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(72) Inventeurs/Inventors:
WOLL, MATTHEW G., US;
CHEN, GUANGMING, US;
CHOI, SOONGYU, US;
DAKKA, AMAL, US;
...

(73) Propriétaires/Owners:

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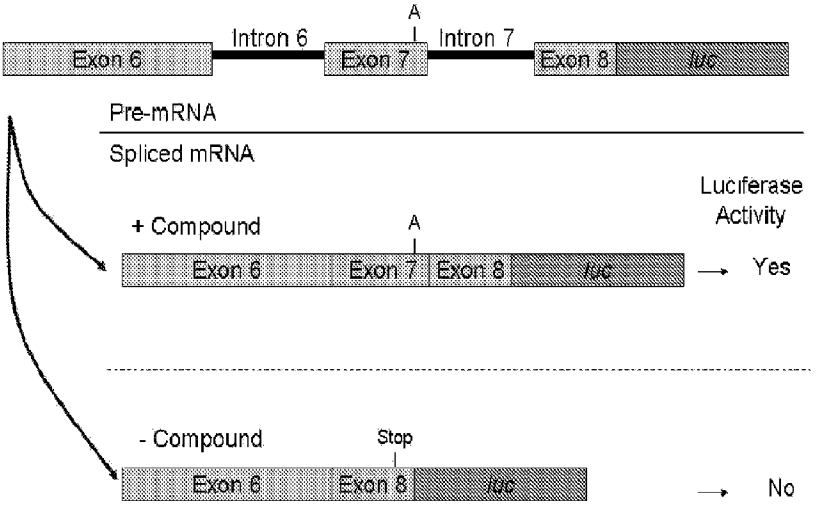

(57) Abrégé/Abstract:
Provided herein are compounds, compositions thereof and uses therewith for treating spinal muscular atrophy. In a specific embodiment, provided herein are compounds of a form that may be used to modulate the inclusion of exon 7 of SMN2 into mRNA

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(72) Inventeurs(suite)/Inventors(continued): HUANG, SONG, US; KARP, GARY MITCHELL, US; LEE, CHANG-SUN, US; LI, CHUNSHI, US; NARASIMHAN, JANA, US; NARYSHKIN, NIKOLAI, US; PAUSHKIN, SERGEY, US; QI, HONGYAN, US; TURPOFF, ANTHONY A., US; WEETALL, MARLA L., US; WELCH, ELLEN, US; YANG, TIANLE, US; ZHANG, NANJING, US; ZHANG, XIAOYAN, US; ZHAO, XIN, US; PINARD, EMMANUEL, FR; RATNI, HASANE, FR

(73) Propriétaires(suite)/Owners(continued):PTC THERAPEUTICS, INC., US; F. HOFFMANN-LA ROCHE AG, CH

(74) Agent: OSLER, HOSKIN & HARCOURT LLP

(57) Abrégé(suite)/Abstract(continued):
that is transcribed from the SMN2 gene. In another specific embodiment, provided herein are compounds of a form 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 a form 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.

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(71) **Applicants**: **PTC THERAPEUTICS, INC.** [US/US]; 100 Corporate Court, Middlesex Business Center, South Plainfield, NJ 07080 (US). **F. HOFFMANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse 124, 4070 Basel (CH).

(72) **Inventors**: **WOLL, Matthew G.**; 413 Mountainview Terrace, Dunellen, NJ 08812 (US). **CHEN, Guangming**; 932 Sunset Ridge, Bridgewater, NJ 08807 (US). **CHOI, Soongyu**; 627 Swain Court, Belle Mead, NJ 08502 (US). **DAKKA, Amal**; 3 Gleim Rd, Whitehouse Station, NJ 08889 (US). **HUANG, Song**; 15682 Anchorage Drive, San Leandro, CA 94579 (US). **KARP, Gary Mitchell**; 37 Cartwright Drive, Princeton Junction, NJ 08550 (US). **LEE, Chang-Sun**; 118 Ketcham Rd., Belle Mead, NJ 08502 (US). **LI, Chunshi**; 10 Albemarle Rd, East Brunswick, NJ 08816 (US). **NARASIMHAN, Jana**; 2257 New York Ave., Scotch Plains, NJ 07076 (US). **NARYSHKIN, Nikolai**; 101 Windsong Circle, East Brunswick, NJ 08816 (US). **PAUSHKIN, Sergey**; 51 Scenic Hills Court, Belle Mead, NJ 08502 (US). **QI, Hongyan**; 30 Birch Drive, Plainsboro, NJ 08536 (US). **TURPOFF, Anthony A.**; 94 Meadowbrook Dr., Hillsborough, NJ 08844 (US). **WEETALL, Marla L.**; 70 Burnham Parkway, Morristown, NJ 07960 (US). **WELCH, Ellen**; 33 Hollow Brook Rd, Califon, NJ 07830 (US). **YANG, Tianle**; 1573 Coles Ave., Mountainside, NJ 07092 (US). **ZHANG, Nanjing**; 4 Pickering Cir, Princeton, NJ 08540 (US). **ZHANG, Xiaoyan**; 7 Livingston Dr., Belle Mead, NJ 08502 (US). **ZHAO, Xin**; 222 Tomahawk Court, Belle Mead, NJ 08502 (US). **PINARD, Emmanuel**; 7, rue de Pujo, F 68480 Linsdort (FR). **RATNI, Hasane**; 4, rue Louis Pasteur, F 68440 Habsheim (FR).

(74) **Agents**: **INSOGNA, Anthony, M.** et al.; Jones Day, 222 East 41st Street, New York, NY 10017-6702 (US).

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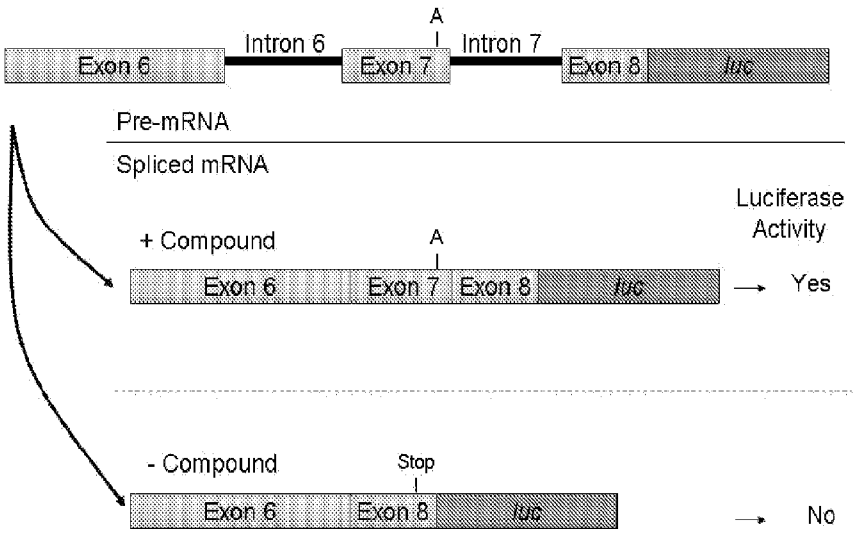
(54) **Title**: COMPOUNDS FOR TREATING SPINAL MUSCULAR ATROPHY



(57) **Abstract**: Provided herein are compounds, compositions thereof and uses therewith for treating spinal muscular atrophy. In a specific embodiment, provided herein are compounds of a form 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 a form 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 a form 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.

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JUMBO APPLICATIONS / PATENTS

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COMPOUNDS FOR TREATING SPINAL MUSCULAR ATROPHY

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

STATEMENT ON JOINT RESEARCH AGREEMENT

[0002] 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;

[0003] the claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and

[0004] 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

[0005] Provided herein are compounds, compositions thereof and uses therewith for treating Spinal Muscular Atrophy.

BACKGROUND

[0006] 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).

[0007] 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.

[0008] (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, newborns have little movement and difficulties with swallowing and breathing.

[0009] (b) Type 1 SMA (Infantile SMA or Werdnig-Hoffmann disease) presents the first symptoms between 0 and 6 months: This type of SMA is also very severe. Patients never achieve the ability to sit, and death usually occurs within the first 2 years without respiratory support.

[0010] (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.

[0011] (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 the course of the disease but often become wheelchair-bound during youth or adulthood.

[0012] (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 onset SMA is much slower and has little or no impact on life expectancy.

[0013] 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.

[0014] Smn 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.

[0015] In most cases, SMA is diagnosed based on clinical symptoms and by the presence of at least on copy of the SMN1 gene test. However, in approximately 5% of cases SMA is caused by mutation in genes other than the inactivation of SMN1, some known and others not yet defined. In some cases, when the SMN1 gene test is not feasible or does not show any abnormality, other tests such as an electromyography (EMG) or muscle biopsy may be indicated.

[0016] 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 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 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.

[0017] 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 # 008714) provides a less severe SMA disease model, with mice having reduced levels of both 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.

[0018] As a result of improved understanding of the genetic basis for SMA, several strategies for treatment have been explored, but none have yet demonstrated success in the clinic.

[0019] 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.

[0020] 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).

[0021] 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 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 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.

[0022] In an alternative approach, neuroprotective agents such as olesoxime have been chosen for investigation. Such strategies are not aimed at producing functional Smn for the treatment of SMA, but instead are being explored to protect the Smn-deficient motor neurons from neurodegeneration.

[0023] 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

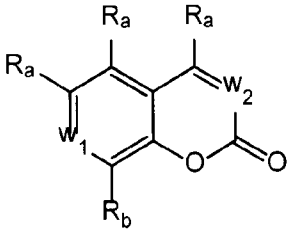
PCT/US2009/004625 filed August 13, 2009 (published as International Publication Number WO2010/019236 and United States Publication Number US2011/0172284).

[0024]

[0025] 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

[0026] In one aspect, provided herein are compounds of Formula (I):



(I)

[0027] or a form thereof, wherein: w_1, w_2, R_a and R_b 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).

[0028] 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 the loss of exon 7 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 the inclusion of exon 7 of SMN1 into mRNA that is transcribed from the SMN1 gene.

[0029] 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.

[0030] 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.

[0031] 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 NOs: 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 NOs: 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 NOs: 1, 2, 3, 7, 8, 9, 10, 11, 12 or 13.

[0032] 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.

[0033] 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.

[0034] 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.

[0035] 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.

[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 SMN1 into mRNA that is transcribed from an SMN1 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 and/or SMN2 into mRNA that is transcribed from an SMN1 and/or SMN2 gene.

[0038] 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.

[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 SMN1 gene and includes exon 7 of SMN1 in a patient sample. In a specific embodiment, the patient is 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 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.

[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, 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.

[0042] 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.

[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 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.

[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 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.

[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 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.

[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 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.

[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 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.

[0048] 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

[0049] Figure 1, referenced in Biological Example 1, is a schematic drawing of the SMN2 minigene construct, which features the two alternatively spliced mRNA transcripts. The nucleotide added to exon 7 of SMN2 after nucleic residue 48 is indicated by the letter "A," which could be adenine, cytosine, or thymine. The presence of one or more stop codon(s) generated in Exon 8 is indicated by "Stop."

[0050] 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 subsequences 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 A insert (position 6008);

6015-6458: intron 7;

6459-6481: part of exon 8;

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

8147-8266: 3'UTR (deg).

[0051] Figure 3, referenced in Biological Example 2, shows the correction of SMN2 minigene alternative splicing in cells treated with rising concentrations of Compound **35** (Figure 3a) and Compound **626** (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.

[0052] 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 **35** (Figure 4a) and Compound **626** (Figure 4b) over a 24 hr period. The levels of full length and Δ7 SMN2 mRNAs were quantified using RT-qPCR. The levels of full length and Δ7 SMN2 mRNAs in compound-treated samples were normalized to those in vehicle-treated samples and plotted as a function of the compound concentration.

[0053] 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 **35** (Figure 5a) and Compound **626** (Figure 5b) over a 24 hr period. The full length and Δ7 SMN2 mRNAs 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 mRNAs respectively. The intensity of each band is proportional to the amount of RNA present in the sample.

[0054] 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 of C/C-allele SMA mouse model treated for 10 days twice per day with 10 mg/kg of Compound **35** (Figure 6a) and Compound **626** (Figure 6b). The levels of full length and Δ7 SMN2 mRNAs 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.

[0055] 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 of C/C-allele SMA mouse model treated for 10 days twice per day with 10 mg/kg of Compound **35** (Figure 7a) and Compound **626** (Figure 7b). The full length and Δ7 SMN2 mRNAs 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 mRNAs respectively. The intensity of each band is proportional to the amount of RNA present in the sample. The GAPDH loading control is shown for Compound **626**.

[0056] 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 **35** (Figure 8a) and Compound **626** (Figure 8b).

[0057] Figure 9, referenced in Biological Example 8, shows an increase in nuclear speckle counts (gems) in Type 1 SMA patient fibroblasts treated with Compound **35** (Figure 9a) and Compound **626** (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.

[0058] 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 **35** (Figure 10a) and Compound **626** (Figure 10b) over a 72 hour period. 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.

[0059] Figure 11, referenced in Biological Example 11, shows increased Smn protein expression in tissues (Brain: Figure 11a; Spinal cord: Figure 11b; and Muscle: Figure 11c) of C/C-allele SMA mouse model treated for 10 days twice per day with 10 mg/kg of Compound **35** and Compound **626**.

[0060] Figure 12, referenced in Biological Example 12, shows a dose dependent increase in Smn protein expression in tissues (Brain: Figure 12a and Figure 12b; Spinal cord: Figure 12c and Figure 12d; and Muscle: Figure 12e and Figure 12f) of neonatal Δ7 SMA mouse model treated for 7 days once per day with indicated doses of Compound **35** and Compound **626**, respectively.

[0061] Figure 13, referenced in Biological Example 13, shows differences in body weight of neonatal Δ7 SMA mouse model treated until postnatal day 66 with Compound **35** (Figure 13a) and until postnatal day 76 with Compound **626** (Figure 13b).

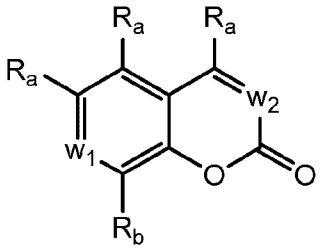
[0062] Figure 14, referenced in Biological Example 14, shows improved righting reflex of neonatal Δ7 SMA mouse model treated with Compound **35**.

[0063] Figure 15, referenced in Biological Example 15, shows improved survival in a neonatal Δ7 SMA mouse model treated with Compound **35** (Figure 15a) and Compound **626** (Figure 15b).

[0064] Figure 16, referenced in Biological Example 15, shows increased Smn protein expression in tissues (Brain: Figure 16a; and Muscle: Figure 16b) in a neonatal Δ7 SMA mouse model treated until postnatal day 47-55 (P47-55) with Compound **35** and until postnatal day 68 (P68) with Compound **626** relative to vehicle treated and age-matched heterozygous mice.

DETAILED DESCRIPTION

[0065] Provided herein are compounds of Formula (I):



(I)

[0066] or a form thereof, wherein:

[0067] w_1 and w_2 are C-R_1 or C-R_2; wherein, one of w_1 and w_2 is C-R_1 and the other is C-R_2, provided that, when w_1 is C-R_1, then w_2 is C-R_2; or, when w_1 is C-R_2, then w_2 is C-R_1;

[0068] 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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl, amino-$C_{1-8}$alkyl-amino, $(amino\text{-}C_{1-8}alkyl)_2$-amino, $(amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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-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-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-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, 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;

[0069] wherein, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two or three R_3 substituents and one additional, optional R_4 substituent; and,

[0070] wherein, alternatively, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

[0071] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[0072] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent;

[0073] R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

[0074] R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

[0075] 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)$_2$-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;

[0076] 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;

[0077] 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;

[0078] 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, amino, C_{1-8}alkyl-amino, (C_{1-8}alkyl)$_2$-amino or C_{1-8}alkyl-thio; and,

[0079] R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

EMBODIMENTS

[0080] In one embodiment of a compound of Formula (I), 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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl, amino-$C_{1-8}$alkyl-amino, $(amino\text{-}C_{1-8}alkyl)_2$-amino, $(amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl-amino, $[(C_{1-8}alkyl)_2\text{-}amino\text{-}C_{1-8}alkyl](C_{1-8}alkyl)$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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkoxy, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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, $(halo\text{-}C_{1-8}alkyl)_2$-amino, $(halo\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, hydroxy-$C_{1-8}$alkyl, hydroxy-$C_{1-8}$alkoxy-$C_{1-8}$alkyl, hydroxy-$C_{1-8}$alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino, $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, hydroxy-$C_{1-8}$alkyl-amino-$C_{1-8}$alkyl, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl, $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl, hydroxy-$C_{1-8}$alkyl-amino-$C_{1-8}$alkoxy, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkoxy, $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkoxy, hydroxy-$C_{1-8}$alkyl-amino-$C_{1-8}$alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)_2$-amino, $(hydroxy\text{-}C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl-amino, $[(hydroxy\text{-}C_{1-8}alkyl)_2\text{-}amino\text{-}C_{1-8}alkyl](C_{1-8}alkyl)$amino, $[(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)\text{amino-}C_{1-8}alkyl](C_{1-8}alkyl)$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, $(heterocyclyl\text{-}C_{1-8}alkyl)_2$-amino, $(heterocyclyl\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, heterocyclyl-$C_{1-8}$alkyl-amino-$C_{1-8}$alkyl, $(heterocyclyl\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl, $(heterocyclyl\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl,

heterocyclyl-carbonyl-oxy, 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 and heteroaryl is optionally substituted.

[0081] In one embodiment of a compound of Formula (I), R_1 is 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, 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-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-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, 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 and heteroaryl is optionally substituted.

[0082] In another embodiment of a compound of Formula (I), 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-(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 or 6,9-diazaspiro[4.5]decyl; wherein, each instance of heterocyclyl is optionally substituted.

[0083] In another embodiment of a compound of Formula (I), 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-3-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-2(1*H*)-yl, hexahydropyrrolo[1,2-*a*]pyrazin-6(2*H*)-one, (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.

[0084] In another embodiment of a compound of Formula (I), R_1 is substituted heterocyclyl selected from (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,
(1R,5S,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.

[0085] 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.

[0086] In one 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.

[0087] 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.

[0088] In one 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.

[0089] 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.

[0090] In one 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.

[0091] 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.

[0092] In one 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.

[0093] 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.

[0094] In one 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.

[0095] 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.

[0096] In one 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-[(thiophenyl-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.

[0097] 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.

[0098] In one 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.

[0099] 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.

[00100] In one 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.

[00101] 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.

[00102] In one 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.

[00103] 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; wherein, each instance of aryl is optionally substituted.

[00104] In one 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.

[00105] 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.

[00106] In one embodiment of a compound of Formula (I), R_1 is heteroaryl selected from pyridin-4-yl; wherein, each instance of heteroaryl is optionally substituted.

[00107] In one embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl, wherein heteroaryl is selected from 1H-imidazolyl; and, wherein, each instance of heteroaryl is optionally substituted.

[00108] In one embodiment of a compound of Formula (I), R_1 is heteroaryl-C_{1-8}alkyl selected from 1H-imidazol-1-yl-methyl; wherein, each instance of heteroaryl is optionally substituted.

[00109] 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.

[00110] In one embodiment of a compound of Formula (I), R_1 is (heteroaryl-C_{1-8}alkyl)(C_{1-8}alkyl)amino selected from (pyridin-3-yl-methyl)(methyl)amino; wherein, each instance of heteroaryl is optionally substituted.

[00111] 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.

[00112] In one 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.

[00113] 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)(C_{1-8}alkyl)amino or (hydroxy-C_{1-8}alkyl)$_2$-amino.

[00114] 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}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)(C_{1-8}alkyl)amino or (hydroxy-C_{1-8}alkyl)$_2$-amino.

[00115] 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.

[00116] In one embodiment of a compound of Formula (I), R_3 is C_{1-8}alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00117] 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.

[00118] 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, trihalo-propyl or dihalo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

[00119] 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.

[00120] In one 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.

[00121] In one embodiment of a compound of Formula (I), R_3 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00122] 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.

[00123] 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.

[00124] 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.

[00125] In one 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.

[00126] 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.

[00127] In one 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.

[00128] 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.

[00129] In one 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.

[00130] 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 each instance of aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted.

[00131] In one 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 selected from phenyl; and, wherein, each instance of aryl is optionally substituted.

[00132] 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.

[00133] In one 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.

[00134] 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.

[00135] In one 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.

[00136] 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.

[00137] In one embodiment of a compound of Formula (I), R_5 is hydroxy.

[00138] 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.

[00139] In one embodiment of a compound of Formula (I), R_5 is C_{1-8}alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00140] 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.

[00141] In one embodiment of a compound of Formula (I), R_5 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00142] 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.

[00143] In one embodiment of a compound of Formula (I), R_2 is aryl selected from phenyl; wherein, each instance of aryl is optionally substituted.

[00144] 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.

[00145] In one embodiment of a compound of Formula (I), R_2 is aryl-amino selected from phenyl-amino; wherein, each instance of aryl is optionally substituted.

[00146] In one embodiment of a compound of Formula (I), R_2 is aryl-amino-carbonyl, wherein aryl is selected from phenyl; wherein, each instance of aryl is optionally substituted.

[00147] In one 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.

[00148] In one embodiment of a compound of Formula (I), R_2 is heterocyclyl selected from 1,2,3,6-tetrahydropyridinyl, 1,3-benzodioxolyl, 3a,7a-dihydrooxazolo[4,5-*b*]pyridinyl or 2,3-dihydro-1,4-benzodioxinyl; wherein, each instance of heterocyclyl is optionally substituted.

[00149] In another embodiment of a compound of Formula (I), 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.

[00150] In one embodiment of a compound of Formula (I), 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, indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzooxazolyl, 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, [1,3]oxazolo[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 or quinoxalinyl; wherein, each instance of heteroaryl is optionally substituted.

[00151] In another embodiment of a compound of Formula (I), 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, indol-5-yl, indol-6-yl, 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, indolizin-2-yl, benzofuran-2-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, pyrrolo[1,2-*b*]pyridazin-6-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*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 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 or quinoxalin-2-yl; wherein, each instance of heteroaryl is optionally substituted.

[00152] In another embodiment of a compound of Formula (I), R_2 is substituted heteroaryl selected from 4-methylthiophen-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, 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, 4-chloro-1,3-benzothiazol-2-yl, 7-chloro-1,3-benzothiazol-2-yl, 2-methyl-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-6-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 or 8-(methylsulfanyl)imidazo[1,2-*a*]pyrazin-2-yl.

[00153] 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.

[00154] 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.

[00155] In one embodiment of a compound of Formula (I), R_6 is selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio

[00156] In one embodiment of a compound of Formula (I), R_6 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

[00157] In one embodiment of a compound of Formula (I), R_6 is C_{1-8}alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00158] 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.

[00159] In one embodiment of a compound of Formula (I), R_6 is C_{2-8}alkenyl selected from ethenyl or allyl.

[00160] 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.

[00161] 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.

[00162] In one 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.

[00163] In one embodiment of a compound of Formula (I), R_6 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00164] 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.

[00165] 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 pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl; and, wherein heteroaryl is selected from thienyl or pyridinyl.

[00166] In one 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.

[00167] In one 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.

[00168] In one embodiment of a compound of Formula (I), R_7 is aryl selected from phenyl.

[00169] In one embodiment of a compound of Formula (I), R_7 is heterocyclyl selected from pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl.

[00170] In one embodiment of a compound of Formula (I), R_7 is heterocyclyl selected from pyrrolidin-1-yl or 1,2,3,6-tetrahydropyridin-4-yl.

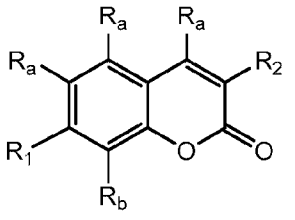
[00171] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from thienyl or pyridinyl.

[00172] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from pyridinyl.

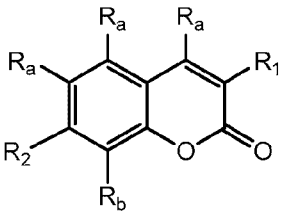
[00173] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from thien-2-yl or pyridin-2-yl.

[00174] In one embodiment of a compound of Formula (I), R_7 is heteroaryl selected from pyridin-2-yl.

[00175] In one embodiment of a compound of Formula (I), the compound is selected from Formula (Ia) or Formula (Ib):



(Ia), and



(Ib);

[00176] or a form thereof, wherein all variables are as previously defined.

[00177] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from (methyl)$_2$-amino and R_2 is benzothiazol-2-yl optionally substituted with one R_6 substituent, then R_6 is other than chloro.

[00178] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from (methyl)$_2$-amino or (2-fluoro-ethyl)(methyl)amino, then R_2 is benzothiazol-2-yl substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent.

[00179] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is piperazin-1-yl substituted with one R_3 substituent selected from methyl, 2-fluoro-ethyl, 2-hydroxy-ethyl or 3-hydroxy-propyl; or, one R_4 substituent selected from 3-(4-methyl-phenyl-sulfonyloxy)-propyl, then R_2 is benzothiazol-2-yl substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent.

[00180] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is piperazin-1-yl substituted with one R_3 substituent selected from 2-fluoro-ethyl and R_2 is imidazo[1,2-*a*]pyridin-2-yl optionally substituted with one R_6 substituent, then R_6 is other than chloro.

[00181] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is (2-fluoro-ethyl)(methyl)amino and R_2 is [1,3,4]oxadiazol-2-yl optionally substituted with one R_7 substituent, then R_7 is other than thien-2-yl.

[00182] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is piperazin-1-yl substituted with one R_3 substituent selected from 3-fluoro-propyl and R_2 is thiazol-2-yl optionally substituted with two R_6 substituents, then R_6 is not simultaneously methyl and buta-1,3-dienyl.

[00183] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from methyl-amino or (methyl)$_2$-amino, then R_2 is benzooxazol-2-yl substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent.

[00184] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from (methyl)$_2$-amino and R_2 is benzooxazol-2-yl optionally substituted with one R_6 substituent, then R_6 is other than chloro.

[00185] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is piperazin-1-yl substituted with one R_3 substituent selected from methyl, then

R_2 is benzooxazol-2-yl substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent.

[00186] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from (methyl)$_2$-amino, then R_2 is 1*H*-benzoimidazol-2-yl substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent.

[00187] In one embodiment of a compound of Formula (I), when w_1 is C-R_1, w_2 is C-R_2 and R_1 is selected from (methyl)$_2$-amino and R_2 is 1*H*-benzoimidazol-2-yl substituted with one R_6 substituent, then R_6 is other than methyl.

[00188] In certain embodiments, the compound of Formula (I) is other than:

3-benzothiazol-2-yl-7-[4-(2-fluoro-ethyl)-piperazin-1-yl]-chromen-2-one,

3-benzothiazol-2-yl-7-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-chromen-2-one,

3-(6-chloro-imidazo[1,2-a]pyridin-2-yl)-7-[4-(2-fluoro-ethyl)-piperazin-1-yl]-chromen-2-one,

3-benzothiazol-2-yl-7-(4-methyl-piperazin-1-yl)-chromen-2-one,

3-benzothiazol-2-yl-7-[(2-fluoro-ethyl)-methyl-amino]-chromen-2-one,

7-[(2-fluoro-ethyl)-methyl-amino]-3-(5-thiophene-2-yl-[1,3,4]oxadiazol-2-yl)-chromen-2-one,

3-(4-buta-1,3-dienyl-5-methyl-thiazol-2-yl)-7-[4-(3-fluoro-propyl)-piperazin-1-yl]-chromen-2-one,

toluene-4-sulfonic acid 3-[4-(3-benzothiazol-2-yl-2-oxo-2H-chromen-7-yl)-piperazin-1-yl]-propyl ester,

3-benzothiazol-2-yl-7-[4-(3-hydroxy-propyl)-piperazin-1-yl]-chromen-2-one,

3-benzooxazol-2-yl-7-(4-methyl-piperazin-1-yl)-chromen-2-one,

7-dimethylamino-3-(1-methyl-1*H*-benzoimidazol-2-yl)-chromen-2-one,

3-(1*H*-benzoimidazol-2-yl)-7-dimethylamino-chromen-2-one,

3-(6-chloro-benzothiazol-2-yl)-7-dimethylamino-chromen-2-one,

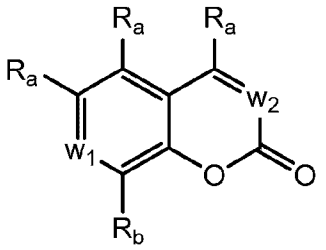
3-benzothiazol-2-yl-7-dimethylamino-chromen-2-one,

3-benzooxazol-2-yl-7-dimethylamino-chromen-2-one,

3-benzooxazol-2-yl-7-methylamino-chromen-2-one, and

3-(5-chloro-benzooxazol-2-yl)-7-dimethylamino-chromen-2-one.

[00189] Further provided herein are compounds of Formula (I):



(I)

[00190] or a form thereof, wherein:

[00191] w_1 and w_2 are C-R_1 or C-R_2; wherein, one of w_1 and w_2 is C-R_1 and the other is C-R_2, provided that, when w_1 is C-R_1, then w_2 is C-R_2; or, when w_1 is C-R_2, then w_2 is C-R_1;

[00192] R_1 is 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, 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)$_2$-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-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino,
(hydroxy-C_{1-8}alkyl)$_2$-amino-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, 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;

[00193] wherein, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two or three R_3 substituents and one additional, optional R_4 substituent; and,

[00194] wherein, alternatively, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

[00195] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00196] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent;

[00197] R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

[00198] R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

[00199] 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, $(C_{1-8}alkyl)_2$-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;

[00200] 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, 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;

[00201] 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;

[00202] R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, halo-C_{1-8}alkyl, hydroxy-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; and,

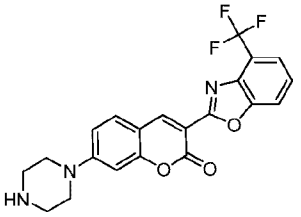
[00203] R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00204] In one embodiment of a compound of Formula (I), R_3 is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, 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}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.

[00205] In one embodiment of a compound of Formula (I), R_6 is, in each instance, independently selected from hydroxy, cyano, nitro, halo-C_{1-8}alkyl, hydroxy-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.

[00206] In one embodiment of a compound of Formula (I), R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl or heterocyclyl.

[00207] In one embodiment of a compound of Formula (I), the compound is selected from the group consisting of:



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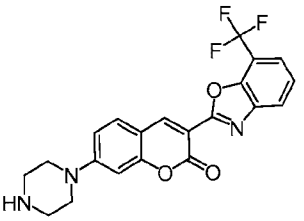

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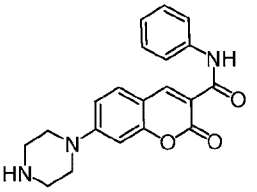

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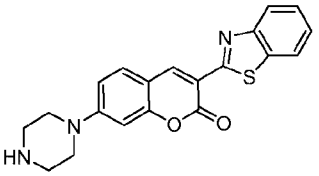

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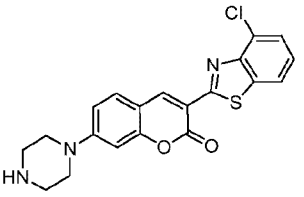

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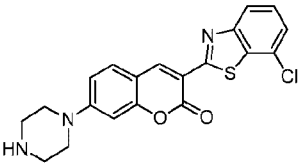

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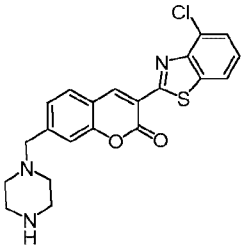

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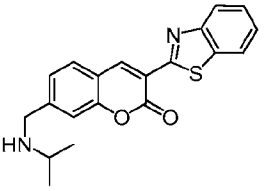

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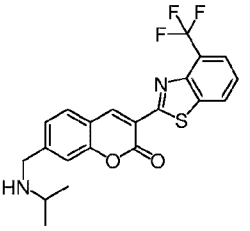

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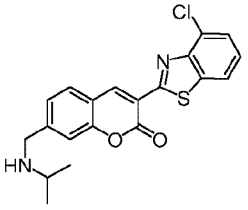

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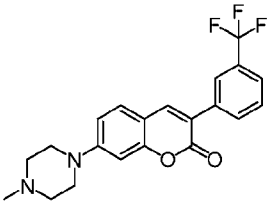

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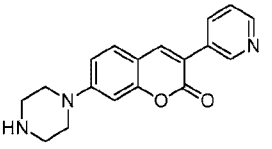

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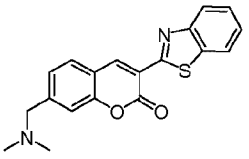

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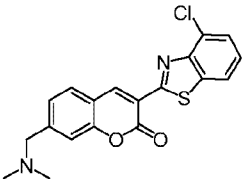

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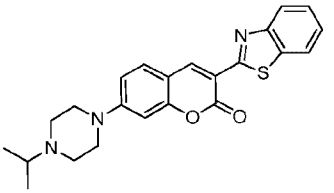

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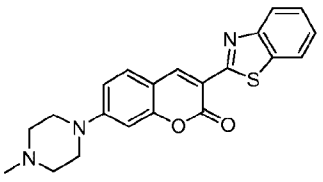

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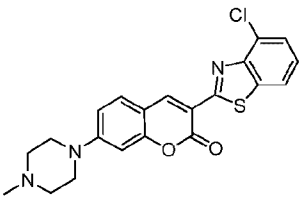

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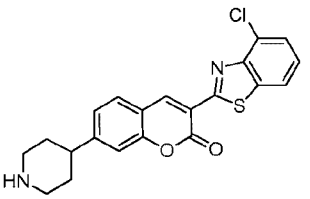

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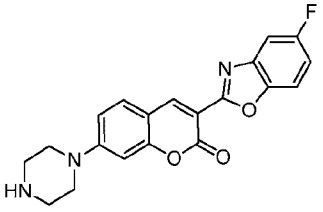

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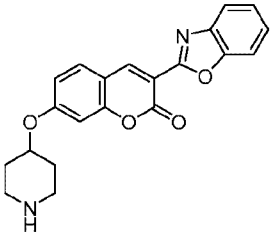

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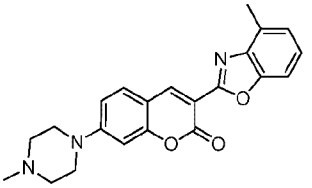

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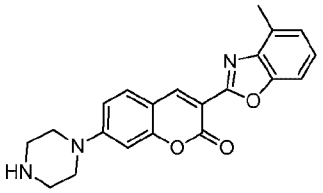

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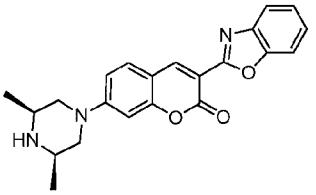

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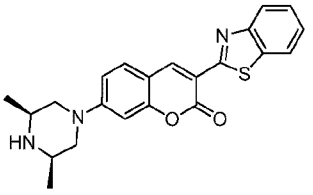

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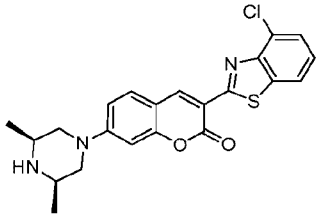

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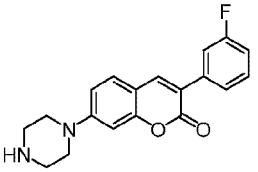

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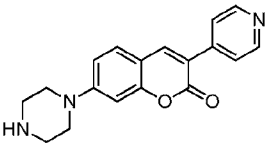

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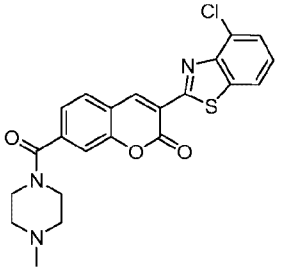

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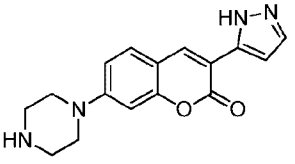

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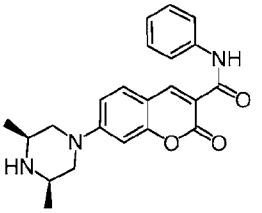

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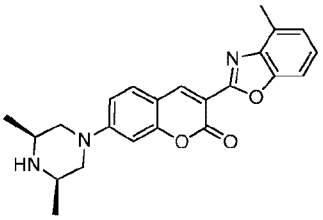

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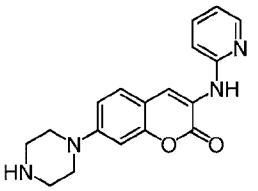

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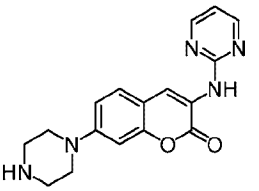

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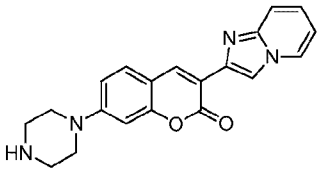

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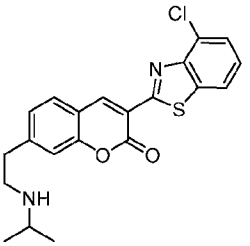

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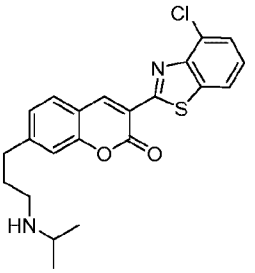

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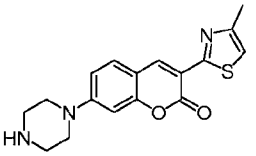

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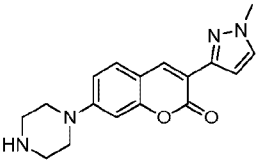

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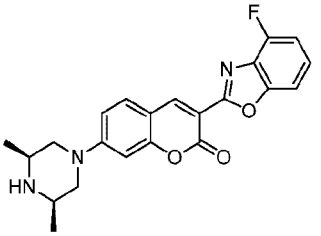

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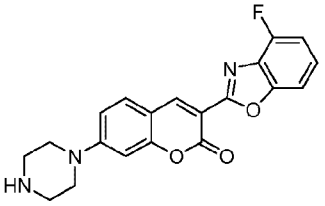

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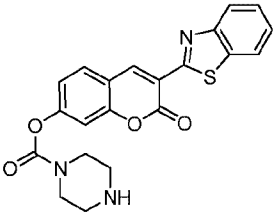

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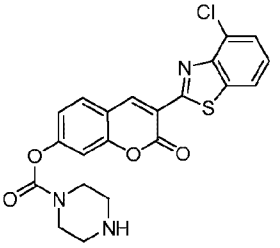

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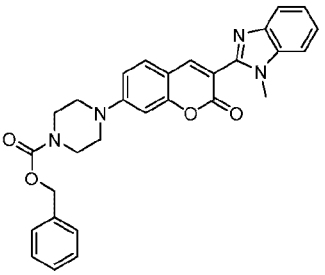

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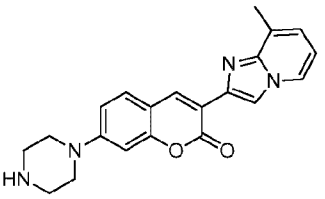

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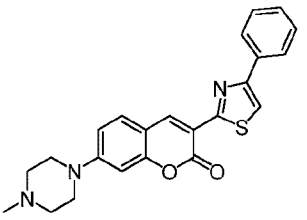

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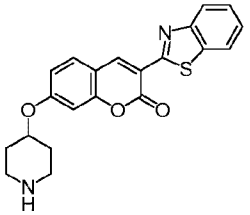

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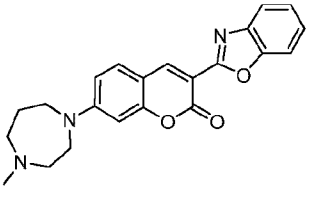

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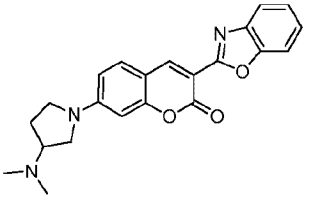

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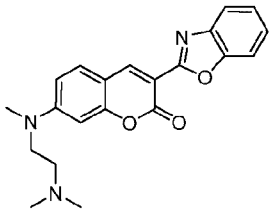

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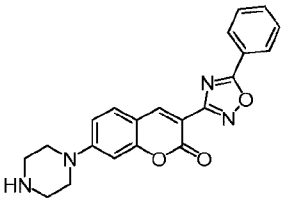

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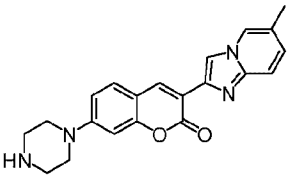

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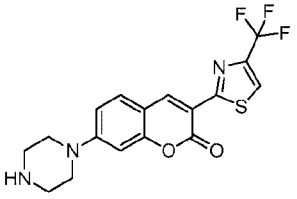

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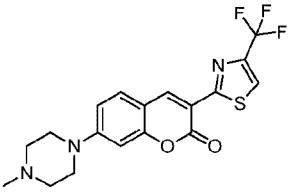

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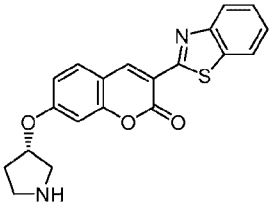

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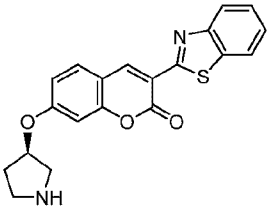

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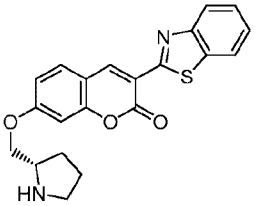

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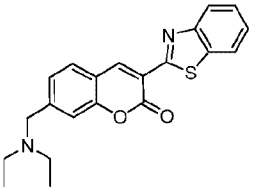

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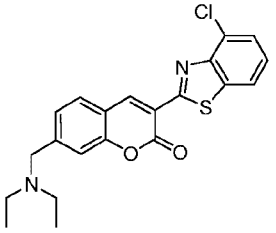

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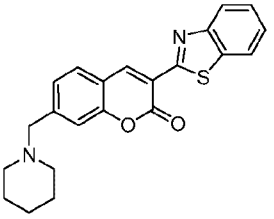

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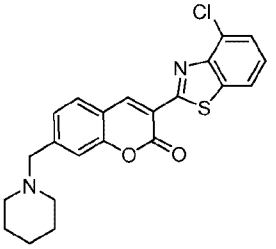

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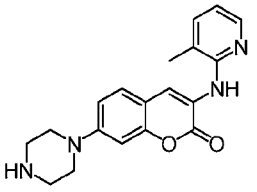

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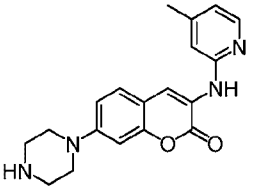

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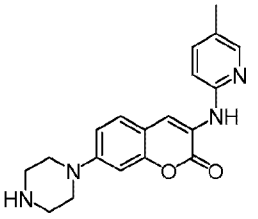

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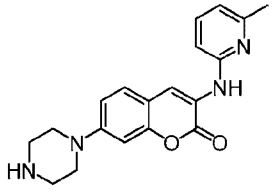

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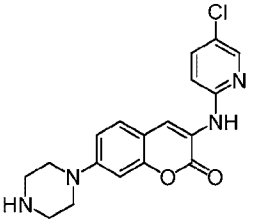

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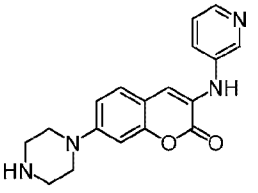

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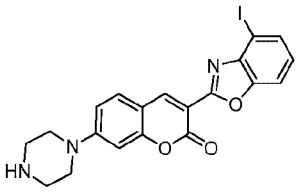

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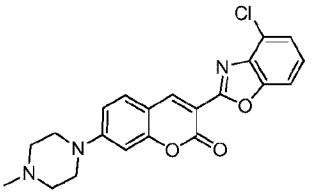

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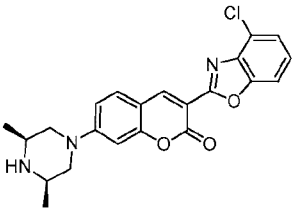

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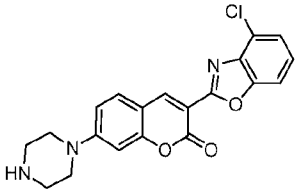

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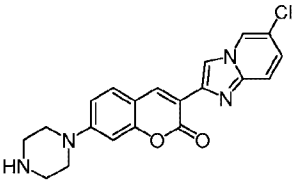

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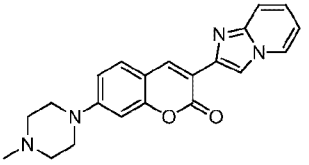

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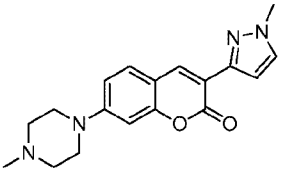

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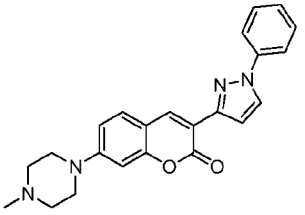

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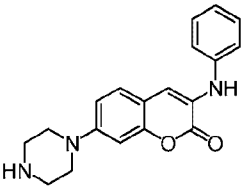

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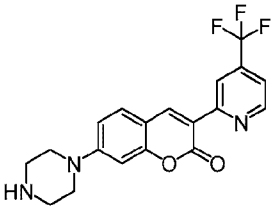

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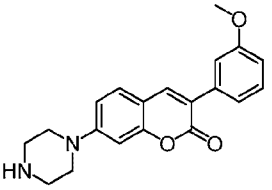

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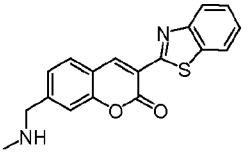

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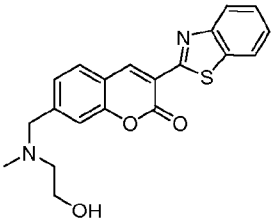

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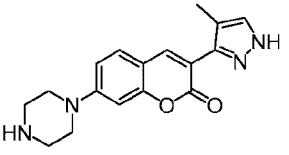

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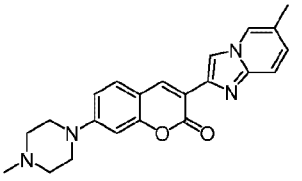

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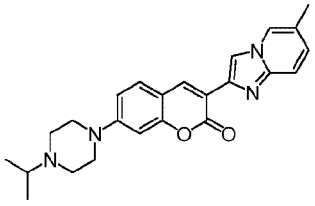

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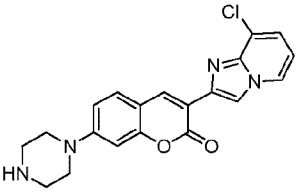

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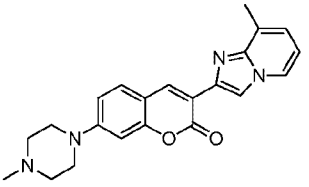

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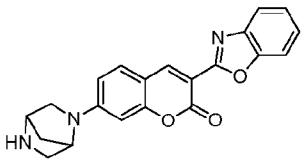

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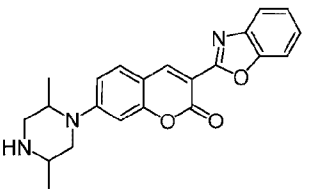

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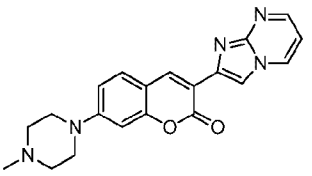

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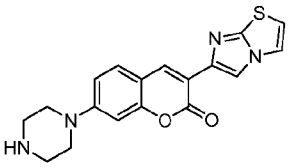

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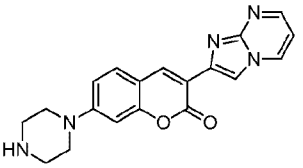

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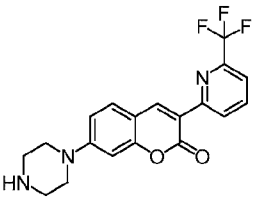

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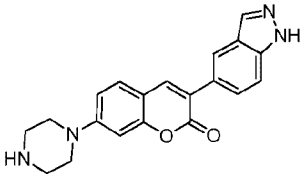

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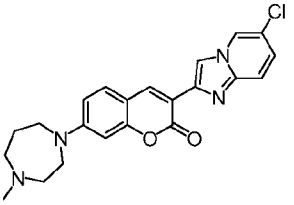

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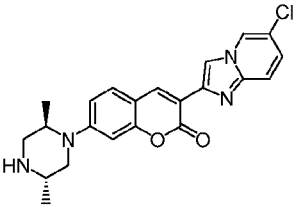

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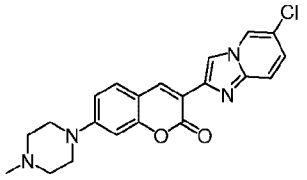

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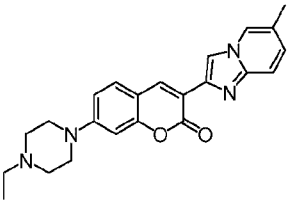

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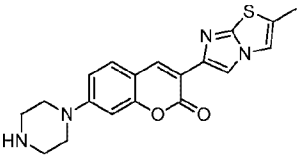

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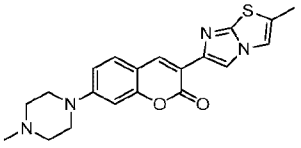

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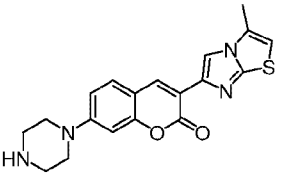

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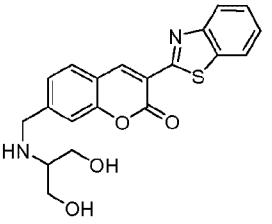

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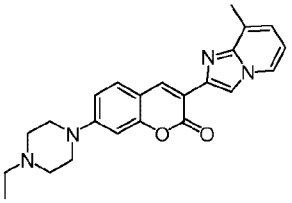

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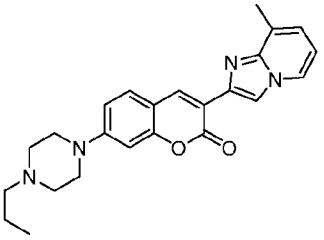

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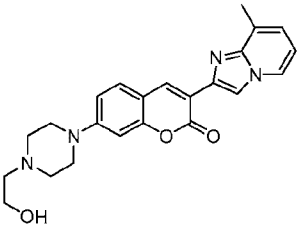

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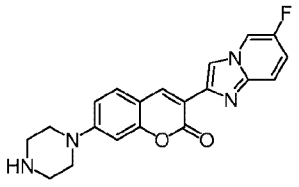

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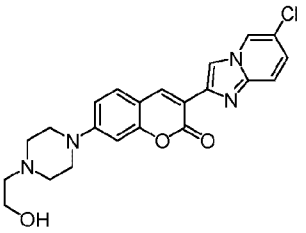

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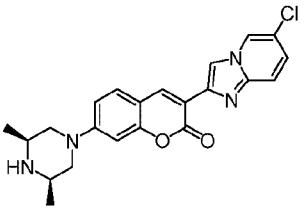

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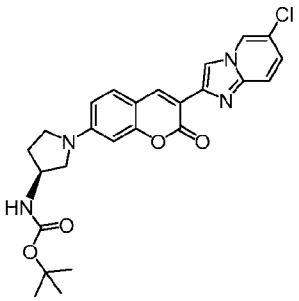

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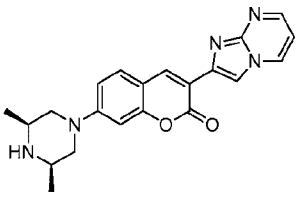

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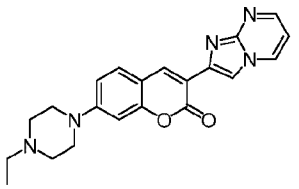

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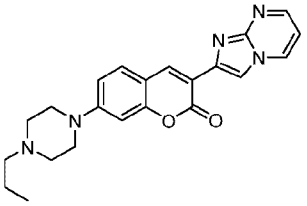

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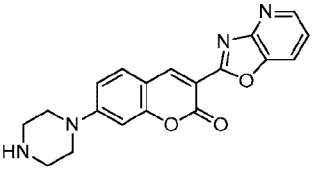

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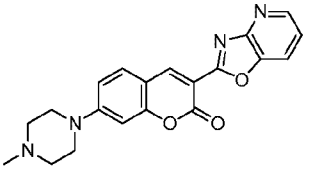

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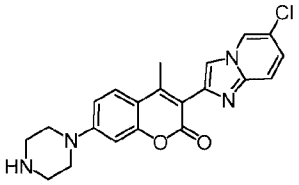

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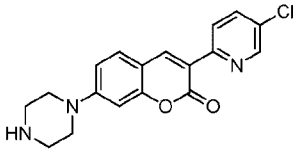

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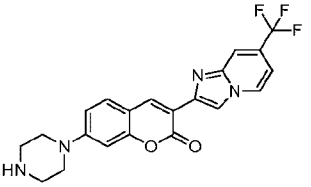

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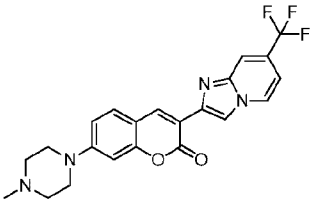

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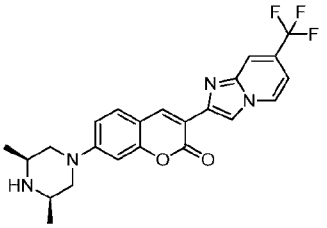

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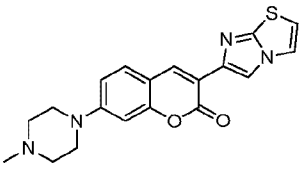

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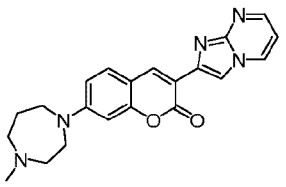

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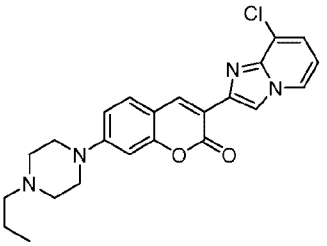

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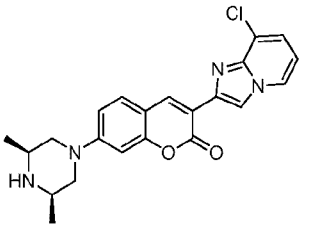

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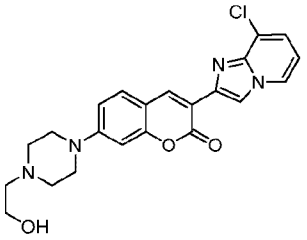

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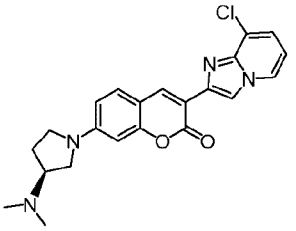

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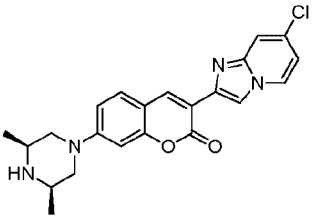

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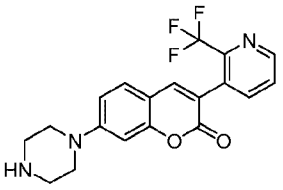

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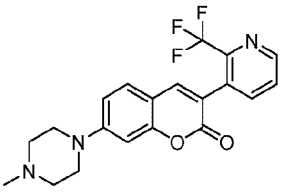

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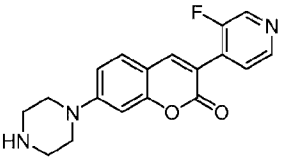

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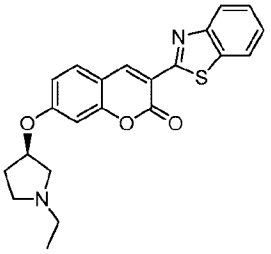

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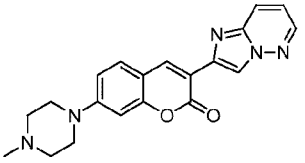

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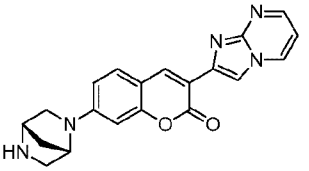

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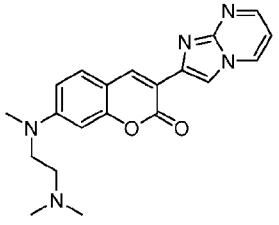

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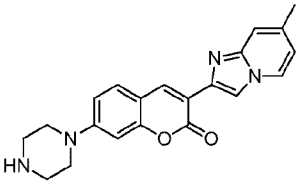

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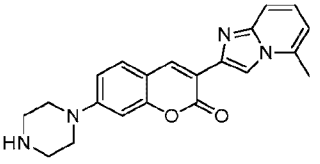

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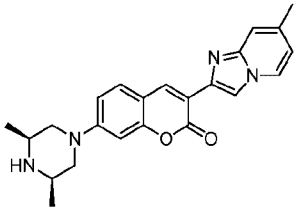

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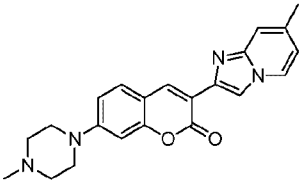

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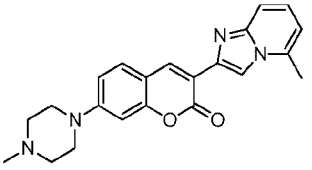

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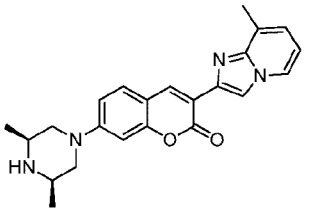

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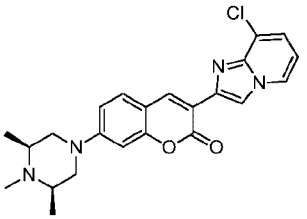

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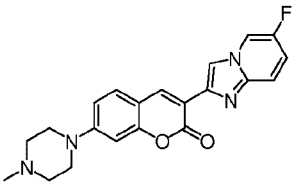

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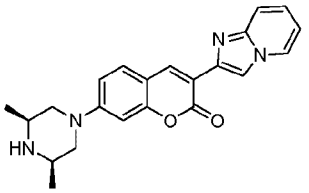

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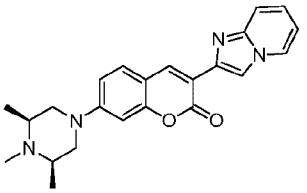

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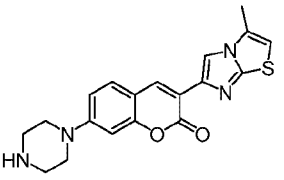

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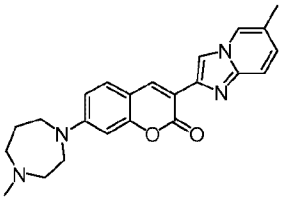

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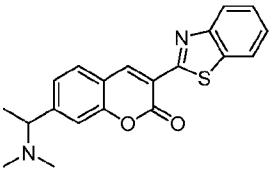

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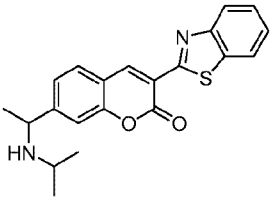

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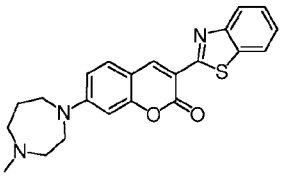

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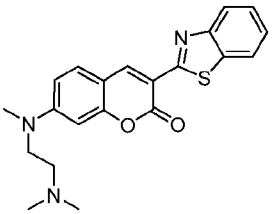

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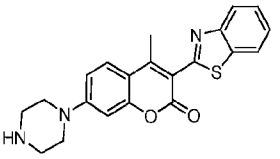

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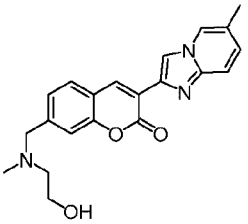

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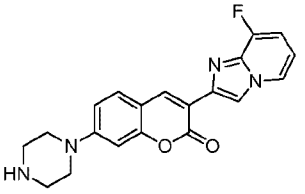

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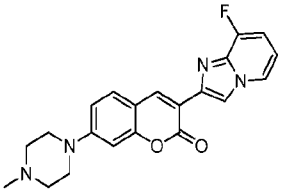

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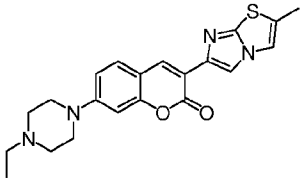

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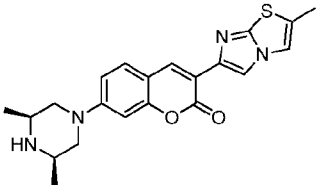

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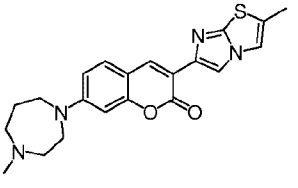

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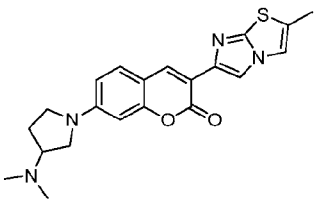

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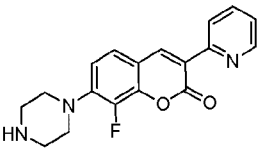

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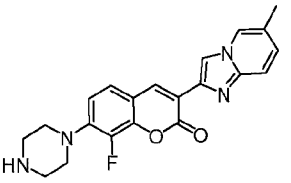

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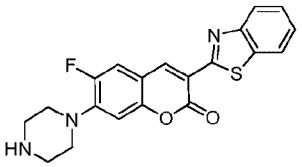

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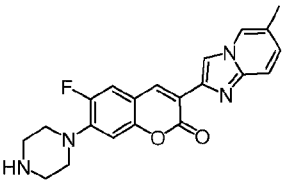

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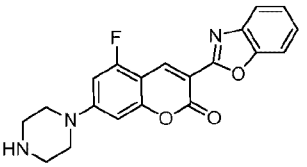

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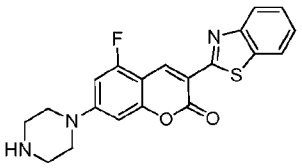

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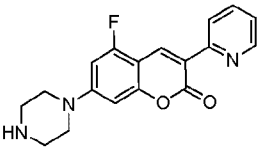

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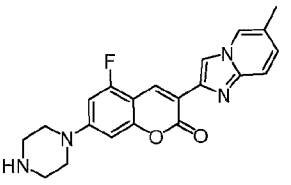

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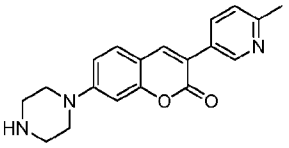

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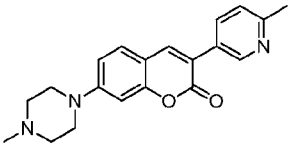

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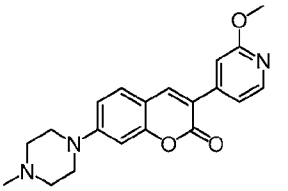

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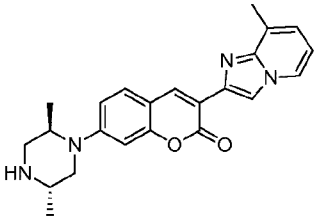

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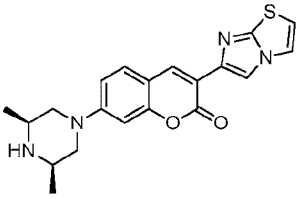

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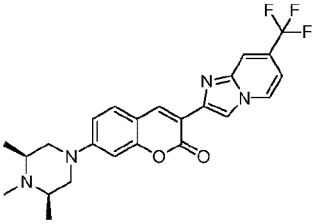

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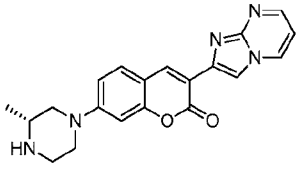

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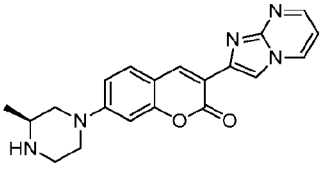

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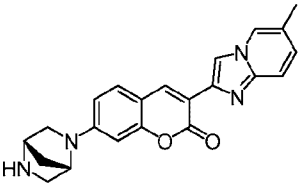

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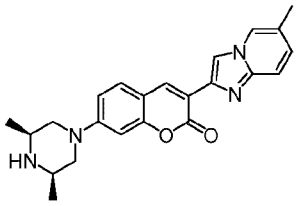

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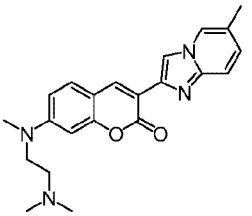

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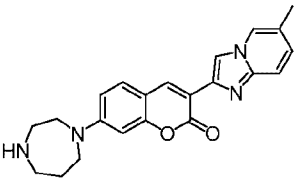

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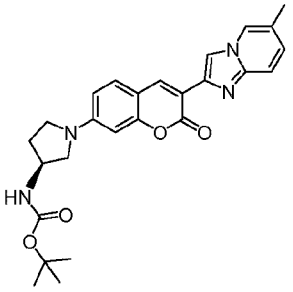

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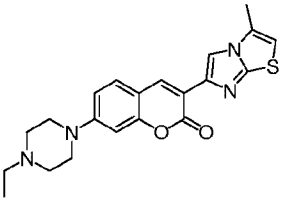

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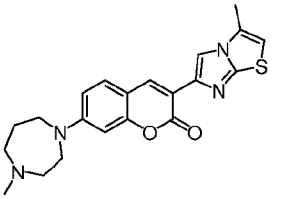

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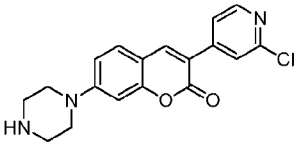

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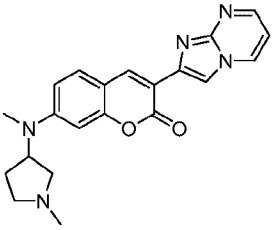

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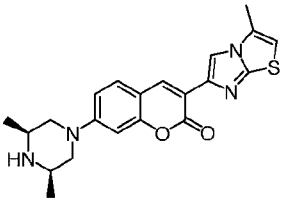

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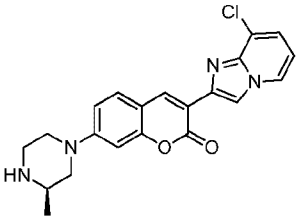

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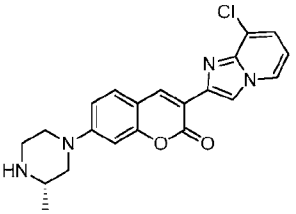

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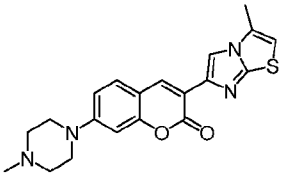

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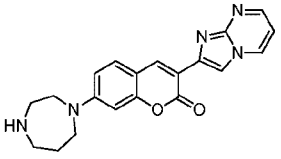

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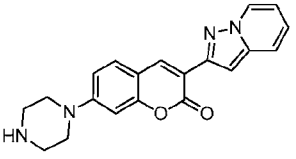

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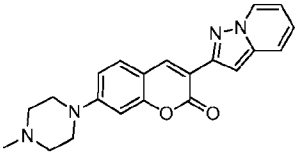

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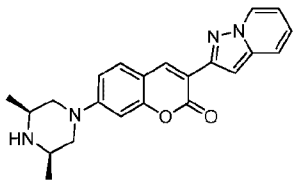

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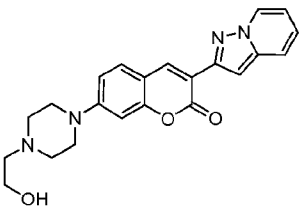

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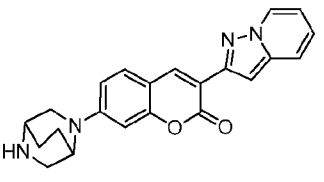

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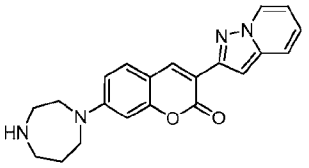

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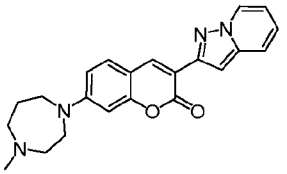

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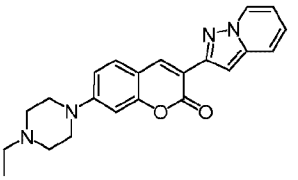

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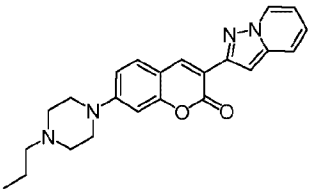

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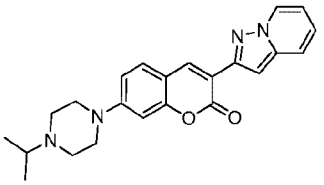

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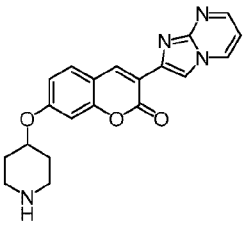

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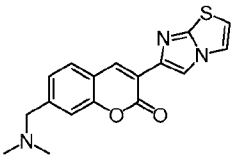

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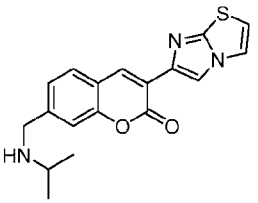

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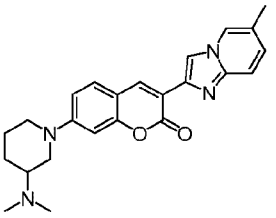

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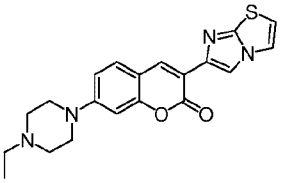

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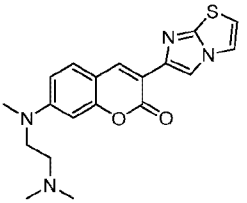

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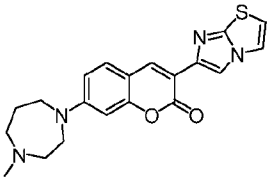

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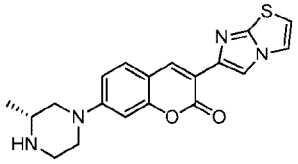

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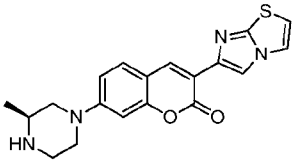

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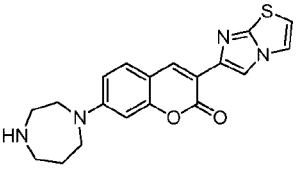

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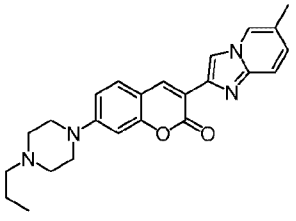

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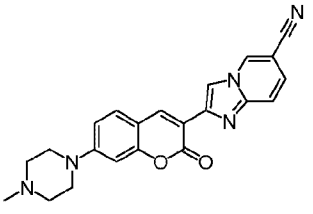

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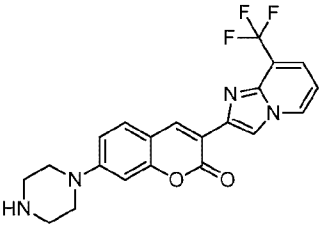

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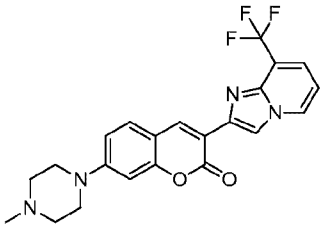

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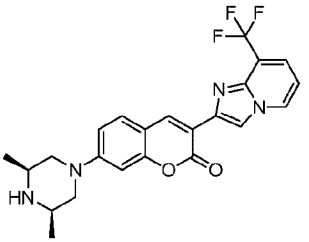

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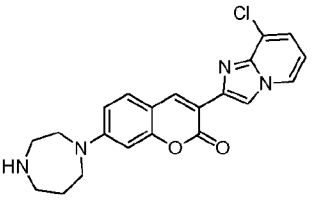

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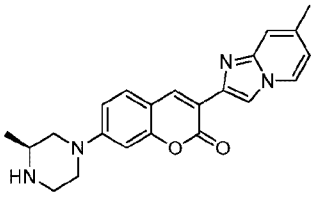

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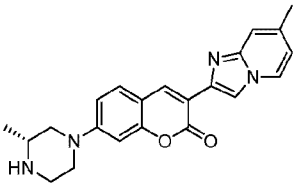

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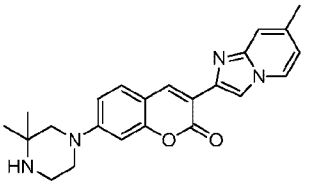

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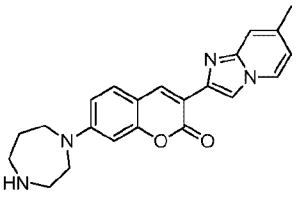

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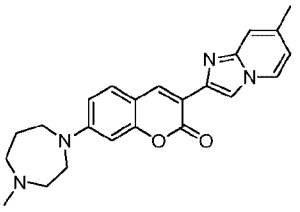

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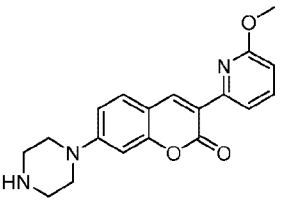

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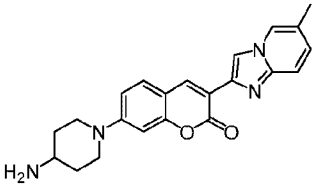

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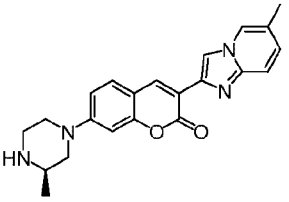

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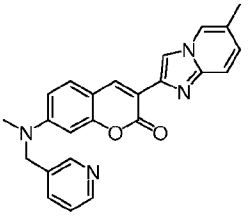

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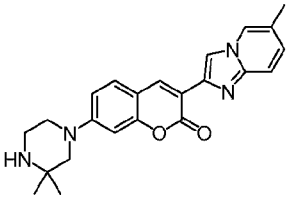

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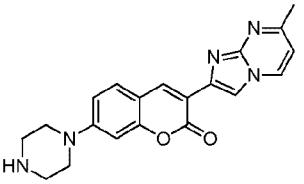

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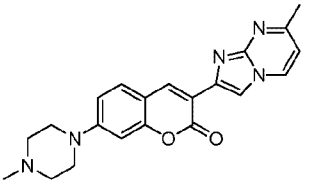

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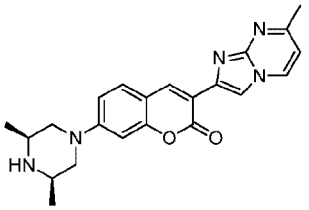

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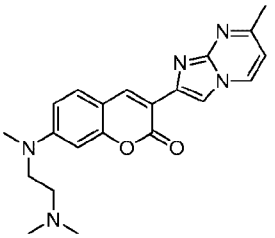

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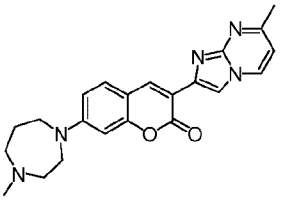

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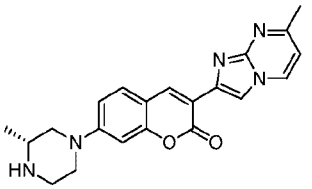

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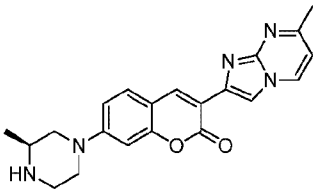

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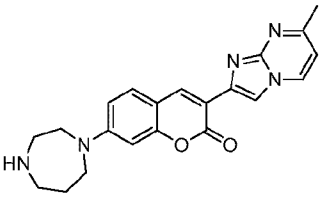

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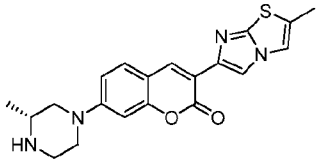

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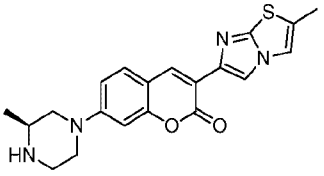

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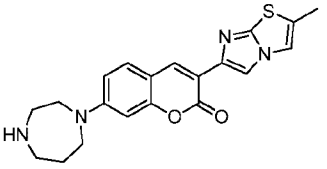

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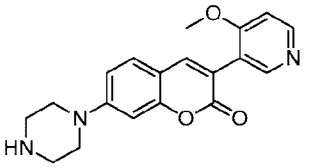

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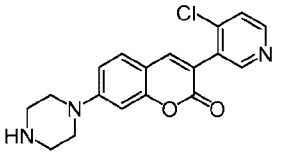

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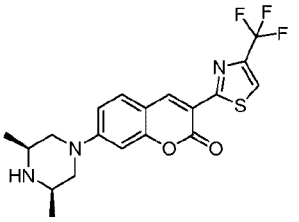

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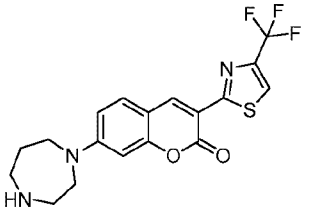

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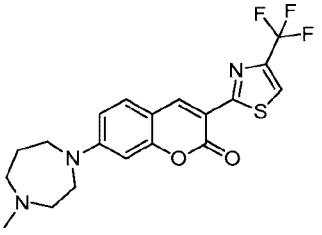

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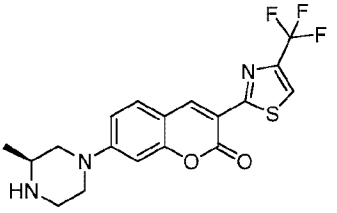

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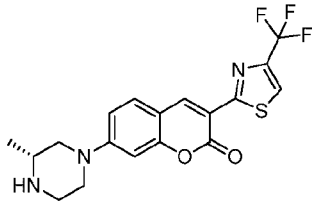

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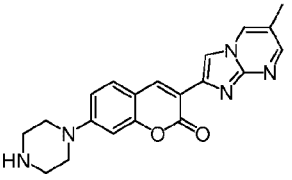

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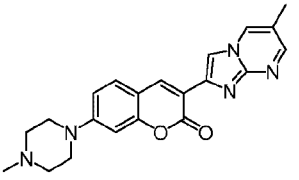

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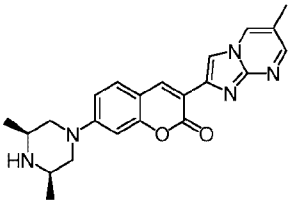

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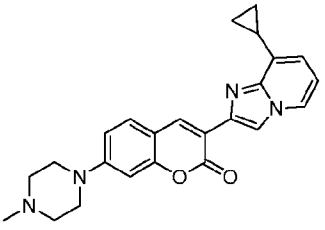

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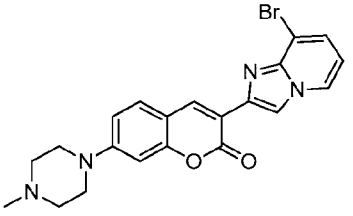

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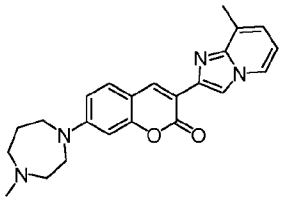

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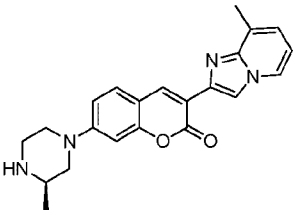

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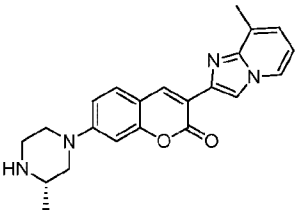

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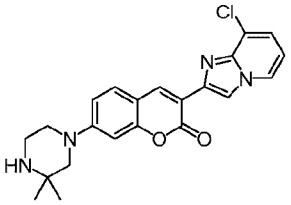

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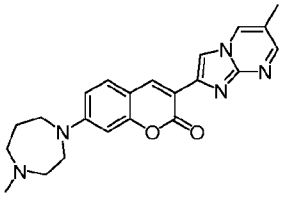

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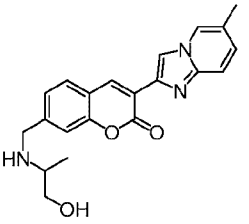

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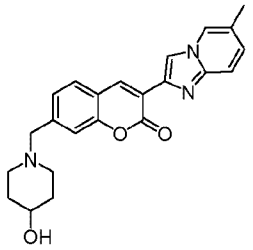

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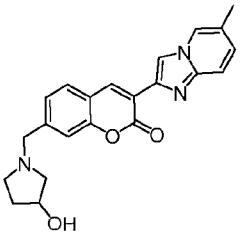

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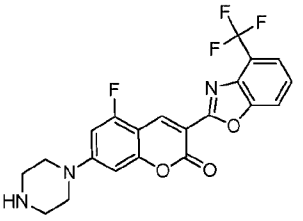

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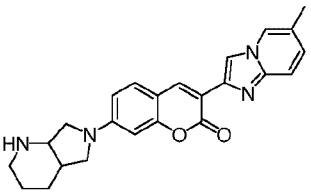

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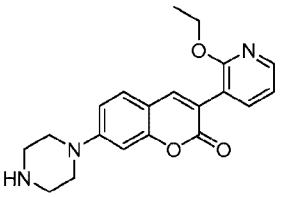

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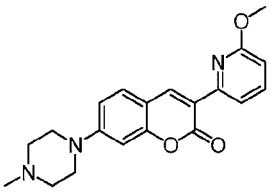

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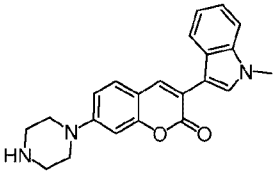

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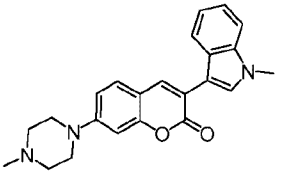

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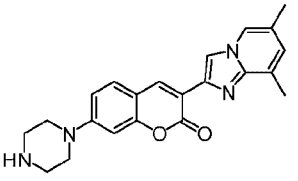

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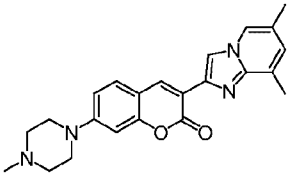

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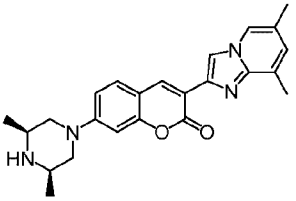

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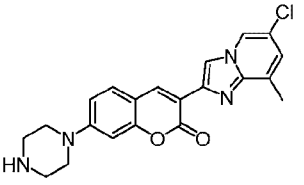

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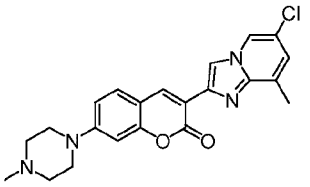

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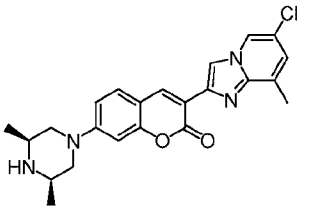

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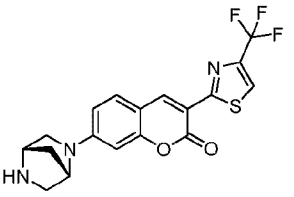

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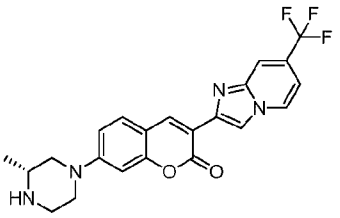

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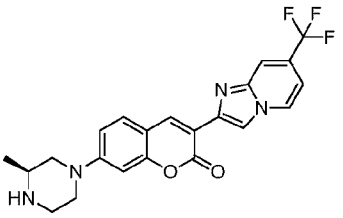

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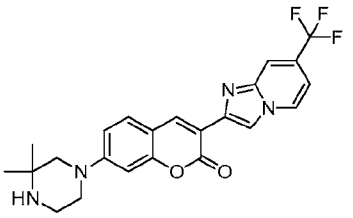

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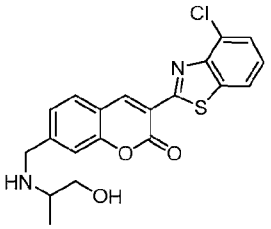

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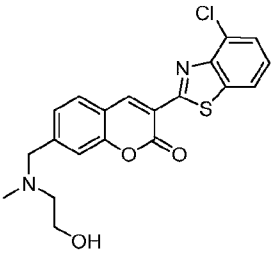

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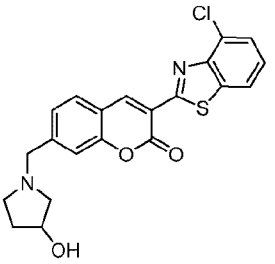

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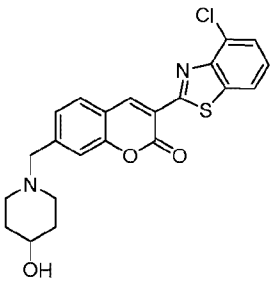

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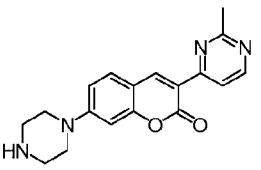

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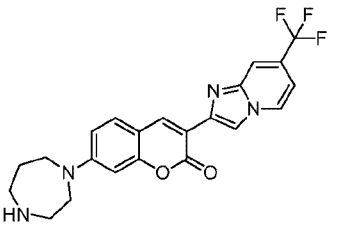

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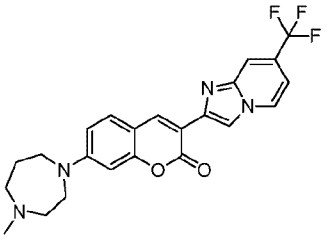

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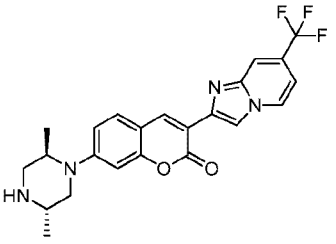

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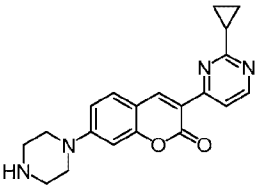

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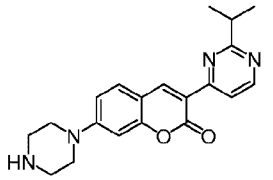

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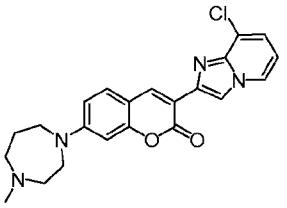

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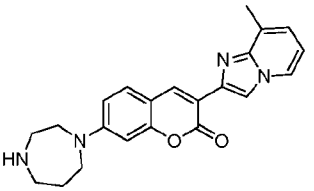

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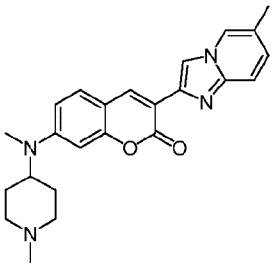

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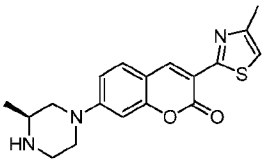

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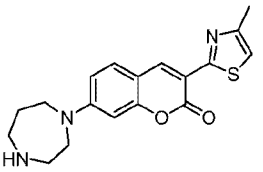

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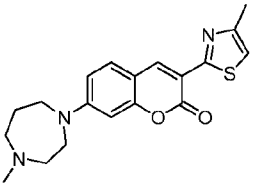

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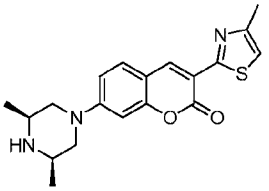

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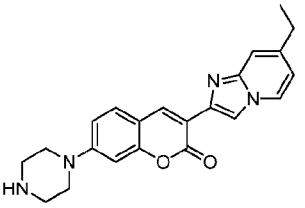

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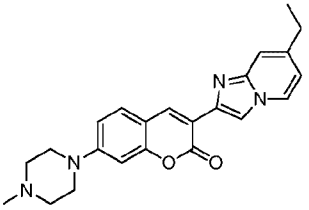

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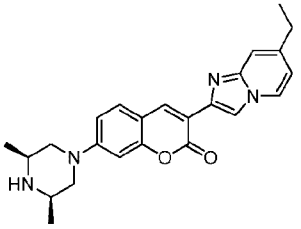

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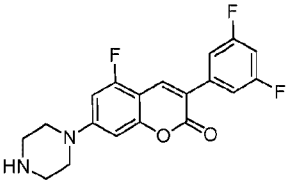

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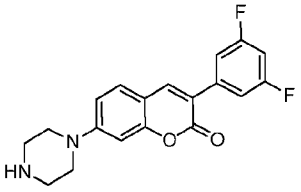

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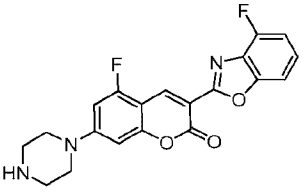

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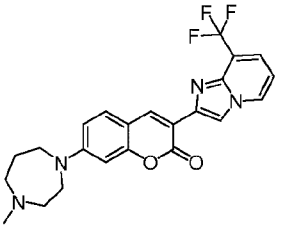

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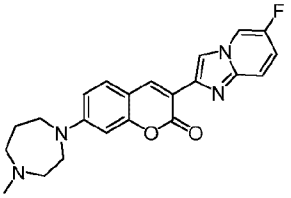

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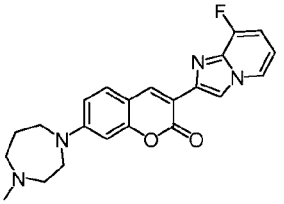

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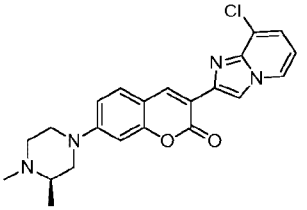

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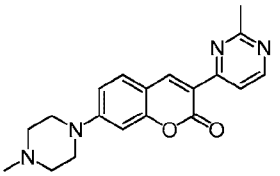

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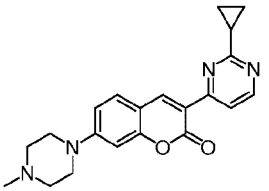

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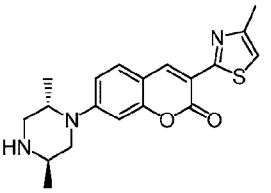

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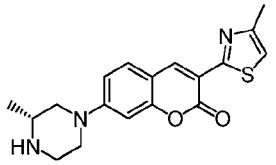

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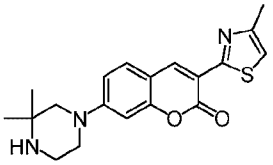

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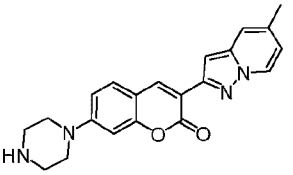

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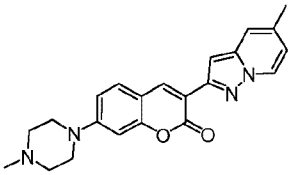

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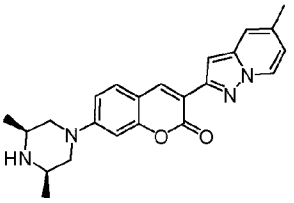

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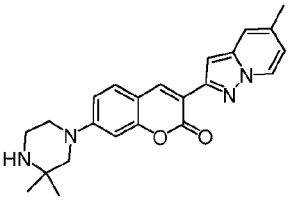

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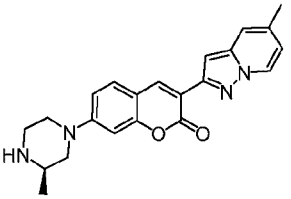

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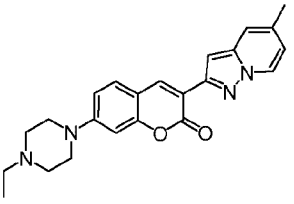

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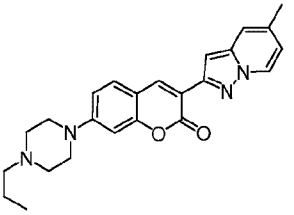

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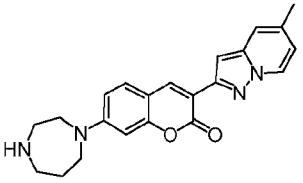

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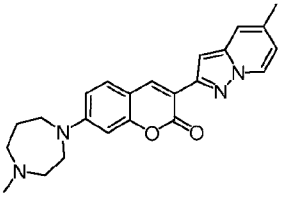

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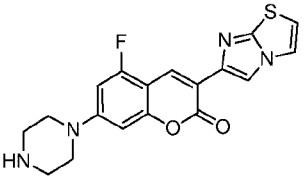

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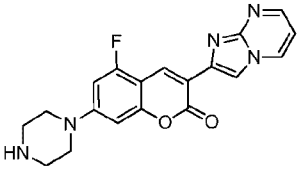

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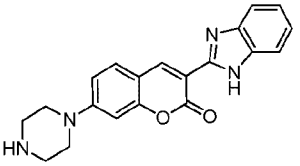

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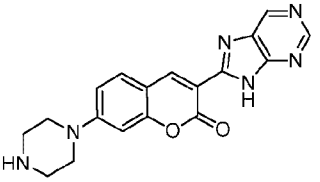

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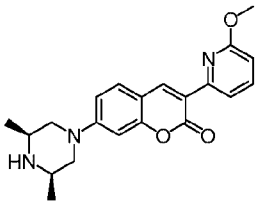

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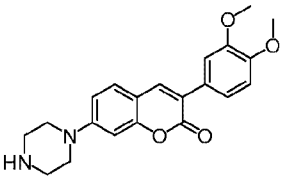

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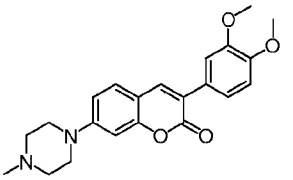

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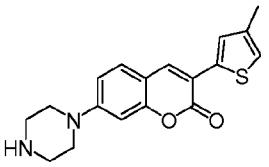

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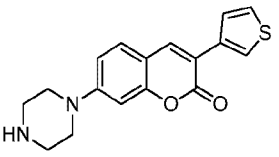

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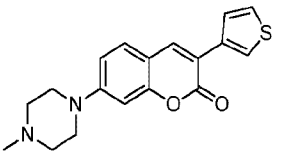

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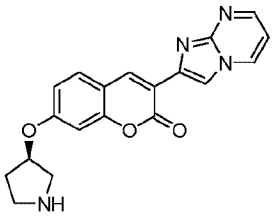

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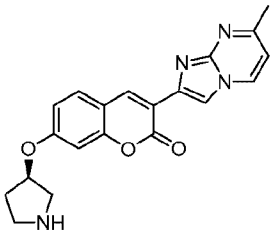

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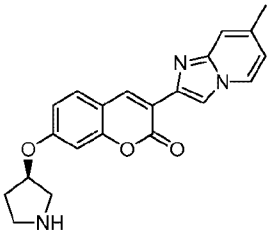

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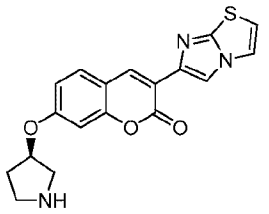

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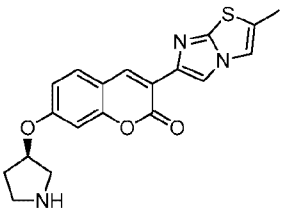

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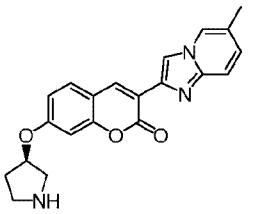

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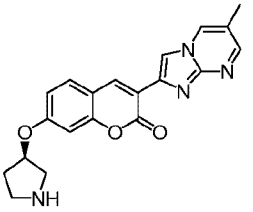

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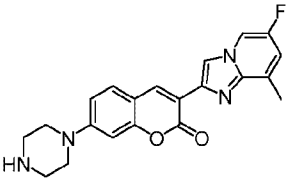

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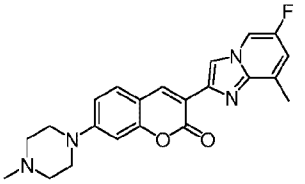

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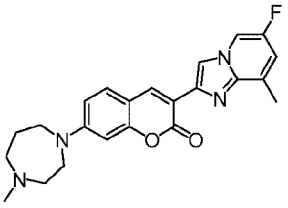

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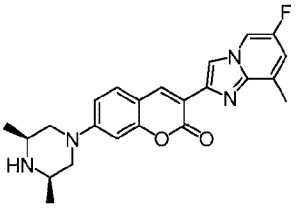

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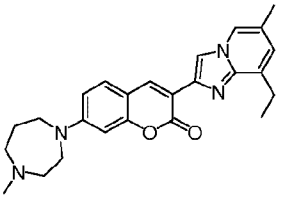

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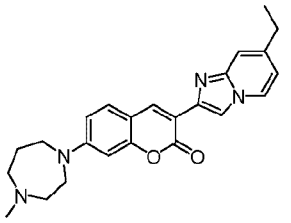

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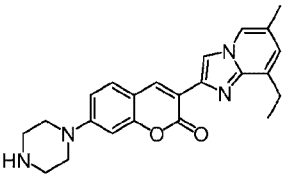

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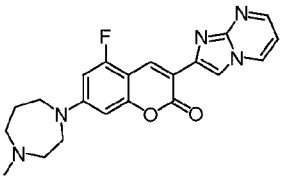

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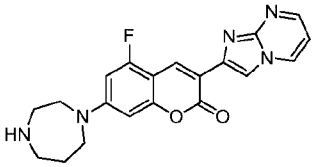

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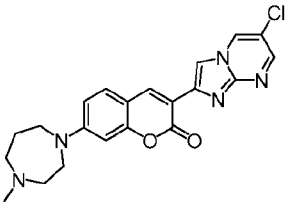

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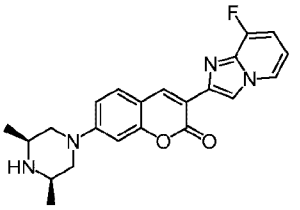

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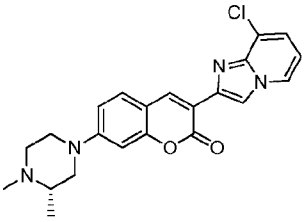

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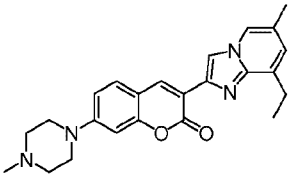

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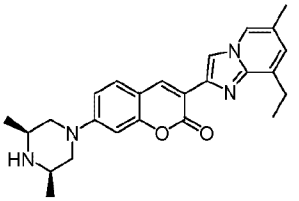

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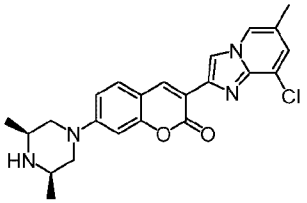

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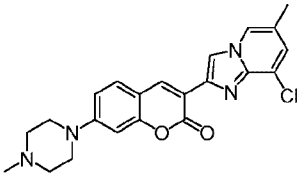

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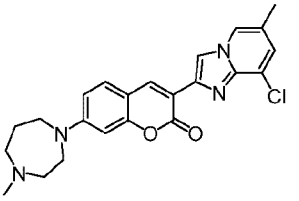

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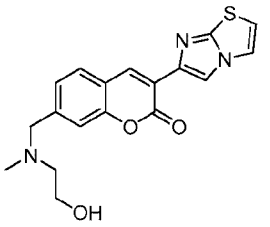

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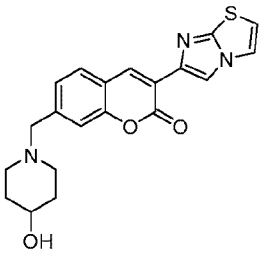

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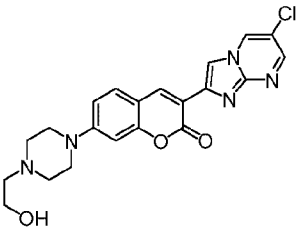

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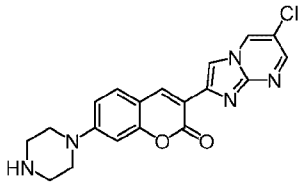

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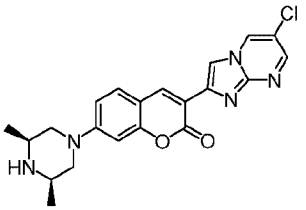

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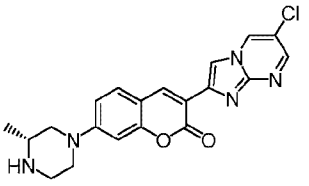

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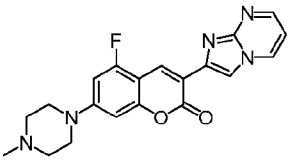

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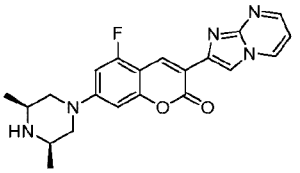

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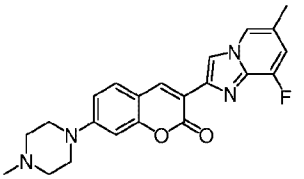

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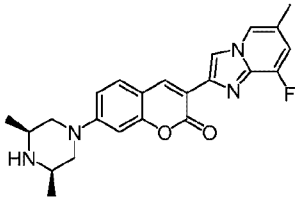

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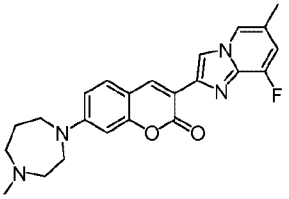

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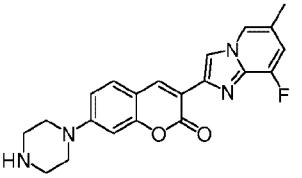

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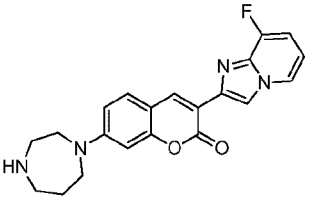

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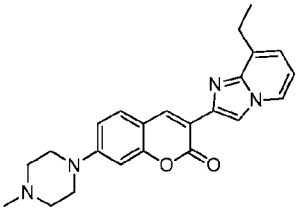

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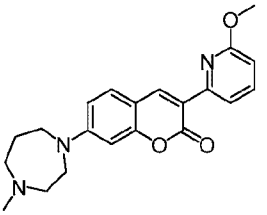

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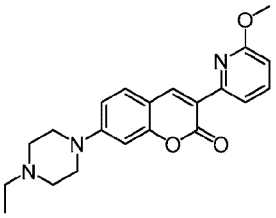

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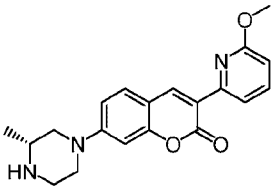

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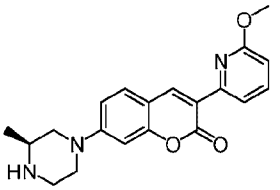

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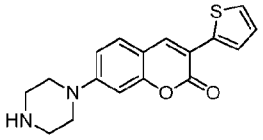

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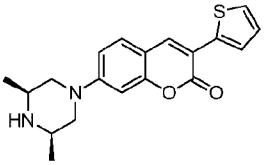

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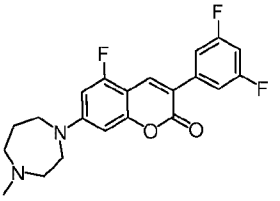

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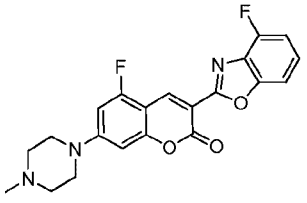

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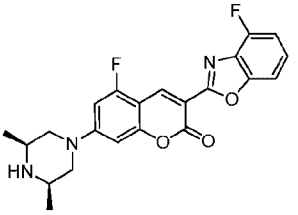

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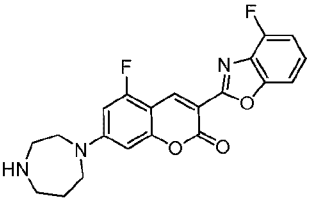

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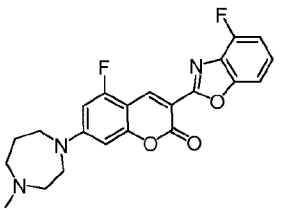

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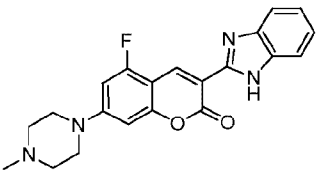

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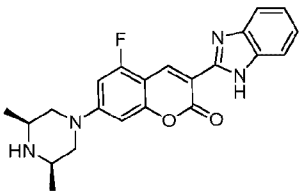

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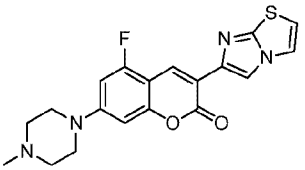

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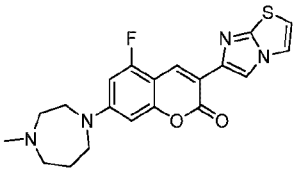

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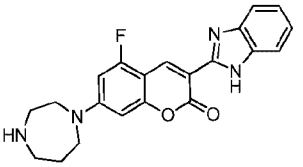

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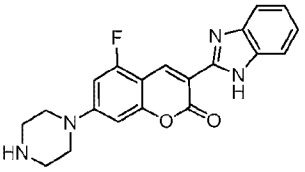

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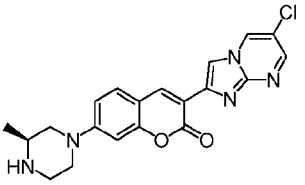

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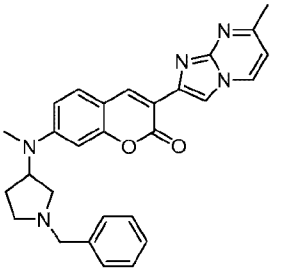

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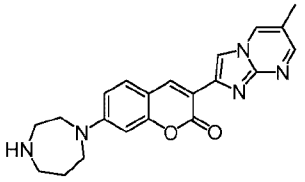

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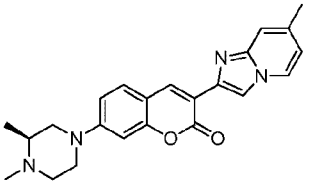

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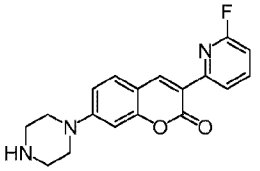

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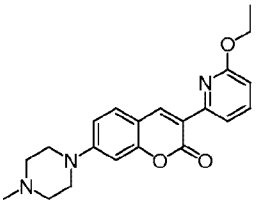

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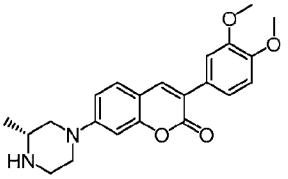

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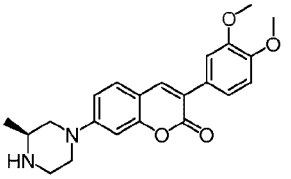

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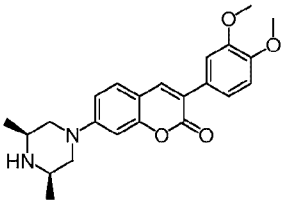

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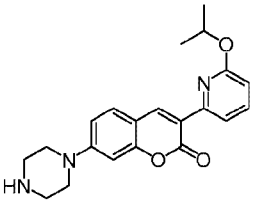

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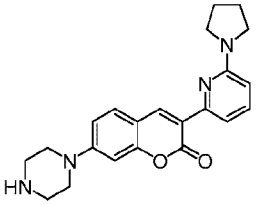

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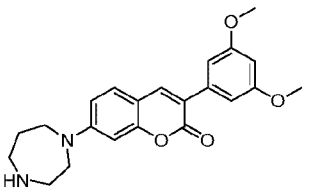

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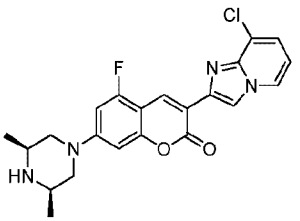

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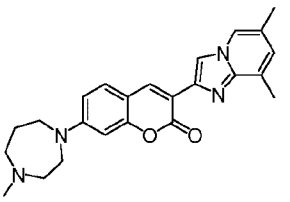

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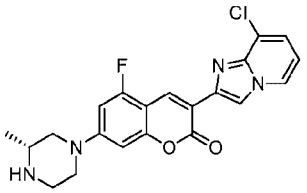

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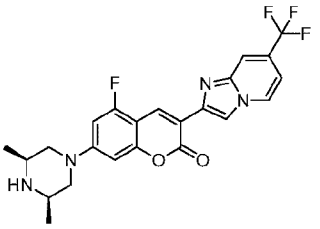

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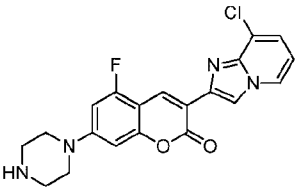

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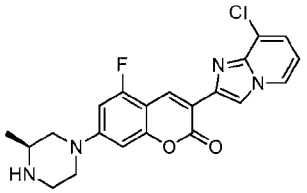

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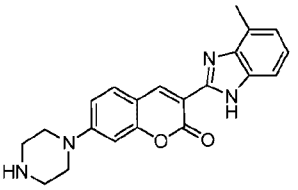

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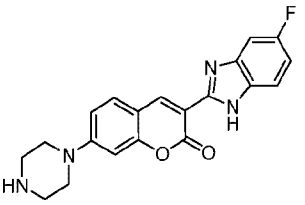

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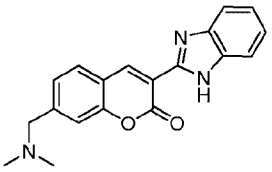

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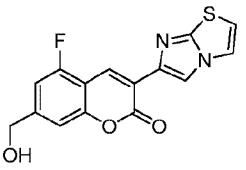

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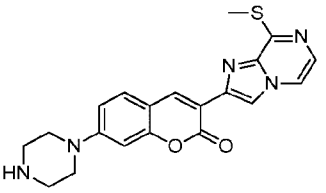

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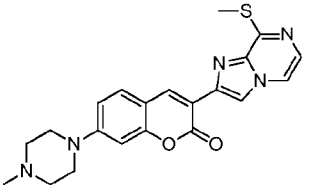

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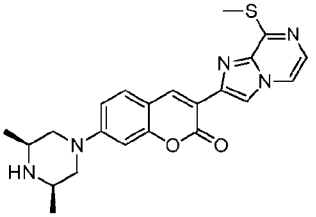

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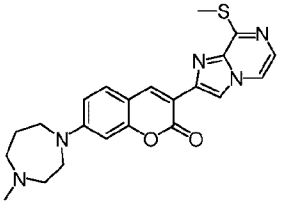

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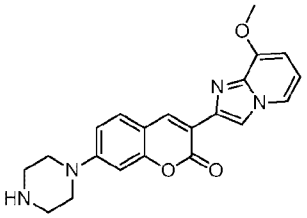

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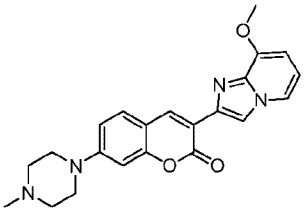

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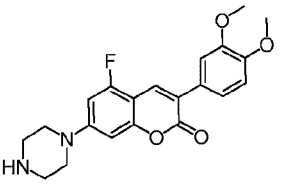

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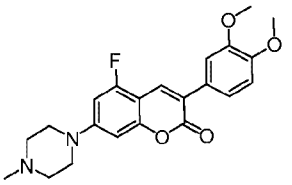

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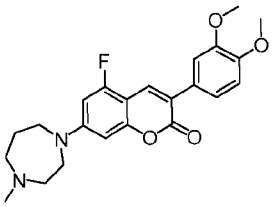

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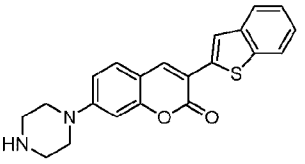

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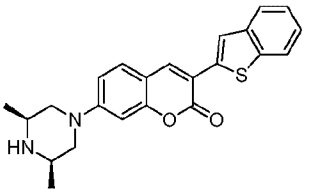

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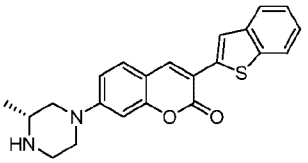

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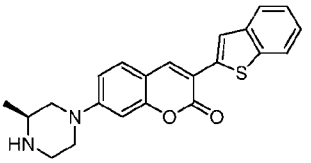

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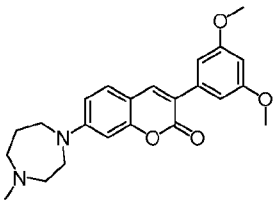

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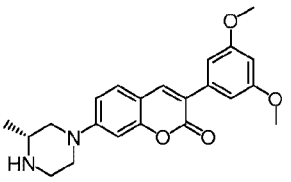

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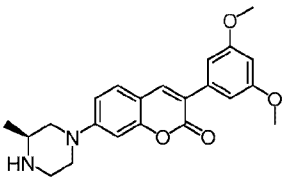

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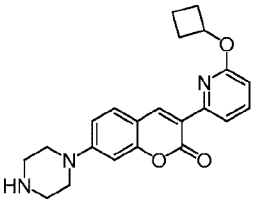

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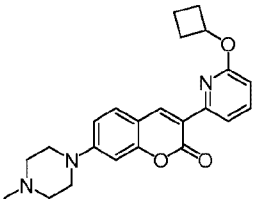

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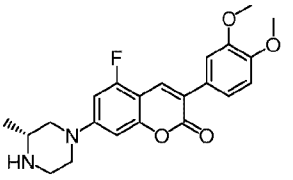

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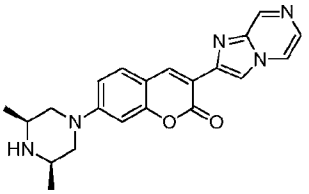

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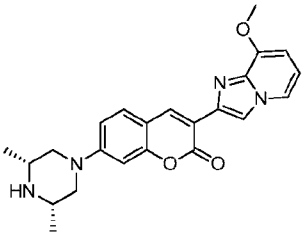

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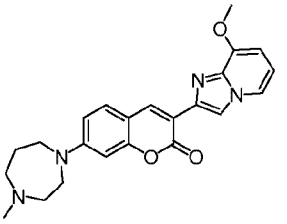

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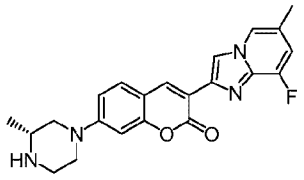

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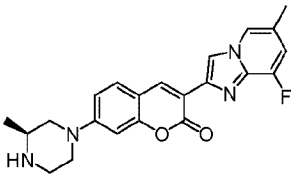

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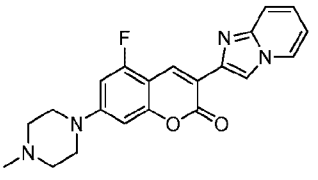

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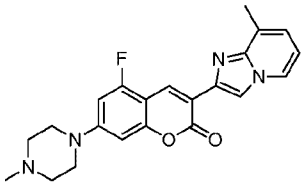

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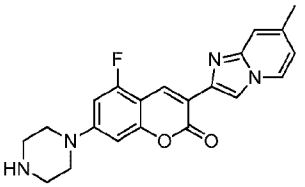

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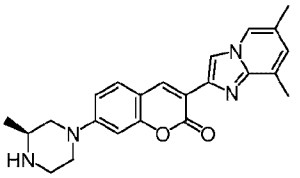

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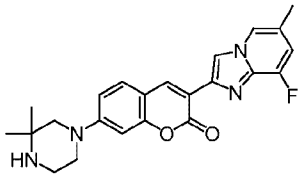

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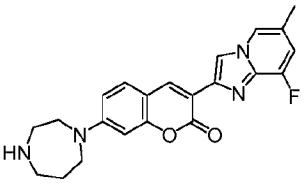

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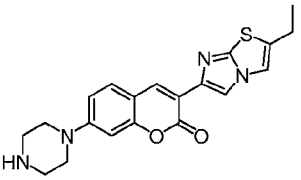

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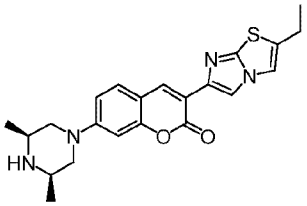

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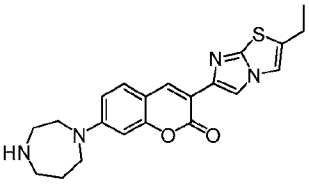

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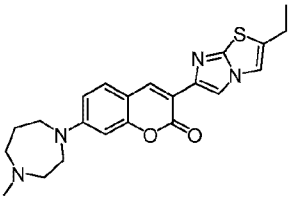

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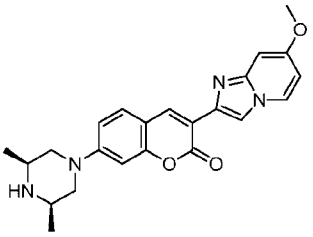

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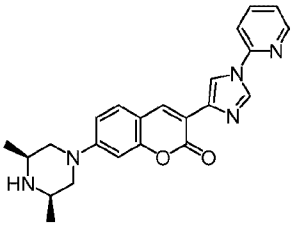

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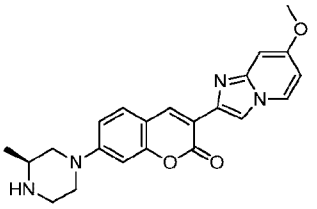

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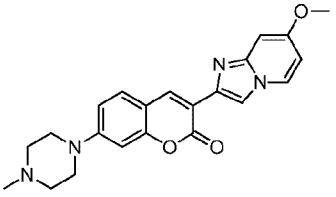

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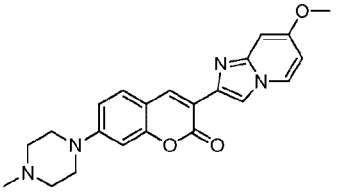

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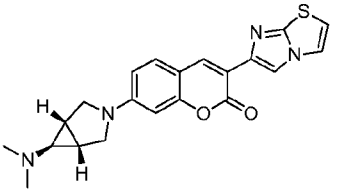

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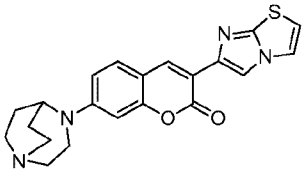

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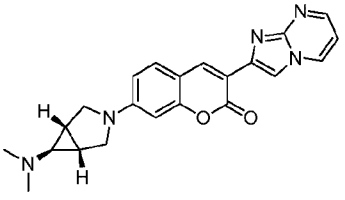

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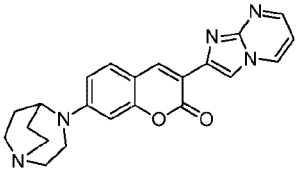

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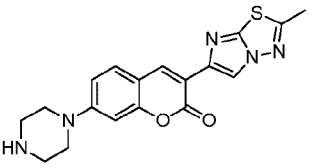

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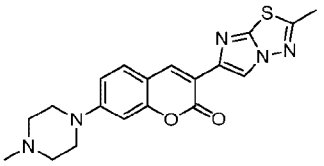

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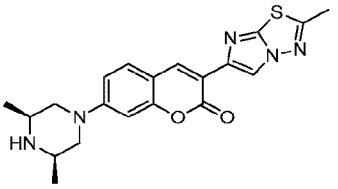

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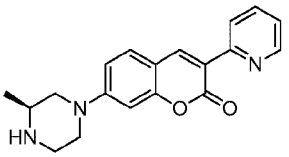

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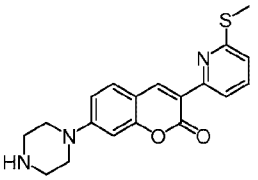

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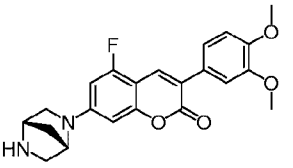

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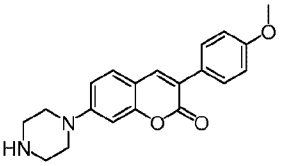

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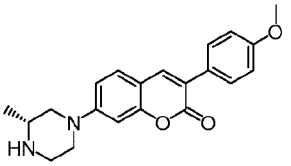

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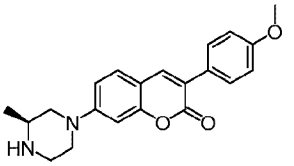

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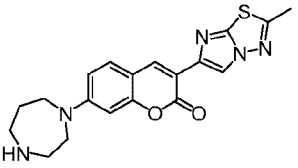

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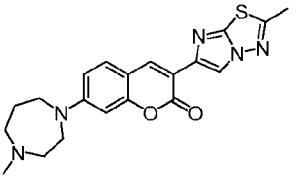

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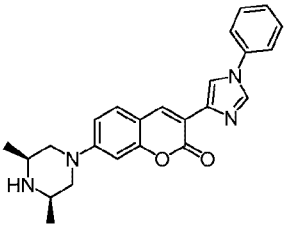

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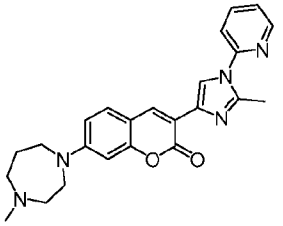

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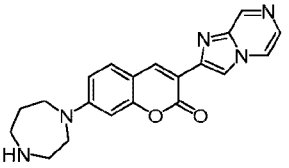

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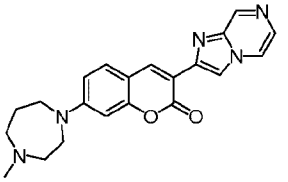

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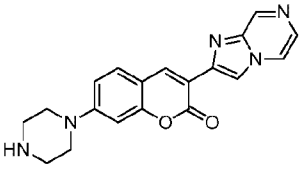

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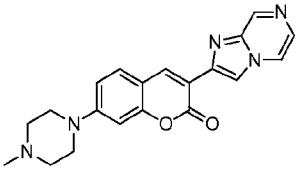

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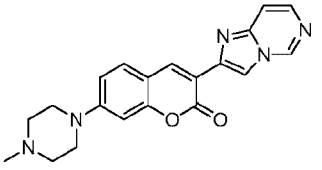

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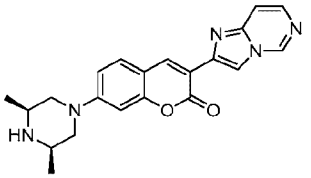

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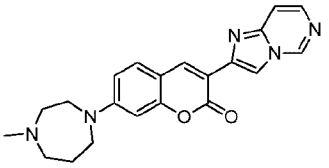

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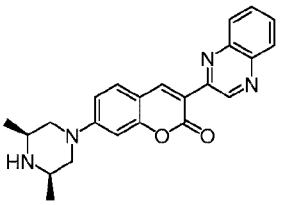

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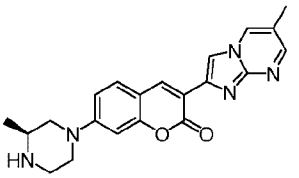

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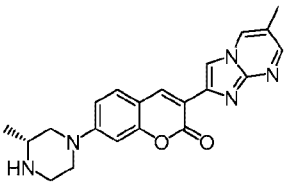

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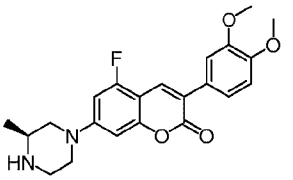

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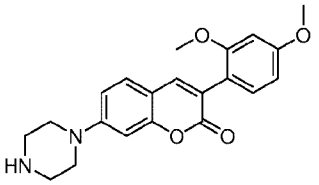

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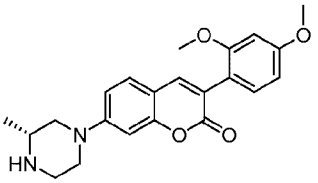

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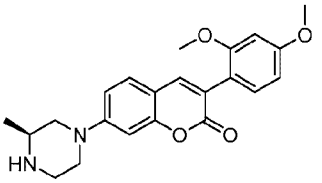

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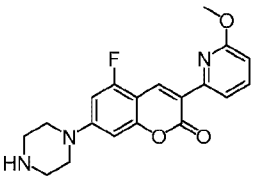

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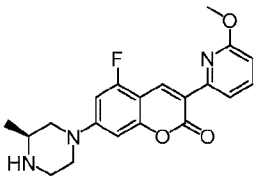

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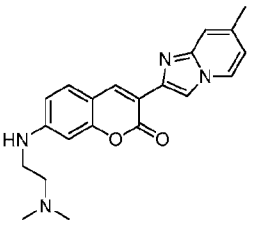

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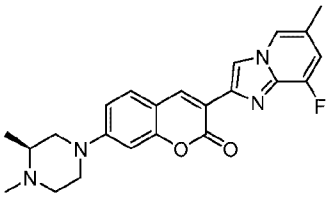

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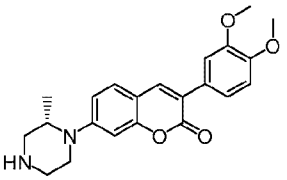

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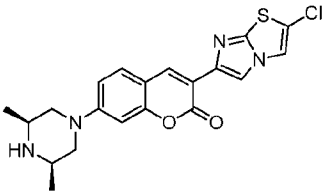

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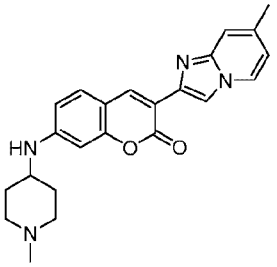

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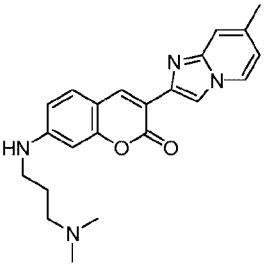

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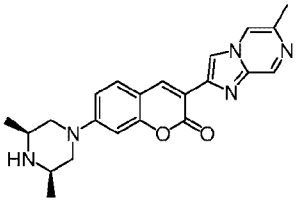

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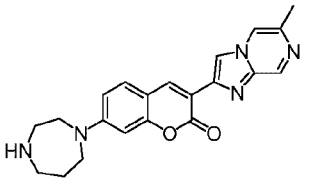

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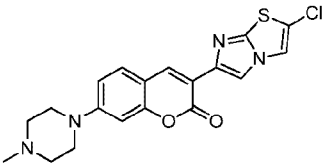

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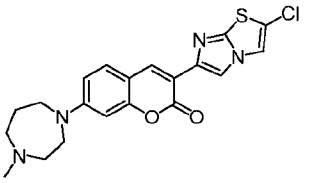

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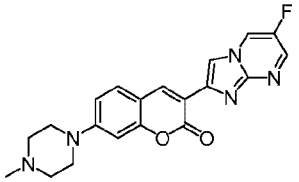

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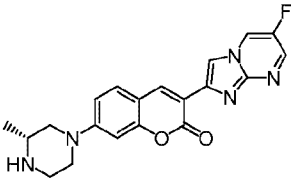

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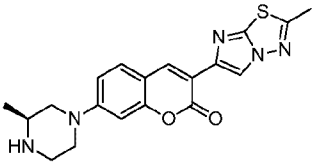

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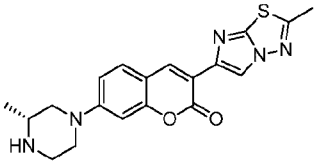

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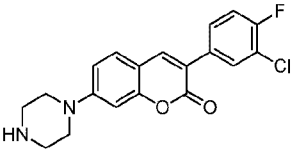

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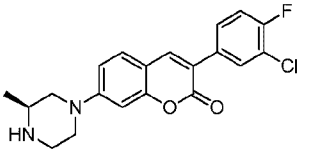

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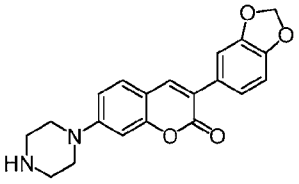

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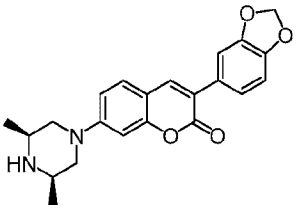

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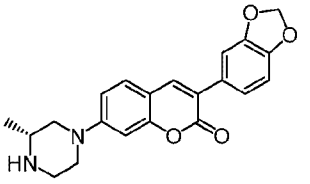

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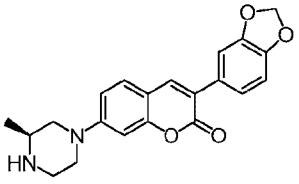

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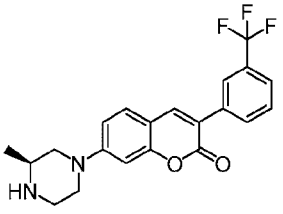

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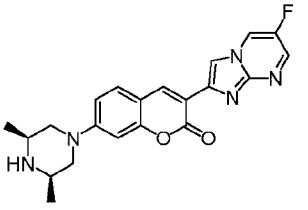

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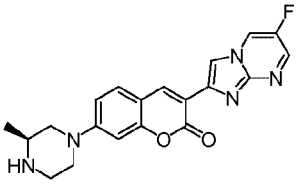

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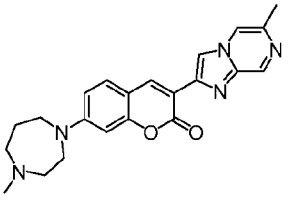

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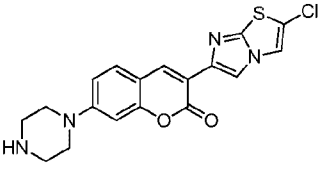

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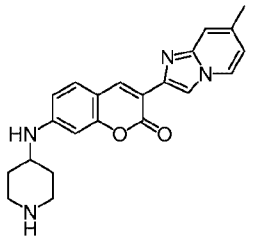

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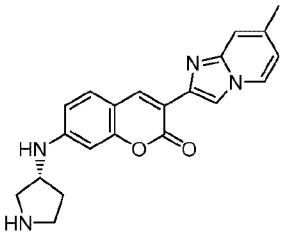

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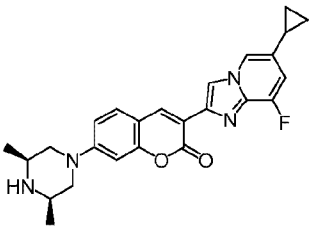

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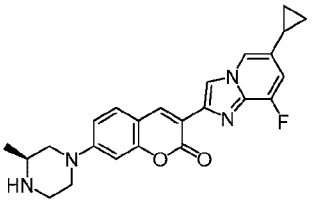

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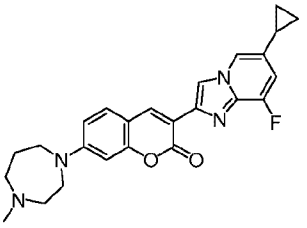

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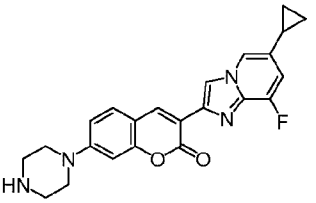

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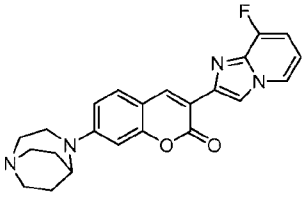

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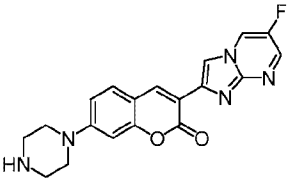

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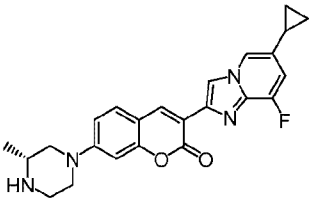

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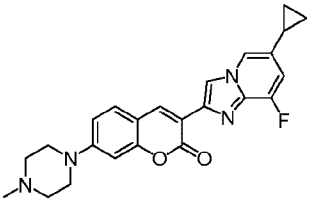

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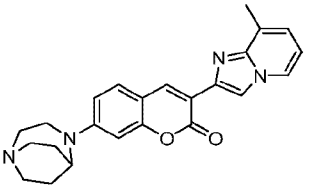

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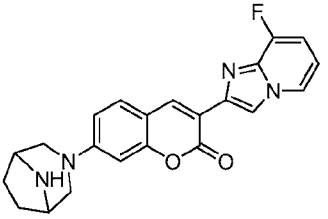

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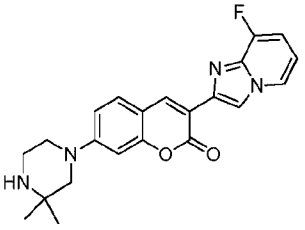

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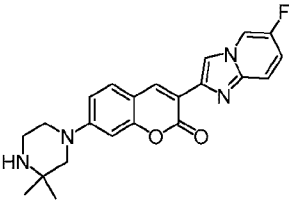

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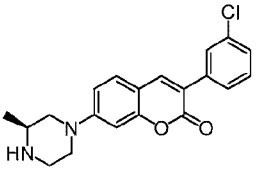

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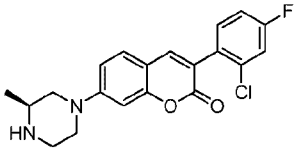

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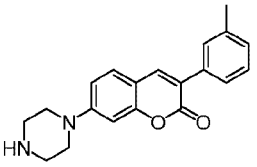

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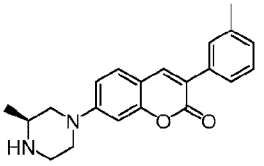

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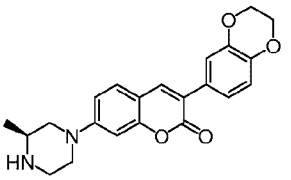

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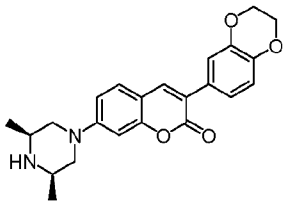

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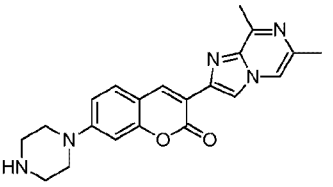

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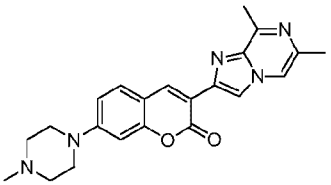

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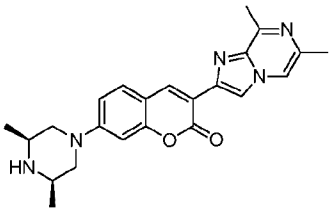

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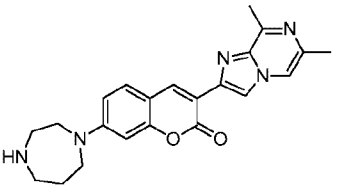

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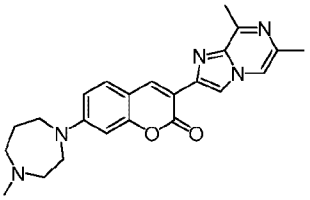

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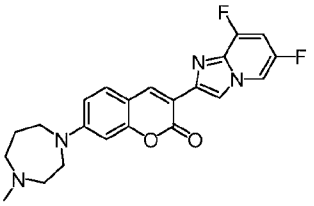

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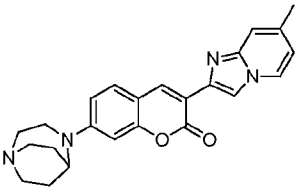

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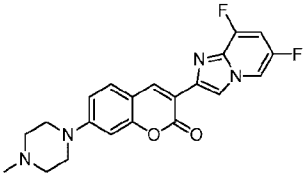

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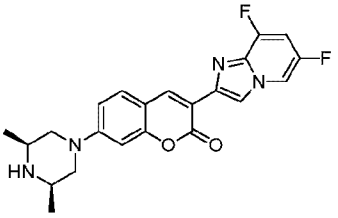

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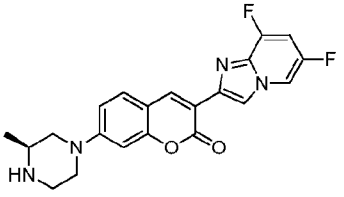

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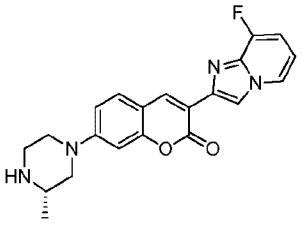

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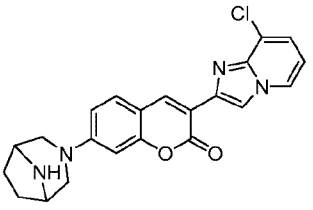

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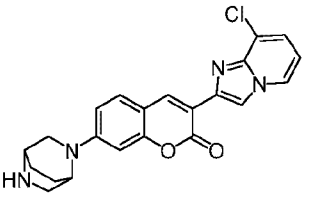

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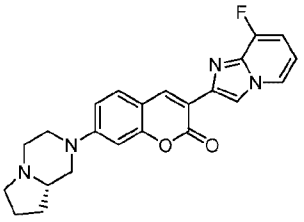

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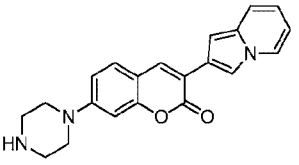

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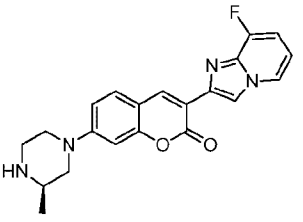

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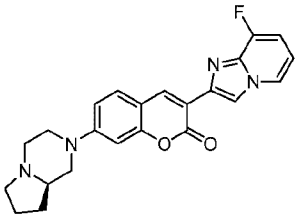

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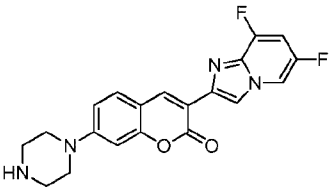

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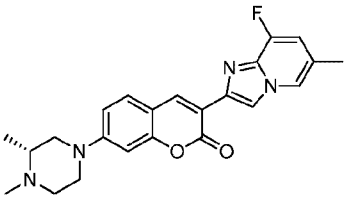

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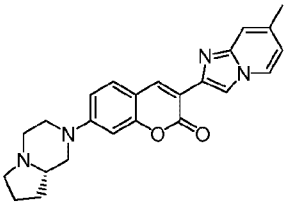

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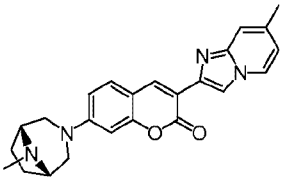

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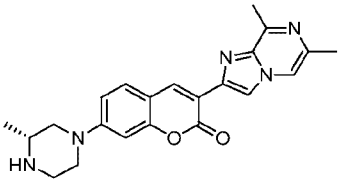

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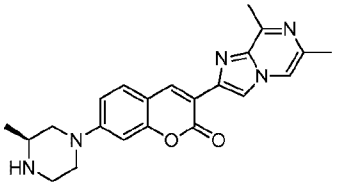

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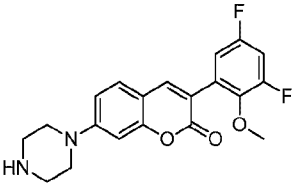

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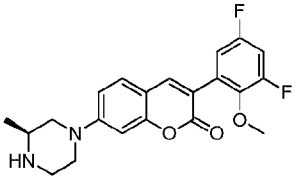

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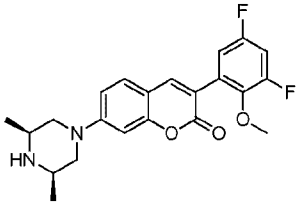

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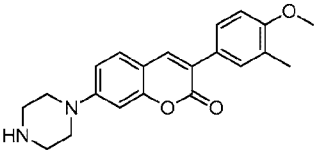

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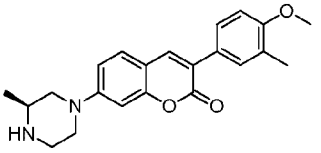

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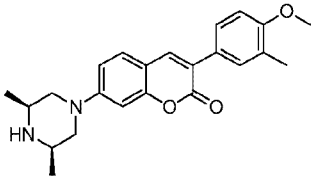

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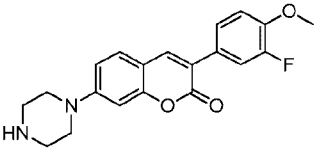

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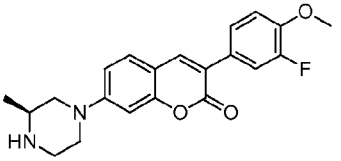

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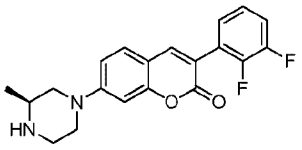

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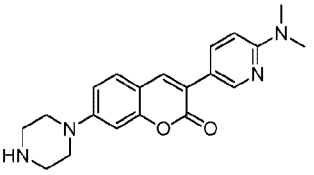

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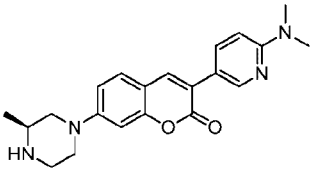

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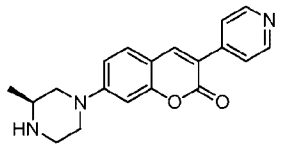

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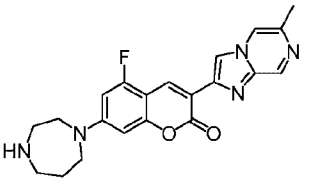

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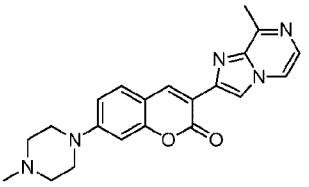

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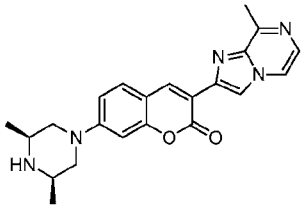

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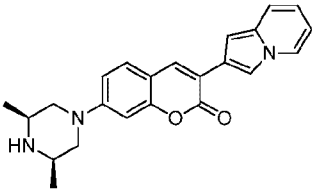

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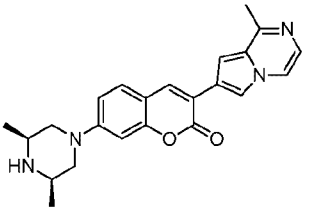

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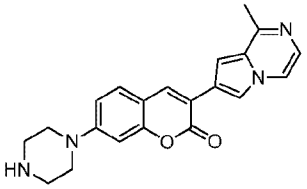

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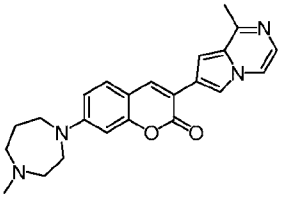

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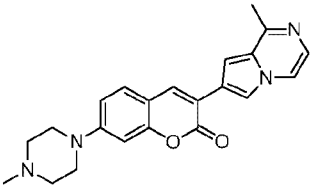

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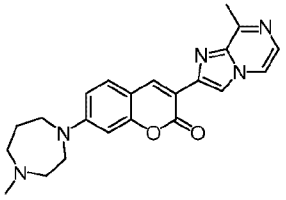

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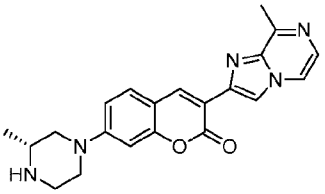

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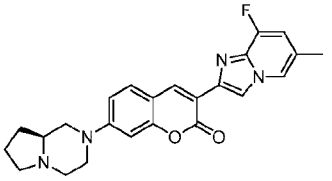

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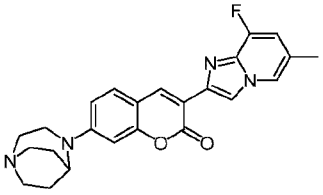

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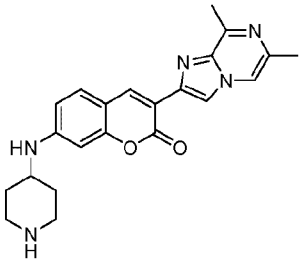

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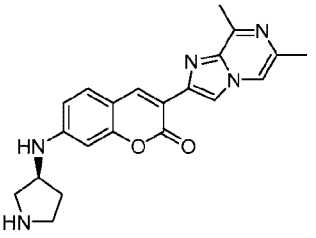

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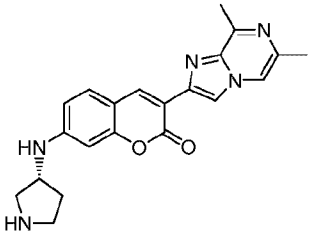

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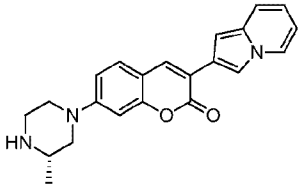

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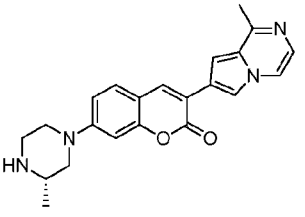

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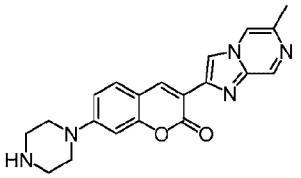

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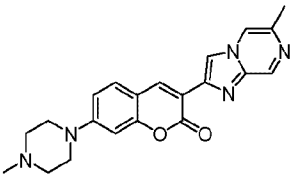

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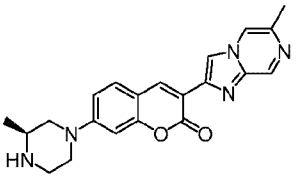

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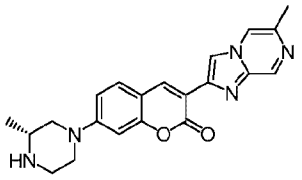

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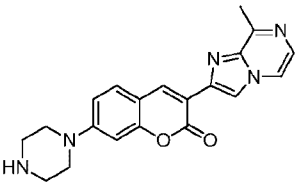

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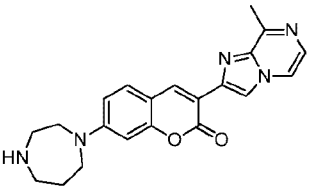

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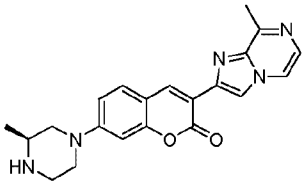

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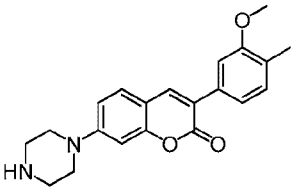

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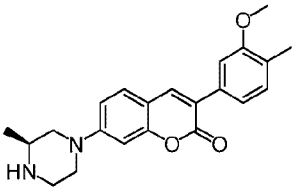

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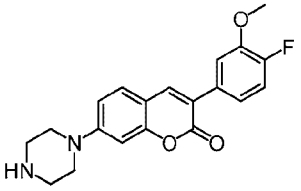

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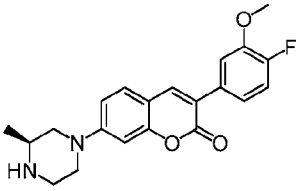

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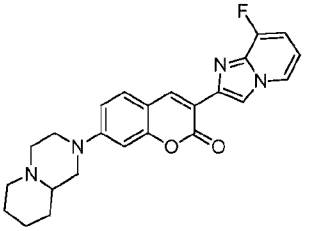

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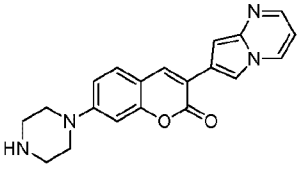

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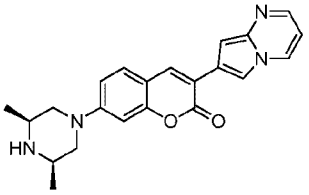

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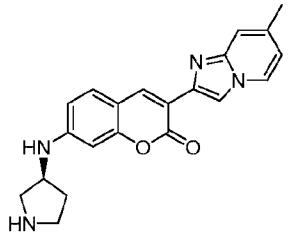

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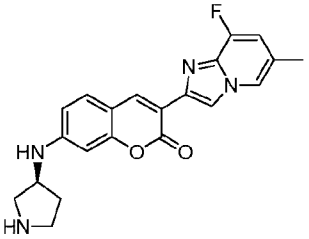

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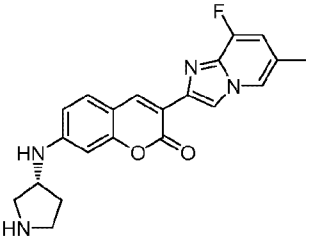

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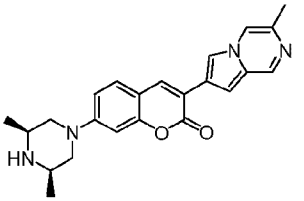

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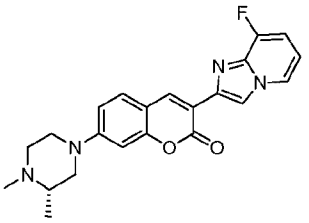

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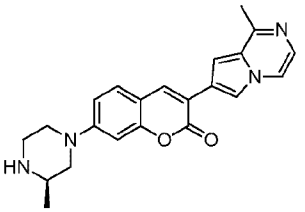

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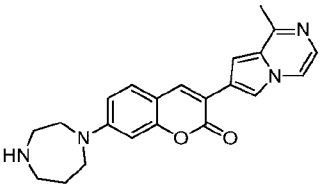

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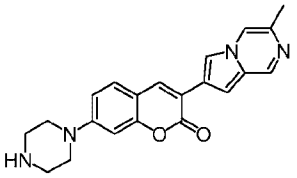

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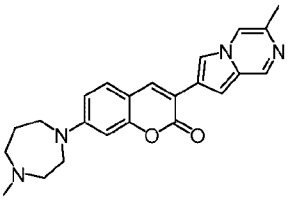

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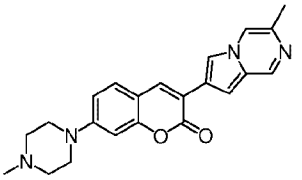

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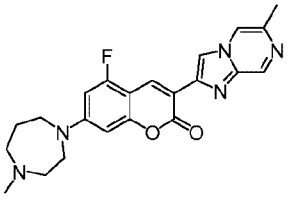

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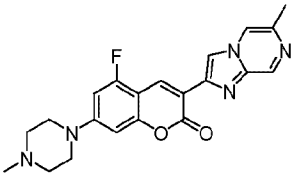

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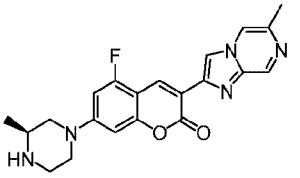

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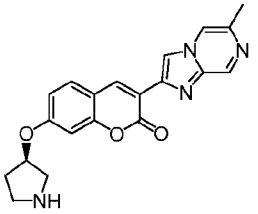

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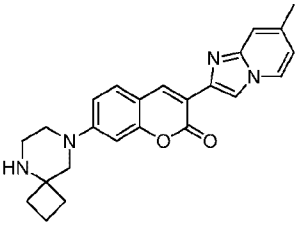

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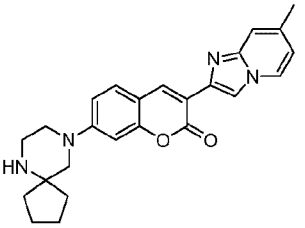

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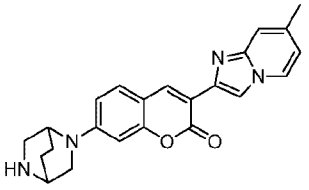

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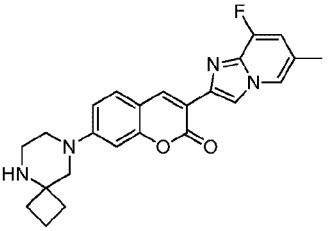

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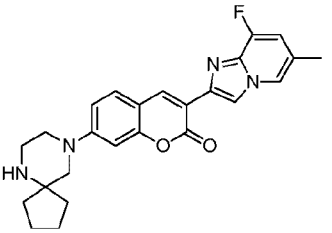

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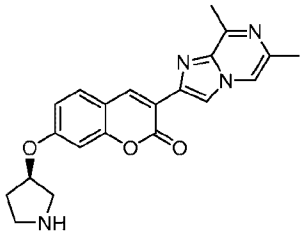

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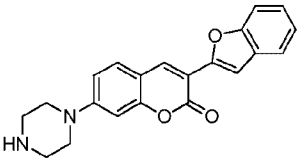

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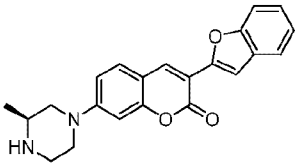

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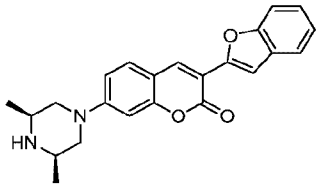

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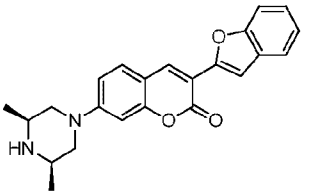

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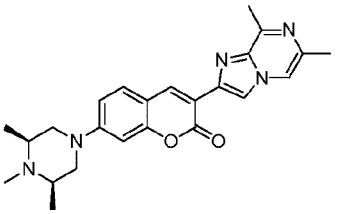

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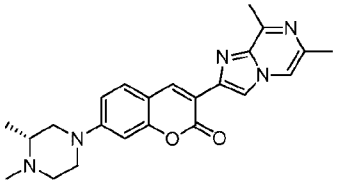

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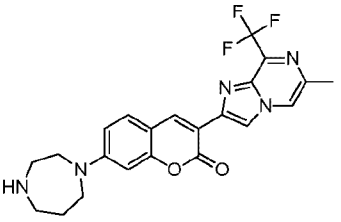

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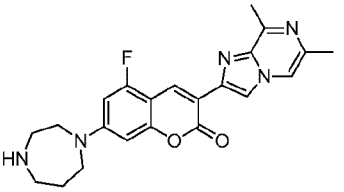

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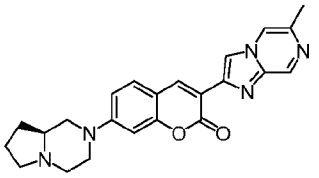

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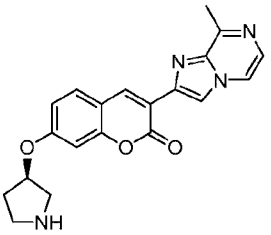

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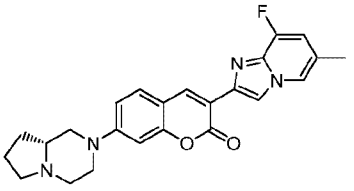

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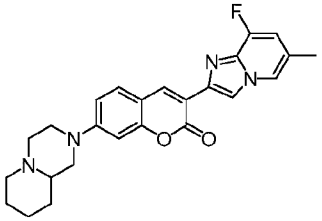

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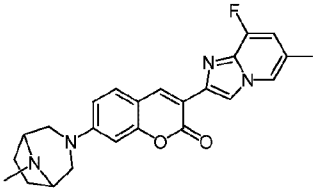

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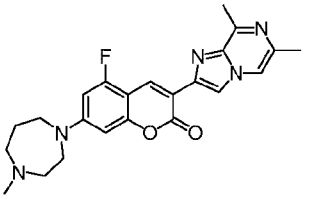

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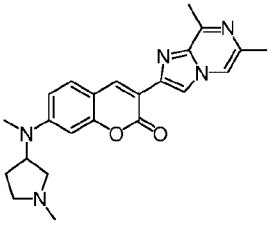

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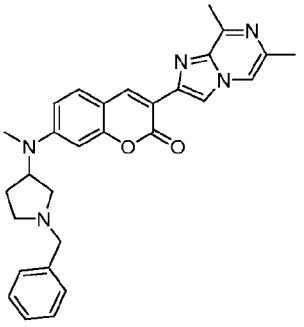

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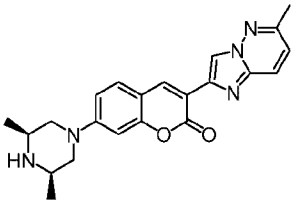

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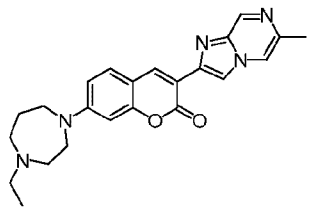

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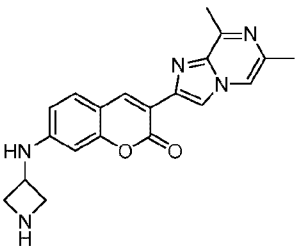

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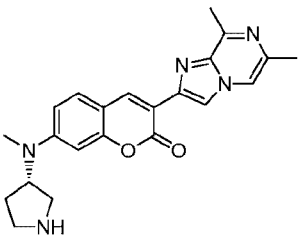

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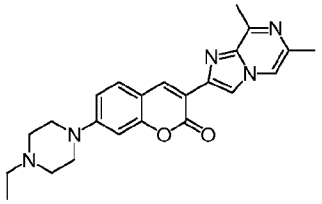

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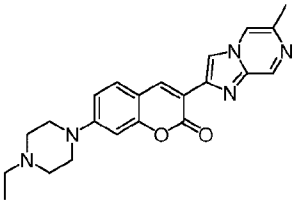

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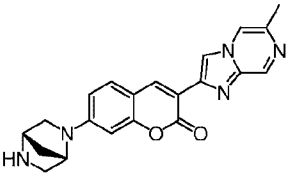

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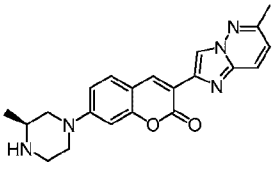

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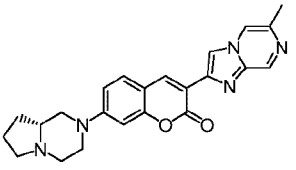

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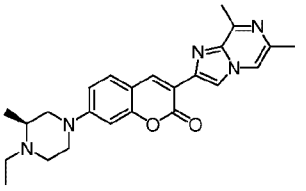

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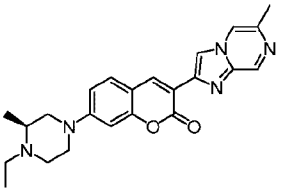

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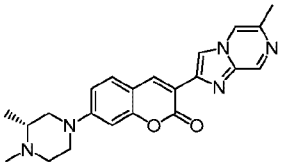

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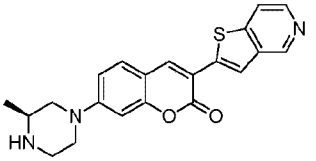

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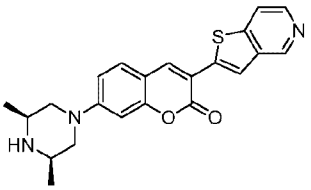

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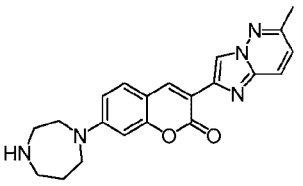

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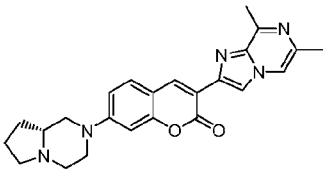

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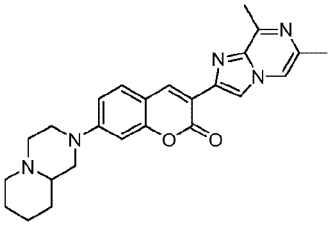

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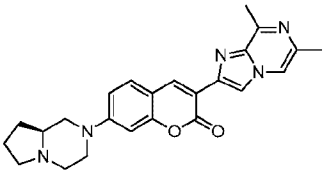

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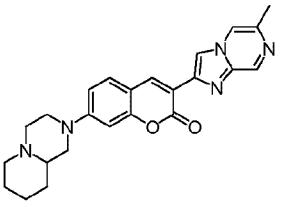

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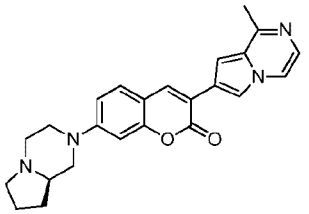

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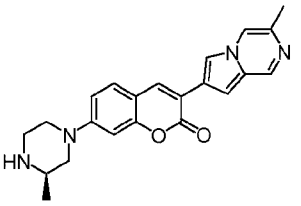

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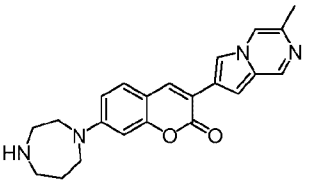

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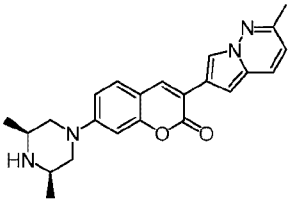

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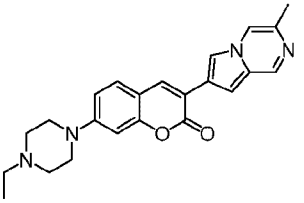

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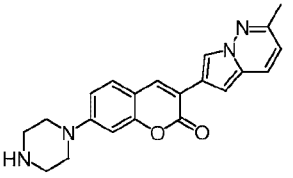

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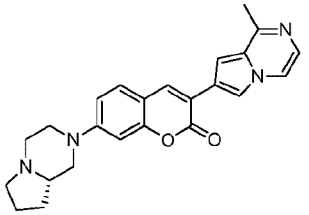

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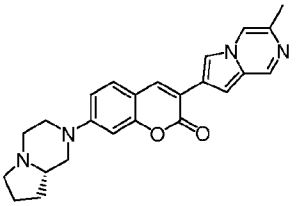

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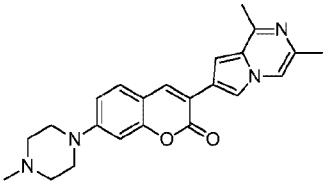

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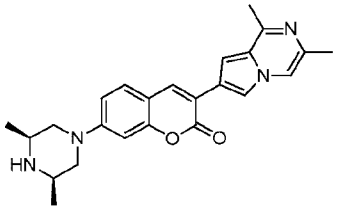

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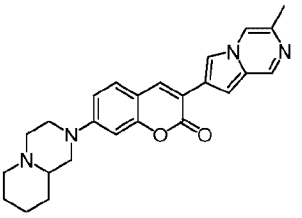

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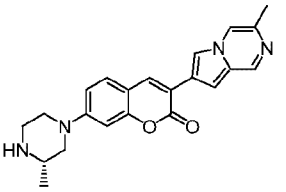

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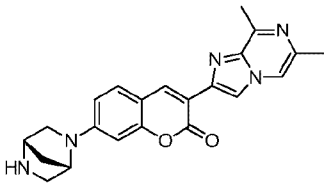

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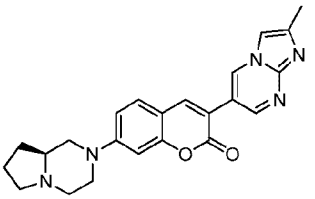

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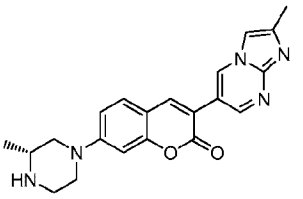

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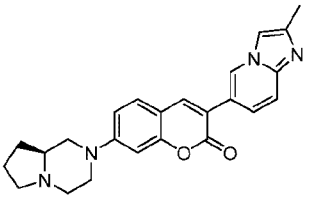

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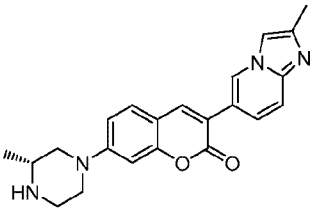

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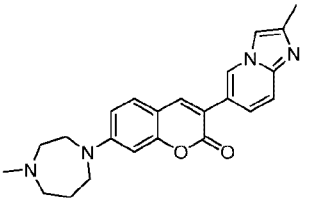

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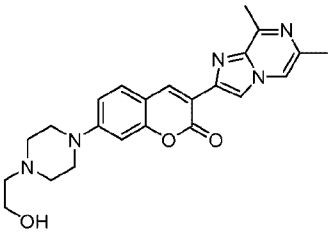

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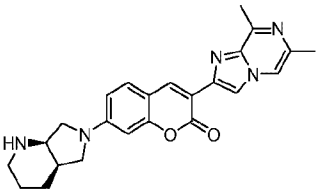

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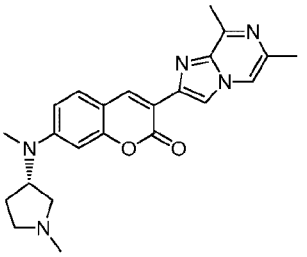

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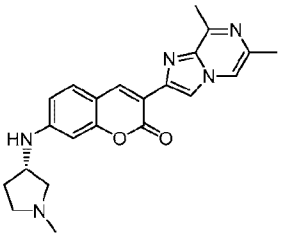

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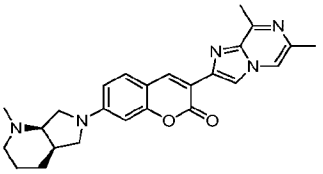

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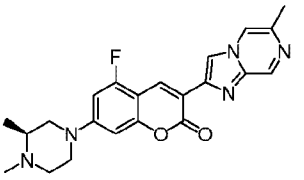

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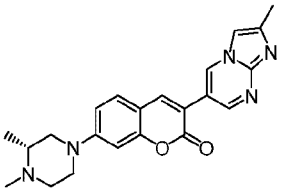

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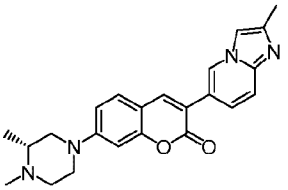

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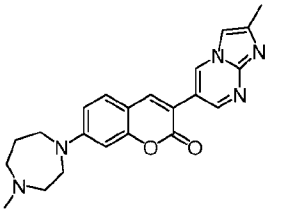

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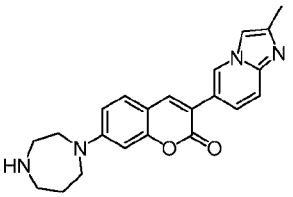

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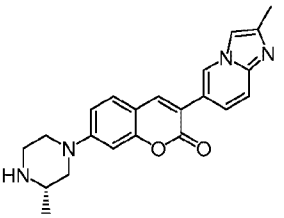

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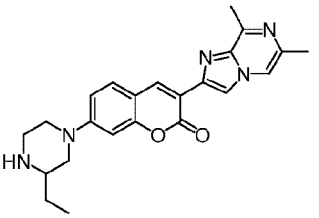

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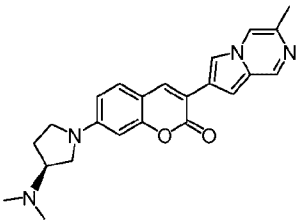

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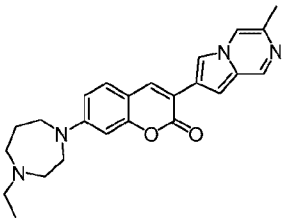

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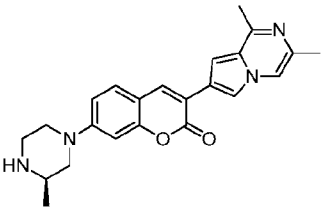

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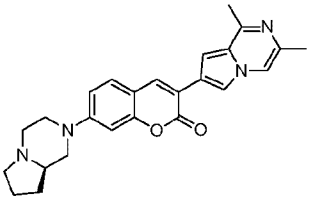

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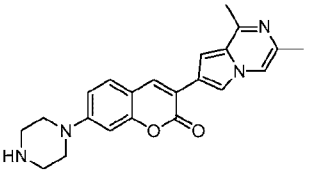

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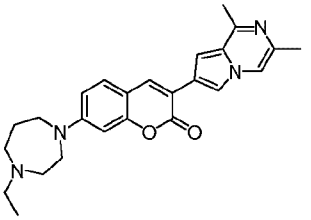

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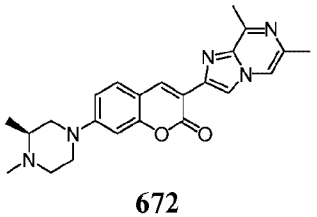

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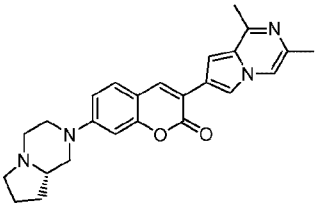

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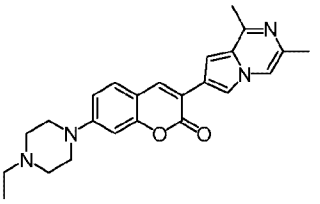

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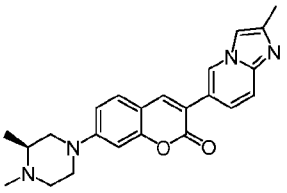

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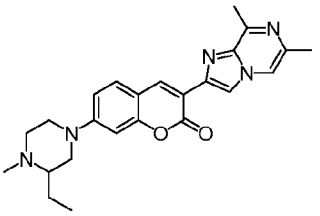

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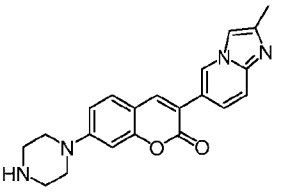

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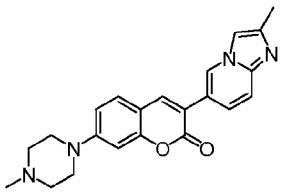

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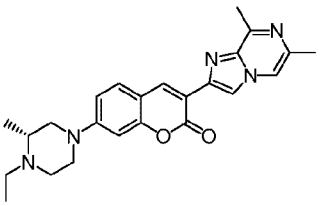

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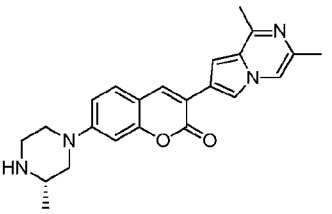

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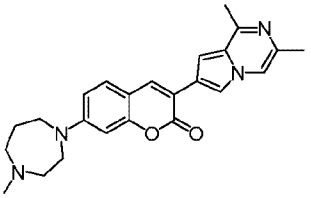

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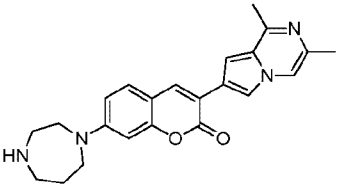

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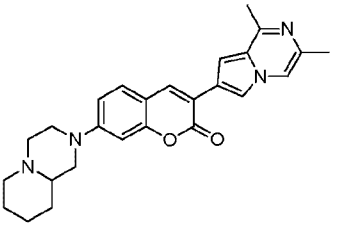

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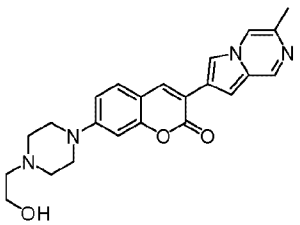

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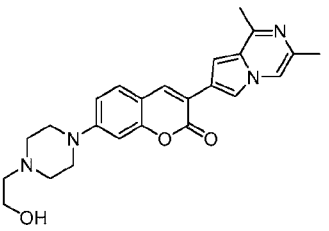

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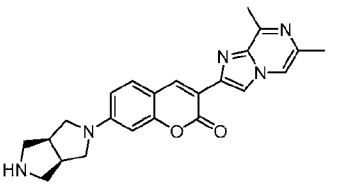

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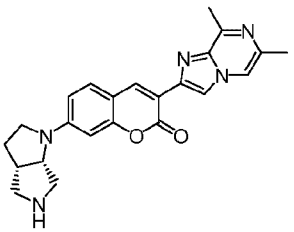

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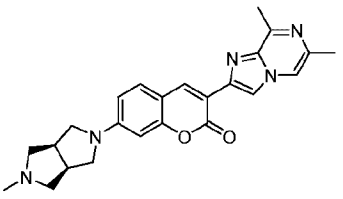

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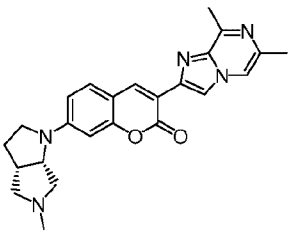

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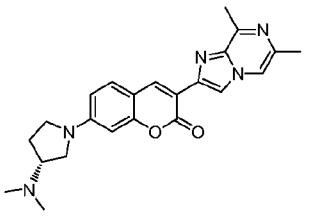

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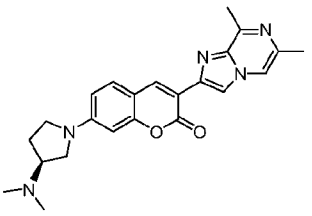

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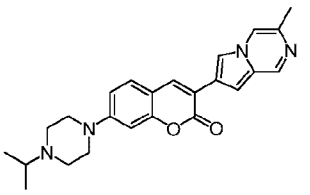

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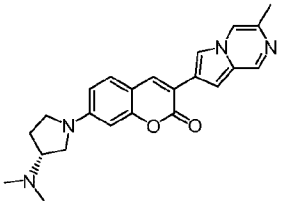

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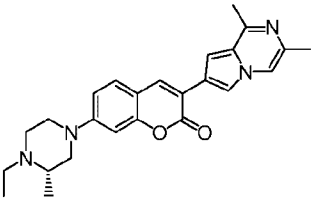

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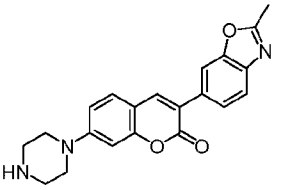

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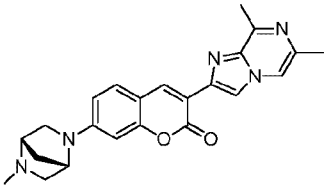

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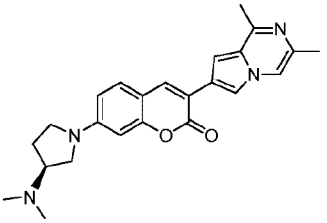

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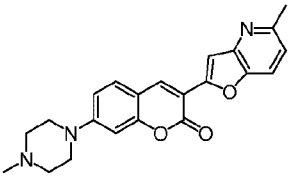

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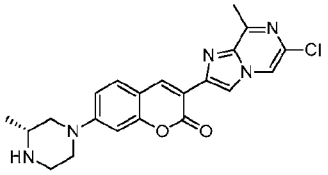

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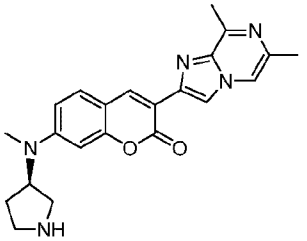

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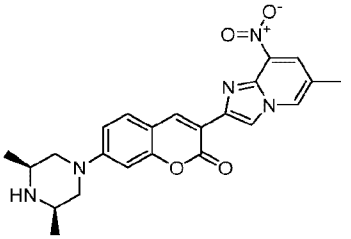

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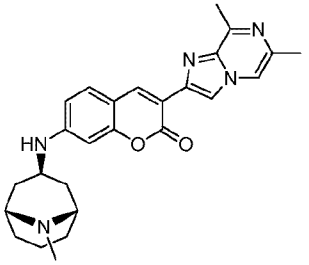

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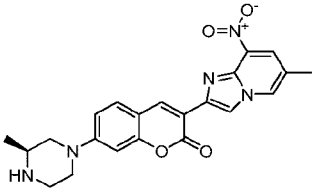

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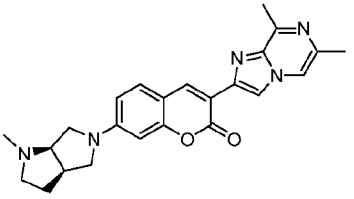

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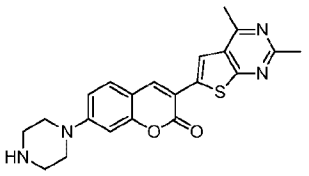

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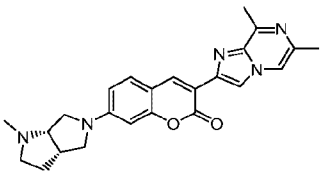

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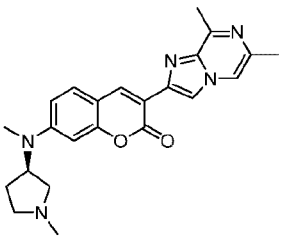

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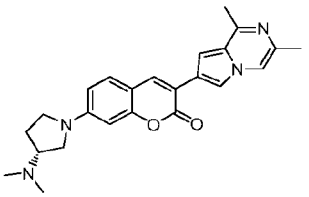

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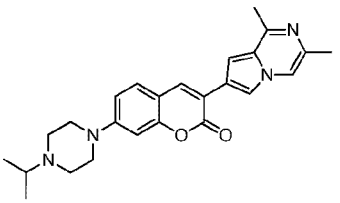

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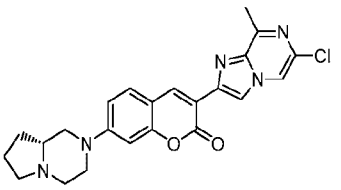

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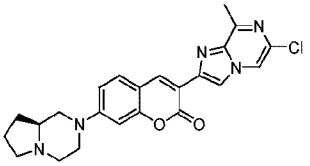

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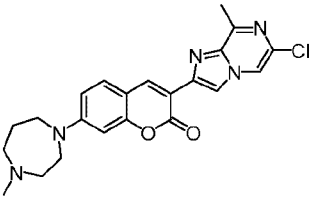

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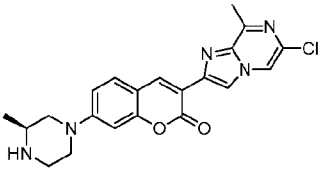

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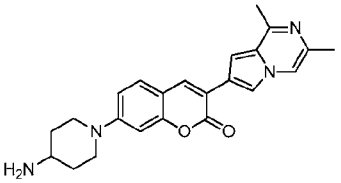

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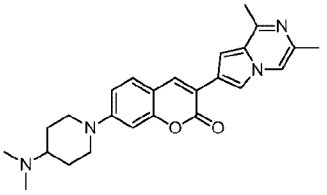

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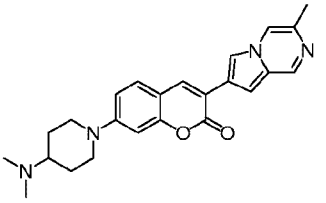

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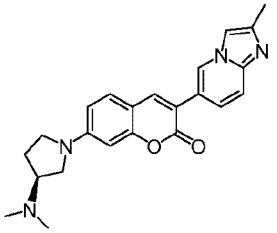

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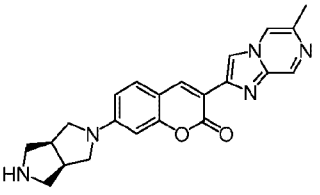

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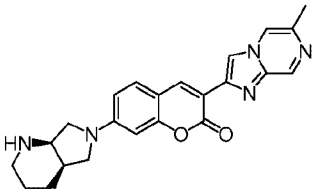

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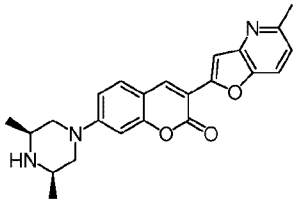

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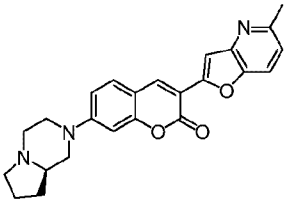

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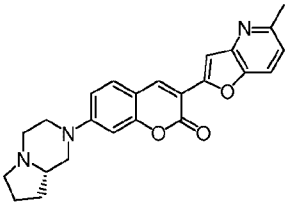

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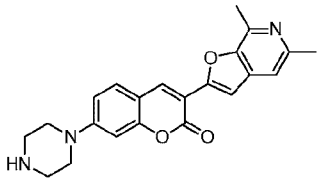

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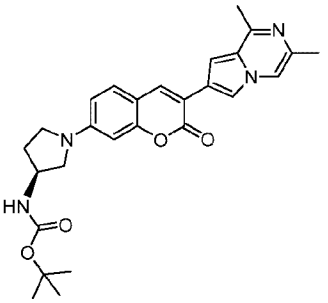

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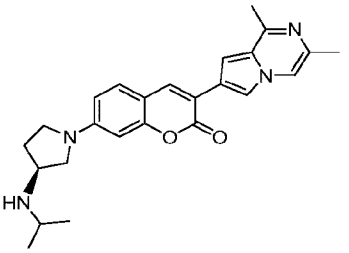

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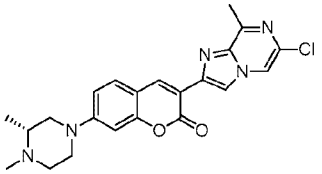

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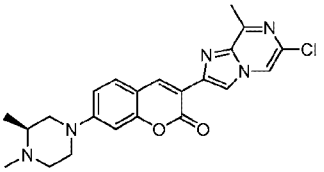

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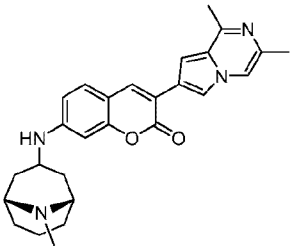

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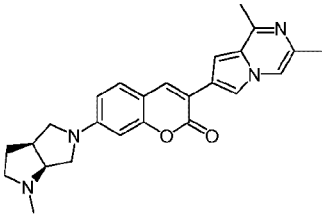

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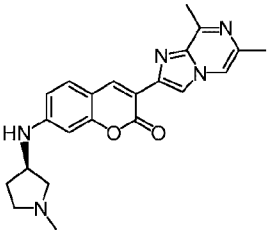

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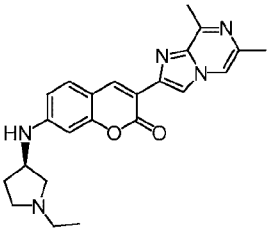

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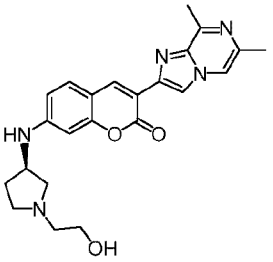

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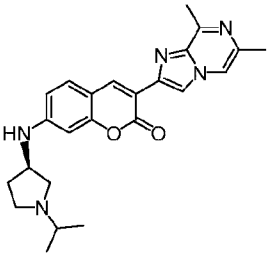

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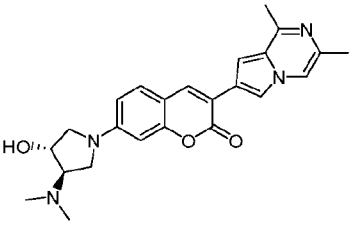

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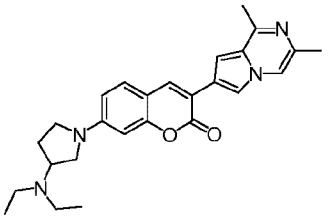

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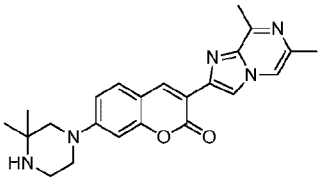

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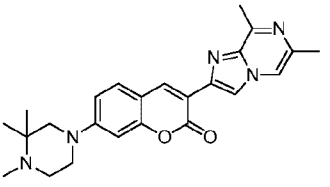

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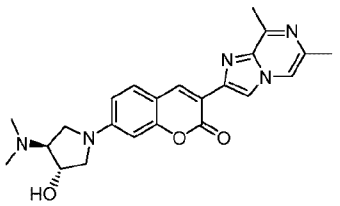

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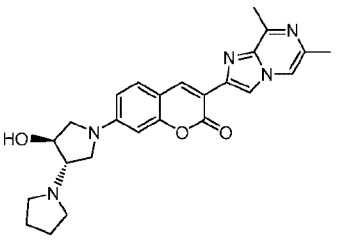

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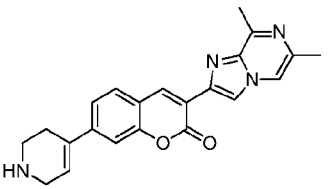

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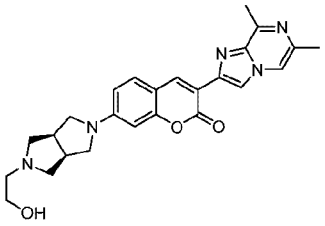

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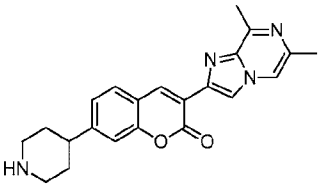

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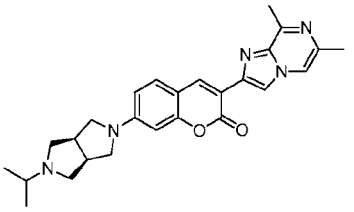

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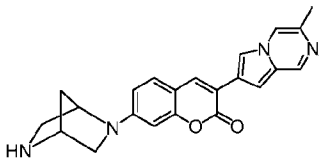

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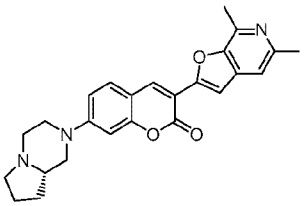

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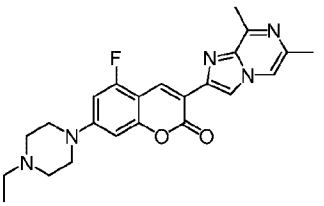

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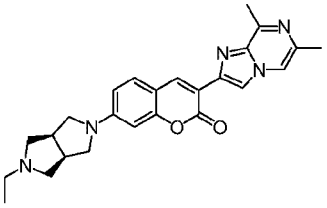

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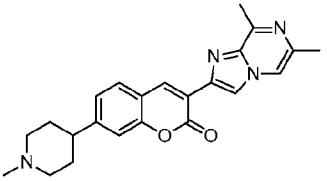

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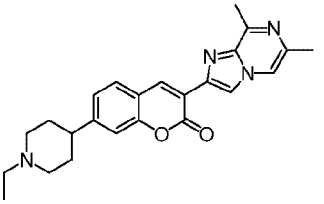

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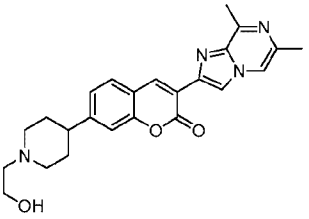

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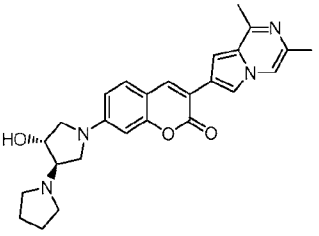

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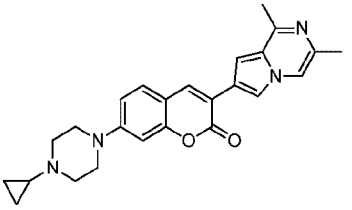

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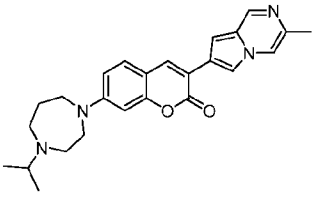

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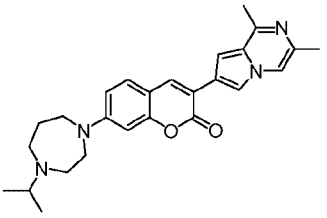

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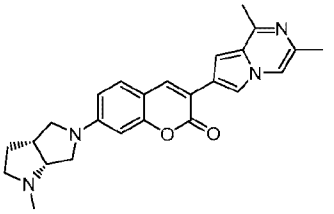

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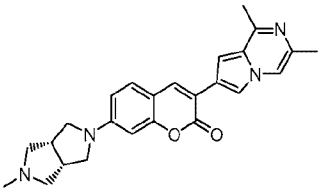

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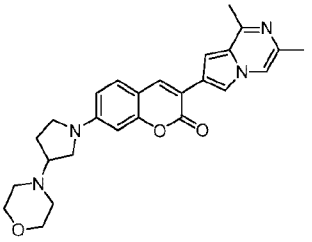

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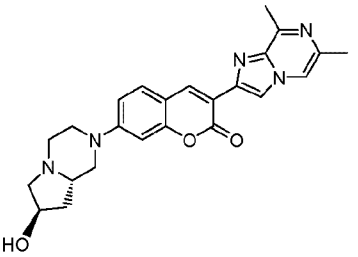

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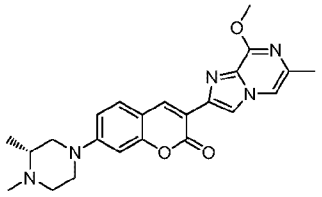

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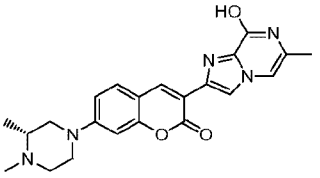

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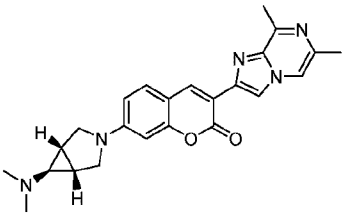

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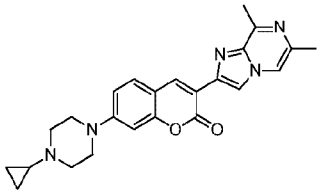

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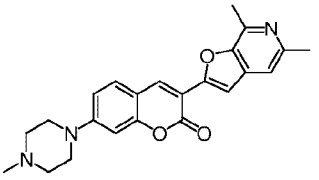

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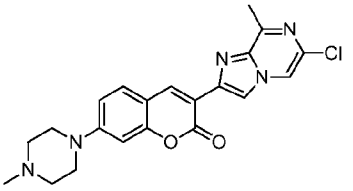

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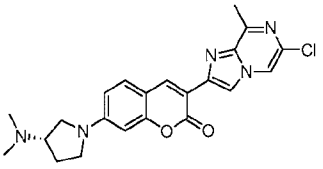

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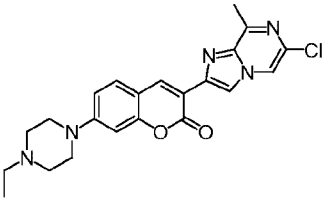

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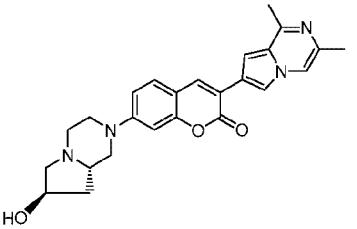

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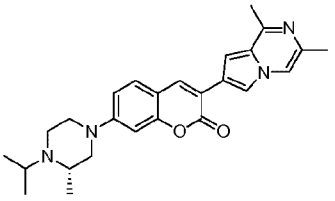

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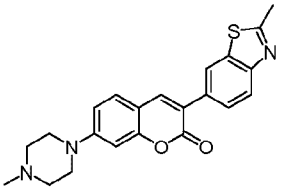

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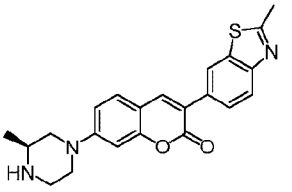

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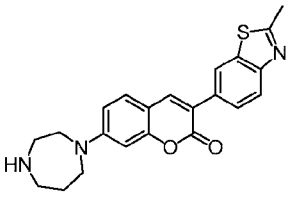

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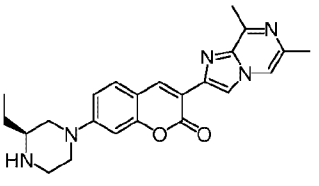

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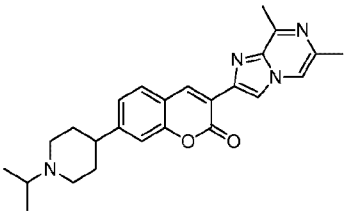

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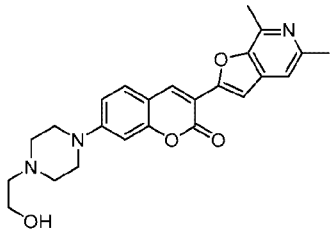

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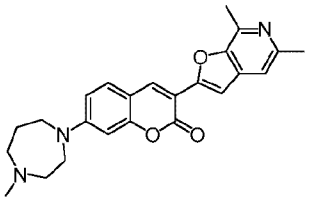

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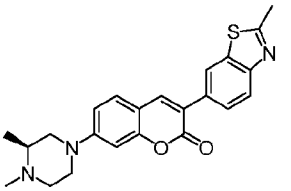

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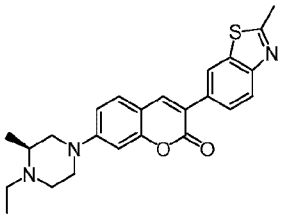

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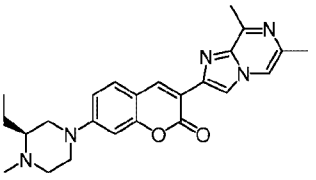

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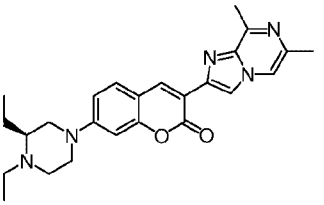

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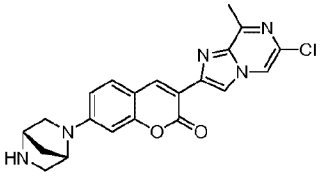

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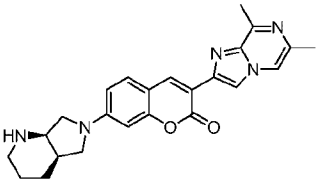

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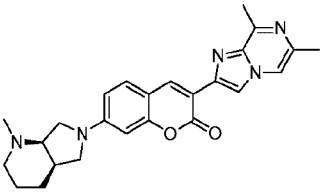

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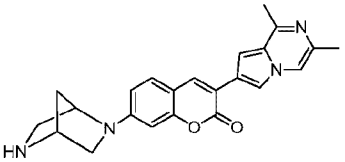

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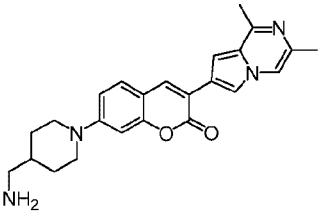

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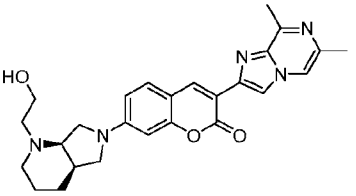

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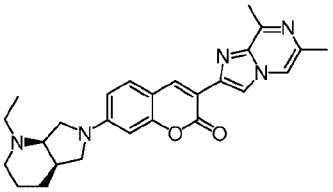

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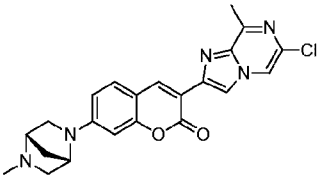

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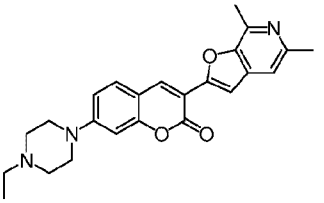

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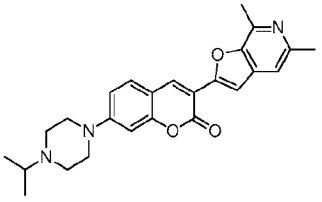

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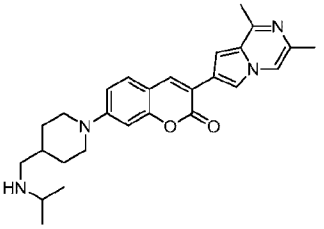

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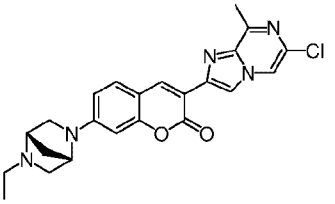

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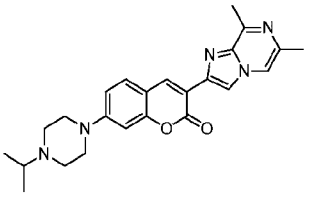

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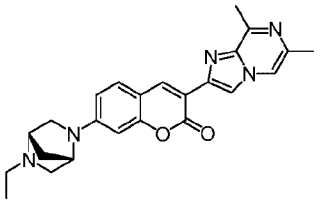

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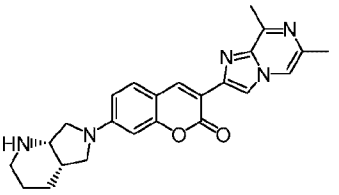

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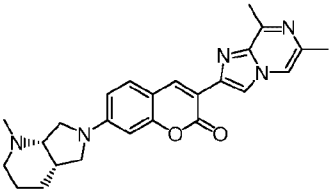

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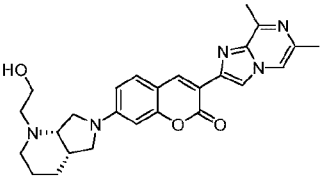

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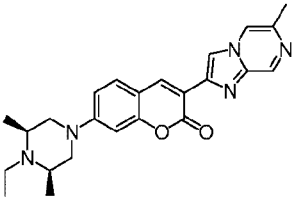

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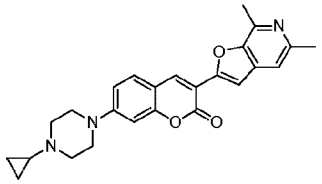

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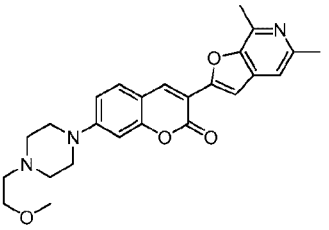

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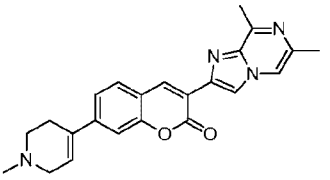

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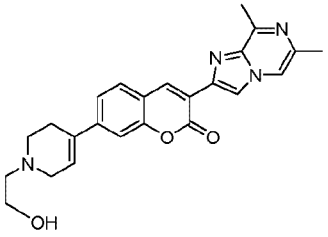

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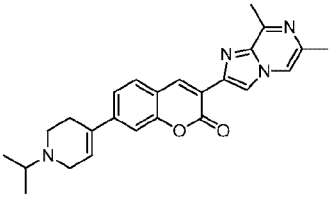

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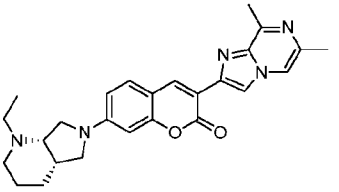

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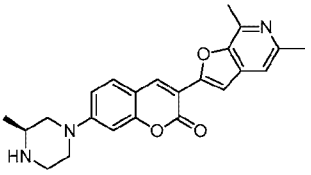

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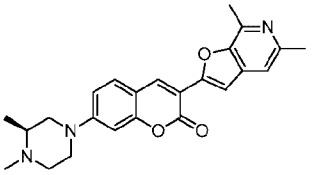

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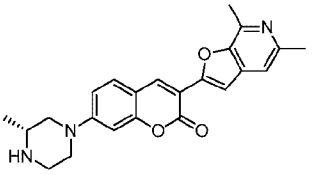

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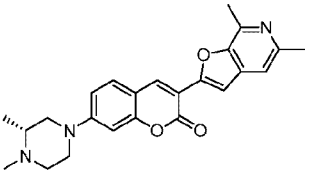

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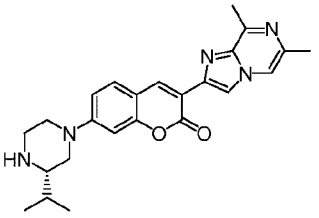

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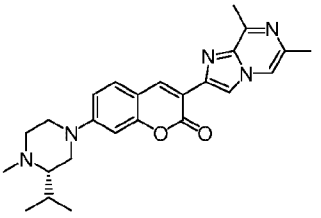

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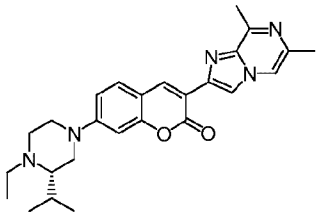

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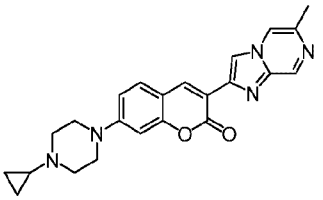

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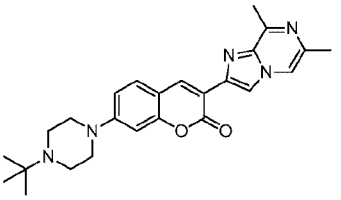

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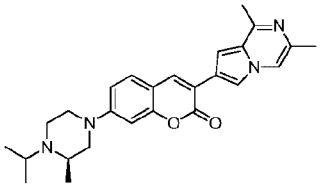

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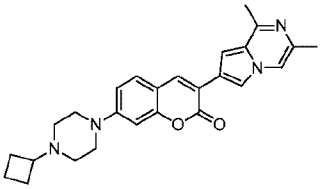

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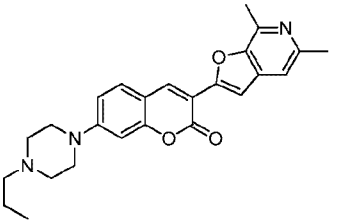

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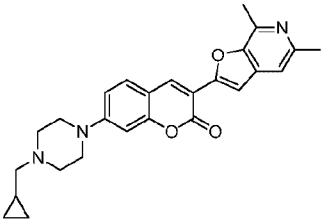

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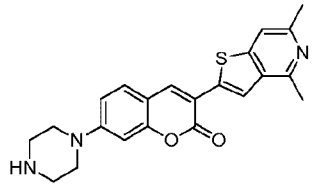

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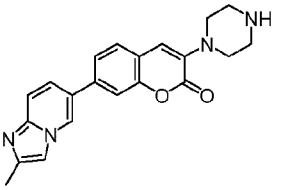

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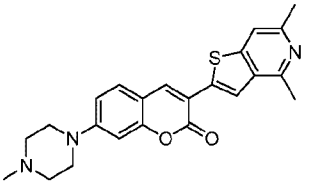

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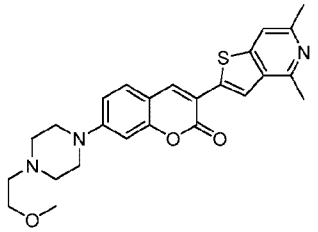

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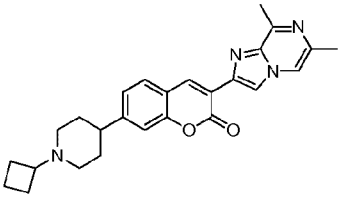

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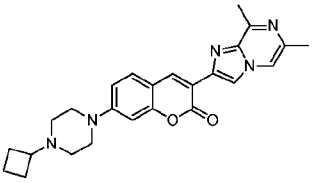

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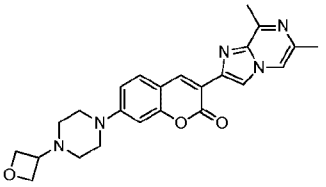

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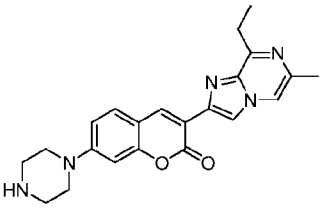

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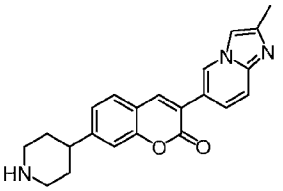

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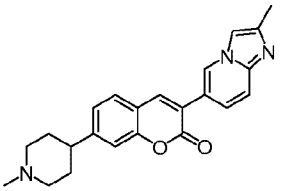

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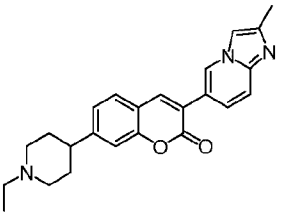

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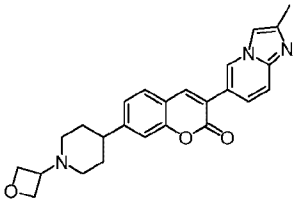

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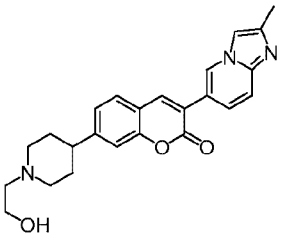

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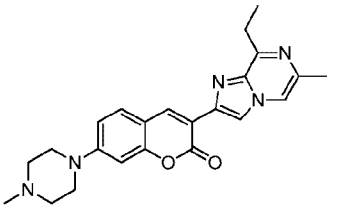

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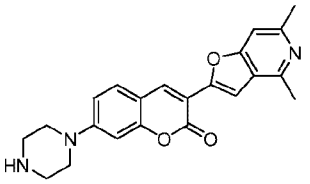

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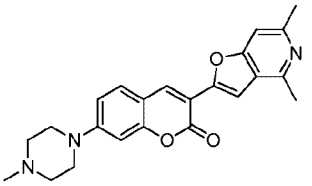

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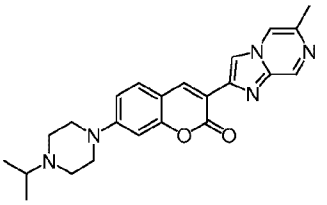

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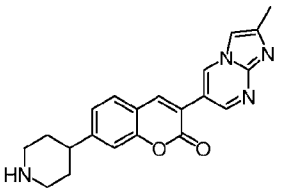

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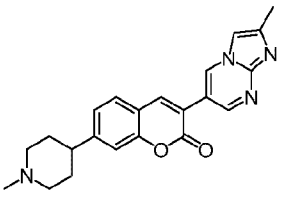

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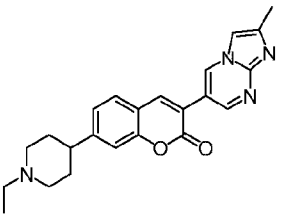

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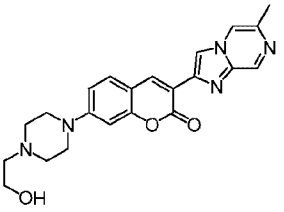

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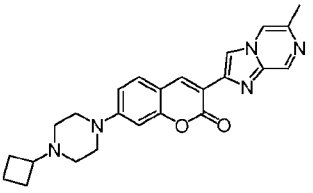

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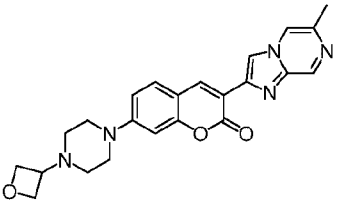

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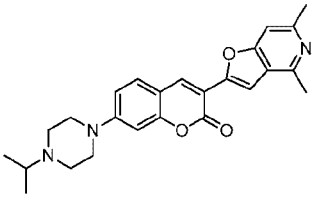

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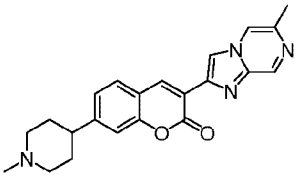

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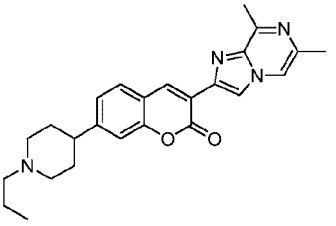

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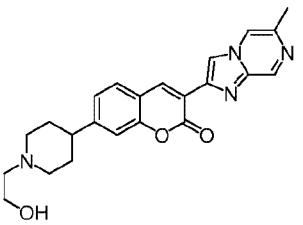

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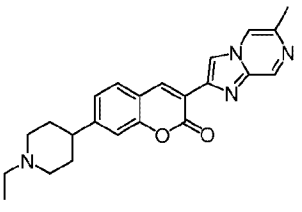

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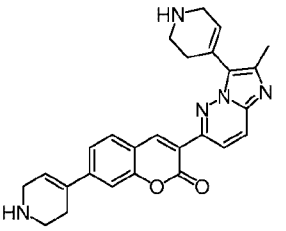

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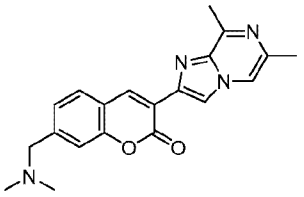

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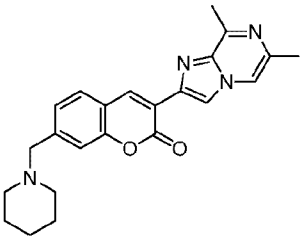

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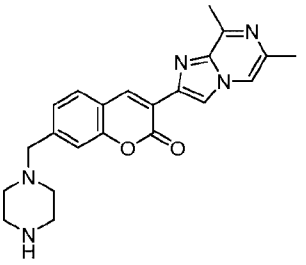

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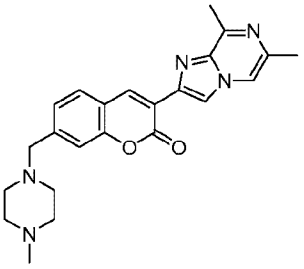

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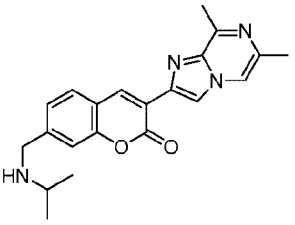

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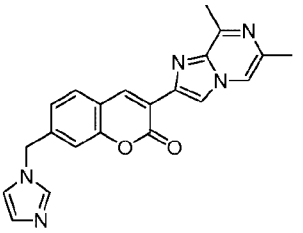

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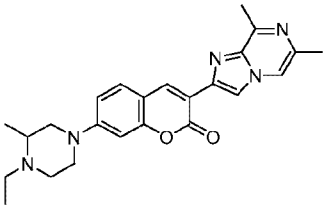

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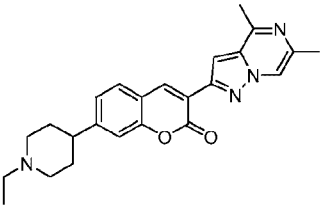

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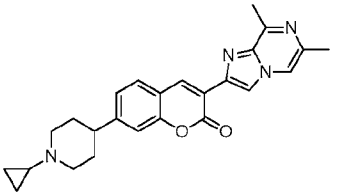

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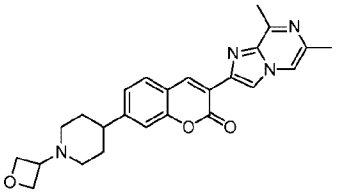

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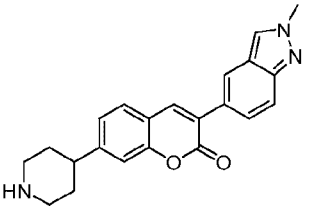

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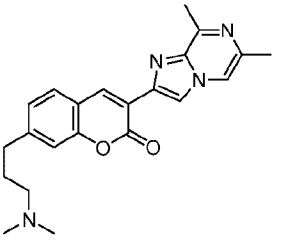

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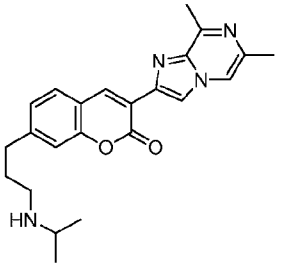

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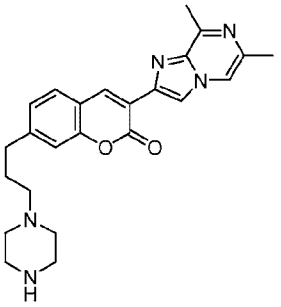

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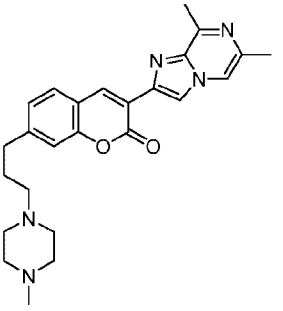

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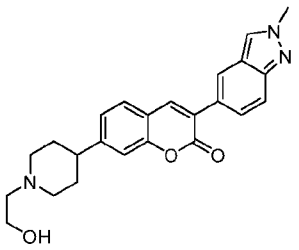

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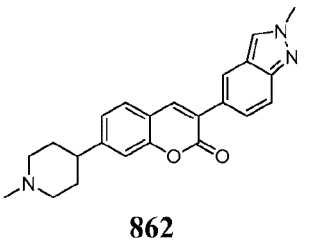

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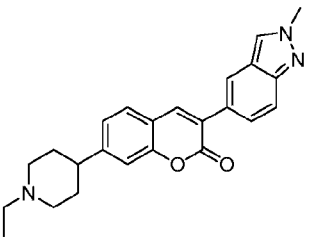

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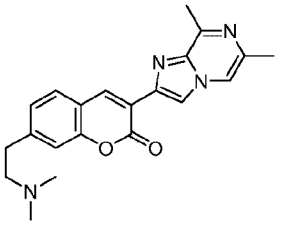

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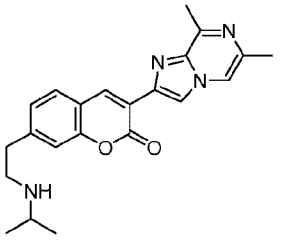

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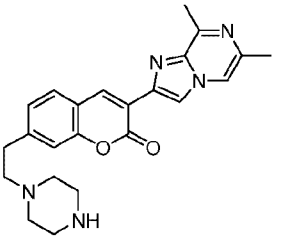

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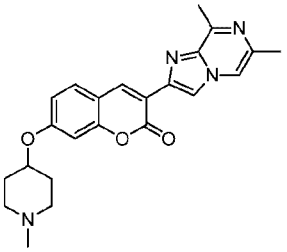

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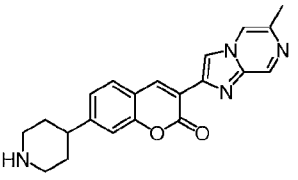

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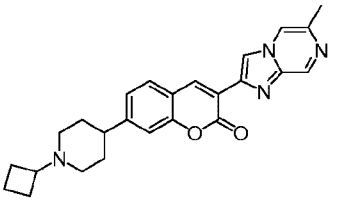

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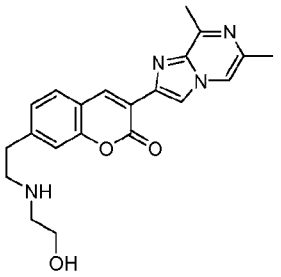

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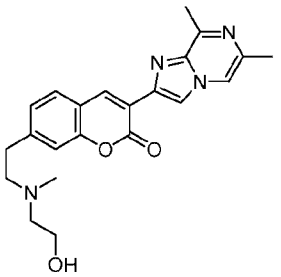

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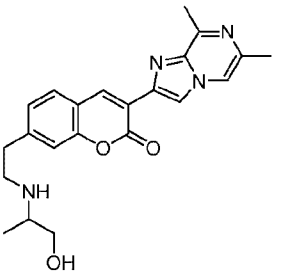

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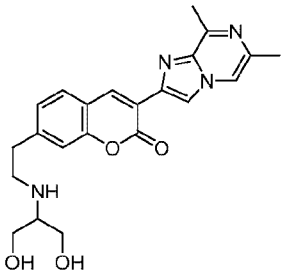

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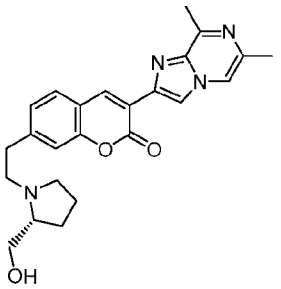

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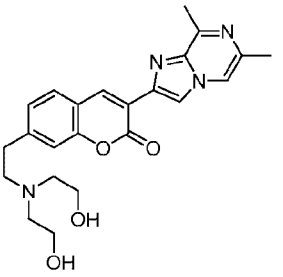

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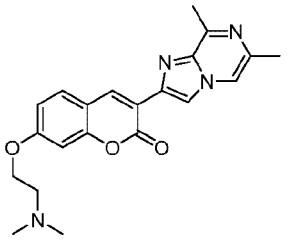

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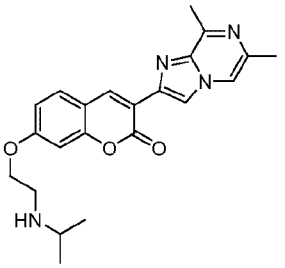

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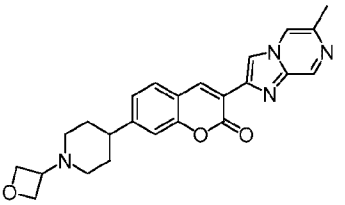

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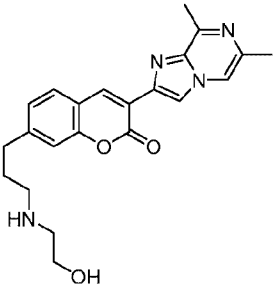

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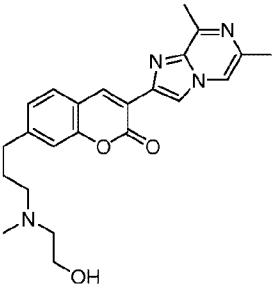

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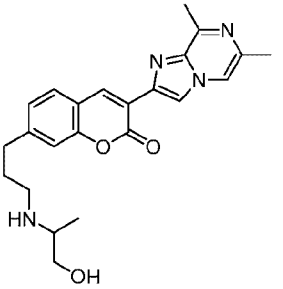

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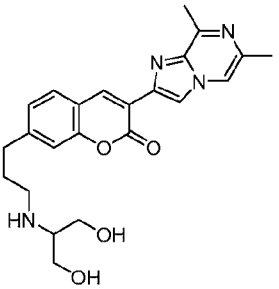

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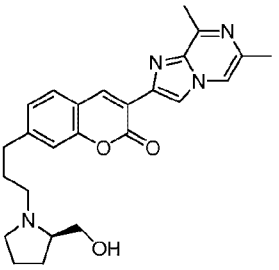

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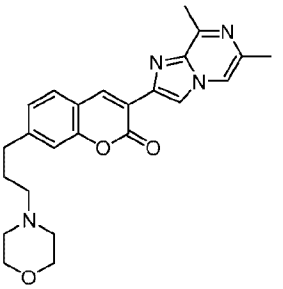

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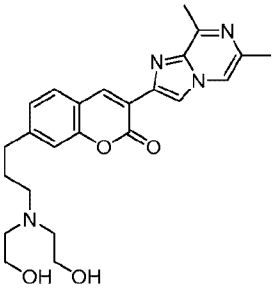

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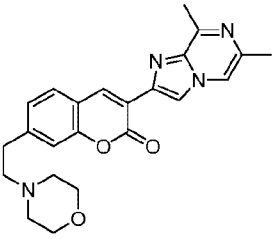

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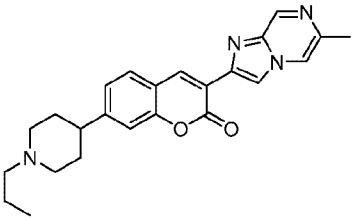

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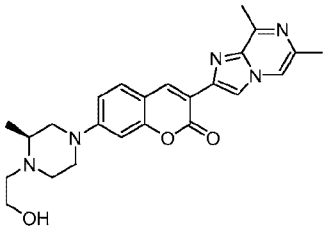

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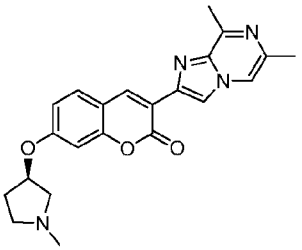

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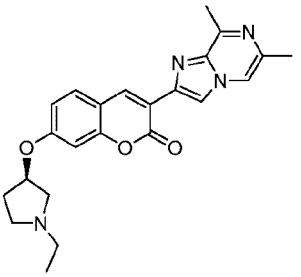

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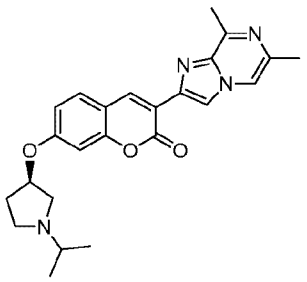

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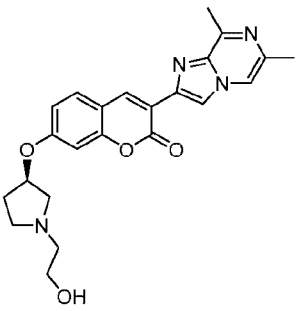

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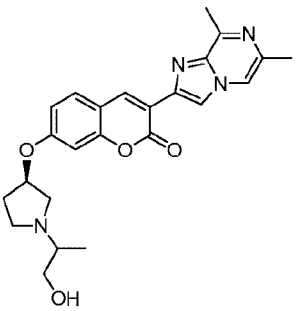

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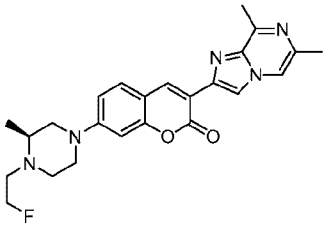

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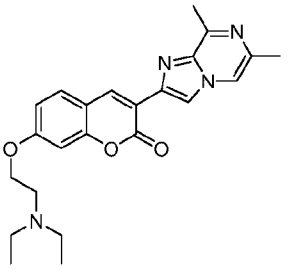

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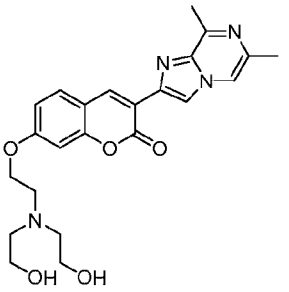

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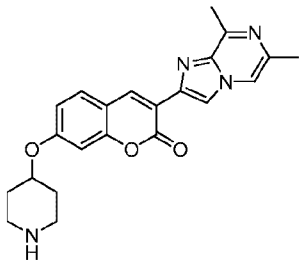

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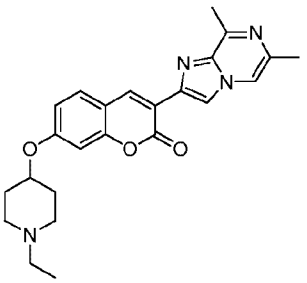

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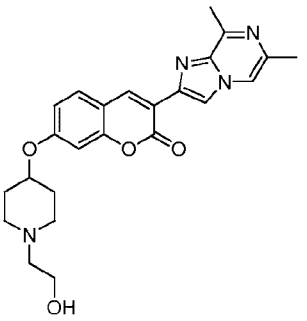

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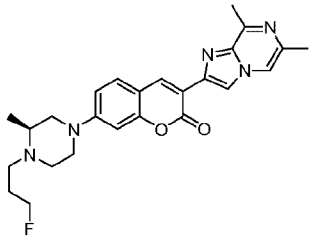

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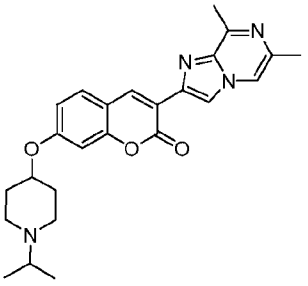

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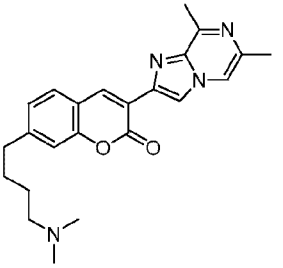

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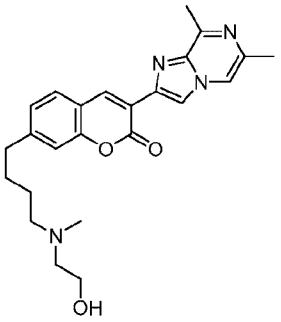

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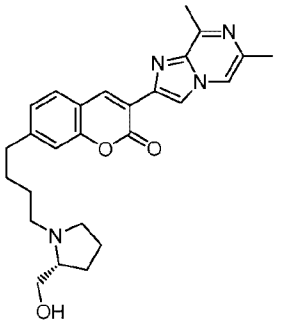

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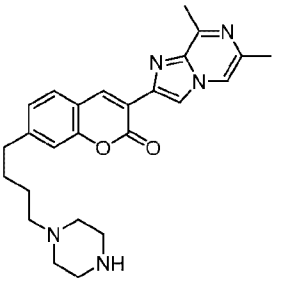

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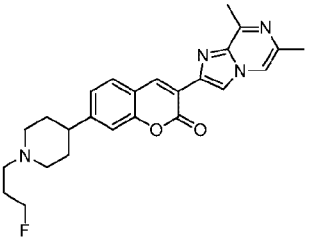

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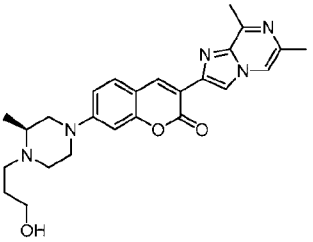

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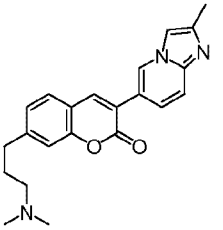

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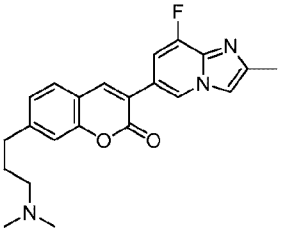

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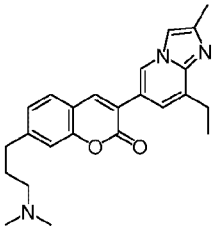

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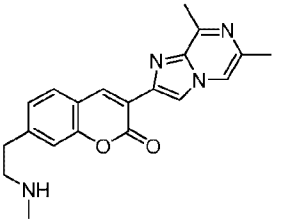

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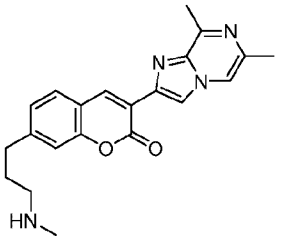

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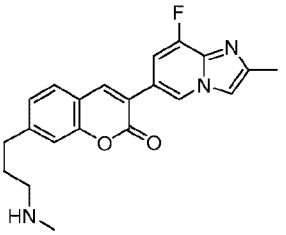

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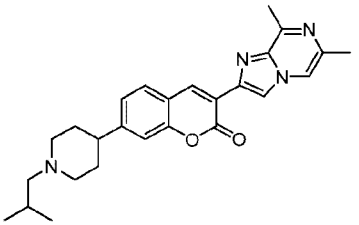

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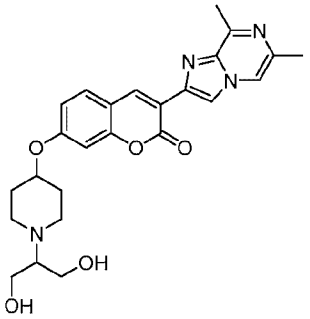

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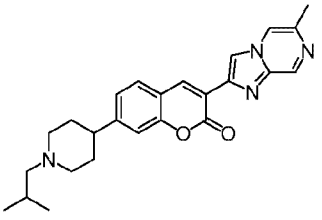

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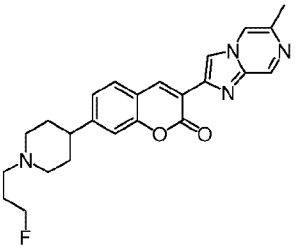

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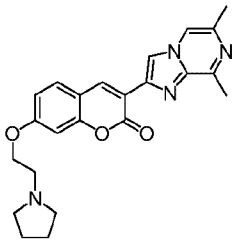

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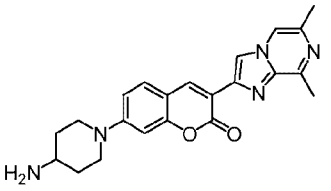

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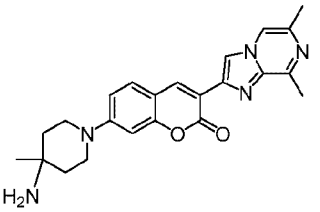

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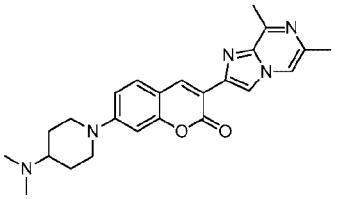

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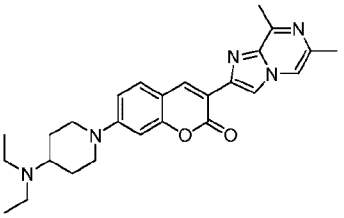

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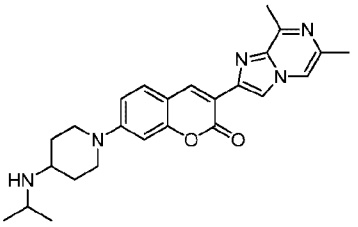

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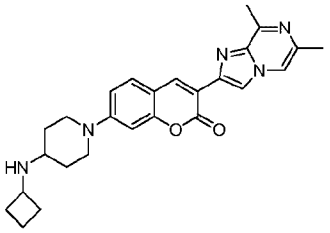

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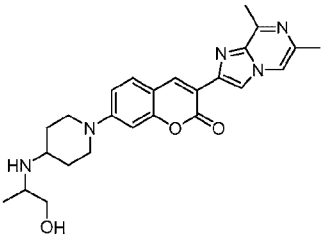

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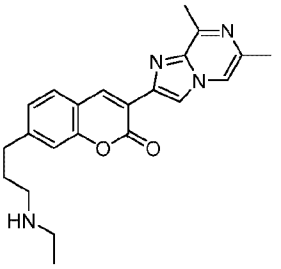

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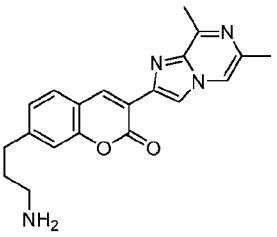

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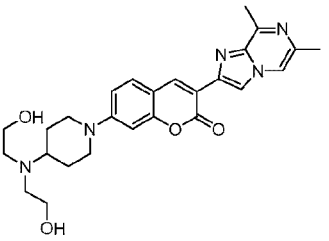

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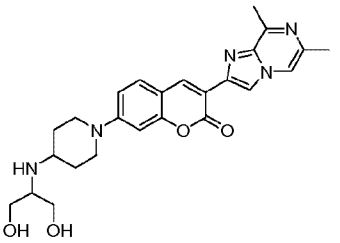

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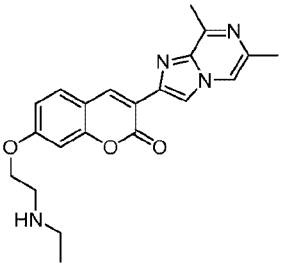

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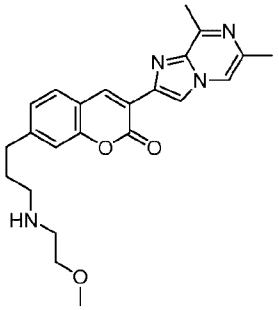

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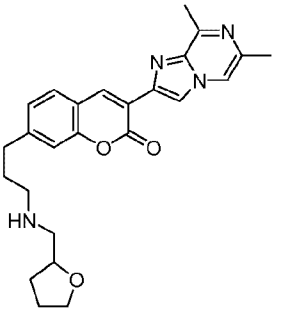

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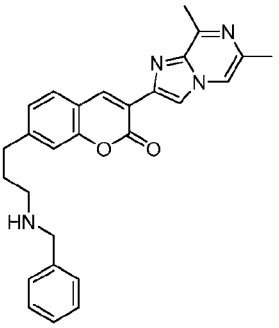

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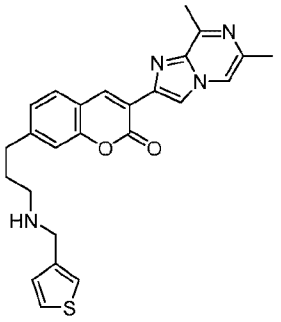

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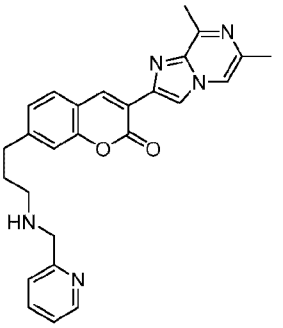

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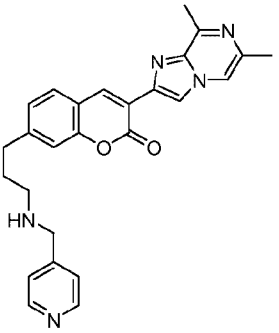

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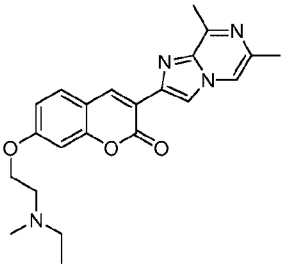

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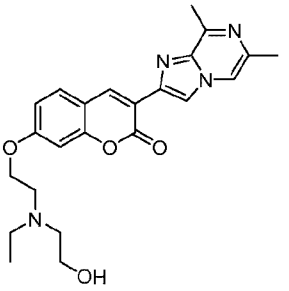

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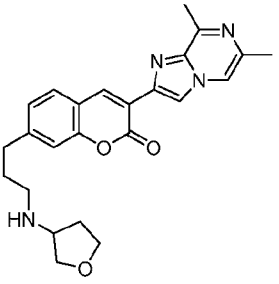

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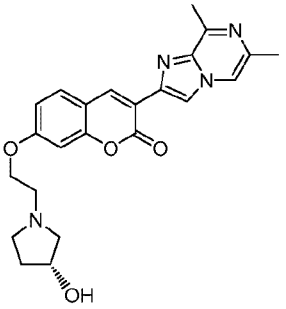

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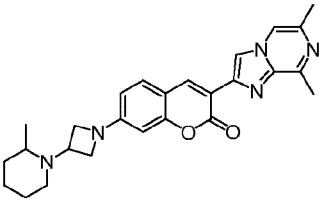

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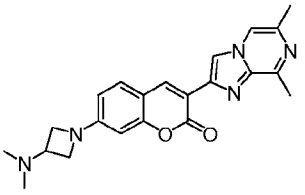

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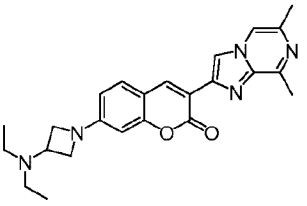

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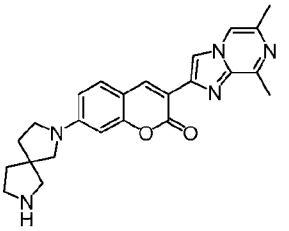

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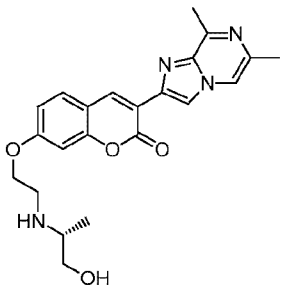

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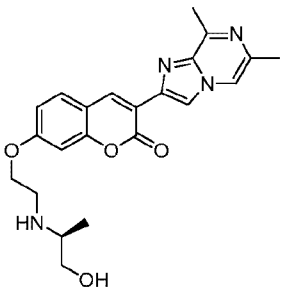

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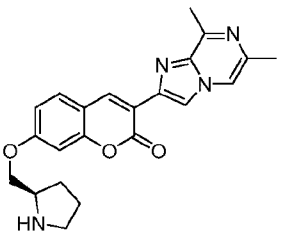

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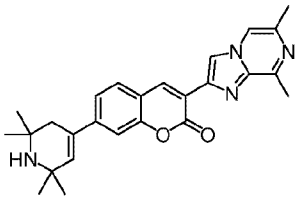

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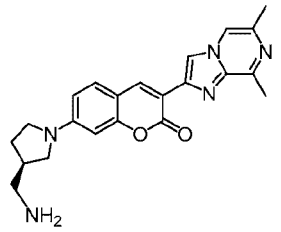

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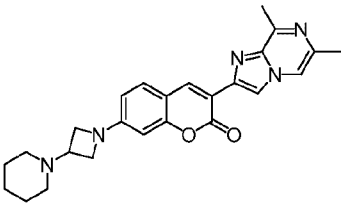

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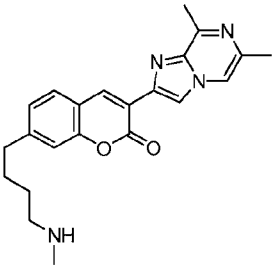

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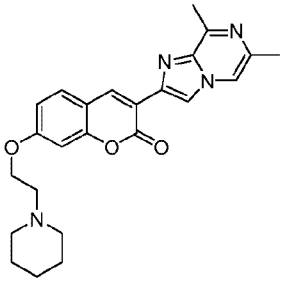

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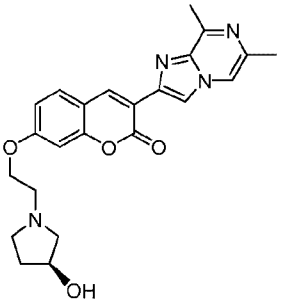

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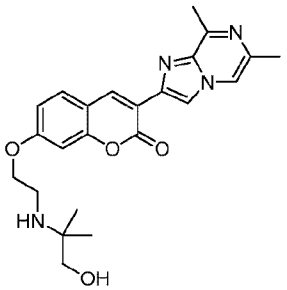

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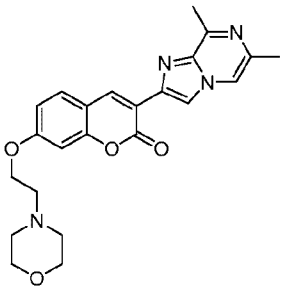

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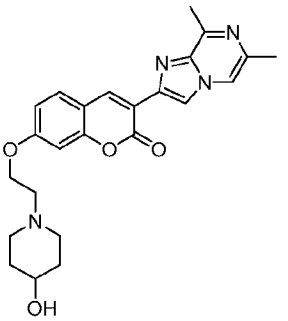

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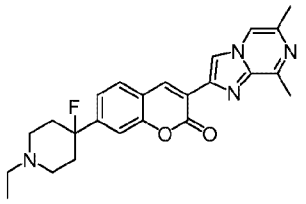

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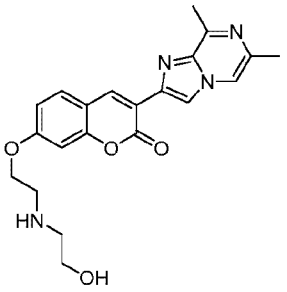

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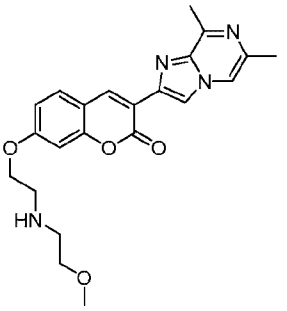

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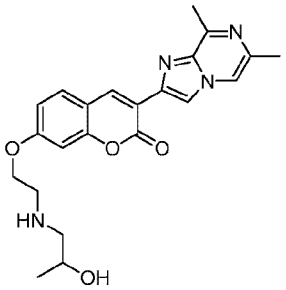

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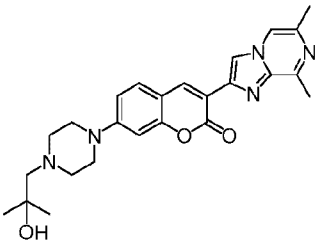

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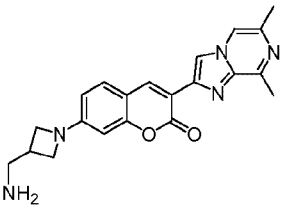

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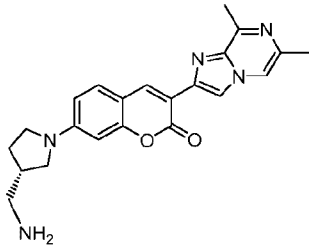

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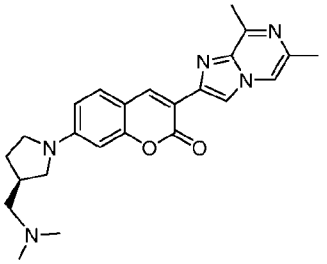

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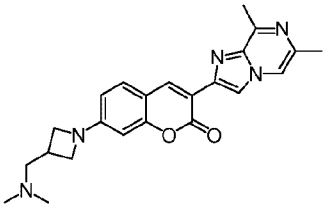

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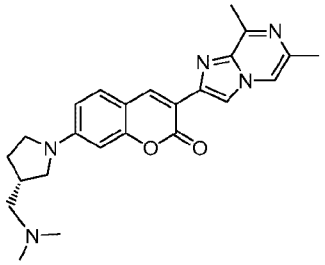

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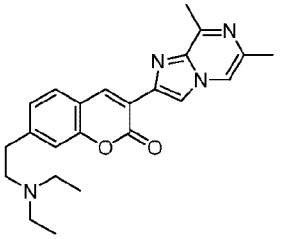

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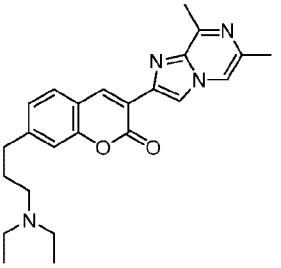

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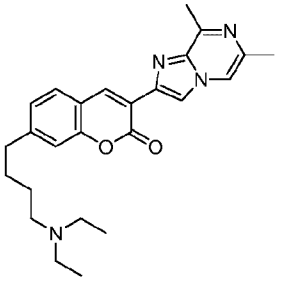

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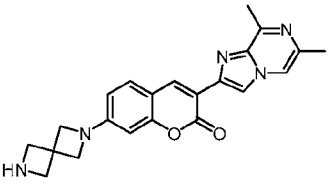

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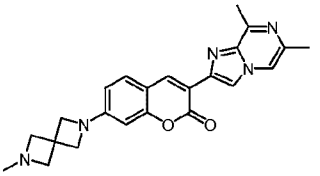

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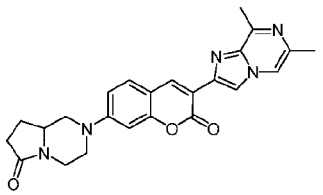

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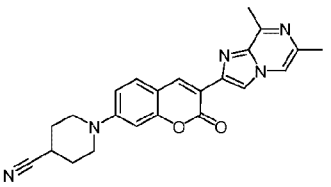

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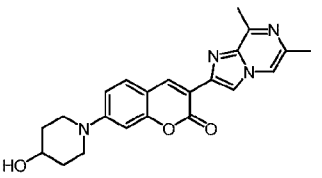

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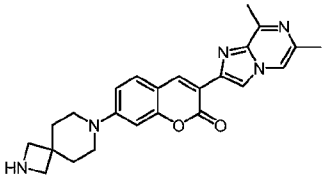

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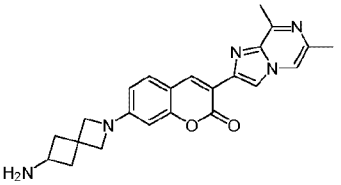

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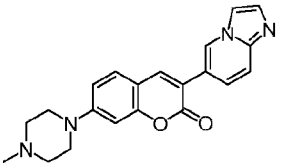

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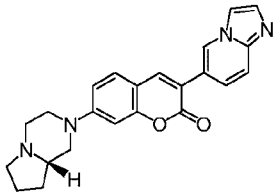

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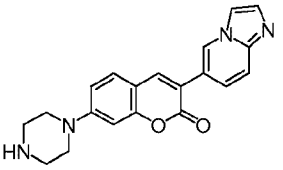

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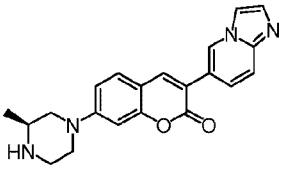

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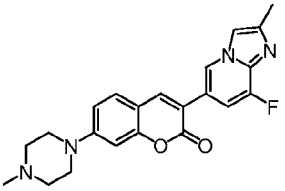

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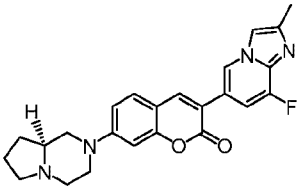

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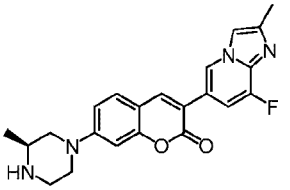

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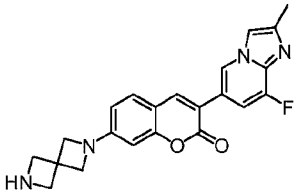

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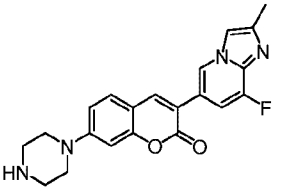

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[00208] or a form thereof.

TERMINOLOGY

[00209] 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.

[00210] 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.

[00211] 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.

[00212] 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 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.

[00213] 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.

[00214] As used herein, the term "C_{3-14}cycloalkyl" generally refers to a saturated monocyclic, bicyclic or polycyclic hydrocarbon radical, including, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 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.

[00215] 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.

[00216] 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, 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, 6H-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*]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, 3H-imidazo[4,5-b]pyridinyl, [1,3]oxazolo[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.

[00217] 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-2H-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-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, 8-azabicyclo[3.2.1]oct-2-enyl, 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 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.

[00218] 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.

[00219] 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.

[00220] 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)$_2$.

[00221] As used herein, the term "(C_{1-8}alkoxy-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-O-C_{1-8}alkyl).

[00222] 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.

[00223] 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)$_2$.

[00224] 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).

[00225] 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.

[00226] 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)$_2$.

[00227] 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).

[00228] As used herein, the term "C_{1-8}alkoxy-carbonyl" refers to a radical of the formula: -C(O)-O-C_{1-8}alkyl.

[00229] 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.

[00230] As used herein, the term "C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl.

[00231] As used herein, the term "(C_{1-8}alkyl)$_2$-amino" refers to a radical of the formula: -N(C_{1-8}alkyl)$_2$.

[00232] 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.

[00233] 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)$_2$.

[00234] 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.

[00235] 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)$_2$.

[00236] 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.

[00237] 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)$_2$.

[00238] 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.

[00239] 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)$_2$.

[00240] 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)$_2$.

[00241] 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).

[00242] 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)$_2$].

[00243] 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.

[00244] 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)$_2$.

[00245] As used herein, the term "C_{1-8}alkyl-carbonyl" refers to a radical of the formula: -C(O)-C_{1-8}alkyl.

[00246] 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.

[00247] As used herein, the term "C_{1-8}alkyl-thio" refers to a radical of the formula: -S-C_{1-8}alkyl.

[00248] As used herein, the term "amino-C_{2-8}alkenyl" refers to a radical of the formula: -C_{2-8}alkenyl-NH_2.

[00249] As used herein, the term "amino-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-NH_2.

[00250] As used herein, the term "amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH_2.

[00251] 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.

[00252] 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)$_2$.

[00253] 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).

[00254] As used herein, the term "amino-C_{2-8}alkynyl" refers to a radical of the formula: -C_{2-8}alkynyl-NH_2.

[00255] 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.

[00256] As used herein, the term "aryl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-aryl.

[00257] As used herein, the term "aryl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-aryl.

[00258] 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)$_2$.

[00259] 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).

[00260] 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.

[00261] 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)$_2$.

[00262] 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).

[00263] As used herein, the term "aryl-amino" refers to a radical of the formula: -NH-aryl.

[00264] As used herein, the term "aryl-amino-carbonyl" refers to a radical of the formula: -C(O)-NH-aryl.

[00265] 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.

[00266] As used herein, the term "benzoxy-carbonyl" refers to a radical of the formula: -C(O)O-CH_2-phenyl.

[00267] 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.

[00268] As used herein, the term "C_{3-14}cycloalkyl-amino" refers to a radical of the formula: -NH-C_{3-14}cycloalkyl.

[00269] As used herein, the term "C_{3-14}cycloalkyl-oxy" refers to a radical of the formula: -O-C_{3-14}cycloalkyl.

[00270] As used herein, the term "halo" or "halogen" generally refers to a halogen atom radical, including fluoro, chloro, bromo and iodo.

[00271] 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.

[00272] 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.

[00273] As used herein, the term "halo-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-halo.

[00274] 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).

[00275] 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)$_2$.

[00276] As used herein, the term "heteroaryl-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-heteroaryl.

[00277] As used herein, the term "heteroaryl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-heteroaryl.

[00278] As used herein, the term "heteroaryl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-heteroaryl.

[00279] 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)$_2$.

[00280] 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).

[00281] 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.

[00282] 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)$_2$.

[00283] 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).

[00284] As used herein, the term "heteroaryl-amino" refers to a radical of the formula: -NH-heteroaryl.

[00285] As used herein, the term "heterocyclyl-C_{1-8}alkoxy" refers to a radical of the formula: -O-C_{1-8}alkyl-heterocyclyl.

[00286] As used herein, the term "heterocyclyl-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-heterocyclyl.

[00287] As used herein, the term "(heterocyclyl)(C_{1-8}alkyl)amino" refers to a radical of the formula: -N(C_{1-8}alkyl)(heterocyclyl).

[00288] As used herein, the term "heterocyclyl-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-heterocyclyl.

[00289] 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)$_2$.

[00290] 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).

[00291] 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.

[00292] 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)$_2$.

[00293] 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).

[00294] As used herein, the term "heterocyclyl-amino" refers to a radical of the formula: -NH-heterocyclyl.

[00295] As used herein, the term "heterocyclyl-amino-C_{1-8}alkyl" refers to a radical of the formula: -C_{1-8}alkyl-NH-heterocyclyl.

[00296] As used herein, the term "heterocyclyl-carbonyl" refers to a radical of the formula: -C(O)-heterocyclyl.

[00297] As used herein, the term "heterocyclyl-carbonyl-oxy" refers to a radical of the formula: -O-C(O)-heterocyclyl.

[00298] As used herein, the term "heterocyclyl-oxy" refers to a radical of the formula: -O-heterocyclyl.

[00299] As used herein, the term "hydroxy" refers to a radical of the formula: -OH.

[00300] 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.

[00301] 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.

[00302] 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).

[00303] As used herein, the term "hydroxy-C_{1-8}alkyl-amino" refers to a radical of the formula: -NH-C_{1-8}alkyl-OH.

[00304] 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)$_2$.

[00305] 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.

[00306] 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).

[00307] 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)$_2$.

[00308] 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.

[00309] 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).

[00310] 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)$_2$.

[00311] 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.

[00312] 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)$_2$.

[00313] 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)$_2$.

[00314] 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).

[00315] 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)$_2$].

[00316] 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).

[00317] 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)].

[00318] 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.

[00319] 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.

[00320] 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 to be included within the scope of the compounds described herein.

[00321] 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.

[00322] 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.

[00323] 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.

[00324] 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.

[00325] 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.

[00326] 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.

[00327] 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:

[00328] 70,241,893 to 70,242,003 exon 6;

[00329] 70,242,004 to 70,247,767 intron 6;

[00330] 70,247,768 to 70,247,821 exon 7;

[00331] 70,247,822 to 70,248,265 intron 7; and,

[00332] 70,248,266 to 70,248,839 exon 8.

[00333] 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.

[00334] The approximate locations of exons 6, 7 and 8 and introns 6 and 7 of SMN2 on human chromosome 5 are as follows:

[00335] 69,366,468 to 69,366,578 exon 6;

[00336] 69,366,579 to 69,372,347 intron 6;

[00337] 69,372,348 to 69,372,401 exon 7;

[00338] 69,372,402 to 69,372,845 intron 7; and,

[00339] 69,372,846 to 69,373,419 exon 8.

[00340] 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.

[00341] 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.

[00342] 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, 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) in need thereof is increased.

[00343] 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, 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.

[00344] As used herein, the term "substantial change" in the context of the amount of mRNA means that the amount of mRNA changes 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.

[00345] 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.

[00346] As used herein, the term "elderly human" refers to a human 65 years old or older.

[00347] As used herein, the term "human adult" refers to a human that is 18 years or older.

[00348] As used herein, the term "human child" refers to a human that is 1 year to 18 years old.

[00349] As used herein, the term "human infant" refers to a newborn to 1 year old year human.

[00350] As used herein, the term "human toddler" refers to a human that is 1 year to 3 years old.

COMPOUND FORMS

[00351] As used herein, the terms "a compound of Formula (Ia)" and "a compound of Formula (Ib)" refer to sub-genuses of the compound of Formula (I) or a form thereof and are defined herein. Rather than repeat embodiments for a compound of Formula (Ia) or a compound of Formula (Ib), in certain embodiments, the term "a compound(s) of Formula (I) or a form thereof" is used to refer to either a compound of Formula (Ia) or a form thereof, a compound of Formula (Ib) or a form thereof, or both. Thus, embodiments and references to "a compound of Formula (I)" are intended to include compounds of Formula (Ia) and Formula (Ib).

[00352] 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.

[00353] 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.

[00354] 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.

[00355] 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.

[00356] In certain embodiments described herein, the form of the compound of Formula (I) is a free acid, free base or salt thereof.

[00357] In certain embodiments described herein, the form of the compound of Formula (I) is an isotopologue thereof.

[00358] In certain embodiments described herein, the form of the compound of Formula (I) is a stereoisomer, racemate, enantiomer or diastereomer thereof.

[00359] In certain embodiments described herein, the form of the compound of Formula (I) is a tautomer thereof.

[00360] In certain embodiments described herein, the form of the compound of Formula (I) is a pharmaceutically acceptable form.

[00361] In certain embodiments described herein, the compound of Formula (I) or a form thereof is isolated for use.

[00362] 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.

[00363] 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.

[00364] Prodrugs of a compound of Formula (I) or a form thereof are also contemplated herein.

[00365] 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.

[00366] 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.

[00367] 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.

[00368] 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.

[00369] 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.

[00370] 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).

[00371] As used herein, the term "hydrate" means a solvate wherein the solvent molecule is water.

[00372] 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.

[00373] 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.

[00374] Pharmaceutically acceptable salts include one or more salts of acidic or basic groups present in compounds described herein. Embodiments of acid addition salts include, and are not limited to, acetate, acid phosphate, ascorbate, benzoate, benzenesulfonate, bisulfate, bitartrate, borate, butyrate, chloride, citrate, camphorate, camphorsulfonate, ethanesulfonate, formate, fumarate, gentisinate, gluconate, glucaronate, glutamate, hydrobromide, hydrochloride, dihydrochloride, hydroiodide, isonicotinate, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, pamoate, pantothenate, phosphate, propionate, saccharate, salicylate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate (also known as tosylate), trifluoroacetate salts and the like. Certain embodiments of mono-acid, di-acid or tri-acid addition salts include a chloride, hydrochloride, dihydrochloride, trihydrochloride, hydrobromide, acetate, diacetate or trifluoroacetate salt. More particular embodiments include a chloride, hydrochloride, dihydrochloride, hydrobromide or trifluoroacetate salt.

[00375] 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* (Food & Drug Administration, Washington, D.C. on their website).

[00376] 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.

[00377] All such acid salts and base salts are intended to be pharmaceutically acceptable salts within the scope of the description herein and all acid and base salts are considered equivalent to the free forms of the corresponding compounds for the purposes described herein.

[00378] Compounds of Formula I and forms thereof may further exist in a tautomeric form (for example, as a keto or enol form such as an embedded enone system). All such tautomeric forms are contemplated herein as part of the present description.

[00379] 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.

[00380] 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.

[00381] 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.

[00382] 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%.

[00383] 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%.

[00384] 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.

[00385] 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.

[00386] 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.

[00387] 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.

[00388] It is also possible that the compounds of Formula (I) may exist in different tautomeric forms, and all such forms are embraced within the scope of this description. Accordingly, all keto-enol and imine-enamine forms of a compound of Formula (I) are included in the description herein.

[00389] 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*.

[00390] 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.

[00391] 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.

[00392] 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.*, H^2) 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.

[00393] When the compounds are enriched with deuterium, the deuterium-to-hydrogen ratio in the deuterated areas of the molecules substantially exceeds the naturally occurring deuterium-to-hydrogen ratio.

[00394] An embodiment described herein may include a compound of Formula (I) and forms thereof, wherein the isotopologue is deuterium.

[00395] 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.

[00396] 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

[00397] 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.

[00398] 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.

[00399] 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 A method for enhancing the inclusion of exon 7 of SMN2 into mRNA transcribed from the SMN2 gene, comprising contacting a human cell with 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. 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*, in a non-human animal or in a human. In a specific embodiment, the human cell is in a human. In another specific embodiment, the human cell is in a human

SMA patient. In another specific embodiment, the human cell is 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).

[00400] 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. 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*, in a non-human animal or in a human. In a specific embodiment, the human cell is in a human. In another specific embodiment, the human cell is in a human SMA patient. In another specific embodiment, the human cell is 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).

[00401] 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. 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*, in a non-human animal or in a human. In a specific embodiment, the human cell is in a human. In another specific embodiment, the human cell is in a human SMA patient.

[00402] 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*, in a non-human animal or in a human. In a specific embodiment, the human cell is in a human. In another specific embodiment, the human cell is in a human SMA patient.

[00403] 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. 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*.

[00404] 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. 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*.

[00405] 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. 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 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.

[00406] 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*, in a non-human animal or in a human. In a specific embodiment, the human cell is in a human. In another specific embodiment, the human cell is in a human SMA patient. In another specific embodiment, the human cell is 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).

[00407] 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.

[00408] 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. 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*.

[00409] 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*).

[00410] 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.

[00411] 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.

[00412] 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.

[00413] 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). 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.

[00414] 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).

[00415] 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.

[00416] 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).

[00417] 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.

[00418] 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 human 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).

[00419] 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).

[00420] 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).

[00421] 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.

[00422] 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.

[00423] 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.

[00424] 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

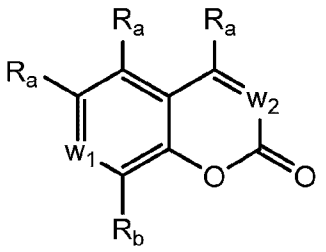
SMN deficient motor neurons from degeneration; (ix) an increase in motor function; (x) an increase in pulmonary function; and/or (xi) a reduction in the loss of pulmonary function.

[00425] 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.

[00426] 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.

[00427] In a specific embodiment, a compound of Formula (I):



(I)

[00428] or a form thereof is used in accordance with a method described herein, wherein:

[00429] w_1 and w_2 are C-R_1 or C-R_2; wherein, one of w_1 and w_2 is C-R_1 and the other is C-R_2, provided that, when w_1 is C-R_1, then w_2 is C-R_2; or, when w_1 is C-R_2, then w_2 is C-R_1;

[00430] 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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkyl, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino-$C_{1-8}$alkyl, amino-$C_{1-8}$alkyl-amino, $(amino\text{-}C_{1-8}alkyl)_2$-amino, $(amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)_2$-amino, $(C_{1-8}alkyl\text{-}amino\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl-amino, $[(C_{1-8}alkyl)_2\text{-amino-}C_{1-8}alkyl](C_{1-8}alkyl)$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, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)_2$-amino-$C_{1-8}$alkoxy, $(C_{1-8}alkoxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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, $(halo\text{-}C_{1-8}alkyl)_2$-amino, $(halo\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$amino, hydroxy-$C_{1-8}$alkyl, hydroxy-$C_{1-8}$alkoxy-$C_{1-8}$alkyl, hydroxy-$C_{1-8}$alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino, $(hydroxy\text{-}C_{1-8}alkyl)(C_{1-8}alkyl)$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-amino-C_{1-8}alkyl)(C_{1-8}alkyl)amino, (hydroxy-C_{1-8}alkyl)$_2$-amino-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, 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;

[00431] wherein, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two or three R_3 substituents and one additional, optional R_4 substituent; and,

[00432] wherein, alternatively, each instance of heterocyclyl and heteroaryl is optionally substituted with one, two, three or four R_3 substituents;

[00433] R_2 is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00434] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R_6 substituents and one additional, optional R_7 substituent;

[00435] R_a is, in each instance, independently selected from hydrogen, halogen or C_{1-8}alkyl;

[00436] R_b is hydrogen, halogen, C_{1-8}alkyl or C_{1-8}alkoxy;

[00437] 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, $(C_{1-8}alkyl)_2$-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;

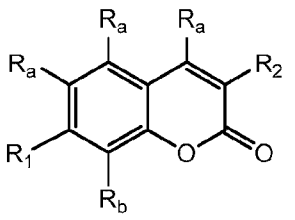
[00438] R_4 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-C_{1-8}alkyl, C_{3-14}cycloalkyl-amino, aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl, aryl-sulfonyloxy-C_{1-8}alkyl, heterocyclyl or heterocyclyl-C_{1-8}alkyl; wherein, each instance of C_{3-14}cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R_5 substituents;

[00439] 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;

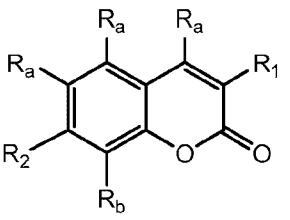
[00440] R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, C_{2-8}alkenyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio; and,

[00441] R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00442] In another specific embodiment, the compound of Formula (I) used in accordance with a method described herein is a compound selected from Formula (Ia) or Formula (Ib):



(Ia), and



(Ib);

[00443] or a form thereof, wherein all variables are as previously defined.

PATIENT POPULATION

[00444] 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, wherein the subject has SMA 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.

[00445] 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.

[00446] 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.

[00447] 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.

[00448] 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. In a specific embodiment, the patient is an SMA patient.

[00449] In some embodiments, a compound of Formula (I) or a form thereof, or a pharmaceutical composition thereof, is administered to a patient to treat or ameliorate SMA in an SMA patient. 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 treat or ameliorate SMA in an SMA patient. 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 advancement of SMA in an SMA patient. 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 treat or ameliorate SMA in an SMA patient. In a specific embodiment, the patient is an SMA patient.

[00450] 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, wherein the subject has SMA 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.

[00451] 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.

[00452] 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.

[00453] 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.

[00454] 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. In a specific embodiment, the patient is an SMA patient.

[00455] In some embodiments, a compound of Formula (I) or a form thereof, or a medicament thereof, is administered to a patient to treat or ameliorate SMA in an SMA patient. 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 treat or ameliorate SMA in an SMA patient. 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 advancement of SMA in an SMA patient. 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 treat or ameliorate SMA in an SMA patient. In a specific embodiment, the patient is an SMA patient.

MODE OF ADMINISTRATION

[00456] 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. In a specific embodiment, the patient is an SMA patient.

[00457] 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

[00458] 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.

[00459] 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.

[00460] 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.

[00461] 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.

[00462] 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.

[00463] 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, intravenous (bolus and infusion), intracerebral, transdermal, and pulmonary routes of administration.

PHARMACEUTICAL COMPOSITIONS

[00464] 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 carrier, excipient or diluent. In a specific embodiment, the human subject is an SMA patient.

[00465] 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.

[00466] 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.

[00467] 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.

[00468] 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.

[00469] 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

[00470] 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 a specific embodiment, the patient is an SMA patient.

[00471] 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 a specific embodiment, the patient is an SMA patient.

[00472] 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.

[00473] 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 that does or does not include exon 7 of SMN1 and/or SMN2.

[00474] 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.

[00475] 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.

[00476] 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 down-stream 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.

[00477] 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 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 that 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.

[00478] 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.

[00479] 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.

[00480] 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.

[00481] 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.

[00482] 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.

[00483] 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.

[00484] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes and 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 does not include exon 7 of SMN1 and SMN2.

[00485] 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.

[00486] 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.

[00487] 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. In a specific embodiment, the patient is an SMA patient.

[00488] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes and 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 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.

[00489] 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.

[00490] 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.

[00491] 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.

[00492] The amount of mRNA that is transcribed from the human SMN1 and SMN2 genes and 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 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.

[00493] 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.

[00494] 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.

[00495] 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.

[00496] 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.

[00497] 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.

[00498] 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.

[00499] 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.

[00500] 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.

[00501] 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.

[00502] 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 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.

[00503] 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.

[00504] 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 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 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.

[00505] 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.

[00506] 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 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 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.

[00507] 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.

[00508] 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 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 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 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.

[00509] 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 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.

[00510] 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 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 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 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.

[00511] 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 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.

[00512] 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 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 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 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.

[00513] 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 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.

[00514] 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) 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 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 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.

[00515] In another specific embodiment, provided herein is a method for monitoring a SMA patient's responsiveness to a compound, comprising: (a) administering a compound to a 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 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.

[00516] 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 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 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 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.

[00517] 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 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.

[00518] 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 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 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 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.

[00519] 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 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.

[00520] 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 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 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 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.

[00521] 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 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.

[00522] In specific embodiments, the SMA in the 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

[00523] 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.

[00524] 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.

[00525] 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).

[00526] 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. In other embodiments, these primers are used as probes in, *e.g.*, hybridization assays, such as Southern blot or Northern blot.

[00527] 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.

[00528] 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.

[00529] 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.

[00530] 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.

[00531] 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.

[00532] 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.

[00533] 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.

[00534] 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.

[00535] 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.

[00536] 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.

[00537] 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.

[00538] 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 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).

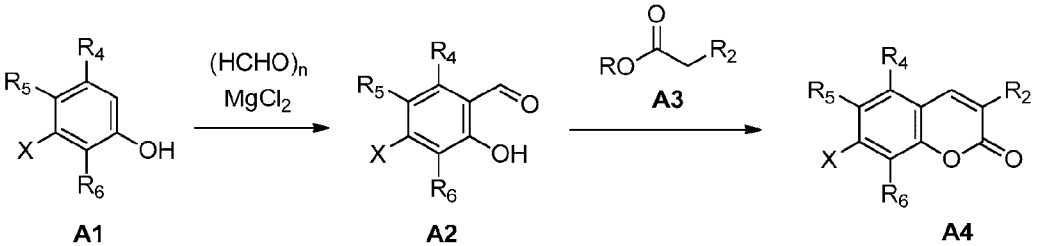
[00539] In another aspect, provided herein is a pharmaceutical kit comprising a compound of Formula (I) or a form thereof, in a container, and instructions for use of the compound or form thereof. In a specific embodiment, provided herein is a pharmaceutical kit comprising a pharmaceutical composition 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.

GENERAL SYNTHETIC METHODS

[00540] 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 reactions steps of the synthetic schemes provided herein in isolation is contemplated.

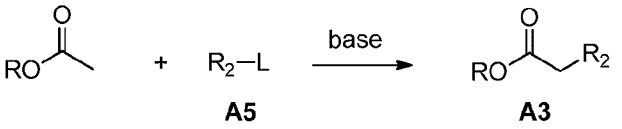
Scheme A

[00541] Compounds of Formula (I), wherein R_2 is an aryl or heteroaryl monocyclic or bicyclic ring system, can be prepared as described in Scheme A below.



[00542] Compound **A1** (where X represents various reactive groups which may be used to prepare R_1 substituents via functional group substitution reactions using techniques known to a

person of ordinary skill in the art) can be regioselectively formylated by treatment with a Lewis acid (such as $MgCl_2$ and the like) and paraformaldehyde in a suitable solvent (such as acetonitrile or THF and the like) to afford Compound **A2**. Compound **A2** is reacted with Compound **A3**, where R is a C_{1-4}alkyl group (such as methyl, ethyl, t-butyl and the like), and in the presence of condensation reagents (such as piperidine/acetic acid and the like) will undergo Knoevenagel condensation followed by lactone formation to afford Compound **A4**.

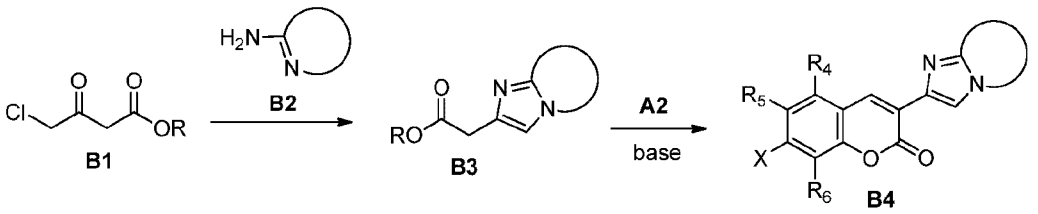


A5 **A3**

[00543] Compound **A3** can be prepared by combining a mixture of acetic acid ester (such as t-butyl acetate and the like) and a base (such as LiHMDS and the like) in a suitable solvent (such as THF and the like) with Compound **A5**, wherein R_2 represents an aryl, heterocycle or heteroaryl and L represents a leaving group.

Scheme B

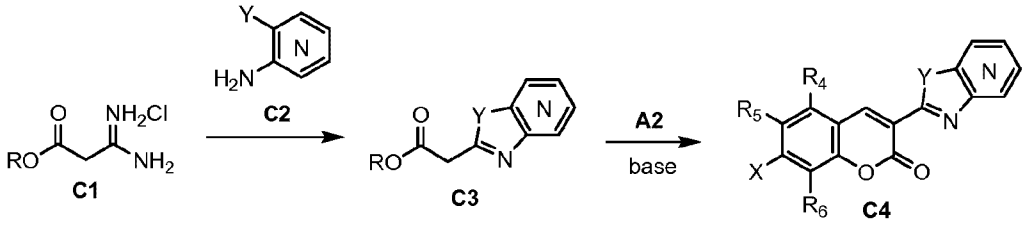
[00544] Compounds of Formula (I), wherein R_2 is a bicyclic heteroaryl ring system, can be prepared as described in Scheme B below.



[00545] Compound **B2**, an optionally substituted monocyclic heteroaryl ring system containing 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) is reacted with Compound **B1** (where R represents a C_{1-4}alkyl group such as methyl, ethyl and the like) in a suitable solvent (such as EtOH and the like) to give Compound **B3**. Compound **B3**, is reacted with Compound **A2**, and in the presence of condensation reagents (such as piperidine/acetic acid and the like), will undergo Knoevenagel condensation followed by lactone formation to afford Compound **B4**.

Scheme C

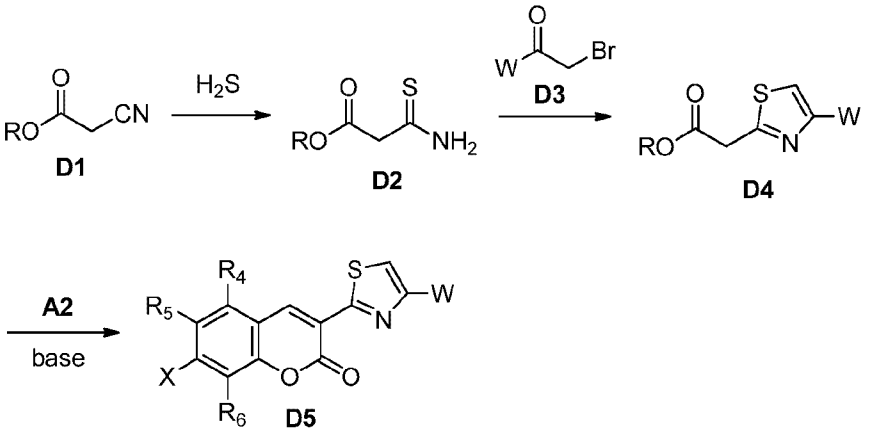
[00546] Compounds of Formula (I), wherein R_2 is a bicyclic heteroaryl ring system, can be prepared as described in Scheme C below.



[00547] Compound **C1** (where R represents a C_{1-4}alkyl group such as methyl, ethyl and the like) is reacted with Compound **C2**, an optionally substituted aniline (where Y can be OH, NH_2, or SH; and, where the aniline ring may have one or more carbon atom ring members replaced with one or more nitrogen atoms, thus making Compound **C2** an optionally substituted ring system such as a pyridine, pyrimidine, pyrazine and the like), and in a suitable solvent (such as EtOH or acetonitrile and the like) affords Compound **C3**. Compound **C3** is reacted with Compound **A2**, and in the presence of condensation reagents (such as piperidine/acetic acid and the like), will undergo Knoevenagel condensation followed by lactone formation to afford Compound **C4**.

Scheme D

[00548] Compounds of Formula (I), wherein R_2 is a monocyclic heteroaryl ring system, can be prepared as described in Scheme D below.

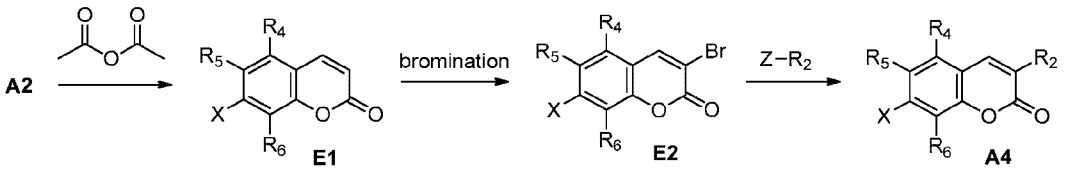


[00549] Compound **D1** (where R represents a C_{1-4}alkyl group such as methyl, ethyl and the like) is reacted with hydrogen sulfide in the presence of an organic base (such as triethylamine and the like) and a suitable solvent (such as pyridine and the like) to give Compound **D2**. Compound **D2** is reacted with Compound **D3**, an α-bromoketone (where W represents a

C_{1-4}alkyl or halo-C_{1-4}alkyl group such as methyl, ethyl, trifluoromethyl and the like), and in an appropriate solvent (such as DMF and the like), undergoes a tandem alkylation dehydrative condensation to give Compound **D4**. Compound **D4** is reacted with Compound **A2**, and in the presence of condensation reagents (such as piperidine/acetic acid and the like), will undergo Knoevenagel condensation followed by lactone formation to afford Compound **D5**.

Scheme E

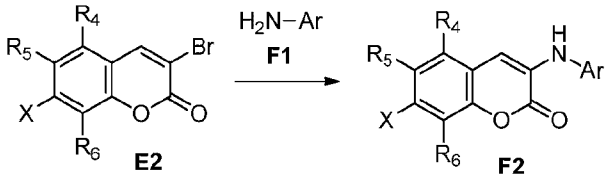
[00550] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl or heteroaryl ring system, can be prepared as described in Scheme E below.



[00551] Compound **A2** is reacted with acetic anhydride, and in the presence of an organic base (such as triethylamine and the like), undergoes Aldol condensation/lactone formation to afford Compound **E1**. Compound **E1** is brominated with an appropriate brominating reagent (such as Br_2 or NBS) to afford Compound **E2**. Compound **E2** is reacted with a boronic acid (where Z represents $B(OH)_2$ and the like) or a trialkyl stannane (where Z represents $SnBu_3$ and the like), and in the presence of a palladium catalyst (such as tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine) palladium(II) dichloride, palladium acetate and the like) and an appropriate phospine ligand will undergo Suzuki or Stille cross coupling to give Compound **A4**.

Scheme F

[00552] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl-amino or heteroaryl-amino, can be prepared as described in Scheme F below.

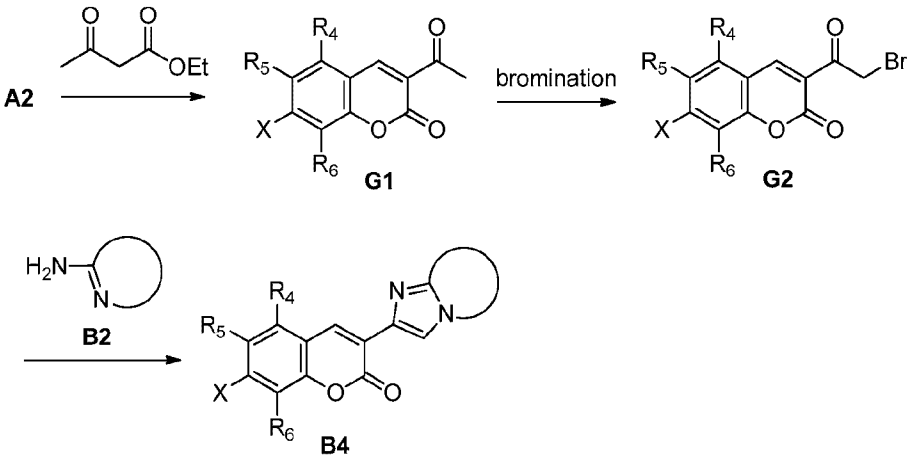


[00553] Compound **E2** is reacted with Compound **F1**, where Ar represents an optionally substituted monocyclic or bicyclic aryl or heteroaryl ring system such as an optionally substituted aniline or amino-heteroaryl, in the presence of a palladium catalyst (such as tris(dibenzylideneacetone)dipalladium(0) and the like), phosphine ligand (such as xantphos and

the like), and an inorganic base (such as cesium carbonate and the like) in an appropriate solvent (such as 1,4-dioxane or toluene and the like) to afford Compound **F2**.

Scheme G

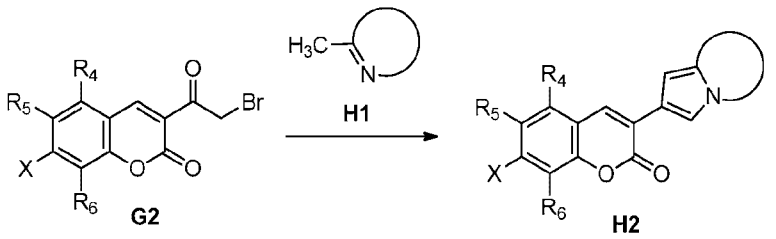
[00554] Compounds of Formula (I), wherein R_2 is a bicyclic heteroaryl ring system, can be prepared as described in Scheme G below.



[00555] Compound **A2** is reacted with ethyl acetoacetate, and in the presence of condensation reagents (such as piperidine/acetic acid and the like), will undergo Knoevenagel condensation followed by lactone formation to afford Compound **G1**. The α-methyl group of Compound **G1** can be selectively brominated with an appropriate brominating reagent (such as Br_2 or NBS and the like) to afford Compound **G2**. Compound **G2** is reacted with Compound **B2**, an optionally substituted monocyclic heteroaryl ring system containing 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 acetonitrile and the like) to give Compound **B4**.

Scheme H

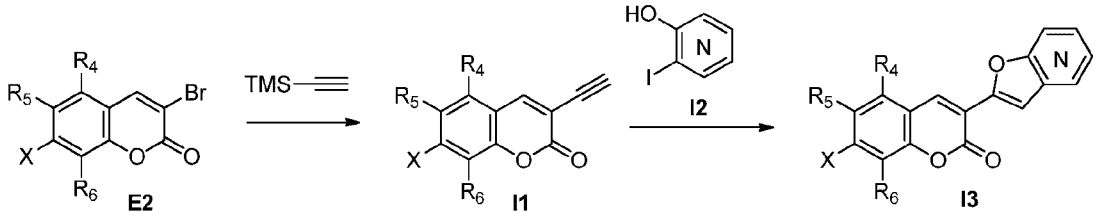
[00556] Compounds of Formula (I), wherein R_2 is a bicyclic heteroaryl ring system, can be prepared as described in Scheme H below.



[00557] Compound **G2** is reacted with Compound **H1**, an optionally substituted monocyclic heteroaryl ring system containing a ketimine-like moiety (such as but not limited to 2-methylpyridine, 2-methylpyrimidine, 2-methylpyrazine, 3-methylpyridazine and the like), and in a suitable solvent (such as acetonitrile and the like), undergoes a tandem alkylation dehydrative cyclization reaction to give Compound **H2**.

Scheme I

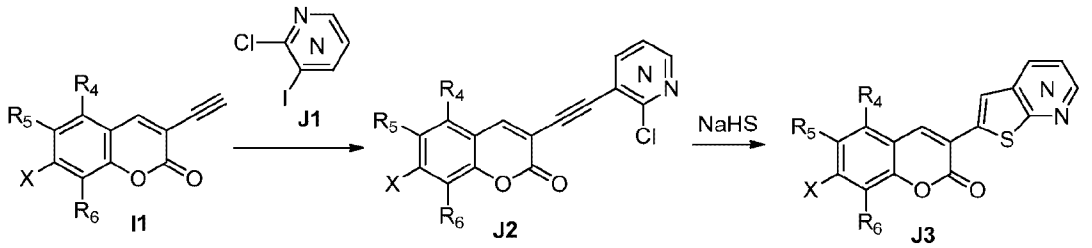
[00558] Compounds of Formula (I), wherein R_2 is a bicyclic heteroaryl ring system, can be prepared as described in Scheme I below.



[00559] Compound **E2** is reacted with trimethylsilylacetylene and an organic base (such as triethylamine and the like) in the presence of copper(I) iodide and a palladium catalyst (such as tetrakis (triphenylphosphine) palladium(0), bis(triphenylphosphine) palladium(II) dichloride, palladium acetate and the like) and, in the presence of an appropriate phospine ligand undergoes a Sonogashira coupling. The resulting trimethylsilylacetylene product when treated with an inorganic base (such as potassium carbonate and the like) in an appropriate solvent (such as methanol and the like) yields Compound **I1**. Compound **I1** can undergo an additional Sonogashira coupling with Compound **I2**, an iodo-hydroxy-substituted monocyclic heteroaryl ring system (where the heteroaryl ring may have one or more additional nitrogen atom ring members, thus making Compound **I2** an iodo-hydroxy-substituted ring system such as a pyridine, pyrimidine, pyrazine and the like, and where the iodo and hydroxy substituents are in an ortho orientation with respect to one another, such as 2-iodopyridin-3-ol, 4-iodopyridin-3-ol and the like) to give Compound **I3**.

Scheme J

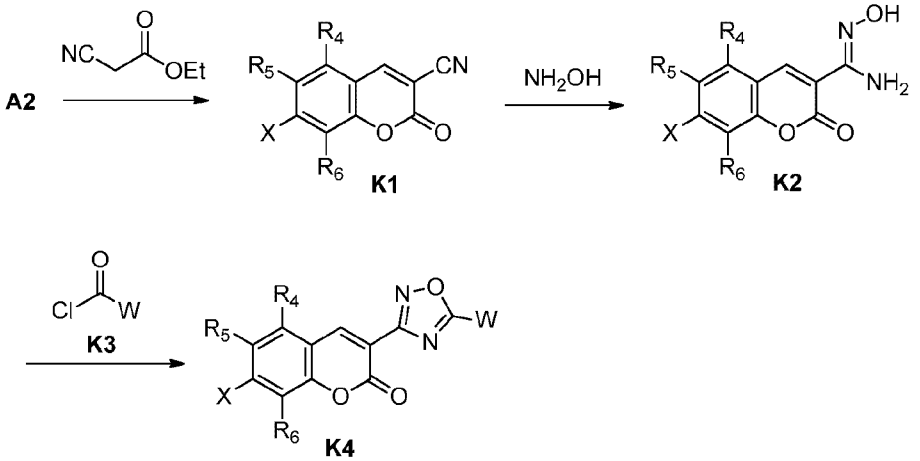
[00560] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic heteroaryl ring system, can be prepared as described in Scheme J below.



[00561] Compound **I1** is reacted with Compound **J1**, a chloro-iodo-substituted monocyclic heteroaryl ring system (where the heteroaryl ring may have one or more additional nitrogen atom ring members, thus making Compound **J1** a chloro-iodo-substituted ring system such as a pyridine, pyrimidine, pyrazine and the like, and where the chloro- and iodo-substituents are in an ortho orientation with respect to one another, such as 2-chloro-3-iodopyridine or 4-chloro-3-iodopyridine and the like), and an organic base (such as triethylamine and the like) in the presence of copper(I) iodide and a palladium catalyst (such as tetrakis (triphenylphosphine) palladium(0), bis(triphenylphosphine) palladium(II) dichloride, palladium acetate and the like) and, in the presence of an appropriate phospine ligand undergoes a Sonogashira coupling to afford Compound **J2**. Compound **J2** treated with sodium hydrosulfide in a suitable solvent (such as EtOH and the like) affords Compound **J3**.

Scheme K

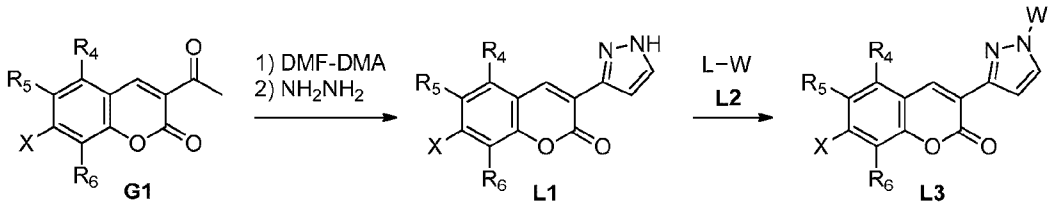
[00562] Compounds of Formula (I), wherein R_2 is an optionally substituted 1,2,4-oxadiazole ring system, can be prepared as described in Scheme K below.



[00563] Compound **A2** is reacted with ethyl cyanoacetate, and in the presence of condensation reagents (such as piperidine/acetic acid and the like) will undergo Knoevenagel condensation followed by lactone formation to afford Compound **K1**. Compound **K1** is reacted with hydroxylamine in a suitable solvent (such as CH_2Cl_2) to give Compound **K2**. Compound **K2** is reacted with Compound **K3** (where W represents a C_{1-4}alkyl, aryl or heteroaryl group), and in the presence of an organic base (such as triethylamine and the like), affords an O-acyl-hydroxyamidine intermediate, that undergoes dehydrative cyclization at elevated temperatures (≥100 °C) to yield Compound **K4**.

Scheme L

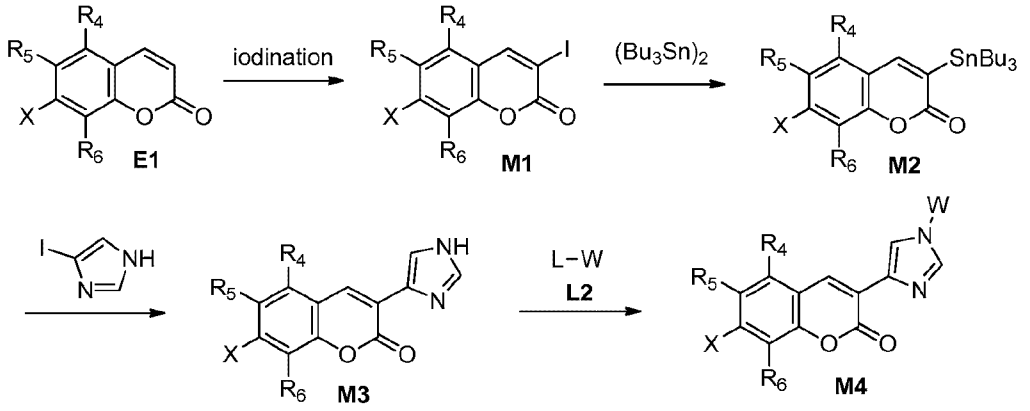
[00564] Compounds of Formula (I), wherein R_2 is a monocyclic heteroaryl ring system, can be prepared as described in Scheme L below.



[00565] Compound **G1** is reacted with dimethylformamide dimethyl acetal and an organic base (such as pyrrolidine and the like) to give an enaminone intermediate, which is then reacted with hydrazine in the presence of an organic acid (such as acetic acid and the like) to afford Compound **L1**. Compound **L1** is reacted with Compound **L2** (where W represents a C_{1-4}alkyl, aryl, or heteroaryl group and L represents a leaving group (such as I or Br and the like), in a suitable solvent (such as DMF and the like), in the presence of an inorganic base (such as Cs_2CO_3 and the like), and an optional catalyst (such as CuI and the like) to afford Compound **L3**.

Scheme M

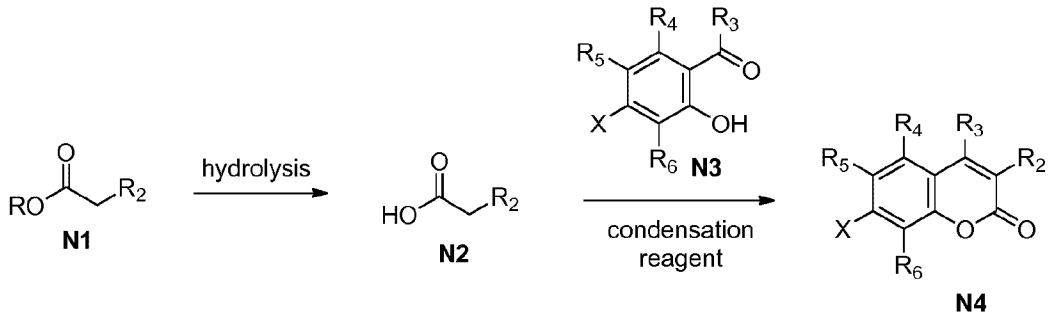
[00566] Compounds of Formula (I), wherein R_2 is a monocyclic heteroaryl ring system, can be prepared as described in Scheme M below.



[00567] Compound **E1** can be regioselectively iodinated with an appropriate iodinating agent (such as iodine or bis(trifluoroacetoxy)iodo]benzene and the like) in an appropriate solvent (such as $CHCl_3$ and the like). Compound **M1**, when treated with hexabutylditin in the presence of a palladium catalyst (such as tetrakis (triphenylphosphine) palladium(0), bis(triphenylphosphine) palladium(II) dichloride, palladium acetate and the like) in an appropriate solvent (such as 1,4-dioxane or toluene), affords Compound **M2**. Compound **M2** is reacted with 5-iodoimidazole, in the presence of a catalyst (such as tetrakis (triphenylphosphine) palladium(0), bis(triphenylphosphine) palladium(II) dichloride, palladium acetate and the like) and a cocatalyst (such as CuI and the like), in an appropriate solvent (such as 1,4-dioxane or toluene and the like) to afford Compound **M3**. Compound **M3** is reacted with Compound **L2** (where W represents a C_{1-4}alkyl, aryl, or heteroaryl group and L represents a leaving group (such as I or Br and the like), in a suitable solvent (such as DMF and the like), in the presence of an inorganic base (such as Cs_2CO_3 and the like), and an optional catalyst (such as CuI and the like) to afford Compound **M4**.

Scheme N

[00568] Compounds of Formula (I), wherein R_2 is a monocyclic or bicyclic aryl or heteroaryl ring system and R_3 is hydrogen or alkyl, can be prepared as described in Scheme N below.



[00569] Compound **N1** is treated under the conditions for ester hydrolysis (such as aqueous NaOH), to afford Compound **N2**. Compound **N2** is reacted with Compound **N3** (where R represents a hydrogen or C_{1-4}alkyl group), and in the presence of a coupling reagent (such as *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride and the like) and an organic base (such as triethylamine and the like), undergoes ester formation followed by Knoevenagel condensation to give Compound **N4**.

SPECIFIC SYNTHETIC EXAMPLES

[00570] 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.

[00571] 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.

[00572] 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

[00573] 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	with heating
AcOH or HOAc	acetic acid
Ac_2O	acetic anhydride
Ar	argon
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
BrettPhos	2-(dicyclohexylphosphino)3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl
°C	degrees Centigrade
CDI	1,1-carbonyldiimidazole or N,N'-carbonyldiimidazole

Abbreviation	Meaning
$(CHO)_n$, $(HCHO)_n$ or HCHO	paraformaldehyde
Cs_2CO_3	cesium carbonate
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	dimethyl acetal
DMAc	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
MeI	iodomethane
Me-THF	2-methyltetrahydrofuran
Me_2Zn	dimethylzinc
MnO_2	manganese dioxide
MS	mass spectroscopy
NaH	sodium hydride
NaHS	sodium hydrosulfide

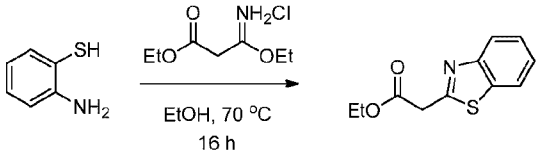
Abbreviation	Meaning
NaHMDS	sodium bis(trimethylsilyl)amide or sodium hexamethyldisilazide
NaI	sodium iodide
NaOAc	sodium acetate
NaOMe	sodium methoxide
NBS	N-bromosuccinimide
NMP	N-methylpyrrolidone
NMR	nuclear magnetic resonance
o/n	overnight
Pd	palladium
Pd/C	palladium on carbon
$Pd(dba)_2$	bis(dibenzylideneacetone)palladium(0)
$Pd_2(dba)_3$ 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 $Pd(pph_3)_4$	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
$POCl_3$	phosphoryl chloride
PPh_3	triphenylphosphine
PPA	polyphosphoric acid
PPTs	pyridinium *p*-toluenesulfonate
psi	pounds per square inch pressure
PyBOP	(benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate
rt	room temperature
RuPhos	2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
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

Abbreviation	Meaning
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilane
TMSCl	trimethylchlorosilane or trimethylsilyl chloride
TMSOK	potassium trimethylsilanolate
t-Bu	tert-butyl
t-BuOAc	tert-butyl acetate
t-BuXPhos Palladacycle	chloro[2-(di-*tert*-butylphosphino)-2′,4′,6′-triisopropyl-1,1′-biphenyl][2-(2-aminoethyl)phenyl)] palladium(II)
TsOH, p-TsOH or *p*TSA	tosylic acid or *p*-toluenesulfonic acid
xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

[00574] **Example 1**

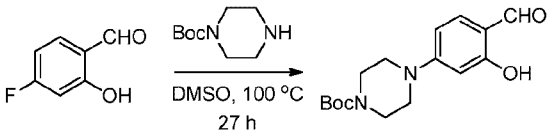
[00575] Preparation of Cpd 4

[00576] Part 1: Preparation of ethyl 2-(benzo[d]thiazol-2-yl)acetate



[00577] A mixture of 2-aminobenzenethiol (5.34 mL, 50 mmol) and 3-ethoxy-3-iminopropanoate hydrochloride (9.75 g, 50 mmol) in EtOH (50 mL) was heated at 70 °C for 16 h. The mixture was partitioned in EtOAc (200 mL) and water (200 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica gel column chromatography (10% EtOAc in hexanes) to give the title compound (6.0 g, 54%) as a yellow oil. MS *m/z* 222.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.05 (1H, d, J = 8.1 Hz), 7.91 (1H, d, J = 8.0 Hz), 7.51 (1H, t, J = 8 Hz), 7.43 (1H, t, J = 8 Hz), 4.28 (2H, q, J = 7.2 Hz), 4.22 (2H, s), 1.33 (3H, t, J = 7.1 Hz).

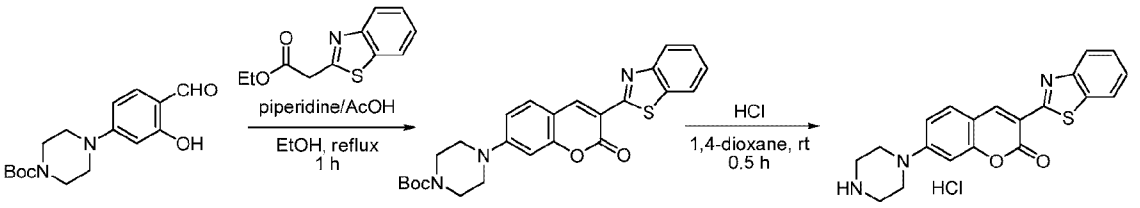
[00578] Part 2: Preparation of tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate



[00579] A mixture of 4-fluoro-2-hydroxybenzaldehyde (10 g, 71.4 mmol), 1-boc-piperazine (15.3 g, 82.2 mmol), and DMSO (100 mL) was heated at 100 °C for 27 h. The reaction mixture

was diluted in an aqueous K_2CO_3 solution and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with hexane/ether (1:1), yielding the title compound (18.8 g, 86%) as a yellow solid. MS *m/z* 307.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 11.50 (1H, s), 9.60 (1H, s), 7.36 (1H, d, *J* = 9 Hz), 6.27 (1H, d, *J* = 2 Hz), 6.45 (1H, dd, *J* = 9 Hz, 2 Hz), 3.58 (4H, m), 3.42 (4H, m), 1.49 (9H, s).

[00580] Part 3: Preparation of Cpd 4



[00581] Step A: tert-Butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (49 mg, 0.16 mmol) and ethyl 2-(benzo[d]thiazol-2-yl)acetate (35 mg, 0.16 mmol) were combined with piperidine (10 μL, 0.1 mmol) and acetic acid (6 μL, 0.1 mmol) in EtOH (1 mL). The mixture was heated at reflux for 1 h. After cooling the mixture to room temperature, a precipitate formed. The solid was collected by vacuum filtration, washed with 1:1 EtOH:H_2O (1 mL) and dried under vacuum to afford tert-butyl 4-(3-(benzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate.

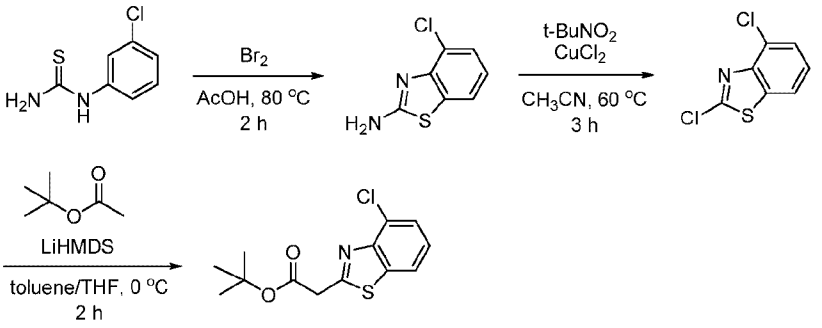
[00582] Step B: tert-butyl 4-(3-(benzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate was suspended in 4N HCl in 1,4-dioxane (1 mL). After stirring the mixture for 30 min at room temperature, the solvent was removed with a stream of nitrogen, to give the title compound (40 mg, 69%) as a yellow powder: m.p. 250 °C (decomp.); MS *m/z* 364.4 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.26 (2H, br s), 9.14 (1H, s), 8.16 (1H, d, *J* = 7.9 Hz), 8.04 (1H, d, *J* = 8.1 Hz), 7.93 (1H, d, *J* = 9.0 Hz), 7.56 (1H, m), 7.47 (1H, m), 7.16 (1H, dd, *J* = 8.9 Hz, 2.3 Hz), 7.09 (1H, d, *J* = 2.3 Hz), 3.76-3.74 (4H, m), 3.25-3.23 (4H, m).

[00583] 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.

[00584] **Example 2**

[00585] Preparation of Cpd 5

[00586] Part 1: Preparation of tert-butyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate

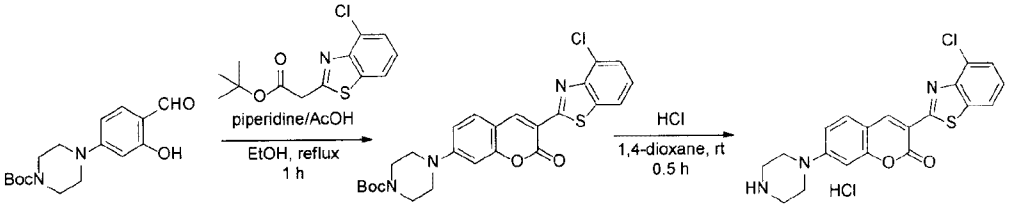


[00587] Step A: To a solution of 1-(3-chlorophenyl)thiourea (5.09 g, 27.2 mmol) in acetic acid (100 mL) was added bromine (1.82 mL, 35.4 mmol) dropwise at 60 °C. The mixture was heated at 80 °C for 2 h and the solvent was removed under reduced pressure. Diethyl ether was added to the mixture to produce a precipitate. The solid was collected and dried to give 4-chlorobenzo[d]thiazol-2-amine (5.7 g, 79%). MS *m/z* 185.9 $[M+H]^+$.

[00588] Step B: To a mixture of 4-chlorobenzo[d]thiazol-2-amine (4.78 g, 25.8 mmol) and copper(II) chloride (4.16 g, 31 mmol) in CH_3CN (25 mL) was added t-butyl nitrite (4.61 mL, 38.8 mmol) at room temperature. The reaction mixture was heated at 60 °C for 30 min, then the solvent was removed from the mixture. The residue was suspended in water, collected by filtration and dried to give 2,4-dichlorobenzo[d]thiazole. (5.3 g, 81%). MS *m/z* 205.9 $[M+H]^+$.

[00589] Step C: To a mixture of t-butyl acetate (4.93 mL, 36.6 mmol) and 2,4-dichlorobenzo[d]thiazole (5 g, 24.4 mmol) in toluene (20mL) was added lithium bis(trimethylsilyl)amide (1M in THF, 66 mL, 66 mmol) at 0 °C. The mixture was stirred at room temperature overnight. Excess reagent was quenched with the addition of aqueous saturated NH_4Cl. The aqueous mixture was extracted with EtOAc. The organic layer was concentrated and purified by silica gel column chromatography (0-5% EtOAC in hexanes) to give the title compound (5.9 g, 85%) as a yellow oil. MS *m/z* 282.1 $[M-H]^-$. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75 (1H, d, *J* = 8.2 Hz), 7.47 (1H, d, *J* = 7.7 Hz), 7.29 (1H, t, *J* = 7.9 Hz), 4.15 (2H, s), 1.48 (9H, s).

[00590] Part 2: Preparation of Cpd 5



[00591] Step A: Following the procedure found in Example 1, Part 3, tert-Butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (49 mg, 0.16 mmol), tert-butyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (35 mg, 0.16 mmol), piperidine (10 µL, 0.1 mmol) and acetic acid (6 µL, 0.1 mmol) in EtOH (1 mL) gave tert-butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate.

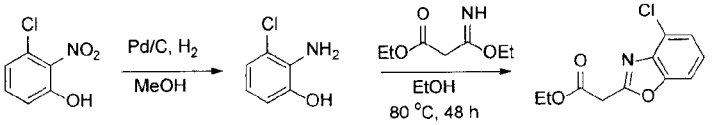
[00592] Step B: Following the procedure found in Example 1, Part 3, tert-butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate and 4N HCl in 1,4-dioxane (1 mL) gave the title compound (62 mg, 97%) as a yellow powder: m.p. 290 °C (decomp.); MS *m/z* 398.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.18 (2H, br s), 9.09 (1H, s), 8.14 (1H, dd, J = 8.0 Hz, 1.0 Hz), 7.99 (1H, d, J = 9.2 Hz), 7.65 (1H, dd, J = 7.7 Hz, 1.0 Hz), 7.44 (1H, t, J = 7.8 Hz), 7.17 (1H, dd, J = 9.0 Hz, 2.4 Hz), 7.09 (1H, d, J = 2.2 Hz), 3.77-3.74 (4H, m), 3.25-3.23 (4H, m).

[00593] 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.

[00594] **Example 3**

[00595] Preparation of Cpd 68

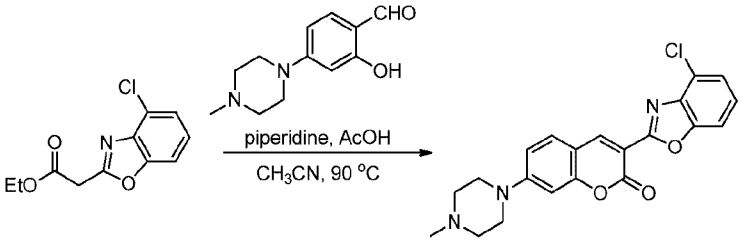
[00596] Part 1: Preparation of ethyl 2-(4-chlorobenzo[d]oxazol-2-yl)acetate



[00597] Step A: A mixture of 3-chloro-2-nitrophenol (18.95 g, 100 mmol) and Pd/C (10%, 0.50 g) in MeOH (300 mL) was stirred under H_2 (1 atm). After 15 h, the mixture was filtered through Celite™. The filtrate was concentrated to give a brown solid, which was washed with CH_2Cl_2 to give 2-amino-3-chlorophenol (7.39 g, 52%) as a light brown solid. MS *m/z* 144.1 $[M+H]^+$.

[00598] Step B: To a solution of 2-amino-3-chlorophenol (2.0 g, 14 mmol) in EtOH (30 mL) was added ethyl 3-ethoxy-3-iminopropanoate hydrochloride (3.01 g, 15.4 mmol). After heating at 80 °C for 2 d, the mixture was concentrated. The residue was partitioned between EtOAc and water. The organic layer was concentrated and purified by silica gel column chromatography (CH_2Cl_2) to give ethyl 2-(4-chlorobenzo[d]oxazol-2-yl)acetate (3.17 g, 94%) as an off-white solid. MS *m/z* 240.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 7.75 (1H, dd, J = 8.0 Hz, 0.9 Hz), 7.49 (1H, dd, J = 8.0 Hz, 0.9 Hz), 7.43 (1H, t, J = 8.0 Hz), 4.28 (2H, s), 4.16 (2H, q, J = 7.2 Hz), 1.21 (3H, t, J = 7.2 Hz).

[00599] Part 2: Preparation of Cpd 68

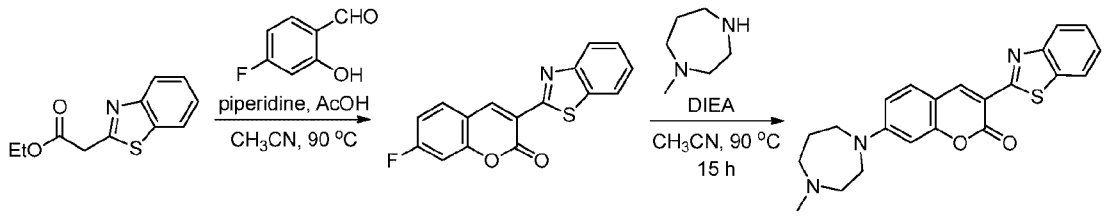


[00600] To a solution of ethyl 2-(4-chlorobenzo[d]oxazol-2-yl)acetate (72 mg, 0.3 mmol, prepared according to Example 1) and 2-hydroxy-4-(4-methylpiperazin-1-yl)benzaldehyde (66 mg, 0.3 mmol, prepared following the procedure in Example 1, Part 2) in CH_3CN (0.5 mL) were added piperidine (3 uL, 0.03 mmol) and AcOH (3.4 uL, 0.06 mmol). After heating at 90 °C for 2 h, the mixture was cooled to room temperature. The product was collected by vacuum filtration, washed with CH_3CN and dried to give the title compound (92 mg, 78%) as a yellow solid: m.p. 229–231 °C; MS *m/z* 396.2, 398.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.91 (1H, s), 8.79 (1H, d, J = 9.1 Hz), 7.76 (1H, dd, J = 8.2 Hz, 0.9 Hz), 7.50 (1H, dd, J = 8.0 Hz, 0.8 Hz), 7.42 (1H, t, J = 8.0 Hz), 7.08 (1H, dd, J = 9.0 Hz, 2.4 Hz), 6.90 (1H, d, J = 2.3 Hz), 3.49 (4H, m), 2.43 (4H, m), 2.26 (3H, s).

[00601] 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.

[00602] **Example 4**

[00603] Preparation of Cpd 145



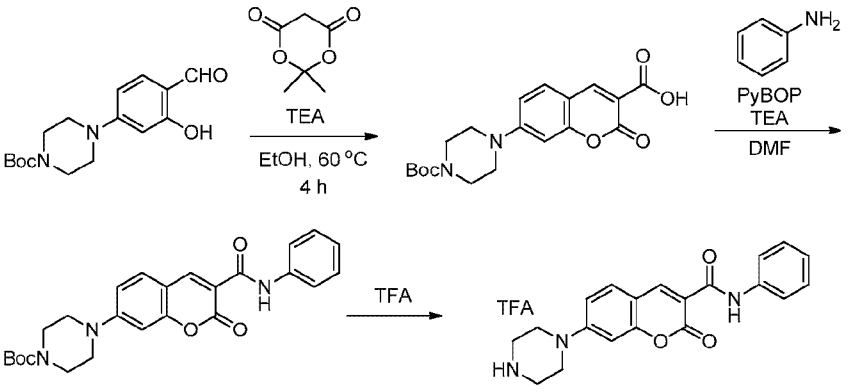
[00604] Step A: A mixture of ethyl 2-(benzo[d]thiazol-2-yl)acetate (0.53 g, 2.4 mmol, prepared in Example 1, Part 1), 4-fluoro-2-hydroxybenzaldehyde (0.336 g, 2.4 mmol), piperidine (80 μL, 0.8 mmol) and acetic acid (92 μL, 0.16 mmol) in CH_3CN (2 mL) was heated at 60 °C for 1 h. The mixture was filtered. The solid material was washed with CH_3CN and dried to give 3-(benzo[d]thiazol-2-yl)-7-fluoro-2H-chromen-2-one (0.57 g, 80%) as a yellow solid. MS *m/z* 298.1 $[M+H]^+$.

[00605] Step B: A mixture of 3-(benzo[d]thiazol-2-yl)-7-fluoro-2H-chromen-2-one (89 mg, 0.3 mmol), 1-methyl-1,4-diazepane (75 μL, 0.6 mmol), N,N-diisopropylethylamine (78 μL, 0.45 mmol) in CH_3CN (1 mL) was heated at 90 °C. After 15 h, the mixture was cooled to room temperature and filtered. The solid material was washed with CH_3CN to give the title compound (110 mg, 94%) as a yellow solid: m.p. 217–220 °C; MS *m/z* 392.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 9.04 (1H, s), 8.12 (1H, d, *J* = 7.7 Hz), 7.99 (1H, d, *J* = 8.1 Hz), 7.79 (1H, d, J = 9.1), 7.54-7.51 (1H, m), 7.43-7.40 (1H, m), 6.93 (1H, dd, *J* = 9.0 Hz, 2.4 Hz), 6.76 (1H, d, *J* = 2.2 Hz), 3.69 (2H, m), 3.61 (2H, t, *J* = 6.2 Hz), 2.64 (2H, m), 2.46 (2H, m), 2.26 (3H, s), 1.91 (2H, m).

[00606] 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.

[00607] **Example 5**

[00608] Preparation of Cpd 3



[00609] Step A: tert-Butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (918 mg, 3 mmol, prepared in Example 1, Part 2), 2,2-dimethyl-1,3-dioxane-4,6-dione (648 mg, 4.5 mmol) and triethylamine (0.14 mL, 1 mmol) were combined in EtOH (6 mL). The mixture was heated at 60 °C for 4 h. The mixture was cooled to room temperature and filtered. The collected material was washed with EtOH and dried under vacuum to afford 7-(4-(tert-butoxycarbonyl)piperazin-1-yl)-2-oxo-2H-chromene-3-carboxylic acid (1.05 g, 94%) as a yellow powder. MS *m/z* 373.2 $[M-H]^-$.

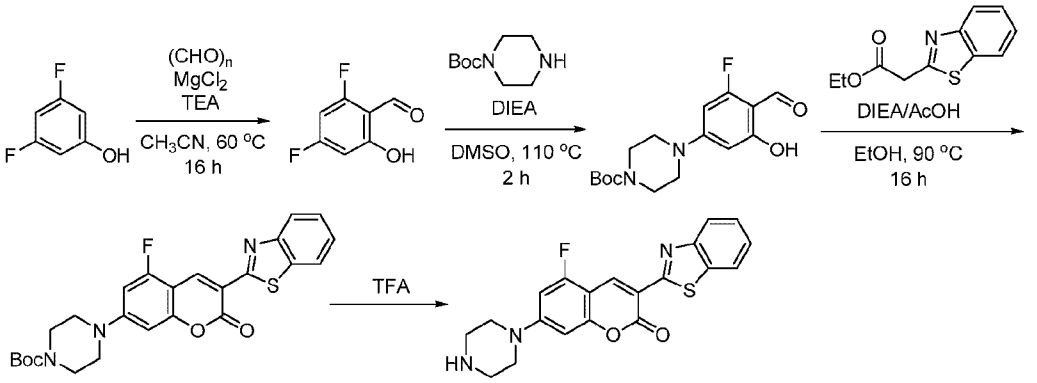
[00610] Step B: 7-(4-(tert-Butoxycarbonyl)piperazin-1-yl)-2-oxo-2H-chromene-3-carboxylic acid (60 mg, 0.16 mmol) was combined with aniline (22 μL, 0.24 mmol), (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (100 mg, 0.19 mmol) and triethylamine (45 μL, 0.32 mmol) in DMF (1 mL). The mixture was stirred at room temperature for 2 h. A solution of 4:1 MeOH:H_2O (1 mL) was added to the mixture. A precipitate formed and was collected by vacuum filtration. The solid was washed with MeOH:H_2O (4:1) and dried under vacuum to afford tert-butyl 4-(2-oxo-3-(phenylcarbamoyl)-2H-chromen-7-yl)piperazine-1-carboxylate.

[00611] Step C: A mixture of tert-butyl 4-(2-oxo-3-(phenylcarbamoyl)-2H-chromen-7-yl)piperazine-1-carboxylate in trifluoroacetic acid (1 mL) was stirred at room temperature for 20 min, then the solvent was removed with a stream of nitrogen to afford the title compound (75 mg, 99%) as a yellow powder: MS *m/z* 350.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 10.73 (1H, s), 8.81 (1H, s), 7.78 (1H, d, J = 9.1 Hz), 7.72 (2H, d, J = 8.6 Hz), 7.38 (2H, m), 7.13 (1H, t, J = 7.4 Hz), 7.09 (1H, dd, J = 9.1 Hz, 2.5 Hz), 6.93 (1H, d, J = 2.3 Hz), 3.43 (4H, m), 2.81 (4H, m).

[00612] 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.

[00613] **Example 6**

[00614] Preparation of Cpd 160



[00615] Step A: 3,5-Difluorophenol (2.6 g, 20 mmol) was dissolved in CH_3CN (50 mL) with triethylamine (14 mL, 100 mmol). Magnesium chloride (3.8 g, 40 mmol) and paraformaldehyde (6.4 g, 200 mmol) were added sequentially. The heterogeneous mixture was stirred vigorously at 60 °C for 16 h. The mixture was diluted with H_2O (200mL) and the pH was adjusted to <2 with aqueous HCl (1 M). The mixture was extracted with EtOAc (200 mL). The organic layer was washed with brine, dried over Na_2SO_4, then filtered and concentrated to afford 2,4-difluoro-6-hydroxybenzaldehyde (2.6 g, 82%) as a red oil. MS *m/z* 157.1 $[M-H]^-$.

[00616] Step B: 2,4-Difluoro-6-hydroxybenzaldehyde (16 mmol) was combined with 1-Boc-piperazine (3.57 g, 19.2 mmol) and N,N-diisopropylethylamine (3.34 mL, 19.2 mmol) in DMSO (4 mL). The mixture was heated to 120 °C for 2 h. The mixture was purified by silica gel column chromatography (0-40% EtOAc in hexanes) to afford tert-butyl 4-(3-fluoro-4-formyl-5-hydroxyphenyl)piperazine-1-carboxylate (1.3 g, 25%) as an off white powder. ^1H NMR (500 MHz, DMSO-d_6): δ 11.93 (1H, s), 9.92 (1H, s), 6.08 (1H, dd, J = 14.2 Hz, 2.4 Hz), 6.04 (1H, d, J = 2.4 Hz), 3.59 (4H, m), 3.43 (4H, m), 1.49 (9H, s).

[00617] Step C: tert-Butyl 4-(3-fluoro-4-formyl-5-hydroxyphenyl)piperazine-1-carboxylate (65 mg, 0.2 mmol) was combined with ethyl 2-(benzo[d]thiazol-2-yl)acetate (22 mg, 0.2 mmol, prepared in Example 1, Part 1), N,N-diisopropylethylamine (35 μL, 0.2 mmol) and acetic acid (11 μL, 0.2 mmol) in EtOH (1 mL). The mixture was heated to 90 °C for 16 h. After cooling the mixture to room temperature, a precipitate was formed. The solid was collected, washed

with 1:1 MeOH:H_2O (1 mL) and dried under vacuum to afford tert-butyl 4-(3-(benzo[d]thiazol-2-yl)-5-fluoro-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate.

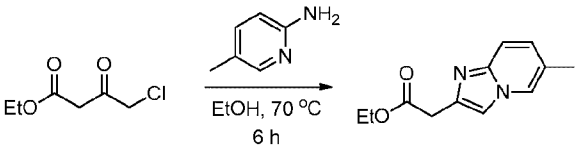
[00618] Step D: A mixture of tert-butyl 4-(3-(benzo[d]thiazol-2-yl)-5-fluoro-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate and trifluoroacetic acid (1 mL) was stirred at room temperature for 15 min, then the solvent was removed with a stream of nitrogen. The residue was partitioned in CH_2Cl_2 (5 mL) and aqueous K_2CO_3 (1 M, 5 mL). The organic layer was collected through a hydrophobic frit and concentrated to afford the title compound (38 mg, 50%) as a yellow powder: m.p. 256–260 °C; MS *m/z* 382.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.89 (1H, s), 8.15 (1H, d, J = 7.8 Hz), 8.05 (1H, d, J = 7.3 Hz), 7.55 (1H, m), 7.44 (1H, m), 7.02 (1H, dd, J = 13.9 Hz, 2.1 Hz), 6.82 (1H, s), 3.45-3.41 (4H, m), 2.82-2.78 (4H, m), 2.46 (1H, s br).

[00619] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 6 by substituting the appropriate starting materials, reagents and reaction conditions.

[00620] **Example 7**

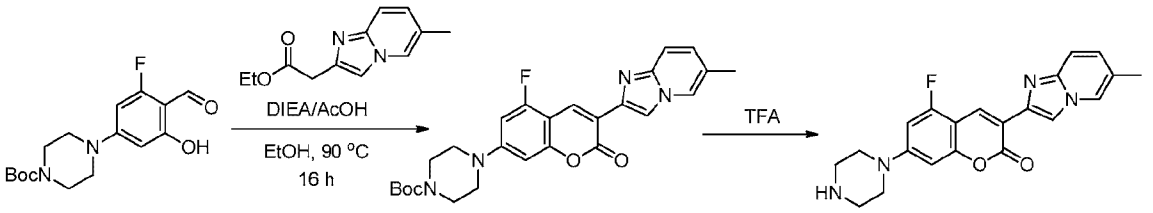
[00621] Preparation of Cpd 162

[00622] Part 1: Preparation of ethyl 2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetate



[00623] A mixture of ethyl 4-chloroacetoacetate (5.4 mL, 40 mmol) and 5-methylpyridin-2-amine (5.18 g, 48 mmol) in EtOH (100 mL) was heated at 70 °C for 6 h. The mixture was partitioned in EtOAc (300 mL) and an aqueous saturated $NaHCO_3$ solution (300 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica gel column chromatography (70% EtOAc in hexanes) to give the title compound (1.6 g, 19%) as a brown oil. ^1H NMR (500 MHz, DMSO-d_6): δ 8.31 (1H, s), 7.74 (1H, s), 7.39 (1H, d, J = 9.2 Hz), 7.08 (1H, d, J = 9.2 Hz), 4.10 (2H, q, J = 7.1 Hz), 3.75 (2H, s), 2.27 (3H, s), 1.20 (3H, t, J = 7.1 Hz).

[00624] Part 2: Preparation of Cpd 162



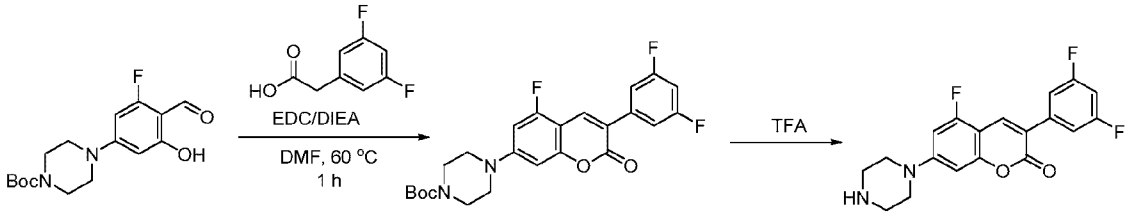
[00625] Step A: Following the procedure in Example 6, Step C, tert-butyl 4-(3-fluoro-4-formyl-5-hydroxyphenyl)piperazine-1-carboxylate (65 mg, 0.2 mmol), ethyl 2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetate (22 mg, 0.2 mmol), N,N-diisopropylethylamine (35 μL, 0.2 mmol) and acetic acid (11 μL, 0.2 mmol) in EtOH (1 mL) gave tert-butyl 4-(5-fluoro-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate.

[00626] Step B: Following the procedure in Example 6, Step D, tert-butyl 4-(5-fluoro-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate and trifluoroacetic acid (1 mL) gave the title compound (18 mg, 24%) as a yellow powder: m.p. 265–270 °C; MS *m/z* 379.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.60 (1H, s), 8.42 (2H, m), 7.49 (1H, d, J = 9.1 Hz), 7.16 (1H, dd, J = 9.3 Hz, 1.6 Hz), 6.93 (1H, dd, J = 11.6 Hz, 2.2 Hz), 6.75 (1H, d, J = 1.9 Hz), 3.33-3.31 (4H, m), 2.82-2.80 (4H, m), 2.28 (3H, s).

[00627] 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.

[00628] **Example 8**

[00629] Preparation of Cpd 290



[00630] Step A: tert-Butyl 4-(3-fluoro-4-formyl-5-hydroxyphenyl)piperazine-1-carboxylate (65 mg, 0.2 mmol, prepared in Example 6, Step B) was combined with 2-(3,5-difluorophenyl)acetic acid (55 mg, 0.2 mmol), *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (57 mg, 0.3 mmol) and N,N-diisopropylethylamine (70 μL, 0.4 mmol) in DMF (1 mL). The mixture was heated to 60 °C for 1 h. After cooling to room temperature, the mixture was filtered. The solid was washed with MeOH:H_2O (1:1) and dried

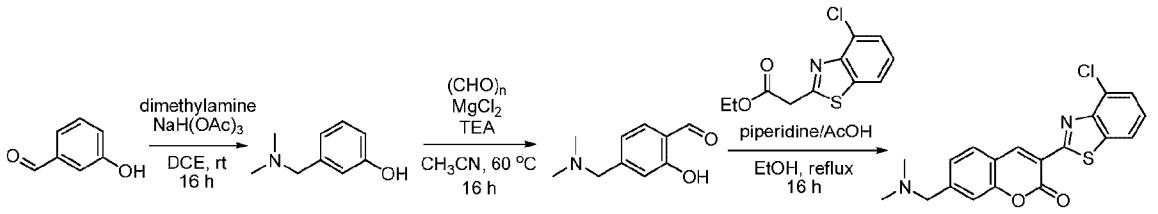
under vacuum to afford tert-butyl 4-(3-(3,5-difluorophenyl)-5-fluoro-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate.

[00631] Step B: A mixture of tert-Butyl 4-(3-(3,5-difluorophenyl)-5-fluoro-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate and trifluoroacetic acid (1 mL) was stirred at room temperature for 15 min, then the solvent was removed with a stream of nitrogen. The residue was partitioned in CH_2Cl_2 (5 mL) and aqueous K_2CO_3 (1 M, 5 mL). The organic layer was collected through a hydrophobic frit and concentrated to afford the title compound (24 mg, 33%) as a yellow powder: m.p. 193–198 °C; MS *m/z* 361.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.11 (1H, s), 7.44 (2H, m), 7.16 (1H, tt, J = 9.3 Hz, 2.4 Hz), 6.82 (1H, dd, J = 13.8 Hz, 2.2 Hz), 6.65 (1H, d, J = 2.4 Hz), 3.26 (4H, m), 2.73 (4H, m).

[00632] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 8 by substituting the appropriate starting materials, reagents and reaction conditions.

[00633] **Example 9**

[00634] Preparation of Cpd 14



[00635] Step A: 3-Hydroxybenzaldehyde (6.1 g, 50 mmol) was combined with dimethylamine (37.5 mL of 2M solution in THF, 75 mmol) in 1,2-dichloroethane (200 mL). Sodium triacetoxyborohydride (15.9 g, 75 mmol) was added slowly at room temperature. Acetic acid (2.86 mL, 50 mmol) was added to the mixture. The mixture was stirred at room temperature for 16 h. To the reaction mixture was added an aqueous saturated $NaHCO_3$ solution (100 mL). The organic layer was removed, dried over Na_2SO_4, then filtered and concentrated to afford crude 3-((dimethylamino)methyl)phenol (~30 mmol, 60%).

[00636] Step B: The crude material (~30 mmol) from Step A was dissolved in CH_3CN (300 mL) and triethylamine (21 mL, 150 mmol). To the solution was added anhydrous magnesium chloride (5.7 g, 60 mmol) and paraformaldehyde (9.0 g, 300 mmol). The mixture was stirred vigorously at 60 °C for 16 h, then diluted with aqueous sodium potassium tartrate (0.1 M, 600 mL). The mixture was extracted three times with CH_2Cl_2 (300 mL). The combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified

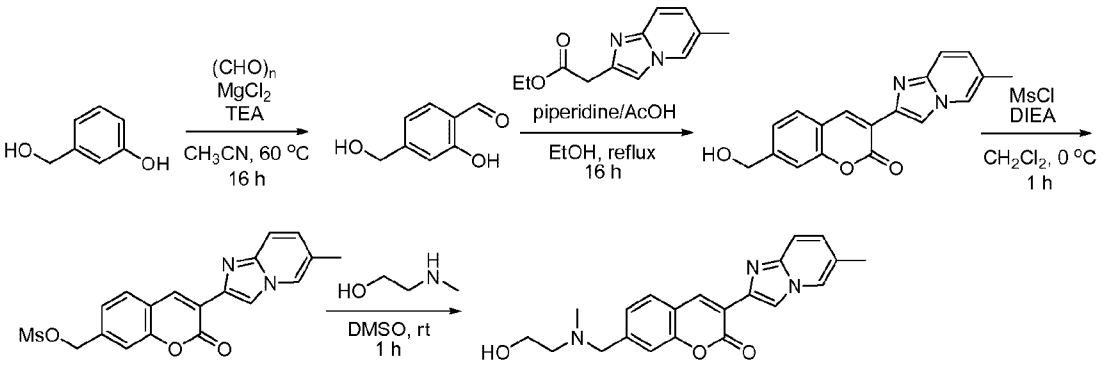
by silica gel column chromatography (0-10% MeOH in CH_2Cl_2) to afford 4-((dimethylamino)methyl)-2-hydroxybenzaldehyde (1.7 g, 32%) as a yellow powder. MS *m/z* 180.1 $[M+H]^+$.

[00637] Step C: A mixture of 4-((dimethylamino)methyl)-2-hydroxybenzaldehyde (0.5 mmol), ethyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (128 mg, 0.5 mmol, prepared as in Example 2, Part 1), piperidine (40 μL, 0.4 mmol) and acetic acid (12 μL, 0.2 mmol) in EtOH (3 mL) was heated at reflux for 16 h. After cooling the mixture to room temperature, a precipitate formed. The solid was collected by vacuum filtration, washed with 1:1 EtOH:H_2O (1 mL) and dried under vacuum to afford the title compound (184 mg, 99%) as a yellow powder: m.p. 179–182 °C; MS *m/z* 371.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.20 (1H, s), 8.18 (1H, d, J = 8.0 Hz), 8.10 (1H, d, J = 8.0 Hz), 7.69 (1H, d, J = 7.7 Hz), 7.48 (2H, m), 7.43 (1H, d, J = 8.0 Hz), 3.57 (2H, s), 2.21 (6H, s).

[00638] 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.

[00639] **Example 10**

[00640] Preparation of Cpd 148



[00641] Step A: Following the procedure in Example 6, Step A, 3-(hydroxymethyl)phenol (6.2 g, 50 mmol), triethylamine (35 mL, 250 mmol), anhydrous magnesium chloride (9.5 g, 100 mmol) and paraformaldehyde (15 g, 500 mmol) in CH_3CN (500 mL) afforded 2-hydroxy-4-(hydroxymethyl)benzaldehyde (2.2 g, 29%). MS *m/z* 151.1 $[M-H]^-$.

[00642] Step B: Following the procedure in Example 9, Step C, 2-hydroxy-4-(hydroxymethyl)benzaldehyde (608 mg, 4.0 mmol), ethyl 2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetate (872 mg, 4.0 mmol, prepared in Example 7, Part 1), piperidine (0.4 mL, 4.0 mmol) and

acetic acid (0.24 mL, 4.0 mmol) in EtOH (4 mL) afforded 7-(hydroxymethyl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (980 mg, 80%). MS *m/z* 307.2 $[M+H]^+$.

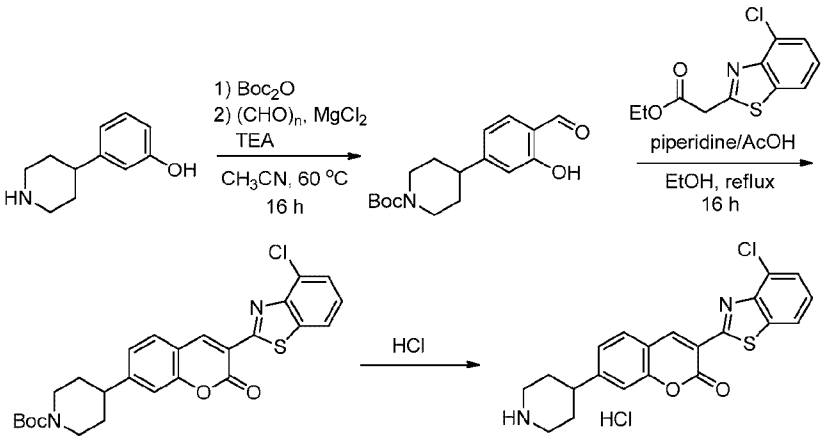
[00643] Step C: 7-(Hydroxymethyl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (900 mg, 2.9 mmol) was combined with N,N-diisopropylethylamine (1.0 mL, 6 mmol) in CH_2Cl_2 (15 mL). The mixture was cooled to 0 °C, before adding methanesulfonyl chloride (0.28 mL, 3.6 mmol) via syringe. The mixture stirred for 1 h at 0 °C, then the solvent was removed from the mixture. The residue was suspended in MeOH (5 mL) and filtered. The collected material was washed with MeOH and dried under vacuum to afford (3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl)methyl methanesulfonate (1.05 g, 92%) as a tan powder. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.86 (1H, s), 8.56 (1H, s), 8.46 (1H, s), 7.99 (1H, d, J = 7.9 Hz), 7.56 (1H, s), 7.51 (1H, d, J = 9.1 Hz), 7.47 (1H, d, J = 8.0 Hz), 7.20 (1H, d, 9.3 Hz), 5.41 (2H, s), 3.32 (3H, s), 2.30 (3H, s).

[00644] Step D: (3-(6-Methylimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl)methyl methanesulfonate (77 mg, 0.2 mmol) was combined with 2-(methylamino)ethanol (75 mg, 1.0 mmol) in DMF (2 mL). The mixture was stirred at room temperature for 1 h. To the mixture was added H_2O (0.25 mL) to produce a precipitate. The solid was collected by vacuum filtration, washed with MeOH:H_2O (1:1) and dried under vacuum to afford the title compound (65 mg, 90%) as an off white powder: m.p. 166–169 °C; MS *m/z* 364.3 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.83 (1H, s), 8.53 (1H, s), 8.46 (1H, s), 7.87 (1H, d, J = 8.0 Hz), 7.50 (1H, d, J = 9.4 Hz), 7.43 (1H, s), 7.37 (1H, d, J = 7.9 Hz), 7.19 (1H, d, J = 9.2 Hz), 4.47 (1H, t, J = 5.4 Hz), 3.64 (2H, s), 3.54 (2H, q, J = 5.5 Hz), 2.47 (2H, t, J = 6.3 Hz), 2.29 (3H, s), 2.21 (3H, s).

[00645] 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.

[00646] **Example 11**

[00647] Preparation of Cpd 18



[00648] Step A: 4-(3-Hydroxyphenyl)piperidine (1.7 g, 10 mmol) was added to a mixture of CH_3CN (20 mL) and di-tert-butyl dicarbonate (2.4 g, 11 mmol). The mixture was stirred for 1 h at room temperature, then triethylamine (7 mL, 50 mmol), anhydrous magnesium chloride (1.9 g, 20 mmol) and paraformaldehyde (3.0 g, 100 mmol) were added. The mixture was stirred vigorously at 60 °C for 2 h, then diluted with H_2O (100 mL). Aqueous HCl (1N) was added to adjust the pH of the mixture to ~2. The mixture was extracted with EtOAc (100 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (0-5% MeOH in CH_2Cl_2) to afford tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperidine-1-carboxylate (1.44 g, 47%) as a white powder. MS *m/z* 304.2 $[M-H]^-$.

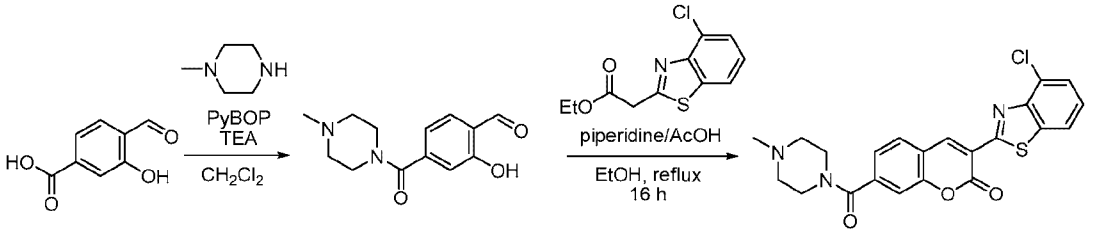
[00649] Step B: Following the procedure in Example 9, Step C, tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperidine-1-carboxylate (61 mg, 0.2 mmol), ethyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (50 mg, 0.2 mmol, prepared according to Example 2, Part 1), piperidine (10 μL, 0.1 mmol) and acetic acid (6 μL, 0.1 mmol) in EtOH (1 mL) afforded tert-butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperidine-1-carboxylate.

[00650] Step C: tert-Butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)piperidine-1-carboxylate was suspended in 4N HCl in 1,4-dioxane (1 mL). The mixture was stirred for 1 h, then the solvent was removed to afford the title compound (73 mg, 92%) as a yellow powder: m.p. 339–341 °C; MS *m/z* 397.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.21 (1H, s), 8.19 (1H, d, J = 8.0), 8.14 (1H, d, J = 8.1), 7.70 (1H, d, J = 7.7 Hz), 7.49 (1H, t, J =

7.8 Hz), 7.43 (1H, s), 7.40 (1H, d, J = 8.2 Hz) 3.41 (2H, m), 3.01-3.07 (3H, m), 2.03 (2H, m), 1.92 (2H, m).

[00651] **Example 12**

[00652] Preparation of Cpd 28

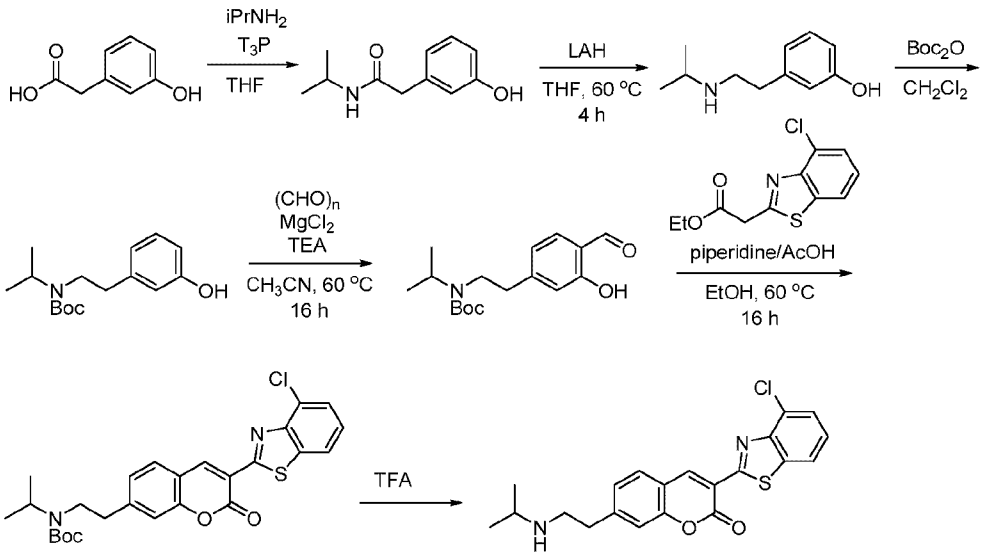


[00653] Step A: 4-Formyl-3-hydroxybenzoic acid (830 mg, 5 mmol) was combined with 1-methylpiperazine (0.61 mL, 5.5 mmol), triethylamine (0.77 mL, 5.5 mmol) and (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (2.86 g, 5.5 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 3h, then concentrated and purified by silica gel column chromatography (0-5% MeOH in CH_2Cl_2) to afford 2-hydroxy-4-(4-methylpiperazine-1-carbonyl)benzaldehyde (1.24 g, 100%). MS *m/z* 249.1 $[M+H]^+$.

[00654] Step B: Following the procedure in Example 9, Step C, 2-hydroxy-4-(4-methylpiperazine-1-carbonyl)benzaldehyde (50 mg, 0.2 mmol), ethyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (50 mg, 0.2 mmol, prepared according to Example 2, Part 1), piperidine (20 μL, 0.2 mmol) and acetic acid (12 μL, 0.2 mmol) in EtOH (1 mL) afforded the title compound (60 mg, 68%) as a yellow powder: m.p. 230–235 °C; MS *m/z* 440.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.26 (1H, s), 8.24 (1H, d, J = 8.0 Hz), 8.21 (1H, d, J = 8.0 Hz), 7.72 (1H, d, J = 7.6 Hz), 7.59 (1H, s), 7.51 (1H, t, J = 7.9 Hz), 7.48 (1H, d, J = 7.9 Hz), 3.65 (2H, m), 3.34 (2H, m), 2.42 (2H, m), 2.31(2H, m), 2.22 (3H, s).

[00655] **Example 13**

[00656] Preparation of Cpd 35



[00657] Step A: 3-Hydroxyphenylacetic acid (2.13 g, 14 mmol) was combined with isopropylamine (3.6 mL, 42 mmol) in THF (20 mL). The solution was cooled to 0 °C before adding propylphosphonic anhydride (9.8 mL, ~50% in DMF, 16 mmol). The solution stirred at room temperature for 16 h. The mixture was partitioned in H_2O (300 mL) and EtOAc (300 mL). The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (50% EtOAc in hexanes) to afford 2-(3-hydroxyphenyl)-N-isopropylacetamide (1.9 g, 70%) as a white powder. MS *m/z* 194.1 $[M+H]^+$.

[00658] Step B: 2-(3-Hydroxyphenyl)-N-isopropylacetamide (1.9 g, 10 mmol) was dissolved in THF (20 mL). Lithium aluminum hydride (10 mL, 1 M in THF, 10 mmol) was added to the solution. The mixture was heated to 60 °C for 2 h with stirring. The excess reagent was quenched by the slow addition of H_2O. After vigorous stirring for 1 h, the mixture was filtered through Celite. The filtrate was concentrated to afford crude 3-(2-(isopropylamino)ethyl)phenol, which was used without further purification.

[00659] Step C: 3-(2-(Isopropylamino)ethyl)phenol (716 mg, 4 mmol) was combined with di-tert-butyl dicarbonate (872 mg, 4 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 16 h, then concentrated and purified by silica gel column chromatography (50% EtOAc in hexanes) to afford tert-butyl 3-hydroxyphenethyl(isopropyl)carbamate (650 mg, 23%) as a white powder.

[00660] Step D: Following the procedure in Example 6, Step A, tert-butyl 3-hydroxyphenethyl(isopropyl)carbamate (650 mg, 2.3 mmol), triethylamine (1.6 mL, 11.5 mmol), anhydrous magnesium chloride (437 mg, 4.6 mmol) and paraformaldehyde (690 mg, 23 mmol) in CH_3CN (8 mL) afforded tert-butyl 4-formyl-3-hydroxyphenethyl(isopropyl)carbamate (520 mg, 73%). MS *m/z* 306.1 $[M-H]^-$.

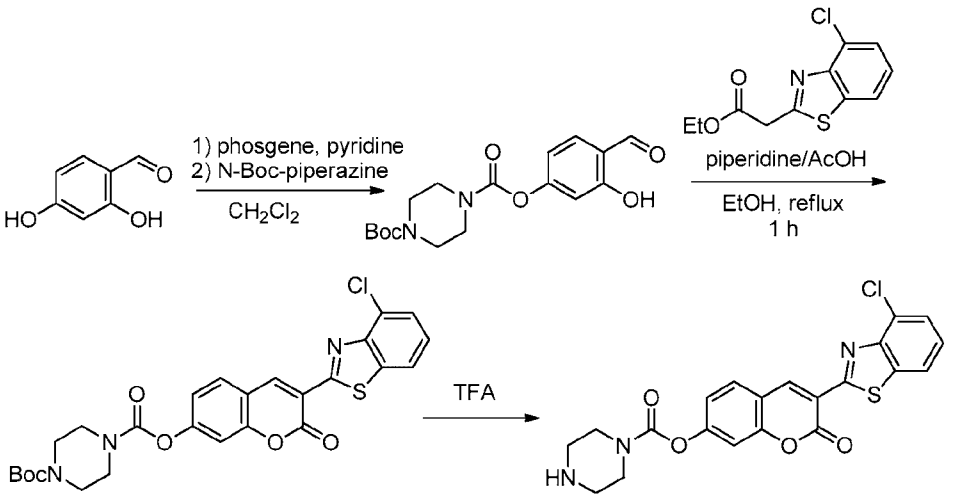
[00661] Step E: Following the procedure in Example 9, Step C, tert-butyl 4-formyl-3-hydroxyphenethyl(isopropyl)carbamate (50 mg, 0.16 mmol), ethyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (50 mg, 0.2 mmol, prepared according to Example 2, Part 1), piperidine (20 μL, 0.2 mmol) and acetic acid (12 μL, 0.2 mmol) in EtOH (1 mL) afforded tert-butyl 2-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)ethyl(isopropyl)carbamate.

[00662] Step F: A mixture of 2-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl)ethyl(isopropyl)carbamate (0.16 mmol) and trifluoroacetic acid (1 mL) was stirred at room temperature for 15 min, then the solvent was removed with a stream of nitrogen. The residue was partitioned in CH_2Cl_2 (5 mL) and aqueous K_2CO_3 (1 M, 5 mL). The organic layer was collected through a hydrophobic frit and concentrated to afford the title compound (42 mg, 66%) as a yellow powder: m.p. 179–182 °C; MS *m/z* 399.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.23 (1H, s), 8.22 (1H, d, J = 7.8 Hz), 8.10 (1H, d, J = 8.0 Hz), 7.73 (1H, d, J = 7.7 Hz), 7.52 (1H, t, J = 7.8 Hz), 7.50 (1H, s), 7.42 (1H, d, J = 8.0 Hz), 2.89 (4H, m), 2.79 (1H, m), 1.02 (6H, d, J = 6.2 Hz).

[00663] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 13 by substituting the appropriate starting materials, reagents and reaction conditions.

[00664] **Example 14**

[00665] Preparation of Cpd 42



[00666] Step A: 2,4-Dihydroxybenzaldehyde (1.38 g, 10 mmol) was dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. To the mixture was added pyridine (0.81 mL, 10 mmol), followed by phosgene (5.0 mL, 20% in toluene, 10 mmol). The mixture was stirred for 5 min at 0 °C. A solution of 1-Boc-piperazine (1.86 g, 10 mmol) and triethylamine (1.4 mL, 10 mmol) in CH_2Cl_2 (5 mL) was added to the mixture at 0 °C. After 5 min, the mixture was washed with an aqueous saturated $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (20% EtOAc in hexanes) to afford 1-tert-butyl 4-(4-formyl-3-hydroxyphenyl) piperazine-1,4-dicarboxylate (480 mg, 14%). MS *m/z* 349.3 $[M-H]^-$.

[00667] Step B: Following the procedure in Example 9, Step C, 1-tert-butyl 4-(4-formyl-3-hydroxyphenyl) piperazine-1,4-dicarboxylate (70 mg, 0.2 mmol), ethyl 2-(4-chlorobenzo[d]thiazol-2-yl)acetate (50 mg, 0.2 mmol, prepared according to Example 2, Part 1), piperidine (20 μL, 0.2 mmol) and acetic acid (12 μL, 0.2 mmol) in EtOH (1 mL) afforded 1-tert-butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl) piperazine-1,4-dicarboxylate.

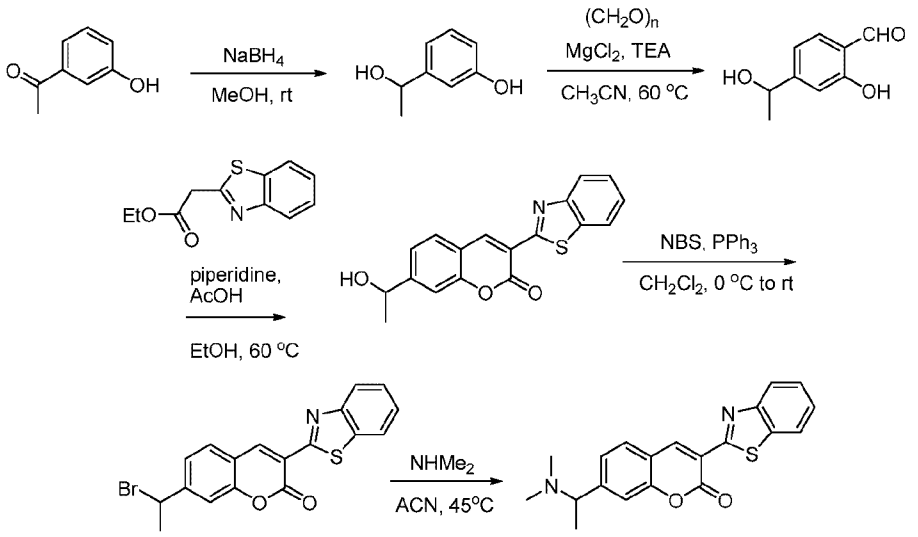
[00668] Step C: A mixture of 1-tert-butyl 4-(3-(4-chlorobenzo[d]thiazol-2-yl)-2-oxo-2H-chromen-7-yl) piperazine-1,4-dicarboxylate (0.2 mmol) and trifluoroacetic acid (1 mL) was stirred at room temperature for 15 min, then the solvent was removed with a stream of nitrogen. The residue was partitioned in CH_2Cl_2 (5 mL) and aqueous K_2CO_3 (1 M, 5 mL). The organic layer was collected through a hydrophobic frit and concentrated to afford the title compound (62 mg, 70%) as an off white powder: m.p. 236–239 °C; MS *m/z* 442.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.23 (1H, s), 8.21-8.18 (2H, m), 7.70 (1H, d, J = 7.72 Hz), 7.49 (1H, t, J =

7.9 Hz), 7.46 (1H, d, J = 2.1 Hz), 7.31 (1H, dd, J = 8.5 Hz, 2.1 Hz), 3.55 (2H, m), 3.39 (2H, m), 2.76 (4H, m).

[00669] 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.

[00670] **Example 15**

[00671] Preparation of Cpd 143



[00672] Step A: To a solution of 3-hydroxyacetophenone (2.72 g, 20 mmol) in MeOH (10mL) was added sodium borohydride (380 mg, 10 mmol). After stirring at room temperature for 2 h, the reaction mixture was acidified to pH <7 with aqueous HCl (1 N). MeOH was removed by rotoevaporation under reduced pressure. The mixture was partitioned in water and EtOAc. The organic layer was washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide 3-(1-hydroxyethyl)phenol (2.15 g, 78%). MS *m/z* 137.1 $[M-H]^-$.

[00673] Step B: To a mixture of 3-(1-hydroxyethyl)phenol (1.38 g, 10 mmol), magnesium chloride (1.94 g, 20.4 mmol) and triethylamine (7 mL, 50 mmol) in CH_3CN (5mL) was added paraformaldehyde (3 g, 100 mmol) at room temperature. The reaction mixture was heated at 60 °C overnight, then the solvent was removed by rotoevaporation under reduced pressure. The residual mixture was acidified to pH ~2 with aqueous HCl (1 N). The aqueous mixture was extracted with EtOAc and the organic layer was concentrated. The residue was purified by silica gel column chromatography (0-20% EtOAc in CH_2Cl_2) to provide 2-hydroxy-4-(1-hydroxyethyl)benzaldehyde (734 mg, 44%).

[00674] Step C: To a mixture of 2-hydroxy-4-(1-hydroxyethyl)benzaldehyde (568 mg, 3.4 mmol), piperidine (674 μL, 6.8 mmol) and acetic acid (194 μL, 3.4 mmol) in EtOH (2 mL) was added ethyl 2-(benzo[d]thiazol-2-yl)acetate (800 mg, 4.1 mmol, prepared in Example 1, Part 1). The mixture was heated at 60 °C overnight. After cooling to room temperature, diethyl ether was added to the mixture to produce a precipitate. The solid was collected by filtration, washed with water and dried under vacuum to give 3-(benzo[d]thiazol-2-yl)-7-(1-hydroxyethyl)-2H-chromen-2-one (493 mg, 45%). MS *m/z* 324.1 $[M+H]^+$.

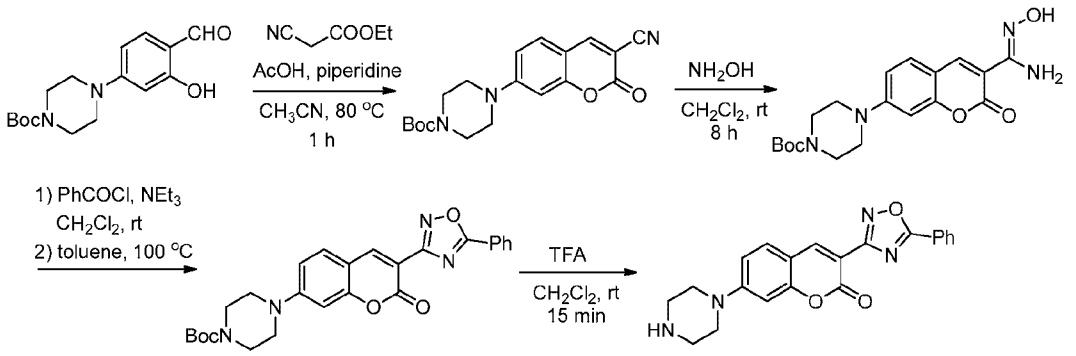
[00675] Step D: To a mixture of 3-(benzo[d]thiazol-2-yl)-7-(1-hydroxyethyl)-2H-chromen-2-one (323 mg, 1 mmol) and triphenylphosphine (525 mg, 2 mmol) in CH_2Cl_2 (2 mL) was added N-bromosuccinimide (456 mg, 2.6 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h. Diethyl ether was added to the mixture to produce a precipitate. The precipitate was collected by vacuum filtration, washed with water and a saturated aqueous $NaHCO_3$ solution, and dried to give 3-(benzo[d]thiazol-2-yl)-7-(1-bromoethyl)-2H-chromen-2-one (193 mg, 50%). MS *m/z* 386.1, 388.1 $[M+H]^+$.

[00676] Step E: To a solution of 3-(benzo[d]thiazol-2-yl)-7-(1-bromoethyl)-2H-chromen-2-one (40 mg, 0.10 mmol) in CH_3CN (0.8 mL) was added dimethylamine (16 mg, 0.36 mmol). The reaction mixture was heated at 45 °C for 2 h. Diethyl ether was added to the mixture to produce a precipitate. The solid was collected by vacuum filtration, washed with water and an aqueous saturated $NaHCO_3$ solution, then dried to afford the title compound (14 mg, 27%) as a yellow solid: m.p. 130–133 °C; MS *m/z* 351.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.25 (1H, s), 8.20 (1H, d, J = 8.1Hz), 8.09 (1H, d, J = 8.1 Hz), 8.03 (1H, d, J = 7.9Hz), 7.59 (1H, t, J = 7.6 Hz), 7.51-7.43 (3H, m), 3.46 (1H, q, J = 6.7 Hz), 2.15 (6H, s), 1.32 (3H, d, J = 6.7 Hz).

[00677] 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.

[00678] **Example 16**

[00679] Preparation of Cpd 50



[00680] Step A: A mixture of tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (6.5 g, 21.2 mmol, prepared in Example 1, Part 2), ethyl cyanoacetate (2.87 mL, 29.6 mmol), piperidine (2.6 mL, 26 mmol), AcOH (1.6 mL, 29.3 mmol) and CH_3CN (50 mL) was heated at 80 °C for 1 h. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (10% EtOAc in CH_2Cl_2), followed by trituration with hexane/EtOAc (1:1), yielding tert-butyl 4-(3-cyano-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (5.05 g, 67%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (1H, s), 7.41 (1H, d, J = 8.5 Hz), 6.84 (1H, dd, J = 8.5 Hz, 2.5 Hz), 6.66 (1H, d, J = 2.5 Hz), 3.65 (4H, m), 3.51 (4H, m), 1.52 (9H, s).

[00681] Step B: A mixture of tert-butyl 4-(3-cyano-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (400 mg, 1.13 mmol), MeOH (2 mL), CH_2Cl_2 (2 mL), and NH_2OH (50% aqueous solution, 200 μL, 3.2 mmol) was stirred at room temperature for 8 h. The reaction mixture was concentrated with a stream of nitrogen until the total volume was halved. The reaction mixture was diluted with MeOH (40 mL) and H_2O (5 mL), generating a precipitate. The precipitate was collected by vacuum filtration and dried, affording tert-butyl 4-(3-(N'-hydroxycarbamimidoyl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (386 mg, 88%) as a tan solid. MS *m/z* 389.2 $[M+H]^+$.

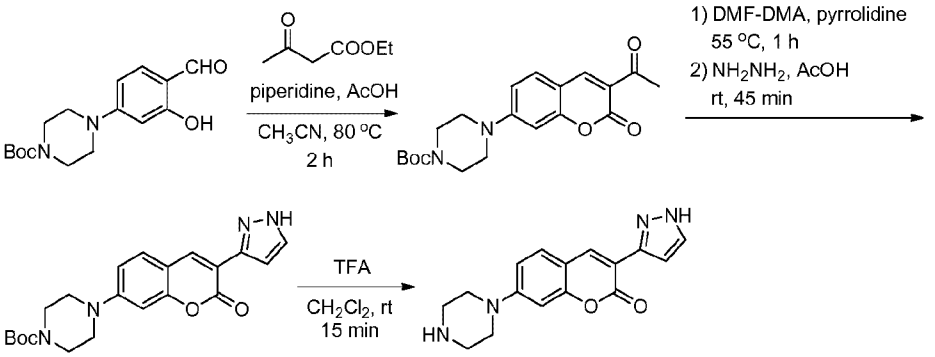
[00682] Step C: tert-Butyl 4-(3-(N'-hydroxycarbamimidoyl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (190 mg, 0.49 mmol) was suspended in CH_2Cl_2 (1.5 mL) and triethylamine (85 μL, 0.6 mmol). Acetyl chloride (40 μL, 0.54 mmol) was added to the mixture. After 10 min, the mixture was diluted in CH_2Cl_2 and washed with aqueous HCl, followed by an aqueous saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, filtered and

concentrated under vacuum. The residue was suspended in toluene (1.5 mL) and heated at 100 °C for 30 h, then the solvent was removed with a stream of nitrogen. The residue was purified by silica gel column chromatography (10% EtOAc in CH_2Cl_2), followed by trituration with 2:1 hexane/acetone, yielding tert-butyl 4-(2-oxo-3-(5-phenyl-1,2,4-oxadiazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (187 mg, 50%) as a yellow solid. MS *m/z* 475.2 $[M+H]^+$.

[00683] Step D: tert-Butyl 4-(2-oxo-3-(5-phenyl-1,2,4-oxadiazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (107 mg, 0.26 mmol) was stirred in a solution of CH_2Cl_2 (2.5 mL) and trifluoroacetic acid (1.0 mL) for 15 min. The reaction mixture was partitioned in CH_2Cl_2 and aqueous K_2CO_3. The organic layer was concentrated under vacuum. The residue was triturated with 2:1 hexane/acetone, yielding the title compound (116 mg, 81%) as a yellow solid: m.p. 214–221 °C; MS *m/z* 375.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.77 (1H, s), 8.18 (2H, m), 7.75 (2H, m), 7.68 (2H, m), 7.04 (1H, dd, J = 9 Hz, 2 Hz), 6.87 (1H, d, J = 2 Hz), 3.38 (4H, m), 2.82 (4H, m).

[00684] **Example 17**

[00685] Preparation of Cpd 29



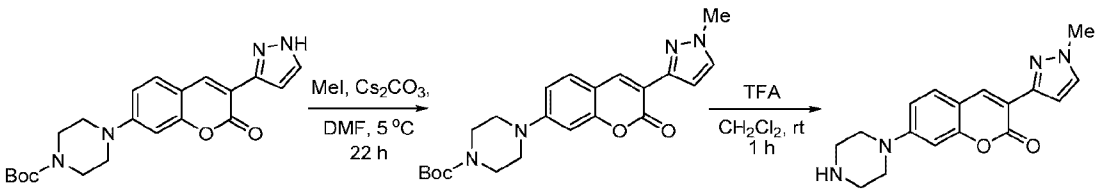
[00686] Step A: A mixture of tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (2.9 g, 9.5 mmol, prepared in Example 1, Part 2), ethyl acetoacetate (1.28 mL, 11.8 mmol), AcOH (725 μL, 13.3 mmol), piperidine (1.16 mL, 11.8 mmol), and CH_3CN (23 mL) were heated at 80 °C for 2 h. The reaction mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (10% EtOAc in CH_2Cl_2), followed by ether trituration, yielding tert-butyl 4-(3-acetyl-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (3.15 g, 89%) as a yellow solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.47 (1H, s), 7.49 (1H, d, J = 9 Hz), 6.83 (1H, dd, J = 9 Hz, 2.5 Hz), 6.67 (1H, d, J = 2.5 Hz), 3.64 (4H, m), 3.47 (4H, m), 2.72 (3H, s), 1.52 (9H, s).

[00687] Step B: A mixture of tert-butyl 4-(3-acetyl-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (300 mg, 0.81 mmol), dimethylformamide dimethyl acetal (900 μL, 7.5 mmol) and pyrrolidine (150 μL, 1.83 mmol) was heated at 55 °C for 1 h, then the solvent was removed with a stream of nitrogen. Hydrazine (70 μL, 2.2 mmol) and AcOH (900 μL) were added. The mixture was stirred at room temperature for 45 min, then partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, then filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (30% EtOAc in CH_2Cl_2), followed by trituration with 2:1 hexane/acetone, yielding tert-butyl 4-(2-oxo-3-(1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (180 mg, 56%) as a yellow solid. MS *m/z* 397.2 $[M+H]^+$.

[00688] Step C: A solution of tert-butyl 4-(2-oxo-3-(1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (180 mg, 0.45 mmol) in CH_2Cl_2 (2.5 mL) and trifluoroacetic acid (1.0 mL) was stirred at room temperature for 15 min. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Trituration of the residue with acetone yielded the title compound (100 mg, 75%) as a yellow solid: m.p. 224–228 °C; MS *m/z* 297.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6:D_2O, 100 °C): δ 8.31 (1H, s), 7.63 (1H, br s), 7.54 (1H, d, J = 9 Hz), 6.94 (1H, dd, J = 9 Hz, 2 Hz), 6.82 (1H, d, J = 2 Hz), 6.77 (1H, d, J = 2 Hz), 3.32 (4H, t, J = 5 Hz), 2.88 (4H, t, J = 5 Hz).

[00689] **Example 18**

[00690] Preparation of Cpd 38



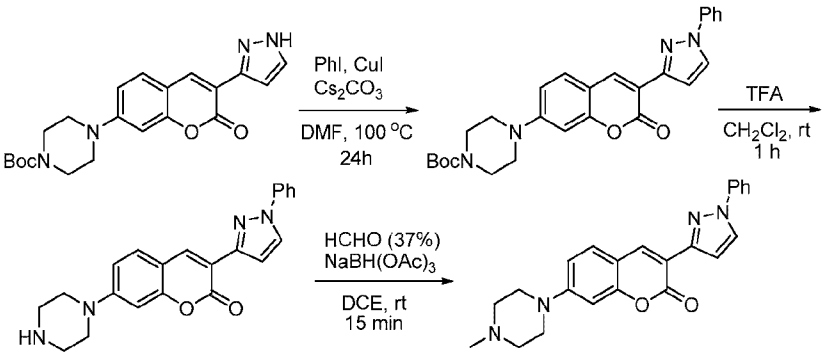
[00691] Step A: A mixture of tert-butyl 4-(2-oxo-3-(1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (300 mg, 0.76 mmol, prepared in Example 17, Step B), Cs_2CO_3 (515 mg, 1.58 mmol), iodomethane (93 μL, 1.5 mmol), and DMF (2.0 mL) was stirred at 5 °C for 22 h. The reaction mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (15% EtOAc in CH_2Cl_2), followed by trituration with ether to give tert-butyl 4-(3-(1-methyl-1H-pyrazol-3-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (215

mg, 69%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (1H, s), 7.41 (2H, m), 7.05 (1H, d, J = 2 Hz), 6.83 (1H, dd, J = 8.5 Hz, 2.5 Hz), 6.74 (1H, d, J = 2 Hz), 3.97 (3H, s), 3.62 (4H, m), 3.33 (4H, m), 1.50 (9H, s).

[00692] Step B: A solution of tert-butyl 4-(3-(1-methyl-1H-pyrazol-3-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (215 mg, 0.52 mmol) in CH_2Cl_2 (2.5 mL) and trifluoroacetic acid (1.0 mL) was stirred at room temperature for 1 h. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with 1:1 hexane/acetone affording the title compound (142 mg, 92%) as a yellow solid: m.p. 224–228 °C; MS *m/z* 311.1 $[M+H]^+$; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (1H, s), 7.42 (2H, m), 7.06 (1H, d, *J* = 2 Hz), 6.85 (1H, dd, *J* = 9 Hz, 2.5 Hz), 6.77 (1H, d, *J* = 2 Hz), 3.99 (3H, s), 3.34 (4H, m), 3.06 (4H, m).

[00693] **Example 19**

[00694] Preparation of Cpd 74



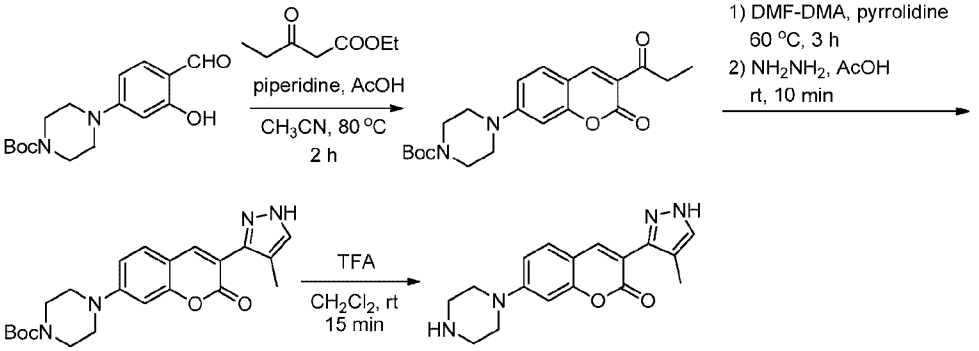
[00695] Step A: A mixture of tert-butyl 4-(2-oxo-3-(1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (250 mg, 0.63 mmol, prepared in Example 17, Step B), Cs_2CO_3 (650 mg, 1.98 mmol), copper(I) iodide (14 mg, 0.073 mmol), iodobenzene (110 μL, 0.97 mmol), and DMF (1.6 mL) was heated at 100 °C for 24 h. The reaction mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (5% EtOAc in CH_2Cl_2), followed by ether trituration to yield tert-butyl 4-(2-oxo-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (129 mg, 43%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (1H, s), 7.97 (1H, d, *J* = 2.5 Hz), 7.77 (2H, d, *J* = 8 Hz), 7.49 (3H, m), 7.32 (2H, m), 6.86 (1H, dd, *J* = 8.5 Hz, 2.5 Hz), 6.77 (1H, d, *J* = 2.5 Hz), 3.62 (4H, m), 3.36 (4H, m), 1.50 (9H, s).

[00696] Step B: A solution of tert-butyl 4-(2-oxo-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (127 mg, 0.27 mmol) in CH_2Cl_2 (2.5 mL) and trifluoroacetic acid (1.0 mL) was stirred at room temperature for 1 h. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with 2:1 hexane/acetone to afford 3-(1-phenyl-1H-pyrazol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one (85 mg, 84%) as a yellow solid. MS *m/z* 373.3 $[M+H]^+$.

[00697] Step C: 3-(1-phenyl-1H-pyrazol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one (55 mg, 0.15 mmol) was combined with aqueous formaldehyde (37%, 200 uL, 2.15 mmol) and sodium triacetoxyborohydride (110 mg, 0.52 mmol) in 1,2-dichloroethane (0.5 mL). The mixture was stirred 20 min at room temperature, and then quenched by the addition of an aqueous saturated $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2. The organic layer was, dried over $NaSO_4$, filtered, concentrated and purified by silica gel column chromatography (10% MeOH in CH_2Cl_2) to give the title compound (34 mg, 58%) as a yellow solid: m.p. 152–159 °C; MS *m/z* 387.3 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.51 (1H, s), 7.97 (1H, d, J = 2.5 Hz), 7.77 (2H, d, J = 7.5 Hz), 7.47 (3H, m), 7.32 (2H, m), 6.86 (1H, dd, J = 8.5 Hz), 6.77 (1H, d, J = 2 Hz), 3.45 (4H, m), 2.66 (4H, br s), 2.43 (3H, s).

[00698] **Example 20**

[00699] Preparation of Cpd 80



[00700] Step A: A mixture of tert-butyl 4-(4-formyl-3-hydroxyphenyl)piperazine-1-carboxylate (3.0 g, 9.8 mmol, prepared in Example 1, Part 2), ethyl 3-oxopentanoate (1.62 mL, 11.3 mmol), AcOH (650 μL, 12 mmol), piperidine (1.1 mL, 11.3 mmol), and CH_3CN (24 mL) were heated at 80 °C for 4 h. The reaction mixture was partitioned between CH_2Cl_2 and H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (10% EtOAc in CH_2Cl_2), followed by ether

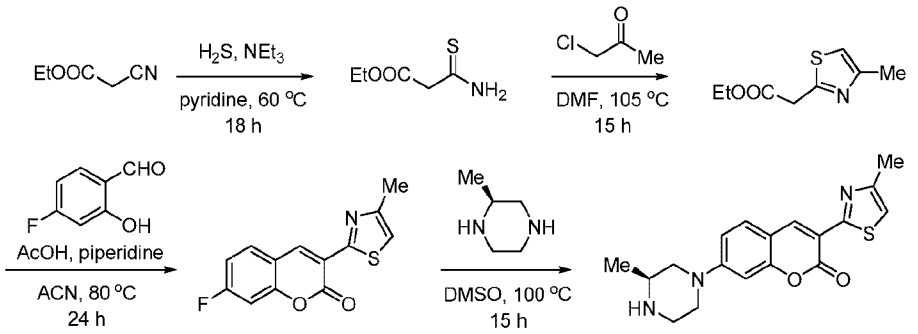
trituration, yielding tert-butyl 4-(2-oxo-3-propionyl-2H-chromen-7-yl)piperazine-1-carboxylate (3.6 g, 95%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (1H, s), 7.50 (1H, d, J = 8.5 Hz), 6.83 (1H, dd, J = 8.5 Hz, 2.5 Hz), 6.67 (1H, d, J = 2 Hz), 3.63 (4H, m), 3.47 (4H, m), 3.16 (2H, q, J = 7 Hz), 1.52 (9H, s), 1.19 (3H, t, J = 7 Hz).

[00701] Step B: A mixture of tert-butyl 4-(2-oxo-3-propionyl-2H-chromen-7-yl)piperazine-1-carboxylate (3.3 g, 8.55 mmol), dimethylformamide dimethyl acetal (10 mL, 830 mmol) and pyrrolidine (1.65 mL, 20.1 mmol) was heated at 60 °C for 3 h, then the solvent was removed under vacuum. The reaction mixture was dissolved in AcOH (10 mL) and cooled to 0 °C. Hydrazine (820 μL, 26 mmol) was added dropwise (mild exotherm). After the addition was complete, the mixture was stirred at room temperature for 10 min. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, then filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (50% EtOAc in CH_2Cl_2), followed by trituration with 2:1 hexane/acetone, yielding tert-butyl 4-(3-(4-methyl-1H-pyrazol-3-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (1.01 g, 29%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (1H, s), 7.48 (1H, s), 7.44 (1H, d, J = 9 Hz), 6.87 (1H, dd, J = 8.5 Hz, 2.5 Hz), 6.74 (1H, d, J = 2.5 Hz), 3.63 (4H, m), 3.38 (4H, m), 2.36 (3H, s), 1.50 (9H, s).

[00702] Step C: A solution of tert-butyl 4-(3-(4-methyl-1H-pyrazol-3-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (250 mg, 0.61mmol) in CH_2Cl_2 (2.5 mL) and trifluoroacetic acid (1.0 mL) was stirred at room temperature for 15 min. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with 1:1 hexane/acetone yielding the title compound (155 mg, 82%) as a yellow solid: m.p. 175-200 °C (decomposition range); MS *m/z* 311.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6:D_2O, 100 °C): δ 7.91 (1H, s), 7.54 (1H, d, J = 9 Hz), 7.41 (1H, br s), 6.95 (1H, d, J = 9 Hz), 6.80 (1H, d, J = 2.5 Hz), 3.35 (4H, m), 2.92 (4H, m), 2.09 (3H, br s).

[00703] **Example 21**

[00704] Preparation of Cpd 283



[00705] Step A: Hydrogen sulfide gas (H_2S) was bubbled into a solution of ethyl cyanoacetate (4.7 mL, 44.3 mmol) in pyridine/triethylamine (500 mL, 1:1 v/v) until it became saturated. The mixture was heated at 60 °C for 18 h, then the solvent was removed under vacuum. The residue was partitioned between EtOAc and aqueous HCl. The organic layer was dried over $MgSO_4$, then filtered and concentrated under vacuum. The resulting oil was filtered to remove solid impurities. Ethyl 3-amino-3-thioxopropanoate (6.25 g, 96%) was obtained as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.92 (1H, br s), 7.75 (1H, br s), 4.21 (2H, q, J = 7 Hz), 3.82 (2H, s), 1.29 (3H, t, J = 7 Hz).

[00706] Step B: A solution of ethyl 3-amino-3-thioxopropanoate (2.0 g, 13.6 mmol) and chloroacetone (1.2 mL, 15.0 mmol) in DMF (230 mL) was heated at 105 °C for 15 h. The reaction mixture was partitioned between EtOAc and H_2O. The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2) yielding ethyl 2-(4-methylthiazol-2-yl)acetate (1.22 g, 48%) as a red oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.86 (1H, s), 4.24 (2H, q, J = 7 Hz), 4.03 (2H, s), 2.44 (3H, s), 1.29 (3H, t, J = 7 Hz).

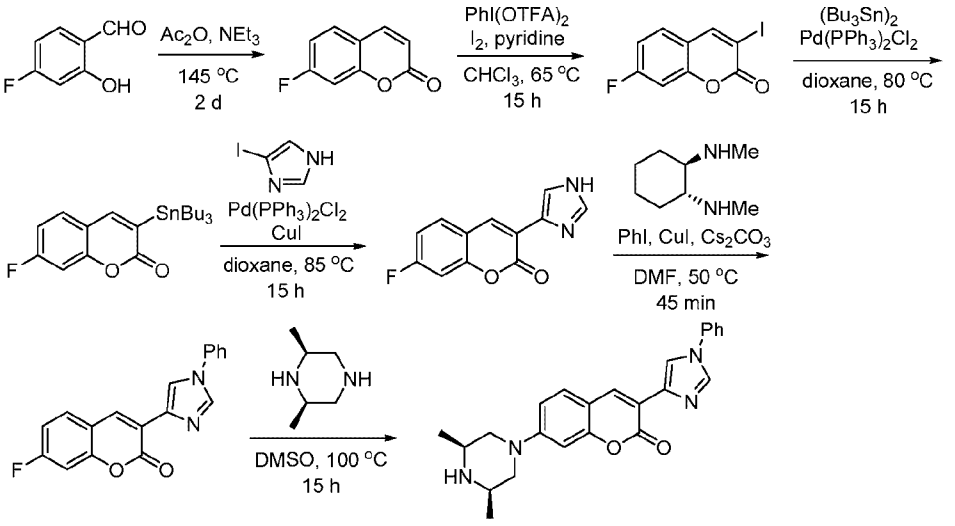
[00707] Step C: A mixture of ethyl 2-(4-methylthiazol-2-yl)acetate (650 mg, 3.5 mmol), 4-fluoro-2-hydroxybenzaldehyde (490 mg, 3.5 mmol), piperidine (15 μL, 0.15 mmol), AcOH (15 μL, 0.27 mmol) and CH_3CN (5 mL) was heated at 80 °C for 24 h. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was triturated with 7:3 hexane/CH_2Cl_2 yielding 7-fluoro-3-(4-methylthiazol-2-yl)-2H-chromen-2-one (642 mg, 70%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (1H, s), 7.69 (1H, dd, J = 8.5 Hz, 6 Hz), 7.15 (3H, m), 2.57 (3H, s).

[00708] Step D: A mixture of 7-fluoro-3-(4-methylthiazol-2-yl)-2H-chromen-2-one (100 mg, 0.38 mmol), (S)-2-methylpiperazine (46 mg, 0.46 mmol) and DMSO (600 μL) was heated at 80 °C for 15 h. The reaction mixture was diluted in an aqueous saturated $NaHCO_3$ solution and filtered. The collected material was purified by silica gel column chromatography (10% MeOH in CH_2Cl_2), followed by trituration with 1:1 hexane/acetone to yield the title compound (103 mg, 79%) as a yellow solid: m.p. 194–199 °C; MS *m/z* 342.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.80 (1H, s), 7.75 (1H, d, *J* = 9 Hz), 7.32 (1H, m), 7.06 (1H, dd, *J* = 9 Hz, 2.5 Hz), 6.91 (1H, d, *J* = 2.5 Hz), 3.88 (2H, t, *J* = 11 Hz), 2.96 (1H, d, *J* = 12 Hz), 2.81 (1H, td, *J* = 12 Hz, 3 Hz), 2.72 (2H, m), 2.45 (4H, m), 2.36 (1H, br s), 1.04 (3H, d, *J* = 6.5 Hz).

[00709] 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.

[00710] **Example 22**

[00711] Preparation of Cpd 452



[00712] Step A: A mixture of 4-fluoro-2-hydroxybenzaldehyde (10 g, 71.4 mmol), acetic anhydride (34 mL, 360 mmol), and triethylamine (11 mL, 79 mmol) was heated at 145 °C for 2 d. The reaction mixture was diluted in aqueous NH_4OH (500 mL) and filtered. The collected material was dried, yielding 7-fluoro-2H-chromen-2-one (10.3 g, 88%) as a brown solid. ^1H NMR (500 MHz. $CDCl_3$): δ 7.69 (1H, d, *J* = 9.5 Hz), 7.48 (1H, dd, *J* = 8.5 Hz, 6 Hz), 7.07 (1H, dd, *J* = 8.5 Hz, 2.5 Hz), 7.03 (1H, td, *J* = 8.5 Hz, 2.5 Hz), 6.38 (1H, d, *J* = 9.5 Hz).

[00713] Step B: A mixture of 7-fluoro-2H-chromen-2-one (4.33 g, 26.4 mmol), [bis(trifluoroacetoxy)iodo]benzene (18.15 g, 42.2 mmol), iodine (10.7 g, 42.2 mmol), pyridine (4.2 mL, 53 mmol), and $CHCl_3$ (25 mL) was heated at 65 °C for 15 h. The reaction mixture was partitioned between aqueous $NaHSO_3$ and CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (50% CH_2Cl_2 in hexanes, then CH_2Cl_2) yielding 7-fluoro-3-iodo-2H-chromen-2-one (5.6 g, 73%) as a tan solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (1H, s), 7.46 (1H, dd, J = 9 Hz, 6 Hz), 7.07 (2H, m).

[00714] Step C: A mixture of 7-fluoro-3-iodo-2H-chromen-2-one (5.6 g, 19.3 mmol), hexabutylditin (13.45 g, 23.2 mmol), bis(triphenylphosphine)palladium(II) dichloride (540 mg, 0.77 mmol) and 1,4-dioxane (55 mL) was heated at 80 °C for 15 h. The reaction mixture was diluted in EtOAc and filtered. The filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (20-40% CH_2Cl_2 in hexanes) yielding 7-fluoro-3-(tributylstannyl)-2H-chromen-2-one (6.79 g, 77%) as a colorless oil.

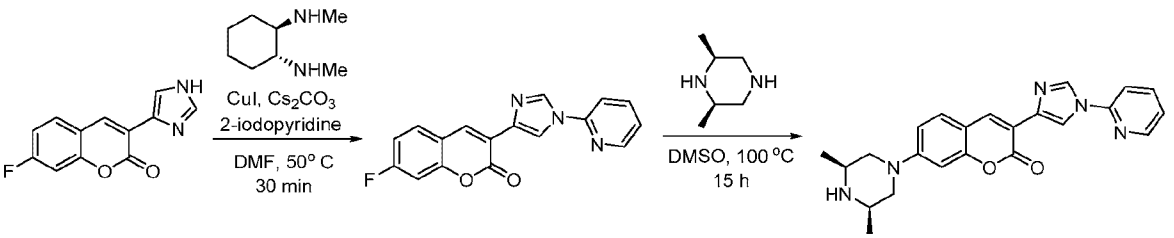
[00715] Step D: A mixture of 7-fluoro-3-(tributylstannyl)-2H-chromen-2-one (1.15 g, 2.53 mmol), 4-iodoimidazole (600 mg, 3.1 mmol), bis(triphenylphosphine)palladium(II) dichloride (285 mg, 0.41 mmol), copper(I) iodide (115 mg, 0.60 mmol), and 1,4-dioxane (7 mL) was heated at 85 °C for 2 d. The reaction mixture was partitioned between NH_4OH and CH_2Cl_2. The organic layer was concentrated under vacuum. The residue was purified by silica gel column chromatography (30% MeOH in CH_2Cl_2). The product was triturated with CH_2Cl_2, yielding 7-fluoro-3-(1H-imidazol-4-yl)-2H-chromen-2-one (298 mg, 51%) as a yellow solid. MS *m/z* 231.1 $[M+H]^+$.

[00716] Step E: A mixture of 7-fluoro-3-(1H-imidazol-4-yl)-2H-chromen-2-one (90 mg, 0.39 mmol), iodobenzene (70 μL, 0.62 mmol), CuI (60 mg, 0.32 mmol), trans-1,2-bis(methylamino)cyclohexane (23 μL, 0.15 mmol), Cs_2CO_3 (585 mg, 1.79 mmol) and DMF (0.9 mL) was heated at 50 °C for 45 min. The reaction mixture was diluted in H_2O and filtered. The solid material was partitioned between aqueous NH_4OH and CH_2Cl_2. The organic layer was concentrated under vacuum. The residue was purified by silica gel chromatography (10% EtOAc in CH_2Cl_2), yielding 7-fluoro-3-(1-phenyl-1H-imidazol-4-yl)-2H-chromen-2-one (52 mg, 43%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58 (1H, s), 8.27 (1H, d, J = 1.5 Hz), 7.94 (1H, d, J = 1.5 Hz), 7.60 (1H, dd, J = 8.5 Hz, 6 Hz), 7.52 (4H, m), 7.42 (1H, m), 7.11 (1H, dd, J = 9 Hz, 2.5 Hz), 7.06 (1H, td, J = 8 Hz, 2.5 Hz).

[00717] Step F: A mixture of 7-fluoro-3-(1-phenyl-1H-imidazol-4-yl)-2H-chromen-2-one (50 mg, 0.16 mmol), cis-2,6-dimethylpiperazine (29 mg, 0.25 mmol) and DMSO (300 μL) were heated at 100 °C for 15 h. The reaction mixture was diluted in an aqueous saturated $NaHCO_3$ solution and filtered. The solid material was purified by silica gel column chromatography (5% MeOH in CH_2Cl_2), yielding the title compound (52 mg, 81%) as a yellow solid: m.p. 260–264 °C; MS *m/z* 401.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.50 (1H, s), 8.41 (1H, d, *J* = 1 Hz), 8.14 (1H, d, *J* = 1 Hz), 7.71 (2H, d, *J* = 8.5 Hz), 7.64 (1H, d, *J* = 9 Hz), 7.55 (2H, t, *J* = 8 Hz), 7.40 (1H, t, *J* = 7.5 Hz), 7.01 (1H, dd, *J* = 9 Hz, 2 Hz), 6.89 (1H, d, *J* = 2 Hz), 3.82 (2H, dd, *J* = 12.5 Hz, 2 Hz), 2.80 (2H, m), 2.31 (2H, t, *J* = 11.5 Hz), 2.25 (1H, br s), 1.04 (6H, d, *J* = 6.5 Hz).

[00718] **Example 23**

[00719] Preparation of Cpd 433



[00720] Step A: A mixture of 7-fluoro-3-(1H-imidazol-4-yl)-2H-chromen-2-one (75 mg, 0.32 mmol, prepared in Example 22, Step D), 2-iodopyridine (55 μL, 0.5 mmol), copper(I) iodide (27 mg, 0.14 mmol), trans-1,2-bis(methylamino)cyclohexane (13 μL, 0.08 mmol), Cs_2CO_3 (330 mg, 1.01 mmol) and DMF (750 μL) was heated at 50 °C for 30 min. The reaction mixture was diluted with H_2O and filtered. The solid material was partitioned between aqueous NH_4OH and CH_2Cl_2. The organic layer was concentrated under vacuum. The residue was purified by silica gel column chromatography (10% acetone in CH_2Cl_2), followed by trituration with 1:1 CH_2Cl_2/hexane, yielding 7-fluoro-3-(1-(pyridin-2-yl)-1H-imidazol-4-yl)-2H-chromen-2-one (62 mg, 63%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.61 (1H, s), 8.56 (1H, d, *J* = 1 Hz), 8.52 (1H, m), 8.50 (1H, d, *J* = 1 Hz), 7.88 (1H, m), 7.60 (1H, dd, *J* = 8.5 Hz, 6 Hz), 7.48 (1H, d, *J* = 8.5 Hz), 7.29 (1H, m), 7.11 (1H, dd, *J* = 9 Hz, 2.5 Hz), 7.06 (1H, td, *J* = 8.5 Hz, 2.5 Hz).

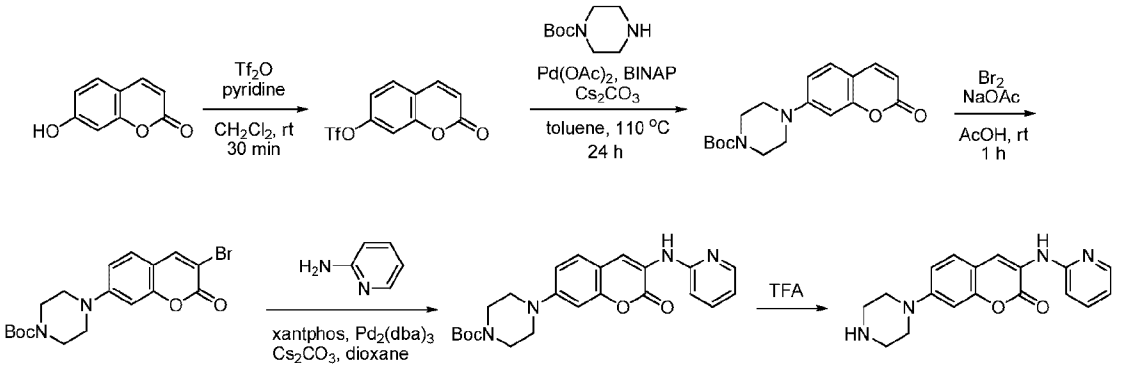
[00721] Step B: Following the procedure from Example 22, Step F, 7-fluoro-3-(1-(pyridin-2-yl)-1H-imidazol-4-yl)-2H-chromen-2-one (40 mg, 0.13 mmol), *cis*-2,6-dimethylpiperazine (23 mg, 0.2 mmol), and DMSO (300 μL) yielded the title compound (46 mg, 88%): m.p. 201–206 °C; MS *m/z* 402.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.71 (1H, d, *J* = 1 Hz), 8.55 (1H,

m), 8.52 (1H, s), 8.45 (1H, d, J = 1 Hz), 8.02 (1H, m), 7.92 (1H, d, J = 8.5 Hz), 7.64 (1H, d, J = 9 Hz), 7.41 (1H, dd, J = 6.5 Hz, 5 Hz), 7.02 (1H, dd, J = 9 Hz, 2 Hz), 6.88 (1H, d, J = 2.5 Hz), 3.82 (2H, d, J = 11.5 Hz), 2.80 (2H, m), 2.32 (2H, t, J = 11.5 Hz), 2.28 (1H, br s), 1.04 (6H, d, J = 6.5 Hz).

[00722] 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.

[00723] **Example 24**

[00724] Preparation of Cpd 32



[00725] Step A: Into a suspension of 7-hydroxycoumarin (16.2 g, 100 mmol) in pyridine (16.3 mL, 200 mmol) and CH_2Cl_2 (250 mL) at 0 °C was added dropwise a solution of triflic anhydride (20.2 mL, 120 mmol) in CH_2Cl_2 (50 mL). The mixture warmed to room temperature over 30 min. The mixture was washed with dilute aqueous HCl, water, brine, and then dried over $NaSO_4$ and concentrated to give a solid 2-oxo-2*H*-chromen-7-yl trifluoromethanesulfonate (28.5 g, 97%) as a tan solid. MS *m/z* 295.0 $[M+H]^+$.

[00726] Step B: A mixture of palladium(II) acetate (0.228 g, 1.02 mmol), 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (1.27 g, 2.04 mmol) and Cs_2CO_3 (8.3 g, 25.5 mmol) in toluene (75 mL) was stirred under Argon at 110 °C for 15 min until a dark red color formed. The mixture was cooled to room temperature, upon which 2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (5.0 g, 17 mmol) and 1-Boc-piperazine (3.8 g, 20.4 mmol) were added. The mixture was stirred at 110 °C for 24 h. The mixture was partitioned in EtOAc and water. The organic layer was dried over $NaSO_4$, filtered, concentrated and purified by silica gel column chromatography (0-15% EtOAc in CH_2Cl_2) to give *tert*-butyl 4-(2-oxo-2*H*-chromen-7-yl)piperazine-1-carboxylate (2.5 g, 45%) as a yellow solid. MS *m/z* 331.2 $[M+H]^+$.

[00727] Step C: Into a mixture of *tert*-butyl 4-(2-oxo-2*H*-chromen-7-yl)piperazine-1-carboxylate (2.5 g, 7.58 mmol) and sodium acetate (1.86 g, 22.7 mmol) in acetic acid (30 mL) at room temperature was added bromine (0.4 mL, 7.95 mmol) dropwise. The mixture was stirred at room temperature for 1 h. Water was added to produce a precipitate. The solid was collected by vacuum filtration, washed with water, dried and purified by silica gel column chromatography (0-25% EtOAc in CH_2Cl_2) to give *tert*-butyl 4-(3-bromo-2-oxo-2*H*-chromen-7-yl)piperazine-1-carboxylate (1.8 g, 58%) as a yellow solid. MS *m/z* 409.1 $[M+H]^+$, 411.1 $[M+2+H]^+$.

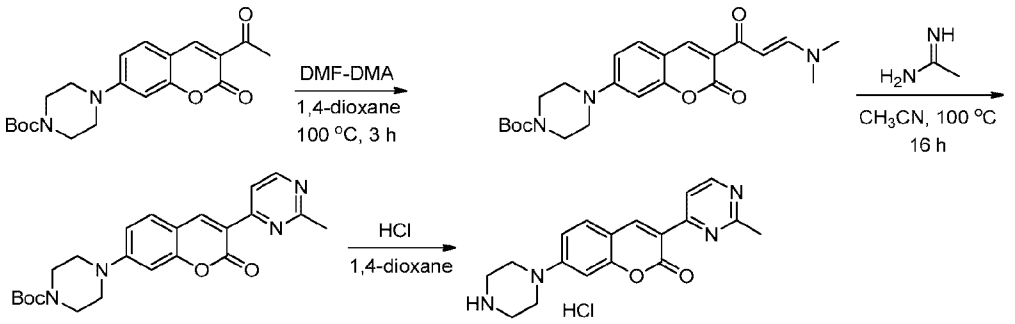
[00728] Step D: A mixture of *tert*-butyl 4-(3-bromo-2-oxo-2*H*-chromen-7-yl)piperazine-1-carboxylate (80 mg, 0.2 mmol), 2-aminopyridine (26 mg, 0.28 mmol), bis(dibenzylideneacetone)palladium(0) (3.7 mg, 0.004 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (5.1 mg, 0.0088 mmol) and Cs_2CO_3 (91 mg, 0.28 mmol) in 1,4-dioxane (1.0 mL) was stirred at 100 °C overnight under Argon, then the solvent was removed. The residue was purified by silica gel column chromatography (0-10% EtOAc in CH_2Cl_2) to give *tert*-butyl 4-(2-oxo-3-(pyridin-2-ylamino)-2*H*-chromen-7-yl)piperazine-1-carboxylate (82 mg, 71%) as a yellow solid. MS *m/z* 423.2 $[M+H]^+$.

[00729] Step E: *tert*-Butyl 4-(2-oxo-3-(pyridin-2-ylamino)-2*H*-chromen-7-yl)piperazine-1-carboxylate (71 mg, 0.168 mmol) was dissolved in trifluoroacetic acid (2.0 mL). The mixture was stirred for 15 min at room temperature, then the solvent was removed with a stream of nitrogen. The residue was partitioned in CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $NaSO_4$, filtered and concentrated to give the title compound (41 mg, 76%) as a yellow solid: m.p. 191–194 °C; MS *m/z* 323.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.78 (1H, s), 8.77 (1H, s), 8.69 (1H, s), 8.24 (1H, dd, J = 5.1 Hz, 1.3 Hz), 7.62-7.57 (1H, m), 7.44 (1H, d, J = 8.8 Hz), 7.27 (1H, d, J = 8.5 Hz), 6.95 (1H, dd, J = 8.8 Hz, 2.2 Hz), 6.85-6.80 (2H, m), 3.20-3.13 (4H, m), 2.86-2.78 (4H, m).

[00730] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 24 by substituting the appropriate starting materials, reagents and reaction conditions.

[00731] **Example 25**

[00732] Preparation of Cpd 274



[00733] Step A: To a solution of *t*-butyl 4-(3-acetyl-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (1.42 g, 3.8 mmol, prepared in Example 17, Step A) in 1,4-dioxane (8 mL) was added *N,N*-dimethylformamide dimethylacetal (6 mL, 44.7 mmol). The mixture was heated at 100 °C for 3 h. The reaction mixture was concentrated under reduced pressure. The residue was triturated with ether-hexane (1:1), producing a precipitate. The solid was collected by vacuum filtration, washed with ether-hexane and dried under nitrogen, affording (E)-tert-butyl 4-(3-(3-(dimethylamino)acryloyl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (1.5g, 92%) as an orange powder. MS *m/z* 428.4 $[M+H]^+$.

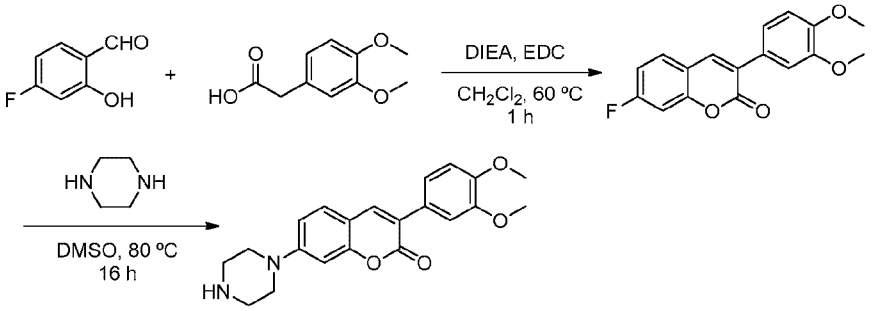
[00734] Step B: To a solution of (E)-*t*-butyl 4-(3-(3-(dimethylamino)acryloyl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (171 mg, 0.40 mmol) and acetamidine hydrochloride (151 mg, 1.6 mmol) in CH_3CN (2 mL) was added K_2CO_3 (110 mg, 0.80 mmol). The mixture was heated to 100 °C for 16 h. After cooling to room temperature, water (10 mL) was added to the mixture, producing a precipitate. The precipitate was collected by vacuum filtration, washed with water and dried under nitrogen to afford *t*-butyl-4-(3-(2-methylpyrimidin-4-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (148 mg, 88 %). MS *m/z* 423.3 $[M+H]^+$.

[00735] Step C: To a suspension of *t*-butyl-4-(3-(2-methylpyrimidin-4-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (182 mg, 0.42 mmol) in CH_2Cl_2 (1 mL) was added 4N HCl in 1,4-dioxane (1 mL). The mixture was stirred for 2 h at room temperature. The suspension was diluted with ether (10 mL) and filtered. The solid was washed with ether and dried under nitrogen to afford the title compound (140 mg, 91%) as a yellow solid: m.p. 200 °C (decomp.); MS *m/z* 323.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 9.13 (2H, br), 9.05 (1H, s), 8.78 (1H, d, J = 5.4 Hz), 8.22 (1H, d, J = 5.4 Hz), 7.88 (1H, d, J = 8.8 Hz), 7.12 (1H, dd, J = 8.8 Hz, 2.5 Hz), 7.03 (1H, d, J = 2.2 Hz), 3.73 (4H, m), 3.24 (4H, m), 2.71 (3H, s).

[00736] 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.

[00737] **Example 26**

[00738] Preparation of Cpd 316



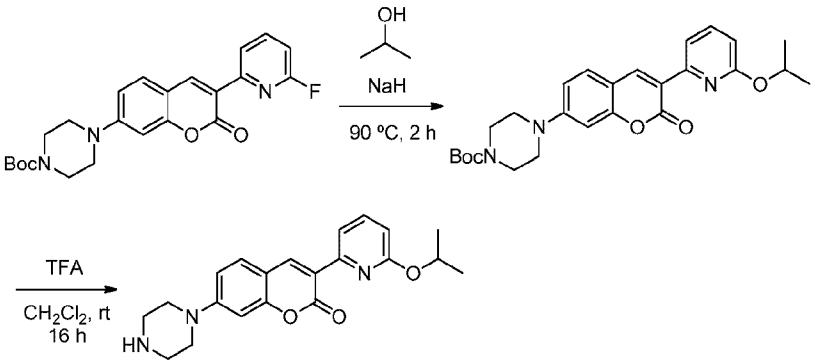
[00739] Step A: To a pressure vessel were added, 4-fluoro-2-hydroxybenzaldehyde (0.5 g, 3.6 mmol), 2-(3,4-dimethoxyphenyl)acetic acid (1.4 g, 7.2 mmol), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (1.5 g, 7.9 mmol), diisopropylethylamine (2.3 mL, 14.3 mmol) and CH_2Cl_2 (10 mL). The mixture was stirred at 60 °C for 1 h, then quenched with an aqueous saturated $NaHCO_3$ solution (50 mL) and extracted with EtOAc three times. The combined extracts were dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column chromatography (0-5% EtOAc in CH_2Cl_2) to give 3-(3,4-dimethoxyphenyl)-7-fluoro-2H-chromen-2-one (1.0 g, 95%). MS *m/z* 301.0 $[M+H]^+$.

[00740] Step B: A mixture of 3-(3,4-dimethoxyphenyl)-7-fluoro-2H-chromen-2-one (40 mg, 0.13 mmol), piperazine (34 mg, 0.40 mmol) and DMSO (0.3 mL) was stirred at 80 °C overnight. After cooling to room temperature, the mixture was diluted with water (5 mL) to produce a precipitate. The precipitate was collected by filtration, washed with water and ethyl ether, and dried to give the title compound (14 mg, 29 %) as yellow powder: m.p. 168–170 °C; MS *m/z* 367.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (1H, s), 7.38 (1H, d, J = 8.8 Hz), 7.31 (1H, d, J = 1.9 Hz), 7.25 (1H, d, J = 2.2 Hz), 6.93 (1H, d, J = 8.5 Hz), 6.85 (1H, dd, J = 8.8 Hz, 2.5 Hz), 6.77 (1H, d, J = 2.5 Hz), 3.95 (3H, s), 3.93 (3H, s), 3.36-3.32 (4H, m), 3.10-3.05 (4H, m).

[00741] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 26 by substituting the appropriate starting materials, reagents and reaction conditions.

[00742] **Example 27**

[00743] Preparation of Cpd 385



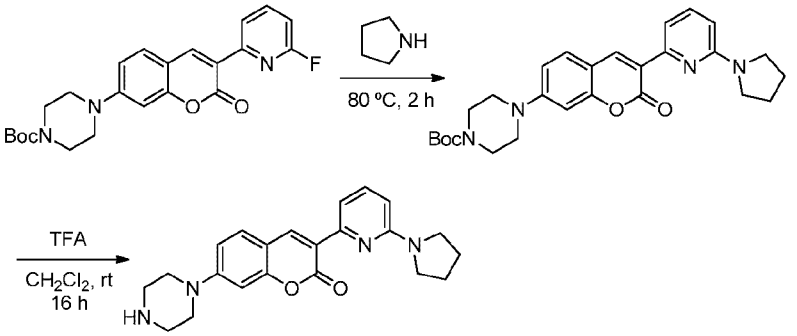
[00744] Step A: To a suspension of tert-butyl 4-(3-(6-fluoropyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (90 mg, 0.21 mmol, prepared according to Example 26) in isopropanol (1 mL) was added NaH (19 mg, 60% in mineral oil, 0.48 mmol). The mixture was stirred at 90 °C for 2 h, diluted with water and extracted with dichloromethane. The organic layer was concentrated and purified by silica gel column chromatography (0-10% MeOH in CH_2Cl_2) to give tert-butyl 4-(3-(6-isopropoxypyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (50 mg, 51%). MS 466.3 *m/z* $[M+H]^+$.

[00745] Step B: tert-Butyl 4-(3-(6-isopropoxypyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (50 mg, 0.11 mmol) was stirred with 50% TFA in CH_2Cl_2 (1.0 mL) at room temperature overnight. Aqueous K_2CO_3 (2M solution) was added to the mixture, until the aqueous layer became basic, pH ~9. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organics were dried over Na_2SO_2 and concentrated to provide the title compound (37 mg, 82%) as a yellow powder: m.p. 177–180 °C; MS 366.3 *m/z* $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.67 (1H, s), 8.06 (1H, dd, *J* = 7.6 Hz, 0.6 Hz), 7.63 (1H, dd, *J* = 8.2 Hz, 7.6 Hz), 7.49 (1H, d, *J* = 8.8 Hz), 6.86 (1H, dd, *J* = 8.7 Hz, 2.4 Hz), 6.75 (1H, d, *J* = 2.2 Hz), 6.65 (1H, dd, *J* = 8.2 Hz, 0.6 Hz), 5.43 (1H, t, *J* = 6.3 Hz), 3.41-3.31 (4H, m), 3.10-3.00 (4H, m), 1.42 (6H, d, *J* = 6.3 Hz).

[00746] 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.

[00747] **Example 28**

[00748] Preparation of Cpd 386

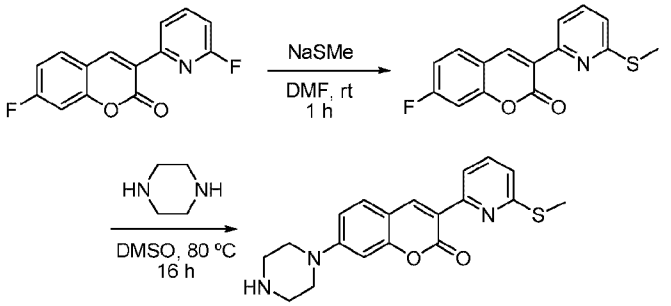


[00749] Step A: A mixture of tert-butyl 4-(3-(6-fluoropyridin-2-yl)-2-oxo-2H-chromen-7-yl)piperazine-1-carboxylate (90 mg, 0.21 mmol, prepared according to Example 26) and pyrrolidine (1 mL) was stirred at 80 °C for 2 h. The mixture was diluted with water (10 mL) and extracted with dichloromethane. The organic layer was concentrated and purified by silica gel column chromatography (0-10% MeOH in CH_2Cl_2) to give tert-butyl 4-(2-oxo-3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-2H-chromen-7-yl)piperazine-1-carboxylate (56 mg, 50 %). MS 477.0 *m/z* $[M+H]^+$.

[00750] Step B: tert-Butyl 4-(2-oxo-3-(6-(pyrrolidin-1-yl)pyridin-2-yl)-2H-chromen-7-yl)piperazine-1-carboxylate was stirred with 50% TFA in CH_2Cl_2 (1.0 mL) at room temperature overnight. Aqueous K_2CO_3 (2M solution) was added to the mixture, until the aqueous layer became basic, pH ~9. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organics were dried over Na_2SO_2 and concentrated to provide the title compound (63 mg, 80 %) as yellow powder: m.p. 190–192 °C; MS 377.3 *m/z* $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.72 (1H, s), 7.73 (1H, d, J = 7.3 Hz), 7.54-7.44 (2H, m), 6.84 (1H, dd, J = 8.8 Hz, 2.5 Hz), 6.75 (1H, d, J = 2.2 Hz), 6.40-6.33 (1H, m), 3.60-3.50 (4H, m), 3.33 (4H, dd, J = 6.2 Hz, 4.3 Hz), 3.10-3.01 (4H, m), 2.04 (4H, dt, J = 6.5 Hz, 3.4 Hz).

[00751] **Example 29**

[00752] Preparation of Cpd 445

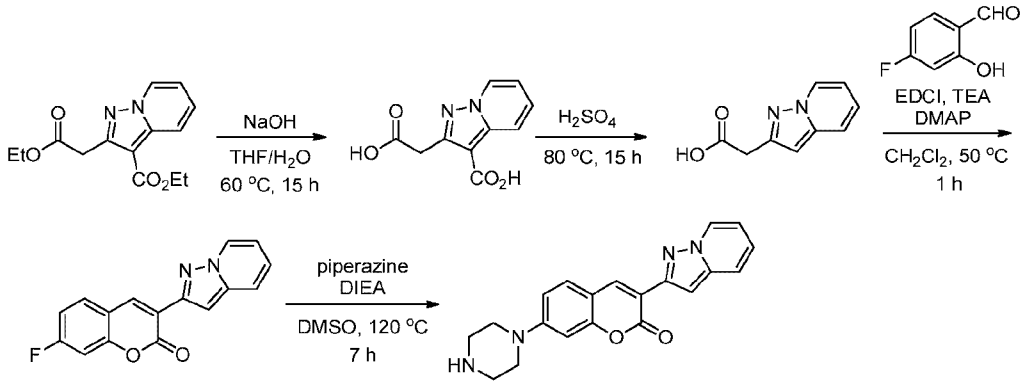


[00753] Step A: A mixture of 7-fluoro-3-(6-fluoropyridin-2-yl)-2H-chromen-2-one (260 mg, 1.0 mmol, prepared according to Example 26) and NaSMe (105 mg, 1.5 mmol) in DMF (2 mL) was stirred at room temperature for 1 h. The mixture was diluted with water (10 mL) to produce a precipitate. The precipitate was collected by filtration, washed with water and CH_2Cl_2, and dried to give 7-fluoro-3-(6-(methylthio)pyridin-2-yl)-2H-chromen-2-one (100 mg, 35 %). MS 288.3 *m/z* $[M+H]^+$.

[00754] Step B: A mixture of 7-fluoro-3-(6-(methylthio)pyridin-2-yl)-2H-chromen-2-one (50 mg, 0.17 mmol), piperazine (44 mg, 0.51 mmol) and DMSO (0.5 mL) was stirred at 80 °C overnight. After cooling to room temperature, the mixture was diluted with water (5 mL) to produce a precipitate. The precipitate was collected by filtration, washed with water and ethyl ether, and dried to give the title compound (18 mg, 30 %): m.p. 180–183 °C; MS *m/z* 354.3 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.69 (1H, s), 7.84 (1H, d, *J* = 7.3 Hz), 7.59 (1H, dd, *J* = 8.5 Hz, 7.6 Hz), 7.53 (1H, d, *J* = 8.8 Hz), 7.17-7.13 (2H, m), 6.71 (1H, s), 3.63-3.61 (4H, m), 3.09-3.03 (4H, m), 2.58-2.54 (3H, m).

[00755] **Example 30**

[00756] Preparation of Cpd 187



[00757] Step A: A mixture of ethyl 2-(2-ethoxy-2-oxoethyl)pyrazolo[1,5-a]pyridine-3-carboxylate (1.2 g, 4.3 mmol, prepared from 1-aminopyridinium iodide and diethyl 3-oxopentanedioate according to the procedure in Japanese Patent 62-267285, 1986), NaOH (3 N, 8.6 mL) and THF (10 mL) was heated at 60 °C for 15 h. The mixture was cooled to room temperature and washed with EtOAc. The aqueous phase was acidified with aqueous HCl (6 N) to pH 3, producing a precipitate. The precipitate was collected by vacuum filtration, washed with water and dried to give 2-(carboxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (0.63 g, 66%) as a white solid. MS *m/z* 221.1 $[M+H]^+$.

[00758] Step B: To a suspension of 2-(carboxymethyl)pyrazolo[1,5-a]pyridine-3-carboxylic acid (0.63 g, 2.9 mmol) in water (5 mL) was added conc. H_2SO_4 (5 mL). The clear solution was heated at 80 °C for 15 h. The solution was cooled to room temperature. Aqueous NaOH (1 N) was added to the solution until pH 2-3 was reached. A precipitate formed. The precipitate was collected by vacuum filtration, washed with water and dried to give 2-(pyrazolo[1,5-a]pyridin-2-yl)acetic acid (0.435 g, 86%) as a white solid. MS *m/z* 177.1 $[M+H]^+$.

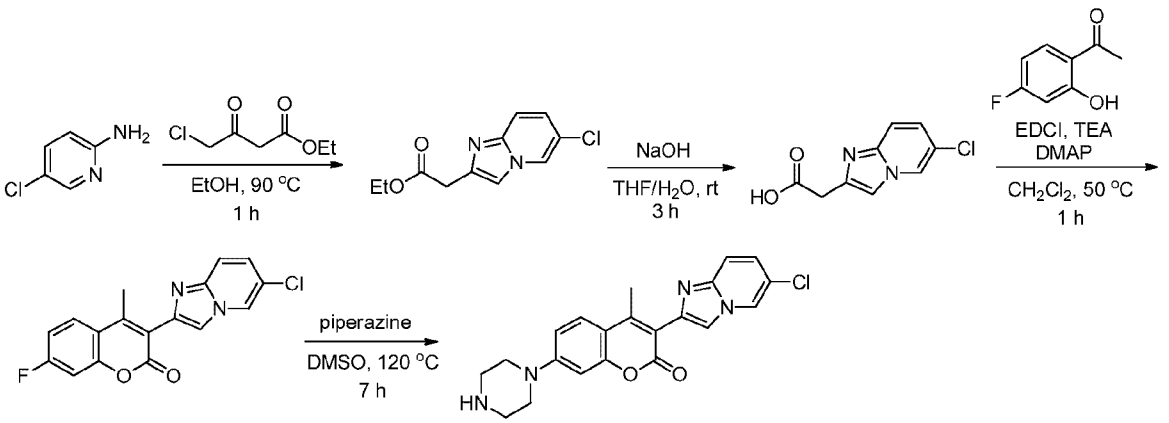
[00759] Step C: A mixture of 2-(pyrazolo[1,5-a]pyridin-2-yl)acetic acid (0.435 g, 2.47 mmol)), 4-fluoro-2-hydroxybenzaldehyde (0.363 g, 2.59 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.57 g, 2.96 mmol), 4-(dimethylamino)pyridine (61 mg, 0.5 mmol) and triethylamine (0.7 mL, 5.0 mmol) in CH_2Cl_2 (8 mL) was heated at 50 °C. After 1 h, the mixture was concentrated. The residue was suspended in CH_3CN, collected by vacuum filtration, washed with CH_3CN and dried to give 7-fluoro-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one (0.66 g, 95%) as a yellow solid. MS *m/z* 281.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.83 (1H, s), 8.71 (1H, dd *J* = 6.9 Hz, 1.0 Hz), 8.03 (1H, dd, *J* = 8.7 Hz, 6.4 Hz), 7.78 (1H, d, *J* = 8.8 Hz), 7.48 (1H, dd, *J* = 9.6 Hz, 2.4 Hz), 7.34-7.24 (1H, m), 7.30 (1H, s), 7.26 (1H, m), 6.98 (1H, td, *J* = 6.9 Hz, 1.4 Hz).

[00760] Step D: A mixture of 7-fluoro-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one (56 mg, 0.2 mmol), piperazine (52 mg, 0.6 mmol) and N,N-diisopropylethylamine (52 μL, 0.3 mmol) in DMSO (0.5 mL) was heated at 120 °C for 7 h. Upon cooling to room temperature, a precipitate formed. The precipitate was collected by vacuum filtration, washed with CH_3CN and dried to give the title compound (60 mg, 87%) as a yellow solid: m.p. 236–238 °C; MS *m/z* 347.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.67 (1H, dd, *J* = 7.0 Hz, 2.3 Hz), 8.5 (1H, s), 7.73 (1H, d, *J* = 8.9 Hz), 7.69 (1H, d, *J* = 8.9 Hz), 7.25-7.20 (2H, m), 7.01 (1H, dd, *J* = 8.9 Hz, 2.4 Hz), 6.92 (1H, td, *J* = 6.8 Hz, 1.4 Hz), 6.86 (1H, d, *J* = 2.3 Hz), 3.32 (4H, m), 2.82 (4H, m).

[00761] 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.

[00762] **Example 31**

[00763] Preparation of Cpd 112



[00764] Step A: A mixture of 5-chloropyridin-2-amine (2.57 g, 20 mmol) and ethyl 4-chloro-3-oxobutanoate (3.95 g, 24 mmol) in EtOH (20 mL) was heated at 90 °C for 15 h, then the solvent was removed. The residue was suspended in CH_3CN, collected by vacuum filtration, washed with CH_3CN and dried to give ethyl 2-(6-chloroimidazo[1,2-a]pyridin-2-yl)acetate (4.14 g, 86%) as a white solid. MS *m/z* 239.1 $[M+H]^+$.

[00765] Step B: To a solution of ethyl 2-(6-chloroimidazo[1,2-a]pyridin-2-yl)acetate (2.38 g, 10 mmol) in THF was added aqueous NaOH (3 N, 6.6 mL, 20 mmol). After stirring at room temperature for 3 h, the mixture was concentrated. The residual mixture was acidified with aqueous HCl (6 N) to pH 3. A precipitate formed. The precipitate was collected by vacuum filtration, washed with water and dried, yielding 2-(6-chloroimidazo[1,2-a]pyridin-2-yl)acetic acid (1.66 g, 79%) as a white solid. MS *m/z* 211.1 $[M+H]^+$.

[00766] Step C: Following the procedure in Example 30, Step C, 2-(6-chloroimidazo[1,2-a]pyridin-2-yl)acetic acid (0.386 g, 2.5 mmol), 1-(4-fluoro-2-hydroxyphenyl)-ethanone (0.525 g, 2.5 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.623 g, 3.25 mmol), 4-(dimethylamino)pyridine (92 mg, 0.75 mmol) and triethylamine (0.91 mL, 7.5 mmol) in CH_2Cl_2 (4 mL) gave 3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-fluoro-4-methyl-2H-chromen-2-one (0.426 g, 52%) as an off-white solid. MS *m/z* 329.1 $[M+H]^+$.

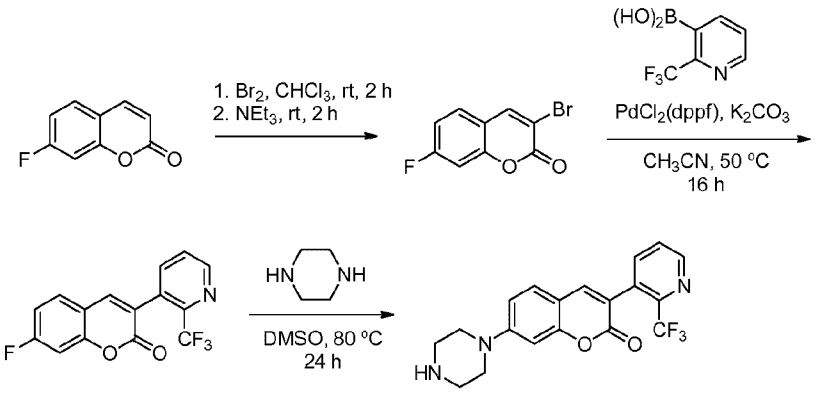
[00767] Step D: Following the procedure in Example 30, Step D, 3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-fluoro-4-methyl-2H-chromen-2-one (82 mg, 0.25 mmol), piperazine (65 mg,

0.75 mmol), DIEA (52 μL, 0.3 mmol) in DMSO (0.5 mL) gave the title compound (64 mg, 65%) as a yellow solid: m.p. 224–227 °C; MS *m/z* 395.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.90 (1H, d, *J* = 2.1 Hz), 8.27 (1H, s), 7.69 (1H, d, *J* = 9.1 Hz), 7.63 (1H, d, *J* = 9.6 Hz), 7.30 (1H, dd, *J* = 9.6 Hz, 2.1 Hz), 7.01 (1H, dd, *J* = 9.1 Hz, 2.4 Hz), 6.82 (1H, d, *J* = 2.5 Hz), 3.28 (4H, m), 2.82 (4H, m), 2.66 (3H, s).

[00768] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 31 by substituting the appropriate starting materials, reagents and reaction conditions.

[00769] **Example 32**

[00770] Preparation of Cpd 124



[00771] Step A: To a stirred solution of 7-fluorocoumarin (3.04 g, 18.5 mmol, prepared in Example 22, Step A) in chloroform (20 mL), at room temperature, was added dropwise, bromine (11.9 g, 3.81 mL, 74 mmol). After the addition, the mixture was stirred at room temperature for an additional 2 hours, then cooled in an ice-water bath and diluted with dichloromethane (100 mL). Triethylamine (22.4 g, 30.7 mL, 222 mmol) was added carefully while stirring. The mixture was stirred at room temperature for an additional 2 h after the addition. The precipitate present in the mixture was removed by filtration and washed with CH_2Cl_2 (3 x 15 mL). The combined filtrate was concentrated and purified by silica gel column chromatography (CH_2Cl_2), yielding 3-bromo-7-fluoro-2H-chromen-2-one (4.07 g, 90%) as white solid. MS *m/z* 242.4, 244.4 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.09 (1H, s), 7.47 (1H, dd, *J* = 8.7 Hz, 5.8 Hz), 7.12-7.03 (2H, m).

[00772] Step B: A reaction tube, equipped with an open-top cap and a septum was charged with 3-bromo-7-fluoro-2H-chromen-2-one (0.49 g, 2.0 mmol), (2-(trifluoromethyl)pyridin-3-yl)boronic acid (0.42 g, 2.2 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II)

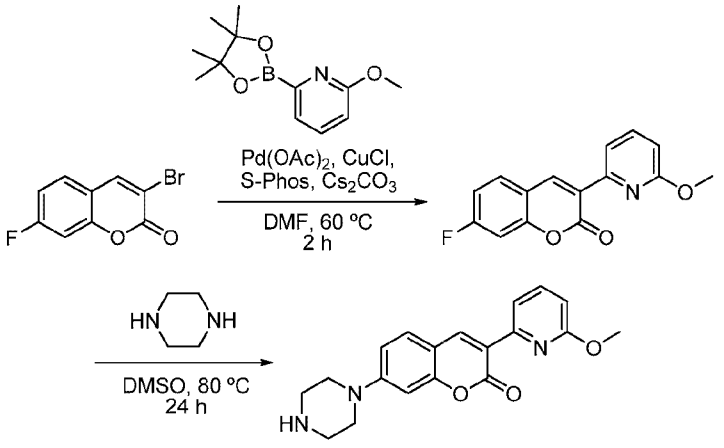
complex with dichloromethane (0.082 g, 0.1 mmol) and CH_3CN (6.0 mL). After purging three times with nitrogen, aqueous K_2CO_3 (2.0 mL, 2.0M, 4.0 mmol) was added and the mixture was stirred at 50 °C overnight, then the solvent was removed. The residue was suspended in CH_2Cl_2 and filtered. The filtrate was concentrated and purified by silica gel column chromatography (0-30% EtOAc in CH_2Cl_2) to give 7-fluoro-3-(2-(trifluoromethyl)pyridin-3-yl)-2H-chromen-2-one (0.21 g, 34%). MS *m/z* 310.2 $[M+H]^+$.

[00773] Step C: A mixture of 7-fluoro-3-(2-(trifluoromethyl)pyridin-3-yl)-2H-chromen-2-one (93 mg, 0.3 mmol) and piperazine (52 mg, 0.6 mmol) in DMSO (0.6 mL) was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was diluted with water (5 mL) to produce a precipitate. The solid was collected by filtration, washed with water and ethyl ether, and dried to give the title compound (100 mg, 89%) as yellow powder: m.p. 197–200 °C; MS *m/z* 376.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.71 (1H, s), 8.53 (1H, d, J = 2.5 Hz), 8.14 (1H, t, J = 7.9 Hz), 7.83 (1H, d, J = 8.5 Hz), 7.75 (1H, d, J = 9.1 Hz), 7.02 (1H, dd, J = 9.0 Hz, 2.4 Hz), 6.85 (1H, d, J = 2.2 Hz), 3.40-3.33 (4H, m), 2.85-2.78 (4H, m).

[00774] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 32 by substituting the appropriate starting materials, reagents and reaction conditions.

[00775] **Example 33**

[00776] Preparation of Cpd 218



[00777] Step A: A mixture of 3-bromo-7-fluorocoumarin (122 mg, 0.5 mmol, prepared in Example 32, Step A), 2-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (235 mg, 1.0 mmol), copper(I) chloride (50 mg, 0.5 mmol), Cs_2CO_3 (652 mg, 2.0 mmol), palladium(II) acetate (5.6 mg, 0.025 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl

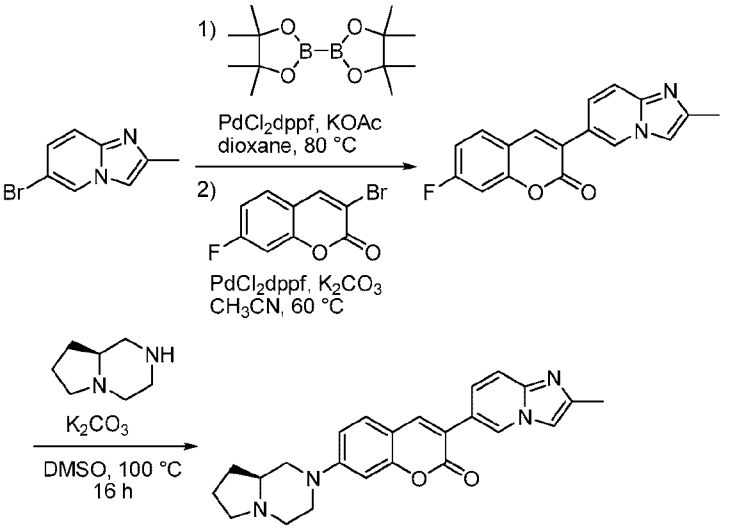
(41 mg, 0.1 mmol) and DMF (2.0 mL) were stirred under an Argon atmosphere at 60 °C for 2 h. After cooling to room temperature, the mixture was diluted with water (10 mL) to produce a precipitate. The solid was washed with water, dried, and purified with silica gel column chromatography (0-10% EtOAc in CH_2Cl_2) to give 7-fluoro-3-(6-methoxypyridin-2-yl)-2H-chromen-2-one (52 mg, 38%). MS *m/z* 272.2 $[M+H]^+$.

[00778] Step B: A mixture of 7-fluoro-3-(6-methoxypyridin-2-yl)-2H-chromen-2-one (52 mg, 0.19 mmol), piperazine (50 mg, 0.57 mmol) and DMSO was stirred at 80 °C overnight. After cooling to room temperature, the mixture was diluted with water (5 mL) to produce a precipitate. The precipitate was collected by filtration, dried and purified by silica gel column chromatography (0-20% MeOH in CH_2Cl_2) to give the title compound (20 mg, 31 %) as yellow powder: m.p. 162–165 °C; MS *m/z* 338.2 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6): δ 8.83 (1H, s), 7.96 (1H, dd, J = 7.6 Hz, 0.9 Hz), 7.75 (1H, dd, J = 8.2, 7.6 Hz), 7.69 (1H, d, J = 8.8 Hz), 7.02 (1H, dd, J = 9.0, 2.4 Hz), 6.85 (1H, d, J = 2.2 Hz), 6.77 (1H, dd, J = 8.2 Hz, 0.6 Hz), 3.98 (3H, s), 3.35-3.28 (4H, m), 2.86-2.78 (4H, m).

[00779] 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.

[00780] **Example 34**

[00781] Preparation of Cpd 651



[00782] Step A: A mixture of 6-bromo-2-methylimidazo[1,2-a]pyridine (0.79 g, 3.75 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (1.14 g, 4.49 mmol), [1,1'-

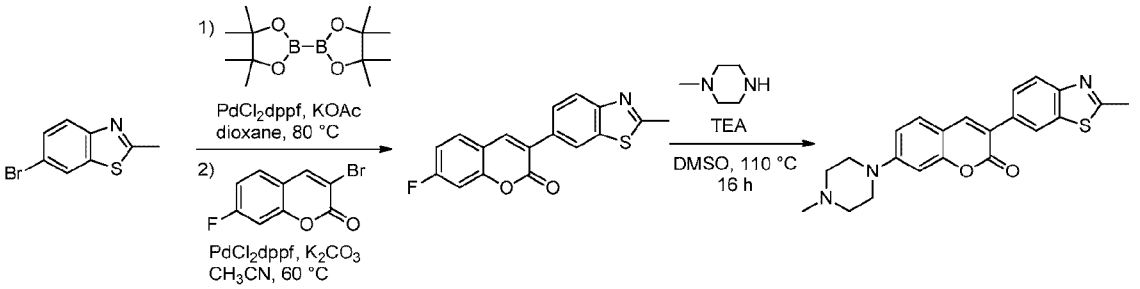
bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (0.15 g, 0.19 mmol), potassium acetate (1.1g, 11.5 mmol) in 1,4-dioxane (7.5 mL) was stirred at 80 °C overnight under Argon. The mixture was diluted with THF (20 mL) and filtered. The filtrate was evaporated to give a dark solid residue, which was used without further purification (MS *m/z* 177.0 $[M+H]^+$). The residue was combined with 3-bromo-7-fluoro-2H-chromen-2-one (0.73 g, 3.0 mmol, prepared in Example 32, Step A), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (0.245 g, 0.3 mmol) and aqueous K_2CO_3 (2.0 M x 4.5 mL, 9.0 mmol) in CH_3CN (9.0 mL). The mixture was stirred at 60 °C overnight under Argon, then diluted with water and filtered. The solid was dissolved in CH_2Cl_2 (10% methanol), dried over Na_2SO_4, filtered, concentrated and purified with by silica gel chromatography (0-10% MeOH in CH_2Cl_2) to give 7-fluoro-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one (0.67 g, 76%). MS *m/z* 295.0 $[M+H]^+$.

[00783] Step B: A mixture of 7-fluoro-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one (90 mg, 0.31 mmol), (S)-octahydropyrrolo[1,2-a]pyrazine (50 mg, 0.40 mmol), K_2CO_3 (125 mg, 0.92 mmol) in DMSO (0.6 mL) was stirred at 100 °C overnight. The mixture was diluted with an aqueous saturated $NaHCO_3$ solution and filtered. The solid was dried and purified by silica gel chromatography (0-10% MeOH in CH_2Cl_2) to give the title compound (56 mg, 46%) as a yellow solid: m.p. 231–233 °C; MS *m/z* 401.5 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.86 (1H, dd, *J*=1.7, 0.8 Hz), 7.83 (1H, s), 7.49 - 7.57 (1H, m), 7.35 - 7.44 (3H, m), 6.87 (1H, d, *J*=8.8 Hz), 6.77 (1H, d, *J*=2.2 Hz), 3.94 (1H, dd, *J*=12.0, 1.6 Hz), 3.80 (1H, d, *J*=12.6 Hz), 3.24-3.06 (3H, m), 2.76 (1H, t, *J*=11.0 Hz), 2.47 (3H, d, *J*=0.6 Hz), 2.45-2.35 (1H, m), 2.30-2.10 (2H, m), 1.99-1.87 (2H, m), 1.86-1.77 (1H, m), 1.61-1.48 (1H, m).

[00784] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 34 by substituting the appropriate starting materials, reagents and reaction conditions.

[00785] **Example 35**

[00786] Preparation of Cpd 769



[00787] Step A: Following the procedure in Example 34, Step A, 6-bromo-2-methylbenzo[d]thiazole (0.47 g, 2.1 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (0.63 g, 2.5 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (84 mg, 0.1 mmol) in dioxane (4.0 mL) followed by reaction of the intermediate formed with 3-bromo-7-fluoro-2H-chromen-2-one (0.45 g, 1.85 mmol), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (0.16 g, 0.2 mmol), aqueous K_2CO_3 (2.0 M x 3.0 mL, 6.0 mmol) in CH_3CN (6.0 mL) yielded 7-fluoro-3-(2-methylbenzo[d]thiazol-6-yl)-2H-chromen-2-one (144 mg, 25%). MS *m/z* 312.0 $[M+H]^+$.

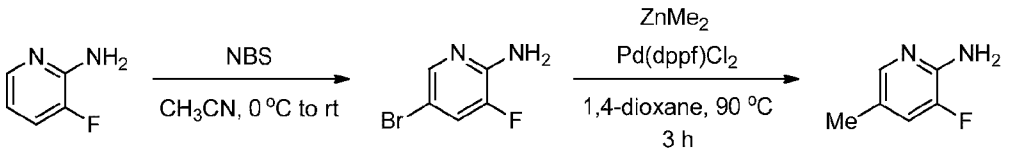
[00788] Step B: A mixture of 7-fluoro-3-(2-methylbenzo[d]thiazol-6-yl)-2H-chromen-2-one (34 mg, 0.11 mmol), 1-methylpiperazine (22 mg, 0.22 mmol), triethylamine (49 mg, 0.49 mmol) in DMSO (0.25 mL) was stirred at 110 °C overnight. The mixture was diluted with an aqueous saturated $NaHCO_3$ solution and filtered. The solid was dried and purified by silica gel chromatography (0-10% MeOH in CH_2Cl_2) to give the title compound (41 mg, 95%) as a yellow solid: m.p. 215–217 °C; MS *m/z* 392.4 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.28 (1H, d, J=1.8 Hz), 7.98 (1H, dd, *J*=8.5, 0.6 Hz), 7.80 (1H, s), 7.73 (1H, dd, *J*=8.5, 1.6 Hz), 7.40 (1H, d, *J*=8.8 Hz), 6.86 (1H, dd, *J*=8.8, 2.5 Hz), 6.78 (1H, d, *J*=2.2 Hz), 3.42 (4H, br. s.), 2.86 (3H, s), 2.62 (4H, s), 2.40 (3H, s)

[00789] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 35 by substituting the appropriate starting materials, reagents and reaction conditions.

[00790] **Example 36**

[00791] Preparation of Cpd 421

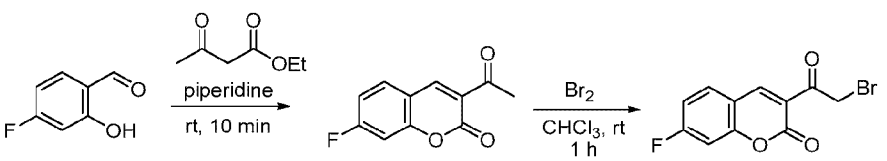
[00792] Part 1: Preparation of 3-fluoro-5-methylpyridin-2-amine



[00793] Step A: A solution of 3-fluoropyridin-2-amine (1.0 g, 8.92 mmol) was dissolved in CH_3CN (300 mL) at 0 °C. N-Bromosuccinimide (800 mg, 4.5 mmol) was added to the solution. The reaction mixture was stirred at 0 °C for 20 min, then at room temperature for 20 min. The mixture was cooled to 0 °C. Additional N-bromosuccinimide (800 mg, 4.5 mmol) was added. The mixture warmed to room temperature over 40 minutes. An aqueous $NaHSO_3$ solution was added to the mixture to quench excess reagent, then the solvent was removed under vacuum. The residue was dissolved in EtOAc, then washed with aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, then filtered and concentrated under vacuum. Trituration of the residue with 2:1 hexanes:ether yielded 5-bromo-3-fluoropyridin-2-amine (1.18 g, 69%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.93 (1H, d, J = 2 Hz), 7.37 (1H, dd, J = 9.5 Hz, 2 Hz), 4.66 (2H, br s), 2.77 (3H, s).

[00794] Step B: A solution of dimethylzinc (15 mL, 1.2 M in toluene, 18 mmol) was added to a mixture of 5-bromo-3-fluoropyridin-2-amine (1.48 g, 7.75 mmol) and [1,1'-bis(diphenylphosphino)-ferrocene]dichloropalladium(II) complex with dichloromethane (150 mg, 0.18 mmol) in 1,4-dioxane (30 mL). The mixture was heated at 95 °C for 2 h. The reaction mixture was cooled to room temperature and quenched with MeOH. The mixture was diluted with aqueous saturated NH_4OH and extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by silica gel column chromatography (20% acetone in CH_2Cl_2), followed by trituration with hexane to give 3-fluoro-5-methylpyridin-2-amine (668 mg, 68%) as a tan solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (1H, s), 7.06 (1H, dd, J = 11.5 Hz, 1.5 Hz), 4.43 (2H, br s), 2.21(3H, s).

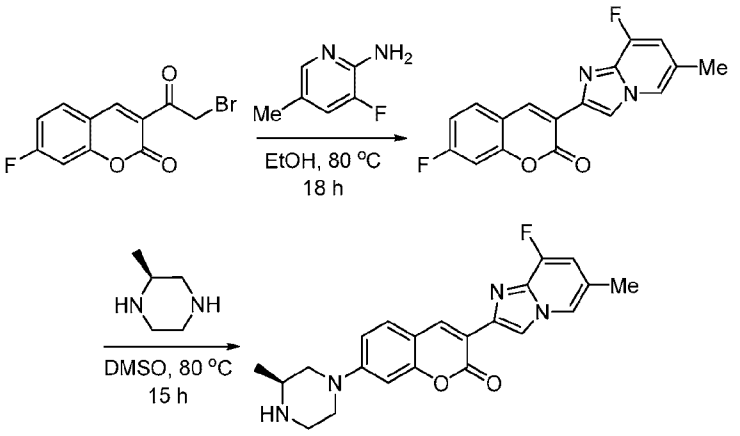
[00795] Part 2: Preparation of 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one



[00796] Step A: Into a mixture of 4-fluoro-2-hydroxybenzaldehyde (1.4 g, 10 mmol) and ethyl 3-oxobutanoate (1.3 g, 10 mmol) was added a few drops of piperidine. The mixture was stirred at room temperature for 10 min. A precipitate formed and was collected by vacuum filtration. The solid was washed with ethanol and aqueous HCl (1 N), filtered and dried to give 3-acetyl-7-fluoro-2*H*-chromen-2-one (1.96 g, 95%) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (1H, s), 7.68 (1H, m), 7.13-7.07 (2H, m), 2.73 (3H, s).

[00797] Step B: Into a solution of 3-acetyl-7-fluoro-2*H*-chromen-2-one (1.96 g, 9.5 mmol) in $CHCl_3$ (20 mL) was added dropwise a solution of bromine (1.6 g, 10 mmol) in $CHCl_3$ (10 mL). The mixture was stirred at room temperature for 1 h and filtered. The solid was washed with $CHCl_3$ and dried to give the title compound (1.96 g, 72%) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (1H, s), 7.72 (1H, m), 7.17-7.10 (2H, m), 4.73 (2H, s).

[00798] Part 3: Preparation of Cpd 421



[00799] Step A: A mixture of 3-(2-bromoacetyl)-7-fluoro-2H-chromen-2-one (500 mg, 1.75 mmol), 3-fluoro-5-methylpyridin-2-amine (240 mg, 1.9 mmol) and EtOH (3 mL) was heated at 95 °C for 18 h. The reaction mixture was partitioned between CH_2Cl_2 and aqueous K_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with 1:1 hexane/acetone, yielding 7-fluoro-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (412 mg, 75%) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (1H, s), 8.50 (1H, d, J = 2.5 Hz), 7.77 (1H, m), 7.63 (1H, dd, J = 9Hz, 6 Hz), 7.11 (1H, dd, J = 9 Hz, 2 Hz), 7.07 (1H, td, J = 8.5 Hz, 2.5 Hz), 6.80 (1H, d, J = 6 Hz), 2.34 (3H, s).

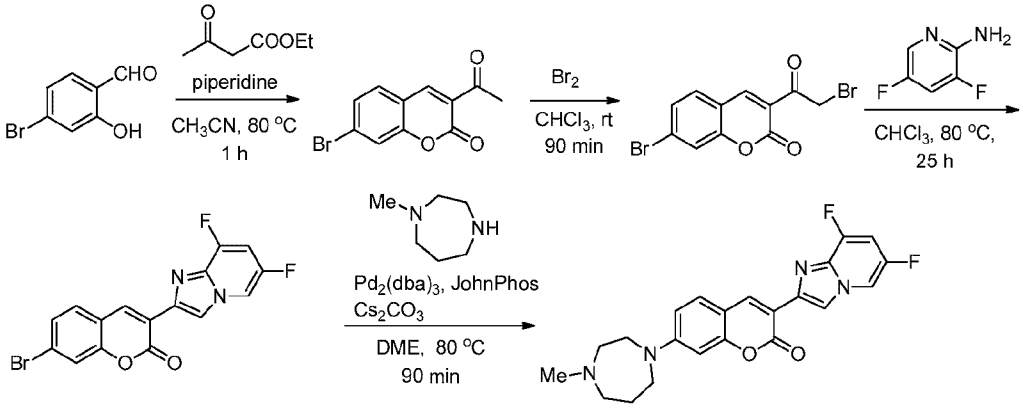
[00800] Step B: A mixture of 7-fluoro-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (120 mg, 0.38 mmol), (S)-2-methylpiperazine (75 mg, 0.75 mmol) and DMSO (900 μL) was heated at 80 °C for 15 h. The mixture was diluted with an aqueous saturated $NaHCO_3$ solution, causing the product to precipitate from solution. The mixture was filtered.

The solid material was purified by silica gel column chromatography (10% MeOH in CH_2Cl_2), yielding the title compound (133 mg, 89%) as a yellow solid: m.p. 250–255 °C; MS *m/z* 393.3 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.73 (1H, s), 8.52 (1H, d, J = 3 Hz), 8.31 (1H, s), 7.72 (1H, d, J = 8.5 Hz), 7.09 (1H, d, J = 12 Hz), 7.02 (1H, dd, J = 9 Hz, 2 Hz), 6.88 (1H, d, J = 2 Hz), 3.81 (2H, m), 2.96 (1H, m), 2.73 (3H, m), 2.39 (1H, t, J = 11 Hz), 2.31 (1H, br s), 2.28 (3H, s), 1.04 (3H, d, J = 6 Hz).

[00801] 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.

[00802] **Example 37**

[00803] Preparation of Cpd 520



[00804] Step A: A mixture of 4-bromo-2-hydroxybenzaldehyde (5.0 g, 24.8 mmol), piperidine (150 μL, 1.5 mmol), ethyl acetoacetate (3.15 mL, 25 mmol) and CH_3CN (2.0 mL) was heated at 80 °C for 1 h. The reaction mixture was partitioned between CH_2Cl_2 and aqueous HCl (1 M). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was triturated with MeOH, yielding 3-acetyl-7-bromo-2H-chromen-2-one (5.45 g, 82%) as a yellow solid. ^1H NMR (500 MHz, $CDCl_3$): δ 8.46 (1H, s), 7.56 (1H, d, J = 1.5 Hz), 7.51 (1H, d, J = 8 Hz), 7.48 (1H, dd, J = 8 Hz, 1.5 Hz), 2.72 (3H, s).

[00805] Step B: A solution of Br_2 (1.1 mL, 21.4 mmol) in $CHCl_3$ (25 mL) was added dropwise to a solution of 3-acetyl-7-bromo-2H-chromen-2-one (5.4 g, 20.2 mmol) in $CHCl_3$ (90 mL) over a period of 90 min. The mixture was filtered. The solid material was washed with $CHCl_3$, yielding 7-bromo-3-(2-bromoacetyl)-2H-chromen-2-one (5.6 g, 80%) as a light pink solid. ^1H

NMR (500 MHz, $CDCl_3$): δ 8.58 (1H, s), 7.60 (1H, d, J = 1.5 Hz), 7.55 (1H, d, J = 8.5 Hz), 7.52 (1H, dd, J = 8.5 Hz, 1.5 Hz), 4.72 (2H, s).

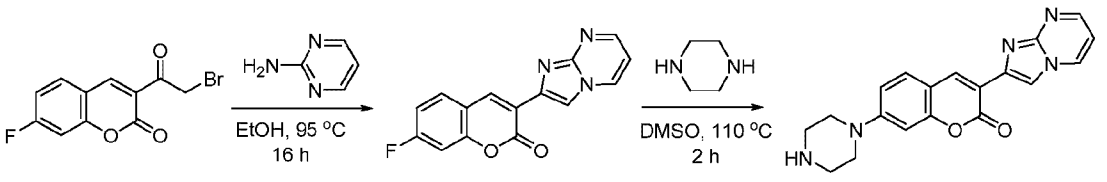
[00806] Step C: A mixture of 7-bromo-3-(2-bromoacetyl)-2H-chromen-2-one (100 mg, 0.29 mmol), 3,5-difluoropyridin-2-amine (48 mg, 0.37 mmol) and $CHCl_3$ (500 μL) was heated at 80 °C for 25 h. The reaction mixture was partitioned between CH_2Cl_2 and an aqueous saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2), yielding 7-bromo-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (96 mg, 88%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (1H, s), 8.64 (1H, d, J = 3 Hz), 8.00 (1H, m), 7.59 (1H, d, J = 1.5 Hz), 7.53 (1H, d, J = 8.5 Hz), 7.47 (1H, dd, J = 8.5 Hz, 1.5 Hz), 6.99 (1H, m).

[00807] Step D: A mixture of 7-bromo-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one (40 mg, 0.11 mmol), (2-biphenyl)-di-t-butylphosphine (6 mg, 0.02 mmol), $Pd_2(dba)_3$ (6 mg, 0.0066 mmol), Cs_2CO_3 (55 mg, 0.17 mmol), 1-methylhomopiperazine (24 μL, 0.18 mmol), and 1,2-dimethoxyethane (450 μL) was heated at 80 °C for 90 min. The reaction mixture was then diluted in CH_2Cl_2 and filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (5-10% MeOH in CH_2Cl_2), followed by trituration with 3:1 hexane/CH_2Cl_2, yielding the title compound (24 mg, 53%) as a yellow solid: m.p. 255–260 °C; MS m/z 411.2 $[M+H]^+$; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.79 (1H, m), 8.73 (1H, s), 8.63 (1H, d, J = 3 Hz), 7.70 (1H, d, J = 9 Hz), 7.55 (1H, m), 6.84 (1H, dd, J = 9 Hz, 2.5 Hz), 6.67 (1H, d, J = 2 Hz), 3.65 (2H, t, J = 5 Hz), 3.57 (2H, t, J = 5.5 Hz), 2.64 (2H, t, J = 5Hz), 2.46 (2H, t, J = 5.5 Hz), 2.27 (3H, s), 1.92 (2H, pentet, J = 5.5 Hz).

[00808] 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.

[00809] **Example 38**

[00810] Preparation of Cpd 89



[00811] Step A: A mixture of 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (0.285 g, 1.0 mmol, prepared in Example 36, Part 2) and 2-aminopyrimidine (0.19 g, 2.0 mmol) in EtOH (2.0 mL) was stirred at 95 °C overnight. The mixture was diluted with water and filtered. The solid was washed with water and dried to afford 7-fluoro-3-(imidazo[1,2-*a*]pyrimidin-2-yl)-2*H*-chromen-2-one hydrobromide (0.28 g, 78%) as a pale yellow solid. MS *m/z* 282.1 $[M+H]^+$.

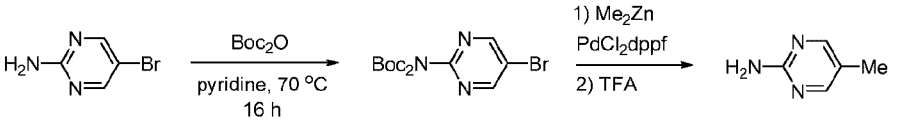
[00812] Step B: A mixture of 7-fluoro-3-(imidazo[1,2-*a*]pyrimidin-2-yl)-2*H*-chromen-2-one hydrobromide (50 mg, 0.18 mmol) and piperazine (61 mg, 0.71 mmol) in DMSO (0.5 mL) was stirred at 110 °C for 2 h. The mixture was diluted with an aqueous saturated $NaHCO_3$ solution and filtered. The solid was washed with water and dried to afford the title compound (40 mg, 64%) as a yellow solid: m.p. 286 °C (decomp.); MS *m/z* 348.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.78 (1H, dd, J = 6.8 Hz, 2.2 Hz), 8.55 (1H, s), 8.46 (1H, dd, J = 4.2 Hz, 2.2 Hz), 8.40 (1H, s), 7.52 (1H, d, J = 8.8 Hz), 6.95-6.91 (2H, m), 6.76 (1H, d, J = 2.2 Hz), 3.33-3.28 (4H, m), 2.91-2.86 (4H, m).

[00813] 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.

[00814] **Example 39**

[00815] Preparation of Cpd 241

[00816] Part 1: Preparation of 5-methylpyrimidin-2-amine

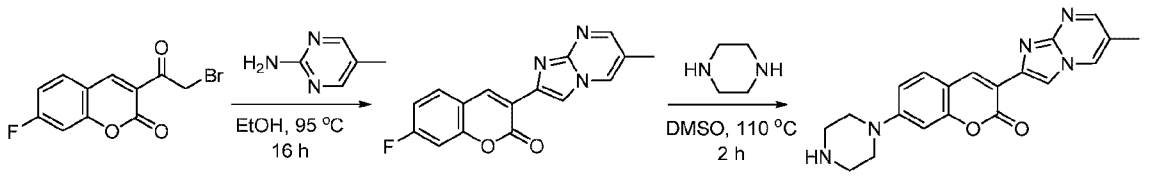


[00817] Step A: A mixture of 2-amino-5-bromopyrimidine (2.75 g, 15.8 mmol) and di-tert-butyl dicarbonate (7.58 g, 34.8 mmol) in pyridine (30 mL) was stirred at 70 °C overnight, then the solvent was removed. The residue was partitioned between EtOAc and aqueous HCl (1 N). The aqueous layer was extracted with EtOAc. The combined organics were dried over $NaSO_4$, then filtered and concentrated to give 2-[bis(*tert*-butoxycarbonyl)amino]-5-bromopyrimidine (5.5 g, 93%) as a white solid. MS *m/z* 398.2 $[M+Na]^+$.

[00818] Step B: A mixture of 2-[bis(*tert*-butoxycarbonyl)amino]-5-bromopyrimidine (3.0 g, 8.0 mmol), dimethylzinc (1.2 M x 8.0 mL, 9.6 mmol) and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (130 mg, 0.16 mmol) in 1,4-dioxane (30 mL) was stirred at 110 °C for 16 h under Argon. The mixture was cooled to room temperature,

diluted with ethyl acetate and washed with saturated NH_4Cl, water and brine. The organic layer was dried over $NaSO_4$, concentrated and purified by silica gel column chromatography (0-35% EtOAc in hexanes) to give a white solid, which was dissolved in trifluoroacetic acid (5.0 mL). After 5 min, the solvent was removed and the residue was partitioned between ethyl acetate and an aqueous saturated $NaHCO_3$ solution. The organic layer was dried over $NaSO_4$, filtered and concentrated to give the title compound (0.7 g, 80%) as a white solid. MS *m/z* 110.1 $[M+H]^+$.

[00819] Part 2: Preparation of Cpd 241



[00820] Step A: Following the procedure in Example 36, Part 3, 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (0.855 g, 3.0 mmol) and 5-methylpyrimidin-2-amine (0.327 g, 3.0 mmol) in EtOH (6.0 mL) gave 7-fluoro-3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one hydrobromide (0.37 g, 42%) as a pale yellow solid. MS *m/z* 296.2 $[M+H]^+$.

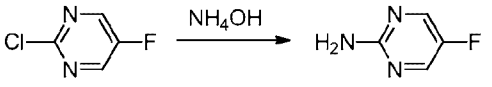
[00821] Step B: Following the procedure in Example 36, Part 3, 7-fluoro-3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one hydrobromide (80 mg, 0.21 mmol) and N-methyl piperizine (93 mg, 1.08 mmol) in DMSO (0.5 mL) gave the title compound (66 mg, 84%) as a yellow solid: m.p. >300 °C; MS *m/z* 362.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.83 (1H, dd, *J* = 2.4 Hz, 1.1 Hz), 8.75 (1H, s), 8.44 (1H, d, *J* = 2.2 Hz), 8.39 (1H, s), 7.71 (1H, d, *J* = 8.8 Hz), 7.02 (1H, dd, *J* = 8.8 Hz, 2.2 Hz), 6.86 (1H, d, *J* = 2.2 Hz), 3.32-3.28 (4H, m), 2.86-2.75 (4H, m), 2.30 (3H, s).

[00822] 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.

[00823] **Example 40**

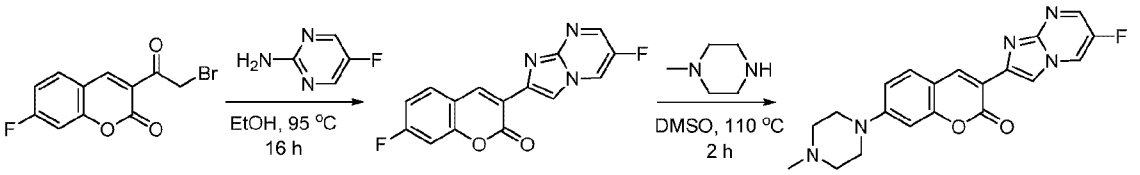
[00824] Preparation of Cpd 480

[00825] Part 1: Preparation of 5-fluoropyrimidin-2-amine



[00826] 2-Chloro-5-fluoropyrimidine (1.34 g, 10 mmol) was stirred with ammonium hydroxide (30%, 15 mL) at 100 °C in a sealed tube overnight. The mixture was cooled to room temperature and filtered. The solid was washed with water and dried to give the title compound (0.95 g, 80%) as a white solid.

[00827] Part 2: Preparation of Cpd 480



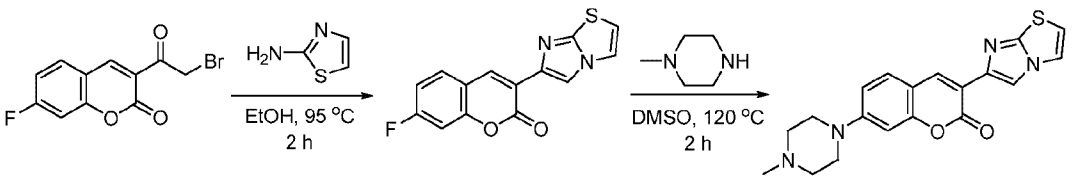
[00828] Step A: Following the procedure in Example 36, Part 3, 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (1.32 g, 4.1 mmol) and 5-fluoropyrimidin-2-amine (0.465 g, 4.1 mmol) in EtOH (12.0 mL) gave 7-fluoro-3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one (0.85 g, 70%) as a pale yellow solid. MS *m/z* 300.1 $[M+H]^+$.

[00829] Step B: Following the procedure in Example 36, Part 3, 7-fluoro-3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one (70 mg, 0.23 mmol) and N-methyl piperizine (46 mg, 0.46 mmol) in DMSO (0.5 mL) gave the title compound (55 mg, 63%) as a yellow solid: m.p. 275–280 °C; MS *m/z* 380.8 $[M+H]^+$; ^{1}H NMR (500 MHz, methanol-d_4): δ 8.95 (1H, dd, J = 3.8 Hz, 2.8 Hz), 8.65 (1H, s), 8.61 (1H, d, J = 2.8 Hz), 8.53 (1H, s), 7.62 (1H, d, J = 8.8 Hz), 7.02 (1H, dd, J = 8.7 Hz, 2.4 Hz), 6.86 (1H, d, J = 2.2 Hz), 3.51 (4H, br s), 2.81 (4H, br s), 2.50 (3H, br s).

[00830] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 40 by substituting the appropriate starting materials, reagents and reaction conditions.

[00831] **Example 41**

[00832] Preparation of Cpd 117



[00833] Step A: A mixture of 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (2.85 g, 10 mmol, prepared in Example 36, Part 2) and 2-aminothiazole (1.0 g, 10 mmol) in EtOH (20 mL) was stirred at 95 °C for 6 h. After cooling to room temperature, ethyl acetate was added, causing

a precipitate to form. The mixture was filtered. The solid was washed with ethyl acetate and dried, affording 6-(7-fluoro-2-oxo-2*H*-chromen-3-yl)imidazo[2,1-*b*]thiazole hydrobromide salt (1.82 g, 64%) as a tan solid. MS *m/z* 287.1 $[M+H]^+$.

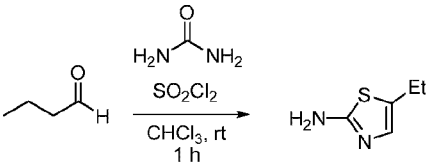
[00834] Step B: A mixture of 6-(7-fluoro-2-oxo-2*H*-chromen-3-yl)imidazo[2,1-*b*]thiazole hydrobromide salt (286 mg, 1.0 mmol) and 1-methylpiperazine (1.0 mL, 3.0 mmol) in DMSO (1.5 mL) was stirred at 110 °C for 2 h. The mixture was cooled to room temperature and diluted with water, producing a precipitate. The precipitate was collected by vacuum filtration, washed with water, dried and purified by silica gel column chromatography (0-10% MeOH in CH_2Cl_2) to give the title compound (185 mg, 51%) as a yellow solid: m.p. 256–258 °C; MS *m/z* 367.2 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.53 (1H, s), 8.31 (1H, s), 7.94 (1H, d, J = 4.4 Hz), 7.64 (1H, d, J = 8.8 Hz), 7.26 (1H, d, J = 4.4 Hz), 7.02 (1H, dd, J = 8.8 Hz, 2.5 Hz), 6.87 (1H, d, J = 2.2 Hz), 3.45-3.23 (4H, m), 2.47-2.39 (4H, m), 2.22 (3H, s).

[00835] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 41 by substituting the appropriate starting materials, reagents and reaction conditions.

[00836] **Example 42**

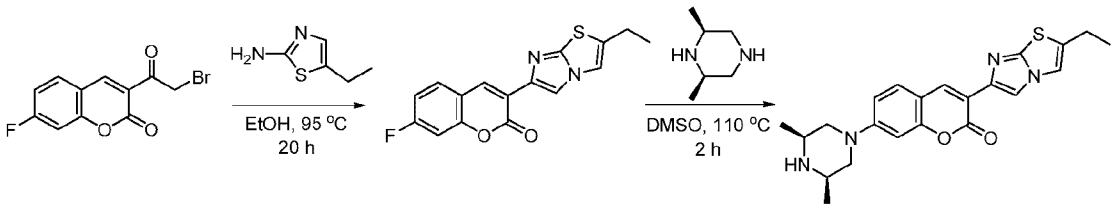
[00837] Preparation of Cpd 429

[00838] Preparation of 5-ethylthiazol-2-amine



[00839] Into a mixture of butyraldehyde (10.8 g, 0.15 mol) and urea (22.8 g, 0.3 mol) in $CHCl_3$ (75 mL) at 0 °C was added sulfuryl chloride (13.5 mL, 0.166 mol) dropwise. The mixture was warmed to room temperature and stirred for 1 h, then the solvent was removed. EtOH (200 mL) was added to the residue, then the mixture was heated at reflux overnight and the solvent was removed. The residue was suspended in water (200 mL) and collected by vacuum filtration to give the title compound (9.5 g, 40%) as a light brown solid. MS *m/z* 129.1 $[M+H]^+$.

[00840] Part 2: Preparation of Cpd 429



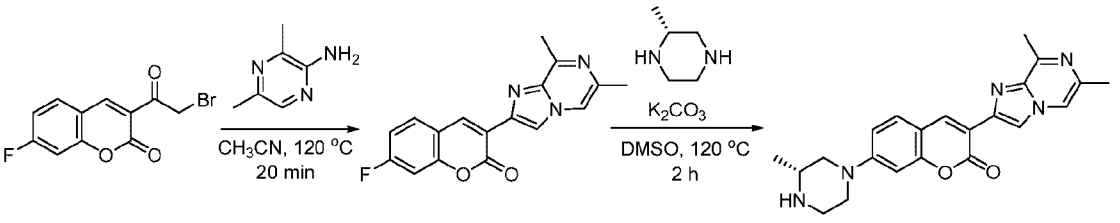
[00841] Step A: Following the procedure in Example 41, Step A, 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (0.76 g, 2.7 mmol) and 5-ethylthiazol-2-amine (0.35 g, 2.7 mmol) in EtOH (20 mL) gave 3-(2-ethylimidazo[2,1-b]thiazol-6-yl)-7-fluoro-2H-chromen-2-one hydrobromide (0.55 g, 66%) as a tan solid. MS *m/z* 315.2 $[M+H]^+$.

[00842] Step B: Following the procedure in Example 41, Step B, 3-(2-ethylimidazo[2,1-b]thiazol-6-yl)-7-fluoro-2H-chromen-2-one hydrobromide (42 mg, 0.13 mmol) and 2,6-cis-dimethylpiperizine (30 mg, 0.26 mmol) in DMSO (0.25 mL) gave the title compound (3.8 mg, 7%) as a yellow solid: m.p. 251-253 °C; MS *m/z* 409.4 $[M+H]^+$; ^{1}H NMR (500 MHz, methanol-d_4) δ 8.32 (1H, s), 8.21 (1H, s), 7.56-7.48 (2H, m), 7.00 (1H, dd, J = 9.0 Hz, 2.4 Hz), 6.82 (1H, d, J = 2.2 Hz), 3.82 (2H, dd, J = 12.5 Hz, 2.4 Hz), 3.00-2.89 (2H, m), 2.82 (2H, qd, J = 7.5, 1.4 Hz), 2.43 (2H, dd, J = 12.5 Hz, 10.9 Hz), 1.34 (3H, t, J = 7.4 Hz), 1.18 (6H, d, J = 6.6 Hz).

[00843] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 42 by substituting the appropriate starting materials, reagents and reaction conditions.

[00844] **Example 43**

[00845] Preparation of Cpd 536



[00846] Step A: A mixture of 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (0.684 g, 2.4 mmol, prepared in Example 36, Part 2) and 3,5-dimethylpyrazin-2-amine (0.246 g, 2.0 mmol) in CH_3CN (10 mL) was stirred at 120 °C in a sealed tube for 20 min. The mixture was cooled to room temperature and diluted with Et_2O to produce a precipitate. The solid was collected by vacuum filtration, washed with Et_2O and dried to give 3-(6,8-dimethylimidazo[1,2-*a*]pyrazin-2-

yl)-7-fluoro-2*H*-chromen-2-one hydrobromide (0.7 g, 90%) as a tan solid. MS *m/z* 310.1 $[M+H]^+$.

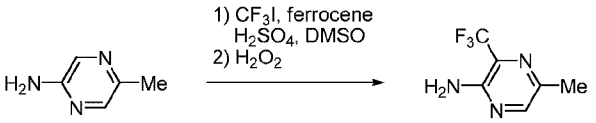
[00847] Step B: 3-(6,8-dimethylimidazo[1,2-*a*]pyrazin-2-yl)-7-fluoro-2*H*-chromen-2-one hydrobromide (100 mg, 0.25 mmol) was stirred with (*R*)-2-methylpiperazine (52 mg, 0.52 mmol) in DMSO (0.5 mL) with K_2CO_3 (0.14 g, 1.0 mmol) at 120 °C for 2 h. The mixture was cooled to room temperature and diluted with water to produce a precipitate. The solid was collected by vacuum filtration and purified by silica gel chromatography (10 % MeOH in CH_2Cl_2) to give the title compound (64 mg, 64%) as a yellow solid. MS *m/z* 390.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.74 (1H, s), 8.45 (1H, s), 7.77 (1H, s), 7.51 (1H, d, *J* = 8.8 Hz), 6.88 (1H, dd, *J* = 8.8 Hz, 2.5 Hz), 6.77 (1H, d, *J* = 2.5 Hz), 3.77-3.67 (2H, m), 3.21-3.14 (2H, m), 3.06-2.92 (3H, m), 2.91 (3H, s), 2.64-2.56 (1H, m), 2.48 (3H, s), 1.20 (3H, d, *J* = 6.3 Hz).

[00848] 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.

[00849] **Example 44**

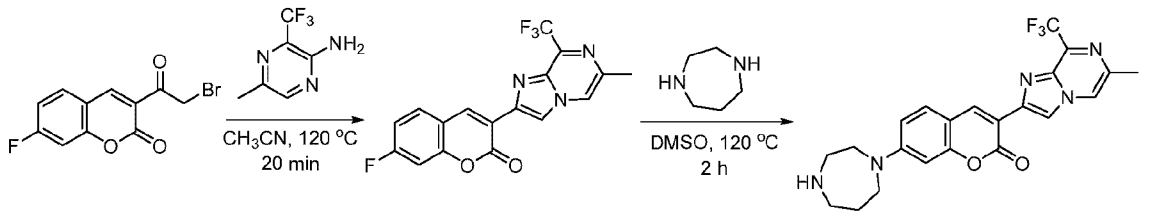
[00850] Preparation of Cpd 607

[00851] Part 1: Preparation of 5-methyl-3-(trifluoromethyl)pyrazin-2-amine



[00852] Into a solution of 5-methylpyrazin-2-amine (0.51 g, 4.72 mmol) and ferrocene (0.263 g, 1.42 mmol) in DMSO (12 mL) was added sulfuric acid (12 mL) and a solution of CF_3I in DMSO (2.4 M, 5.9 mL, 14.2 mmol). Aqueous hydrogen peroxide (30%, 0.94 mL) was added dropwise to the mixture. After stirring for 30 min at room temperature, excess reagent was quenched with ice water. The mixture was diluted with water and extracted with EtOAc. The organic layer was dried over $NaSO_4$, filtered, concentrated and purified by silica gel column chromatography (0-20% EtOAc in CH_2Cl_2) to give the title compound (86 mg, 8%) as a white solid. MS *m/z* 219.1 $[M+H]^+$.

[00853] Part 2: Preparation of Cpd 607



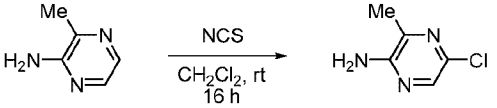
[00854] Step A: Following the procedure in Example 43, Step A, 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (138 g, 0.49 mmol) and 5-methyl-3-(trifluoromethyl)pyrazin-2-amine (86 g, 0.49 mmol) in CH_3CN (1.0 mL) gave 7-fluoro-3-(6-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one hydrobromide (44 mg, 20%) as a tan solid.

[00855] Step B: Following the procedure in Example 43, Step B, 7-fluoro-3-(6-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one hydrobromide (44 mg, 0.10 mmol) and 1,4-diazepane (44 mg, 0.44 mmol) in DMSO (0.25 mL) gave the title compound (43 mg, 99%) as a yellow solid: m.p. >300 °C; MS *m/z* 444.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.79 (1H, s), 8.59 (1H, s), 8.09 (1H, s), 7.50 (1H, d, J = 9.1 Hz), 6.69 (1H, dd, J = 8.8 Hz, 2.2 Hz), 6.57 (1H, d, J = 1.9 Hz), 3.70-3.61 (4H, m), 3.10-3.01 (2H, m), 2.88-2.83 (2H, m), 2.55 (3H, s), 2.03-1.90 (2H, m).

[00856] **Example 45**

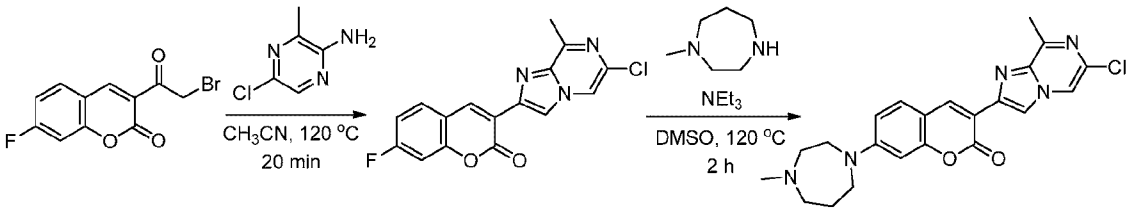
[00857] Preparation of Cpd 712

[00858] Part 1: Preparation of 5-chloro-3-methylpyrazin-2-amine



[00859] A mixture of 3-methylpyrazin-2-amine (109 mg, 1.0 mmol) and N-chlorosuccinimide (136 mg, 1.0 mmol) in CH_2Cl_2 (6.0 mL) was stirred at room temperature overnight. The mixture was washed with aqueous K_2CO_3 (2.0 M, 6.0 mL). The organic layer was dried over $NaSO_4$, filtered, concentrated and purified by silica gel column chromatography (0-35% EtOAc in hexanes) to give the title compound (136 mg, 80%) as a white solid. MS *m/z* 144.0 $[M+H]^+$.

[00860] Part 2: Preparation of Cpd 712



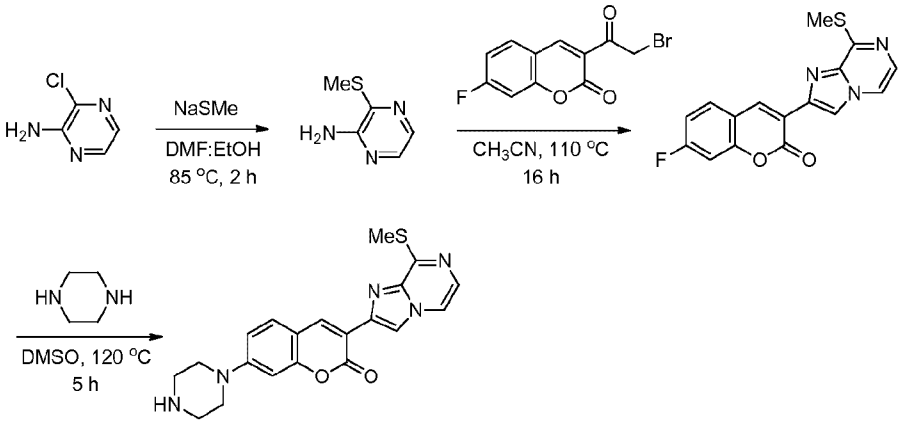
[00861] Step A: Following the procedure in Example 43, Step A, 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (0.233 g, 0.81 mmol) and 5-chloro-3-methylpyrazin-2-amine (0.117 g, 0.81 mmol) in CH_3CN (3.0 mL) gave 3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-fluoro-2H-chromen-2-one hydrobromide (0.18 g, 67%) as a tan solid. MS *m/z* 330.1 $[M+H]^+$.

[00862] Step B: Following the procedure in Example 43, Step B, 3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-fluoro-2H-chromen-2-one hydrobromide (67 mg, 0.2 mmol), N-methyl homopiperizine (28 mg, 0.24 mmol) and triethylamine (100 mg, 1.0 mmol) in DMSO (0.5 mL) gave the title compound (70 mg, 83%) as a yellow solid: m.p. 212–218 °C; MS *m/z* 424 $[M+H]^+$; ^1H NMR (500 MHz, methanol-d_4) δ 8.71 (1H, s), 8.55 (1H, s), 8.42 (1H, d, J = 0.9 Hz), 7.56 (1H, d, J = 8.8 Hz), 6.84 (1H, dd, J = 8.8 Hz, 2.5 Hz), 6.67 (1H, d, J = 2.2 Hz), 3.86-3.77 (2H, m), 3.65 (2H, t, J = 6.3 Hz), 3.16 (2H, d, J = 1.6 Hz), 3.04 (2H, br s), 2.89-2.82 (3H, m), 2.69 (3H, s), 2.27-2.14 (2H, m).

[00863] 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.

[00864] **Example 46**

[00865] Preparation of Cpd 398



[00866] Step A: A mixture of 3-chloropyrazin-2-amine (1.29 g, 10 mmol) and sodium methanethiolate (1.05 g, 15 mmol) in DMF (10 mL) and EtOH (10 mL) was stirred at 85 °C for 2 h, and then concentrated. The mixture was diluted with water and filtered. The filtrate was extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, filtered and concentrated. The residue was combined with the material collected from filtration, affording the desired product 3-(methylthio)pyrazin-2-amine (1.33 g, 94%) as a white solid. MS *m/z* 142.1 $[M+H]^+$.

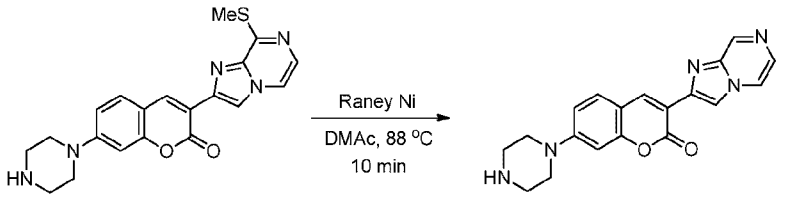
[00867] Step B: A mixture of 3-(2-bromoacetyl)-7-fluoro-2*H*-chromen-2-one (2.85 g, 10 mmol, prepared in Example 36, Part 2) and 3-(methylthio)pyrazin-2-amine (1.5 g, 10 mmol) in CH_3CN (40 mL) was stirred at 110 °C overnight. The mixture was cooled to room temperature and diluted with ethyl acetate to generate a precipitate. The solid was collected by vacuum filtration, washed with ethyl acetate and dried, yielding 7-fluoro-3-(8-(methylthio)imidazo[1,2-*a*]pyrazin-2-yl)-2*H*-chromen-2-one hydrobromide salt (2.15 g, 66%) as a tan solid. MS *m/z* 328.1 $[M+H]^+$.

[00868] Step C: A mixture of 7-fluoro-3-(8-(methylthio)imidazo[1,2-*a*]pyrazin-2-yl)-2*H*-chromen-2-one hydrobromide (100 mg, 0.24 mmol) and piperazine (60 mg, 0.6 mmol) in DMSO (0.5 mL) was stirred at 120 °C for 5 h. The mixture was cooled to room temperature and diluted with water to produce a precipitate. The solid was collected by vacuum filtration, washed with water, dried and purified with silica gel column chromatography (5-10% MeOH in CH_2Cl_2) to give the title compound (52 mg, 55%) as a yellow solid. MS *m/z* 394.3 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 8.81 (1H, s), 8.50 (1H, s), 7.81 (1H, d, *J* = 4.4 Hz), 7.70 (1H, d, *J* = 4.7 Hz), 7.52 (1H, d, *J* = 8.8 Hz), 6.88 (1H, dd, *J* = 8.8 Hz, 2.5 Hz), 6.77 (1H, d, *J* = 2.2 Hz), 3.50 (1H, s), 3.38-3.30 (4H, m), 3.09-3.01 (4H, m), 2.71 (3H, s).

[00869] 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.

[00870] **Example 47**

[00871] Preparation of Cpd 456

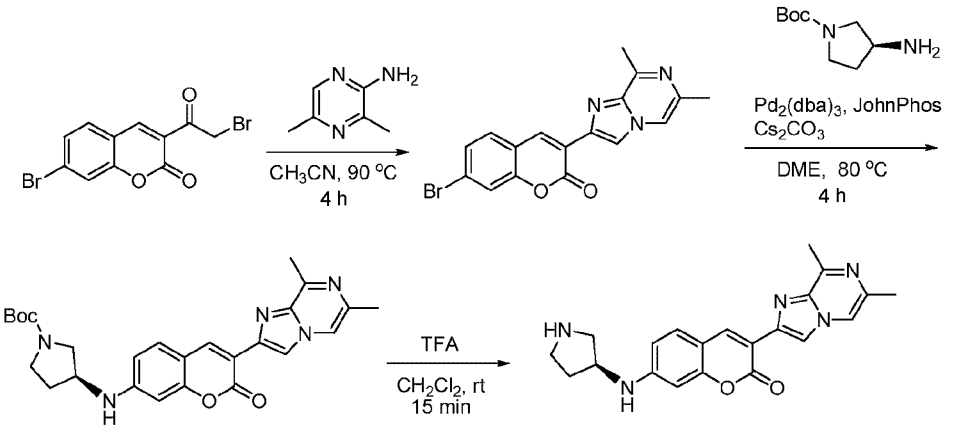


[00872] Into a solution of 7-(4-methylpiperazin-1-yl)-3-(7-(methylthio)imidazo[1,2-*c*]pyrimidin-2-yl)-2*H*-chromen-2-one (30 mg, 0.076 mmol) in dimethylacetamide (2.0 mL) at 88 °C was added a large excess of Raney Nickle. The mixture was stirred until gas evolution ceased (~10 min). The mixture was diluted with MeOH and filtered through Celite. The filtrate was concentrated under a stream of nitrogen. The residue was purified with silica gel column chromatography (5-10% MeOH in CH_2Cl_2) to give the title compound (32 mg, 55%) as a yellow solid: m.p. 258–260 °C; MS *m/z* 348.2 $[M+H]^+$; ^1H NMR (500 MHz, $CDCl_3$): δ 9.07 (1H, s), 8.75 (1H, s), 8.60 (1H, d, J = 0.6 Hz), 8.09 (1H, dd, J = 4.6 Hz, 1.4 Hz), 7.88 (1H, d, J = 4.4 Hz), 7.50 (1H, d, J = 8.8 Hz), 6.88 (1H, dd, J = 8.8 Hz, 2.2 Hz), 6.78 (1H, d, J = 2.5 Hz), 3.36 (4H, dd, J = 6.1 Hz, 4.3 Hz), 3.05 (4H, dd, J = 6.1 Hz, 4.3 Hz)

[00873] 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.

[00874] **Example 48**

[00875] Preparation of Cpd 563



[00876] Step A: A mixture of 7-bromo-3-(2-bromoacetyl)-2H-chromen-2-one (2.0 g, 5.78 mmol, prepared in Example 37, Step B), 2-amino-3,5-dimethylpyrazine (825 mg, 6.71 mmol) and CH_3CN (22 mL) was heated at 90 °C for 4 h. The addition of an aqueous saturated $NaHCO_3$ solution to the mixture resulted in the formation of a precipitate. The precipitate was collected by vacuum filtration and triturated with 1:1 hexane/acetone, yielding 7-bromo-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one (1.9 g, 88%) as an orange solid. ^1H NMR (500 MHz, DMSO-d_6): δ 8.81 (1H, s), 8.61 (1H, s), 8.31 (1H, s), 7.93 (1H, d, J = 8 Hz), 7.76 (1H, d, J = 1.5 Hz), 7.58 (1H, dd, J = 8 Hz, 1.5 Hz), 2.76 (3H, s), 2.37 (3H, s).

[00877] Step B: A mixture of 7-bromo-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one (150 mg, 0.40 mmol), (2-biphenyl)-di-t-butylphosphine (10 mg, 0.033 mmol), $Pd_2(dba)_3$ (10 mg, 0.011 mmol), Cs_2CO_3 (170 mg, 0.52 mmol), (S)-1-Boc-3-aminopyrrolidine (105 μL, 0.60 mmol) and 1,2-dimethoxyethane (1.4 mL) was heated at 80 °C for 4 h. The reaction mixture was diluted with CH_2Cl_2 and filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (30-50% acetone in CH_2Cl_2), followed by trituration with 1:1 hexane/acetone, yielding (S)-tert-butyl 3-(3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2-oxo-2H-chromen-7-ylamino)pyrrolidine-1-carboxylate (109 mg, 57%) as a yellow solid. MS *m/z* 476.3 $[M+H]^+$.

[00878] Step C: A mixture of (S)-tert-butyl 3-(3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2-oxo-2H-chromen-7-ylamino)pyrrolidine-1-carboxylate (105 mg, 0.22 mmol) was stirred in a solution of trifluoroacetic acid (1.0 mL) in CH_2Cl_2 (4.0 mL) for 15 min. The reaction mixture was poured into dilute aqueous NaOH. The mixture was extracted with CH_2Cl_2 (EtOH added to improve the solubility). The organic layer was collected and concentrated under reduced pressure, yielding the title compound (70 mg, 85%) as a yellow solid: m.p. 132 °C (decomp.); MS *m/z* 376.1 $[M+H]^+$; ^1H NMR (500 MHz, DMSO-d_6): δ 8.70 (1H, s), 8.50 (1H, s), 8.32 (1H, s), 7.68 (1H, d, J = 9 Hz), 7.06 (1H, d, J = 6.5 Hz), 6.68 (1H, dd, J = 9 Hz, 2 Hz), 6.55 (1H, d, J = 2 Hz), 4.12 (1H, m), 3.37 (1H, dd, J = 12 Hz, 6 Hz), 3.18 (1H, m), 3.11 (1H, m), 2.94 (1H, dd, J = 12 Hz, 4 Hz), 2.76 (3H, s), 2.37 (3H, s), 2.22 (1H, m), 1.82 (1H, m).

[00879] As shown in Table 1 below, additional compounds disclosed herein may be prepared according to Example 48 by substituting the appropriate starting materials, reagents and reaction conditions.

DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME __1___ DE __2___

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

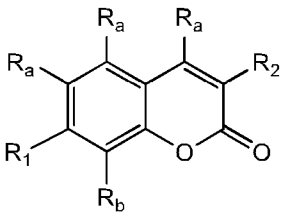
THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

NOTE: For additional volumes please contact the Canadian Patent Office.

The embodiments of the present invention for which an exclusive property or privilege is claimed are defined as follows:

1. A compound selected from Formula (Ia):



(Ia)

or a free acid, free base, salt, stereoisomer, racemate, enantiomer, diastereomer or tautomer form thereof, wherein:

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-3-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-2(1*H*)-yl, hexahydropyrrolo[1,2-*a*]pyrazin-6(2*H*)-one, (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,

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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 and 6,9-diazaspiro[4.5]dec-9-yl optionally substituted with one, two or three R_3 substituents and/or one optional R_4 substituent;

R_2 is heteroaryl selected from thien-2-yl, thien-3-yl, 1*H*-pyrazol-4-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1,2,4-oxadiazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-4-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl, indol-5-yl, indol-6-yl, 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, indolizin-2-yl, benzofuran-2-yl, benzothien-2-yl, benzothien-3-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-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, pyrrolo[1,2-*b*]pyridazin-6-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*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, 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-*b*]pyridazin-6-yl, imidazo[1,2-*a*]pyrazin-2-yl and quinoxalin-2-yl;

wherein, R_2 is optionally substituted with one, two or three R_6 substituents and/or one optional 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_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,

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$(C_{1-8}alkyl)_2$-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;

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, 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, halo-C_{1-8}alkyl, hydroxy-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; 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 salt is a chloride, hydrochloride, dihydrochloride, hydrobromide, acetate, or trifluoroacetate salt.

3. A compound, wherein the compound is selected from:

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one
7-(piperazin-1-yl)-3-[7-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one
2-oxo-N-phenyl-7-(piperazin-1-yl)-2H-chromene-3-carboxamide
3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one
3-(7-chloro-1,3-benzothiazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one
3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperazin-1-ylmethyl)-2H-chromen-2-one
3-(1,3-benzothiazol-2-yl)-7-[(propan-2-ylamino)methyl]-2H-chromen-2-one
7-[(propan-2-ylamino)methyl]-3-[4-(trifluoromethyl)-1,3-benzothiazol-2-yl]-2H-chromen-2-one
3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(propan-2-ylamino)methyl]-2H-chromen-2-one
7-(4-methylpiperazin-1-yl)-3-[3-(trifluoromethyl)phenyl]-2H-chromen-2-one
7-(piperazin-1-yl)-3-(pyridin-3-yl)-2H-chromen-2-one

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3-(1,3-benzothiazol-2-yl)-7-[(dimethylamino)methyl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(dimethylamino)methyl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

3-(5-fluoro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-(piperidin-4-yloxy)-2H-chromen-2-one

3-(4-methyl-1,3-benzoxazol-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4-methyl-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(3-fluorophenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyridin-4-yl)-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(4-methylpiperazin-1-yl)carbonyl]-2H-chromen-2-one

7-(piperazin-1-yl)-3-(1H-pyrazol-5-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-oxo-N-phenyl-2H-chromene-3-carboxamide

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(4-methyl-1,3-benzoxazol-2-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyridin-2-ylamino)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyrimidin-2-ylamino)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[2-(propan-2-ylamino)ethyl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[3-(propan-2-ylamino)propyl]-2H-chromen-2-one

3-(4-methyl-1,3-thiazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1-methyl-1H-pyrazol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(4-fluoro-1,3-benzoxazol-2-yl)-2H-chromen-2-one

3-(4-fluoro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-2-oxo-2H-chromen-7-yl piperazine-1-carboxylate

3-(4-chloro-1,3-benzothiazol-2-yl)-2-oxo-2H-chromen-7-yl piperazine-1-carboxylate

benzyl 4-[3-(1-methyl-1H-benzimidazol-2-yl)-2-oxo-2H-chromen-7-yl]piperazine-1-carboxylate

3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(4-phenyl-1,3-thiazol-2-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-(piperidin-4-yloxy)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

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3-(1,3-benzoxazol-2-yl)-7-[3-(dimethylamino)pyrrolidin-1-yl]-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-{[2-(dimethylamino)ethyl](methyl)amino}-2H-chromen-2-one

3-(5-phenyl-1,2,4-oxadiazol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(3S)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(2S)-pyrrolidin-2-ylmethoxy]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(diethylamino)methyl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(diethylamino)methyl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-(piperidin-1-ylmethyl)-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperidin-1-ylmethyl)-2H-chromen-2-one

3-[(3-methylpyridin-2-yl)amino]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[(4-methylpyridin-2-yl)amino]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[(5-methylpyridin-2-yl)amino]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[(6-methylpyridin-2-yl)amino]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[(5-chloropyridin-2-yl)amino]-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyridin-3-ylamino)-2H-chromen-2-one

3-(4-iodo-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-chloro-1,3-benzoxazol-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4-chloro-1,3-benzoxazol-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(4-chloro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(1-methyl-1H-pyrazol-3-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(1-phenyl-1H-pyrazol-3-yl)-2H-chromen-2-one

3-(phenylamino)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)pyridin-2-yl]-2H-chromen-2-one

3-(3-methoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[(methylamino)methyl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-{[(2-hydroxyethyl)(methyl)amino]methyl}-2H-chromen-2-one

3-(4-methyl-1H-pyrazol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

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3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-(2,5-diazabicyclo[2.2.1]hept-2-yl)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-7-(2,5-dimethylpiperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-[6-(trifluoromethyl)pyridin-2-yl]-2H-chromen-2-one

3-(1H-indazol-5-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(2R,5S)-2,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-{[(1,3-dihydroxypropan-2-yl)amino]methyl}-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

tert-butyl {(3S)-1-[3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl]pyrrolidin-3-yl}carbamate

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

3-([1,3]oxazolo[4,5-b]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-([1,3]oxazolo[4,5-b]pyridin-2-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyridin-2-yl)-4-methyl-7-(piperazin-1-yl)-2H-chromen-2-one

3-(5-chloropyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

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7-(4-methylpiperazin-1-yl)-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2H-chromen-2-one

3-(7-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-(piperazin-1-yl)-3-[2-(trifluoromethyl)pyridin-3-yl]-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-[2-(trifluoromethyl)pyridin-3-yl]-2H-chromen-2-one

3-(3-fluoropyridin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-{[(3R)-1-ethylpyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(imidazo[1,2-b]pyridazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-{[2-(dimethylamino)ethyl](methyl)amino}-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(5-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(5-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(imidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-2H-chromen-2-one

3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

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3-(1,3-benzothiazol-2-yl)-7-[1-(dimethylamino)ethyl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-[1-(propan-2-ylamino)ethyl]-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-7-{[2-(dimethylamino)ethyl](methyl)amino}-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-4-methyl-7-(piperazin-1-yl)-2H-chromen-2-one

7-{[(2-hydroxyethyl)(methyl)amino]methyl}-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-[3-(dimethylamino)pyrrolidin-1-yl]-3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

8-fluoro-7-(piperazin-1-yl)-3-(pyridin-2-yl)-2H-chromen-2-one

8-fluoro-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-6-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

6-fluoro-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzoxazol-2-yl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzothiazol-2-yl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

5-fluoro-7-(piperazin-1-yl)-3-(pyridin-2-yl)-2H-chromen-2-one

5-fluoro-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methylpyridin-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(6-methylpyridin-3-yl)-2H-chromen-2-one

3-(2-methoxypyridin-4-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

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7-{[2-(dimethylamino)ethyl](methyl)amino}-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

tert-butyl {(3S)-1-[3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2-oxo-2H-chromen-7-yl]pyrrolidin-3-yl}carbamate

7-(4-ethylpiperazin-1-yl)-3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(2-chloropyridin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-[methyl(1-methylpyrrolidin-3-yl)amino]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(2,5-diazabicyclo[2.2.2]oct-2-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-propylpiperazin-1-yl)-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-[4-(propan-2-yl)piperazin-1-yl]-3-(pyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(piperidin-4-yloxy)-2H-chromen-2-one

7-[(dimethylamino)methyl]-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-[(propan-2-ylamino)methyl]-2H-chromen-2-one

7-[3-(dimethylamino)piperidin-1-yl]-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-{[2-(dimethylamino)ethyl](methyl)amino}-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

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3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

2-[7-(4-methylpiperazin-1-yl)-2-oxo-2H-chromen-3-yl]imidazo[1,2-a]pyridine-6-carbonitrile

7-(piperazin-1-yl)-3-[8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-[8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-[8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(1,4-diazepan-1-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-methoxypyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-aminopiperidin-1-yl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[methyl(pyridin-3-ylmethyl)amino]-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-{[2-(dimethylamino)ethyl](methyl)amino}-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

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3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(4-methoxypyridin-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-chloropyridin-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(8-cyclopropylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(8-bromoimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(3,3-dimethylpiperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-{[(1-hydroxypropan-2-yl)amino]methyl}-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

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7-[(4-hydroxypiperidin-1-yl)methyl]-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3-hydroxypyrrolidin-1-yl)methyl]-3-(6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

5-fluoro-7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-2H-chromen-2-one

3-(2-ethoxypyridin-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methoxypyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(1-methyl-1H-indol-3-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1-methyl-1H-indol-3-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-{[(1-hydroxypropan-2-yl)amino]methyl}-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-{[(2-hydroxyethyl)(methyl)amino]methyl}-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(3-hydroxypyrrolidin-1-yl)methyl]-2H-chromen-2-one

3-(4-chloro-1,3-benzothiazol-2-yl)-7-[(4-hydroxypiperidin-1-yl)methyl]-2H-chromen-2-one

3-(2-methylpyrimidin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

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7-(4-methyl-1,4-diazepan-1-yl)-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

7-[(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(2-cyclopropylpyrimidin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-[2-(propan-2-yl)pyrimidin-4-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[methyl(1-methylpiperidin-4-yl)amino]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

3-(7-ethylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(7-ethylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(7-ethylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(3,5-difluorophenyl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3,5-difluorophenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(4-fluoro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-[8-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(2-methylpyrimidin-4-yl)-2H-chromen-2-one

3-(2-cyclopropylpyrimidin-4-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(2S,5R)-2,5-dimethylpiperazin-1-yl]-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(4-methyl-1,3-thiazol-2-yl)-2H-chromen-2-one

3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

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7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(5-methylpyrazolo[1,5-a]pyridin-2-yl)-2H-chromen-2-one

5-fluoro-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(9H-purin-8-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methoxypyridin-2-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4-methylthiophen-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(thiophen-3-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(thiophen-3-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(6-fluoro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-fluoro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-fluoro-8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-fluoro-8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

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3-(8-ethyl-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(7-ethylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-ethyl-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-5-fluoro-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyrimidin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(8-ethyl-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-ethyl-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-chloro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(8-chloro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(8-chloro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-{[(2-hydroxyethyl)(methyl)amino]methyl}-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-[(4-hydroxypiperidin-1-yl)methyl]-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

5-fluoro-3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-fluoro-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

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3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-ethylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-methoxypyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(6-methoxypyridin-2-yl)-2H-chromen-2-one

3-(6-methoxypyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-methoxypyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(piperazin-1-yl)-3-(thiophen-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(thiophen-2-yl)-2H-chromen-2-one

3-(3,5-difluorophenyl)-5-fluoro-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

5-fluoro-3-(4-fluoro-1,3-benzoxazol-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-fluoro-3-(4-fluoro-1,3-benzoxazol-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-5-fluoro-3-(4-fluoro-1,3-benzoxazol-2-yl)-2H-chromen-2-one

5-fluoro-3-(4-fluoro-1,3-benzoxazol-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-5-fluoro-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-fluoro-2H-chromen-2-one

5-fluoro-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-7-(1,4-diazepan-1-yl)-5-fluoro-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-chloroimidazo[1,2-a]pyrimidin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(1-benzylpyrrolidin-3-yl)(methyl)amino]-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-fluoropyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-ethoxypyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-(piperazin-1-yl)-3-[6-(propan-2-yloxy)pyridin-2-yl]-2H-chromen-2-one

7-(piperazin-1-yl)-3-[6-(pyrrolidin-1-yl)pyridin-2-yl]-2H-chromen-2-one

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7-(1,4-diazepan-1-yl)-3-(3,5-dimethoxyphenyl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-fluoro-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-5-fluoro-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-5-fluoro-3-[7-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-5-fluoro-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(4-methyl-1H-benzimidazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(5-fluoro-1H-benzimidazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1H-benzimidazol-2-yl)-7-[(dimethylamino)methyl]-2H-chromen-2-one

5-fluoro-7-(hydroxymethyl)-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-[8-(methylsulfanyl)imidazo[1,2-a]pyrazin-2-yl]-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-[8-(methylsulfanyl)imidazo[1,2-a]pyrazin-2-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-[8-(methylsulfanyl)imidazo[1,2-a]pyrazin-2-yl]-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-[8-(methylsulfanyl)imidazo[1,2-a]pyrazin-2-yl]-2H-chromen-2-one

3-(8-methoxyimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(8-methoxyimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-5-fluoro-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-5-fluoro-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-5-fluoro-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(1-benzothiophen-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1-benzothiophen-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(1-benzothiophen-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1-benzothiophen-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,5-dimethoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(3,5-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,5-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-[6-(cyclobutyloxy)pyridin-2-yl]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[6-(cyclobutyloxy)pyridin-2-yl]-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-5-fluoro-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

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7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(imidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-methoxyimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(8-methoxyimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

5-fluoro-3-(imidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(2-ethylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(2-ethylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(2-ethylimidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

3-(2-ethylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(7-methoxyimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-[1-(pyridin-2-yl)-1H-imidazol-4-yl]-2H-chromen-2-one

3-(7-methoxyimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(7-methoxyimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(7-methoxyimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(1R,5S,6s)-6-(dimethylamino)-3-azabicyclo[3.1.0]hex-3-yl]-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(imidazo[2,1-b][1,3]thiazol-6-yl)-2H-chromen-2-one

7-[(1R,5S,6s)-6-(dimethylamino)-3-azabicyclo[3.1.0]hex-3-yl]-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

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7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(pyridin-2-yl)-2H-chromen-2-one

3-[6-(methylsulfanyl)pyridin-2-yl]-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(3,4-dimethoxyphenyl)-5-fluoro-2H-chromen-2-one

3-(4-methoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(1-phenyl-1H-imidazol-4-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-[2-methyl-1-(pyridin-2-yl)-1H-imidazol-4-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(imidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-c]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(imidazo[1,2-c]pyrimidin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-c]pyrimidin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(quinoxalin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-5-fluoro-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2,4-dimethoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(2,4-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

5-fluoro-3-(6-methoxypyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

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5-fluoro-3-(6-methoxypyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-{[2-(dimethylamino)ethyl]amino}-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(3,4-dimethoxyphenyl)-7-[(2S)-2-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-chloroimidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(1-methylpiperidin-4-yl)amino]-2H-chromen-2-one

7-{[3-(dimethylamino)propyl]amino}-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(2-chloroimidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(2-chloroimidazo[2,1-b][1,3]thiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3-chloro-4-fluorophenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3-chloro-4-fluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-benzodioxol-5-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-benzodioxol-5-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-benzodioxol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-benzodioxol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-[3-(trifluoromethyl)phenyl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(2-chloroimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

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3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperidin-4-ylamino)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-ylamino]-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6-fluoroimidazo[1,2-a]pyrimidin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-cyclopropyl-8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(8-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(3,8-diazabicyclo[3.2.1]oct-3-yl)-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(3,3-dimethylpiperazin-1-yl)-3-(6-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(3-chlorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-chloro-4-fluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3-methylphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

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3-(6,8-difluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6,8-difluoroimidazo[1,2-a]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-difluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-difluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(3,8-diazabicyclo[3.2.1]oct-3-yl)-2H-chromen-2-one

3-(8-chloroimidazo[1,2-a]pyridin-2-yl)-7-(2,5-diazabicyclo[2.2.2]oct-2-yl)-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(indolizin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(6,8-difluoroimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(1R,5S)-8-methyl-3,8-diazabicyclo[3.2.1]oct-3-yl]-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,5-difluoro-2-methoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3,5-difluoro-2-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3,5-difluoro-2-methoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(4-methoxy-3-methylphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-methoxy-3-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(4-methoxy-3-methylphenyl)-2H-chromen-2-one

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3-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2,3-difluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-[6-(dimethylamino)pyridin-3-yl]-7-(piperazin-1-yl)-2H-chromen-2-one

3-[6-(dimethylamino)pyridin-3-yl]-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(pyridin-4-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-5-fluoro-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(indolizin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

7-(1,4-diazabicyclo[3.2.2]non-4-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperidin-4-ylamino)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-pyrrolidin-3-ylamino]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-pyrrolidin-3-ylamino]-2H-chromen-2-one

3-(indolizin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

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7-(1,4-diazepan-1-yl)-3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(3-methoxy-4-methylphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(3-methoxy-4-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(4-fluoro-3-methoxyphenyl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4-fluoro-3-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(piperazin-1-yl)-3-(pyrrolo[1,2-a]pyrimidin-7-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(pyrrolo[1,2-a]pyrimidin-7-yl)-2H-chromen-2-one

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-pyrrolidin-3-ylamino]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-pyrrolidin-3-ylamino]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-ylamino]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(8-fluoroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(4-methylpiperazin-1-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

5-fluoro-7-(4-methyl-1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

5-fluoro-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

5-fluoro-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

7-(5,8-diazaspiro[3.5]non-8-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(6,9-diazaspiro[4.5]dec-9-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

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7-(2,5-diazabicyclo[2.2.2]oct-2-yl)-3-(7-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(5,8-diazaspiro[3.5]non-8-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(6,9-diazaspiro[4.5]dec-9-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

7-(2,5-diazabicyclo[2.2.2]oct-2-yl)-3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(1-benzofuran-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1-benzofuran-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1-benzofuran-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-[6-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyrazin-2-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-5-fluoro-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(8-fluoro-6-methylimidazo[1,2-a]pyridin-2-yl)-7-(8-methyl-3,8-diazabicyclo[3.2.1]oct-3-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-5-fluoro-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[methyl(1-methylpyrrolidin-3-yl)amino]-2H-chromen-2-one

7-[(1-benzylpyrrolidin-3-yl)(methyl)amino]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-b]pyridazin-2-yl)-2H-chromen-2-one

7-(4-ethyl-1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(azetidin-3-ylamino)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{methyl[(3S)-pyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-b]pyridazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(thieno[3,2-c]pyridin-2-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(thieno[3,2-c]pyridin-2-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(6-methylimidazo[1,2-b]pyridazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(3R)-3-methylpiperazin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(2-methylpyrrolo[1,2-b]pyridazin-6-yl)-2H-chromen-2-one

7-(4-ethylpiperazin-1-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(2-methylpyrrolo[1,2-b]pyridazin-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(1-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

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3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3S)-3-methylpiperazin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{methyl[(3S)-1-methylpyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3S)-1-methylpyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-5-fluoro-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

7-(4-methyl-1,4-diazepan-1-yl)-3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(3-ethylpiperazin-1-yl)-2H-chromen-2-one

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7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-(4-ethyl-1,4-diazepan-1-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(4-ethyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(4-ethylpiperazin-1-yl)-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(3-ethyl-4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(octahydro-2H-pyrido[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aS,6aS)-hexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aS,6aS)-5-methylhexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl]-2H-chromen-2-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2H-chromen-2-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(5-methylfuro[3,2-b]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{methyl[(3R)-pyrrolidin-3-yl]amino}-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(6-methyl-8-nitroimidazo[1,2-a]pyridin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3-exo)-9-methyl-9-azabicyclo[3.3.1]non-3-yl]amino}-2H-chromen-2-one

3-(6-methyl-8-nitroimidazo[1,2-a]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-2H-chromen-2-one

3-(2,4-dimethylthieno[2,3-d]pyrimidin-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{methyl[(3R)-1-methylpyrrolidin-3-yl]amino}-2H-chromen-2-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

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3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(4-aminopiperidin-1-yl)-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[4-(dimethylamino)piperidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[4-(dimethylamino)piperidin-1-yl]-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-3-(5-methylfuro[3,2-b]pyridin-2-yl)-2H-chromen-2-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(5-methylfuro[3,2-b]pyridin-2-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(5-methylfuro[3,2-b]pyridin-2-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

tert-butyl {(3S)-1-[3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2-oxo-2H-chromen-7-yl]pyrrolidin-3-yl}carbamate

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3S)-3-(propan-2-ylamino)pyrrolidin-1-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-{[(1R,5S)-9-methyl-9-azabicyclo[3.3.1]non-3-yl]amino}-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-methylpyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-ethylpyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-(2-hydroxyethyl)pyrrolidin-3-yl]amino}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-(propan-2-yl)pyrrolidin-3-yl]amino}-2H-chromen-2-one

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7-[(3R,4R)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[3-(diethylamino)pyrrolidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(3,3-dimethylpiperazin-1-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(3,3,4-trimethylpiperazin-1-yl)-2H-chromen-2-one

7-[(3S,4S)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3'S,4'S)-4'-hydroxy-1,3'-bipyrrolidin-1'-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-(propan-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

7-(2,5-diazabicyclo[2.2.1]hept-2-yl)-3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-5-fluoro-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-ethylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3'R,4'R)-4'-hydroxy-1,3'-bipyrrolidin-1'-yl]-2H-chromen-2-one

7-(4-cyclopropylpiperazin-1-yl)-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-[4-(propan-2-yl)-1,4-diazepan-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[4-(propan-2-yl)-1,4-diazepan-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-2H-chromen-2-one

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3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[3-(morpholin-4-yl)pyrrolidin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(7R,8aS)-7-hydroxyhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(8-methoxy-6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(8-hydroxy-6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(1R,5S,6s)-6-(dimethylamino)-3-azabicyclo[3.1.0]hex-3-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-cyclopropylpiperazin-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(7R,8aS)-7-hydroxyhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(2-methyl-1,3-benzothiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(1,4-diazepan-1-yl)-3-(2-methyl-1,3-benzothiazol-6-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-ethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-2H-chromen-2-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(2-methyl-1,3-benzothiazol-6-yl)-2H-chromen-2-one

7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-3-(2-methyl-1,3-benzothiazol-6-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-ethyl-4-methylpiperazin-1-yl]-2H-chromen-2-one

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7-[(3S)-3,4-diethylpiperazin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

7-(2,5-diazabicyclo[2.2.1]hept-2-yl)-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

7-[4-(aminomethyl)piperidin-1-yl]-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-1-(2-hydroxyethyl)octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aR,7aR)-1-ethyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-ethylpiperazin-1-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-{4-[(propan-2-ylamino)methyl]piperidin-1-yl}-2H-chromen-2-one

3-(6-chloro-8-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aS,7aS)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aS,7aS)-1-(2-hydroxyethyl)octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

7-[(3R,5S)-4-ethyl-3,5-dimethylpiperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-cyclopropylpiperazin-1-yl)-3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(2-methoxyethyl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4aS,7aS)-1-ethyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-methyl-3-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-ethyl-3-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

7-(4-cyclopropylpiperazin-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-tert-butylpiperazin-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

7-(4-cyclobutylpiperazin-1-yl)-3-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-2H-chromen-2-one

3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-propylpiperazin-1-yl)-2H-chromen-2-one

7-[4-(cyclopropylmethyl)piperazin-1-yl]-3-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-2H-chromen-2-one

3-(4,6-dimethylthieno[3,2-c]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-3-(piperazin-1-yl)-2H-chromen-2-one

3-(4,6-dimethylthieno[3,2-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4,6-dimethylthieno[3,2-c]pyridin-2-yl)-7-[4-(2-methoxyethyl)piperazin-1-yl]-2H-chromen-2-one

7-(1-cyclobutylpiperidin-4-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-cyclobutylpiperazin-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(oxetan-3-yl)piperazin-1-yl]-2H-chromen-2-one

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3-(8-ethyl-6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-2H-chromen-2-one

7-(1-ethylpiperidin-4-yl)-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-2H-chromen-2-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(8-ethyl-6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4,6-dimethylfuro[3,2-c]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(4,6-dimethylfuro[3,2-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-7-(1-methylpiperidin-4-yl)-2H-chromen-2-one

7-(1-ethylpiperidin-4-yl)-3-(2-methylimidazo[1,2-a]pyrimidin-6-yl)-2H-chromen-2-one

7-[4-(2-hydroxyethyl)piperazin-1-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-cyclobutylpiperazin-1-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(oxetan-3-yl)piperazin-1-yl]-2H-chromen-2-one

3-(4,6-dimethylfuro[3,2-c]pyridin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-2H-chromen-2-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(1-ethylpiperidin-4-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-[2-methyl-3-(1,2,3,6-tetrahydropyridin-4-yl)imidazo[1,2-b]pyridazin-6-yl]-7-(1,2,3,6-tetrahydropyridin-4-yl)-2H-chromen-2-one

7-[(dimethylamino)methyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperidin-1-ylmethyl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-ylmethyl)-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(4-methylpiperazin-1-yl)methyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(propan-2-ylamino)methyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1H-imidazol-1-ylmethyl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-ethyl-3-methylpiperazin-1-yl)-2H-chromen-2-one

3-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-2H-chromen-2-one

7-(1-cyclopropylpiperidin-4-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-2H-chromen-2-one

3-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

7-[3-(dimethylamino)propyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(propan-2-ylamino)propyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(piperazin-1-yl)propyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(4-methylpiperazin-1-yl)propyl]-2H-chromen-2-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-3-(2-methyl-2H-indazol-5-yl)-2H-chromen-2-one

3-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-2H-chromen-2-one

7-(1-ethylpiperidin-4-yl)-3-(2-methyl-2H-indazol-5-yl)-2H-chromen-2-one

7-[2-(dimethylamino)ethyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(propan-2-ylamino)ethyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(piperazin-1-yl)ethyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(1-methylpiperidin-4-yl)oxy]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperidin-4-yl)-2H-chromen-2-one

7-(1-cyclobutylpiperidin-4-yl)-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2-hydroxyethyl)amino]ethyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2-hydroxyethyl)(methyl)amino]ethyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(1-hydroxypropan-2-yl)amino]ethyl}-2H-chromen-2-one

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7-{2-[(1,3-dihydroxypropan-2-yl)amino]ethyl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]ethyl}-2H-chromen-2-one

7-{2-[bis(2-hydroxyethyl)amino]ethyl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[2-(dimethylamino)ethoxy]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(propan-2-ylamino)ethoxy]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(2-hydroxyethyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(2-hydroxyethyl)(methyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(1-hydroxypropan-2-yl)amino]propyl}-2H-chromen-2-one

7-{3-[(1,3-dihydroxypropan-2-yl)amino]propyl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(morpholin-4-yl)propyl]-2H-chromen-2-one

7-{3-[bis(2-hydroxyethyl)amino]propyl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(morpholin-4-yl)ethyl]-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-methylpyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-ethylpyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-(propan-2-yl)pyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-(2-hydroxyethyl)pyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[(3R)-1-(1-hydroxypropan-2-yl)pyrrolidin-3-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-(2-fluoroethyl)-3-methylpiperazin-1-yl]-2H-chromen-2-one

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7-[2-(diethylamino)ethoxy]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{2-[bis(2-hydroxyethyl)amino]ethoxy}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperidin-4-yloxy)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(1-ethylpiperidin-4-yl)oxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[1-(2-hydroxyethyl)piperidin-4-yl]oxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-(3-fluoropropyl)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{[1-(propan-2-yl)piperidin-4-yl]oxy}-2H-chromen-2-one

7-[4-(dimethylamino)butyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)(methyl)amino]butyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{4-[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]butyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(piperazin-1-yl)butyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-4-(3-hydroxypropyl)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-[3-(dimethylamino)propyl]-3-(2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

7-[3-(dimethylamino)propyl]-3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

7-[3-(dimethylamino)propyl]-3-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(methylamino)ethyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(methylamino)propyl]-2H-chromen-2-one

3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[3-(methylamino)propyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(2-methylpropyl)piperidin-4-yl]-2H-chromen-2-one

7-{[1-(1,3-dihydroxypropan-2-yl)piperidin-4-yl]oxy}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[1-(2-methylpropyl)piperidin-4-yl]-2H-chromen-2-one

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7-[1-(3-fluoropropyl)piperidin-4-yl]-3-(6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(pyrrolidin-1-yl)ethoxy]-2H-chromen-2-one

7-(4-aminopiperidin-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(4-amino-4-methylpiperidin-1-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[4-(dimethylamino)piperidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[4-(diethylamino)piperidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(propan-2-ylamino)piperidin-1-yl]-2H-chromen-2-one

7-[4-(cyclobutylamino)piperidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{4-[(1-hydroxypropan-2-yl)amino]piperidin-1-yl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(ethylamino)propyl]-2H-chromen-2-one

7-(3-aminopropyl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{4-[bis(2-hydroxyethyl)amino]piperidin-1-yl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{4-[(1,3-dihydroxypropan-2-yl)amino]piperidin-1-yl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(ethylamino)ethoxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(2-methoxyethyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(tetrahydrofuran-2-ylmethyl)amino]propyl}-2H-chromen-2-one

7-[3-(benzylamino)propyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(thiophen-3-ylmethyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(pyridin-2-ylmethyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{3-[(pyridin-4-ylmethyl)amino]propyl}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[ethyl(methyl)amino]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[ethyl(2-hydroxyethyl)amino]ethoxy}-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(tetrahydrofuran-3-ylamino)propyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(3R)-3-hydroxypyrrolidin-1-yl]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(2-methylpiperidin-1-yl)azetidin-1-yl]-2H-chromen-2-one

7-[3-(dimethylamino)azetidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[3-(diethylamino)azetidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(2,7-diazaspiro[4.4]non-2-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(2-{[(2R)-1-hydroxypropan-2-yl]amino}ethoxy)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(2-{[(2S)-1-hydroxypropan-2-yl]amino}ethoxy)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(2R)-pyrrolidin-2-ylmethoxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-2H-chromen-2-one

7-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[3-(piperidin-1-yl)azetidin-1-yl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(methylamino)butyl]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(piperidin-1-yl)ethoxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(3S)-3-hydroxypyrrolidin-1-yl]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(1-hydroxy-2-methylpropan-2-yl)amino]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(morpholin-4-yl)ethoxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[2-(4-hydroxypiperidin-1-yl)ethoxy]-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(1-ethyl-4-fluoropiperidin-4-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2-hydroxyethyl)amino]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2-methoxyethyl)amino]ethoxy}-2H-chromen-2-one

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3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-{2-[(2-hydroxypropyl)amino]ethoxy}-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[4-(2-hydroxy-2-methylpropyl)piperazin-1-yl]-2H-chromen-2-one

7-[3-(aminomethyl)azetidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{(3R)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{3-[(dimethylamino)methyl]azetidin-1-yl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-{(3S)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[2-(diethylamino)ethyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[3-(diethylamino)propyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-[4-(diethylamino)butyl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(2,6-diazaspiro[3.3]hept-2-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(6-methyl-2,6-diazaspiro[3.3]hept-2-yl)-2H-chromen-2-one

2-[3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2-oxo-2H-chromen-7-yl]hexahydropyrrolo[1,2-a]pyrazin-6(2H)-one

1-[3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2-oxo-2H-chromen-7-yl]piperidine-4-carbonitrile

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(4-hydroxypiperidin-1-yl)-2H-chromen-2-one

7-(2,7-diazaspiro[3.5]non-7-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

7-(6-amino-2-azaspiro[3.3]hept-2-yl)-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-(imidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one

3-(imidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-2H-chromen-2-one

3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2H-chromen-2-one

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3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-2H-chromen-2-one

7-(2,6-diazaspiro[3.3]hept-2-yl)-3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2H-chromen-2-one, and

3-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one;

or a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

4. The compound of claim 3, wherein the compound is selected from:

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one trifluoroacetate

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one hydrochloride

7-(piperazin-1-yl)-3-[7-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one trifluoroacetate

7-(piperazin-1-yl)-3-[7-(trifluoromethyl)-1,3-benzoxazol-2-yl]-2H-chromen-2-one hydrochloride

2-oxo-N-phenyl-7-(piperazin-1-yl)-2H-chromene-3-carboxamide trifluoroacetate

3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(7-chloro-1,3-benzothiazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(4-chloro-1,3-benzothiazol-2-yl)-7-(piperidin-4-yl)-2H-chromen-2-one hydrochloride

3-(5-fluoro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(4-methyl-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(4-fluoro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one trifluoroacetate

7-(piperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one hydrochloride

7-(4-methylpiperazin-1-yl)-3-[4-(trifluoromethyl)-1,3-thiazol-2-yl]-2H-chromen-2-one trifluoroacetate

3-(4-iodo-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(4-chloro-1,3-benzoxazol-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-([1,3]oxazolo[4,5-b]pyridin-2-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one hydrochloride (1:3)

3-(3-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride (1:3)

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7-(1,4-diazepan-1-yl)-3-(imidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one hydrochloride

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-(piperidin-4-yloxy)-2H-chromen-2-one hydrochloride

3-(2-methylpyrimidin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

3-(2-cyclopropylpyrimidin-4-yl)-7-(piperazin-1-yl)-2H-chromen-2-one hydrochloride

7-(piperazin-1-yl)-3-[2-(propan-2-yl)pyrimidin-4-yl]-2H-chromen-2-one hydrochloride

3-(imidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(7-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(imidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(2-methylimidazo[2,1-b][1,3]thiazol-6-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

3-(6-methylimidazo[1,2-a]pyrimidin-2-yl)-7-[(3R)-pyrrolidin-3-yloxy]-2H-chromen-2-one hydrochloride (1:2)

7-[(1-benzylpyrrolidin-3-yl)(methyl)amino]-3-(7-methylimidazo[1,2-a]pyrimidin-2-yl)-2H-chromen-2-one acetate

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(8-methoxy-6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one acetate (1:2)

7-[(3R)-3,4-dimethylpiperazin-1-yl]-3-(8-hydroxy-6-methylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one acetate

7-[(3S)-3,4-dimethylpiperazin-1-yl]-3-(2-methyl-1,3-benzothiazol-6-yl)-2H-chromen-2-one acetate (2:1)

7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-3-(2-methyl-1,3-benzothiazol-6-yl)-2H-chromen-2-one acetate

3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-ethyl-4-methylpiperazin-1-yl]-2H-chromen-2-one acetate, and

7-[(3S)-3,4-diethylpiperazin-1-yl]-3-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-2H-chromen-2-one acetate (1:2);

or a free base, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

5. A compound selected from Formula (Ia) :

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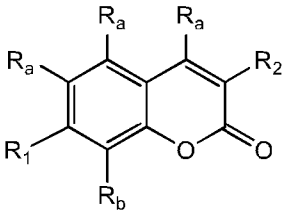

(Ia)

or a free acid, free base, salt, stereoisomer, racemate, enantiomer, diastereomer or tautomer form thereof, wherein:

R_1 is heterocyclyl selected from azetidin-1-yl, tetrahydrofuran-3-yl, piperidin-1-yl, piperidin-4-yl, piperazin-1-yl, 1,4-diazepan-1-yl, 1,2,5,6-tetrahydropyridin-3-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-2(1*H*)-yl, hexahydropyrrolo[1,2-*a*]pyrazin-6(2*H*)-one, (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,

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(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 and 6,9-diazaspiro[4.5]dec-9-yl optionally substituted with one, two or three R_3 substituents and one additional, optional R_4 substituent;

R_2 is heteroaryl selected from thien-2-yl, thien-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1,2,4-oxadiazol-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-4-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl, indol-5-yl, indol-6-yl, 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, indolizin-2-yl, benzofuran-2-yl, benzothien-2-yl, benzothien-3-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-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, pyrrolo[1,2-*b*]pyridazin-6-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*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, 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-*b*]pyridazin-6-yl, imidazo[1,2-*a*]pyrazin-2-yl and quinoxalin-2-yl;

wherein, each heteroaryl is optionally substituted with one, two or three R_6 substituents and one additional, optional 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_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, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl-amino,

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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;

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, 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, halo-C_{1-8}alkyl, hydroxy-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; and,

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

6. A pharmaceutical composition for use in the treatment of spinal muscular atrophy comprising the compound of claim 1, 3 or 5 and a pharmaceutically acceptable carrier, excipient or diluent.

7. A pharmaceutical composition for enhancing the inclusion of exon 7 of SMN2 into mRNA that is transcribed from the SMN2 gene, comprising the compound of any one of claims 1, 3 or 5 and a pharmaceutically acceptable carrier, excipient or diluent.

8. A pharmaceutical composition for increasing the amount of Smn protein, comprising the compound of any one of claims 1, 3 or 5 and a pharmaceutically acceptable carrier, excipient or diluent.

9. The compound of claim 5, wherein the salt is a chloride, hydrochloride, dihydrochloride, hydrobromide, acetate or trifluoroacetate salt.

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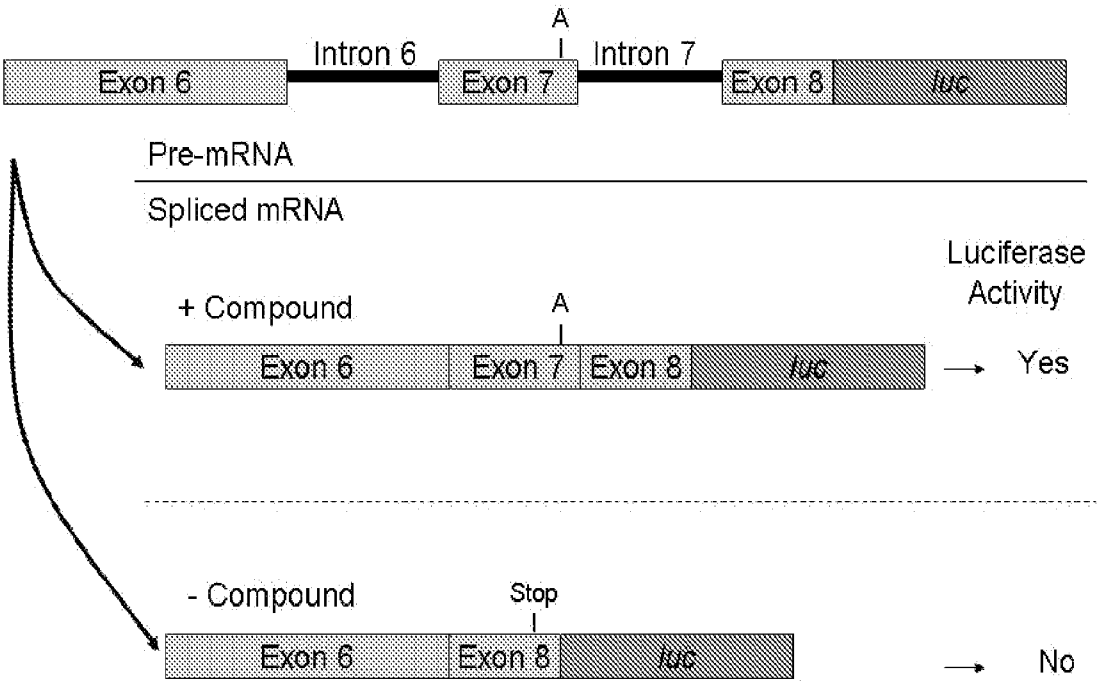
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Figure 1

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SEQ ID NO. 21
Figure 2a

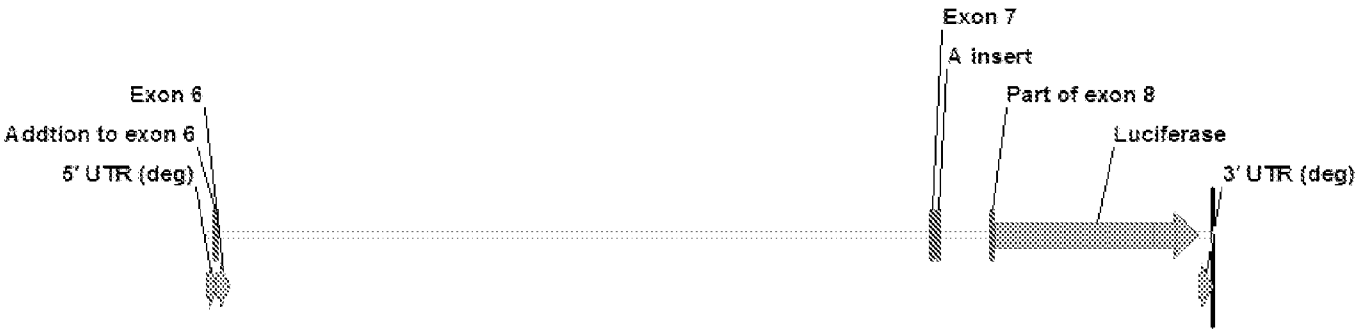

Exon 7
A insert
Exon 6
Part of exon 8
Addtion to exon 6
Luciferase
5' UTR (deg)
3' UTR (deg)

Figure 2b

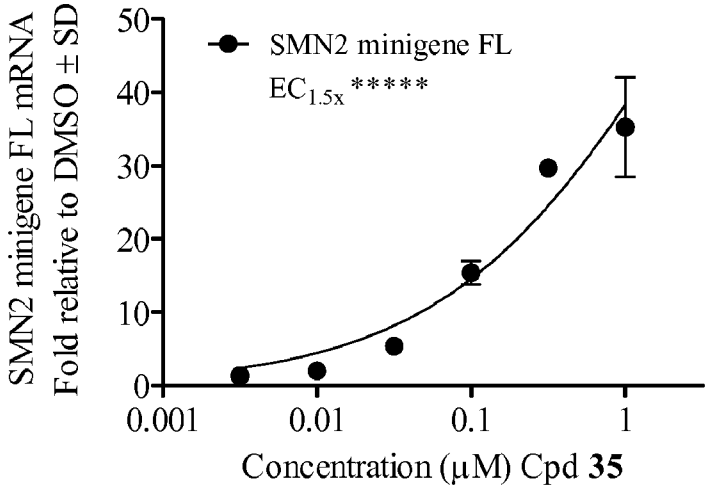


Figure 3a

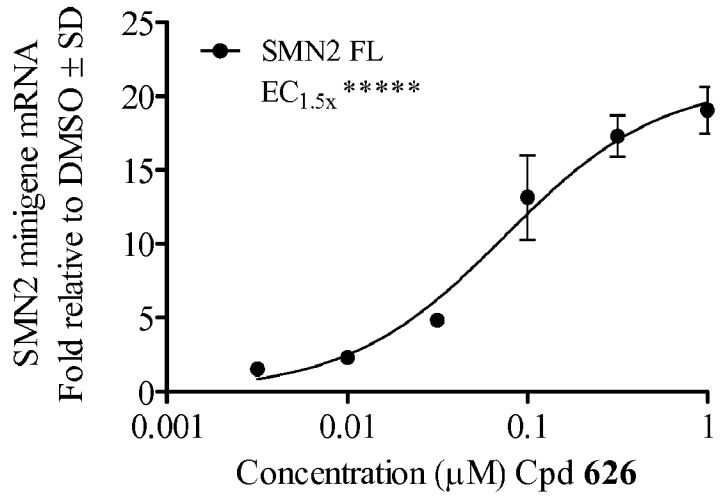


Figure 3b

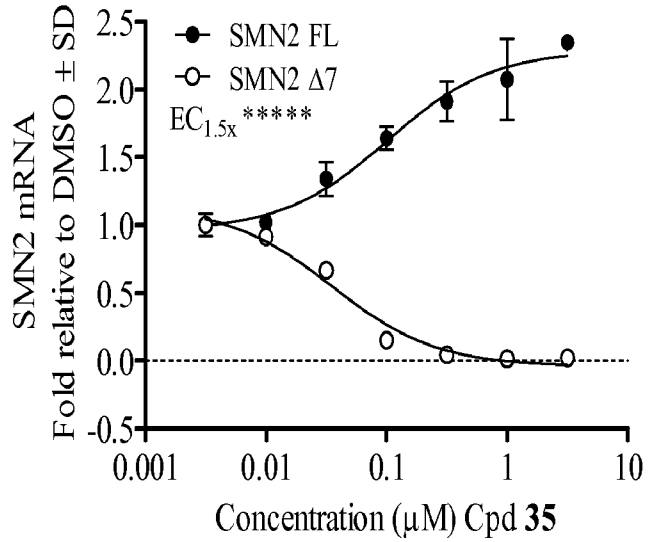


Figure 4a

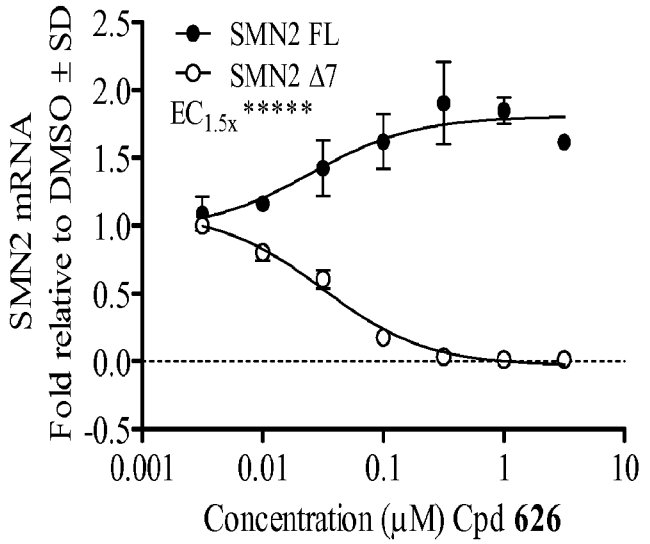


Figure 4b

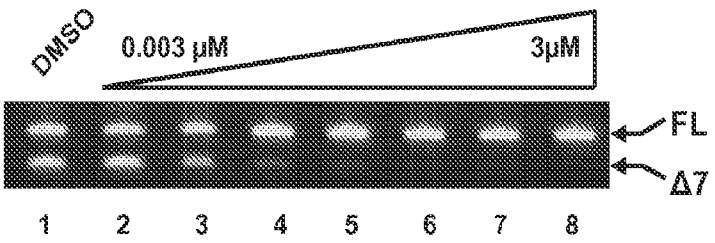


Figure 5a

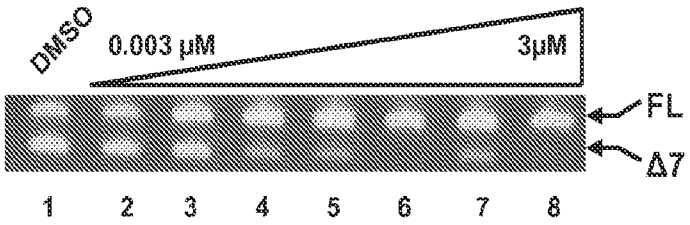


Figure 5b

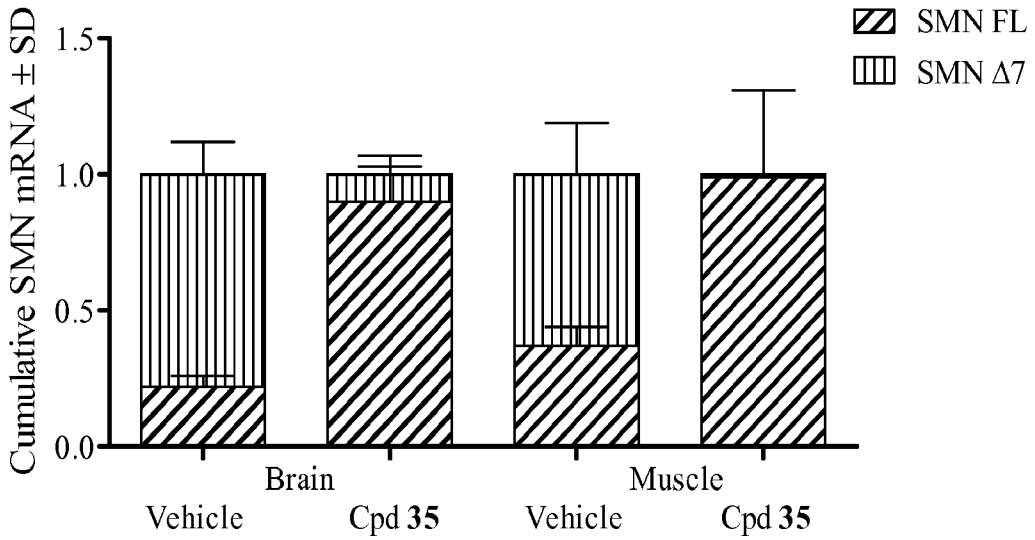


Figure 6a

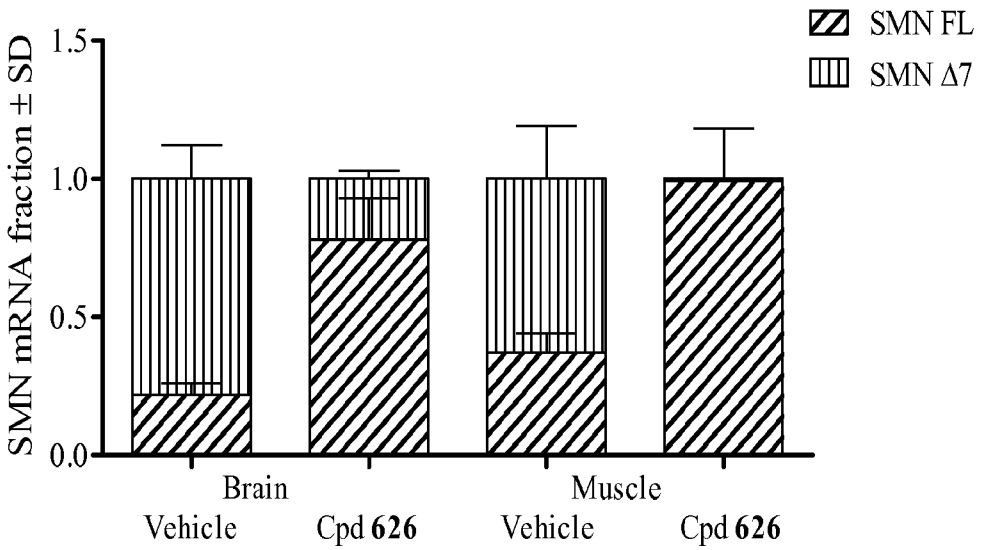


Figure 6b

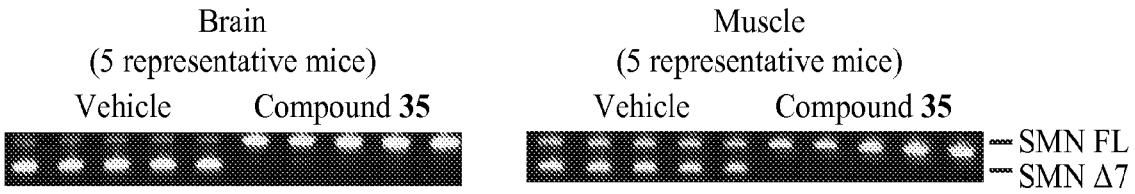


Figure 7a

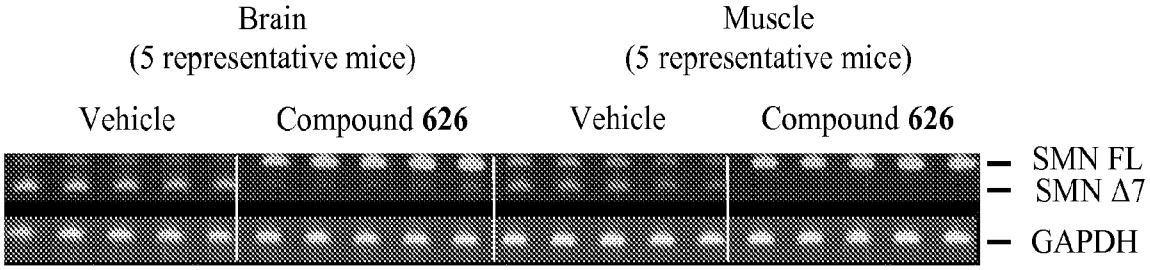


Figure 7b

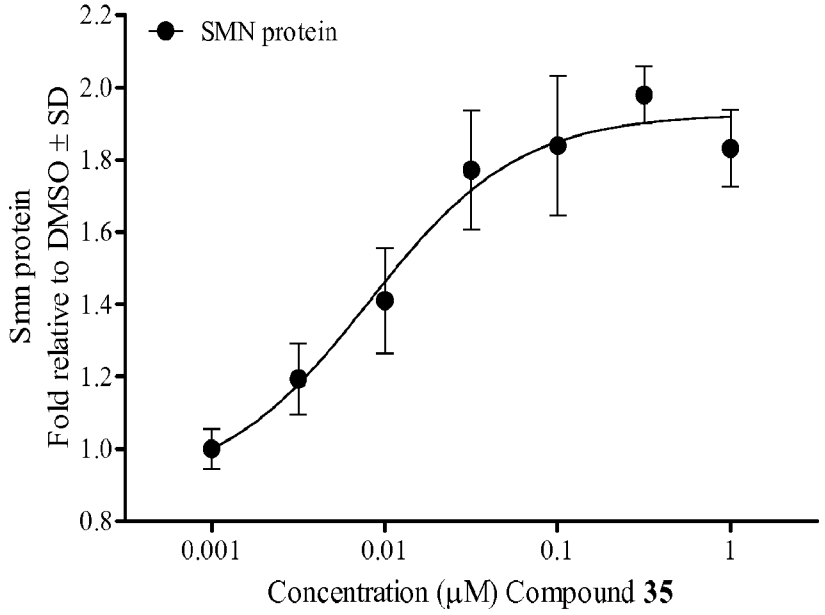


Figure 8a

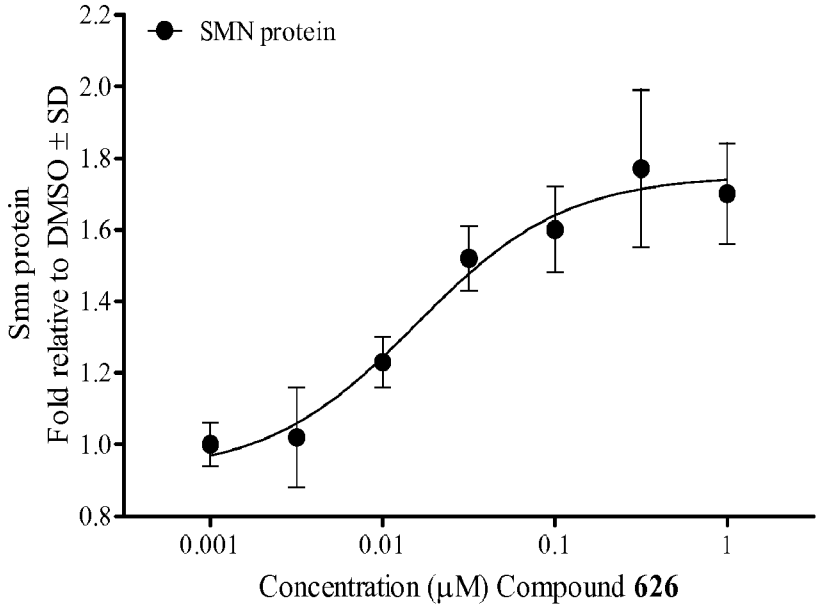


Figure 8b

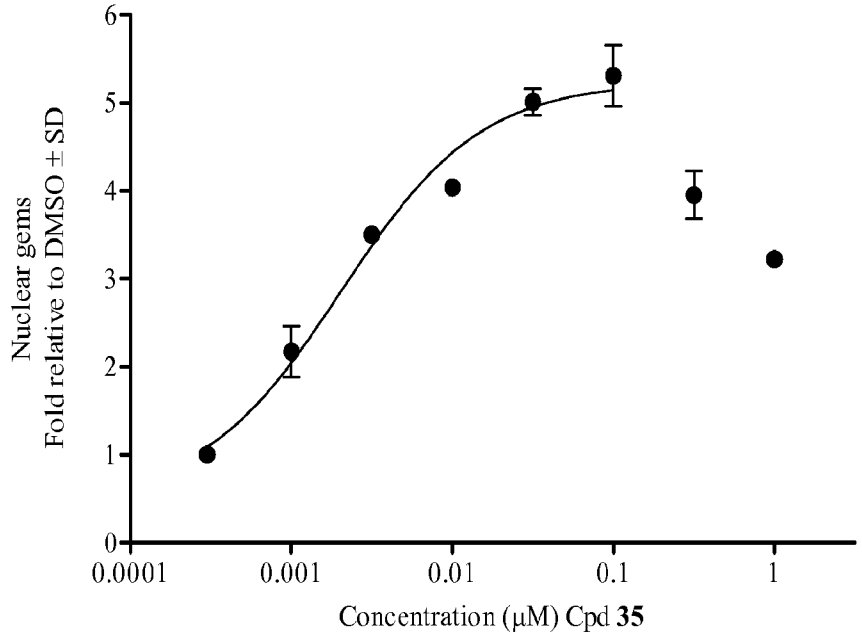


Figure 9a

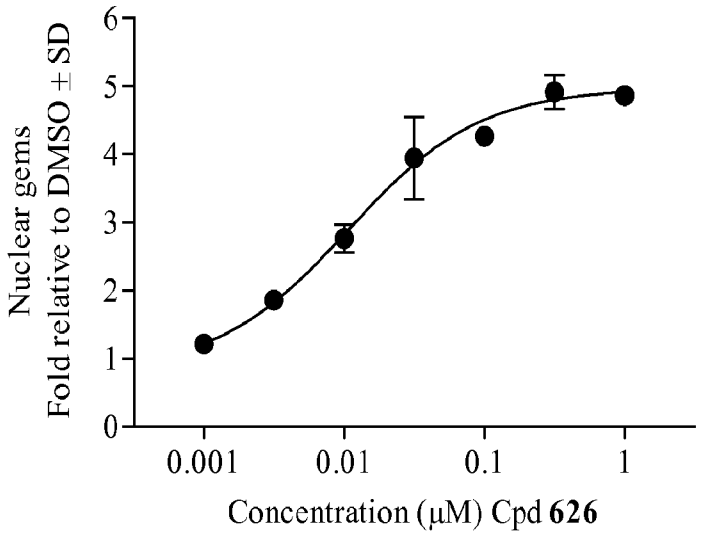


Figure 9b

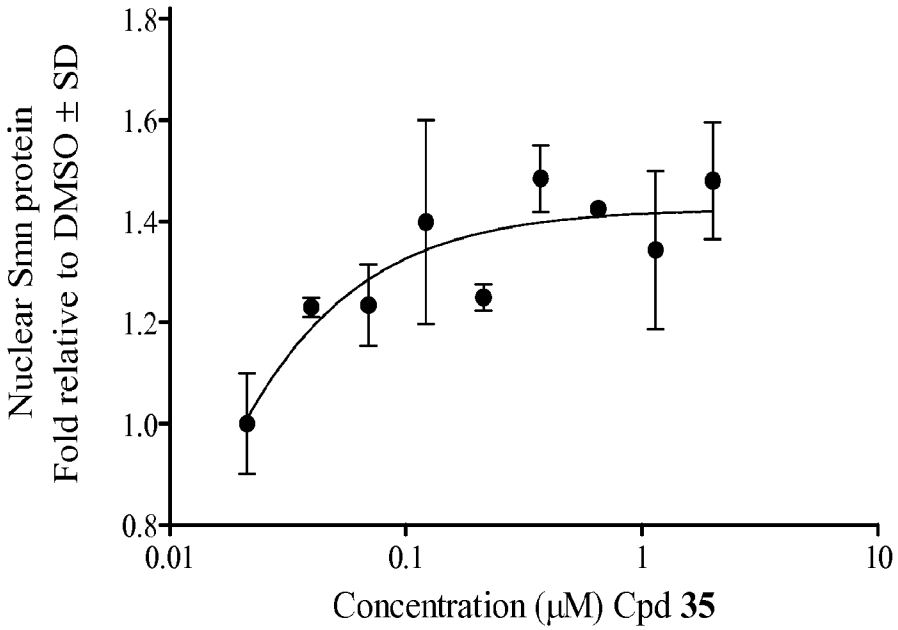


Figure 10a

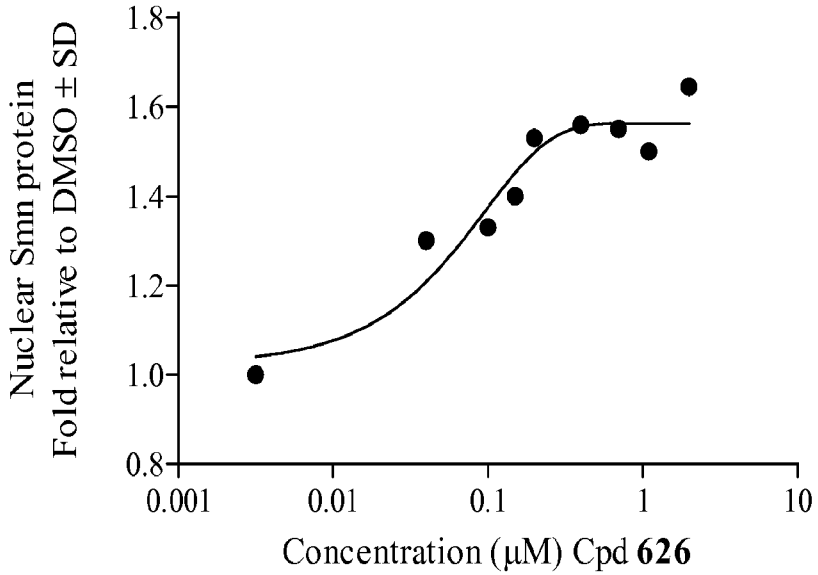


Figure 10b

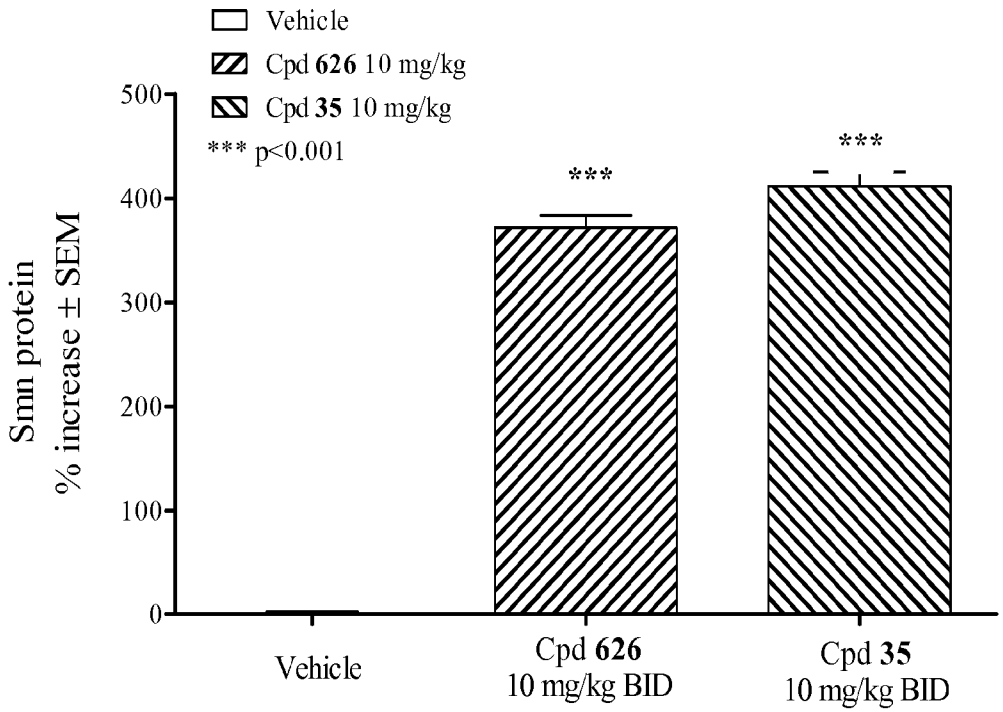

Vehicle
Cpd 626 10 mg/kg
Cpd 35 10 mg/kg
*** p<0.001
Smn protein
% increase ± SEM
500
400
300
200
100
0
***
***
Vehicle
Cpd 626
10 mg/kg BID
Cpd 35
10 mg/kg BID

Figure 11a

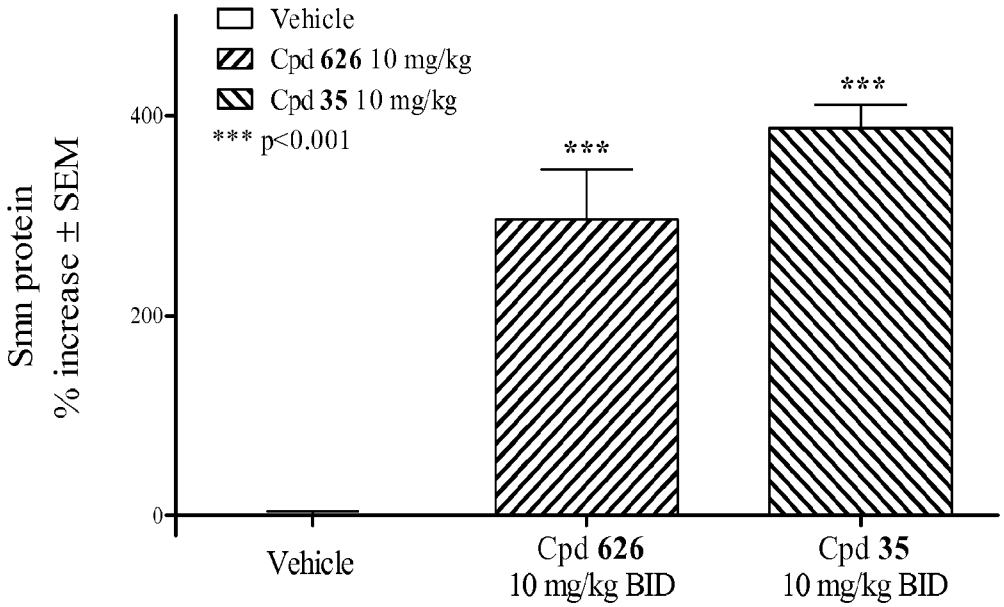

Vehicle
Cpd 626 10 mg/kg
Cpd 35 10 mg/kg
*** p<0.001
Smn protein
% increase ± SEM
400
200
0
***
***
Vehicle
Cpd 626
10 mg/kg BID
Cpd 35
10 mg/kg BID

Figure 11b

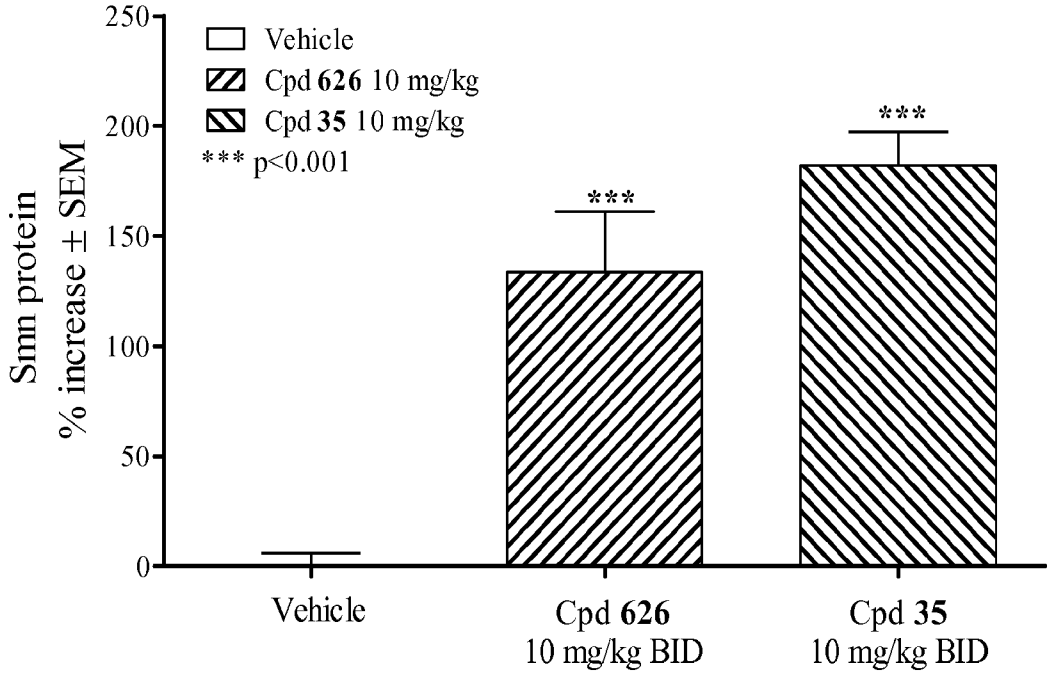

Vehicle
Cpd 626 10 mg/kg
Cpd 35 10 mg/kg
*** p<0.001
Smn protein
% increase ± SEM
250
200
150
100
50
0
***
***
Vehicle
Cpd 626
10 mg/kg BID
Cpd 35
10 mg/kg BID

Figure 11c

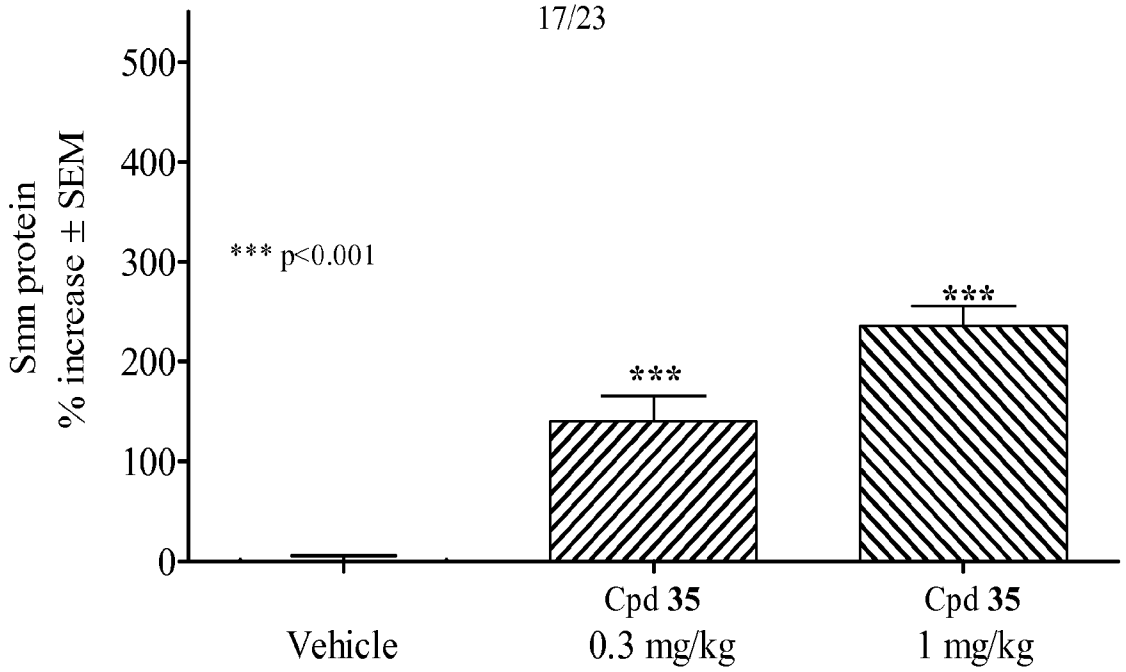


Figure 12a

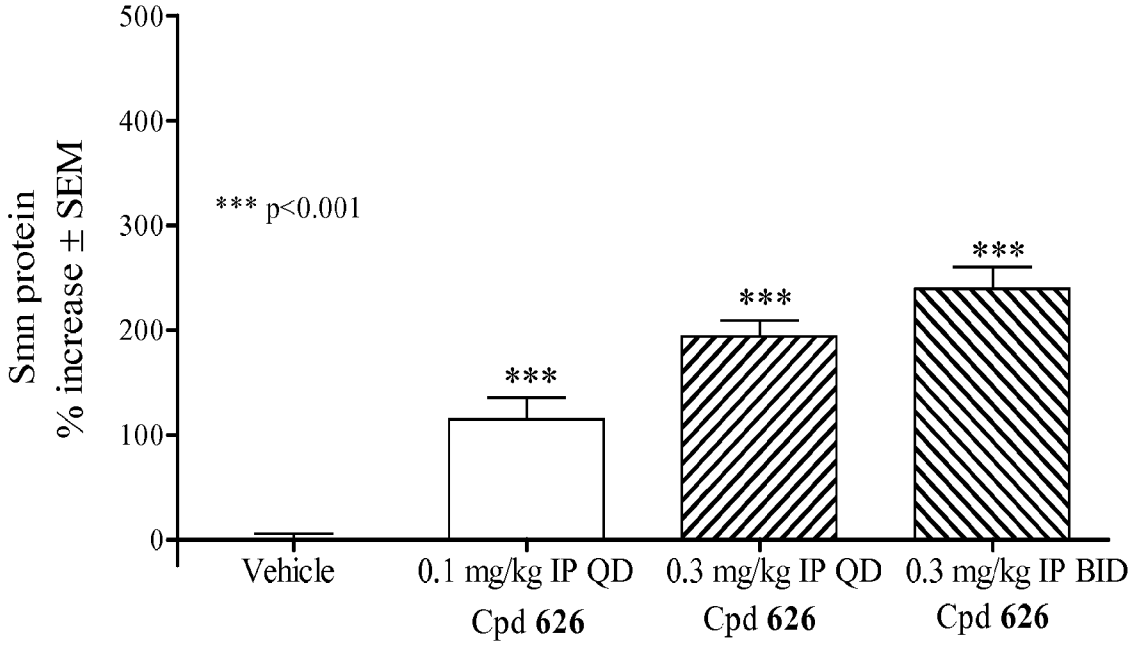


Figure 12b

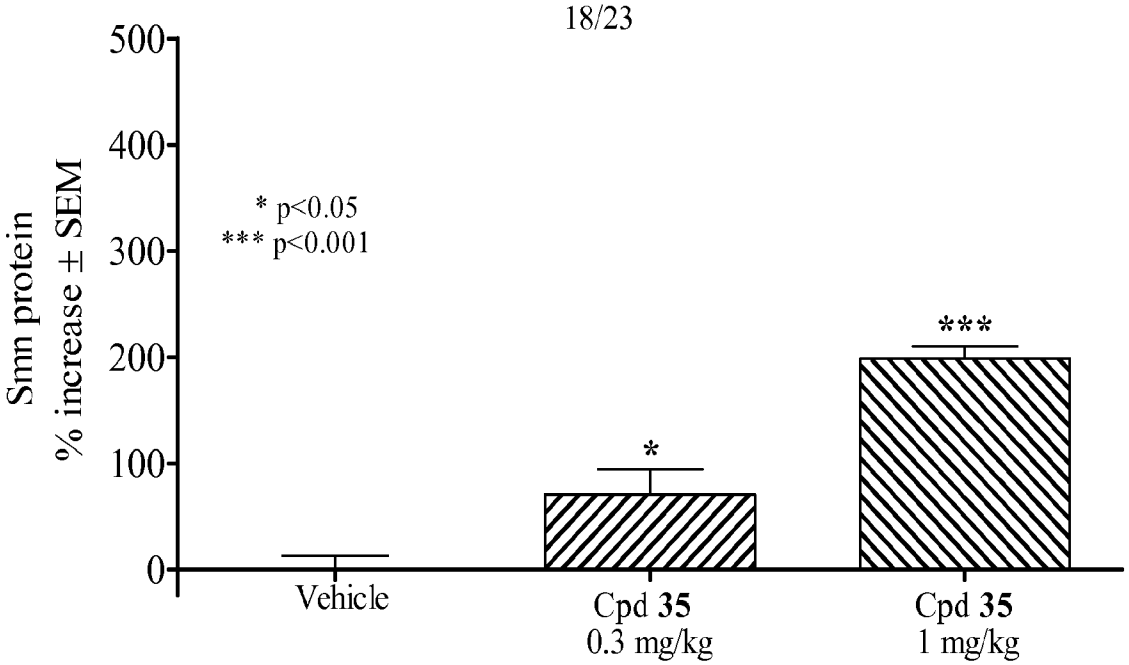


Figure 12c

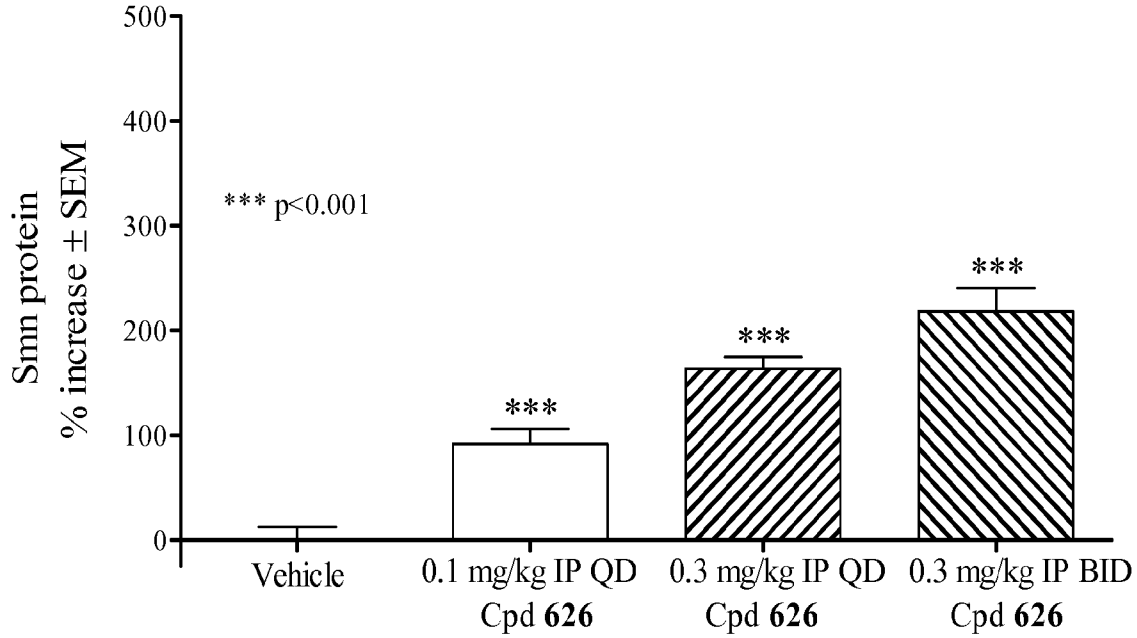


Figure 12d

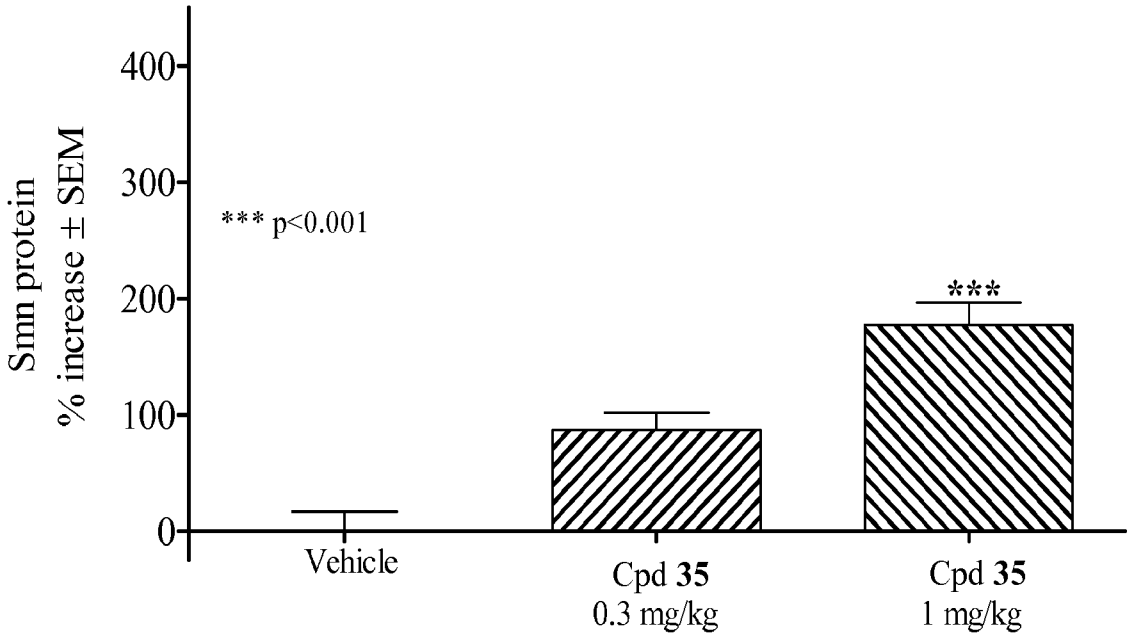


Figure 12e

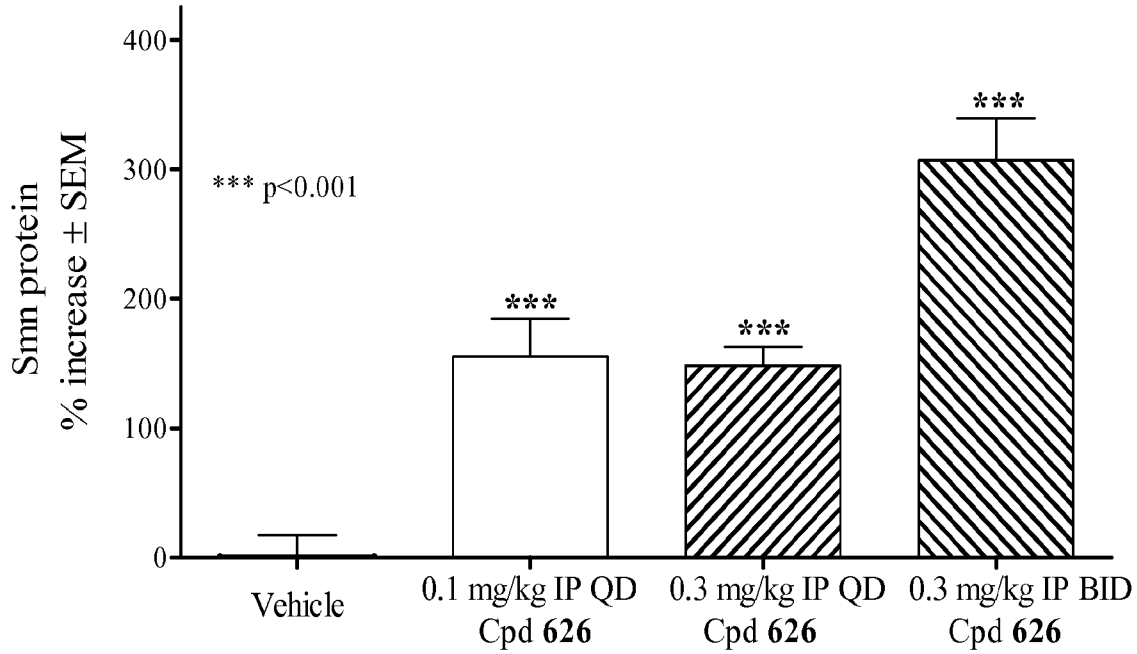


Figure 12f

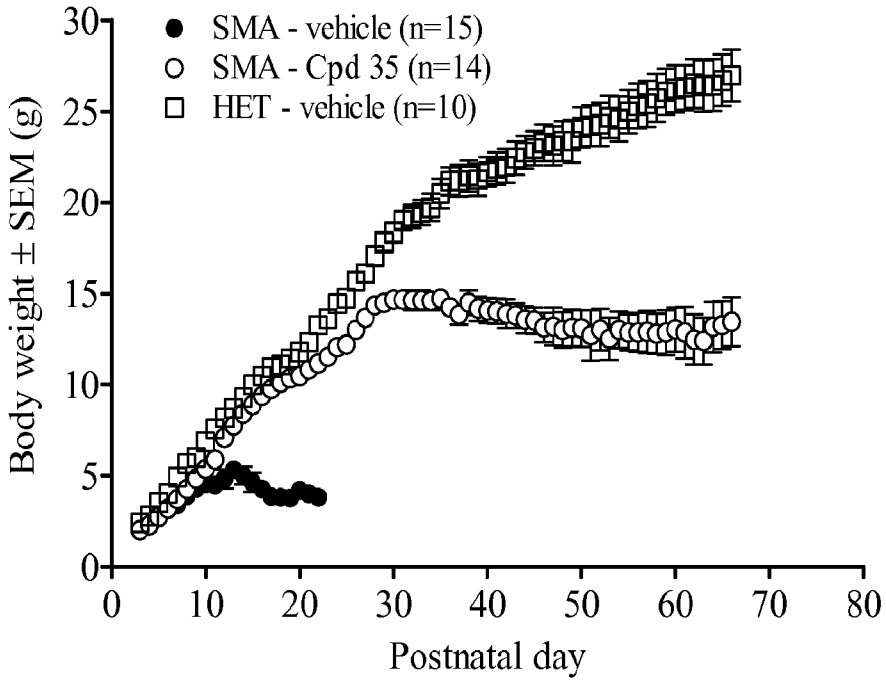


Figure 13a

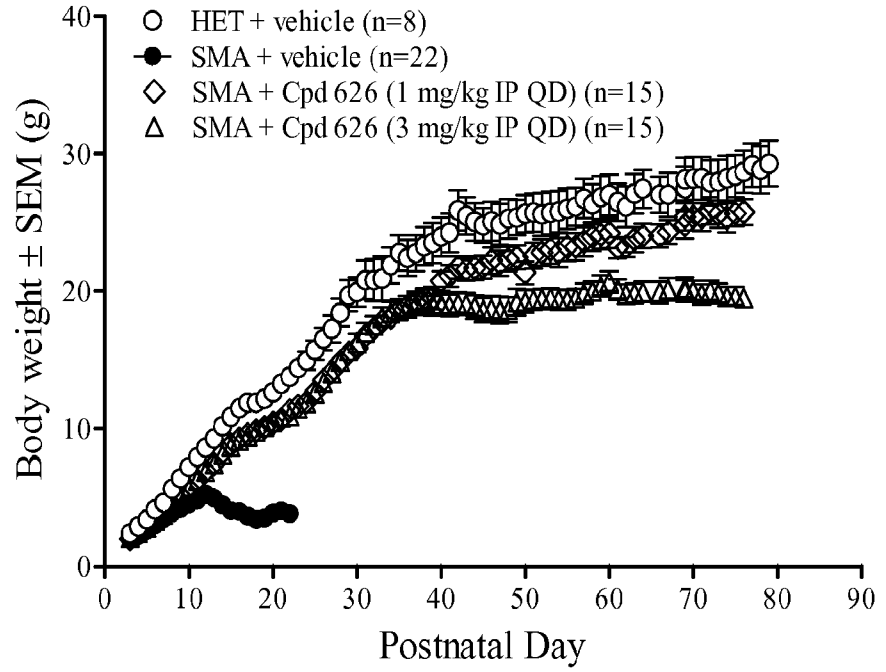


Figure 13b

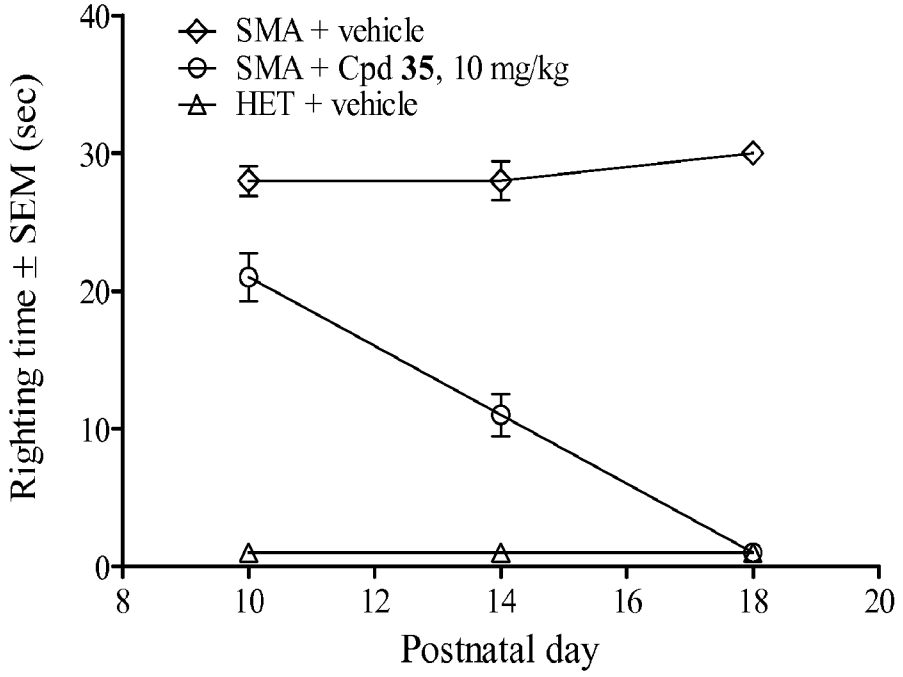

SMA + vehicle
SMA + Cpd 35, 10 mg/kg
HET + vehicle
Righting time ± SEM (sec)
40
30
20
10
0
8
10
12
14
16
18
20
Postnatal day

Figure 14

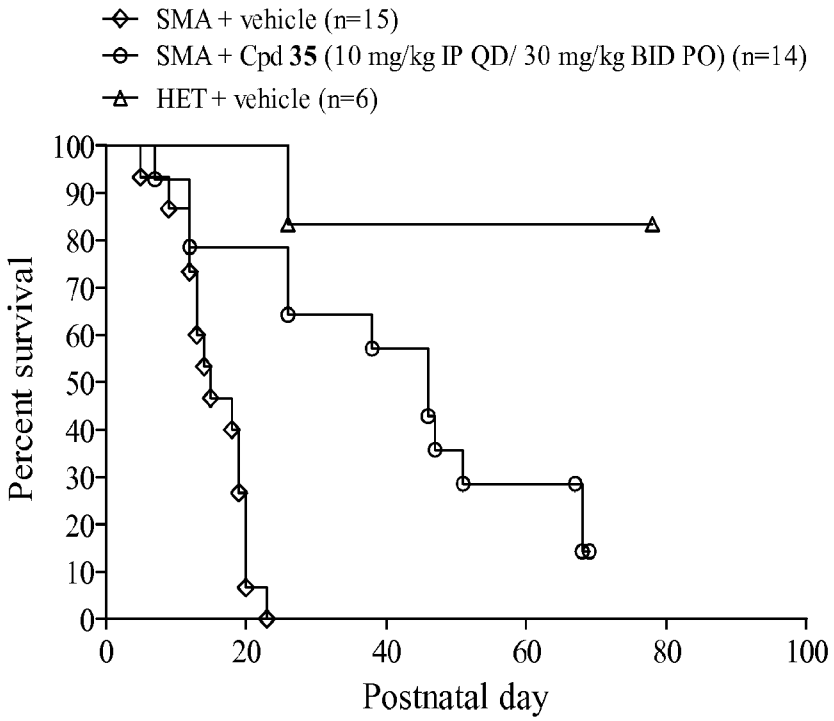


Figure 15a

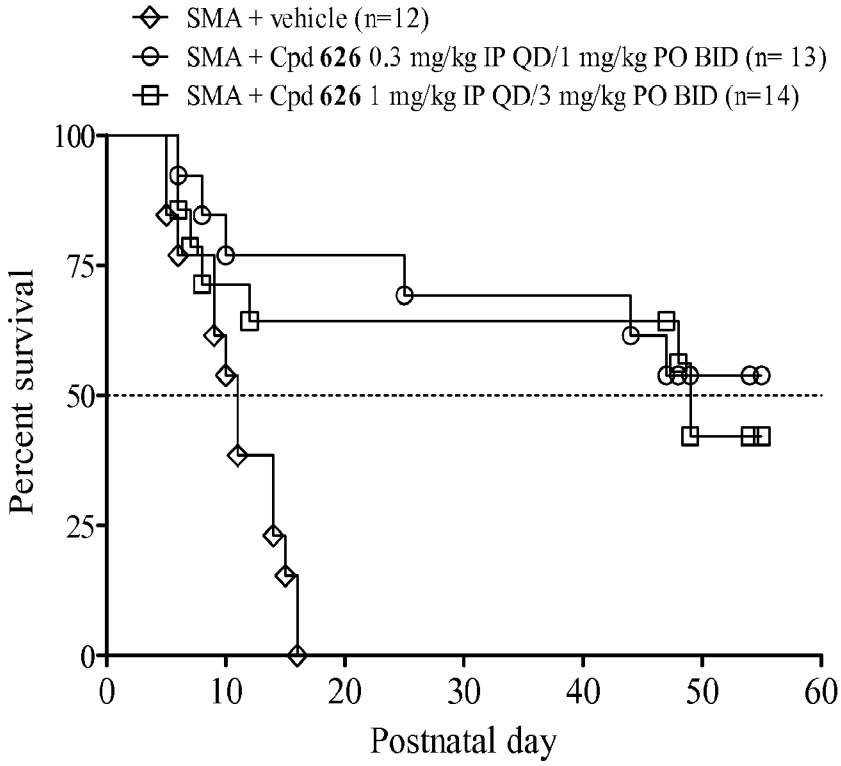


Figure 15b

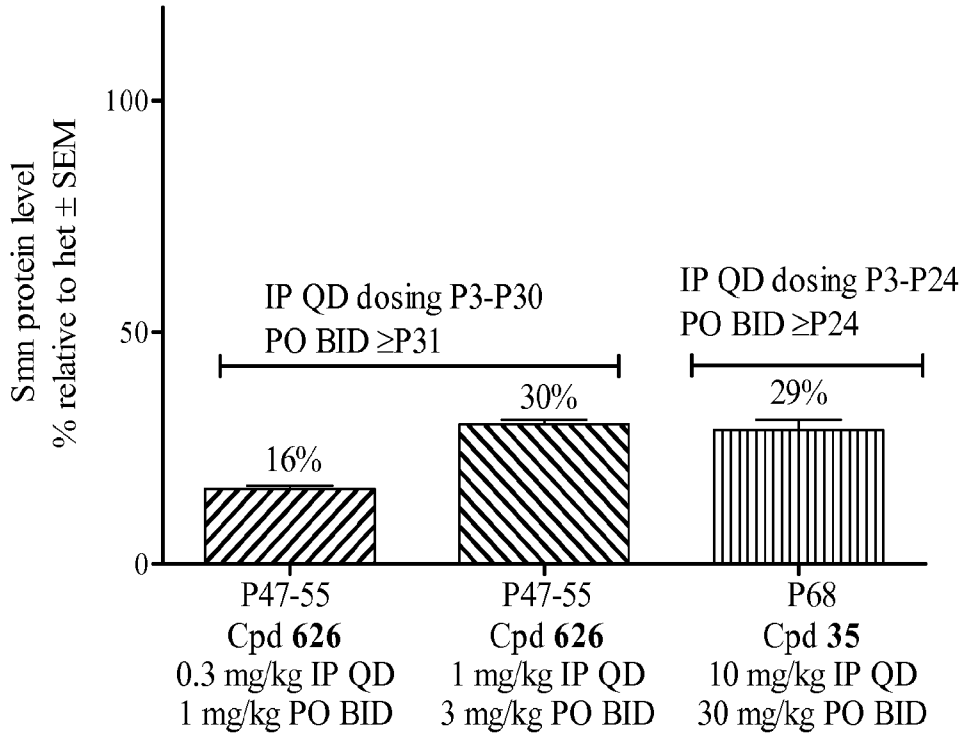


Figure 16a

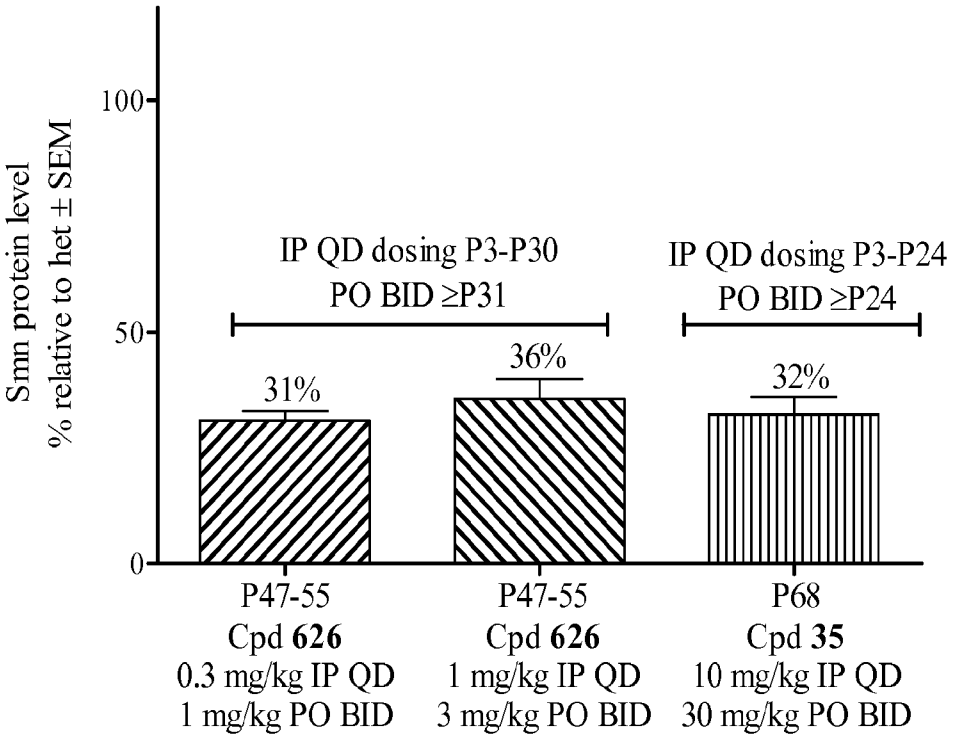
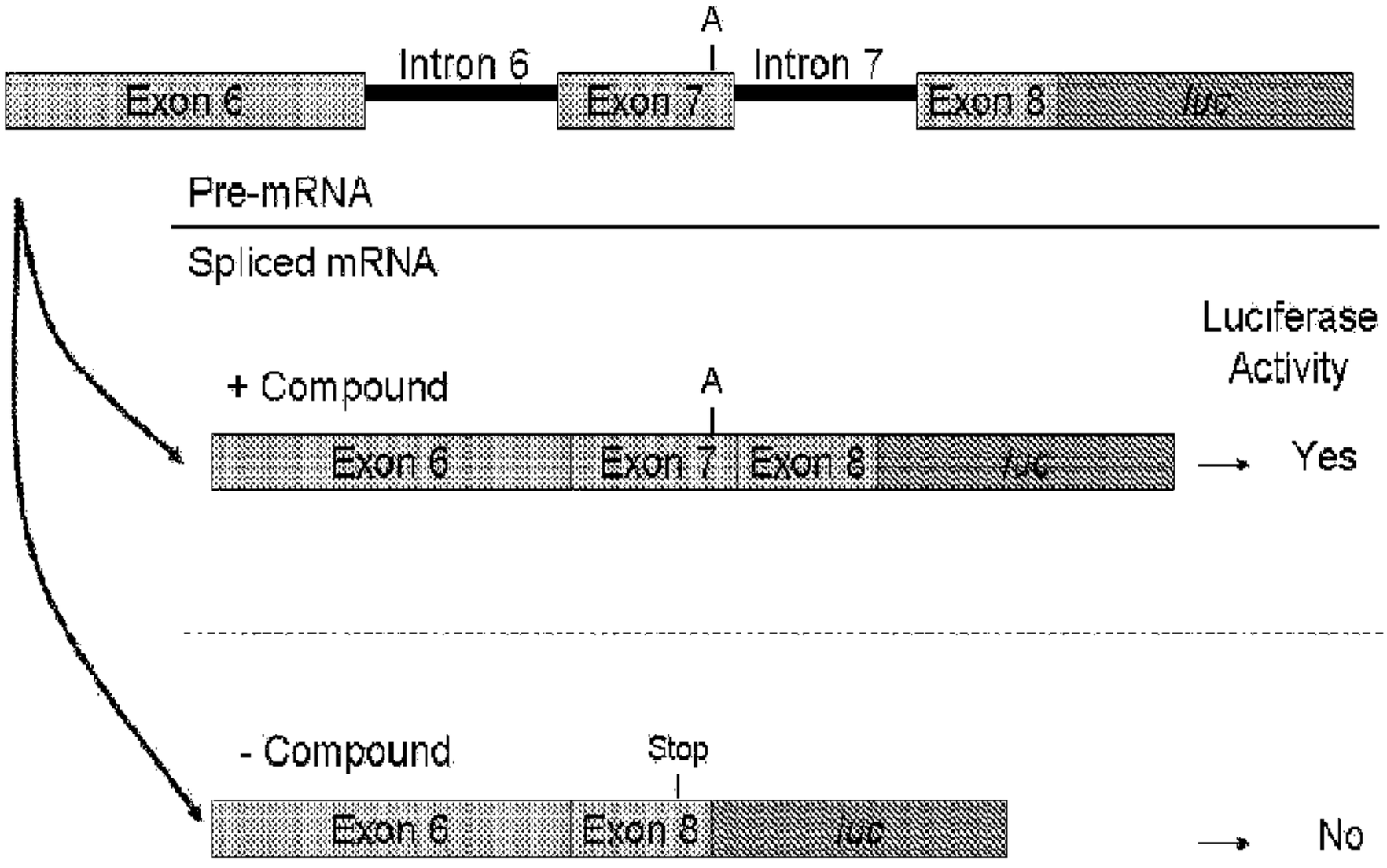


Figure 16b


A
Intron 6
Intron 7
Exon 6
Exon 7
Exon 8
luc
Pre-mRNA
Spliced mRNA
Luciferase Activity
+ Compound
A
Exon 6
Exon 7
Exon 8
luc
Yes
- Compound
Stop
Exon 6
Exon 8
luc
No