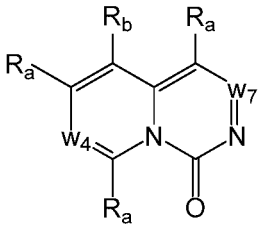
[00410] Another embodiment of the compound of Formula (VI) is a compound of Formula (VIa):



(VIa)

[00411] or a form thereof.

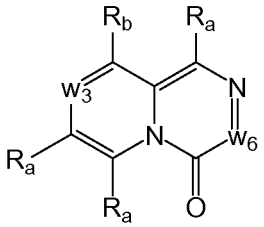
[00412] Another embodiment of the compound of Formula (VII) is a compound of Formula (VIIa):



(VIIa)

[00413] or a form thereof.

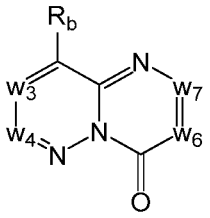
[00414] Another embodiment of the compound of Formula (VIII) is a compound of Formula (VIIIa):



(VIIIa)

[00415] or a form thereof.

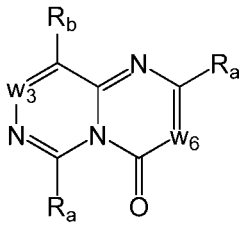
[00416] Another embodiment of the compound of Formula (IX) is a compound of Formula (IXa):



(IXa)

[00417] or a form thereof.

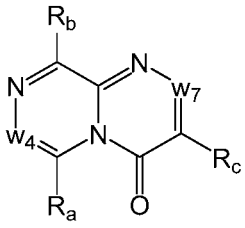
[00418] Another embodiment of the compound of Formula (X) is a compound of Formula (Xa):



(Xa)

[00419] or a form thereof.

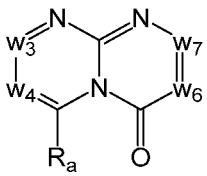
[00420] Another embodiment of the compound of Formula (XI) is a compound of Formula (XIa):



(XIa)

[00421] or a form thereof.

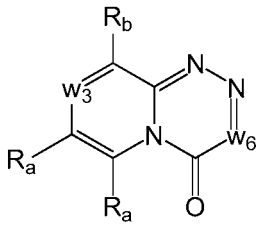
[00422] Another embodiment of the compound of Formula (XII) is a compound of Formula (XIIa):



(XIIa)

[00423] or a form thereof.

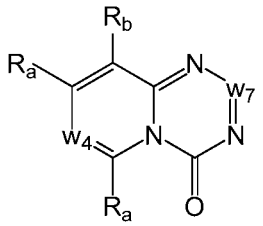
[00424] Another embodiment of the compound of Formula (XIII) is a compound of Formula (XIIIa):



(XIIIa)

[00425] or a form thereof.

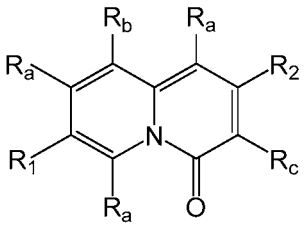
[00426] Another embodiment of the compound of Formula (XIV) is a compound of Formula (XIVa):



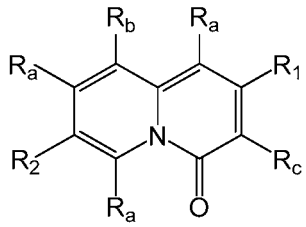
(XIVa)

[00427] or a form thereof.

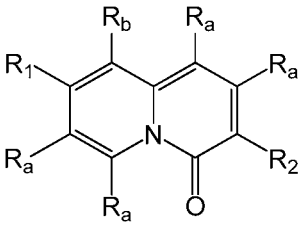
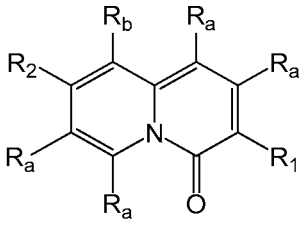
[00428] An embodiment of the compound of Formula (Ia) is a compound of Formula (Ia1), Formula (Ia2), Formula (Ia3) or Formula (Ia4):



(Ia1),



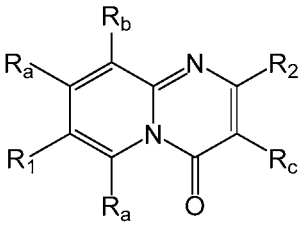
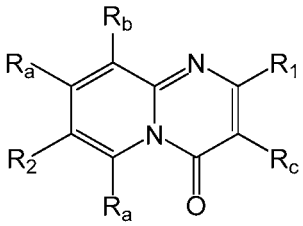
(Ia2),

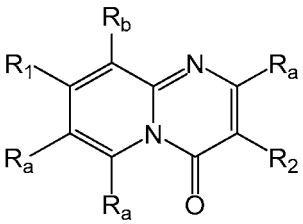
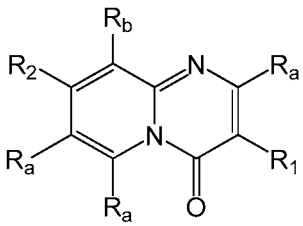
(Ia3) or (Ia4)

[00429] or a form thereof.

[00430] An embodiment of the compound of Formula (IIa) is a compound of Formula (IIa1), Formula (IIa2), Formula (IIa3) or Formula (IIa4):

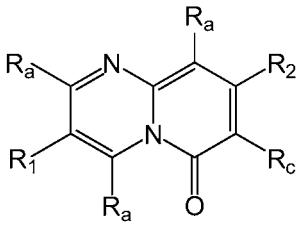
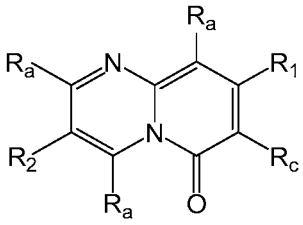
(IIa1), (IIa2),

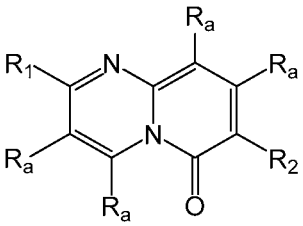
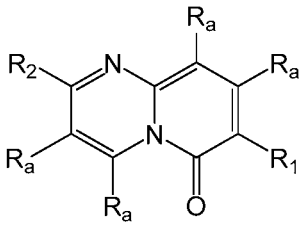
(IIa3) or (IIa4)

[00431] or a form thereof.

[00432] An embodiment of the compound of Formula (IIIa) is a compound of Formula (IIIa1), Formula (IIIa2), Formula (IIIa3) or Formula (IIIa4):

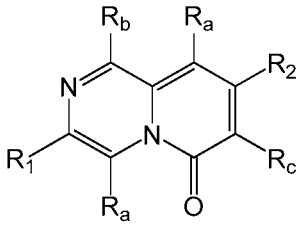
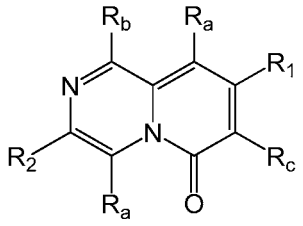
(IIIa1), (IIIa2),

(IIIa3) or (IIIa4)

[00433] or a form thereof.

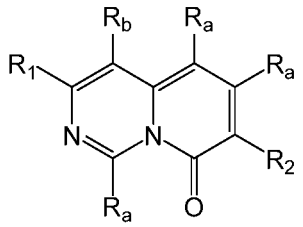
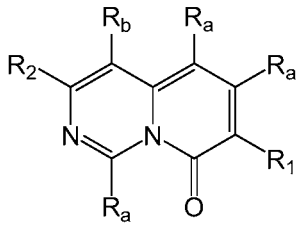
[00434] An embodiment of the compound of Formula (IVa) includes a compound of Formula (IVa1) or Formula (IVa2):

(IVa1) or (IVa2)

[00435] or a form thereof.

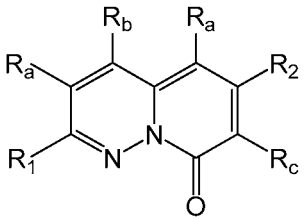
[00436] An embodiment of the compound of Formula (Va) is a compound of Formula (Va1) or Formula (Va2):

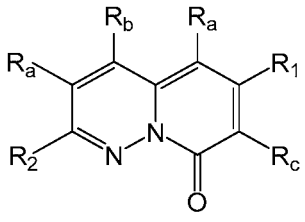
(Va1) or (Va2)

[00437] or a form thereof.

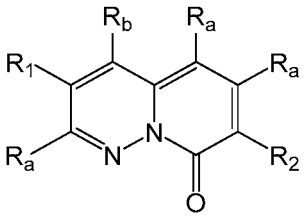
[00438] An embodiment of the compound of Formula (VIa) is a compound of Formula (VIa1), Formula (VIa2), Formula (VIa3) or Formula (VIa4):



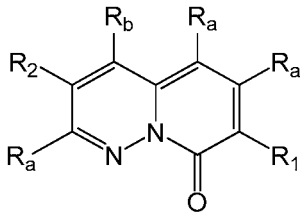
(VIa1),



(VIa2),



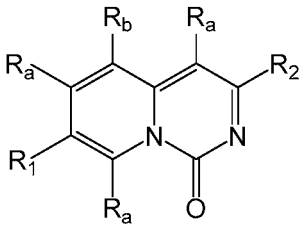
(VIa3) or



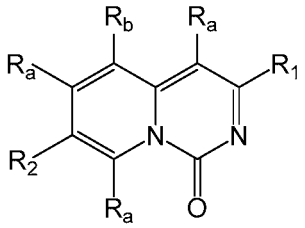
(VIa4)

[00439] or a form thereof.

[00440] An embodiment of the compound of Formula (VIIa) includes a compound of Formula (VIIa1) or Formula (VIIa2):



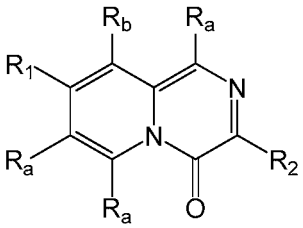
(VIIa1) or



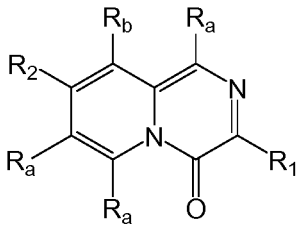
(VIIa2)

[00441] or a form thereof.

[00442] An embodiment of the compound of Formula (VIIIa) is a compound of Formula (VIIIa1) or Formula (VIIIa2):



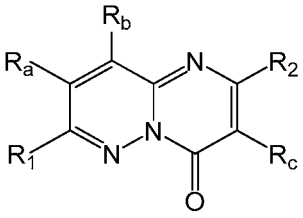
(VIIIa1) or



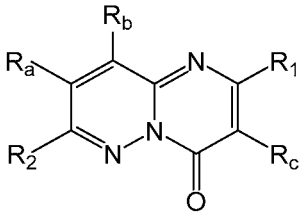
(VIIIa2)

[00443] or a form thereof.

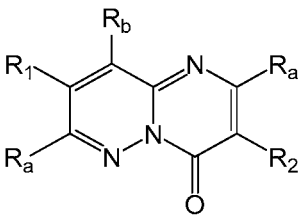
[00444] An embodiment of the compound of Formula (IXa) is a compound of Formula (IXa1), Formula (IXa2), Formula (IXa3) or Formula (IXa4):



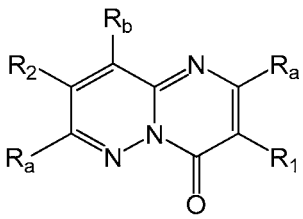
(IXa1),



(IXa2),



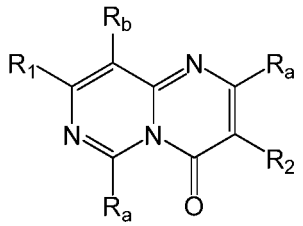
(IXa3) or



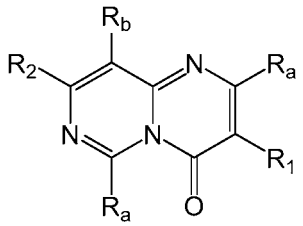
(IXa4)

[00445] or a form thereof.

[00446] An embodiment of the compound of Formula (Xa) is a compound of Formula (Xa1) or Formula (Xa2):



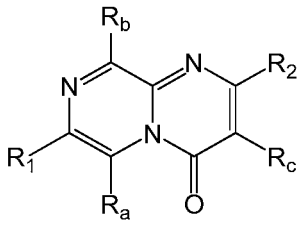
(Xa1) or



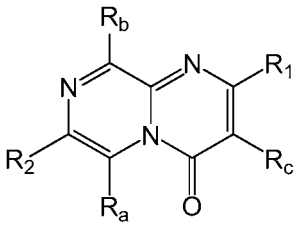
(Xa2)

[00447] or a form thereof.

[00448] An embodiment of the compound of Formula (XIa) is a compound of Formula (XIa1) or Formula (XIa2):



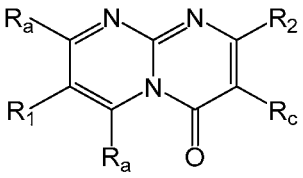
(XIa1) or



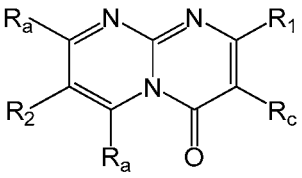
(XIa2)

[00449] or a form thereof.

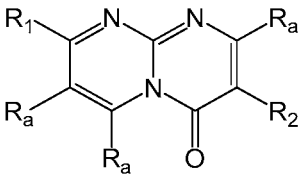
[00450] An embodiment of the compound of Formula (XIIa) is a compound of Formula (XIIa1), Formula (XIIa2), Formula (XIIa3) or Formula (XIIa4):



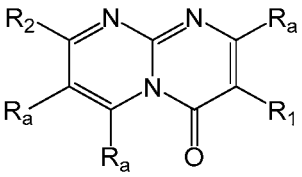
(XIIa1),



(XIIa2),



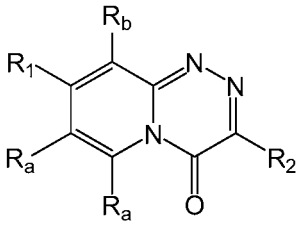
(XIIa3) or



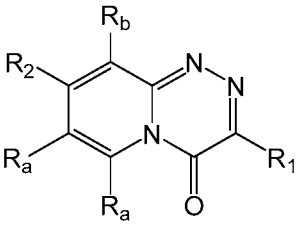
(XIIa4)

[00451] or a form thereof.

[00452] An embodiment of the compound of Formula (XIIIa) is a compound of Formula (XIIIa1) or Formula (XIIIa2):



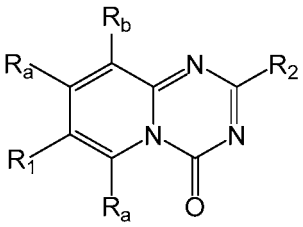
(XIIIa1) or



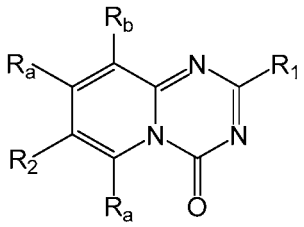
(XIIIa2)

[00453] or a form thereof.

[00454] An embodiment of the compound of Formula (XIVa) is a compound of Formula (XIVa1) or Formula (XIVa2):



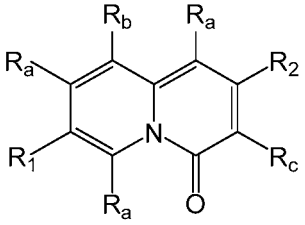
(XIVa1) or



(XIVa2)

[00455] or a form thereof.

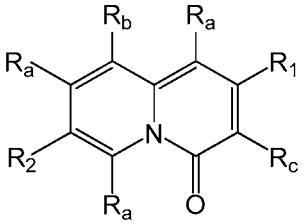
[00456] An embodiment of the compound of Formula (Ia) is a compound of Formula (Ia1):



(Ia1)

[00457] or a form thereof.

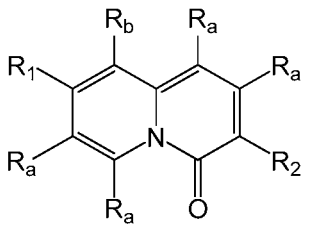
[00458] An embodiment of the compound of Formula (Ia) is a compound of Formula (Ia2):



(Ia2)

[00459] or a form thereof.

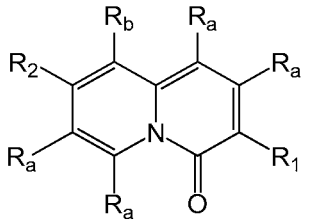
[00460] An embodiment of the compound of Formula (Ia) is a compound of Formula (Ia3):



(Ia3)

[00461] or a form thereof.

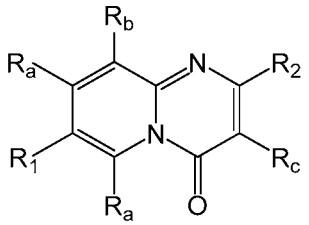
[00462] An embodiment of the compound of Formula (Ia) is a compound of Formula (Ia4):



(Ia4)

[00463] or a form thereof.

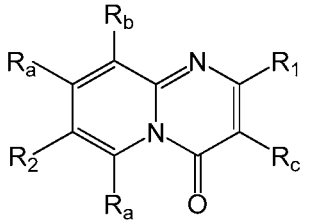
[00464] An embodiment of the compound of Formula (IIa) is a compound of Formula (IIa1):



(IIa1)

[00465] or a form thereof.

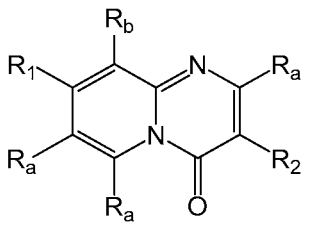
[00466] An embodiment of the compound of Formula (IIa) is a compound of Formula (IIa2):



(IIa2)

[00467] or a form thereof.

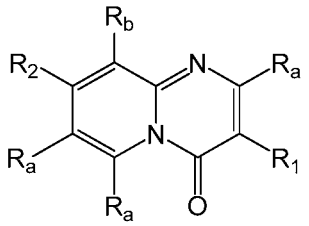
[00468] An embodiment of the compound of Formula (IIa) is a compound of Formula (IIa3):



(IIa3)

[00469] or a form thereof.

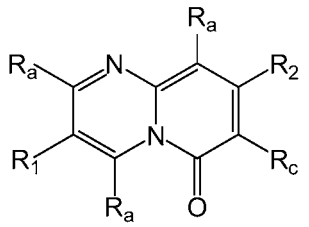
[00470] An embodiment of the compound of Formula (IIa) is a compound of Formula (IIa4):



(IIa4)

[00471] or a form thereof.

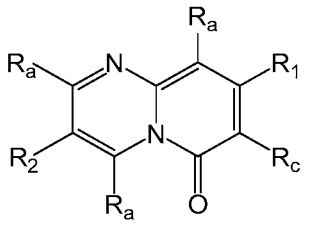
[00472] An embodiment of the compound of Formula (IIIa) is a compound of Formula (IIIa1):



(IIIa1)

[00473] or a form thereof.

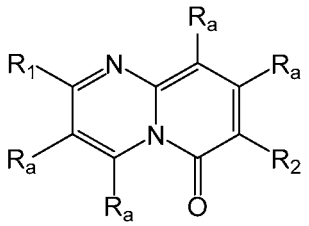
[00474] An embodiment of the compound of Formula (IIIa) is a compound of Formula (IIIa2):



(IIIa2)

[00475] or a form thereof.

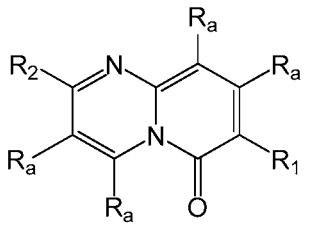
[00476] An embodiment of the compound of Formula (IIIa) is a compound of Formula (IIIa3):



(IIIa3)

[00477] or a form thereof.

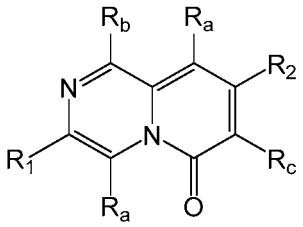
[00478] An embodiment of the compound of Formula (IIIa) is a compound of Formula (IIIa4):



(IIIa4)

[00479] or a form thereof.

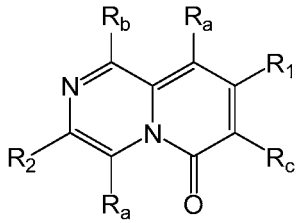
[00480] An embodiment of the compound of Formula (IVa) is a compound of Formula (IVa1):



(IVa1)

[00481] or a form thereof.

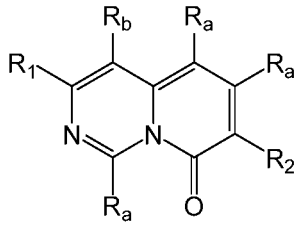
[00482] An embodiment of the compound of Formula (IVa) is a compound of Formula (IVa2):



(IVa2)

[00483] or a form thereof.

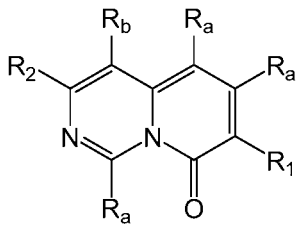
[00484] An embodiment of the compound of Formula (Va) is a compound of Formula (Va1):



(Va1)

[00485] or a form thereof.

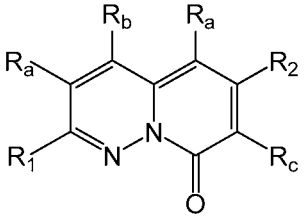
[00486] An embodiment of the compound of Formula (Va) is a compound of Formula (Va2):



(Va2)

[00487] or a form thereof.

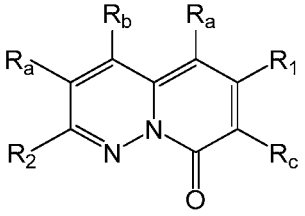
[00488] An embodiment of the compound of Formula (VIa) is a compound of Formula (VIa1):



(VIa1)

[00489] or a form thereof.

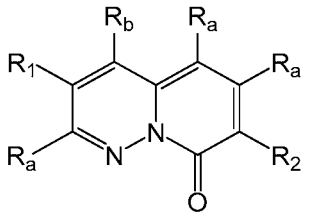
[00490] An embodiment of the compound of Formula (VIa) is a compound of Formula (VIa2):



(VIa2)

[00491] or a form thereof.

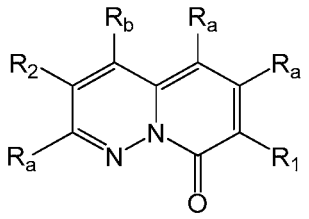
[00492] An embodiment of the compound of Formula (VIa) is a compound of Formula Formula (VIa3):



(VIa3)

[00493] or a form thereof.

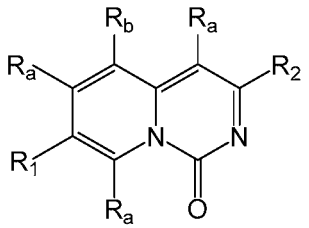
[00494] An embodiment of the compound of Formula (VIa) is a compound of Formula (VIa4):



(VIa4)

[00495] or a form thereof.

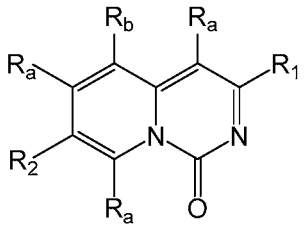
[00496] An embodiment of the compound of Formula (VIIa) is a compound of Formula (VIIa1):



(VIIa1)

[00497] or a form thereof.

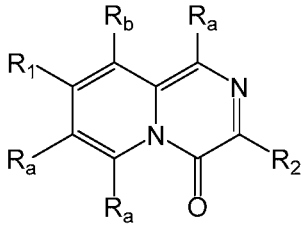
[00498] An embodiment of the compound of Formula (VIIa) is a compound of Formula (VIIa2):



(VIIa2)

[00499] or a form thereof.

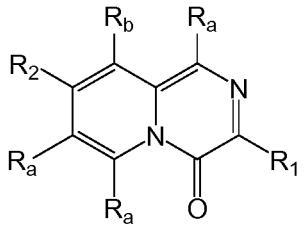
[00500] An embodiment of the compound of Formula (VIIIa) is a compound of Formula (VIIIa1):



(VIIIa1)

[00501] or a form thereof.

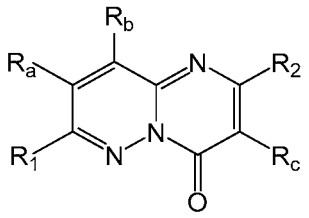
[00502] An embodiment of the compound of Formula (VIIIa) is a compound of Formula (VIIIa2):



(VIIIa2)

[00503] or a form thereof.

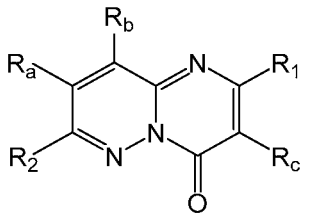
[00504] An embodiment of the compound of Formula (IXa) is a compound of Formula (IXa1):



(IXa1)

[00505] or a form thereof.

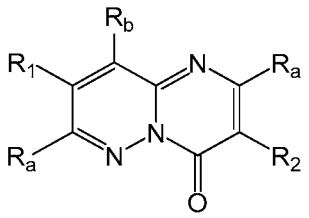
[00506] An embodiment of the compound of Formula (IXa) is a compound of Formula (IXa2):



(IXa2)

[00507] or a form thereof.

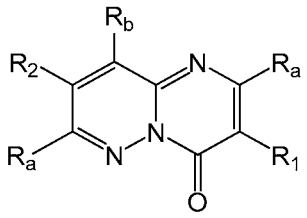
[00508] An embodiment of the compound of Formula (IXa) is a compound of Formula (IXa3):



(IXa3)

[00509] or a form thereof.

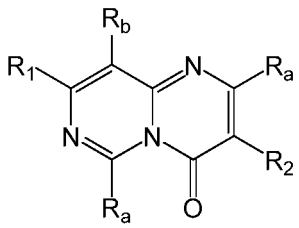
[00510] An embodiment of the compound of Formula (IXa) is a compound of Formula (IXa4):



(IXa4)

[00511] or a form thereof.

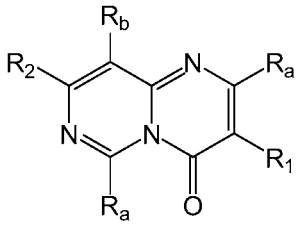
[00512] An embodiment of the compound of Formula (Xa) is a compound of Formula (Xa1):



(Xa1)

[00513] or a form thereof.

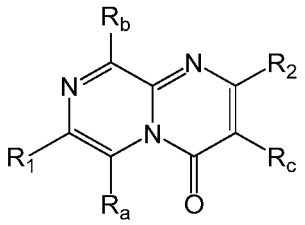
[00514] An embodiment of the compound of Formula (Xa) is a compound of Formula (Xa2):



(Xa2)

[00515] or a form thereof.

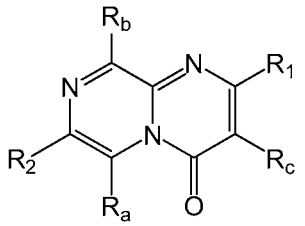
[00516] An embodiment of the compound of Formula (XIa) is a compound of Formula (XIa1):



(XIa1)

[00517] or a form thereof.

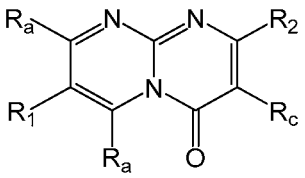
[00518] An embodiment of the compound of Formula (XIa) is a compound of Formula (XIa2):



(XIa2)

[00519] or a form thereof.

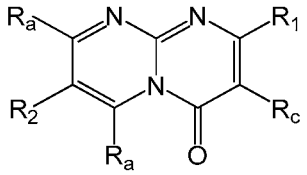
[00520] An embodiment of the compound of Formula (XIIa) is a compound of Formula (XIIa1):



(XIIa1)

[00521] or a form thereof.

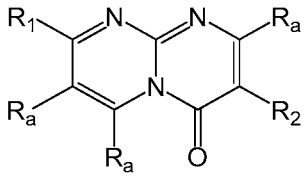
[00522] An embodiment of the compound of Formula (XIIa) is a compound of Formula (XIIa2):



(XIIa2)

[00523] or a form thereof.

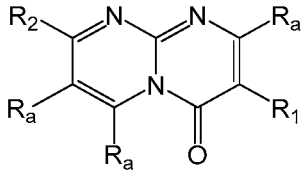
[00524] An embodiment of the compound of Formula (XIIa) is a compound of Formula (XIIa3):



(XIIa3)

[00525] or a form thereof.

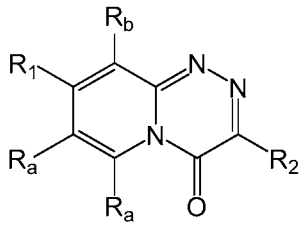
[00526] An embodiment of the compound of Formula (XIIa) is a compound of Formula (XIIa4):



(XIIa4)

[00527] or a form thereof.

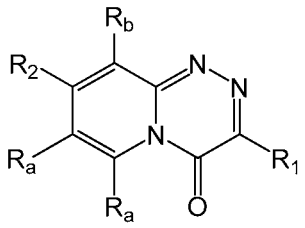
[00528] An embodiment of the compound of Formula (XIIIa) is a compound of Formula (XIIIa1):



(XIIIa1)

[00529] or a form thereof.

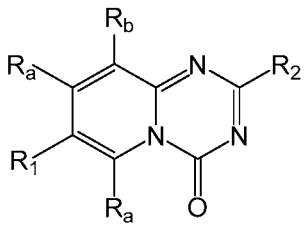
[00530] An embodiment of the compound of Formula (XIIIa) is a compound of Formula (XIIIa2):



(XIIIa2)

[00531] or a form thereof.

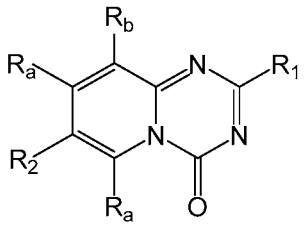
[00532] An embodiment of the compound of Formula (XIVa) is a compound of Formula (XIVa1):



(XIVa1)

[00533] or a form thereof.

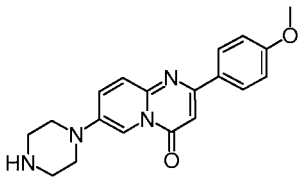
[00534] An embodiment of the compound of Formula (XIVa) is a compound of Formula (XIVa2):



(XIVa2)

[00535] or a form thereof.

[00536] An embodiment of the compound of Formula (I) is a compound selected from the group consisting of:



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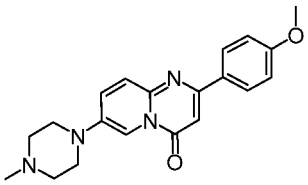

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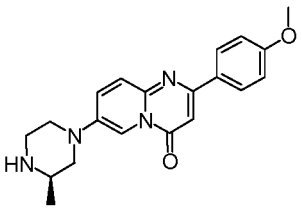

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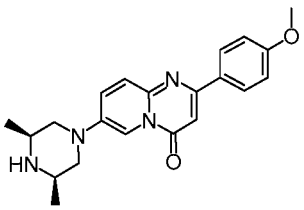

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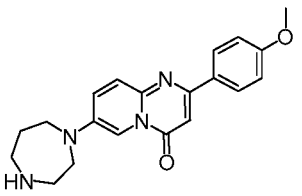

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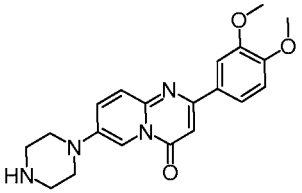

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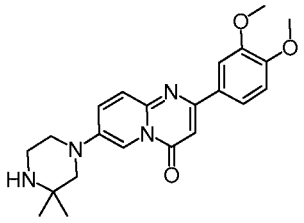

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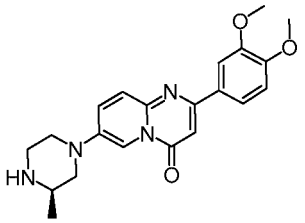

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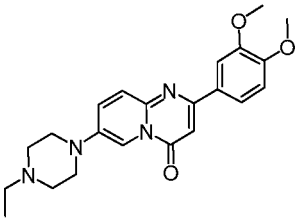

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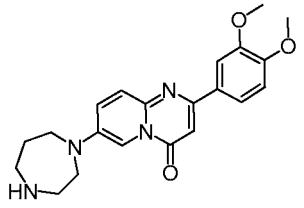

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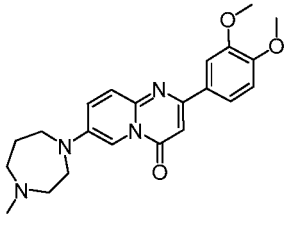

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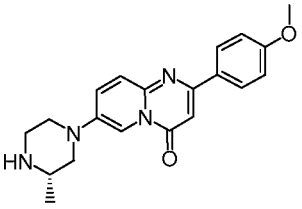

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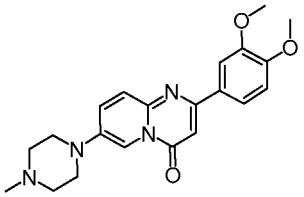

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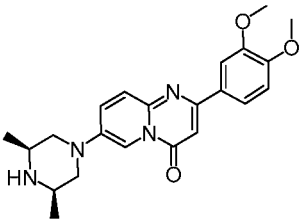

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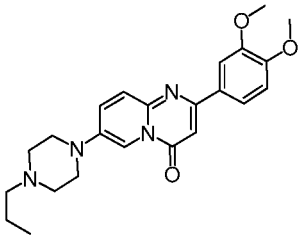

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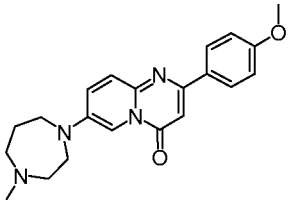

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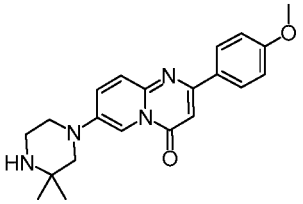

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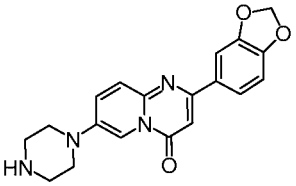

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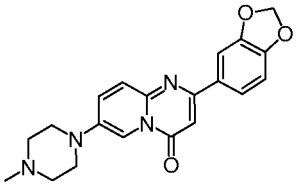

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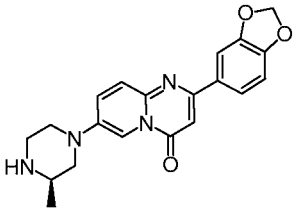

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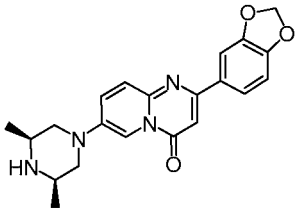

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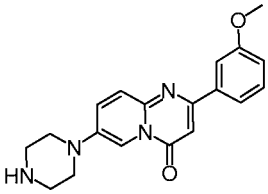

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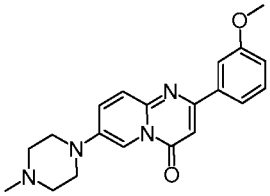

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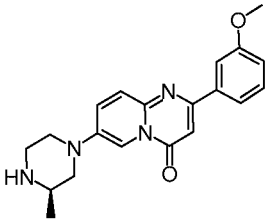

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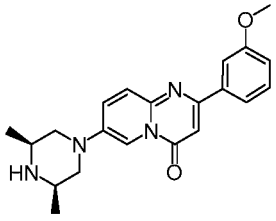

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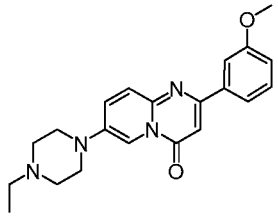

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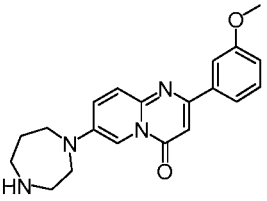

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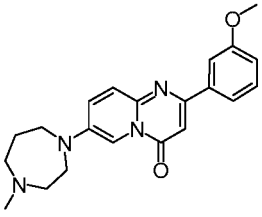

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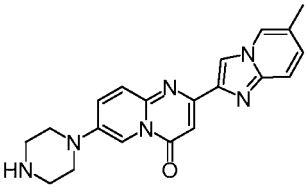

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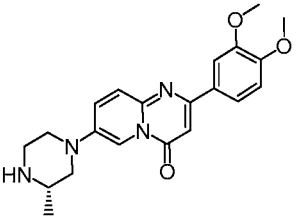

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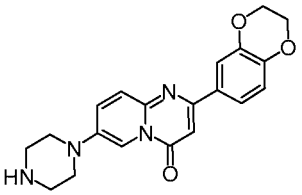

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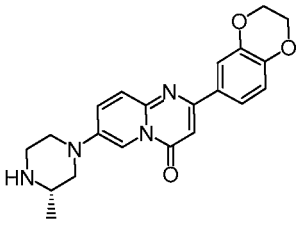

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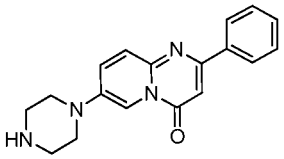

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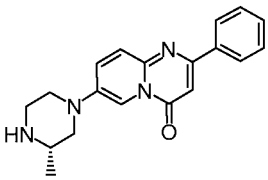

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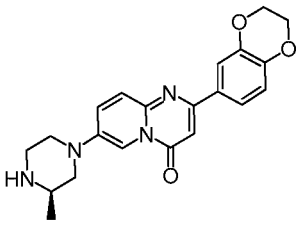

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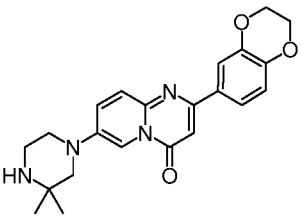

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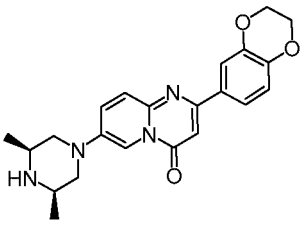

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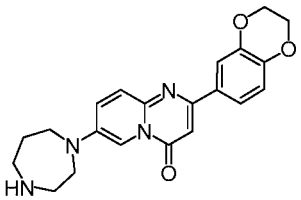

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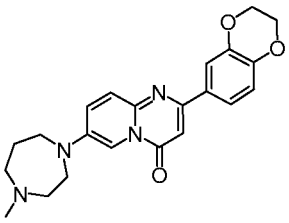

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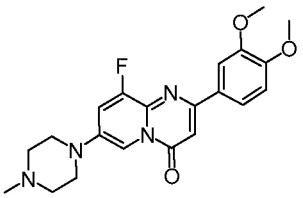

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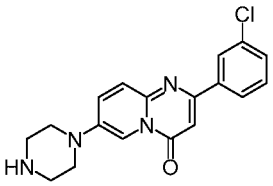

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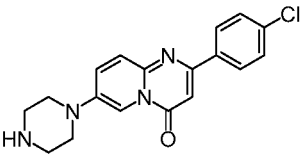

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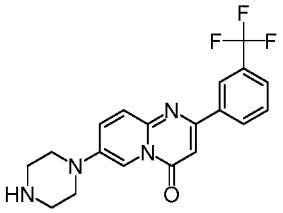

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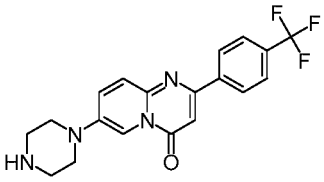

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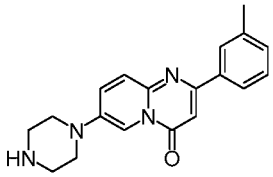

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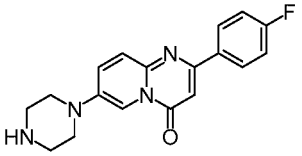

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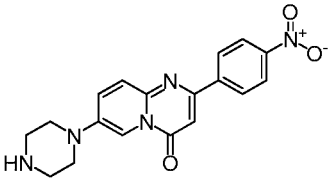

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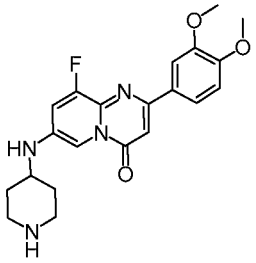

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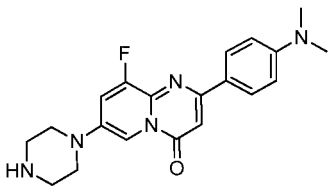

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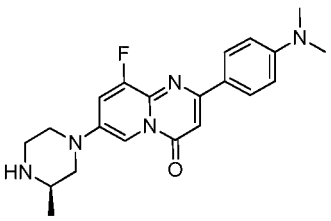

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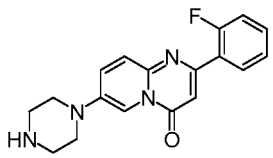

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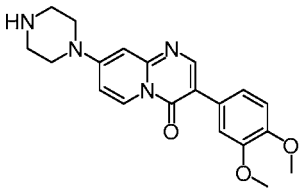

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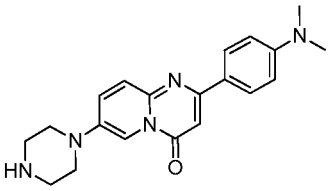

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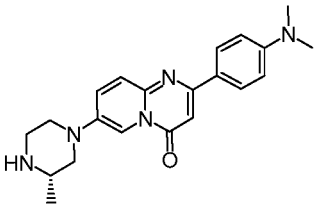

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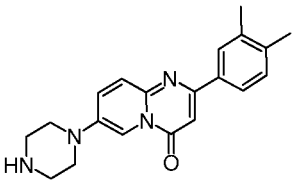

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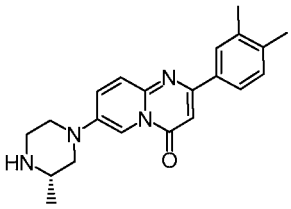

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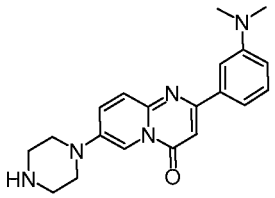

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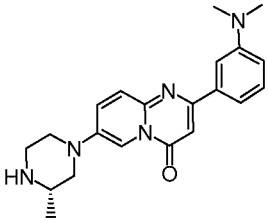

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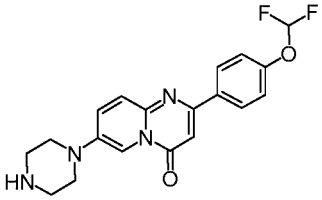

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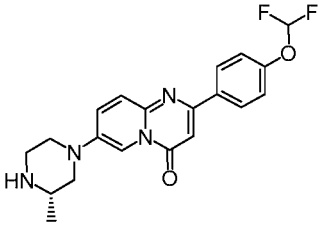

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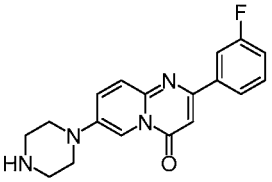

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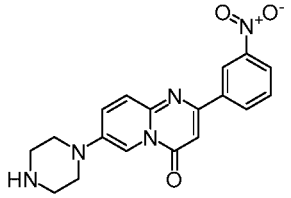

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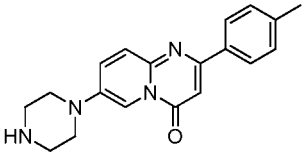

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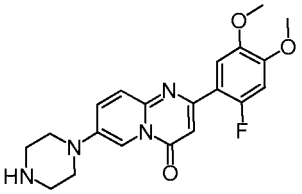

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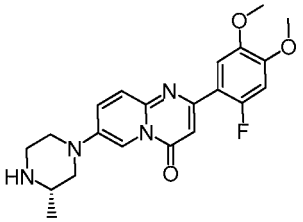

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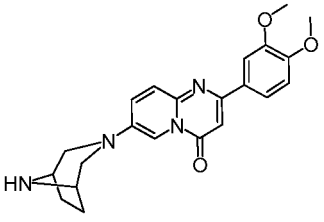

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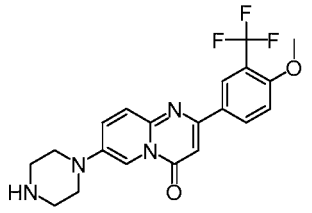

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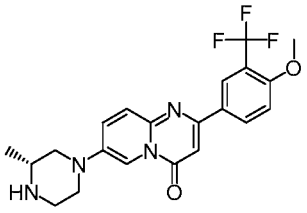

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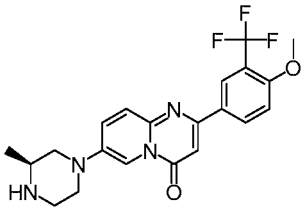

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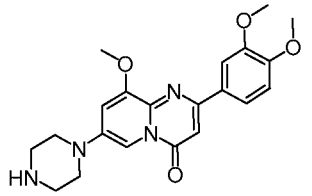

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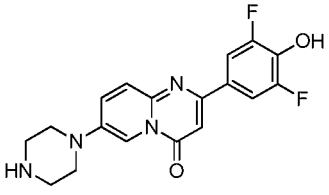

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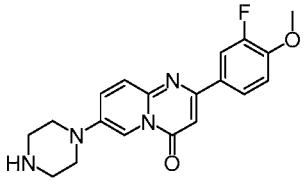

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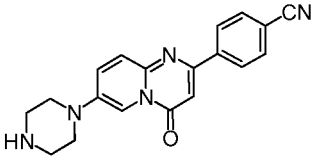

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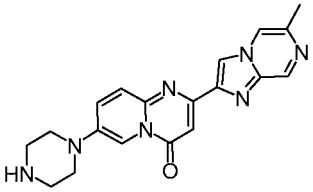

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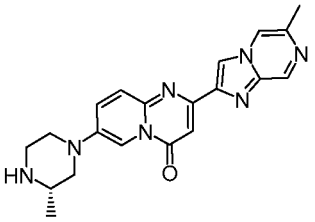

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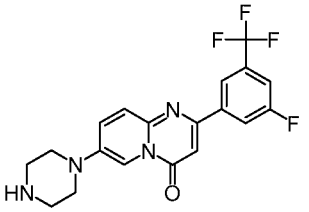

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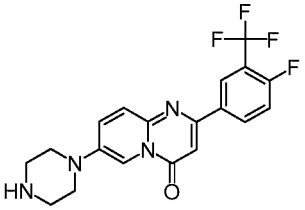

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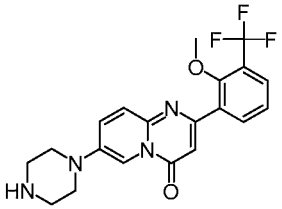

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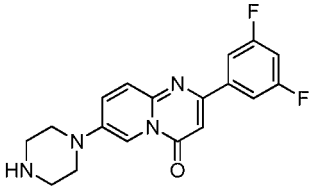

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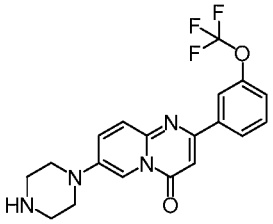

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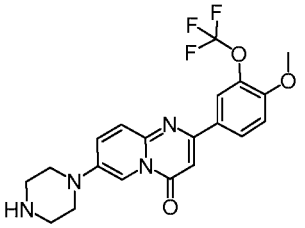

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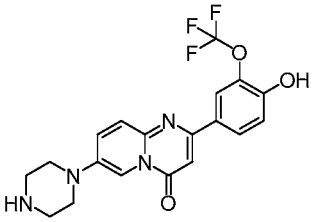

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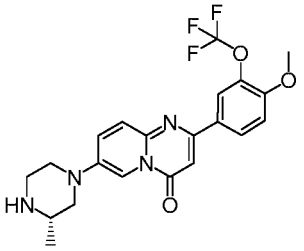

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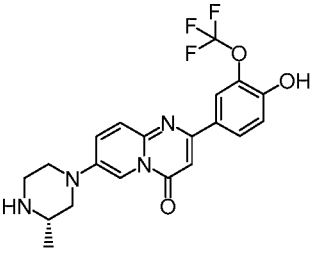

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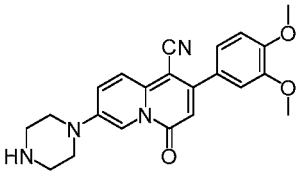

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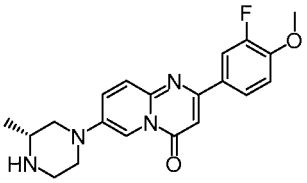

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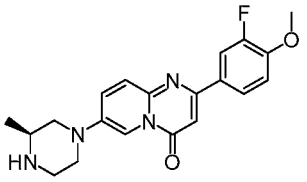

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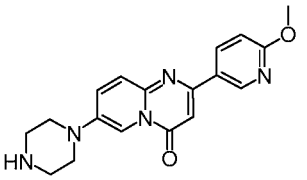

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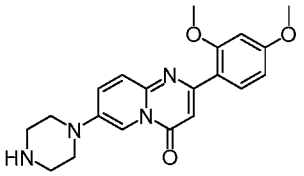

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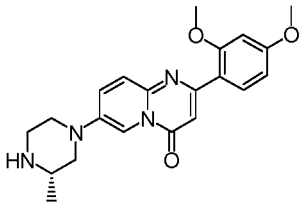

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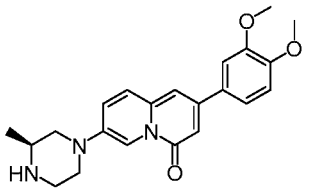

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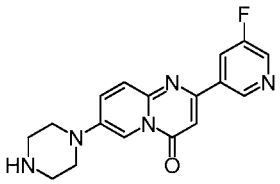

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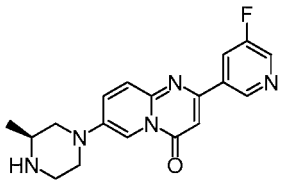

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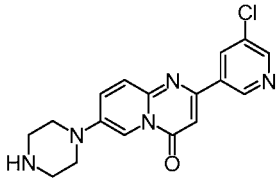

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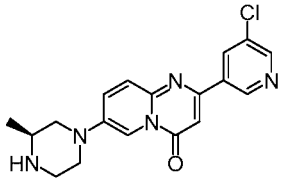

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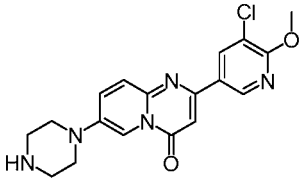

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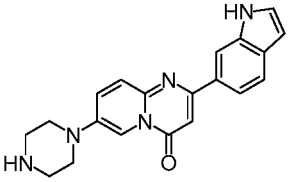

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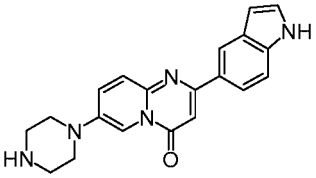

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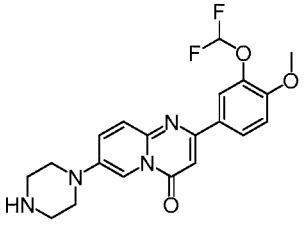

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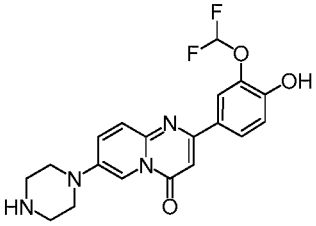

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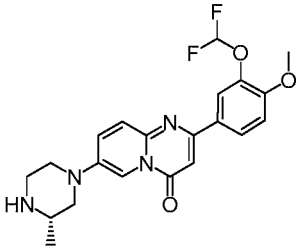

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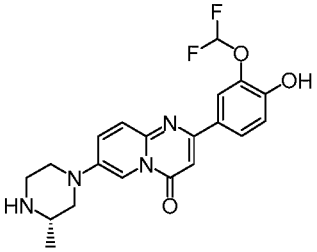

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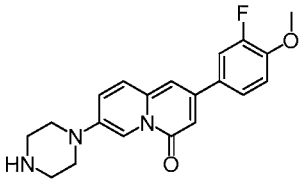

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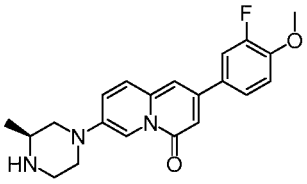

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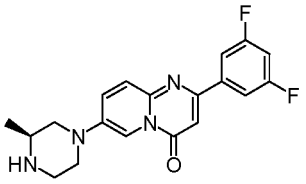

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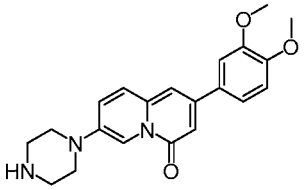

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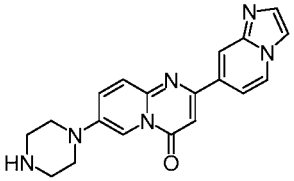

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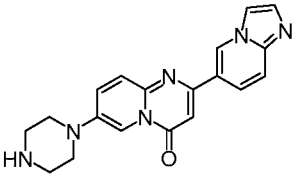

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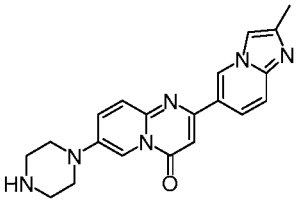

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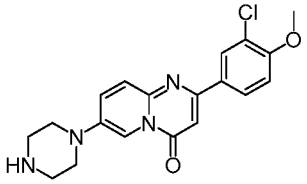

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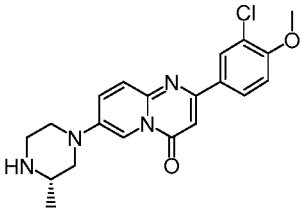

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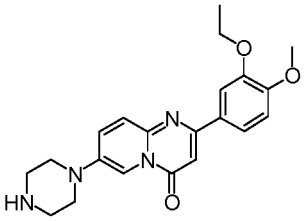

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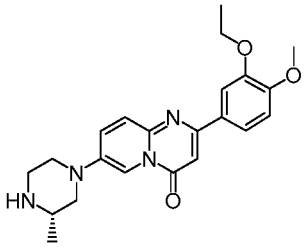

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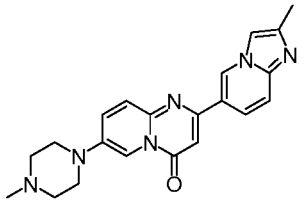

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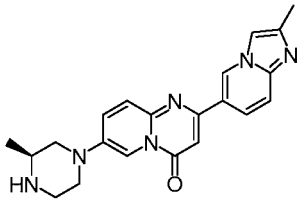

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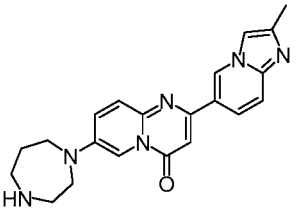

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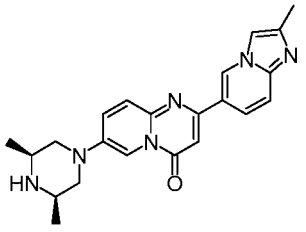

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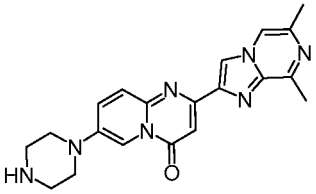

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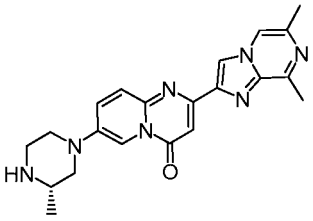

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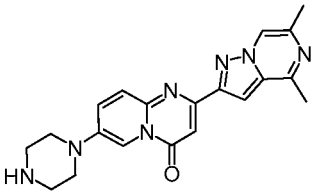

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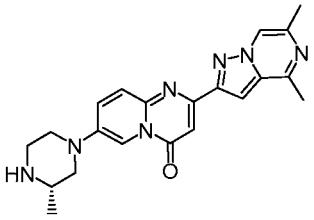

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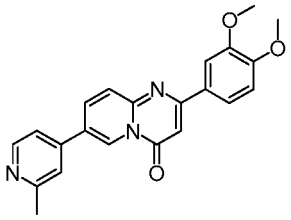

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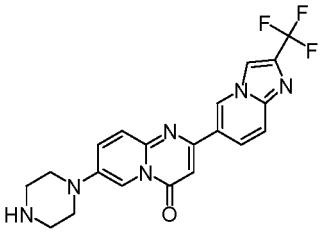

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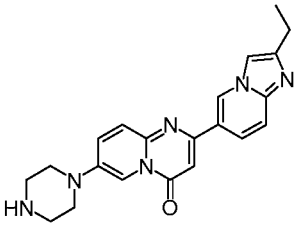

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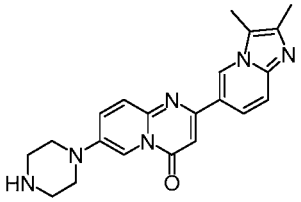

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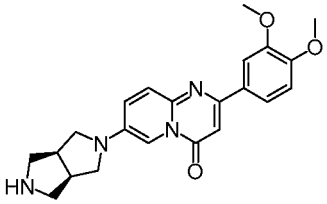

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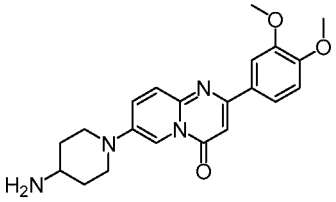

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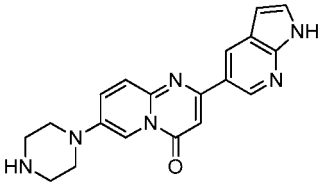

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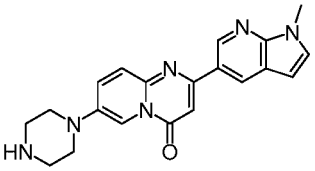

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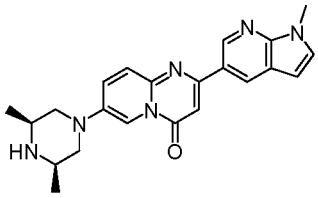

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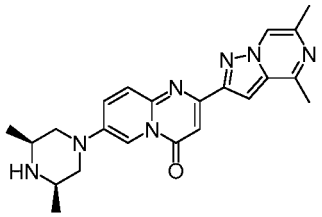

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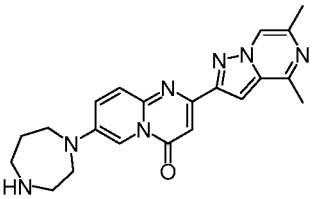

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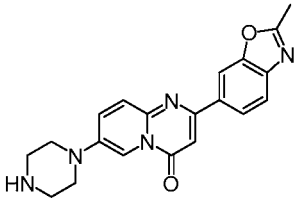

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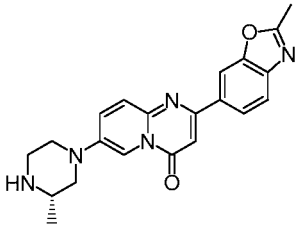

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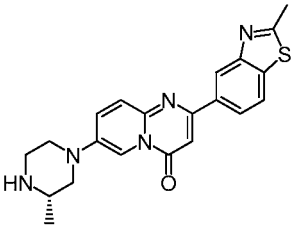

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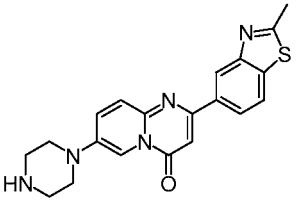

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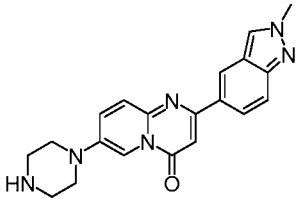

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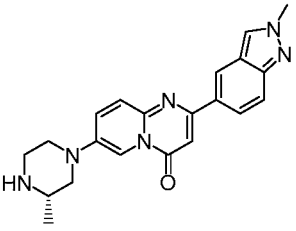

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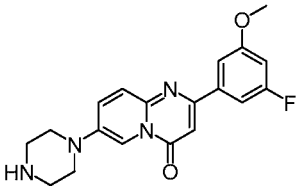

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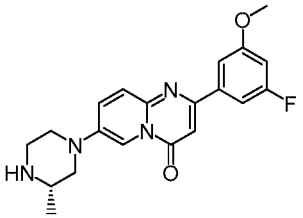

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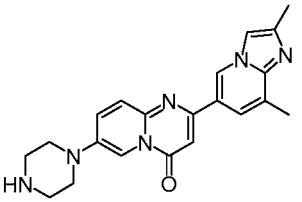

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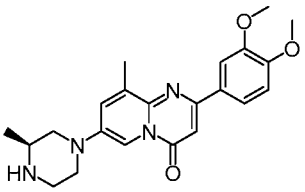

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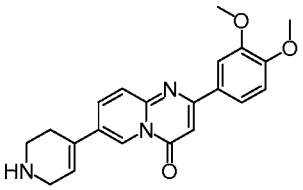

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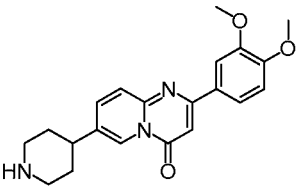

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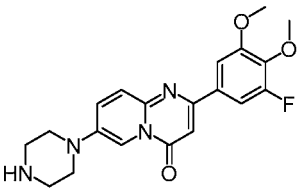

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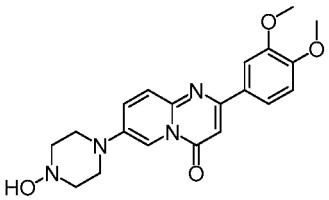

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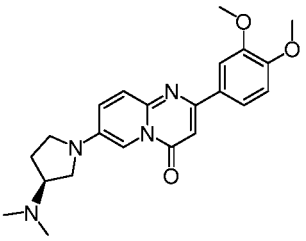

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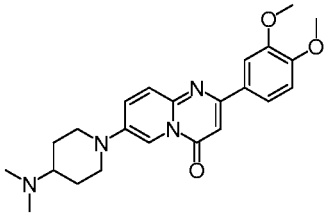

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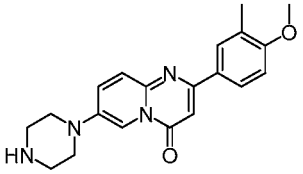

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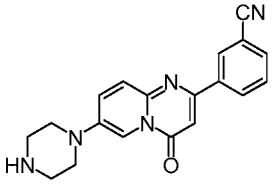

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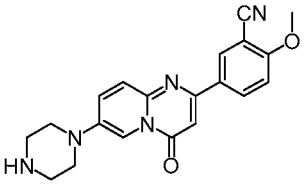

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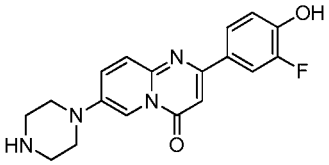

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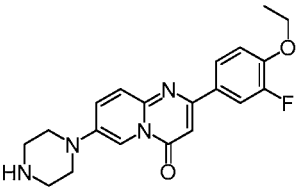

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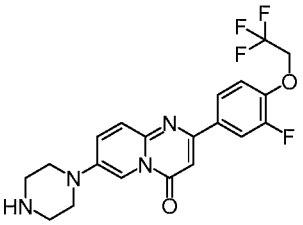

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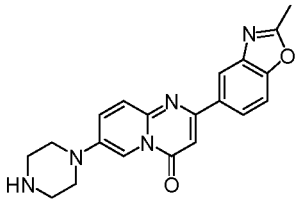

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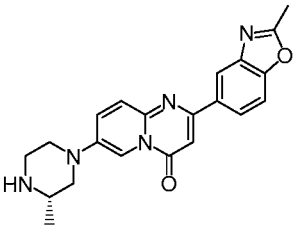

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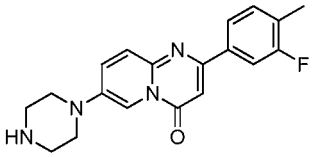

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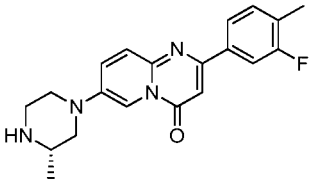

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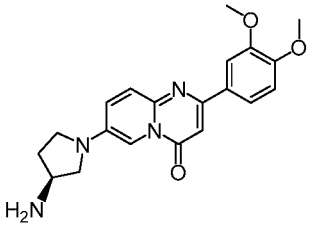

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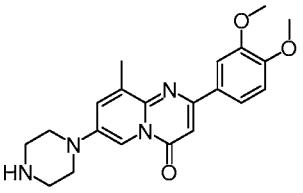

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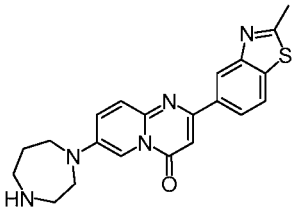

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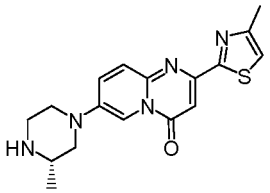

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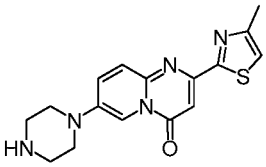

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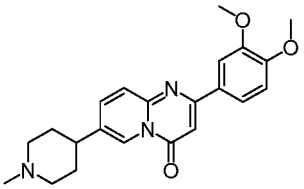

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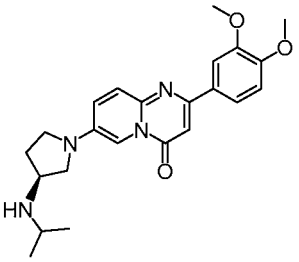

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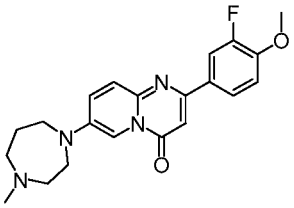

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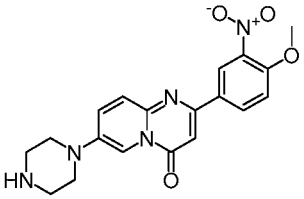

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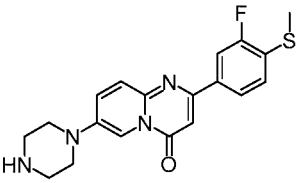

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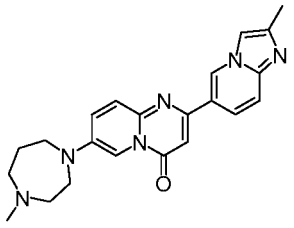

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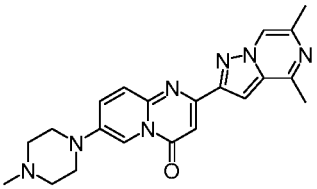

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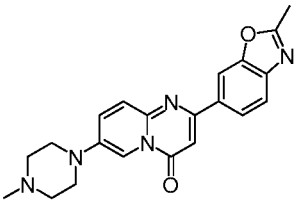

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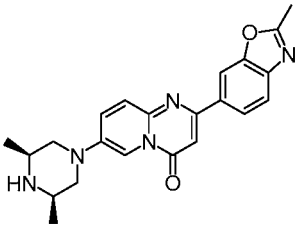

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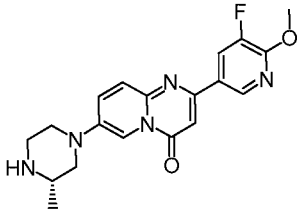

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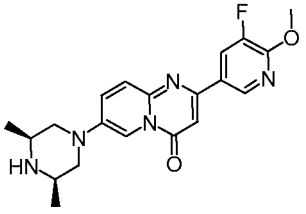

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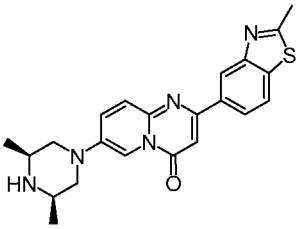

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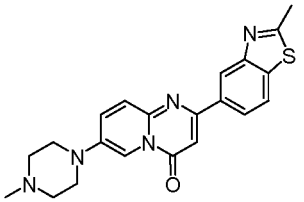

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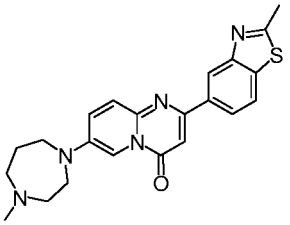

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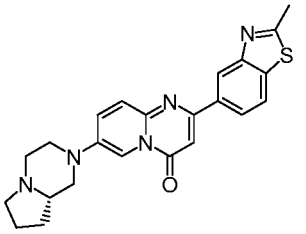

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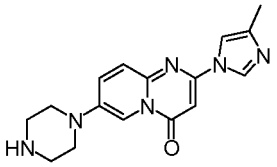

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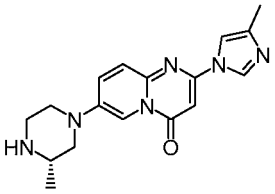

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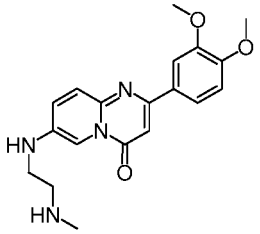

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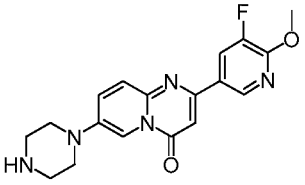

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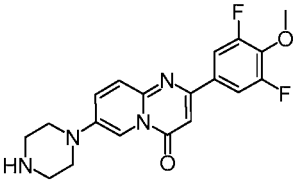

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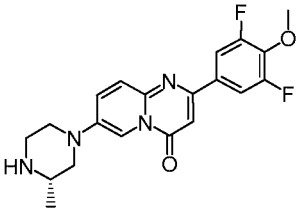

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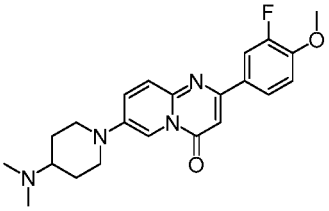

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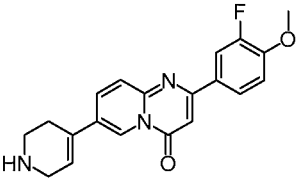

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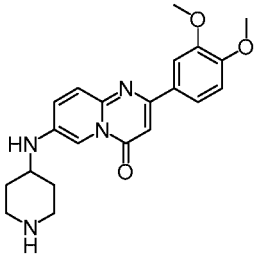

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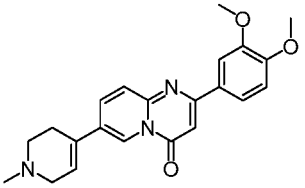

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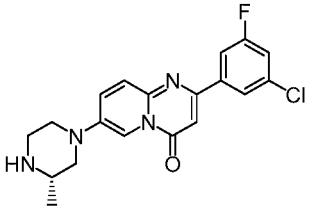

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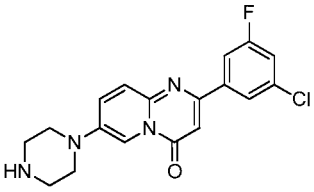

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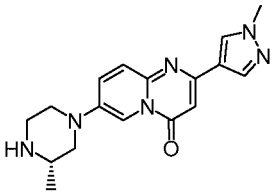

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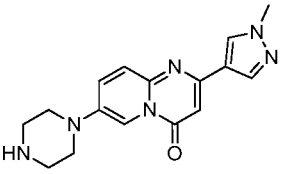

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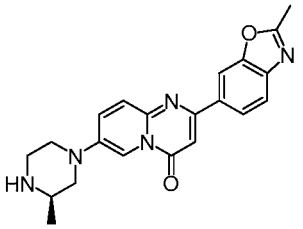

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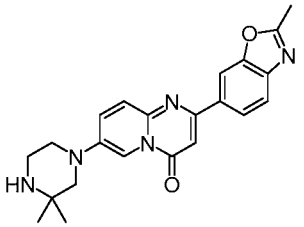

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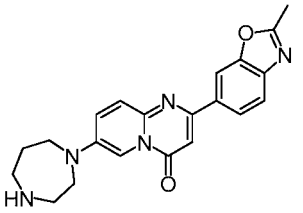

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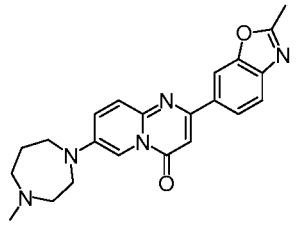

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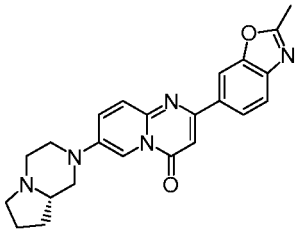

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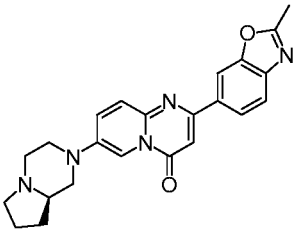

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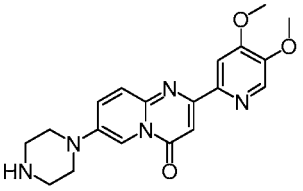

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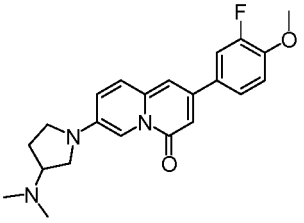

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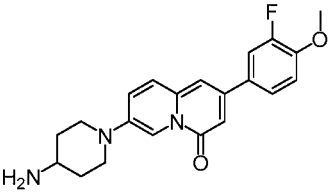

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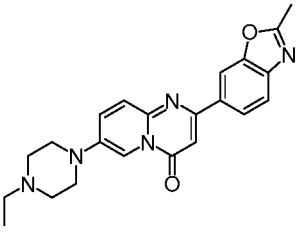

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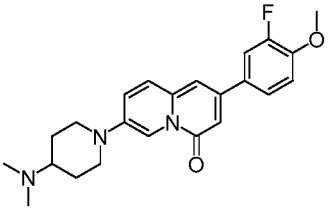

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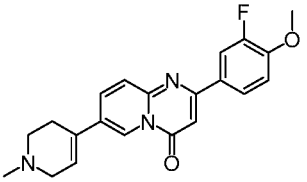

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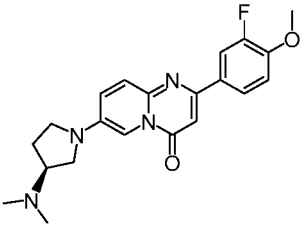

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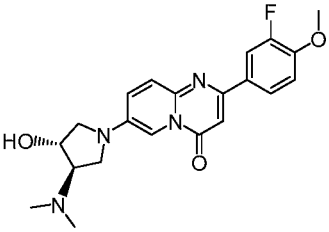

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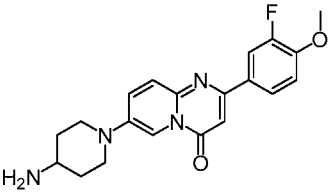

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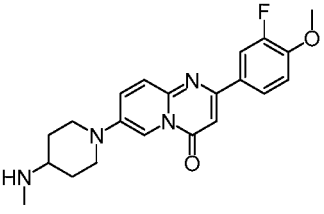

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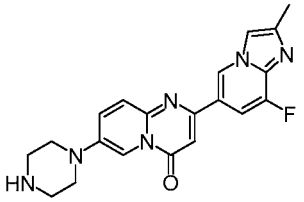

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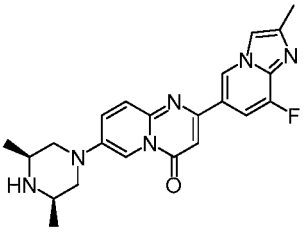

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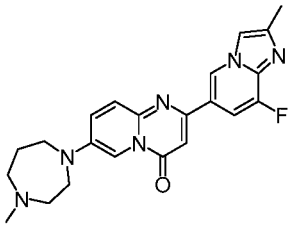

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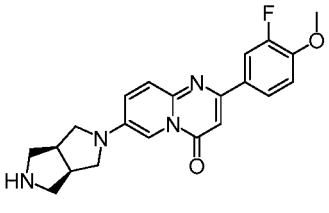

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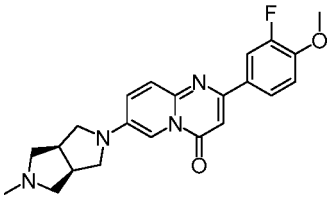

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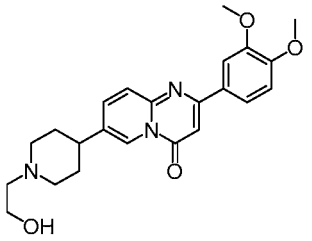

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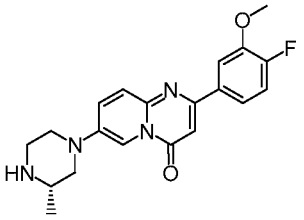

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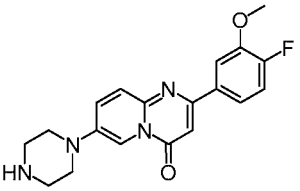

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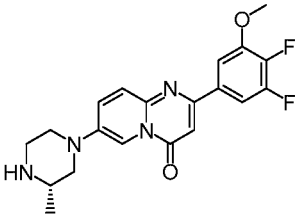

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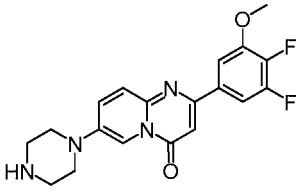

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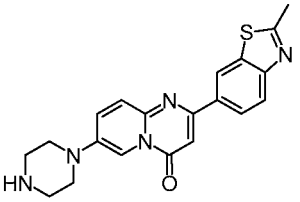

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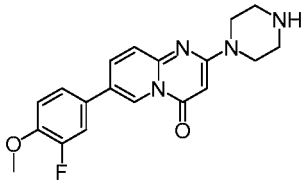

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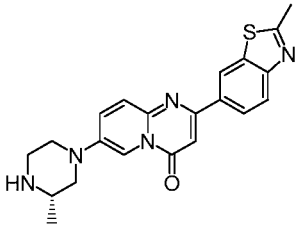

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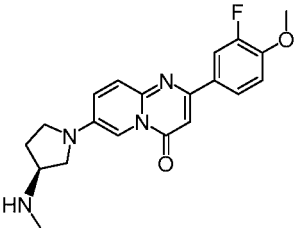

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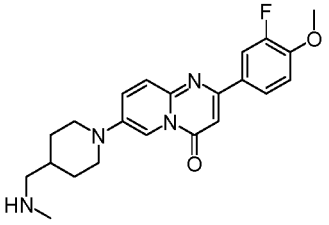

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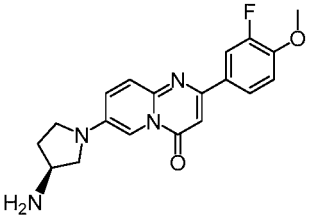

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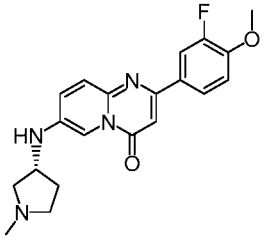

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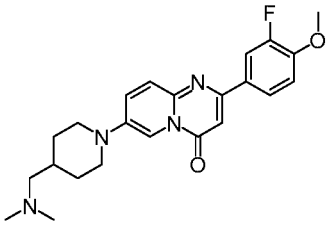

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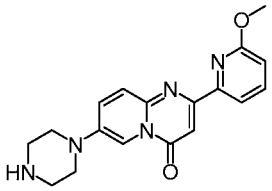

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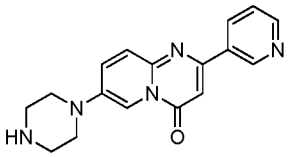

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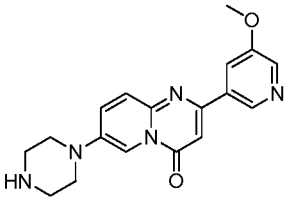

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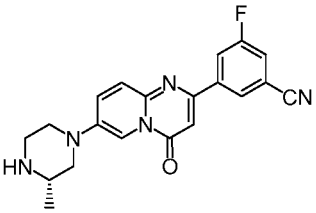

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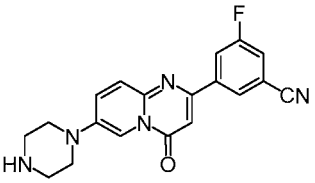

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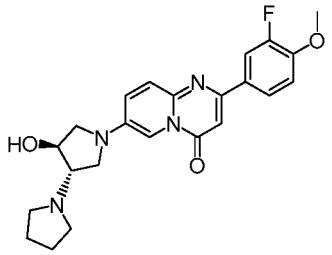

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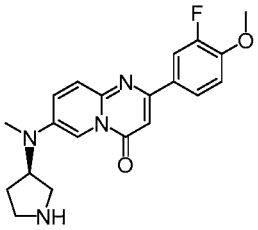

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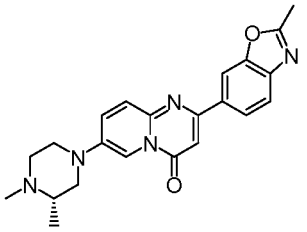

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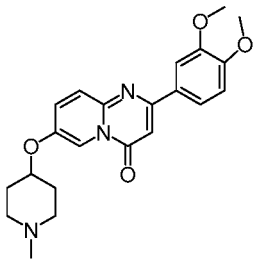

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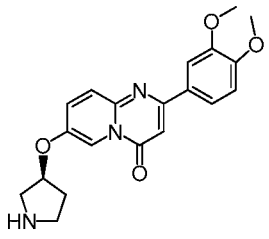

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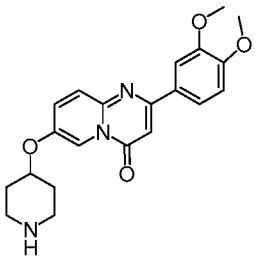

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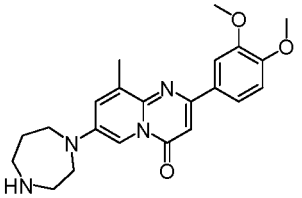

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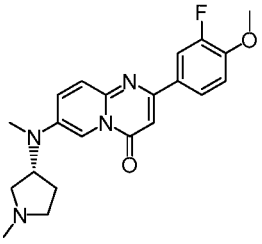

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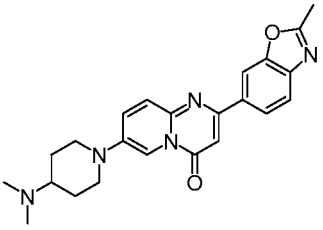

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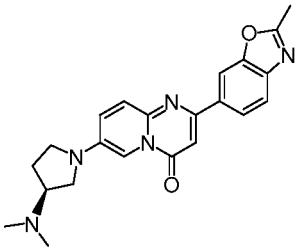

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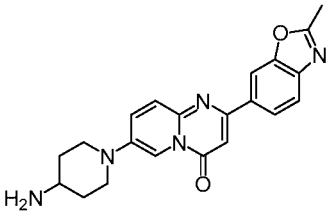

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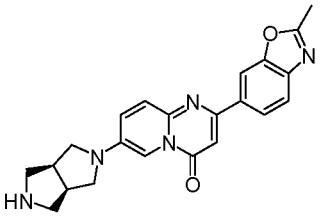

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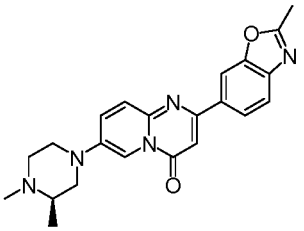

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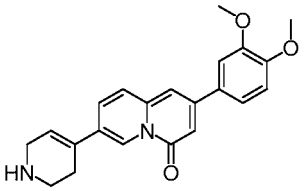

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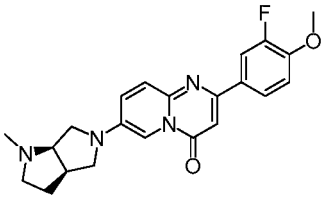

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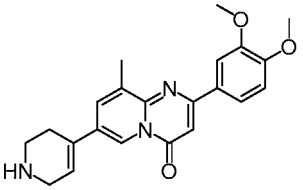

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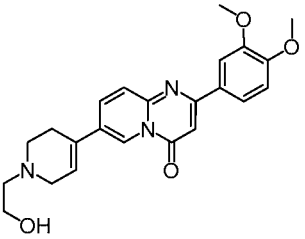

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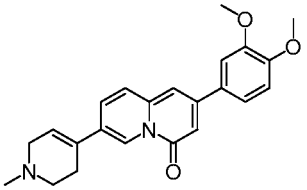

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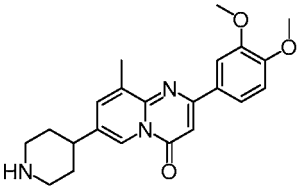

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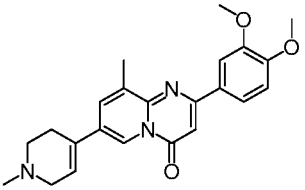

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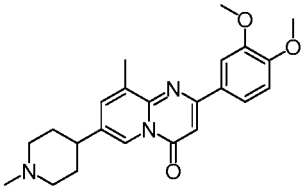

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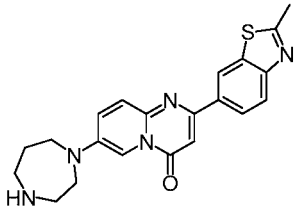

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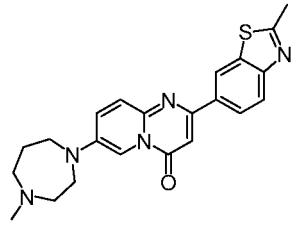

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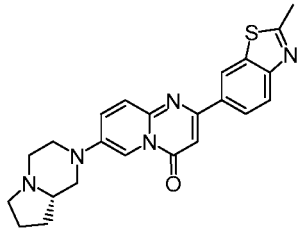

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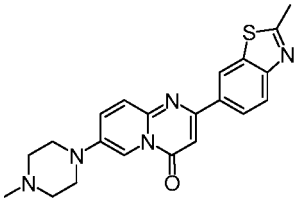

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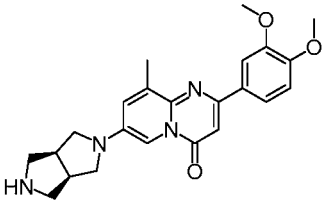

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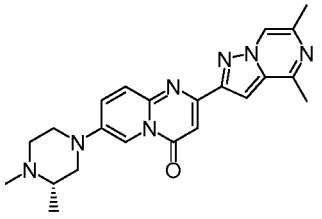

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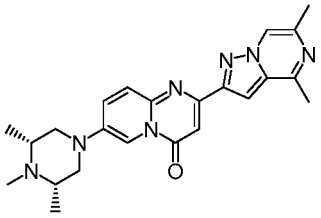

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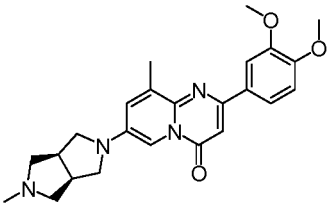

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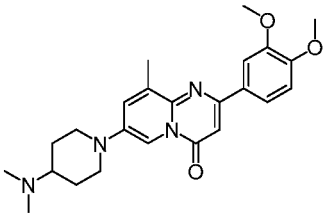

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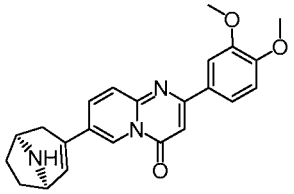

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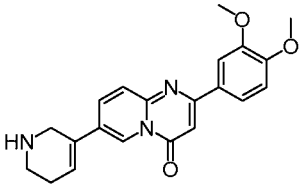

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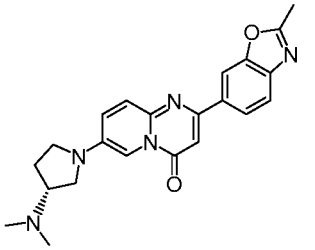

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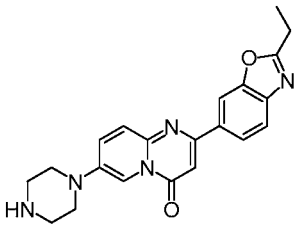

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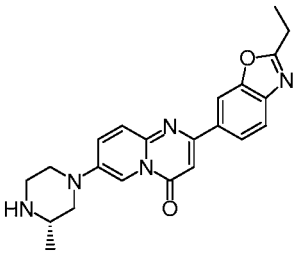

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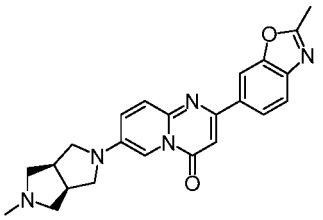

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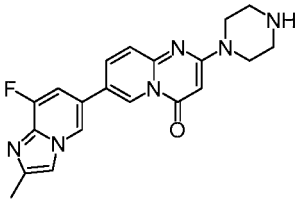

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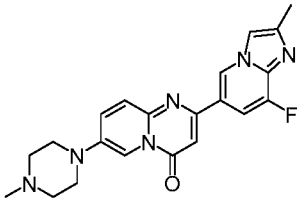

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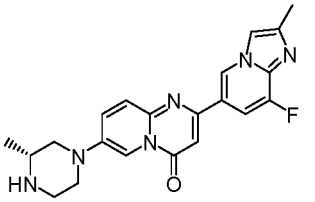

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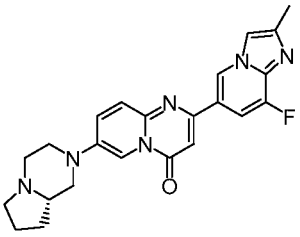

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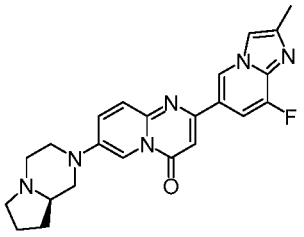

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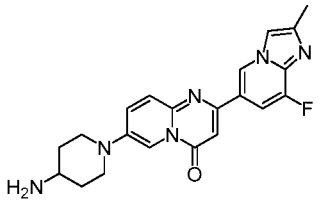

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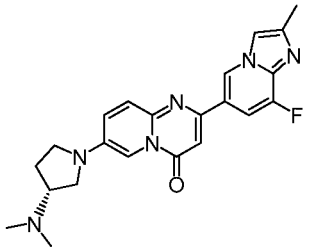

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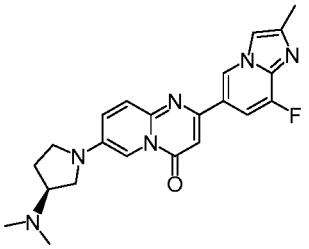

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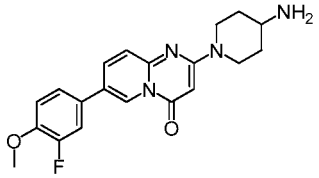

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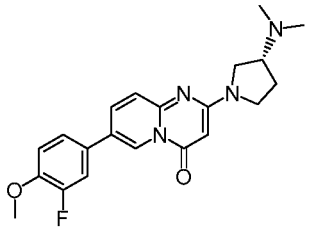

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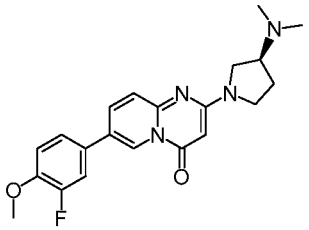

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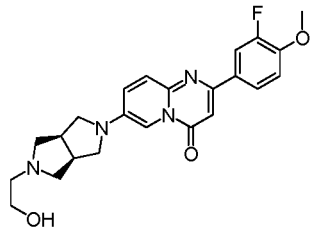

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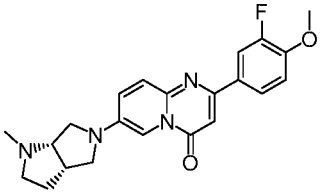

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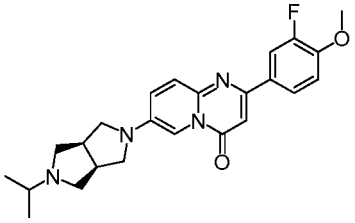

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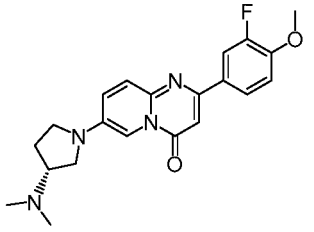

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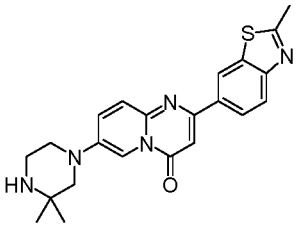

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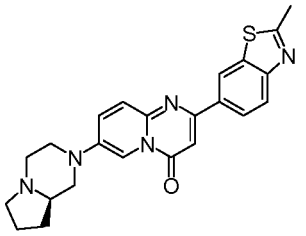

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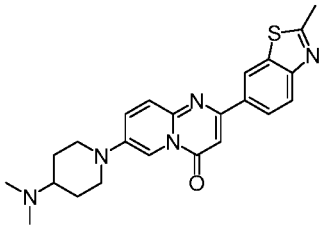

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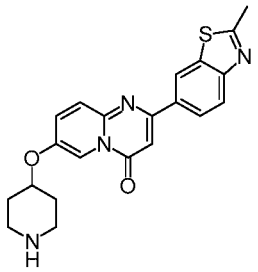

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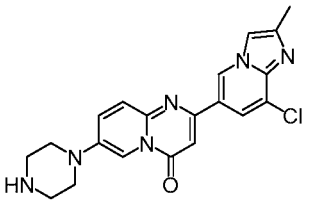

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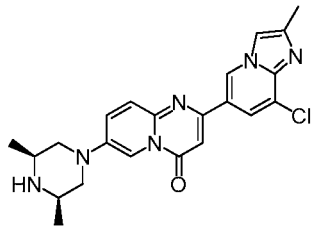

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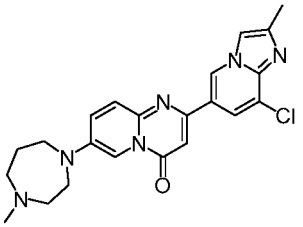

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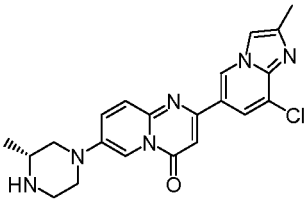

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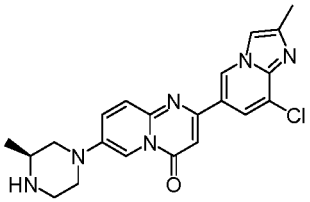

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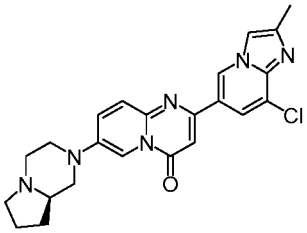

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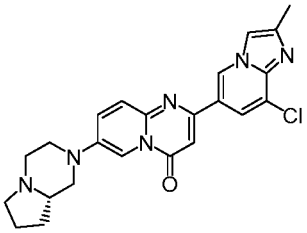

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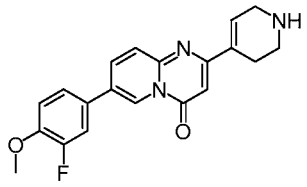

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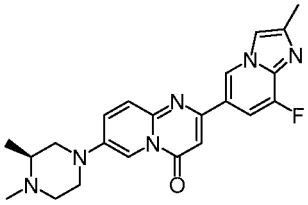

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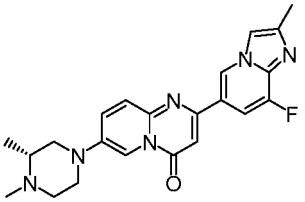

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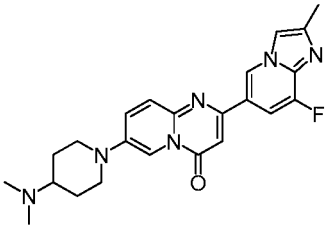

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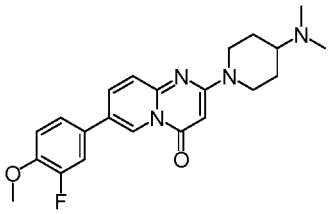

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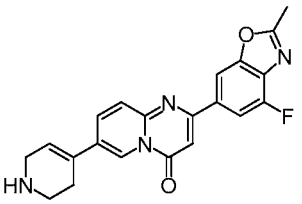

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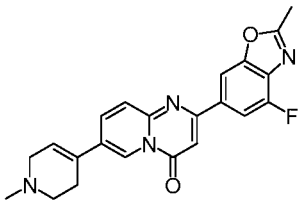

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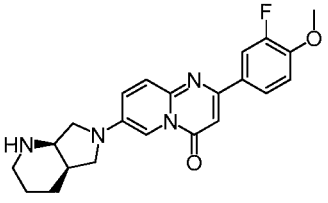

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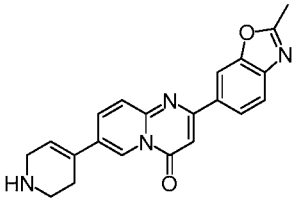

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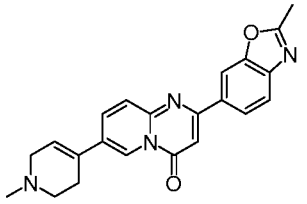

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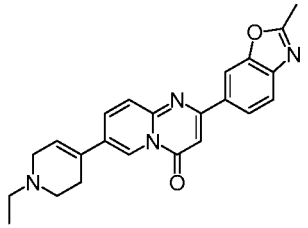

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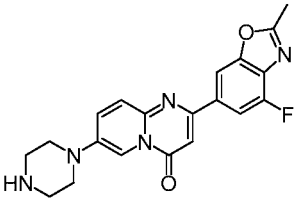

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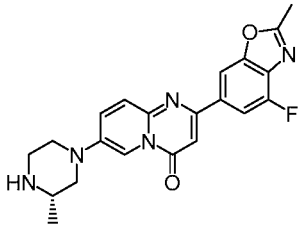

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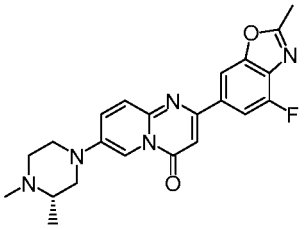

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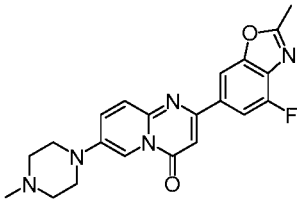

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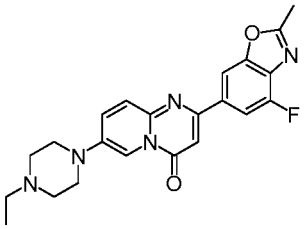

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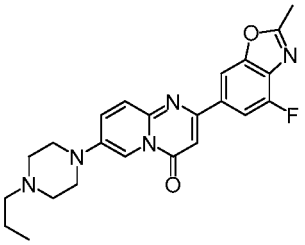

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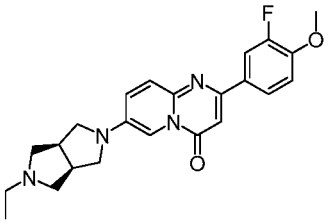

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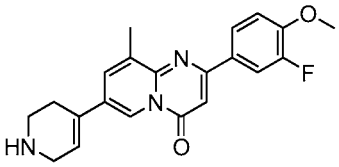

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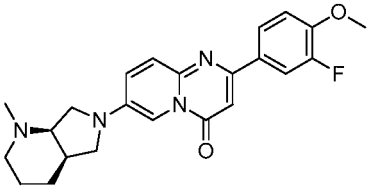

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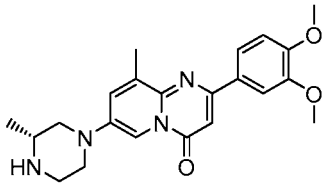

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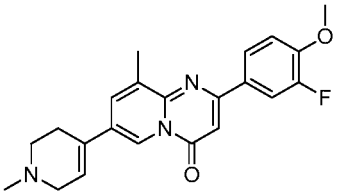

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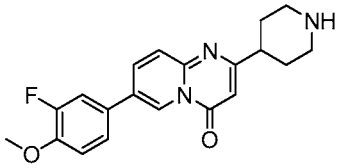

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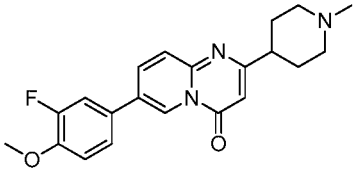

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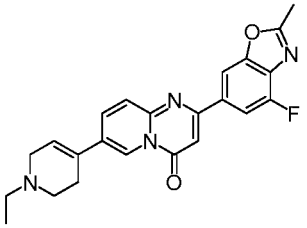

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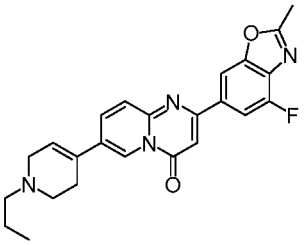

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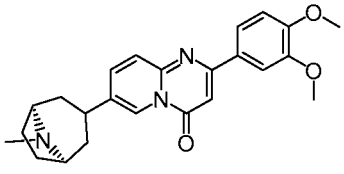

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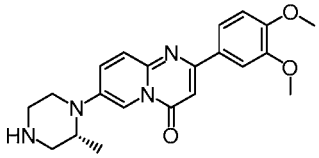

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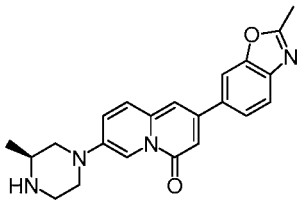

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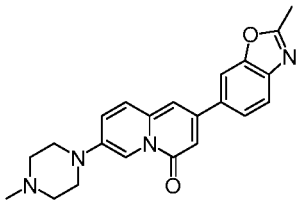

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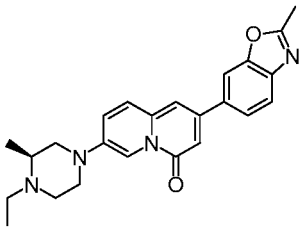

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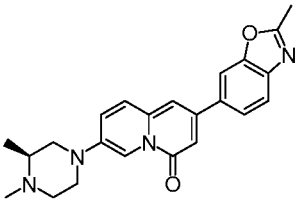

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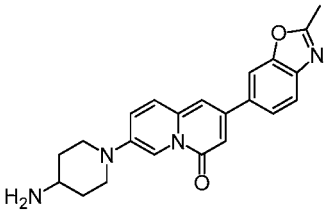

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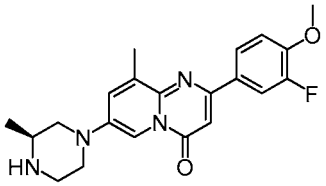

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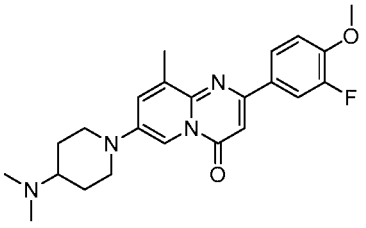

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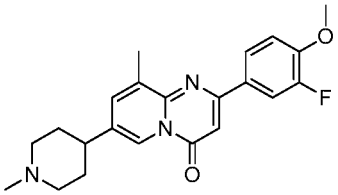

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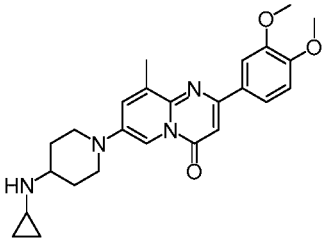

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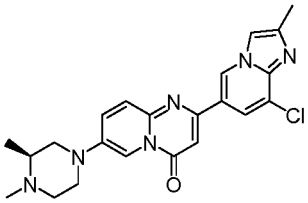

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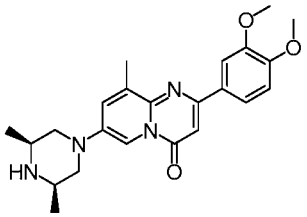

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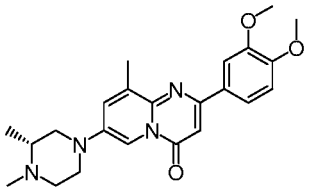

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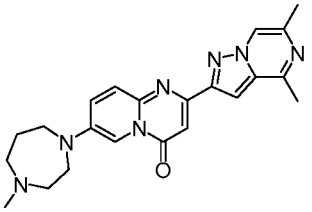

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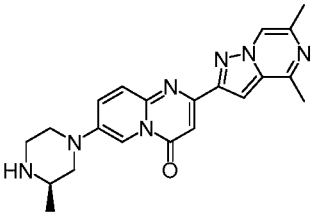

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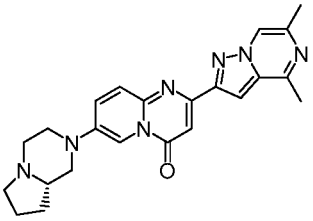

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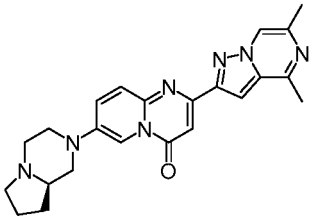

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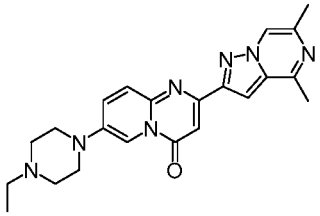

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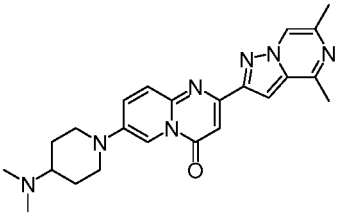

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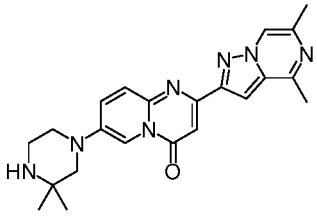

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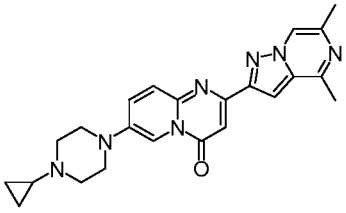

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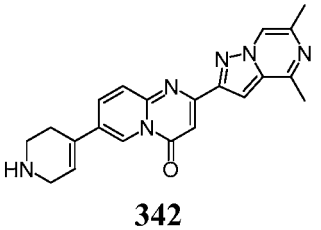

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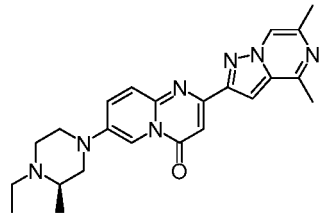

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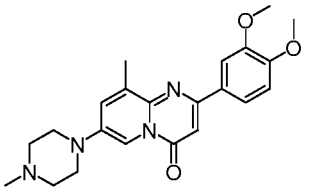

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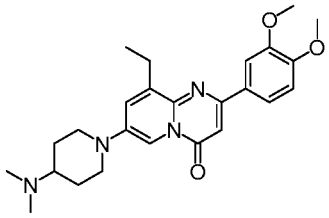

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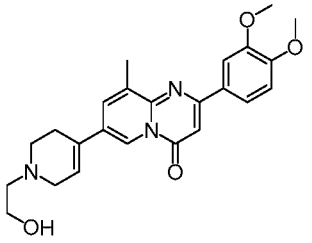

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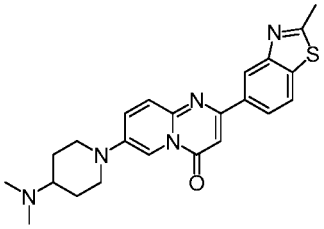

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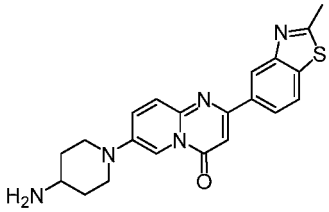

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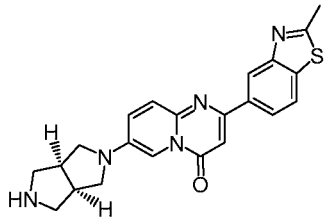

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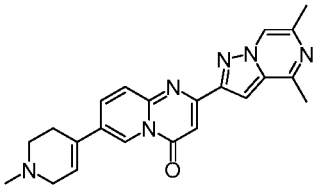

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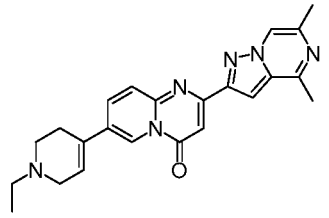

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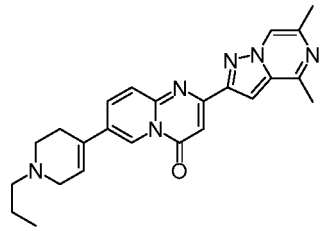

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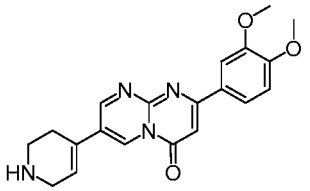

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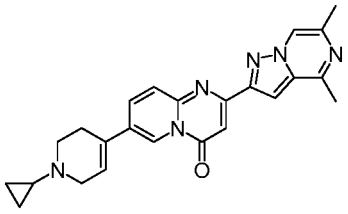

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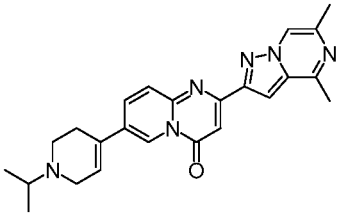

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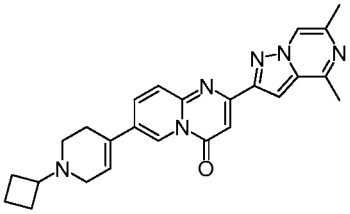

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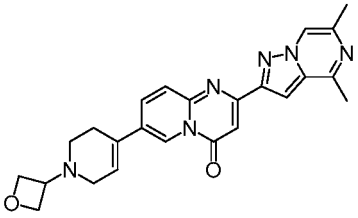

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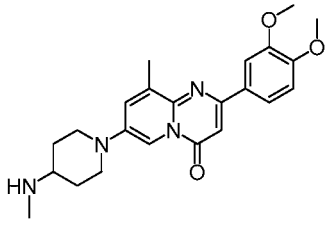

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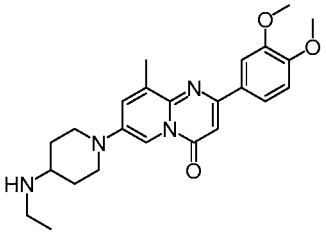

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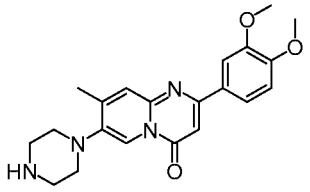

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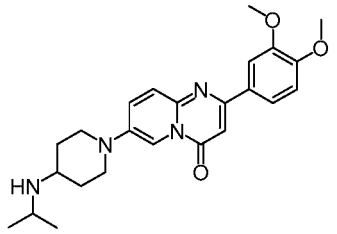

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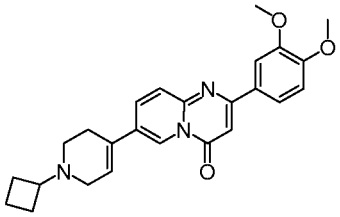

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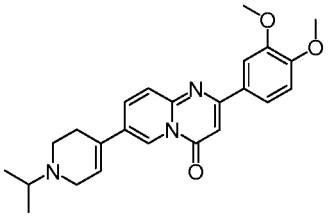

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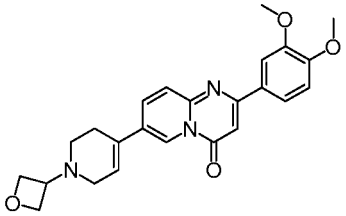

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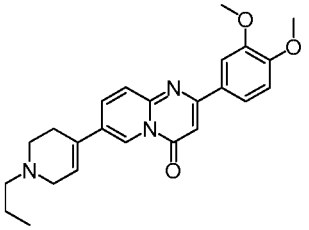

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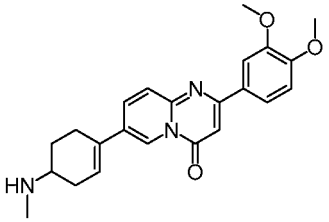

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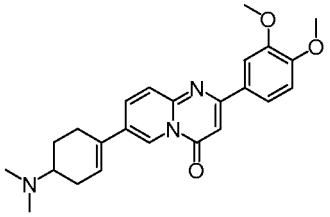

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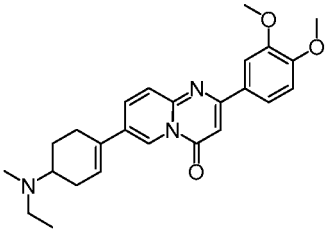

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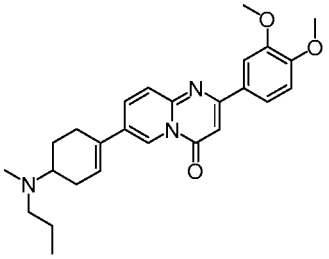

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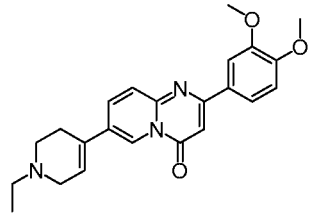

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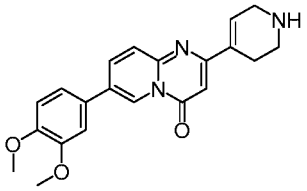

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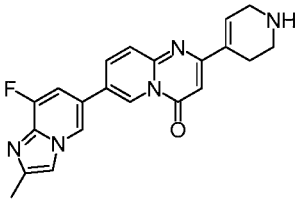

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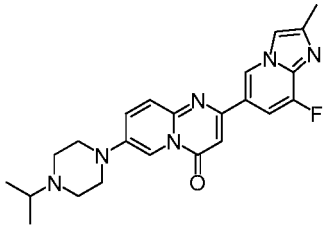

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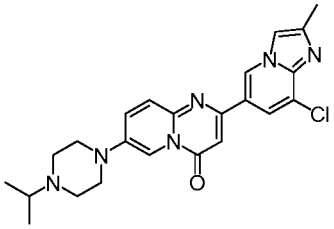

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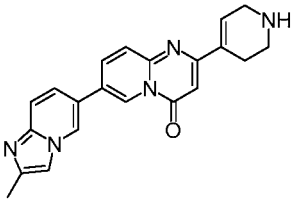

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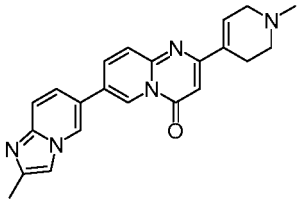

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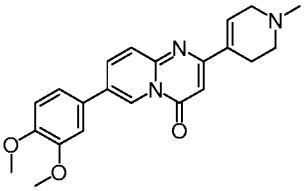

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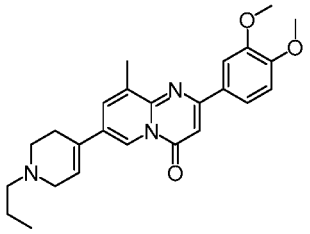

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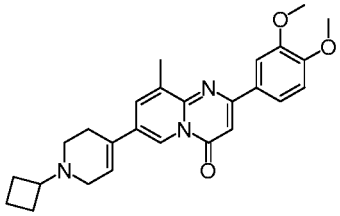

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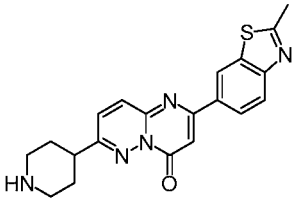

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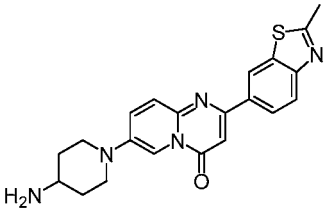

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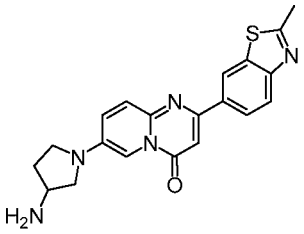

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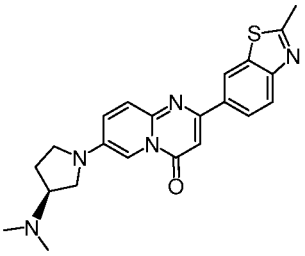

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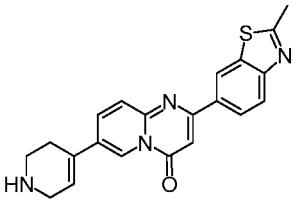

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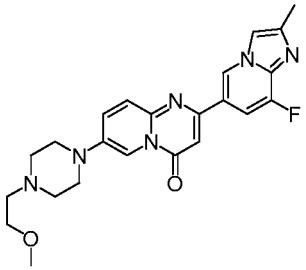

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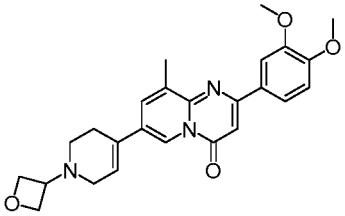

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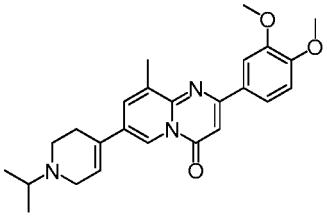

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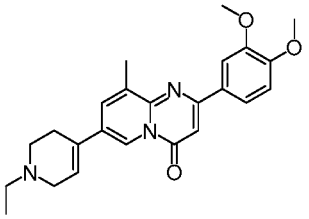

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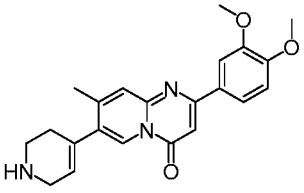

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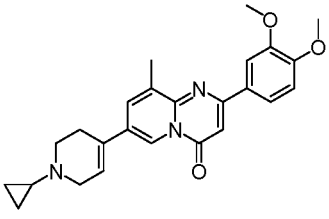

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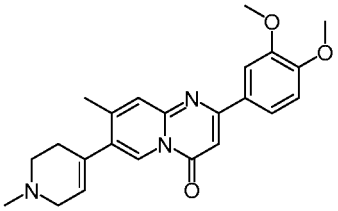

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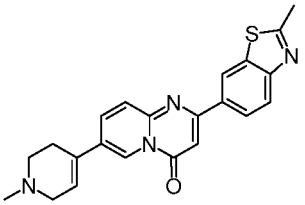

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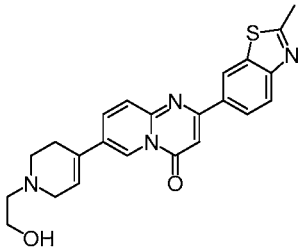

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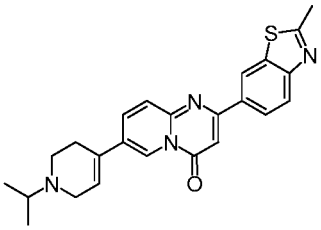

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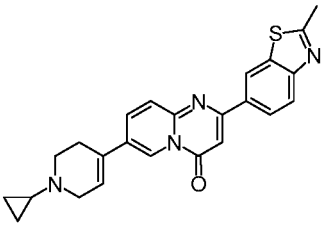

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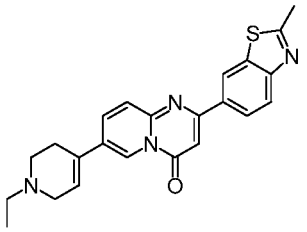

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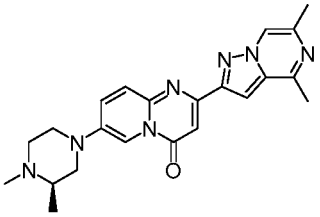

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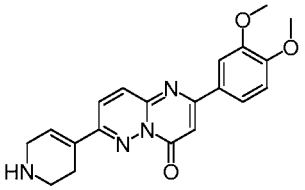

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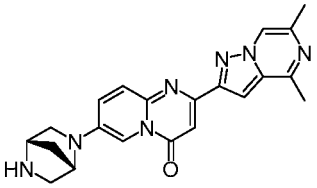

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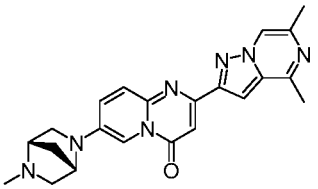

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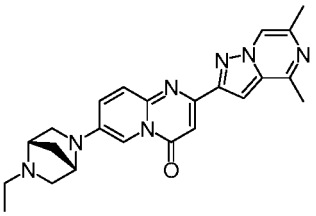

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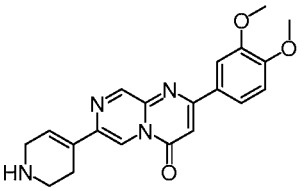

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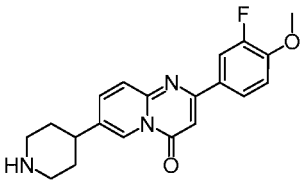

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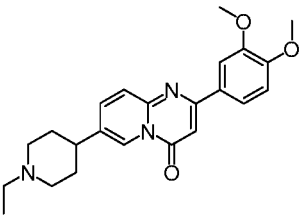

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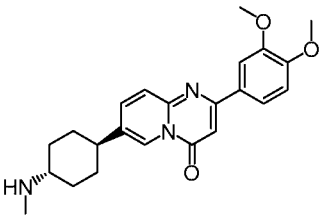

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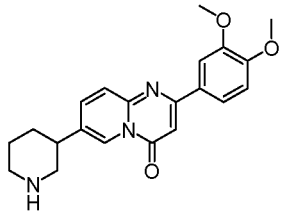

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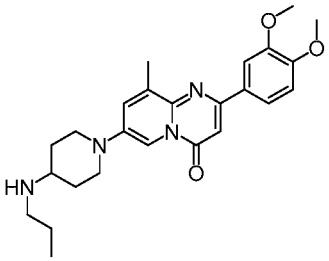

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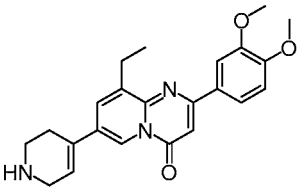

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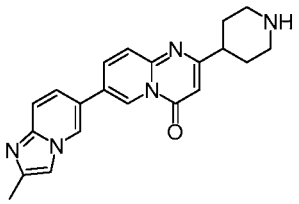

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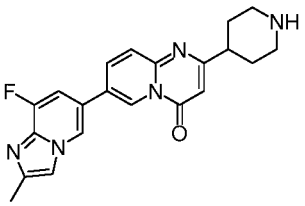

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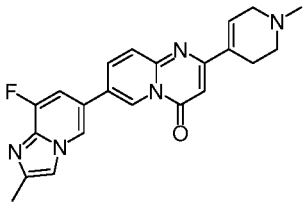

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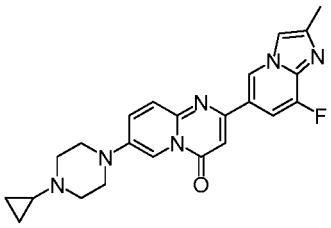

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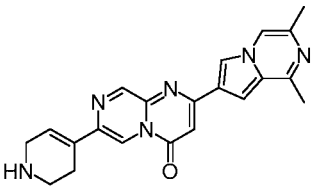

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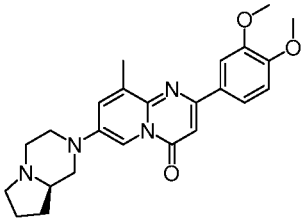

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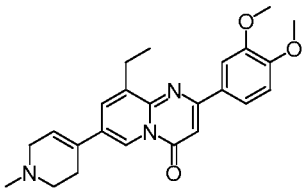

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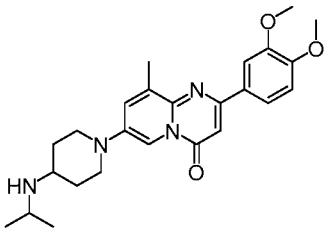

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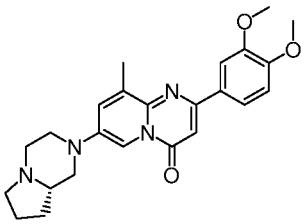

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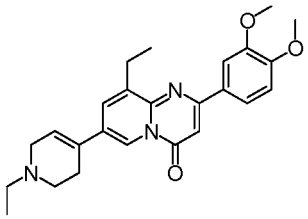

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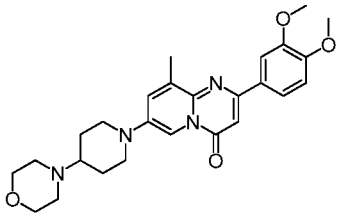

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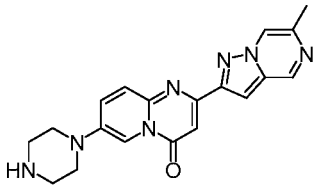

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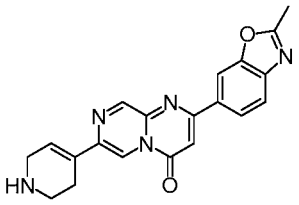

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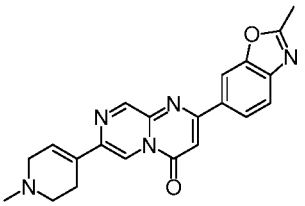

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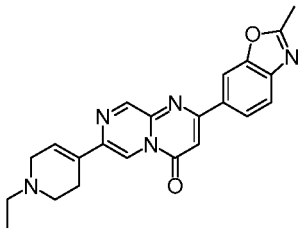

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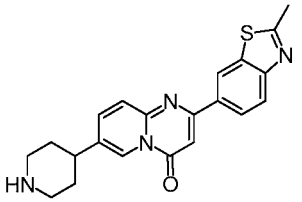

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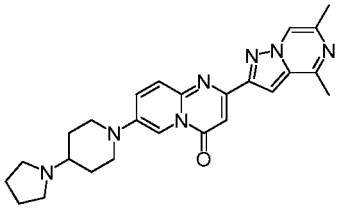

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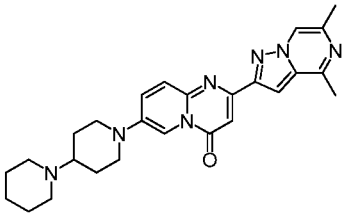

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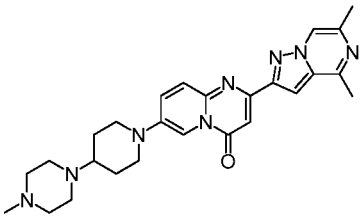

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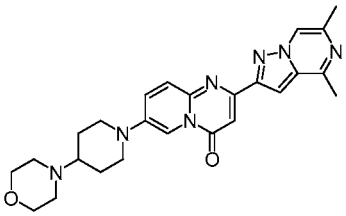

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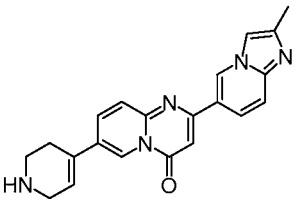

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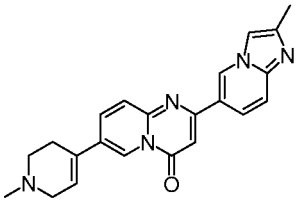

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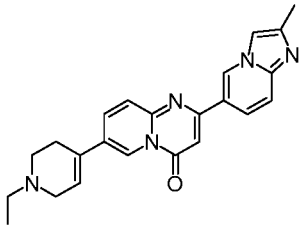

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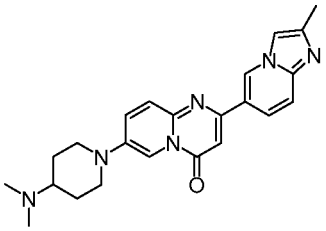

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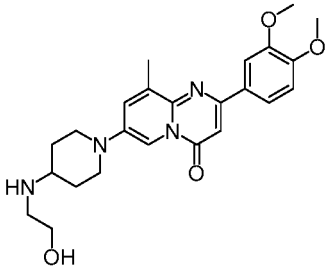

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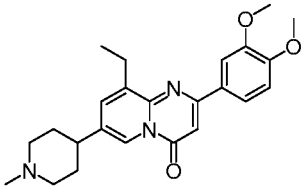

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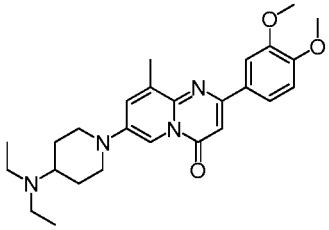

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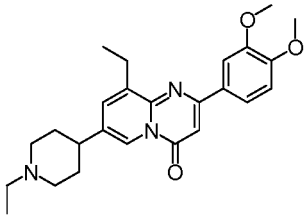

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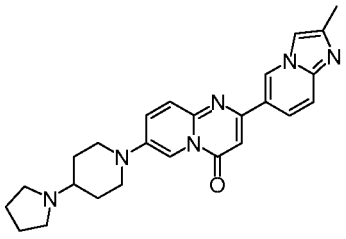

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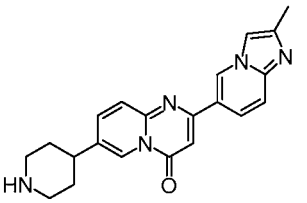

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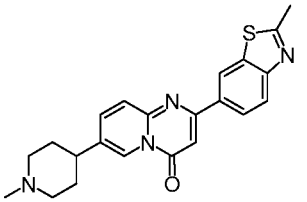

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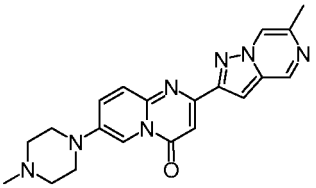

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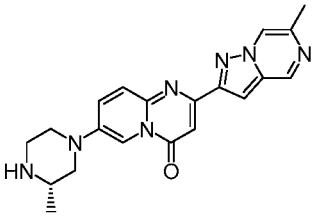

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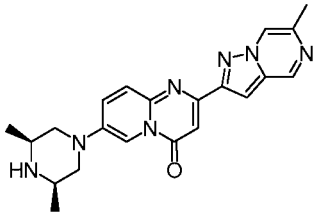

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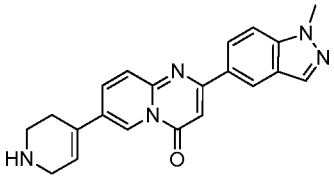

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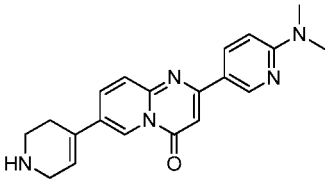

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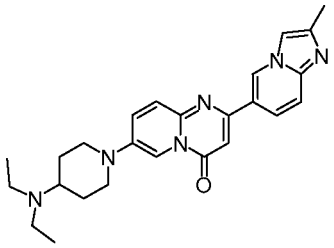

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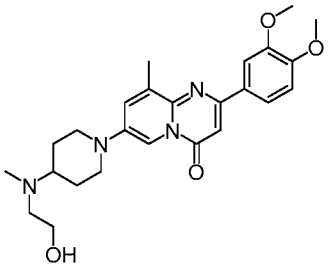

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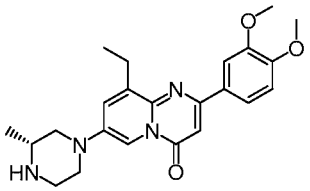

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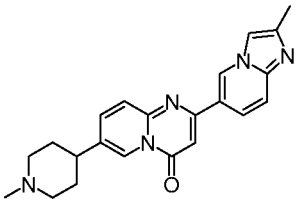

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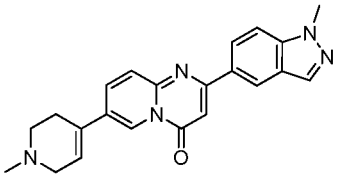

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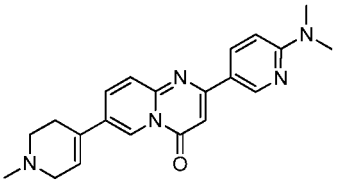

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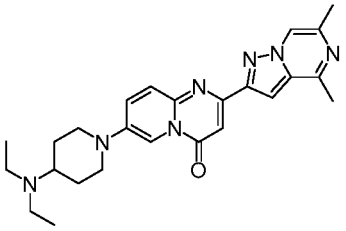

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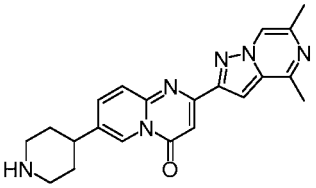

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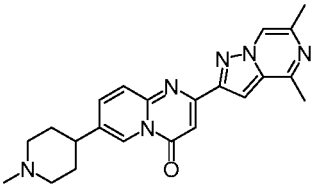

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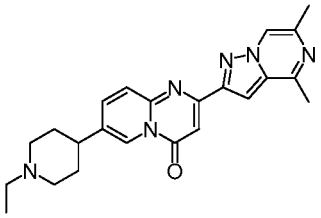

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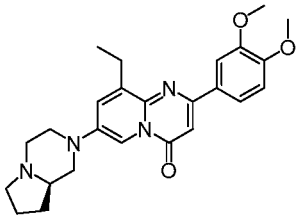

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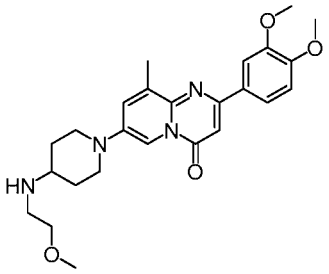

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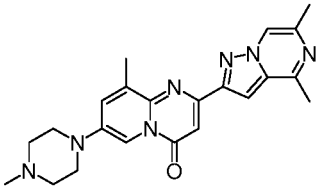

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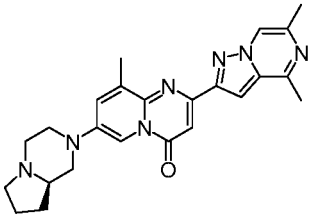

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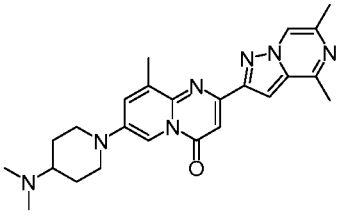

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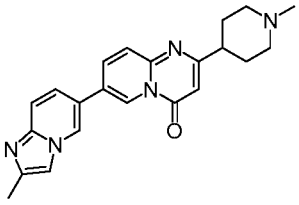

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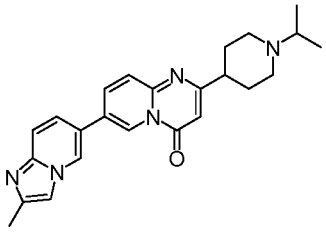

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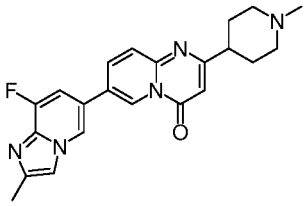

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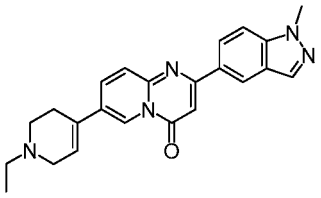

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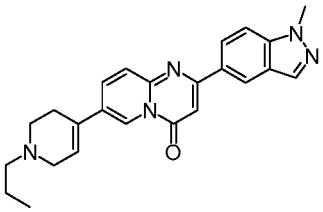

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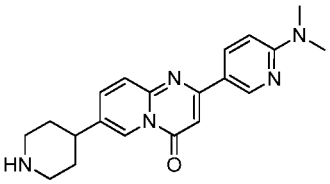

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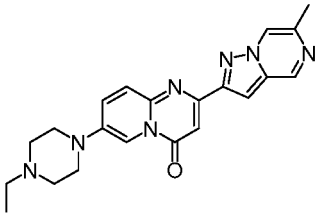

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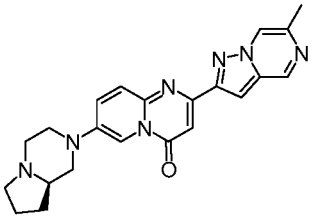

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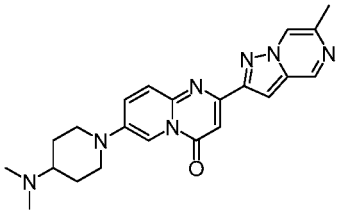

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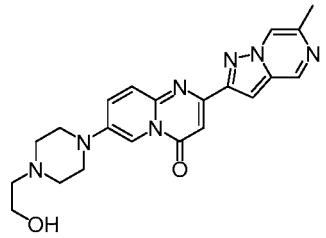

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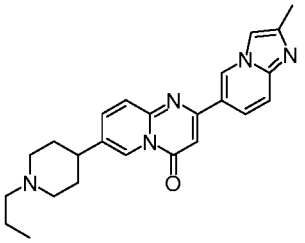

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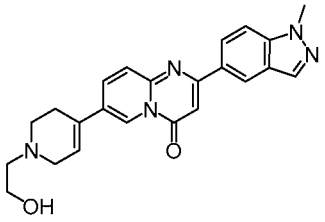

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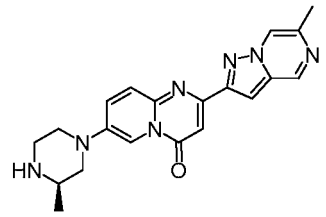

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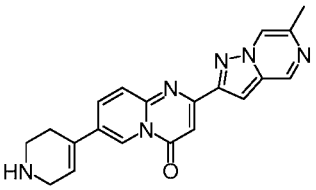

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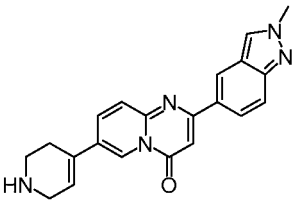

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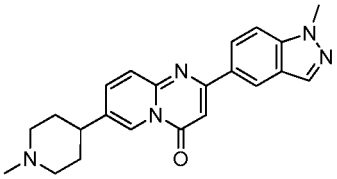

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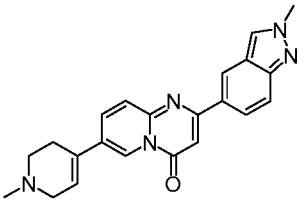

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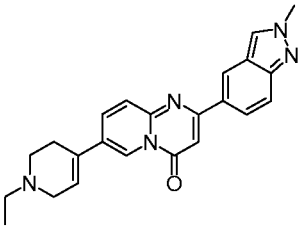

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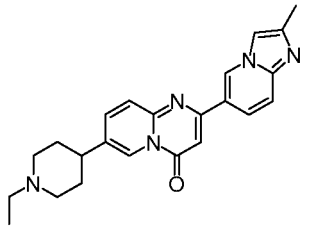

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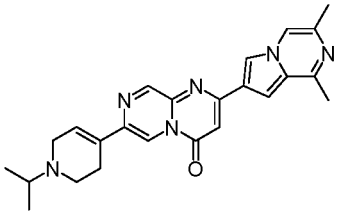

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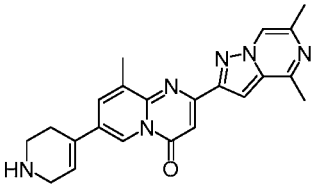

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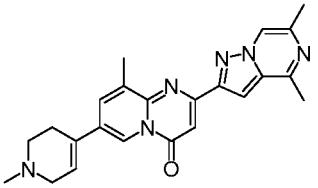

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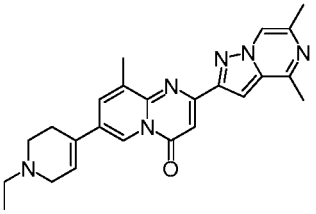

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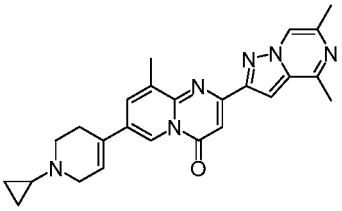

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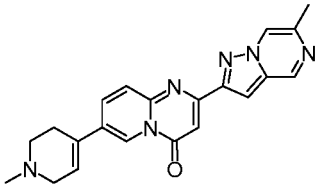

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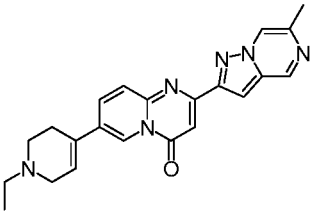

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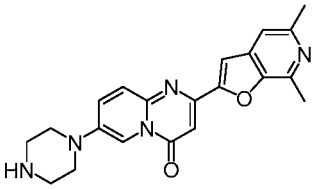

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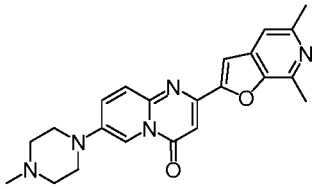

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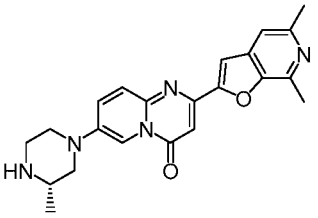

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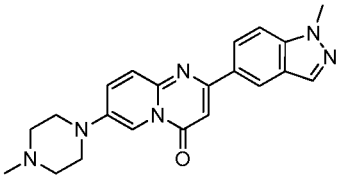

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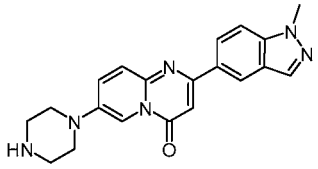

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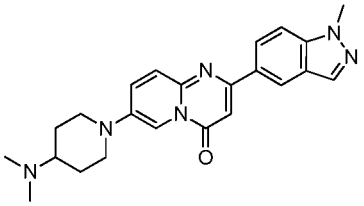

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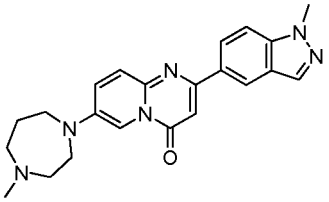

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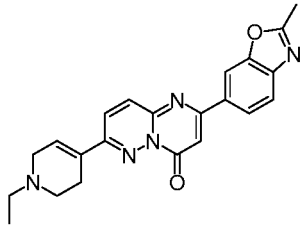

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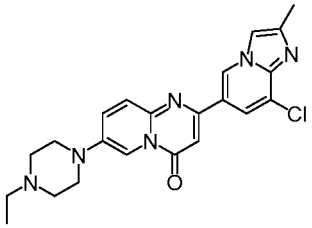

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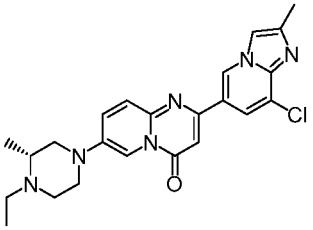

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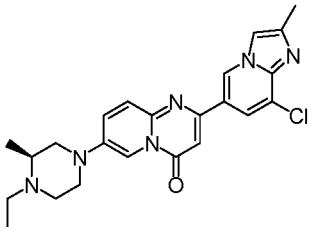

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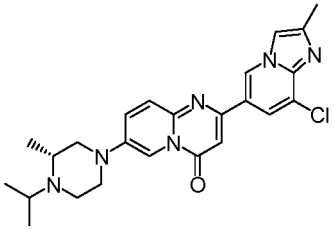

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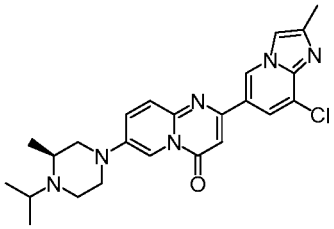

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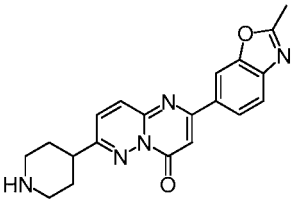

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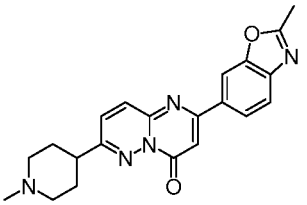

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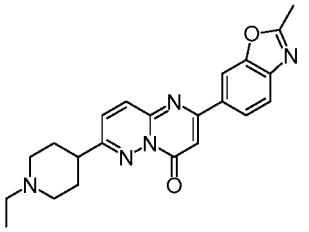

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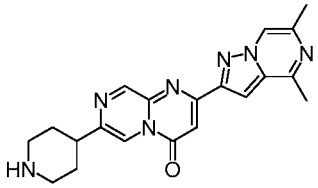

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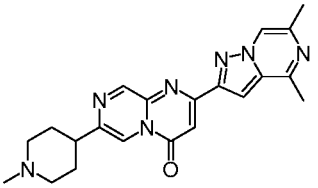

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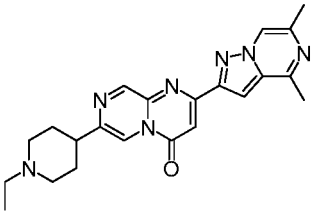

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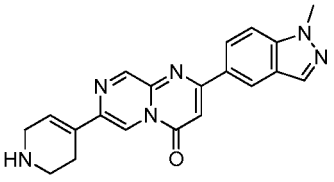

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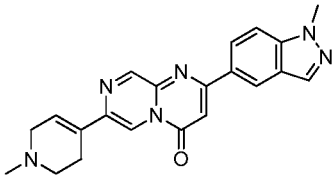

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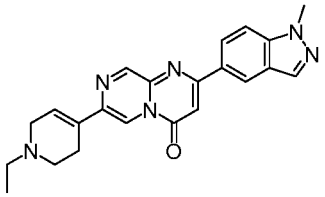

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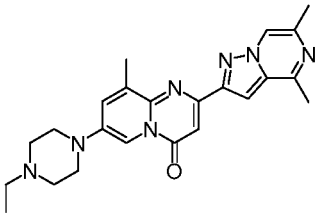

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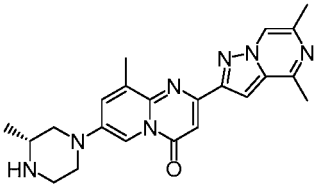

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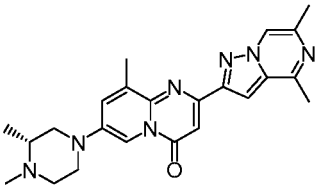

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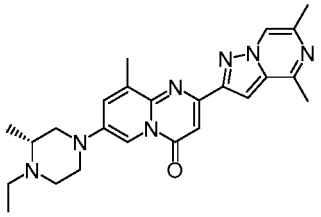

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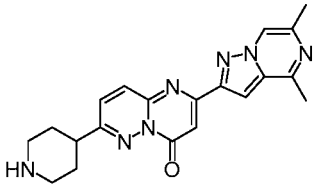

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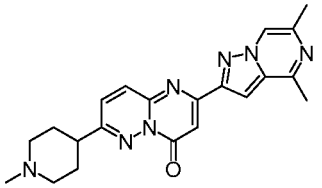

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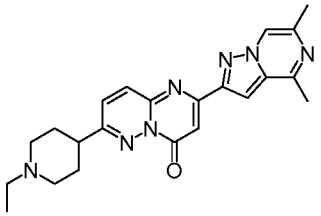

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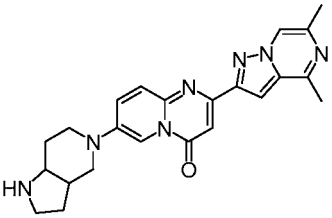

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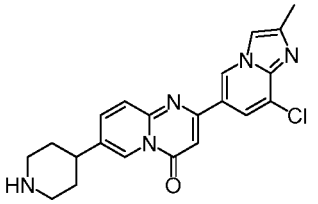

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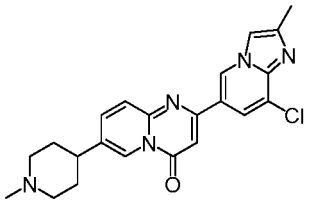

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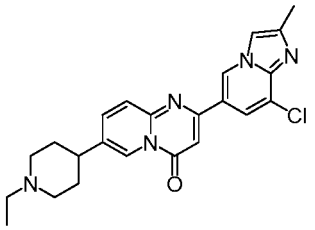

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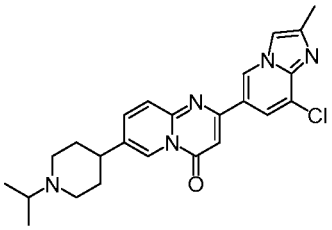

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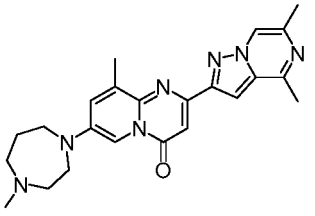

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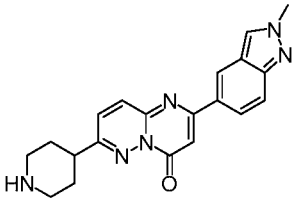

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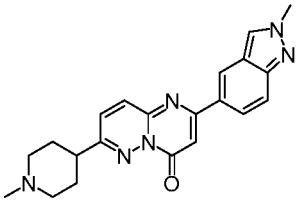

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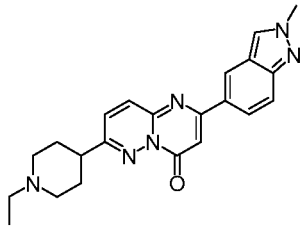

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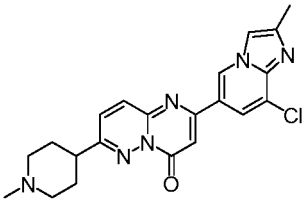

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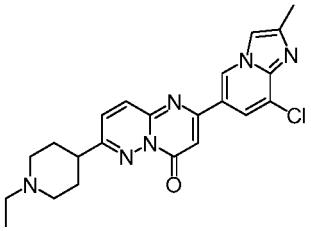

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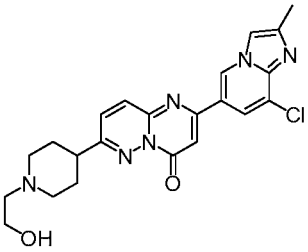

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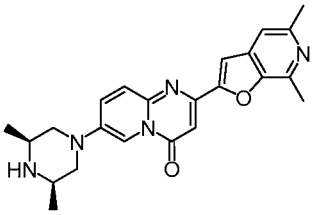

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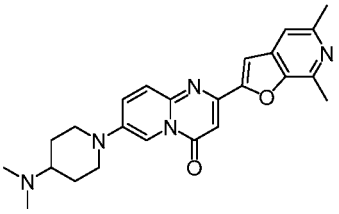

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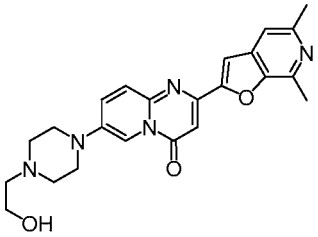

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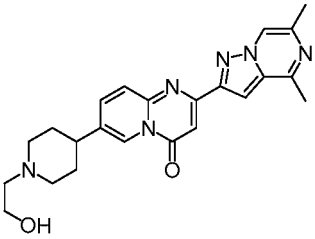

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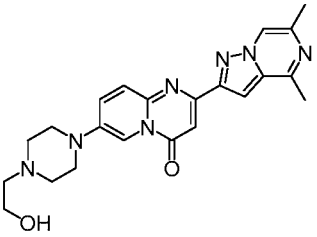

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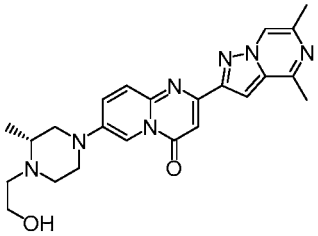

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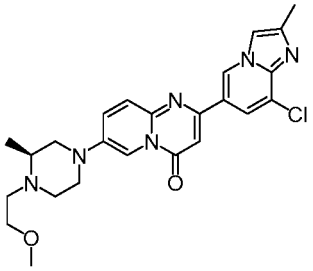

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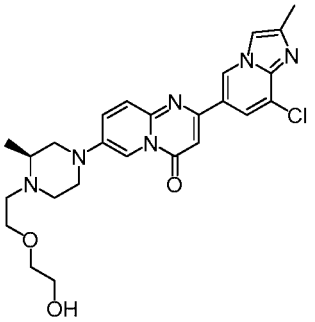

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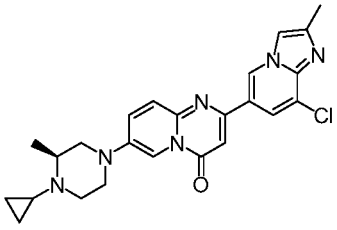

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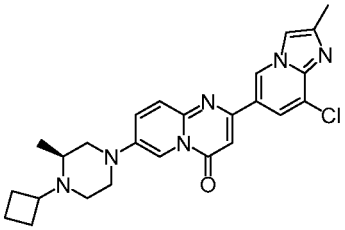

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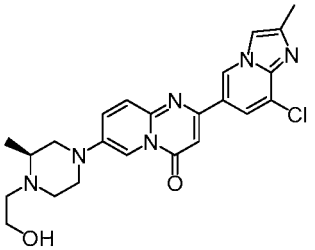

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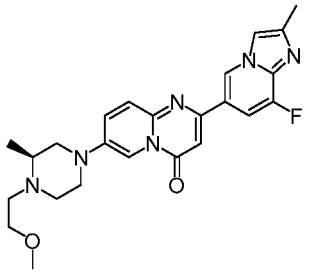

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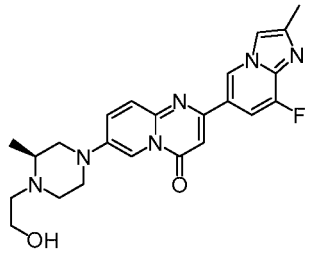

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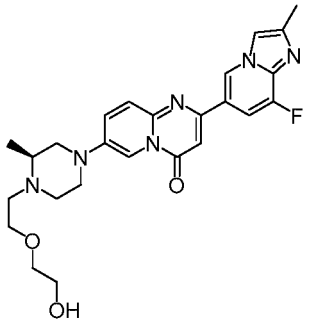

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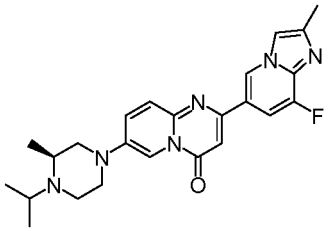

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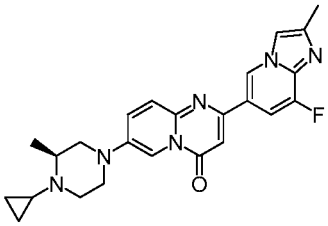

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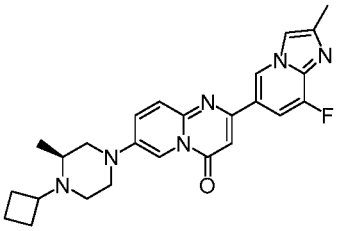

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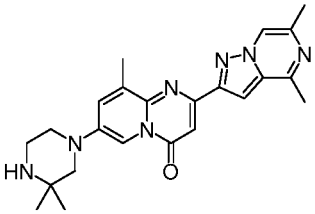

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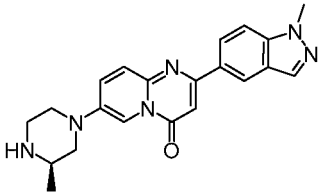

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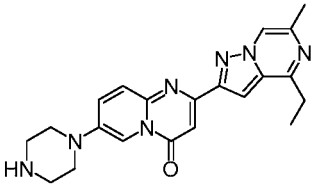

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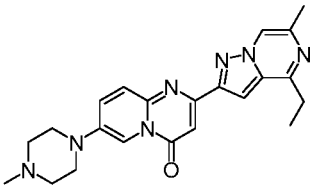

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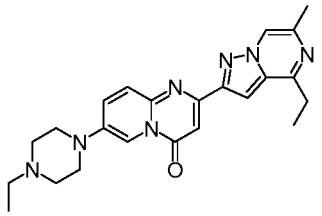

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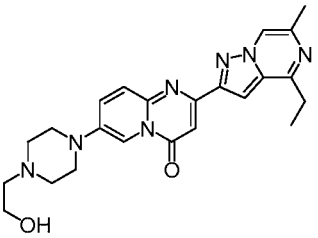

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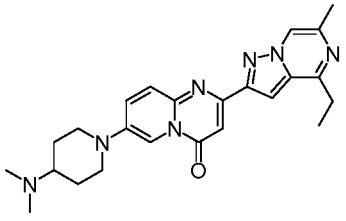

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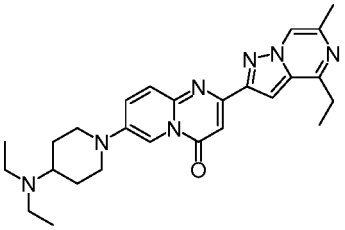

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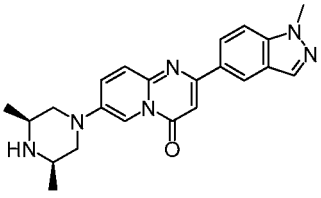

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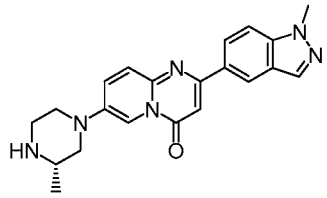

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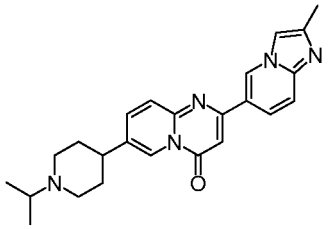

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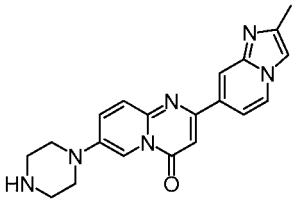

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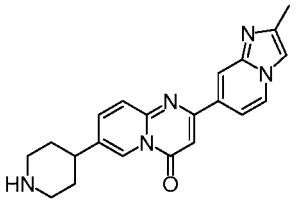

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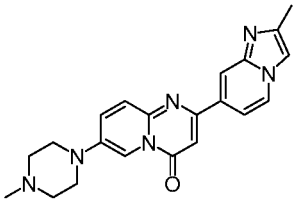

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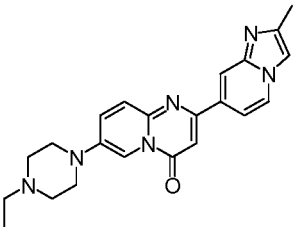

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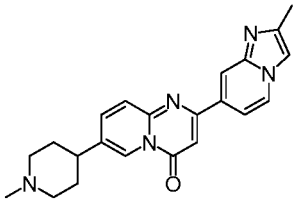

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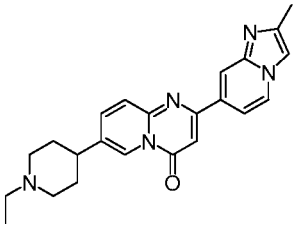

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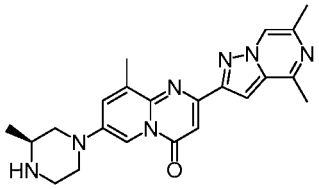

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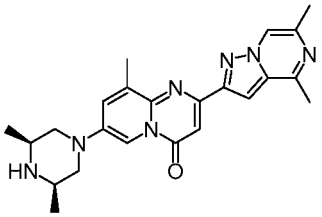

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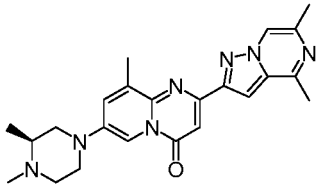

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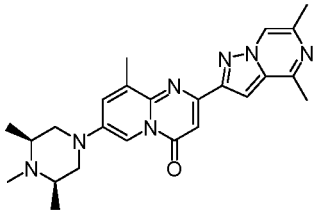

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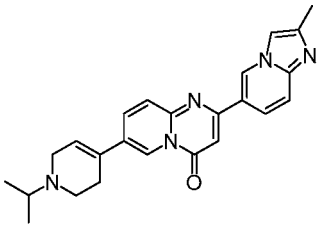

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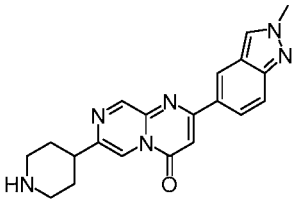

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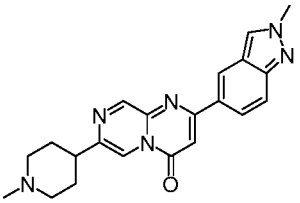

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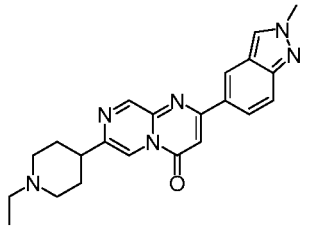

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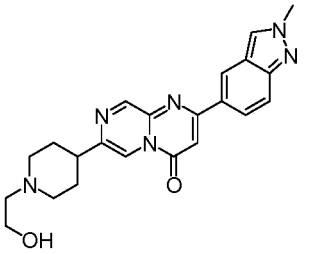

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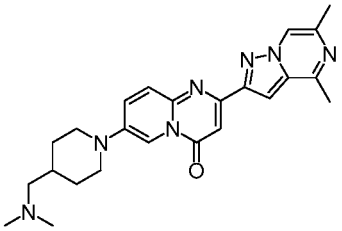

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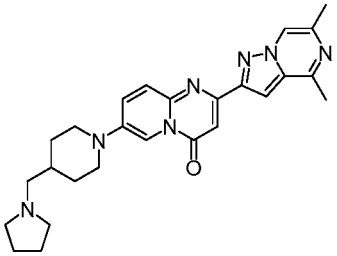

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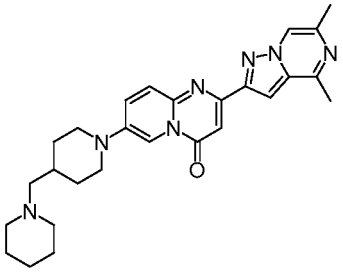

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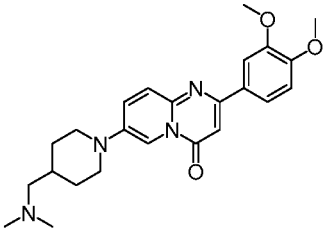

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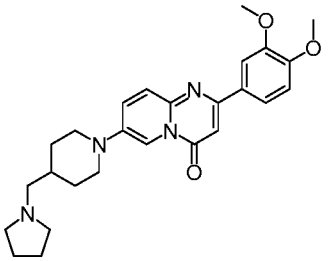

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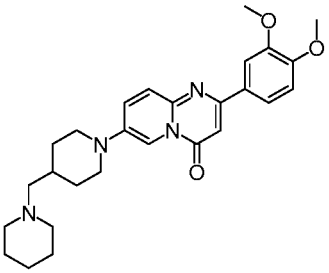

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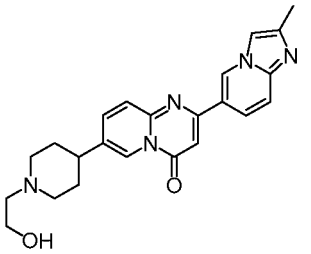

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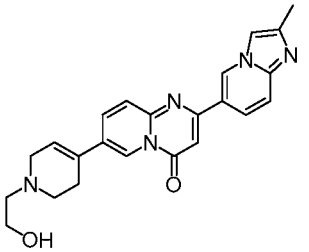

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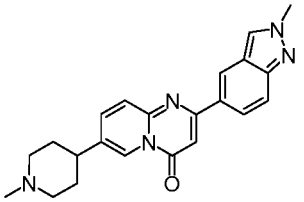

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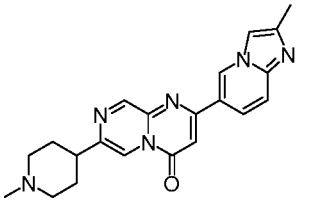

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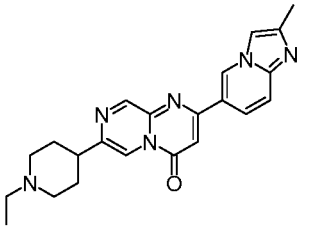

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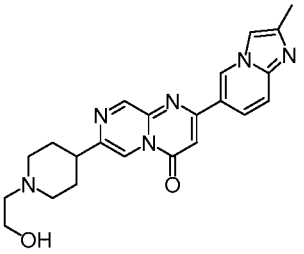

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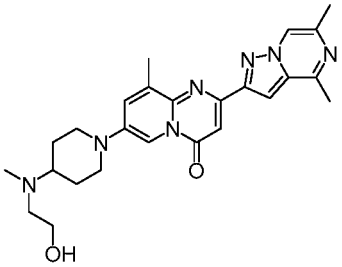

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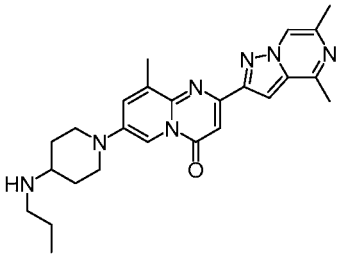

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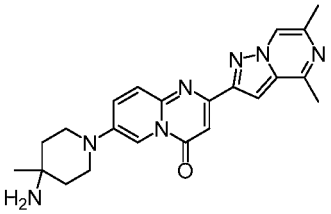

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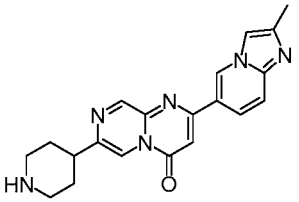

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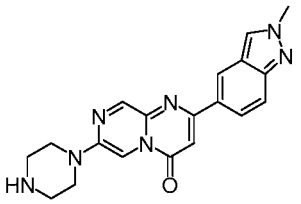

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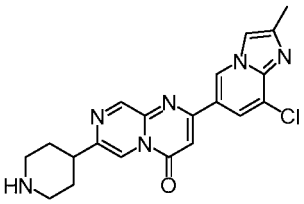

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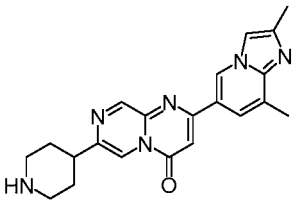

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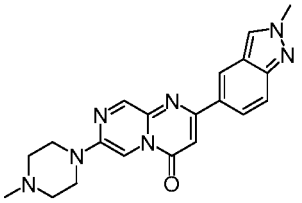

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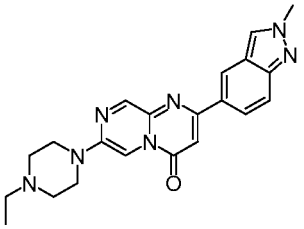

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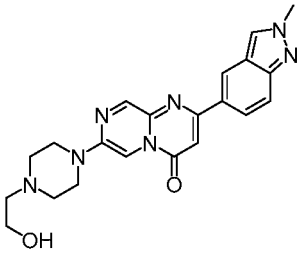

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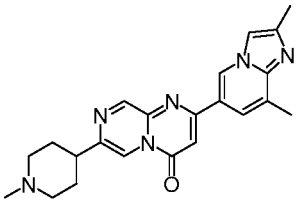

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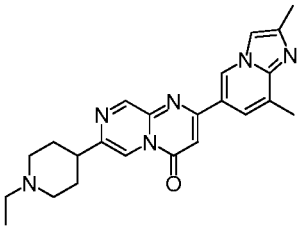

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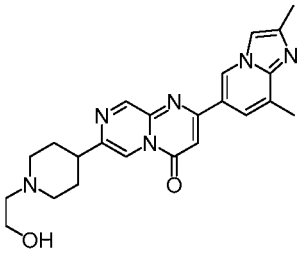

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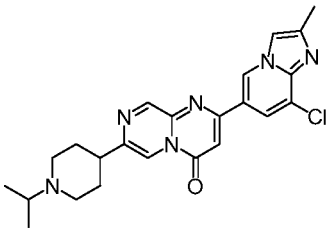

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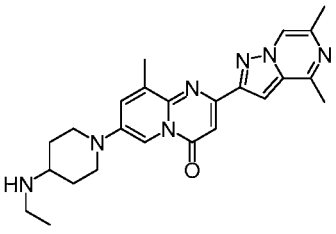

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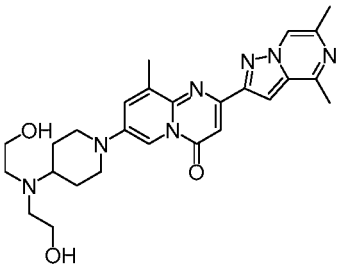

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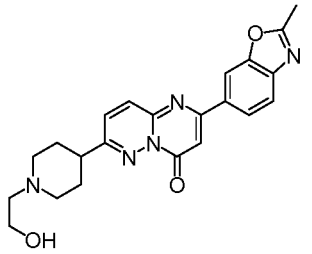

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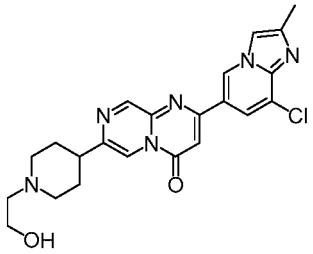

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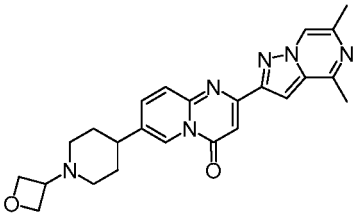

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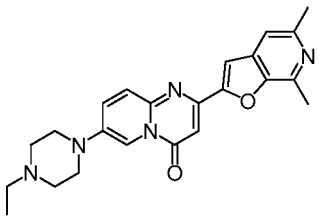

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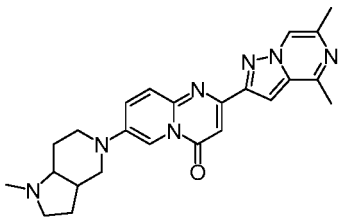

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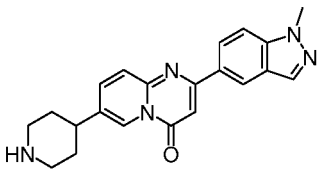

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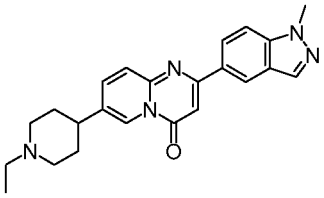

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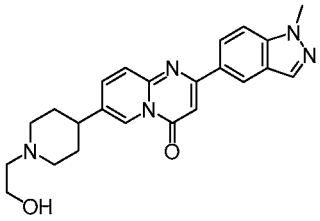

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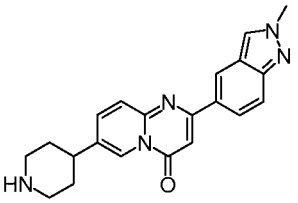

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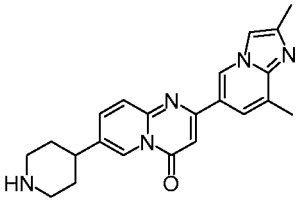

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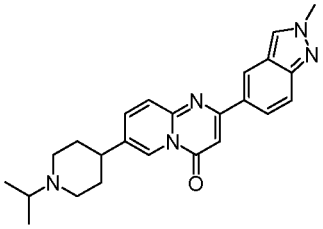

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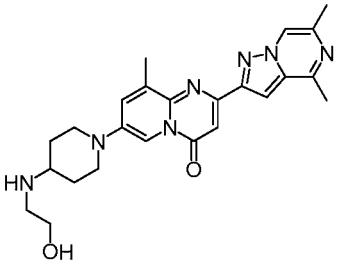

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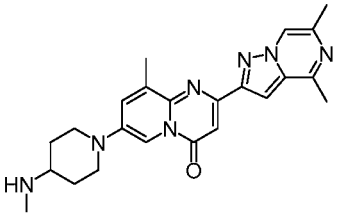

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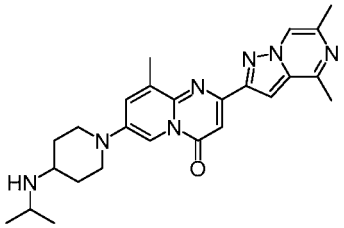

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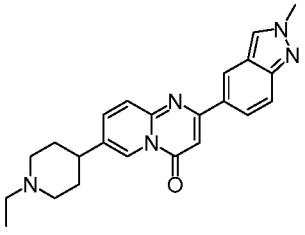

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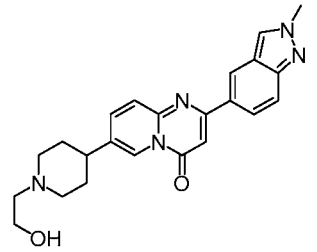

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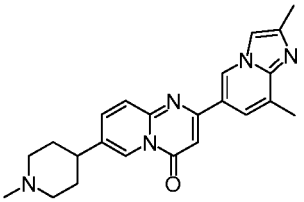

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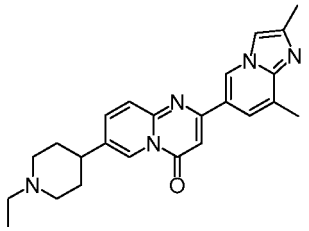

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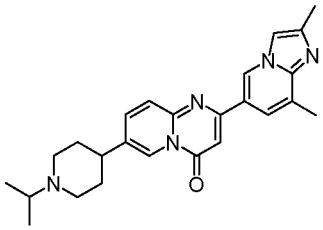

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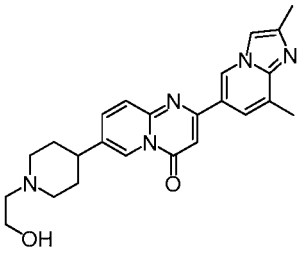

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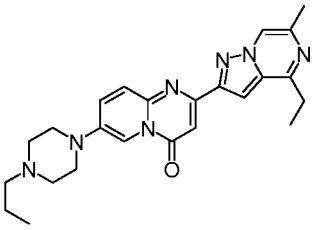

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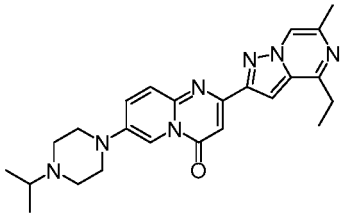

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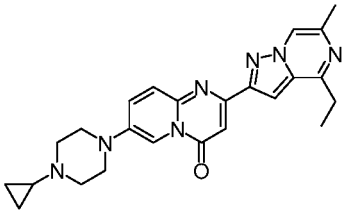

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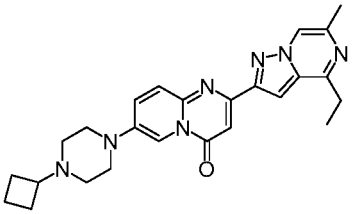

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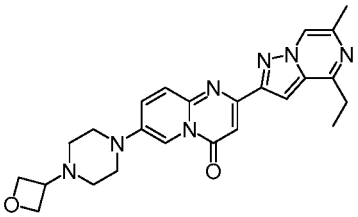

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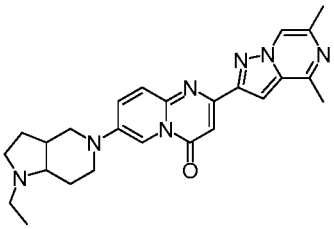

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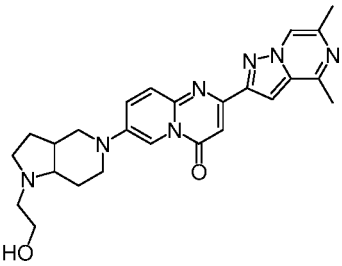

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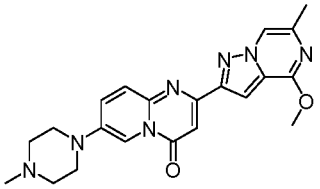

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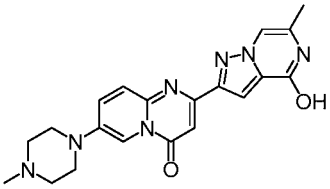

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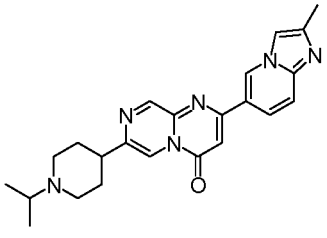

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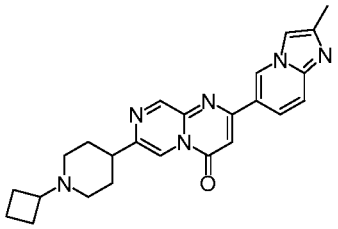

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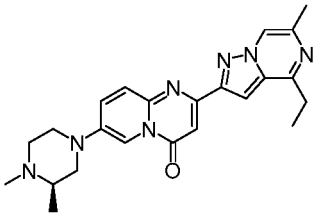

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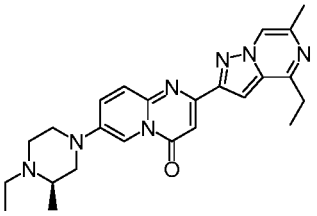

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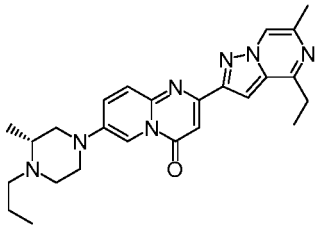

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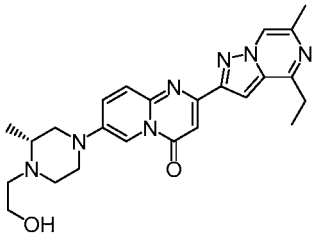

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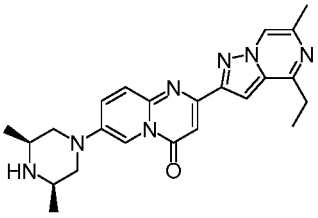

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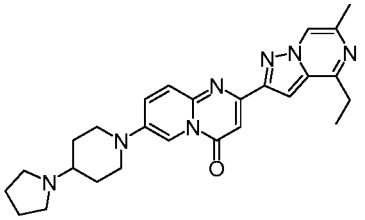

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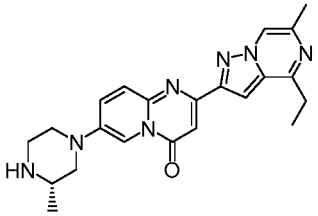

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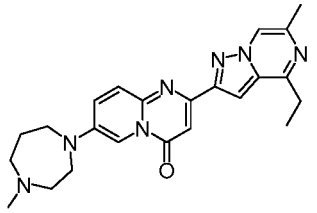

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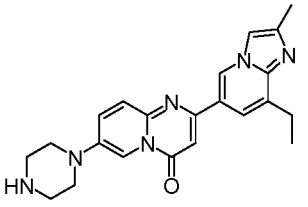

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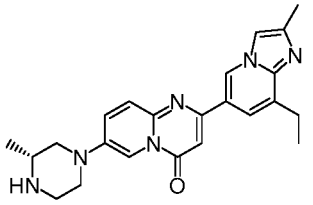

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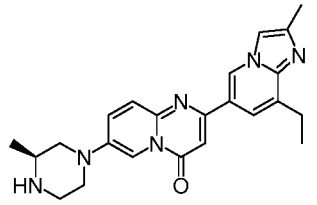

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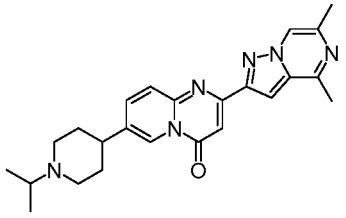

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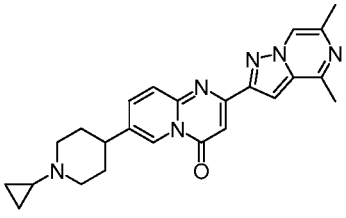

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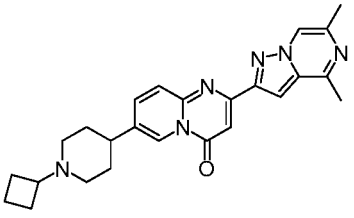

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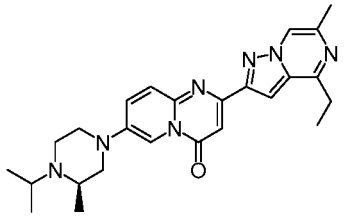

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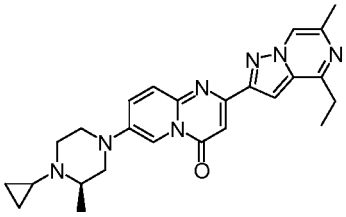

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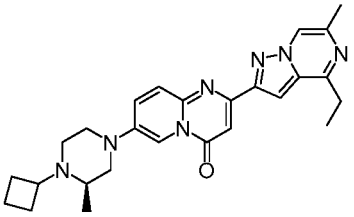

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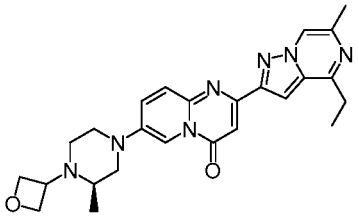

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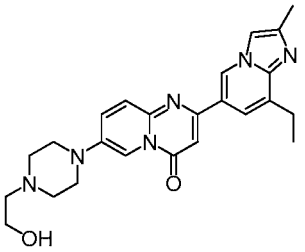

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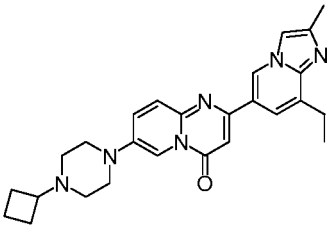

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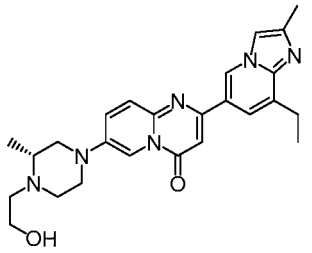

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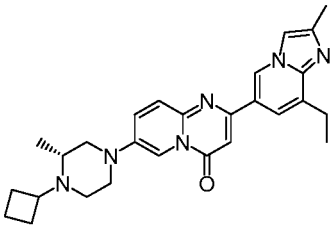

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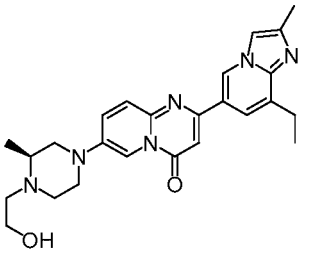

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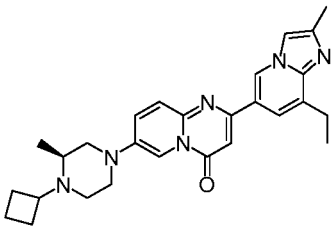

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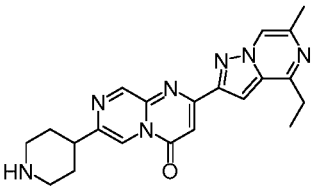

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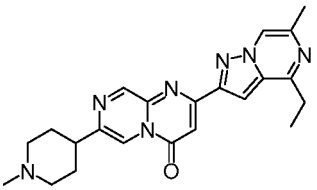

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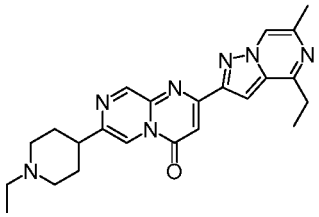

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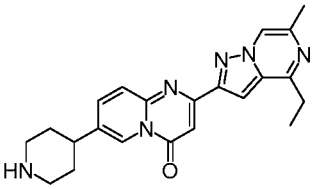

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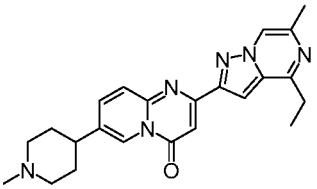

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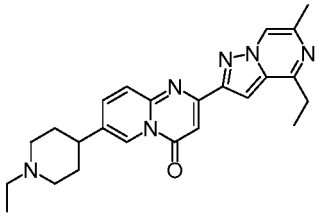

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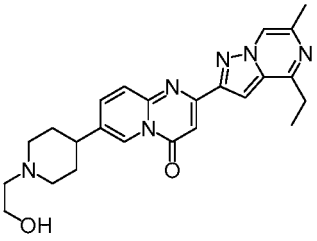

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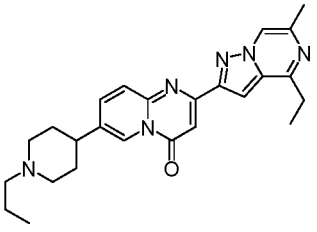

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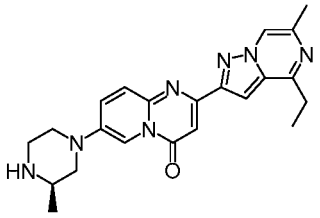

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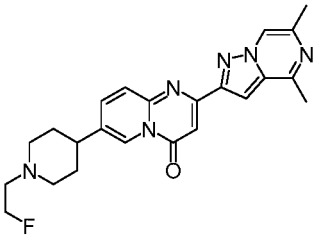

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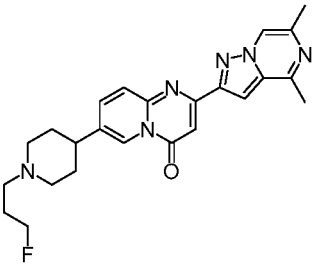

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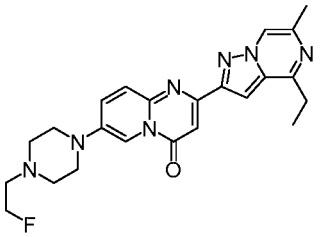

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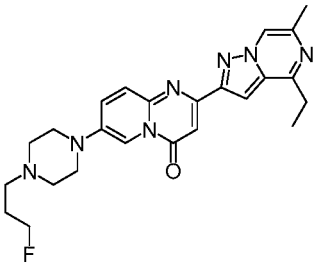

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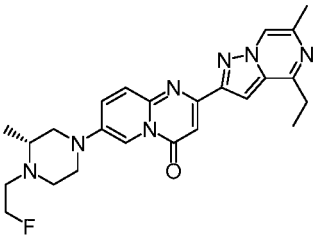

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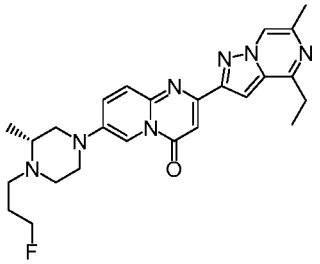

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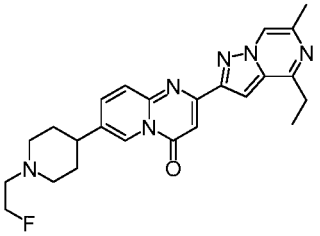

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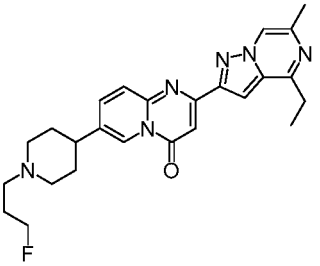

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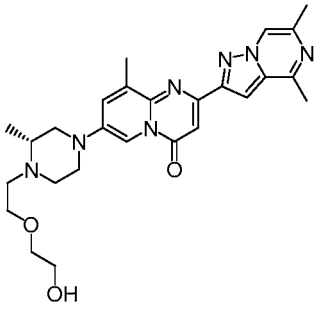

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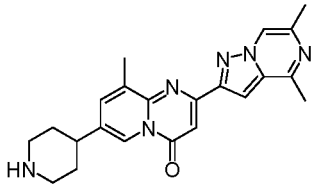

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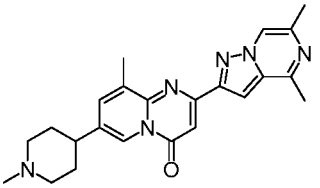

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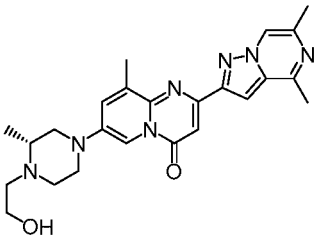

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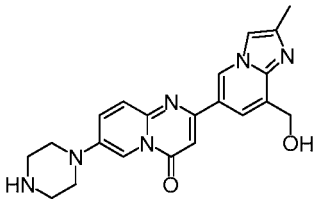

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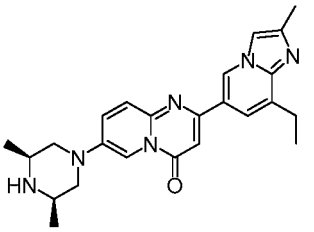

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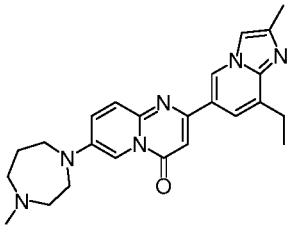

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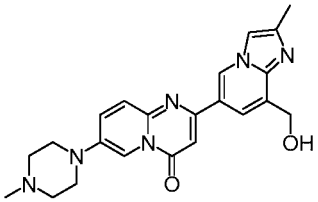

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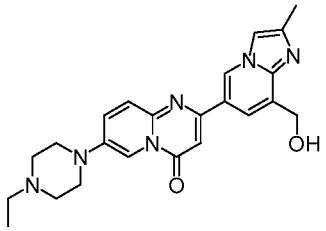

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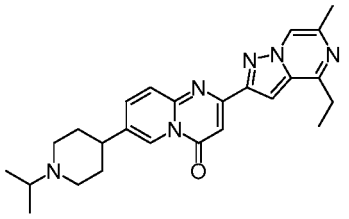

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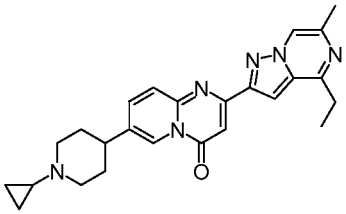

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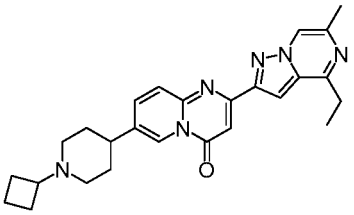

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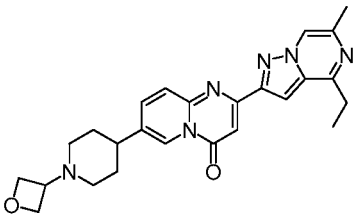

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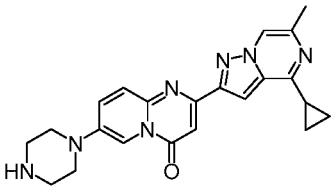

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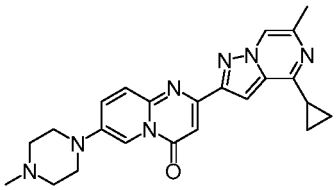

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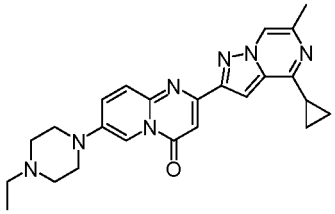

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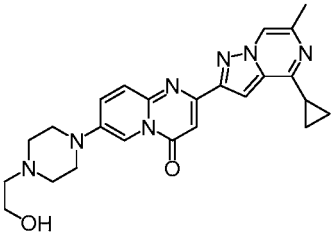

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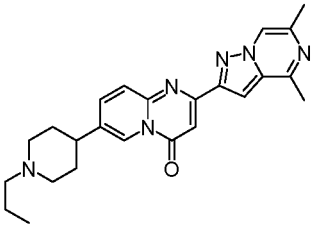

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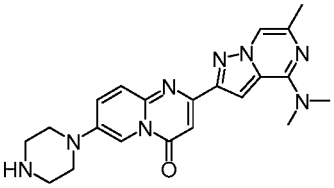

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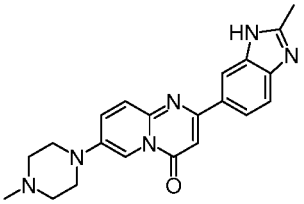

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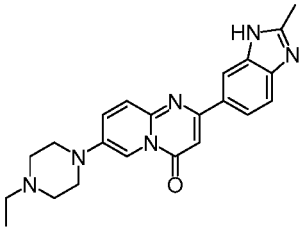

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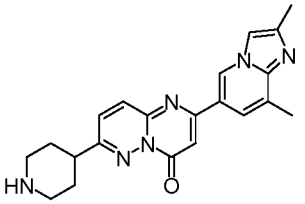

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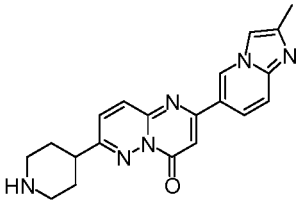

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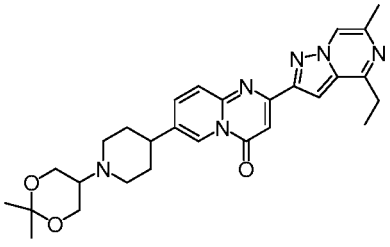

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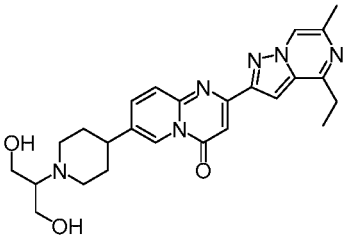

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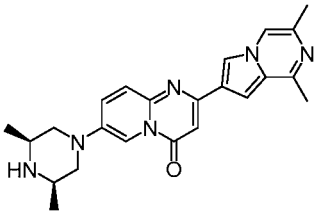

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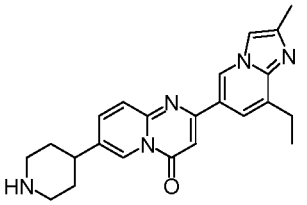

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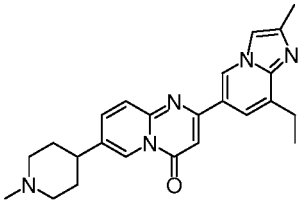

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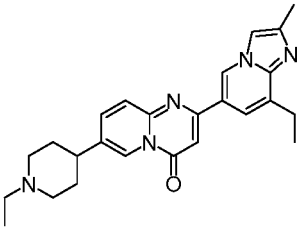

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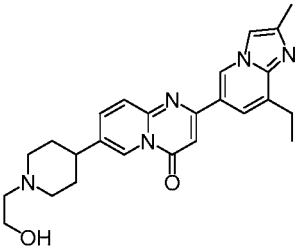

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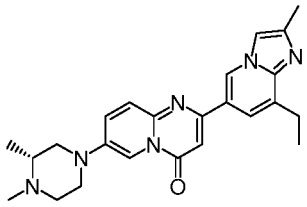

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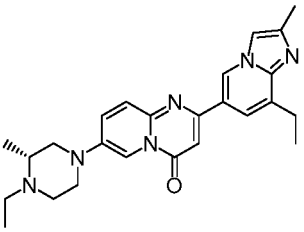

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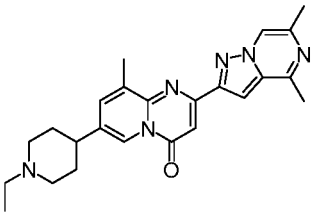

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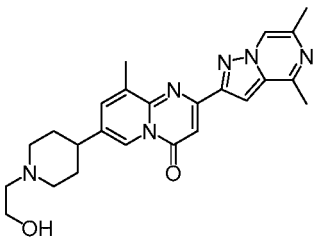

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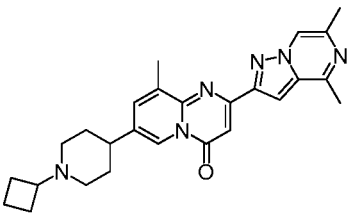

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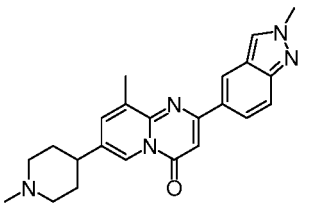

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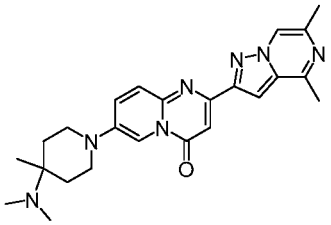

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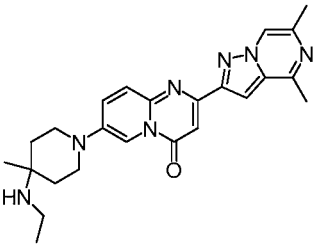

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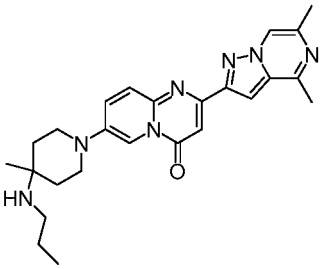

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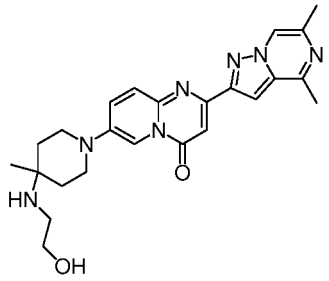

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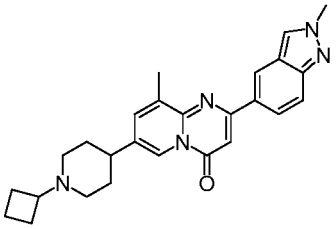

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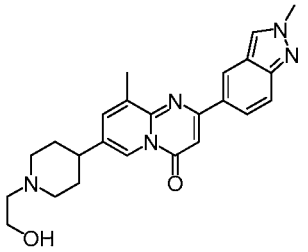

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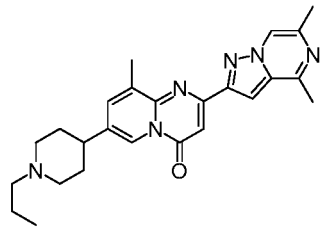

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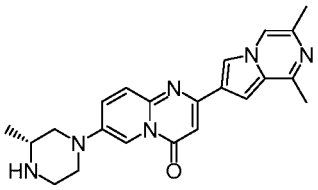

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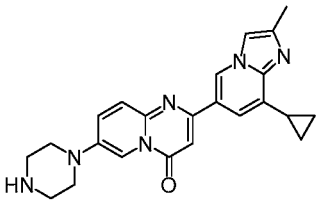

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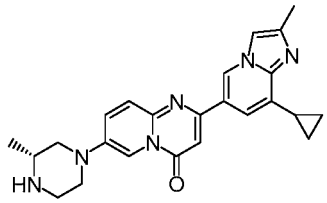

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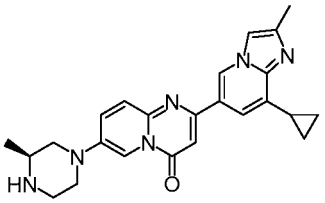

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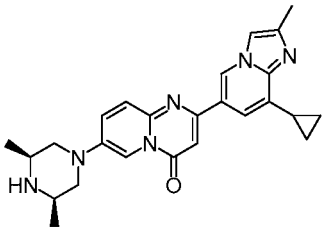

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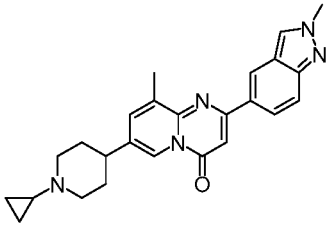

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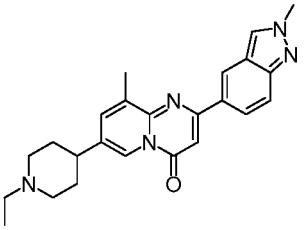

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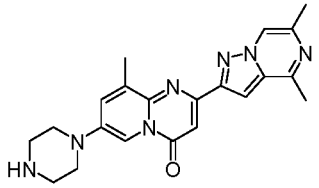

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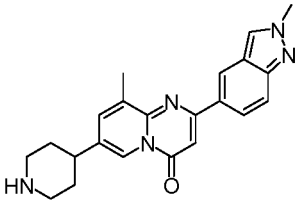

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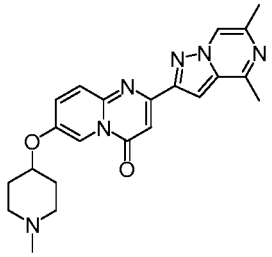

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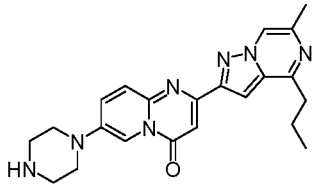

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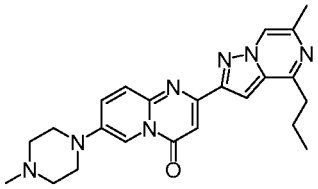

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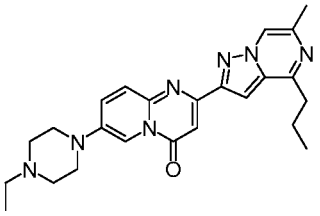

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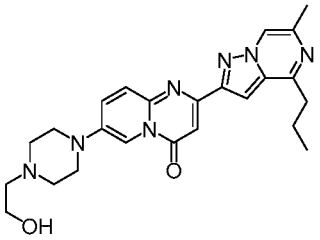

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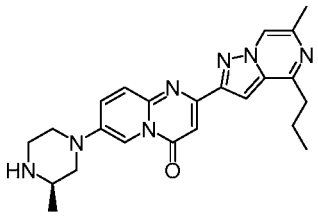

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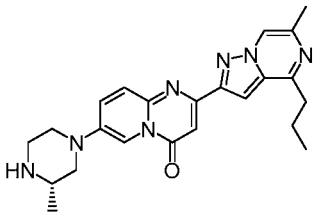

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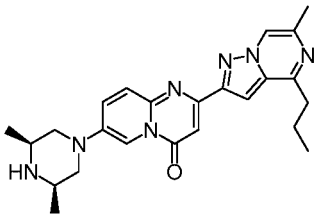

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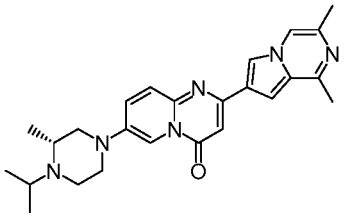

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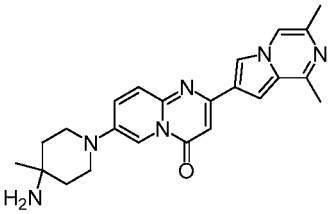

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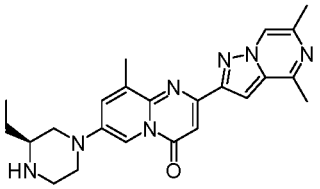

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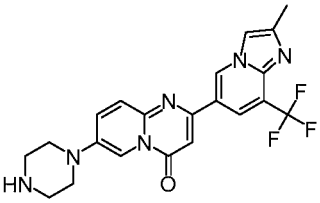

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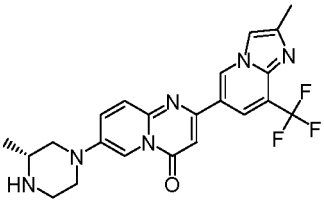

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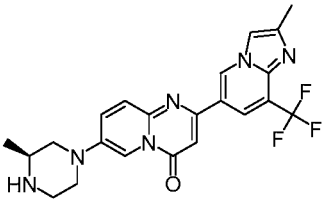

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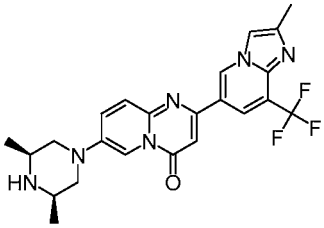

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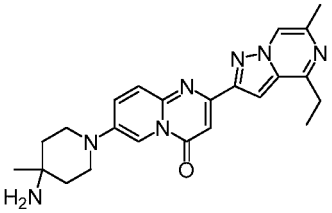

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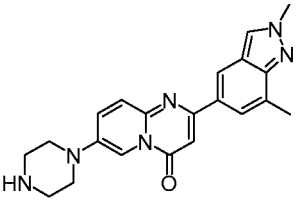

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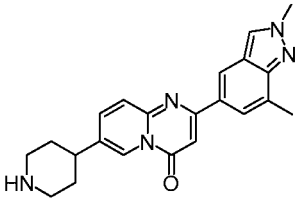

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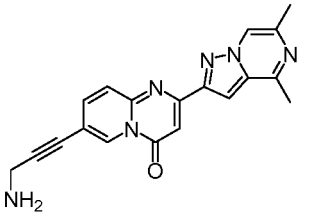

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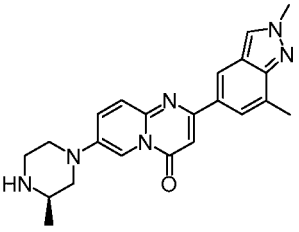

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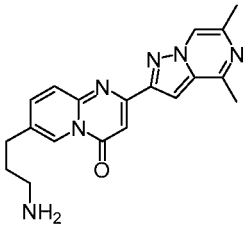

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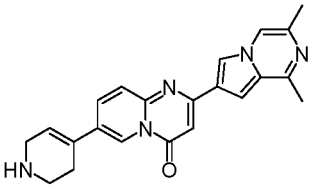

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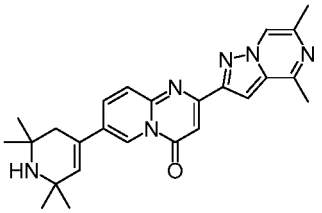

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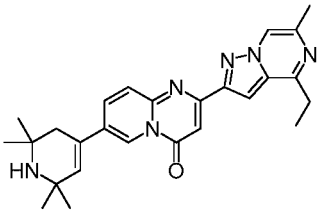

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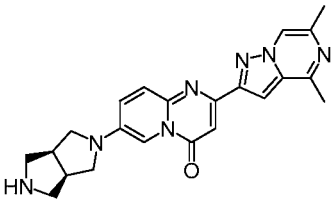

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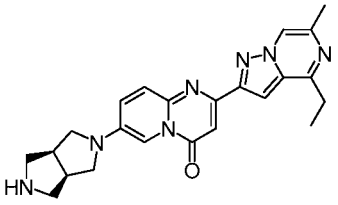

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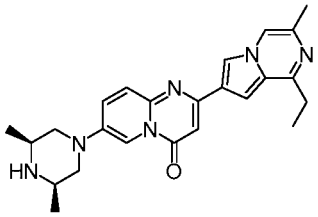

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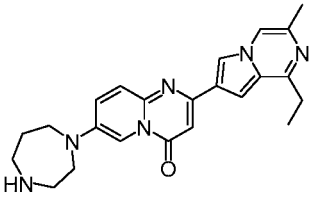

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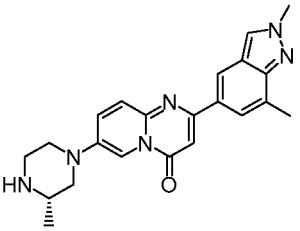

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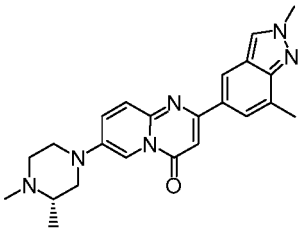

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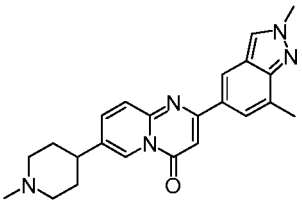

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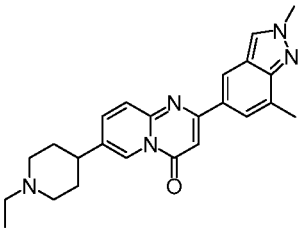

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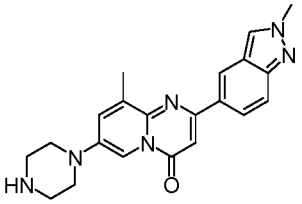

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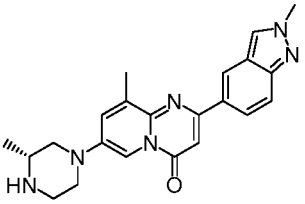

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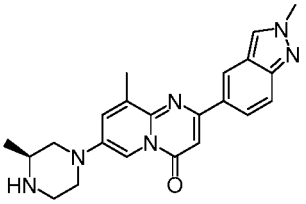

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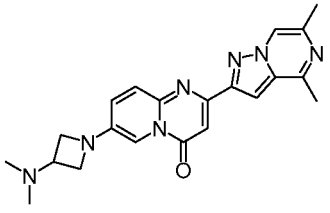

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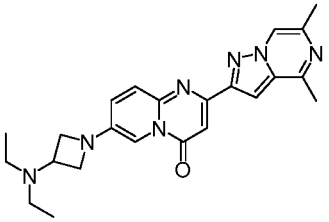

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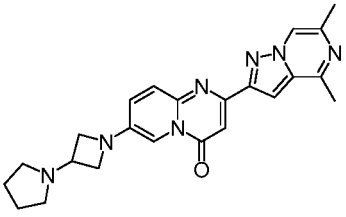

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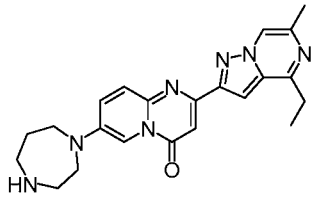

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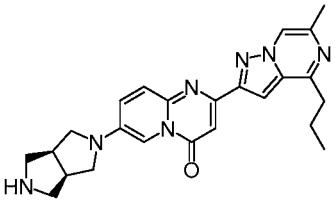

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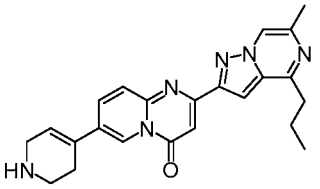

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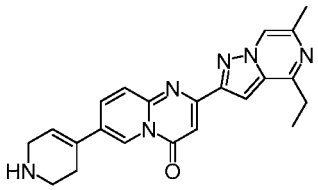

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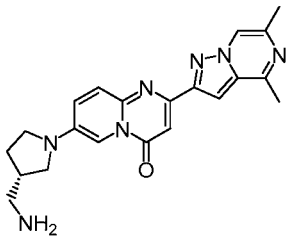

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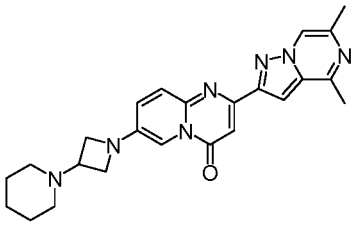

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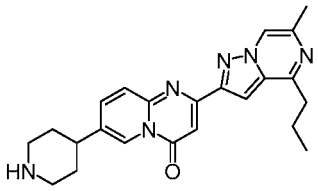

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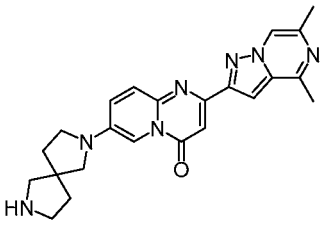

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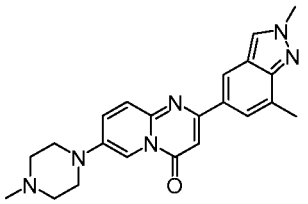

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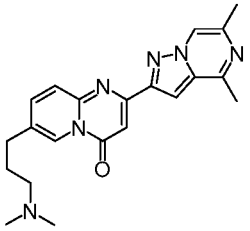

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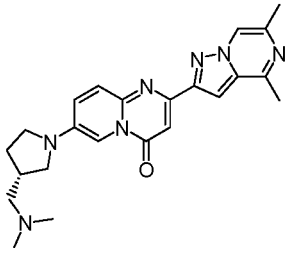

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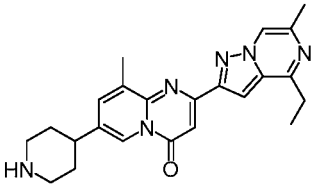

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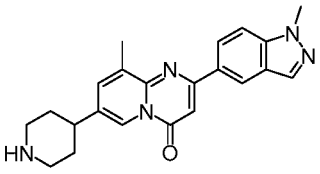

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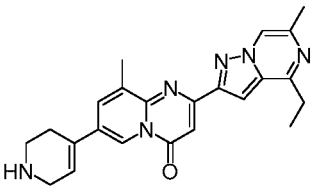

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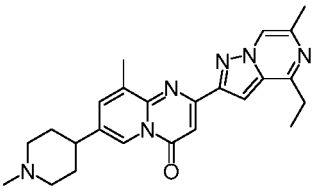

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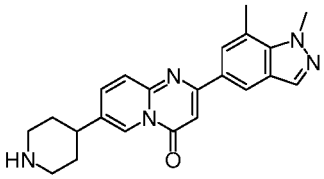

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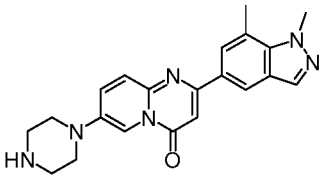

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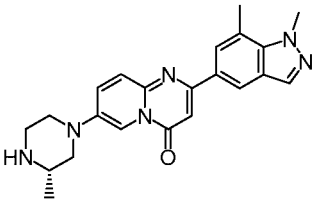

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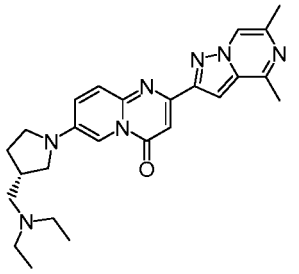

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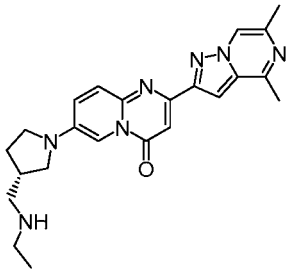

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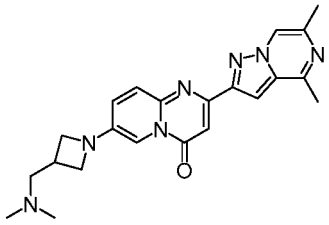

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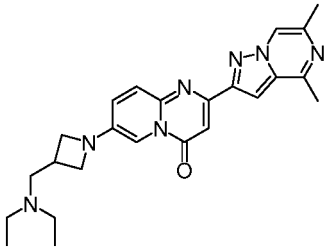

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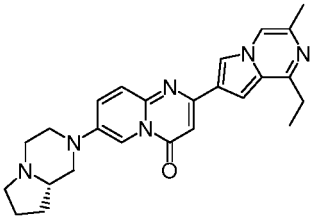

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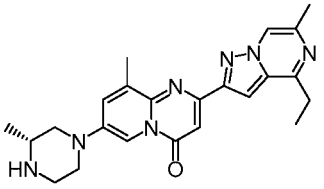

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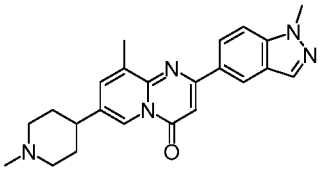

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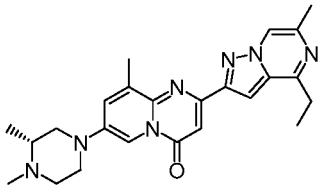

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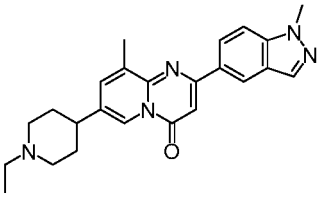

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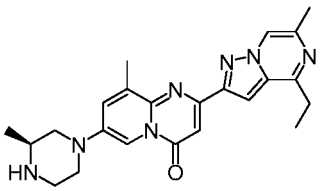

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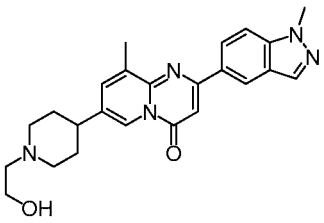

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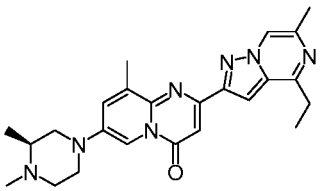

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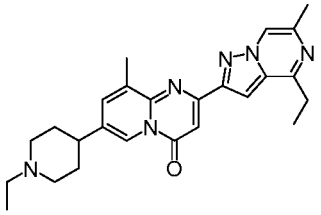

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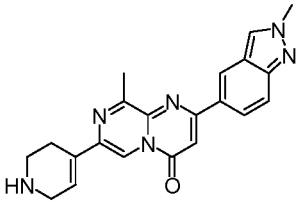

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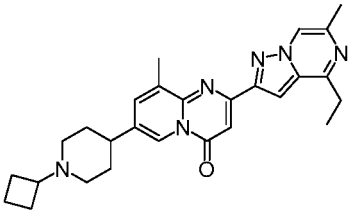

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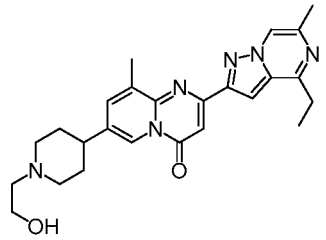

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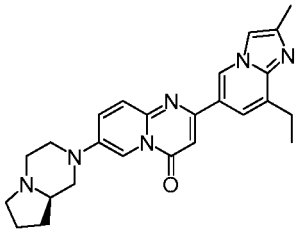

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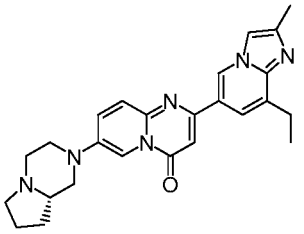

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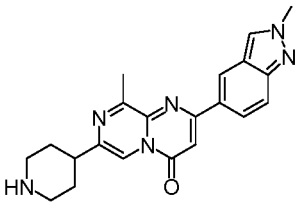

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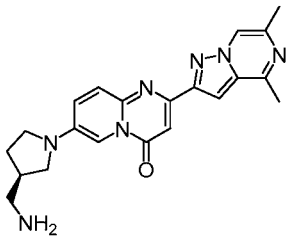

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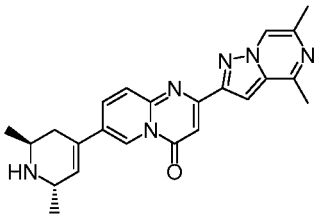

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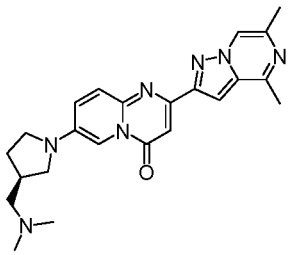

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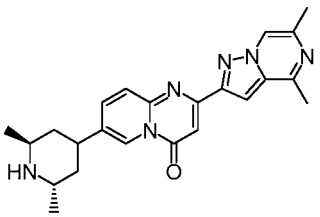

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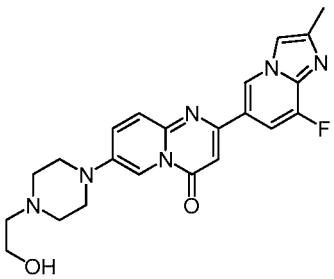

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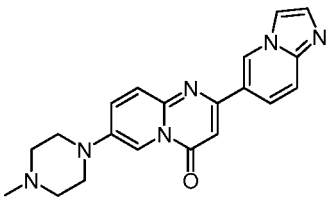

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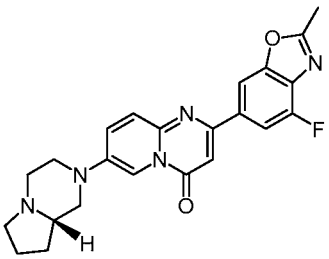

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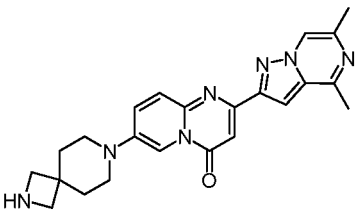

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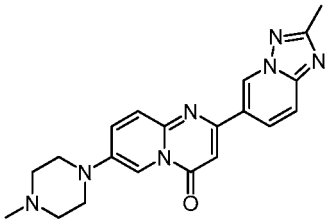

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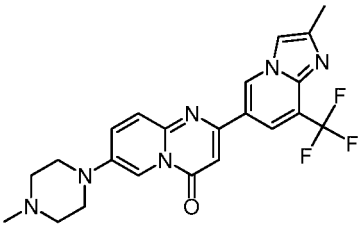

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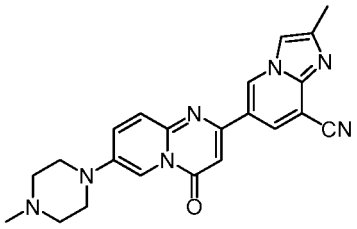

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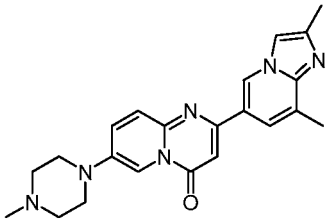

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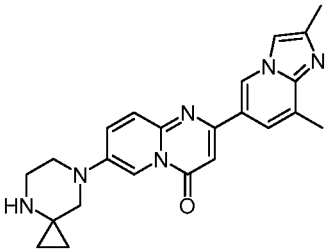

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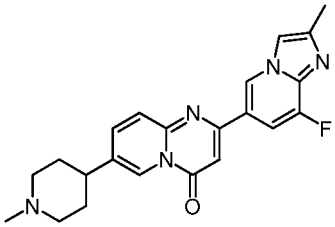

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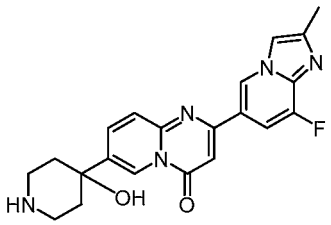

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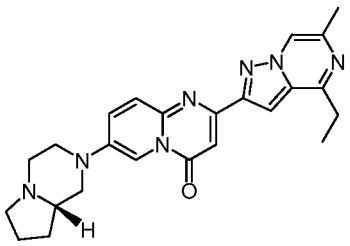

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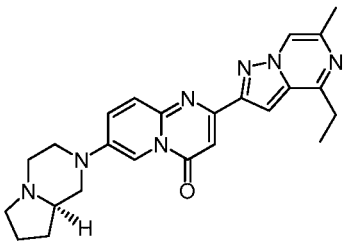

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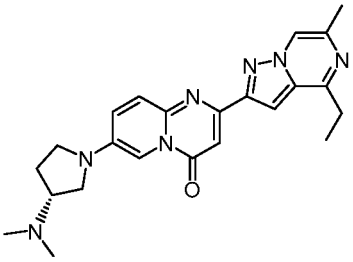

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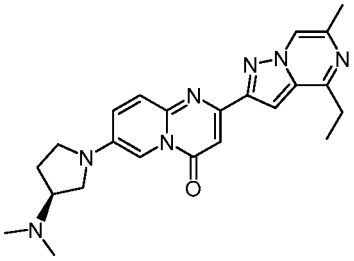

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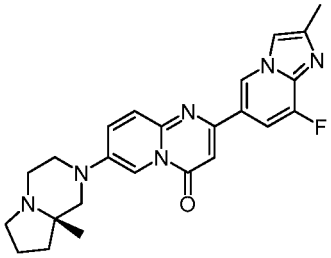

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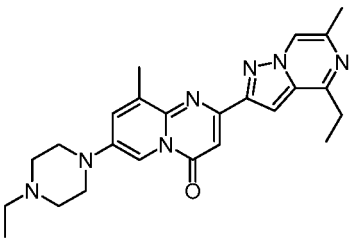

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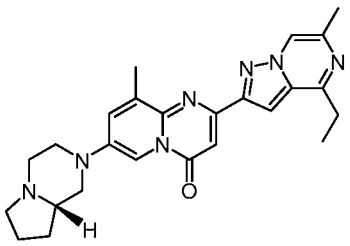

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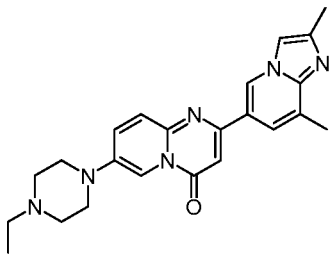

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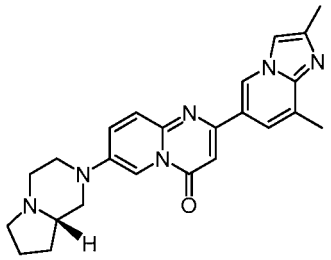

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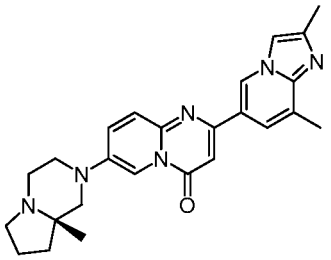

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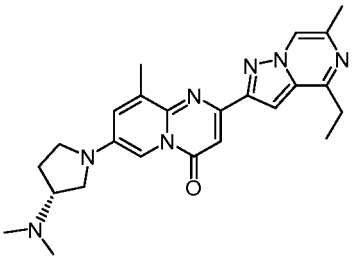

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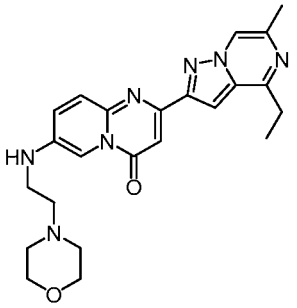

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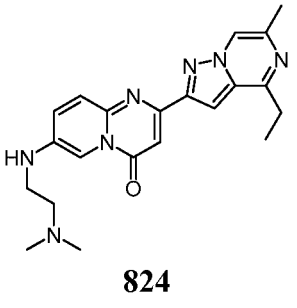

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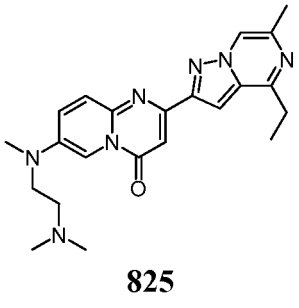

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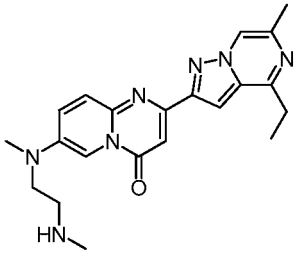

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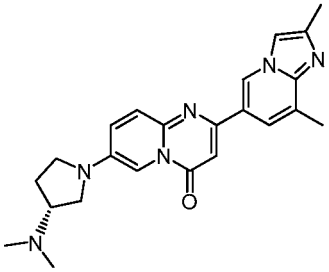

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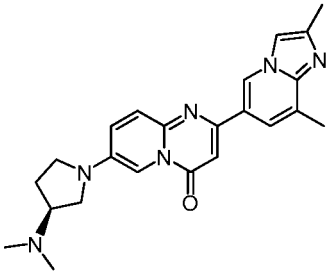

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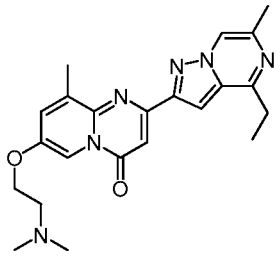

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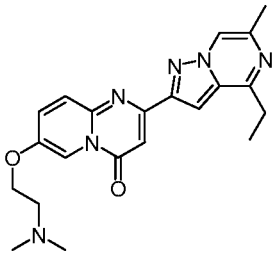

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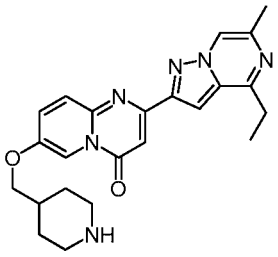

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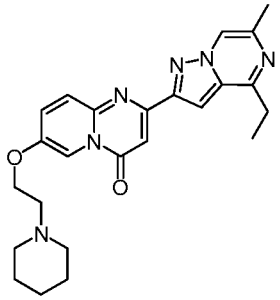

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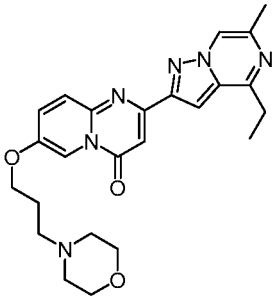

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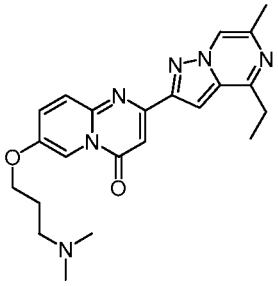

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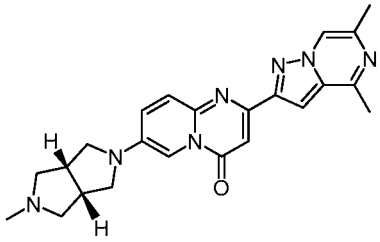

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[00537] or a form thereof.

TERMINOLOGY

[00538] The chemical terms used above and throughout the description herein, unless specifically defined otherwise, shall be understood by one of ordinary skill in the art to have the following indicated meanings.

[00539] As used herein, the term "C_{1-8}alkyl" generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration, including, but not limited to, methyl, ethyl, n-propyl (also referred to as propyl or propanyl), isopropyl, n-butyl (also referred to as butyl or butanyl), isobutyl, sec-butyl, tert-butyl, n-pentyl (also referred to as pentyl or pentanyl), n-hexyl (also referred to as hexyl or hexanyl), n-heptyl (also referred to as heptyl or heptanyl), n-octyl and the like. In some embodiments, C_{1-8}alkyl includes, but is not limited to, C_{1-6}alkyl, C_{1-4}alkyl and the like. A C_{1-8}alkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00540] As used herein, the term "C_{2-8}alkenyl" generally refers to partially unsaturated hydrocarbon radicals having from two to eight carbon atoms in a straight or branched chain configuration and one or more carbon-carbon double bonds therein, including, but not limited to, ethenyl (also referred to as vinyl), allyl, propenyl and the like. In some embodiments, C_{2-8}alkenyl includes, but is not limited to, C_{2-6}alkenyl, C_{2-4}alkenyl and the like. A C_{2-8}alkenyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00541] As used herein, the term "C_{2-8}alkynyl" generally refers to partially unsaturated hydrocarbon radicals having from two to eight carbon atoms in a straight or branched chain configuration and one or more carbon-carbon triple bonds therein, including, but not limited to, ethynyl, propynyl, butynyl and the like. In some embodiments, C_{2-8}alkynyl includes, but is not limited to, C_{2-6}alkynyl, C_{2-4}alkynyl and the like. A C_{2-8}alkynyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00542] As used herein, the term "C_{1-8}alkoxy" generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration of the formula: -O-C_{1-8}alkyl, including, but not limited to, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentoxy, n-hexoxy and the like. In some

embodiments, C_{1-8}alkoxy includes, but is not limited to, C_{1-6}alkoxy, C_{1-4}alkoxy and the like. A C_{1-8}alkoxy radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00543] As used herein, the term "C_{3-14}cycloalkyl" generally refers to a saturated or partially unsaturated monocyclic, bicyclic or polycyclic hydrocarbon radical, including, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctyl, 1*H*-indanyl, indenyl, tetrahydro-naphthalenyl and the like. In some embodiments, C_{3-14}cycloalkyl includes, but is not limited to, C_{3-8}cycloalkyl, C_{5-8}cycloalkyl, C_{3-10}cycloalkyl and the like. A C_{3-14}cycloalkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00544] As used herein, the term "aryl" generally refers to a monocyclic, bicyclic or polycyclic aromatic carbon atom ring structure radical, including, but not limited to, phenyl, naphthyl, anthracenyl, fluorenyl, azulenyl, phenanthrenyl and the like. An aryl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00545] As used herein, the term "heteroaryl" generally refers to a monocyclic, bicyclic or polycyclic aromatic carbon atom ring structure radical in which one or more carbon atom ring members have been replaced, where allowed by structural stability, with one or more heteroatoms, such as an O, S or N atom, including, but not limited to, furanyl (also referred to as furyl), thienyl (also referred to as thiophenyl), pyrrolyl, 2*H*-pyrrolyl, 3*H*-pyrrolyl, pyrazolyl, 1*H*-pyrazolyl, imidazolyl, 1*H*-imidazolyl, isoxazolyl, isothiazolyl, oxazolyl, 1,3-thiazolyl, triazolyl (such as 1*H*-1,2,3-triazolyl and the like), oxadiazolyl (such as 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl and the like), thiadiazolyl, tetrazolyl (such as 1*H*-tetrazolyl, 2*H*-tetrazolyl and the like), pyridinyl (also referred to as pyridyl), pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, 1*H*-indolyl, indazolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, isoindolyl, benzofuranyl, benzothienyl (also referred to as benzothiophenyl), benzoimidazolyl, 1*H*-benzoimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl (also referred to as 1,3-benzooxazolyl), purinyl, 9*H*-purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 1,3-diazinyl, 1,2-diazinyl, 1,2-diazolyl, 1,4-diazanaphthalenyl, acridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, 6*H*-thieno[2,3-*b*]pyrrolyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, 1*H*-pyrrolo[3,2-*b*]pyridinyl,

pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, 3*H*-imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl and the like. A heteroaryl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

[00546] As used herein, the term "heterocyclyl" generally refers to a saturated or partially unsaturated monocyclic, bicyclic or polycyclic carbon atom ring structure radical in which one or more carbon atom ring members have been replaced, where allowed by structural stability, with a heteroatom, such as an O, S or N atom, including, but not limited to, oxiranyl, oxetanyl, azetidinyl, tetrahydrofuranyl, pyrrolinyl, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, isoxazolinyl, isoxazolidinyl, isothiazolinyl, isothiazolidinyl, oxazolinyl, oxazolidinyl, thiazolinyl, thiazolidinyl, triazolinyl, triazolidinyl, oxadiazolinyl, oxadiazolidinyl, thiadiazolinyl, thiadiazolidinyl, tetrazolinyl, tetrazolidinyl, pyranyl, dihydro-2*H*-pyranyl, thiopyranyl, 1,3-dioxanyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,4-diazepanyl, 1,3-benzodioxolyl (also referred to as benzo[*d*][1,3]dioxolyl), 1,4-benzodioxanyl, 2,3-dihydro-1,4-benzodioxinyl (also referred to as 2,3-dihydrobenzo[*b*][1,4]dioxinyl), hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, octahydro-2*H*-pyrido[1,2-*a*]pyrazinyl,

3-azabicyclo[3.1.0]hexyl, (1*R*,5*S*)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl, (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl, 6,9-diazaspiro[4.5]decyl and the like. A heterocyclyl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

[00547] As used herein, the term "C_{1-8}alkoxy-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-O-C_{1-8}alkyl.

[00548] As used herein, the term "C_{1-8}alkoxy-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-O-C_{1-8}alkyl.

[00549] As used herein, the term "(C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-O-C_{1-8}alkyl)$_2$.

[00550] As used herein, the term "C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-NH-C_{1-8}alkyl-O-C_{1-8}alkyl.

[00551] As used herein, the term "(C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-N(C_{1-8}alkyl-O-C_{1-8}alkyl)$_2$.

[00552] As used herein, the term "(C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-O-C_{1-8}alkyl).

[00553] As used herein, the term "C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl-O-C_{1-8}alkyl.

[00554] As used herein, the term "(C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl-O-C_{1-8}alkyl)$_2$.

[00555] As used herein, the term "(C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-O-C_{1-8}alkyl).

[00556] As used herein, the term "C_{1-8}alkoxy-carbonyl" refers to a radical of the formula: -C(O)-O-C_{1-8}alkyl.

[00557] As used herein, the term "C_{1-8}alkoxy-carbonyl-C_{2-8}alkenyl" refers to a radical of the formula: -C_{2-8}alkenyl-C(O)-O-C_{1-8}alkyl.

[00558] As used herein, the term "C_{1-8}alkoxy-carbonyl-amino" refers to a radical of the formula: -NH-C(O)-O-C_{1-8}alkyl.

[00559] As used herein, the term "C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl.

[00560] As used herein, the term "(C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl)$_2$.

[00561] As used herein, the term "C_{1-8}alkyl-amino-C_{2-8}alkenyl" refers to a radical of the formula: -C_{2-8}alkenyl-NH-C_{1-8}alkyl.

[00562] As used herein, the term "(C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl" refers to a radical of the formula: -C_{2-8}alkenyl-N(C_{1-8}alkyl)$_2$.

[00563] As used herein, the term "C_{1-8}alkyl-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-NH-C_{1-8}alkyl.

[00564] As used herein, the term "(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-N(C_{1-8}alkyl)$_2$.

[00565] As used herein, the term "C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl.

[00566] As used herein, the term "(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)$_2$.

[00567] As used herein, the term "C_{1-8}alkyl-amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-NH-C_{1-8}alkyl.

[00568] As used herein, the term "(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-N(C_{1-8}alkyl)$_2$.

[00569] As used herein, the term "(C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-NH-C_{1-8}alkyl)$_2$.

[00570] As used herein, the term "[(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl]$_2$-amino" refers to a radical of the formula: -N[C_{1-8}alkyl-N(C_{1-8}alkyl)$_2$]$_2$.

[00571] As used herein, the term "(C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-NH-C_{1-8}alkyl).

[00572] As used herein, the term "[$(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)[C_{1-8}alkyl-N(C_{1-8}alkyl)$_2$].

[00573] As used herein, the term "C_{1-8}alkyl-amino-C_{2-8}alkynyl" refers to a radical of the formula: -C_{2-8}alkynyl-NH-C_{1-8}alkyl.

[00574] As used herein, the term "$(C_{1-8}alkyl)_2$-amino-C_{2-8}alkynyl" refers to a radical of the formula: -C_{2-8}alkynyl-N(C_{1-8}alkyl)$_2$.

[00575] As used herein, the term "C_{1-8}alkyl-carbonyl" refers to a radical of the formula: -C(O)-C_{1-8}alkyl.

[00576] As used herein, the term "C_{1-8}alkyl-carbonyl-amino" refers to a radical of the formula: -NH-C(O)-C_{1-8}alkyl.

[00577] As used herein, the term "C_{1-8}alkyl-thio" refers to a radical of the formula: -S-C_{1-8}alkyl.

[00578] As used herein, the term "amino-C_{2-8}alkenyl" refers to a radical of the formula: -C_{2-8}alkenyl-NH_2.

[00579] As used herein, the term "amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-NH_2.

[00580] As used herein, the term "amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH_2.

[00581] As used herein, the term "amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-NH_2.

[00582] As used herein, the term "(amino-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-NH_2)$_2$.

[00583] As used herein, the term "(amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-NH_2).

[00584] As used herein, the term "amino-C_{2-8}alkynyl" refers to a radical of the formula: -C_{2-8}alkynyl-NH_2.

[00585] As used herein, the term "aryl-C_{1-8}alkoxy-carbonyl" refers to a radical of the formula: -C(O)-O-C_{1-8}alkyl-aryl.

[00586] As used herein, the term "aryl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-aryl.

[00587] As used herein, the term "aryl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-aryl.

[00588] As used herein, the term "(aryl-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-aryl)$_2$.

[00589] As used herein, the term "(aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-aryl).

[00590] As used herein, the term "aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl-aryl.

[00591] As used herein, the term "(aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl-aryl)$_2$.

[00592] As used herein, the term "(aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-aryl).

[00593] As used herein, the term "aryl-amino" refers to a radical of the formula: -NH-aryl.

[00594] As used herein, the term "aryl-amino-carbonyl" refers to a radical of the formula: -C(O)-NH-aryl.

[00595] As used herein, the term "aryl-sulfonyloxy-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-O-SO_2-aryl.

[00596] As used herein, the term "benzoxy-carbonyl" refers to a radical of the formula: -C(O)-O-CH_2-phenyl.

[00597] As used herein, the term "C_{3-14}cycloalkyl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-C_{3-14}cycloalkyl.

[00598] As used herein, the term "C_{3-14}cycloalkyl-amino" refers to a radical of the formula: -NH-C_{3-14}cycloalkyl.

[00599] As used herein, the term "C_{3-14}cycloalkyl-oxy" refers to a radical of the formula: -O-C_{3-14}cycloalkyl.

[00600] As used herein, the term "halo" or "halogen" generally refers to a halogen atom radical, including fluoro, chloro, bromo and iodo.

[00601] As used herein, the term "halo-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-halo, wherein C_{1-8}alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

[00602] As used herein, the term "halo-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-halo, wherein C_{1-8}alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

[00603] As used herein, the term "halo-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-halo.

[00604] As used herein, the term "(halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-halo).

[00605] As used herein, the term "(halo-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-halo)$_2$.

[00606] As used herein, the term "heteroaryl-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-heteroaryl.

[00607] As used herein, the term "heteroaryl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-heteroaryl.

[00608] As used herein, the term "heteroaryl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-heteroaryl.

[00609] As used herein, the term "(heteroaryl-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-heteroaryl)$_2$.

[00610] As used herein, the term "(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-heteroaryl).

[00611] As used herein, the term "heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl-heteroaryl.

[00612] As used herein, the term "(heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl-heteroaryl)$_2$.

[00613] As used herein, the term "(heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-heteroaryl).

[00614] As used herein, the term "heteroaryl-amino" refers to a radical of the formula: -NH-heteroaryl.

[00615] As used herein, the term "heterocyclyl-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-heterocyclyl.

[00616] As used herein, the term "heterocyclyl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-heterocyclyl.

[00617] As used herein, the term "heterocyclyl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-heterocyclyl.

[00618] As used herein, the term "(heterocyclyl-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-heterocyclyl)$_2$.

[00619] As used herein, the term "(heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-heterocyclyl).

[00620] As used herein, the term "heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl-heterocyclyl.

[00621] As used herein, the term "(heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl-heterocyclyl)$_2$.

[00622] As used herein, the term "(heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-heterocyclyl).

[00623] As used herein, the term "heterocyclyl-amino" refers to a radical of the formula: -NH-heterocyclyl.

[00624] As used herein, the term "(heterocyclyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(heterocyclyl).

[00625] As used herein, the term "heterocyclyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-heterocyclyl.

[00626] As used herein, the term "heterocyclyl-carbonyl" refers to a radical of the formula: -C(O)-heterocyclyl.

[00627] As used herein, the term "heterocyclyl-carbonyl-oxy" refers to a radical of the formula: -O-C(O)-heterocyclyl.

[00628] As used herein, the term "heterocyclyl-oxy" refers to a radical of the formula: -O-heterocyclyl.

[00629] As used herein, the term "hydroxy" refers to a radical of the formula: -OH.

[00630] As used herein, the term "hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-O-C_{1-8}alkyl-OH.

[00631] As used herein, the term "hydroxy-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-OH, wherein C_{1-8}alkyl is partially or completely substituted with one or more hydroxy radicals where allowed by available valences.

[00632] As used herein, the term "hydroxy-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-OH.

[00633] As used herein, the term "(hydroxy-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-OH)$_2$.

[00634] As used herein, the term "(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-OH).

[00635] As used herein, the term "hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-C_{1-8}alkyl-OH.

[00636] As used herein, the term "(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl-OH)$_2$.

[00637] As used herein, the term "(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-OH).

[00638] As used herein, the term "hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-NH-C_{1-8}alkyl-OH.

[00639] As used herein, the term "(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-N(C_{1-8}alkyl-OH)$_2$.

[00640] As used herein, the term "(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-OH).

[00641] As used herein, the term "hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-NH-C_{1-8}alkyl-OH.

[00642] As used herein, the term "(hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl-NH-C_{1-8}alkyl-OH)$_2$.

[00643] As used herein, the term "(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-N(C_{1-8}alkyl-OH)$_2$.

[00644] As used herein, the term "(hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(C_{1-8}alkyl-NH-C_{1-8}alkyl-OH).

[00645] As used herein, the term "[(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)[C_{1-8}alkyl-N(C_{1-8}alkyl-OH)$_2$].

[00646] As used herein, the term "(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-N(C_{1-8}alkyl,C_{1-8}alkyl-OH).

[00647] As used herein, the term "[(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)[C_{1-8}alkyl-N(C_{1-8}alkyl)(C_{1-8}alkyl-OH)].

[00648] As used herein, the term "substituent" means positional variables on the atoms of a core molecule that are attached at a designated atom position, replacing one or more hydrogen atoms on the designated atom, provided that the atom of attachment does not exceed the available valence or shared valences, such that the substitution results in a stable compound. Accordingly, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. It should also be noted that any carbon as well as heteroatom with a valence level that appears to be unsatisfied as described or shown herein is assumed to have a sufficient number of hydrogen atom(s) to satisfy the valences described or shown.

[00649] For the purposes of this description, where one or more substituent variables for a compound of Formula (I) encompass functionalities incorporated into a compound of Formula (I), each functionality appearing at any location within the disclosed compound may be independently selected, and as appropriate, independently and/or optionally substituted.

[00650] As used herein, the terms "independently selected," or "each selected" refer to functional variables in a substituent list that may be attached more than once on the structure of a core molecule, where the pattern of substitution at each occurrence is independent of the pattern at any other occurrence. Further, the use of a generic substituent on a core structure for a compound provided herein is understood to include the replacement of the generic substituent with specie substituents that are included within the particular genus, e.g., aryl may be independently replaced with phenyl or naphthalenyl (also referred to as naphthyl) and the like, such that the resulting compound is intended to be included within the scope of the compounds described herein.

[00651] As used herein, the term "each instance of" when used in a phrase such as "…aryl, aryl-C_{1-8}alkyl, heterocyclyl and heterocyclyl-C_{1-8}alkyl, wherein each instance of aryl and heterocyclyl is optionally substituted with one or two substituents…" is intended to include optional, independent substitution on each of the aryl and heterocyclyl rings and on the aryl and heterocyclyl portions of aryl-C_{1-8}alkyl and heterocyclyl-C_{1-8}alkyl.

[00652] As used herein, the term "optionally substituted" means that the specified substituent variables, groups, radicals or moieties represent the scope of the genus and may be independently chosen as needed to replace one or more hydrogen atoms on the designated atom of attachment of a core molecule.

[00653] As used herein, the terms "stable compound' or "stable structure" mean a compound that is sufficiently robust to be isolated to a useful degree of purity from a reaction mixture and formulations thereof into an efficacious therapeutic agent.

[00654] Compound names provided herein were obtained using ACD Labs Index Name software provided by ACD Labs and/or ChemDraw Ultra software provided by CambridgeSoft®. When the compound name disclosed herein conflicts with the structure depicted, the structure shown will supercede the use of the name to define the compound intended. Nomenclature for substituent radicals defined herein may differ slightly from the chemical name from which they are derived; one skilled in the art will recognize that the definition of the substituent radical is intended to include the radical as found in the chemical name.

[00655] The term "SMN," unless otherwise specified herein, refers to the human SMN1 gene, DNA or RNA, and/or human SMN2 gene, DNA or RNA. In a specific embodiment, the term "SMN1" refers to the human SMN1 gene, DNA or RNA. In another specific embodiment, the term "SMN2" refers to the human SMN2 gene, DNA or RNA.

[00656] Nucleic acid sequences for the human SMN1 and SMN2 genes are known in the art. For nucleic acid sequences of human SMN1, *see, e.g.*, GenBank Accession Nos. DQ894095, NM_000344, NM_022874, and BC062723. For nucleic acid sequences of human SMN2, see, e.g., NM_022875, NM_022876, NM_022877, NM_017411, DQ894734 (Life Technologies, Inc. (formerly Invitrogen), Carlsbad, Calif.), BC000908, BC070242, CR595484, CR598529, CR609539, U21914, and BC015308.

[00657] The SMN1 gene can be found on the forward strand of human chromosome 5 from approximately nucleotide 70,220,768 to approximately nucleotide 70,249,769. The approximate locations of exons 6, 7 and 8 and introns 6 and 7 of SMN1 on human chromosome 5 are as follows:

[00658] 70,241,893 to 70,242,003 exon 6;

[00659] 70,242,004 to 70,247,767 intron 6;

[00660] 70,247,768 to 70,247,821 exon 7;

[00661] 70,247,822 to 70,248,265 intron 7; and,

[00662] 70,248,266 to 70,248,839 exon 8.

[00663] The SMN2 gene can be found on the forward strand of human chromosome 5 from approximately nucleotide 69,345,350 to approximately nucleotide 69,374,349.

[00664] The approximate locations of exons 6, 7 and 8 and introns 6 and 7 of SMN2 on human chromosome 5 are as follows:

[00665] 69,366,468 to 69,366,578 exon 6;

[00666] 69,366,579 to 69,372,347 intron 6;

[00667] 69,372,348 to 69,372,401 exon 7;

[00668] 69,372,402 to 69,372,845 intron 7; and,

[00669] 69,372,846 to 69,373,419 exon 8.

[00670] In specific embodiments, the nucleotide sequences delineated above for exons 6, 7 and 8 and introns 6 and 7 of SMN1 are used in the SMN1 minigene nucleic acid constructs described herein. In other specific embodiments, the nucleotide sequences of exons 6, 7 and 8 and introns 6 and 7 of SMN2 in the examples provided herein are used in the SMN2 minigene nucleic acid constructs described herein.

[00671] The term "Smn" or "Smn protein," unless otherwise specified herein, refers to a human Smn protein that contains the amino acid residues encoded by exons 1 through 7 of the SMN1 gene and/or SMN2 gene. In a specific embodiment, the Smn protein is stable and functional *in vitro* and/or *in vivo* as assessed by methods known to one of skill in the art. In another specific embodiment, the Smn protein is the full-length protein encoded by the human SMN1 gene and/or SMN2 gene. In another specific embodiment, the Smn protein has the amino acid sequence found at GenBank Accession No. NP_000335, AAC50473.1, AAA66242.1, or NP_059107.

[00672] As used herein, the term "enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene," and analogous terms, unless otherwise specified herein, refers to the inclusion of the complete, intact, non-truncated sequence of exon 7 of SMN2 into the mature mRNA that is transcribed from the SMN2 gene (*i.e.*, resulting in the production of full-length SMN2 mRNA) *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art, such that increased levels of Smn protein are produced from the SMN2 gene *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that increased

expression of stable and functional Smn protein is produced from the SMN2 gene *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that expression of the fusion protein encoded by the minigene is increased *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that expression of Smn protein produced from the SMN2 gene in a subject (e.g., an animal model for SMA or a human subject or an SMA patient) in need thereof is increased.

[00673] As used herein, the term "enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene," and analogous terms, unless otherwise specified herein, refers to the inclusion of the complete, intact, non-truncated sequence of exon 7 of SMN1 into the mature mRNA that is transcribed from the SMN1 gene (*i.e.*, resulting in the production of full-length SMN1 mRNA) *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art, such that increased levels of Smn protein are produced from the SMN1 gene *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that increased expression of stable and functional Smn protein is produced from the SMN1 gene *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that expression of the fusion protein encoded by the minigene is increased *in vitro* and/or *in vivo*, as assessed by methods known to one of skill in the art; or, that expression of Smn protein produced from the SMN1 gene in a subject (*e.g.*, an animal model for SMA or a human subject) in need thereof is increased.

[00674] As used herein, the term "substantial change" in the context of the amount of mRNA means that the amount of mRNA does not change by a statistically significant amount, *e.g.*, a p value less than a value selected from 0.1, 0.05, 0.01, 0.005, 0.001, 0.0005, 0.0001, 0.00005 or 0.00001.

[00675] As used herein, the terms "subject" and "patient" are used interchangeably to refer to an animal or any living organism having sensation and the power of voluntary movement, and which requires for its existence oxygen and organic food. Nonlimiting examples include members of the human, equine, porcine, bovine, rattus, murine, canine and feline species. In some embodiments, the subject is a mammal or a warm-blooded vertebrate animal. In certain embodiments, the subject is a non-human animal. In specific embodiments, the subject is a human. In one specific embodiment, the subject is a human SMA patient.

[00676] As used herein, the term "elderly human" refers to a human 65 years old or older.

[00677] As used herein, the term "human adult" refers to a human that is 18 years or older.

[00678] As used herein, the term "human child" refers to a human that is 1 year to 18 years old.

[00679] As used herein, the term "human infant" refers to a newborn to 1 year old year human.

[00680] As used herein, the term "human toddler" refers to a human that is 1 year to 3 years old.

COMPOUND FORMS

[00681] As used herein, the terms "a compound of Formula (Ia)," "a compound of Formula (Ia1)," "a compound of Formula (Ia2)," "a compound of Formula (Ia3)," "a compound of Formula (Ia4)," "a compound of Formula (II)," "a compound of Formula (IIa)," "a compound of Formula (IIa1)," "a compound of Formula (IIa2)," "a compound of Formula (IIa3)," "a compound of Formula (IIa4)," "a compound of Formula (III)," "a compound of Formula (IIIa)," "a compound of Formula (IIIa1)," "a compound of Formula (IIIa2)," "a compound of Formula (IIIa3)," "a compound of Formula (IIIa4)," "a compound of Formula (IV)," "a compound of Formula (IVa)," "a compound of Formula (IVa1)," "a compound of Formula (IVa2)," "a compound of Formula (V)," "a compound of Formula (Va)," "a compound of Formula (Va1)," "a compound of Formula (Va2)," "a compound of Formula (VI)," "a compound of Formula (VIa)," "a compound of Formula (VIa1)," "a compound of Formula (VIa2)," "a compound of Formula (VIa3)," "a compound of Formula (VIa4)," "a compound of Formula (VII)," "a compound of Formula (VIIa)," "a compound of Formula (VIIa1)," "a compound of Formula (VIIa2)," "a compound of Formula (VIII)," "a compound of Formula (VIIIa)," "a compound of Formula (VIIIa1)," "a compound of Formula (VIIIa2)," "a compound of Formula (IX)," "a compound of Formula (IXa)," "a compound of Formula (IXa1)," "a compound of Formula (IXa2)," "a compound of Formula (IXa3)," "a compound of Formula (IXa4)," "a compound of Formula (X)," "a compound of Formula (Xa)," "a compound of Formula (Xa1)," "a compound of Formula (Xa2)," "a compound of Formula (XI)," "a compound of Formula (XIa)," "a compound of Formula (XIa1)," "a compound of Formula (XIa2)," "a compound of Formula (XII)," "a compound of Formula (XIIa)," "a compound of Formula (XIIa1)," "a compound of Formula (XIIa2)," "a compound of Formula (XIIa3)," "a compound of Formula (XIIa4)," "a

compound of Formula (XIII)," "a compound of Formula (XIIIa)," "a compound of Formula (XIIIa1)," "a compound of Formula (XIIIa2)," "a compound of Formula (XIV)," "a compound of Formula (XIVa)," "a compound of Formula (XIVa1)," and "a compound of Formula (XIVa2)," each refer to subgenera of the compound of Formula (I) or a form thereof.

[00682] Rather than repeat embodiments for the various subgenera of the compound of Formula (I), in certain embodiments, the term "a compound of Formula (I) or a form thereof" is used to inclusively to refer to a compound of Formula (Ia) or a form thereof, a compound of Formula (Ia1) or a form thereof, a compound of Formula (Ia2) or a form thereof, a compound of Formula (Ia3) or a form thereof, a compound of Formula (Ia4) or a form thereof, a compound of Formula (II) or a form thereof, a compound of Formula (IIa) or a form thereof, a compound of Formula (IIa1) or a form thereof, a compound of Formula (IIa2) or a form thereof, a compound of Formula (IIa3) or a form thereof, a compound of Formula (IIa4) or a form thereof, a compound of Formula (III) or a form thereof, a compound of Formula (IIIa) or a form thereof, a compound of Formula (IIIa1) or a form thereof, a compound of Formula (IIIa2) or a form thereof, a compound of Formula (IIIa3) or a form thereof, a compound of Formula (IIIa4) or a form thereof, a compound of Formula (IV) or a form thereof, a compound of Formula (IVa) or a form thereof, a compound of Formula (IVa1) or a form thereof, a compound of Formula (IVa2) or a form thereof, a compound of Formula (V) or a form thereof, a compound of Formula (Va) or a form thereof, a compound of Formula (Va1) or a form thereof, a compound of Formula (Va2) or a form thereof, a compound of Formula (VI) or a form thereof, a compound of Formula (VIa) or a form thereof, a compound of Formula (VIa1) or a form thereof, a compound of Formula (VIa2) or a form thereof, a compound of Formula (VIa3) or a form thereof, a compound of Formula (VIa4) or a form thereof, a compound of Formula (VII) or a form thereof, a compound of Formula (VIIa) or a form thereof, a compound of Formula (VIIa1) or a form thereof, a compound of Formula (VIIa2) or a form thereof, a compound of Formula (VIII) or a form thereof, a compound of Formula (VIIIa) or a form thereof, a compound of Formula (VIIIa1) or a form thereof, a compound of Formula (VIIIa2) or a form thereof, a compound of Formula (IX) or a form thereof, a compound of Formula (IXa) or a form thereof, a compound of Formula (IXa1) or a form thereof, a compound of Formula (IXa2) or a form thereof, a compound of Formula (IXa3) or a form thereof, a compound of Formula (IXa4) or a form thereof, a compound of Formula (X) or a form thereof, a compound of Formula (Xa) or a form thereof, a compound of

Formula (Xa1) or a form thereof, a compound of Formula (Xa2) or a form thereof, a compound of Formula (XI) or a form thereof, a compound of Formula (XIa) or a form thereof, a compound of Formula (XIa1) or a form thereof, a compound of Formula (XIa2) or a form thereof, a compound of Formula (XII) or a form thereof, a compound of Formula (XIIa) or a form thereof, a compound of Formula (XIIa1) or a form thereof, a compound of Formula (XIIa2) or a form thereof, a compound of Formula (XIIa3) or a form thereof, a compound of Formula (XIIa4) or a form thereof, a compound of Formula (XIII) or a form thereof, a compound of Formula (XIIIa) or a form thereof, a compound of Formula (XIIIa1) or a form thereof, a compound of Formula (XIIIa2) or a form thereof, a compound of Formula (XIV) or a form thereof, a compound of Formula (XIVa) or a form thereof, a compound of Formula (XIVa1) or a form thereof or a compound of Formula (XIVa2) or a form thereof, either separately or together.

[00683] Thus, embodiments and references to "a compound of Formula (I)" are intended to be inclusive of compounds of Formula (Ia), Formula (Ia1), Formula (Ia2), Formula (Ia3), Formula (Ia4), Formula (II), Formula (IIa), Formula (IIa1), Formula (IIa2), Formula (IIa3), Formula (IIa4), Formula (III), Formula (IIIa), Formula (IIIa1), Formula (IIIa2), Formula (IIIa3), Formula (IIIa4), Formula (IV), Formula (IVa), Formula (IVa1), Formula (IVa2), Formula (V), Formula (Va), Formula (Va1), Formula (Va2), Formula (VI), Formula (VIa), Formula (VIa1), Formula (VIa2), Formula (VIa3), Formula (VIa4), Formula (VII), Formula (VIIa), Formula (VIIa1), Formula (VIIa2), Formula (VIII), Formula (VIIIa), Formula (VIIIa1), Formula (VIIIa2), Formula (IX), Formula (IXa), Formula (IXa1), Formula (IXa2), Formula (IXa3), Formula (IXa4), Formula (X), Formula (Xa), Formula (Xa1), Formula (Xa2), Formula (XI), Formula (XIa), Formula (XIa1), Formula (XIa2), Formula (XII), Formula (XIIa), Formula (XIIa1), Formula (XIIa2), Formula (XIIa3), Formula (XIIa4), Formula (XIII), Formula (XIIIa), Formula (XIIIa1), Formula (XIIIa2), Formula (XIV), Formula (XIVa), Formula (XIVa1) and Formula (XIVa2).

[00684] As used herein, the term "form" means a compound of Formula (I) selected from a free acid, free base, salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer, or tautomer thereof.

[00685] In certain embodiments described herein, the form of the compound of Formula (I) is a selected from a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00686] In certain embodiments described herein, the form of the compound of Formula (I) is a selected from a free acid, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00687] In certain embodiments described herein, the form of the compound of Formula (I) is a selected from a free base, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00688] In certain embodiments described herein, the form of the compound of Formula (I) is a free acid, free base or salt thereof.

[00689] In certain embodiments described herein, the form of the compound of Formula (I) is an isotopologue thereof.

[00690] In certain embodiments described herein, the form of the compound of Formula (I) is a stereoisomer, racemate, enantiomer or diastereomer thereof.

[00691] In certain embodiments described herein, the form of the compound of Formula (I) is a tautomer thereof.

[00692] In certain embodiments described herein, the form of the compound of Formula (I) is a pharmaceutically acceptable form.

[00693] In certain embodiments described herein, the compound of Formula (I) or a form thereof is isolated for use.

[00694] As used herein, the term "isolated" means the physical state of a compound of Formula (I) or a form thereof after being isolated and/or purified from a synthetic process (*e.g.*, from a reaction mixture) or natural source or combination thereof according to an isolation or purification process or processes described herein or which are well known to the skilled artisan (e.g., chromatography, recrystallization and the like) in sufficient purity to be characterizable by standard analytical techniques described herein or well known to the skilled artisan.

[00695] As used herein, the term "protected" means that a functional group on a compound of Formula (I) is in a form modified to preclude undesired side reactions at the protected site when the compound is subjected to a reaction. Suitable protecting groups will be recognized by those with ordinary skill in the art as well as by reference to standard textbooks such as, for example, T. W. Greene *et al*, *Protective Groups in Organic Synthesis* (1991), Wiley, New York.

[00696] Prodrugs of a compound of Formula (I) or a form thereof are also contemplated herein.

[00697] As used herein, the term "prodrug" means that a functional group on a compound of Formula (I) is in a form (*e.g.*, acting as an active or inactive drug precursor) that is transformed *in vivo* to yield an active or more active compound of Formula (I) or a form thereof. The transformation may occur by various mechanisms (*e.g.*, by metabolic and/or non-metabolic chemical processes), such as, for example, by hydrolysis and/or metabolism in blood, liver and/or other organs and tissues. A discussion of the use of prodrugs is provided by V.J.. Stella, et. al., "Biotechnology: Pharmaceutical Aspects, Prodrugs: Challenges and Rewards,"American Association of Pharmaceutical Scientists and Springer Press, 2007.

[00698] In one example, when a compound of Formula (I) or a form thereof contains a carboxylic acid functional group, a prodrug can comprise an ester formed by the replacement of the hydrogen atom of the acid group with a functional group such as alkyl and the like. In another example, when a compound of Formula (I) or a form thereof contains an alcohol functional group, a prodrug can be formed by the replacement of the hydrogen atom of the alcohol group with a functional group such as alkyl or substituted carbonyl and the like. In another example, when a compound of Formula (I) or a form thereof contains an amine functional group, a prodrug can be formed by the replacement of one or more amine hydrogen atoms with a functional group such as alkyl or substituted carbonyl. In another example, when a compound of Formula (I) or a form thereof contains a hydrogen substituent, a prodrug can be formed by the replacement of one or more hydrogen atoms with an alkyl substituent.

[00699] Pharmaceutically acceptable prodrugs of compounds of Formula (I) or a form thereof include those compounds substituted with one or more of the following groups: carboxylic acid esters, sulfonate esters, amino acid esters phosphonate esters, mono-, di- or triphosphate esters or alkyl substituents where appropriate. As described herein, it is understood by a person of ordinary skill in the art that one or more of such substituents may be used to provide a compound of Formula (I) or a form thereof for use as a prodrug.

[00700] The compounds of Formula (I) can form salts which are intended to be included within the scope of this description. Reference to a compound of Formula (I) herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula (I) contains both a basic moiety, such as, but not limited to a pyridine or imidazole, and

an acidic moiety, such as, but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein.

[00701] The term "pharmaceutically acceptable salt(s)", as used herein, means those salts of compounds described herein that are safe and effective (*i.e.*, non-toxic, physiologically acceptable) for use in mammals and that possess biological activity, although other salts are also useful. Salts of the compounds of Formula (I) may be formed, for example, by reacting a compound of Formula (I) with an amount of acid or base, such as an equivalent or stoichiometric amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

[00702] Pharmaceutically acceptable salts include one or more salts of acidic or basic groups present in compounds described herein. Embodiments of acid addition salts include, but are not limited to, an acetate, diacetate, acid phosphate, ascorbate, benzoate, benzenesulfonate, bisulfate, bitartrate, borate, butyrate, chloride, citrate, camphorate, camphorsulfonate, ethanesulfonate, formate, fumarate, gentisinate, gluconate, glucaronate, glutamate, hydrobromide, hydrochloride, dihydrochloride, trihydrochloride, hydroiodide, isonicotinate, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, pamoate, pantothenate, phosphate, propionate, saccharate, salicylate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate (also known as tosylate), trifluoroacetate, trifluoroacetic acid salt and the like. One or more embodiments of acid addition salts include chloride, hydrobromide, hydrochloride, dihydrochloride, trihydrochloride, acetate, diacetate, trifluoroacetate, trifluoroacetic acid salt and the like. More particular embodiments include a chloride, hydrobromide, hydrochloride, dihydrochloride, trifluoroacetate, trifluoroacetic acid salt and the like.

[00703] Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use.* (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33, 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (see, website for Food & Drug Administration, Washington, D.C.). These disclosures are incorporated herein by reference thereto.

[00704] Suitable basic salts include, but are not limited to, aluminum, ammonium, calcium, lithium, magnesium, potassium, sodium, zinc, and diethanolamine salts. Certain compounds described herein can also form pharmaceutically acceptable salts with organic bases (for example, organic amines) such as, but not limited to, dicyclohexylamines, *tert*-butyl amines and the like, and with various amino acids such as, but not limited to, arginine, lysine and the like. Basic nitrogen-containing groups may be quarternized with agents such as lower alkyl halides (*e.g.*, methyl, ethyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (*e.g.*, dimethyl, diethyl, and dibutyl sulfates), long chain halides (*e.g.*, decyl, lauryl, and stearyl chlorides, bromides and iodides), aralkyl halides (*e.g.*, benzyl and phenethyl bromides), and others.

[00705] All such acid salts and base salts are intended to be pharmaceutically acceptable salts within the scope of the description herein and all such acid and base salts are considered equivalent to the free forms of the corresponding compounds for the purposes described herein.

[00706] Compounds of Formula I and forms thereof may further exist in a tautomeric form. All such tautomeric forms are contemplated herein as part of the present description.

[00707] The compounds of Formula (I) may contain asymmetric or chiral centers, and, therefore, may exist in different stereoisomeric forms. The present description is intended to include all stereoisomeric forms of the compounds of Formula (I) as well as mixtures thereof, including racemic mixtures.

[00708] The compounds of Formula (I) described herein may include one or more chiral centers, and as such may exist as racemic mixtures (*R/S*) or as substantially pure enantiomers and diastereomers. The compounds may also exist as substantially pure (*R*) or (*S*) enantiomers (when one chiral center is present). In one embodiment, the compounds of Formula (I) described herein are (*S*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*S*) isomer. In another embodiment, the compounds of Formula (I) described herein are (*R*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*R*) isomer. As one of skill in the art will recognize, when more than one chiral center is present, the compounds of Formula (I) described herein may also include portions described as an (*R,R*), (*R,S*), (*S,R*) or (*S,S*) isomer, as defined by *IUPAC* Nomenclature Recommendations.

[00709] As used herein, the term "substantially pure" refers to compounds consisting substantially of a single isomer in an amount greater than or equal to 90%, in an amount greater

than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100% of the single isomer.

[00710] In one aspect, a compound of Formula (I) is a substantially pure (*S*) enantiomer present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

[00711] In one aspect, a compound of Formula (I) is a substantially pure (*R*) enantiomer present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

[00712] As used herein, a "racemate" is any mixture of isometric forms that are not "enantiomerically pure", including mixtures such as, without limitation, in a ratio of about 50/50, about 60/40, about 70/30, about 80/20, about 85/15 or about 90/10.

[00713] In addition, the present description embraces all geometric and positional isomers. For example, if a compound of Formula (I) incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures, are embraced within the scope of the description herein.

[00714] Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as, for example, by chromatography and/or fractional crystallization. Enantiomers can be separated by use of chiral HPLC column or other chromatographic methods known to those skilled in the art.

[00715] Enantiomers can also be separated by converting the enantiomeric mixture into a diastereomeric mixture by reaction with an appropriate optically active compound (e.g., chiral auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereomers and converting (e.g., hydrolyzing) the individual diastereomers to the corresponding pure enantiomers. Also, some of the compounds of Formula (I) may be atropisomers (e.g., substituted biaryls) and are considered part of this description.

[00716] All stereoisomer forms (for example, geometric isomers, optical isomers, positional isomers and the like) of the present compounds (including salts, solvates, esters and prodrugs and

transformed prodrugs thereof) which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons), rotameric forms, atropisomers, diastereomeric forms and regioisomeric forms are contemplated within the scope of the description herein. For example, if a compound of Formula (I) incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures thereof, are embraced within the scope of the description herein. Also, for example, all keto-enol and imine-enamine tautomeric forms of the compounds are included in the description herein. Individual stereoisomers of the compounds of Formula (I) described herein may, for example, be substantially free of other isomers, or may be present in a racemic mixture, as described *supra*.

[00717] The use of the terms "salt," "prodrug" and "transformed prodrug" are intended to equally apply to the salts, prodrugs and transformed prodrugs of all contemplated isotopologues, stereoisomers, racemates or tautomers of the instant compounds.

[00718] The term "isotopologue" refers to isotopically-enriched compounds which are identical to those recited herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds described herein include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and chlorine, such as H^2, H^3, C^{13}, C^{14}, N^{15}, O^{18}, O^{17}, P^{31}, P^{32}, S^{35}, F^{18}, Cl^{35} and Cl^{36}, respectively, each of which is also within the scope of this description.

[00719] Certain isotopically-enriched compounds described herein (*e.g.,* those labeled with H^3 and C^{14}) are useful in compound and/or substrate tissue distribution assays. Tritiated (*i.e.*, H^3) and carbon-14 (*i.e.*, C^{14}) isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium (*i.e.*, "deuterium enriched") may afford certain therapeutic advantages resulting from greater metabolic stability (*e.g.*, increased in vivo half-life or reduced dosage requirements) and hence may be preferred in some circumstances. Isotopically-enriched compounds of Formula (I) can generally be prepared using procedures known to persons of ordinary skill in the art by substituting an appropriate isotopically-enriched reagent for a non-isotopically-enriched reagent.

[00720] When the compounds are enriched with deuterium, the deuterium-to-hydrogen ratio on the deuterated atoms of the molecule substantially exceeds the naturally occurring deuterium-to-hydrogen ratio.

[00721] An embodiment described herein may include an isotopologue form of the compound of Formula (I), wherein the isotopologue is substituted on one or more atom members of the compound of Formula (I) with one or more deuterium atoms in place of one or more hydrogen atoms.

[00722] An embodiment described herein may include a compound of Formula (I) and forms thereof, wherein a carbon atom may have from 1 to 3 hydrogen atoms optionally replaced with deuterium.

[00723] One or more compounds described herein may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like, and the description herein is intended to embrace both solvated and unsolvated forms.

[00724] As used herein, the term "solvate" means a physical association of a compound described herein with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. As used herein, "solvate" encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like.

[00725] One or more compounds described herein may optionally be converted to a solvate. Preparation of solvates is generally known. A typical, non-limiting process involves dissolving a compound in a desired amount of the desired solvent (organic or water or mixtures thereof) at a higher than ambient temperature, and cooling the solution at a rate sufficient to form crystals which are then isolated by standard methods. Analytical techniques such as, for example infrared spectroscopy, show the presence of the solvent (or water) in the crystals as a solvate (or hydrate).

[00726] As used herein, the term "hydrate" means a solvate wherein the solvent molecule is water.

[00727] Polymorphic crystalline and amorphous forms of the compounds of Formula (I), and of the salts, solvates, esters and prodrugs of the compounds of Formula (I), are further intended to be included in the scope of the compounds described herein.

COMPOUND USES

[00728] Compounds of Formula (I) or a form thereof that enhance inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene are described herein. Such compounds of Formula (I) or a form thereof have been shown to enhance the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene using the assays described herein (see Biological example section, *infra*). Accordingly, compounds of Formula (I) or a form thereof have utility as enhancers for the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene.

[00729] Compounds of Formula (I) or a form thereof for enhancing inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene are described herein. Such compounds of Formula (I) or a form thereof may enhance inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene using, *e.g.*, an SMN1 minigene assay. Accordingly, compounds of Formula (I) or a form thereof may have utility as enhancers for the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene.

[00730] In one aspect, provided herein are methods for modulating the inclusion of exon 7 of SMN2 into RNA transcribed from the SMN2 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein are methods for modulating the inclusion of exon 7 of SMN2 into RNA transcribed from the SMN2 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof that modulates the expression of an SMN2 minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In another embodiment, the minigene is the minigene described in Biological Example 1, *infra*. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro* and/or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific embodiment, the human cell is from or in a human. In another specific embodiment, the human cell is from or in a human SMA patient. In another specific embodiment, the human cell is from or in a human SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In another embodiment, the human cell is a human cell from a human

SMA patient. In certain embodiments, the human cell is from a cell line, such as GM03813, GM00232, GM09677, and/or GM23240 (available from Coriell Institute). In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00731] In a specific embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In another embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof that enhances the expression of an SMN2 minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In another embodiment, the minigene is the minigene described in Biological Example 1, *infra*. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro* and/or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific embodiment, the human cell is from or in a human. In another specific embodiment, the human cell is from or in a human SMA patient. In another specific embodiment, the human cell is from or in a human SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In another embodiment, the human cell is a human cell from a human SMA patient. In certain embodiments, the human cell is from a cell line, such as GM03813, GM00232, GM09677, and/or GM23240 (available from Coriell Institute). In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00732] In another aspect, provided herein are methods for enhancing the inclusion of exon 7 of SMN1 into RNA transcribed from the SMN1 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein are methods for enhancing the inclusion of exon 7 of SMN1 into RNA transcribed from the SMN1 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In another specific embodiment, provided herein are methods for enhancing the inclusion of exon 7 of SMN1 into RNA transcribed from the SMN1 gene, comprising contacting a human cell with a compound of Formula (I) or a form thereof that modulates the expression of an SMN1 minigene

described in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro* and/or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific embodiment, the human cell is from or in a human. In another specific embodiment, the human cell is from or in a human SMA patient. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00733] In specific embodiments, provided herein are methods for enhancing the inclusion of exon 7 of SMN1 and SMN2 into RNA transcribed from the SMN1 and SMN2 genes, comprising contacting a human cell with a compound of Formula (I) or a form thereof. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro* and/or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific embodiment, the human cell is from or in a human. In another specific embodiment, the human cell is from or in a human SMA patient. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00734] In another aspect, provided herein is a method for modulating the inclusion of exon 7 of SMN2 into RNA transcribed from the SMN2 gene, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for modulating the inclusion of exon 7 of SMN2 into RNA transcribed from the SMN2 gene, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof that modulates the expression of an SMN2 minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In another embodiment, the minigene is the minigene described in Biological Example 1, *infra*. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00735] In a specific embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising administering

to a non-human animal model for SMA a compound of Formula (I) or a form thereof. In another specific embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof that enhances the expression of an SMN2 minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In another embodiment, the minigene is the minigene described in Biological Example 1, *infra*. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00736] In another aspect, provided herein is a method for enhancing the inclusion of exon 7 of SMN1 into RNA transcribed from the SMN1 gene, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN1 into RNA transcribed from the SMN1 gene, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof that modulates the expression of an SMN1 minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In one embodiment, the minigene is a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00737] In specific embodiments, provided herein is a method for enhancing the inclusion of exon 7 of SMN1 and SMN2 into RNA transcribed from the SMN1 and SMN2 genes, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00738] In another aspect, provided herein is a method for increasing the amount of Smn protein, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for increasing the amount of Smn protein,

comprising contacting a human cell with a compound of Formula (I) that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. In another specific embodiment, provided herein is a method for increasing the amount of Smn protein, comprising contacting a human cell with a compound of Formula (I) that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro* and/or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific embodiment, the human cell is from or in a human. In another specific embodiment, the human cell is from or in a human SMA patient. In another specific embodiment, the human cell is from or in a human SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In another embodiment, the human cell is a human cell from a human SMA patient. In certain embodiments, the human cell is from a cell line, such as GM03813, GM00232, GM09677, and/or GM23240 (available from Coriell Institute). In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00739] In another aspect, provided herein is a method for increasing the amount of Smn protein, comprising administering to a non-human animal model for SMA a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for increasing the amount of Smn protein, comprising administering to a non-human animal model for SMA a compound of Formula (I) that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in, *e.g.*, a cell-based or cell-free assay, such as described in the Biological Examples, *infra*. In another specific embodiment, provided herein is a method for increasing the amount of Smn protein, comprising administering to a non-human animal model for SMA a compound of Formula (I) that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene in, *e.g.*, a cell-based or cell-free assay.

[00740] In one embodiment, the compound of Formula (I) enhances the expression of a minigene described herein or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In a specific embodiment, the compound of Formula (I) enhances the expression of a minigene described in the Examples of International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In another specific embodiment, the

compound of Formula (I) enhances the expression of a minigene described in Biological Example 1, *infra*. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00741] In one embodiment, provided herein is the use of a compound of Formula (I) or a form thereof for the preparation of a medicament that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. In another embodiment, provided herein is the use of a compound of Formula (I) or a form thereof for the preparation of a medicament that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, thereby increasing expression of Smn protein in a human subject in need thereof. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00742] In one embodiment, provided herein is the use of a compound of Formula (I) or a form thereof for the preparation of a medicament that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene. In another embodiment, provided herein is the use of a compound of Formula (I) or a form thereof for the preparation of a medicament that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene, thereby increasing expression of Smn protein in a human subject in need thereof. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00743] In another aspect, provided herein are methods for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in a human subject in need thereof, comprising administering to the human subject an effective amount of a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in a human subject in need thereof, comprising administering to the human subject an effective amount a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In specific embodiments, the effective amount of the compound of Formula (I) or a form thereof is administered to the human subject in a

pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient or diluent. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In a specific embodiment, the human subject is a human SMA patient. In another specific embodiment, the human subject is a human SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00744] In another aspect, provided herein are methods for enhancing the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene in a human subject in need thereof, comprising administering to the human subject an effective amount of a compound of Formula (I) or a form thereof. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene in an assay described in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833. In specific embodiments, the effective amount of the compound of Formula (I) or a form thereof is administered to the human subject in a pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient or diluent. In a specific embodiment, the human subject is a human SMA patient. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00745] In another aspect, provided herein is a method for enhancing the inclusion of exon 7 of SMN1 and SMN2 into mRNA that is transcribed from the SMN1 and SMN2 genes in a human subject in need thereof, comprising administering to the human subject an effective amount a compound of Formula (I) or a form thereof. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene in an assay(s) described in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (see, *e.g.*, the Examples in those publications), each of which is incorporated herein by reference in its entirety. In specific embodiments, the effective amount of the compound of Formula (I) or a form thereof is administered to the human subject in a pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient or diluent. In a specific embodiment, the human subject is a human SMA patient. In another specific embodiment, the human subject is a human

SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00746] In another aspect, provided herein are methods for enhancing the expression of Smn protein in a human subject in need thereof, comprising administering to the human subject an effective amount of a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for enhancing the expression of Smn protein in a human subject in need thereof, comprising administering to the human subject an effective amount a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. In another specific embodiment, provided herein is a method for enhancing the expression of Smn protein in a human subject in need thereof, comprising administering to the human subject an effective amount a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene. In specific embodiments, the effective amount of the compound of Formula (I) or a form thereof is administered to the human subject in a pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient or diluent. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*) or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (see, *e.g.*, the Examples in those publications), each of which is incorporated herein by reference in its entirety.

[00747] In a specific embodiment, the human subject is a human SMA patient. In another specific embodiment, the human subject is a human SMA patient, wherein SMA is caused by an inactivating mutation or deletion in the teleomeric copy of the SMN1 gene in both chromosomes, resulting in a loss of SMN1 gene function. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00748] In another embodiment, provided herein is the use of a compound of Formula (I) or a form thereof for the preparation of a medicament that enhances expression of Smn protein in a human subject in need thereof. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the

SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In another embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*) or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (see, *e.g.*, the Examples in those publications), each of which is incorporated herein by reference in its entirety. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00749] In another aspect, provided herein are methods for treating spinal muscular atrophy (SMA), comprising administering to a subject an effective amount of a compound of Formula (I) or a form thereof. In a specific embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject an effective amount of a compound of Formula (I) or a form thereof. In another specific embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising an effective amount of a compound of Formula (I) or a form thereof, and a pharmaceutically acceptable carrier, excipient or diluent. In one embodiment, the compound is a compound of Formula (I) or a form thereof.

[00750] In another embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject an effective amount of a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene. In a specific embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising an effective amount of a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, and a pharmaceutically acceptable carrier, excipient or diluent. In another specific embodiment, provided herein is a method for treating SMA in a human subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising an effective amount of a compound of Formula (I) or a form thereof that enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene, and a pharmaceutically acceptable carrier, excipient or diluent. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of

exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In another embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*) or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (see, *e.g.*, the Examples in those publications), each of which is incorporated herein by reference in its entirety. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00751] In another embodiment, provided herein is the use of a compound of Formula (I) or a form thereof in the manufacture of a medicament for treating SMA in a human subject in need thereof. In a particular embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*). In another embodiment, the compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene as determined in an assay described herein (*see*, *e.g.*, the Biological Examples, *infra*) or in International Publication No. WO2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (see, *e.g.*, the Examples in those publications), each of which is incorporated herein by reference in its entirety. In a specific embodiment, the compound is a compound of Formula (I) or a form thereof.

[00752] In an embodiment of a use or method provided herein, compounds of Formula (I) or a form thereof are used in combination with one or more additional agents. A compound(s) of Formula (I) or a form thereof can be administered to a subject or contacted with a cell prior to, concurrently with, or subsequent to administering to the subject or contacting the cell with an additional agent(s). A compound(s) of Formula (I) or a form thereof and an additional agent(s) can be administered to a subject or contacted with a cell in single composition or different compositions. In a specific embodiments, a compound(s) of Formula (I) or a form thereof is used in combination with gene replacement of SMN1 (using, *e.g.*, viral delivery vectors). In another specific embodiments, a compound(s) of Formula (I) or a form thereof are used in combination with cell replacement using differentiated $SMN1^{+/+}$ and/or $SMN2^{+/+}$ stem cells. In another specific embodiments, a compound(s) of Formula (I) or a form thereof are used in

combination with cell replacement using differentiated $SMN1^{+/+}$ stem cells. In another specific embodiments, a compound(s) of Formula (I) or a form thereof are used in combination with cell replacement using differentiated $SMN2^{+/+}$ stem cells. In another specific embodiment, a compound(s) of Formula (I) or a form thereof are used in combination with aclarubicin. In another specific embodiment, a compound(s) of Formula (I) or a form thereof are used in combination with a transcription activator such as a histone deacetylase ("HDAC") inhibitor (*e.g.*, butyrates, valproic acid, and hydroxyurea), and mRNA stabilizers (*e.g.*, mRNA decapping inhibitor RG3039 from Repligen).

[00753] In one embodiment, provided herein is the use of compounds of Formula (I) or a form thereof in combination with supportive therapy, including respiratory, nutritional or rehabilitation care.

[00754] In certain embodiments, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) has a therapeutic effect and/or beneficial effect. In a specific embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in one, two or more of the following effects: (i) reduces or ameliorates the severity of SMA; (ii) delays onset of SMA; (iii) inhibits the progression of SMA; (iv) reduces hospitalization of a subject; (v) reduces hospitalization length for a subject; (vi) increases the survival of a subject; (vii) improves the quality of life of a subject; (viii) reduces the number of symptoms associated with SMA; (ix) reduces or ameliorates the severity of a symptom(s) associated with SMA; (x) reduces the duration of a symptom associated with SMA; (xi) prevents the recurrence of a symptom associated with SMA; (xii) inhibits the development or onset of a symptom of SMA; and/or (xiii) inhibits of the progression of a symptom associated with SMA.

[00755] Symptoms of SMA include muscle weakness, poor muscle tone, weak cry, weak cough, limpness or a tendency to flop, difficulty sucking or swallowing, difficulty breathing, accumulation of secretions in the lungs or throat, clenched fists with sweaty hand, flickering/vibrating of the tongue, head often tilted to one side, even when lying down, legs that tend to be weaker than the arms, legs frequently assuming a "frog legs" position, feeding difficulties, increased susceptibility to respiratory tract infections, bowel/bladder weakness, lower-than-normal weight, inability to sit without support, failure to walk, failure to crawl, and

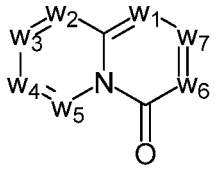
hypotonia, areflexia, and multiple congenital contractures (arthrogryposis) associated with loss of anterior horn cells.

[00756] In a specific embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in one,two or more of the following effects: (i) a reduction in the loss of muscle strength; (ii) an increase in muscle strength; (iii) a reduction in muscle atrophy; (iv) a reduction in the loss of motor function; (v) an increase in motor neurons; (vii) a reduction in the loss of motor neurons; (viii) protection of SMN deficient motor neurons from degeneration; (ix) an increase in motor function; (x) an increase in pulmonary function; and/or (xi) a reduction in the loss of pulmonary function.

[00757] In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant or a human toddler to sit up. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to stand up unaided. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to walk unaided. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to run unaided. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to breathe unaided. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to turn during sleep unaided. In another embodiment, treating SMA with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) results in the functional ability or helps retain the functional ability for a human infant, a human toddler, a human child or a human adult to swallow unaided.

[00758] In certain embodiments, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot, to determine whether a compound of Formula (I) or a form thereof enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from an SMN1 and/or SMN2 gene. In some embodiments, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 8, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification, Northern blot or Southern blot, or a pharmaceutical or assay kit as described *infra*, to monitor patient responses to a compound of Formula (I) or a form thereof.

[00759] In one embodiment, a compound of Formula (I):



(I)

[00760] or a form thereof is used as described herein, wherein:

[00761] w_1 and w_5 are independently C-R_a or N;

[00762] w_2 is C-R_b or N;

[00763] w_3, w_4 and w_7 are independently C-R_1, C-R_2, C-R_a or N;

[00764] w_6 is C-R_1, C-R_2, C-R_c or N;

[00765] wherein one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00766] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00767] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00768] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00769] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N; and,

[00770] wherein any one, two or three of w_1, w_2, w_3, w_4, w_5, w_6 and w_7 may optionally be N;

[00771] R_1 is $C_{1\text{-}8}$alkyl, amino, $C_{1\text{-}8}$alkyl-amino, ($C_{1\text{-}8}$alkyl)$_2$-amino, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)$_2$-amino,

(C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, (amino-C_{1-8}alkyl)$_2$-amino, (amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, amino-C_{1-8}alkoxy, C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, amino-C_{2-8}alkenyl, C_{1-8}alkyl-amino-C_{2-8}alkenyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkenyl, amino-C_{2-8}alkynyl, C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl,

(heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino, (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl;

[00772] wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or,

[00773] wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

[00774] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00775] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent;

[00776] R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

[00777] R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

[00778] R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkyl-carbonyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl]$_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, [(C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino,

(C_{1-8}alkoxy-C_{1-8}alkyl)$_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-carbonyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino or (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino;

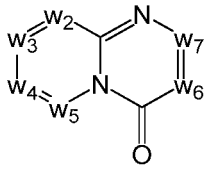
[00779] R_4 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-C_{1-8}alkyl, C_{3-14}cycloalkyl-amino, aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl, aryl-sulfonyloxy-C_{1-8}alkyl, heterocyclyl or heterocyclyl-C_{1-8}alkyl; wherein, each instance of C_{3-14}cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R_5 substituents;

[00780] R_5 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino or C_{1-8}alkyl-thio;

[00781] R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, C_{2-8}alkenyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino or C_{1-8}alkyl-thio; and,

[00782] R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00783] An embodiment of the use of the compound of Formula (I) is the use of a compound selected from Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV):



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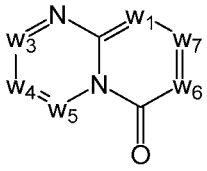

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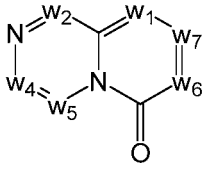

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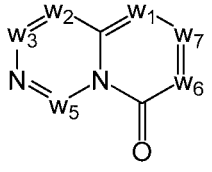

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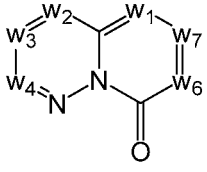

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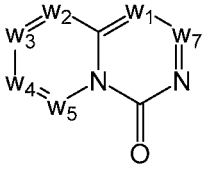

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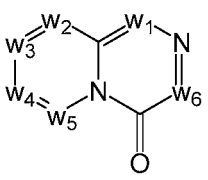

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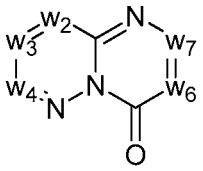

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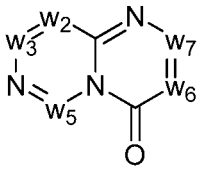

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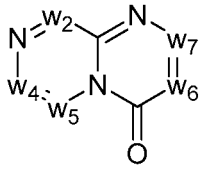

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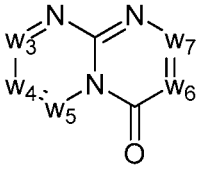

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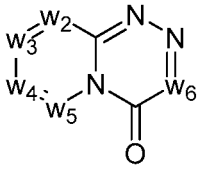
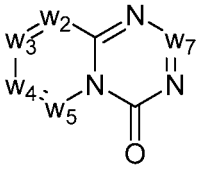


(XIII) or



(XIV)

[00784] or a form thereof.

[00785] In an embodiment of the use of the compound of Formula (I), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00786] In another embodiment of the use of the compound of Formula (I), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00787] In another embodiment of the use of the compound of Formula (I), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00788] In another embodiment of the use of the compound of Formula (I), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00789] In an embodiment of the use of the compound of Formula (II), w_3 is C-R_1, w_6 is C-R_2, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00790] In another embodiment of the use of the compound of Formula (II), w_3 is C-R_2, w_6 is C-R_1, w_4, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00791] In another embodiment of the use of the compound of Formula (II), w_4 is C-R_1, w_7 is C-R_2, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00792] In another embodiment of the use of the compound of Formula (II), w_4 is C-R_2, w_7 is C-R_1, w_3 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00793] In an embodiment of the use of the compound of Formula (III), w_3 is C-R_1, w_6 is C-R_2 and w_1, w_4, w_5 and w_7 are independently C-R_a or N.

[00794] In another embodiment of the use of the compound of Formula (III), w_3 is C-R_2, w_6 is C-R_1 and w_1, w_4, w_5 and w_7 are independently C-R_a or N.

[00795] In another embodiment of the use of the compound of Formula (III), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00796] In another embodiment of the use of the compound of Formula (III), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00797] In an embodiment of the use of the compound of Formula (IV), w_4 is C-R_1, w_7 is C-R_2, w_1 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00798] In another embodiment of the use of the compound of Formula (IV), w_4 is C-R_2, w_7 is C-R_1, w_1 and w_5 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00799] In an embodiment of the use of the compound of Formula (V), w_3 is C-R_1, w_6 is C-R_2, w_1, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00800] In another embodiment of the use of the compound of Formula (V), w_3 is C-R_2, w_6 is C-R_1, w_1, w_5 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00801] In an embodiment of the use of the compound of Formula (VI), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00802] In another embodiment of the use of the compound of Formula (VI), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00803] In another embodiment of the use of the compound of Formula (VI), w_4 is C-R_1, w_7 is C-R_2, w_1 and w_3 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00804] In another embodiment of the use of the compound of Formula (VI), w_4 is C-R_2, w_7 is C-R_1, w_1 and w_3 are independently C-R_a or N, w_2 is C-R_b or N and w_6 is C-R_c or N.

[00805] In another embodiment of the use of the compound of Formula (VII), w_4 is C-R_1, w_7 is C-R_2, w_1, w_3 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00806] In another embodiment of the use of the compound of Formula (VII), w_4 is C-R_2, w_7 is C-R_1, w_1, w_3 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00807] In another embodiment of the use of the compound of Formula (VIII), w_3 is C-R_1, w_6 is C-R_2, w_1, w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00808] In another embodiment of the use of the compound of Formula (VIII), w_3 is C-R_2, w_6 is C-R_1, w_1, w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00809] In an embodiment of the use of the compound of Formula (IX), w_3 is C-R_1, w_6 is C-R_2, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00810] In another embodiment of the use of the compound of Formula (IX), w_3 is C-R_2, w_6 is C-R_1, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00811] In another embodiment of the use of the compound of Formula (IX), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00812] In another embodiment of the use of the compound of Formula (IX), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00813] In an embodiment of the use of the compound of Formula (X), w_3 is C-R_1, w_6 is C-R_2, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00814] In another embodiment of the use of the compound of Formula (X), w_3 is C-R_2, w_6 is C-R_1, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00815] In an embodiment of the use of the compound of Formula (XI), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00816] In another embodiment of the use of the compound of Formula (XI), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00817] In an embodiment of the use of the compound of Formula (XII), w_3 is C-R_1, w_6 is C-R_2 and w_4, w_5 and w_7 are independently C-R_a or N.

[00818] In another embodiment of the use of the compound of Formula (XII), w_3 is C-R_2, w_6 is C-R_1 and w_4, w_5 and w_7 are independently C-R_a or N.

[00819] In another embodiment of the use of the compound of Formula (XII), w_4 is C-R_1, w_7 is C-R_2, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00820] In another embodiment of the use of the compound of Formula (XII), w_4 is C-R_2, w_7 is C-R_1, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

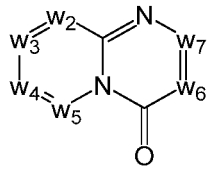
[00821] In an embodiment of the use of the compound of Formula (XIII), w_3 is C-R_1, w_6 is C-R_2, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

[00822] In another embodiment of the use of the compound of Formula (XIII), w_3 is C-R_2, w_6 is C-R_1, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

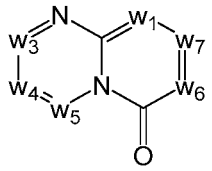
[00823] In an embodiment of the use of the compound of Formula (XIV), w_4 is C-R_1, w_7 is C-R_2, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

[00824] In another embodiment of the use of the compound of Formula (XIV), w_4 is C-R_2, w_7 is C-R_1, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

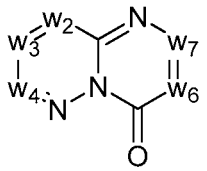
[00825] Another embodiment of the use of the compound of Formula (I) is the use of the compound selected from Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII):



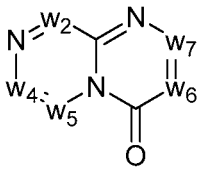
(II),



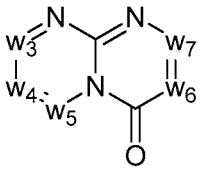
(III),



(IX),



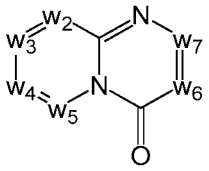
(XI), or



(XII)

[00826] or a form thereof.

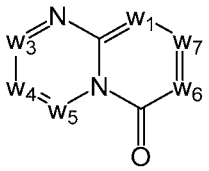
[00827] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (II):



(II)

[00828] or a form thereof.

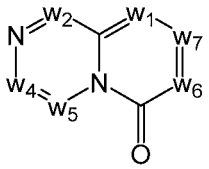
[00829] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (III):



(III)

[00830] or a form thereof.

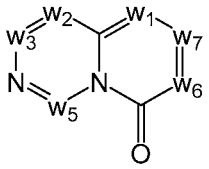
[00831] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (IV):



(IV)

[00832] or a form thereof.

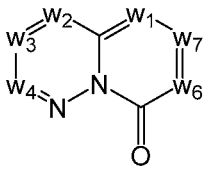
[00833] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (V):



(V)

[00834] or a form thereof.

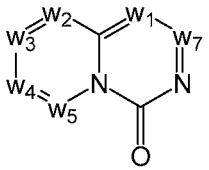
[00835] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (VI):



(VI)

[00836] or a form thereof.

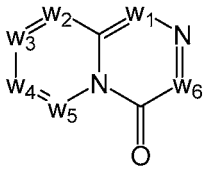
[00837] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (VII):



(VII)

[00838] or a form thereof.

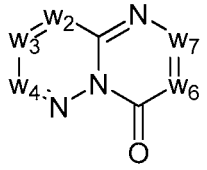
[00839] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (VIII):



(VIII)

[00840] or a form thereof.

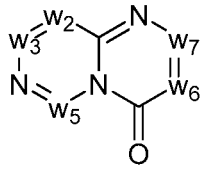
[00841] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (IX):



(IX)

[00842] or a form thereof.

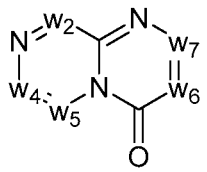
[00843] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (X):



(X)

[00844] or a form thereof.

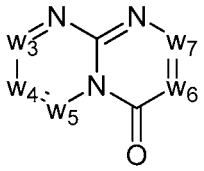
[00845] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (XI):



(XI)

[00846] or a form thereof.

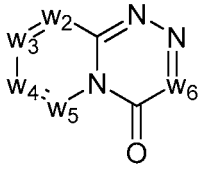
[00847] Another embodiment of the compound of Formula (I) is the use of the compound of Formula (XII):



(XII)

[00848] or a form thereof.

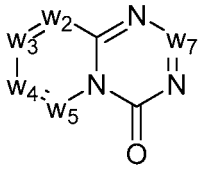
[00849] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (XIII):



(XIII)

[00850] or a form thereof.

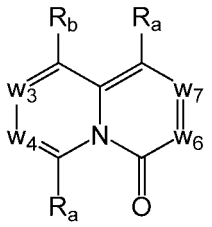
[00851] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (XIV):



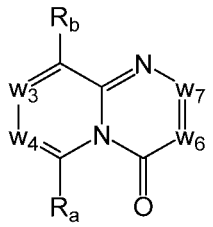
(XIV)

[00852] or a form thereof.

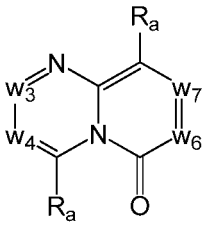
[00853] An embodiment of the use of the compound of Formula (I), Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV) is the use of a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IVa), Formula (Va), Formula (VIa), Formula (VIIa), Formula (VIIIa), Formula (IXa), Formula (Xa), Formula (XIa), Formula (XIIa), Formula (XIIIa) or Formula (XIVa), respectively:



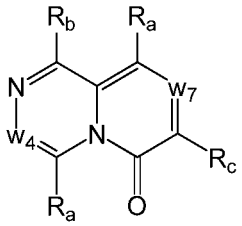
(Ia),



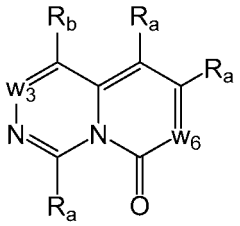
(IIa),



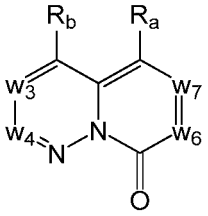
(IIIa),



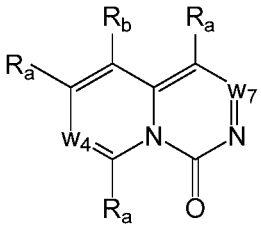
(IVa),



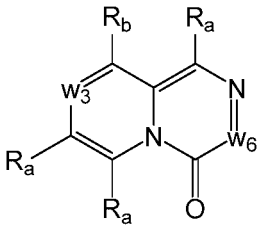
(Va),



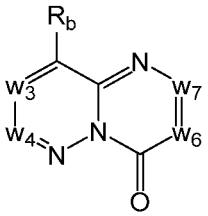
(VIa)



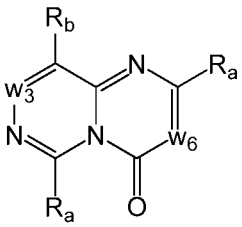
(VIIa),



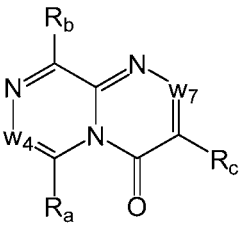
(VIIIa),



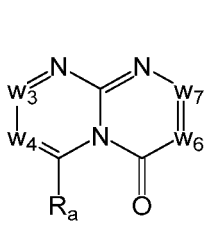
(IXa),



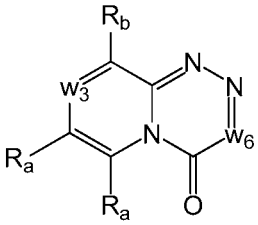
(Xa),



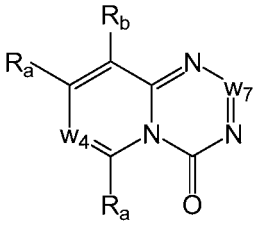
(XIa),



(XIIa),



(XIIIa), or



(XIVa)

[00854] or a form thereof.

[00855] In an embodiment of the use of the compound of Formula (Ia), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00856] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00857] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00858] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00859] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00860] In an embodiment of the use of the compound of Formula (IIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00861] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00862] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00863] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00864] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00865] In an embodiment of the use of the compound of Formula (IIIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00866] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00867] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00868] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00869] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00870] In an embodiment of the use of the compound of Formula (IVa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00871] In an embodiment of the use of the compound of Formula (Va), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00872] In an embodiment of the use of the compound of Formula (VIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00873] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00874] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00875] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00876] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00877] In an embodiment of the use of the compound of Formula (VIIa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00878] In an embodiment of the use of the compound of Formula (VIIIa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00879] In an embodiment of the use of the compound of Formula (IXa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00880] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00881] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

[00882] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00883] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

[00884] In an embodiment of the use of the compound of Formula (Xa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00885] In an embodiment of the use of the compound of Formula (XIa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

[00886] In an embodiment of the use of the compound of Formula (XIIa), one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

[00887] when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

[00888] when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

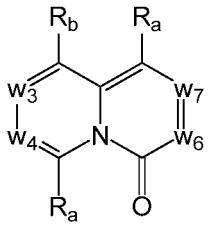
[00889] when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

[00890] when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N.

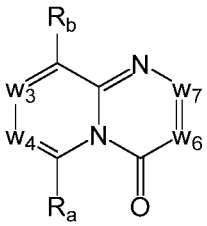
[00891] In an embodiment of the use of the compound of Formula (XIIIa), one of w_3 and w_6 is C-R_1 and the other is C-R_2, provided that, when w_3 is C-R_1, then w_6 is C-R_2; or, when w_3 is C-R_2, then w_6 is C-R_1.

[00892] In an embodiment of the use of the compound of Formula (XIVa), one of w_4 and w_7 is C-R_1 and the other is C-R_2, provided that, when w_4 is C-R_1, then w_7 is C-R_2; or, when w_4 is C-R_2, then w_7 is C-R_1.

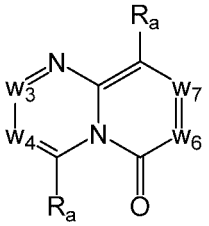
[00893] An embodiment of the use of the compound of Formula (I), Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII) is the use of the compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IXa), Formula (XIa) or Formula (XIIa), respectively:



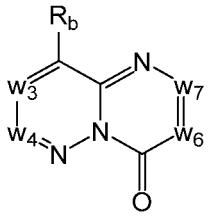
(Ia),



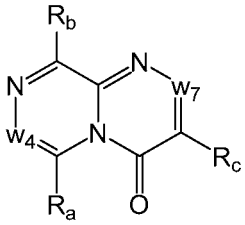
(IIa),



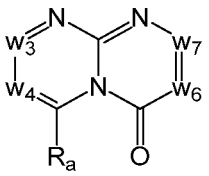
(IIIa),



(IXa),



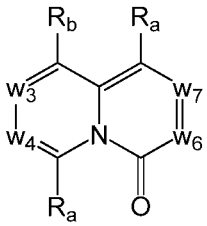
(XIa), or



(XIIa)

[00894] or a form thereof.

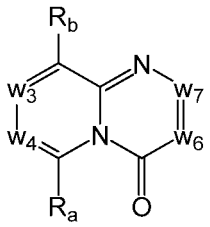
[00895] Another embodiment of the use of the compound of Formula (I) is the use of the compound of Formula (Ia):



(Ia)

[00896] or a form thereof.

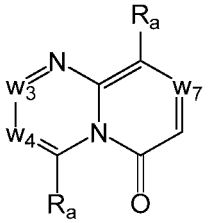
[00897] Another embodiment of the use of the compound of Formula (II) is the use of the compound of Formula (IIa):



(IIa)

[00898] or a form thereof.

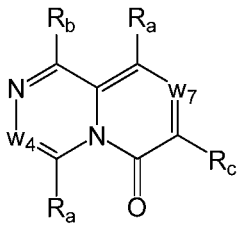
[00899] Another embodiment of the use of the compound of Formula (III) is the use of the compound of Formula (IIIa):



(IIIa)

[00900] or a form thereof.

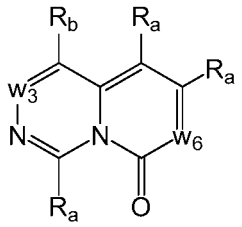
[00901] Another embodiment of the use of the compound of Formula (IV) is the use of the compound of Formula (IVa):



(IVa)

[00902] or a form thereof.

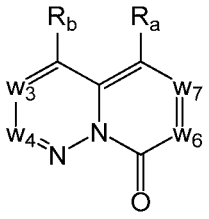
[00903] Another embodiment of the use of the compound of Formula (V) is the use of the compound of Formula (Va):



(Va)

[00904] or a form thereof.

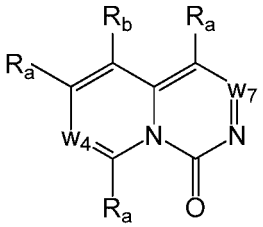
[00905] Another embodiment of the use of the compound of Formula (VI) is the use of the compound of Formula (VIa):



(VIa)

[00906] or a form thereof.

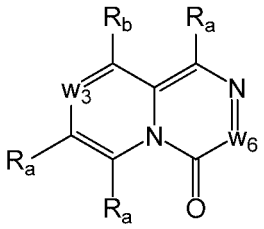
[00907] Another embodiment of the use of the compound of Formula (VII) is the use of the compound of Formula (VIIa):



(VIIa)

[00908] or a form thereof.

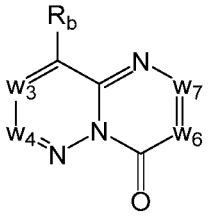
[00909] Another embodiment of the use of the compound of Formula (VIII) is the use of the compound of Formula (VIIIa):



(VIIIa)

[00910] or a form thereof.

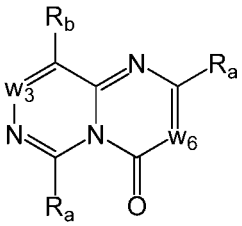
[00911] Another embodiment of the use of the compound of Formula (IX) is the use of the compound of Formula (IXa):



(IXa)

[00912] or a form thereof.

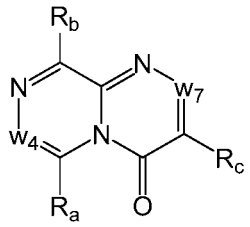
[00913] Another embodiment of the use of the compound of Formula (X) is the use of the compound of Formula (Xa):



(Xa)

[00914] or a form thereof.

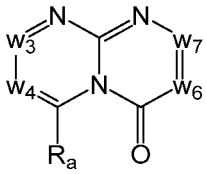
[00915] Another embodiment of the use of the compound of Formula (XI) is the use of the compound of Formula (XIa):



(XIa)

[00916] or a form thereof.

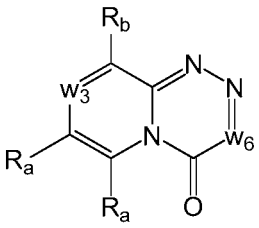
[00917] Another embodiment of the use of the compound of Formula (XII) is the use of the compound of Formula (XIIa):



(XIIa)

[00918] or a form thereof.

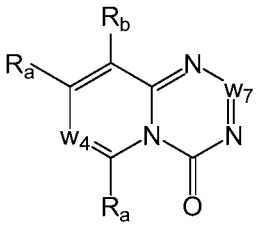
[00919] Another embodiment of the use of the compound of Formula (XIII) is the use of the compound of Formula (XIIIa):



(XIIIa)

[00920] or a form thereof.

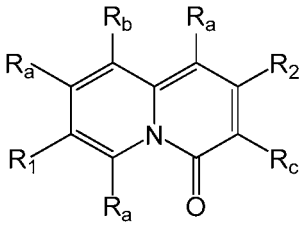
[00921] Another embodiment of the use of the compound of Formula (XIV) is the use of the compound of Formula (XIVa):



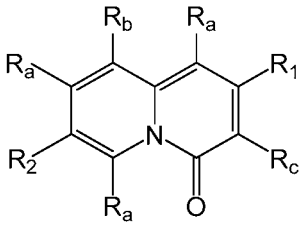
(XIVa)

[00922] or a form thereof.

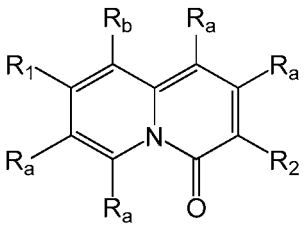
[00923] An embodiment of the use of the compound of Formula (Ia) is the use of a compound of Formula (Ia1), Formula (Ia2), Formula (Ia3) or Formula (Ia4):



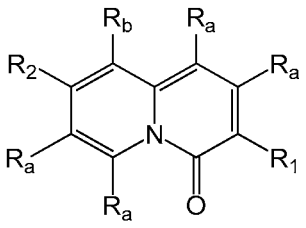
(Ia1),



(Ia2),



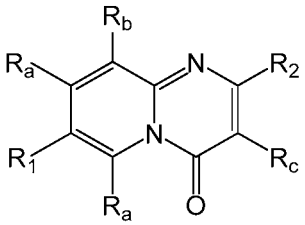
(Ia3) or



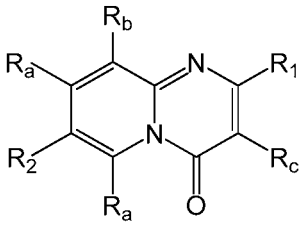
(Ia4)

[00924] or a form thereof.

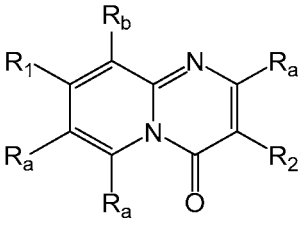
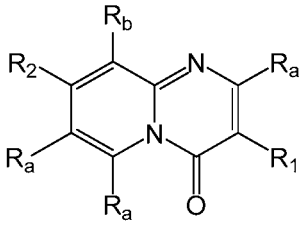
[00925] An embodiment of the use of the compound of Formula (IIa) is the use of a compound of Formula (IIa1), Formula (IIa2), Formula (IIa3) or Formula (IIa4):



(IIa1),



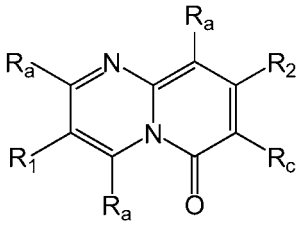
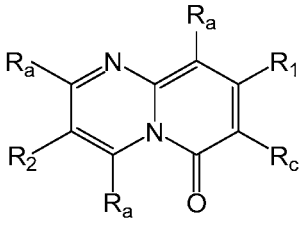
(IIa2),

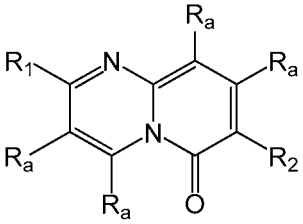
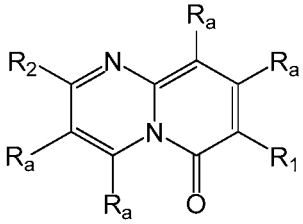
(IIa3) or (IIa4)

[00926] or a form thereof.

[00927] An embodiment of the use of the compound of Formula (IIIa) is the use of a compound of Formula (IIIa1), Formula (IIIa2), Formula (IIIa3) or Formula (IIIa4):

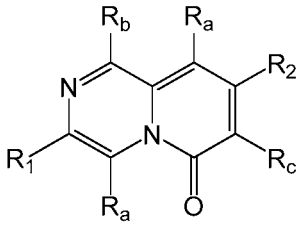
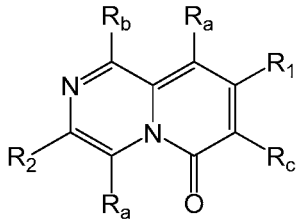
(IIIa1), (IIIa2),

(IIIa3) or (IIIa4)

[00928] or a form thereof.

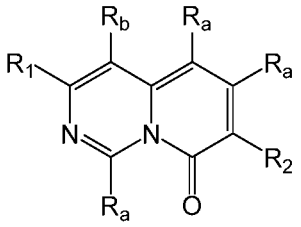
[00929] An embodiment of the use of the compound of Formula (IVa) is the use of a compound of Formula (IVa1) or Formula (IVa2):

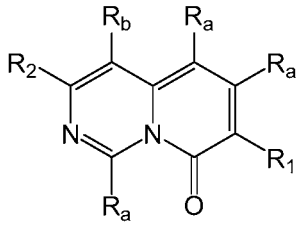
(IVa1) or (IVa2)

[00930] or a form thereof.

[00931] An embodiment of the use of the compound of Formula (Va) is the use of a compound of Formula (Va1) or Formula (Va2):



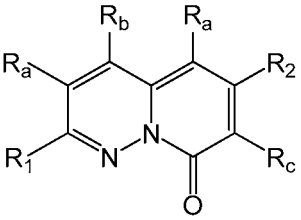
(Va1) or



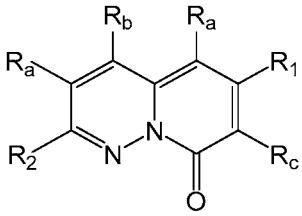
(Va2)

[00932] or a form thereof.

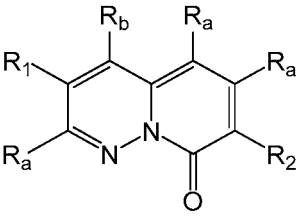
[00933] An embodiment of the use of the compound of Formula (VIa) is the use of a compound of Formula (VIa1), Formula (VIa2), Formula (VIa3) or Formula (VIa2):



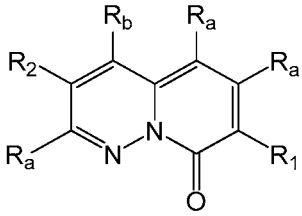
(VIa1),



(VIa2),



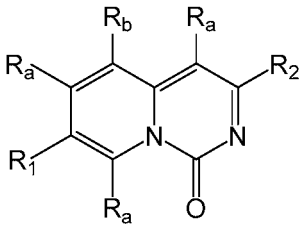
(VIa3) or



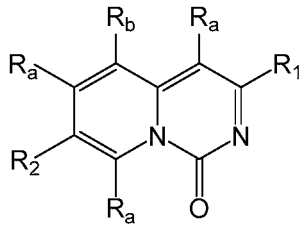
(VIa4)

[00934] or a form thereof.

[00935] An embodiment of the use of the compound of Formula (VIIa) is the use of a compound of Formula (VIIa1) or Formula (VIIa2):



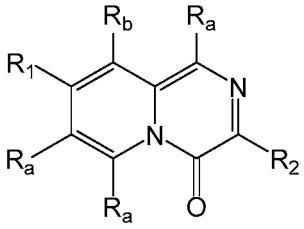
(VIIa1) or



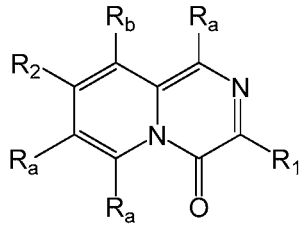
(VIIa2)

[00936] or a form thereof.

[00937] An embodiment of the use of the compound of Formula (VIIIa) is the use of a compound of Formula (VIIIa1) or Formula (VIIIa2):



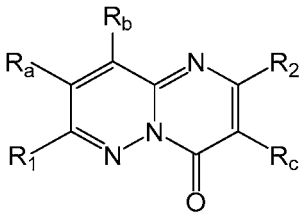
(VIIIa1) or



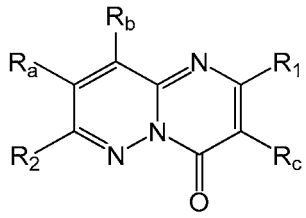
(VIIIa2)

[00938] or a form thereof.

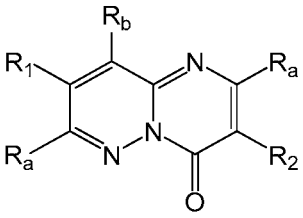
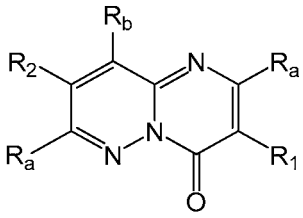
[00939] An embodiment of the use of the compound of Formula (IXa) is the use of a compound of Formula (IXa1), Formula (IXa2), Formula (IXa3) or Formula (IXa4):



(IXa1),



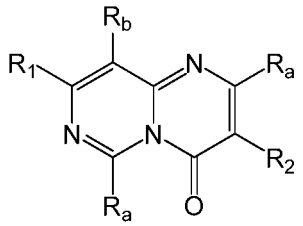
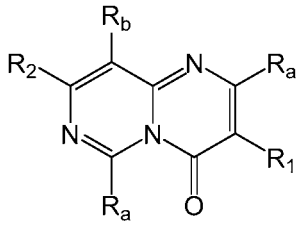
(IXa2),

(IXa3) or (IXa4)

[00940] or a form thereof.

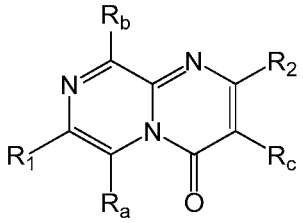
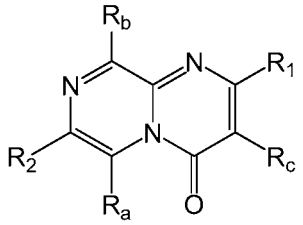
[00941] An embodiment of the use of the compound of Formula (Xa) is the use of a compound of Formula (Xa1) or Formula (Xa2):

(Xa1) or (Xa2)

[00942] or a form thereof.

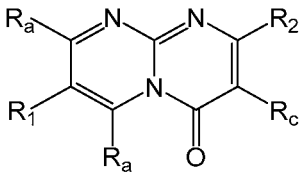
[00943] An embodiment of the use of the compound of Formula (XIa) is the use of a compound of Formula (XIa1) or Formula (XIa2):

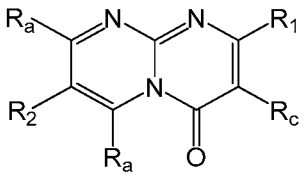
(XIa1) or (XIa2)

[00944] or a form thereof.

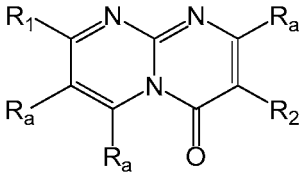
[00945] An embodiment of the use of the compound of Formula (XIIa) is the use of a compound of Formula (XIIa1), Formula (XIIa2), Formula (XIIa3) or Formula (XIIa4):



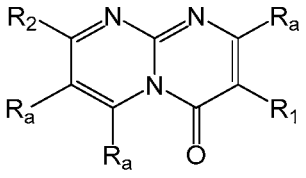
(XIIa1),



(XIIa2),



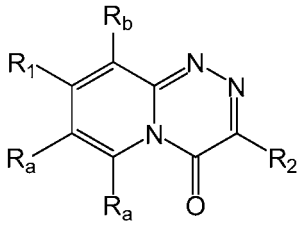
(XIIa3) or



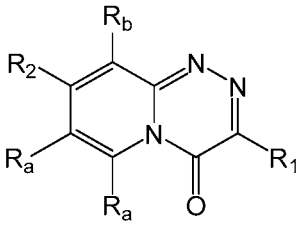
(XIIa4)

[00946] or a form thereof.

[00947] An embodiment of the use of the compound of Formula (XIIIa) is the use of a compound of Formula (XIIIa1) or Formula (XIIIa2):



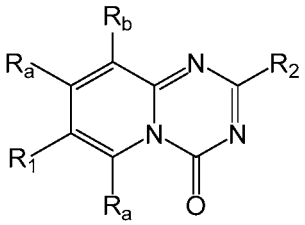
(XIIIa1) or



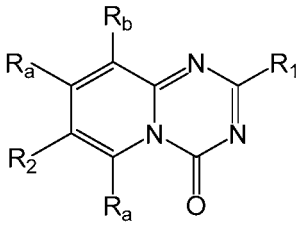
(XIIIa2)

[00948] or a form thereof.

[00949] An embodiment of the use of the compound of Formula (XIVa) is the use of a compound of Formula (XIVa1) or Formula (XIVa2):



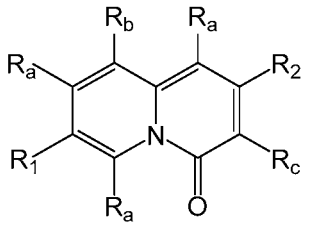
(XIVa1) or



(XIVa2)

[00950] or a form thereof.

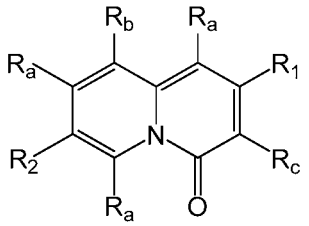
[00951] An embodiment of the use of the compound of Formula (Ia) is the use of the compound of Formula (Ia1):



(Ia1)

[00952] or a form thereof.

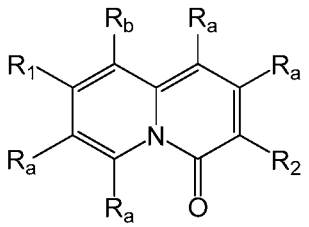
[00953] An embodiment of the use of the compound of Formula (Ia) is the use of the compound of Formula (Ia2):



(Ia2)

[00954] or a form thereof.

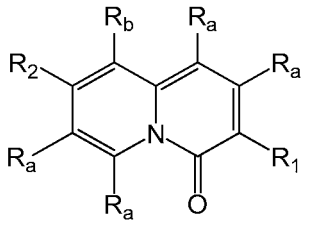
[00955] An embodiment of the use of the compound of Formula (Ia) is the use of the compound of Formula (Ia3):



(Ia3)

[00956] or a form thereof.

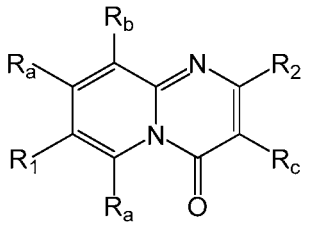
[00957] An embodiment of the use of the compound of Formula (Ia) is the use of the compound of Formula (Ia4):



(Ia4)

[00958] or a form thereof.

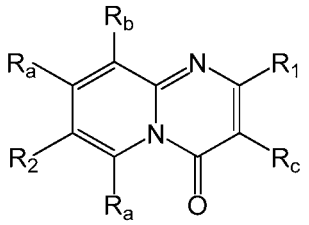
[00959] An embodiment of the use of the compound of Formula (IIa) is the use of the compound of Formula (IIa1):



(IIa1)

[00960] or a form thereof.

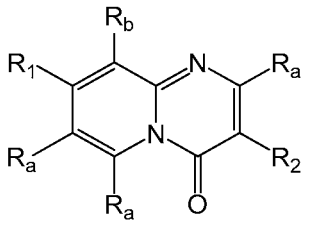
[00961] An embodiment of the use of the compound of Formula (IIa) is the use of the compound of Formula (IIa2):



(IIa2)

[00962] or a form thereof.

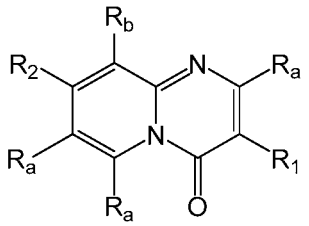
[00963] An embodiment of the use of the compound of Formula (IIa) is the use of the compound of Formula (IIa3):



(IIa3)

[00964] or a form thereof.

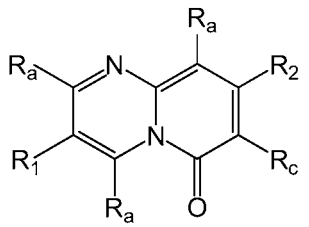
[00965] An embodiment of the use of the compound of Formula (IIa) is the use of the compound of Formula (IIa4):



(IIa4)

[00966] or a form thereof.

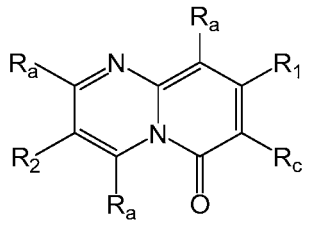
[00967] An embodiment of the use of the compound of Formula (IIIa) is the use of the compound of Formula (IIIa1):



(IIIa1)

[00968] or a form thereof.

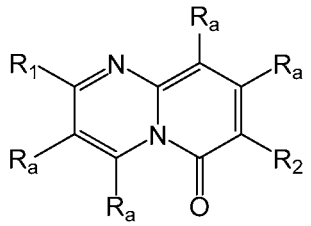
[00969] An embodiment of the use of the compound of Formula (IIIa) is the use of the compound of Formula (IIIa2):



(IIIa2)

[00970] or a form thereof.

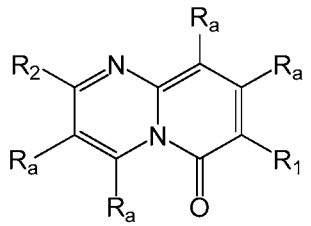
[00971] An embodiment of the use of the compound of Formula (IIIa) is the use of the compound of Formula (IIIa3):



(IIIa3)

[00972] or a form thereof.

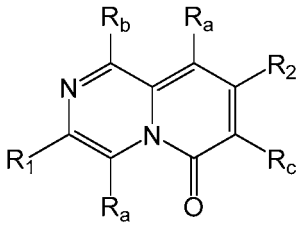
[00973] An embodiment of the use of the compound of Formula (IIIa) is the use of the compound of Formula (IIIa4):



(IIIa4)

[00974] or a form thereof.

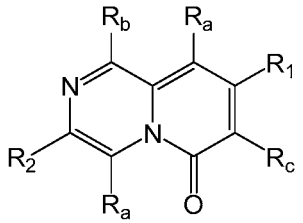
[00975] An embodiment of the use of the compound of Formula (IVa) is the use of the compound of Formula (IVa1):



(IVa1)

[00976] or a form thereof.

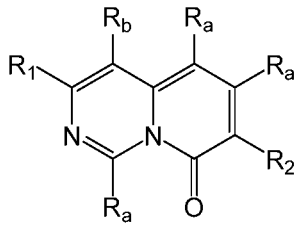
[00977] An embodiment of the use of the compound of Formula (IVa) is the use of the compound of Formula (IVa2):



(IVa2)

[00978] or a form thereof.

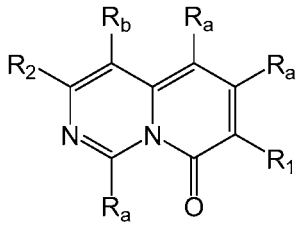
[00979] An embodiment of the use of the compound of Formula (Va) is the use of the compound of Formula (Va1):



(Va1)

[00980] or a form thereof.

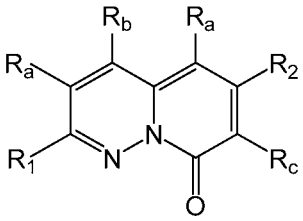
[00981] An embodiment of the use of the compound of Formula (Va) is the use of the compound of Formula (Va2):



(Va2)

[00982] or a form thereof.

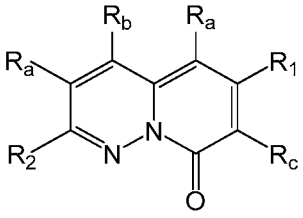
[00983] An embodiment of the use of the compound of Formula (VIa) is the use of the compound of Formula (VIa1):



(VIa1)

[00984] or a form thereof.

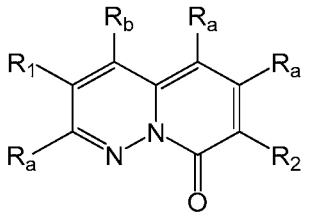
[00985] An embodiment of the use of the compound of Formula (VIa) is the use of the compound of Formula (VIa2):



(VIa2)

[00986] or a form thereof.

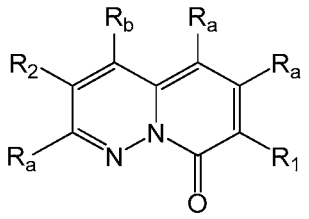
[00987] An embodiment of the use of the compound of Formula (VIa) is the use of the compound of Formula Formula (VIa3):



(VIa3)

[00988] or a form thereof.

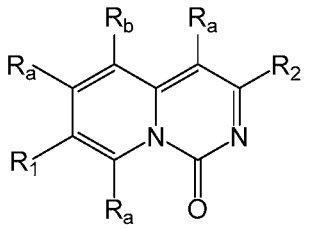
[00989] An embodiment of the use of the compound of Formula (VIa) is the use of the compound of Formula (VIa4):



(VIa4)

[00990] or a form thereof.

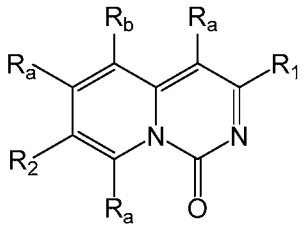
[00991] An embodiment of the use of the compound of Formula (VIIa) is the use of the compound of Formula (VIIa1):



(VIIa1)

[00992] or a form thereof.

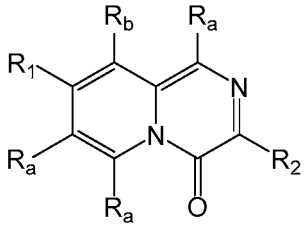
[00993] An embodiment of the use of the compound of Formula (VIIa) is the use of the compound of Formula (VIIa2):



(VIIa2)

[00994] or a form thereof.

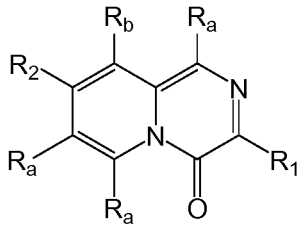
[00995] An embodiment of the use of the compound of Formula (VIIIa) is the use of the compound of Formula (VIIIa1):



(VIIIa1)

[00996] or a form thereof.

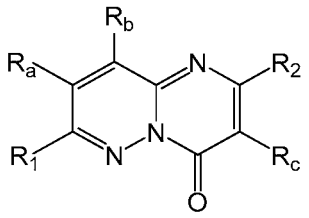
[00997] An embodiment of the use of the compound of Formula (VIIIa) is the use of the compound of Formula (VIIIa2):



(VIIIa2)

[00998] or a form thereof.

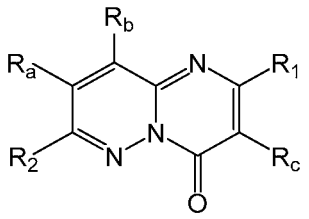
[00999] An embodiment of the use of the compound of Formula (IXa) is the use of the compound of Formula (IXa1):



(IXa1)

[001000] or a form thereof.

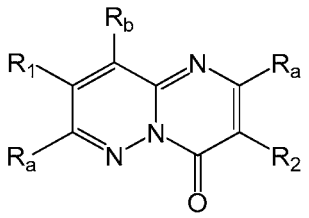
[001001] An embodiment of the use of the compound of Formula (IXa) is the use of the compound of Formula (IXa2):



(IXa2)

[001002] or a form thereof.

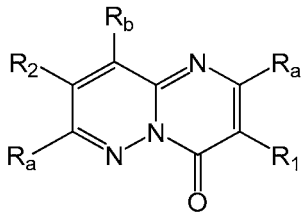
[001003] An embodiment of the use of the compound of Formula (IXa) is the use of the compound of Formula (IXa3):



(IXa3)

[001004] or a form thereof.

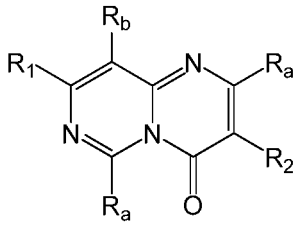
[001005] An embodiment of the use of the compound of Formula (IXa) is the use of the compound of Formula (IXa4):



(IXa4)

[001006] or a form thereof.

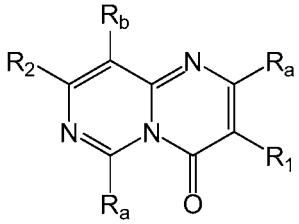
[001007] An embodiment of the use of the compound of Formula (Xa) is the use of the compound of Formula (Xa1):



(Xa1)

[001008] or a form thereof.

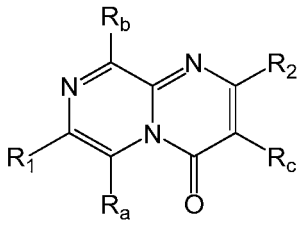
[001009] An embodiment of the use of the compound of Formula (Xa) is the use of the compound of Formula (Xa2):



(Xa2)

[001010] or a form thereof.

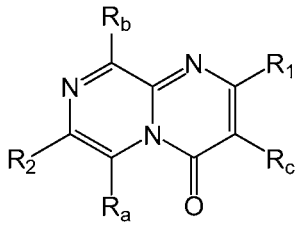
[001011] An embodiment of the use of the compound of Formula (XIa) is the use of the compound of Formula (XIa1):



(XIa1)

[001012] or a form thereof.

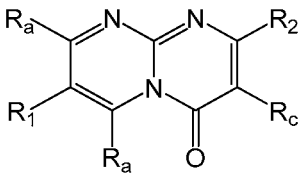
[001013] An embodiment of the use of the compound of Formula (XIa) is the use of the compound of Formula (XIa2):



(XIa2)

[001014] or a form thereof.

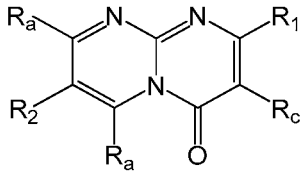
[001015] An embodiment of the use of the compound of Formula (XIIa) is the use of the compound of Formula (XIIa1):



(XIIa1)

[001016] or a form thereof.

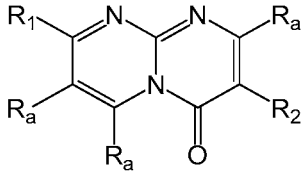
[001017] An embodiment of the use of the compound of Formula (XIIa) is the use of the compound of Formula (XIIa2):



(XIIa2)

[001018] or a form thereof.

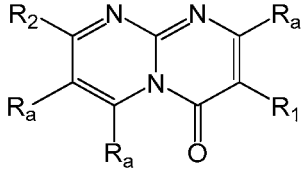
[001019] An embodiment of the use of the compound of Formula (XIIa) is the use of the compound of Formula (XIIa3):



(XIIa3)

[001020] or a form thereof.

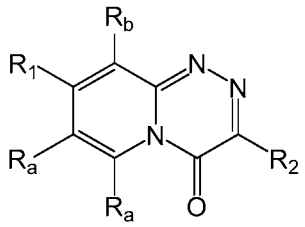
[001021] An embodiment of the use of the compound of Formula (XIIa) is the use of the compound of Formula (XIIa4):



(XIIa4)

[001022] or a form thereof.

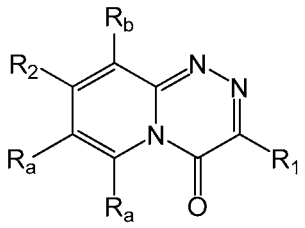
[001023] An embodiment of the use of the compound of Formula (XIIIa) is the use of the compound of Formula (XIIIa1):



(XIIIa1)

[001024] or a form thereof.

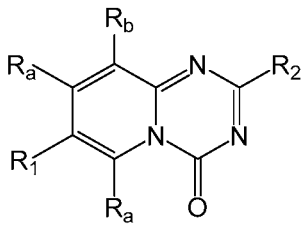
[001025] An embodiment of the use of the compound of Formula (XIIIa) is the use of the compound of Formula (XIIIa2):



(XIIIa2)

[001026] or a form thereof.

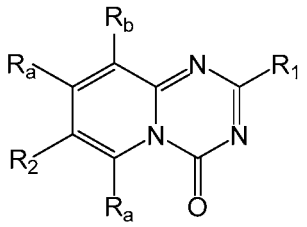
[001027] An embodiment of the use of the compound of Formula (XIVa) is the use of the compound of Formula (XIVa1):



(XIVa1)

[001028] or a form thereof.

[001029] An embodiment of the use of the compound of Formula (XIVa) is the use of the compound of Formula (XIVa2):



(XIVa2)

[001030] or a form thereof.

PATIENT POPULATION

[001031] In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject suffering from SMA. In other embodiments, a compound of Formula (I) or a form thereof, is administered to a subject predisposed or susceptible to SMA. In a specific embodiment, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human subject having SMA, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In certain embodiments, the human subject is genotyped prior to administration of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof to determine whether the subject has an inactivating mutation or deletion in the teleomeric copy of the SMN1 gene in both chromosomes, which results in a loss of SMN1 gene function. In some embodiments, a compound of Formula (I) or a form thereof, or pharmaceutical composition thereof is administered to a subject with Type 0 SMA. In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject with Type 1 SMA. In other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject with Type 2 SMA. In other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject with Type 3 SMA. In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject with Type 4 SMA. In certain embodiments, the human subject is an SMA patient.

[001032] In certain embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject that will or might benefit from enhanced inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene. In specific embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a subject that will or may benefit from enhanced Smn protein expression.

[001033] In certain embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human that has an age in a range of from about 0 months to about 6 months old, from about 6 to about 12 months old, from about 6 to about 18 months old, from about 18 to about 36 months old, from about 1 to about 5 years old, from about 5 to about 10 years old, from about 10 to about 15 years old, from about 15 to about 20 years old, from about 20 to about 25 years old, from about 25 to about 30 years old, from about 30 to about 35 years old, from about 35 to about 40 years old, from about 40 to about 45 years old, from about 45 to about 50 years old, from about 50 to about 55 years old, from about 55 to about 60 years old, from about 60 to about 65 years old, from about 65 to about 70 years old, from about 70 to about 75 years old, from about 75 to about 80 years old, from about 80 to about 85 years old, from about 85 to about 90 years old, from about 90 to about 95 years old or from about 95 to about 100 years old.

[001034] In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human infant. In other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human toddler. In other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human child. In other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to a human adult. In yet other embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof is administered to an elderly human.

[001035] In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other embodiments, an effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other

embodiments, a prophylactically effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other embodiments, a therapeutically effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA.

[001036] In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to an SMA patient to treat or ameliorate SMA. In other embodiments, an effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to an SMA patient to treat or ameliorate SMA. In other embodiments, a prophylactically effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to an SMA patient to prevent advancement of SMA. In other embodiments, a therapeutically effective amount of a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to an SMA patient to treat or ameliorate SMA.

[001037] In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject suffering from SMA. In other embodiments, a compound of Formula (I) or a form thereof, is administered to a subject predisposed or susceptible to SMA. In a specific embodiment, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human subject having SMA, wherein SMA is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function. In certain embodiments, the human subject is genotyped prior to administration of a compound of Formula (I) or a form thereof, or a medicament thereof to determine whether the subject has an inactivating mutation or deletion in the teleomeric copy of the SMN1 gene in both chromosomes, which results in a loss of SMN1 gene function. In some embodiments, a compound of Formula (I) or a form thereof, or medicament thereof is administered to a subject with Type 0 SMA. In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject with Type 1 SMA. In other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject with Type 2 SMA. In other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject with Type 3 SMA. In some embodiments, a

compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject with Type 4 SMA. In certain embodiments, the human subject is an SMA patient.

[001038] In certain embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject that will or might benefit from enhanced inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene. In specific embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a subject that will or may benefit from enhanced Smn protein expression.

[001039] In certain embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human that has an age in a range of from about 0 months to about 6 months old, from about 6 to about 12 months old, from about 6 to about 18 months old, from about 18 to about 36 months old, from about 1 to about 5 years old, from about 5 to about 10 years old, from about 10 to about 15 years old, from about 15 to about 20 years old, from about 20 to about 25 years old, from about 25 to about 30 years old, from about 30 to about 35 years old, from about 35 to about 40 years old, from about 40 to about 45 years old, from about 45 to about 50 years old, from about 50 to about 55 years old, from about 55 to about 60 years old, from about 60 to about 65 years old, from about 65 to about 70 years old, from about 70 to about 75 years old, from about 75 to about 80 years old, from about 80 to about 85 years old, from about 85 to about 90 years old, from about 90 to about 95 years old or from about 95 to about 100 years old.

[001040] In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human infant. In other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human toddler. In other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human child. In other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a human adult. In yet other embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to an elderly human.

[001041] In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other embodiments, an effective amount of a compound of Formula (I) or a form

thereof, or a medicament thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other embodiments, a prophylactically effective amount of a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA. In other embodiments, a therapeutically effective amount of a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to a patient to prevent the onset of SMA in a patient at risk of developing SMA.

[001042] In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to an SMA patient to treat or ameliorate SMA. In other embodiments, an effective amount of a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to an SMA patient to treat or ameliorate SMA. In other embodiments, a prophylactically effective amount of a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to an SMA patient to prevent advancement of SMA. In other embodiments, a therapeutically effective amount of a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to an SMA patient to treat or ameliorate SMA.

MODE OF ADMINISTRATION

[001043] When administered to a patient, a compound of Formula (I) or a form thereof is preferably administered as a component of a composition that optionally comprises a pharmaceutically acceptable carrier, excipient or diluent. The composition can be administered orally, or by any other convenient route, for example, by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.*, oral mucosa, rectal, and intestinal mucosa) and may be administered together with another biologically active agent. Administration can be systemic or local. Various delivery systems are known, *e.g.*, encapsulation in liposomes, microparticles, microcapsules, capsules, and can be used to administer the compound.

[001044] Methods of administration include but are not limited to parenteral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intranasal, intracerebral, intravaginal, transdermal, rectally, by inhalation, or topically, particularly to the ears, nose, eyes, or skin. The mode of administration is left to the discretion of

the practitioner. In most instances, administration will result in the release of a compound into the bloodstream. In a specific embodiment, a compound is administered orally.

DOSAGE AND DOSAGE FORMS

[001045] The amount of a compound of Formula (I) or a form thereof that will be effective in the treatment of SMA depend, *e.g.*, on the route of administration, the type of SMA, the general health of the subject, ethnicity, age, weight, and gender of the subject, diet, time, and the severity of SMA, and should be decided according to the judgment of the practitioner and each patient's or subject's circumstances.

[001046] In specific embodiments, an "effective amount," "prophylactically effective amount" or "therapeutically effective amount" in the context of the administration of a compound of Formula (I) or a form thereof, or composition or medicament thereof refers to an amount of a compound of Formula (I) which has a therapeutic effect and/or beneficial effect. In certain specific embodiments, an "effective amount," "prophylactically effective amount" or "therapeutically effective amount" in the context of the administration of a compound of Formula (I) or a form thereof, or composition or medicament thereof results in one, two or more of the following effects: (i) reduces or ameliorates the severity of SMA; (ii) delays onset of SMA; (iii) inhibits the progression of SMA; (iv) reduces hospitalization of a subject; (v) reduces hospitalization length for a subject; (vi) increases the survival of a subject; (vii) improves the quality of life of a subject; (viii) reduces the number of symptoms associated with SMA; (ix) reduces or ameliorates the severity of a symptom(s) associated with SMA; (x) reduces the duration of a symptom associated with SMA; (xi) prevents the recurrence of a symptom associated with SMA; (xii) inhibits the development or onset of a symptom of SMA; and/or (xiii) inhibits of the progression of a symptom associated with SMA. In certain embodiments, an effective amount of a compound of Formula (I) or a form thereof is an amount effective to enhance inclusion of exon 7 of SMN2 into SMN2 mRNA that is transcribed from the SMN2 gene and increases the levels of Smn protein produced from the SMN2 gene and thus producing a desired beneficial effect in a subject in need thereof. In some instances, the desired effect can be determined by analyzing or quantifying: (1) the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene; or (2) the levels of Smn protein produced from the SMN2

gene. Non-limiting examples of effective amounts of a compound of Formula (I) or a form thereof are described herein.

[001047] For example, the effective amount may be the amount required to treat SMA in a human subject in need thereof, or the amount required to enhance inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene in a human subject in need thereof, or the amount required to increase levels of Smn protein produced from the SMN2 gene in a human subject in need thereof. In a specific embodiment, the human subject is an SMA patient.

[001048] In general, the effective amount will be in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day for a patient or subject having a weight in a range of between about 1 kg to about 200 kg. The typical adult subject is expected to have a median weight in a range of between about 70 and about 100 kg.

[001049] Within the scope of the present description, the "effective amount" of a compound of Formula (I) or a form thereof for use in the manufacture of a medicament, the preparation of a pharmaceutical kit or in a method for treating SMA in a human subject in need thereof, is intended to include an amount in a range of from about 0.001 mg to about 35,000 mg. In a specific embodiment, the human subject is an SMA patient.

[001050] The compositions described herein are formulated for administration to the subject via any drug delivery route known in the art. Nonlimiting examples include oral, ocular, rectal, buccal, topical, nasal, ophthalmic, subcutaneous, intramuscular, intraveneous (bolus and infusion), intracerebral, transdermal, and pulmonary routes of administration.

PHARMACEUTICAL COMPOSITIONS

[001051] Embodiments described herein include the use of a compound of Formula (I) or a form thereof in a pharmaceutical composition. In a specific embodiment, described herein is the use of a compound of Formula (I) or a form thereof in a pharmaceutical composition for treating SMA in a human subject in need thereof comprising administering an effective amount of a compound of Formula (I) or a form thereof in admixture with a pharmaceutically acceptable excipient. In a specific embodiment, the human subject is an SMA patient.

[001052] A compound of Formula (I) or a form thereof may optionally be in the form of a composition comprising the compound or a form thereof and an optional carrier, excipient or diluent. Other embodiments provided herein include pharmaceutical compositions comprising

an effective amount of a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient, or diluent. In a specific embodiment, the pharmaceutical compositions are suitable for veterinary and/or human administration. The pharmaceutical compositions provided herein can be in any form that allows for the composition to be administered to a subject.

[001053] In a specific embodiment and in this context, the term "pharmaceutically acceptable carrier, excipient or diluent" means a carrier, excipient or diluent approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant (*e.g.*, Freund's adjuvant (complete and incomplete)), excipient, or vehicle with which a therapeutic agent is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a specific carrier for intravenously administered pharmaceutical compositions. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions.

[001054] Typical compositions and dosage forms comprise one or more excipients. Suitable excipients are well-known to those skilled in the art of pharmacy, and non limiting examples of suitable excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. Whether a particular excipient is suitable for incorporation into a pharmaceutical composition or dosage form depends on a variety of factors well known in the art including, but not limited to, the way in which the dosage form will be administered to a patient and the specific active ingredients in the dosage form. Further provided herein are anhydrous pharmaceutical compositions and dosage forms comprising one or more compounds of Formula (I) or a form thereof as described herein. The compositions and single unit dosage forms can take the form of solutions or syrups (optionally with a flavoring agent), suspensions (optionally with a flavoring agent), emulsions, tablets (*e.g.*, chewable tablets), pills, capsules, granules, powder (optionally for reconstitution), taste-masked or sustained-release formulations and the like.

[001055] Pharmaceutical compositions provided herein that are suitable for oral administration can be presented as discrete dosage forms, such as, but are not limited to, tablets, caplets, capsules, granules, powder, and liquids. Such dosage forms contain predetermined amounts of active ingredients, and may be prepared by methods of pharmacy well known to those skilled in the art.

[001056] Examples of excipients that can be used in oral dosage forms provided herein include, but are not limited to, binders, fillers, disintegrants, and lubricants.

BIOMARKERS

[001057] In certain embodiments, the amount of mRNA that is transcribed from the SMN1 gene and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 is used as a biomarker for SMA. In certain embodiments, the amount of mRNA that is transcribed from the SMN1 gene and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 is used as a biomarker for SMA. In other embodiments, the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 is used as a biomarker for an SMA patient being treated with a compound, such as disclosed herein. In other embodiments, the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 is used as a biomarker for an SMA patient being treated with a compound, such as disclosed herein. In some embodiments, a change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and a corresponding change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 is a biomarker for a patient being treated with a compound, such as disclosed herein. In a specific embodiment, the patient is an SMA patient.

[001058] In a specific embodiment, an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and a corresponding decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 after the administration of a compound (*e.g.*, a compound of Formula (I) disclosed herein) indicates that the compound may be effective to treat SMA. In another specific embodiment, a decrease in the amount of mRNA that is transcribed from the SMN2 gene and includes exon 7 of SMN2 and a corresponding

increase in the amount of mRNA that is transcribed from the SMN2 gene and does not include exon 7 of SMN2 after the administration of a compound (*e.g.*, a compound of Formula (I) disclosed herein) indicates that the compound will not be effective to treat SMA. In accordance with these embodiments, an SMN primer(s) and/or an SMN probe described below can be used in assays, such as PCR (e.g., qPCR) and RT-PCR (e.g., RT-qPCR or endpoint RT-PCR) to assess and/or quantify the amount of mRNA that is transcribed from the SMN1 gene and/or SMN2 gene and does or does not include exon 7 of SMN1 and/or SMN2.

[001059] In one embodiment, provided herein are SMN primers and/or SMN probes (*e.g.*, a forward primer having the nucleotide sequence of SEQ ID NO. 1, 7, 8, 11 or 13; and/or a reverse primer having the nucleotide sequence of SEQ ID NO. 9 or 12; and/or an SMN probe such as a SEQ ID NO. 3 or 10) for amplifying nucleic acids encoding or encoded by human SMN1 and/or SMN2. These primers can be used as primers in, *e.g.*, RT-PCR (such as RT-PCR, endpoint RT-PCR and/or RT-qPCR as described herein or as known to one skilled in the art), PCR (such as qPCR) or rolling circle amplification, and as probes in hybridization assays, such as a Northern blot and/or a Southern blot assay. As utilized in the Biological Examples herein, endpoint RT-PCR is a reverse transcription-polymerase chain reaction that is carried out for a certain number of amplification cycles (or until starting materials are exhausted) following by a quantification of each of the DNA products using, *e.g.*, gel electrophoretic separation, staining with a fluorescent dye, quantification of fluorescence and the like.

[001060] SEQ ID NO. 1 hybridizes to DNA or RNA comprising nucleotides corresponding to nucleotides 22 to 40 of exon 7 of SMN1 and/or SMN2, SEQ ID NO. 2 hybridizes to DNA or RNA comprising nucleotides corresponding to nucleotides 4 to 26 of the firefly luciferase coding sequence; SEQ ID NO. 7 hydridizes to nucleic acid sequences (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding to nucleotides 32 to 54 of exon 7 of SMN1 and/or SMN2 and nucleotides 1 to 4 of exon 8 of SMN1 and/or SMN2, SEQ ID NO. 8 hybridizes to nucleic acid sequences (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding, in order, to nucleotides 87 to 111 of exon 7 of SMN1 and/or SMN2 and nucleotides 1 to 3 of exon 8 of SMN1 and/or SMN2, SEQ ID NO. 9 hybridizes to nucleic acid sequences (*e.g.*, the antisense strand of DNA or RNA) comprising nucleotides corresponding to nucleotides 39 to 62 of exon 8 of SMN1 and/or SMN2, SEQ ID NO. 11 hybridizes to nucleic acid sequences (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding to nucleotides 43 to 63 of exon 6 of

SMN1 and/or SMN2, SEQ ID NO. 12 hybridizes to nucleic acid sequences (*e.g.*, the antisense strand of DNA or RNA) comprising nucleotides corresponding to nucleotides 51 to 73 of exon 8 of SMN1 and/or SMN2, and SEQ ID NO. 13 hybridizes to nucleic acid sequence (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding to nucleotides 22 to 46 of exon 6 of SMN1 and/or SMN2.

[001061] Accordingly, an oligonucleotide corresponding to SEQ ID NO. 9, 11, 12 and/or 13 can be used in an amplification reaction to amplify nucleic acids encoding or encoded by human SMN1 and/or SMN2 lacking exon 7 of human SMN1 and/or SMN2 and nucleic acid encoding or encoded by human SMN1 and/or SMN2 and includes exon 7 of human SMN1 and/or SMN2. In contrast, an oligonucleotide corresponding to SEQ ID NO. 8 in conjunction with a downstream reverse primer (*e.g.*, SEQ ID NO. 9 or 12) can be used to amplify nucleic acids encoding or encoded by human SMN1 and/or SMN2 lacking exon 7 of human SMN1 and/or SMN2 and an oligonucleotide corresponding to SEQ ID NO. 1 and 7 in conjunction with a downstream reverse primer (*e.g.*, SEQ ID NO. 9 or 12) can be used to amplify nucleic acids encoding or encoded by human SMN1 and/or human SMN2 and includes exon 7 of SMN1 and/or SMN2.

[001062] SEQ ID NO. 3 hybridizes to nucleic acid sequences (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding, in order, to nucleotides 50 to 54 of exon 7 of human SMN1 and/or SMN2 and nucleotides 1 to 21 of exon 8 of human SMN1 and/or SMN2, and SEQ ID NO. 10 hybridizes to nucleic acid sequences (*e.g.*, the sense strand of DNA) comprising nucleotides corresponding to nucleotides 7 to 36 of exon 8 of human SMN1 and/or SMN2. SEQ ID NO. 3 is useful as a probe to detect mRNA that is transcribed from the minigene and includes exon 7 of SMN1 and/or SMN2, described herein or described in International Publication No. WO 2009/151546 or U.S. Patent Application Publication No. 2011/0086833 (each of which is incorporated herein by reference in its entirety) and to detect mRNA that is transcribed from human SMN1 and/or SMN2 and includes exon 7 of SMN1 and/or SMN2. In addition, SEQ ID NO. 10 is useful as a probe to detect mRNA that is transcribed from the minigene and does or does not include exon 7 of SMN1 and/or SMN2 and to detect mRNA that is transcribed from human SMN1 and/or SMN2, described herein or as described in International Publication No. WO 2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety.

[001063] In a specific embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 11 or 13 and/or SEQ ID NO. 2, 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to determine whether a compound (*e.g.*, a compound of Formula (I) or a form thereof) enhances the inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from an SMN1 and/or SMN2 gene.

[001064] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in a patient sample. In a specific embodiment, the patient is an SMA patient.

[001065] In another embodiment, a primer and/or probe described below in the Biological Examples (*e.g.*, SMN primers such as SEQ ID NO. 1, 7, 11 or 13 and/or SEQ ID NO. 9 or 12, and/or SMN probes such as a SEQ ID NO. 3 or 10) is used in an assay, such as RT-PCR, RT-qPCR, endpoint RT-PCR, PCR, qPCR, rolling circle amplification and, as applicable, Northern blot or Southern blot (*e.g.*, an assay such as described below in the Biological Examples), to monitor a patient's response to a compound (*e.g.*, a compound of Formula (I) or a form thereof). In a specific embodiment, the patient is an SMA patient.

[001066] A sample (*e.g.*, a blood sample, PBMC sample, or tissue sample, such as a skin or muscle tissue sample) from a patient can be obtained using techniques known to one skilled in the art and the primers and/or probes described in the Biological Examples below can be used in assays (*e.g.*, PCR, RT-PCR, RT-qPCR, qPCR, endpoint RT-PCR, rolling circle amplification, Northern blot and Southern blot) to determine the amount of mRNA that is transcribed from the SMN1 and/or SMN2 genes (*e.g.*, the amount of mRNA that includes exon 7 of SMN2 transcribed from the SMN2 gene). A sample derived from a patient refers to a sample that is processed and/or manipulated after being obtained from the patient using techniques known to

one skilled in the art. For example, a sample from a patient can be processed to, *e.g.*, extract RNA, using techniques known to one of skill in the art. A sample from a patient can be processed to, *e.g.*, extract RNA and the RNA is reversed transcribed to produce cDNA. In a specific embodiment, the patient is an SMA patient.

[001067] In a specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001068] In another specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (e.g., SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001069] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes that includes exon 7 of SMN1 and SMN2 and the amount of mRNA that is transcribed from the human SMN1 and SMN2 genes and does not include exon 7 of SMN1 and SMN2 can be differentiated from each other by, *e.g.*, size of the RNA or DNA fragment generated from SMN1

and SMN2 mRNA that includes exon 7 of SMN1 and SMN2 and from SMN1 and SMN2 mRNA that do not include exon 7 of SMN1 and SMN2.

[001070] In another specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001071] In another specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with an SMN probe described below (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components, *e.g.*, of an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR), rolling circle amplification and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001072] In another specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with an SMN probe described below (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR), rolling circle amplification

and, as applicable, Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes.

[001073] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes that includes exon 7 of SMN1 and SMN2 and the amount of mRNA that is transcribed from the human SMN1 and SMN2 genes and does not include exon 7 of SMN1 and SMN2 can be differentiated from each other by, *e.g.*, size of the RNA or DNA fragment generated from SMN1 and SMN2 mRNA that includes exon 7 of SMN1 and SMN2 and from SMN1 and SMN2 mRNA that do not include exon 7 of SMN1 and SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001074] In another specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with an SMN probe described below (*e.g.*, SEQ ID NO. 10) along with applicable components for, *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR), rolling circle amplification, or Northern blot or Southern blot; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001075] In a specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is

from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001076] In a specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe described herein (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, as applicable; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and SMN2 genes. In a specific embodiment, the patient is an SMA patient.

[001077] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes that includes exon 7 of SMN1 and SMN2 and the amount of mRNA that is transcribed from the human SMN1 and SMN2 genes that do not include exon 7 of SMN1 and SMN2 can be differentiated from each other by, *e.g.*, size of the RNA or DNA fragment generated from SMN1 and SMN2 mRNA that includes exon 7 of SMN1 and SMN2 and from SMN1 and SMN2 mRNA that does not include exon 7 of SMN1 and SMN2. In certain embodiments, the sample is from or derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001078] In a specific embodiment, provided herein is a method for detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, comprising: (a) contacting a patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from a patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe described herein (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, an RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2. In certain embodiments, the sample is from or

derived from a patient administered a compound, such as a compound of Formula (I) or a form thereof as described herein. In a specific embodiment, the patient is an SMA patient.

[001079] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001080] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient

with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (e.g., from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001081] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (e.g., SEQ ID NO. 3 or 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1

and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001082] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of

therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001083] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of

tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001084] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after

administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001085] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001086] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient;

(b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (e.g., from the same type of tissue sample) from the patient prior to administration of the compound indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001087] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as

described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001088] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient;

(b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for e.g., RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months,

9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001089] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an

analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001090] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is

transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001091] In a specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR) or PCR (*e.g.*, qPCR), wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is responsive to the compound and

that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001092] In another specific embodiment, provided herein is a method for assessing an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does

not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound, indicate that the SMN1 and/or patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is assessed 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001093] In a specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for *e.g.*, RT-PCR(*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2,

wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001094] In another specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable

components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (e.g., from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001095] In a specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*,

blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound

of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001096] In another specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 1, 7, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 3 or 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2, wherein (1) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7,

8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001097] In a specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value

to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001098] In another specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include

exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored continuous administration of a compound over a period of days, weeks, months or years, such as a compound of Formula (I) or a form thereof as described herein.

[001099] In a specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample o*r* tissue sample*)* or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from a patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the

compound or a certain number of do*ses* of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (e.g., from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001100] In another specific embodiment, provided herein is a method for monitoring an SMA patient's responsiveness to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 8, 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1) a decrease in the amount of mRNA that is transcribed from the

SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to the administration of the compound or a certain number of doses of the compound, or a certain earlier date indicates that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001101] In a specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (e.g., blood sample or tissue sample) or a sample derived from an SMA patient (e.g., a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (e.g., SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9

or 12) along with applicable components for, *e.g.*, RT-PCR (e.g., endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain

embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001102] In another specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR), or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the

compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001103] In a specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with an SMN probe (*e.g.*, SEQ ID NO. 10)

along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of S SMN1 and/or MN2 in an analogous sample (e.g., from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain

embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001104] In another specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with an SMN probe (*e.g.*, SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound

and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001105] In a specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) contacting an SMA patient sample (*e.g.*, blood sample or tissue sample) or a sample derived from an SMA patient (*e.g.*, a blood sample or tissue sample that has been processed to extract RNA) with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (e.g., SEQ ID NO. 9

or 12) and/or an SMN probe (SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification, wherein the sample is from or derived from an SMA patient administered a compound (*e.g.*, a compound of Formula (I) or a form thereof as described herein); and (b) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic

value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001106] In another specific embodiment, provided herein is a method for monitoring an SMA patient's response to a compound, comprising: (a) administering a compound to an SMA patient; (b) contacting a sample (*e.g.*, blood sample or tissue sample) obtained or derived from the patient with a forward SMN primer described below (*e.g.*, SEQ ID NO. 11 or 13) and/or a reverse SMN primer described herein (*e.g.*, SEQ ID NO. 9 or 12) and/or an SMN probe (SEQ ID NO. 10) along with applicable components for, *e.g.*, RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification; and (c) detecting the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, wherein (1)(i) an increase in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) a decrease in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an

analogous sample (*e.g.*, from the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is responsive to the compound and that the compound may be or is beneficial and/or of therapeutic value to the patient; and (2)(i) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, and (ii) no change or no substantial change in the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in the patient sample relative to the amount of mRNA that is transcribed from the SMN2 gene and does not include exon 7 of SMN1 and/or SMN2 in an analogous sample (*e.g.*, the same type of tissue sample) from the patient prior to administration of the compound or a certain number of doses of the compound, or a certain earlier date, indicate that the patient is not responsive to the compound and that the compound is not beneficial and/or of therapeutic value to the patient. In certain embodiments, the patient's response is monitored 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, 20 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 7 days, 14 days, 28 days, 1 month, 2 months, 3 months, 6 months, 9 months, 12 months or more after administration of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the patient has received 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored after the administration of 1-5, 5-10, 10-15, 15-20, 20-30, 30-40, 40-50, or 50-100 doses of a compound, such as a compound of Formula (I) or a form thereof as described herein. In some embodiments, the patient's response is monitored over a period of days, weeks, months or years during or after the continuous administration of a compound, such as a compound of Formula (I) or a form thereof as described herein.

[001107] In specific embodiments, SMA in a patient is caused by an inactivating mutation or deletion in the SMN1 gene on both chromosomes, resulting in a loss of SMN1 gene function.

KITS

[001108] In one aspect, provided herein are pharmaceutical or assay kits comprising an SMN primer or probe described herein, in one or more containers, and instructions for use. In one embodiment, a pharmaceutical or assay kit comprises, in a container, one or more SMN reverse primers (*e.g.*, SEQ ID NO. 2, 9 and/or 12) and/or one or more SMN forward primers (SEQ ID NO. 1, 7, 8, 11 and/or 13)) and instructions for use. In another embodiment, a pharmaceutical or assay kit comprises, in one container, an SMN reverse primer (*e.g.*, SEQ ID NO. 2, 9 or 12), an SMN forward primer (SEQ ID NO. 1, 7, 8, 11 or 13)) and instructions for use.

[001109] In one embodiment, a pharmaceutical or assay kit comprises, in separate containers, one SMN reverse primer (*e.g.*, SEQ ID NO. 2, 9 or 12) in one container, another SMN forward primer (*e.g.*, SEQ ID NO. 1, 7, 8, 11 or 13)) in another container, and instructions for use.

[001110] In certain embodiments, applicable components needed for a PCR (*e.g.*, qPCR), RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR) or rolling circle amplification, such as polymerase, deoxynucleoside triphosphates, etc., are included in such kits. In some embodiments, components needed for hybridization are included in such kits. A pharmaceutical or assay kit containing such primers can be used in PCR and RT-PCR to, *e.g.*,: (i) assess whether a therapeutic agent (*e.g.*, a compound of Formula (I) or a form thereof) enhances inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene, (ii) monitor the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 of SMN1 and/or SMN2 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1 and/or SMN2, and/or (iii) monitor a subject's response to a therapeutic agent (*e.g.*, a compound of Formula (I) or a form thereof). In other embodiments, the subject is a human subject. In other embodiments, the human subject is a human patient. In certain other embodiments, the human patient is a human SMA patient.

[001111] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the sequence found in SEQ ID NO. 1, in a container, and the reverse primer with the sequence found in SEQ ID NO. 2, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by a human SMN1 minigene or human SMN2 minigene, such as described those described herein or in International

Publication No. WO 2009/151546 or U.S. Patent Application Publication No. 2011/0086833, each of which is incorporated herein by reference in its entirety. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001112] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 7, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001113] In another specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 8, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by the endogenous human SMN2 gene. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001114] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 7, in a container, the forward primer with the nucleotide sequence found in SEQ ID NO. 8, in another container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001115] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 11, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 12, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by

endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001116] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 11, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001117] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 13, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 12, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001118] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 13, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001119] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 1, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 9, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001120] In a specific embodiment, a pharmaceutical or assay kit comprises the forward primer with the nucleotide sequence found in SEQ ID NO. 1, in a container, and the reverse primer with the nucleotide sequence found in SEQ ID NO. 12, in another container. In certain embodiments, these primers are used in RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR), PCR (*e.g.*, qPCR) or rolling circle amplification for amplifying nucleotide sequences encoded by endogenous human SMN1 and SMN2 genes. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[001121] In another embodiment, a pharmaceutical or assay kit comprises an SMN probe described herein (*e.g.*, SEQ ID NO. 3 or 10), in one container. In other embodiments, the probe is used in, *e.g.*, a hybridization assay, such as a Southern blot or Northern blot. In a specific embodiment, the probe is used in RT-qPCR or qPCR. In certain embodiments, components needed for a PCR (*e.g.*, qPCR), RT-PCR (*e.g.*, endpoint RT-PCR and/or RT-qPCR) or rolling circle amplification, such as polymerase, deoxynucleoside triphosphates, primers, etc., are included in such kits. In some embodiments, components needed for hybridization are included in such kits.

[001122] In one embodiment, a pharmaceutical or assay kit comprises an SMN reverse primer (*e.g.*, SEQ ID NO. 2, 9 or 12) in one container, an SMN forward primer (*e.g.*, SEQ ID NO. 1, 7, 8, 11 or 13) in another container, and an SMN probe (*e.g.*, SEQ ID NO. 3 or 10) in another container, and instructions for use. In another embodiment, a pharmaceutical or assay kit comprises one or more SMN reverse primers (*e.g.*, SEQ ID NO. 2, 9 and/or 12) in one container, one or more SMN forward primers (*e.g.*, SEQ ID NO. 1, 7, 8, 11 and/or 13) in another container, and one or more SMN probe (*e.g.*, SEQ ID NO. 3 and/or 10) in another container, and instructions for use.

[001123] In certain embodiments, components needed to run a PCR, RT-PCR or rolling circle amplification, such as polymerase, deoxynucleoside triphosphates, etc., are included in such kits. A pharmaceutical or assay kit containing such probes and/or primers can be used in PCR and RT-PCR to, *e.g.*,: (i) assess whether a therapeutic agent (*e.g.*, a compound of Formula (I) or a form thereof) enhances inclusion of exon 7 of SMN1 and/or SMN2 into mRNA that is transcribed from the SMN1 and/or SMN2 gene, (ii) monitor the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and includes exon 7 and the amount of mRNA that is transcribed from the SMN1 and/or SMN2 gene and does not include exon 7 of SMN1

and/or SMN2, and/or (iii) monitor a subject's response to a therapeutic agent (e.g., a compound of Formula (I) or a form thereof). In other embodiments, the subject is a human subject. In other embodiments, the human subject is a human patient. In certain other embodiments, the human patient is a human SMA patient.

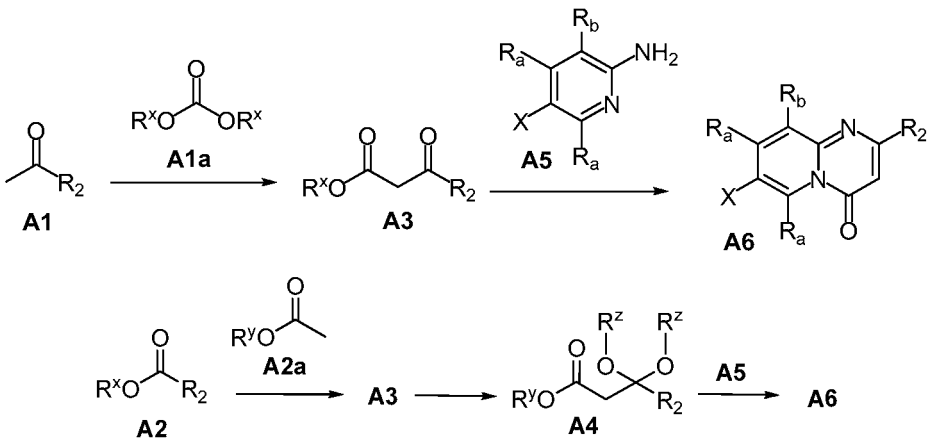
[001124] In another aspect, provided herein is a pharmaceutical kit comprising a compound of Formula (I) or a form thereof, in a container, and instructions for use of the compound or form thereof. In a specific embodiment, provided herein is a pharmaceutical kit comprising a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent, and instructions for use. In another specific embodiment, provided herein is a pharmaceutical kit comprising a pharmaceutical composition comprising an effective amount of a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent, and instructions for use. In one embodiment, the instructions for use explain one, two or more of the following: the dose, route of administration, frequency of administration and side effects of administration of a compound of Formula (I) or a form thereof to a subject. In other embodiments, the subject is a human subject. In other embodiments, the human subject is a human patient. In certain other embodiments, the human patient is a human SMA patient.

[001125] As disclosed herein, general methods for preparing the compounds of Formula (I) or a form thereof as described herein are available via standard, well-known synthetic methodology. Many of the starting materials are commercially available or, when not available, can be prepared using the routes described below using techniques known to those skilled in the art. The synthetic schemes provided herein comprise multiple reaction steps, each of which is intended to stand on its own and can be carried out with or without any preceding or succeeding step(s). In other words, each of the individual reaction steps of the synthetic schemes provided herein in isolation is contemplated.

GENERAL SYNTHETIC METHODS

[001126] **Scheme A**

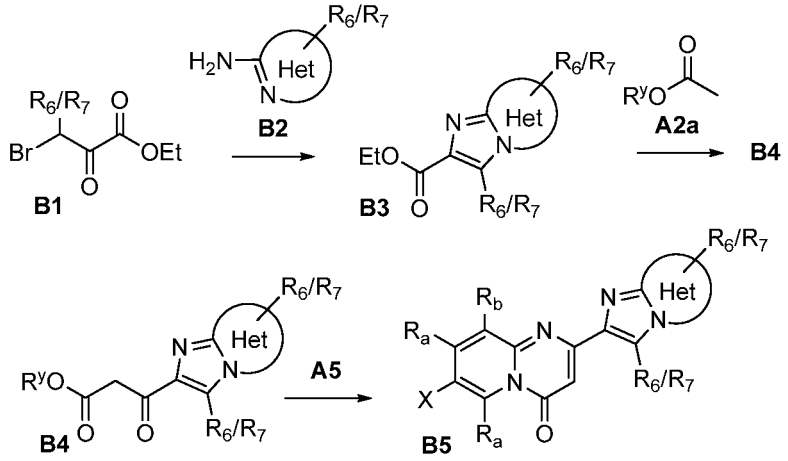
[001127] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl, heterocyclyl or heteroaryl ring system, may be prepared as described in **Scheme A** below.



[001128] Methyl ketone Compound **A1** is reacted with dialkyl carbonate Compound **A1a** (where R^x is C_{1-4}alkyl and the like) in the presence of a base (such as NaH and the like) in a suitable solvent (such as THF and the like) to provide Compound **A3**. Alternatively, ester Compound **A2** is reacted with acetic acid ester Compound **A2a** (where R^y is C_{1-4}alkyl and the like) in the presence of a base (such as LDA and the like) in a suitable solvent (such as THF and the like) to provide Compound **A3**. Compound **A3** is further reacted in the presence of an alcohol (such as MeOH and the like) and an acid catalyst (such as p-TsOH and the like) to provide acetal Compound **A4** (where R^z is C_{1-4}alkyl and the like). Either Compound **A3** or Compound **A4** is reacted with Compound **A5** (where X represents various reactive groups, which may be used to provide a plurality of R_1 functional group substituents by reacting suitable starting materials with Compound **A5** or Compound **A6** using techniques known to a person of ordinary skill in the art) in the presence of an acid (such as PPA, p-TsOH and the like) and a suitable solvent (such as DMA and the like) to afford Compound **A6**.

[001129] **Scheme B**

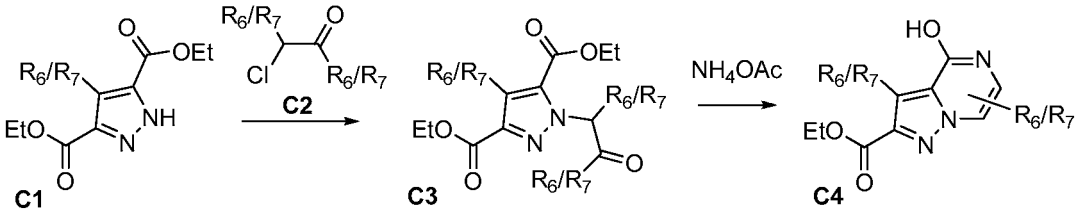
[001130] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heterocyclyl or heteroaryl ring system, may be prepared as described in **Scheme B** below.

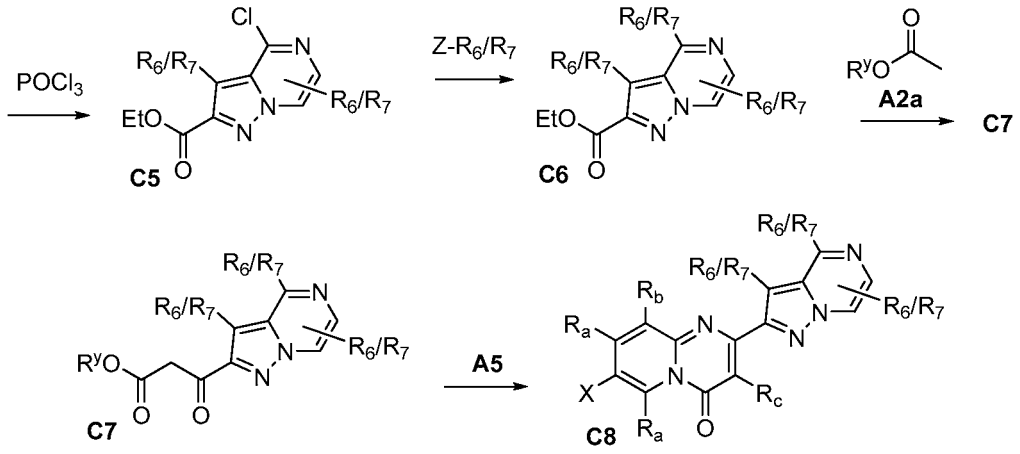


[001131] Compound **B1** is reacted with Compound **B2**, an optionally substituted heterocyclyl or heteroaryl ring system (wherein the term "Het" refers to an amidine-like moiety such as, but not limited to, 2-aminopyridine, 2-aminopyrimidine, 2-aminopyrazine, 3-aminopyridazine, 2-aminothiazole, 4-aminothiazole, 4-aminopyrimidine and the like), in a suitable solvent (such as MeOH and the like) to provide Compound **B3**. Compound **B3** is reacted with acetic acid ester Compound **A2a** (where R^y is C_{1-4}alkyl and the like) in the presence of a base (such as LDA and the like) in a suitable solvent (such as THF and the like) to afford Compound **B4**. Compound **B4** is reacted with Compound **A5** in the presence of an acid (such as PPA, p-TsOH and the like) and a suitable solvent (such as DMA and the like) to afford Compound **B5**.

[001132] **Scheme C**

[001133] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heteroaryl ring system, may be prepared as described in **Scheme C** below.

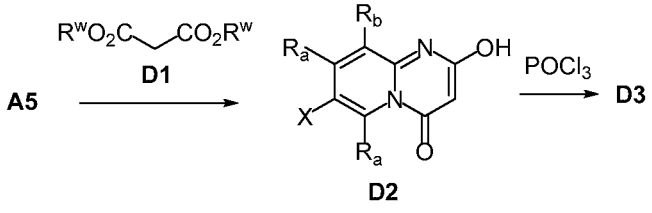


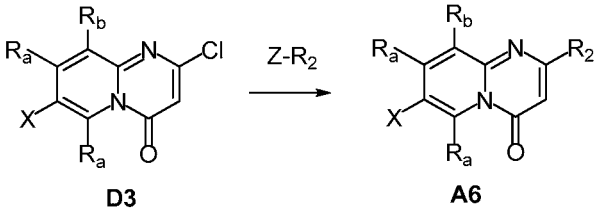


[001134] A 2,4-diester pyrazole Compound **C1** is reacted with an α-chloro ketone Compound **C2** in the presence of a base (such as K_2CO_3 and the like) and a suitable solvent (such as acetone and the like) to afford Compound **C3**. Compound **C3** is treated with ammonium acetate in a suitable solvent (such as AcOH and the like) to provide Compound **C4**. Compound **C4** is treated with a chlorinating reagent (such as $POCl_3$ and the like) to provide Compound **C5**. Compound **C5** is reacted with an alkyl boronic acid (where Z is $B(OH)_2$ and R^z is C_{1-4}alkyl and the like) or an alkyl boronic acid ester (where Z is $B_2(pin)_2$ also referred to as bis(pinacolato)diboron and R^z is C_{1-4}alkyl and the like) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to give Compound **C6**. Compound **C6** is reacted with acetic acid ester Compound **A2a** (where R^y is C_{1-4}alkyl and the like) in the presence of a base (such as LDA and the like) in a suitable solvent (such as THF and the like) to afford Compound **C7**. Compound **C7** is reacted with Compound **A5** in the presence of an acid (such as p-TsOH, PPTs and the like) and a suitable solvent to afford Compound **C8**.

[001135] **Scheme D**

[001136] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl or heteroaryl ring system, may be prepared as described in **Scheme D** below.



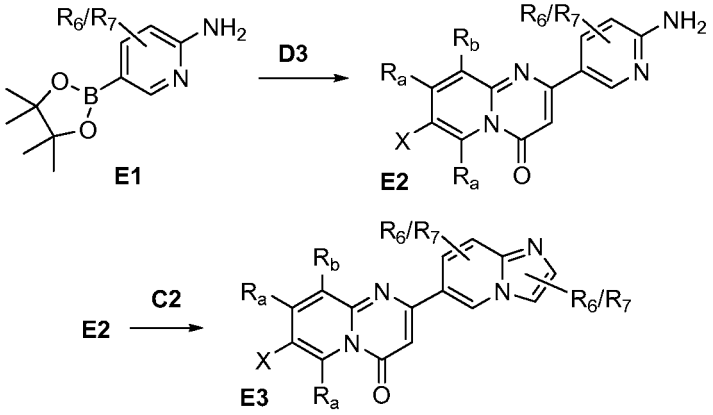


D3 A6

[001137] Compound **A5** is reacted with malonic ester Compound **D1** (where R^w is C_{1-4}alkyl, 2,4,6-trichlorophenyl and the like) to afford Compound **D2**. Compound **D2** is treated with a chlorinating reagent (such as $POCl_3$ and the like) to provide Compound **D3**. Compound **D3** is reacted with an R_2 substituted alkyl boronic acid (where Z is $B(OH)_2$) or an alkyl boronic acid ester (where Z is $B_2(pin)_2$), wherein R_2 is aryl or heteroaryl, in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to give Compound **A6**.

[001138] **Scheme E**

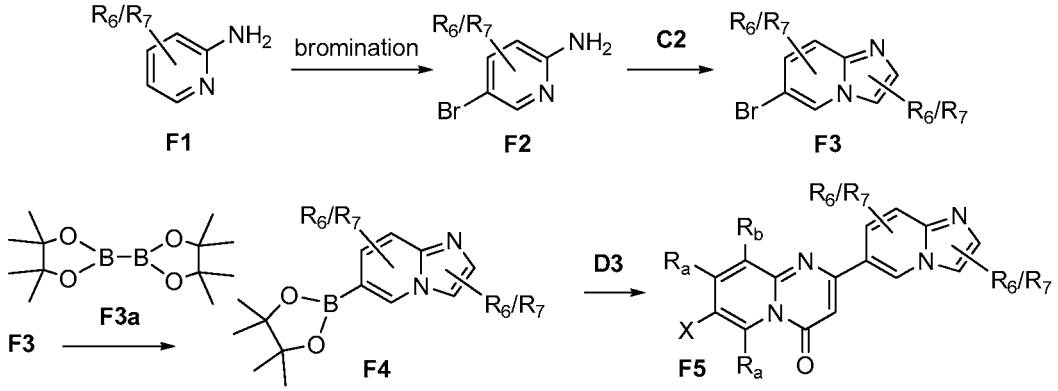
[001139] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heteroaryl ring system, may be prepared as described in **Scheme E** below.



[001140] Compound **E1** is reacted with Compound **D3** in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to give Compound **E2**. Compound **E2** is reacted with Compound **C2** in a suitable solvent (such as DMSO and the like) to afford Compound **E3**.

[001141] **Scheme F**

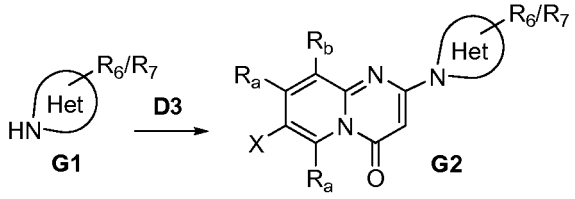
[001142] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heteroaryl ring system, may be prepared as described in **Scheme F** below.



[001143] An optionally substituted 2-aminopyridine Compound **F1** is reacted with a brominating reagent (such as Br_2 and NBS and the like) to provide Compound **F2.** Compound **F2** is reacted with Compound **C2** in a suitable solvent (such as DMSO and the like) to afford Compound **F3**. Compound **F3** is reacted with Compound **F3a** in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as KOAc and the like) in a suitable solvent (such as acetonitrile and the like) to provide Compound **F4**. Compound **F4** is reacted with Compound **D3** in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to give Compound **F5**.

[001144] **Scheme G**

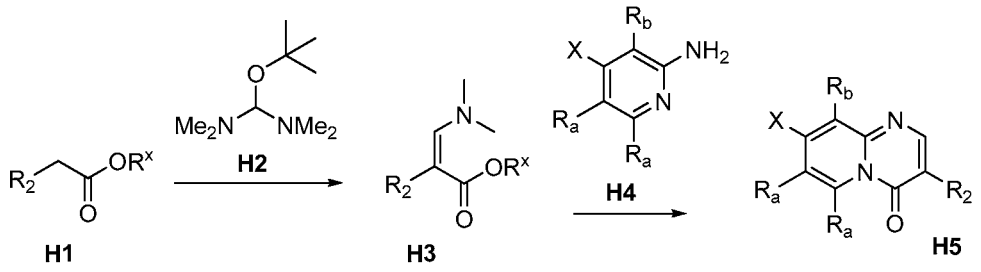
[001145] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heteroaryl ring system, may be prepared as described in **Scheme G** below.



[001146] An optionally substituted azole Compound **G1** (wherein the term "Het" refers to the azole ring system optionally further containing one, two or three additional nitrogen ring members where allowed by available valences) is reacted with Compound **D3** in a suitable solvent (such as DMSO and the like) to provide Compound **G2**.

[001147] **Scheme H**

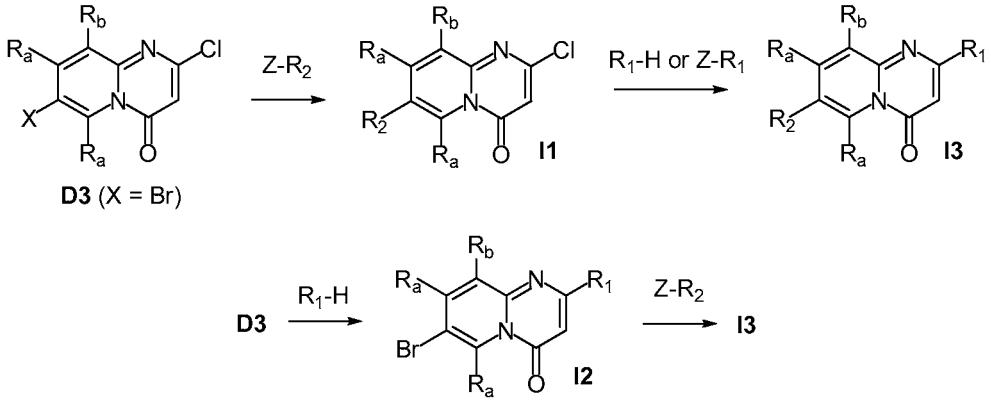
[001148] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl, heterocyclyl or heteroaryl ring system, may be prepared as described in **Scheme H** below.



[001149] Compound **H1** (where R_2 is a monocyclic or bicyclic aryl, heterocyclyl or heteroaryl ring system) is reacted with Bredereck's reagent Compound **H2** (or DMF-DMA and the like) to form Compound **H3**. Compound **H3** is reacted with Compound **H4** (where X represents various reactive groups, which may be used to provide a plurality of R_1 functional group substituents by reacting suitable starting materials with Compound **H4** or Compound **H5** using techniques known to a person of ordinary skill in the art) to provide Compound **H5**.

[001150] **Scheme I**

[001151] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl or heteroaryl ring system, may be prepared as described in **Scheme I** below.



[001152] Compound **D3** (where X is bromo and the like) is reacted with an R_2 substituted alkyl boronic acid (where Z is $B(OH)_2$) or an alkyl boronic acid ester (where Z is $B_2(pin)_2$), wherein R_2 is a monocyclic or bicyclic aryl or heteroaryl ring system and the like, in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to provide Compound **I1**.

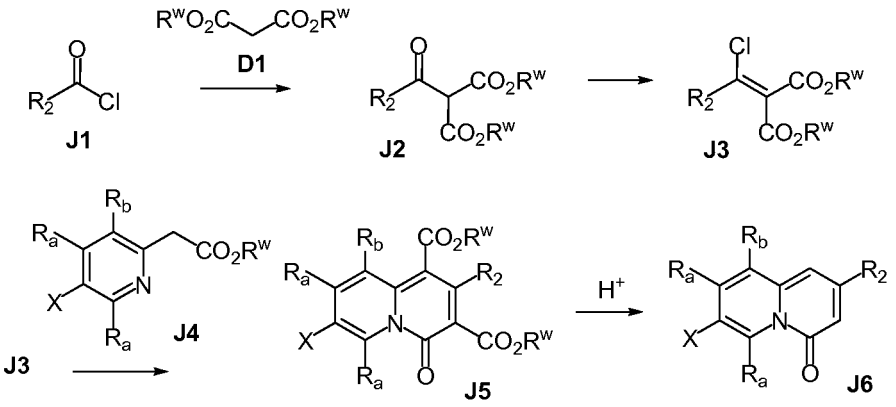
Compound **I1** is reacted with R_1-H (wherein R_1 contains a nucleophilic amino or hydroxyl group and the like) in a suitable solvent (such as DMSO and the like) to provide Compound **I3**.

[001153] Compound **I1** may also be reacted with an R_1 substituted alkyl boronic acid (where Z is $B(OH)_2$) or an alkyl boronic acid ester (where Z is $B_2(pin)_2$) in the presence of a palladium catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like) undergoing Suzuki coupling to provide Compound **I3**.

[001154] Alternatively, Compound **D3** (where X is bromo and the like) may be reacted with R_1-H (wherein R_1 contains a nucleophilic amino or hydroxyl group and the like) in a suitable solvent (such as DMSO and the like) to provide Compound **I2**. Compound **I2** is reacted with an R_2 substituted alkyl boronic acid (where Z is $B(OH)_2$) or an alkyl boronic acid ester (where Z is $B_2(pin)_2$) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as DMF and the like), undergoing Suzuki cross coupling to give Compound **I3**.

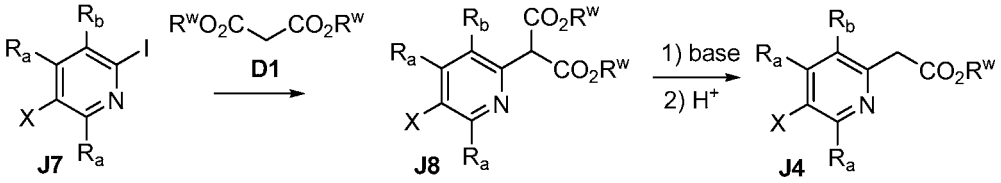
[001155] **Scheme J**

[001156] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl, heterocyclyl or heteroaryl ring system, may be prepared as described in **Scheme J** below.



[001157] Compound **J1** (where R_2 is a monocyclic or bicyclic aryl, heterocyclyl or heteroaryl ring system) is reacted with malonic ester Compound **D1** in the presence of a base (such as TEA or DIEA and the like), a Lewis acid (such as $MgCl_2$ and the like) and a suitable solvent (such as ACN and the like) to provide Compound **J2**. Compound **J2** is treated with a chlorinating reagent (such as $POCl_3$ and the like) in the presence of a base (such as Hünig's base and the like) to provide Compound **J3**.

[001158] Compound **J3** is reacted with Compound **J4** (where X represents various reactive groups, which may be used to provide a plurality of R_1 functional group substituents by reacting suitable starting materials with Compound **J4**, Compound **J5** or Compound **J6** using techniques known to a person of ordinary skill in the art) in the presence of a base (such as NaH and the like) and a suitable solvent (such as DMF and the like) to afford Compound **J5**. The carboxylic ester groups of Compound **J5** may be hydrolyzed and decarboxylated under acidic conditions (such as TFA and the like) in a suitable solvent (such as water and the like) to give Compound **J6**.



[001159] Compound **J7** (where X represents various reactive groups, which may be used to provide a plurality of R_1 functional group substituents by reacting suitable starting materials with Compound **J7**, Compound **J8** or Compound **J4** using techniques known to a person of ordinary skill in the art) is reacted with malonic diester Compound **D1** the presence of a base (such as Cs_2CO_3 and the like), a metal catalyst (such as CuI and the like) and a ligand (such as 2-nicotinic acid and the like) in the presence of a suitable solvent (such as 1,4-dioxane and the like) to afford the diester Compound **J8**. The carboxylic ester groups of Compound **J8** may be hydrolyzed using a base (such as NaOH and the like) in a suitable solvent system (such as MeOH and water and the like), then decarboxylated and acidified using an acid (such as HCl and the like) in a suitable solvent (such as water and the like) to give Compound **J4.**

SPECIFIC SYNTHETIC EXAMPLES

[001160] To describe in more detail and assist in understanding, the following non-limiting examples are offered to more fully illustrate the scope of compounds described herein and are not to be construed as specifically limiting the scope thereof. Such variations of the compounds described herein that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the compounds as described herein and hereinafter claimed. These examples illustrate the preparation of certain compounds. Those of skill in the art will understand that the techniques described in these examples represent techniques, as described by those of ordinary skill in the art, that function

well in synthetic practice, and as such constitute preferred modes for the practice thereof. However, it should be appreciated that those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific methods that are disclosed and still obtain a like or similar result without departing from the spirit and scope of the present description.

[001161] Other than in the following examples of the embodied compounds, unless indicated to the contrary, all numbers expressing quantities of ingredients, reaction conditions, experimental data, and so forth used in the specification and claims are to be understood as being modified by the term "about". Accordingly, all such numbers represent approximations that may vary depending upon the desired properties sought to be obtained by a reaction or as a result of variable experimental conditions. Therefore, within an expected range of experimental reproducibility, the term "about" in the context of the resulting data, refers to a range for data provided that may vary according to a standard deviation from the mean. As well, for experimental results provided, the resulting data may be rounded up or down to present data consistently, without loss of significant figures. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should be construed in light of the number of significant digits and rounding techniques used by those of skill in the art.

[001162] While the numerical ranges and parameters setting forth the broad scope of the present description are approximations, the numerical values set forth in the examples set forth below are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

COMPOUND EXAMPLES

[001163] As used above, and throughout the present description, the following abbreviations, unless otherwise indicated, shall be understood to have the following meanings:

Abbreviation	Meaning
Δ	heating (chemistry) or deletion (biology)
AcOH or HOAc	acetic acid
Ac_2O	acetic anhydride
Ar	argon

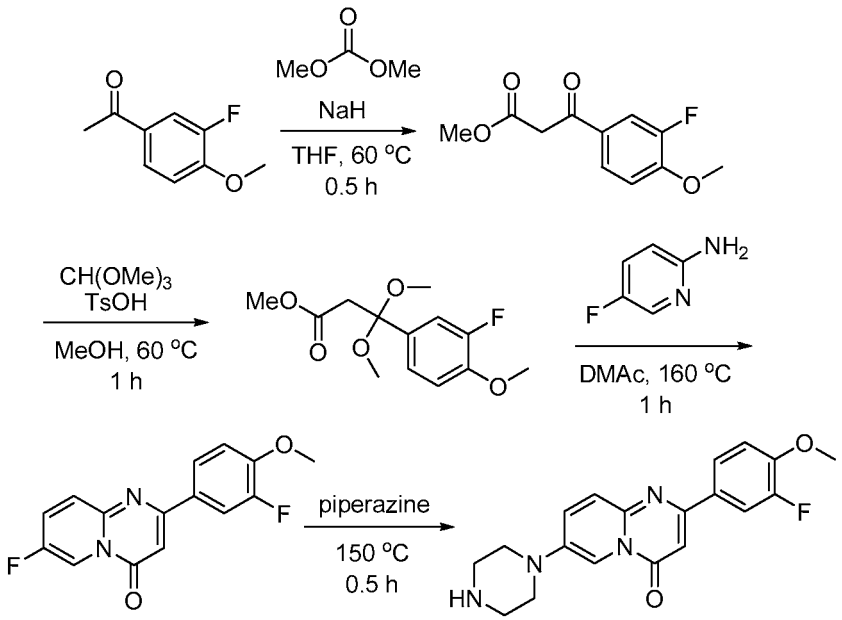
Abbreviation	Meaning
ACN	acetonitrile
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthalene
$B(OiPr)_3$	triisopropyl borate
Boc	tert-butoxy-carbonyl
Boc_2O	di-tert-butyl dicarbonate
BuOH	*n*-butanol
°C	degrees Centigrade
CDI	1,1-carbonyldiimidazole or N,N'-carbonyldiimidazole
$(CHO)_n$ or $(HCHO)_n$	paraformaldehyde
d/h/hr/hrs/min/s	day(d)/hour(h, hr or hrs)/minute(min)/second(s)
DavePhos	2-dicyclohexylphosphino-2′-(N,N-dimethylamino)biphenyl
DCE	1,2-dichloroethane
DCM	dichloromethane (CH_2Cl_2)
DIAD	diisopropyl azodicarboxylate
DIEA or DIPEA	N,N-diisopropylethylamine
DMA	dimethylacetamide
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EDC or EDCI	*N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride
EtOAc	ethyl acetate
EtOH	ethanol
Et_2O	diethyl ether
HCOH	formaldehyde
iPrI	iodopropane
JohnPhos	(2-biphenyl)-di-t-butylphosphine
KOAc	potassium acetate
LAH	lithium aluminum hydride
LC/MS, LCMS or LC-MS	liquid chromatographic mass spectroscopy
LDA	lithium diisopropylamine
LiHMDS or LHMDS	lithium bis(trimethylsilyl)amide
MeOH	methanol

Abbreviation	Meaning
MeI	iodomethane
Me-THF	2-methyltetrahydrofuran
Me_2Zn	dimethylzinc
MnO_2	manganese dioxide
MS	mass spectroscopy
NaH	sodium hydride
NaHS	sodium hydrosulfide
NaHMDS	sodium bis(trimethylsilyl)amide or sodium hexamethyldisilazide
NaI	sodium iodide
NaOAc	sodium acetate
NaOMe	sodium methoxide
NBS	N-bromosuccinimide
NMP	N-methylpyrrolidone
NMR	nuclear magnetic resonance
o/n	overnight
Pd	palladium
Pd/C	palladium on carbon
$Pd(dba)_2$	bis(dibenzylideneacetone)palladium
$Pd_2(dba)_3$ or Pd_2dba_3	tris(dibenzylideneacetone)dipalladium(0)
$PdCl_2(PhCN)_2$	trans-bis(benzonitrile)dichloropalladium(II)
$PdCl_2(dppf)$, $PdCl_2dppf$ or $Pd(dppf)Cl_2$	[1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)
$Pd(OAc)_2$	palladium(II) acetate
$Pd(PPh_3)_4$ or $Pd(Ph_3P)_4$	tetrakis(triphenylphosphine)palladium(0)
$Pd(PPh_3)_2Cl_2$, $PdCl_2(PPh_3)_2$ or $PdCl_2(Ph_3P)_2$	bis(triphenylphosphine)palladium(II) dichloride
$PHBu_3BF_4$ or tBu_3PHBF_4	tri-tert-butylphosphonium tetrafluoroborate
PhI	iodobenzene
$PhI(OTFA)_2$	[bis(trifluoroacetoxy)iodo]benzene
PhMe	toluene
Ph-NTf2 or $PhNTf_2$	N-phenyl triflimide, also referred to as N-phenyl-bis(trifluoromethanesulfonimide)
$POCl_3$	phosphoryl chloride
PPh_3	triphenylphosphine
PPA	polyphosphoric acid

Abbreviation	Meaning
PPTs	pyridinium *p*-toluenesulfonate
Psi	pounds per square inch pressure
PyBOP	(benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate
rt	room temperature
S-Phos, SPhos or Sphos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
T_3P	propylphosphonic anhydride
TEA, Et_3N or NEt_3	triethylamine
Tf_2O	triflic anhydride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilane
TMSCl	trimethylchlorosilane or trimethylsilyl chloride
TMSOK	potassium trimethylsilanolate
t-Bu	tert-butyl
TsOH, p-TsOH or *p*TSA	tosylic acid or *p*-toluenesulfonic acid
xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

[001164] **Example 1**

[001165] Preparation of Cpd 72



[001166] Step A: 3′-Fluoro-4′-methoxyacetophenone (336 mg, 2 mmol) was dissolved in THF (4 mL). To the solution was added dimethyl carbonate (0.42 mL, 5 mmol) and sodium hydride (200 mg, 5 mmol, 60% dispersion in mineral oil) sequentially. The mixture was heated to 60 °C for 30 minutes. After cooling the mixture to 0 °C, the remaining sodium hydride was quenched with 1N aqueous HCl (20 mL). The mixture was extracted with EtOAc (20 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was eluted from silica gel with EtOAc (25%) in hexanes, affording methyl 3-(3-fluoro-4-methoxyphenyl)-3-oxopropanoate as a pale yellow oil (405 mg, 89%). MS *m/z* 227.2 $[M+H]^+$; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.76 (1H, dd, J = 8.6 Hz, 2.1 Hz), 7.72 (1H, dd, J = 11.7 Hz, 2.2 Hz), 7.04 (1H, t, J = 8.4 Hz), 3.99 (3H, s), 3.97 (2H, s), 3.78 (3H, s).

[001167] Step B: methyl 3-(3-fluoro-4-methoxyphenyl)-3-oxopropanoate (405 mg, 1.8 mmol) was dissolved in methanol (1 mL). p-Toluenesulfonic acid monohydrate (17 mg, 0.09 mmol) was added to the solution, followed by trimethylorthoformate (0.30 mL, 2.7 mmol). The solution was stirred at 60 °C for 1 hour. Volatiles were removed with a stream of nitrogen providing crude methyl 3-(3-fluoro-4-methoxyphenyl)-3,3-dimethoxypropanoate. ^1H NMR (DMSO-d_6, 500 MHz): δ 7.18-7.15 (3H, m), 3.85 (3H, s), 3.38 (3H, s), 3.10 (6H, s), 2.98 (2H, s).

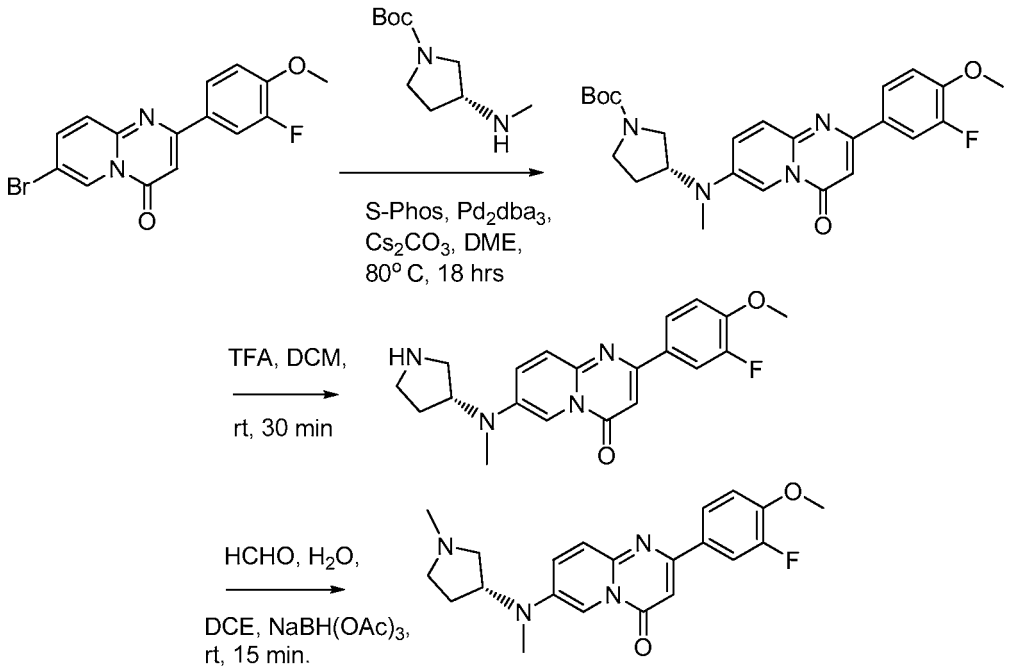
[001168] Step C: To the crude material (1.8 mmol) from Step B was added 5-fluoropyridin-2-amine (213 mg, 1.9 mmol). The mixture was heated neat to 160 °C for 1 hour to provide 7-fluoro-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (475 mg, 92%). MS *m/z* 289.2 $[M+H]^+$; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.99 (1H, m), 7.92 (1H, dd, J = 12.5 Hz, 2.2 Hz), 7.90 (1H, d, 8.5 Hz), 7.88 (1H, m), 7.73 (1H, m), 7.10 (1H, t, J = 8.5 Hz), 6.85 (1H, s), 3.99 (3H, s).

[001169] Step D: 7-Fluoro-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (200 mg, 0.7 mmol) was combined with piperazine (430 mg, 3.5 mmol) in dimethylacetamide (0.5 mL). The mixture was stirred at 150 °C for 0.5 hours, then chromatographed on silica gel, eluting with 0% to 8% MeOH (3% NH_3) in CH_2Cl_2. The title compound was obtained as a yellow powder (175 mg, 71%). M.P. 191-195 °C; MS *m/z* 355.0 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.20 (1H, d, J = 2.7 Hz), 8.07-8.02 (3H, m), 7.67 (1H, d, J = 9.7 Hz), 7.28 (1H, t, J = 8.7 Hz), 6.93 (1H, s), 3.13 (4H, m), 2.90 (3H, s), 2.88 (4H, m), 2.34 (1H, br s).

[001170] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 1 by substituting the appropriate starting materials, reagents and reaction conditions.

[001171] **Example 2**

[001172] Preparation of Cpd 239



[001173] Step A: A mixture of 7-bromo-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (250 mg, 0.72 mmol), (R)-tert-butyl 3-(methylamino)pyrrolidine-1-carboxylate (180 mg, 0.90 mmol), Pd_2dba_3 (61 mg, 0.065 mmol), dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine (SPhos, 78 mg, 0.19 mmol), Cs_2CO_3 (500 mg, 1.53 mmol), and 1,2-dimethoxyethane (DME, 2.0 mL) were stirred under an argon atmosphere at 80° C for 18 hours. The reaction mixture was then diluted with CH_2Cl_2/MeOH (9:1) and was filtered to remove solids. The filtrate was concentrated under vacuum. Purification by silica gel chromatography (10% to 20% acetone in CH_2Cl_2), followed by an ether wash, yielded (R)-tert-butyl 3-((2-(3-fluoro-4-methoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)(methyl)amino)pyrrolidine-1-carboxylate (132 mg, 39%) as a light tan solid. MS *m/z* 469.0 $[M+H]^+$.

[001174] Step B: A solution of (R)-tert-butyl 3-((2-(3-fluoro-4-methoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)(methyl)amino)pyrrolidine-1-carboxylate (130 mg, 0.28 mmol) in

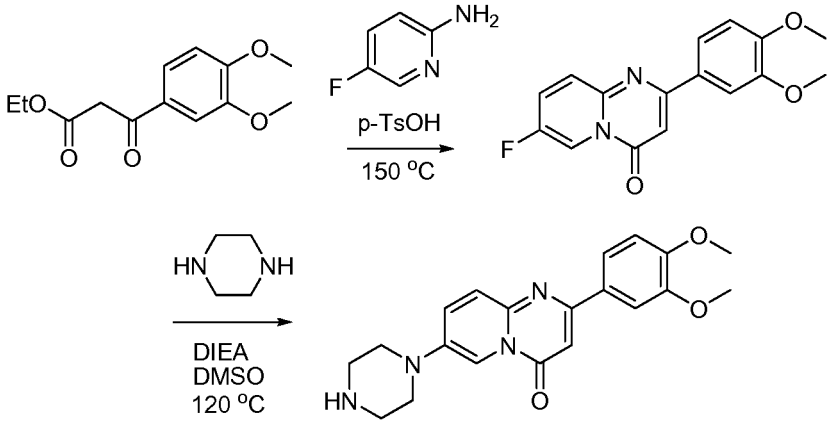
CH_2Cl_2 (2.0 mL) and TFA (500 μL) was stirred at room temperature for 30 minutes. The mixture was poured into 1N NaOH solution (50 mL). The product was extracted into CH_2Cl_2/EtOH (9:1). The organic layer was concentrated under vacuum. Purification by silica gel chromatography (CH_2Cl_2/MeOH/NH_4OH = 9/1/0.1) yielded (R)-2-(3-fluoro-4-methoxyphenyl)-7-(methyl(pyrrolidin-3-yl)amino)-4H-pyrido[1,2-a]pyrimidin-4-one (82 mg, 79%) as a yellow solid. MS *m/z* 369.1 $[M+H]^+$.

[001175] Step C: A mixture of (R)-2-(3-fluoro-4-methoxyphenyl)-7-(methyl(pyrrolidin-3-yl)amino)-4H-pyrido[1,2-a]pyrimidin-4-one (45 mg, 0.12 mmol), DCE (500 μL), formaldehyde (37% w/w in H_2O, 200 μL), and $NaBH(OAc)_3$ (85 mg, 0.40 mmol) was stirred at room temperature for 15 minutes. The reaction mixture was added to an aqueous K_2CO_3 solution, and the title product was extracted into CH_2Cl_2. The organic layer was concentrated under vacuum. Purification by silica gel chromatography (10% MeOH in CH_2Cl_2) yielded the title compound (39 mg, 85%) as an off-white solid. M.P. 143-149 °C; MS *m/z* 383.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.13 (d, 1H, J = 3 Hz), 8.0-8.1 (m, 3H),.7.69 (d, 1H, J = 10 Hz), 7.29 (t, 1H, J = 9.0 Hz), 6.90 (s, 1H), 4.58 (m, 1H), 3.92 (s, 3H), 2.93 (3H, s), 2.81 (m, 1H), 2.75 (m, 1H), 2.49 (m, 1H, obscured by DMSO-d_6), 2.20 (m, 2H), 2.28 (s, 3H), 1.76 (m, 1H).

[001176] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 2 by substituting the appropriate starting materials, reagents and reaction conditions.

[001177] **Example 3**

[001178] Preparation of Cpd 6



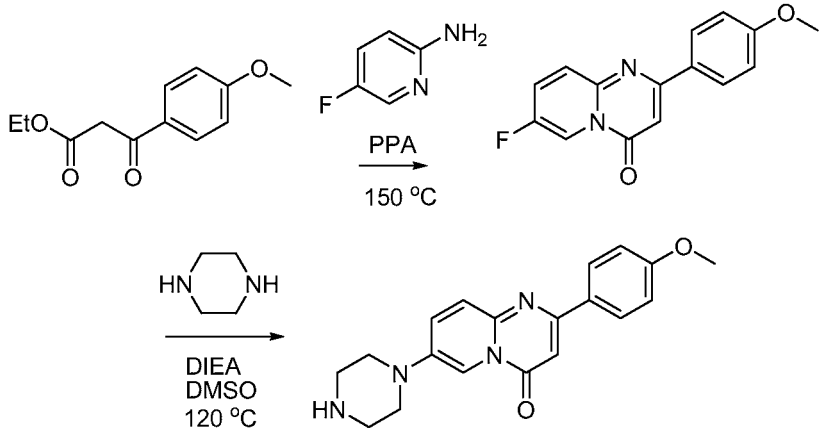
Step A: A mixture of ethyl 3-(3,4-dimethoxyphenyl)-3-oxopropanoate (2.02 g, 8.0 mmol), 2-amino-5-fluoropyridine (0.897 g, 8.0 mmol) and *p*-TsOH (152 mg, 0.8 mmol) was heated at 150 °C. The mixture was melted and then solidified. After1 hour, the mixture was cooled to room temperature and washed with MeCN to give 2-(3,4-dimethoxyphenyl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (1.356 g, 56%). MS *m/z* 367.5 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.92 (1H, dd, *J* = 2.9 Hz, 4.8 Hz), 8.11-8.07 (1H, m), 7.85-7.82 (1H, m),7.77 (1H, d, *J* = 2.1 Hz), 7.09 (1H, d, *J* = 8.6 Hz), 7.06 (1H, s), 6.93 (1H, s), 3.88 (3H, s), 3.84 (3H, s),

[001179] Step B: A mixture of 2-(3,4-dimethoxyphenyl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (1.50 g, 5.0 mmol), piperazine (1.29 g, 15 mmol) and DIEA (1.3 mL, 7.5 mmol) in DMSO (10 mL) was heated at 120 °C. After 15 hours, the volatiles were removed and the residue was washed with MeCN to give the title compound as a yellow solid (1.674 g, 91%).
M.P. 182-184 °C; MS *m/z* 367.5 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (1H, d, J = 2.7 Hz), 8.04 (1H, dd, *J* = 2.8 Hz, 9.8 Hz), 7.79 (1H, dd, *J* = 2.1 Hz, 8.5 Hz), 7.74 (1H, d, J = 2.1 Hz), 7.67 (1H, d, *J* = 9.7 Hz), 7.07 (1H, d, *J* = 8.5 Hz), 6.93 (1H, s), 3.87 (3H, s), 3.83 (3H, s), 3.12 (4H, m), 2.88 (4H, m).

[001180] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 3 by substituting the appropriate starting materials, reagents and reaction conditions.

[001181] **Example 4**

[001182] Preparation of Cpd 1



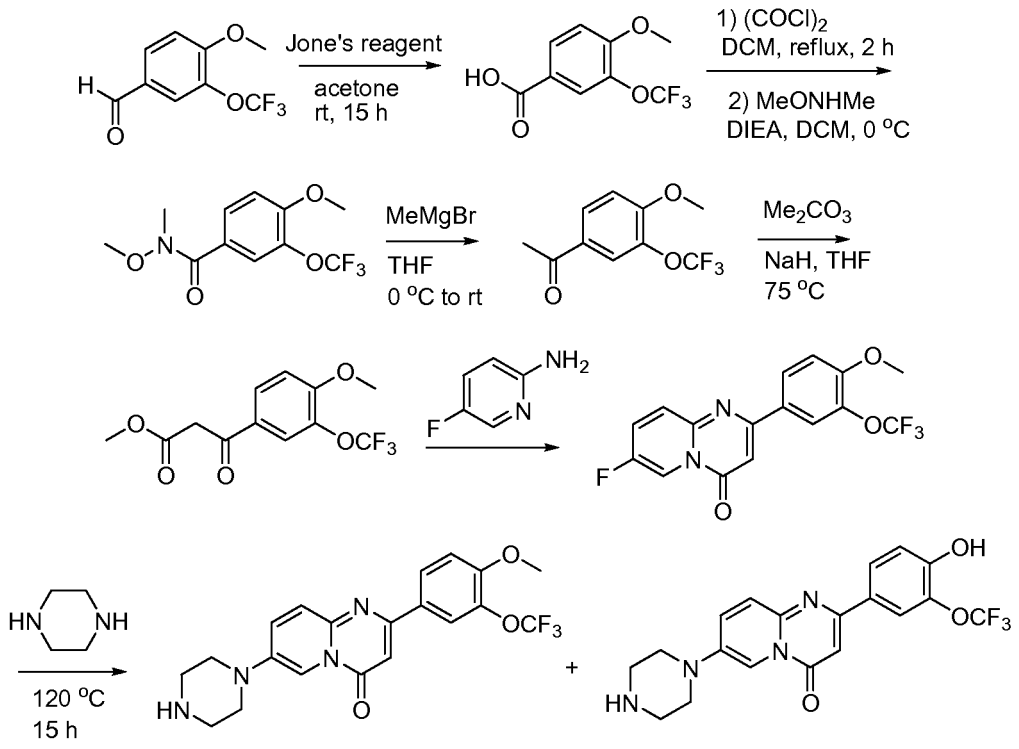
[001183] Step A: A mixture of ethyl 3-(3-methoxyphenyl)-3-oxopropanoate (2.68 mL, 14.0 mmol) and 2-amino-5-fluoropyridine (1.12 g, 10.0 mmol) in PPA (~5 g) was heated at 120 °C. After 0.5 hours, the dark purple mixture was cooled to room temperature and treated with ice-water. The precipitate was filtered, washed with water and MeCN to give 2-(4-methoxyphenyl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a slightly yellow solid (1.758 g, 65%). MS *m/z* 271.2 $[M+H]^+$.

[001184] Step B: Following the procedure in Example 3, Step B, 7-fluoro-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (81 mg, 0.3 mmol) and piperazine (129 mg, 1.5 mmol) in DMSO (1 mL) gave the title compound as a yellow solid (66 mg, 66%). M.P. 182-184 °C; MS *m/z* 337.3 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (1H, d, J = 2.6 Hz), 8.16 (2H, dd, J = 2.0 Hz, 7.0 Hz), 8.05 (1H, dd, J = 2.7 Hz, 9.7 Hz), 7.67 (1H, d, J = 9.7 Hz), 7.05 (2H, d, J = 1.9 Hz, 7.0 Hz), 6.86 (1H, s), 3.83 (3H, s), 3.12 (4H, m), 2.87 (4H, m).

[001185] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 4 by substituting the appropriate starting materials, reagents and reaction conditions.

[001186] **Example 5**

[001187] Preparation of Cpd 81 and Cpd 82



[001188] Step A: To a solution of 4-methoxy-3-(trifluoromethoxy)benzaldehyde (1.0 g, 4.5 mmol) in acetone (30 mL) was added Jone's reagent (5 mL). After stirring at room temperature for 15 hours, methanol (2 mL) was added and the mixture was filtered. The filtrate was concentrated, dissolved in EtOAc and washed with water. The organics were dried and concentrated to give 4-methoxy-3-(trifluoromethoxy)-benzoic acid as a white solid (1.02 g, 96%), MS *m/z* 235.2 $[M-H]^-$.

[001189] Step B: To a solution of 4-methoxy-3-(trifluoromethoxy)benzoic acid (1.02 g, 4.32 mmol) in DCM (10 mL) was added oxalyl chloride (5 mL). After refluxing for 6 hours, the solution was concentrated to give 4-methoxy-3-(trifluoromethoxy)-benzoyl chloride. The crude acid chloride was dissolved in DCM (10 mL) and cooled to 0 °C. Diisopropylethylamine (1.56 mL, 9.0 mmol) and N,O-dimethylhydroxylamine (0.658 g, 6.7 mmol) were added. After stirring at room temperature for 2 hours, the mixture was washed with water. The organics were dried, concentrated and chromatographed (5% EtOAc in CH_2Cl_2) to give 4-dimethoxy-N-methyl-3-(trifluoromethoxy)benzamide as an amber oil (0.58 g, 48%).

[001190] Step C: To a solution of 4-dimethoxy-N-methyl-3-(trifluoromethoxy)-benzamide (0.58 g, 2.08 mmol) in THF (8 mL) at 0 °C was added MeMgBr (3.0 M, 0.83 mL, 2.5 mmol). After stirring at room temperature for 15 hours, the solution was washed with water. The organics were dried and concentrated to give 11-(4-methoxy-3-(trifluoromethoxy)phenyl)ethanone as a white solid (0.45 g, 96%).

[001191] Step D: To a solution of the crude 1-(2-fluoro-4,5-dimethoxyphenyl)-ethanone (0.45 g, 2.0 mmol) and dimethyl carbonate (1.5 mL, 18.2 mmol) in THF (8 mL) at room temperature was added NaH (60%, 0.44 g, 10.9 mmol). After heating at 75 °C for 20 minutes, the mixture was quenched with NH_4Cl (satd.). The pH of the mixture was adjusted to neutral with 1N HCl. The mixture was extracted with EtOAc. The organics were dried and concentrated to give methyl 3-(4-methoxy-3-(trifluoromethoxy)phenyl)-3-oxopropanoate. MS *m/z* 299.1 $[M+H]^+$. The crude product was used directly in the next step.

[001192] Step E: A solution of the crude methyl 3-(4-methoxy-3-(trifluoromethoxy)phenyl)-3-oxopropanoate (2 mmol) from step D, *p*-TsOH (38 mg, 0.2 mmol) and trimethoxymethane in MeOH (4 mL) was heated at 60 °C. After 1 hour, the volatiles were removed and 2-amino-5-fluoropyridine (0.224 g, 2.0 mmol) was added. The mixture was heated at 150 °C for 1 hour, cooled to room temperature and washed with MeCN to give 7-fluoro-2-(4-methoxy-3-(trifluoromethoxy)phenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (146 mg, 21%). MS *m/z* 355.1 $[M+H]^+$.

[001193] Step F: A mixture of 7-fluoro-2-(4-methoxy-3-(trifluoromethoxy)phenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (71 mg, 0.2 mmol), piperazine (38 mg, 0.4 mmol) and diisopropylethylamine (69 uL, 0.4 mmol) in DMSO (0.5 mL) was heated at 120 °C. After 15 hours, the volatiles were removed and the residue was chromatographed (20% MeOH in DCM) to give two products:

[001194] Cpd 81 (8 mg, 9%) was obtained as a yellow solid. M.P. 158-162 °C; MS *m/z* 421.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.26 (1H, d, J = 2.6 Hz), 8.24 (1H, dd, J = 2.2 Hz, 8.8 Hz), 8.19 (1H, m), 8.08 (1H, dd, J = 2.8 Hz, 9.7 Hz), 7.75 (1H, d, J = 9.7 Hz), 7.37 (1H, d, J = 8.8 Hz), 6.99 (1H, s), 3.94 (3H, s), 3.07 (4H, m), 2.50 (4H, m, obscured by DMSO-d_6; and,

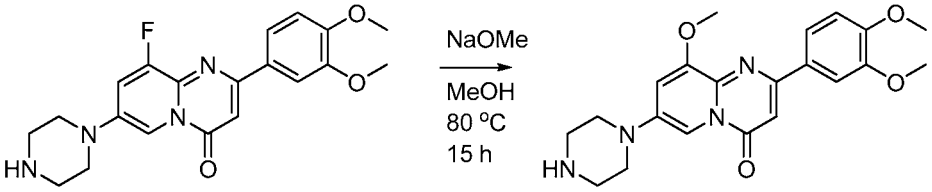
[001195] Cpd 82 (9 mg, 11%) was obtained as a yellow solid. M.P. 245-248 °C; MS *m/z* 407.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.21 (1H, d, J = 2.7 Hz), 8.11 (1H, m), 8.07-8.03

(2H, m), 7.68 (1H, d, J = 9.7 Hz), 7.11 (1H, d, *J* = 8.6 Hz), 6.87 (1H, s), 3.14 (4H, m), 2.88 (4H, m).

[001196] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 5 by substituting the appropriate starting materials, reagents and reaction conditions.

[001197] **Example 6**

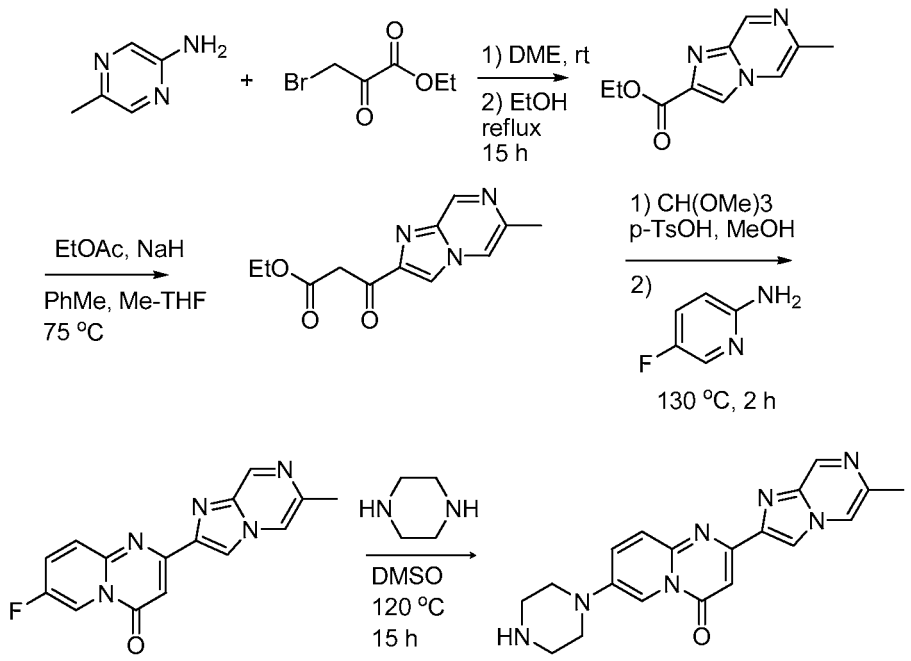
[001198] Preparation of Cpd 70



[001199] To a suspension of 2-(3,4-dimethoxyphenyl)-9-fluoro-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (38 mg, 0.1 mmol, prepared by following the procedures in Example 3, Steps A and B in MeOH (0.5 mL) was added NaOMe (0.5 M in MeOH, 1 mL, 0.5 mmol). After heating at 80 °C for 15 hours, the volatiles were removed and the residue was chromatographed (10-15% MeOH/CH_2Cl_2) to give the title compound as a yellow solid (18 mg, 45%). M.P. 185-187 °C; MS *m/z* 397.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.20 (1H, d, J = 2.5 Hz), 7.80 (2H, m), 7.08 (1H, d, *J* = 9.0 Hz), 7.00 (1H, s), 6.97 (1H, d, *J* = 2.5 Hz), 3.89 (3H, s), 3.87 (3H, s), 3.83 (3H, s), 3.30 (4H, m), 2.98 (4H, m).

[001200] **Example 7**

[001201] Preparation of Cpd 74



[001202] Step A: To a solution of 2-amino-5-methylpyrazine (1.09 g, 10 mmol) in DME (10 mL) was added ethyl 3-bromo-2-oxopropanoate (1.57 mL, 12.5 mmol). The mixture was stirred at room temperature for 45 minutes. The precipitate was filtered, washed with Et_2O and dried to give a yellow solid. The solid was suspended in EtOH (20 mL) and heated at 90 °C. After 1.5 hours, the resulting brown solution was concentrated and adjusted to pH 7. The mixture was extracted with EtOAc. The organics were concentrated and the residue was triturated and washed with MeCN to give ethyl 6-methylimidazo[1,2-a]pyrazine-2-carboxylate as a brown solid (0.993 g, 48%). MS *m/z* 206.2 $[M+H]^+$.

[001203] Step B: To a solution of ethyl 6-methylimidazo[1,2-a]pyrazine-2-carboxylate (0.971 g, 4.73 mmol) and EtOAc (0.98 mL, 10 mmol) in toluene (2 mL) and Me-THF (8 mL) at room temperature was added NaH (60%, 0.503 mg, 12.6 mmol). After heating at 70 °C for 30 minutes, the mixture was cooled to room temperature, quenched with ice, adjusted to pH 7 with 1N HCl and extracted with EtOAc. The organics were combined, dried, concentrated and chromatographed to give ethyl 3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-3-oxopropanoate as a brownish oil (0.93 g, 78%).

[001204] Step C: Following the procedure in Example 1 Step B, ethyl 3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-3-oxopropanoate (0.913 g, 3.7 mmol), p-toluenesulfonic acid monohydrate (70 mg, 0.37 mmol) and trimethylorthoformate (0.81 mL, 7.4 mmol) in MeOH (10 mL) afforded the ketal which was used directly in the next step.

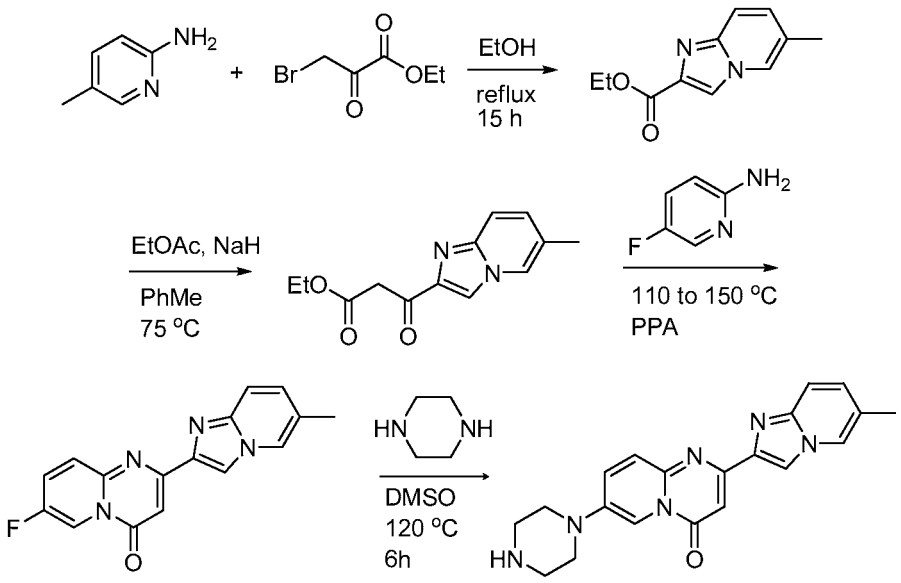
[001205] Step D: Following the procedure in Example 1 Step C, the crude dimethoxypropanoate (from Step C and 2-amino-5-fluoro-pyridine (0.422 g, 3.7 mmol) gave 7-fluoro-2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a brownish solid (0.344 g, 31%). MS *m/z* 295.9 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.09 (1H, s), 8.97-8.96 (1H, m), 8.67 (1H, s), 8.47 (1H, s), 8.15-8.11 (1H, m), 7.85-7.82 (1H, m), 7.08 (1H, s), 2.42 (3H, S).

[001206] Step E: Following the procedure in Example 3, Step B, 7-fluoro-2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (59 mg, 0.2 mmol) and piperazine (52 mg, 0.6 mmol) in DMSO (0.5 mL) gave the title compound as a yellow solid (28 mg, 39%). M.P. 221-225 °C; MS *m/z* 362.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.07 (1H, s), 8.62 (1H, s), 8.46 (1H, s), 8.25 (1H, d, J = 2.6 Hz), 8.09 (1H, d, J = 2.7 Hz, 9.7 Hz), 7.67 (1H, d, J = 9.7 Hz), 7.00 (1H, s), 3.16 (4H, m), 2.90 (4H, m), 2.44 (3H, s).

[001207] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 7 by substituting the appropriate starting materials, reagents and reaction conditions.

[001208] **Example 8**

[001209] Preparation of Cpd 29



[001210] Step A: Following the procedure in Example 7, Step A, 2-amino-5-methylpyridine (5.41 g, 50 mmol) and ethyl 3-bromo-2-oxopropanoate (7.0 mL, 50 mmol) in MeOH (50 mL) gave ethyl 6-methylimidazo[1,2-a]pyridine-2-carboxylate as a yellowish solid (9.50 g, 93%), MS *m/z* 205.1 $[M+H]^+$.

[001211] Step B: Following the procedure in Example 7, Step B, ethyl 6-methylimidazo[1,2-a]pyridine-2-carboxylate (0.55 g, 2.5 mmol), EtOAc (0.29 mL, 5.0 mmol) and NaH (60%, 0.20 g, 5 mmol) in toluene (5 mL) gave ethyl 3-(6-methylimidazo[1,2-a]pyridin-2-yl)-3-oxopropanoate as a yellow solid (0.62 g, 100%), MS *m/z* 243.1 $[M+H]^+$.

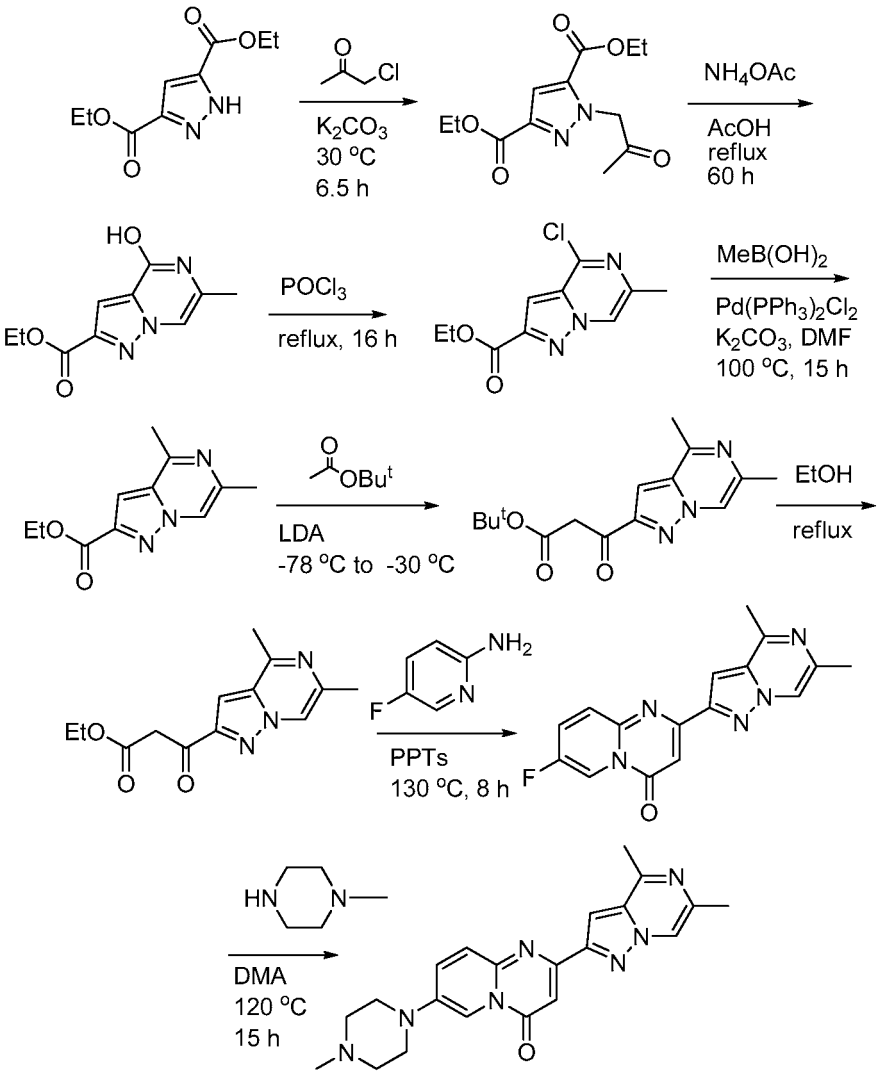
[001212] Step C: Following the procedure in Example 4, Step A, ethyl 3-(6-methylimidazo[1,2-a]pyridin-2-yl)-3-oxopropanoate (246 mg, 1.0 mmol) and 2-amino-5-fluoropyridine (334 mg, 1.2 mmol) in PPA (~5 g) gave 7-fluoro-2-(6-methylimidazo[1,2-a]pyridin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (17 mg, 6%), MS *m/z* 295.2 $[M+H]^+$.

[001213] Step D: Following the procedure in Example 3, Step B, 7-fluoro-2-(6-methylimidazo[1,2-a]pyridin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (17 mg, 0.06 mmol) and piperazine (30 mg, 0.3 mmol) in DMSO (10 mL) gave the title compound as a light brown solid (19 mg, 83%). M.P. 193-198 °C; MS *m/z* 361.3 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.48 (1H, s), 8.41 (1H, s), 8.25 (1H, d, J = 2.6 Hz), 8.06 (1H, dd, J = 2.7 Hz, 9.7 Hz), 7.66 (1H,

d, J = 9.7 Hz), 7.55 (1H, d, 9.3 Hz), 7.18 (1H, d, *J* = 9.3 Hz), 6.96 (1H, s), 3.23 (4H, m), 3.01 (4H, m), 2.29 (3H, s).

[001214] **Example 9**

[001215] Preparation of Cpd 170



[001216] Step A: To a solution of diethyl 1H-pyrazole-3,5-dicarboxylate (10.0 g, 47 mmol) and chloroacetone (3.76 mL, 47 mmol) in acetone (200 mL) was added potassium carbonate (7.2 g, 52 mmol). After heating at 30 °C for 6 hours, the mixture was concentrated to remove the volatiles. The residue was taken into EtOAc and washed with water. The organics were dried over $MgSO_4$ and concentrated to give diethyl 1-(2-oxopropyl)-1H-pyrazole-3,5-dicarboxylate as a light brown solid, which was used directly in the next step, MS *m/z* 269.1 $[M+H]^+$.

[001217] Step B: To a solution of diethyl 1-(2-oxopropyl)-1H-pyrazole-3,5-dicarboxylate (~47 mmol) in acetic acid (300 mL) was added ammonium acetate (72 g, 940 mmol). After refluxing for 48 hours, the mixture was concentrated to minimum volume and diluted with water. The precipitate was filtered, washed with water and MeCN to give ethyl 4-hydroxy-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate as a tan solid (6.7 g, 64%), MS *m/z* 222.1 $[M+H]^+$.

[001218] Step C: A mixture of ethyl 4-hydroxy-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (7.18 g, 32.5 mmol) in $POCl_3$ (80 mL) was refluxed for 15 hours. The dark mixture was concentrated and washed with MeCN to give ethyl 4-chloro-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (5.197 g) as an off-white solid. The filtrate was concentrated and chromatographed to give an additional 1.42 g product (6.617 g, 85%) MS *m/z* 240.1 $[M+H]^+$, 242.1 $[M+2+H]^+$.

[001219] Step D: A mixture of ethyl 4-chloro-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (5.197 g, 21.7 mmol), $MeB(OH)_2$ (3.90 g, 65.1 mmol), K_2CO_3 (14.8 g, 107.5 mmol) and $Pd(PPh_3)_2Cl_2$ in (456 mg, 0.65 mmol) DMF (100 mL) was degassed and heated under N_2 for 15 hours. The mixture was concentrated on a rotovap to remove most of the DMF and washed with water. The residue was chromatographed (2% to 5% MeOH in CH_2Cl_2) to give ethyl 4,6-dimethylpyrazolo[1,5-a]pyrazine-2-carboxylate as a yellow solid (3.90 g, 82%), MS *m/z* 220.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.54 (1H, s), 7.49 (1H, s), 4.36 (2H, q, J = 7.2 Hz), 2.70 (3H, s), 2.42 (3H, s), 1.34 (3H, t, J = 7.2Hz).

[001220] Step E: To a solution of t-butyl acetate (1.63 mL, 12.1 mmol) in THF (50 mL) at -78 °C was added LDA (1.5 M, 0.97 mL, 14.5 mmol). After 0.5 hours, the solution was cannulated to a solution of ethyl 4,6-dimethylpyrazolo[1,5-a]pyrazine-2-carboxylate (1.33 g, 6.07 mmol) in THF (100 mL) at -30 °C. After 1 hour, the mixture was quenched with saturated NH_4Cl, adjusted to pH 5-6 and extracted with EtOAc. The combined organics were dried and concentrated. The residue was chromatographed (2% to 4% MeOH/ CH_2Cl_2) to give t-butyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate as a yellow oil (1.696 g, 97%), MS *m/z* 290.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.57 (1H, s), 7.50 (1H, s), 4.02 (2H, s), 2.70 (3H, s), 2.43 (3H, s), 1.38 (9H, s).

[001221] Step F: A solution of t-butyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (4.86 g, 16.8 mmol) in EtOH (30 mmol) was heated at 120 °C in a capped tube. After 1 hour, the solution was cooled to room temperature and the volatiles were removed to

give ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate as a yellow solid (4.44 g, 98%), MS *m/z* 262.2 $[M+H]^+$.

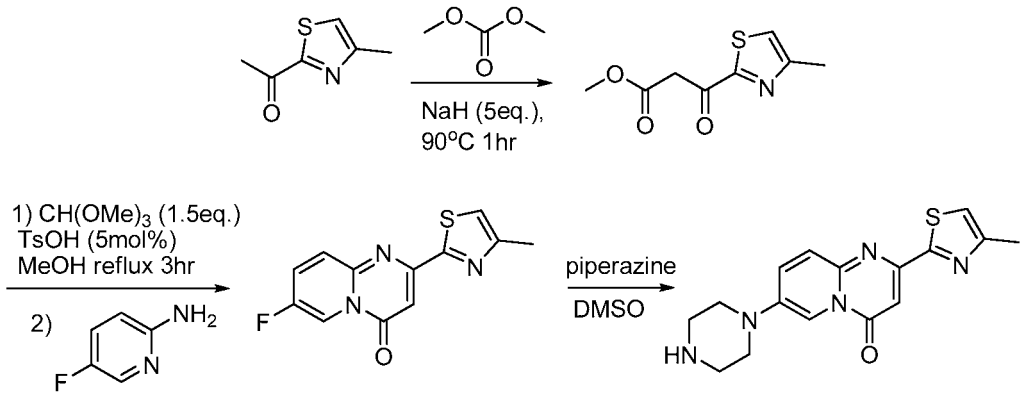
[001222] Step G: A mixture of 2-amino-5-fluoro-pyridine (134 mg, 1.2 mmol), ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (261 mg, 1.0 mmol) and PPTs (12.6 mg, 0.05 mmol) was heated at 130 °C. After 8 hours, the mixture was cooled to room temperature and chromatographed to give 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (220 mg, 71%). MS *m/z* 310.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.97-8.95 (1H, m), 8.55 (1H, s), 8.16-8.12 (1H, m), 7.87-7.85 (1H, m), 7.56 (1H, s), 7.03 (1H, s), 2.73, (3H, s), 2.43 (3H, s).

[001223] Step H: Following the procedure in Example 3, Step B, 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (309 mg, 1.0 mmol) and piperazine (1.1 mL, 10 mmol) in DMA (1.0 mL) gave the title compound as a yellow solid (313 mg, 80%). M.P. 254-256 °C; MS *m/z* 390.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.55 (1H, s), 8.27 (1H, d, J = 2.7 Hz), 8.12 (1H, dd, J = 2.8 Hz, 9.7 Hz), 7.71 (1H, d, J = 9.7 Hz), 7.54 (1H, s), 6.95 (1H, s), 3.25 (4H, m), 2.72 (3H, s), 2.51 (4H, m, obscured by DMSO-d_6), 2.43 (3H, s), 2.25 (3H, s).

[001224] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 9 by substituting the appropriate starting materials, reagents and reaction conditions.

[001225] **Example 10**

[001226] Preparation of Cpd 163



[001227] Step A: Following the procedure in Example 5, Step E, 2-acetyl-4-methylthiazole (706 mg, 5 mmol), dimethyl carbonate (15 mL, 178 mmol) and NaH (60% dispersion in mineral oil, 1.14 g, 28.5 mmol) provided methyl 3-(4-methylthiazol-2-yl)-3-oxopropanoate. The crude product was used directly in the next step. MS *m/z* 200.1 $[M+H]^+$.

[001228] Step B: Following the procedure in Example 1, Step B, 3-(4-methylthiazol-2-yl)-3-oxopropanoate (199 mg, 1.0 mmo), trimethylorthoformate (0.25 mL, 2.25 mmol) and toluenesulfonic acid monohydrate (14.3 mg, 0.075 mmol) in MeOH (1.5 mL) afforded the dimethoxypropanoate.

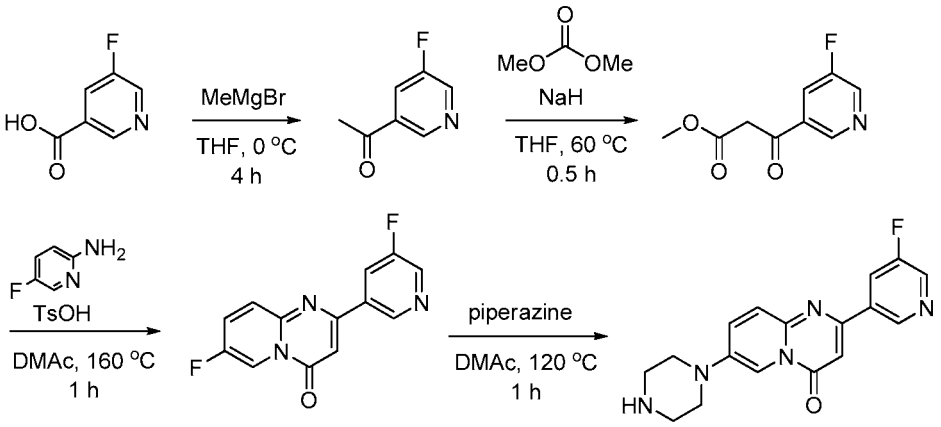
[001229] Step C: Following the procedure in Example 1, Step C the dimethoxypropanoate from Step B and 2-amino-4-fluoro-pyridine (201.8 mg, 1.8 mmol) in DMA (1.5 mL) provided 7-fluoro-2-(4-methylthiazol-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (175.5 mg, 67%). MS *m/z* 262.1 $[M+H]^+$.

[001230] Step D: Following the procedure in Example 3, Step B, 7-fluoro-2-(4-methylthiazol-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (52.2 mg, 0.2 mmol) and piperazine (86 mg, 1 mmol) in DMSO (0.8 mL) provided the title compound (20 mg, 30%). M.P. 142-147 °C; MS *m/z* 328.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.27 (1H, dd, J = 2.7 Hz, 18.6 Hz), 8.11-8.16 (1H, m), 7.73 (1H, t, J = 9.2 Hz), 7.56 (1H, s), 6.88 (1H, d, J = 3.2 Hz), 3.29-3.31 (2H, m), 3.16-3.18 (2H, m), 2.89-2.91 (2H, m), 2.67-2.69 (2H, m), 2.47 (3H, s).

[001231] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 10 by substituting the appropriate starting materials, reagents and reaction conditions.

[001232] **Example 11**

[001233] Preparation of Cpd 92



[001234] Step A: 5-Fluoronicotinic acid (1.0 g, 7.1 mmol) was dissolved in THF (10 mL) and cooled to 0 °C. A 1.4 M solution of methylmagnesium bromide in THF:toluene (3:1) (11.2 mL, 15.6 mmol) was added drop wise to the solution. The solution was allowed to warm to room temperature. The solution was stirred at room temperature for 4 hours, upon which 1N aqueous HCl (50 mL) was slowly added. The mixture was partitioned into EtOAc (200 mL) and aqueous 1N NaOH (200 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed on silica, eluting with EtOAc (0% to 50%) in hexanes to afford 1-(5-fluoropyridin-3-yl)ethanone as a white powder (290 mg, 29%).

[001235] Step B: Following the procedure in Example 5, Step D, the methyl ketone from Step A, dimethyl carbonate (0.44 mL, 5.25 mmol) and sodium hydride (210 mg, 60% dispersion in mineral oil, 5.25 mmol) in THF (6 mL) afforded methyl 3-(5-fluoropyridin-3-yl)-3-oxopropanoate as an off white powder (278 mg, 67%).

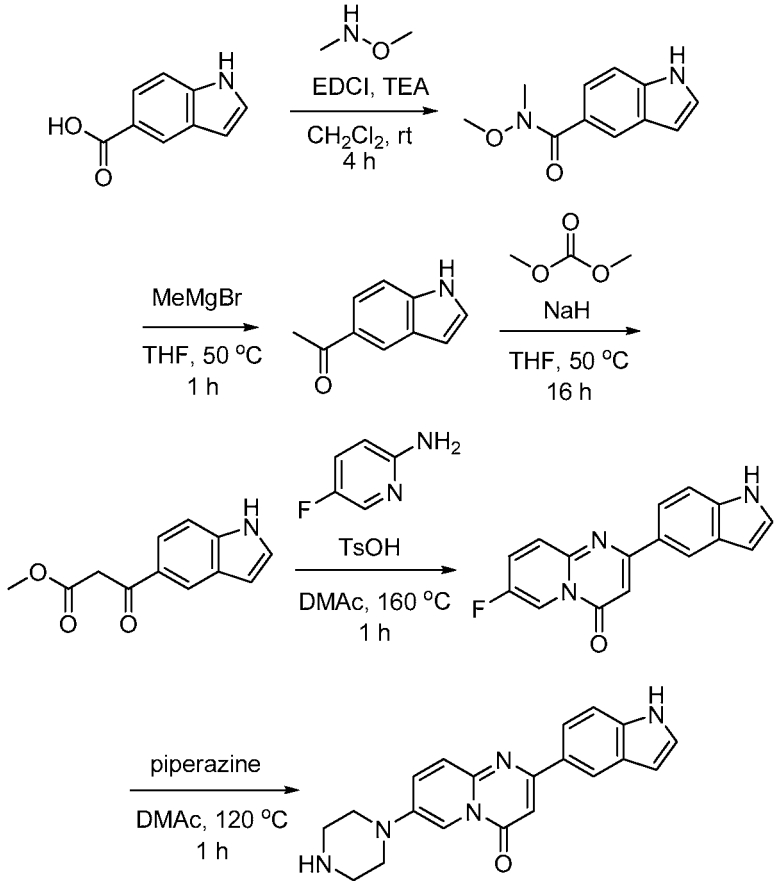
[001236] Step C: Methyl 3-(5-fluoropyridin-3-yl)-3-oxopropanoate (138 mg, 0.7 mmol) was combined with 5-fluoropyridin-2-amine (90 mg, 0.8 mmol) and toluenesulfonic acid monohydrate (6 mg, 0.03 mmol) in dimethylacetamide (0.5 mL). The mixture was heated to 160 °C for 1 hour. The mixture was cooled to 120 °C, before adding piperazine (300 mg, 3.5 mmol). The mixture was stirred at 120 °C for 1 hour. The mixture was loaded onto silica in CH_2Cl_2 and eluted with 0% to 8% MeOH (3% NH_3) in CH_2Cl_2. The title compound was obtained as a yellow powder (37 mg, 16%). M.P. 201-208 °C; MS *m/z* 326.2 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.25 (1H, s), 8.70 (1H, d, J = 2.8 Hz), 8.42 (1H, d, J = 10.2 Hz), 8.22 (1H, d, 2.7

Hz), 8.12 (1H, dd, J = 9.8 Hz, 2.8 Hz), 7.74 (1H, d, J = 9.7 Hz), 7.11 (1H, s), 3.16 (4H, m), 2.89 (4H, m), 2.37 (1H, br s).

[001237] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 11 by substituting the appropriate starting materials, reagents and reaction conditions.

[001238] **Example 12**

[001239] Preparation of Cpd 98



[001240] Step A: 1H-Indole-5-carboxylic acid (1.0 g, 6.2 mmol) was combined with N,O-dimethylhydroxylamine hydrochloride (907 mg, 9.3 mmol), N-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (1.78 g, 9.3 mmol) and N,N-diisopropylethylamine (3.2 mL, 18.6 mmol) in CH_2Cl_2 (12 mL). After stirring for 4 hours at room temperature, the mixture was washed with aqueous HCl (1N, 20 mL). The organic layer was dried over Na_2SO_4 and concentrated. The crude product was used directly in the next step.

[001241] Step B: The crude product from Step A was dissolved in THF (20 mL). A 1.4 M solution of methylmagnesium bromide (11.2 mL, 15.6 mmol) in THF:toluene (3:1), was added drop wise to the solution. The solution was allowed to warm to room temperature. The solution was stirred at 50 °C for 1 hour, upon which 1N aqueous HCl (50 mL) was slowly added. The mixture was partitioned into EtOAc (200 mL) and aqueous 1N NaOH (200 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed on silica, eluting with EtOAc (0% to 50%) in hexanes to afford 1-(1H-indol-5-yl)ethanone as a white powder (323 mg, 33%).

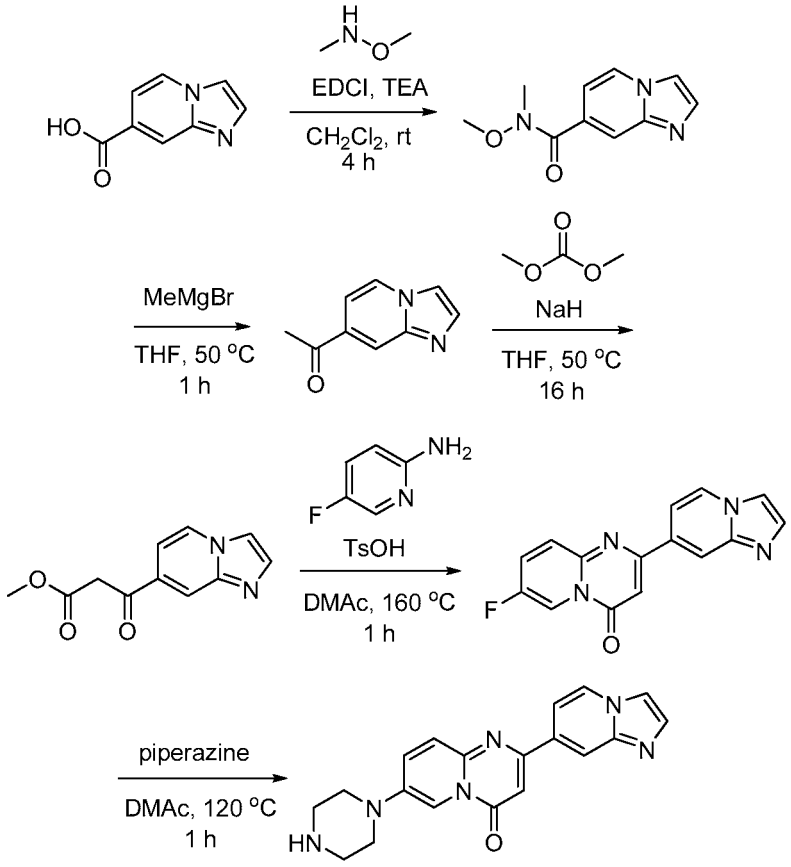
[001242] Step C: Following the procedure in Example 5, Step E, the methyl ketone from Step B, dimethyl carbonate (0.46 mL, 5.5 mmol) and sodium hydride (220 mg, 60% dispersion in mineral oil, 5.5 mmol) in THF (6 mL) afforded methyl methyl 3-(1H-indol-5-yl)-3-oxopropanoate as an off white powder (120 mg, 27%). MS *m/z* 216.1 $[M-H]^-$.

[001243] Step D: Following the procedure of Example 11, Step C, methyl 3-(1H-indol-5-yl)-3-oxopropanoate (98 mg, 0.45 mmol), 5-fluoropyridin-2-amine (56 mg, 0.5 mmol), toluenesulfonic acid monohydrate (9 mg, 0.05 mmol) and piperazine (194 mg, 2.25 mmol) in dimethylacetamide (0.5 mL) afforded the title compound as an off-white powder (40 mg, 26%). M.P. 266-272 °C.MS *m/z* 346.2 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 11.3 (1H, s), 8.46 (1H, s), 8.22 (1H, d, J = 2.8 Hz), 8.04 (1H, dd, J = 9.7 Hz, 2.8 Hz), 7.95 (1H, d, J = 8.7 Hz), 7.69 (1H, d, J = 9.7 Hz), 7.49 (1H, d, J = 8.6 Hz), 7.42 (1H, t, J = 2.7 Hz), 6.90 (1H, s), 6.57 (1H, m), 3.14 (4H, m), 2.89 (4H, m), 2.36 (1H, br s).

[001244] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 12 by substituting the appropriate starting materials, reagents and reaction conditions.

[001245] **Example 13**

[001246] Preparation of Cpd 107



[001247] Step A: Following the procedure in Example 12, Step A, imidazo[1,2-a]pyridine-7-carboxylic acid (1.0 g, 6.2 mmol), N,O-dimethylhydroxylamine hydrochloride (907 mg, 9.3 mmol), N-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (1.78 g, 9.3 mmol) and N,N-diisopropylethylamine (3.2 mL, 18.6 mmol) in CH_2Cl_2 (12 mL) gave N-methoxy-N-methylimidazo[1,2-a]pyridine-7-carboxamide (505 mg, 40%).

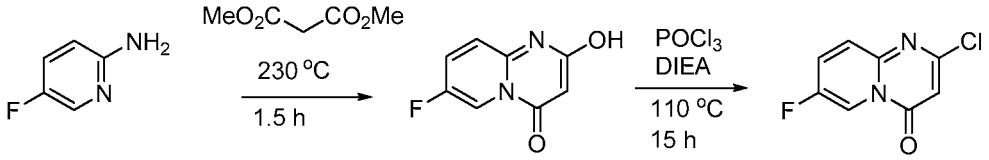
[001248] Step B: Following the procedure in Example 12, Step B, the product from Step A (505 mg, 2.5 mmol), methylmagnesium bromide (3.6 mmol) in THF (10 mL) afforded 1-(imidazo[1,2-a]pyridin-7-yl)ethanone (275 mg, 70%).

[001249] Step C: Following the procedure in Example 5, Step E, the methyl ketone from Step B (275 mg, 1.7 mmol), dimethyl carbonate (0.35 mL, 4.25 mmol) and sodium hydride (170 mg, 60% dispersion in mineral oil, 4.25 mmol) in THF (5 mL) afforded methyl 3-(imidazo[1,2-a]pyridin-7-yl)-3-oxopropanoate as an off-white powder (215 mg, 58%).

[001250] Step D: Following the procedure of Example 11, Step C, methyl 3-(imidazo[1,2-a]pyridin-7-yl)-3-oxopropanoate (215 mg, 1.0 mmol), 5-fluoropyridin-2-amine (123 mg, 1.1 mmol), toluenesulfonic acid monohydrate (19 mg, 0.1 mmol) and piperazine (430 mg, 5 mmol) in dimethylacetamide (1.0 mL) afforded the title compound as an off-white powder (40 mg, 12%). M.P. 258-270 °C; MS *m/z* 347.0 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.65 (1H, d, J = 7.2 Hz), 8.46 (1H, s), 8.24 (1H, d, J = 2.7 Hz), 8.11 (1H, dd, J = 9.7 Hz, 2.7 Hz), 8.06 (1H, s), 7.75 (1H, d, J = 9.7 Hz), 7.73 (1H, dd, J = 7.2 Hz, 2.7 Hz), 7.71 (1H, s), 7.10 (1H, s), 3.16 (4H, m), 2.89 (4H, m), 2.34 (1H, br s).

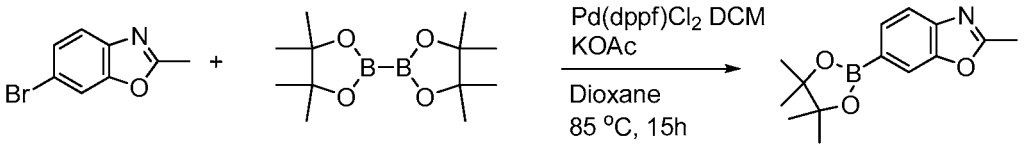
[001251] **Example 14**

[001252] Preparation of Cpd 171

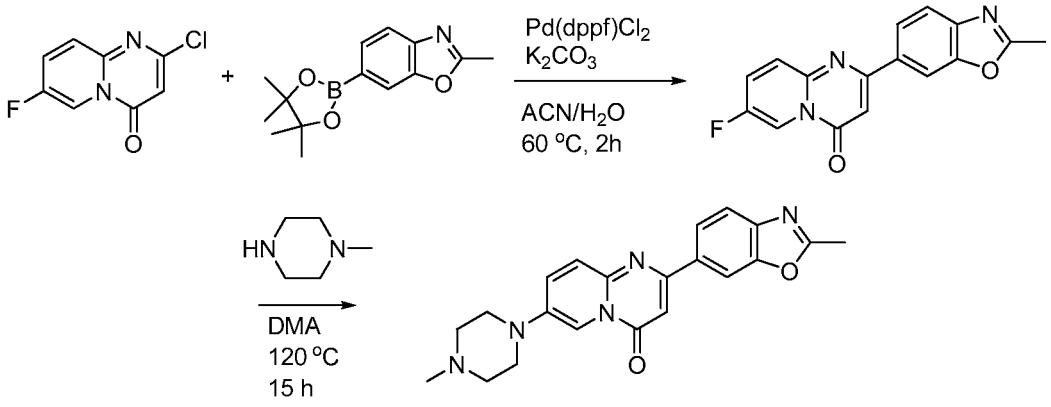


[001253] Part 1, Step A: A mixture of 2-amino-5-fluoropyridine (11.20 g, 0.10 mol) and dimethyl malonate (57.0 mL, 0.50 mol) was heated at 230 °C for 1.5 hours. After cooling to room temperature, the precipitate was filtered and washed with ACN (3x) to give 7-fluoro-2-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one as a dark solid (14 g), which was used directly in the next step. MS *m/z* 181.3 $[M+H]^+$.

[001254] Part 1, Step B: A dark mixture of crude 7-fluoro-2-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one (14g, ~77 mmol) in $POCl_3$ (50 mL) and DIEA (13.3 mL, 77 mmol) was heated at 110 °C for 15 hours. The volatiles were removed and the dark residue was treated with ice-water, washed with water (3x) and dried to give a brown solid. The crude brown solid was chromatographed (5% MeOH in CH_2Cl_2) to give 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (9.84 g, 50%, 2 steps), MS *m/z* 199.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.99 (1H, dd, J = 2.8 Hz, 4.7 Hz), 8.27-8.23 (1H, m), 7.85 (1H, dd, *J* = 5.4 Hz, 9.8 Hz), 6.56 (1H, s).



[001255] Part 2: A mixture of 6-bromo-2-methylbenzo[d]oxazole (1.06 g, 5.0 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.40 g, 5.5 mmol), KOAc (1.47 g, 15 mmol) and Pd(dppf)Cl_2•CH_2Cl_2 (122 mg, 0.15 mmol) in dioxane (8 mL) was degassed and heated under N_2 at 85 °C. After 15 hours, the mixture was diluted with EtOAc, filtered through celite and concentrated. The residue was chromatographed to give 2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]oxazole as a light orange solid (1.30 g, 100%), MS *m/z* 260.4 $[M+H]^+$.



[001256] Part 3, Step A: A mixture of 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.436 g, 2.2 mmol), 2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[d]oxazole (0.647 g, 2.5 mmol), Pd(dppf)Cl_2 in DCM (90 mg, 0.11 mmol), K_2CO_3 (2M, 3.0 mL, 6.0mmol), and ACN (6 mL) was degassed and then heated under N_2 at 60 °C for 3.5 hours. The volatiles were removed and the residue was chromatographed (2.5% MeOH/CH_2Cl_2) to give 7-fluoro-2-(2-methylbenzo[d]oxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as an off-white solid (0.64 g, 98%). MS *m/z* 296.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.96-8.95 (1H, m), 8.51 (1H, d, J = 1.6 Hz), 8.26 (1H, dd, *J* = 8.5 Hz, 1.6 Hz), 8.16-8.12 (1H, m), 7.91-7.88 (1H, m), 7.78 (1H, d, J = 8.4 Hz), 7.17 (1H, s), 2.67 (3H, s).

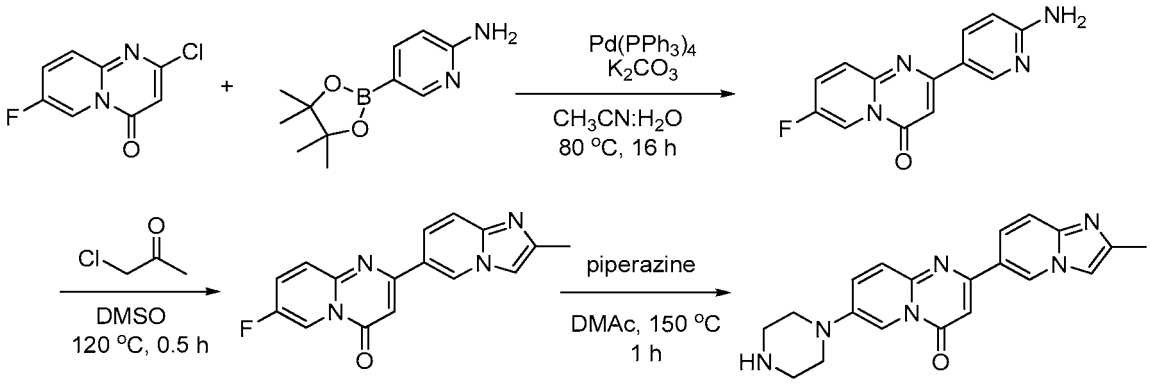
[001257] Part 3, Step B: A mixture of 7-fluoro-2-(2-methylbenzo[d]oxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (60 mg, 0.2 mmol) and 1-Methyl piperazine (0.11 mL, 1.0 mmol) in DMA (0.3 mL) was heated at 120 °C for 15 hours. The volatiles were removed and the residue was chromatographed to give the title compound as a yellow solid (46 mg, 61%).

M.P. 178-183 °C; MS *m/z* 376.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.47 (1H, d, *J* = 1.5 Hz), 8.25 (1H, d, J = 2.7 Hz), 8.23 (1H, dd, *J* = 1.6 Hz, 8.4 Hz), 8.11 (1H, dd, *J* = 2.8 Hz, 9.7 Hz), 7.76 (1H, d, J = 8.6 Hz), 7.74 (1H, d, *J* = 9.9 Hz), 7.06 (1H, s), 3.25 (4H, m), 2.66 (3H, s), 2.25 (3H, s).

[001258] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 14 by substituting the appropriate starting materials, reagents and reaction conditions.

[001259] **Example 15**

[001260] Preparation of 109



[001261] Step A: 2-Chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (990 mg, 5 mmol, prepared according to the procedure in Example 14, Part 1) was combined with 2-aminopyridine-5-boronic acid pinacol ester (1.21 g, 5.5 mmol), tetrakis(triphenylphosphine) palladium(0) (281 mg, 0.25 mmol), CH_3CN (10 mL) and aqueous K_2CO_3 (1M, 10 mL). The mixture was heated to 80 °C for 6 hours. The mixture was cooled to room temperature, and then filtered. The collected precipitate was washed with CH_3CN and dried under vacuum, providing 2-(6-aminopyridin-3-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow powder (1.13 g, 88%). MS *m/z* 257.0 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.90 (1H, m), 8.83 (1H, d, J = 2.1 Hz), 8.17 (1H, dd, J = 8.8 Hz, 2.5 Hz), 8.07 (1H, m), 7.78 (1H, dd, J = 9.8 Hz, 5.3 Hz), 6.87 (1H, s), 6.58 (2H, s), 6.53 (1H, d, 8.9 Hz).

[001262] Step B. 2-(6-Aminopyridin-3-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (254 mg, 1.0 mmol) was combined with chloroacetone (100 μL, 1.2 mmol) in DMSO (360 μL, 1.65 mmol). The mixture was heated to 120 °C for 30 minutes. After cooling to room temperature,

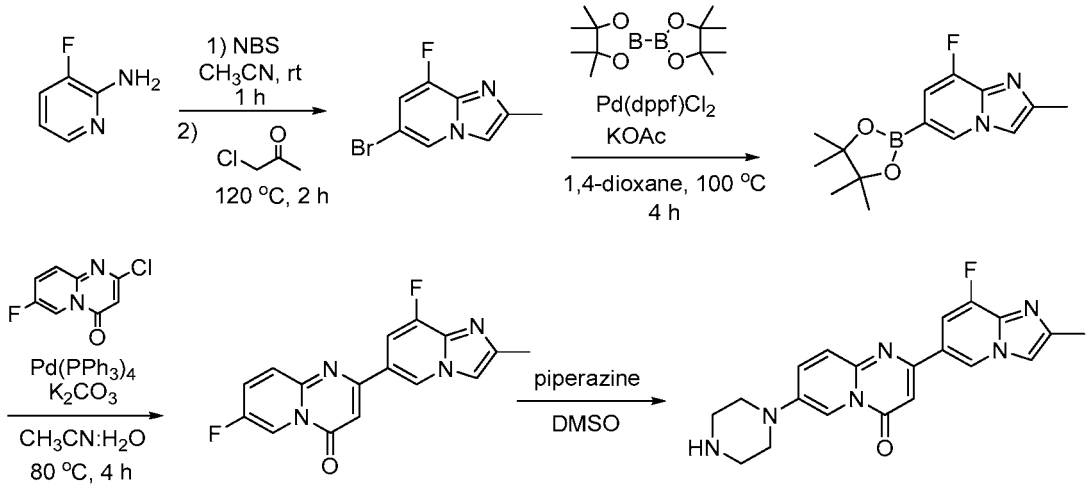
the mixture was partitioned in CH_2Cl_2 and saturated aqueous $NaHCO_3$. The organic layer was concentrated. The residue was eluted from silica with MeOH (0% to 6%) in CH_2Cl_2, affording 7-fluoro-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a tan powder (136 mg, 46%). MS *m/z* 295.0 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.40 (1H, s), 8.95 (1H, m), 8.14 (1H, m), 7.96 (1H, dd, J = 9.5 Hz, 1.9 Hz), 7.85 (2H, m), 7.54 (1H, J = 9.4), 7.08 (1H, s), 2.36 (3H, s).

[001263] Step C: 7-Fluoro-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (45 mg, 0.15 mmol) was combined with piperazine (65 mg, 0.75 mmol) in dimethylacetamide (0.5 mL). The mixture was heated to 150 °C for 1 hour. The mixture was loaded onto silica and eluted with 0% to 8% MeOH (3% NH_3) in CH_2Cl_2 to afford the title compound as a tan powder (33 mg, 61%). M.P. 259-267 °C; MS *m/z* 361.1 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.36 (1H, s), 8.23 (1H, d, J = 2.7 Hz), 8.10 (1H, dd, J = 9.7 Hz, 2.7 Hz), 7.94 (1H, dd, J = 9.5 Hz, 1.8 Hz), 7.82 (1H, s), 7.70 (1H, d, J = 9.7 Hz), 7.52 (1H, d, J = 9.5 Hz), 6.96 (1H, s), 3.15 (4H, m), 2.89 (4H, m), 2.36 (3H, s).

[001264] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 15 by substituting the appropriate starting materials, reagents and reaction conditions.

[001265] **Example 16**

[001266] Preparation of Cpd 209



[001267] Step A: 3-Fluoropyridin-2-amine (5.0 g, 45 mmol) was combined with N-bromosuccinimide (8.0 g, 45 mmol) in CH_3CN (40 mL). The mixture was stirred at room

temperature for 30 minutes. Chloroacetone (4.3 mL, 54 mmol) was added to the mixture. The mixture was heated to 100 °C, allowing the CH_3CN to evaporate. After 1 hour, the temperature was raised to 120 °C for 2 hours. The mixture solidified upon cooling. The solid material was dissolved in H_2O (50 mL). To the aqueous solution was added 100 mL of saturated aqueous $NaHCO_3$. A precipitate formed, and was collected by vacuum filtration. The solid material was washed with H_2O and dried under vacuum. The material was loaded onto silica in CH_2Cl_2 and eluted with EtOAc (0% to 30%) in CH_2Cl_2, providing 6-bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine as a tan powder (4.65 g, 45%). MS *m/z* 229.2 $[M+H]^+$, 231.2 $[M+2+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.72 (1H, s), 7.79 (1H, s), 7.39 (1H, d, J = 10.7 Hz), 2.35 (3H, s).

[001268] Step B: Following the procedure in Example 14, Part 2, 6-Bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine (912 mg, 4 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.32 g, 4.8 mmol), [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (163 mg, 0.2 mmol) and potassium acetate (784 mg, 8 mmol) provided 8-fluoro-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine. The crude product was used directly in the next step.

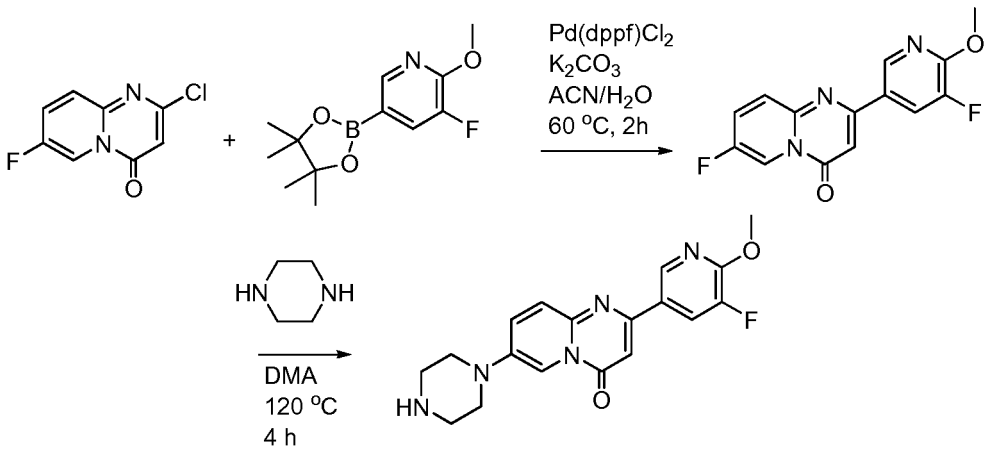
[001269] Step C: Following the procedure in Example 14, Part 3, Step A, the crude product of 8-fluoro-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine from step A and 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (4 mmol, prepared in Example 14, Part 1, Step B), tetrakis(triphenylphosphine) palladium(0) (225 mg, 0.2 mmol) and aqueous K_2CO_3 (1M, 8 mL) provided 7-fluoro-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a tan powder (860 mg, 69%). MS *m/z* 313.0 $[M+H]^+$.

[001270] Step D: Following the procedure in Example 14, Part 3, Step B, 7-Fluoro-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (65 mg, 0.21 mmol) and piperazine (90 mg, 1.05 mmol) afforded the title compound as a tan powder (34 mg, 43%). M.P. 282-288 °C; MS *m/z* 379.4 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.26 (1H, s), 8.21 (1H, d, J = 2.6 Hz), 8.10 (1H, dd, J = 9.7 Hz, 2.7 Hz), 7.93 (1H, d, J = 2.3 Hz), 7.84 (1H, d, J = 12.7 Hz), 7.68 (1H, d, J = 9.8 Hz), 6.98 (1H, s), 3.14 (4H, m), 2.88 (4H, m), 2.39 (3H, s), 2.35 (1H, br s).

[001271] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 16 by substituting the appropriate starting materials, reagents and reaction conditions.

[001272] **Example 17**

[001273] Preparation of Cpd 182



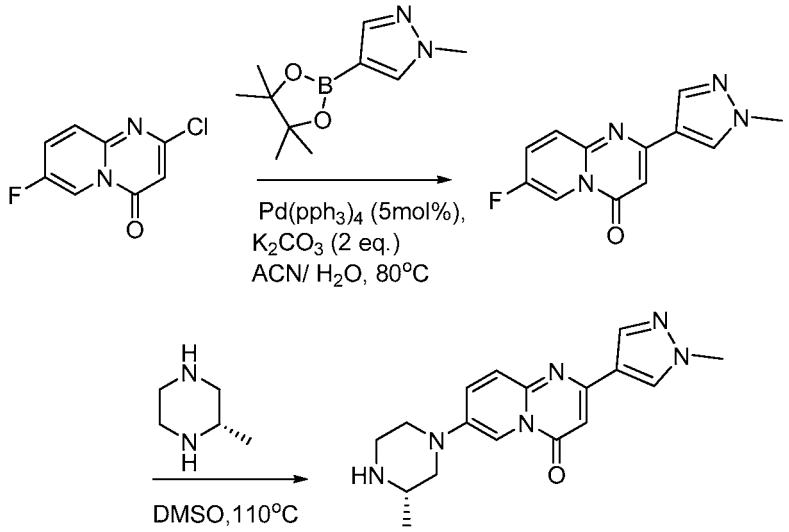
[001274] Step A: Following the procedure for Example 14, Part 3, Step A, 3-fluoro-2-methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (~4.85 mmol, crude product prepared by the procedure in Example 14, Part 2) and 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.64 g, 3.23 mmol, prepared in Example 14, Part 1) gave 7-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (1.0 g, 100%) as a brown solid, MS *m/z* 290.4 $[M+H]^+$.

[001275] Step B: A mixture of 7-fluoro-2-(5-fluoro-6-methoxypyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (145 mg, 0.5 mmol) and piperazine (43 mg, 0.5 mmol) in DMA (1 mL) was heated at 120 °C. After 4 hours, the volatiles were removed and the residue was chromatographed (20% MeOH/CH_2Cl_2) to give the title compound as a yellow solid (63 mg, 36%). M.P. 166-170 °C; MS *m/z* 356.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.83 (1H,d, *J* = 1.9 Hz), 8.39 (1H, dd, J = 1.9 Hz, 11.8 Hz), 8.23 (1H, d, *J* = 2.6 Hz), 8.10 (1H, dd, *J* = 2.7 Hz, 9.7 Hz), 7.71 (1H, d, J = 9.7 Hz), 7.02 (1H, s), 4.03 (3H, s), 3.20 (4H, m), 2.94 (4H, m).

[001276] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 17 by substituting the appropriate starting materials, reagents and reaction conditions.

[001277] **Example 18**

[001278] Preparation of Cpd 191



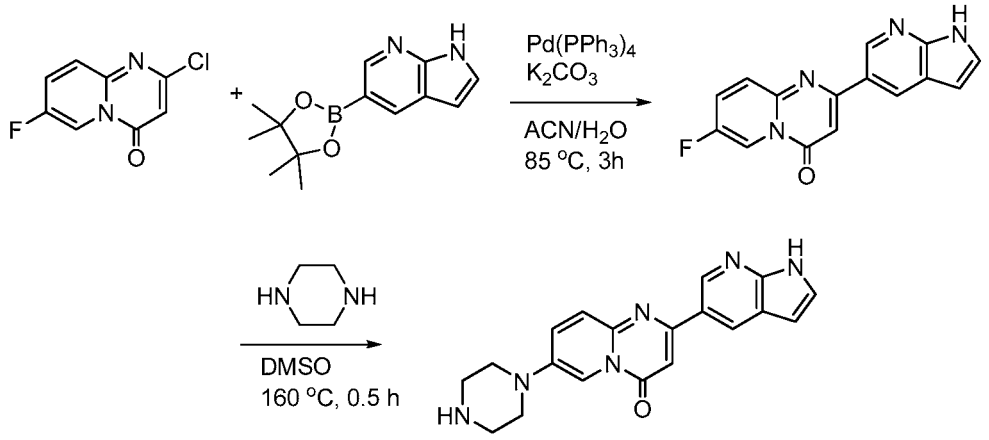
[001279] Step A: Following the procedure of Example 14, Part 3, Step A, 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (199 mg, 1 mmol, prepared in Example 14, Part 1), 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (239.2 mg 1.15 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol) and K_2CO_3 (276.4 mg, 2 mmol) in CH_3CN/H_2O (1.0 mL/1.0 mL) gave 7-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (97.6mg, 40%). MS *m/z* 245.1 $[M+H]^+$.

[001280] Step B: Following the procedure of Example 14, Part 3, Step B, 7-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (48.8 mg, 0.2 mmol) and (S)-2-methylpiperazine (100 mg, 1 mmol) in DMSO (0.5 mL) gave the title compound (32.1mg, 49.5%). M.P. 168-170 °C; MS *m/z* 325.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.35 (1H, s), 8.18 (1H, d, J = 2.8 Hz), 8.06 (1H, s), 8.02 (1H, dd, J = 9.7 Hz, 2.6 Hz), 7.56 (1H, d, J = 9.8 Hz), 6.63 (1H, s), 3.89 (3H, s), 3.54-3.57 (2H, m), 2.99-3.02 (1H, m), 2.80-2.85 (2H, m), 2.58-2.64 (1H, m), 2.24-2.28 (1H, m), 1.05 (3H, d, J = 6.3 Hz).

[001281] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 18 by substituting the appropriate starting materials, reagents and reaction conditions.

[001282] **Example 19**

[001283] Preparation of Cpd 128



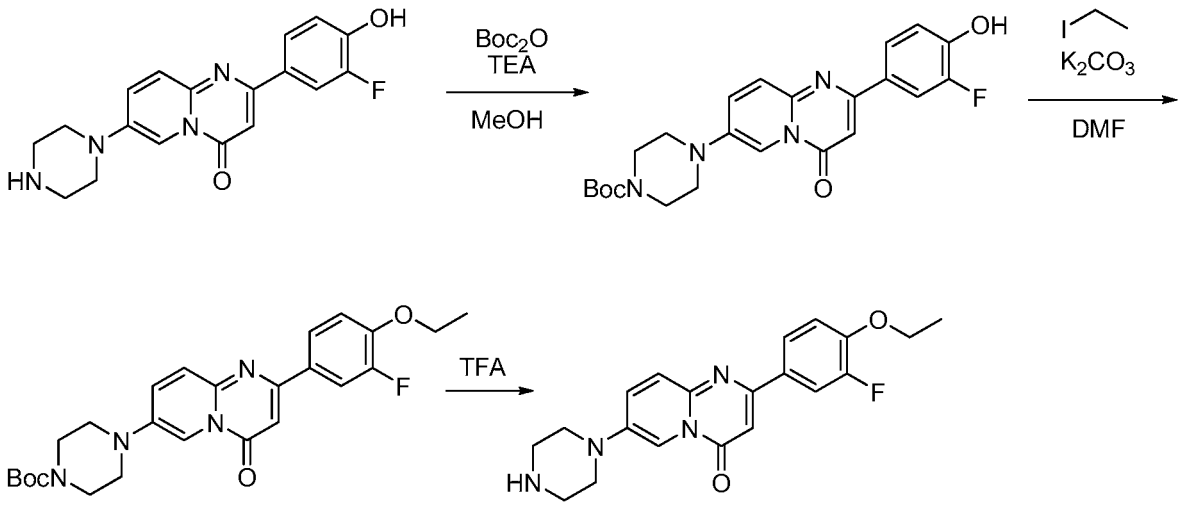
[001284] Step A: To a solution of 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (199 mg, 1.0 mmol, prepared in Example 14, Part 1) in 2 mL of acetonitrile were added 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine (293 mg, 1.2 mmol), tetrakistriphenylphosphine Pd (0) (57.8 mg, 0.05 mmol) and aqueous K_2CO_3 (1M in water, 2 mmol) at room temperature. The mixture was stirred at 85°C for 3 hours and cooled to room temperature. The solid was filtered off and washed with dichloromethane, water and acetonitrile to give 7-fluoro-2-(1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (249 mg, 89%). MS *m/z* 281.1 $[M+H]^+$.

[001285] Step B: A solution of 7-fluoro-2-(1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (100 mg, 0.36 mmol) in DMSO (1 mL) was treated with piperazine (154 mg, 1.79 mmol) at room temperature. The solution was stirred at 160°C for 30 minutes and cooled to room temperature. The reaction mixture was loaded on silica gel without concentration and eluted with MeOH (0% to 20%) in CH_2Cl_2 to provide the title compound (74.8 mg, 60%). M.P. 252-255 °C; MS *m/z* 347.1 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz) δ 11.8 (1H, s), 8.95 (1H, d, J = 2.0 Hz)), 8.64 (1H, d, J = 1.7 Hz), 8.14 (1H, d, J = 2.3 Hz), 8.0-7.9 (1H, m), 7.62 (1H, d, J = 9.6 Hz), 7.45 (1H, m), 6.9 (1H, s), 6.48 (1H, br. m). 3.1 (4H, m), 2.85 (4H, m).

[001286] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 19 by substituting the appropriate starting materials, reagents and reaction conditions.

[001287] **Example 20**

[001288] Preparation of Cpd 153



[001289] Step A: 2-(3-Fluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (180 mg, 0.53 mmol), prepared by Suzuki coupling according to the procedure in Example 14, Part 3, Step A, was combined with di-tert-butyl dicarbonate (131 mg, 0.6 mmol) and triethylamine (85 μL, 0.6 mmol) in MeOH (4 mL). The mixture was stirred at 50 °C for 2 hours. The mixture was filtered, leaving a yellow powder, which was washed with MeOH and dried under vacuum, affording tert-butyl 4-(2-(3-fluoro-4-hydroxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (230 mg, 99%). MS *m/z* 441.0 $[M+H]^+$.

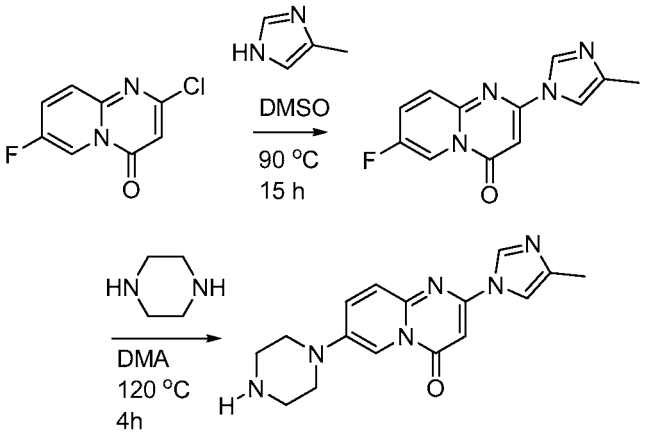
[001290] Step B: tert-Butyl 4-(2-(3-fluoro-4-hydroxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (60 mg, 0.14 mmol) was combined with K_2CO_3 (39 mg, 0.28 mmol) and iodoethane (48 μL, 0.21 mmol) in DMF (1 mL). The mixture was stirred at 50 °C for 1 hour. After cooling to room temperature, H_2O (0.5 mL) was added drop wise to the mixture. The precipitate was collected, washed with H_2O, and dried under vacuum.

[001291] Step C: To the crude product from Step B was added trifluoroacetic acid (1 mL). After standing for 10 minutes, volatiles were removed. The residue was partitioned in CH_2Cl_2 (4 mL) and aqueous K_2CO_3 (1M, 2 mL). The organic layer was removed and concentrated, providing the title compound (36 mg, 70%). M.P. 180-186 °C; MS *m/z* 369.1 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.21 (1H, d, J = 2.7 Hz), 8.02 (3H, m), 7.68 (1H, d, J = 9.7 Hz), 7.27 (1H, t, J = 8.8 Hz), 6.93 (1H, s), 4.20 (2H, q, J = 7.0 Hz), 3.14 (4H, m), 2.88 (4H, m), 2.36 (1H, br), 1.39 (3H, t, J = 7.0 Hz).

[001292] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 20 by substituting the appropriate starting materials, reagents and reaction conditions.

[001293] **Example 21**

[001294] Preparation of Cpd 179



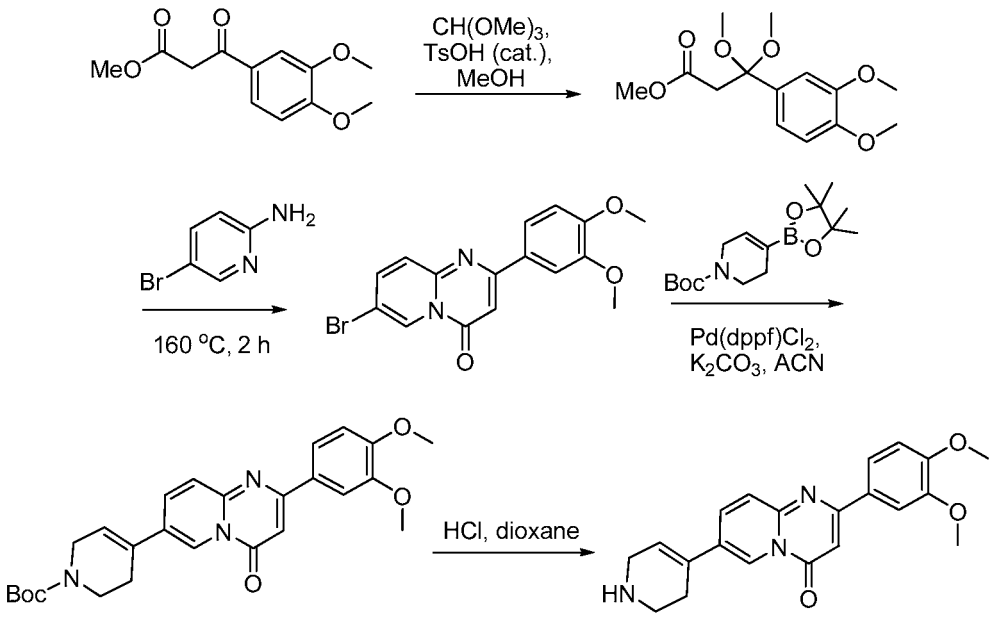
[001295] Step A: A mixture of 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (300 mg, 1.5 mmol) and 4-methyl-1H-imidazole (429 mg, 6.0 mmol) in DMSO (1.5 mL) was heated at 90 °C for 15 hours. The mixture was cooled to room temperature and diluted with CH_3CN. The precipitate was filtered, washed with CH_3CN (3x) and dried to give 2-(4-methyl-1H-imidazol-1-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as an off-white solid (225 mg, 61%). MS *m/z* 345.4 $[M+H]^+$.

[001296] Step B: A mixture of 2-(4-methyl-1H-imidazol-1-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (73 mg, 0.3 mmol) and piperazine (129 mg, 1.5 mmol) in DMA (0.6 mL) was heated at 120 °C for 4 hours. The DMA was removed and the mixture was diluted with CH_3CN. The precipitate was filtered, washed with CH_3CN (3x) and dried to give the title compound as a yellow solid (310 mg, 95%). M.P. 204-206°C; MS *m/z* 311.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.47 (1H,d, J = 1.2 Hz), 8.22 (1H, d, J = 2.7 Hz), 8.13 (1H, dd, J = 2.8 Hz, 9.6 Hz), 7.69 (1H, d, J = 1.1 Hz), 7.63 (1H, d, J = 9.6 Hz), 6.68 (1H, s), 3.14 (4H, m), 2.87 (4H, m), 2.16 (3H, s).

[001297] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 21 by substituting the appropriate starting materials, reagents and reaction conditions.

[001298] **Example 22**

[001299] Preparation of Cpd 143



[001300] Step A: Following the procedure in Example 1, Step A, methyl 3-(3,4-dimethoxyphenyl)-3-oxopropanoate (5.0 gram, 20 mmol), trimethylorthoformate (3.5 mL, 30 mmol) and p-toluenesulfonic acid monohydrate (380 mg, 2 mmol) in methanol (50 mL) provided methyl 3-(3,4-dimethoxyphenyl)-3,3-dimethoxypropanoate. The crude product was used directly in the next step without purification. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.93 (3H, m), 3.82 (2H, q, J = 7.2 Hz), 3.75 (3H, s), 3.73 (3H, s), 3.12 (6H, s), 2.92 (2H, s), 0.92 (3H, t, J = 7.1 Hz).

[001301] Step B: To the above ketal intermediate was added 5-bromopyridin-2-amine (3.5 g, 20 mmol). The mixture was heated to 150 °C for 2 hours, then cooled to room temperature. The crude product was triturated with acetonitrile and filtered to provide the title compound as a white solid (6.8 gram, 94%). MS *m/z* 360.9 $[M+H]^+$, 362.9 $[M+2+H]^+$.

[001302] Step C: Following the procedure in Example 14, Part 3, Step A, 7-bromo-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (181 mg, 0.5 mmol), tert-butyl 4-(4,4,5,5-

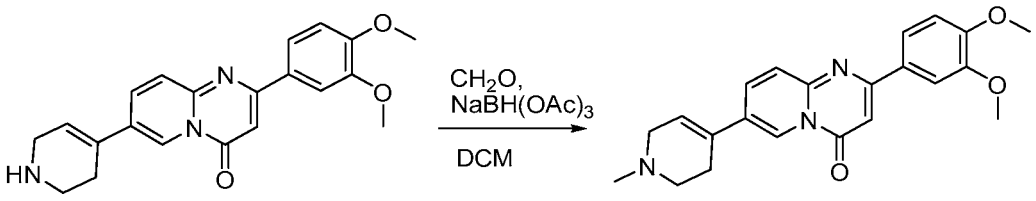
tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (170 mg, 0.55 mmol), potassium carbonate (207 mg, 1.5 mmol) and Pd(dppf)Cl_2 (36.5 mg, 0.05 mmol) in acetonitrile (2 mL) provided tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a white solid (0.22 mg, 95%). MS *m/z* 464.1 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (s, 1H), 8.24 (dd, J = 1.5, 9 Hz, 1H), 7.85 (dd, J = 2, 8.5 Hz, 1H), 7.78 (d, J = 2 Hz, 1H), 7.73 (d, J = 9.5 Hz, 1H), 7.10 (d, J = 9 Hz, 1H), 7.05 (s, 1H), 6.54 (s, 1H), 4.09 (bs, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.60-3.59 (m, 2H), 2.64-2.63 (m, 2H), 1.45 (s, 9H).

[001303] Step D: The intermediate obtained from Step A was suspended in a solution of HCl in dioxane (4M, 4 mL). The reaction mixture was stirred at room temperature for 2 hours. The mixture was concentrated and the residue was partitioned between dichloromethane and saturated aqueous sodium bicarbonate. The organics were dried, concentrated and chromatographed on a basic alumina column, eluting with dichloromethane with methanol (10%) to provide the title compound as a white solid (150 mg, 88%). M.P. 196-198 °C; MS *m/z* 364.1 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.77 (d, J = 2 Hz, 1H), 8.24 (dd, J = 2, 9.5 Hz, 1H), 7.85 (dd, J = 2, 8.5 Hz, 1H), 7.78 (d, J = 2 Hz, 1H), 7.71 (d, J = 9.5 Hz, 1H), 7.09 (d, J = 8.5 Hz, 1H), 7.03 (s, 1H), 6.60 (s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.45 (d, J = 2.5 Hz, 2H), 2.97 (t, J = 5.5 Hz, 2H), 2.41 (bs, 2H).

[001304] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 22 by substituting the appropriate starting materials, reagents and reaction conditions.

[001305] **Example 23**

[001306] Preparation of Cpd 188



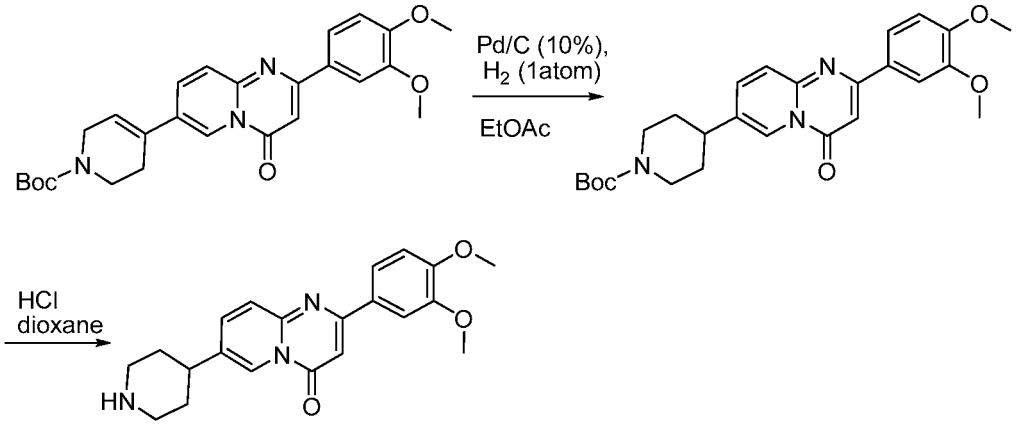
[001307] A mixture of 2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (30 mg, 0.08 mmol), formaldehyde (0.05 mL, 37%, ~ 0.8 mmol) and sodium triacetoxyborohydride (50 mg, 0.24 mmol) was stirred in dichloromethane (1 mL)

for 2 hr. The reaction mixture was diluted with dichloromethane and neutralized with sodium bicarbonate. The organics were dried and concentrated to provide the title compound as a white solid (26 mg, 83%). M.P. 165-168 °C; MS *m/z* 378.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (d, J = 2 Hz, 1H), 8.25 (dd, J = 2, 9.5 Hz, 1H), 7.85 (dd, J = 2, 8.5 Hz, 1H), 7.78 (d, J = 2 Hz, 1H), 7.71 (d, J = 9.5 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 7.04 (s, 1H), 6.56 (s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.09 (bs, 2H), 2.64-2.61 (m, 2H), 2.56 (bs, 2H), 2.51 (s, 3H).

[001308] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 23 by substituting the appropriate starting materials, reagents and reaction conditions.

[001309] **Example 24**

[001310] Preparation of Cpd 144

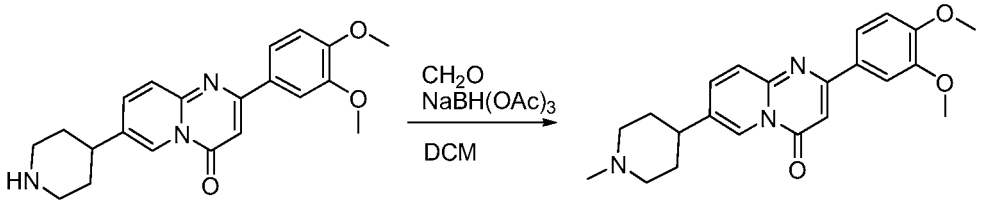


[001311] Step A: A mixture of tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (100 mg, 0.22 mmol, prepared as depicted in Example 22, Step C) and Pd/C (10%) (10 mg) in ethyl acetate (25 mL) was stirred under 1 atmosphere of hydrogen overnight. The reaction mixture was filtered through celite, concentrated and chromatographed on a silica column, eluting with EtOAc/CH_2Cl_2 (30/70) to provide tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate as a white solid (75 mg, 75%), which was used directly in the next step without further purification. MS *m/z* 466.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 7.80 (dd, J = 2.5, 9.5 Hz, 1H), 7.64 (dd, J = 2, 8.5 Hz, 1H), 7.57 (d, J = 2 Hz, 1H), 7.53 (d, J = 9 Hz, 1H), 6.9 (d, J = 9 Hz, 1H), 6.82 (s, 1H), 3.92 (bs, 2H), 3.69 (s, 3H), 3.65 (s, 3H), 2.78-2.71 (m, 2H), 2.69-2.65 (1H, m), 1.69-1.67 (m, 2H), 1.41-1.38 (m, 2H), 1.24 (s, 9H).

[001312] Step B: Following the procedure in Example 22, Step D, the above product from Step A and HCl in dioxane (4M, 3 mL) provided the title compound as a white solid (49 mg, 83%). M.P. 214-217 °C; MS *m/z* 366.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.88 (d, J = 2 Hz, 1H), 8.09 (dd, J = 2, 9.5 Hz, 1H), 7.98 (dd, J = 2, 8.5 Hz, 1H), 7.91 (d, J = 2 Hz, 1H), 7.88 (d, J = 9 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.15 (s, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.30 (d, J = 11.5 Hz, 2H), 3.01 (tt, J = 2 Hz, 12 Hz, 1H), 2.87 (t, J = 12 Hz, 2H), 2.02 (d, J = 12.5 Hz, 2H), 1.80-1.73 (m, 2H).

[001313] **Example 25**

[001314] Preparation of Cpd 164

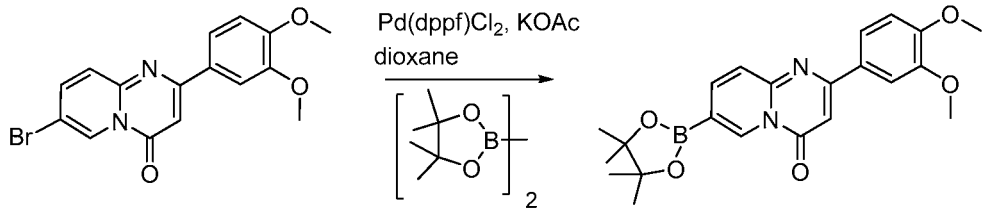


[001315] Following the procedure in Example 23, 2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (10 mg, 0.027 mmol), formaldehyde (10 μL, 37%, 0.13 mmol) and sodium triacetoxyborohydride (17 mg, 5.7 mmol) in dichloromethane (0.5 mL) provided the title compound as a white solid (7.6 mg, 73%). M.P. 181-183 °C; MS *m/z* 380.1 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.76 (d, J = 2 Hz, 1H), 8.0 (dd, J = 2, 9 Hz, 1H), 7.84 (dd, J = 2, 8.5 Hz, 1H), 7.77 (d, J = 2 Hz, 1H), 7.72 (d, J = 9.5 Hz, 1H), 7.09 (d, J = 8.5 Hz, 1H), 7.01 (s, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 2.91 (d, J = 9.5 Hz, 2H), 2.73-2.64 (m, 1H), 2.22 (s, 3H), 2.01 (t, J = 8.5 Hz, 2H), 1.88-1.85 (m, 2H), 1.71-1.69 (m, 2H).

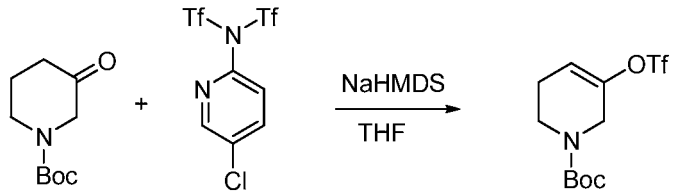
[001316] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 25 by substituting the appropriate starting materials, reagents and reaction conditions.

[001317] **Example 26**

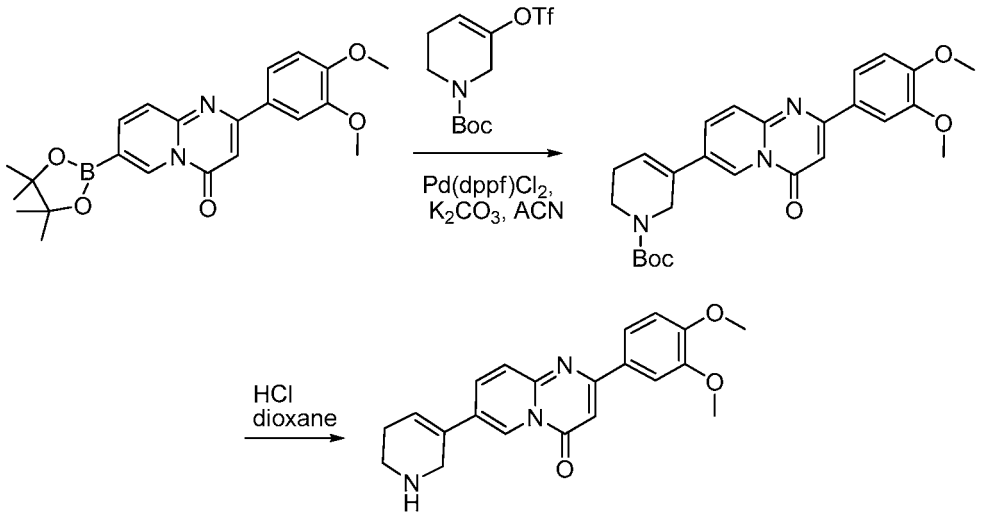
[001318] Preparation of Cpd 263



[001319] Part 1: Following the procedure in Example 14, Part 2, 7-Bromo-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (661 mg, 1.8 mmol), prepared in Example 22, Step B, KOAc (530 mg, 5.4 mmol), bis(pincolato)diboron (700 mg, 2.7 mmol), and $Pd(dppf)Cl_2$ (60 mg, 0.09 mmol) in dioxane (5 mL) provided 2-(3,4-dimethoxyphenyl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a white solid (560 mg, 76%). MS *m/z* 327.1 $[M+H]^+$ for boronic acid.



[001320] Part 2: To a solution of tert-butyl 3-oxopiperidine-1-carboxylate (482 mg, 2.4 mmol) in 2-methyltetrahydrofuran (2.5 mL) was added drop wise a solution of sodium bis(trimethylsilyl)amide (2.6 mL, 2.6 mmol, 1.0M in THF) at -78°C under argon. The mixture was stirred at -78°C for 1 hr, followed by the addition of a solution of N-(5-chloropyridin-2-yl)-1,1,1-trifluoro-N-(trifluoromethylsulfonyl)-methanesulfonamide (1.0 gram, 2.5 mmol) in 2-methyltetrahydrofuran (2.5 mL), and then the reaction was allowed to warm to room temperature over 2 hours. After stirring at room temperature overnight, the reaction was quenched with saturated aqueous sodium carbonate, diluted with ether, and the organics were washed with water, dried and concentrated. The crude product was chromatographed on a basic alumina column, eluting with 5% ethyl acetate in hexane to provide the title compound as a colorless oil (290 mg, 37%).

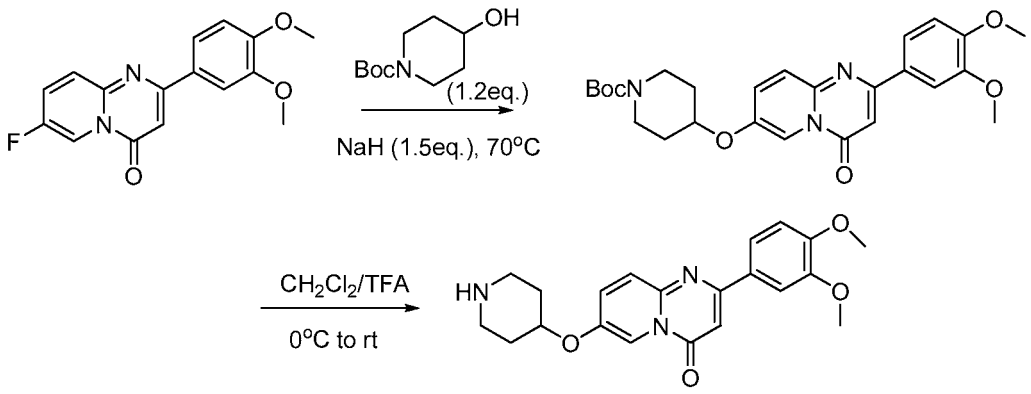


[001321] Part 3, Step A: Following the procedure of Example 14, Part 3, Step A, 2-(3,4-dimethoxyphenyl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (370 mg, 0.91 mmol), tert-butyl 3-(trifluoromethylsulfonyloxy)-5,6-dihydropyridine-1(2H)-carboxylate (290 mg, 0.88 mmol), potassium carbonate (364 mg, 2.6 mmol) and $Pd(dppf)Cl_2$ (58 mg, 0.08 mmol) in acetonitrile (4 mL) provided tert-butyl 3-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a white solid (0.22 mg, 62%). MS *m/z* 464.3 $[M+H]^+$.

[001322] Part 3, Step B: Following the procedure in Example 22, Step B, tert-butyl 3-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (220 mg, 0.47 mmol) and HCl in dioxane (4M, 5 mL) provided the title compound (160 mg, 79%). M.P. 146-150 °C; MS *m/z* 364.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.73 (d, J = 2 Hz, 1H), 8.23 (dd, J = 2, 9.5 Hz, 1H), 7.85 (dd, J = 2, 8.5 Hz, 1H), 7.78 (d, J = 2.5 Hz, 1H), 7.71 (d, J = 9.5 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 7.05 (s, 1H), 6.60 (s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.29 (bs, 2H), 2.40-2.36 (m, 4H).

[001323] **Example 27**

[001324] Preparation of Cpd 237



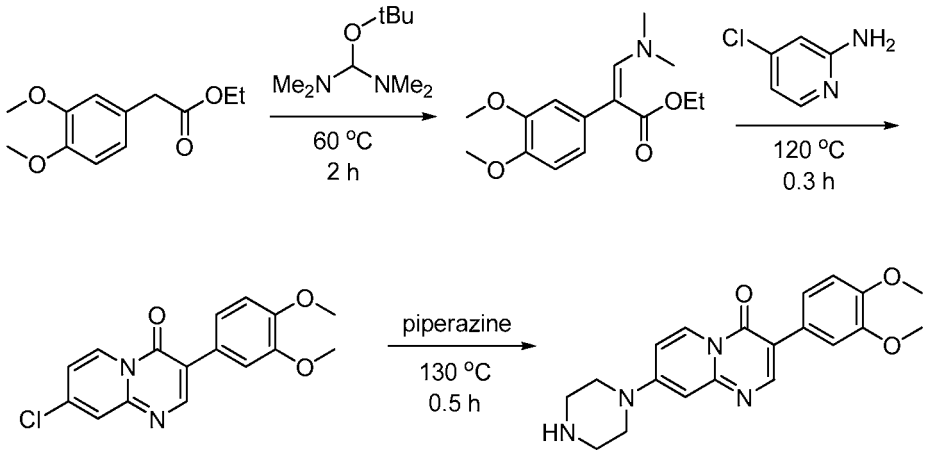
[001325] Step A: NaH (60% dispersion in mineral oil, 12mg, 0.3 mmol) was added slowly to 1-Boc-4-hydroxypiperidine (48.3 mg, 0.24 mmol) in anhydrous THF at room temperature. The reaction mixture was stirred at room temperature for 10 minutes, and 2-(3,4-dimethoxyphenyl)-7-F-4H-pyrido[1,2-a]pyrimidin-4-one (60 mg, 0.2 mmol) was added. The reaction mixture was then heated at 70°C for 3 hours. A small amount of ice water was added to quench the reaction. After most of the THF was evaporated, ether was added to the mixture, and the precipitate was filtered and dried to provide tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yloxy)piperidine-1-carboxylate, which was used in the next step without further purification.

[001326] Step B: tert-Butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yloxy)piperidine-1-carboxylate was dissolved into CH_2Cl_2/TFA (0.5 mL / 0.5 mL) at 0 °C. The mixture was stirred at 0 °C for 2 hours, until the starting material disappeared. After most of the TFA was evaporated, ice cold saturated $NaHCO_3$ was added to the reaction mixture. The mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and concentrated to provide the title compound (57 mg, 74.8% for 2 steps). M.P. 221-224 °C; MS *m/z* 382.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.58 (1H, d, J = 2.9 Hz),,7.81-7.86 (2H, m), 7.73-7.78 (2H, m), 7.08 (1H, d, J = 8.7 Hz), 7.01 (1H, s), 4.82-4.86 (1H, m), 3.87 (3H, s), 3.83 (3H, s), 3.23-3.27 (2H, m), 3.04-3.09 (2H, m), 2.13-2.18 (2H, m), 1.85-1.91 (2H, m).

[001327] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 27 by substituting the appropriate starting materials, reagents and reaction conditions.

[001328] **Example 28**

[001329] Preparation of Cpd 52



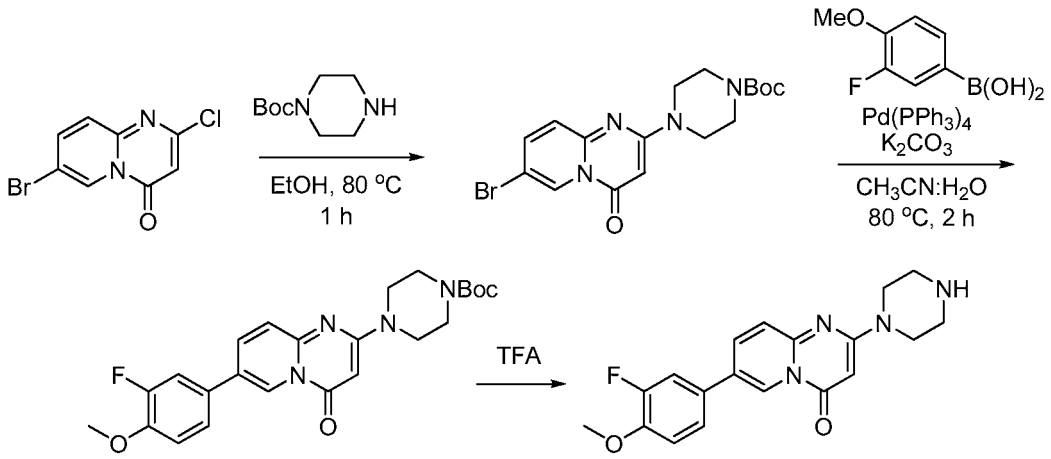
[001330] Step A: Ethyl 2-(3,4-dimethoxyphenyl)acetate (673 mg, 3 mmol) was combined with 1-tert-butoxy-N,N,N',N'-tetramethylmethanediamine (0.68 mL, 3.3 mmol). The mixture was heated to 60 °C for 2 hours. The mixture was used directly in the next step without work-up.

[001331] Step B: 4-Chloropyridin-2-amine (424 mg, 3.3 mmol) was added directly to the mixture. The mixture was heated to 120 °C for 20 minutes. The mixture was used directly in the next step without work-up.

[001332] Step C: Piperazine (1.3 g, 15 mmol) was added to the mixture from Step B, which stirred for an additional 30 minutes at 120 °C. The mixture was chromatographed on silica with 10% MeOH (1% triethylamine) in CH_2Cl_2 affording the title compound as a yellow powder (120 mg, 11%). M.P. 175-179 °C; MS *m/z* 367.2 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.84 (1H, d, J = 8.2 Hz), 8.40 (1H, s), 7.44 (1H, d, J = 2.1 Hz), 7.34 (1H, dd, J = 8.4 Hz, 2.1 Hz), 7.28 (1H, dd, J = 8.2 Hz, 2.8 Hz), 6.99 (1H, d, J = 8.5 Hz), 6.73 (1H, d, J = 2.8 Hz), 3.80 (3H, s), 3.78 (3H, s), 3.48 (4H, m), 2.82 (4H, m).

[001333] **Example 29**

[001334] Preparation of Cpd 220



[001335] Step A: 7-Bromo-2-chloro-4H-pyrido[1,2-a]pyrimidin-4-one (130 mg, 0.5 mmol), prepared according to Example 14, Part 1, was combined with tert-butyl piperazine-1-carboxylate (140 mg, 0.75 mmol) and triethylamine (0.14 mL, 1.0 mmol) in EtOH (2 mL). The mixture was heated to 80 °C for 1 hour. The reaction mixture was cooled to room temperature, and then filtered. The collected material was chromatographed on silica with 0% to 50% EtOAc in CH_2Cl_2, providing tert-butyl 4-(7-bromo-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)piperazine-1-carboxylate (130 mg, 64%). MS *m/z* 409.4 $[M+H]^+$.

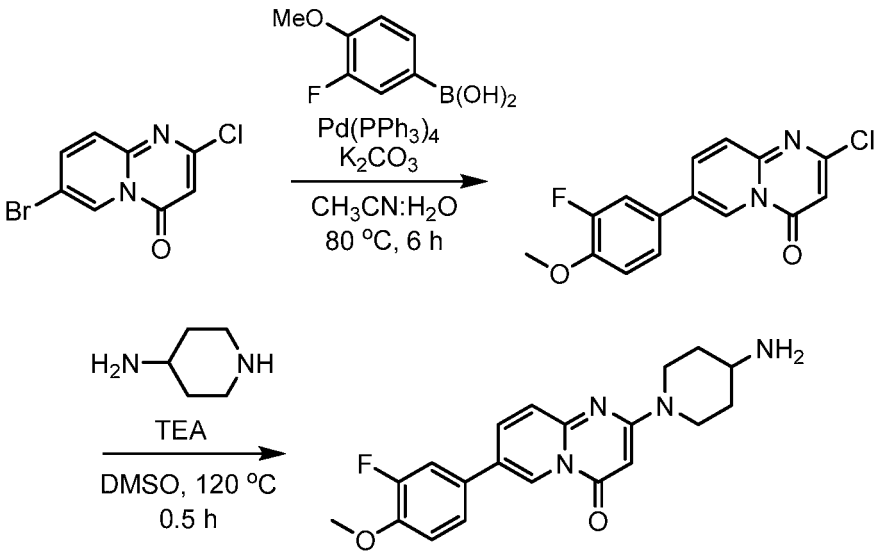
[001336] Step B: The intermediate (0.3 mmol) from Step A was combined with 3-fluoro-4-methoxyphenylboronic acid (77 mg, 0.45 mmol) and tetrakis(triphenylphosphine) palladium(0) (35 mg, 0.03 mmol) in CH_3CN (2 mL) and aqueous K_2CO_3 (1M, 2 mL). The mixture was heated at 80 °C with vigorous stirring under argon for 2 hours. The organic layer was removed and concentrated. The residue was chromatographed on silica with 0% to 50% EtOAc in CH_2Cl_2.

[001337] Step C: The Boc-protected intermediate from Step B was dissolved in trifluoroacetic acid (1 mL). After 20 minutes, volatiles were removed. The residue was partitioned in CH_2Cl_2 and aqueous K_2CO_3 (1M). The organic layer was removed and concentrated, affording the title compound as a white powder (30 mg, 17%). M.P. 202-206 °C; MS *m/z* 355.0 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 8.93 (1H, d, J = 2.0 Hz), 8.15 (1H, dd, J = 9.3 Hz, 2.3 Hz), 7.67 (1H, dd, J = 12.7 Hz, 2.3 Hz), 7.54 (1H, m), 7.37 (1H, d, J = 9.2), 7.30 (1H, t, J = 8.8 Hz), 5.62 (1H, s), 3.90 (3H, s), 3.57 (4H, m), 2.75 (4H, m), 2.42 (1H, br s).

[001338] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 29 by substituting the appropriate starting materials, reagents and reaction conditions.

[001339] **Example 30**

[001340] Preparation of Cpd 276



[001341] Step A. 7-Bromo-2-chloro-4H-pyrido[1,2-a]pyrimidin-4-one (1.29 g, 5 mmol) was combined with 3-fluoro-4-methoxyphenylboronic acid (850 mg, 5 mmol), tetrakis(triphenylphosphine) palladium(0) (281 mg, 0.25 mmol), CH_3CN (10 mL) and aqueous K_2CO_3 (1M, 10 mL). The mixture was heated to 80 °C for 6 hours. After cooling to room temperature, the mixture was partitioned in CH_2Cl_2 (75 mL) and H_2O (50 mL). The organic layer was collected and concentrated. The residue was chromatographed on silica, eluting with EtOAc (0% to 50%) in CH_2Cl_2, to afford 2-chloro-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one as a white powder (520 mg, 34%). MS *m/z* 305.0 $[M+H]^+$.

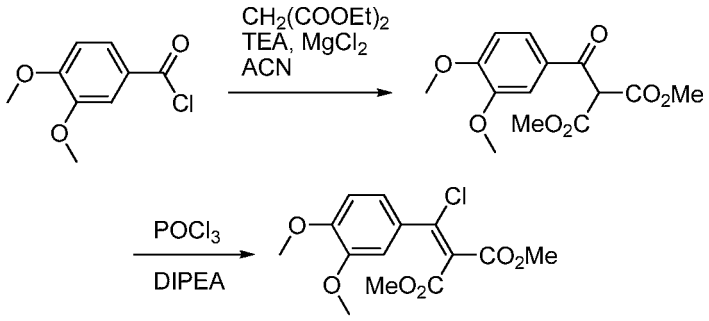
[001342] Step B. 2-Chloro-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (180 mg, 0.6 mmol) was combined with 4-aminopiperidine (90 mg, 0.9 mmol) and triethylamine (165 µL, 1.2 mmol) in DMSO (0.75 mL). The mixture was heated to 120 °C for 30 minutes. After cooling to room temperature, CH_3CN (2 mL) was added to the mixture. The mixture was filtered. The collected material was washed with CH_3CN and dried under vacuum, affording the title compound as a white powder (115 mg, 52%). M.P. 268-283 °C; MS *m/z* 369.3 $[M+H]^+$; ^1H

NMR (DMSO-d_6, 500 MHz): δ 8.94 (1H, d, J = 2.0 Hz), 8.16 (1H, dd, J = 9.3 Hz, 2.3 Hz), 7.68 (1H, dd, J = 12.7 Hz, 2.3 Hz), 7.55 (1H, d, J = 8.5 Hz), 7.39 (1H, d, J = 9.2), 7.30 (1H, t, J = 8.9 Hz), 5.70 (1H, s), 5.20 (2H, br), 4.36 (2H, br), 3.92 (3H, s), 3.04 (3H, m), 1.87 (2H, m), 1.32 (2H, m).

[001343] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 30 by substituting the appropriate starting materials, reagents and reaction conditions.

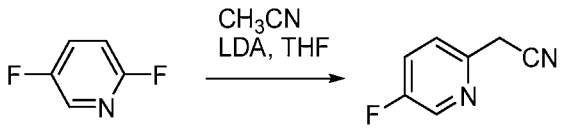
[001344] **Example 31**

[001345] Preparation of Cpd 85

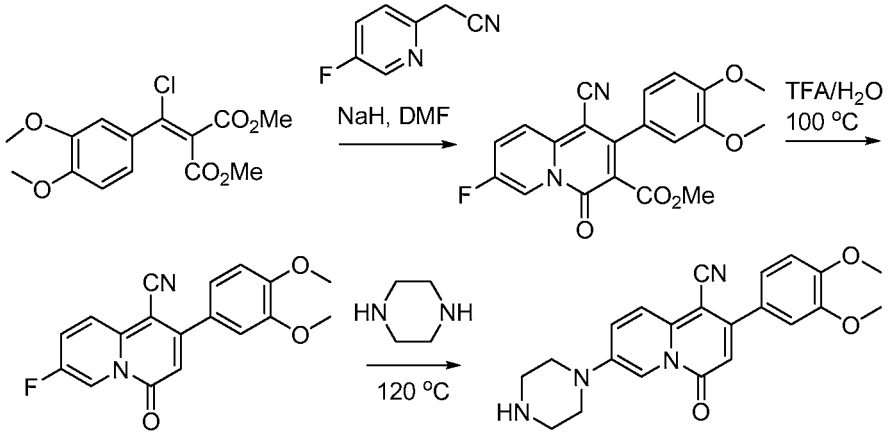


[001346] Part 1, Step A: To a suspension of $MgCl_2$ (2.85 g, 30 mmol) in acetonitrile (27 mL) at 0 °C was added dropwise diethyl malonate (3.4 mL, 30 mmol) and triethylamine (8.3 mL, 60 mmol). The mixture was stirred at 0 °C for 30 minutes. 3,4-dimethoxybenzoyl chloride (5.0 g, 25 mmol) was then added portionwise. The mixture was allowed to stir at room temperature overnight, after which it was treated with 1N HCl, extracted with ether, dried and evaporated. The residue was purified on silica with ethyl acetate (5% to 40%) in hexanes to give dimethyl 2-(3,4-dimethoxybenzoyl)malonate (7.38 g, 100%). MS *m/z* 297.1 $[M+H]^+$.

[001347] Part 1, Step B: To a solution of dimethyl 2-(3,4-dimethoxybenzoyl)malonate (2.96 g, 10 mmol) in $POCl_3$ (9.4 mL, 100 mmol) at room temperature was added DIPEA (2.75 mL, 16.7 mmol) dropwise. The mixture was then stirred at 100 °C for 3 hours. $POCl_3$ was removed under vacuum and the residue was treated with ice-water and extracted with ether. The organic layer was washed with 1N HCl, dried and evaporated. The residue was purified on silica with ethyl acetate (5% to 50%) in hexanes to give the title compound (2.0 g, 64%). MS *m/z* 282.9 $[M+H]^+$.



[001348] Part 2: To a solution of LDA (1.5 M, 13.3 mL, 20 mmol) in THF (15 mL) at -78 °C was added dropwise a solution of 2,5-difluoropyridine (1.15 g, 10 mmol) in THF (10 mL). The temperature was then allowed to rise to room temperature, and the mixture was stirred at room temperature for 2 hours before the reaction was quenched with aqueous NH4Cl. The mixture was extracted with ethyl acetate, dried, and evaporated. The residue was purified on silica with ethyl acetate (5% to 50%) in hexanes to give 2-(5-fluoropyridin-2-yl)acetonitrile (0.8 g, 59%). MS *m/z* 137.0 $[M+H]^+$.



[001349] Part 3, Step A: To a solution of 2-(5-fluoropyridin-2-yl)acetonitrile (44 mg, 0.325 mmol) in DMF (0.5 mL) was added 60% NaH (20 mg, 0.325 mmol). The mixture was stirred at room temperature for 10 minutes and then treated with dimethyl 2-(chloro(3,4-dimethoxyphenyl)methylene)malonate (102 mg, 0.325 mmol). The mixture was stirred for 15 minutes, and the reaction was quenched with saturated NH_4Cl solution. The mixture was filtered. The solid was washed with water and used directly in the next step without further purification.

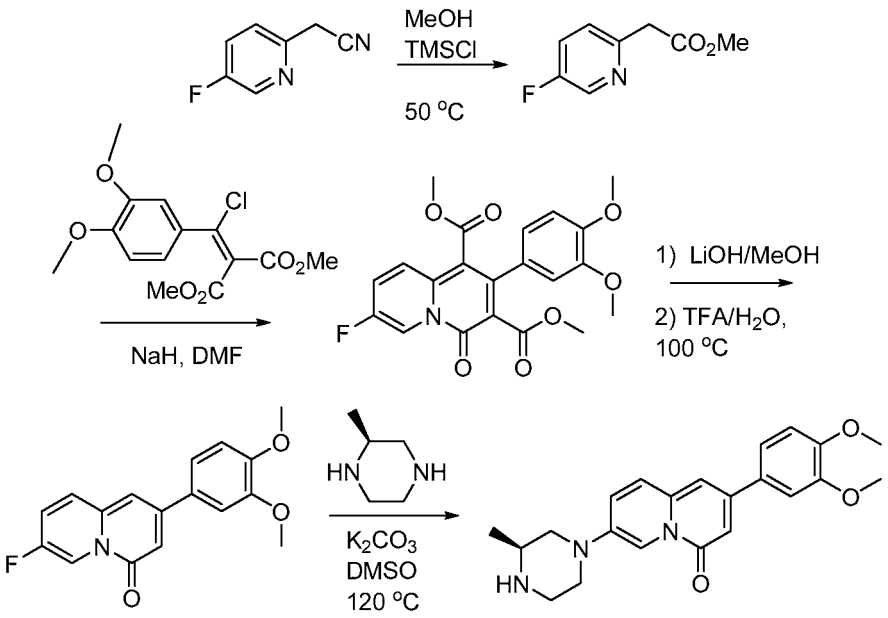
[001350] Part 3, Step B: The crude solid from Step A was treated with TFA (2.0 mL) and water (0.2 mL). The mixture was stirred at 100 °C overnight. The solvent was then removed under vacuum and the crude product was used in the next step without further purification.

[001351] Part 3, Step C: The crude product from Step B was heated with piperazine (86 mg, 1.0 mmol) in DMSO (1.0 mL) at 120 °C overnight. Removal of the solvent by N_2 followed by

purification over silica with methanol (10%) in dichloromethane provided the title compound (30 mg, 25%). M.P. 199-202 °C; MS *m/z* 391.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.60 (1H, d, J = 2.2 Hz), 7.98 (1H, d, *J* = 9.8 Hz), 7.59 (1H, dd, *J* = 9.5, 2.5 Hz), 7.20 (1H, dd, J = 8.5, 2.2 Hz), 7.12 (1H, d, *J* = 2.2 Hz), 6.93 (1H, d, *J* = 8.2 Hz), 6.52 (1H, s), 3.89 (3H, s), 3.88 (3H, s), 3.23-3.21 (4H, m), 3.05-3.03 (4H, m).

[001352] **Example 32**

[001353] Preparation of Cpd 91



[001354] Step A: To a solution of 2-(5-fluoropyridin-2-yl)acetonitrile (0.78 g, 5.7 mmol) in MeOH (15 mL) was added trimethysilyl chloride (4.4 mL, 34.4 mmol) dropwise. The mixture was stirred at 50 °C overnight. Organic volatiles were removed under vacuum and the residue was partitioned between ether and aqueous sodium bicarbonate. The aqueous layer was extracted with ether. The ether extractions were combined, dried and evaporated to give methyl 2-(5-fluoropyridin-2-yl)acetate as an oil (0.9 g, 93%), which was used without further purification. MS *m/z* 170.1 $[M+H]^+$.

[001355] Step B: Following the procedure in Example 31, Part 3, Step A, methyl 2-(5-fluoropyridin-2-yl)acetate (0.34 g, 2.0 mmol), 60% NaH (176 mg, 4.4 mmol) and dimethyl 2-(chloro(3,4-dimethoxyphenyl)methylene)malonate (0.69 g, 2.2 mmol, prepared in Example 31,

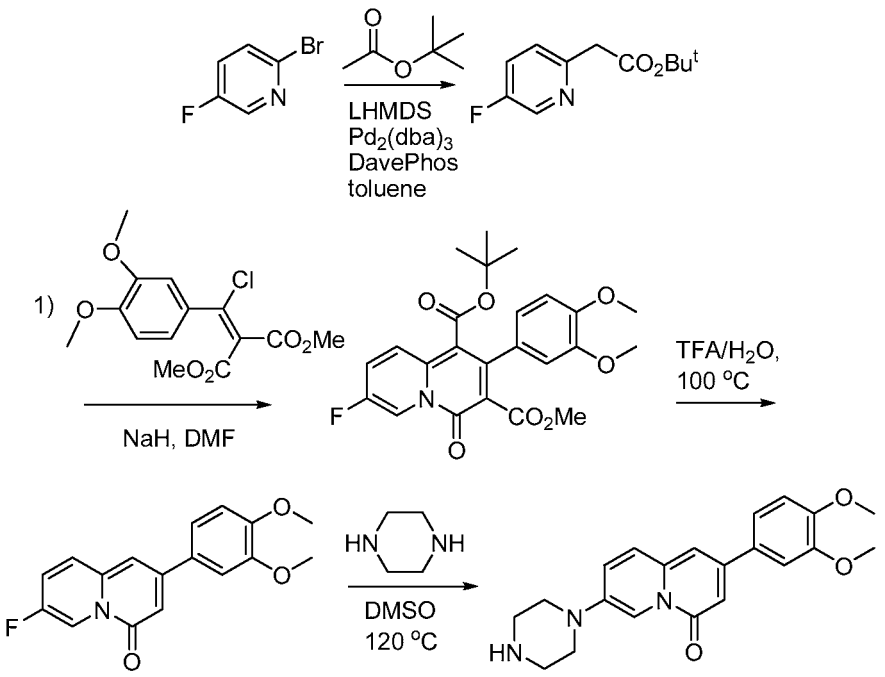
Part 1, Step B) in DMF (3.0 mL) provided the desired dimethyl 2-(3,4-dimethoxyphenyl)-7-fluoro-4-oxo-4*H*-quinolizine-1,3-dicarboxylate (0.2 g, 24%). MS *m/z* 416.1 $[M+H]^+$.

[001356] Step C: A solution of dimethyl 2-(3,4-dimethoxyphenyl)-7-fluoro-4-oxo-4*H*-quinolizine-1,3-dicarboxylate (0.2 g, 0.48 mmol) in methanol (6.0 mL) was treated with aqueous LiOH (2.0 N, 2.0 mL, 4.0 mmol) and stirred at 90 °C for 2 hours. Aqueous workup followed by evaporation provided a dark residue, which was treated with TFA (2.0 mL) and water (0.2 mL) and stirred at 100 °C for 1 hour. Removal of the solvents by N_2 followed by chromatography with ethyl acetate (25% to 75%) in hexanes provided 2-(3,4-dimethoxyphenyl)-7-fluoro-4*H*-quinolizin-4-one (30 mg, 21%). MS *m/z* 300.2 $[M+H]^+$.

[001357] Step D: A solution of 2-(3,4-dimethoxyphenyl)-7-fluoro-4*H*-quinolizin-4-one (30 mg, 0.1 mmol), (*S*)-2-methyl piperazine (30 mg, 0.3 mmol) and K_2CO_3 (27 mg, 0.2 mmol) in DMSO (0.2 mL) was stirred at 120 °C for 48 hours. Removal of the solvents by N_2 followed by purification by dichloromethane and methanol (10%) provided the title compound (24 mg, 63%). M.P. 243-245 °C; MS *m/z* 380.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.52 (1H, d, J = 2.2 Hz), 7.46 (1H, d, *J* = 9.8 Hz), 7.30 (2H, dt, *J* = 10.4, 2.2 Hz), 7.22 (1H, d, *J* = 1.9 Hz), 6.98 (1H, d, J = 8.5 Hz), 6.84 (2H, s), 3.96 (3H, s), 3.95 (3H, s), 3.58-3.54 (2H, m), 3.50 (1H, s), 3.21-3.19 (1H, m), 3.12-3.04 (2H, m), 2.85-2.80 (1H, m), 2.49 (1H, t, *J* = 11.1 Hz), 1.20 (3H, d, J = 6.6 Hz).

[001358] **Example 33**

[001359] Preparation of Cpd 106



[001360] Step A: To a mixture of $Pd_2(dba)_3$ (0.55 g, 0.6 mmol) and DavePhos (0.50 g, 1.26 mmol) in toluene (40 mL) at room temperature under an argon atmosphere was added a solution of LHMDS in hexane (1.0 M x 50 mL, 50 mmol) dropwise. The mixture was stirred for 10 minutes and then cooled to -10 °C, into which *tert*-butyl acetate (6.2 mL, 46 mmol) was added and stirred for another 10 minutes. 2-Bromo-5-fluoropyridine (3.52 g, 20 mmol) was then added portionwise. Upon completion of the addition, the temperature was allowed to rise to room temperature and the mixture was stirred for another 1 hour. The reaction was then quenched by saturated NH_4Cl solution. Aqueous workup followed by chromatography with ethyl acetate (0% to 20%) in hexanes provided *tert*-butyl 2-(5-fluoropyridin-2-yl)acetate (2.6 g, 62%).

[001361] Step B: Following the procedure in Example 31 Part 3, Step A, *tert*-butyl 2-(5-fluoropyridin-2-yl)acetate, 60% NaH (80 mg, 2.0 mmol) and dimethyl 2-(chloro(3,4-dimethoxyphenyl)-methylene)malonate (0.32 g, 1.0 mmol, prepared in Example 31, Part 2, Step B) in DMF (1.0 mL) provided 1-tert-butyl 3-methyl 2-(3,4-dimethoxyphenyl)-7-fluoro-4-oxo-4H-quinolizine-1,3-dicarboxylate. The crude solid was used directly in the next step without purification.

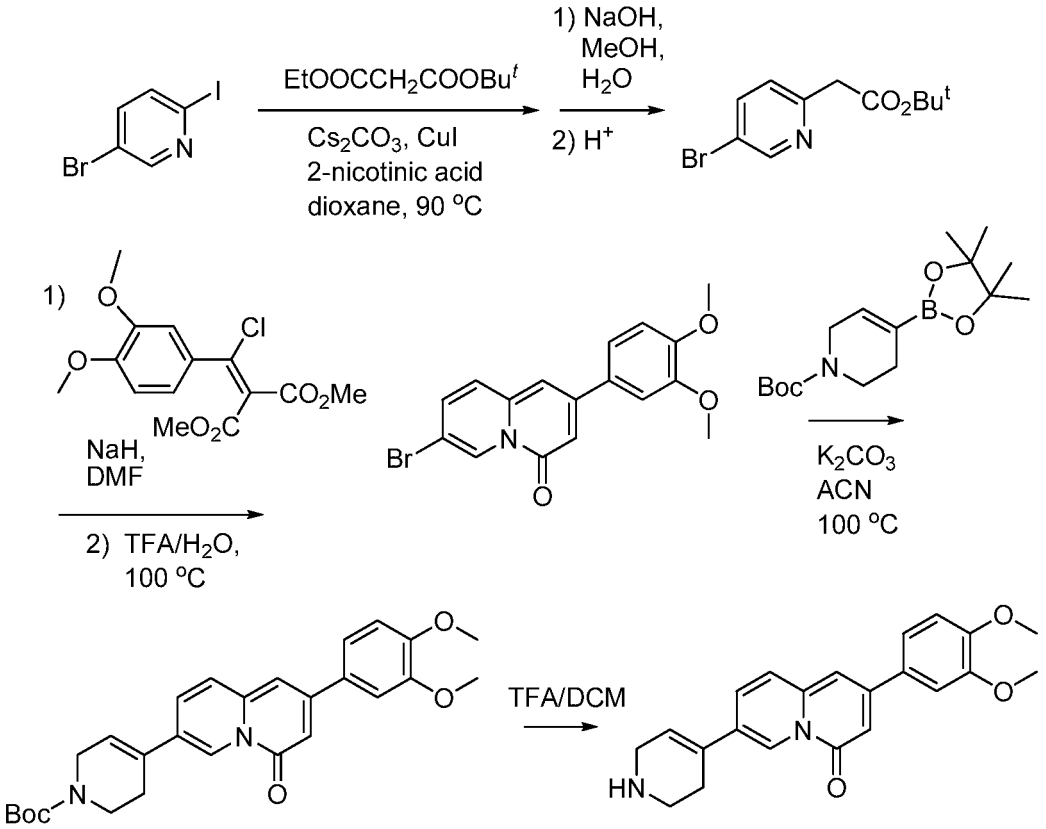
[001362] Step C: Following the procedure in Example 31 Part 3, Step B, The crude solid from Step B, TFA (5 mL) and water (2 mL) provided 2-(3,4-dimethoxyphenyl)-7-fluoro-4*H*-quinolizin-4-one (145 mg, 48%). MS *m/z* 300.2 $[M+H]^+$.

[001363] Step D: Following the procedure in Example 31 Part 3, Step C, 2-(3,4-dimethoxyphenyl)-7-fluoro-4*H*-quinolizin-4-one (75 mg, 0.25 mmol) and piperazine (75 mg, 0.87 mmol) in DMSO (0.5 mL) provided the title compound (30 mg, 33%). M.P. 170-172 °C; MS *m/z* 366.1 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.53 (1H, d, *J* = 2.2 Hz), 7.46 (1H, d, *J* = 9.5 Hz), 7.32-7.27 (2H, m), 7.22 (1H, d, *J* = 1.9 Hz), 6.97 (1H, d, J = 8.5 Hz), 6.84 (2H, s), 3.98 (3H, s), 3.95 (3H, s), 3.25-3.20 (4H, m), 3.13-3.07 (4H, m).

[001364] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 33 by substituting the appropriate starting materials, reagents and reaction conditions.

[001365] **Example 34**

[001366] Preparation of Cpd 245



[001367] Step A: A mixture of 5-bromo-2-iodopyridine (2.84 g, 10 mmol), *tert*-butyl ethyl malonate (3.76 g, 20 mmol), Cs_2CO_3 (9.77 g, 30 mmol), CuI (0.19 g, 1.0 mmol) and 2-nicotinic acid (0.246 g, 2.0 mmol) in dioxane (20 mmol) was stirred at 90 °C overnight under nitrogen atmosphere. The mixture was then treated with water, extracted with ethyl acetate, dried and evaporated. The residue was dissolved in MeOH (100 mL) and water (40 mL) and NaOH (1.2 g, 30 mmol) were added. The mixture was stirred at room temperature for 3 hours, then acidified with 1N HCl to pH 4, extracted with ethyl acetate, dried and chromatographed with ethyl acetate (10% to 50%) in hexanes to give *tert*-butyl 2-(5-bromopyridin-2-yl)acetate (1.2 g, 44%).

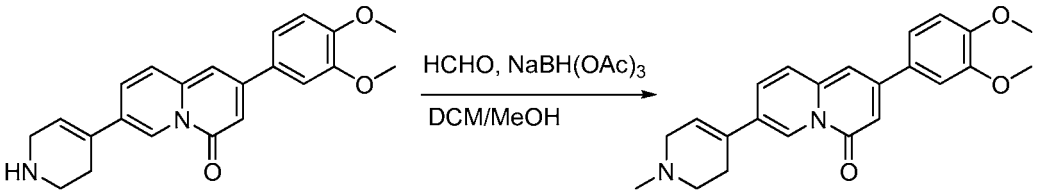
[001368] Step B: Following the procedure in Example 33, Step B and C, *tert*-butyl 2-(5-bromopyridin-2-yl)acetate (0.54 g, 2.0 mmol) was treated with NaH (60% in mineral oil, 0.16 g, 4.0 mmol) in DMF (2.0 mL) followed by reaction with 2-(chloro(3,4-dimethoxyphenyl)methylene)malonate (2.0 mmol). Deprotection and decarboxylation in TFA (5.0 mL) and water (2.0 mL) at 100 °C afforded 7-bromo-2-(3,4-dimethoxyphenyl)-4*H*-quinolizin-4-one (0.17 g, 68%). MS *m/z* 360.1 $[M+H]^+$, 362.0 $[M+2+H]^+$.

[001369] Step C: A mixture of 7-bromo-2-(3,4-dimethoxyphenyl)-4*H*-quinolizin-4-one (0.17 g, 0.47 mmol), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (0.18 g, 0.57 mmol), $PdCl_2$dppf (38 mg, 0.047 mmol), K_2CO_3 (2.0 M x 0.75 mL, 1.5 mmol) in acetonitrile (1.5 mL) was stirred at 100 °C for 16 hours. The mixture was then treated with water, extracted with dichloromethane, dried and chromatographed with ethyl acetate (20% to 100%) in dichloromethane to give *tert*-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4*H*-quinolizin-7-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (0.16 g, 73%). MS *m/z* 463.3 $[M+H]^+$.

[001370] Step D: *tert*-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4*H*-quinolizin-7-yl)-5,6-dihydropyridine-1(2*H*)-carboxylate (80 mg, 0.17 mmol) was treated with dichloromethane (1.0 mL) and TFA (1.0 mL) and stirred at room temperature for 1 hour. The mixture was then evaporated, treated with dichloromethane and washed with saturated aqueous sodium bicarbonate solution. The organic layer was dried and evaporated to give the title compound (63 mg, 100%). M.P. 174-176 °C; MS *m/z* 363.2 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.04 (1H, s), 7.53 (1H, dd, *J* = 9.2, 1.9 Hz), 7.47 (1H, d, *J* = 9.2 Hz), 7.31 (1H, dd, *J* = 8.5, 2.2 Hz), 7.23 (1H, d, *J* = 2.2 Hz), 6.99 (1H, J = 8.2 Hz), 6.86 (2H, br s), 6.36 (1H, s), 3.99 (3H, s), 3.97 (3H, s), 3.67-3.60 (2H, m), 3.24-3.13 (2H, m), 2.62-2.55 (2H, m), 2.21 (1H, br s).

[001371] **Example 35**

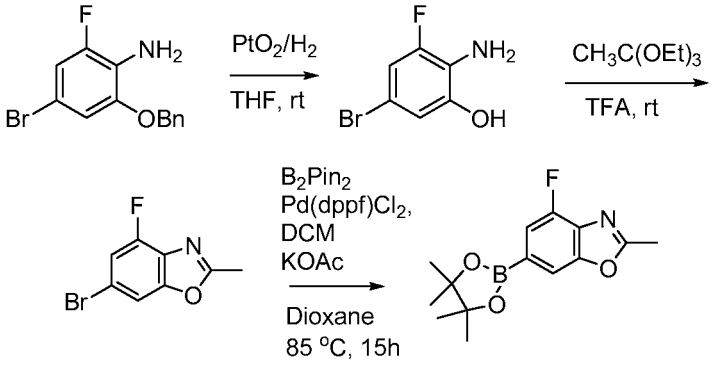
[001372] Preparation of Cpd 249



[001373] Following the procedure in Example 23, 2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4*H*-quinolizin-4-one (30 mg, 0.083 mmol), sodium triacetoxyborohydride (53 mg, 0.25 mmol) and aqueous solution of formaldehyde (30%, 14 μL, 0.166 mmol) in 10% methanol in dichloromethane (1.0 mL) gave the title compound (26 mg, 83%). M.P. 194-196 °C; MS *m/z* 377.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ: 9.03 (1H, s), 7.51-7.44 (2H, m), 7.29 (1H, dd, *J* = 8.5, 2.2 Hz), 7.21 (1H, d, *J* = 1.9 Hz), 6.98 (1H, *J* = 8.2 Hz), 6.87-6.82 (2H, m), 6.26 (1H, s), 3.98 (3H, s), 3.95 (3H, s), 3.48 (2H, br s), 3.06-2.97 (2H, m), 2.90-2.80 (2H, m), 2.65 (3H, s).

[001374] **Example 36**

[001375] Preparation of Cpd 306

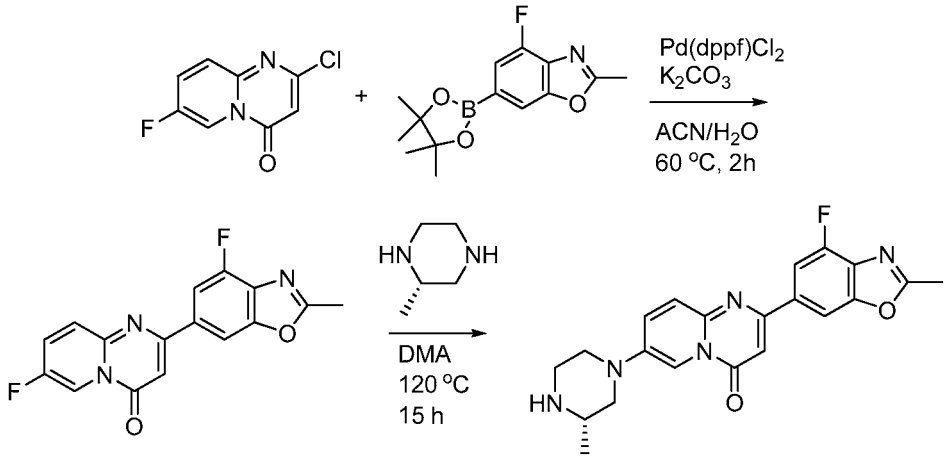


[001376] Part 1, Step A: To a solution of 2-(benzyloxy)-4-bromo-6-fluoroaniline (3.74 g, 12.6 mmol) in THF (25 mL), prepared from 1,3-difluoro-2-nitrobenzene in 3 steps according to known procedures (WO2007/067612), was added PtO_2 (0.23 g, 1.0 mmol). After stirring under hydrogen (1 atm, balloon) at room temperature for 23 hours, the mixture was filtered through celite. The filtrate was concentrated to give 2-amino-5-bromo-3-fluorophenol as a brown solid,

which was used in the next step without further purification. MS *m/z* 206.1 $[M+H]^+$, 208.0 $[M+2+H]^+$.

[001377] Part 1, Step B: To a solution of the crude 2-amino-5-bromo-3-fluorophenol from Step A in 1,1,1-triethoxyethane (10 mL) was added TFA (0.96 mL, 12.6 mmol) at room temperature. After 15 hours, the mixture was neutralized with Na_2CO_3 and filtered. The filtrated was concentrated and chromatographed with CH_2Cl_2 to give 6-bromo-4-fluoro-2-methylbenzo[d]oxazole as a tan solid (2.531 g, 88%). MS *m/z* 230.0 $[M+H]^+$, 232.1 $[M+2+H]^+$.

[001378] Part 1, Step C: A mixture of 6-bromo-4-fluoro-2-methylbenzo[d]oxazole (2.531 g, 11.0 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (3.087 g, 12.2 mmol), KOAc (3.25 g, 33.2 mmol) and $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (449 mg, 0.55 mmol) in dioxane (25 mL) was degassed and heated under N_2 at 85 °C. After 15 hours, LC-MS indicated disappearance of the starting material and the products as a mixture of boronic acid and boronic pinacol ester in a ratio of ~2/1: boronic acid product: MS *m/z* 196.1 $[M+H]^+$; pinacol boronic ester product: MS *m/z* 278.2 $[M+H]^+$. The reaction mixture was concentrated to dryness and used as is in the next step.



[001379] Part 2, Step A: A mixture of crude boronic pinacol ester/boronic acid from Part 1 (~ 4 g, ~ 4 mmol), 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.792 g, 4.0 mmol, prepared in Example 14, Part 1), $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (146 mg, 0.20 mmol), K_2CO_3 (2M, 6.0 mL, 12.0 mmol), and CH_3CN (12 mL) was degassed and then heated under N_2 at 60 °C for 2.5 hours. The volatiles were removed and the residue was washed with water and CH_3CN to give 7-fluoro-2-(4-fluoro-2-methylbenzo[d]oxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a

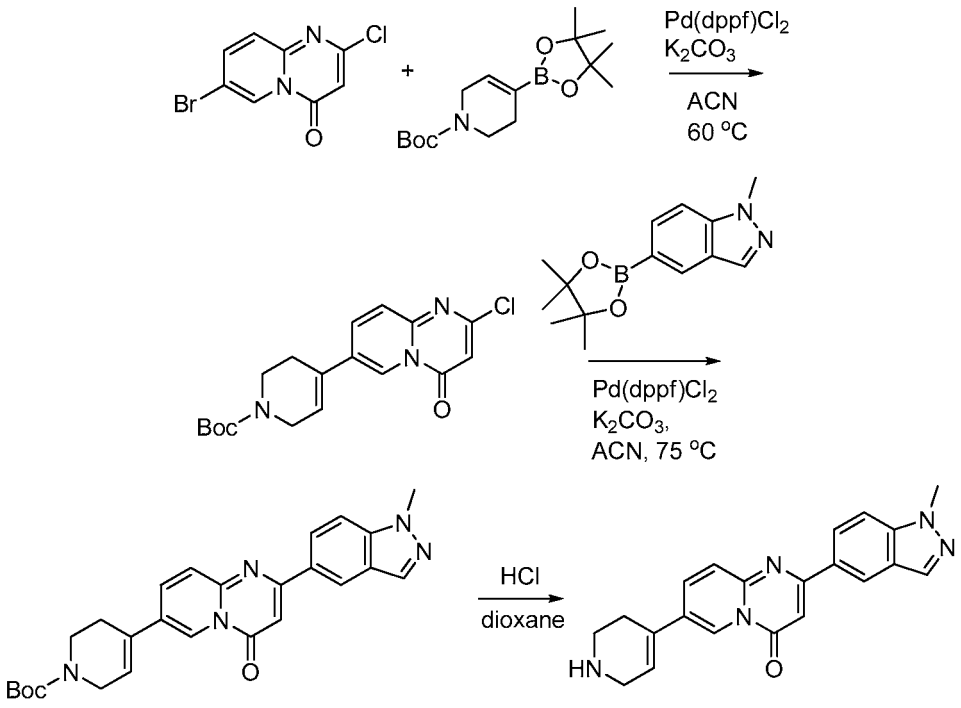
grayish solid (1.119 g, 89%). MS *m/z* 314.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 - 9.01 (1H, m), 8.39 - 8.48 (1H, m), 8.11 - 8.20 (2H, m), 7.86 - 7.96 (1H, m), 7.21 - 7.29 (1H, m), 2.69 (3H, s).

[001380] Part 2, Step B: A mixture of 7-fluoro-2-(4-fluoro-2-methylbenzo[d]oxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (63 mg, 0.2 mmol) and (S)-2-methylpiperazine (30 mg, 0.3 mmol) in DMA (0.5 mL) was heated at 120 °C for 15 hours. The volatiles were removed and the residue was chromatographed (10-15% MeOH in CH_2Cl_2) to give the title compound as a yellow solid (26 mg, 33%). M.P. 207-209 °C; MS *m/z* 394.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.39 (1H, d, J = 1.3 Hz), 8.20 - 8.24 (1H, m), 8.05 - 8.16 (2H, m), 7.71 - 7.77 (1H, m), 7.11 (1H, s), 3.56 - 3.68 (2H, m), 2.98 - 3.06 (1H, m), 2.78 - 2.88 (2H, m), 2.68 (3H, s), 2.62 - 2.68 (1H, m), 2.27 - 2.34 (1H, m), 1.06 (3H, d, J = 6.3 Hz).

[001381] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 36 by substituting the appropriate starting materials, reagents and reaction conditions.

[001382] Example 37

[001383] Preparation of Cpd 443



[001384] Step A: A mixture of 7-bromo-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (516 mg, 2.0 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (740 mg, 2.4 mmol), potassium carbonate (828 mg, 6.0 mmol) and $Pd(dppf)Cl_2$ (144 mg, 0.2 mmol) in acetonitrile (4 mL) was degassed and then heated under N_2 at 60 °C overnight. The volatiles were removed and the residue was chromatographed (30% EtOAc/CH_2Cl_2) to give tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a yellow solid (579 mg, 80%). MS m/z 362.8 $[M+H]^+$.

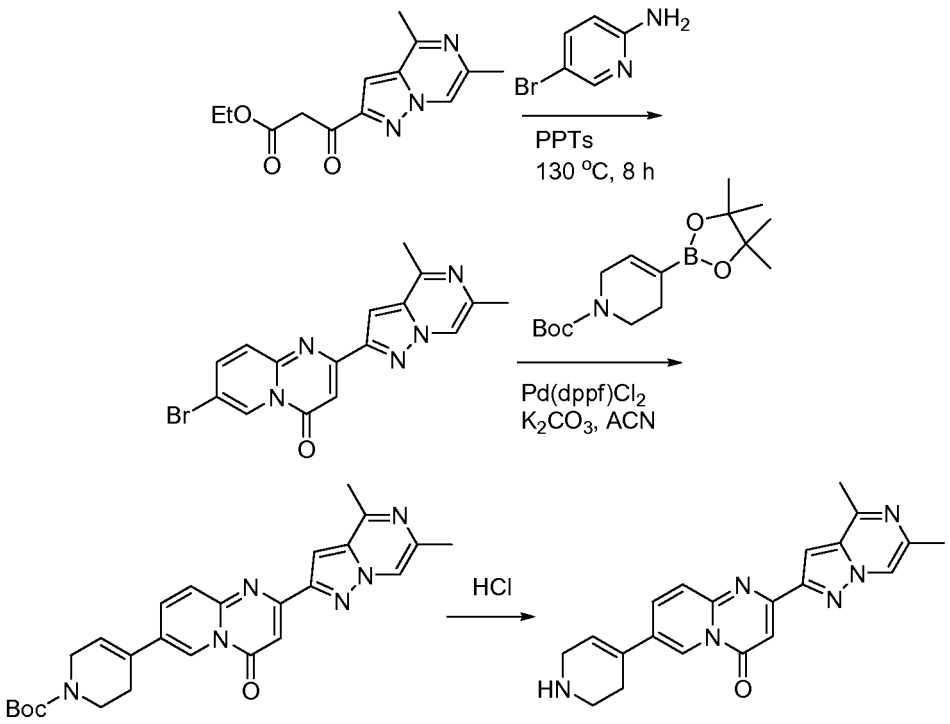
[001385] Step B: To the product from Step A (400 mg, 1.1 mmol) was added 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (220 mg, 1.2 mmol), $Pd(dppf)Cl_2$ (40 mg, 0.05 mmol), potassium carbonate (455 mg, 3.3 mmol) and CH_3CN (2 mL). The mixture was degassed and then heated at 75 °C overnight. The mixture was washed with water and CH_3CN. The volatiles were removed and the residue was chromatographed with 0-2% MeOH in CH_2Cl_2 to give tert-butyl 4-(2-(1-methyl-1H-indazol-5-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate as an off-white solid (327 mg, 65%). MS m/z 458.5 $[M+H]^+$.

[001386] Step C: Following the procedure in Example 22, Step D, the above product from Step B (327 mg, 0.72 mmol) and HCl in dioxane (4 M, 5 mL) provided the title compound as an off-white solid (194 mg, 76%). M.P. 200-203 °C; MS m/z 358.2 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz) δ 8.80 (d, J = 1.6 Hz, 1H), 8.72 (d, J = 1.6 Hz, 1H), 8.30-8.26 (m, 2H), 8.22 (d, J = 1.6 Hz, 1H), 7.77 (d, J = 1.6 Hz, 2H), 7.09 (s, 1H), 6.62 (s, 1H), 4.11 (s, 3H), 3.46-3.44 (m, 2H), 2.98-2.96 (m, 2H), 2.43-2.39 (m, 2H).

[001387] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 37 by substituting the appropriate starting materials, reagents and reaction conditions.

[001388] **Example 38**

[001389] Preparation of Cpd 342



[001390] Step A: Following the procedure in Example 9, Step G, 2-amino-5-bromo-pyridine (415 mg, 2.4 mmol), ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (520 mg, 2.0 mmol) and PPTs (25 mg, 0.1 mmol) gave 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-bromo-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (498 mg, 67%). MS *m/z* 370.2 $[M+H]^+$, 372.2 $[M+2+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.99 - 9.09 (1H, m), 8.53 - 8.62 (1H, m), 8.08 - 8.18 (1H, m), 7.68 - 7.75 (1H, m), 7.55 - 7.63 (1H, m), 7.01 - 7.09 (1H, m), 2.74 (3H, s), 2.44 (3H, s).

[001391] Step B: Following the procedure in Example 22, Step C, 7-bromo-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (498 mg, 1.3 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (482 mg, 1.56 mmol), potassium carbonate (538 mg, 3.9 mmol) and Pd(dppf)Cl_2 (95 mg, 0.13 mmol) in acetonitrile (3 mL) gave tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate as an off-white solid (0.57 g, 84%). MS *m/z* 473.5 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.80 - 8.89 (1H, m), 8.53 - 8.61 (1H, m), 8.23 - 8.32 (1H, m), 7.71 - 7.79 (1H, m), 7.55 - 7.61 (1H, m), 6.99 -

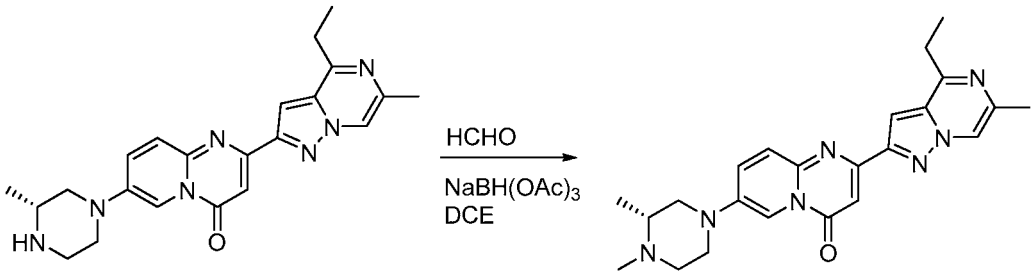
7.04 (1H, m), 4.03 - 4.14 (2H, m), 3.55 - 3.65 (2H, m), 2.74 (3H, s), 2.53 - 2.58 (2H, m), 2.43 (3H, s), 1.44 (9H, s).

[001392] Step C: Following the procedure in example 22, Step D, tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate, HCl (2 mL, 4N in dioxane) in CH_2Cl_2 (4 mL) gave the title compound as an off-white solid (234 mg, 84%). M.P. 207-210 °C; MS *m/z* 373.4 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.80 (1H, s), 8.55 - 8.60 (1H, m), 8.27 - 8.32 (1H, m), 7.73 - 7.78 (1H, m), 7.58 - 7.63 (1H, m), 7.00 - 7.05 (1H, m), 6.57 - 6.65 (1H, m), 3.42 - 3.47 (2H, m), 2.93 - 2.98 (2H, m), 2.72 - 2.76 (2H, m), 2.44 (3H, s), 2.39 (3H, s).

[001393] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 38 by substituting the appropriate starting materials, reagents and reaction conditions.

[001394] **Example 39**

[001395] Preparation of Cpd 629

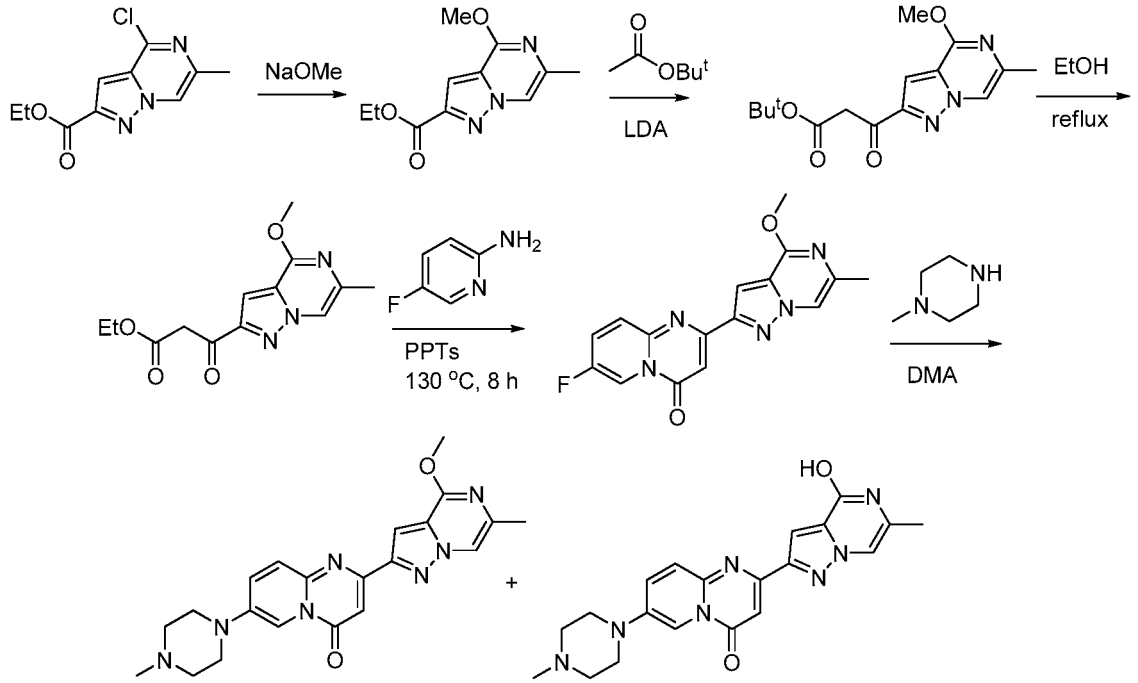


[001396] A mixture of (R)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (48 mg, 0.12 mmol, prepared according to Example 9), formaldehyde (0.039 ml, 0.48 mmol, 37% in water) and sodium triacetoxyborohydride (51 mg, 0.24 mmol) was stirred in dichloromethane (1 mL) for 1 hour. The reaction mixture was diluted with dichloromethane and neutralized with sodium bicarbonate. The organics were dried, concentrated and chromatographed with 0-5% MeOH/CH_2Cl_2 to provide the title compound as a yellow solid (45 mg, 90%). M.P. 257-259 °C; MS *m/z* 418.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.56 (1H, s), 8.25 - 8.26 (1H, m), 8.12 - 8.14 (1H, m), 7.72 - 7.74 (1H, m), 7.55 (1H, s), 6.95 (1H, s), 3.60 - 3.65 (2H, m), 3.08 (2H, q, J = 7.6 Hz), 2.84 - 2.89 (2H, m), 2.43-2.52 (2H, m, obscured by DMSO-d_6), 2.45 (3H, s), 2.29 – 2.31 (1H, m), 2.24 (3H, s), 1.33 (3H, t, J = 7.6 Hz), 1.91 (3H, d, J = 6.2 Hz).

[001397] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 39 by substituting the appropriate starting materials, reagents and reaction conditions.

[001398] **Example 40**

[001399] Preparation of Cpd 625 and Cpd 626



[001400] Step A: A mixture of ethyl 4-chloro-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (2.39 g, 10 mmol, prepared in Example 9, Step C) and sodium methoxide (60 mL, 30 mmol, 0.5 M in MeOH) was stirred at 30 °C for 1 hour. The mixture was concentrated to remove most of the methanol, diluted with water and neutralized with 6 N HCl. A white solid precipitated out and was filtered, washed with water and CH_3CN, and dried to give ethyl 4-methoxy-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate as a white solid (1.387 g, 62%). MS *m/z* 222.2 $[M-CH_3+H]^+$.

[001401] Step B: Following the procedure in Example 9, Step E, tert-butyl acetate (1.6 mL, 12.3 mmol), LDA (10.2 mL, 15.4 mmol, 1.5 M in THF) and ethyl 4-methoxy-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (1.387 g, 6.2 mmol) gave tert-butyl 3-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate as an oil (1.35 g, 72%). MS *m/z* 306.3

$[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.35 (1H, s), 7.27 (1H, s) 4.05 (3H, s), 4.01 (2H, s), 2.36 (3H, s), 1.38 (9H, s).

[001402] Step C: : Following the procedure in Example 9, Step F, tert-butyl 3-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (1.35 g, 4.43 mmol) and EtOH (10 mL) gave ethyl 3-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate as a yellowish solid, which was used directly in the next step without further purification. MS *m/z* 278.3 $[M+H]^+$.

[001403] Step D: A mixture of ethyl 3-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (~4.43 mmol), 2-amino-5-fluoro-pyridine (0.596 g, 5.3 mmol), PPTs (100 mg, 0.4 mmol) and tetraethyl orthosilicate (1.0 mL, 4.43 mmol) in m-xylene (2.2 mL) was heated at 130 °C. After 15 hours, the mixture was cooled to room temperature and washed with CH_2Cl_2 to give 7-fluoro-2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (1.015 g, 70%). MS *m/z* 326.3 $[M+H]^+$.

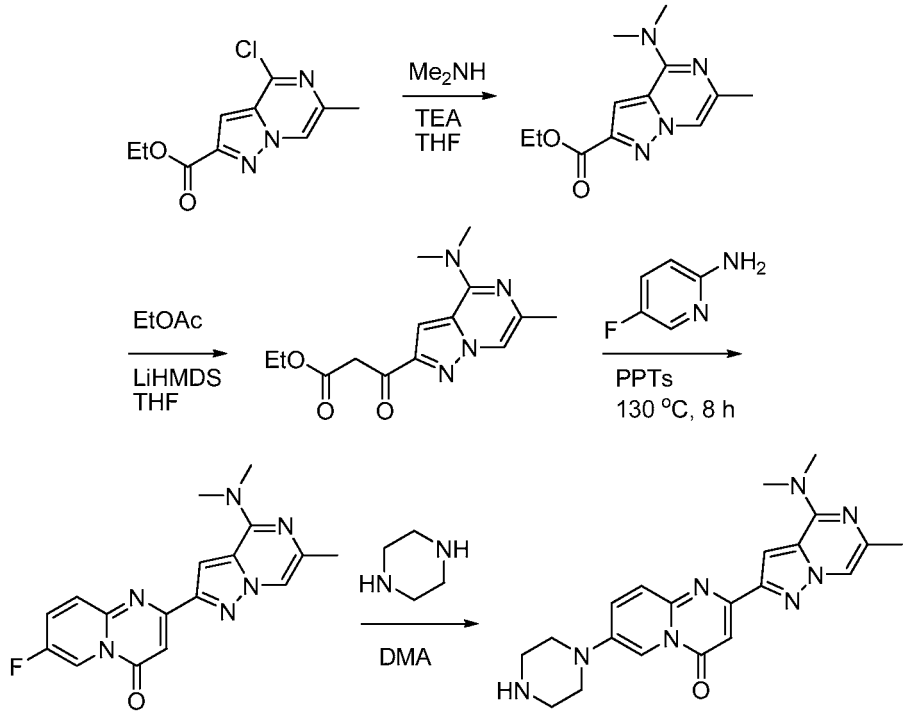
[001404] Step E: A mixture of 7-fluoro-2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (98 mg, 0.30 mmol) and N-methyl-piperazine (150 mg, 1.5 mmol) in DMA (0.6 mL) was heated at 130 °C. After 6 hours, the mixture was cooled to room temperature and chromatographed with 5% MeOH/ CH_2Cl_2 and 10% 3.5 N NH_3 in MeOH/ CH_2Cl_2 to give Cpd 625 (12 mg, 10%) and Cpd 626 (8.5 mg, 7%), each as yellow solids.

[001405] Cpd 625: M.P. 242-244 °C; MS *m/z* 406.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.33 - 8.38 (1H, m), 8.24 - 8.30 (1H, m), 8.09 - 8.15 (1H, m), 7.70 - 7.74 (1H, m), 7.34 - 7.39 (1H, m), 6.92 - 6.96 (1H, m), 4.07 (3H, s), 3.21 - 3.29 (4H, m), 2.5 (4H, m, obscured by DMSO-d_6), 2.37 (3H, s), 2.26 (3H, s).

[001406] Cpd 626: M.P. 280-283 °C; MS *m/z* 392.4 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 11.4 (1H, s), 8.24 - 8.28 (1H, m), 8.09 - 8.14 (1H, m), 7.70 - 7.75 (1H, m), 7.63 - 7.67 (1H, m), 7.48 (1H, s), 6.88 (1H, s), 3.22 - 3.29 (4H, m), 2.51 - 2.56 (4H, m), 2.24 - 2.30 (3H, s), 2.15 (3H, s).

[001407] **Example 41**

[001408] Preparation of Cpd 688



[001409] Step A: A mixture of ethyl 4-chloro-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (0.956 g, 4 mmol, prepared in Example 9, Step C), dimethylamine (2.1 mL, 4.2 mmol, 2.0 M in THF) and Et_3N (0.84 mL, 6.0 mmol) was heated at 60 °C. After 15 hours, the mixture was concentrated, the residue was dissolved in EtOAc, washed with water, dried and concentrated to give ethyl 4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate as an off-white solid (0.99 g, 99%). MS *m/z* 249.3 $[M+H]^+$.

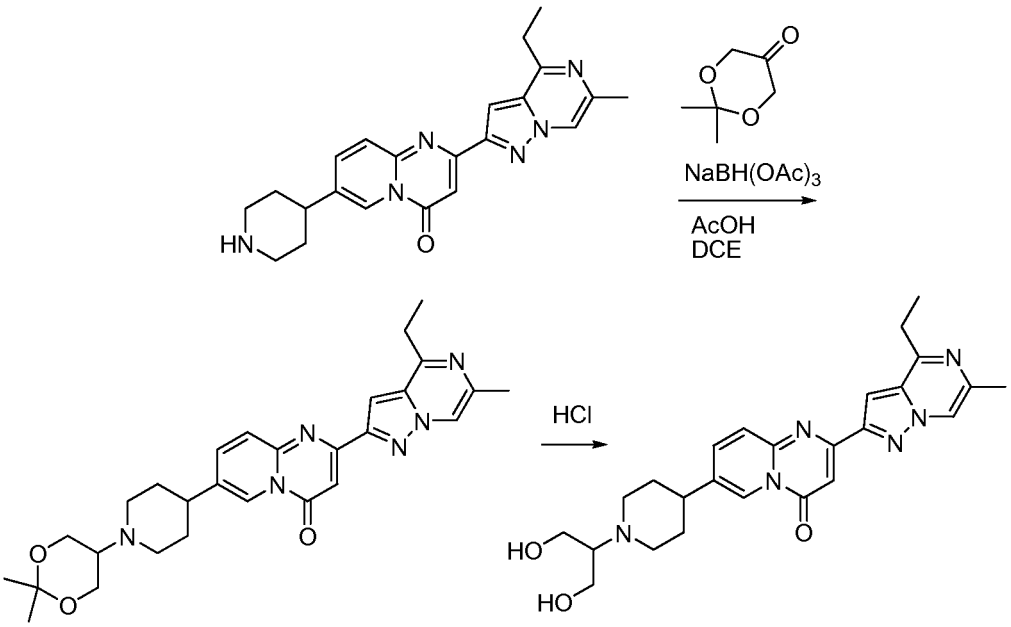
[001410] Step B: To a solution of ethyl 4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazine-2-carboxylate (0.99 g, 4.0 mmol) and EtOAc (1.95 mL, 20 mmol) in THF (30 mL) at -20 °C was added LiHMDS (11.1 mL, 10 mmol, 0.9 M in THF). After 1 hours, the mixture was quenched with saturated NH_4Cl, extracted with EtOAc. The organics were concentrated and chromatographed with 2% MeOH/DCM to give ethyl 3-(4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate as a pale yellow oil (0.48 g, 40%). MS *m/z* 291.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 7.73 (1H, s), 7.05 (1H, s), 5.43 (2H, s), 3.96 (2H, q, *J* = 7.0 Hz), 3.28 (6H, s), 2.20 (3H, s), 1.16 (3H, t, J = 7.0 Hz)

[001411] Step C: Following the procedure in Example 40, Step D, ethyl 3-(4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (0.48 g, 1.6 mmol), 2-amino-5-fluoro-pyridine (179 mg, 1.6 mmol), PPTs (40 mg, 0.16 mmol) and tetraethyl orthosilicate (0.36 mL, 1.6 mmol) in m-xylene (0.8 mL) gave 2-(4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a yellow solid (0.39 g, 72%). MS *m/z* 339.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.92 - 9.00 (1H, m), 8.06 - 8.18 (1H, m), 7.91 - 7.94 (1H, m), 7.85 - 7.91 (1H, m), 7.55 - 7.61 (1H, m), 6.98 - 7.08 (1H, m), 3.36 (6H, s), 2.25 (3H, s).

[001412] Step D: A mixture of 7-fluoro-2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (50 mg, 0.15 mmol) and piperazine (86 mg, 1.0 mmol) in DMA (0.5 mL) was heated at 150 °C. After 2 hours, the mixture was cooled to room temperature and washed with CH_3CN to give the title compound as a yellow solid (60 mg, 98%). M.P. 245-248 °C; MS *m/z* 405.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 - 8.28 (1H, m), 8.06 - 8.11 (1H, m), 7.89 - 7.92 (1H, m), 7.69 - 7.75 (1H, m), 7.50 - 7.55 (1H, m), 6.92 (1H, s), 3.35 (6H, s), 3.12 - 3.19 (4H, m), 2.87 - 2.92 (4H, m), 2.80 (1H, s), 2.24 (3H, s).

[001413] **Example 42**

[001414] Preparation of Cpd 694



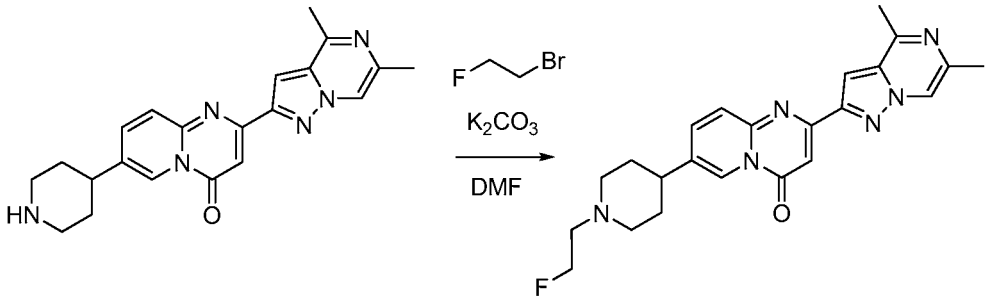
[001415] Step A: To a mixture of 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (78 mg, 0.2 mmol, prepared according to the

procedure in Examples 38 and 24) and 2,2-dimethyl-1,3-dioxan-5-one (72 mg, 0.5 mmol, 90% tech grade) in dichloroethane (1 mL) were added $NaBH(OAc)_3$ (106 mg, 0.5 mmol) and 1 drop of AcOH. The mixture was stirred at 60 °C. After 1 hour, the mixture was quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2, concentrated and chromatographed (2-5% MeOH/ CH_2Cl_2) to give 7-(1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a white solid (70 mg, 70%). MS *m/z* 503.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.75 - 8.82 (1H, m), 8.54 - 8.61 (1H, m), 8.00 - 8.10 (1H, m), 7.72 - 7.79 (1H, m), 7.58 - 7.63 (1H, m), 6.99 - 7.03 (1H, m), 3.86 - 3.95 (2H, m), 3.71 - 3.81 (2H, m), 3.06 - 3.15 (2H, m), 3.00 - 3.06 (2H, m), 2.70 - 2.80 (1H, m), 2.53 - 2.59 (1H, m), 2.45 (3H, s), 2.28 - 2.38 (2H, m), 1.82 - 1.90 (2H, m), 1.59 - 1.71 (2H, m), 1.32 - 1.37 (6H, m), 1.27 (3H, s).

[001416] Step B: To a mixture of 7-(1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (50 mg, 0.1 mmol) in THF (10 mL) was added HCl (1.3 mL, 2.6 mmol, 2 N). The mixture was stirred at room temperature. After 15 hours, the mixture was treated with excess of 7N NH_3 in MeOH, concentrated and chromatographed (10% 2.5 N NH_3 in MeOH/ CH_2Cl_2) to give the title compound as a yellow solid (45 mg, 97%). M.P. 228-230 °C; MS *m/z* 463.6 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6) δ 8.77 - 8.84 (1H, m), 8.54 - 8.61 (1H, m), 8.02 - 8.10 (1H, m), 7.90 - 7.94 (1H, m), 7.74 - 7.79 (1H, m), 7.57 - 7.63 (1H, m), 6.99 - 7.05 (1H, m), 4.21 - 4.31 (2H, m), 3.42 - 3.59 (4H, m), 3.10 (2H, q, J = 7.5 Hz), 2.89 - 3.00 (2H, m), 2.70-2.72 (1H, m), 2.57 - 2.62 (1H, m), 2.45 (3H, s), 1.79 - 1.89 (2H, m), 1.63 - 1.75 (2H, m), 1.34 (3H, t, *J* = 7.5 Hz).

[001417] **Example 43**

[001418] Preparation of Cpd 662

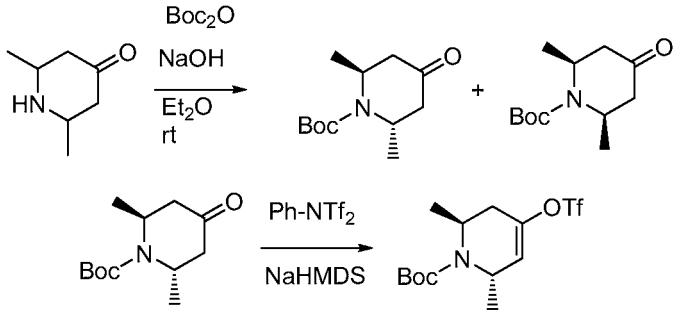


[001419] A mixture of 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (56 mg, 0.15 mmol, prepared according to the procedure in Example 24), 1-bromo-2-fluoroethane (23 mg, 0.18 mmol) and K_2CO_3 (23 mg, 0.18 mmol) in DMF (1 mL) was heated at 80 °C. After 7 hours, the mixture was cooled to room temperature and chromatographed (5% MeOH/CH_2Cl_2) to give the title compound as a yellow solid (29 mg, 44%). M.P. 197-199 °C; MS *m/z* 421.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 - 8.85 (1H, m), 8.55 - 8.60 (1H, m), 8.05 - 8.11 (1H, m), 7.73 - 7.80 (1H, m), 7.57 - 7.62 (1H, m), 7.02 (1H, s), 4.59 - 4.65 (1H, m), 4.48 - 4.55 (1H, m), 3.01 - 3.07 (2H, m), 2.69-2.75 (1H, m), 2.74 (3H, s), 2.68 - 2.72 (1H, m), 2.62 - 2.67 (1H, m), 2.43 (3H, s), 2.12 - 2.21 (2H, m), 1.85-1.88 (2H, m), 1.70-1.88 (2H, m).

[001420] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 43 by substituting the appropriate starting materials, reagents and reaction conditions.

[001421] **Example 44**

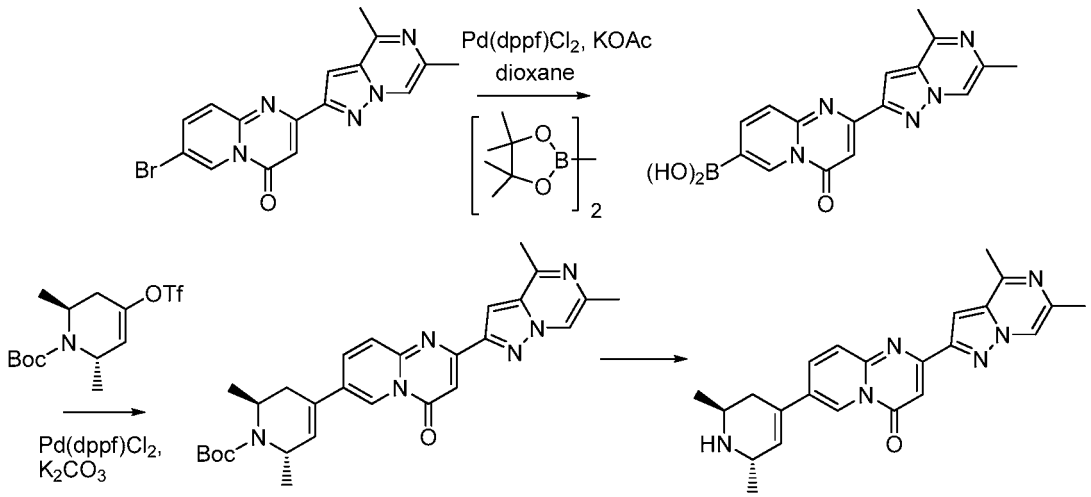
[001422] Preparation of Cpd 798



[001423] Part 1, Step A: To a solution of 2,6-dimethylpiperidin-4-one (1.27 g, 10 mmol, a mixture of trans/cis isomers in a ratio of ~1.5/1) and di-tert-butyl dicarbonate (2.40 g, 11 mmol) in ether was added NaOH (11 mL, 11 mmol, 1 N in water). The mixture was stirred at room temperature. After 36 hours, the mixture was extracted with ether. The organics were concentrated and chromatographed (5-30% EtOAc/Hexanes) to give a mixture of tert-butyl 2,6-dimethyl-4-oxopiperidine-1-carboxylate as a Tran/cis mixture in a ratio of ~1.2/1 (1.99 g, 87%, clear oil). Upon standing overnight, a solid precipitated from the oil, which was filtered and washed with ether to give the tert-butyl *trans*-2,6-dimethyl-4-oxopiperidine-1-carboxylate (0.376 g, 16%)(95% trans by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.33 - 4.45 (2H, m), 2.80 - 2.90

(2H, m), 2.33 - 2.44 (2H, m), 1.50 (9H, s), 1.26 (6H, d, J = 6.9 Hz). The ^{1}H NMR is consistent with that of the trans-isomer in a mixture of cis and trans-isomers (US200839454, JOC, 1993, 58, 1109-1117).

[001424] Part 1, Step B: To a solution of the tert-butyl *trans*-2,6-dimethyl-4-oxopiperidine-1-carboxylate (266 mg, 1.17 mmol) in THF (7 mL) at -78 °C was added NaHMDS. After 1 hour, N-Phenyl-bis(trifluoromethanesulfonimide) (0.50 g, 1.4 mmol) in THF (3 mL) was added. The reaction mixture was stirred at room temperature for 2 hours, quenched with saturated NH_4Cl and extracted with ether. The organics were concentrated and chromatographed with 1% EtOAc/Hexanes to give tert-butyl-trans-2,6-dimethyl-4-(trifluoromethylsulfonyloxy)-5,6-dihydropyridine-1(2H)-carboxylate (0.415 g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 - 5.85 (1H, m), 4.29 - 4.44 (2H, m), 2.81 - 2.90 (1H, m), 2.15 - 2.23 (1H, m), 1.48 (9H, s), 1.37 (3H, d, J = 6.6 Hz), 1.24 (3H, d, J = 6.6 Hz).



[001425] Part 2, Step A: Following the procedure of Example 14, Part 2, 7-bromo-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (0.74 g, 2.0 mmol, prepared in Example 38, Step A), KOAc (590 mg, 6.0 mmol), bis(pincolato)diboron (560 mg, 2.2 mmol), and $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (82 mg, 0.1 mmol) in dioxane (6 mL) provided 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-ylboronic acid. The crude intermediate was used directly in the next step. MS m/z 336.3 $[M+H]^+$.

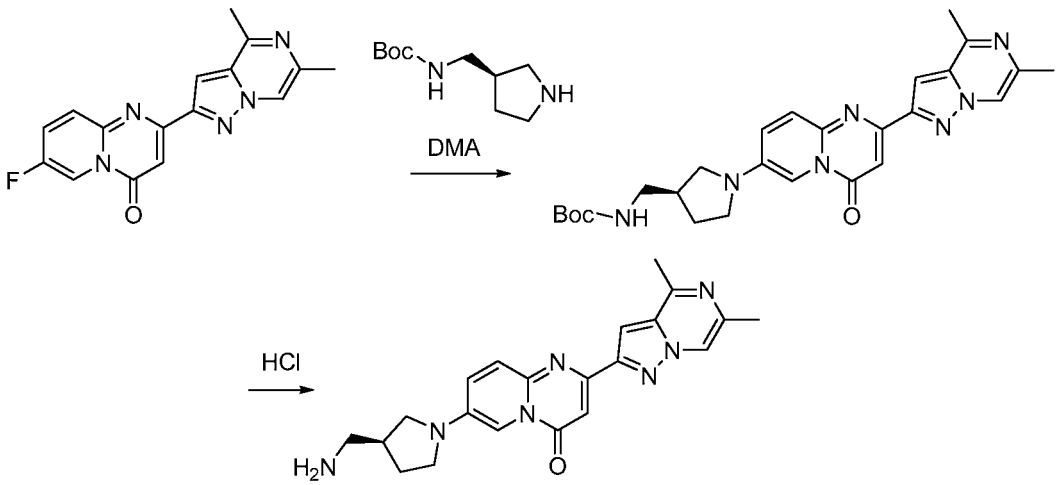
[001426] Part 2, Step B: Following the procedure of Example 14, Part 3, Step A, 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-ylboronic acid (~2 mmol), tert-butyl-trans- 2,6-dimethyl-4-(trifluoromethylsulfonyloxy)-5,6-dihydropyridine-

1(2H)-carboxylate (0.415 g, 1.15 mmol), potassium carbonate (3.5 mL, 2.0M) and Pd(dppf)Cl_2• CH_2Cl_2 (82 mg, 0.1 mmol) in acetonitrile (10 mL) provided tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-trans-2,6-dimethyl-5,6-dihydropyridine-1(2H)-carboxylate as a yellow solid (0.5 g, 87%). MS m/z 501.4 $[M+H]^+$.

[001427] Part 2, Step C: Following the procedure in Example 38, Step C, tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-trans-2,6-dimethyl-5,6-dihydropyridine-1(2H)-carboxylate (50 mg, 0.1 mmol) and HCl in dioxane (4 M, 0.5 mL) provided the title compound as a yellow solid (25 mg, 62%). M.P. 228-231 °C; MS m/z 401.3 $[M+H]^+$; ^{1}HNMR (500 MHz, DMSO-d_6) δ 8.77 - 8.82 (1H, m), 8.54 - 8.58 (1H, m), 8.25 - 8.32 (1H, m), 7.70 - 7.76 (1H, m), 7.57 (1H, s), 7.02 (1H, s), 6.50 - 6.58 (1H, m), 3.64 - 3.75 (1H, m), 3.08 - 3.18 (1H, m), 2.73 (3H, s), 2.41-2.44 (1H, m), 2.43 (3H, s), 1.99 - 2.08 (1H, m), 1.21 (3H, d, J = 6.6 Hz), 1.16 (3H, d, J = 6.3 Hz).

[001428] **Example 45**

[001429] Preparation of Cpd 764



[001430] Step A: Following the procedure in Example 9, Step H, 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (618 mg, 2.0 mmol), (R)-tert-butyl pyrrolidin-3-ylmethylcarbamate (481 mg, 2.4 mmol) and DMA (2.0 mL) provided (S)-tert-butyl (1-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)pyrrolidin-3-yl)methylcarbamate (0.90 g, 92%) as a yellow solid. MS *m/z* 490.5 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 - 8.59 (1H, m), 7.97 - 8.03 (1H, m), 7.72 - 7.82 (2H, m),

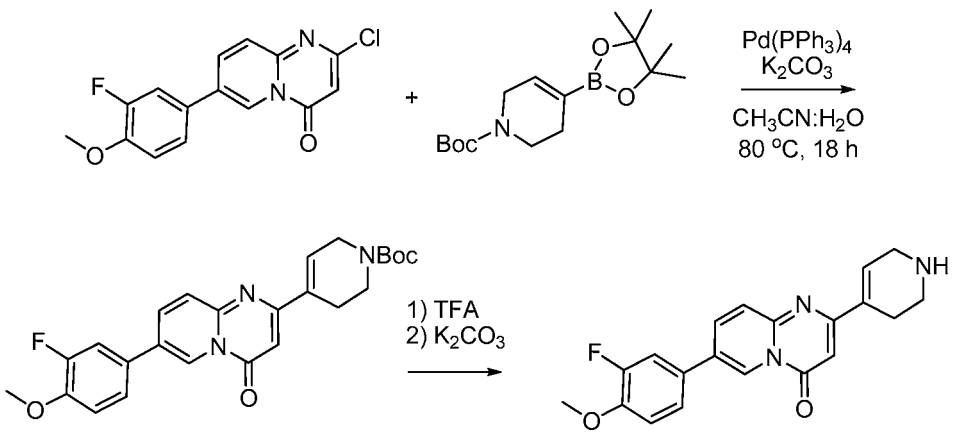
7.48 - 7.57 (1H, m), 7.04-7.08 (1H, m), 6.87 - 6.94 (1H, m), 3.41 - 3.50 (2H, m), 3.35 - 3.41 (1H, m), 2.97 - 3.16 (3H, m), 2.73 (3H, s), 2.47-2.51 (1H, m, obscured by DMSO- d_6), 2.43 (3H, s), 2.04 - 2.16 (1H, m), 1.71 - 1.83 (1H, m), 1.39 (9H, s).

[001431] Step B: Following the procedure in Example 38, Step C, (S)-tert-butyl (1-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)pyrrolidin-3-yl)methylcarbamate (0.39 g, 0.8 mmol), HCl (2.0 mL, 4 M in dioxane) and CH_2Cl_2 (10 mL) provided the title compound as a yellow solid (0.19 g, 62%). M.P. 244-246 °C; MS *m/z* 390.4 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 - 8.57 (1H, m), 7.96 - 8.03 (1H, m), 7.73 - 7.80 (2H, m), 7.52 (1H, s), 6.90 (1H, s), 3.42 - 3.50 (2H, m), 3.34 - 3.41 (1H, m), 3.10 - 3.18 (1H, m), 2.73 (3H, s), 2.59 - 2.70 (2H, m), 2.43 (3H, s), 2.34 - 2.42 (1H, m), 2.09 - 2.16 (1H, m), 1.73 - 1.82 (1H, m).

[001432] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 45 by substituting the appropriate starting materials, reagents and reaction conditions.

[001433] **Example 46**

[001434] Preparation of Cpd 294



[001435] Step A: 2-chloro-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (182 mg, 0.6 mmol), prepared according to Example 30, Step A, was combined with tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (222 mg, 0.72 mmol), tetrakis(triphenylphosphine) palladium(0) (67 mg, 0.06 mmol), CH_3CN (2 mL) and aqueous K_2CO_3 (1 M, 2 mL). The mixture was heated at 80 °C for 18 hours. After cooling to room temperature, the mixture was filtered, providing tert-butyl 4-(7-(3-fluoro-4-

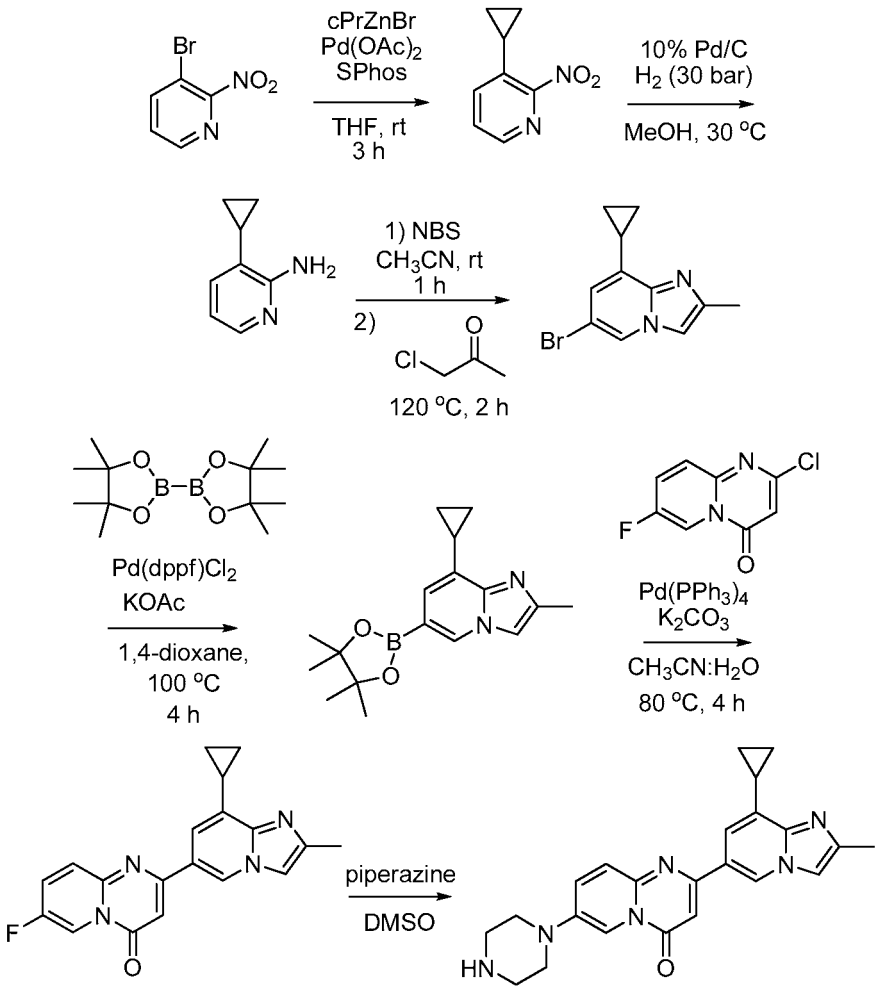
methoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a crude product that was used directly in the next step.

[001436] Step B: The tert-butyl 4-(7-(3-fluoro-4-methoxyphenyl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate from step A was dissolved in TFA (2 mL). After 10 minutes, volatiles were removed with a nitrogen stream. The residue was partitioned in CH_2Cl_2 and aqueous K_2CO_3 (1 M). The organic layer was loaded onto silica gel, eluting with 0-10% MeOH (3% NH_3) in CH_2Cl_2, affording the title compound as a white powder (150 mg, 72%). M.P. 188-192 °C; MS *m/z* 352.1 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.05 (1H, d, J = 2.3 Hz), 8.28 (1H, dd, J = 9.4 Hz, 2.2 Hz), 7.76 (1H, dd, J = 12.7 Hz, 2.3 Hz), 7.70 (1H, d, J = 9.3 Hz), 7.63 (1H, m), 7.33 (1H, t, J = 8.8 Hz), 7.14 (1H, m), 6.44 (1H, s), 3.92 (3H, s), 3.46 (2H, m), 2.91 (2H, m), 2.39 (2H, m).

[001437] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 46 by substituting the appropriate starting materials, reagents and reaction conditions.

[001438] **Example 47**

[001439] Preparation of Cpd 714



[001440] Step A: 3-Bromo-2-nitropyridine (2.0 g, 10 mmol) was dissolved in THF (20 mL). 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl (205 mg, 0.5 mmol) and palladium(II) acetate (113 mg, 0.5 mmol) were added to the mixture. To the mixture was added cyclopropylzinc bromide (15 mmol, 0.5 M in THF). The mixture was stirred at room temperature for 3 hours. The mixture was concentrated and chromatographed on silica gel, eluting with 0-5% EtOAc in CH_2Cl_2 to provide 3-cyclopropyl-2-nitropyridine (1.1 g, 67%) as a white solid. MS *m/z* 165.2 $[M+H]^+$.

[001441] Step B: 3-Cyclopropyl-2-nitropyridine (1.1 g, 6.7 mmol) was dissolved in MeOH (150 mL). The solution was passed over a cartridge containing 10% Pd/C under H_2 (30 bar) at

30 °C. The solution was concentrated leaving 3-cyclopropyl-2-aminopyridine (898 mg, quant.) as colorless oil. MS *m/z* 135.1 $[M+H]^+$.

[001442] Step C: Following the procedure in Example 16, Step A, 3-cyclopropyl-2-aminopyridine (898 mg, 6.7 mmol), N-bromosuccinimide (1.3 g, 7.4 mmol), CH_3CN (15 mL) and chloroacetone (0.81 mL, 10 mmol) provided 6-bromo-8-cyclopropyl-2-methylimidazo[1,2-a]pyridine as a tan powder (255 mg, 15%). MS *m/z* 251.1 $[M+H]^+$, 253.1 $[M+2+H]^+$.

[001443] Step D: Following the procedure in Example 14, Part 2, 6-Bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine (255 mg, 1.0 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (380 mg, 1.5 mmol), [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (41 mg, 0.05 mmol) and potassium acetate (196 mg, 2 mmol) provided 8-cyclopropyl-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine. The crude product was used directly in the next step.

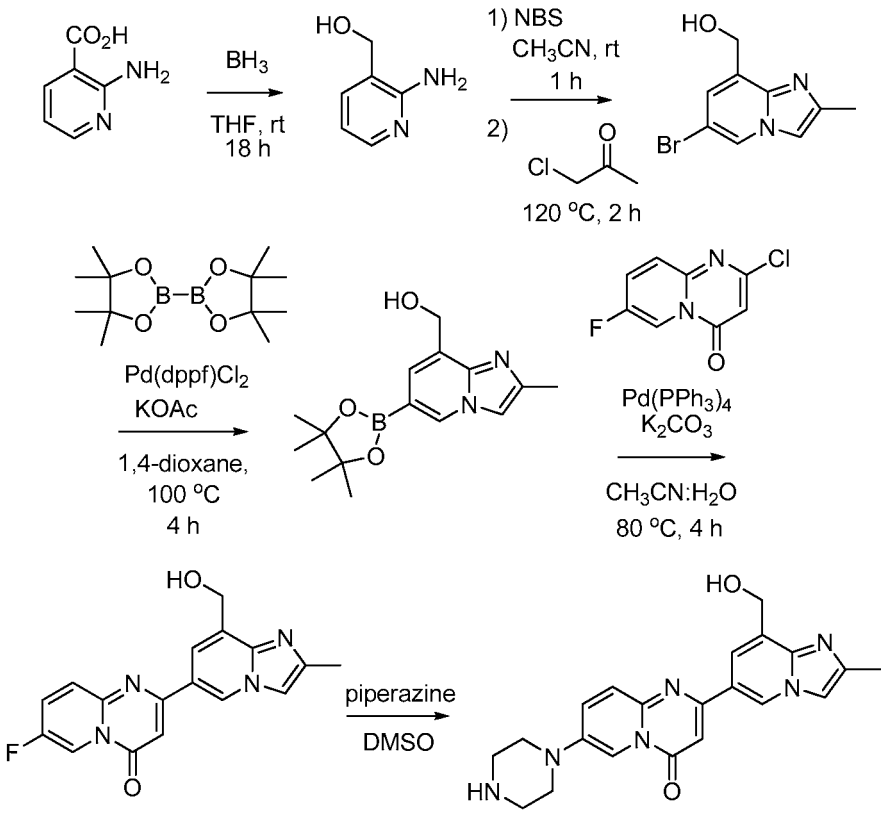
[001444] Step E: Following the procedure in Example 14, Part 3, Step A, the crude product of 8-cyclopropyl-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine from Step D and 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (1 mmol, prepared in Example 14, Part 1, Step B), tetrakis(triphenylphosphine) palladium(0) (112 mg, 0.1 mmol), CH_3CN (4 mL) and aqueous K_2CO_3 (1M, 4 mL) provided 2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one as a tan powder (330 mg, 99%). MS *m/z* 335.2 $[M+H]^+$.

[001445] Step F: Following the procedure in Example 14, Part 3, Step B, 2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (50 mg, 0.15 mmol) and piperazine (65 mg, 0.75 mmol) afforded the title compound as a tan powder (38 mg, 63%). M.P. 274-277 °C; MS *m/z* 401.4 $[M+H]^+$; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.14 (1H, d, J = 1.7 Hz), 8.21 (1H, d, J = 2.9 Hz), 8.07 (1H, dd, J = 9.7 Hz, 2.8 Hz), 7.79 (1H, d, J = 1.0 Hz), 7.67 (1H, d, J = 9.2 Hz), 7.43 (1H, m), 6.99 (1H, s), 3.14 (4H, m), 2.89 (4H, m), 2.48 (1H, m), 2.37 (3H, s), 2.35 (1H, br s), 1.13 (2H, m), 1.04 (2H, m).

[001446] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 47 by substituting the appropriate starting materials, reagents and reaction conditions.

[001447] **Example 48**

[001448] Preparation of Cpd 674



[001449] Step A: 2-Aminonicotinic acid (4.8 g, 35 mmol) was suspended in THF (100 mL). To the mixture was added borane THF complex (40 mmol, 1 M in THF). The mixture was stirred at room temperature for 18 hours. The excess reagent was quenched by the addition of aqueous potassium hydroxide (2 M, 15 mL). The mixture was stirred vigorously for 10 minutes. The organic layer was collected and concentrated. The residue was chromatographed on silica gel, eluting with 0-10% MeOH in CH_2Cl_2 to provide (2-aminopyridin-3-yl)methanol (1.0 g, 23%) as a white solid. MS *m/z* 125.1 $[M+H]^+$.

[001450] Step B: Following the procedure in Example 16, Step A, (2-aminopyridin-3-yl)methanol (1.0 g, 8 mmol), N-bromosuccinimide (1.57 g, 8.8 mmol), CH_3CN (16 mL) and chloroacetone (0.81 mL, 10 mmol) provided (6-bromo-2-methylimidazo[1,2-a]pyridin-8-yl)methanol as a tan powder (82 mg, 4%). MS *m/z* 241.1 $[M+H]^+$, 243.1 $[M+2+H]^+$.

[001451] Step C: Following the procedure in Example 14, Part 2, 6-Bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine (85 mg, 0.35 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-

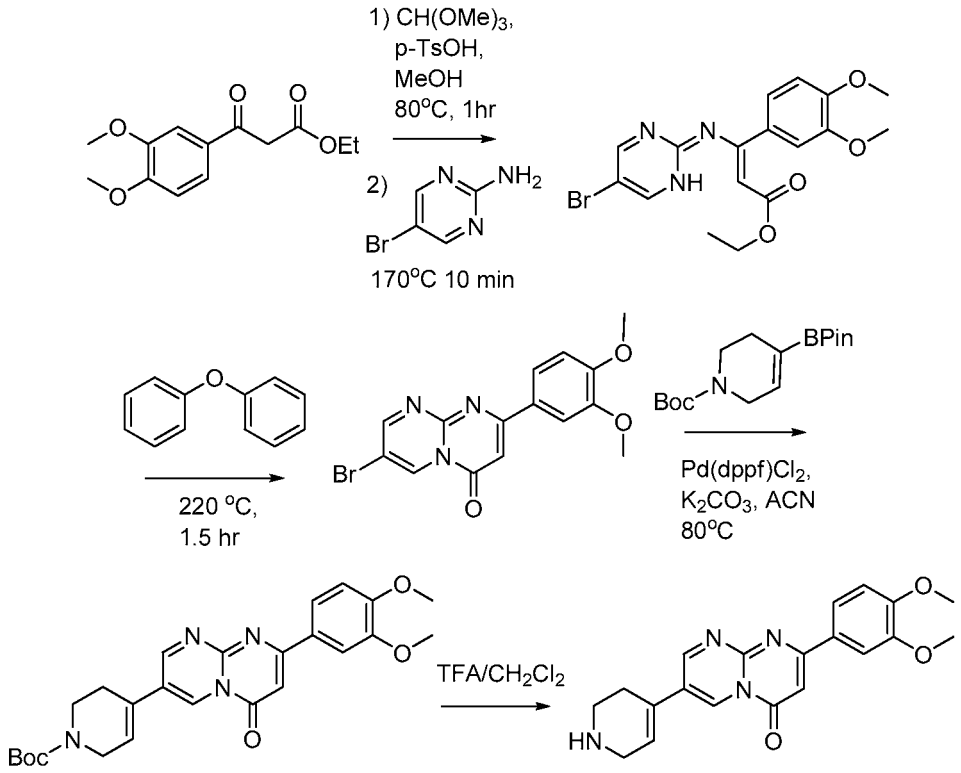
dioxaborolane) (133 mg, 0.53 mmol), [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (30 mg, 0.035 mmol) and potassium acetate (69 mg, 0.7 mmol) provided (2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridin-8-yl)methanol. The crude product was used directly in the next step.

[001452] Step D: Following the procedure in Example 14, Part 3, Step A, the crude product of (2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridin-8-yl)methanol from Step C and 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.35 mmol, prepared in Example 14, Part 1, Step B,, tetrakis(triphenylphosphine) palladium(0) (39 mg, 0.035 mmol), CH_3CN (2 mL) and aqueous K_2CO_3 (1 M, 2 mL) provided 7-fluoro-2-(8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a tan powder (100 mg, 88%). MS *m/z* 325.2 $[M+H]^+$.

[001453] Step E: Following the procedure in Example 14, Part 3, Step B, 7-fluoro-2-(8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (120 mg, 0.15 mmol) and piperazine (65 mg, 0.75 mmol) afforded the title compound as a tan powder (120 mg, 99%). M.P. >320 °C; MS *m/z* 391.3 $[M+H]^+$; ^1H NMR (DMSO-d_6, 500 MHz): δ 9.23 (1H, s), 8.24 (1H, d, J = 2.6 Hz), 8.07 (1H, dd, J = 9.7 Hz, 2.6 Hz), 7.96 (1H, s), 7.79 (1H, s), 7.73 (1H, d, J = 6.7 Hz), 6.87 (1H, s), 4.86 (2H, s), 3.14 (4H, m), 2.89 (4H, m), 2.37 (3H, s).

[001454] **Example 49**

[001455] Preparation of Cpd 353



[001456] Step A: Ethyl 3-(3,4-dimethoxyphenyl)-3-oxopropanoate (907 mg, 3.6 mmol) was dissolved in methanol (2 mL). p-Toluenesulfonic acid monohydrate (34.2 mg, 0.18 mmol) was added to the solution, followed by trimethylorthoformate (0.59 mL, 5.4 mmol). The solution was stirred at 80 °C for 1 hour. Volatiles were removed with a stream of nitrogen. To the crude material were added 5-bromopyrimidin-2-amine (550 mg, 3.1 mmol) and diphenyl ether (2 mL). The mixture was heated at 170 °C for 10 minutes. The reaction mixture was passed through a through a flash silica column (33% Hexanes/CH_2Cl_2) to give ethyl-3-(-5-bromopyrimidin-2(1H)-ylideneamino)-3-(3,4-dimethoxyphenyl)acrylate as a yellow solid. MS *m/z* 408.0 $[M+H]^+$, 410.0 $[M+2+H]^+$.

[001457] Step B: To ethyl-3-(-5-bromopyrimidin-2(1H)-ylideneamino)-3-(3,4-dimethoxyphenyl)acrylate was added diphenyl ether (2 mL). The reaction was heated to 220 °C for 1.5 hours. The mixture was purified by chromatography (100% CH_2Cl_2) to provide 7-bromo-2-(3,4-dimethoxyphenyl)-4H-pyrimido[1,2-a]pyrimidin-4-one (314 mg, 28% for 2 steps) as a yellow solid. MS *m/z* 361.9 $[M+H]^+$, 363.9 $[M+2+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.30

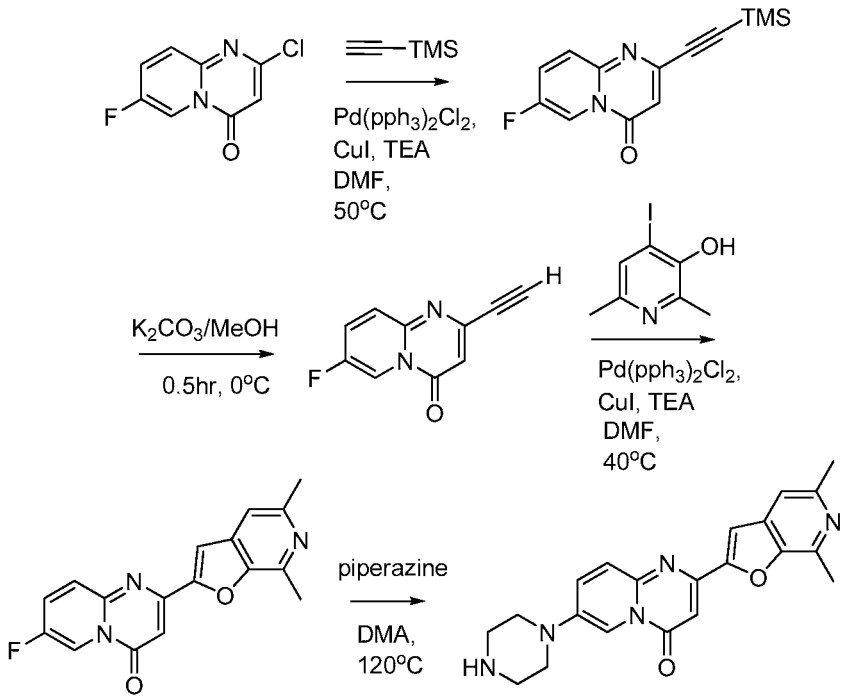
(1H, d, J = 2.7 Hz), 9.20 (1H, d, *J* = 2.9 Hz), 7.88 (1H, dd, *J* = 8.5 Hz, 2.6 Hz), 7.79 (1H, d, J = 2.2 Hz), 7.15 (1H, s), 7.11 (1H, d, *J* = 8.5 Hz), 3.88 (3H, s), 3.85 (3H, s).

[001458] Step C: A mixture of 7-bromo-2-(3,4-dimethoxyphenyl)-4H-pyrimido[1,2-a]pyrimidin-4-one (53.7 mg, 0.15 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (50.5 mg, 0.016 mmol), $Pd(dppf)Cl_2$ (11 mg, 0.015 mmol), K_2CO_3 (62.2 mg, 0.45 mmol), and ACN (1 mL) was degassed and then heated under N_2 at 80 °C overnight. The volatiles were removed and the residue was used in the next step without purification. MS *m/z* 465.4 $[M+H]^+$.

[001459] Step D: A solution of tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrimido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate in CH_2Cl_2/TFA (0.5 mL / 0.5 mL) was stirred at 0 °C for 2 hours. After most of the TFA and CH_2Cl_2 were removed by rotary evaporation, ice-cold saturated $NaHCO_3$ was added to the reaction mixture. The mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, concentrated, and chromatographed (5% MeOH/CH_2Cl_2) to provide the title compound as a yellow solid. MS *m/z* 365.1 $[M+H^+]$.

[001460] **Example 50**

[001461] Preparation of Cpd 486



[001462] Step A: A mixture of 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (995 mg, 5 mmol, prepared in Example 14, Part 1), CuI (19.0 mg, 0.1 mmol), $PdCl_2(PPh_3)_2$ (70.2 mg, 0.1 mmol), ethynyltrimethylsilane (2.1 mL, 15 mmol), triethylamine (2.1 mL, 15 mmol) in DMF (10 mL) was degassed and then heated under N_2 at 50 °C overnight. The volatiles were removed and the crude 7-fluoro-2-((trimethylsilyl)ethynyl)-4H-pyrido[1,2-a]pyrimidin-4-one was used directly for the next step. MS *m/z* 261.1 [M+H$^+$].

[001463] Step B: Potassium carbonate (1.0 g, 7.5 mmol) was added to the solution of crude 7-fluoro-2-((trimethylsilyl)ethynyl)-4H-pyrido[1,2-a]pyrimidin-4-one in MeOH (33 mL). The mixture was stirred at 0 °C for 0.5 hours. After MeOH was removed by rotary evaporation, water was added. The precipitate was filtered and purified by silica chromatography (8% EtOAc/CH_2Cl_2) to give 2-ethynyl-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (192.1 mg, 20% for 2 steps) as a yellow solid. MS *m/z* 189.1 [M+H$^+$].

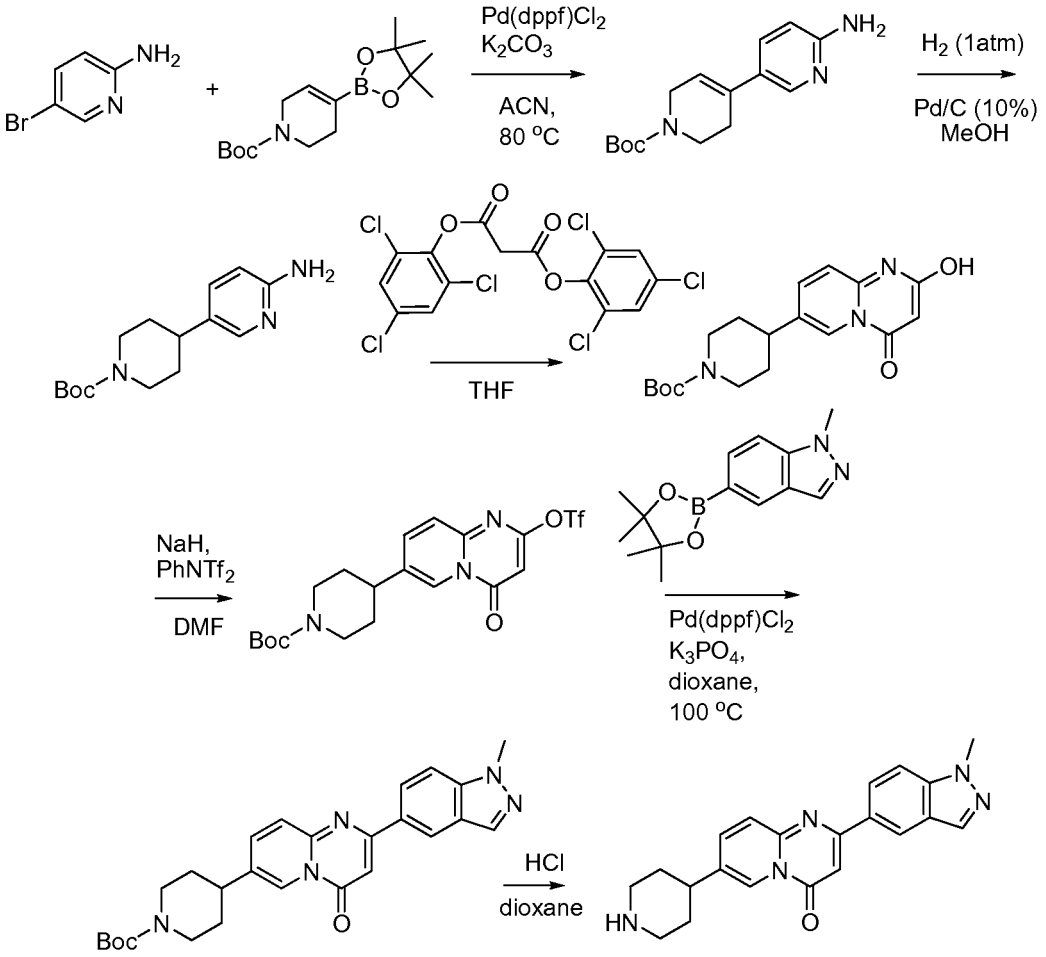
[001464] Step C: A mixture of 2-ethynyl-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (192.1 mg, 1.0 mmol), 4-iodo-2,6-dimethylpyridin-3-ol (305.3 mg, 1.2 mmol), CuI (9.7 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (35.8 mg, 0.05 mmol), triethylamine (288 μL, 2 mmol) in DMF (1.7 mL) was degassed and then heated under N_2 at 40 °C overnight. After most of the DMF was removed, water was added. The precipitate was filtered and purified by chromatography (14% EtOAC/CH_2Cl_2) to give 2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (126.3mg, 41%) as a yellow solid. MS *m/z* 310.1 [M+H$^+$].

[001465] Step D: Piperazine (64.6 mg, 0.75 mmol) was added to a solution of 2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (46.4 mg, 0.15 mmol) in DMA (0.5 mL). The reaction mixture was heated at 120 °C for 2 hours. After most of the DMA was removed, CH_3CN was added to the reaction mixture, and a precipitate was formed. The precipitate was filtered, washed with water and dried to provide the title compound as a yellow solid (30 mg, 53%). M.P.198-200 °C; MS *m/z* 376.3 [M+H$^+$]; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.25 (1H, d, J = 2.5 Hz), 8.13 (1H, dd, J = 9.9 Hz, 2.5 Hz), 7.73 (1H, d, J = 9.8 Hz), 7.64 (1H, s), 7.41 (1H, s), 6.94 (1H, s), 3.17 (4H, m), 2.90 (4H, m), 2.71 (3H, s), 2.51 (3H, s), 2.07 (1H, s).

[001466] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 50 by substituting the appropriate starting materials, reagents and reaction conditions.

[001467] Example 51

[001468] Preparation of Cpd 603



[001469] Step A: A mixture of 5-bromopyridin-2-amine (433 mg, 2.5 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (928 mg, 3.0 mmol), $PdCl_2dppf$ (204 mg, 0.25 mmol), K_2CO_3 (1.04 g, 7.5 mmol) in acetonitrile (8.0 mL) was degassed and then stirred at 80 °C overnight. The volatiles were removed and the residue was chromatographed with 7% MeOH in CH_2Cl_2 to provide tert-butyl 4-(6-aminopyridin-3-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a light yellow oil (599 mg, 87%). MS m/z 276.3 $[M+H]^+$.

[001470] Step B: A solution of the product from Step A (599 mg, 2.2 mmol) in methanol (10 mL) was hydrogenated using Pd/C (10%, 60 mg) in a Parr shaker (60 psi) overnight. The mixture was filtered through Celite, evaporated and chromatographed with 7% MeOH in DCM

to provide tert-butyl 4-(6-aminopyridin-3-yl)piperidine-1-carboxylate as a brown oil (600 mg, 99%). MS m/z 278.3 $[M+H]^+$.

[001471] Step C: A mixture of the product from Step B (600 mg, 2.2 mmol) and bis(2,4,6-trichlorophenyl) malonate (1.0 g, 2.2 mmol) in THF (8.0 mL) was stirred at room temperature for 1 hour. The mixture was then filtered and the solid was washed with DCM. The cake was collected and dried to give tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate as an off-white solid (455 mg, 63%). MS m/z 346.4 $[M+H]^+$.

[001472] Step D: Into a solution of the product from Step C (455 mg, 1.3 mmol) in DMF (6 mL) at room temperature was added NaH (60%, 62 mg, 1.6 mmol). The mixture was stirred for 15 minutes, then N-phenylbis(trifluoromethanesulfonimide) (511 mg, 1.4 mmol) was added in one portion. The mixture was stirred at room temperature overnight. Aqueous workup followed by purification with 3% MeOH in CH_2Cl_2 provided tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate as an off-white solid (521 mg, 84%).

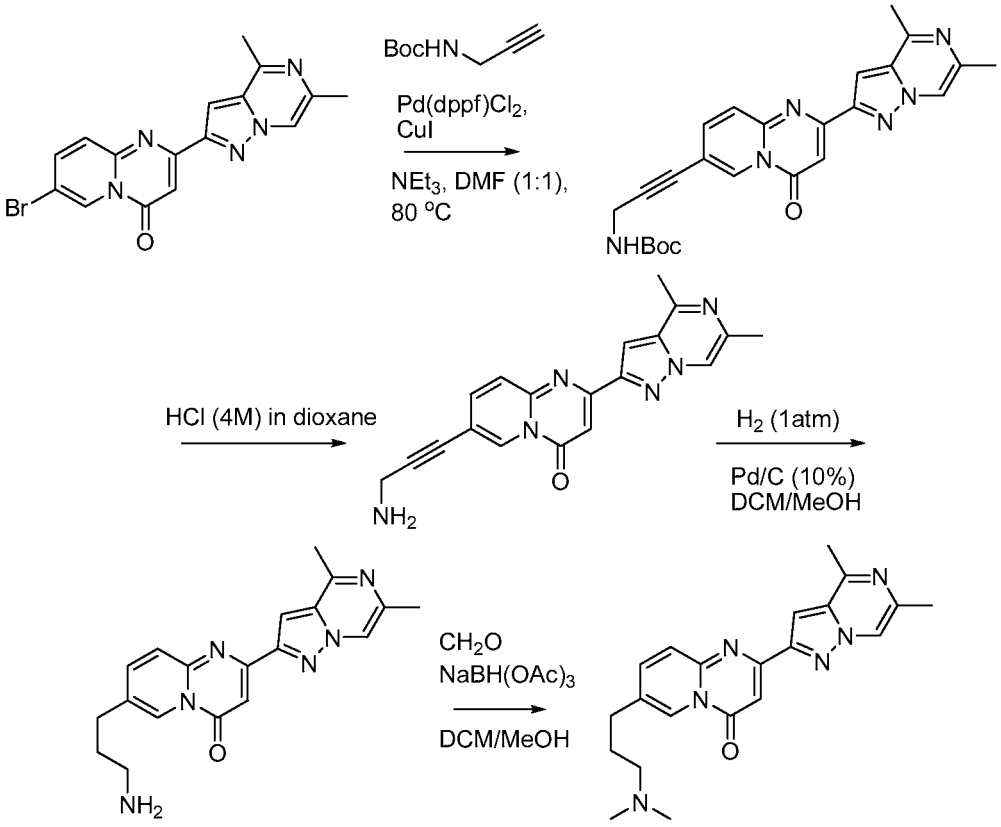
[001473] Step E: A mixture of the product from Step D (300 mg, 0.62 mmol), 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (142 mg, 0.81 mmol), $PdCl_2$dppf (51 mg, 0.062 mmol), K_3PO_4 (193 mg, 0.93 mmol) in dioxane (2.0 mL) was degassed and then stirred at 100 °C overnight. The volatiles were removed and the residue was chromatographed with 10% MeOH in CH_2Cl_2 to give tert-butyl 4-(2-(1-methyl-1H-indazol-5-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate with some impurities (~ 300 mg), which was used directly in the next step. MS m/z 460.5 $[M+H]^+$.

[001474] Step F: Following the procedure in Example 22, Step D, the above product from Step E (~ 300 mg) and HCl in dioxane (4 M, 5 mL) provided the title compound as a white solid (196 mg, 88%, in two steps). M.P. 268-270 °C; MS m/z 360.4 $[M+H]^+$; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.75 (s, 1H), 8.70 (s, 1H), 8.27 (dd, J = 9.0 Hz, 1.6 Hz, 1H), 8.21 (s, 1H), 8.00 (dd, J = 9 Hz, 1.6 Hz, 1H), 7.76 (d, J = 9 Hz, 2H), 7.06 (s, 1H), 4.10 (s, 3H), 3.06 (d, J = 10 Hz, 2H), 2.84-2.79 (m, 1H), 2.64-2.59 (m, 2H), 2.04 (bs, 1H), 1.81 (d, J = 10 Hz, 2H), 1.56-1.53 (m, 2H).

[001475] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 51 by substituting the appropriate starting materials, reagents and reaction conditions.

[001476] **Example 52**

[001477] Preparation of Cpd769



[001478] Step A: To an oven dried, argon filled flask was added 7-bromo-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (270 mg, 0.73 mmol, prepared in Example 38, Step A), CuI (3.4 mg, 5%), $PdCl_2(PPh_3)_2$ (30 mg, 5%), triethylamine (1 mL) and DMF (1 mL). The resulting mixture was purged with argon three times and then a solution of tert-butyl prop-2-ynylcarbamate (0.14 g, 0.88 mmol) in DMF (1 mL) was added. The mixture was heated at 80 °C overnight, then cooled to room temperature. After addition of water, the resulting solids were filtered and washed with water and CH_3CN sequentially to provide tert-butyl 3-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)prop-2-ynylcarbamate (260 mg, 80%). MS *m/z* 445.2 $[M+H]^+$.

[001479] Step B: Following the procedure in Example 22, Step D, the above product from Step A (100 mg, 0.23 mmol) and HCl in dioxane (4 M, 3 mL) provided 7-(3-aminoprop-1-ynyl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as an off-white solid (50 mg, 66%). MS m/z 345.4 $[M+H]^+$.

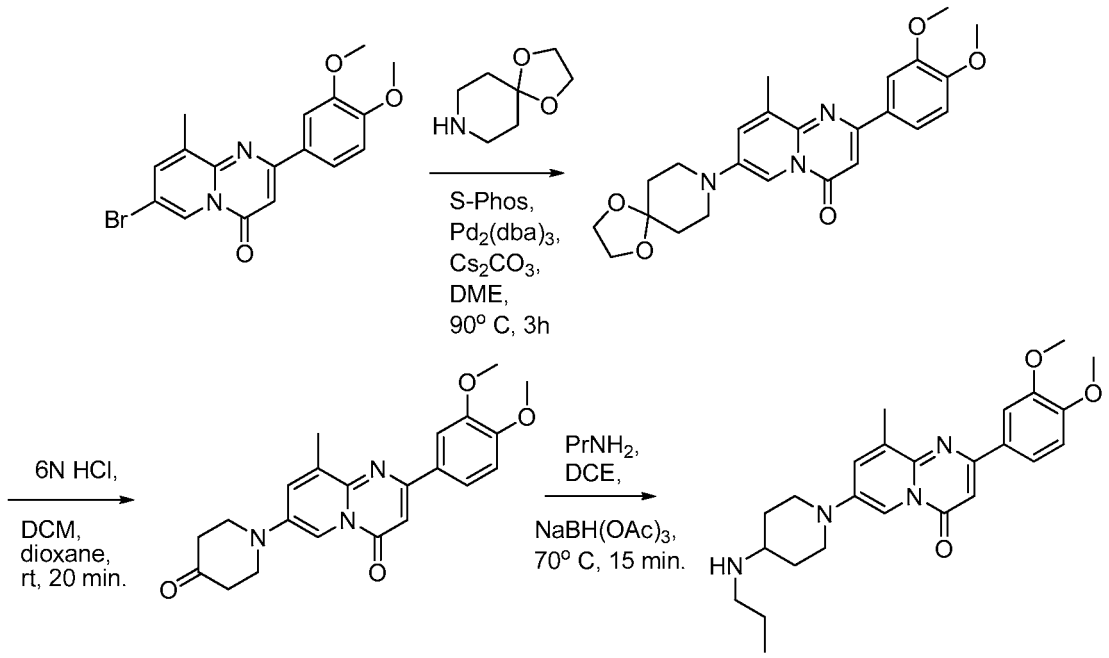
[001480] Step C: The above product from Step C (50 mg, 0.15 mmol) was mixed with Pd/C (10%, 5 mg) in dichloromethane/methanol (1:1, 2 mL) and stirred under 1 atmosphere of hydrogen overnight. The reaction mixture was filtered through celite, concentrated and chromatographed on a silica column, eluting with CH_2Cl_2 / MeOH (85/15) to provide 7-(3-aminopropyl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (45 mg, 89%). MS *m/z* 349.3 $[M+H]^+$.

[001481] Step D: Following the procedure in Example 23, the above product from Step B (45 mg, 0.13 mmol), formaldehyde (0.05 mL, 37%, ~ 0.8 mmol) and sodium triacetoxyborohydride (50 mg, 0.24 mmol) in dichloromethane/methanol (10:1, 1 mL) provided the title compound as a white solid (20 mg, 41%). M.P.136-138 °C; MS m/z 377.3 $[M+H]^+$; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 8.84 (d, *J* = 1.6 Hz, 1H), 8.58 (d, *J* = 1.6 Hz, 1H), 8.00 (d, *J* = 9 Hz, 1H), 7.77 (d, J = 9 Hz, 1H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.02 (s, 1H), 2.79-2.75 (m, 5H), 2.45 (s, 3H), 2.25 (t, J = 10 Hz, 2H), 2.15 (bs, 6H), 1.83-1.76 (m, 2H).

[001482] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 52 by substituting the appropriate starting materials, reagents and reaction conditions.

[001483] **Example 53**

[001484] Preparation of Cpd 407



[001485] Step A: A mixture of 7-bromo-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (1.5 g, 4.0 mmol, prepared in a manner exemplified in Example 22, Steps A and B), 1,4-dioxa-8-azaspiro[4.5]decane (660 μL, 5.05 mmol), S-Phos (140 mg, 0.34 mmol), $Pd_2(dba)_3$ (92 mg, 0.1 mmol), Cs_2CO_3 (3.0 g, 9.2 mmol), and DME (12 mL) was heated under argon at 90° C for 3 hours. The reaction mixture was then suspended in a solution of CH_2Cl_2 and acetone, and was filtered. The filtrate was concentrated under vacuum. Purification by silica gel chromatography (1:1 CH_2Cl_2 / EtOAc, then 20% acetone in CH_2Cl_2), followed by trituration with 1:1 hexanes / ether, yielded 2-(3,4-dimethoxyphenyl)-9-methyl-7-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (878 mg, 50%) as a yellow solid. MS *m/z* 438.2 $[M+H]^+$.

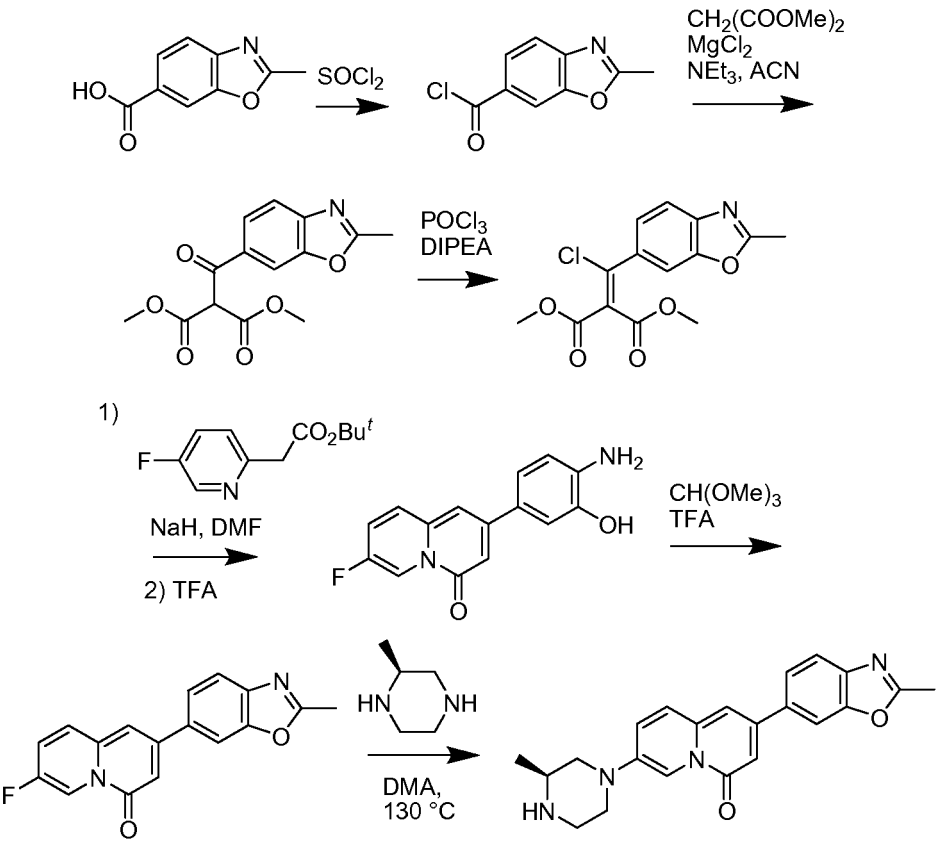
[001486] Step B: A solution of 2-(3,4-dimethoxyphenyl)-9-methyl-7-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (875 mg, 2.0 mmol) in CH_2Cl_2 / dioxane (1:1 v/v, 28 mL) was treated with 6 N HCl (7 mL). The mixture was stirred at room temperature for 20 minutes, then made basic with aqueous K_2CO_3. The mixture was extracted into CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Trituration with 1:1 hexanes / acetone yielded 2-(3,4-dimethoxyphenyl)-9-methyl-7-(4-oxopiperidin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (758 mg, 96%) as a yellow solid. MS *m/z* 394.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.27 (1H, d *J* = 2.5 Hz), 8.08 (1H, s), 7.85 (1H, dd, J = 8.5 Hz, 2.5 Hz), 7.81 (1H, m), 7.09 (1H, d, J = 8.5 Hz), 6.96 (1H, s), 3.88 (3H, s), 3.84 (3H, s), 3.67 (4H, t, J = 6 Hz), 2.64 (3H, s), 2.53 (4H, m, obscured by DMSO- d_6).

[001487] Step C: A mixture of 2-(3,4-dimethoxyphenyl)-9-methyl-7-(4-oxopiperidin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (50 mg, 0.13 mmol), $NaBH(OAc)_3$ (65 mg, 0.31 mmol), DCE (500 μL), and n-propylamine (40 μL, 0.49 mmol) was heated at 70° C for 15 minutes. The reaction mixture was partitioned between aqueous K_2CO_3 and CH_2Cl_2. The organic layer was concentrated under vacuum. Purification by silica gel chromatography (10% MeOH in CH_2Cl_2, followed by 9:1:0.1 CH_2Cl_2 : MeOH: NH_4OH) yielded the title compound (47 mg, 87%) as a yellow solid. M.P.178-184 °C; MS *m/z* 437.5 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.17 (1H, d, J = 3 Hz), 8.00 (1H, m), 7.84 (1H, dd, J = 8.5 Hz, 2 Hz), 7.80 (1H, d, J = 2 Hz), 7.08 (1H, d, J = 8.5 Hz), 6.95 (1H, s), 3.88 (3H, s), 3.84 (3H, s), 3.67 (2H, d, J = 12.5 Hz), 2.84 (2H, t, J = 12.5 Hz), 2.61 (3H, s), 2.57 (1H, m), 2.54 (2H, m, obscured by DMSO- d_6 peak), 1.95 (2H, d, J = 12.5 Hz), 1.41 (4H, m), 0.89 (3H, t, J = 7.5 Hz).

[001488] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 53 by substituting the appropriate starting materials, reagents and reaction conditions.

[001489] **Example 54**

[001490] Preparation of Cpd 322



[001491] Step A: Into a mixture of 2-methylbenzo[d]oxazole-6-carboxylic acid (2.54 g, 14.4 mmol) and $SOCl_2$ (2.05 g, 17.2 mmol) in toluene (70 mL) was added 6 drops of DMF. The mixture was then stirred at 70 °C for 3 hours, cooled and evaporated to give 2-methylbenzo[d]oxazole-6-carbonyl chloride as an oil, which solidified on standing (2.9 g, 100%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 - 8.30 (1H, m), 8.13 (1H, dd, *J*=8.4, 1.7 Hz), 7.74 (1H, dd, *J*=8.5, 0.6 Hz), 2.73 (3H, s).

[001492] Step B: Following the procedure in Example 31, Part 1, Step A, reaction of 2-methylbenzo[d]oxazole-6-carbonyl chloride (2.9 g, 14.4 mmol), dimethylmalonate (1.9 g, 14.4 mmol), $MgCl_2$ (1.37 g, 14.4 mmol), and triethylamine (2.9 mL, 28.8 mmol) in acetonitrile (15

mL) provided dimethyl 2-(2-methylbenzo[d]oxazole-6-carbonyl)malonate (2.75 g, 66%). MS m/z 292.0 $[M+H]^+$.

[001493] Step C: Following the procedure in Example 31, Part 1, Step B, reaction of dimethyl 2-(2-methylbenzo[d]oxazole-6-carbonyl)malonate (2.75 g, 9.5 mmol), $POCl_3$ (10 mL) and DIPEA (2.6 mL, 15.8 mmol) provided dimethyl 2-(chloro(2-methylbenzo[d]oxazol-6-yl)methylene)malonate (0.7 g, 24%). MS m/z 310.1 $[M+H]^+$.

[001494] Step D: Following the procedure in Example 33, Step B and C, reaction of dimethyl 2-(chloro(2-methylbenzo[d]oxazol-6-yl)methylene)malonate (0.7 g, 2.3 mmol), tert-butyl 2-(5-fluoropyridin-2-yl)acetate (0.57 g, 2.7 mmol), prepared as in Example 33, Step A, NaH (0.18 g, 4.5 mmol) in DMF followed by reaction with TFA and water at 100 °C provided 2-(4-amino-3-hydroxyphenyl)-7-fluoro-4H-quinolizin-4-one (0.3 g, 48%). MS m/z 271.2 $[M+H]^+$.

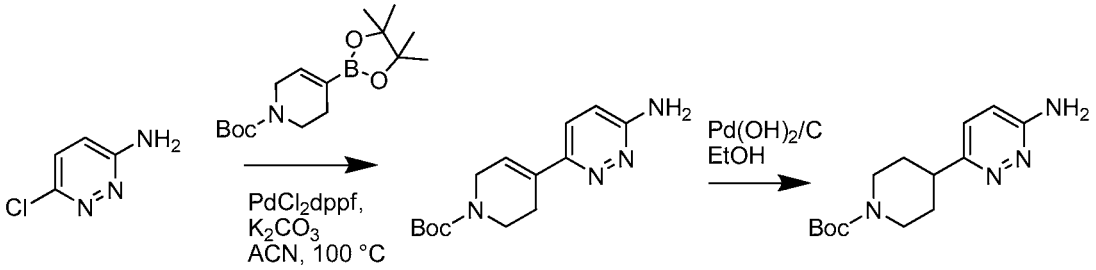
[001495] Step E: Into a mixture of 2-(4-amino-3-hydroxyphenyl)-7-fluoro-4H-quinolizin-4-one (0.3 g, 1.1 mmol) and trimethyl orthoformate (1.4 mL, 11.1 mmol) was added TFA (0.13 mL, 1.8 mmol). The mixture was stirred for 2 hours at room temperature and then evaporated to give 7-fluoro-2-(2-methylbenzo[d]oxazol-6-yl)-4H-quinolizin-4-one (0.3 g, 99%). MS m/z 295.2 $[M+H]^+$.

[001496] Step F: A mixture of 7-fluoro-2-(2-methylbenzo[d]oxazol-6-yl)-4H-quinolizin-4-one (0.15 g, 0.51 mmol) and (S)-2-methylpiperazine (0.2 g, 2.0 mmol) in DMA (1.0 mL) was stirred at 130 °C overnight. The solvent was removed by a stream of nitrogen and the residue was purified with methanol in dichloromethane (10%) to give the title compound as a yellow solid (69 mg, 36%). M.P. 115-117 °C; MS m/z 375.3 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$) δ 8.55 (1H, d, *J*=2.2 Hz), 7.79 (1H, d, *J*=1.3 Hz), 7.73 (1H, d, *J*=7.9 Hz), 7.64 (1H, dd, *J*=8.2, 1.6 Hz), 7.49 (1H, d, *J*=9.5 Hz), 7.33 (1H, d, *J*=2.5 Hz), 6.86 - 6.91 (2H, m), 3.60 (2H, br. s.), 3.25 - 3.34 (1H, m), 3.10 - 3.22 (2H, m), 2.93 - 3.03 (1H, m), 2.62 - 2.70 (4H, m), 1.31 (3H, d, *J*=6.3 Hz).

[001497] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 54 by substituting the appropriate starting materials, reagents and reaction conditions.

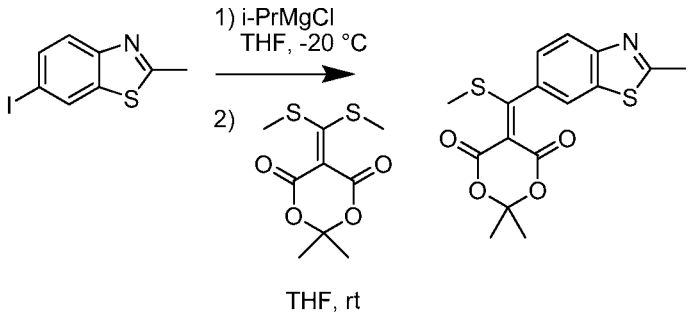
[001498] **Example 55**

[001499] Preparation of Cpd 380



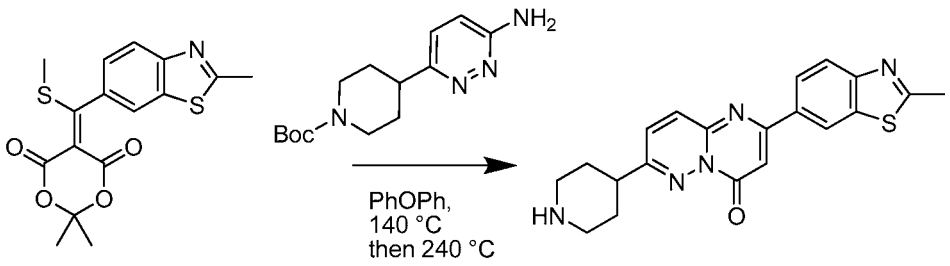
[001500] Part 1, Step A: A mixture of 6-chloropyridazin-3-amine (0.26 g, 2.0 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.62 g, 2.0 mmol), $PdCl_2dppf$ (0.16 g, 0.2 mmol), K_2CO_3 (2.0 M, 3.0 mL, 6.0 mmol) in acetonitrile (6.0 mL) was stirred at 100 °C overnight. Aqueous workup followed by purification with methanol in dichloromethane (0-10%) provided tert-butyl 4-(6-aminopyridazin-3-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.51 g, 93%). MS m/z 277.2 $[M+H]^+$.

[001501] Part 1, Step B: A solution of tert-butyl 4-(6-aminopyridazin-3-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.4 g, 1.4 mmol) in ethanol (25 mL) was hydrogenated using $Pd(OH)_2$ on carbon (20%, 0.2 g) in a Parr shaker (60 psi) overnight. The mixture was filtered through Celite, evaporated and purified with methanol in dichloromethane (0-10%) to give tert-butyl 4-(6-aminopyridazin-3-yl)piperidine-1-carboxylate (0.25 g, 62%). MS m/z 279.2 $[M+H]^+$.



[001502] Part 2, Into a solution of 6-iodo-2-methylbenzo[d]thiazole (2.24 g, 7.3 mmol) in THF (15 mL) at -20 °C was added i-PrMgCl in THF (2.0 M, 3.7 mL, 7.4 mmol). The mixture was kept between -10 °C to -20 °C for 1 hour, then transferred via a cannula to a solution of 5-(bis(methylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (1.4 g, 5.6 mmol) in THF (15 mL). The reaction was slightly exothermic. The mixture was stirred at room temperature for 90

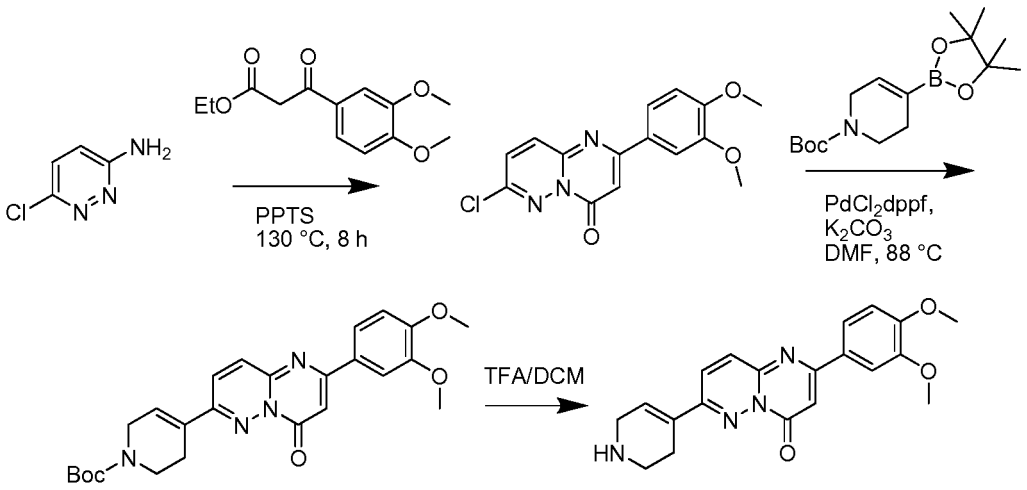
minutes before quenching with aqueous NH_4Cl solution. Aqueous workup followed by purification with ethyl acetate in dichloromethane (0-10%) provided 2,2-dimethyl-5-((2-methylbenzo[d]thiazol-6-yl)(methylthio)methylene)-1,3-dioxane-4,6-dione (1.26 g, 64%). MS m/z 350.1 $[M+H]^+$.



[001503] Part 3, A mixture of 2,2-dimethyl-5-((2-methylbenzo[d]thiazol-6-yl)(methylthio)methylene)-1,3-dioxane-4,6-dione (0.13 g, 0.36 mmol) and tert-butyl 4-(6-aminopyridazin-3-yl)piperidine-1-carboxylate (0.1 g, 0.36 mmol) in diphenyl ether (2.0 mL) was stirred at 140 °C for 1 hour. The temperature was then raised to 240 °C and stirred for 30 minutes. The mixture was evaporated and the residue was purified by prep HPLC to give the title compound as a yellow solid (33 mg, 24%) trifluoroacetic acid salt. M.P. 230-235 °C; MS m/z 378.2 $[M+H]^+$; ^1H NMR (500 MHz, *DMSO-d_6*) δ 8.87 - 8.92 (1H, m), 8.28 - 8.33 (1H, m), 8.08 (1H, d, *J*=9.1 Hz), 7.99 - 8.04 (1H, m), 7.79 (1H, s), 7.26 (1H, s), 3.41 - 3.48 (2H, m), 3.22 - 3.32 (1H, m), 3.03 - 3.11 (2H, m), 2.84 (3H, s), 2.14 - 2.22 (2H, m), 2.08 (1H, s), 1.92 - 2.03 (2H, m).

[001504] **Example 56**

[001505] Preparation of Cpd 398



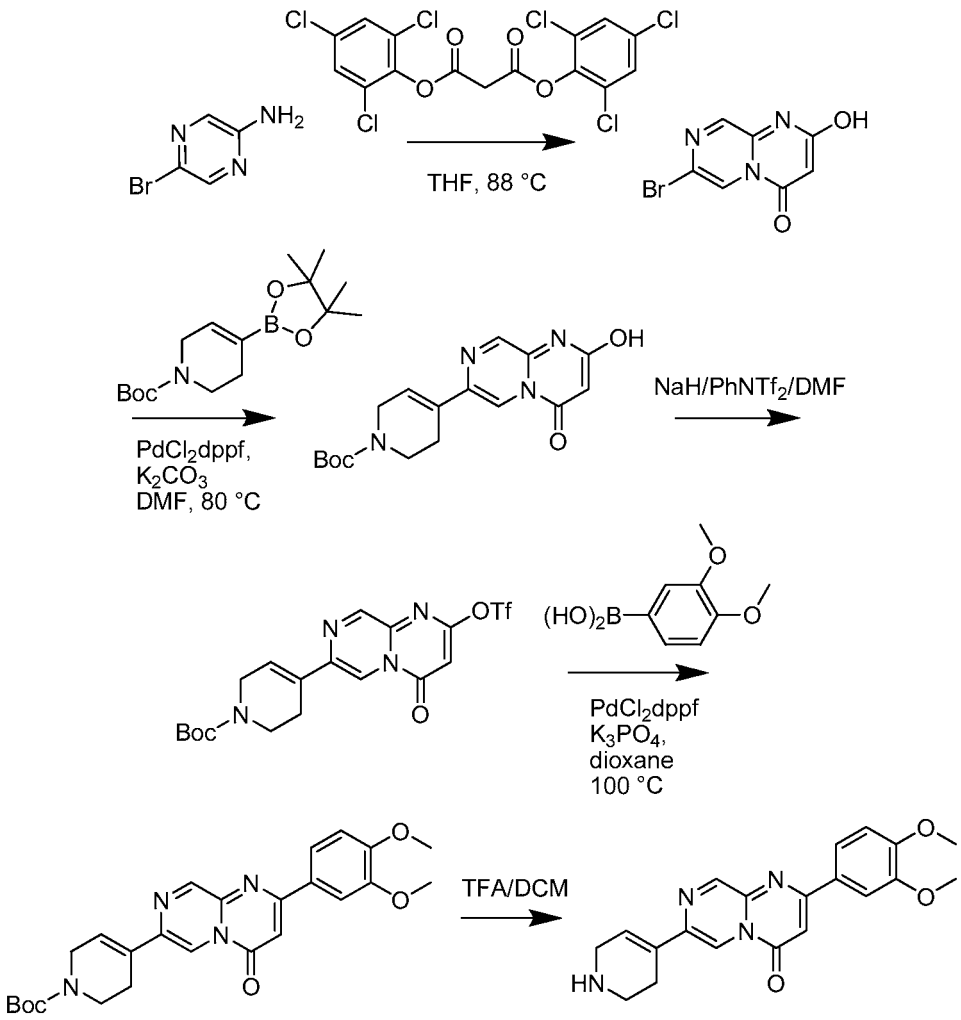
[001506] Step A: Following the procedure of Example 9, Step G, reaction of 6-chloropyridazin-3-amine (0.65 g, 5.0 mmol), ethyl 3-(3,4-dimethoxyphenyl)-3-oxopropanoate (1.77 g, 7.0 mmol) and PPTs (63 mg, 0.25 mmol) provided 7-chloro-2-(3,4-dimethoxyphenyl)-4H-pyrimido[1,2-b]pyridazin-4-one (0.23 g, 14%). MS m/z 318.1 $[M+H]^+$.

[001507] Step B: Following the procedure of Example 34, Step C, reaction of 7-chloro-2-(3,4-dimethoxyphenyl)-4H-pyrimido[1,2-b]pyridazin-4-one (0.12 g, 0.38 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.14 g, 0.45 mmol), $PdCl_2dppf$ (35 mg, 0.038 mmol), K_2CO_3 (2.0 M, 0.6 mL, 1.2 mmol) in acetonitrile (1.2 mL) provided tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (100 mg, 56%). MS m/z 465.3 $[M+H]^+$.

[001508] Step C: Following the procedure of Example 34, Step D, treatment of tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (100 mg, 0.21 mmol) with TFA (1.0 mL) and dichloromethane (1.0 mL) provided the title compound as a yellow solid (50 mg, 65%). M.P.195-200 °C; MS m/z 365.3 $[M+H]^+$; ^1H NMR (500 MHz, *DMSO-d_6*) δ 8.13 (1H, d, *J*=9.8 Hz), 7.96 (1H, d, *J*=9.8 Hz), 7.82 (1H, dd, *J*=8.5, 2.2 Hz), 7.74 (1H, d, *J*=2.2 Hz), 7.15 (1H, s), 7.08 (1H, d, *J*=8.8 Hz), 7.01 (1H, br. s.), 3.87 (3H, s), 3.83 (3H, s), 3.57 (2H, br. s.), 3.00 (2H, br. s.), 2.58 (2H, br. s.).

[001509] **Example 57**

[001510] Preparation of Cpd 402



[001511] Step A: A mixture of 5-bromopyrazin-2-amine (0.17 g, 1.0 mmol) and bis(2,4,6-trichlorophenyl)malonate (0.56 g, 1.2 mmol) in THF (4.0 mL) was stirred at 88 °C for 1 hour. The mixture was then filtered and the solid was washed with ethyl acetate. The cake was collected and dried to give 7-bromo-2-hydroxy-4H-pyrazino[1,2-a]pyrimidin-4-one (0.18 g, 74%). MS m/z 242.0 $[M+H]^+$, 244.0 $[M+2+H]^+$.

[001512] Step B: Following the procedure of Example 34, Step C, reaction of 7-bromo-2-hydroxy-4H-pyrazino[1,2-a]pyrimidin-4-one (0.18 g, 0.74 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.27 g, 0.89 mmol), $PdCl_2dppf$ (60 mg, 0.074 mmol), K_2CO_3 (0.31 g, 2.2 mmol) in DMF (2.5 mL) provided

tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.18 g, 70%). MS m/z 345.3 $[M+H]^+$.

[001513] Step C: Into a solution of tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.18 g, 0.52 mmol) in DMF (3.0 mL) at room temperature was added NaH (60%, 23 mg, 0.57 mmol). The mixture was stirred for 15 minutes then $PhNTf_2$ (0.22 g, 0.62 mmol) was added in one portion. The mixture was stirred overnight. Aqueous workup followed by purification with ethyl acetate in dichloromethane (0-20%) provided tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.1 g, 40%). MS m/z 377.1 $[M-Boc+H]^+$.

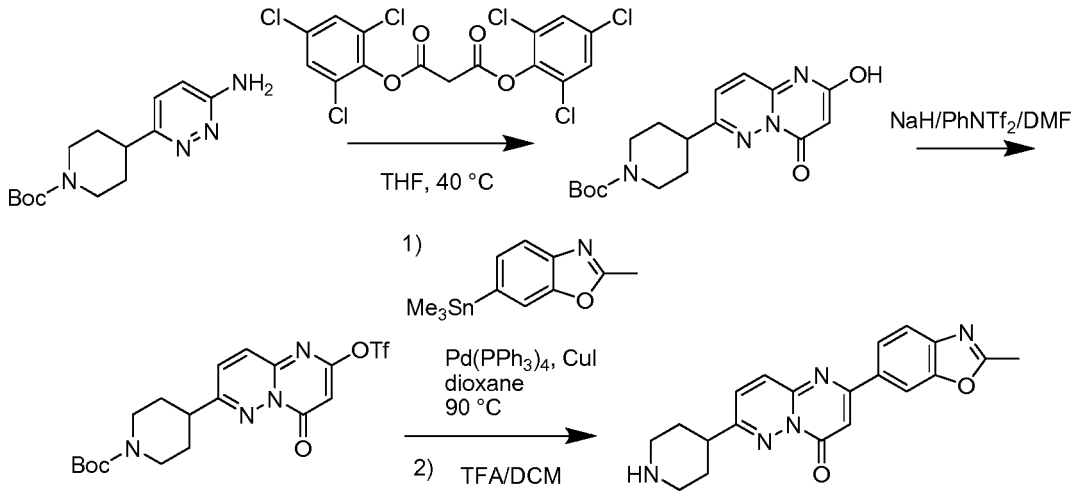
[001514] Step D: A mixture of tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (80 mg, 0.17 mmol), 3,4-dimethoxyphenylboronic acid (46 mg, 0.25 mmol), $PdCl_2dppf$ (14 mg, 0.017 mmol), K_3PO_4 (54 mg, 0.25 mmol) in dioxane (2.0 mL) was stirred at 100 °C for 24 hours. The mixture was filtered, evaporated and purified with ethyl acetate in dichloromethane (0-20%) to give tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (43 mg, 55%). ^1H NMR (500 MHz, $CDCl_3$) δ 9.10 (1H, s), 8.61 (1H, s), 7.72 (1H, s), 7.70 (1H, d, J = 1.8 Hz), 7.00 (3H, m), 4.19 - 4.26 (2H, m), 4.03 (3H, s), 3.98 (3H, s), 3.69 - 3.76 (2H, m), 2.56 - 2.67 (2H, m), 1.51 (9H, s).

[001515] Step E: Following the procedure of Example 34, Step D, treatment of tert-butyl 4-(2-(3,4-dimethoxyphenyl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (43 mg, 0.09 mmol) with TFA (1.0 mL) and dichloromethane (1.0 mL) provided the title compound as a yellow solid (34 mg, 100%). M.P. 205-208 °C; MS m/z 365.4 $[M+H]^+$; ^1H NMR (500 MHz, *DMSO-d_6*) δ 9.15 (1H, d, J=0.9 Hz), 8.41 (1H, s), 7.85 - 7.94 (1H, m), 7.78 (1H, d, J=1.9 Hz), 7.27 (1H, s), 7.11 (1H, d, J=8.5 Hz), 6.97 - 7.05 (1H, m), 3.89 (3H, s), 3.84 (3H, s), 3.58 (2H, br. s.), 3.21 - 3.42 (3H, m), 3.07 (2H, t, J=5.7 Hz).

[001516] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 57 by substituting the appropriate starting materials, reagents and reaction conditions.

[001517] **Example 58**

[001518] Preparation of Cpd 499



[001519] Step A: A mixture of tert-butyl 4-(6-aminopyridazin-3-yl)piperidine-1-carboxylate (0.88 g, 3.2 mmol) and bis(2,4,6-trichlorophenyl) malonate (1.76 g, 3.8 mmol) in THF (12 mL) was stirred at 40 °C for 1 hour. The mixture was then evaporated and purified with methanol in dichloromethane (0-10%) to give tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (0.69 g, 63%). MS m/z 347.2 $[M+H]^+$.

[001520] Step B: Following the procedure of Example 57, Step C, reaction of tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (0.69 g, 2.0 mmol), NaH (60%, 88 mg, 2.2 mmol), $PhNTf_2$ (0.79 g, 2.2 mmol) in DMF (12 mL) provided tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (0.87 g, 91%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (1H, d, *J*=9.5 Hz), 7.61 (1H, d, *J*=9.5 Hz), 6.45 (1H, s), 4.28 - 4.36 (2H, m), 3.20 - 3.30 (1H, m), 2.82 - 2.93 (2H, m), 1.94 - 2.02 (2H, m), 1.75 - 1.85 (2H, m), 1.49 (9H, s).

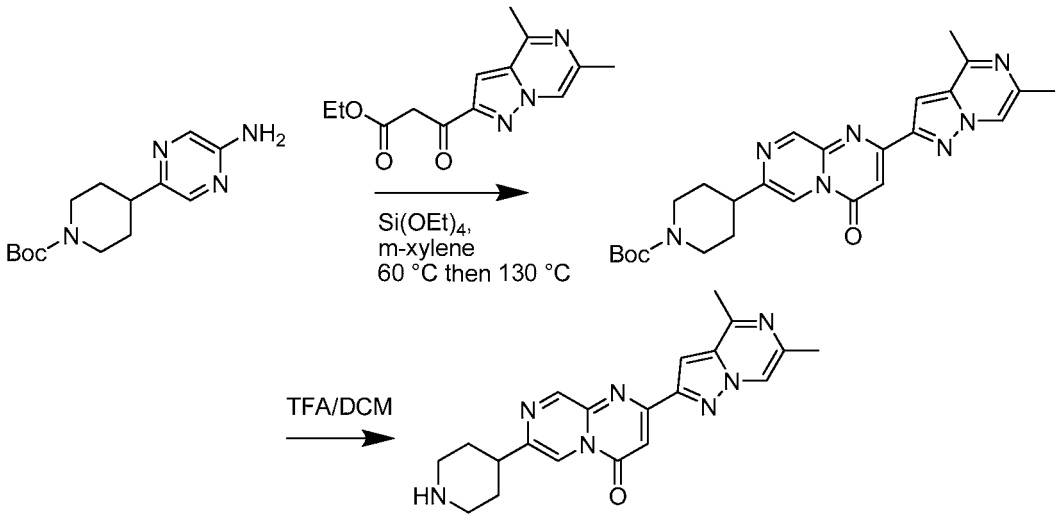
[001521] Step C: A mixture of tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (0.24 g, 0.5 mmol), 2-methyl-6-(trimethylstannyl)benzo[d]oxazole (0.18 g, 0.6 mmol), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol), CuI (23 mg, 0.12 mmol) in dioxane (2.0 mL) was stirred at 90 °C overnight. The mixture was concentrated and purified with methanol in dichloromethane (0-10%). The desired fractions were combined and evaporated. The residue was treated with TFA (1.0 mL) and dichloromethane (1.0 mL) and worked up as described in Example 34, Step D to give the title

compound as a yellow solid (86 mg, 48%). M.P. 126-128 °C; MS m/z 362.2 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 8.20 (1H, s), 7.91 - 7.99 (2H, m), 7.67 (2H, d, *J*=8.2 Hz), 7.07 (1H, s), 3.45 (2H, d, *J*=12.3 Hz), 3.07 - 3.21 (2H, m), 3.30 – 3.24 (1H, m), 2.61 (3H, s), 2.14 (4H, br. s.).

[001522] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 58 by substituting the appropriate starting materials, reagents and reaction conditions.

[001523] **Example 59**

[001524] Preparation of Cpd 502



[001525] Step A: A mixture of tert-butyl 4-(5-aminopyrazin-2-yl)piperidine-1-carboxylate (0.2 g, 0.72 mmol), ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (0.21 g, 0.79 mmol), $Si(OEt)_4$ (0.16 mL, 0.72 mmol), PPTs (18 mg, 0.072 mmol) in m-xylene (0.36 mL) was stirred at 60 °C for 1 hour then 130 °C overnight. The mixture was cooled and loaded directly onto a silica column and purified with methanol in dichloromethane (0-10%). Further purification with ethyl acetate in dichloromethane (20-100%) provided tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate (0.117 g, 34%). MS m/z 476.4 $[M+H]^+$.

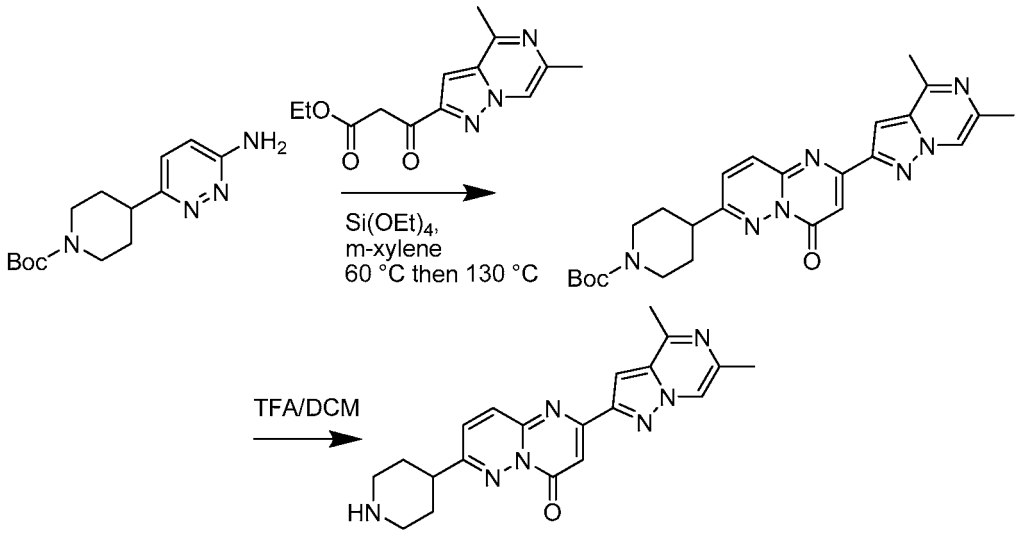
[001526] Step B: Following the procedure of Example 34, Step D, treatment of tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate (117 mg, 0.25 mmol) with TFA (1.0 mL) and dichloromethane (2.0 mL) provided

the title compound as a yellow solid (93 mg, 100%). MS m/z 376.4 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 9.13 (1H, d, *J*=1.3 Hz), 8.53 (1H, s), 8.27 (1H, d, *J*=0.6 Hz), 7.55 (1H, d, *J*=1.3 Hz), 7.28 (1H, s), 3.27 – 3.34 (2H, m), 2.99 - 3.09 (1H, m), 2.85 - 2.96 (2H, m), 2.75 (3H, s), 2.47 (3H, d, *J*=0.9 Hz), 2.05 - 2.14 (2H, m), 1.84 - 1.95 (2H, m).

[001527] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 59 by substituting the appropriate starting materials, reagents and reaction conditions.

[001528] **Example 60**

[001529] Preparation of Cpd 512



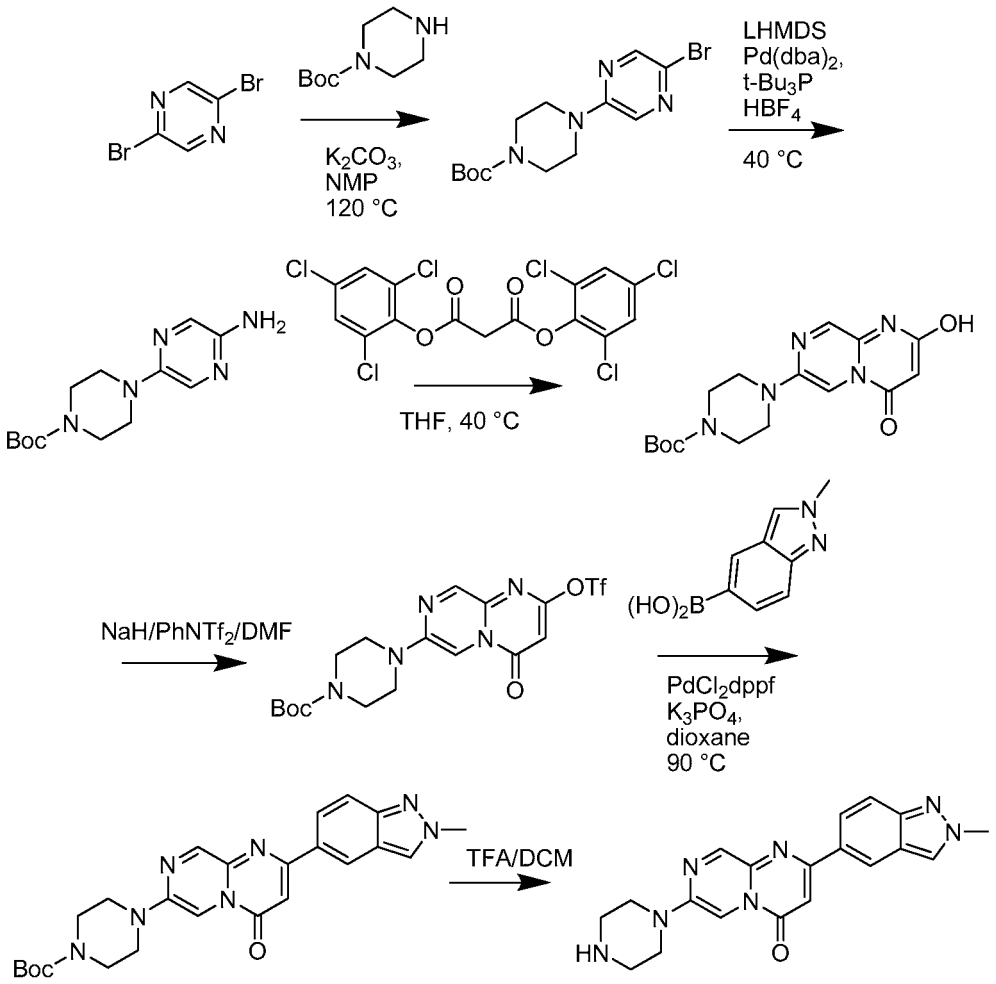
[001530] Step A: Following the procedure of Example 59, Step A, the reaction of tert-butyl 4-(6-aminopyridazin-3-yl)piperidine-1-carboxylate (0.28 g, 1.0 mmol), ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (0.28 g, 1.1 mmol), $Si(OEt)_4$ (0.22 mL, 1.0 mL), PPTs (25 mg, 0.1 mmol) in m-xylene (0.5 mL) provided tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (60 mg, 13%). MS m/z 476.4 $[M+H]^+$.

[001531] Step B: Following the procedure of Example 34, Step D, treatment of tert-butyl 4-(2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4-oxo-4H-pyrimido[1,2-b]pyridazin-7-yl)piperidine-1-carboxylate (60 mg, 0.13 mmol) with TFA (1.0 mL) and dichloromethane (1.0 mL) provided the title compound as a yellow solid (47 mg, 100%). MS m/z 376.4 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 8.27 - 8.31 (1H, m), 8.06 (1H, d, *J*=9.5 Hz), 7.78 (1H, s), 7.57 (1H, d,

J=0.9 Hz), 7.39 (1H, s), 3.25 - 3.30 (2H, m), 3.15 - 3.23 (1H, m), 2.82 - 2.90 (2H, m), 2.79 (3H, s), 2.51 (3H, d, *J*=0.9 Hz), 2.02 - 2.09 (2H, m), 1.85 - 1.96 (2H, m).

[001532] **Example 61**

[001533] Preparation of Cpd 586



[001534] Step A: A mixture of 2,5-dibromopyrazine (1.45 g, 6.1 mmol), tert-butyl piperazine-1-carboxylate (1.13 g, 6.1 mmol) and K_2CO_3 (1.26 g, 9.2 mmol) in NMP (6.0 mL) was stirred at 120 °C overnight. The mixture was cooled, then aqueous workup followed by purification with ethyl acetate in dichloromethane (0-15%) provided tert-butyl 4-(5-bromopyrazin-2-yl)piperazine-1-carboxylate (1.45 g, 69%). MS m/z 343.3 $[M+H]^+$, 345.3 $[M+2+H]^+$.

[001535] Step B: A mixture of tert-butyl 4-(5-bromopyrazin-2-yl)piperazine-1-carboxylate (1.25 g, 3.6 mmol), LiHMDS (1.0 M, 4.4 mL, 4.4 mmol), $Pd(dba)_2$ (105 mg, 0.18 mmol), P^tBu_3 HBF_4 (53 mg, 0.18 mmol) in toluene (4.4 mL) was stirred at 40 °C overnight under an Ar

atmosphere. The mixture was then cooled, treated with acetonitrile (2.0 mL) and 1N HCl (0.2 mL), stirred for 15 minutes and purified over silica gel with methanol in dichloromethane (0-10%) to give tert-butyl 4-(5-aminopyrazin-2-yl)piperazine-1-carboxylate (0.96 g, 94%). MS m/z 280.2 $[M+H]^+$.

[001536] Step C: A mixture of tert-butyl 4-(5-aminopyrazin-2-yl)piperazine-1-carboxylate (0.68 g, 2.4 mmol), bis(2,4,6-trichlorophenyl) malonate (1.36 g, 2.9 mmol) in THF (15 mL) was stirred at room temperature for 64 hours. The mixture was then filtered. The solid was washed with ethyl acetate and dried to give tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.65 g, 77%). MS m/z 348.3 $[M+H]^+$.

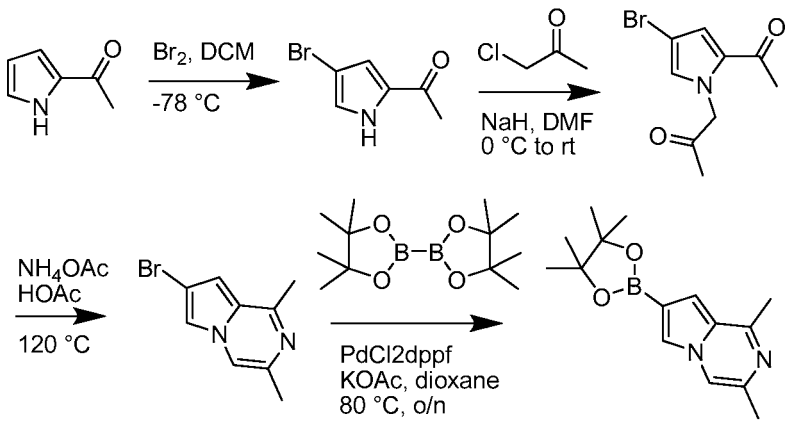
[001537] Step D: Following the procedure in Example 57, Step C, reaction of tert-butyl 4-(2-hydroxy-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.65 g, 1.9 mmol), NaH (60%, 82 mg, 2.1 mmol) and $PhNTf_2$ (0.74 g, 2.1 mmol) in DMF (10 mL) provided tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.72 g, 80%). MS m/z 480.2 $[M+H]^+$.

[001538] Step E: Following the procedure in Example 57, Step D, reaction of tert-butyl 4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.38 g, 0.79 mmol) and 2-methyl-2H-indazol-5-ylboronic acid (0.21 g, 1.2 mmol) in the presence of $PdCl_2dppf$ (64 mg, 0.08 mmol) an K_3PO_4 (0.25 g, 1.2 mmol) in dioxane (6.0 mL) provided tert-butyl 4-(2-(2-methyl-2H-indazol-5-yl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.22 g, 60%). MS m/z 462.3 $[M+H]^+$.

[001539] Step F: Following the procedure of Example 34, Step D, treatment of tert-butyl 4-(2-(2-methyl-2H-indazol-5-yl)-4-oxo-4H-pyrazino[1,2-a]pyrimidin-7-yl)piperazine-1-carboxylate (0.22 g, 0.48 mmol) with TFA (1.0 mL) and dichloromethane (1.0 mL) provided the title compound as a yellow solid (0.17 mg, 99%). M.P. 160-162 °C; MS m/z 362.3 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 9.04 (1H, d, J=1.3 Hz), 8.50 (1H, dd, J=1.6, 0.9 Hz), 8.18 (1H, s), 7.97 - 8.02 (2H, m), 7.71 (1H, d, J=9.1 Hz), 7.01 (1H, s), 4.23 (3H, s), 3.61 - 3.67 (4H, m), 3.13-3.20 (4H, m).

[001540] **Example 62**

[001541] Preparation of Cpd 695



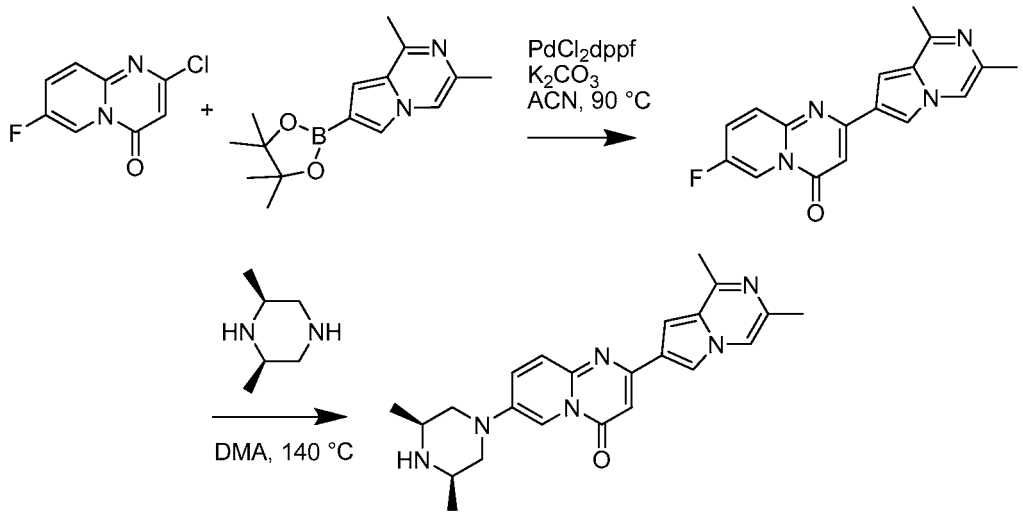
[001542] Part 1, Step A: Into a suspension of 1-(1H-pyrrol-2-yl)ethanone (2.18 g, 20 mmol) in dichloromethane (100 mL) at -78 °C was added a solution of bromine (1.23 mL, 24 mmol) in dichloromethane (25 mL) dropwise over 30 minutes. The mixture was stirred for 10 minutes at -78 °C after the addition and then poured into ice-water. The aqueous layer was extracted with dichloromethane. The organic extracts were combined, dried and evaporated. The residue was purified with ethyl acetate in dichloromethane (0-20%) to give 1-(4-bromo-1H-pyrrol-2-yl)ethanone (3.48 g, 92%). MS m/z 188.0 $[M+H]^+$, 190.0 $[M+2+H]^+$.

[001543] Part 1, Step B: Into a solution of 1-(4-bromo-1H-pyrrol-2-yl)ethanone (3.48 g, 18.5 mmol) in DMF (40 mL) at 0 °C was added NaH (60%, 0.81 g, 20.4 mmol) portionwise. The temperature was allowed to rise to room temperature and 1-chloropropan-2-one (1.54 mL, 19.4 mmol) was added dropwise. The mixture was stirred at room temperature overnight. Aqueous workup followed by purification with ethyl acetate in hexane (5-30%) provided 1-(2-acetyl-4-bromo-1H-pyrrol-1-yl)propan-2-one (2.9 g, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (1H, d, *J*=1.9 Hz), 6.77 (1H, d, *J*=1.6 Hz), 5.00 (2H, s), 2.39 (3H, s), 2.25 (3H, s).

[001544] Part 1, Step C: A mixture of 1-(2-acetyl-4-bromo-1H-pyrrol-1-yl)propan-2-one (2.9 g, 11.9 mmol) and ammonium acetate (18 g, 238 mmol) in acetic acid (100 mL) was stirred at 120 °C overnight. The acetic acid was then removed by rotary evaporation, then ice water was added to the residue and the mixture was made basic with NaOH to pH 9. The mixture was extracted with ethyl acetate. The organic extracts were combined, dried, and evaporated. The

residue was purified with ethyl acetate in dichloromethane (0-10%) to provide 7-bromo-1,3-dimethylpyrrolo[1,2-a]pyrazine (2.4 g, 90%). MS m/z 225.1 $[M+H]^+$, 227.1 $[M+2+H]^+$.

[001545] Part 1, Step D: Following the procedure in Example 14, Part 2, reaction of 7-bromo-1,3-dimethylpyrrolo[1,2-a]pyrazine (0.67 g, 3.0 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (0.99 g, 3.9 mmol), $PdCl_2$dppf (0.24 g, 0.3 mmol), KOAc (0.88 g, 9.0 mmol) in dioxane (10 mL) provided 1,3-dimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolo[1,2-a]pyrazine, which was used directly in the next step without further purification. MS m/z 191.2 $[M\text{-pinacol}+H]^+$.



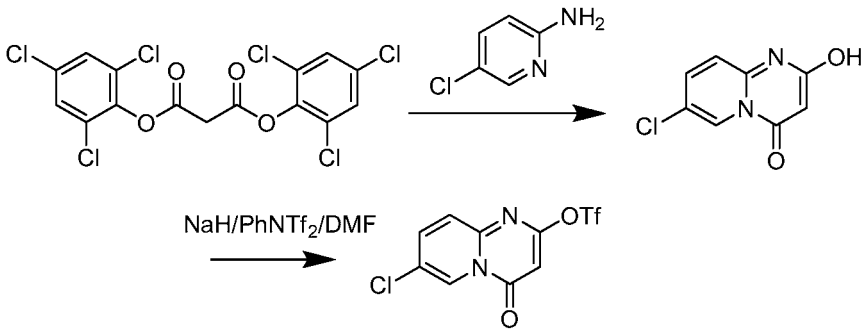
[001546] Part 2, Step A: Following the procedure in Example 14, Part 3, Step A, reaction of 2-chloro-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.3 g, 1.5 mmol) with1,3-dimethyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolo[1,2-a]pyrazine (1.5 mmol) provided 2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.34 g, 74%). MS m/z 309.2 $[M+H]^+$.

[001547] Part 2, Step B: Following the procedure in Example 14, Part 3, Step B, reaction of 2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-fluoro-4H-pyrido[1,2-a]pyrimidin-4-one (0.14 g, 0.45 mmol) with 2,6-dimethylpiperazine (0.26 g, 2.27 mmol) provided the title compound as a yellow solid (57 mg, 32%). M.P. 254-256 °C; MS m/z 403.4 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 8.20 (1H, d, J=2.8 Hz), 7.99 (1H, d, J=1.6 Hz), 7.84 - 7.90 (1H, m), 7.72 (1H, d, J=0.6 Hz), 7.58 (1H, d, J=9.5 Hz), 7.25 (1H, t, J=1.1 Hz), 6.69 (1H, s), 3.60 (2H, d, J=9.5 Hz), 3.03 - 3.11 (2H, m), 2.62 (3H, s), 2.37 (2H, t, J=11.3 Hz), 2.31 (3H, d, J=0.9 Hz), 1.21 (6H, d, J=6.3 Hz).

[001548] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 62 by substituting the appropriate starting materials, reagents and reaction conditions.

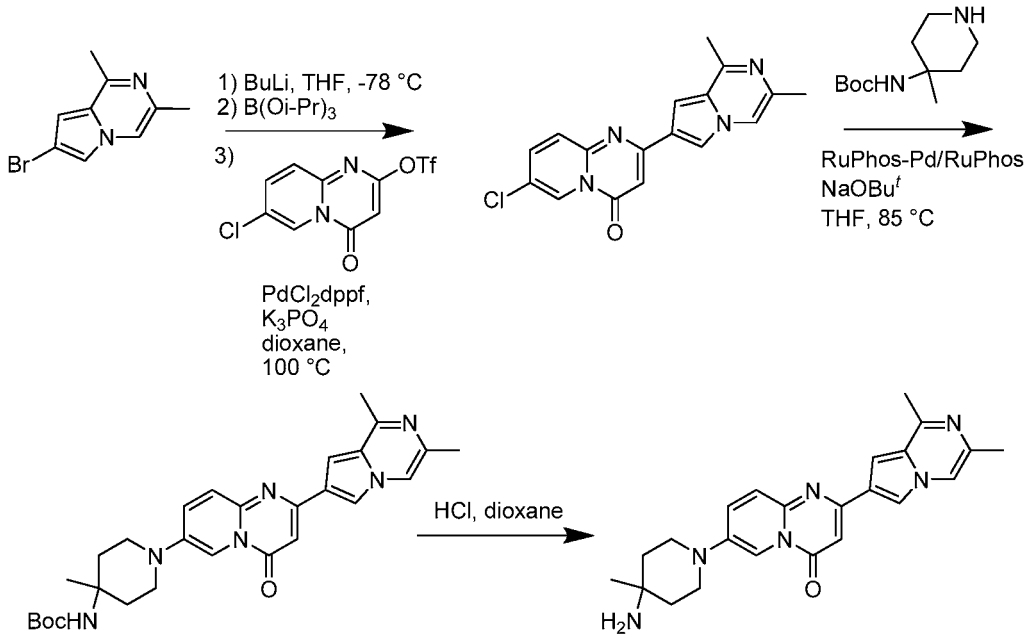
[001549] **Example 63**

[001550] Preparation of Cpd 731



[001551] Part 1, Step A: Following the procedure in Example 57, Step A, reaction of 5-chloropyridin-2-amine (2.57 g, 20 mmol) and bis(2,4,6-trichlorophenyl) malonate (10.2 g, 22 mmol) in THF (100 mL) provided 7-chloro-2-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one (3.89 g, 97%). ^{1}H NMR (500 MHz, *DMSO-d$_6$*) δ 12.01 (1H, br. s.), 8.89 (1H, d, *J*=2.2 Hz), 8.10 (1H, dd, *J*=9.3, 2.4 Hz), 7.44 (1H, d, *J*=9.5 Hz), 5.19 (1H, br. s.).

[001552] Part 1, Step B: Following the procedure in Example 57, Step C, reaction of 7-chloro-2-hydroxy-4H-pyrido[1,2-a]pyrimidin-4-one (3.89 g, 19.8 mmol) with NaH (60%, 0.87 g, 21.8 mmol) and $PhNTf_2$ (7.78 g, 21.8 mmol) in DMF (50 mL) provided 7-chloro-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl trifluoromethanesulfonate (5.9 g, 91%). MS m/z 370.0 $[M+H]^+$.



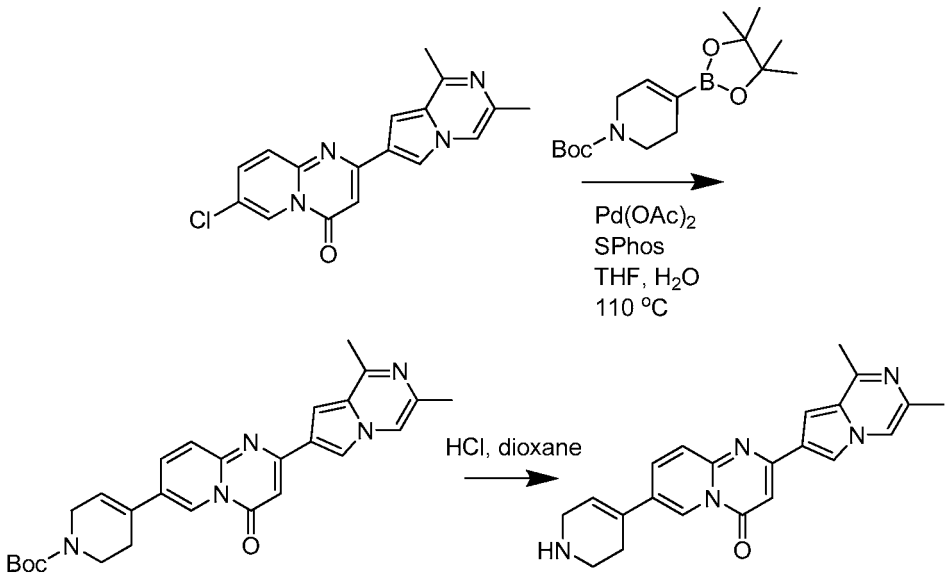
[001553] Part 2, Step A: Into a solution of 7-bromo-1,3-dimethylpyrrolo[1,2-a]pyrazine (1.1 g, 4.9 mmol) in THF (20 mL) at -78 °C was added BuLi (1.6 M, 4.7 mL, 7.5 mmol) dropwise. The mixture was stirred at -78 °C for 30 minutes, triisopropyl borate (1.7 mL, 7.4 mmol) was added. The temperature was allowed to rise to room temperature slowly. The reaction was quenched with water (1.0 mL) and the mixture was evaporated to dryness under vacuum. Into the residue was added 7-chloro-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl trifluoromethanesulfonate (1.6 g, 4.9 mmol), $PdCl_2$dppf (0.4 g, 0.49 mmol), K_3PO_4 (1.55 g, 7.3 mmol) and dioxane (40 mL). The mixture was stirred at 100 °C overnight under an Ar atmosphere, after which the mixture was cooled, evaporated and purified through silica with methanol in dichloromethane (0-10%) to give 7-chloro-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (0.34 g, 22%). MS m/z 325.2 $[M+H]^+$.

[001554] Part 2, Step B: A mixture of 7-chloro-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (0.2 g, 0.62 mmol), tert-butyl 4-methylpiperidin-4-ylcarbamate (0.17 g, 0.8 mmol), RuPhos-Pd (22 mg, 0.031 mmol), RuPhos (14 mg, 0.031 mmol) and sodium t-butoxide (83 mg, 0.87 mmol) in THF (1.5 mL) was stirred at 85 °C overnight under an Ar atmosphere. The mixture was then cooled, into which was added acetic acid (1.4 eq) and then purified over silica with methanol in dichloromethane (0-10%) to give tert-butyl 1-(2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-4-methylpiperidin-4-ylcarbamate (70 mg, 22%). MS m/z 503.4 $[M+H]^+$.

[001555] Part 2, Step C: The compound tert-butyl 1-(2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-4-methylpiperidin-4-ylcarbamate (70 mg, 0.14 mmol) was treated with HCl in dioxane (4 N, 1.0 mL) for 30 minutes. The solvent was then removed. The residue was re-treated with ammonia in methanol and evaporated. The residue was purified with methanol in dichloromethane (0-10%) to give the title compound as a yellow solid (36 mg, 64%). M.P. 244-246 °C; MS m/z 403.3 $[M+H]^+$; ^1H NMR (500 MHz, *DMSO-d*$_6$) δ 8.22 - 8.27 (2H, m), 8.04 (1H, dd, *J*=9.8, 2.8 Hz), 7.96 (1H, s), 7.60 (1H, d, *J*=9.8 Hz), 7.41 (1H, t, *J*=1.3 Hz), 6.82 (1H, s), 3.25 - 3.30 (4H, m), 2.58 (3H, s), 2.27 (3H, d, *J*=0.9 Hz), 1.47 - 1.65 (6H, m), 1.10 (3H, s).

[001556] **Example 64**

[001557] Preparation of Cpd 743

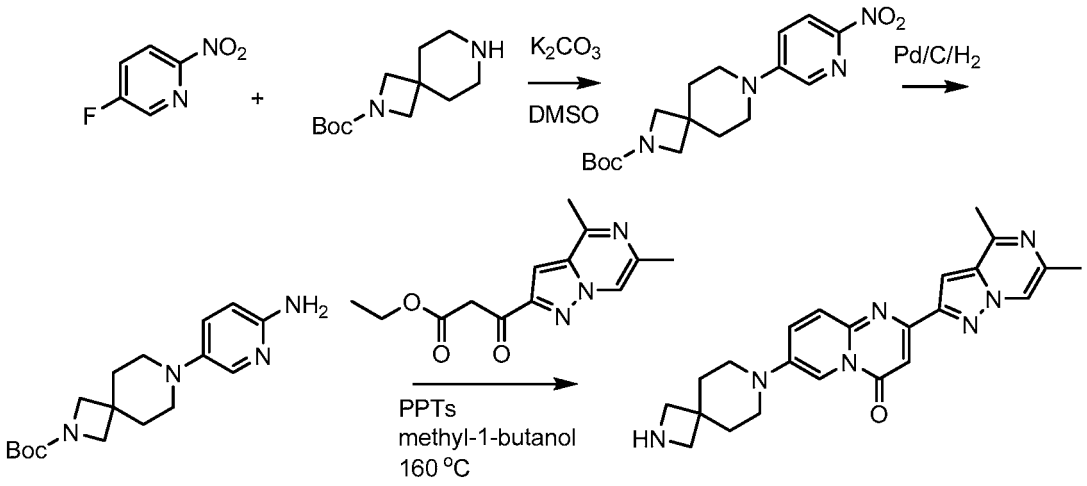


[001558] Step A: A mixture of 7-chloro-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (0.14 g, 0.43 mmol) and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.2 g, 0.65 mmol), $Pd(OAc)_2$ (1.9 mg, 0.0086 mmol), SPhos (7.0 mg, 0.0172 mmol) and K_3PO_4 (0.18 g, 0.86 mmol) in THF (1.0 mL) and water (0.5 mL) was stirred at 110 °C overnight. Aqueous workup followed by purification with methanol in dichloromethane (0-10%) provided tert-butyl 4-(2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.13 g, 65%). MS m/z 472.3 $[M+H]^+$.

[001559] Step B: Following the procedure in Example 63, Part 2, Step C, treatment of tert-butyl 4-(2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-5,6-dihydropyridine-1(2H)-carboxylate (0.13 g, 0.28 mmol) with HCl in dioxane (1.0 mL) provided the title compound as a yellow solid (5 mg, 5%). M.P. 189-191 °C; MS m/z 372.3 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 8.81 (1H, d, *J*=1.9 Hz), 8.03 (2H, d, *J*=1.6 Hz), 7.71 (1H, s), 7.62 (1H, d, *J*=9.5 Hz), 7.28 (1H, s), 6.76 (1H, s), 6.41 - 6.50 (1H, m), 3.58 (2H, d, *J*=2.5 Hz), 3.15 (2H, t, *J*=5.8 Hz), 2.63 (3H, s), 2.54 (2H, br. s.), 2.32 (3H, d, *J*=0.6 Hz).

[001560] **Example 65**

[001561] Preparation of Cpd 804



[001562] Step A: 5-fluoro-2-nitropyridine (200 mg, 1.41 mmol), tert-butyl 2,7-diazaspiro[3.5]-nonane-2-carboxylate (319 mg, 1.41 mmol) and K_2CO_3 (195 mg, 1.41 mmol) were combined in DMSO (8 mL). The reaction mixture was heated at 70°C for 15 hours and cooled to room temperature, before the solvent was evaporated. An extraction (CH_2Cl_2 and H_2O) followed by chromatography with silica gel (CH_2Cl_2/MeOH: 98/2) gave 7-(6-nitro-pyridin-3-yl)-2,7-diaza-spiro[3.5]nonane-2-carboxylic acid tert-butyl ester (320 mg, 65%) as a yellow solid. MS *m/z* 349.5 $[M+H]^+$.

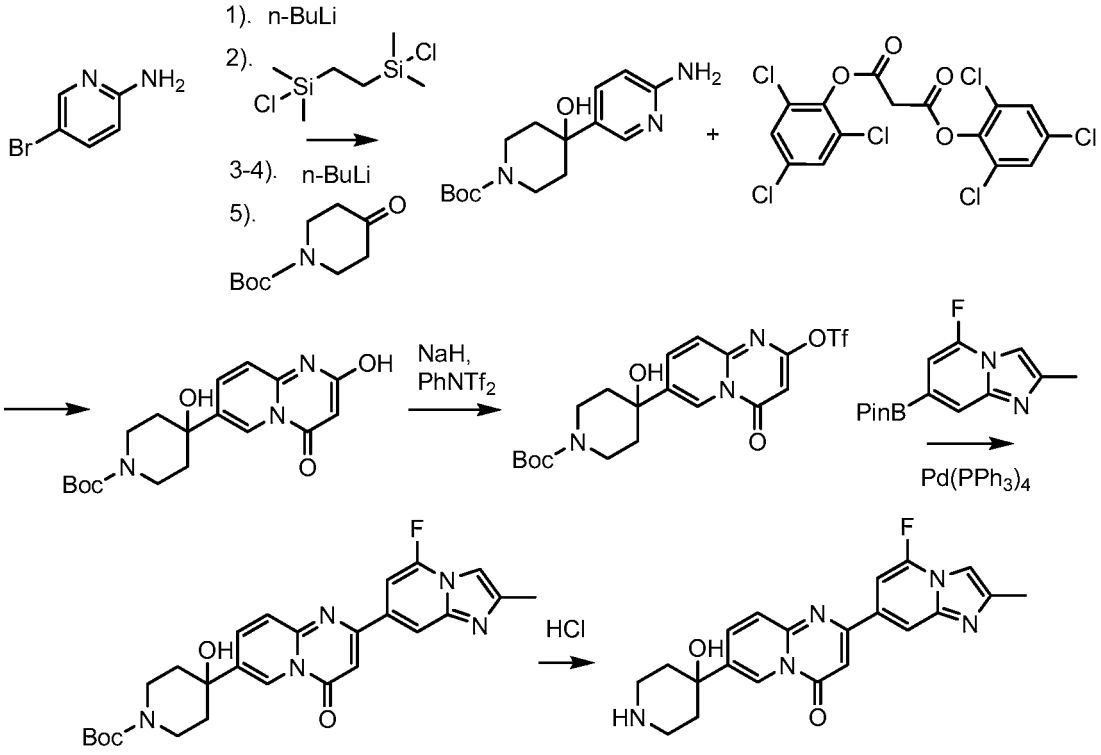
[001563] Step B: 7-(6-nitro-pyridin-3-yl)-2,7-diaza-spiro[3.5]nonane-2-carboxylic acid tert-butyl ester (315 mg, 0.90 mmol) and Pd/C (32 mg) were combined in MeOH (40 mL) and placed under a hydrogen atmosphere (H_2 balloon) for 15 hours. The reaction mixture was filtered through celite and chromatographed with silica gel (CH_2Cl_2/MeOH: 98/2) to give 7-(6-amino-

pyridin-3-yl)-2,7-diaza-spiro [3.5]nonane-2-carboxylic acid tert-butyl ester (227 mg, 78%) as an off-white solid. MS *m/z* 319.6 $[M+H]^+$.

[001564] Step C: A mixture of 7-(6-amino-pyridin-3-yl)-2,7-diaza-spiro[3.5]nonane-2-carboxylic acid tert-butyl ester (100 mg, 0.31 mmol), ethyl 3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-3-oxopropanoate (90 mg, 0.31 mmol, preparation described in Example 9, Steps A to F) and PPTs (87 mg, 0.345 mmol) in methyl-1-butanol (2 mL) was heated at 160°C for 15 hours. The mixture was cooled to room temperature, poured into an aqueous NaOH (1M) solution and extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and the residue was chromatographed with silica gel (CH_2Cl_2/MeOH: 9/1; and, 1% aqueous NH_3) to give the title product (40 mg, 31%) as a yellow solid. MS *m/z* 416.2 $[M+H]^+$. ^1H NMR ($CDCl_3$, 600 MHz) δ 8.18 (d, J=1.1 Hz, 1H), 8.15 (s, 1H), 7.45 (dd, 1H) 7.80 (d, 1H), 7.32 (s, 1H), 7.11 (s, 1H), 3.51 (m, 2H), 3.42 (d, 1H), 3.36 (d, 1H), 3.15 (m, 2H), 3.00 (d, 1H), 2.97 (d, 1H), 2.79 (s, 3H), 2.52 (s, 3H), 2.10 (m, 2H), 1.89 (m, 2H).

[001565] **Example 66**

[001566] Preparation of Cpd 811



[001567] Step A: 5-Bromopyridin-2-amine (1.0 g, 5.8 mmol) in THF (20 mL), cooled to -78°C under Ar, was combined with n-BuLi (3.6 ml, 5.8 mmol, 1.6 M in hexanes) and stirred for 0.5 hours. 1,2-Bis(chlorodimethylsilyl)ethane (1.2 g, 5.8 mmol) in THF (10 mL) was added and the mixture was allowed to warm to ambient temperature over 1 hour. The mixture was then re-cooled to -78°C and a second equivalent of n-BuLi (3.6 ml, 5.8 mmol, 1.6 M in hexanes) was added. The mixture was stirred for 0.5 hours at -78°C and then allowed to warm to ambient temperature over 1 hour. The mixture was then re-cooled to -78°C and a third equivalent of n-BuLi (3.6 ml, 5.8 mmol, 1.6 M in hexanes) was added. The mixture was stirred for 1 hour at -78°C, then tert-butyl 4-oxopiperidine-1-carboxylate (1.3 g, 6.4 mmol) in THF (10 mL) was added and the reaction was allowed to come to ambient temperature. The mixture was diluted with EtOAc, washed with brine, dried (Na_2SO_4) and concentrated. The residue was eluted from silica with EtOAc (0-100%) in n-heptane to afford tert-butyl 4-(6-aminopyridin-3-yl)-4-hydroxypiperidine-1-carboxylate as a light yellow solid (1.1 g, 64%). MS *m/z* 294.2 $[M+H]^+$.

[001568] Step B: A mixture of bis(2,4,6-trichlorophenyl) malonate (0.80 g, 1.7 mmol) and tert-butyl 4-(6-aminopyridin-3-yl)-4-hydroxypiperidine-1-carboxylate (0.50 g, 1.7 mmol) was heated in toluene (10 mL) at 60°C for 2 hours. The reaction was concentrated to remove the volatiles. The residue was eluted from silica with MeOH (0-20%) in CH_2Cl_2 to afford tert-butyl 4-hydroxy-4-(2-hydroxy-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate as a light yellow solid (0.43 g, 70%). MS *m/z* 362.3 $[M+H]^+$.

[001569] Step C: A mixture of tert-butyl 4-hydroxy-4-(2-hydroxy-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate (0.17 g, 0.5 mmol), 1,1,1-trifluoro-N-phenyl-N-(trifluoromethylsulfonyl)methanesulfonamide (0.19 g, 0.5 mmol) and potassium carbonate (0.13 g, 0.9 mmol) in DMF (3 mL) was stirred at ambient temperature. After 1 hour, the mixture was diluted with EtOAc, washed with water, brine, dried (Na_2SO_4) and concentrated. The residue was eluted from silica with EtOAc (10-50%) in n-heptane to afford tert-butyl 4-hydroxy-4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate as a crystalline yellow solid (0.08 g, 35%). MS *m/z* 494.3 $[M+H]^+$.

[001570] Step D: Following the procedure in Example 15, Step A, tert-butyl 4-hydroxy-4-(4-oxo-2-(trifluoromethylsulfonyloxy)-4H-pyrido[1,2-a]pyrimidin-7-yl)piperidine-1-carboxylate (80 mg, 0.16 mmol), 8-fluoro-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine (67 mg, 0.24 mmol, Prepared in Example 16, Step B),

tetrakis(triphenylphosphine)palladium(0) (9 mg, 0.01 mmol) and K_2CO_3 (31 mg, 0.32 mmol) in MeCN/water (2 ml/ 0.3 mL) provided tert-butyl 4-(2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-7-yl)-4-hydroxypiperidine-1-carboxylate as an off-white crystalline solid (60 mg, 75%). MS *m/z* 494.5 $[M+H]^+$.

[001571] Step E: Following the procedure in Example 24, Step B, the above product from Step D and HCl in dioxane (4M, 2 mL) provided 2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-hydroxypiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one as a white solid (11 mg, 49%). MS *m/z* 394.4 $[M+H]^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 9.31 (d, J= 1.2 Hz, 1H), 9.01 (d, J = 1.8 Hz, 1H), 8.12 (dd, J = 9.3, 1.8 Hz, 1H), 7.96 (d, J = 2.4Hz, 1H), 7.88 (dd, J = 12.6, 1.2 Hz, 1H), 7.75 (d, J = 9.3 Hz, 1H), 7.06 (s, 1H), 5.34 (br s, 1H), 2.91 (apparent t, J = 12.0 Hz, 2H), 2.79 (d, J = 12.0 Hz, 2H), 2.39 (s, 3H), 1.89-1.84 (m, 2H), 1.60 (d, J = 12.0 Hz, 2H).

[001572] Table 1 provides isolated compounds of a free base form of a compound of Formula (I) that may be prepared according to the procedures of the indicated Example by substituting the appropriate starting materials, reagents and reaction conditions. The preparation of any salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer from a free base form of a compound of Formula (I) is also contemplated and further included within the scope of the description herein. Where a free base form of the compound was not isolated from the salt form, a person of ordinary skill in the art could be expected to perform the required reactions to prepare and isolate the free base form of the compound.

[001573] The term "Cpd" represents Compound number, the term "Ex" represents "Example Number" (wherein * indicates that the corresponding Example for the Compound is provided above), the term "M.P." represents "Melting Point (°C)," the term "MS" represents "Mass Spectroscopy Peak(s) *m/z* $[M+H]^+$, $[M+2+H]^+$, $[M-H]^-$ or $[M+2-H]^-$," the term "D" represents "Decomposition/Decomposed," the term "DR" represents "Decomposition Range," the term "S" represents "Softens," the term "ND" indicates that the value was "Not Determined" and the term "NI" indicates that the compound was "Not Isolated."

[001574] Table 1

Ex	Cpd	Name	M.P.	MS
4*	**1**	2-(4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	182-184	337.3

Ex	Cpd	Name	M.P.	MS
4	2	2-(4-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-182	351.3
4	3	2-(4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	152-154	351.3
4	4	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	185-187	365.3
4	5	7-(1,4-diazepan-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	149-152	351.3
3*	6	2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	182-184	367.5
3	7	2-(3,4-dimethoxyphenyl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	138-140	395.3
3	8	2-(3,4-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	181-184	381.3
3	9	2-(3,4-dimethoxyphenyl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	159-162	395.3
3	10	7-(1,4-diazepan-1-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	381.3
3	11	2-(3,4-dimethoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	166-168	395.3
3	12	2-(4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	158-160	351.3
3	13	2-(3,4-dimethoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	183-185	381.3
3	14	2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	182-187	395.3
3	15	2-(3,4-dimethoxyphenyl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	185-189	409.3
4	16	2-(4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	137-141	365.3
4	17	7-(3,3-dimethylpiperazin-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	365.3
4	18	2-(1,3-benzodioxol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-201	351.3
4	19	2-(1,3-benzodioxol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	235-237	365.2
4	20	2-(1,3-benzodioxol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	195-197	365.3

Ex	Cpd	Name	M.P.	MS
4	21	2-(1,3-benzodioxol-5-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	198-201	379.3
4	22	2-(3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	147-149	337.2
4	23	2-(3-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	173-175	351.2
4	24	2-(3-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	164-166	351.2
4	25	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-191	365.3
4	26	7-(4-ethylpiperazin-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-160	365.3
4	27	7-(1,4-diazepan-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	351.2
4	28	2-(3-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	130-132	365.2
8*	29	2-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	193-198	361.3
3	30	2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	153-158	381.3
4	31	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	230-232	365.3
4	32	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-207	379.3
3	33	2-phenyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	151-153	307.2
3	34	7-[(3S)-3-methylpiperazin-1-yl]-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one	170-173	321.3
4	35	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	212-214	379.2
4	36	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-198	393.3
4	37	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	247-250	393.3

Ex	Cpd	Name	M.P.	MS
4	38	7-(1,4-diazepan-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	180-182	379.3
4	39	2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	150-152	393.3
1	40	2-(3,4-dimethoxyphenyl)-9-fluoro-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	183-185	399.3
1	41	2-(3-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	185-189	341.2
1	42	2-(4-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	207-212	341.2
1	43	7-(piperazin-1-yl)-2-[3-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one	199-207	375.2
1	44	7-(piperazin-1-yl)-2-[4-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one	285 (D)	375.2
1	45	2-(3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	183-187	321.2
1	46	2-(4-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-218	325.2
1	47	2-(4-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	237-242	352.2
1	48	2-(3,4-dimethoxyphenyl)-9-fluoro-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one	224-226	399.3
3	49	2-[4-(dimethylamino)phenyl]-9-fluoro-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-218	368.3
3	50	2-[4-(dimethylamino)phenyl]-9-fluoro-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-207	382.3
1	51	2-(2-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	142-146	325.2
28*	52	3-(3,4-dimethoxyphenyl)-8-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175-179	367.2
3	53	2-[4-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	211-215	350.3
3	54	2-[4-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	199-202	364.3
3	55	2-(3,4-dimethylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	186-188	335.2

Ex	Cpd	Name	M.P.	MS
3	56	2-(3,4-dimethylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	207-209	349.3
3	57	2-[3-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-180	350.2
3	58	2-[3-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	144-146	364.3
3	59	2-[4-(difluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	131-133	373.5
3	60	2-[4-(difluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	166-168	387.2
1	61	2-(3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	153-156	325.2
1	62	2-(3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175 (D)	352.2
1	63	2-(4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	192-195	321.2
3	64	2-(2-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	177-180	385.2
3	65	2-(2-fluoro-4,5-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	167-170	399.2
3	66	7-(3,8-diazabicyclo[3.2.1]oct-3-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-161	393.3
1	67	2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	177-181	405.1
1	68	2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-212	419.3
1	69	2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	195-200	419.3
6*	70	2-(3,4-dimethoxyphenyl)-9-methoxy-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	185-187	397.3
11	71a	2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	NI	NI
1*	72	2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	191-195	355.0

Ex	Cpd	Name	M.P.	MS
3	**73**	4-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile	146-151	332.1
7*	**74**	2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	221-225	362.2
7	**75**	2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	235-238	376.2
1	**76**	2-[3-fluoro-5-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	393
1	**77**	2-[4-fluoro-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-217	393.1
1	**78**	2-[2-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-200	405.1
1	**79**	2-(3,5-difluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	195-198	343
1	**80**	7-(piperazin-1-yl)-2-[3-(trifluoromethoxy)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one	140-143	391
5*	**81**	2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-162	421.1
5*	**82**	2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	245-248	407.2
5	**83**	2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	176-178	435.9
5	**84**	2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	152-155	421.2
31*	**85**	2-(3,4-dimethoxyphenyl)-4-oxo-7-(piperazin-1-yl)-4H-quinolizine-1-carbonitrile	199-202	391.2
1	**86**	2-(3-fluoro-4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-178	369.1
1	**87**	2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-178	369.1
1	**88**	2-(6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	173-178	338.2
1	**89**	2-(2,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	171-173	367.3

Ex	Cpd	Name	M.P.	MS
1	90	2-(2,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	172-177	381.2
32*	91	2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one	243-245	380.2
11*	92	2-(5-fluoropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	201-208	326.2
11	93	2-(5-fluoropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	191-199	340.1
11	94	2-(5-chloropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-218	342
11	95	2-(5-chloropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	227-232	356
1	96	2-(5-chloro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	201-209	372.1
12	97	2-(1H-indol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-206	346.2
12*	98	2-(1H-indol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	266-272	346.2
3	99	2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	403.4
3	100	2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	233-237	389.2
3	101	2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	167-169	417
3	102	2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	192-197	403.2
33	103	2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one	200-202	354.1
33	104	2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one	188-192	368.1
1	105	2-(3,5-difluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	189-194	357.2
33*	106	2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one	170-172	366.1
13*	107	2-(imidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	258-270	347
12	108	2-(imidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	347

Ex	Cpd	Name	M.P.	MS
15*	**109**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	259-267	361.1
3	**110**	2-(3-chloro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	201-203	371.4, 373.4
3	**111**	2-(3-chloro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	187-189	385.5, 387.5
1	**112**	2-(3-ethoxy-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	381.1
1	**113**	2-(3-ethoxy-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	159-162	395.1
15	**114**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	375.1
15	**115**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	375.1
15	**116**	7-(1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	375.1
15	**117**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	181-186	389.1
7	**118**	2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-192	376.5
7	**119**	2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	202-208	390.5
9	**120**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	195-200	376.5
9	**121**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	192-194	390.5
22	**122**	2-(3,4-dimethoxyphenyl)-7-(2-methylpyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	197-200	374
15	**123**	7-(piperazin-1-yl)-2-[2-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	250-255	415.5
15	**124**	2-(2-ethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-232	375.5

Ex	Cpd	Name	M.P.	MS
15	**125**	2-(2,3-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-240	375.5
2	**126**	2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	286-290	393.1
2	**127**	7-(4-aminopiperidin-1-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	182-185	381.1
19*	**128**	7-(piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	252-255	347.1
19	**129**	2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	230-233	361.1
19	**130**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	265-268	389.1
9	**131**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	404.5
9	**132**	7-(1,4-diazepan-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	390.5
14	**133**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	219-222	362.5
14	**134**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	191-193	376.5
14	**135**	2-(2-methyl-1,3-benzothiazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	174-180	392.2
14	**136**	2-(2-methyl-1,3-benzothiazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	378.1
14	**137**	2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175-180	361.5
14	**138**	2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	166-170	375.5
14	**139**	2-(3-fluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	168-170	355.5
14	**140**	2-(3-fluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	154-156	369.5

Ex	Cpd	Name	M.P.	MS
16	**141**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	270-274	375.1
2	**142**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	176-182	395.5
22*	**143**	2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-198	364.1
24*	**144**	2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-217	366.4
1	**145**	2-(3-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	385.5
3	**146**	2-(3,4-dimethoxyphenyl)-7-(4-hydroxypiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	383.5
2	**147**	2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	156-158	395.4
2	**148**	2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	158-161	409.1
14	**149**	2-(4-methoxy-3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-203	351.5
14	**150**	3-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile	224-231	332.1
14	**151**	2-methoxy-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile	191-197	362
14	**152**	2-(3-fluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	259-266	341.5
20*	**153**	2-(4-ethoxy-3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	180-186	369.1
20	**154**	2-[3-fluoro-4-(2,2,2-trifluoroethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-201	423.1
14	**155**	2-(2-methyl-1,3-benzoxazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-183	362
14	**156**	2-(2-methyl-1,3-benzoxazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	376.5
14	**157**	2-(3-fluoro-4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	174-176	339.5

Ex	Cpd	Name	M.P.	MS
14	**158**	2-(3-fluoro-4-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-178	353.5
2	**159**	7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	148-151	367.1
2	**160**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175 (S), 216-222	381.1
14	**161**	7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-212	392.2
10	**162**	7-[(3S)-3-methylpiperazin-1-yl]-2-(4-methyl-1,3-thiazol-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	225-230	342.1
10*	**163**	2-(4-methyl-1,3-thiazol-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	142-147	328.2
25*	**164**	2-(3,4-dimethoxyphenyl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	181-183	380.1
2	**165**	2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(propan-2-ylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	169-172	409.1
1	**166**	2-(3-fluoro-4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	176-178	383.1
14	**167**	2-(4-methoxy-3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	183-187	382.5
14	**168**	2-[3-fluoro-4-(methylsulfanyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	174-176	371.1
15	**169**	7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-213	389.1
9*	**170**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-256	390.4
14*	**171**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-183	376.5
14	**172**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	233-235	390.3
17	**173**	2-(5-fluoro-6-methoxypyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-180	370.5

Ex	Cpd	Name	M.P.	MS
17	**174**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-fluoro-6-methoxypyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	160-165	384.5
14	**175**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-212	406.1
14	**176**	2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-218	392.1
14	**177**	2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	165-170	406.1
14	**178**	7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-256	418.1
21*	**179**	2-(4-methyl-1H-imidazol-1-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	204-206	311.1
21	**180**	2-(4-methyl-1H-imidazol-1-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	204-206	325.5
2	**181**	2-(3,4-dimethoxyphenyl)-7-{[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	135-138	355
17*	**182**	2-(5-fluoro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	166-170	356.4
17	**183**	2-(3,5-difluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	167-169	373.4
17	**184**	2-(3,5-difluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	182-184	387.5
2	**185**	7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-201	397.1
2	**186**	2-(3-fluoro-4-methoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	182-184	352
2	**187**	2-(3,4-dimethoxyphenyl)-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	381.1
23*	**188**	2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	165-168	378.3

Ex	Cpd	Name	M.P.	MS
14	**189**	2-(3-chloro-5-fluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	188-190	373
14	**190**	2-(3-chloro-5-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	180-184	359.1
18*	**191**	7-[(3S)-3-methylpiperazin-1-yl]-2-(1-methyl-1H-pyrazol-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	168-170	325.2
18	**192**	2-(1-methyl-1H-pyrazol-4-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	311.1
14	**193**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-177	376.5
14	**194**	7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	160-162	390.5
14	**195**	7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	134-137	376.5
14	**196**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	146-150	390.5
14	**197**	7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-217	402.5
14	**198**	7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-199	402.5
14	**199**	2-(4,5-dimethoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	207-209	368.4
33	**200**	7-[3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one	259-261	382.1
33	**201**	7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one	ND	368.2
14	**202**	7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	212-216	390.5
33	**203a**	7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one	NI	NI
23	**204**	2-(3-fluoro-4-methoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	129-132	366
2	**205**	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	187-192	383.1

Ex	Cpd	Name	M.P.	MS
2	**206**	7-[(3R,4R)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	223-228	399
2	**207**	7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	173-179	369.1
2	**208**	2-(3-fluoro-4-methoxyphenyl)-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	167-171	383.1
16*	**209**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	282-288	379.4
16	**210**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-259	407.1
16	**211**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	262-266	407.6
2	**212**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	195-200	381.1
2	**213**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	204-210	395.1
25	**214**	2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	145-148	410
14	**215**	2-(4-fluoro-3-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	130-135	369.2
14	**216**	2-(4-fluoro-3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	355.2
14	**217**	2-(3,4-difluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	160-164	387.1
14	**218**	2-(3,4-difluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	155-160	373.1
14	**219**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-220	378.1
29*	**220**	7-(3-fluoro-4-methoxyphenyl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-206	355

Ex	Cpd	Name	M.P.	MS
14	**221**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	214-216	392.1
2	**222**	2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-(methylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	208-216	369.1
2	**223**	2-(3-fluoro-4-methoxyphenyl)-7-{4-[(methylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	163-170	397.1
2	**224**	7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	193-198	355
2	**225**	2-(3-fluoro-4-methoxyphenyl)-7-{[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	197-202	369.1
2	**226**	7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-185	411.1
14	**227**	2-(6-methoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-218	338.1
14	**228**	7-(piperazin-1-yl)-2-(pyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175-178	308
14	**229**	2-(5-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	192-195	338
14	**230**	3-fluoro-5-{7-[(3S)-3-methylpiperazin-1-yl]-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl}benzonitrile	185-188	364.2
14	**231**	3-fluoro-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile	238-244	350.1
2	**232**	2-(3-fluoro-4-methoxyphenyl)-7-[(3'S,4'S)-4'-hydroxy-1,3'-bipyrrolidin-1'-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	226-232	425.1
2	**233**	2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-pyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	143-147	369.1
14	**234**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	205-209	390.6
27	**235**	2-(3,4-dimethoxyphenyl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	396.2
27	**236**	2-(3,4-dimethoxyphenyl)-7-[(3S)-pyrrolidin-3-yloxy]-4H-pyrido[1,2-a]pyrimidin-4-one	164-166	368.1

Ex	Cpd	Name	M.P.	MS
27*	**237**	2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one	221-224	382.2
2	**238**	7-(1,4-diazepan-1-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	160-177	395.5
2*	**239**	2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	143-149	383.5
14	**240**	7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	206-210	404.5
14	**241**	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-193	390.5
14	**242**	7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	376.2
14	**243**	7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	388.3
14	**244**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	181-187	390.5
34*	**245**	2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one	174-176	363.2
2	**246**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-209	395.2
2	**247**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	186-191	378.2
23	**248**	2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	134-137	408.2
35*	**249**	2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one	194-196	377.2
24	**250**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	176-181	380.3
23	**251**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	187-196	392.2

Ex	Cpd	Name	M.P.	MS
25	**252**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-174	394.2
14	**253**	7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	205-207	392.2
14	**254**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-160	406.1
14	**255**	7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	250-260 (DR)	418.1
14	**256**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	230-234	392.1
2	**257**	2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	215 (S), 246-251	407.3
9	**258**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-223	404.3
9	**259**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	254-260	418.3
2	**260**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	212-218	421.2
2	**261**	2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	167-171	423.3
22	**262**	7-[(1R,5S)-8-azabicyclo[3.2.1]oct-2-en-3-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	191-194	390.2
26*	**263**	2-(3,4-dimethoxyphenyl)-7-(1,2,5,6-tetrahydropyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	146-150	364.2
14	**264**	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	203-207	390.2
14	**265**	2-(2-ethyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-175	376.2
14	**266**	2-(2-ethyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	168-170	390.2

Ex	Cpd	Name	M.P.	MS
14	**267**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	200-204	402.2
29	**268**	7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	308 (D)	379.2
16	**269**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	283-286	393.3
16	**270**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	393.3
16	**271**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	270-274	419.3
16	**272**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	277-280	419.2
16	**273**	7-(4-aminopiperidin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	393.3
16	**274**	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	300 (D)	407.3
16	**275**	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	294-297	407.3
30*	**276**	2-(4-aminopiperidin-1-yl)-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	268-283	369.3
30	**277**	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	167-170	383.2
30	**278**	2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	167-169	383.2
2	**279**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	180-186	425.3
2	**280**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	207-211	395.3

Ex	Cpd	Name	M.P.	MS
2	**281**	2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(propan-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	189-192	423.3
2	**282**	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	188-191	383.3
14	**283**	7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-202	406.3
14	**284**	7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-256	418.2
14	**285**	7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	420.2
27	**286**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one	218-220	393.1
16	**287**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	245-251	395.2
16	**288**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	289-295	423.1
16	**289**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	239-244	423.2
16	**290**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	236-239	409.1
16	**291**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	236-239	409.1
16	**292**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	274-280	435.2
16	**293**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	269-275	435.2
46*	**294**	7-(3-fluoro-4-methoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	188-192	352.1

Ex	Cpd	Name	M.P.	MS
39	**295**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	269-275	407.3
39	**296**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	279-282	407.3
39	**297**	7-[4-(dimethylamino)piperidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	250-257	421.3
39	**298**	2-[4-(dimethylamino)piperidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	157-160	397.2
37	**299**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	177-180	377.2
23	**300**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-181	391.3
2	**301**	2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	194-201	395.2
37	**302**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	359.2
23	**303**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	132-135	373.3
23	**304**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	128-131	387.3
36	**305**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	184-186	380.3
36*	**306**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	207-209	394.3
39	**307**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	408.3
36	**308**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	219-221	394.1

Ex	Cpd	Name	M.P.	MS
36	**309**	7-(4-ethylpiperazin-1-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	212-214	408.2
36	**310**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175-178	422.1
2	**311**	7-[(3aR,6aS)-5-ethylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	157-167	409.1
22	**312**	2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	211-215	366.1
2	**313**	2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	223-227	409.1
2	**314**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	177-184	395.2
23	**315**	2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	184-190	380.1
24	**316**	7-(3-fluoro-4-methoxyphenyl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	278-281	354.1
25	**317**	7-(3-fluoro-4-methoxyphenyl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-205	368.1
23	**318**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	151-154	405.2
23	**319**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	159-162	419.3
25	**320**	2-(3,4-dimethoxyphenyl)-7-[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	406.2
2	**321**	2-(3,4-dimethoxyphenyl)-7-[(2R)-2-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	381.1
54*	**322**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one	115-117	375.3
54	**323**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-quinolizin-4-one	ND	375.1

Ex	Cpd	Name	M.P.	MS
39	**324**	7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one	288-290	403.2
39	**325**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one	>300	389.2
45	**326**	7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one	288-290	375.2
2	**327**	2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	198-202	383.1
2	**328**	7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	141-145	411.2
25	**329**	2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-203	382.2
53	**330**	7-[4-(cyclopropylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	141 (S), 158-161	435.3
39	**331**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	258-262	423.2
2	**332**	2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	225-233	409.3
2	**333**	2-(3,4-dimethoxyphenyl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	148 (S), 168-177	409.3
9	**334**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	169-171	404.4
9	**335**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	390.4
9	**336**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	215-218	416.3
9	**337**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	416.4

Ex	Cpd	Name	M.P.	MS
9	**338**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	251-253	404.4
9	**339**	7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-210	418.4
9	**340**	7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	195-197	404.4
9	**341**	7-(4-cyclopropylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-192	416.4
38*	**342**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	207-210	373.3
39	**343**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.4
2	**344**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	191-198	395.3
2	**345**	2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-ethyl-4H-pyrido[1,2-a]pyrimidin-4-one	146-150	437.3
23	**346**	2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	169-179	422.3
14	**347**	7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-220	420.2
45	**348**	7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	190-192	392.1
45	**349**	7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	404.1
23	**350**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	193-197	387.4
23	**351**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	401.4

Ex	Cpd	Name	M.P.	MS
23	**352**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	191-193	415.5
49*	**353**	2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-a]pyrimidin-4-one	ND	365.1
23	**354**	7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	413.4
23	**355**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	186-189	415.4
23	**356**	7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	191-193	427.4
23	**357**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	429.3
53	**358**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	409.3
53	**359**	2-(3,4-dimethoxyphenyl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	423.4
2	**360**	2-(3,4-dimethoxyphenyl)-8-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	161-169	381.3
39	**361**	2-(3,4-dimethoxyphenyl)-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	423.3
23	**362**	7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one	152-154	418.3
23	**363**	2-(3,4-dimethoxyphenyl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	116-118	406.3
23	**364**	2-(3,4-dimethoxyphenyl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	178-180	420.3
23	**365**	2-(3,4-dimethoxyphenyl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-160	406.2

Ex	Cpd	Name	M.P.	MS
22	**366**	2-(3,4-dimethoxyphenyl)-7-[4-(methylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	232-235	392.3
23	**367**	2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	162-164	406.2
23	**368**	2-(3,4-dimethoxyphenyl)-7-{4-[ethyl(methyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	132-134	420.4
23	**369**	2-(3,4-dimethoxyphenyl)-7-{4-[methyl(propyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	116-118	434.4
23	**370**	2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	392.3
46	**371**	7-(3,4-dimethoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	172-178	364.3
46	**372**	7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	376.2
16	**373**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	260-264	421.3
16	**374**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	287-292	437.4
46	**375**	7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	197-201	358.2
23	**376**	7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	203-207	372.2
23	**377**	7-(3,4-dimethoxyphenyl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	149-152	378.3
23	**378**	2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	171-177	420.3

Ex	Cpd	Name	M.P.	MS
23	**379**	7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	167-178	432.3
55	**380a**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	NI	NI
45	**381**	7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	190-194	392.2
45	**382**	7-(3-aminopyrrolidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-200	378.2
14	**383**	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	235-240	406.3
37	**384**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	124-126	375.2
16	**385**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-methoxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	258-262	437.5
23	**386**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	180-195 (DR)	434.3
23	**387**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	153-163	420.4
23	**388**	2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	406.4
22	**389**	2-(3,4-dimethoxyphenyl)-8-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175 (D)	378.3
23	**390**	7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	180-189	418.4
23	**391**	2-(3,4-dimethoxyphenyl)-8-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	174-178	392.4
23	**392**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	389.2

Ex	Cpd	Name	M.P.	MS
23	**393**	7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	178-180	419.2
23	**394**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	168-170	417.2
23	**395**	7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	158-160	415.3
23	**396**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	128-130 (DR)	403.2
39	**397**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	247-249	404.5
56*	**398**	2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	195-200	365.3
9	**399**	7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-221	388.3
39	**400**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	188-191	402.3
39	**401**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	175-177	416.4
57*	**402**	2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	205-208	365.4
24	**403**	2-(3-fluoro-4-methoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	122-125	354.3
25	**404**	2-(3,4-dimethoxyphenyl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	155-157	394.4
24	**405**	2-(3,4-dimethoxyphenyl)-7-[cis-4-(methylamino)cyclohexyl]-4H-pyrido[1,2-a]pyrimidin-4-one	156-158	394.4
24	**406**	2-(3,4-dimethoxyphenyl)-7-(piperidin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	126-129	366.3

Ex	Cpd	Name	M.P.	MS
53*	**407**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	178-184	437.5
22	**408**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	171-177	392.4
24	**409**	7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-258	360.4
24	**410**	7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	295-298	378.4
23	**411**	7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-222	390.4
16	**412**	7-(4-cyclopropylpiperazin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-258	419.4
57	**413a**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	NI	NI
2	**414**	2-(3,4-dimethoxyphenyl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	421.4
23	**415**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	177-182	406.4
53	**416**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	178-183	437.5
2	**417**	2-(3,4-dimethoxyphenyl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	183-189	421.4
23	**418**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	148-153	420.5
53	**419**	2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	219-224	465.5
9	**420**	2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	362.2

Ex	Cpd	Name	M.P.	MS
57	**421**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:1)	ND	360.1
23	**422**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	240-242	374.3
23	**423**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	225-227	388.4
24	**424**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	222-224	377.1
9	**425**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	215-218	444.4
9	**426**	7-(1,4'-bipiperidin-1'-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-238	458.4
9	**427**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	198-200	473.5
9	**428**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	192-195	460.4
37	**429**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	206-208	358.4
23	**430**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	137-140	372.2
23	**431**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-223	386.4
14	**432**	7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	204-206	403.4
53	**433**	2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	185-193	439.4
25	**434**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	146 (S), 166-169	408.4

Ex	Cpd	Name	M.P.	MS
53	**435**	7-[4-(diethylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	149-155	451.5
25	**436**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	157-162	422.4
14	**437**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	230-232	429.4
51	**438**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	298-300	360.1
25	**439**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-242	391.4
9	**440**	7-(4-methylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	230-240 (DR)	376.2
9	**441**	7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	235-240 (DR)	376.2
9	**442**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	258-260	390.3
37*	**443**	2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-203	358.2
37	**444**	2-[6-(dimethylamino)pyridin-3-yl]-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-257	348.4
37	**445**	7-[4-(diethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-210	431.4
53	**446**	2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	164-171	453.5
2	**447**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	140-147	409.2
25	**448**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-220	374.3

Ex	Cpd	Name	M.P.	MS
23	**449**	2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	148-150	372.3
23	**450**	2-[6-(dimethylamino)pyridin-3-yl]-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-216	362.4
9	**451**	7-[4-(diethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	232-235	446.5
24	**452**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	375.4
25	**453**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-222	389.3
25	**454**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	403.3
2	**455**	2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	180-184	435.3
53	**456**	2-(3,4-dimethoxyphenyl)-7-{4-[(2-methoxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	178-182	453.3
9	**457**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	262-271	404.2
2	**458**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	244-256	430.3
2	**459**	7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	231-241	432.4
25	**460**	7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	227-230	374.3
25	**461**	7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	215-218	402.3
25	**462**	7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	235-238	392.3

Ex	Cpd	Name	M.P.	MS
23	**463**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	172-174	386.3
23	**464**	2-(1-methyl-1H-indazol-5-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	152-154	400.4
24	**465**	2-[6-(dimethylamino)pyridin-3-yl]-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-210	350.3
9	**466**	7-(4-ethylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-230 (DR)	390.3
9	**467**	7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-250 (DR)	402.3
9	**468**	7-[4-(dimethylamino)piperidin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-242	404.3
9	**469**	7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-256	406.3
25	**470**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	159-161	402.4
23	**471**	7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	402.3
9	**472**	7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-244	376.2
38	**473**	2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	260-265 (DR)	359.2
37	**474**	2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	239-241	358.4
37	**475**	2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-218	374.4
25	**476**	2-(2-methyl-2H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	226-228	372.3

Ex	Cpd	Name	M.P.	MS
23	**477**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-200	386.4
23	**478**	7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	190-192	388.4
23	**479**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one	220-222	415.3
22	**480**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	> 300	387.4
23	**481**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	401.4
23	**482**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	415.5
23	**483**	7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	427.4
23	**484**	2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	126-128 (DR)	373.2
23	**485**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	387.3
50*	**486**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-200	376.3
50	**487**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	256-258	390.2
50	**488**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	390.3
14	**489**	2-(1-methyl-1H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	375.3
14	**490**	2-(1-methyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	206-208	361.3
14	**491**	7-[4-(dimethylamino)piperidin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	209-212	403.5

Ex	Cpd	Name	M.P.	MS
14	**492**	7-(4-methyl-1,4-diazepan-1-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	389.4
23	**493**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	205-207	388.4
16	**494**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	264-268	423.4
39	**495**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	239-245	437.5
39	**496**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	234-245	437.5
39	**497**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	278-281	451.3
39	**498**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	264-270	451.3
58*	**499**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	126-128	362.2
25	**500**	2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	272-275	376.4
25	**501**	7-(1-ethylpiperidin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	284-286	390.4
59*	**502**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	376.4
25	**503**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	257-259	390.3
25	**504**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	404.3
57	**505**	2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	228-230	359.2

Ex	Cpd	Name	M.P.	MS
23	**506**	2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	234-236	373.3
23	**507**	7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	387.4
2	**508**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	241-252	418.5
2	**509**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	213-222	404.5
2	**510**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	244-253	418.4
2	**511**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	240-245	432.5
60*	**512**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	ND	376.4
25	**513**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	265-267	390.3
25	**514**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	283-285	404.4
2	**515**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	198-200	416.3
24	**516**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	287-293	394.2
25	**517**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	292-296	408.3
25	**518**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-246	422.3
25	**519**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	279-285	436.5

Ex	Cpd	Name	M.P.	MS
2	**520**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.3
58	**521**	2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	ND	361.4
25	**522**	2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	260-262	375.2
25	**523**	7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	253-255	389.3
25	**524**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	289-291	409.3
25	**525**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	284-286	423.2
25	**526**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrimido[1,2-b]pyridazin-4-one	255-257	439.3
50	**527**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	260-262	404.3
50	**528**	7-[4-(dimethylamino)piperidin-1-yl]-2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-202	418.3
50	**529**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	256-258	420.3
25	**530**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	419.3
9	**531**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	246-248	420.4
39	**532**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	238-240	434.3
43	**533**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-methoxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	179-183	467.3

Ex	Cpd	Name	M.P.	MS
43	**534**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	201-205	497.3
39	**535**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-cyclopropyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	253-257	449.3
39	**536**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-232	463.3
43	**537**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-234	453.3
43	**538**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-methoxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	215-219	451.3
43	**539**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	270-274	437.3
43	**540**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	175-181	481.3
39	**541**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	191-194	435.3
39	**542**	7-[(3S)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	242-246	433.4
39	**543**	7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	264-267	447.3
2	**544**	7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.3
14	**545**	2-(1-methyl-1H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	190-192	375.3
9	**546**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	230-233	390.5

Ex	Cpd	Name	M.P.	MS
9	547	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	250-252	404.5
9	548	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	250-252	418.5
9	549	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	240-242	434.5
9	550	7-[4-(dimethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	258-260	432.5
9	551	7-[4-(diethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	232-235	460.6
14	552	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	240-242	389.5
14	553	2-(1-methyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	206-208	375.4
25	554	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	218-220	402.4
16	555	2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	272-277	361.3
24	556	2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	257-260	360.3
39	557	2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	285-288	375.3
39	558	7-(4-ethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	219-222	389.3
25	559	2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-260	374.3
25	560	7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	229-233	388.4
2	561	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	210-219	404.4

Ex	Cpd	Name	M.P.	MS
2	562	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	273-283	418.4
2	563	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	244-253	418.4
2	564	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	297-310	432.4
23	565	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	230-232	400.5
58	566	2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	235-237	361.3
25	567	2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	275-277	375.3
25	568	7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	198-200	389.3
25	569	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	230-232	405.3
9	570	7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	206-208	432.3
9	571	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	177-180	458.5
9	572	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	192-195	472.6
9	573	2-(3,4-dimethoxyphenyl)-7-{4-[(dimethylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	182-184	423.3
9	574	2-(3,4-dimethoxyphenyl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	449.5
9	575	2-(3,4-dimethoxyphenyl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	184-186	463.5
25	576	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-202	404.4

Ex	Cpd	Name	M.P.	MS
23	**577**	7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	248-250	402.2
25	**578**	2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	256-258	374.3
25	**579**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	277-280	375.3
25	**580**	7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	255-258	389.3
25	**581**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	250-252	405.3
53	**582**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	250-259	462.4
53	**583**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	231-241	446.4
2	**584**	7-(4-amino-4-methylpiperidin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-203	404.5
58	**585**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	361.3
61*	**586**	2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	160-162	362.3
58	**587**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	395.3
58	**588**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	375.4
39	**589**	2-(2-methyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	376.4
39	**590**	7-(4-ethylpiperazin-1-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	214-216	390.4
39	**591**	7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	200-202	406.4
25	**592**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	249-251	389.3

Ex	Cpd	Name	M.P.	MS
25	**593**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	242-244	403.4
25	**594**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one	242-244	419.4
25	**595**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one	243-245	437.3
53	**596**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	228-236	432.4
53	**597**	7-{4-[bis(2-hydroxyethyl)amino]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	218-227	492.4
25	**598**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	205-207	406.3
25	**599**	2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one	266-268	439.3
25	**600**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	150-152	431.3
50	**601**	2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	404.3
39	**602**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	210-212	430.3
51*	**603**	2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	268-270	360.4
25	**604**	7-(1-ethylpiperidin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	184-186	388.5
25	**605**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	204-206	404.5
24	**606**	2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	360.4
24	**607**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	282-284	374.3

Ex	Cpd	Name	M.P.	MS
25	**608**	2-(2-methyl-2H-indazol-5-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	402.5
53	**609**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	221-232	448.4
53	**610**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	218-227	418.4
53	**611**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	215-225	446.4
25	**612**	7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	388.5
25	**613**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	404.5
25	**614**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-202	388.5
25	**615**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	402.5
25	**616**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	242-244	416.5
25	**617**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.5
9	**618**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	243-245	432.5
9	**619**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	255-258	432.5
9	**620**	7-(4-cyclopropylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	258-260	430.5
39	**621**	7-(4-cyclobutylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	275-278	444.5

Ex	Cpd	Name	M.P.	MS
39	**622**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-208	446.5
39	**623**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	176-178	444.5
39	**624**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	184-187	460.5
40*	**625**	2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	242-244	406.5
40*	**626**	2-(4-hydroxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	280-283	392.4
25	**627**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one	229-231	403.3
25	**628**	7-(1-cyclobutylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	249-251	415.2
39*	**629**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	257-259	418.5
39	**630**	7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	256-258	432.5
39	**631**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-propylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	243-245	446.5
39	**632**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	238-241	448.5
9	**633**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	258-260	418.4
9	**634**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	229-232	458.6

Ex	Cpd	Name	M.P.	MS
9	635	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	404.4
9	636	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	175-180	418.4
16	637	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	264-271	389.4
16	638	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	230-234	403.4
16	639	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	232-236	403.4
25	640	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	196-198	417.5
25	641	7-(1-cyclopropylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	180-183	415.5
25	642	7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-191	429.5
39	643	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	242-244	446.5
39	644	7-[(3R)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	244-247	444.5
39	645	7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	261-264	458.6
39	646	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	216-219	460.5
39	647	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	248-253	433.3
39	648	7-(4-cyclobutylpiperazin-1-yl)-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	274-279	443.5

Ex	Cpd	Name	M.P.	MS
39	**649**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	217-220	447.4
39	**650**	7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	209-212	457.4
39	**651**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	220-223	447.4
39	**652**	7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	457.5
59	**653**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	ND	390.4
25	**654**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	261-263	404.5
25	**655**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	273-275	418.3
24	**656**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-238	389.4
25	**657**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	190-192	403.5
25	**658**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	417.5
25	**659**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	207-209	433.5
25	**660**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	203-204	431.5
9	**661**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	185-188	404.5
43*	**662**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	197-199	421.5

Ex	Cpd	Name	M.P.	MS
43	**663**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	186-188	435.5
43	**664**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-fluoroethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	245-247	436.5
43	**665**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(3-fluoropropyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	240-242	450.6
43	**666**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-fluoroethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	255-257	450.6
43	**667**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(3-fluoropropyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	244-246	464.6
43	**668**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	206-208	435.6
43	**669**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	216-218	449.6
43	**670**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3R)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	492.4
24	**671**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	247-255	389.3
25	**672**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	237-248	403.4
39	**673**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	273-281	448.4
48*	**674**	2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	>320	391.3
16	**675**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	417.4

Ex	Cpd	Name	M.P.	MS
16	**676**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	417.3
39	**677**	2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	262-266	405.3
39	**678**	7-(4-ethylpiperazin-1-yl)-2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	258-262	419.3
25	**679**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	431.5
25	**680**	7-(1-cyclopropylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-199	429.5
25	**681**	7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	227-229	443.5
25	**682**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	190-192	445.5
9	**683**	2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	226-229	402.4
9	**684**	2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	238-240	416.5
9	**685**	2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-238	430.5
9	**686**	2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	239-241	446.5
25	**687**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	185-187	417.4
41*	**688**	2-[4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	245-248	405.4

Ex	Cpd	Name	M.P.	MS
14	**689**	2-(2-methyl-1H-benzimidazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	292-294	375.3
39	**690**	7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1H-benzimidazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	283-285	389.3
58	**691**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	215-217	375.4
58	**692**	2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one	249-251	361.3
25	**693**	7-[1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-238	503.5
42*	**694**	7-[1-(1,3-dihydroxypropan-2-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	463.6
62*	**695**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-256	403.4
24	**696**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	221-224	388.3
25	**697**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-218	402.4
25	**698**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	196-200	416.5
25	**699**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	244-247	432.4
39	**700**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	217-220	417.4
39	**701**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	179-182	431.4
25	**702**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	231-240	417.4
25	**703**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	224-233	433.3

Ex	Cpd	Name	M.P.	MS
25	**704**	7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	228-237	443.5
25	**705**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	222-227	388.3
2	**706**	7-[4-(dimethylamino)-4-methylpiperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	237-239	432.4
2	**707**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)-4-methylpiperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	187-189	432.4
2	**708**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-methyl-4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	181-183	446.4
2	**709**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]-4-methylpiperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	196-198	448.4
25	**710**	7-(1-cyclobutylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	232-235	428.4
25	**711**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-222	418.4
25	**712**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-223	431.4
62	**713**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	389.3
47*	**714**	2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	274-277	401.4
47	**715**	2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	246-250	415.4
47	**716**	2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	246-250	415.4

Ex	Cpd	Name	M.P.	MS
47	**717**	2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	205-209	429.5
25	**718**	7-(1-cyclopropylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	226-231	414.4
25	**719**	7-(1-ethylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	237-241	402.5
2	**720**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	254-264	390.4
24	**721**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	211 (S), 223-227	374.3
27	**722**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one	249-252	405.4
9	**723**	2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	250-252	404.4
9	**724**	7-(4-methylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	246-248	418.4
9	**725**	7-(4-ethylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	231-233	432.5
9	**726**	7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	225-227	448.4
9	**727**	7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	195-197	418.4
9	**728**	7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	195-197	418.4
9	**729**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	249-251	432.5
39	**730**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	249-251	431.3

Ex	Cpd	Name	M.P.	MS
63*	**731**	7-(4-amino-4-methylpiperidin-1-yl)-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	244-246	403.3
2	**732**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-ethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	243-251	418.5
16	**733**	2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	325-328	429.3
16	**734**	7-[(3R)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	303-306	443.2
16	**735**	7-[(3S)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	>320	443.2
16	**736**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	293-296	457.3
2	**737**	7-(4-amino-4-methylpiperidin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-218	418.5
14	**738**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	375.4
24	**739**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	374.4
52	**740**	7-(3-aminoprop-1-yn-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	242-244	345.4
14	**741**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	170-172	389.4
52	**742**	7-(3-aminopropyl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	349.3
64*	**743**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	189-191	372.3
38	**744**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	218-221	429.5

Ex	Cpd	Name	M.P.	MS
38	**745**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-258	443.5
45	**746**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	239-242	402.4
2	**747**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	246-249	416.4
62	**748**	7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	238-241	417.4
62	**749**	7-(1,4-diazepan-1-yl)-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	200-202	403.4
14	**750**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	308-310	389.4
39	**751**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	202-204	403.4
25	**752**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-210	388.3
25	**753**	2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	162-164	402.4
2	**754**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	233-243	375.3
2	**755**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	389.4
2	**756**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	389.3
2	**757**	7-[3-(dimethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	226-228	390.4
2	**758**	7-[3-(diethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	231-233	418.5

Ex	Cpd	Name	M.P.	MS
2	759	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(pyrrolidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	235-237	416.4
9	760	7-(1,4-diazepan-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	212-214	404.4
45	761	7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	212-214	430.4
38	762	2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	257-260	401.4
38	763	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	287-289	387.4
45*	764	7-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	244-246	390.4
2	765	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(piperidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	220-223	430.5
24	766	2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	403.4
2	767	7-(2,7-diazaspiro[4.4]non-2-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	208-210	416.4
14	768	2-(2,7-dimethyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	216-218	389.5
52*	769	7-[3-(dimethylamino)propyl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	136-138	377.3
39	770	7-{(3S)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	239-241	418.4
24	771	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	241-249	403.4
24	772	9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	212-217	374.3

Ex	Cpd	Name	M.P.	MS
22	**773**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	265 (D)	401.3
25	**774**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-227	417.3
51	**775**	2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	220-222	374.2
14	**776**	2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	160-163	375.3
14	**777**	2-(1,7-dimethyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	248-250	389.3
39	**778**	7-{(3S)-3-[(diethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	194-196	446.4
39	**779**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3S)-3-[(ethylamino)methyl]pyrrolidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.4
2	**780**	7-{3-[(dimethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	228-230	404.4
2	**781**	7-{3-[(diethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	205-207	432.4
62	**782**	2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	220-222	429.3
2	**783**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	223-233	418.4
25	**784**	9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	255-263	388.3
39	**785**	7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	234-240	432.4
25	**786**	7-(1-ethylpiperidin-4-yl)-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	236-240	402.4

Ex	Cpd	Name	M.P.	MS
2	**787**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	227-236	418.4
2	**788**	7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	225-228	418.4
2	**789**	7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	235-241	432.4
25	**790**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	201-208	431.4
22	**791**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	> 240 (D)	373.3
25	**792**	7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	231-237	457.3
25	**793**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	210-216	447.4
16	**794**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	231-235	429.3
16	**795**	2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	229-233	429.3
51	**796**	9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one	229-235	375.3
2	**797**	7-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	214-217	390.4
44*	**798**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	228-231	401.3
2	**799**	7-{(3R)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	229-231	418.4
24	**800**	7-[(2S,6S)-2,6-dimethylpiperidin-4-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	248-250	403.3

Ex	Cpd	Name	M.P.	MS
16	**801**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	423.5
16	**802**	2-(imidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	361.5
36	**803**	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	420.6
65*	**804**	7-(2,7-diazaspiro[3.5]non-7-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	416.2
14	**805**	7-(4-methylpiperazin-1-yl)-2-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	376.1
16	**806**	7-(4-methylpiperazin-1-yl)-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	443.6
16	**807**	2-methyl-6-[7-(4-methylpiperazin-1-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]imidazo[1,2-a]pyridine-8-carbonitrile	ND	400.6
16	**808**	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	389.5
16	**809**	7-(4,7-diazaspiro[2.5]oct-7-yl)-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	401.4
25	**810**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	392.4
66*	**811**	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-hydroxypiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	394.4
9	**812**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	430.7
9	**813**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	430.6
9	**814**	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.7

Ex	Cpd	Name	M.P.	MS
9	815	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	418.7
16	816	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	433.6
9	817	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	432.6
9	818	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	444.6
16	819	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	403.7
16	820	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	415.7
16	821	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	429.7
9	822	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	432.6
9	823	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{[2-(morpholin-4-yl)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	ND	434.6
9	824	7-{[2-(dimethylamino)ethyl]amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	392.6
9	825	7-{[2-(dimethylamino)ethyl](methyl)amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	406.6
9	826	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{methyl[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one	ND	392.6
16	827	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	403.7

Ex	Cpd	Name	M.P.	MS
16	**828**	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	403.7
27	**829**	7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one	ND	407.6
27	**830**	7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	393.6
27	**831**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-ylmethoxy)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	419.5
27	**832**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[2-(piperidin-1-yl)ethoxy]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	433.6
27	**833**	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(morpholin-4-yl)propoxy]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	449.6
27	**834**	7-[3-(dimethylamino)propoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one	ND	407.6
9	**835**	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one	ND	416.5

[001575] or a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[001576] Table 2 further provides certain isolated compounds of a salt form of a compound of Formula (I) that may be prepared according to the procedures of the indicated Example by using the appropriate reactants, reagents and reaction conditions. The preparation of any free base, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer from a salt form of a compound of Formula (I) is also contemplated and further included within the scope of the description herein. Where a free base form of the compound was not isolated from the salt form, a person of ordinary skill in the art could be expected to perform the required reactions to prepare and isolate the free base form of the compound.

[001577] The term "Cpd" represents Compound number, the term "Ex" represents "Example Number" (wherein * indicates that the corresponding Example for the Compound is provided

above), the term "M.P." represents "Melting Point (°C)," the term "MS" represents "Mass Spectroscopy Peak(s) *m/z* $[M+H]^+$, $[M+2+H]^+$, $[M-H]^-$ or $[M+2-H]^-$," the term "D" represents "Decomposition/Decomposed," the term "DR" represents "Decomposition Range," the term "S" represents "Softens" and the term "ND" indicates that the value was "Not Determined."

[001578] Table 2

Ex	Cpd	Name	M.P.	MS
1	**71**	2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one hydrochloride	290 (D)	359.2
33	**203**	7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one acetate	188-192	396.2
55*	**380**	2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one trifluoroacetate (1:1)	230-235	378.2
57	**413**	2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:2)	>300	373.3

[001579] or a free base, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

BIOLOGICAL EXAMPLES

[001580] To describe in more detail and assist in understanding the present description, the following non-limiting biological examples are offered to more fully illustrate the scope of the description and are not to be construed as specifically limiting the scope thereof. Such variations of the present description that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the present description and as hereinafter claimed. These examples illustrate the testing of certain compounds described herein *in vitro* and/or *in vivo* and demonstrate the usefulness of the compounds for treating of SMA by enhancing the inclusion of exon 7 of SMN2 into mRNA transcribed from the SMN2 gene. Compounds of Formula (I) enhance inclusion of exon 7 of SMN2 into mRNA transcribed from the SMN2 gene and increase levels of Smn protein produced from the SMN2 gene, and thus can be used to treat SMA in a human subject in need thereof.

[001581] **Example 1**

[001582] **SMN2 Minigene Construct**

[001583] **Preparation of the Minigene Constructs**

[001584] DNA corresponding to a region of the *SMN2* gene starting from the 5' end of exon 6 (ATAATTCCCCC) (**SEQ ID NO. 14**) and ending at nucleic acid residue 23 of exon 8 (CAGCAC) (**SEQ ID NO. 15**) was amplified by PCR using the following primers:

[001585] Forward primer: 5'-CGCGGATCCATAATTCCCCCACCACCTC-3' (**SEQ ID NO. 16**)

[001586] Reverse primer: 5'-CGCGGATCCGTGCTGCTCTATGCCAGCA-3' (**SEQ ID NO. 17**)

[001587] The 5' end of each primer was designed to add a BamHI restriction endonuclease recognition site at both the 5' end of exon 6 (GGATCC) (**SEQ ID NO. 18**) and the 3' end after the 23rd nucleotide of exon 8. Using the BamHI restriction endonuclease recognition sites, the PCR fragment was cloned into a derivative of the original pcDNA 3.1/Hygro vector which was modified as disclosed in United States Patent Publication US2005/0048549.

[001588] New UTRs were added to the modified vector using the HindIII site and the BamHI restriction sites comprising a 5´DEG UTR: 5'-TAGCTTCTTACCCGTACTCCACCGTTGGCAGCACGATCGCACGTCCCACGTGAAC CATTGGTAAACCCTG-3' (**SEQ ID NO. 19**) cloned into the modified pcDNA3.1/Hygro vector together with a start codon upstream of the BamHI restriction site, and;

[001589] a 3´DEG UTR: 5'-ATCGAAAGTACAGGACTAGCCTTCCTAGCAACCGCGGGCTGGGAGTCTGAGACAT CACTCAAGATATATGCTCGGTAACGTATGCTCTAGCCATCTAACTATTCCCTATGTCT TATAGGG-3' (**SEQ ID NO. 20**) cloned into the modified pcDNA3.1/Hygro vector using the NotI restriction endonuclease recognition site and the XhoI restriction endonuclease recognition site with a stop codon immediately downstream of the NotI restriction site. In addition, a firefly luciferase gene lacking the start codon was cloned into the vector using the BamHI and NotI restriction sites.

[001590] The resulting minigene comprises, in 5' to 3' order: the 5'-DEG UTR, the start codon, six additional nucleotides forming a BamHI restriction site, the nucleic acid residues of exon 6, the nucleic acid residues of intron 6 of SMN2, the nucleic acid residues of exon 7 of

SMN2, the nucleic acid residues of intron 7 of SMN2, and the first 23 nucleic acid residues of exon 8 of *SMN2*, an additional six nucleotides forming a BamHI restriction site and the firefly luciferase gene lacking the start codon.

[001591] A single adenine residue was inserted after nucleotide 48 of exon 7 of SMN2 by site-directed mutagenesis. This minigene construct is referred to as SMN2-A.

[001592] SMN2 transcripts derived from minigenes containing exon 6 through 8 and the intervening introns recapitulate the splicing of their endogenous pre-mRNA (Lorson et al, Proc. Natl. Acad. Sci. U.S.A., 1999, 96 (11), 6307). An SMN2-alternative splicing reporter construct which contains exons 6 through 8 and the intervening introns followed by a luciferase reporter gene was generated. Salient features of this construct are the lack of the start codon in the luciferase gene, inactivation of the termination codon (in the open reading frame that encodes the SMN protein) of exon 7 by insertion of a nucleotide after nucleic acid 48 of exon 7 and addition of a start codon (ATG) immediately upstream of exon 6. A single adenine (SMN2-A) was inserted after nucleic residue 48 of exon 7.

[001593] The SMN2 minigene was designed such that the luciferase reporter is in frame with the ATG start codon immediately upstream of exon 6 when exon 7 is present in the mRNA and the luciferase reporter is out of frame with the ATG start codon immediately upstream of exon 6 if exon 7 of SMN2 is removed during splicing of the pre-mRNA. In addition, in the absence of exon 7, the open reading frame that starts from the ATG start codon immediately upstream of exon 6 contains a stop codon in the fragment of exon 8 of SMN. Thus, in the presence of compounds that increase the inclusion of exon 7 of SMN2 into mRNA transcribed from the SMN2 gene, more transcripts containing exon 7 and more functional reporter are produced. A schematic illustration of this description can be found in Figure 1.

[001594] The DNA sequence of the minigene from the SMN2-A construct **SEQ ID NO. 21** is provided in Figure 2a. A picture of the minigene SMN2-A subsequences is shown in Figure 2b.

[001595] **Example 2**

[001596] **SMN2 minigene mRNA splicing RT-qPCR assay in cultured cells**

[001597] The reverse transcription-quantitative PCR-based (RT-qPCR) assay is used to quantify the level of the full length SMN2 minigene mRNA containing SMN2 exon 7 in a HEK293H cell line stably transfected with said minigene and treated with a test compound.

[001598] Materials

Material	Source
HEK293H cells	ATCC Catalog No. CRL-1573
Cells-To-Ct lysis buffer	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4399002
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
96-well flat-bottom plates	Becton Dickinson Catalog No.: 353072
RT-PCR Enzyme Mix	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388520 (also included in AgPath-ID Kit Catalog No.: 4387391)
RT-PCR buffer	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388519 (also included in AgPath-ID Kit Catalog No.: 4387391)
AgPath-ID One-Step RT-PCR Kit	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4387391
Thermocycler	Life Technologies, Inc. (formerly Applied Biosystems) 7900HT

[001599] Protocol. HEK293H cells stably transfected with the SMN2-A minigene construct described above (10,000 cells/well) are seeded in 200 μL of cell culture medium (DMEM plus 10% FBS, with 200 μg/mL hygromycin) in 96-well flat-bottom plates and the plate is immediately swirled to ensure proper dispersal of cells, forming an even monolayer of cells. Cells are allowed to attach for at least 4-6 hours. Test compounds are serially diluted 3.16-fold in 100% DMSO to generate a 7-point concentration curve. A solution of test compound (1 μL, 200x in DMSO) is added to each cell-containing well and the plate is incubated for 24 hours in a cell culture incubator (37°C, 5% CO_2, 100% relative humidity). 2 replicates are prepared for each test compound concentration. The cells are then lysed in Cells-To-Ct lysis buffer and the lysate is stored at −80°C.

[001600] Full length SMN2-A minigene and GAPDH mRNA are quantified using the following primers and probes provided in Table 3. Primer SMN Forward A (SEQ ID NO. 1) hybridizes to a nucleotide sequence in exon 7 (nucleotide 22 to nucleotide 40), primer SMN Reverse A (SEQ ID NO. 2) hybridizes to a nucleotide sequence in the coding sequence of Firefly luciferase, SMN Probe A (SEQ ID NO. 3) hybridizes to a nucleotide sequence in exon 7 (nucleotide 50 to nucleotide 54) and exon 8 (nucleotide 1 to nucleotide 21). The combination of these three oligonucleotides detects only SMN1 or SMN2 minigenes (RT-qPCR) and will not detect endogenous SMN1 or SMN2 genes.

[001601] Table 3

Primers/Probes	Sequence	Source
SMN Forward Primer A	**SEQ ID NO.1:** GAAGGAAGGTGCTCACATT	PTC[1]
SMN Reverse Primer A	**SEQ ID NO.2:** TCTTTATGTTTTTGGCGTCTTC	PTC[1]
SMN Forward Probe A	**SEQ ID NO.3:** 6FAM-AAGGAGAAATGCTGGCATAGAGCAGC-TAMRA	PTC[1]
hGAPDH Forward Probe	**SEQ ID NO.4:** VIC-CGCCTGGTCACCAGGGCTGCT–TAMRA	LTI[2]
hGAPDH Forward Primer	**SEQ ID NO.5:** CAACGGATTTGGTCGTATTGG	LTI[2]
hGAPDH Reverse Primer	**SEQ ID NO.6:** TGATGGCAACAATATCCACTTTACC	LTI[2]

[001602] [1] Primers and probe designed by PTC Therapeutics, Inc.; [2] Commercially available from Life Technologies, Inc. (formerly Invitrogen).

[001603] The SMN forward and reverse primers are used at final concentrations of 0.4 μM. The SMN probe is used at a final concentration of 0.15 μM. The GAPDH primers are used at final concentrations of 0.2 μM and the probe at 0.15 μM.

[001604] The SMN2-minigene GAPDH mix (15 μL total volume) is prepared by combining 7.5 μL of 2x RT-PCR buffer, 0.4 μL of 25x RT-PCR enzyme mix, 0.75 μL of 20x GAPDH primer-probe mix, 4.0075 μL of water, 2 μL of 10-fold diluted cell lysate, 0.06 μL of 100 μM SMN forward primer, 0.06 μL of 100 μM SMN reverse primer, and 0.225 μL of 100 μM SMN probe.

[001605] PCR is carried out at the following temperatures for the indicated time: Step 1: 48°C (15 min); Step 2: 95°C (10 min); Step 3: 95°C (15 sec); Step 4: 60°C (1 min); then repeat Steps 3 and 4 for a total of 40 cycles.

[001606] Each reaction mixture contains both SMN2-A minigene and GAPDH primers/probe sets (multiplex design), allowing simultaneous measurement of the levels of two transcripts.

[001607] Two SMN spliced products are generated from the SMN2 minigene. The first spliced product containing exon 7, corresponding to full length SMN2 mRNA, is referred to herein using the term "SMN2 minigene FL." The second spliced product lacking exon 7 is referred to herein using the term "SMN2 minigene Δ7."

[001608] The increase of SMN2 minigene FL mRNA relative to that in cells treated with vehicle control is determined from real-time PCR data using a modified ΔΔCt method (as described in Livak and Schmittgen, Methods, 2001, 25:402-8). The amplification efficiency (E) is calculated from the slope of the amplification curve for SMN2 minigene FL and GAPDH individually. The abundances of SMN2 minigene FL and GAPDH are then calculated as $(1 + E)^{-Ct}$, where Ct is the threshold value for each amplicon. The abundance of SMN2 minigene FL is normalized to GAPDH abundance. The normalized SMN2 minigene FL abundance from test compound-treated samples is then divided by normalized SMN2 minigene FL abundance from vehicle-treated cells to determine the level of SMN2 FL mRNA relative to vehicle control.

[001609] **Results.** As seen in Figure 3, cells treated with Compound **6** (Figure 3a) and Compound **170** (Figure 3b) increased SMN2 minigene FL mRNA at low concentrations. The two test compounds fully restored exon 7 inclusion relative to untreated cells.

[001610] For compounds of Formula (I) or a form thereof disclosed herein, Table 4 provides the $EC_{1.5x}$ for production of full length SMN2 mRNA that was obtained from the 7-point concentration data generated for each test compound according to the procedure of Biological Example 2. The term "$EC_{1.5x}$ for production of full length SMN2 mRNA" is defined as that concentration of test compound that is effective in increasing the amount of full length SMN2 mRNA to a level 1.5-fold greater relative to that in vehicle-treated cells. An $EC_{1.5x}$ for production of full length SMN2 mRNA between > 3 μM and ≤ 30 μM is indicated by one star (*), an $EC_{1.5x}$ between > 1 μM and ≤ 3 μM is indicated by two stars (**), an $EC_{1.5x}$ between > 0.3 μM and ≤ 1 μM is indicated by three stars (***), an $EC_{1.5x}$ between > 0.1 μM and ≤ 0.3 μM is indicated by four stars (****) and an $EC_{1.5x}$ ≤ 0.1 μM is indicated by five stars (*****).

[001611] **Table 4**

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
1	***	**280**	**	**558**	**
2	**	**281**	****	**559**	**
3	***	**282**	***	**560**	**
4	**	**283**	*****	**561**	*****
5	*	**284**	***	**562**	***
6	*****	**285**	*****	**563**	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
7	***	286	***	564	**
8	****	287	*****	565	*****
9	**	288	*****	566	*****
10	**	289	*****	567	****
11	***	290	*****	568	*****
12	***	291	*****	569	*****
13	**	292	*****	570	***
14	**	293	*****	571	***
15	**	294	*****	572	***
16	**	295	*****	573	***
17	**	296	*****	574	***
18	***	297	*****	575	***
19	**	298	***	576	*****
20	**	299	*****	577	*****
21	*	300	*****	578	*****
22	***	301	**	579	****
23	*	302	*****	580	*****
24	**	303	*****	581	****
25	**	304	*****	582	*****
26	*	305	*****	583	*****
27	*	306	*****	584	*****
28	*	307	*****	585	*****
29	*	308	*****	586	****
30	*****	309	*****	587	*****
31	**	310	*****	588	*****
32	**	311	****	589	****
33	**	312	*****	590	***
34	**	313	**	591	***
35	*	314	*****	592	****
36	*	315	*****	593	*****
37	**	316	****	594	****
38	*	317	***	595	*****
39	*	318	*****	596	*****
40	*	319	*****	597	****
41	***	320	***	598	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
42	**	321	**	599	*****
43	****	322	*****	600	****
44	**	323	****	601	*****
45	*	324	***	602	*****
46	**	325	***	603	****
47	**	326	**	604	***
48	*	327	*****	605	***
49	*	328	*****	606	*****
50	*	329	*****	607	*****
51	*	330	****	608	****
52	*	331	*****	609	*****
53	**	332	***	610	*****
54	**	333	****	611	***
55	**	334	*****	612	*****
56	**	335	*****	613	*****
57	*	336	****	614	*****
58	*	337	*****	615	*****
59	**	338	*****	616	*****
60	**	339	*****	617	*****
61	***	340	*****	618	*****
62	****	341	***	619	****
63	**	342	*****	620	***
64	*	343	*****	621	***
65	*	344	****	622	**
66	***	345	*****	623	*****
67	****	346	*****	624	*****
68	****	347	*****	625	**
69	***	348	****	626	***
70	**	349	*****	627	****
71	**	350	*****	628	***
72	*****	351	*****	629	*****
73	*	352	*****	630	*****
74	*****	353	****	631	****
75	*****	354	*****	632	*****
76	***	355	*****	633	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
77	***	356	*****	634	*****
78	**	357	****	635	*****
79	****	358	*****	636	*****
80	**	359	*****	637	*****
81	***	360	**	638	*****
82	**	361	****	639	*****
83	***	362	***	640	*****
84	**	363	***	641	*****
85	**	364	**	642	*****
86	****	365	****	643	****
87	****	366	*****	644	****
88	**	367	*****	645	*****
89	**	368	*****	646	***
90	**	369	*****	647	*****
91	**	370	****	648	*****
92	**	371	****	649	*****
93	**	372	*****	650	*****
94	**	373	*****	651	*****
95	**	374	*****	652	*****
96	***	375	*****	653	*****
97	**	376	*****	654	*****
98	**	377	***	655	*****
99	***	378	*****	656	*****
100	***	379	****	657	*****
101	***	380	****	658	*****
102	***	381	****	659	*****
103	***	382	*****	660	*****
104	***	383	***	661	*****
105	****	384	*****	662	*****
106	***	385	*****	663	*****
107	***	386	***	664	***
108	****	387	***	665	****
109	*****	388	*****	666	****
110	****	389	**	667	*****
111	****	390	***	668	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
112	***	391	**	669	*****
113	**	392	****	670	*****
114	**	393	*****	671	*****
115	*****	394	****	672	*****
116	****	395	***	673	*****
117	*****	396	****	674	*****
118	****	397	*****	675	*****
119	****	398	***	676	*****
120	*****	399	***	677	*****
121	*****	400	****	678	*****
122	**	401	****	679	*****
123	**	402	*****	680	*****
124	***	403	*****	681	*****
125	***	404	***	682	***
126	****	405	****	683	*****
127	***	406	***	684	****
128	***	407	*****	685	****
129	***	408	*****	686	***
130	**	409	*****	687	*****
131	*****	410	*****	688	**
132	*****	411	*****	689	****
133	*****	412	*****	690	*****
134	*****	413	*****	691	*****
135	*****	414	*****	692	****
136	*****	415	*****	693	**
137	****	416	*****	694	*****
138	****	417	****	695	*****
139	**	418	*****	696	*****
140	**	419	****	697	*****
141	*****	420	*****	698	*****
142	***	421	*****	699	*****
143	*****	422	*****	700	*****
144	*****	423	*****	701	*****
145	**	424	*****	702	*****
146	**	425	*****	703	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
147	**	426	***	704	****
148	****	427	**	705	*****
149	***	428	***	706	*****
150	***	429	*****	707	*****
151	****	430	*****	708	*****
152	****	431	*****	709	*****
153	***	432	*****	710	*****
154	**	433	*****	711	*****
155	****	434	***	712	*****
156	***	435	****	713	*****
157	**	436	***	714	*****
158	**	437	****	715	*****
159	**	438	*****	716	*****
160	*****	439	****	717	****
161	***	440	*****	718	*****
162	***	441	*****	719	*****
163	**	442	*****	720	*****
164	***	443	*****	721	*****
165	**	444	***	722	*****
166	***	445	*****	723	*****
167	*****	446	*****	724	***
168	***	447	****	725	****
169	*****	448	*****	726	***
170	*****	449	*****	727	*****
171	*****	450	***	728	****
172	*****	451	*****	729	****
173	***	452	*****	730	*****
174	**	453	*****	731	*****
175	*****	454	*****	732	***
176	***	455	****	733	*****
177	****	456	****	734	*****
178	***	457	*****	735	*****
179	***	458	*****	736	*****
180	**	459	*****	737	*****
181	**	460	****	738	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
182	***	461	***	739	*****
183	**	462	*****	740	***
184	**	463	*****	741	*****
185	*****	464	****	742	****
186	*****	465	***	743	*****
187	**	466	*****	744	*****
188	****	467	*****	745	*****
189	***	468	*****	746	*****
190	***	469	****	747	*****
191	**	470	*****	748	*****
192	**	471	*****	749	*****
193	*****	472	*****	750	*****
194	*****	473	*****	751	*****
195	*****	474	*****	752	*****
196	*****	475	***	753	*****
197	****	476	*****	754	*****
198	*****	477	*****	755	*****
199	***	478	*****	756	*****
200	**	479	*****	757	***
201	*****	480	*****	758	***
202	***	481	*****	759	****
203	**	482	*****	760	*****
204	*****	483	*****	761	*****
205	***	484	*****	762	*****
206	**	485	*****	763	*****
207	*****	486	*****	764	**
208	*****	487	****	765	**
209	*****	488	*****	766	*****
210	*****	489	****	767	*****
211	*****	490	*****	768	*****
212	****	491	***	769	****
213	****	492	***	770	*****
214	***	493	*****	771	*****
215	***	494	*****	772	*****
216	***	495	*****	773	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
217	***	496	*****	774	*****
218	****	497	*****	775	***
219	*****	498	*****	776	**
220	***	499	*****	777	**
221	*****	500	****	778	*****
222	***	501	****	779	*****
223	***	502	*****	780	*****
224	***	503	*****	781	*****
225	**	504	*****	782	*****
226	***	505	*****	783	*****
227	**	506	*****	784	****
228	**	507	****	785	*****
229	***	508	*****	786	****
230	***	509	*****	787	*****
231	***	510	*****	788	*****
232	**	511	*****	789	*****
233	***	512	*****	790	*****
234	*****	513	****	791	*****
235	***	514	****	792	*****
236	**	515	*****	793	*****
237	**	516	*****	794	*****
238	***	517	*****	795	*****
239	**	518	*****	796	*****
240	*****	519	*****	797	**
241	****	520	****	798	*****
242	*****	521	****	799	*****
243	*****	522	*****	800	*****
244	*****	523	*****	801	****
245	***	524	****	802	**
246	**	525	****	803	*****
247	*****	526	***	804	*****
248	***	527	*****	805	****
249	***	528	*****	806	*****
250	*****	529	*****	807	*****
251	*****	530	*****	808	*****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
252	****	531	****	809	*****
253	**	532	*****	810	*****
254	****	533	*****	811	***
255	***	534	*****	812	*****
256	***	535	*****	813	*****
257	*****	536	*****	814	*****
258	*****	537	*****	815	*****
259	*****	538	*****	816	*****
260	****	539	*****	817	*****
261	*****	540	*****	818	****
262	****	541	****	819	*****
263	***	542	*****	820	*****
264	*****	543	*****	821	*****
265	**	544	*****	822	****
266	**	545	****	823	*
267	*****	546	*****	824	***
268	*****	547	*****	825	***
269	*****	548	*****	826	****
270	*****	549	*****	827	*****
271	*****	550	*****	828	*****
272	*****	551	****	829	****
273	*****	552	***	830	*****
274	*****	553	****	831	****
275	*****	554	****	832	****
276	***	555	**	833	*****
277	**	556	***	834	*****
278	**	557	**	835	*****
279	****				

[001612] **Example 3**

[001613] **Endogenous SMN2 mRNA RT-qPCR splicing assay in cultured cells**

[001614] The reverse transcription-quantitative PCR-based (RT-qPCR) assay is used to quantify the levels of the full length and Δ7 SMN2 mRNA in primary cells and cell lines containing the SMN2 gene treated with a test compound.

[001615] Materials

Material	Source
SMA Type 1 human cells	GM03813 (Coriell Institute)
Cells-To-Ct lysis buffer	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4399002
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
96-well flat-bottom plates	Becton Dickinson Catalog # 353072
RT-PCR Enzyme Mix	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388520 (also included in AgPath-ID Kit Catalog No.: 4387391)
RT-PCR buffer	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388519 (also included in AgPath-ID Kit Catalog No.: 4387391)
AgPath-ID One-Step RT-PCR Kit	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4387391
Thermocycler	Life Technologies, Inc. (formerly Applied Biosystems) 7900HT

[001616] Protocol. GM03813 SMA patient cells (5,000 cells/well) are seeded in 200 μL of cell culture medium (DMEM plus 10% FBS) in 96-well flat-bottom plates and the plate is immediately swirled to ensure proper dispersal of cells, forming an even monolayer of cells. Cells are allowed to attach for at least 4-6 hrs. Test compounds are serially diluted 3.16-fold in 100% DMSO to generate a 7-point concentration curve. A solution of test compound (1 μL, 200x in DMSO) is added to each test well and 1 μL DMSO is added to each control well. The plate is incubated for 24 hrs in a cell culture incubator (37°C, 5% CO_2, 100% relative humidity). The cells are then lysed in Cells-To-Ct lysis buffer and the lysate is stored at −80°C.

[001617] SMN2-specific spliced products and GAPDH mRNA are identified using the following primers and probes in Table 5. Primer SMN FL Forward B (SEQ ID NO. 7) hybridizes to a nucleotide sequence in exon 7 (nucleotide 32 to nucleotide 54) and exon 8 (nucleotide 1 to nucleotide 4), primer SMN Δ7 Forward B (SEQ ID NO. 8) hybridizes to a nucleotide sequence in exon 6 (nucleotide 87 to nucleotide 111) and exon 8 (nucleotide 1 to nucleotide 3), primer SMN Reverse B (SEQ ID NO. 9) hybridizes to a nucleotide sequence in exon 8 (nucleotide 39 to nucleotide 62), probe SMN Probe B (SEQ ID NO. 10) hybridizes to a nucleotide sequence in exon 8 (nucleotide 7 to nucleotide 36). These primers and probes hybridize to nucleotide sequences common to human SMN1 and SMN2 mRNA. Since the SMA patient cells used in Example 3 contain only the SMN2 gene, RT-qPCR can quantify only SMN2 full-length and Δ7 mRNA.

[001618] Table 5

Primer/Probe	Sequence	Source
SMN FL Forward Primer B	**SEQ ID NO.7:** GCTCACATTCCTTAAATTAAGGAGAAA	PTC[1]
SMN Δ7 Forward Primer B	**SEQ ID NO.8:** TGGCTATCATACTGGCTATTATATGGAA	PTC[1]
SMN Reverse Primer B	**SEQ ID NO.9:** TCCAGATCTGTCTGATCGTTTCTT	PTC[1]
SMN Forward Probe B	**SEQ ID NO.10:** 6FAM-CTGGCATAGAGCAGCACTAAATGACACCAC-TAMRA	PTC[1]
hGAPDH Forward Probe	**SEQ ID NO.4:** VIC-CGCCTGGTCACCAGGGCTGCT–TAMRA	LTI[2]
hGAPDH Forward Primer	**SEQ ID NO.5:** CAACGGATTTGGTCGTATTGG	LTI[2]
hGAPDH Reverse Primer	**SEQ ID NO.6:** TGATGGCAACAATATCCACTTTACC	LTI[2]

[001619] [1] Primers and probe designed by PTC Therapeutics, Inc.; [2] Commercially available from Life Technologies, Inc. (formerly Invitrogen).

[001620] The SMN forward and reverse primers are used at final concentrations of 0.4 μM. The SMN probe is used at a final concentration of 0.15 μM. GAPDH primers are used at final concentrations of 0.1 μM and the probe at 0.075 μM.

[001621] The SMN-GAPDH mix (10 μL total volume) is prepared by combining 5 μL of 2x RT-PCR buffer, 0.4 μL of 25x RT-PCR enzyme mix, 0.25 μL of 20x GAPDH primer-probe mix, 1.755 μL water, 2.5 μL of cell lysate, 0.04 μL of 100 μM SMN FL or SMN Δ7 forward primer, 0.04 μL of 100 μM SMN reverse primer, and 0.015 μL of 100 μM probe.

[001622] PCR is carried out at the following temperatures for the indicated time: Step 1: 48°C (15 min); Step 2: 95°C (10 min); Step 3: 95°C (15 sec); Step 4: 60°C (1 min); then, repeat Steps 3 and 4 for a total of 40 cycles.

[001623] Each reaction mixture contains either SMN2 FL and GAPDH or SMN2 Δ7 and GAPDH primers/probe sets (multiplex design), allowing simultaneous measurement of the levels of two transcripts.

[001624] The endogenous SMN2 gene gives rise to two alternatively spliced mRNA. The full length SMN2 mRNA that contains exon 7 is referred to herein using the term "SMN2 FL." The truncated mRNA that lacks exon 7 is referred to herein using the term "SMN2 Δ7."

[001625] The increase of SMN2 FL and decrease in SMN2 Δ7 mRNA relative to those in cells treated with vehicle control are determined from real-time PCR data using a modified ΔΔCt method (as described in Livak and Schmittgen, Methods, 2001, 25:402-8). The amplification efficiency (E) is calculated from the slope of the amplification curve for SMN2 FL, SMN2 Δ7, and GAPDH individually. The abundances of SMN2 FL, SMN2 Δ7, and GAPDH are then calculated as $(1 + E)^{-Ct}$, where Ct is the threshold value for each amplicon. The abundances of SMN2 FL and SMN2 Δ7 are normalized to GAPDH abundance. The normalized SMN2 FL and SMN2 Δ7 abundances from test compound-treated samples are then divided by normalized SMN2 FL and SMN2 Δ7 abundances, respectively, from vehicle-treated cells to determine the levels of SMN2 FL and SMN2 Δ7 mRNA relative to vehicle control.

[001626] **Results.** As seen in Figure 4, cells treated with increasing concentrations of Compound **6** (Figure 4a) and Compound **170** (Figure 4b) contain progressively more SMN2 FL mRNA and less SMN2 Δ7 mRNA than those treated with vehicle, indicating a correction of SMN2 alternative splicing.

[001627] **Example 4**

[001628] **Endogenous SMN2 mRNA end-point semi-quantitative RT-PCR splicing assay in cultured cells**

[001629] The endpoint reverse transcription-PCR splicing assay is used to visualize and quantify the levels of the full length and Δ7 SMN2 mRNA in primary cells and cell lines containing the SMN2 gene treated with a test compound.

[001630] **Materials**

Material	Source
SMA Type 1 human cells	GM03813 (Coriell Institute)
Cells-To-Ct lysis buffer	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4399002
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
96-well flat-bottom plates	Becton Dickinson Catalog No.: 353072
Platinum Taq HiFi DNA Polymerase Super Mix	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11304-016
iScript RT enzyme Kit	BioRad: Catalog No.: 170-8890
Ethidium bromide 2% agarose E gels 48-Well Double Comb	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: G8008-02

Material	Source
Gel Documentation System	UVP Gel Doc It 310 Imaging system

[001631] **Protocol.** GM03813 SMA patient cells (5,000 cells/well) are seeded in 200 μL of cell culture medium (DMEM plus 10% FBS) in 96-well flat-bottom plates and the plate is immediately swirled to ensure proper dispersal of cells, forming an even monolayer of cells. Cells are allowed to attach for at least 4-6 hrs. Test compounds are serially diluted 3.16-fold in 100% DMSO to generate a 7-point concentration curve. A solution of test compound (1 μL, 200x in DMSO) is added to each test well and 1 μL DMSO is added to each control well. The plate is incubated for 24 hrs in a cell culture incubator (37°C, 5% CO_2, 100% relative humidity). The cells are then lysed in Cells-To-Ct lysis buffer and the lysate is stored at −80°C.

[001632] SMN FL and Δ7 mRNA are identified using the following primers in Table 6. These primers hybridize to a nucleotide sequence in exon 6 (SMN Forward C, SEQ ID NO. 11) (nucleotide 43 to nucleotide 63) and exon 8 (SMN Reverse C, SEQ ID NO. 12) (nucleotide 51 to nucleotide 73) common to human SMN1 and SMN2 mRNA. Since the SMA patient cells used in Example 4 contain only the SMN2 gene, RT-PCR can visualize and quantify only SMN2 full-length and SMN2 Δ7 mRNA.

[001633] **Table 6**

Primer	Sequence	Source
SMN Forward C	**SEQ ID NO.11:** GATGCTGATGCTTTGGGAAGT	PTC[1]
SMN Reverse C	**SEQ ID NO.12:** CGCTTCACATTCCAGATCTGTC	PTC[1]

[001634] [1] Primers designed by PTC Therapeutics, Inc.

[001635] To synthesize cDNA, 5 μL of lysate, 4 μL of 5x iScript reaction mix, 1 μL of reverse transcriptase, and 10 μL of water are combined and incubated 5 min at 25°C followed by 30 min at 42°C, followed by 5 min at 85°C. The cDNA solution is stored at -20°C.

[001636] To perform endpoint PCR, 5 μL of cDNA, 0.2 μL of 100 μM forward primer, 0.2 μL of 100 μM reverse primer, and 22.5 μL of polymerase super mix are combined in a 96 well semiskirted PCR plate. PCR is carried out at the following temperatures for the indicated time: Step 1: 94°C (2 min), Step 2: 94°C (30 sec), Step 3: 55°C (30 sec), Step 4: 68°C (1 min), then repeat Steps 2 to 4 for a total of 33 cycles, then hold at 4°C.

[001637] 10 μL of each PCR sample is electrophoretically separated on a 2% agarose E-gel for 14 minutes stained with double-stranded DNA (dsDNA) staining reagents (e.g., ethidium bromide) and visualized using a gel imager.

[001638] **Results.** As seen in Figure 5, cells treated with increasing concentrations of Compound **6** (Figure 5a) or Compound **170** (Figure 5b) contain progressively more SMN2 FL mRNA and less SMN2 Δ7 mRNA, indicating a correction of SMN2 alternative splicing.

[001639] **Example 5**

[001640] **SMN2 mRNA RT-qPCR splicing assay in animal tissues**

[001641] The reverse transcription-quantitative PCR-based (RT-qPCR) assay is used to quantify the levels of the full length and Δ7 SMN2 mRNA in tissues from mice treated with test compound.

[001642] **Materials**

Material	Source
Tissues from C/C-allele SMA mice	The Jackson Laboratory, strain No.: 008714 (B6.129-*Smn1*$^{tm5(Smn1/SMN2)Mrph}$/J)
Tissues from Δ7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)
RT-PCR Enzyme Mix	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388520 (also included in AgPath-ID Kit Catalog No.: 4387391)
RT-PCR buffer	Life Technologies, Inc. (formerly Applied Biosystems) Part No.: 4388519 (also included in AgPath-ID Kit Catalog No.: 4387391)
AgPath-ID One-Step RT-PCR Kit	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4387391
Mouse GAPDH primers and probes	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4352339E
QIAzol Lysis Reagent	Qiagen Catalog No.: 79306
RNeasy Lipid Tissue Mini Kit	Qiagen Catalog No.: 74804
5 mm Stainless Steel Bead	Qiagen Catalog No.: 69989
TissueLyzer II	Qiagen Catalog No.: 85300
Thermocycler	Life Technologies, Inc. (formerly Applied Biosystems) 7900HT

[001643] **Protocol.** C/C-allele SMA mice are treated by oral gavage two times per day (BID) for 10 days with test compounds re-suspended in 0.5% HPMC and 0.1% Tween-80. Tissue samples were collected and snap frozen for RNA purification.

[001644] Tissue samples (20-40 mg) are homogenized in QIAzol Lysis Reagent for 2 minutes at 20 Hz in the TissueLyser II using one stainless steel bead. After addition of chloroform, the homogenate is separated into aqueous and organic phases by centrifugation. RNA partitioned to the upper, aqueous phase is extracted and ethanol is added to provide appropriate binding conditions. The sample is then applied to the RNeasy spin column from the RNeasy Mini Kit, where total RNA binds to the membrane. The RNA is eluted in RNase-free water then stored at -20°C and subsequently analyzed using the TaqMan RT-qPCR on the 7900HT Thermocycler. Total RNA is diluted ten fold and 2.5 μL of the diluted sample is added to the TaqMan RT-qPCR mixture.

[001645] SMN2 spliced products are identified using the following primers and probe in Table 7. Primer SMN FL Forward B (SEQ ID NO. 7) hybridizes to a nucleotide sequence in exons 7 and 8, primer SMN Δ7 Forward B (SEQ ID NO. 8) hybridizes to a nucleotide sequence in exons 6 and 8, primer SMN Reverse B (SEQ ID NO. 9) hybridizes to a nucleotide sequence in exon 8, probe SMN Probe B (SEQ ID NO. 10) hybridizes to a nucleotide sequence in exon 8. These primers and probe hybridize to nucleotide sequences common to human SMN1 and SMN2 mRNA. Since the SMA patient cells used in Example 5 contain only the SMN2 gene, RT-qPCR can quantify only SMN2 full-length and Δ7 mRNA.

[001646] **Table 7**

Primer/Probe	Sequence	Source
SMN FL Forward Primer B	**SEQ ID NO.7:** GCTCACATTCCTTAAATTAAGGAGAAA	PTC[1]
SMN Δ7 Forward Primer B	**SEQ ID NO.8:** TGGCTATCATACTGGCTATTATATGGAA	PTC[1]
SMN Reverse Primer B	**SEQ ID NO.9:** TCCAGATCTGTCTGATCGTTTCTT	PTC[1]
SMN Forward Probe B	**SEQ ID NO.10:** 6FAM-CTGGCATAGAGCAGCACTAAATGACACCAC-TAMRA	PTC[1]

[001647] [1] Primers and probe designed by PTC Therapeutics, Inc.

[001648] The SMN forward and reverse primers are used at final concentrations of 0.4 μM. The SMN probe is used at a final concentration of 0.15 μM. The SMN-GAPDH Mix (10 μL total volume) is prepared by combining 5 μL of 2x RT-PCR buffer, 0.4 μL of 25x RT-PCR enzyme mix, 0.5 μL of 20x GAPDH primer-probe mix, 1.505 μL of water, 2.5 μL of RNA solution, 0.04 μL of 100 μM forward primer, 0.04 μL of 100 μM reverse primer, and 0.015 μL of 100 μM SMN probe.

[001649] Each PCR cycle was carried out at the following temperatures for the indicated time: Step 1: 48°C (15 min); Step 2: 95°C (10 min); Step 3: 95°C (15 sec); Step 4: 60°C (1 min); then, repeat Steps 3 and 4 for a total of 40 cycles.

[001650] Each reaction mixture contains either SMN2 FL and mGAPDH or SMN2 Δ7 and mGAPDH primers/probe sets (multiplex design), allowing simultaneous measurement of the levels of two transcripts.

[001651] The increase of SMN2 FL and decrease in SMN2 Δ7 mRNA relative to those in tissues from animals treated with vehicle control are determined from real-time PCR data using a modified ΔΔCt method (as described in Livak and Schmittgen, Methods, 2001, 25:402-8). The amplification efficiency (E) is calculated from the slope of the amplification curve for SMN2 FL, SMN2 Δ7, and GAPDH individually. The abundances of SMN2 FL, SMN2 Δ7, and GAPDH are then calculated as $(1 + E)^{-Ct}$, where Ct is the threshold value for each amplicon. The abundances of SMN2 FL and SMN2 Δ7 are normalized to GAPDH abundance. The normalized SMN2 FL and SMN2 Δ7 abundances from test compound-treated samples are then divided by normalized SMN2 FL and SMN2 Δ7 abundances, respectively, from vehicle-treated cells to determine the levels of SMN2 FL and SMN2 Δ7 mRNA relative to vehicle control.

[001652] **Results.** As seen in Figure 6, tissues of animals treated with Compound **6** (Figure 6a) and Compound **170** (Figure 6b) contain substantially more SMN2 FL mRNA and less SMN2 Δ7 mRNA than those treated with vehicle, indicating a correction of SMN2 alternative splicing.

[001653] **Example 6**

[001654] **Endogenous SMN2 mRNA end-point semi-quantitative RT-PCR splicing assay in animal tissues**

[001655] The endpoint reverse transcription-PCR (RT-PCR) splicing assay is used to quantify the levels of the full length and Δ7 SMN2 mRNA in tissues from mice treated with test compound.

[001656] **Materials**

Material	Source
Tissues from C/C-allele SMA mice	The Jackson Laboratory, strain No.: 008714 (B6.129-*Smn1*$^{tm5(Smn1/SMN2)Mrph}$/J)
Tissues from ΔExon7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)
Qiagen RNeasy lipid Kit	Qiagen Catalog No.: 74804
Platinum Taq HiFi DNA Polymerase Super Mix	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11304-016
iScript RT enzyme Kit	BioRad Catalog No.: 170-8890
Twin.tec 96-Well Semiskirted PCR Plate	Eppendorf Catalog No.: 951020389
Ethidium bromide 2% agarose E gels 48-Well Double Comb	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: G8008-02
Gel Documentation System	UVP Gel Doc It 310 Imaging system

[001657] **Protocol.** C/C-allele SMA mice are treated by oral gavage BID for 10 days with test compounds in 0.5% HPMC and 0.1% Tween-80. Tissue samples are collected and snap frozen for RNA purification.

[001658] Tissue samples (20-40 mg) are homogenized in QIAzol Lysis Reagent for 2 minutes at 20Hz in the TissueLyser II using one stainless steel bead. After addition of chloroform, the homogenate is separated into aqueous and organic phases by centrifugation. RNA partitioned to the upper, aqueous phase is extracted and ethanol is added to provide appropriate binding conditions. The sample is then applied to the RNeasy spin column from the RNeasy Mini Kit, where total RNA binds to the membrane. The RNA is eluted in RNase-free water then stored at -20°C.

[001659] SMN2 spliced products are identified using the following amplification primers in Table 8. These primers hybridize to a nucleotide sequence in exon 6 (SMN Forward D, SEQ ID

NO. 13) (nucleotide 22 to nucleotide 46) and exon 8 (SMN Reverse C, SEQ ID NO. 12), common to human SMN1 and SMN2 mRNA.

[001660] Table 8

Primer	Sequence	Source
SMN Forward D	**SEQ ID NO.13:** ATATGTCCAGATTCTCTTGATGATG	PTC[1]
SMN Reverse C	**SEQ ID NO.12:** CGCTTCACATTCCAGATCTGTC	PTC[1]

[001661] [1] Primers designed by PTC Therapeutics, Inc.

[001662] To synthesize cDNA, combine 1 μL of RNA solution (25-50 ng), 4 μL of 5x iScript reaction mix, 1 μL of reverse transcriptase, and 10 μL of water are combined and incubates 25°C for 5 min followed by 42°C for 30 min followed by 85°C for 5 min. The cDNA solution is stored at -20°C.

[001663] To perform endpoint PCR, 5 μL of cDNA, 0.2 μL of 100 μM forward primer, 0.2 μL of 100 μM reverse primer, and 22.5 μL of polymerase super mix are combined in a 96 well semiskirted PCR plate. PCR is carried out at the following temperatures for the indicated time: Step 1: 94°C (2 min), Step 2: 94°C (30 sec), Step 3: 55°C (30 sec), Step 4: 68°C (1 min), then repeat Steps 2 to 4 for a total of 33 cycles, then hold at 4°C.

[001664] 10 μL of each PCR sample is electrophoretically separated on a 2% agarose E-gel for 14 minutes stained with dsDNA staining reagents (e.g., ethidium bromide) and visualized using a gel imager.

[001665] **Results.** As seen in Figure 7**,** tissues from mice treated with increasing concentrations of Compound **6** (Figure 7a) and Compound **170** (Figure 7b) contain progressively more SMN2 FL mRNA and less SMN2 Δ7 mRNA, indicating a correction of SMN2 alternative splicing.

[001666] **Example 7**

[001667] **Smn protein assay in cultured cells**

[001668] The SMN HTRF (homogeneous time resolved fluorescence) assay is used to quantify the level of Smn protein in SMA patient fibroblast cells treated with test compounds. The results of the assay are shown in Table 9.

[001669] Materials

Material	Source
SMA Type 1 human cells	GM03813 (Coriell Institute)
Protease inhibitor cocktail	Roche Applied Science Catalog No.: 11836145001
Anti-SMN d2	Blue cap Cisbio Catalog No.: 63IDC002-SMN
Anti-SMN kryptate	Red cap Cisbio Catalog No.: 63IDC002-SMN
SMN reconstitution buffer	Cisbio Catalog No.: 63IDC002-SMN-Buffer
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
RIPA Lysis Buffer	20 mM Tris-HCl pH 7.5, 150 mM NaCl, 1 mM EDTA, 1% NP-40, 1% Sodium deoxycholate
Diluent Buffer	20 mM Tris-HCl pH 7.5, 150 mM NaCl
Envision Plate Reader	Perkin Elmer Model No.: 2103

[001670] Protocol. Cells are thawed and cultured in DMEM-10% FBS for 72 hours. Cells are trypsinized, counted and re-suspended to a concentration of 25,000 cells/mL in DMEM-10% FBS. The cell suspension is plated at 5,000 cells per well in a 96 well microtiter plate and incubated for 3 to 5 hours. To provide a control signal, three (3) wells in the 96 well plate do not receive cells and, thus, serve as Blank control wells. Test compounds are serially diluted 3.16-fold in 100% DMSO to generate a 7-point concentration curve. 1 μL of test compound solution is transferred to cell-containing wells and cells are incubated for 48 hours in a cell culture incubator (37°C, 5% CO_2, 100% relateive humidity). Triplicate samples are set up for each test compound concentration. After 48 hours, the supernatant is removed from the wells and 25 μL of the RIPA lysis buffer, containing protease inhibitors, is added to the wells and incubated with shaking at room temperature for 1 hour. 25 μL of the diluent is added and then 35 μL of the resulting lysate is transferred to a 384-well plate, where each well contains 5 μL of the antibody solution (1:100 dilution of anti-SMN d2 and anti-SMN kryptate in SMN reconstitution buffer). The plate is centrifuged for 1 minute to bring the solution to the bottom of the wells, then incubated overnight at room temperature. Fluorescence for each well of the plate at 665 nm and 620 nm is measured on an EnVision multilabel plate reader (Perkin-Elmer).

[001671] The normalized fluorescence signal is calculated for each sample, Blank and vehicle control well by dividing the signal at 665 nm by the signal at 620 nm. Normalizing the signal accounts for possible fluorescence quenching due to the matrix effect of the lysate. The ΔF value (a measurement of Smn protein abundance as a percent value) for each sample well is

calculated by subtracting the normalized average fluorescence for the Blank control wells from the normalized fluorescence for each sample well, then dividing this difference by the normalized average fluorescence for the Blank control wells and multiplying the resulting value by 100. The ΔF value for each sample well represents the Smn protein abundance from test compound-treated samples. The ΔF value for each sample well is divided by the ΔF value for the vehicle control wells to calculate the fold increase in Smn protein abundance relative to the vehicle control.

[001672] **Results.** As seen in Figure 8, SMA Type 1 patient fibroblast cells treated with Compound **6** (Figure 8a) and Compound **170** (Figure 8b) show a dose dependent increase in Smn protein expression as measured by the SMN HTRF assay.

[001673] For compounds of Formula (I) or a form thereof disclosed herein, Table 9 provides the $EC_{1.5x}$ for Smn protein expression that was obtained from the 7-point concentration data generated for each test compound according to the procedure of Biological Example 7. The term "$EC_{1.5x}$ for Smn protein expression" is defined as that concentration of test compound that is effective in producing 1.5 times the amount of Smn protein in an SMA patient fibroblast cell compared to the amount produced from the DMSO vehicle control. An $EC_{1.5x}$ for Smn protein expression between > 3 μM and ≤ 10 μM is indicated by one star (*), an $EC_{1.5x}$ between > 1 μM and ≤ 3 μM is indicated by two stars (**), an $EC_{1.5x}$ between > 0.3 μM and ≤ 1 μM is indicated by three stars (***) and an $EC_{1.5x}$ ≤ 0.3 μM is indicated by four stars (****).

[001674] **Table 9**

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
3	**	**380**	***	**626**	**
6	***	**381**	*	**627**	**
8	**	**382**	***	**628**	*
18	**	**384**	****	**629**	****
20	**	**385**	***	**630**	****
22	**	**393**	***	**631**	***
24	*	**396**	***	**632**	****
30	**	**397**	****	**633**	****
43	**	**398**	**	**634**	****
61	***	**399**	***	**635**	****
62	***	**400**	***	**636**	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
66	*	401	***	637	****
67	***	402	**	638	****
69	***	403	**	639	****
71	*	404	**	640	****
72	***	405	***	641	****
74	***	406	*	642	****
75	****	409	****	643	***
79	***	410	****	644	***
82	**	412	****	645	****
84	**	413	****	646	**
85	*	414	***	647	****
86	****	416	**	648	****
87	***	417	**	649	****
90	*	420	****	650	****
95	**	422	**	651	****
96	***	423	***	652	****
99	***	424	****	653	****
100	***	425	****	654	****
102	***	426	***	655	****
105	***	427	*	656	****
106	**	428	**	657	****
109	****	429	****	658	****
115	****	430	****	659	****
116	*	431	****	660	****
117	****	432	****	661	****
118	***	437	***	662	****
119	***	438	****	663	****
120	****	439	**	664	***
121	****	440	****	665	****
127	*	441	****	666	***
129	*	442	****	667	****
130	*	443	****	668	****
131	**	444	**	669	****
132	****	445	***	670	****
133	****	446	**	671	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
134	****	448	****	672	****
135	****	449	****	673	****
136	****	451	***	674	****
137	***	452	****	675	****
138	***	453	****	676	***
141	****	454	****	677	***
143	****	457	****	678	****
144	****	458	***	679	****
148	**	460	***	680	****
150	**	461	**	681	****
152	****	462	****	682	**
160	***	463	***	683	***
161	**	464	**	684	***
162	**	466	***	685	**
164	**	467	****	686	**
167	**	468	***	687	****
169	****	469	***	688	**
170	****	470	****	689	***
171	****	471	****	690	***
172	****	472	****	691	****
175	***	473	****	692	***
176	*	474	****	693	**
179	***	475	**	694	****
180	**	476	****	695	****
182	***	477	****	696	****
186	***	478	****	697	****
188	***	480	****	698	****
189	***	481	****	699	****
190	**	482	*	700	****
191	**	484	****	701	****
192	**	485	****	702	****
193	****	486	****	703	****
194	****	487	****	704	****
195	***	488	****	705	****
196	****	489	**	706	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
197	****	490	***	707	****
198	****	491	**	708	****
199	**	492	**	709	****
201	***	493	***	710	****
204	****	494	****	711	****
208	***	495	****	712	****
209	****	496	****	713	****
210	****	497	***	714	****
211	****	498	****	715	****
212	****	499	****	716	***
213	****	500	***	717	***
214	**	501	***	718	***
218	**	502	****	719	****
219	****	503	****	720	****
221	****	504	****	721	****
224	***	505	****	722	****
229	*	506	****	723	****
230	**	507	***	724	***
231	**	508	***	725	***
234	****	509	***	726	**
235	**	510	****	727	****
236	*	511	**	728	****
240	****	512	****	729	***
241	****	513	****	730	****
242	****	514	**	731	****
243	****	515	****	732	***
244	****	516	****	733	****
247	****	517	****	734	****
248	***	518	****	735	****
250	****	519	****	736	****
251	****	520	****	737	****
252	***	521	****	738	****
254	**	522	***	739	****
256	**	523	****	740	***
257	**	524	***	741	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
258	***	525	***	742	***
259	***	526	**	743	****
260	**	527	****	744	***
261	****	528	****	745	****
262	***	529	***	746	****
263	***	530	****	747	****
264	****	531	***	748	****
267	****	532	****	749	****
268	****	533	***	750	****
269	****	534	****	751	****
270	****	535	***	752	****
271	****	536	****	753	****
272	****	537	****	754	****
273	****	538	***	755	****
274	****	539	****	756	****
275	****	541	***	757	***
283	****	542	***	759	***
284	***	543	****	760	****
285	****	544	***	761	****
286	***	545	****	762	****
287	****	546	****	763	****
288	****	547	****	764	*
289	****	548	****	765	**
290	****	549	****	766	****
291	****	550	****	767	****
292	****	551	****	768	****
293	****	552	***	769	***
294	*	553	****	770	***
295	****	554	****	771	****
296	****	555	**	772	****
297	****	556	**	773	****
299	****	561	****	774	****
300	****	563	****	777	**
302	****	565	***	778	***
303	****	566	****	779	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
304	****	567	***	780	****
305	****	568	****	781	****
306	****	569	****	782	****
307	****	570	**	783	****
308	****	571	**	784	***
309	****	572	**	785	****
310	***	573	**	786	***
312	****	576	****	787	****
314	***	577	****	788	****
316	**	578	****	789	****
317	**	579	***	790	****
318	****	580	***	791	****
319	****	581	***	792	***
320	**	582	****	793	****
322	***	583	****	794	****
323	**	584	****	795	****
326	**	585	****	796	****
327	****	586	****	797	*
329	**	587	****	798	****
331	****	588	****	799	****
333	**	589	***	800	****
334	****	590	**	801	***
335	****	591	**	802	*
336	****	592	***	803	****
337	****	593	****	804	****
338	****	594	***	805	***
339	****	595	****	806	****
340	****	596	****	807	****
341	***	597	***	808	****
342	****	598	***	809	****
343	****	599	****	810	****
344	***	600	**	811	***
346	****	601	***	812	****
349	**	602	****	813	****
350	****	603	***	814	****

Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$	Cpd	$EC_{1.5x}$
351	****	604	****	815	****
352	****	605	***	816	****
354	***	606	**	817	****
355	***	607	****	818	***
356	***	608	**	819	****
357	***	609	****	820	****
358	**	610	****	821	****
359	**	612	****	822	***
366	****	613	****	824	*
367	*	614	****	825	**
368	***	615	****	826	**
369	**	616	****	827	***
370	***	617	****	828	****
371	***	618	****	829	**
372	****	619	***	830	***
373	****	620	**	831	**
374	****	621	****	832	***
375	****	622	**	833	**
376	***	623	****	834	****
377	**	624	****	835	****
378	**				

[001675] For compounds of Formula (I) or a form thereof disclosed herein, Table 10 provides the maximum fold (Fold) increase of Smn protein that was obtained from the 7-point concentration data generated for each test compound according to the procedure of Biological Example 7. A maximum fold increase of ≤ 1.2 is indicated by one star (*), a fold increase between > 1.2 and ≤ 1.35 is indicated by two stars (**), a fold increase between > 1.35 and ≤ 1.5 is indicated by three stars (***), a fold increase between > 1.5 and ≤ 1.65 is indicated by four stars (****) and a fold increase > 1.65 is indicated by five stars (*****).

[001676] Table 10

Cpd	Fold	Cpd	Fold	Cpd	Fold
1	**	280	*	558	**
2	**	281	**	559	*
3	***	282	**	560	*

Cpd	Fold	Cpd	Fold	Cpd	Fold
4	*	283	****	561	****
5	*	284	****	562	**
6	****	285	*****	563	*****
7	***	286	****	564	*
8	****	287	*****	565	****
9	***	288	*****	566	*****
10	**	289	****	567	****
11	***	290	*****	568	*****
12	***	291	*****	569	*****
13	**	292	****	570	****
14	***	293	*****	571	****
15	***	294	***	572	****
16	*	295	****	573	****
17	*	296	*****	574	**
18	****	297	*****	575	***
19	**	298	***	576	*****
20	****	299	*****	577	*****
21	*	300	*****	578	*****
22	***	301	*	579	*****
23	***	302	*****	580	*****
24	***	303	****	581	*****
25	*	304	*****	582	*****
26	**	305	*****	583	*****
27	*	306	*****	584	*****
28	**	307	****	585	*****
29	***	308	*****	586	*****
30	****	309	****	587	****
31	*	310	***	588	*****
32	*	311	**	589	****
33	*	312	****	590	****
34	**	313	*	591	****
35	*	314	****	592	*****
36	*	315	***	593	*****
37	*	316	*****	594	****
38	*	317	****	595	****

Cpd	Fold	Cpd	Fold	Cpd	Fold
39	*	318	*****	596	****
40	*	319	****	597	****
41	***	320	****	598	*****
42	*	321	***	599	*****
43	***	322	****	600	****
44	*	323	***	601	****
45	**	324	***	602	****
46	***	325	***	603	*****
47	***	326	***	604	*****
48	*	327	****	605	*****
49	*	328	***	606	****
50	**	329	****	607	*****
51	**	330	**	608	****
52	*	331	*****	609	*****
53	*	332	*	610	*****
54	*	333	****	611	***
55	*	334	*****	612	*****
56	*	335	*****	613	*****
57	*	336	*****	614	*****
58	*	337	*****	615	****
59	*	338	*****	616	*****
60	*	339	*****	617	*****
61	****	340	*****	618	*****
62	*****	341	*****	619	*****
63	**	342	*****	620	***
64	**	343	*****	621	*****
65	**	344	*****	622	****
66	***	345	***	623	*****
67	***	346	****	624	*****
68	**	347	***	625	**
69	****	348	**	626	*****
70	*	349	***	627	****
71	****	350	*****	628	****
72	***	351	*****	629	*****
73	**	352	****	630	*****

Cpd	Fold	Cpd	Fold	Cpd	Fold
74	*****	353	**	631	*****
75	*****	354	****	632	*****
76	**	355	****	633	*****
77	**	356	****	634	*****
78	*	357	****	635	*****
79	****	358	***	636	*****
80	*	359	***	637	*****
81	**	360	*	638	*****
82	*****	361	***	639	*****
83	*	362	***	640	****
84	*****	363	**	641	*****
85	***	364	*	642	*****
86	****	365	***	643	*****
87	****	366	****	644	*****
88	**	367	***	645	*****
89	***	368	****	646	*****
90	***	369	***	647	*****
91	**	370	*****	648	*****
92	**	371	****	649	*****
93	**	372	*****	650	*****
94	***	373	****	651	*****
95	****	374	*****	652	*****
96	****	375	****	653	*****
97	**	376	***	654	*****
98	***	377	****	655	****
99	****	378	****	656	****
100	*****	379	***	657	*****
101	***	380	****	658	*****
102	*****	381	***	659	*****
103	***	382	****	660	****
104	***	383	**	661	*****
105	****	384	*****	662	*****
106	****	385	*****	663	*****
107	**	386	*	664	*****
108	***	387	**	665	*****

Cpd	Fold	Cpd	Fold	Cpd	Fold
109	****	388	***	666	*****
110	***	389	**	667	*****
111	***	390	*	668	*****
112	***	391	*	669	*****
113	***	392	***	670	*****
114	***	393	***	671	*****
115	****	394	**	672	*****
116	***	395	**	673	****
117	****	396	****	674	*****
118	*****	397	*****	675	*****
119	*****	398	*****	676	*****
120	*****	399	****	677	*****
121	*****	400	****	678	*****
122	***	401	*****	679	*****
123	*	402	****	680	*****
124	**	403	****	681	*****
125	***	404	****	682	*****
126	**	405	****	683	*****
127	***	406	***	684	*****
128	***	407	***	685	****
129	***	408	**	686	*****
130	***	409	*****	687	****
131	***	410	*****	688	***
132	*****	411	***	689	****
133	****	412	*****	690	****
134	*****	413	****	691	*****
135	****	414	*****	692	*****
136	*****	415	***	693	****
137	*****	416	***	694	*****
138	*****	417	****	695	*****
139	***	418	***	696	*****
140	***	419	**	697	*****
141	*****	420	****	698	*****
142	***	421	***	699	*****
143	*****	422	***	700	*****

Cpd	Fold	Cpd	Fold	Cpd	Fold
144	****	423	****	701	*****
145	*	424	*****	702	*****
146	*	425	*****	703	*****
147	*	426	*****	704	****
148	***	427	***	705	*****
149	**	428	***	706	*****
150	****	429	****	707	*****
151	***	430	****	708	*****
152	*****	431	*****	709	*****
153	**	432	*****	710	*****
154	*	433	***	711	*****
155	**	434	**	712	*****
156	***	435	***	713	*****
157	**	436	**	714	*****
158	*	437	****	715	*****
159	***	438	*****	716	*****
160	***	439	***	717	*****
161	***	440	****	718	****
162	****	441	*****	719	****
163	***	442	*****	720	*****
164	****	443	*****	721	*****
165	**	444	***	722	*****
166	**	445	***	723	*****
167	***	446	***	724	*****
168	*	447	*	725	*****
169	****	448	*****	726	****
170	*****	449	****	727	*****
171	*****	450	**	728	*****
172	*****	451	*****	729	*****
173	**	452	*****	730	*****
174	**	453	*****	731	*****
175	****	454	*****	732	****
176	***	455	**	733	*****
177	***	456	***	734	*****
178	**	457	*****	735	****

Cpd	Fold	Cpd	Fold	Cpd	Fold
179	*****	458	****	736	*****
180	****	459	***	737	*****
181	*	460	****	738	*****
182	****	461	****	739	*****
183	**	462	*****	740	*****
184	**	463	*****	741	*****
185	***	464	****	742	*****
186	****	465	***	743	*****
187	**	466	*****	744	***
188	*****	467	*****	745	*****
189	****	468	****	746	*****
190	****	469	*****	747	*****
191	****	470	****	748	*****
192	*****	471	*****	749	*****
193	*****	472	*****	750	*****
194	*****	473	*****	751	*****
195	****	474	****	752	*****
196	****	475	***	753	*****
197	*****	476	*****	754	*****
198	****	477	****	755	*****
199	****	478	*****	756	*****
200	*	479	**	757	****
201	***	480	*****	758	***
202	**	481	****	759	*****
203	*	482	***	760	*****
204	****	483	**	761	*****
205	**	484	*****	762	*****
206	**	485	*****	763	*****
207	***	486	****	764	***
208	***	487	****	765	****
209	****	488	****	766	*****
210	****	489	****	767	*****
211	****	490	*****	768	*****
212	****	491	****	769	*****
213	***	492	****	770	****

Cpd	Fold	Cpd	Fold	Cpd	Fold
214	****	493	****	771	*****
215	***	494	****	772	*****
216	***	495	*****	773	*****
217	***	496	*****	774	*****
218	***	497	****	775	***
219	****	498	*****	776	**
220	**	499	*****	777	***
221	*****	500	*****	778	*****
222	***	501	*****	779	*****
223	***	502	*****	780	*****
224	****	503	*****	781	*****
225	*	504	*****	782	*****
226	*	505	****	783	*****
227	***	506	****	784	****
228	**	507	****	785	*****
229	***	508	****	786	****
230	****	509	****	787	*****
231	****	510	*****	788	*****
232	*	511	****	789	*****
233	*	512	*****	790	*****
234	*****	513	*****	791	*****
235	****	514	*****	792	*****
236	***	515	*****	793	*****
237	***	516	****	794	*****
238	**	517	*****	795	*****
239	*	518	****	796	*****
240	****	519	*****	797	***
241	*****	520	****	798	*****
242	****	521	*****	799	*****
243	****	522	*****	800	*****
244	****	523	*****	801	*****
245	**	524	*****	802	*****
246	*	525	*****	803	*****
247	*****	526	*****	804	*****
248	****	527	*****	805	*****

Cpd	Fold	Cpd	Fold	Cpd	Fold
249	*	528	****	806	*****
250	*****	529	*****	807	*****
251	*****	530	*****	808	*****
252	****	531	*****	809	*****
253	*	532	*****	810	*****
254	***	533	*****	811	*****
255	**	534	*****	812	*****
256	****	535	*****	813	*****
257	****	536	****	814	*****
258	****	537	****	815	*****
259	****	538	****	816	****
260	***	539	****	817	*****
261	****	540	***	818	*****
262	*****	541	*****	819	*****
263	****	542	*****	820	*****
264	*****	543	*****	821	*****
265	***	544	****	822	****
266	**	545	*****	823	**
267	*****	546	*****	824	****
268	*****	547	*****	825	*****
269	*****	548	*****	826	*****
270	****	549	*****	827	*****
271	*****	550	*****	828	*****
272	*****	551	*****	829	*****
273	*****	552	****	830	*****
274	*****	553	*****	831	****
275	*****	554	*****	832	*****
276	*	555	***	833	*****
277	***	556	***	834	*****
278	**	557	*	835	*****
279	**				

[001677] **Example 8**

[001678] **Gems count (Smn-dependent nuclear speckle count) assay**

[001679] The level of Smn protein directly correlates with the amount of nuclear foci, also known as gems, produced upon staining the cell with a fluorescently labeled anti-Smn antibody (Liu and Dreyfuss, EMBO J., 1996, 15:3555). Gems are multi-protein complexes whose formation is nucleated by the Smn protein and the gems count assay is used to evaluate the level of Smn protein in the cell. As described herein, the gems count assay is used to quantify the level of Smn protein in SMA patient fibroblast cells treated with a test compound.

[001680] **Materials**

Material	Source
SMA Type 1 human cells	GM03813 (Coriell Institute)
Primary Antibody- mouse anti-SMN clone 2B1	Sigma Catalog No.: S2944
Secondary Antibody- anti-mouse Alexa Fluor 555	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: A21422
Bovine Serum Albumin (BSA)	Sigma Catalog No.: A3294
4% Paraformaldehyde	Electron Microscopy Sciences Catalog No.: 15710
Bortezomib	LC Labs, Catalog No.: B-1408
0.05% Triton X-100	Sigma Catalog No.: 93443-100mL
Mounting medium- ProLong Gold Antifade Reagent with DAPI	Life Technologies, Inc. (formerly Invitrogen) Catalog Nos.: P7481 and P36935
22x22 #1 sterile Cover slips	Fisher Catalog No.: 12-548-B
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
PBS	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 10010-031
Clear-coat nail polish	Revlon brand Catalog No.: 1271-76
Zeiss Axovert 135 Fluorescence microscope	Zeiss

[001681] **Protocol:** Cells are thawed and incubated in DMEM-10% FBS for 72 hours, then trypsinized, counted and resuspended to 100,000 cells/mL in DMEM-10% FBS. The cell suspension (2 mL) is plated in a 6-well cell culture plate with a sterile cover slip and incubated for 3 to 5 hours. Test compounds are serially diluted 3.16-fold in 100% DMSO to generate a 7-point dilution curve. 10 μL of test compound solution is added to each cell-containing well and incubated for 48 hours in a cell culture incubator (37°C, 5% CO_2, 100% relative humidity).

Duplicates are set up for each test compound concentration. Cells containing DMSO at a final concentration of 0.5% are used as controls.

[001682] Cell culture medium is aspirated from the wells containing cover slips and gently washed three times with cold PBS. The cells are fixed by incubation for 20 minutes at room temperature while in paraformaldehyde. The cells are then washed two times with cold PBS followed by incubation for 5 minutes at room temperature with 0.05% Triton X-100 in PBS to permeabilize the cells. After the fixed cells are washed three times with cold PBS, they are blocked with 10% FBS for 1 hour. 60 μL of primary antibody diluted 1:1000 in blocking buffer is added and the mixture is incubated for one hour at room temperature. The cells are washed three times with PBS and 60 μL of secondary antibody diluted 1:5000 in blocking buffer is added, then the mixture is incubated for one hour at room temperature. The cover slips are mounted onto the slides with the aid of mounting medium and allowed to dry overnight. Nail polish is applied to the sides of the cover slip and the slides are stored, protected from light. A Zeiss Axovert 135 with a 63x Plan-Apochromat, NA=1.4 objective is used for immunofluorescence detection and counting. The number of gems is counted per ≥150 nuclei and % activation is calculated using DMSO and 10 nM bortezomib as controls. For each test compound, the cells are examined at all wavelengths to identify test compounds with inherent fluorescence.

[001683] **Results.** As seen in Figure 9, SMA Type 1 patient cells treated with Compound **6** (Figure 9a) and Compound **170** (Figure 9b) contain progressively more gems relative to cells treated with DMSO.

[001684] **Example 9**

[001685] **Smn protein assay in human motor neurons**

[001686] Smn immunofluorescent confocal microscopy is used to quantify the level of Smn protein in human motor neurons treated with test compounds.

[001687] **Protocol.** Human motor neurons derived from SMA iPS cells (Ebert et al., Nature, 2009, 457:2770; and, Rubin et al., BMC Biology, 2011, 9:42) are treated with test compound at various concentrations for 72 hours. The level of Smn protein in the cell nucleus is quantified using Smn immunostaining and confocal fluorescence microscopy essentially as described in Makhortova et al., Nature Chemical Biology, 2011, 7:544. The level of Smn protein in

compound-treated samples is normalized to that in vehicle-treated samples and plotted as a function of the compound concentration.

[001688] Results. As seen in Figure 10, human motor neurons treated for 72 hours with increasing concentrations of Compound **6** contain progressively more Smn protein in the nucleus.

[001689] Example 10

[001690] Smn protein assay in animal tissues

[001691] This Smn protein assay compares tissues from test compound treated mice with those from DMSO vehicle treated mice to determine the increase in levels of Smn protein produced from the human SMN2 gene.

[001692] Materials

Material	Source
Tissues from C/C-allele SMA mice	The Jackson Laboratory, strain No.: 008714 (B6.129-*Smn1*$^{tm5(Smn1/SMN2)Mrph}$/J)
Tissues from Δ7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)
Protease inhibitor cocktail	Roche Applied Science Catalog No.: 11836145001
Anti-SMN d2	Blue cap Cisbio Catalog No.: 63IDC002-SMN
Anti-SMN kryptate	Red cap Cisbio Catalog No.: 63IDC002-SMN
SMN reconstitution buffer	Cisbio Catalog No.: 63IDC002-SMN-Buffer
RIPA Lysis Buffer	20 mM Tris-HCl pH 7.5, 150 mM NaCl, 1 mM EDTA, 1% NP-40, 1% Sodium deoxycholate
Diluent Buffer	20 mM Tris-HCl pH 7.5, 150 mM NaCl
BCA protein assay Kit	Pierce Catalog No.: 23225
White 384 well plate	Nunc Catalog No.: 351190
Polypropylene V-bottom plate	Falcon Catalog No.: 165195
Clear 96 well polystyrene plate	Nunc Catalog No.: 442404
5 mm Stainless Steel Beads	Qiagen Catalog No.: 69989
Safe-Lock Tubes 2.0 mL	Eppendorf Catalog No.: 022363352
Twin.tec 96-Well Semiskirted PCR Plate	Eppendorf Catalog No.: 951020389
TissueLyzer II	Qiagen Catalog No.: 85300
Envision Plate Reader	Perkin Elmer Model No.: 2103

[001693] **Protocol.** The tissue samples in Safe-Lock tubes are weighed and the volume of RIPA buffer containing the protease inhibitor cocktail is added based on the weight to volume ratios for each type of tissue: Brain (50 mg/mL), Muscle (50 mg/mL) and Spinal Cord (25 mg/mL).

[001694] Tissues are homogenized using the TissueLyzer by bead milling. 5 mm stainless steel beads are added to the sample and shaken vigorously for 5 minutes at 30 Hz in the TissueLyzer. The samples are then centrifuged for 20 minutes at 14,000 x g in a microcentrifuge and the homogenates transferred to the PCR plate. The homogenates are diluted in RIPA buffer to approximately 1 mg/mL for HTRF and approximately 0.5 mg/mL for total protein measurement using the BCA protein assay. For the SMN HTRF assay, 35 μL of the tissue homogenate is transferred to a 384-well plate containing 5 μL of the antibody solution (1:100 dilution of each of the anti-SMNd2 and anti-SMN Kryptate in reconstitution buffer). To provide a control signal, three (3) wells in the plate contain only RIPA Lysis Buffer and, thus, serve as Blank control wells. The plate is centrifuged for 1 minute to bring the solution to the bottom of the wells and then incubated overnight at room temperature. Fluorescence for each well of the plate at 665 nm and 620 nm is measured on an EnVision multilabel plate reader (Perkin-Elmer). The total protein in the tissue homogenate is measured using the BCA assay according to the manufacturer's protocol.

[001695] The normalized fluorescence signal is calculated for each sample, Blank and vehicle control well by dividing the signal at 665 nm by the signal at 620 nm. Normalizing the signal accounts for possible fluorescence quenching due to the matrix effect of the tissue homogenate. The ΔF value (a measurement of Smn protein abundance as a percent value) for each tissue sample well is calculated by subtracting the normalized average fluorescence for the Blank control wells from the normalized fluorescence for each tissue sample well, then dividing this difference by the normalized average fluorescence for the Blank control wells and multiplying the resulting value by 100. The ΔF value for each tissue sample well is divided by the total protein quantity (determined using the BCA assay) for that tissue sample. The change in Smn protein abundance for each tissue sample relative to the vehicle control is calculated as the percent difference in the ΔF value of the tissue sample in the presence of the test compound and the averaged ΔF value of the vehicle control signal divided by the averaged ΔF value of the vehicle control signal.

[001696] **Example 11**

[001697] **Smn protein assay in tissues of adult C/C-allele SMA mice**

[001698] The tissues for use in the assay for Smn protein in adult C/C-allele SMA mice are prepared as described in Example 10. The assay assesses whether treatment of C/C-allele SMA mice with a test compound for 10 days increases levels of Smn protein produced from the SMN2 gene.

[001699] **Materials**

Material	Source
Tissues from C/C-allele SMA mice	The Jackson Laboratory, strain No.: 008714 (B6.129-*Smn1*$^{tm5(Smn1/SMN2)Mrph}$/J)

[001700] **Protocol.** C/C-allele SMA mice are dosed BID orally (in 0.5% hydroxypropylmethyl cellulose (HPMC) with 0.1% Tween-80) with a test compound or vehicle at 10 mg/kg for 10 days. Age-matched heterozygous mice are dosed with vehicle for use as a control. Tissues are collected for analysis of protein levels according to Example 10.

[001701] **Results.** As seen in Figure 11, total protein-normalized Smn level was increased in brain, spinal cord, and muscle tissues of adult C/C-allele SMA mice treated at 100 mg/kg BID for 10 days with Compound **6** (Figure 11a) or treated at 10 mg/kg BID for 10 days with Compound **170** (Figure 11b) relative to the vehicle group.

[001702] **Example 12**

[001703] **Smn protein in tissues of neonatal Δ7 SMA mice**

[001704] The assay for Smn protein in neonatal SMA mice tissues is used to determine whether treatment with a test compound increases Smn protein levels produced from the SMN2 gene.

[001705] **Materials**

Material	Source
Tissues from Δ7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)

[001706] **Protocol.** SMA Δ7 homozygous knockout mice are dosed once a day (QD) intraperitoneally (IP) with a test compound or vehicle (100% DMSO) from postnatal day (PND) 3 to PND 9. Tissues are collected for analysis of protein levels according to Example 10.

[001707] **Results.** As seen in Figure 12, total protein normalized Smn level was dose dependently increased in brain, spinal cord, muscle, and skin tissues of neonatal SMA Δ7

homozygous knockout mice treated with Compound **6** (Figures 12a, 12b, 12c and 12d, respectively) and in brain, spinal cord, and muscle of neonatal SMA Δ7 homozygous knockout mice treated with Compound **170** (Figures 12e, 12f and 12g respectively).

[001708] **Example 13**

[001709] **Body weight of neonatal Δ7 SMA mice**

[001710] The change in body weight of neonatal SMA mice is used to determine whether treatment with a test compound improves body weight.

[001711] **Materials**

Material	Source
Tissues from ΔExon7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)

[001712] **Protocol.** SMA Δ7 homozygous knockout mice are dosed intraperitoneally (IP) with test compound or vehicle (100% DMSO) QD from PND 3 until the dose regimen is switched to an oral dose BID in 0.5% hydroxypropylmethyl cellulose (HPMC) with 0.1% Tween-80 at a dose 3.16-fold higher than the dose used for IP. Body weights of SMA Δ7 mice treated with test compound or vehicle and age matched heterozygous mice are recorded every day.

[001713] **Results.** As seen in Figure 13, body weight of neonatal SMA Δ7 homozygous knockout mice treated with Compound **6**, dosed IP QD from PND 3 to PND 30, then orally BID from PND 31 until study end (Figure 13a) and Compound **170**, dosed IP QD from PND 3 to PND 23, then orally BID from PND 24 until study end (Figure 13b), improved compared to vehicle treated mice.

[001714] **Example 14**

[001715] **Righting reflex in neonatal Δ7 SMA mice**

[001716] The functional change in righting reflex of neonatal SMA mice is used to determine whether treatment with a test compound improves righting reflex.

[001717] **Materials**

Material	Source
Tissues from ΔExon7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)

[001718] **Protocol.** SMA Δ7 homozygous knockout mice are dosed intraperitoneally (IP) with test compound or vehicle (100% DMSO) QD from PND 3 until the dose regimen is switched to

an oral dose BID in 0.5% hydroxypropylmethyl cellulose (HPMC) with 0.1% Tween-80 at a dose 3.16-fold higher than the dose used for IP. The righting reflex time is measured as the time taken by a mouse to flip over onto its feet after being laid on its back. Righting reflex is measured five times for each mouse (allowing a maximal time of 30 sec for each try) with 5 minutes between each measurement. The righting reflex time for SMA Δ7 homozygous knockout mice treated with test compound or vehicle and age-matched heterozygous mice is measured on PND 10, 14 and 18 and plotted.

[001719] Results. As seen in Figure 14, the righting reflex of neonatal SMA Δ7 homozygous knockout mice treated with Compound **6** (Figure 14a) and Compound **170** (Figure 14b) dosed IP QD from PND 3 improved compared to vehicle treated mice. The righting time of the compound treated neonatal SMA Δ7 homozygous knockout mice was similar to that of the age matched heterozygous mice on PND 18.

[001720] Example 15

[001721] Survival of neonatal Δ7 SMA mice

[001722] The change in the number of surviving mice over time is used to determine whether treatment with a test compound improves survival.

[001723] Materials

Material	Source
Tissues from Δ7 SMA mice	The Jackson Laboratory, strain No.: 005025 (FVB.Cg-Tg(SMN2*delta7)4299Ahmb Tg(SMN2)89Ahmb *Smn1*^{tm1Msd}/J)

[001724] Protocol. SMA Δ7 homozygous knockout mice are dosed intraperitoneally (IP) with test compound or vehicle (100% DMSO) QD from PND 3 until the dose regimen is switched to an oral dose BID in 0.5% hydroxypropylmethyl cellulose (HPMC) with 0.1% Tween-80 at a dose 3.16-fold higher than the dose used for IP and later switched to an oral dose QD in 0.5% hydroxypropylmethyl cellulose (HPMC) with 0.1% Tween-80 at a dose 6.32-fold higher than the dose used for IP. The number of surviving mice in each group is recorded every day and plotted as a percent of total number of mice. Tissues of SMA Δ7 and age-matched heterozygous mice are collected for the measurement of Smn protein levels and processed as detailed in Example 10. The total protein normalized Smn protein levels measured in the tissues are plotted as a percent of those in the age-matched heterozygous mice tissues, with the Smn level in heterozygous mice set to 100 percent. The level of Smn protein in the test compound treated

mice tissue relative to that in heterozygous mice tissue is indicated as a percent value above each bar in the graph.

[001725] Results. As seen in Figure 15, survival of neonatal SMA Δ7 homozygous knockout mice treated with Compound **6** (Figure 15a), dosed IP QD from PND 3 to PND 30, then orally BID from PND 31 until study end, and Compound **170** (Figure 15b), dosed IP QD from PND 3 to PND 23, then orally BID from PND 24 until study end, improved compared to vehicle treated mice. As seen in Figure 16, Smn protein levels in brain, spinal cord, and muscle tissues of SMA Δ7 homozygous knockout mice after treatment with Compound **6** dosed IP 10 mg/kg QD from PND 3 to PND 30, then orally 30 mg/kg BID from PND 31 to PND 156 (Figure 16a) and Compound **170** dosed IP 3 mg/kg QD from PND 3 to PND 23, then orally 10 mg/kg BID from PND 24 to PND 88, orally 20 mg/kg QD from PND 89 to PND185 (Figure 16b) was measured and plotted relative to vehicle treated and age-matched heterozygous mice.

[001726] Example 16

[001727] Human SMN1 minigene mRNA end-point semi-quantitative RT-PCR splicing assay in cultured cells

[001728] The RT-PCR assay is used to visualize and quantify the levels of the human SMN1 minigene full length and Δ7 mRNA in primary cells and cell lines expressing the human SMN1 minigene construct treated with a test compound.

[001729] Materials

Material	Source
HEK293H cells	ATCC Catalog No.: CRL-1573
Cells-To-Ct lysis buffer	Life Technologies, Inc. (formerly Applied Biosystems) Catalog No.: 4399002
FuGENE-6 lipid transfection reagent	Roche Applied Science, Catalog No.: 11 814 443 001
DMEM	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11960-044
96-well flat-bottom plates	Becton Dickinson Catalog No.: 353072
Platinum Taq HiFi DNA Polymerase Super Mix	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: 11304-016
iScript RT enzyme Kit	BioRad Catalog No.: 170-8890
Ethidium bromide 2% agarose E gels 48-Well Double Comb	Life Technologies, Inc. (formerly Invitrogen) Catalog No.: G8008-02
Gel Documentation System	UVP Gel Doc It 310 Imaging system

[001730] SMN1 Minigene Construct

[001731] Preparation of the Minigene Constructs

[001732] Using the procedure for the preparation of the SMN2 minigene construct described in Biological Example 1, the SMN1 version of the minigene is generated by replacing the sixth nucleotide of exon 7 (a thymine residue) of the SMN2-A minigene construct to cytosine using site-directed mutagenesis. Thus, similar to the SMN2-A minigene construct, the SMN1 minigene construct has a single adenine residue inserted after nucleic residue 48 of exon 7. The SMN1 minigene construct is referred to as SMN1-A.

[001733] Protocol. HEK293H cells (10,000 cells/well/199 μL) were transfected, using FuGENE-6 reagent, in a 96-well plate with 15 ng of the SMN1-A minigene reporter plasmid per well. Cells were incubated for 24 hours following transfection. Test compounds were serially diluted 3.16-fold in 100% DMSO to generate a 7-point concentration curve. A solution of test compound (1 μL, 200x in DMSO) was added to each test well. 1 μL DMSO was added to each control well. The plate was incubated for 7 hours in a cell culture incubator (37°C, 5% CO_2, 100% relative humidity). The cells were then lysed in Cells-To-Ct lysis buffer and the lysates were stored at −80°C.

[001734] Two SMN spliced mRNA are generated from the SMN1 minigene. The term "SMN1 minigene FL" refers to the first spliced product containing exon 7, corresponding to full length SMN1 mRNA. The term "SMN1 minigene Δ7" refers to the second product lacking exon 7.

[001735] SMN minigene FL and Δ7 mRNA are amplified using the primers in Table 11. Primer SMN Forward C (SEQ ID NO. 11) hybridizes to a nucleotide sequence in exon 6 (nucleotide 43 to nucleotide 63), primer SMN Reverse A (SEQ ID NO. 2) hybridizes to a nucleotide sequence in the coding sequence of Firefly luciferase. The combination of these two oligonucleotides detects only SMN1 or SMN2 minigenes (RT-PCR) and will not detect endogenous SMN1 or SMN2 genes. Since the HEK293H cells used in Example 16 were transfected with only the human SMN1 minigene, RT-PCR can visualize and quantify only SMN1 minigene full-length and SMN1 minigene Δ7 mRNA.

[001736] Table 11

Primer	Sequence	Source
SMN Forward C	**SEQ ID NO.11:** GATGCTGATGCTTTGGGAAGT	PTC[1]
SMN Reverse A	**SEQ ID NO.2:** CGCTTCACATTCCAGATCTGTC	PTC[1]

[001737] [1] Primers designed by PTC Therapeutics, Inc.

[001738] To synthesize cDNA, 5 μL of lysate, 4 μL of 5x iScript reaction mix, 1 μL of reverse transcriptase, and 10 μL of water are combined and incubated 5 min at 25°C followed by 30 min at 42°C, followed by 5 min at 85°C. The cDNA solution is stored at -20°C.

[001739] To perform endpoint PCR, 5 μL of cDNA, 0.2 μL of 100 μM forward primer, 0.2 μL of 100 μM reverse primer, and 22.5 μL of polymerase super mix are combined in a 96 well semiskirted PCR plate. PCR is carried out at the following temperatures for the indicated time: Step 1: 94°C (2 min), Step 2: 94°C (30 sec), Step 3: 55°C (30 sec), Step 4: 68°C (1 min), then repeat Steps 2 to 4 for a total of 33 cycles, then hold at 4°C.

[001740] 10 μL of each PCR sample is electrophoretically separated on a 2% agarose E-gel for 14 minutes stained with dsDNA staining reagents (e.g., ethidium bromide) and visualized using a gel imager.

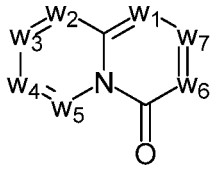
[001741] **Results.** As seen in Figure 17, cells treated with increasing concentrations of Compound **6** (Figure 17a) and Compound **170** (Figure 17b) contain progressively more SMN1 minigene FL mRNA and less SMN1 minigene Δ7 mRNA, indicating a correction of SMN1 alternative splicing.

[001742] Without regard to whether a document cited herein was specifically and individually indicated as being incorporated by reference, all documents referred to herein are incorporated by reference into the present application for any and all purposes to the same extent as if each individual reference was fully set forth herein.

[001743] Although certain embodiments have been described in detail above, those having ordinary skill in the art will clearly understand that many modifications are possible in the embodiments without departing from the teachings thereof. All such modifications are intended to be encompassed within the claims as described herein.

What is claimed is:

1. A compound of Formula (I):



(I)

or a form thereof, wherein:

w_1 and w_5 are independently C-R_a or N;

w_2 is C-R_b or N;

w_3, w_4 and w_7 are independently C-R_1, C-R_2, C-R_a or N;

w_6 is C-R_1, C-R_2, C-R_c or N;

wherein one of w_3, w_4, w_6 and w_7 is C-R_1 and one other of w_3, w_4, w_6 and w_7 is C-R_2, provided that,

when w_3 is C-R_1, then w_6 is C-R_2 and w_4 and w_7 are independently C-R_a or N; or,

when w_3 is C-R_2, then w_6 is C-R_1 and w_4 and w_7 are independently C-R_a or N; or,

when w_4 is C-R_1, then w_7 is C-R_2 and w_3 is C-R_a or N and w_6 is C-R_c or N; or,

when w_4 is C-R_2, then w_7 is C-R_1 and w_3 is C-R_a or N and w_6 is C-R_c or N; and,

wherein any one, two or three of w_1, w_2, w_3, w_4, w_5, w_6 and w_7 may optionally be N;

R_1 is $C_{1\text{-}8}$alkyl, amino, $C_{1\text{-}8}$alkyl-amino, ($C_{1\text{-}8}$alkyl)$_2$-amino, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)$_2$-amino, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino, amino-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl, ($C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino-$C_{1\text{-}8}$alkyl, amino-$C_{1\text{-}8}$alkyl-amino, (amino-$C_{1\text{-}8}$alkyl)$_2$-amino, (amino-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino, $C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl-amino, ($C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl)$_2$-amino, ($C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino, ($C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl-amino, [($C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkyl]($C_{1\text{-}8}$alkyl)amino, amino-$C_{1\text{-}8}$alkoxy, $C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkoxy, ($C_{1\text{-}8}$alkyl)$_2$-amino-$C_{1\text{-}8}$alkoxy, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkoxy, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkoxy, ($C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino-$C_{1\text{-}8}$alkoxy, amino-$C_{2\text{-}8}$alkenyl, $C_{1\text{-}8}$alkyl-amino-$C_{2\text{-}8}$alkenyl, ($C_{1\text{-}8}$alkyl)$_2$-amino-$C_{2\text{-}8}$alkenyl, amino-$C_{2\text{-}8}$alkynyl,

C_{1-8}alkyl-amino-C_{2-8}alkynyl, (C_{1-8}alkyl)$_2$-amino-C_{2-8}alkynyl, halo-C_{1-8}alkyl-amino, (halo-C_{1-8}alkyl)$_2$-amino, (halo-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkoxy, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkoxy, hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)$_2$-amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl-amino, (hydroxy-C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl-amino, [(hydroxy-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, [(hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, heterocyclyl, heterocyclyl-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkoxy, heterocyclyl-amino, (heterocyclyl)(C_{1-8}alkyl)amino, heterocyclyl-amino-C_{1-8}alkyl, heterocyclyl-C_{1-8}alkyl-amino, (heterocyclyl-C_{1-8}alkyl)$_2$-amino, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heterocyclyl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (heterocyclyl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C_{3-14}cycloalkyl, aryl-C_{1-8}alkyl-amino, (aryl-C_{1-8}alkyl)$_2$-amino, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, aryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl, (aryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl, heteroaryl, heteroaryl-C_{1-8}alkyl, heteroaryl-C_{1-8}alkoxy, heteroaryl-amino, heteroaryl-C_{1-8}alkyl-amino, (heteroaryl-C_{1-8}alkyl)$_2$-amino, (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino, heteroaryl-C_{1-8}alkyl-amino-C_{1-8}alkyl, (heteroaryl-C_{1-8}alkyl)$_2$-amino-C_{1-8}alkyl or (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino-C_{1-8}alkyl;

wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or,

wherein, each instance of heterocyclyl, C_{3-14}cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent;

R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

R_c is hydrogen, halogen or C_{1-8}alkyl;

R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkyl-carbonyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl, amino-C_{1-8}alkyl-amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, (C_{1-8}alkyl-amino-$C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl-amino, $[(C_{1-8}alkyl)_2$-amino-$C_{1-8}alkyl]_2$-amino, (C_{1-8}alkyl-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, $[(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl](C_{1-8}alkyl)amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, (C_{1-8}alkoxy-$C_{1-8}alkyl)_2$-amino, (C_{1-8}alkoxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino, C_{1-8}alkyl-carbonyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, (hydroxy-$C_{1-8}alkyl)_2$-amino or (hydroxy-C_{1-8}alkyl)(C_{1-8}alkyl)amino;

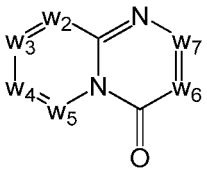
R_4 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-C_{1-8}alkyl, C_{3-14}cycloalkyl-amino, aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl, aryl-sulfonyloxy-C_{1-8}alkyl, heterocyclyl or heterocyclyl-C_{1-8}alkyl; wherein, each instance of C_{3-14}cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R_5 substituents;

R_5 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio;

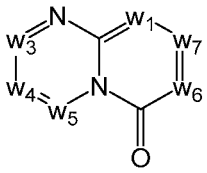
R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, C_{2-8}alkenyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio; and,

R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

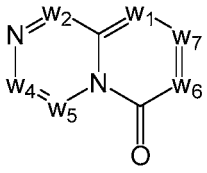
2. The compound of claim 1, wherein the compound is selected from Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV):



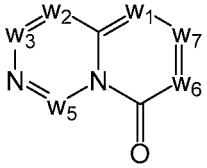
(II),



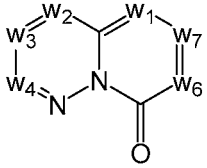
(III),



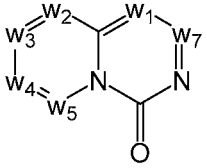
(IV),



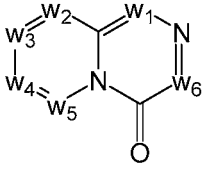
(V),



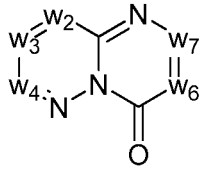
(VI),



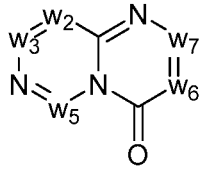
(VII),



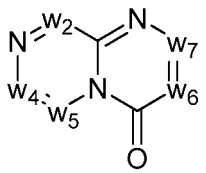
(VIII),



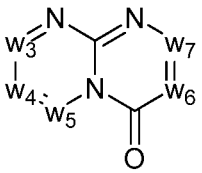
(IX),



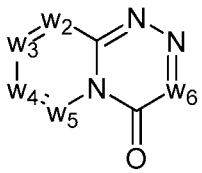
(X),



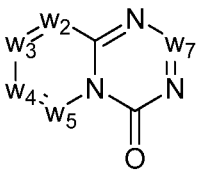
(XI),



(XII),



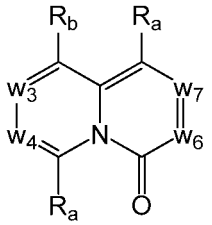
(XIII), or



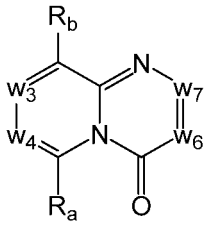
(XIV)

or a form thereof.

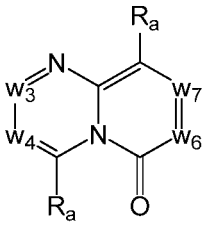
3. The compound of claim 2, wherein the compound of Formula (I), Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV) is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IVa), Formula (Va), Formula (VIa), Formula (VIIa), Formula (VIIIa), Formula (IXa), Formula (Xa), Formula (XIa), Formula (XIIa), Formula (XIIIa) or Formula (XIVa), respectively:



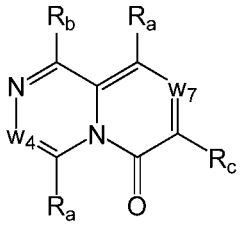
(Ia),



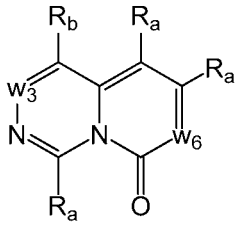
(IIa),



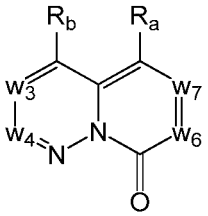
(IIIa),



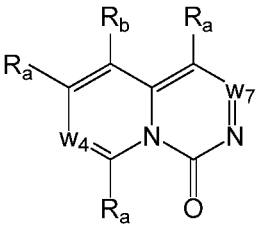
(IVa),



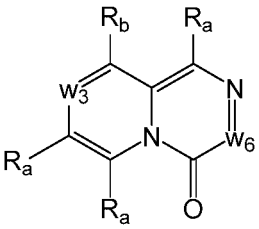
(Va),



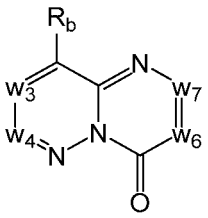
(VIa),



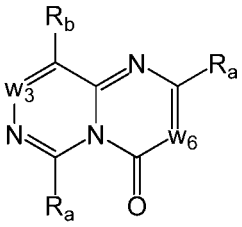
(VIIa),



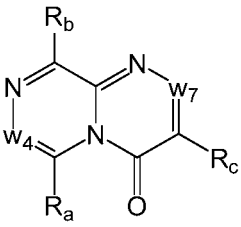
(VIIIa),



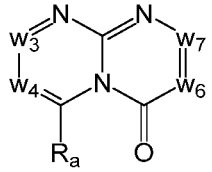
(IXa),



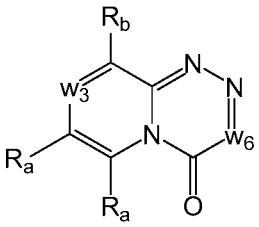
(Xa),



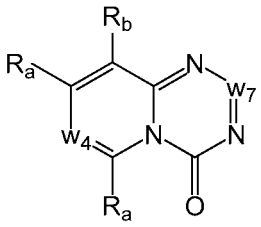
(XIa),



(XIIa),



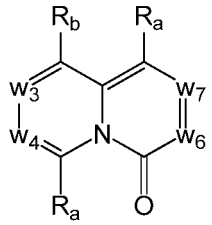
(XIIIa), or



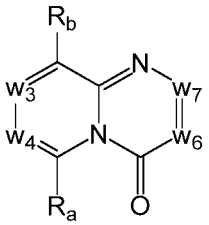
(XIVa)

or a form thereof.

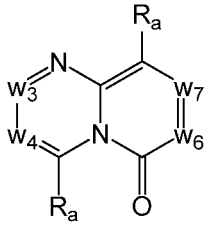
4. The compound of claim 3, wherein the compound of Formula (I), Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII) is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IXa), Formula (XIa) or Formula (XIIa), respectively:



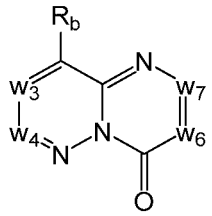
(Ia),



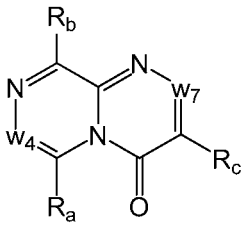
(IIa),



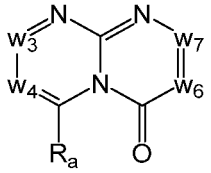
(IIIa),



(IXa),



(XIa), or



(XIIa)

or a form thereof.

5. The compound of claim 1, wherein the form is selected from a free acid, free base, salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

6. The compound of claim 5, wherein the salt form is a chloride, hydrobromide, hydrochloride, dihydrochloride, acetate, trifluoroacetate or trifluoroacetic acid salt.

7. The compound of claim 1, wherein the compound is selected from the group consisting of:

2-(4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-benzodioxol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-benzodioxol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-benzodioxol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-benzodioxol-5-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-phenyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-fluoro-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-[3-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-[4-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-fluoro-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)phenyl]-9-fluoro-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)phenyl]-9-fluoro-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

3-(3,4-dimethoxyphenyl)-8-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(difluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(difluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-fluoro-4,5-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,8-diazabicyclo[3.2.1]oct-3-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methoxy-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

4-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile

2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-fluoro-5-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-fluoro-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[2-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-[3-(trifluoromethoxy)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-4-oxo-7-(piperazin-1-yl)-4H-quinolizine-1-carbonitrile

2-(3-fluoro-4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one

2-(5-fluoropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-fluoropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-chloropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-chloropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-chloro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1H-indol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1H-indol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one

2-(3,5-difluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one

2-(imidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(imidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-ethoxy-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-ethoxy-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(2-methylpyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-[2-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-ethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,3-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(4-hydroxypiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxy-3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

3-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile

2-methoxy-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile

2-(3-fluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethoxy-3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-fluoro-4-(2,2,2-trifluoroethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-(4-methyl-1,3-thiazol-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methyl-1,3-thiazol-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(propan-2-ylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxy-3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-fluoro-4-(methylsulfanyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-fluoro-6-methoxypyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-fluoro-6-methoxypyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methyl-1H-imidazol-1-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methyl-1H-imidazol-1-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-fluoro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-5-fluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-5-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-(1-methyl-1H-pyrazol-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-pyrazol-4-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,5-dimethoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one

7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,4R)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-3-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-difluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-difluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-fluoro-4-methoxyphenyl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-(methylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-{4-[(methylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-{[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-(pyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

3-fluoro-5-{7-[(3S)-3-methylpiperazin-1-yl]-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl}benzonitrile

3-fluoro-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile

2-(3-fluoro-4-methoxyphenyl)-7-[(3'S,4'S)-4'-hydroxy-1,3'-bipyrrolidin-1'-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-pyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3S)-pyrrolidin-3-yloxy]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(1R,5S)-8-azabicyclo[3.2.1]oct-2-en-3-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,5,6-tetrahydropyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-ethyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-ethyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-aminopiperidin-1-yl)-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(propan-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-fluoro-4-methoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)piperidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3aR,6aS)-5-ethylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-fluoro-4-methoxyphenyl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-fluoro-4-methoxyphenyl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(2R)-2-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-quinolizin-4-one

7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one

2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(cyclopropylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclopropylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-ethyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(methylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[ethyl(methyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[methyl(propyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,4-dimethoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,4-dimethoxyphenyl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminopyrrolidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-methoxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[cis-4-(methylamino)cyclohexyl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclopropylpiperazin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:1)

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4'-bipiperidin-1'-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(diethylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[6-(dimethylamino)pyridin-3-yl]-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(diethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[6-(dimethylamino)pyridin-3-yl]-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(diethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(2-methoxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[6-(dimethylamino)pyridin-3-yl]-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methyl-1,4-diazepan-1-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrimido[1,2-b]pyridazin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-methoxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-cyclopropyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-methoxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(diethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(dimethylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-amino-4-methylpiperidin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-{4-[bis(2-hydroxyethyl)amino]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclopropylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclobutylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-hydroxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-propylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclobutylpiperazin-1-yl)-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-fluoroethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(3-fluoropropyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-fluoroethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(3-fluoropropyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3R)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1H-benzimidazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1H-benzimidazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-[1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(1,3-dihydroxypropan-2-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)-4-methylpiperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)-4-methylpiperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-methyl-4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]-4-methylpiperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-amino-4-methylpiperidin-1-yl)-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-ethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-amino-4-methylpiperidin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminoprop-1-yn-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminopropyl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(diethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(pyrrolidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(piperidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2,7-diazaspiro[4.4]non-2-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)propyl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-{(3S)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,7-dimethyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-{(3S)-3-[(diethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3S)-3-[(ethylamino)methyl]pyrrolidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

7-{3-[(dimethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-{3-[(diethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-{(3R)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(2S,6S)-2,6-dimethylpiperidin-4-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(imidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2,7-diazaspiro[3.5]non-7-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-methyl-6-[7-(4-methylpiperazin-1-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]imidazo[1,2-a]pyridine-8-carbonitrile

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4,7-diazaspiro[2.5]oct-7-yl)-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-hydroxypiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{[2-(morpholin-4-yl)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-{[2-(dimethylamino)ethyl]amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-{[2-(dimethylamino)ethyl](methyl)amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{methyl[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-ylmethoxy)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[2-(piperidin-1-yl)ethoxy]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(morpholin-4-yl)propoxy]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)propoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one, or

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

or a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

8. The compound of claim 7, wherein the compound is selected from the group consisting of:

2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one hydrochloride

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one acetate

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one trifluoroacetate (1:1), or

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:2)

or a free base, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

9. A pharmaceutical composition comprising an effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier, excipient or diluent.

10. The pharmaceutical composition of claim 9 for use in the treatment of spinal muscular atrophy (SMA).

11. A method for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising contacting a human cell with the compound of claim 1.

12. A method for increasing the amount of Smn protein, comprising contacting a human cell with the compound of claim 1.

13. The method of claim 11 or 12, wherein the human cell is a human cell from a human SMA patient.

14. A method for treating SMA in a human subject in need thereof, comprising administering to the subject an effective amount of the compound of claim 1.

15. A method for treating SMA in a human subject in need thereof, comprising administering to the subject the pharmaceutical composition of claim 9.