



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

(13) **A1**

(86) Date de dépôt PCT/PCT Filing Date: 2017/11/27
(87) Date publication PCT/PCT Publication Date: 2018/05/31
(85) Entrée phase nationale/National Entry: 2019/05/13
(86) N° demande PCT/PCT Application No.: US 2017/063323
(87) N° publication PCT/PCT Publication No.: 2018/098446
(30) Priorité/Priority: 2016/11/28 (US62/426,619)

(51) Cl.Int./Int.Cl. *A01N 43/90* (2006.01),
A61K 31/519 (2006.01), *C07D 239/70* (2006.01)

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(54) Titre : PROCÉDES DE MODULATION DE L'ÉPISSAGE DE L'ARN

(54) Title: METHODS FOR MODULATING RNA SPLICING

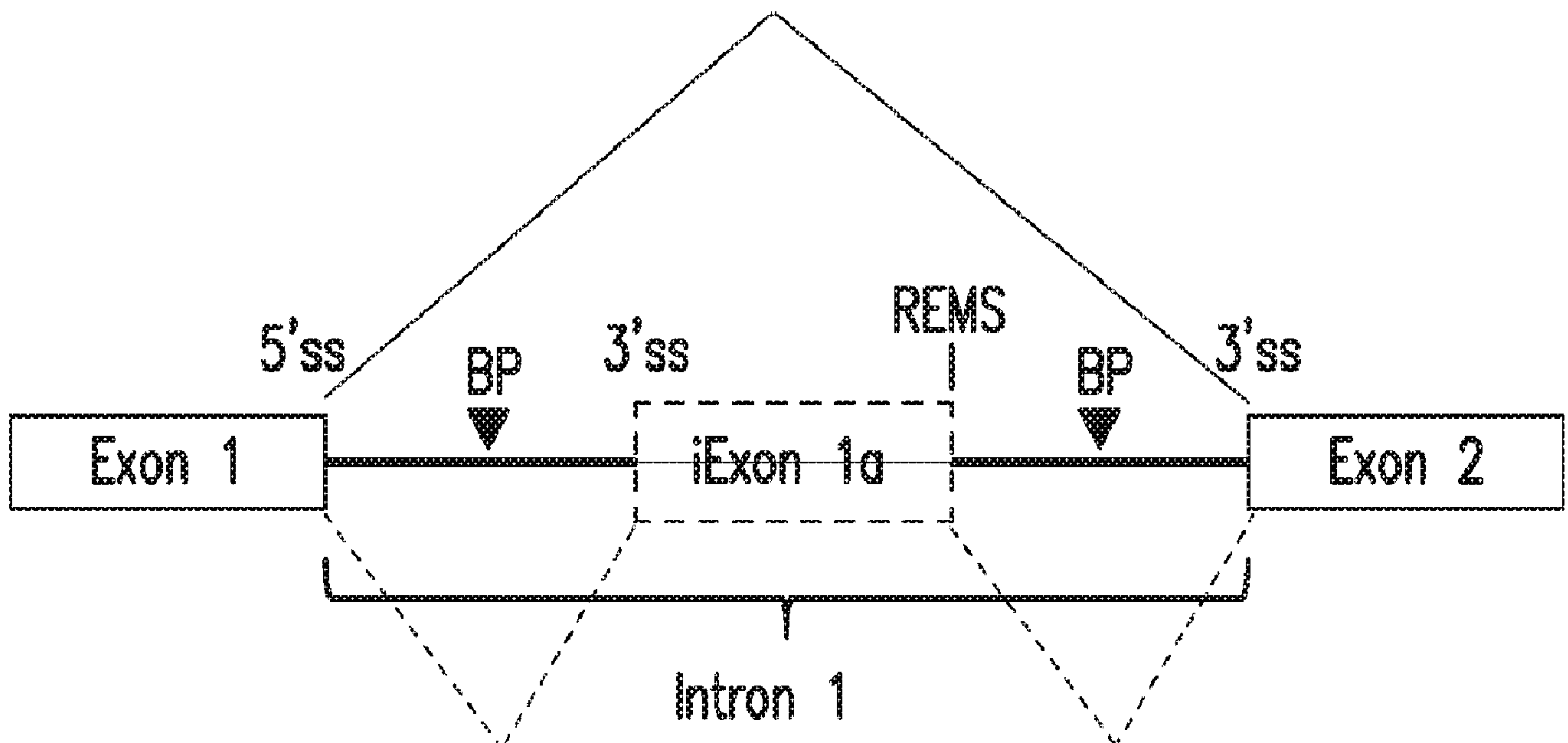


FIG. 1A

(57) Abrégé/Abstract:

In one aspect, described herein is an intronic recognition element for splicing modifier (iREMS) that can be recognized by a compound provided herein. In another aspect, described herein are methods for modulating the amount of a product of a gene,

(57) Abrégé(suite)/Abstract(continued):

wherein a precursor RNA transcript transcribed from the gene contains an intronic REMS, and the methods utilizing a compound described herein. More particularly, described herein are methods for modulating the amount of an RNA transcript or protein product encoded by a gene, wherein a precursor RNA transcript transcribed from the gene comprises an intronic REMS, and the methods utilizing a compound described herein. In another aspect, provided herein are artificial gene constructs comprising an intronic REMS, and uses of those artificial gene constructs to modulate protein production. In another aspect, provided herein are methods for altering endogenous genes to comprise an intronic REMS, and the use of a compound described herein to modulate protein produced from such altered endogenous genes.

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

(19) World Intellectual Property
Organization
International Bureau(43) International Publication Date
31 May 2018 (31.05.2018)(10) International Publication Number
WO 2018/098446 A1

(51) International Patent Classification:

A01N 43/90 (2006.01) C07D 239/70 (2006.01)
A61K 31/519 (2006.01)

(21) International Application Number:

PCT/US2017/063323

(22) International Filing Date:

27 November 2017 (27.11.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/426,619 28 November 2016 (28.11.2016) US

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

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,

(54) Title: METHODS FOR MODULATING RNA SPLICING

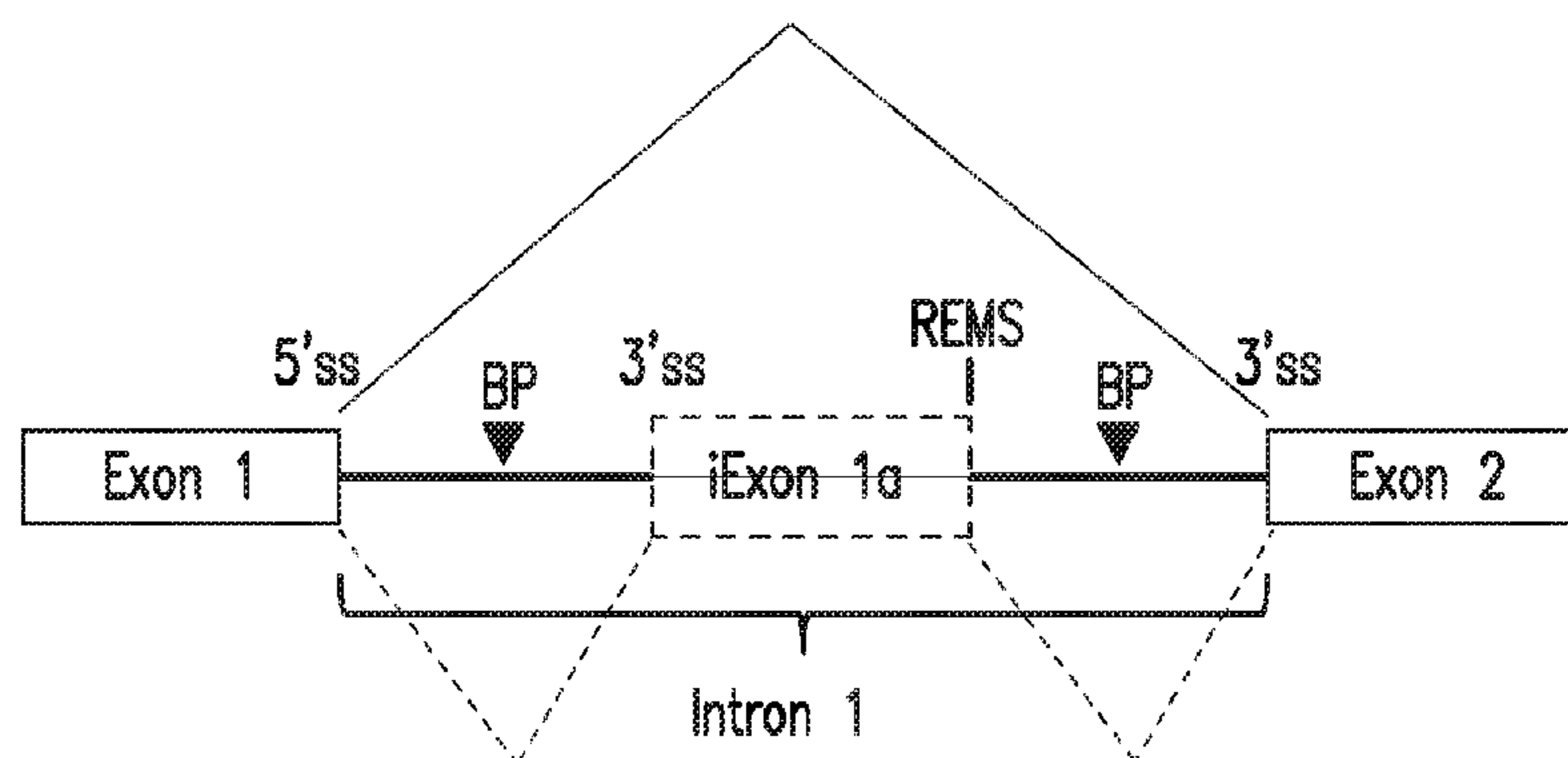


FIG. 1A

(57) Abstract: In one aspect, described herein is an intronic recognition element for splicing modifier (iREMS) that can be recognized by a compound provided herein. In another aspect, described herein are methods for modulating the amount of a product of a gene, wherein a precursor RNA transcript transcribed from the gene contains an intronic REMS, and the methods utilizing a compound described herein. More particularly, described herein are methods for modulating the amount of an RNA transcript or protein product encoded by a gene, wherein a precursor RNA transcript transcribed from the gene comprises an intronic REMS, and the methods utilizing a compound described herein. In another aspect, provided herein are artificial gene constructs comprising an intronic REMS, and uses of those artificial gene constructs to modulate protein production. In another aspect, provided herein are methods for altering endogenous genes to comprise an intronic REMS, and the use of a compound described herein to modulate protein produced from such altered endogenous genes.

[Continued on next page]

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

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with sequence listing part of description (Rule 5.2(a))*

DEMANDE OU BREVET VOLUMINEUX

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

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CONTENANT LES PAGES 1 À 346

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JUMBO APPLICATIONS/PATENTS

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

THIS IS VOLUME 1 OF 2
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NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

Methods for Modulating RNA Splicing

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of provisional application No. 62/426,619, filed on November 28, 2016, which is incorporated by reference herein in its entirety.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] This application incorporates by reference a Sequence Listing submitted with this application as a text file entitled “10589-275-228_Sequence_Listing.txt” created on November 18, 2017 and having a size of 1,112 kilobytes.

INTRODUCTION

[0003] In one aspect, described herein is a recognition element for splicing modifier (REMS) present in an intron (i.e., an “intronic REMS” or iREMS) that can be recognized as a 5’ splice site by the U1 snRNP and/or other components of the pre-mRNA splicing machinery in the presence of a small molecule splicing modifier, wherein gene expression is modulated by inducing alternative splicing of intronic exons (iExons) in the transcribed RNA. In another aspect, described herein are methods for modulating the amount of a product of a gene, wherein a precursor RNA transcript transcribed from the gene contains an intronic REMS, a branch point and a 3’ splice site, and the methods utilize a small molecule compound described herein to induce alternative splicing of iExons. More particularly, described herein are methods for modulating the amount of an RNA transcript or protein product encoded by a gene via alternative splicing of iExons, wherein a precursor RNA transcript transcribed from the gene comprises an endogenous or non-endogenous intronic REMS, and the methods utilize a compound described herein to induce iExon alternative splicing. In another aspect, provided herein are artificial gene constructs comprising an intronic REMS (including an endogenous or non-endogenous intronic REMS), and uses of those artificial gene constructs to modulate protein production via iExon alternative splicing in the presence of a small molecule splicing modifier compound. In another aspect, provided herein are methods for altering genes to comprise an endogenous or non-endogenous intronic REMS, and the use of a small molecule compound described herein to induce alternative splicing of iExons, subsequently modulating the amount and type of protein produced from such altered endogenous or non-endogenous gene transcripts.

BACKGROUND

[0004] Diseases associated with expression of an aberrant gene product (*e.g.*, where the production of an aberrant RNA transcript or protein causes a disease) are often treated with a focus on affecting aberrant protein expression. However, targeting components of the splicing process responsible for production of aberrant RNA before the aberrant protein is expressed by using a small molecule may affect the underlying cause of a disease or disorder, and thus more efficiently prevent or ameliorate the disease or disorder caused by expression of the aberrant gene product. Accordingly, there is a need for methods of modulating the expression of aberrant RNA transcripts encoded by certain genes using small molecules to prevent or treat diseases associated with expression of aberrant RNA transcripts or associated proteins.

SUMMARY

[0005] In one aspect, provided herein is a recognition element for splicing modifier (otherwise referred to as “REMS”) present in an intron (*i.e.*, an “intronic REMS”) capable of being recognized by the U1 snRNP and/or other components of the pre-mRNA splicing machinery in the presence of a small molecule splicing modifier, whereby elements of the splicing reaction are affected as further described herein. In a specific embodiment, the intronic REMS comprises the nucleotide sequence GAgurngn (SEQ ID NO: 2) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n is any nucleotide. In another specific embodiment, the intronic REMS comprises the nucleotide sequence GAguragu (SEQ ID NO: 3866) at the RNA level, wherein r is adenine or guanine. In a specific embodiment, the intronic REMS comprises the nucleotide sequence NNGAgurngn (SEQ ID NO: 1) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n or N is any nucleotide. In another specific embodiment, the intronic REMS comprises the nucleotide sequence NNGAguragu (SEQ ID NO: 3862) at the RNA level, wherein r is adenine or guanine and N is any nucleotide. In one or more of such specific embodiments provided herein, N is adenine or guanine.

[0006] In another aspect, in addition to the intronic REMS sequence, the RNA transcript comprises an upstream branch point and a functional upstream iExon 3' splice site. In certain embodiments including, but not limited to, iExons, an exon 5' splice site, a branch point and the functional iExon 3' splice site upstream from the intronic REMS are further linked to a

downstream branch point and 3' splice site of a downstream exon (see, for example, Figure 1A). In other embodiments including, but not limited to, extended exons, the branch point and the functional 3' splice site for an exon are downstream from the intronic REMS sequences (see, for example, Figures 1B and 1C). In a particular embodiment, an RNA sequence comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, and wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site (also referred to as an iExon 3' splice site), an iREMS, a second branch point, and a second 3' splice site. In the presence of a compound described herein, the iREMS sequence functions as a 5' splice site, causing the NNGA (SEQ ID NO: 3863) nucleotides of the iREMS and the intronic nucleotides downstream of the first 3' splice site to be retained and spliced as an intronic exon to provide a non-wild-type mRNA. In other words, the nucleotides between the iREMS and the first 3' splice site are retained and form the intronic exon, which results in the expression of a non-wild-type mRNA sequence. In the presence of a compound described herein, the iREMS sequence functions as a 5' splice site, causing the NNGA (SEQ ID NO: 3863) nucleotides of the iREMS and the intronic nucleotides between the 3' iExon splice site to be retained and spliced as an intronic exon to provide a non-wild-type mRNA. In other aspects, in the presence of a compound described herein and a downstream branch point, the intronic REMS will undergo splicing with the 3' splice site of a downstream exon. In this aspect, the intronic REMS is located downstream of an exon such that there is no intervening upstream branch point and iExon 3' splice site between the exon and the REMS sequence. In the presence of a compound described herein, the exon 5' splice site does not undergo splicing with the downstream 3' splice site. Instead, functioning as a 5' splice site in the presence of a compound described herein, the iREMS sequence undergoes splicing with the downstream 3' splice site. In other embodiments, in the presence of a compound described herein, an upstream exon 5' splice site, an upstream branch point, and a functional iExon 3' splice site upstream from the intronic REMS, will undergo splicing. In certain embodiments, one or more sequence elements necessary to form an iExon splice junction may be present endogenously or non-endogenously. For example, one or more of the following sequence elements may be present naturally in an intron or an intron may be engineered to comprise one or more of the following sequences in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point, and a second 3' splice site. In certain

embodiments, one or more snRNPs and trans factor elements necessary for splicing may be present beyond endogenous levels as a result of the presence of a compound described herein at various splice inducing sequence combinations. Without being bound by any theory or mechanism, the small molecule compounds described herein, in conjunction with the iREMS sequence, initiate the assembly of a splicing-competent spliceosome around a weak or incompletely defined exon (i.e., a nascent iExon). Splicing modifier compounds most likely enable a functional U1 snRNP – REMS interaction and, at least, have been shown to increase the affinity of one or more snRNPs and trans factor elements necessary for splicing, including U1, U2, U4, U5 and U6, whereby the interaction between the U1 snRNP, as well as other components of the pre-mRNA splicing machinery, and the nucleotides NNGA (SEQ ID NO: 3863) of the REMS are enhanced. In fact, we have discovered that the interaction of the U1 snRNP, the iREMS and the small molecule splicing modifier compounds described herein serve to define nascent exons by increasing the binding affinity of the pre-mRNA splicing machinery to the iREMS sequence, stabilizing U1 binding with the iREMS sequence, activating a 3' splice site and a branch point upstream from the iREMS and recruiting U2 snRNP and other trans-acting splicing factors such as U2AF (U2AF65 and U2AF35) and SF3A (SF3A1, SF3A2 and SF3A3) to the upstream branch point and 3' splice site. The branch point and 3' splice site may or may not be fully occupied in the absence of the compound but have been shown to become occupied after the compound has enabled the formation of a functional U1 snRNP – REMS complex. We have elaborated on the interaction of these key splicing machinery elements, showing that, in the presence of small molecule splicing modifier compounds such as, but certainly not limited to, those described herein, the mechanism of intronic spliceosome assembly can be mediated by iREMS interaction with such compounds, such that the intronic REMS sequence functions as a U1 snRNP binding site, resulting in intronic nucleotides spliced in the mature RNA transcript as an intronic exon.

[0007] In Figure 1A, the intronic REMS is located in Intron 1 downstream from an Exon 1 5' splice site (i.e., a 5' splice site at the 3' end of Exon 1), a first branch point (BP) sequence and a first 3' splice site sequence and upstream from a second branch point sequence and a second 3' splice site sequence of Exon 2 in an RNA transcript (i.e., the precursor mRNA). In the presence of a small molecule splicing modifier compound described herein the intronic REMS functions as a 5' splice site, whereby the nucleotides between the Exon 1 5' splice site

and the first 3' splice site are removed to form a splice junction between Exon 1 and a nascent intronic exon and the nucleotides between the intronic REMS and the second 3' splice site sequence are removed to form a splice junction between iExon 1a and Exon 2, and allowing Exon 2 and the portion of the intron comprising nucleotides from the first 3' splice site up to and including NNGA (SEQ ID NO: 3863) of the intronic REMS to be joined, thus introducing an intron-derived iExon 1a, generating a non-wildtype mRNA. In certain embodiments of Figure 1A, one or more elements necessary to form a splice junction may be present endogenously or introduced, wherein the one or more elements are selected from the group consisting of the first branch point, the first 3' splice site, the intronic REMS, the second branch point and the second 3' splice site. While illustrated for Intron 1 here, this concept is generally applicable to any other intron in a pre-mRNA transcript.

[0008] In Figure 1B, the intronic REMS is located in an intron of an RNA transcript downstream from an Exon 1 5' splice site (*i.e.*, a 5' splice site at the 3' end of Exon 1) and upstream from an Intron 1 branch point sequence and a 3' splice site sequence of Exon 2 (*i.e.*, a 3' splice site at the 5' end of Exon 2). In the presence of a small molecule splicing modifier compound described herein, the nucleotides between the Exon 1 5' splice site and the intronic REMS are retained and those between the intronic REMS and the Intron 1 3' splice site sequence (except the NNGA (SEQ ID NO: 3863) nucleotides of the intronic REMS) are removed, allowing Exon 1 and the portion of the intron comprising nucleotides from those adjacent to the Exon 1 5' splice site up to and including NNGA (SEQ ID NO: 3863) of the intronic REMS and the Exon 2 nucleotides to be joined. The scope of the invention described herein is merely illustrated in this configuration for Exon 1 but is generally applicable to any other nascent iExon in an intronic sequence. The elements necessary to induce splicing of an iExon may be present in any configuration capable of recognition by the splicing machinery as an "exon."

Accordingly, in the presence of a splicing modifier compound, the spliceosome recognizes the elements as exonic boundaries for removal of intervening intronic nucleotides between those boundaries. The configuration in this instance results in an iExon spliced between at least one upstream exon and one downstream exon of the same pre-mRNA transcript.

[0009] In Figure 1C, the intronic REMS is located in Intron 2 downstream from an Exon 2 5' splice site (*i.e.*, a 5' splice site at the 3' end of Exon 2) and upstream from an Intron 2 branch point sequence and a 3' splice site sequence of Exon 3 (*i.e.*, a 3' splice site at the 5' end of Exon

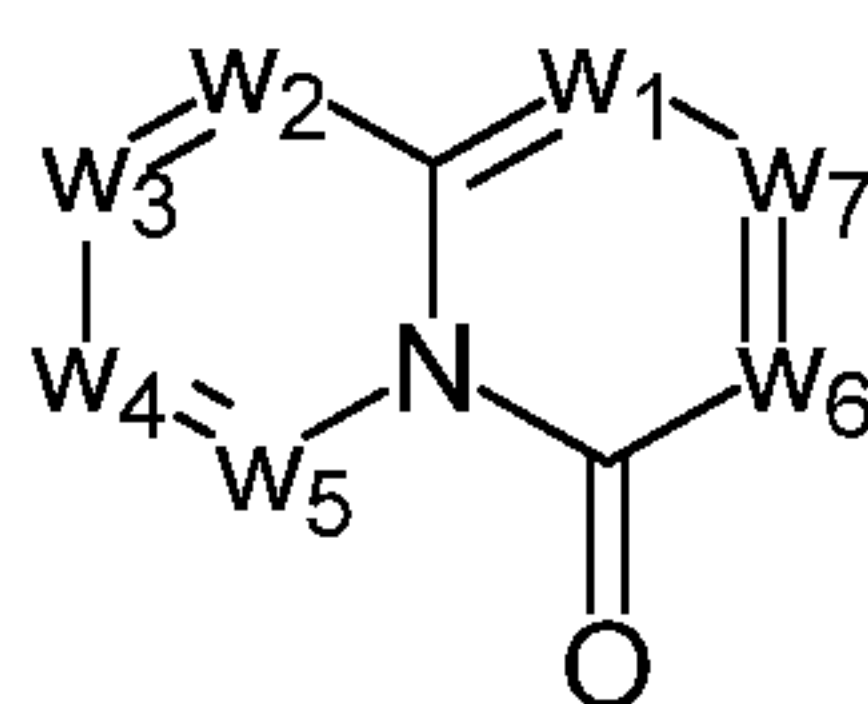
3) in an RNA transcript. In the presence of a small molecule splicing modifier compound described herein, the nucleotides between the intronic REMS and the Exon 3 3' splice site sequence are removed, allowing Exon 3 and the portion of the intron comprising nucleotides from those adjacent to the Exon 2 5' splice site up to and including NNGA (SEQ ID NO: 3863) of the intronic REMS to be joined. In this example, the endogenous splicing reaction between Exon 1 and Exon 2 is unaffected by the presence of a compound described herein, resulting in the complete removal of Intron 1. While illustrated for Exon 2 here, this concept is generally applicable to any other internal nascent intronic exon, i.e., an exon that is located between at least one upstream exon and one downstream exon of the same pre-mRNA transcript.

[0010] As used herein, an “exon 5' splice site”, a “5' splice site of an exon” or the like refers to a 5' splice site at the 3' end of the exon, while an “exon 3' splice site”, a “3' splice site of an exon” or the like refers to a 3' splice site at the 5' end of the exon.

[0011] In the presence of a small molecule splicing modifier compound described herein, the iREMS nucleotides retained in the formation of an iExon are selected from the group consisting of ANGA (SEQ ID NO: 5), CNGA (SEQ ID NO: 11), GNGA (SEQ ID NO: 17), UNGA (SEQ ID NO: 23), NAGA (SEQ ID NO: 6), NCGA (SEQ ID NO: 12), NGGA (SEQ ID NO: 18), NUGA (SEQ ID NO: 24), AAGA (SEQ ID NO: 7), ACGA (SEQ ID NO: 13), AGGA (SEQ ID NO: 19), AUGA (SEQ ID NO: 25), CAGA (SEQ ID NO: 8), CCGA (SEQ ID NO: 14), CGGA (SEQ ID NO: 20), CUGA (SEQ ID NO: 26), GAGA (SEQ ID NO: 9), GCGA (SEQ ID NO: 15), GGGA (SEQ ID NO: 21), GUGA (SEQ ID NO: 27), UAGA (SEQ ID NO: 10), UCGA (SEQ ID NO: 16), UGGA (SEQ ID NO: 22) and UUGA (SEQ ID NO: 28). The formation of an iExon may result in an RNA transcript having a non-functional open reading frame due to the inclusion of a frameshift, premature stop codon or internal deletions within the open reading frame. In other embodiments, the inclusion of an iExon may result in the mature mRNA having a functional open reading frame, producing a novel protein which may or may not be functional. RNA transcripts having a non-functional open reading frame due to the inclusion of a frameshift, premature stop codon or internal deletions within the open reading frame can be substrates for nonsense-mediated decay and thus have low abundance. Any intronic REMS-mediated alternative splicing modified RNA transcripts may also have altered stability, altered intracellular transport, altered 3' end formation efficiency and altered translation efficiency.

[0012] Accordingly, in one aspect, provided herein are methods for modulating the amount of RNA transcripts produced from precursor RNA containing an endogenous or non-endogenous intronic REMS. In another aspect, provided herein are artificial gene constructs comprising an endogenous or non-endogenous intronic REMS, which may be used in the context of, *e.g.*, gene therapy or reporter assays. In another aspect, provided herein are methods for altering endogenous genes so that they contain an intronic REMS or an additional intronic REMS.

[0013] In another aspect, provided herein are methods for modulating the amount of one or more RNA transcripts (*e.g.*, mRNA transcripts) or proteins thereof expressed as the product of one or more genes, wherein precursor RNA transcripts transcribed by the one or more genes comprise an intronic REMS, the methods comprising contacting a cell with a compound of Formula (I)



(I)

or a form thereof, wherein w_1 , w_2 , w_3 , w_4 , w_5 , w_6 and w_7 are as defined herein. In one embodiment, provided herein is a method for modulating the amount of an RNA transcript produced from precursor RNA containing an intronic recognition element for splicing modifier (REMS), the method comprising contacting a cell containing the precursor RNA with a compound of Formula (I) or a form thereof, wherein the intronic REMS comprises the sequence NNGAgurngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide, wherein the precursor RNA is a gene in Table 1. In certain embodiments, the precursor RNA is a gene in Table 7. In another embodiment, provided herein is a method for modulating the amount of an RNA transcript produced from precursor RNA containing an intronic recognition element for splicing modifier (REMS), the method comprising contacting the precursor RNA with a compound of Formula (I) or a form thereof, wherein the intronic REMS comprises the sequence NNGAgurngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide, wherein the precursor RNA is a gene in Table 1. In some embodiments, the intronic REMS comprises the sequence NNGAguragu (SEQ ID NO: 3862) at the RNA level, wherein r is adenine or guanine and N is any nucleotide. In certain embodiments, the intronic REMS

comprises a sequence selected from the group consisting of ANGAgurngn (SEQ ID NO: 29), CNGAgurngn (SEQ ID NO: 35), GNGAgurngn (SEQ ID NO: 41), UNGAgurngn (SEQ ID NO: 47), NAGAgurngn (SEQ ID NO: 30), NCGAgurngn (SEQ ID NO: 36), NGGAgurngn (SEQ ID NO: 42), NUGAgurngn (SEQ ID NO: 48), AAGAgurngn (SEQ ID NO: 31), ACGAgurngn (SEQ ID NO: 37), AGGAgurngn (SEQ ID NO: 43), AUGAgurngn (SEQ ID NO: 49), CAGAgurngn (SEQ ID NO: 32), CCGAgurngn (SEQ ID NO: 38), CGGAgurngn (SEQ ID NO: 44), CUGAgurngn (SEQ ID NO: 50), GAGAgurngn (SEQ ID NO: 33), GCGAgurngn (SEQ ID NO: 39), GGGAgurngn (SEQ ID NO: 45), GUGAgurngn (SEQ ID NO: 51), UAGAgurngn (SEQ ID NO: 34), UCGAgurngn (SEQ ID NO: 40), UGGAgurngn (SEQ ID NO: 46) and UUGAgurngn (SEQ ID NO: 52), wherein r is adenine or guanine and n or N is any nucleotide.

In some embodiments, the intronic REMS comprises a sequence selected from the group consisting of ANGAguragu (SEQ ID NO: 437), CNGAguragu (SEQ ID NO: 443), GNGAguragu (SEQ ID NO: 449), UNGAguragu (SEQ ID NO: 455), NAGAguragu (SEQ ID NO: 438), NCGAguragu (SEQ ID NO: 444), NGGAguragu (SEQ ID NO: 450), NUGAguragu (SEQ ID NO: 456), AAGAguragu (SEQ ID NO: 439), ACGAguragu (SEQ ID NO: 445), AGGAguragu (SEQ ID NO: 451), AUGAguragu (SEQ ID NO: 457), CAGAguragu (SEQ ID NO: 440), CCGAguragu (SEQ ID NO: 446), CGGAguragu (SEQ ID NO: 452), CUGAguragu (SEQ ID NO: 458), GAGAguragu (SEQ ID NO: 441), GCGAguragu (SEQ ID NO: 447), GGGAguragu (SEQ ID NO: 453), GUGAguragu (SEQ ID NO: 459), UAGAguragu (SEQ ID NO: 442), UCGAguragu (SEQ ID NO: 448), UGGAguragu (SEQ ID NO: 454) and UUGAguragu (SEQ ID NO: 460) at the RNA level, wherein r is adenine or guanine, and N is any nucleotide. In one or more embodiments provided herein, N is adenine or guanine.

[0014] In a specific embodiment, the intronic REMS referred to in a method or artificial gene construct described herein comprises, at the RNA level, a sequence presented in the following table (wherein r is adenine or guanine, and n or N is any nucleotide):

[0015] Table 13. Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
29	ANGAgurngn	35	CNGAgurngn	41	GNGAgurngn	47	UNGAgurngn
30	NAGAgurngn	36	NCGAgurngn	42	NGGAgurngn	48	NUGAgurngn
31	AAGAgurngn	37	ACGAgurngn	43	AGGAgurngn	49	AUGAgurngn
32	CAGAgurngn	38	CCGAgurngn	44	CGGAgurngn	50	CUGAgurngn
33	GAGAgurngn	39	GCGAgurngn	45	GGGAgurngn	51	GUGAgurngn
34	UAGAgurngn	40	UCGAgurngn	46	UGGAgurngn	52	UUGAgurngn

[0016] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
53	ANGAguragn	77	ANGAgurcgn	101	ANGAgurggn	125	ANGAgurugn
54	NAGAguragn	78	NAGAgurcgn	102	NAGAgurggn	126	NAGAgurugn
55	AAGAguragn	79	AAGAgurcgn	103	AAGAgurggn	127	AAGAgurugn
56	CAGAguragn	80	CAGAgurcgn	104	CAGAgurggn	128	CAGAgurugn
57	GAGAguragn	81	GAGAgurcgn	105	GAGAgurggn	129	GAGAgurugn
58	UAGAguragn	82	UAGAgurcgn	106	UAGAgurggn	130	UAGAgurugn
59	CNGAguragn	83	CNGAgurcgn	107	CNGAgurggn	131	CNGAgurugn
60	NCGAguragn	84	NCGAgurcgn	108	NCGAgurggn	132	NCGAgurugn
61	ACGAguragn	85	ACGAgurcgn	109	ACGAgurggn	133	ACGAgurugn
62	CCGAguragn	86	CCGAgurcgn	110	CCGAgurggn	134	CCGAgurugn
63	GCGAguragn	87	GCGAgurcgn	111	GCGAgurggn	135	GCGAgurugn
64	UCGAguragn	88	UCGAgurcgn	112	UCGAgurggn	136	UCGAgurugn
65	GNGAguragn	89	GNGAgurcgn	113	GNGAgurggn	137	GNGAgurugn
66	NGGAguragn	90	NGGAgurcgn	114	NGGAgurggn	138	NGGAgurugn
67	AGGAguragn	91	AGGAgurcgn	115	AGGAgurggn	139	AGGAgurugn
68	CGGAguragn	92	CGGAgurcgn	116	CGGAgurggn	140	CGGAgurugn
69	GGGAguragn	93	GGGAgurcgn	117	GGGAgurggn	141	GGGAgurugn
70	UGGAguragn	94	UGGAgurcgn	118	UGGAgurggn	142	UGGAgurugn
71	UNGAguragn	95	UNGAgurcgn	119	UNGAgurggn	143	UNGAgurugn
72	NUGAguragn	96	NUGAgurcgn	120	NUGAgurggn	144	NUGAgurugn
73	AUGAguragn	97	AUGAgurcgn	121	AUGAgurggn	145	AUGAgurugn
74	CUGAguragn	98	CUGAgurcgn	122	CUGAgurggn	146	CUGAgurugn
75	GUGAguragn	99	GUGAgurcgn	123	GUGAgurggn	147	GUGAgurugn
76	UUGAguragn	100	UUGAgurcgn	124	UUGAgurggn	148	UUGAgurugn

[0017] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
149	ANGAguraga	173	ANGAgurcga	197	ANGAgurgga	221	ANGAguruga
150	NAGAguraga	174	NAGAgurcga	198	NAGAgurgga	222	NAGAguruga
151	AAGAguraga	175	AAGAgurcga	199	AAGAgurgga	223	AAGAguruga
152	CAGAguraga	176	CAGAgurcga	200	CAGAgurgga	224	CAGAguruga
153	GAGAguraga	177	GAGAgurcga	201	GAGAgurgga	225	GAGAguruga
154	UAGAguraga	178	UAGAgurcga	202	UAGAgurgga	226	UAGAguruga
155	CNGAguraga	179	CNGAgurcga	203	CNGAgurgga	227	CNGAguruga
156	NCGAguraga	180	NCGAgurcga	204	NCGAgurgga	228	NCGAguruga
157	ACGAguraga	181	ACGAgurcga	205	ACGAgurgga	229	ACGAguruga
158	CCGAguraga	182	CCGAgurcga	206	CCGAgurgga	230	CCGAguruga
159	GCGAguraga	183	GCGAgurcga	207	GCGAgurgga	231	GCGAguruga
160	UCGAguraga	184	UCGAgurcga	208	UCGAgurgga	232	UCGAguruga
161	GNGAguraga	185	GNGAgurcga	209	GNGAgurgga	233	GNGAguruga
162	NGGAguraga	186	NGGAgurcga	210	NGGAgurgga	234	NGGAguruga
163	AGGAguraga	187	AGGAgurcga	211	AGGAgurgga	235	AGGAguruga
164	CGGAguraga	188	CGGAgurcga	212	CGGAgurgga	236	CGGAguruga
165	GGGAguraga	189	GGGAgurcga	213	GGGAgurgga	237	GGGAguruga
166	UGGAguraga	190	UGGAgurcga	214	UGGAgurgga	238	UGGAguruga
167	UNGAguraga	191	UNGAgurcga	215	UNGAgurgga	239	UNGAguruga
168	NUGAguraga	192	NUGAgurcga	216	NUGAgurgga	240	NUGAguruga
169	AUGAguraga	193	AUGAgurcga	217	AUGAgurgga	241	AUGAguruga
170	CUGAguraga	194	CUGAgurcga	218	CUGAgurgga	242	CUGAguruga
171	GUGAguraga	195	GUGAgurcga	219	GUGAgurgga	243	GUGAguruga
172	UUGAguraga	196	UUGAgurcga	220	UUGAgurgga	244	UUGAguruga

[0018] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
245	ANGAguragc	269	ANGAgurcgc	293	ANGAgurggc	317	ANGAgurugc
246	NAGAguragc	270	NAGAgurcgc	294	NAGAgurggc	318	NAGAgurugc
247	AAGAguragc	271	AAGAgurcgc	295	AAGAgurggc	319	AAGAgurugc
248	CAGAguragc	272	CAGAgurcgc	296	CAGAgurggc	320	CAGAgurugc
249	GAGAguragc	273	GAGAgurcgc	297	GAGAgurggc	321	GAGAgurugc
250	UAGAguragc	274	UAGAgurcgc	298	UAGAgurggc	322	UAGAgurugc
251	CNGAguragc	275	CNGAgurcgc	299	CNGAgurggc	323	CNGAgurugc
252	NCGAguragc	276	NCGAgurcgc	300	NCGAgurggc	324	NCGAgurugc
253	ACGAguragc	277	ACGAgurcgc	301	ACGAgurggc	325	ACGAgurugc
254	CCGAguragc	278	CCGAgurcgc	302	CCGAgurggc	326	CCGAgurugc
255	GCGAguragc	279	GCGAgurcgc	303	GCGAgurggc	327	GCGAgurugc
256	UCGAguragc	280	UCGAgurcgc	304	UCGAgurggc	328	UCGAgurugc
257	GNGAguragc	281	GNGAgurcgc	305	GNGAgurggc	329	GNGAgurugc
258	NGGAguragc	282	NGGAgurcgc	306	NGGAgurggc	330	NGGAgurugc
259	AGGAguragc	283	AGGAgurcgc	307	AGGAgurggc	331	AGGAgurugc
260	CGGAguragc	284	CGGAgurcgc	308	CGGAgurggc	332	CGGAgurugc
261	GGGAguragc	285	GGGAgurcgc	309	GGGAgurggc	333	GGGAgurugc
262	UGGAguragc	286	UGGAgurcgc	310	UGGAgurggc	334	UGGAgurugc
263	UNGAguragc	287	UNGAgurcgc	311	UNGAgurggc	335	UNGAgurugc
264	NUGAguragc	288	NUGAgurcgc	312	NUGAgurggc	336	NUGAgurugc
265	AUGAguragc	289	AUGAgurcgc	313	AUGAgurggc	337	AUGAgurugc
266	CUGAguragc	290	CUGAgurcgc	314	CUGAgurggc	338	CUGAgurugc
267	GUGAguragc	291	GUGAgurcgc	315	GUGAgurggc	339	GUGAgurugc
268	UUGAguragc	292	UUGAgurcgc	316	UUGAgurggc	340	UUGAgurugc

[0019] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
341	ANGAguragg	365	ANGAgurcgg	389	ANGAgurggg	413	ANGAgurugg
342	NAGAguragg	366	NAGAgurcgg	390	NAGAgurggg	414	NAGAgurugg
343	AAGAguragg	367	AAGAgurcgg	391	AAGAgurggg	415	AAGAgurugg
344	CAGAguragg	368	CAGAgurcgg	392	CAGAgurggg	416	CAGAgurugg
345	GAGAguragg	369	GAGAgurcgg	393	GAGAgurggg	417	GAGAgurugg
346	UAGAguragg	370	UAGAgurcgg	394	UAGAgurggg	418	UAGAgurugg
347	CNGAguragg	371	CNGAgurcgg	395	CNGAgurggg	419	CNGAgurugg
348	NCGAguragg	372	NCGAgurcgg	396	NCGAgurggg	420	NCGAgurugg
349	ACGAguragg	373	ACGAgurcgg	397	ACGAgurggg	421	ACGAgurugg
350	CCGAguragg	374	CCGAgurcgg	398	CCGAgurggg	422	CCGAgurugg
351	GCGAguragg	375	GCGAgurcgg	399	GCGAgurggg	423	GCGAgurugg
352	UCGAguragg	376	UCGAgurcgg	400	UCGAgurggg	424	UCGAgurugg
353	GNGAguragg	377	GNGAgurcgg	401	GNGAgurggg	425	GNGAgurugg
354	NGGAguragg	378	NGGAgurcgg	402	NGGAgurggg	426	NGGAgurugg
355	AGGAguragg	379	AGGAgurcgg	403	AGGAgurggg	427	AGGAgurugg
356	CGGAguragg	380	CGGAgurcgg	404	CGGAgurggg	428	CGGAgurugg
357	GGGAguragg	381	GGGAgurcgg	405	GGGAgurggg	429	GGGAgurugg
358	UGGAguragg	382	UGGAgurcgg	406	UGGAgurggg	430	UGGAgurugg
359	UNGAguragg	383	UNGAgurcgg	407	UNGAgurggg	431	UNGAgurugg
360	NUGAguragg	384	NUGAgurcgg	408	NUGAgurggg	432	NUGAgurugg
361	AUGAguragg	385	AUGAgurcgg	409	AUGAgurggg	433	AUGAgurugg
362	CUGAguragg	386	CUGAgurcgg	410	CUGAgurggg	434	CUGAgurugg
363	GUGAguragg	387	GUGAgurcgg	411	GUGAgurggg	435	GUGAgurugg
364	UUGAguragg	388	UUGAgurcgg	412	UUGAgurggg	436	UUGAgurugg

[0020] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
437	ANGAguragu	461	ANGAgurcgu	485	ANGAgurggu	509	ANGAgurugu
438	NAGAguragu	462	NAGAgurcgu	486	NAGAgurggu	510	NAGAgurugu
439	AAGAguragu	463	AAGAgurcgu	487	AAGAgurggu	511	AAGAgurugu
440	CAGAguragu	464	CAGAgurcgu	488	CAGAgurggu	512	CAGAgurugu
441	GAGAguragu	465	GAGAgurcgu	489	GAGAgurggu	513	GAGAgurugu
442	UAGAguragu	466	UAGAgurcgu	490	UAGAgurggu	514	UAGAgurugu
443	CNGAguragu	467	CNGAgurcgu	491	CNGAgurggu	515	CNGAgurugu
444	NCGAguragu	468	NCGAgurcgu	492	NCGAgurggu	516	NCGAgurugu
445	ACGAguragu	469	ACGAgurcgu	493	ACGAgurggu	517	ACGAgurugu
446	CCGAguragu	470	CCGAgurcgu	494	CCGAgurggu	518	CCGAgurugu
447	GCGAguragu	471	GCGAgurcgu	495	GCGAgurggu	519	GCGAgurugu
448	UCGAguragu	472	UCGAgurcgu	496	UCGAgurggu	520	UCGAgurugu
449	GNGAguragu	473	GNGAgurcgu	497	GNGAgurggu	521	GNGAgurugu
450	NGGAguragu	474	NGGAgurcgu	498	NGGAgurggu	522	NGGAgurugu
451	AGGAguragu	475	AGGAgurcgu	499	AGGAgurggu	523	AGGAgurugu
452	CGGAguragu	476	CGGAgurcgu	500	CGGAgurggu	524	CGGAgurugu
453	GGGAguragu	477	GGGAgurcgu	501	GGGAgurggu	525	GGGAgurugu
454	UGGAguragu	478	UGGAgurcgu	502	UGGAgurggu	526	UGGAgurugu
455	UNGAguragu	479	UNGAgurcgu	503	UNGAgurggu	527	UNGAgurugu
456	NUGAguragu	480	NUGAgurcgu	504	NUGAgurggu	528	NUGAgurugu
457	AUGAguragu	481	AUGAgurcgu	505	AUGAgurggu	529	AUGAgurugu
458	CUGAguragu	482	CUGAgurcgu	506	CUGAgurggu	530	CUGAgurugu
459	GUGAguragu	483	GUGAgurcgu	507	GUGAgurggu	531	GUGAgurugu
460	UUGAguragu	484	UUGAgurcgu	508	UUGAgurggu	532	UUGAgurugu

[0021] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
533	ANGAgurnga	557	ANGAgurngc	581	ANGAgurngg	605	ANGAgurngu
534	NAGAgurnga	558	NAGAgurngc	582	NAGAgurngg	606	NAGAgurngu
535	AAGAgurnga	559	AAGAgurngc	583	AAGAgurngg	607	AAGAgurngu
536	CAGAgurnga	560	CAGAgurngc	584	CAGAgurngg	608	CAGAgurngu
537	GAGAgurnga	561	GAGAgurngc	585	GAGAgurngg	609	GAGAgurngu
538	UAGAgurnga	562	UAGAgurngc	586	UAGAgurngg	610	UAGAgurngu
539	CNGAgurnga	563	CNGAgurngc	587	CNGAgurngg	611	CNGAgurngu
540	NCGAgurnga	564	NCGAgurngc	588	NCGAgurngg	612	NCGAgurngu
541	ACGAgurnga	565	ACGAgurngc	589	ACGAgurngg	613	ACGAgurngu
542	CCGAgurnga	566	CCGAgurngc	590	CCGAgurngg	614	CCGAgurngu
543	GCGAgurnga	567	GCGAgurngc	591	GCGAgurngg	615	GCGAgurngu
544	UCGAgurnga	568	UCGAgurngc	592	UCGAgurngg	616	UCGAgurngu
545	GNGAgurnga	569	GNGAgurngc	593	GNGAgurngg	617	GNGAgurngu
546	NGGAgurnga	570	NGGAgurngc	594	NGGAgurngg	618	NGGAgurngu
547	AGGAgurnga	571	AGGAgurngc	595	AGGAgurngg	619	AGGAgurngu
548	CGGAgurnga	572	CGGAgurngc	596	CGGAgurngg	620	CGGAgurngu
549	GGGAgurnga	573	GGGAgurngc	597	GGGAgurngg	621	GGGAgurngu
550	UGGAgurnga	574	UGGAgurngc	598	UGGAgurngg	622	UGGAgurngu
551	UNGAgurnga	575	UNGAgurngc	599	UNGAgurngg	623	UNGAgurngu
552	NUGAgurnga	576	NUGAgurngc	600	NUGAgurngg	624	NUGAgurngu
553	AUGAgurnga	577	AUGAgurngc	601	AUGAgurngg	625	AUGAgurngu
554	CUGAgurnga	578	CUGAgurngc	602	CUGAgurngg	626	CUGAgurngu
555	GUGAgurnga	579	GUGAgurngc	603	GUGAgurngg	627	GUGAgurngu
556	UUGAgurnga	580	UUGAgurngc	604	UUGAgurngg	628	UUGAgurngu

[0022] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
629	ANGAguangn	653	ANGAguaagn	677	ANGAguacgn	701	ANGAguaggn
630	NAGAguangn	654	NAGAguaagn	678	NAGAguacgn	702	NAGAguaggn
631	AAGAguangn	655	AAGAguaagn	679	AAGAguacgn	703	AAGAguaggn
632	CAGAguangn	656	CAGAguaagn	680	CAGAguacgn	704	CAGAguaggn
633	GAGAguangn	657	GAGAguaagn	681	GAGAguacgn	705	GAGAguaggn
634	UAGAguangn	658	UAGAguaagn	682	UAGAguacgn	706	UAGAguaggn
635	CNGAguangn	659	CNGAguaagn	683	CNGAguacgn	707	CNGAguaggn
636	NCGAguangn	660	NCGAguaagn	684	NCGAguacgn	708	NCGAguaggn
637	ACGAguangn	661	ACGAguaagn	685	ACGAguacgn	709	ACGAguaggn
638	CCGAguangn	662	CCGAguaagn	686	CCGAguacgn	710	CCGAguaggn
639	GCGAguangn	663	GCGAguaagn	687	GCGAguacgn	711	GCGAguaggn
640	UCGAguangn	664	UCGAguaagn	688	UCGAguacgn	712	UCGAguaggn
641	GNGAguangn	665	GNGAguaagn	689	GNGAguacgn	713	GNGAguaggn
642	NGGAguangn	666	NGGAguaagn	690	NGGAguacgn	714	NGGAguaggn
643	AGGAguangn	667	AGGAguaagn	691	AGGAguacgn	715	AGGAguaggn
644	CGGAguangn	668	CGGAguaagn	692	CGGAguacgn	716	CGGAguaggn
645	GGGAguangn	669	GGGAguaagn	693	GGGAguacgn	717	GGGAguaggn
646	UGGAguangn	670	UGGAguaagn	694	UGGAguacgn	718	UGGAguaggn
647	UNGAguangn	671	UNGAguaagn	695	UNGAguacgn	719	UNGAguaggn
648	NUGAguangn	672	NUGAguaagn	696	NUGAguacgn	720	NUGAguaggn
649	AUGAguangn	673	AUGAguaagn	697	AUGAguacgn	721	AUGAguaggn
650	CUGAguangn	674	CUGAguaagn	698	CUGAguacgn	722	CUGAguaggn
651	GUGAguangn	675	GUGAguaagn	699	GUGAguacgn	723	GUGAguaggn
652	UUGAguangn	676	UUGAguaagn	700	UUGAguacgn	724	UUGAguaggn

[0023] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
725	ANGAguaugn	749	ANGAguaaaga	773	ANGAguacga	797	ANGAguagga
726	NAGAguaugn	750	NAGAguaaaga	774	NAGAguacga	798	NAGAguagga
727	AAGAguaugn	751	AAGAguaaaga	775	AAGAguacga	799	AAGAguagga
728	CAGAguaugn	752	CAGAguaaaga	776	CAGAguacga	800	CAGAguagga
729	GAGAguaugn	753	GAGAguaaaga	777	GAGAguacga	801	GAGAguagga
730	UAGAguaugn	754	UAGAguaaaga	778	UAGAguacga	802	UAGAguagga
731	CNGAguaugn	755	CNGAguaaaga	779	CNGAguacga	803	CNGAguagga
732	NCGAguaugn	756	NCGAguaaaga	780	NCGAguacga	804	NCGAguagga
733	ACGAguaugn	757	ACGAguaaaga	781	ACGAguacga	805	ACGAguagga
734	CCGAguaugn	758	CCGAguaaaga	782	CCGAguacga	806	CCGAguagga
735	GCGAguaugn	759	GCGAguaaaga	783	GCGAguacga	807	GCGAguagga
736	UCGAguaugn	760	UCGAguaaaga	784	UCGAguacga	808	UCGAguagga
737	GNGAguaugn	761	GNGAguaaaga	785	GNGAguacga	809	GNGAguagga
738	NGGAguaugn	762	NGGAguaaaga	786	NGGAguacga	810	NGGAguagga
739	AGGAguaugn	763	AGGAguaaaga	787	AGGAguacga	811	AGGAguagga
740	CGGAguaugn	764	CGGAguaaaga	788	CGGAguacga	812	CGGAguagga
741	GGGAguaugn	765	GGGAguaaaga	789	GGGAguacga	813	GGGAguagga
742	UGGAguaugn	766	UGGAguaaaga	790	UGGAguacga	814	UGGAguagga
743	UNGAguaugn	767	UNGAguaaaga	791	UNGAguacga	815	UNGAguagga
744	NUGAguaugn	768	NUGAguaaaga	792	NUGAguacga	816	NUGAguagga
745	AUGAguaugn	769	AUGAguaaaga	793	AUGAguacga	817	AUGAguagga
746	CUGAguaugn	770	CUGAguaaaga	794	CUGAguacga	818	CUGAguagga
747	GUGAguaugn	771	GUGAguaaaga	795	GUGAguacga	819	GUGAguagga
748	UUGAguaugn	772	UUGAguaaaga	796	UUGAguacga	820	UUGAguagga

[0024] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
821	ANGAuauga	845	ANGAuaagc	869	ANGAuaacgc	893	ANGAuaaggc
822	NAGAuauga	846	NAGAuaagc	870	NAGAuaacgc	894	NAGAuaaggc
823	AAGAuauga	847	AAGAuaagc	871	AAGAuaacgc	895	AAGAuaaggc
824	CAGAuauga	848	CAGAuaagc	872	CAGAuaacgc	896	CAGAuaaggc
825	GAGAuauga	849	GAGAuaagc	873	GAGAuaacgc	897	GAGAuaaggc
826	UAGAuauga	850	UAGAuaagc	874	UAGAuaacgc	898	UAGAuaaggc
827	CNGAuauga	851	CNGAuaagc	875	CNGAuaacgc	899	CNGAuaaggc
828	NCGAuauga	852	NCGAuaagc	876	NCGAuaacgc	900	NCGAuaaggc
829	ACGAuauga	853	ACGAuaagc	877	ACGAuaacgc	901	ACGAuaaggc
830	CCGAuauga	854	CCGAuaagc	878	CCGAuaacgc	902	CCGAuaaggc
831	GCGAuauga	855	GCGAuaagc	879	GCGAuaacgc	903	GCGAuaaggc
832	UCGAuauga	856	UCGAuaagc	880	UCGAuaacgc	904	UCGAuaaggc
833	GNGAuauga	857	GNGAuaagc	881	GNGAuaacgc	905	GNGAuaaggc
834	NGGAuauga	858	NGGAuaagc	882	NGGAuaacgc	906	NGGAuaaggc
835	AGGAuauga	859	AGGAuaagc	883	AGGAuaacgc	907	AGGAuaaggc
836	CGGAuauga	860	CGGAuaagc	884	CGGAuaacgc	908	CGGAuaaggc
837	GGGAuauga	861	GGGAuaagc	885	GGGAuaacgc	909	GGGAuaaggc
838	UGGAuauga	862	UGGAuaagc	886	UGGAuaacgc	910	UGGAuaaggc
839	UNGAuauga	863	UNGAuaagc	887	UNGAuaacgc	911	UNGAuaaggc
840	NUGAuauga	864	NUGAuaagc	888	NUGAuaacgc	912	NUGAuaaggc
841	AUGAuauga	865	AUGAuaagc	889	AUGAuaacgc	913	AUGAuaaggc
842	CUGAuauga	866	CUGAuaagc	890	CUGAuaacgc	914	CUGAuaaggc
843	GUGAuauga	867	GUGAuaagc	891	GUGAuaacgc	915	GUGAuaaggc
844	UUGAuauga	868	UUGAuaagc	892	UUGAuaacgc	916	UUGAuaaggc

[0025] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
917	ANGAguaucg	941	ANGAguaaagg	965	ANGAguacgg	989	ANGAguagggg
918	NAGAguaucg	942	NAGAguaaagg	966	NAGAguacgg	990	NAGAguagggg
919	AAGAguaucg	943	AAGAguaaagg	967	AAGAguacgg	991	AAGAguagggg
920	CAGAguaucg	944	CAGAguaaagg	968	CAGAguacgg	992	CAGAguagggg
921	GAGAguaucg	945	GAGAguaaagg	969	GAGAguacgg	993	GAGAguagggg
922	UAGAguaucg	946	UAGAguaaagg	970	UAGAguacgg	994	UAGAguagggg
923	CNGAguaucg	947	CNGAguaaagg	971	CNGAguacgg	995	CNGAguagggg
924	NCGAguaucg	948	NCGAguaaagg	972	NCGAguacgg	996	NCGAguagggg
925	ACGAguaucg	949	ACGAguaaagg	973	ACGAguacgg	997	ACGAguagggg
926	CCGAguaucg	950	CCGAguaaagg	974	CCGAguacgg	998	CCGAguagggg
927	GCGAguaucg	951	GCGAguaaagg	975	GCGAguacgg	999	GCGAguagggg
928	UCGAguaucg	952	UCGAguaaagg	976	UCGAguacgg	1000	UCGAguagggg
929	GNGAguaucg	953	GNGAguaaagg	977	GNGAguacgg	1001	GNGAguagggg
930	NGGAguaucg	954	NGGAguaaagg	978	NGGAguacgg	1002	NGGAguagggg
931	AGGAguaucg	955	AGGAguaaagg	979	AGGAguacgg	1003	AGGAguagggg
932	CGGAguaucg	956	CGGAguaaagg	980	CGGAguacgg	1004	CGGAguagggg
933	GGGAguaucg	957	GGGAguaaagg	981	GGGAguacgg	1005	GGGAguagggg
934	UGGAguaucg	958	UGGAguaaagg	982	UGGAguacgg	1006	UGGAguagggg
935	UNGAguaucg	959	UNGAguaaagg	983	UNGAguacgg	1007	UNGAguagggg
936	NUGAguaucg	960	NUGAguaaagg	984	NUGAguacgg	1008	NUGAguagggg
937	AUGAguaucg	961	AUGAguaaagg	985	AUGAguacgg	1009	AUGAguagggg
938	CUGAguaucg	962	CUGAguaaagg	986	CUGAguacgg	1010	CUGAguagggg
939	GUGAguaucg	963	GUGAguaaagg	987	GUGAguacgg	1011	GUGAguagggg
940	UUGAguaucg	964	UUGAguaaagg	988	UUGAguacgg	1012	UUGAguagggg

[0026] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1013	ANGAguauagg	1037	ANGAguaaagu	1061	ANGAguuacgu	1085	ANGAguuaggu
1014	NAGAguauagg	1038	NAGAguaaagu	1062	NAGAguuacgu	1086	NAGAguuaggu
1015	AAGAguauagg	1039	AAGAguaaagu	1063	AAGAguuacgu	1087	AAGAguuaggu
1016	CAGAguauagg	1040	CAGAguaaagu	1064	CAGAguuacgu	1088	CAGAguuaggu
1017	GAGAguauagg	1041	GAGAguaaagu	1065	GAGAguuacgu	1089	GAGAguuaggu
1018	UAGAguauagg	1042	UAGAguaaagu	1066	UAGAguuacgu	1090	UAGAguuaggu
1019	CNGAguauagg	1043	CNGAguaaagu	1067	CNGAguuacgu	1091	CNGAguuaggu
1020	NCGAguauagg	1044	NCGAguaaagu	1068	NCGAguuacgu	1092	NCGAguuaggu
1021	ACGAguauagg	1045	ACGAguaaagu	1069	ACGAguuacgu	1093	ACGAguuaggu
1022	CCGAguauagg	1046	CCGAguaaagu	1070	CCGAguuacgu	1094	CCGAguuaggu
1023	GCGAguauagg	1047	GCGAguaaagu	1071	GCGAguuacgu	1095	GCGAguuaggu
1024	UCGAguauagg	1048	UCGAguaaagu	1072	UCGAguuacgu	1096	UCGAguuaggu
1025	GNGAguauagg	1049	GNGAguaaagu	1073	GNGAguuacgu	1097	GNGAguuaggu
1026	NGGAguauagg	1050	NGGAguaaagu	1074	NGGAguuacgu	1098	NGGAguuaggu
1027	AGGAguauagg	1051	AGGAguaaagu	1075	AGGAguuacgu	1099	AGGAguuaggu
1028	CGGAguauagg	1052	CGGAguaaagu	1076	CGGAguuacgu	1100	CGGAguuaggu
1029	GGGAguauagg	1053	GGGAguaaagu	1077	GGGAguuacgu	1101	GGGAguuaggu
1030	UGGAguauagg	1054	UGGAguaaagu	1078	UGGAguuacgu	1102	UGGAguuaggu
1031	UNGAguauagg	1055	UNGAguaaagu	1079	UNGAguuacgu	1103	UNGAguuaggu
1032	NUGAguauagg	1056	NUGAguaaagu	1080	NUGAguuacgu	1104	NUGAguuaggu
1033	AUGAguauagg	1057	AUGAguaaagu	1081	AUGAguuacgu	1105	AUGAguuaggu
1034	CUGAguauagg	1058	CUGAguaaagu	1082	CUGAguuacgu	1106	CUGAguuaggu
1035	GUGAguauagg	1059	GUGAguaaagu	1083	GUGAguuacgu	1107	GUGAguuaggu
1036	UUGAguauagg	1060	UUGAguaaagu	1084	UUGAguuacgu	1108	UUGAguuaggu

[0027] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1109	ANGAguaugu	1133	ANGAguanga	1157	ANGAguangc	1181	ANGAguanggg
1110	NAGAguaugu	1134	NAGAguanga	1158	NAGAguangc	1182	NAGAguanggg
1111	AAGAguaugu	1135	AAGAguanga	1159	AAGAguangc	1183	AAGAguanggg
1112	CAGAguaugu	1136	CAGAguanga	1160	CAGAguangc	1184	CAGAguanggg
1113	GAGAguaugu	1137	GAGAguanga	1161	GAGAguangc	1185	GAGAguanggg
1114	UAGAguaugu	1138	UAGAguanga	1162	UAGAguangc	1186	UAGAguanggg
1115	CNGAguaugu	1139	CNGAguanga	1163	CNGAguangc	1187	CNGAguanggg
1116	NCGAguaugu	1140	NCGAguanga	1164	NCGAguangc	1188	NCGAguanggg
1117	ACGAguaugu	1141	ACGAguanga	1165	ACGAguangc	1189	ACGAguanggg
1118	CCGAguaugu	1142	CCGAguanga	1166	CCGAguangc	1190	CCGAguanggg
1119	GCGAguaugu	1143	GCGAguanga	1167	GCGAguangc	1191	GCGAguanggg
1120	UCGAguaugu	1144	UCGAguanga	1168	UCGAguangc	1192	UCGAguanggg
1121	GNGAguaugu	1145	GNGAguanga	1169	GNGAguangc	1193	GNGAguanggg
1122	NGGAguaugu	1146	NGGAguanga	1170	NGGAguangc	1194	NGGAguanggg
1123	AGGAguaugu	1147	AGGAguanga	1171	AGGAguangc	1195	AGGAguanggg
1124	CGGAguaugu	1148	CGGAguanga	1172	CGGAguangc	1196	CGGAguanggg
1125	GGGAguaugu	1149	GGGAguanga	1173	GGGAguangc	1197	GGGAguanggg
1126	UGGAguaugu	1150	UGGAguanga	1174	UGGAguangc	1198	UGGAguanggg
1127	UNGAguaugu	1151	UNGAguanga	1175	UNGAguangc	1199	UNGAguanggg
1128	NUGAguaugu	1152	NUGAguanga	1176	NUGAguangc	1200	NUGAguanggg
1129	AUGAguaugu	1153	AUGAguanga	1177	AUGAguangc	1201	AUGAguanggg
1130	CUGAguaugu	1154	CUGAguanga	1178	CUGAguangc	1202	CUGAguanggg
1131	GUGAguaugu	1155	GUGAguanga	1179	GUGAguangc	1203	GUGAguanggg
1132	UUGAguaugu	1156	UUGAguanga	1180	UUGAguangc	1204	UUGAguanggg

[0028] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1205	ANGAguangu	1229	ANGAgugngn	1253	ANGAgugagn	1277	ANGAgugcgn
1206	NAGAguangu	1230	NAGAgugngn	1254	NAGAgugagn	1278	NAGAgugcgn
1207	AAGAguangu	1231	AAGAgugngn	1255	AAGAgugagn	1279	AAGAgugcgn
1208	CAGAguangu	1232	CAGAgugngn	1256	CAGAgugagn	1280	CAGAgugcgn
1209	GAGAguangu	1233	GAGAgugngn	1257	GAGAgugagn	1281	GAGAgugcgn
1210	UAGAguangu	1234	UAGAgugngn	1258	UAGAgugagn	1282	UAGAgugcgn
1211	CNGAguangu	1235	CNGAgugngn	1259	CNGAgugagn	1283	CNGAgugcgn
1212	NCGAguangu	1236	NCGAgugngn	1260	NCGAgugagn	1284	NCGAgugcgn
1213	ACGAguangu	1237	ACGAgugngn	1261	ACGAgugagn	1285	ACGAgugcgn
1214	CCGAguangu	1238	CCGAgugngn	1262	CCGAgugagn	1286	CCGAgugcgn
1215	GCGAguangu	1239	GCGAgugngn	1263	GCGAgugagn	1287	GCGAgugcgn
1216	UCGAguangu	1240	UCGAgugngn	1264	UCGAgugagn	1288	UCGAgugcgn
1217	GNGAguangu	1241	GNGAgugngn	1265	GNGAgugagn	1289	GNGAgugcgn
1218	NGGAguangu	1242	NGGAgugngn	1266	NGGAgugagn	1290	NGGAgugcgn
1219	AGGAguangu	1243	AGGAgugngn	1267	AGGAgugagn	1291	AGGAgugcgn
1220	CGGAguangu	1244	CGGAgugngn	1268	CGGAgugagn	1292	CGGAgugcgn
1221	GGGAguangu	1245	GGGAgugngn	1269	GGGAgugagn	1293	GGGAgugcgn
1222	UGGAguangu	1246	UGGAgugngn	1270	UGGAgugagn	1294	UGGAgugcgn
1223	UNGAguangu	1247	UNGAgugngn	1271	UNGAgugagn	1295	UNGAgugcgn
1224	NUGAguangu	1248	NUGAgugngn	1272	NUGAgugagn	1296	NUGAgugcgn
1225	AUGAguangu	1249	AUGAgugngn	1273	AUGAgugagn	1297	AUGAgugcgn
1226	CUGAguangu	1250	CUGAgugngn	1274	CUGAgugagn	1298	CUGAgugcgn
1227	GUGAguangu	1251	GUGAgugngn	1275	GUGAgugagn	1299	GUGAgugcgn
1228	UUGAguangu	1252	UUGAgugngn	1276	UUGAgugagn	1300	UUGAgugcgn

[0029] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1301	ANGAgugggn	1325	ANGAgugugn	1349	ANGAgugaga	1373	ANGAgugcga
1302	NAGAgugggn	1326	NAGAgugugn	1350	NAGAgugaga	1374	NAGAgugcga
1303	AAGAgugggn	1327	AAGAgugugn	1351	AAGAgugaga	1375	AAGAgugcga
1304	CAGAgugggn	1328	CAGAgugugn	1352	CAGAgugaga	1376	CAGAgugcga
1305	GAGAgugggn	1329	GAGAgugugn	1353	GAGAgugaga	1377	GAGAgugcga
1306	UAGAgugggn	1330	UAGAgugugn	1354	UAGAgugaga	1378	UAGAgugcga
1307	CNGAgugggn	1331	CNGAgugugn	1355	CNGAgugaga	1379	CNGAgugcga
1308	NCGAgugggn	1332	NCGAgugugn	1356	NCGAgugaga	1380	NCGAgugcga
1309	ACGAgugggn	1333	ACGAgugugn	1357	ACGAgugaga	1381	ACGAgugcga
1310	CCGAgugggn	1334	CCGAgugugn	1358	CCGAgugaga	1382	CCGAgugcga
1311	GCGAgugggn	1335	GCGAgugugn	1359	GCGAgugaga	1383	GCGAgugcga
1312	UCGAgugggn	1336	UCGAgugugn	1360	UCGAgugaga	1384	UCGAgugcga
1313	GNGAgugggn	1337	GNGAgugugn	1361	GNGAgugaga	1385	GNGAgugcga
1314	NGGAgugggn	1338	NGGAgugugn	1362	NGGAgugaga	1386	NGGAgugcga
1315	AGGAgugggn	1339	AGGAgugugn	1363	AGGAgugaga	1387	AGGAgugcga
1316	CGGAgugggn	1340	CGGAgugugn	1364	CGGAgugaga	1388	CGGAgugcga
1317	GGGAgugggn	1341	GGGAgugugn	1365	GGGAgugaga	1389	GGGAgugcga
1318	UGGAgugggn	1342	UGGAgugugn	1366	UGGAgugaga	1390	UGGAgugcga
1319	UNGAgugggn	1343	UNGAgugugn	1367	UNGAgugaga	1391	UNGAgugcga
1320	NUGAgugggn	1344	NUGAgugugn	1368	NUGAgugaga	1392	NUGAgugcga
1321	AUGAgugggn	1345	AUGAgugugn	1369	AUGAgugaga	1393	AUGAgugcga
1322	CUGAgugggn	1346	CUGAgugugn	1370	CUGAgugaga	1394	CUGAgugcga
1323	GUGAgugggn	1347	GUGAgugugn	1371	GUGAgugaga	1395	GUGAgugcga
1324	UUGAgugggn	1348	UUGAgugugn	1372	UUGAgugaga	1396	UUGAgugcga

[0030] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1397	ANGAguggga	1421	ANGAguguga	1445	ANGAgugagc	1469	ANGAgugcgc
1398	NAGAguggga	1422	NAGAguguga	1446	NAGAgugagc	1470	NAGAgugcgc
1399	AAGAguggga	1423	AAGAguguga	1447	AAGAgugagc	1471	AAGAgugcgc
1400	CAGAguggga	1424	CAGAguguga	1448	CAGAgugagc	1472	CAGAgugcgc
1401	GAGAguggga	1425	GAGAguguga	1449	GAGAgugagc	1473	GAGAgugcgc
1402	UAGAguggga	1426	UAGAguguga	1450	UAGAgugagc	1474	UAGAgugcgc
1403	CNGAguggga	1427	CNGAguguga	1451	CNGAgugagc	1475	CNGAgugcgc
1404	NCGAguggga	1428	NCGAguguga	1452	NCGAgugagc	1476	NCGAgugcgc
1405	ACGAguggga	1429	ACGAguguga	1453	ACGAgugagc	1477	ACGAgugcgc
1406	CCGAguggga	1430	CCGAguguga	1454	CCGAgugagc	1478	CCGAgugcgc
1407	GCGAguggga	1431	GCGAguguga	1455	GCGAgugagc	1479	GCGAgugcgc
1408	UCGAguggga	1432	UCGAguguga	1456	UCGAgugagc	1480	UCGAgugcgc
1409	GNGAguggga	1433	GNGAguguga	1457	GNGAgugagc	1481	GNGAgugcgc
1410	NGGAguggga	1434	NGGAguguga	1458	NGGAgugagc	1482	NGGAgugcgc
1411	AGGAguggga	1435	AGGAguguga	1459	AGGAgugagc	1483	AGGAgugcgc
1412	CGGAguggga	1436	CGGAguguga	1460	CGGAgugagc	1484	CGGAgugcgc
1413	GGGAguggga	1437	GGGAguguga	1461	GGGAgugagc	1485	GGGAgugcgc
1414	UGGAguggga	1438	UGGAguguga	1462	UGGAgugagc	1486	UGGAgugcgc
1415	UNGAguggga	1439	UNGAguguga	1463	UNGAgugagc	1487	UNGAgugcgc
1416	NUGAguggga	1440	NUGAguguga	1464	NUGAgugagc	1488	NUGAgugcgc
1417	AUGAguggga	1441	AUGAguguga	1465	AUGAgugagc	1489	AUGAgugcgc
1418	CUGAguggga	1442	CUGAguguga	1466	CUGAgugagc	1490	CUGAgugcgc
1419	GUGAguggga	1443	GUGAguguga	1467	GUGAgugagc	1491	GUGAgugcgc
1420	UUGAguggga	1444	UUGAguguga	1468	UUGAgugagc	1492	UUGAgugcgc

[0031] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1493	ANGAgugggc	1517	ANGAgugugc	1541	ANGAgugagg	1565	ANGAgugcgg
1494	NAGAgugggc	1518	NAGAgugugc	1542	NAGAgugagg	1566	NAGAgugcgg
1495	AAGAgugggc	1519	AAGAgugugc	1543	AAGAgugagg	1567	AAGAgugcgg
1496	CAGAgugggc	1520	CAGAgugugc	1544	CAGAgugagg	1568	CAGAgugcgg
1497	GAGAgugggc	1521	GAGAgugugc	1545	GAGAgugagg	1569	GAGAgugcgg
1498	UAGAgugggc	1522	UAGAgugugc	1546	UAGAgugagg	1570	UAGAgugcgg
1499	CNGAgugggc	1523	CNGAgugugc	1547	CNGAgugagg	1571	CNGAgugcgg
1500	NCGAgugggc	1524	NCGAgugugc	1548	NCGAgugagg	1572	NCGAgugcgg
1501	ACGAgugggc	1525	ACGAgugugc	1549	ACGAgugagg	1573	ACGAgugcgg
1502	CCGAgugggc	1526	CCGAgugugc	1550	CCGAgugagg	1574	CCGAgugcgg
1503	GCGAgugggc	1527	GCGAgugugc	1551	GCGAgugagg	1575	GCGAgugcgg
1504	UCGAgugggc	1528	UCGAgugugc	1552	UCGAgugagg	1576	UCGAgugcgg
1505	GNGAgugggc	1529	GNGAgugugc	1553	GNGAgugagg	1577	GNGAgugcgg
1506	NGGAgugggc	1530	NGGAgugugc	1554	NGGAgugagg	1578	NGGAgugcgg
1507	AGGAgugggc	1531	AGGAgugugc	1555	AGGAgugagg	1579	AGGAgugcgg
1508	CGGAgugggc	1532	CGGAgugugc	1556	CGGAgugagg	1580	CGGAgugcgg
1509	GGGAgugggc	1533	GGGAgugugc	1557	GGGAgugagg	1581	GGGAgugcgg
1510	UGGAgugggc	1534	UGGAgugugc	1558	UGGAgugagg	1582	UGGAgugcgg
1511	UNGAgugggc	1535	UNGAgugugc	1559	UNGAgugagg	1583	UNGAgugcgg
1512	NUGAgugggc	1536	NUGAgugugc	1560	NUGAgugagg	1584	NUGAgugcgg
1513	AUGAgugggc	1537	AUGAgugugc	1561	AUGAgugagg	1585	AUGAgugcgg
1514	CUGAgugggc	1538	CUGAgugugc	1562	CUGAgugagg	1586	CUGAgugcgg
1515	GUGAgugggc	1539	GUGAgugugc	1563	GUGAgugagg	1587	GUGAgugcgg
1516	UUGAgugggc	1540	UUGAgugugc	1564	UUGAgugagg	1588	UUGAgugcgg

[0032] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1589	ANGAgugggg	1613	ANGAgugugg	1637	ANGAgugagu	1661	ANGAgugcgu
1590	NAGAgugggg	1614	NAGAgugugg	1638	NAGAgugagu	1662	NAGAgugcgu
1591	AAGAgugggg	1615	AAGAgugugg	1639	AAGAgugagu	1663	AAGAgugcgu
1592	CAGAgugggg	1616	CAGAgugugg	1640	CAGAgugagu	1664	CAGAgugcgu
1593	GAGAgugggg	1617	GAGAgugugg	1641	GAGAgugagu	1665	GAGAgugcgu
1594	UAGAgugggg	1618	UAGAgugugg	1642	UAGAgugagu	1666	UAGAgugcgu
1595	CNGAgugggg	1619	CNGAgugugg	1643	CNGAgugagu	1667	CNGAgugcgu
1596	NCGAgugggg	1620	NCGAgugugg	1644	NCGAgugagu	1668	NCGAgugcgu
1597	ACGAgugggg	1621	ACGAgugugg	1645	ACGAgugagu	1669	ACGAgugcgu
1598	CCGAgugggg	1622	CCGAgugugg	1646	CCGAgugagu	1670	CCGAgugcgu
1599	GCGAgugggg	1623	GCGAgugugg	1647	GCGAgugagu	1671	GCGAgugcgu
1600	UCGAgugggg	1624	UCGAgugugg	1648	UCGAgugagu	1672	UCGAgugcgu
1601	GNGAgugggg	1625	GNGAgugugg	1649	GNGAgugagu	1673	GNGAgugcgu
1602	NGGAgugggg	1626	NGGAgugugg	1650	NGGAgugagu	1674	NGGAgugcgu
1603	AGGAgugggg	1627	AGGAgugugg	1651	AGGAgugagu	1675	AGGAgugcgu
1604	CGGAgugggg	1628	CGGAgugugg	1652	CGGAgugagu	1676	CGGAgugcgu
1605	GGGAgugggg	1629	GGGAgugugg	1653	GGGAgugagu	1677	GGGAgugcgu
1606	UGGAgugggg	1630	UGGAgugugg	1654	UGGAgugagu	1678	UGGAgugcgu
1607	UNGAgugggg	1631	UNGAgugugg	1655	UNGAgugagu	1679	UNGAgugcgu
1608	NUGAgugggg	1632	NUGAgugugg	1656	NUGAgugagu	1680	NUGAgugcgu
1609	AUGAgugggg	1633	AUGAgugugg	1657	AUGAgugagu	1681	AUGAgugcgu
1610	CUGAgugggg	1634	CUGAgugugg	1658	CUGAgugagu	1682	CUGAgugcgu
1611	GUGAgugggg	1635	GUGAgugugg	1659	GUGAgugagu	1683	GUGAgugcgu
1612	UUGAgugggg	1636	UUGAgugugg	1660	UUGAgugagu	1684	UUGAgugcgu

[0033] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1685	ANGAgugggu	1709	ANGAgugugu	1733	ANGAgugnga	1757	ANGAgugngc
1686	NAGAgugggu	1710	NAGAgugugu	1734	NAGAgugnga	1758	NAGAgugngc
1687	AAGAgugggu	1711	AAGAgugugu	1735	AAGAgugnga	1759	AAGAgugngc
1688	CAGAgugggu	1712	CAGAgugugu	1736	CAGAgugnga	1760	CAGAgugngc
1689	GAGAgugggu	1713	GAGAgugugu	1737	GAGAgugnga	1761	GAGAgugngc
1690	UAGAgugggu	1714	UAGAgugugu	1738	UAGAgugnga	1762	UAGAgugngc
1691	CNGAgugggu	1715	CNGAgugugu	1739	CNGAgugnga	1763	CNGAgugngc
1692	NCGAgugggu	1716	NCGAgugugu	1740	NCGAgugnga	1764	NCGAgugngc
1693	ACGAgugggu	1717	ACGAgugugu	1741	ACGAgugnga	1765	ACGAgugngc
1694	CCGAgugggu	1718	CCGAgugugu	1742	CCGAgugnga	1766	CCGAgugngc
1695	GCGAgugggu	1719	GCGAgugugu	1743	GCGAgugnga	1767	GCGAgugngc
1696	UCGAgugggu	1720	UCGAgugugu	1744	UCGAgugnga	1768	UCGAgugngc
1697	GNGAgugggu	1721	GNGAgugugu	1745	GNGAgugnga	1769	GNGAgugngc
1698	NGGAgugggu	1722	NGGAgugugu	1746	NGGAgugnga	1770	NGGAgugngc
1699	AGGAgugggu	1723	AGGAgugugu	1747	AGGAgugnga	1771	AGGAgugngc
1700	CGGAgugggu	1724	CGGAgugugu	1748	CGGAgugnga	1772	CGGAgugngc
1701	GGGAgugggu	1725	GGGAgugugu	1749	GGGAgugnga	1773	GGGAgugngc
1702	UGGAgugggu	1726	UGGAgugugu	1750	UGGAgugnga	1774	UGGAgugngc
1703	UNGAgugggu	1727	UNGAgugugu	1751	UNGAgugnga	1775	UNGAgugngc
1704	NUGAgugggu	1728	NUGAgugugu	1752	NUGAgugnga	1776	NUGAgugngc
1705	AUGAgugggu	1729	AUGAgugugu	1753	AUGAgugnga	1777	AUGAgugngc
1706	CUGAgugggu	1730	CUGAgugugu	1754	CUGAgugnga	1778	CUGAgugngc
1707	GUGAgugggu	1731	GUGAgugugu	1755	GUGAgugnga	1779	GUGAgugngc
1708	UUGAgugggu	1732	UUGAgugugu	1756	UUGAgugnga	1780	UUGAgugngc

[0034] Table 13 (cont). Intronic REMS RNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1781	ANGAgugngg	1793	GNGAgugngg	1805	ANGAgugngu	1817	GNGAgugngu
1782	NAGAgugngg	1794	NGGAgugngg	1806	NAGAgugngu	1818	NGGAgugngu
1783	AAGAgugngg	1795	AGGAgugngg	1807	AAGAgugngu	1819	AGGAgugngu
1784	CAGAgugngg	1796	CGGAgugngg	1808	CAGAgugngu	1820	CGGAgugngu
1785	GAGAgugngg	1797	GGGAgugngg	1809	GAGAgugngu	1821	GGGAgugngu
1786	UAGAgugngg	1798	UGGAgugngg	1810	UAGAgugngu	1822	UGGAgugngu
1787	CNGAgugngg	1799	UNGAgugngg	1811	CNGAgugngu	1823	UNGAgugngu
1788	NCGAgugngg	1800	NUGAgugngg	1812	NCGAgugngu	1824	NUGAgugngu
1789	ACGAgugngg	1801	AUGAgugngg	1813	ACGAgugngu	1825	AUGAgugngu
1790	CCGAgugngg	1802	CUGAgugngg	1814	CCGAgugngu	1826	CUGAgugngu
1791	GCGAgugngg	1803	GUGAgugngg	1815	GCGAgugngu	1827	GUGAgugngu
1792	UCGAgugngg	1804	UUGAgugngg	1816	UCGAgugngu	1828	UUGAgugngu

[0035] In one embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, by way of nonlimiting example, disclosed in Table 1, *infra*, the method comprising contacting a cell with a compound of Formula (I) or a form thereof. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in Table 16 or Tables 2-7, *infra*, wherein the precursor transcript transcribed from the gene comprises an intronic REMS, the method comprising contacting a cell with a compound of Formula (I) or a form thereof. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in International Patent Application No. PCT/US2014/071252 (International Publication No. WO 2015/105657), wherein the precursor transcript transcribed from the gene comprises an intronic REMS, the method comprising contacting a cell with a compound of Formula (I) or a form thereof. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in International Patent Application No. PCT/US2016/034864 (International Publication No. WO 2016/196386), wherein the precursor transcript transcribed from the gene comprises an intronic REMS, the method comprising contacting a cell with a compound of Formula (I) or a form thereof.

[0036] In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in Table 1, *infra*, wherein the precursor transcript transcribed from the gene comprises an intronic REMS, the method comprising contacting a cell with a compound of Formula (I) or a form thereof. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene disclosed in Table 7, *infra*, comprising contacting a cell with a compound of Formula (I) or a form thereof. See the example section for additional information regarding the genes in Table 7. In certain embodiments, the cell is contacted with the compound of Formula (I) or a form thereof in a cell culture. In other embodiments, the cell is contacted with the compound of Formula (I) or a form thereof in a subject (*e.g.*, a non-human animal subject or a human subject). In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described *infra*. In some embodiments, a compound of Formula (I) is a compound selected from a compound described herein.

[0037] In another aspect, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In one embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, by way of nonlimiting example, disclosed in Table 1, *infra*, the methods comprising administering to a human or non-human subject thereof a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0038] In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in Tables 2-7, *infra*, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject thereof a compound of Formula (I)

or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0039] In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in International Patent Application No. PCT/US2014/071252 (International Publication No. WO 2015/105657), wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in International Patent Application No. PCT/US2016/034864 (International Publication No. WO 2016/196386), wherein the precursor transcript transcribed from the gene comprises an intronic REMS, the method comprising contacting a cell with a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene, disclosed in Table 1, *infra*, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0040] In another embodiment, provided herein are methods for modulating the amount of one, two, three or more RNA transcripts of a gene disclosed in Table 7, *infra*, comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. *See* the example section for additional information regarding the genes in Table 7. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described *infra*. In some embodiments, a compound of Formula (I) is a compound selected from a compound described herein.

[0041] In another embodiment, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), and wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer).

[0042] In another embodiment, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: a first branch point, a first 3' splice site, and an iREMS, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), and wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer).

[0043] In another embodiment, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, and wherein the RNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1A, the method comprising contacting the RNA transcript with a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer).

[0044] In another embodiment, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, and wherein the RNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1B, the method comprising contacting the RNA transcript with a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer).

[0045] In another embodiment, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises three exons and two introns, and wherein the RNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1C, the method comprising contacting the RNA transcript with a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer).

[0046] In a specific embodiment, the RNA transcript is the RNA transcript of a gene described in a table in this disclosure.

[0047] In another embodiment, provided herein is a method for modulating the amount of the product of a gene (such as an RNA transcript or a protein) in a subject, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the DNA nucleotide sequence encoding the intron comprises in 5' to 3' order: a nucleotide sequence encoding a first 5' splice site, a nucleotide sequence encoding a first branch point, a nucleotide sequence encoding a first 3' splice site, a nucleotide sequence encoding an iREMS, a nucleotide sequence encoding a second branch point and a nucleotide sequence encoding a second 3' splice site, wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), and wherein r is adenine or guanine and n is any nucleotide, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0048] In another embodiment, provided herein is a method for modulating the amount of the product of a gene (such as an RNA transcript or protein) in a subject, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the DNA nucleotide sequence of the intron comprises in 5' to 3' order: a nucleotide sequence encoding a first branch point, a nucleotide sequence encoding a first 3' splice site, and a nucleotide sequence encoding an iREMS, wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), and wherein r is adenine or guanine and n is any nucleotide, the

method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0049] In another embodiment, provided herein is a method for modulating the amount of the product of a gene (such as an RNA transcript or protein) in a subject, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1A, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0050] In another embodiment, provided herein is a method for modulating the amount of the product of a gene (such as an RNA transcript or protein) in a subject, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1B, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0051] In another embodiment, provided herein is a method for modulating the amount of the product of a gene (such as an RNA transcript or protein) in a subject, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1C, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0052] In a specific embodiment, the gene is a gene described in a table in this disclosure.

[0053] In another aspect, provided herein are methods for preventing and/or treating a disease associated with the aberrant expression of a product of a gene (e.g., an mRNA transcript or protein), wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In one embodiment, provided herein are methods for preventing and/or treating a disease associated with aberrant expression of a product of a gene (e.g., an mRNA, RNA transcript or protein), by way of nonlimiting example, disclosed in Table 1, *infra*, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a

form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease associated with aberrant expression of a product of a gene (*e.g.*, an mRNA, RNA transcript or protein), disclosed in Tables 2-7, *infra*, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease associated with aberrant expression of a product of a gene (*e.g.*, an mRNA, RNA transcript or protein), by way of nonlimiting example, disclosed in International Patent Application No. PCT/US2014/071252 (International Publication No. WO 2015/105657), wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease associated with aberrant expression of a product of a gene (*e.g.*, an mRNA, RNA transcript or protein), by way of nonlimiting example, disclosed in International Patent Application No. PCT/US2016/034864 (International Publication No. WO 2016/196386), wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease associated with aberrant expression of a product of a gene (*e.g.*, an mRNA, RNA transcript or protein), disclosed in Table 1, *infra*, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease associated

with aberrant expression of a product of a gene disclosed in Table 7, *infra*, (*e.g.*, an mRNA, RNA transcript or protein), comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. *See* the example section for additional information regarding the genes in Table 7. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described *infra*. In some embodiments, a compound of Formula (I) is a compound selected from a compound described herein.

[0054] In another aspect, provided herein are methods for preventing and/or treating a disease in which a change in the level of expression of one, two, three or more RNA isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In one embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene, by way of nonlimiting example, disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0055] In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene, disclosed in Tables 2-7, *infra*, is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical

composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0056] In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene, disclosed in International Patent Application No. PCT/US2014/071252 (International Publication No. WO 2015/105657), is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene, disclosed in International Patent Application No. PCT/US2016/034864 (International Publication No. WO 2016/196386), is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene, disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more RNA isoforms encoded by a gene disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or 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, one, two, three or more RNA isoforms encoded by a gene disclosed in Table 7, *infra*, are decreased following administration of a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. See the example section for additional information regarding the genes in Table 7. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described *infra*. In some embodiments, a compound of Formula (I) is a compound selected from a compound described herein.

[0057] In another aspect, provided herein are methods for preventing and/or treating a disease in which a change in the level of expression of one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In one embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, by way of nonlimiting example, disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0058] In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, disclosed in Tables 2-7, *infra*, is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically

acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, disclosed in International Patent Application No. PCT/US2014/071252 (International Publication No. WO 2015/105657), is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, disclosed in International Patent Application No. PCT/US2016/034864 (International Publication No. WO 2016/196386), is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, wherein the precursor RNA transcript transcribed from the gene comprises an intronic REMS, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or a pharmaceutical composition comprising a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent.

[0059] In another embodiment, provided herein are methods for preventing and/or treating a disease in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene, disclosed in Table 1, *infra*, is beneficial to the prevention and/or treatment of the disease, the methods comprising administering to a human or non-human subject a compound of Formula (I) or a form thereof, or 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, one, two, three or more RNA isoforms encoded by a gene, disclosed in Table 7, *infra*, are decreased following administration of a compound of Formula (I) or a form thereof and a pharmaceutically acceptable carrier, excipient or diluent. See the example section for additional information regarding the genes in Table 7. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described *infra*. In some embodiments, a compound of Formula (I) is a compound selected from a compound described herein.

[0060] In another embodiment, provided herein is a method for either preventing, treating or preventing and treating a disease in a subject in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the DNA nucleotide sequence encoding the intron comprises in 5' to 3' order: a nucleotide sequence encoding a first 5' splice site, a nucleotide sequence encoding a first branch point, a nucleotide sequence encoding a first 3' splice site, a nucleotide sequence encoding an iREMS, a nucleotide sequence encoding a second branch point and a nucleotide sequence encoding a second 3' splice site, wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), and wherein r is adenine or guanine and n is any nucleotide, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0061] In another embodiment, provided herein is a method for either preventing, treating or preventing and treating a disease in a subject in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the DNA

nucleotide sequence of the intron comprises in 5' to 3' order: a nucleotide sequence encoding a first branch point, a nucleotide sequence encoding a first 3' splice site, and a nucleotide sequence encoding an iREMS, wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), and wherein r is adenine or guanine and n is any nucleotide, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0062] In another embodiment, provided herein is a method for either preventing, treating or preventing and treating a disease in a subject in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1A, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0063] In another embodiment, provided herein is a method for either preventing, treating or preventing and treating a disease in a subject in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1B, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0064] In another embodiment, provided herein is a method for either preventing, treating or preventing and treating a disease in a subject in which the alteration (*e.g.*, increase or decrease) in the expression one, two, three or more protein isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, wherein the gene comprises a DNA nucleotide sequence encoding two exons and an intron, and wherein the DNA nucleotide sequence comprises exonic and intronic elements illustrated in Figure 1C, the method comprising administering a compound described herein (for example, a compound of Formula (I) or a form thereof or another splicing inducer) to the subject.

[0065] In a specific embodiment, the gene is a gene described in a table in this disclosure.

[0066] In another aspect, provided herein are artificial gene constructs. In one embodiment, provided herein is an artificial gene construct comprising endogenous DNA is modified to introduce a non-endogenous nucleotide sequence encoding an intron comprising a 3' splice site(s) and a branch point(s) and an intronic REMS. In another embodiment, provided herein is an artificial gene construct comprising DNA encoding exons and one, two or more introns, wherein a nucleotide sequence encoding an intronic REMS, functioning as a 5' splice site in the presence of a compound described herein, which may be upstream of an endogenous nucleotide sequence encoding a branch point and an endogenous nucleotide sequence encoding a 3' splice site, is modified to introduce a nucleotide sequence encoding a non-endogenous branch point and a non-endogenous 3' splice site further upstream from the endogenous intronic REMS. In another embodiment, provided herein is an artificial gene construct comprising DNA encoding exons and one, two or more introns, wherein a nucleotide sequence encoding an intronic REMS 5' splice site, which may be downstream of an endogenous nucleotide sequence encoding a branch point and an endogenous nucleotide sequence encoding a 3' splice site, is modified to introduce a nucleotide sequence encoding a non-endogenous branch point and a non-endogenous 3' splice site further downstream from the endogenous intronic REMS. In another embodiment, provided herein is an artificial gene construct comprising DNA encoding an intronic REMS, comprising nucleotides encoding an intronic REMS having one or more 5' splice site(s), 3' splice site(s) and branch point(s). In certain embodiments, the artificial gene construct encodes a frameshift or premature stop codon or internal insertions or deletions within the open reading frame. In other embodiments, the artificial gene construct encodes a mature mRNA having a functional open reading frame, producing a novel protein which may or may not be functional. In some embodiments, the artificial gene construct encodes a detectable reporter protein. RNA transcripts having a non-functional open reading frame due to the inclusion of a frameshift, premature stop codon or internal insertions or deletions within the open reading frame can be substrates for nonsense-mediated decay and thus have low abundance. Any intronic REMS-mediated alternative splicing modified RNA transcripts may also have altered stability, altered intracellular transport, altered 3' end formation efficiency and altered translation efficiency.

[0067] In a specific embodiment, the nucleotide sequence of the intronic REMS introduced into the nucleotide sequence of the artificial gene construct comprises the sequence NNGAgtrngn (SEQ ID NO: 3), wherein r is adenine or guanine and n or N is any nucleotide. In

a specific embodiment, in the context of DNA, the nucleotide sequence encoding the intronic REMS comprises a sequence selected from the group consisting of
 ANGAgtrngn (SEQ ID NO: 1829), CNGAgtrngn (SEQ ID NO: 1835),
 GNGAgtrngn (SEQ ID NO: 1841), TNGAgtrngn (SEQ ID NO: 1847),
 NAGAgtrngn (SEQ ID NO: 1830), NCGAgtrngn (SEQ ID NO: 1836),
 NGGAgtrngn (SEQ ID NO: 1842), NTGAgtrngn (SEQ ID NO: 1848),
 AAGAgtrngn (SEQ ID NO: 1831), ACGAgtrngn (SEQ ID NO: 1837),
 AGGAgtrngn (SEQ ID NO: 1843), ATGAgtrngn (SEQ ID NO: 1849),
 CAGAgtrngn (SEQ ID NO: 1832), CCGAgtrngn (SEQ ID NO: 1838),
 CGGAgtrngn (SEQ ID NO: 1844), CTGAgtrngn (SEQ ID NO: 1850),
 GAGAgtrngn (SEQ ID NO: 1833), GCGAgtrngn (SEQ ID NO: 1839),
 GGGAgtrngn (SEQ ID NO: 1845), GTGAgtrngn (SEQ ID NO: 1851),
 TAGAgtrngn (SEQ ID NO: 1834), TCGAgtrngn (SEQ ID NO: 1840),
 TGGAgtrngn (SEQ ID NO: 1846) and TTGAgtrngn (SEQ ID NO: 1852), wherein r is adenine or
 guanine and n or N is any nucleotide.

[0068] In a further specific embodiment, in the context of DNA, the nucleotide sequence encoding the intronic REMS comprises a sequence selected from the group consisting of
 ANGAgtragt (SEQ ID NO: 2237), CNGAgtragt (SEQ ID NO: 2243),
 GNGAgtragt (SEQ ID NO: 2249), TNGAgtragt (SEQ ID NO: 2255),
 NAGAgtragt (SEQ ID NO: 2238), NCGAgtragt (SEQ ID NO: 2244),
 NGGAgtragt (SEQ ID NO: 2250), NTGAgtragt (SEQ ID NO: 2256),
 AAGAgtragt (SEQ ID NO: 2239), ACGAgtragt (SEQ ID NO: 2245),
 AGGAgtragt (SEQ ID NO: 2251), ATGAgtragt (SEQ ID NO: 2257),
 CAGAgtragt (SEQ ID NO: 2240), CCGAgtragt (SEQ ID NO: 2246),
 CGGAgtragt (SEQ ID NO: 2252), CTGAgtragt (SEQ ID NO: 2258),
 GAGAgtragt (SEQ ID NO: 2241), GCGAgtragt (SEQ ID NO: 2247),
 GGGAgtragt (SEQ ID NO: 2253), GTGAgtragt (SEQ ID NO: 2259),
 TAGAgtragt (SEQ ID NO: 2242), TCGAgtragt (SEQ ID NO: 2248),
 TGGAgtragt (SEQ ID NO: 2254) and TTGAgtragt (SEQ ID NO: 2260), wherein r is adenine or
 guanine and N is any nucleotide. In one or more embodiments provided herein, N is adenine or
 guanine. In various specific embodiments, the nucleotide sequence encoding the intronic REMS

is a nucleotide sequence encoding a non-endogenous intronic REMS, i.e., a precursor RNA transcript comprising the non-endogenous intronic REMS not naturally found in the DNA sequence of the artificial construct.

[0069] In a specific embodiment, the intronic REMS referred to in a method or artificial gene construct described herein comprises, at the DNA level, a sequence presented in the following table (wherein r is adenine or guanine, and n or N is any nucleotide):

[0070] Table 14. Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1829	ANGAgtrngn	1835	CNGAgtrngn	1841	GNGAgtrngn	1847	TNGAgtrngn
1830	NAGAgtrngn	1836	NCGAgtrngn	1842	NGGAgtrngn	1848	NTGAgtrngn
1831	AAGAgtrngn	1837	ACGAgtrngn	1843	AGGAgtrngn	1849	ATGAgtrngn
1832	CAGAgtrngn	1838	CCGAgtrngn	1844	CGGAgtrngn	1850	CTGAgtrngn
1833	GAGAgtrngn	1839	GCGAgtrngn	1845	GGGAgtrngn	1851	GTGAgtrngn
1834	TAGAgtrngn	1840	TCGAgtrngn	1846	TGGAgtrngn	1852	TTGAgtrngn

[0071] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1853	ANGAgtragn	1877	ANGAgtrcgn	1901	ANGAgtrggn	1925	ANGAgtrtgn
1854	NAGAgtragn	1878	NAGAgtrcgn	1902	NAGAgtrggn	1926	NAGAgtrtgn
1855	AAGAgtragn	1879	AAGAgtrcgn	1903	AAGAgtrggn	1927	AAGAgtrtgn
1856	CAGAgtragn	1880	CAGAgtrcgn	1904	CAGAgtrggn	1928	CAGAgtrtgn
1857	GAGAgtragn	1881	GAGAgtrcgn	1905	GAGAgtrggn	1929	GAGAgtrtgn
1858	TAGAgtragn	1882	TAGAgtrcgn	1906	TAGAgtrggn	1930	TAGAgtrtgn
1859	CNGAgtragn	1883	CNGAgtrcgn	1907	CNGAgtrggn	1931	CNGAgtrtgn
1860	NCGAgtragn	1884	NCGAgtrcgn	1908	NCGAgtrggn	1932	NCGAgtrtgn
1861	ACGAgtragn	1885	ACGAgtrcgn	1909	ACGAgtrggn	1933	ACGAgtrtgn
1862	CCGAgtragn	1886	CCGAgtrcgn	1910	CCGAgtrggn	1934	CCGAgtrtgn
1863	GCGAgtragn	1887	GCGAgtrcgn	1911	GCGAgtrggn	1935	GCGAgtrtgn
1864	TCGAgtragn	1888	TCGAgtrcgn	1912	TCGAgtrggn	1936	TCGAgtrtgn
1865	GNGAgtragn	1889	GNGAgtrcgn	1913	GNGAgtrggn	1937	GNGAgtrtgn
1866	NGGAgtragn	1890	NGGAgtrcgn	1914	NGGAgtrggn	1938	NGGAgtrtgn
1867	AGGAgtragn	1891	AGGAgtrcgn	1915	AGGAgtrggn	1939	AGGAgtrtgn
1868	CGGAgtragn	1892	CGGAgtrcgn	1916	CGGAgtrggn	1940	CGGAgtrtgn
1869	GGGAgtragn	1893	GGGAgtrcgn	1917	GGGAgtrggn	1941	GGGAgtrtgn
1870	TGGAgtragn	1894	TGGAgtrcgn	1918	TGGAgtrggn	1942	TGGAgtrtgn
1871	TNGAgtragn	1895	TNGAgtrcgn	1919	TNGAgtrggn	1943	TNGAgtrtgn
1872	NTGAgtragn	1896	NTGAgtrcgn	1920	NTGAgtrggn	1944	NTGAgtrtgn
1873	ATGAgtragn	1897	ATGAgtrcgn	1921	ATGAgtrggn	1945	ATGAgtrtgn
1874	CTGAgtragn	1898	CTGAgtrcgn	1922	CTGAgtrggn	1946	CTGAgtrtgn
1875	GTGAgtragn	1899	GTGAgtrcgn	1923	GTGAgtrggn	1947	GTGAgtrtgn
1876	TTGAgtragn	1900	TTGAgtrcgn	1924	TTGAgtrggn	1948	TTGAgtrtgn

[0072] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
1949	ANGAgtraga	1973	ANGAgtrcga	1997	ANGAgtrgga	2021	ANGAgtrtga
1950	NAGAgtraga	1974	NAGAgtrcga	1998	NAGAgtrgga	2022	NAGAgtrtga
1951	AAGAgtraga	1975	AAGAgtrcga	1999	AAGAgtrgga	2023	AAGAgtrtga
1952	CAGAgtraga	1976	CAGAgtrcga	2000	CAGAgtrgga	2024	CAGAgtrtga
1953	GAGAgtraga	1977	GAGAgtrcga	2001	GAGAgtrgga	2025	GAGAgtrtga
1954	TAGAgtraga	1978	TAGAgtrcga	2002	TAGAgtrgga	2026	TAGAgtrtga
1955	CNGAgtraga	1979	CNGAgtrcga	2003	CNGAgtrgga	2027	CNGAgtrtga
1956	NCGAgtraga	1980	NCGAgtrcga	2004	NCGAgtrgga	2028	NCGAgtrtga
1957	ACGAgtraga	1981	ACGAgtrcga	2005	ACGAgtrgga	2029	ACGAgtrtga
1958	CCGAgtraga	1982	CCGAgtrcga	2006	CCGAgtrgga	2030	CCGAgtrtga
1959	GCGAgtraga	1983	GCGAgtrcga	2007	GCGAgtrgga	2031	GCGAgtrtga
1960	TCGAgtraga	1984	TCGAgtrcga	2008	TCGAgtrgga	2032	TCGAgtrtga
1961	GNGAgtraga	1985	GNGAgtrcga	2009	GNGAgtrgga	2033	GNGAgtrtga
1962	NGGAgtraga	1986	NGGAgtrcga	2010	NGGAgtrgga	2034	NGGAgtrtga
1963	AGGAgtraga	1987	AGGAgtrcga	2011	AGGAgtrgga	2035	AGGAgtrtga
1964	CGGAgtraga	1988	CGGAgtrcga	2012	CGGAgtrgga	2036	CGGAgtrtga
1965	GGGAgtraga	1989	GGGAgtrcga	2013	GGGAgtrgga	2037	GGGAgtrtga
1966	TGGAgtraga	1990	TGGAgtrcga	2014	TGGAgtrgga	2038	TGGAgtrtga
1967	TNGAgtraga	1991	TNGAgtrcga	2015	TNGAgtrgga	2039	TNGAgtrtga
1968	NTGAgtraga	1992	NTGAgtrcga	2016	NTGAgtrgga	2040	NTGAgtrtga
1969	ATGAgtraga	1993	ATGAgtrcga	2017	ATGAgtrgga	2041	ATGAgtrtga
1970	CTGAgtraga	1994	CTGAgtrcga	2018	CTGAgtrgga	2042	CTGAgtrtga
1971	GTGAgtraga	1995	GTGAgtrcga	2019	GTGAgtrgga	2043	GTGAgtrtga
1972	TTGAgtraga	1996	TTGAgtrcga	2020	TTGAgtrgga	2044	TTGAgtrtga

[0073] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2045	ANGAgtragc	2069	ANGAgtrcgc	2093	ANGAgtrggc	2117	ANGAgtrtgc
2046	NAGAgtragc	2070	NAGAgtrcgc	2094	NAGAgtrggc	2118	NAGAgtrtgc
2047	AAGAgtragc	2071	AAGAgtrcgc	2095	AAGAgtrggc	2119	AAGAgtrtgc
2048	CAGAgtragc	2072	CAGAgtrcgc	2096	CAGAgtrggc	2120	CAGAgtrtgc
2049	GAGAgtragc	2073	GAGAgtrcgc	2097	GAGAgtrggc	2121	GAGAgtrtgc
2050	TAGAgtragc	2074	TAGAgtrcgc	2098	TAGAgtrggc	2122	TAGAgtrtgc
2051	CNGAgtragc	2075	CNGAgtrcgc	2099	CNGAgtrggc	2123	CNGAgtrtgc
2052	NCGAgtragc	2076	NCGAgtrcgc	2100	NCGAgtrggc	2124	NCGAgtrtgc
2053	ACGAgtragc	2077	ACGAgtrcgc	2101	ACGAgtrggc	2125	ACGAgtrtgc
2054	CCGAgtragc	2078	CCGAgtrcgc	2102	CCGAgtrggc	2126	CCGAgtrtgc
2055	GCGAgtragc	2079	GCGAgtrcgc	2103	GCGAgtrggc	2127	GCGAgtrtgc
2056	TCGAgtragc	2080	TCGAgtrcgc	2104	TCGAgtrggc	2128	TCGAgtrtgc
2057	GNGAgtragc	2081	GNGAgtrcgc	2105	GNGAgtrggc	2129	GNGAgtrtgc
2058	NGGAgtragc	2082	NGGAgtrcgc	2106	NGGAgtrggc	2130	NGGAgtrtgc
2059	AGGAgtragc	2083	AGGAgtrcgc	2107	AGGAgtrggc	2131	AGGAgtrtgc
2060	CGGAgtragc	2084	CGGAgtrcgc	2108	CGGAgtrggc	2132	CGGAgtrtgc
2061	GGGAgtragc	2085	GGGAgtrcgc	2109	GGGAgtrggc	2133	GGGAgtrtgc
2062	TGGAgtragc	2086	TGGAgtrcgc	2110	TGGAgtrggc	2134	TGGAgtrtgc
2063	TNGAgtragc	2087	TNGAgtrcgc	2111	TNGAgtrggc	2135	TNGAgtrtgc
2064	NTGAgtragc	2088	NTGAgtrcgc	2112	NTGAgtrggc	2136	NTGAgtrtgc
2065	ATGAgtragc	2089	ATGAgtrcgc	2113	ATGAgtrggc	2137	ATGAgtrtgc
2066	CTGAgtragc	2090	CTGAgtrcgc	2114	CTGAgtrggc	2138	CTGAgtrtgc
2067	GTGAgtragc	2091	GTGAgtrcgc	2115	GTGAgtrggc	2139	GTGAgtrtgc
2068	TTGAgtragc	2092	TTGAgtrcgc	2116	TTGAgtrggc	2140	TTGAgtrtgc

[0074] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2141	ANGAgtragg	2165	ANGAgtrcgg	2189	ANGAgtrggg	2213	ANGAgtrtgg
2142	NAGAgtragg	2166	NAGAgtrcgg	2190	NAGAgtrggg	2214	NAGAgtrtgg
2143	AAGAgtragg	2167	AAGAgtrcgg	2191	AAGAgtrggg	2215	AAGAgtrtgg
2144	CAGAgtragg	2168	CAGAgtrcgg	2192	CAGAgtrggg	2216	CAGAgtrtgg
2145	GAGAgtragg	2169	GAGAgtrcgg	2193	GAGAgtrggg	2217	GAGAgtrtgg
2146	TAGAgtragg	2170	TAGAgtrcgg	2194	TAGAgtrggg	2218	TAGAgtrtgg
2147	CNGAgtragg	2171	CNGAgtrcgg	2195	CNGAgtrggg	2219	CNGAgtrtgg
2148	NCGAgtragg	2172	NCGAgtrcgg	2196	NCGAgtrggg	2220	NCGAgtrtgg
2149	ACGAgtragg	2173	ACGAgtrcgg	2197	ACGAgtrggg	2221	ACGAgtrtgg
2150	CCGAgtragg	2174	CCGAgtrcgg	2198	CCGAgtrggg	2222	CCGAgtrtgg
2151	GCGAgtragg	2175	GCGAgtrcgg	2199	GCGAgtrggg	2223	GCGAgtrtgg
2152	TCGAgtragg	2176	TCGAgtrcgg	2200	TCGAgtrggg	2224	TCGAgtrtgg
2153	GNGAgtragg	2177	GNGAgtrcgg	2201	GNGAgtrggg	2225	GNGAgtrtgg
2154	NGGAgtragg	2178	NGGAgtrcgg	2202	NGGAgtrggg	2226	NGGAgtrtgg
2155	AGGAgtragg	2179	AGGAgtrcgg	2203	AGGAgtrggg	2227	AGGAgtrtgg
2156	CGGAgtragg	2180	CGGAgtrcgg	2204	CGGAgtrggg	2228	CGGAgtrtgg
2157	GGGAgtragg	2181	GGGAgtrcgg	2205	GGGAgtrggg	2229	GGGAgtrtgg
2158	TGGAgtragg	2182	TGGAgtrcgg	2206	TGGAgtrggg	2230	TGGAgtrtgg
2159	TNGAgtragg	2183	TNGAgtrcgg	2207	TNGAgtrggg	2231	TNGAgtrtgg
2160	NTGAgtragg	2184	NTGAgtrcgg	2208	NTGAgtrggg	2232	NTGAgtrtgg
2161	ATGAgtragg	2185	ATGAgtrcgg	2209	ATGAgtrggg	2233	ATGAgtrtgg
2162	CTGAgtragg	2186	CTGAgtrcgg	2210	CTGAgtrggg	2234	CTGAgtrtgg
2163	GTGAgtragg	2187	GTGAgtrcgg	2211	GTGAgtrggg	2235	GTGAgtrtgg
2164	TTGAgtragg	2188	TTGAgtrcgg	2212	TTGAgtrggg	2236	TTGAgtrtgg

[0075] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2237	ANGAgtragt	2261	ANGAgtrcgt	2285	ANGAgtrggt	2309	ANGAgtrtgt
2238	NAGAgtragt	2262	NAGAgtrcgt	2286	NAGAgtrggt	2310	NAGAgtrtgt
2239	AAGAgtragt	2263	AAGAgtrcgt	2287	AAGAgtrggt	2311	AAGAgtrtgt
2240	CAGAgtragt	2264	CAGAgtrcgt	2288	CAGAgtrggt	2312	CAGAgtrtgt
2241	GAGAgtragt	2265	GAGAgtrcgt	2289	GAGAgtrggt	2313	GAGAgtrtgt
2242	TAGAgtragt	2266	TAGAgtrcgt	2290	TAGAgtrggt	2314	TAGAgtrtgt
2243	CNGAgtragt	2267	CNGAgtrcgt	2291	CNGAgtrggt	2315	CNGAgtrtgt
2244	NCGAgtragt	2268	NCGAgtrcgt	2292	NCGAgtrggt	2316	NCGAgtrtgt
2245	ACGAgtragt	2269	ACGAgtrcgt	2293	ACGAgtrggt	2317	ACGAgtrtgt
2246	CCGAgtragt	2270	CCGAgtrcgt	2294	CCGAgtrggt	2318	CCGAgtrtgt
2247	GCGAgtragt	2271	GCGAgtrcgt	2295	GCGAgtrggt	2319	GCGAgtrtgt
2248	TCGAgtragt	2272	TCGAgtrcgt	2296	TCGAgtrggt	2320	TCGAgtrtgt
2249	GNGAgtragt	2273	GNGAgtrcgt	2297	GNGAgtrggt	2321	GNGAgtrtgt
2250	NGGAgtragt	2274	NGGAgtrcgt	2298	NGGAgtrggt	2322	NGGAgtrtgt
2251	AGGAgtragt	2275	AGGAgtrcgt	2299	AGGAgtrggt	2323	AGGAgtrtgt
2252	CGGAgtragt	2276	CGGAgtrcgt	2300	CGGAgtrggt	2324	CGGAgtrtgt
2253	GGGAgtragt	2277	GGGAgtrcgt	2301	GGGAgtrggt	2325	GGGAgtrtgt
2254	TGGAgtragt	2278	TGGAgtrcgt	2302	TGGAgtrggt	2326	TGGAgtrtgt
2255	TNGAgtragt	2279	TNGAgtrcgt	2303	TNGAgtrggt	2327	TNGAgtrtgt
2256	NTGAgtragt	2280	NTGAgtrcgt	2304	NTGAgtrggt	2328	NTGAgtrtgt
2257	ATGAgtragt	2281	ATGAgtrcgt	2305	ATGAgtrggt	2329	ATGAgtrtgt
2258	CTGAgtragt	2282	CTGAgtrcgt	2306	CTGAgtrggt	2330	CTGAgtrtgt
2259	GTGAgtragt	2283	GTGAgtrcgt	2307	GTGAgtrggt	2331	GTGAgtrtgt
2260	TTGAgtragt	2284	TTGAgtrcgt	2308	TTGAgtrggt	2332	TTGAgtrtgt

[0076] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2333	ANGAgtrnga	2357	ANGAgtrngc	2381	ANGAgtrngg	2405	ANGAgtrngt
2334	NAGAgtrnga	2358	NAGAgtrngc	2382	NAGAgtrngg	2406	NAGAgtrngt
2335	AAGAgtrnga	2359	AAGAgtrngc	2383	AAGAgtrngg	2407	AAGAgtrngt
2336	CAGAgtrnga	2360	CAGAgtrngc	2384	CAGAgtrngg	2408	CAGAgtrngt
2337	GAGAgtrnga	2361	GAGAgtrngc	2385	GAGAgtrngg	2409	GAGAgtrngt
2338	TAGAgtrnga	2362	TAGAgtrngc	2386	TAGAgtrngg	2410	TAGAgtrngt
2339	CNGAgtrnga	2363	CNGAgtrngc	2387	CNGAgtrngg	2411	CNGAgtrngt
2340	NCGAgtrnga	2364	NCGAgtrngc	2388	NCGAgtrngg	2412	NCGAgtrngt
2341	ACGAgtrnga	2365	ACGAgtrngc	2389	ACGAgtrngg	2413	ACGAgtrngt
2342	CCGAgtrnga	2366	CCGAgtrngc	2390	CCGAgtrngg	2414	CCGAgtrngt
2343	GCGAgtrnga	2367	GCGAgtrngc	2391	GCGAgtrngg	2415	GCGAgtrngt
2344	TCGAgtrnga	2368	TCGAgtrngc	2392	TCGAgtrngg	2416	TCGAgtrngt
2345	GNGAgtrnga	2369	GNGAgtrngc	2393	GNGAgtrngg	2417	GNGAgtrngt
2346	NGGAgtrnga	2370	NGGAgtrngc	2394	NGGAgtrngg	2418	NGGAgtrngt
2347	AGGAgtrnga	2371	AGGAgtrngc	2395	AGGAgtrngg	2419	AGGAgtrngt
2348	CGGAgtrnga	2372	CGGAgtrngc	2396	CGGAgtrngg	2420	CGGAgtrngt
2349	GGGAgtrnga	2373	GGGAgtrngc	2397	GGGAgtrngg	2421	GGGAgtrngt
2350	TGGAgtrnga	2374	TGGAgtrngc	2398	TGGAgtrngg	2422	TGGAgtrngt
2351	TNGAgtrnga	2375	TNGAgtrngc	2399	TNGAgtrngg	2423	TNGAgtrngt
2352	NTGAgtrnga	2376	NTGAgtrngc	2400	NTGAgtrngg	2424	NTGAgtrngt
2353	ATGAgtrnga	2377	ATGAgtrngc	2401	ATGAgtrngg	2425	ATGAgtrngt
2354	CTGAgtrnga	2378	CTGAgtrngc	2402	CTGAgtrngg	2426	CTGAgtrngt
2355	GTGAgtrnga	2379	GTGAgtrngc	2403	GTGAgtrngg	2427	GTGAgtrngt
2356	TTGAgtrnga	2380	TTGAgtrngc	2404	TTGAgtrngg	2428	TTGAgtrngt

[0077] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2429	ANGAgtangn	2453	ANGAgttaagn	2477	ANGAgttacgn	2501	ANGAgttaggn
2430	NAGAgtangn	2454	NAGAgttaagn	2478	NAGAgttacgn	2502	NAGAgttaggn
2431	AAGAgtangn	2455	AAGAgttaagn	2479	AAGAgttacgn	2503	AAGAgttaggn
2432	CAGAgtangn	2456	CAGAgttaagn	2480	CAGAgttacgn	2504	CAGAgttaggn
2433	GAGAgtangn	2457	GAGAgttaagn	2481	GAGAgttacgn	2505	GAGAgttaggn
2434	TAGAgtangn	2458	TAGAgttaagn	2482	TAGAgttacgn	2506	TAGAgttaggn
2435	CNGAgtangn	2459	CNGAgttaagn	2483	CNGAgttacgn	2507	CNGAgttaggn
2436	NCGAgtangn	2460	NCGAgttaagn	2484	NCGAgttacgn	2508	NCGAgttaggn
2437	ACGAgtangn	2461	ACGAgttaagn	2485	ACGAgttacgn	2509	ACGAgttaggn
2438	CCGAgtangn	2462	CCGAgttaagn	2486	CCGAgttacgn	2510	CCGAgttaggn
2439	GCGAgtangn	2463	GCGAgttaagn	2487	GCGAgttacgn	2511	GCGAgttaggn
2440	TCGAgtangn	2464	TCGAgttaagn	2488	TCGAgttacgn	2512	TCGAgttaggn
2441	GNGAgtangn	2465	GNGAgttaagn	2489	GNGAgttacgn	2513	GNGAgttaggn
2442	NGGAgtangn	2466	NGGAgttaagn	2490	NGGAgttacgn	2514	NGGAgttaggn
2443	AGGAgtangn	2467	AGGAgttaagn	2491	AGGAgttacgn	2515	AGGAgttaggn
2444	CGGAgtangn	2468	CGGAgttaagn	2492	CGGAgttacgn	2516	CGGAgttaggn
2445	GGGAgtangn	2469	GGGAgttaagn	2493	GGGAgttacgn	2517	GGGAgttaggn
2446	TGGAgtangn	2470	TGGAgttaagn	2494	TGGAgttacgn	2518	TGGAgttaggn
2447	TNGAgtangn	2471	TNGAgttaagn	2495	TNGAgttacgn	2519	TNGAgttaggn
2448	NTGAgtangn	2472	NTGAgttaagn	2496	NTGAgttacgn	2520	NTGAgttaggn
2449	ATGAgtangn	2473	ATGAgttaagn	2497	ATGAgttacgn	2521	ATGAgttaggn
2450	CTGAgtangn	2474	CTGAgttaagn	2498	CTGAgttacgn	2522	CTGAgttaggn
2451	GTGAgtangn	2475	GTGAgttaagn	2499	GTGAgttacgn	2523	GTGAgttaggn
2452	TTGAgtangn	2476	TTGAgttaagn	2500	TTGAgttacgn	2524	TTGAgttaggn

[0078] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2525	ANGAgtatgn	2549	ANGAgttaaga	2573	ANGAgtacga	2597	ANGAgttagga
2526	NAGAgtatgn	2550	NAGAgttaaga	2574	NAGAgtacga	2598	NAGAgttagga
2527	AAGAgtatgn	2551	AAGAgttaaga	2575	AAGAgtacga	2599	AAGAgttagga
2528	CAGAgtatgn	2552	CAGAgttaaga	2576	CAGAgtacga	2600	CAGAgttagga
2529	GAGAgtatgn	2553	GAGAgttaaga	2577	GAGAgtacga	2601	GAGAgttagga
2530	TAGAgtatgn	2554	TAGAgttaaga	2578	TAGAgtacga	2602	TAGAgttagga
2531	CNGAgtatgn	2555	CNGAgttaaga	2579	CNGAgtacga	2603	CNGAgttagga
2532	NCGAgtatgn	2556	NCGAgttaaga	2580	NCGAgtacga	2604	NCGAgttagga
2533	ACGAgtatgn	2557	ACGAgttaaga	2581	ACGAgtacga	2605	ACGAgttagga
2534	CCGAgtatgn	2558	CCGAgttaaga	2582	CCGAgtacga	2606	CCGAgttagga
2535	GCGAgtatgn	2559	GCGAgttaaga	2583	GCGAgtacga	2607	GCGAgttagga
2536	TCGAgtatgn	2560	TCGAgttaaga	2584	TCGAgtacga	2608	TCGAgttagga
2537	GNGAgtatgn	2561	GNGAgttaaga	2585	GNGAgtacga	2609	GNGAgttagga
2538	NGGAgtatgn	2562	NGGAgttaaga	2586	NGGAgtacga	2610	NGGAgttagga
2539	AGGAgtatgn	2563	AGGAgttaaga	2587	AGGAgtacga	2611	AGGAgttagga
2540	CGGAgtatgn	2564	CGGAgttaaga	2588	CGGAgtacga	2612	CGGAgttagga
2541	GGGAgtatgn	2565	GGGAgttaaga	2589	GGGAgtacga	2613	GGGAgttagga
2542	TGGAgtatgn	2566	TGGAgttaaga	2590	TGGAgtacga	2614	TGGAgttagga
2543	TNGAgtatgn	2567	TNGAgttaaga	2591	TNGAgtacga	2615	TNGAgttagga
2544	NTGAgtatgn	2568	NTGAgttaaga	2592	NTGAgtacga	2616	NTGAgttagga
2545	ATGAgtatgn	2569	ATGAgttaaga	2593	ATGAgtacga	2617	ATGAgttagga
2546	CTGAgtatgn	2570	CTGAgttaaga	2594	CTGAgtacga	2618	CTGAgttagga
2547	GTGAgtatgn	2571	GTGAgttaaga	2595	GTGAgtacga	2619	GTGAgttagga
2548	TTGAgtatgn	2572	TTGAgttaaga	2596	TTGAgtacga	2620	TTGAgttagga

[0079] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2621	ANGAgtatga	2645	ANGAgtaaagc	2669	ANGAgtacgc	2693	ANGAgtaggc
2622	NAGAgtatga	2646	NAGAgtaaagc	2670	NAGAgtacgc	2694	NAGAgtaggc
2623	AAGAgtatga	2647	AAGAgtaaagc	2671	AAGAgtacgc	2695	AAGAgtaggc
2624	CAGAgtatga	2648	CAGAgtaaagc	2672	CAGAgtacgc	2696	CAGAgtaggc
2625	GAGAgtatga	2649	GAGAgtaaagc	2673	GAGAgtacgc	2697	GAGAgtaggc
2626	TAGAgtatga	2650	TAGAgtaaagc	2674	TAGAgtacgc	2698	TAGAgtaggc
2627	CNGAgtatga	2651	CNGAgtaaagc	2675	CNGAgtacgc	2699	CNGAgtaggc
2628	NCGAgtatga	2652	NCGAgtaaagc	2676	NCGAgtacgc	2700	NCGAgtaggc
2629	ACGAgtatga	2653	ACGAgtaaagc	2677	ACGAgtacgc	2701	ACGAgtaggc
2630	CCGAgtatga	2654	CCGAgtaaagc	2678	CCGAgtacgc	2702	CCGAgtaggc
2631	GCGAgtatga	2655	GCGAgtaaagc	2679	GCGAgtacgc	2703	GCGAgtaggc
2632	TCGAgtatga	2656	TCGAgtaaagc	2680	TCGAgtacgc	2704	TCGAgtaggc
2633	GNGAgtatga	2657	GNGAgtaaagc	2681	GNGAgtacgc	2705	GNGAgtaggc
2634	NGGAgtatga	2658	NGGAgtaaagc	2682	NGGAgtacgc	2706	NGGAgtaggc
2635	AGGAgtatga	2659	AGGAgtaaagc	2683	AGGAgtacgc	2707	AGGAgtaggc
2636	CGGAgtatga	2660	CGGAgtaaagc	2684	CGGAgtacgc	2708	CGGAgtaggc
2637	GGGAgtatga	2661	GGGAgtaaagc	2685	GGGAgtacgc	2709	GGGAgtaggc
2638	TGGAgtatga	2662	TGGAgtaaagc	2686	TGGAgtacgc	2710	TGGAgtaggc
2639	TNGAgtatga	2663	TNGAgtaaagc	2687	TNGAgtacgc	2711	TNGAgtaggc
2640	NTGAgtatga	2664	NTGAgtaaagc	2688	NTGAgtacgc	2712	NTGAgtaggc
2641	ATGAgtatga	2665	ATGAgtaaagc	2689	ATGAgtacgc	2713	ATGAgtaggc
2642	CTGAgtatga	2666	CTGAgtaaagc	2690	CTGAgtacgc	2714	CTGAgtaggc
2643	GTGAgtatga	2667	GTGAgtaaagc	2691	GTGAgtacgc	2715	GTGAgtaggc
2644	TTGAgtatga	2668	TTGAgtaaagc	2692	TTGAgtacgc	2716	TTGAgtaggc

[0080] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2717	ANGAgtatgc	2741	ANGAgttaagg	2765	ANGAgttacgg	2789	ANGAgttaggg
2718	NAGAgtatgc	2742	NAGAgttaagg	2766	NAGAgttacgg	2790	NAGAgttaggg
2719	AAGAgtatgc	2743	AAGAgttaagg	2767	AAGAgttacgg	2791	AAGAgttaggg
2720	CAGAgtatgc	2744	CAGAgttaagg	2768	CAGAgttacgg	2792	CAGAgttaggg
2721	GAGAgtatgc	2745	GAGAgttaagg	2769	GAGAgttacgg	2793	GAGAgttaggg
2722	TAGAgtatgc	2746	TAGAgttaagg	2770	TAGAgttacgg	2794	TAGAgttaggg
2723	CNGAgtatgc	2747	CNGAgttaagg	2771	CNGAgttacgg	2795	CNGAgttaggg
2724	NCGAgtatgc	2748	NCGAgttaagg	2772	NCGAgttacgg	2796	NCGAgttaggg
2725	ACGAgtatgc	2749	ACGAgttaagg	2773	ACGAgttacgg	2797	ACGAgttaggg
2726	CCGAgtatgc	2750	CCGAgttaagg	2774	CCGAgttacgg	2798	CCGAgttaggg
2727	GCGAgtatgc	2751	GCGAgttaagg	2775	GCGAgttacgg	2799	GCGAgttaggg
2728	TCGAgtatgc	2752	TCGAgttaagg	2776	TCGAgttacgg	2800	TCGAgttaggg
2729	GNGAgtatgc	2753	GNGAgttaagg	2777	GNGAgttacgg	2801	GNGAgttaggg
2730	NGGAgtatgc	2754	NGGAgttaagg	2778	NGGAgttacgg	2802	NGGAgttaggg
2731	AGGAgtatgc	2755	AGGAgttaagg	2779	AGGAgttacgg	2803	AGGAgttaggg
2732	CGGAgtatgc	2756	CGGAgttaagg	2780	CGGAgttacgg	2804	CGGAgttaggg
2733	GGGAgtatgc	2757	GGGAgttaagg	2781	GGGAgttacgg	2805	GGGAgttaggg
2734	TGGAgtatgc	2758	TGGAgttaagg	2782	TGGAgttacgg	2806	TGGAgttaggg
2735	TNGAgtatgc	2759	TNGAgttaagg	2783	TNGAgttacgg	2807	TNGAgttaggg
2736	NTGAgtatgc	2760	NTGAgttaagg	2784	NTGAgttacgg	2808	NTGAgttaggg
2737	ATGAgtatgc	2761	ATGAgttaagg	2785	ATGAgttacgg	2809	ATGAgttaggg
2738	CTGAgtatgc	2762	CTGAgttaagg	2786	CTGAgttacgg	2810	CTGAgttaggg
2739	GTGAgtatgc	2763	GTGAgttaagg	2787	GTGAgttacgg	2811	GTGAgttaggg
2740	TTGAgtatgc	2764	TTGAgttaagg	2788	TTGAgttacgg	2812	TTGAgttaggg

[0081] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2813	ANGAgtatgg	2837	ANGAgttaagt	2861	ANGAgtacgt	2885	ANGAgttaggt
2814	NAGAgtatgg	2838	NAGAgttaagt	2862	NAGAgtacgt	2886	NAGAgttaggt
2815	AAGAgtatgg	2839	AAGAgttaagt	2863	AAGAgtacgt	2887	AAGAgttaggt
2816	CAGAgtatgg	2840	CAGAgttaagt	2864	CAGAgtacgt	2888	CAGAgttaggt
2817	GAGAgtatgg	2841	GAGAgttaagt	2865	GAGAgtacgt	2889	GAGAgttaggt
2818	TAGAgtatgg	2842	TAGAgttaagt	2866	TAGAgtacgt	2890	TAGAgttaggt
2819	CNGAgtatgg	2843	CNGAgttaagt	2867	CNGAgtacgt	2891	CNGAgttaggt
2820	NCGAgtatgg	2844	NCGAgttaagt	2868	NCGAgtacgt	2892	NCGAgttaggt
2821	ACGAgtatgg	2845	ACGAgttaagt	2869	ACGAgtacgt	2893	ACGAgttaggt
2822	CCGAgtatgg	2846	CCGAgttaagt	2870	CCGAgtacgt	2894	CCGAgttaggt
2823	GCGAgtatgg	2847	GCGAgttaagt	2871	GCGAgtacgt	2895	GCGAgttaggt
2824	TCGAgtatgg	2848	TCGAgttaagt	2872	TCGAgtacgt	2896	TCGAgttaggt
2825	GNGAgtatgg	2849	GNGAgttaagt	2873	GNGAgtacgt	2897	GNGAgttaggt
2826	NGGAgtatgg	2850	NGGAgttaagt	2874	NGGAgtacgt	2898	NGGAgttaggt
2827	AGGAgtatgg	2851	AGGAgttaagt	2875	AGGAgtacgt	2899	AGGAgttaggt
2828	CGGAgtatgg	2852	CGGAgttaagt	2876	CGGAgtacgt	2900	CGGAgttaggt
2829	GGGAgtatgg	2853	GGGAgttaagt	2877	GGGAgtacgt	2901	GGGAgttaggt
2830	TGGAgtatgg	2854	TGGAgttaagt	2878	TGGAgtacgt	2902	TGGAgttaggt
2831	TNGAgtatgg	2855	TNGAgttaagt	2879	TNGAgtacgt	2903	TNGAgttaggt
2832	NTGAgtatgg	2856	NTGAgttaagt	2880	NTGAgtacgt	2904	NTGAgttaggt
2833	ATGAgtatgg	2857	ATGAgttaagt	2881	ATGAgtacgt	2905	ATGAgttaggt
2834	CTGAgtatgg	2858	CTGAgttaagt	2882	CTGAgtacgt	2906	CTGAgttaggt
2835	GTGAgtatgg	2859	GTGAgttaagt	2883	GTGAgtacgt	2907	GTGAgttaggt
2836	TTGAgtatgg	2860	TTGAgttaagt	2884	TTGAgtacgt	2908	TTGAgttaggt

[0082] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
2909	ANGAgtatgt	2933	ANGAgtanga	2957	ANGAgtangc	2981	ANGAgtangg
2910	NAGAgtatgt	2934	NAGAgtanga	2958	NAGAgtangc	2982	NAGAgtangg
2911	AAGAgtatgt	2935	AAGAgtanga	2959	AAGAgtangc	2983	AAGAgtangg
2912	CAGAgtatgt	2936	CAGAgtanga	2960	CAGAgtangc	2984	CAGAgtangg
2913	GAGAgtatgt	2937	GAGAgtanga	2961	GAGAgtangc	2985	GAGAgtangg
2914	TAGAgtatgt	2938	TAGAgtanga	2962	TAGAgtangc	2986	TAGAgtangg
2915	CNGAgtatgt	2939	CNGAgtanga	2963	CNGAgtangc	2987	CNGAgtangg
2916	NCGAgtatgt	2940	NCGAgtanga	2964	NCGAgtangc	2988	NCGAgtangg
2917	ACGAgtatgt	2941	ACGAgtanga	2965	ACGAgtangc	2989	ACGAgtangg
2918	CCGAgtatgt	2942	CCGAgtanga	2966	CCGAgtangc	2990	CCGAgtangg
2919	GCGAgtatgt	2943	GCGAgtanga	2967	GCGAgtangc	2991	GCGAgtangg
2920	TCGAgtatgt	2944	TCGAgtanga	2968	TCGAgtangc	2992	TCGAgtangg
2921	GNGAgtatgt	2945	GNGAgtanga	2969	GNGAgtangc	2993	GNGAgtangg
2922	NGGAgtatgt	2946	NGGAgtanga	2970	NGGAgtangc	2994	NGGAgtangg
2923	AGGAgtatgt	2947	AGGAgtanga	2971	AGGAgtangc	2995	AGGAgtangg
2924	CGGAgtatgt	2948	CGGAgtanga	2972	CGGAgtangc	2996	CGGAgtangg
2925	GGGAgtatgt	2949	GGGAgtanga	2973	GGGAgtangc	2997	GGGAgtangg
2926	TGGAgtatgt	2950	TGGAgtanga	2974	TGGAgtangc	2998	TGGAgtangg
2927	TNGAgtatgt	2951	TNGAgtanga	2975	TNGAgtangc	2999	TNGAgtangg
2928	NTGAgtatgt	2952	NTGAgtanga	2976	NTGAgtangc	3000	NTGAgtangg
2929	ATGAgtatgt	2953	ATGAgtanga	2977	ATGAgtangc	3001	ATGAgtangg
2930	CTGAgtatgt	2954	CTGAgtanga	2978	CTGAgtangc	3002	CTGAgtangg
2931	GTGAgtatgt	2955	GTGAgtanga	2979	GTGAgtangc	3003	GTGAgtangg
2932	TTGAgtatgt	2956	TTGAgtanga	2980	TTGAgtangc	3004	TTGAgtangg

[0083] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3005	ANGAgtangt	3029	ANGAgtgngn	3053	ANGAgtgagn	3077	ANGAgtgcgn
3006	NAGAgtangt	3030	NAGAgtgngn	3054	NAGAgtgagn	3078	NAGAgtgcgn
3007	AAGAgtangt	3031	AAGAgtgngn	3055	AAGAgtgagn	3079	AAGAgtgcgn
3008	CAGAgtangt	3032	CAGAgtgngn	3056	CAGAgtgagn	3080	CAGAgtgcgn
3009	GAGAgtangt	3033	GAGAgtgngn	3057	GAGAgtgagn	3081	GAGAgtgcgn
3010	TAGAgtangt	3034	TAGAgtgngn	3058	TAGAgtgagn	3082	TAGAgtgcgn
3011	CNGAgtangt	3035	CNGAgtgngn	3059	CNGAgtgagn	3083	CNGAgtgcgn
3012	NCGAgtangt	3036	NCGAgtgngn	3060	NCGAgtgagn	3084	NCGAgtgcgn
3013	ACGAgtangt	3037	ACGAgtgngn	3061	ACGAgtgagn	3085	ACGAgtgcgn
3014	CCGAgtangt	3038	CCGAgtgngn	3062	CCGAgtgagn	3086	CCGAgtgcgn
3015	GCGAgtangt	3039	GCGAgtgngn	3063	GCGAgtgagn	3087	GCGAgtgcgn
3016	TCGAgtangt	3040	TCGAgtgngn	3064	TCGAgtgagn	3088	TCGAgtgcgn
3017	GNGAgtangt	3041	GNGAgtgngn	3065	GNGAgtgagn	3089	GNGAgtgcgn
3018	NGGAgtangt	3042	NGGAgtgngn	3066	NGGAgtgagn	3090	NGGAgtgcgn
3019	AGGAgtangt	3043	AGGAgtgngn	3067	AGGAgtgagn	3091	AGGAgtgcgn
3020	CGGAgtangt	3044	CGGAgtgngn	3068	CGGAgtgagn	3092	CGGAgtgcgn
3021	GGGAgtangt	3045	GGGAgtgngn	3069	GGGAgtgagn	3093	GGGAgtgcgn
3022	TGGAgtangt	3046	TGGAgtgngn	3070	TGGAgtgagn	3094	TGGAgtgcgn
3023	TNGAgtangt	3047	TNGAgtgngn	3071	TNGAgtgagn	3095	TNGAgtgcgn
3024	NTGAgtangt	3048	NTGAgtgngn	3072	NTGAgtgagn	3096	NTGAgtgcgn
3025	ATGAgtangt	3049	ATGAgtgngn	3073	ATGAgtgagn	3097	ATGAgtgcgn
3026	CTGAgtangt	3050	CTGAgtgngn	3074	CTGAgtgagn	3098	CTGAgtgcgn
3027	GTGAgtangt	3051	GTGAgtgngn	3075	GTGAgtgagn	3099	GTGAgtgcgn
3028	TTGAgtangt	3052	TTGAgtgngn	3076	TTGAgtgagn	3100	TTGAgtgcgn

[0084] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3101	ANGAgtgggn	3125	ANGAgtgtgn	3149	ANGAgtgaga	3173	ANGAgtgcga
3102	NAGAgtgggn	3126	NAGAgtgtgn	3150	NAGAgtgaga	3174	NAGAgtgcga
3103	AAGAgtgggn	3127	AAGAgtgtgn	3151	AAGAgtgaga	3175	AAGAgtgcga
3104	CAGAgtgggn	3128	CAGAgtgtgn	3152	CAGAgtgaga	3176	CAGAgtgcga
3105	GAGAgtgggn	3129	GAGAgtgtgn	3153	GAGAgtgaga	3177	GAGAgtgcga
3106	TAGAgtgggn	3130	TAGAgtgtgn	3154	TAGAgtgaga	3178	TAGAgtgcga
3107	CNGAgtgggn	3131	CNGAgtgtgn	3155	CNGAgtgaga	3179	CNGAgtgcga
3108	NCGAgtgggn	3132	NCGAgtgtgn	3156	NCGAgtgaga	3180	NCGAgtgcga
3109	ACGAgtgggn	3133	ACGAgtgtgn	3157	ACGAgtgaga	3181	ACGAgtgcga
3110	CCGAgtgggn	3134	CCGAgtgtgn	3158	CCGAgtgaga	3182	CCGAgtgcga
3111	GCGAgtgggn	3135	GCGAgtgtgn	3159	GCGAgtgaga	3183	GCGAgtgcga
3112	TCGAgtgggn	3136	TCGAgtgtgn	3160	TCGAgtgaga	3184	TCGAgtgcga
3113	GNGAgtgggn	3137	GNGAgtgtgn	3161	GNGAgtgaga	3185	GNGAgtgcga
3114	NGGAgtgggn	3138	NGGAgtgtgn	3162	NGGAgtgaga	3186	NGGAgtgcga
3115	AGGAgtgggn	3139	AGGAgtgtgn	3163	AGGAgtgaga	3187	AGGAgtgcga
3116	CGGAgtgggn	3140	CGGAgtgtgn	3164	CGGAgtgaga	3188	CGGAgtgcga
3117	GGGAgtgggn	3141	GGGAgtgtgn	3165	GGGAgtgaga	3189	GGGAgtgcga
3118	TGGAgtgggn	3142	TGGAgtgtgn	3166	TGGAgtgaga	3190	TGGAgtgcga
3119	TNGAgtgggn	3143	TNGAgtgtgn	3167	TNGAgtgaga	3191	TNGAgtgcga
3120	NTGAgtgggn	3144	NTGAgtgtgn	3168	NTGAgtgaga	3192	NTGAgtgcga
3121	ATGAgtgggn	3145	ATGAgtgtgn	3169	ATGAgtgaga	3193	ATGAgtgcga
3122	CTGAgtgggn	3146	CTGAgtgtgn	3170	CTGAgtgaga	3194	CTGAgtgcga
3123	GTGAgtgggn	3147	GTGAgtgtgn	3171	GTGAgtgaga	3195	GTGAgtgcga
3124	TTGAgtgggn	3148	TTGAgtgtgn	3172	TTGAgtgaga	3196	TTGAgtgcga

[0085] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3197	ANGAgtggga	3221	ANGAgtgtga	3245	ANGAgtgagc	3269	ANGAgtgcgc
3198	NAGAgtggga	3222	NAGAgtgtga	3246	NAGAgtgagc	3270	NAGAgtgcgc
3199	AAGAgtggga	3223	AAGAgtgtga	3247	AAGAgtgagc	3271	AAGAgtgcgc
3200	CAGAgtggga	3224	CAGAgtgtga	3248	CAGAgtgagc	3272	CAGAgtgcgc
3201	GAGAgtggga	3225	GAGAgtgtga	3249	GAGAgtgagc	3273	GAGAgtgcgc
3202	TAGAgtggga	3226	TAGAgtgtga	3250	TAGAgtgagc	3274	TAGAgtgcgc
3203	CNGAgtggga	3227	CNGAgtgtga	3251	CNGAgtgagc	3275	CNGAgtgcgc
3204	NCGAgtggga	3228	NCGAgtgtga	3252	NCGAgtgagc	3276	NCGAgtgcgc
3205	ACGAgtggga	3229	ACGAgtgtga	3253	ACGAgtgagc	3277	ACGAgtgcgc
3206	CCGAgtggga	3230	CCGAgtgtga	3254	CCGAgtgagc	3278	CCGAgtgcgc
3207	GCGAgtggga	3231	GCGAgtgtga	3255	GCGAgtgagc	3279	GCGAgtgcgc
3208	TCGAgtggga	3232	TCGAgtgtga	3256	TCGAgtgagc	3280	TCGAgtgcgc
3209	GNGAgtggga	3233	GNGAgtgtga	3257	GNGAgtgagc	3281	GNGAgtgcgc
3210	NGGAgtggga	3234	NGGAgtgtga	3258	NGGAgtgagc	3282	NGGAgtgcgc
3211	AGGAgtggga	3235	AGGAgtgtga	3259	AGGAgtgagc	3283	AGGAgtgcgc
3212	CGGAgtggga	3236	CGGAgtgtga	3260	CGGAgtgagc	3284	CGGAgtgcgc
3213	GGGAgtggga	3237	GGGAgtgtga	3261	GGGAgtgagc	3285	GGGAgtgcgc
3214	TGGAgtggga	3238	TGGAgtgtga	3262	TGGAgtgagc	3286	TGGAgtgcgc
3215	TNGAgtggga	3239	TNGAgtgtga	3263	TNGAgtgagc	3287	TNGAgtgcgc
3216	NTGAgtggga	3240	NTGAgtgtga	3264	NTGAgtgagc	3288	NTGAgtgcgc
3217	ATGAgtggga	3241	ATGAgtgtga	3265	ATGAgtgagc	3289	ATGAgtgcgc
3218	CTGAgtggga	3242	CTGAgtgtga	3266	CTGAgtgagc	3290	CTGAgtgcgc
3219	GTGAgtggga	3243	GTGAgtgtga	3267	GTGAgtgagc	3291	GTGAgtgcgc
3220	TTGAgtggga	3244	TTGAgtgtga	3268	TTGAgtgagc	3292	TTGAgtgcgc

[0086] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3293	ANGAgtgggc	3317	ANGAgtgtgc	3341	ANGAgtgagg	3365	ANGAgtgcgg
3294	NAGAgtgggc	3318	NAGAgtgtgc	3342	NAGAgtgagg	3366	NAGAgtgcgg
3295	AAGAgtgggc	3319	AAGAgtgtgc	3343	AAGAgtgagg	3367	AAGAgtgcgg
3296	CAGAgtgggc	3320	CAGAgtgtgc	3344	CAGAgtgagg	3368	CAGAgtgcgg
3297	GAGAgtgggc	3321	GAGAgtgtgc	3345	GAGAgtgagg	3369	GAGAgtgcgg
3298	TAGAgtgggc	3322	TAGAgtgtgc	3346	TAGAgtgagg	3370	TAGAgtgcgg
3299	CNGAgtgggc	3323	CNGAgtgtgc	3347	CNGAgtgagg	3371	CNGAgtgcgg
3300	NCGAgtgggc	3324	NCGAgtgtgc	3348	NCGAgtgagg	3372	NCGAgtgcgg
3301	ACGAgtgggc	3325	ACGAgtgtgc	3349	ACGAgtgagg	3373	ACGAgtgcgg
3302	CCGAgtgggc	3326	CCGAgtgtgc	3350	CCGAgtgagg	3374	CCGAgtgcgg
3303	GCGAgtgggc	3327	GCGAgtgtgc	3351	GCGAgtgagg	3375	GCGAgtgcgg
3304	TCGAgtgggc	3328	TCGAgtgtgc	3352	TCGAgtgagg	3376	TCGAgtgcgg
3305	GNGAgtgggc	3329	GNGAgtgtgc	3353	GNGAgtgagg	3377	GNGAgtgcgg
3306	NGGAgtgggc	3330	NGGAgtgtgc	3354	NGGAgtgagg	3378	NGGAgtgcgg
3307	AGGAgtgggc	3331	AGGAgtgtgc	3355	AGGAgtgagg	3379	AGGAgtgcgg
3308	CGGAgtgggc	3332	CGGAgtgtgc	3356	CGGAgtgagg	3380	CGGAgtgcgg
3309	GGGAgtgggc	3333	GGGAgtgtgc	3357	GGGAgtgagg	3381	GGGAgtgcgg
3310	TGGAgtgggc	3334	TGGAgtgtgc	3358	TGGAgtgagg	3382	TGGAgtgcgg
3311	TNGAgtgggc	3335	TNGAgtgtgc	3359	TNGAgtgagg	3383	TNGAgtgcgg
3312	NTGAgtgggc	3336	NTGAgtgtgc	3360	NTGAgtgagg	3384	NTGAgtgcgg
3313	ATGAgtgggc	3337	ATGAgtgtgc	3361	ATGAgtgagg	3385	ATGAgtgcgg
3314	CTGAgtgggc	3338	CTGAgtgtgc	3362	CTGAgtgagg	3386	CTGAgtgcgg
3315	GTGAgtgggc	3339	GTGAgtgtgc	3363	GTGAgtgagg	3387	GTGAgtgcgg
3316	TTGAgtgggc	3340	TTGAgtgtgc	3364	TTGAgtgagg	3388	TTGAgtgcgg

[0087] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3389	ANGAgtgggg	3413	ANGAgtgtgg	3437	ANGAgtgagt	3461	ANGAgtgcgt
3390	NAGAgtgggg	3414	NAGAgtgtgg	3438	NAGAgtgagt	3462	NAGAgtgcgt
3391	AAGAgtgggg	3415	AAGAgtgtgg	3439	AAGAgtgagt	3463	AAGAgtgcgt
3392	CAGAgtgggg	3416	CAGAgtgtgg	3440	CAGAgtgagt	3464	CAGAgtgcgt
3393	GAGAgtgggg	3417	GAGAgtgtgg	3441	GAGAgtgagt	3465	GAGAgtgcgt
3394	TAGAgtgggg	3418	TAGAgtgtgg	3442	TAGAgtgagt	3466	TAGAgtgcgt
3395	CNGAgtgggg	3419	CNGAgtgtgg	3443	CNGAgtgagt	3467	CNGAgtgcgt
3396	NCGAgtgggg	3420	NCGAgtgtgg	3444	NCGAgtgagt	3468	NCGAgtgcgt
3397	ACGAgtgggg	3421	ACGAgtgtgg	3445	ACGAgtgagt	3469	ACGAgtgcgt
3398	CCGAgtgggg	3422	CCGAgtgtgg	3446	CCGAgtgagt	3470	CCGAgtgcgt
3399	GCGAgtgggg	3423	GCGAgtgtgg	3447	GCGAgtgagt	3471	GCGAgtgcgt
3400	TCGAgtgggg	3424	TCGAgtgtgg	3448	TCGAgtgagt	3472	TCGAgtgcgt
3401	GNGAgtgggg	3425	GNGAgtgtgg	3449	GNGAgtgagt	3473	GNGAgtgcgt
3402	NGGAgtgggg	3426	NGGAgtgtgg	3450	NGGAgtgagt	3474	NGGAgtgcgt
3403	AGGAgtgggg	3427	AGGAgtgtgg	3451	AGGAgtgagt	3475	AGGAgtgcgt
3404	CGGAgtgggg	3428	CGGAgtgtgg	3452	CGGAgtgagt	3476	CGGAgtgcgt
3405	GGGAgtgggg	3429	GGGAgtgtgg	3453	GGGAgtgagt	3477	GGGAgtgcgt
3406	TGGAgtgggg	3430	TGGAgtgtgg	3454	TGGAgtgagt	3478	TGGAgtgcgt
3407	TNGAgtgggg	3431	TNGAgtgtgg	3455	TNGAgtgagt	3479	TNGAgtgcgt
3408	NTGAgtgggg	3432	NTGAgtgtgg	3456	NTGAgtgagt	3480	NTGAgtgcgt
3409	ATGAgtgggg	3433	ATGAgtgtgg	3457	ATGAgtgagt	3481	ATGAgtgcgt
3410	CTGAgtgggg	3434	CTGAgtgtgg	3458	CTGAgtgagt	3482	CTGAgtgcgt
3411	GTGAgtgggg	3435	GTGAgtgtgg	3459	GTGAgtgagt	3483	GTGAgtgcgt
3412	TTGAgtgggg	3436	TTGAgtgtgg	3460	TTGAgtgagt	3484	TTGAgtgcgt

[0088] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3485	ANGAgtgggt	3509	ANGAgttgtgt	3533	ANGAgtgnga	3557	ANGAgtgngc
3486	NAGAgtgggt	3510	NAGAgttgtgt	3534	NAGAgtgnga	3558	NAGAgtgngc
3487	AAGAgtgggt	3511	AAGAgttgtgt	3535	AAGAgtgnga	3559	AAGAgtgngc
3488	CAGAgtgggt	3512	CAGAgttgtgt	3536	CAGAgtgnga	3560	CAGAgtgngc
3489	GAGAgtgggt	3513	GAGAgttgtgt	3537	GAGAgtgnga	3561	GAGAgtgngc
3490	TAGAgtgggt	3514	TAGAgttgtgt	3538	TAGAgtgnga	3562	TAGAgtgngc
3491	CNGAgtgggt	3515	CNGAgttgtgt	3539	CNGAgtgnga	3563	CNGAgtgngc
3492	NCGAgtgggt	3516	NCGAgttgtgt	3540	NCGAgtgnga	3564	NCGAgtgngc
3493	ACGAgtgggt	3517	ACGAgttgtgt	3541	ACGAgtgnga	3565	ACGAgtgngc
3494	CCGAgtgggt	3518	CCGAgttgtgt	3542	CCGAgtgnga	3566	CCGAgtgngc
3495	GCGAgtgggt	3519	GCGAgttgtgt	3543	GCGAgtgnga	3567	GCGAgtgngc
3496	TCGAgtgggt	3520	TCGAgttgtgt	3544	TCGAgtgnga	3568	TCGAgtgngc
3497	GNGAgtgggt	3521	GNGAgttgtgt	3545	GNGAgtgnga	3569	GNGAgtgngc
3498	NGGAgtgggt	3522	NGGAgttgtgt	3546	NGGAgtgnga	3570	NGGAgtgngc
3499	AGGAgtgggt	3523	AGGAgttgtgt	3547	AGGAgtgnga	3571	AGGAgtgngc
3500	CGGAgtgggt	3524	CGGAgttgtgt	3548	CGGAgtgnga	3572	CGGAgtgngc
3501	GGGAgtgggt	3525	GGGAgttgtgt	3549	GGGAgtgnga	3573	GGGAgtgngc
3502	TGGAgtgggt	3526	TGGAgttgtgt	3550	TGGAgtgnga	3574	TGGAgtgngc
3503	TNGAgtgggt	3527	TNGAgttgtgt	3551	TNGAgtgnga	3575	TNGAgtgngc
3504	NTGAgtgggt	3528	NTGAgttgtgt	3552	NTGAgtgnga	3576	NTGAgtgngc
3505	ATGAgtgggt	3529	ATGAgttgtgt	3553	ATGAgtgnga	3577	ATGAgtgngc
3506	CTGAgtgggt	3530	CTGAgttgtgt	3554	CTGAgtgnga	3578	CTGAgtgngc
3507	GTGAgtgggt	3531	GTGAgttgtgt	3555	GTGAgtgnga	3579	GTGAgtgngc
3508	TTGAgtgggt	3532	TTGAgttgtgt	3556	TTGAgtgnga	3580	TTGAgtgngc

[0089] Table 14 (cont). Intronic REMS DNA sequence (wherein r is adenine or guanine, and n or N is any nucleotide)

SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence	SEQ ID NO.	Sequence
3581	ANGAgtgngg	3593	GNGAgtgngg	3605	ANGAgtgngt	3617	GNGAgtgngt
3582	NAGAgtgngg	3594	NGGAgtgngg	3606	NAGAgtgngt	3618	NGGAgtgngt
3583	AAGAgtgngg	3595	AGGAgtgngg	3607	AAGAgtgngt	3619	AGGAgtgngt
3584	CAGAgtgngg	3596	CGGAgtgngg	3608	CAGAgtgngt	3620	CGGAgtgngt
3585	GAGAgtgngg	3597	GGGAgtgngg	3609	GAGAgtgngt	3621	GGGAgtgngt
3586	TAGAgtgngg	3598	TGGAgtgngg	3610	TAGAgtgngt	3622	TGGAgtgngt
3587	CNGAgtgngg	3599	TNGAgtgngg	3611	CNGAgtgngt	3623	TNGAgtgngt
3588	NCGAgtgngg	3600	NTGAgtgngg	3612	NCGAgtgngt	3624	NTGAgtgngt
3589	ACGAgtgngg	3601	ATGAgtgngg	3613	ACGAgtgngt	3625	ATGAgtgngt
3590	CCGAgtgngg	3602	CTGAgtgngg	3614	CCGAgtgngt	3626	CTGAgtgngt
3591	GCGAgtgngg	3603	GTGAgtgngg	3615	GCGAgtgngt	3627	GTGAgtgngt
3592	TCGAgtgngg	3604	TTGAgtgngg	3616	TCGAgtgngt	3628	TTGAgtgngt

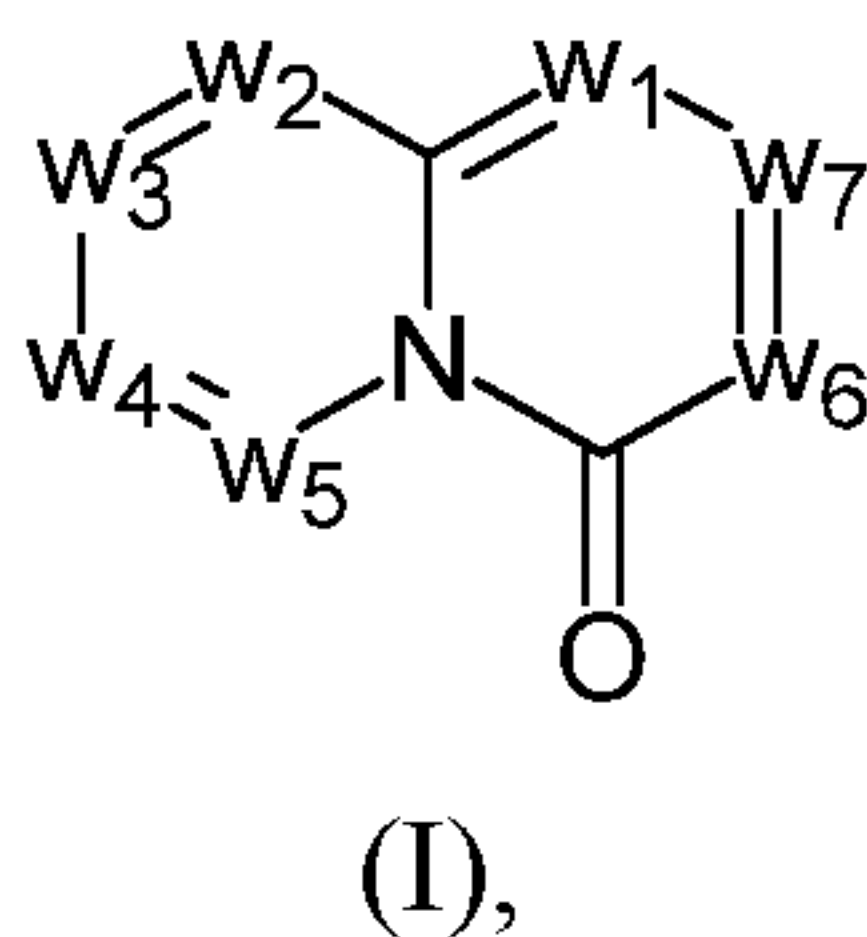
[0090] In certain embodiments, provided herein is a vector comprising the artificial gene construct described herein. In some embodiments, provided herein is a cell comprising an artificial gene construct described herein or a vector comprising an artificial gene construct described herein.

[0091] In another aspect, provided herein is a method of modulating the amount and type of a protein produced by a cell containing an artificial gene construct described herein. In one embodiment, provided herein is a method of modulating the amount and type of a protein produced by a cell containing an artificial gene construct described herein, the method comprising contacting the cell with a compound of Formula (I) or a form thereof. In certain embodiments, the artificial gene construct encodes a therapeutic protein. In certain embodiments, the artificial gene construct encodes a non-functional protein. In some embodiments producing a therapeutic protein, the artificial gene construct may also encode a detectable reporter protein. In some embodiments producing a non-functional protein, the artificial gene construct may also encode a detectable reporter protein.

[0092] In another aspect, provided herein is a method of modulating the amount of a protein produced by a subject, wherein the subject is or was administered an artificial gene construct described herein. In one embodiment, provided herein is method of regulating the amount of a protein produced by a subject, the method comprising: (a) administering an artificial gene

construct or a vector comprising the artificial gene construct described herein to the subject; and (b) administering a compound of Formula (I) or a form thereof to the subject. In another embodiment, provided herein is a method of regulating the amount of a protein produced by a subject, the method comprising administering a compound of Formula (I) or a form thereof to a subject carrying a gene containing a nucleotide sequence encoding an intronic REMS. In another embodiment, provided herein is a method of regulating the amount of a protein produced by a subject, the method comprising administering a compound of Formula (I) to the subject, wherein the subject was previously administered an artificial gene construct described herein. In certain embodiments, the artificial gene construct may encode a therapeutic or a non-functional protein. In some embodiments, the artificial gene construct encodes a detectable reporter protein. In certain embodiments, the subject is a non-human. In specific embodiments, the subject is a human.

[0093] In another aspect, provided herein is a method for modulating the amount of an RNA transcript produced from precursor RNA containing an endogenous or non-endogenous intronic recognition element for splicing modifier (REMS), the method comprising contacting the precursor RNA with a compound of Formula (I) or a form thereof, wherein the endogenous or non-endogenous intronic REMS comprises the sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein Formula (I) is



wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w_3 is C-R₂, then w_6 is C-R₁ and w_4 and w_7 are independently C-R_a or N; or,
 when w_4 is C-R₁, then w_7 is C-R₂ and w_3 is C-R_a or N and w_6 is C-R_c or N; or,
 when w_4 is C-R₂, then w_7 is C-R₁ and w_3 is C-R_a or N and w_6 is C-R_c or N; and,
 wherein any one, two or three of w_1 , w_2 , w_3 , w_4 , w_5 , w_6 and w_7 may optionally be N;
 R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,
 (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,
 C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,
 (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,

(heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

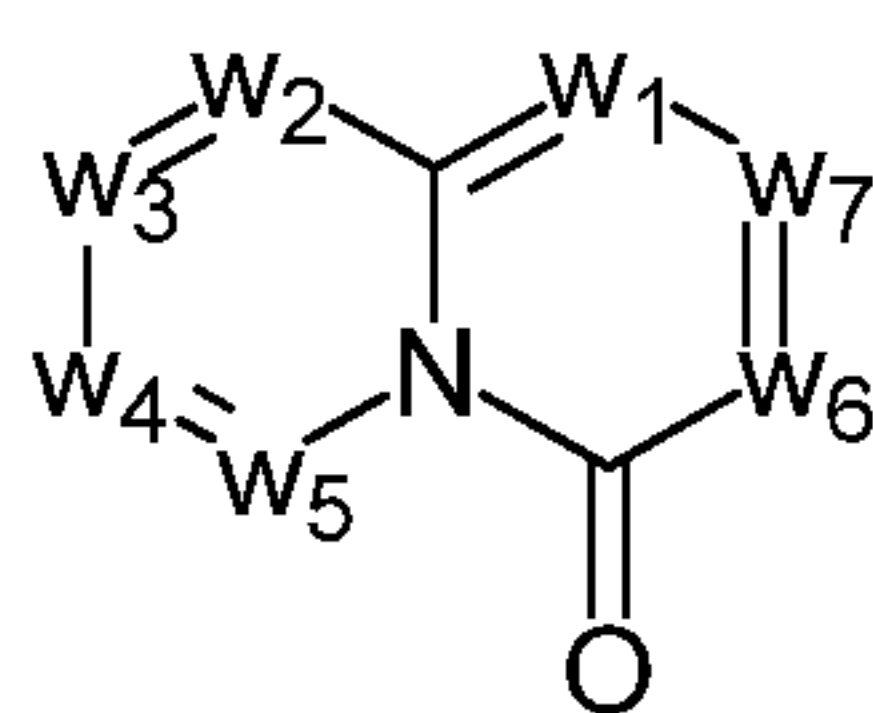
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[0094] In another aspect, provided herein is a method for modulating the amount of an RNA transcript produced from precursor RNA containing an endogenous or non-endogenous intronic recognition element for splicing modifier (REMS), the method comprising contacting the precursor RNA with a compound of Formula (I) or a form thereof, wherein the endogenous or non-endogenous intronic REMS comprises the sequence NNGAgurngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide, and wherein Formula (I) is



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

(hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

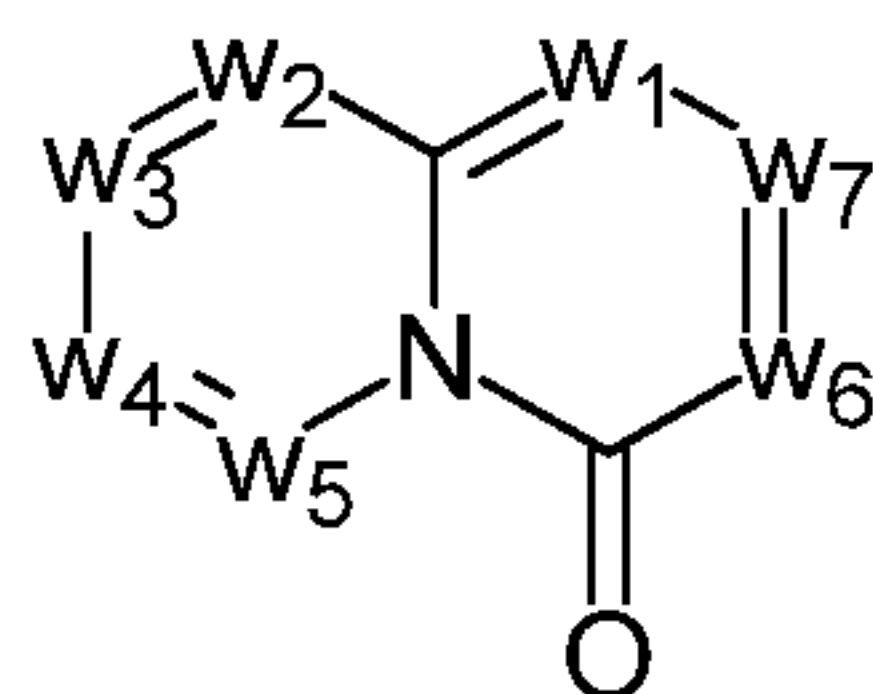
R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[0095] In another aspect, provided herein is a method of regulating the amount and type of a protein produced by a gene comprising a nucleotide sequence encoding an endogenous or non-endogenous intronic REMS in a subject, wherein the nucleotide sequence encoding the endogenous or non-endogenous intronic REMS comprises the sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide, the method comprising administering a compound of Formula (I) to the subject, wherein Formula (I) is



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or

(heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl,

aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or

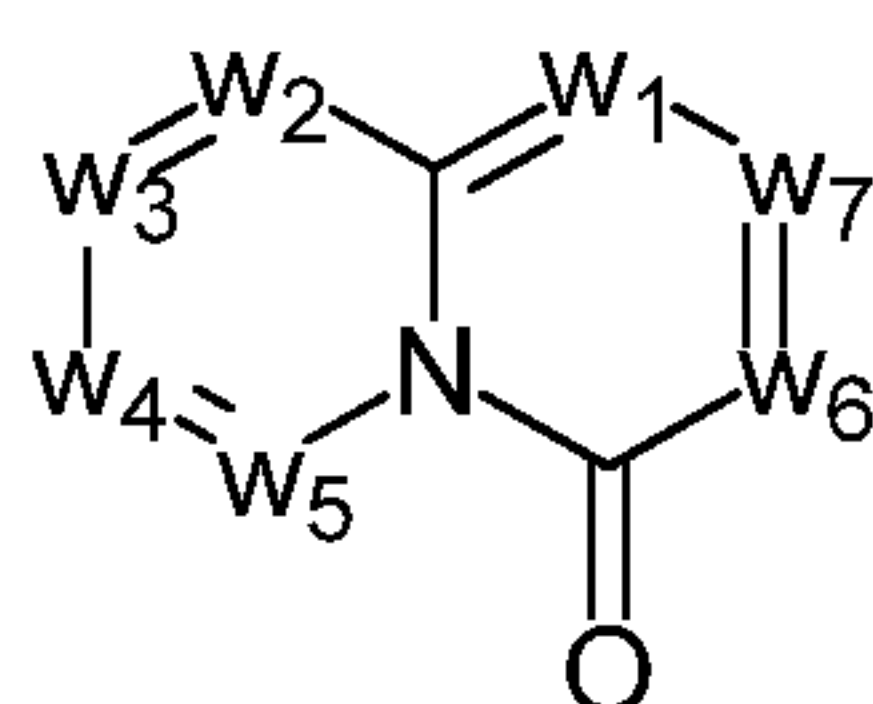
heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[0096] In another aspect, provided herein is a method of regulating the amount and type of a protein produced by a gene comprising a nucleotide sequence encoding an endogenous or non-endogenous intronic REMS in a subject, wherein the nucleotide sequence encoding the endogenous or non-endogenous intronic REMS comprises the sequence NNGAgtrngn (SEQ ID NO: 3), wherein r is adenine or guanine and n or N is any nucleotide, the method comprising administering a compound of Formula (I) to the subject, wherein Formula (I) is



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

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

(heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[0097] In specific embodiments of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCA1, ABCA10, ABCB7, ABCB8, ABCC1, ABCC3, ABHD10, ABL2, ABLIM3, ACACA, ACADVL, ACAT2, ACTA2, ADAL, ADAM12, ADAM15, ADAM17, ADAM33, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF2, AFF3, AGK, AGPAT3, AGPAT4, AGPS, AHCYL2, AHDC1, AHRR, AJUBA, AK021888, AK310472, AKAP1, AKAP3, AKAP9, AKNA, ALCAM, ALDH4A1, AMPD2, ANK1, ANK2, ANK3, ANKFY1, ANKHD1-EIF4EBP3, ANKRA2, ANKRD17, ANKRD33B, ANKRD36, ANKS6, ANP32A, ANXA11, ANXA6, AP2B1, AP4B1-AS1, APAF1, APIP, APLP2, APP, APPL2, APTX, ARHGAP1, ARHGAP12, ARHGAP22, ARHGEF16, ARID1A, ARID2, ARID5B, ARL9, ARL15, ARMCX3, ARMCX6, ASAP1, ASIC1, ASL, ASNS, ASPH, ATAD2B, ATF7IP, ATG5, ATG9A, ATMIN, ATP2A3, ATP2C1, ATXN1, ATXN3, AURKA, AXIN1, B3GALT2, B3GNT6, B4GALT2, BACE1, BAG2, BASP1, BC033281, BCAR3, BCL2L15, BCYRN1, BECN1, BEND6, BHMT2, BICD1, BIN1, BIN3-IT1, BIRC3, BIRC6, BNC1, BRD2, BRPF1, BSCL2, BTBD10, BTG2, BTN3A1, BZW1, C1orf86, C10orf54, C11orf30, C11orf70, C11orf73, C11orf94, C12orf4, C12orf56, C14orf132, C17orf76-AS1, C19orf47, C3, C4orf27, C5orf24, C6orf48, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, C9orf69, CA13, CA3, CAB39, CACNA2D2, CACNB1,

CADM1, CALU, CAMKK1, CAND2, CAPNS1, CASC3, CASP7, CASP8AP2, CAV1, CCAR1, CCDC77, CCDC79, CCDC88A, CCDC92, CCDC122, CCER2, CCNF, CCT6A, CD276, CD46, CDC25B, CDC40, CDC42BPA, CDCA7, CDH11, CDH13, CDK11B, CDK16, CDKAL1, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CEP68, CFH, CFLAR, CHD8, CHEK1, CIITA, CIZ1, CLDN23, CLIC1, CLK4, CLTA, CMAHP, CNGA4, CNOT1, CNRIP1, CNTD1, COG1, COL1A1, COL11A1, COL12A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A1, COL6A6, COL8A1, COLEC12, COMP, COPS7B, CPA4, CPEB2, CPQ, CPSF4, CREB5, CRISPLD2, CRLF1, CRLS1, CRTAP, CRYBG3, CRYL1, CSDE1, CSNK1A1, CSNK1E, CSNK1G1, CTDSP2, CTNND1, CUL2, CUL4A, CUX1, CYB5B, CYB5R2, CYBRD1, CYGB, CYP1B1, CYP51A1, DAB2, DACT1, DAGLB, DARS, DAXX, DCAF10, DCAF11, DCAF17, DCBLD2, DCLK1, DCN, DCUN1D4, DDAH1, DDAH2, DDHD2, DDIT4L, DDR1, DDX39B, DDX42, DDX50, DEGS1, DENND1A, DENND1B, DENND5A, DEPTOR, DFNBS9, DGCR2, DGKA, DHCR24, DHCR7, DHFR, DHX9, DIAPH1, DIAPH3, DIRAS3, DIS3L, DKFZp434M1735, DKK3, DLC1, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNM2, DNMBP, DOCK1, DOCK11, DPP8, DSEL, DST, DSTN, DYNC1H1, DYRK1A, DZIP1L, EBF1, EEA1, EEF1A1, EFCAB14, EFEMP1, EGR1, EGR3, EHMT2, EIF2B3, EIF4G1, EIF4G2, EIF4G3, ELF2, ELN, ELP4, EMX2OS, ENAH, ENG, ENPP1, ENPP2, ENSA, EP300, EPN1, EPT1, ERC1, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, ETV5, EVC, EVC2, EXO1, EXTL2, EYA3, F2R, FADS1, FADS2, FAF1, FAIM, FAM111A, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM198B, FAM20A, FAM219A, FAM219B, FAM3C, FAM46B, FAM65A, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXO9, FBXL6, FBXO10, FBXO18, FBXO31, FBXO34, FBXO9, FCHO1, FDFT1, FDPS, FER, FEZ1, FGD5-AS1, FGFR2, FGFR1, FGL2, FHOD3, FLII, FLNB, FLT1, FN1, FNBP1, FOCAD, FOS, FOSB, FOSL1, FOXK1, FOXM1, FRAS1, FSCN2, FUS, FYN, GABPB1, GAL3ST4, GALC, GALNT1, GALNT15, GAS7, GATA6, GBA2, GBGT1, GCFC2, GCNT1, GDF6, GGACT, GGCT, GHDC, GIGYF2, GJC1, GLCE, GMIP, GNA13, GNAQ, GNAS, GNL3L, GOLGA2, GOLGA4, GOLGB1, GORASP1, GPR1, GPR183, GPR50, GPR89A, GPRC5A, GPRC5B, GPSM2, GREM1, GRK6, GRTP1, GSE1, GTF2H2B, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS2, HAS3, HAT1, HAUS3, HAUS6, HAVCR2, HDAC5, HDAC7, HDX, HECTD2-AS1, HEG1, HEPH, HEY1, HLA-A, HLA-E, HLTF, HMGA1, HMGA2, HMGB1, HMGCR, HMGN3-AS1, HMGCS1, HOOK3, HMOX1, HNMT, HNRNPR,

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 PRPF31, PRPH2, PRRG4, PRSS23, PRUNE2, PSMA4, PSMC1, PSMD6, PSMD6-AS2,
 PTGIS, PTK2B, PTPN14, PTX3, PUF60, PUS7, PVR, P XK, PXN, QKI, RAB23, RAB2B,
 RAB30, RAB34, RAB38, RAB44, RAD1, RAD9B, RAD23B, RAF1, RALB, RAP1A,
 RAP1GDS1, RAPGEF1, RARG, RARS, RARS2, RASSF8, RBBP8, RBCK1, RBFOX2, RBKS,
 RBM10, RCC1, RDX, RERE, RFTN1, RFWD2, RFX3-AS1, RGCC, RGS10, RGS3, RIF1,
 RNF14, RNF19A, RNF38, RNFT1, ROR1, ROR2, RPA1, RPL10, RPS10, RPS6KB2,
 RPS6KC1, RRBP1, RWDD4, SAMD4A, SAMD9, SAMD9L, SAR1A, SART3, SCAF4,
 SCAF8, SCARNA9, SCD, SCLT1, SCO1, SDCBP, SEC14L1, SEC22A, SEC24A, SEC24B,
 SEC61A1, SENP6, SEPT9, SERGEF, SERPINE2, SF1, SGK3, SGOL2, SH3RF1, SH3YL1,
 SHROOM3, SIGLEC10, SKA2, SKIL, SLC12A2, SLC24A3, SLC25A17, SLC35F3, SLC39A3,
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 SLC7A8, SLC7A11, SLC9A3, SLIT3, SMARCA4, SMARCC2, SMC4, SMC6, SMCHD1,
 SMG1, SMG1P3, SMN2, SMPD4, SMTN, SMYD3, SMYD5, SNAP23, SNED1, SNHG16,
 SNX7, SNX14, SOCS2, SON, SORBS2, SORCS2, SOS2, SOX7, SPATA18, SPATA20,
 SPATA5, SPATS2, SPDYA, SPEF2, SPG20, SPIDR, SPRED2, SPRYD7, SQLE, SQRDL,
 SQSTM1, SRCAP, SREBF1, SREK1, SRGAP1, SRRM1, SRSF3, STAC2, STARD4, STAT1,
 STAT3, STAT4, STAU1, STC2, STEAP2, STK32B, STRIP1, STRN3, STRN4, STS, STX16,
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 TOPORS, TP53AIP1, TP53INP1, TPRG1, TRAF3, TRAK1, TRAPPC12, TRIB1, TRIM2,
 TRIM23, TRIM26, TRIM28, TRIM65, TRIM66, TRMT1L, TRPC4, TRPS1, TSC2, TSHZ1,

TSHZ2, TSPAN11, TSPAN18, TSPAN2, TSPAN7, TSSK3, TTC7A, TTC7B, TUBB2C, TUBB3, TUBE1, TXNIP, TXNL1, TXNRD1, TYW5, U2SURP, UBAP2L, UBE2G2, UBE2V1, UBQLN4, UCHL5, UHMK1, UHRF1BP1L, UNC5B, URGCP, USP19, USP7, USP27X, UVRAG, VANGL1, VARS2, VAV2, VCL, VIM-AS1, VIPAS39, VPS13A, VPS29, VPS41, VPS51, VSTM2L, VWA8, VWF, WDR19, WDR27, WDR37, WDR48, WDR91, WIPF1, WISP1, WNK1, WNT5B, WNT10B, WSB1, WWTR1, XIAP, XRN2, YAP1, YDJC, YES1, YPEL5, YTHDF3, Z24749, ZAK, ZBTB10, ZBTB24, ZBTB26, ZBTB7A, ZC3H12C, ZC3H14, ZC3H18, ZCCHC5, ZCCHC8, ZCCHC11, ZEB1, ZEB2, ZFAND1, ZFAND5, ZFP82, ZHX3, ZMIZ1, ZMIZ1-AS1, ZMYM2, ZNF12, ZNF138, ZNF148, ZNF212, ZNF219, ZNF227, ZNF232, ZNF24, ZNF268, ZNF28, ZNF281, ZNF335, ZNF350, ZNF37A, ZNF37BP, ZNF395, ZNF431, ZNF583, ZNF621, ZNF652, ZNF655, ZNF660, ZNF674, ZNF680, ZNF74, ZNF764, ZNF778, ZNF780A, ZNF79, ZNF827, ZNF837, ZNF839 or ZNF91.

[0098] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARMCX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15,

GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B,

YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837.

[0099] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is not described in International Publication No. WO 2015/105657. In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is not described in International Publication No. WO 2016/196386. In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is not described in International Publication No. WO 2015/105657 and not described in International Publication No. WO 2016/196386.

[00100] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCA1, ABCB7, ABCC1, ABHD10, ABL2, ABLIM3, ACACA, ACADVL, ACAT2, ADAM12, ADAM15, ADAM17, ADAM33, AFF2, AGK, AGPAT3, AGPS, AHCYL2, AHDC1, AHRR, AJUBA, AK021888, AK310472, AKAP1, AKAP9, AKNA, ALCAM, ALDH4A1, AMPD2, ANK2, ANKFY1, ANKHD1-EIF4EBP3, ANKRD17, ANKS6, ANP32A, ANXA11, ANXA6, AP2B1, APAF1, APLP2, APP, APPL2, APTX, ARHGAP22, ARID1A, ARID2, ARMCX3, ASAP1, ASL, ASNS, ASPH, ATAD2B, ATF7IP, ATG9A, ATMIN, ATP2C1, ATXN3, AURKA, AXIN1, B4GALT2, BACE1, BAG2, BASP1, BC033281, BCAR3, BEND6, BICD1, BIN1, BNC1, BRD2, BRPF1, BSCL2, BTBD10, BZW1, C11orf30, C11orf73, C17orf76-AS1, C4orf27, C5orf24, C6orf48, C9orf69, CAB39, CALU, CAMKK1, CAPNS1, CASC3, CASP8AP2, CAV1, CCAR1, CCDC77, CCDC88A, CCDC92, CCT6A, CD276, CD46, CDC25B, CDC40, CDC42BPA, CDCA7, CDH11, CDH13, CDK11B, CDK16, CDKAL1, CEP68, CFLAR, CHD8, CIZ1, CLIC1, CLK4, CNOT1, COG1, COL12A1, COL1A1, COL6A1, COPS7B, CPEB2, CREB5, CRLS1, CRTAP, CSDE1, CSNK1A1, CTDSP2, CTNND1, CUL2, CUL4A, CUX1, CYB5B, CYBRD1, CYP51A1, DAB2, DACT1, DARS, DAXX, DCAF10, DCAF11, DCBLD2, DCUN1D4, DDAH1, DDAH2, DDHD2, DDR1, DDX39B, DDX42, DENND1A, DENND1B, DENND5A, DGCR2, DGKA, DHCR24, DHCR7, DHFR, DHX9, DIAPH1, DIAPH3, DIS3L, DKFZp434M1735, DKK3, DLC1, DNM2, DOCK1, DPP8, DSEL, DST, DSTN, EBF1, EEA1, EEF1A1, EFCAB14, EGR1, EHMT2, EIF2B3, EIF4G1, EIF4G2, EIF4G3, ELF2, ENG, ENPP2, ENSA, EPN1, EPT1, ERC1, ERGIC3, ETV5, EXO1, EXTL2,

EYA3, FADS1, FADS2, FAF1, FAM111A, FAM198B, FAM219A, FAM219B, FAM3C, FAM65A, FBXO10, FBXO18, FBXO31, FBXO34, FBXO9, FDFT1, FDPS, FER, FEZ1, FGD5-AS1, FGFRL1, FHOD3, FLII, FLNB, FN1, FNBP1, FOCAD, FOS, FOSB, FOSL1, FOXK1, FOXM1, FUS, FYN, GABPB1, GALT, GALNT1, GAS7, GBA2, GCFC2, GGCT, GHDC, GIGYF2, GJC1, GMIP, GNA13, GNAS, GNL3L, GOLGA2, GOLGA4, GOLGB1, GORASP1, GPR1, GPR89A, GPSM2, GREM1, GRK6, GSE1, GTF2H2B, HAS2, HAT1, HAUS3, HAUS6, HDAC7, HEG1, HLA-A, HLA-E, HLTf, HMGA1, HMGB1, HMGCR, HMGCS1, HMOX1, HNRNPR, HNRNPUL1, HP1BP3, HRH1, HSD17B12, HSD17B4, HTT, IARS, IDH1, IDI1, IGF2BP2, IL6ST, INHBA, INSIG1, IQCE, ITGAV, ITGB5, ITM2C, ITSN1, KANSL3, KCNK2, KIAA1033, KIAA1143, KIAA1199, KIAA1522, KIAA1524, KIAA1549, KIAA1715, KIF14, KIF2A, KIF3A, KLC1, KLC2, KLF6, KLHL7, KRT18, KRT19, KRT34, KRTAP2-3, LAMA2, LAMB1, LARP4, LARP7, LATS2, LDLR, LEMD3, LGALS8, LIMS1, LINC00341, LINC00657, LMAN2L, LMO7, LONP1, LOX, LRCH4, LRIG1, LRP8, LRRC8A, LSS, LTBR, LUC7L2, LZTS2, MADD, MAGED4, MAGED4B, MAN1A2, MAP4K4, MBD1, MBOAT7, MDM2, MED1, MEDAG, MEF2D, MEIS2, MEMO1, MEPCE, MFGE8, MICAL2, MINPP1, MKL1, MKLN1, MKNK2, MLLT4, MLST8, MMAB, MMS19, MMS22L, MPPE1, MPZL1, MRPL3, MSANTD3, MSC, MSH2, MSH6, MSL3, MSMO1, MSRB3, MTAP, MTERFD1, MTHFD1L, MTMR9, MTRR, MUM1, MVD, MVK, MYADM, MYLK, MYO1D, MYO9B, MYOF, NAA35, NADK, NASP, NAV1, NAV2, NCOA1, NCOA3, NCOA4, NCSTN, NELFA, NEO1, NEURL1B, NF2, NFE2L1, NFX1, NID1, NID2, NIPA1, NKX3-1, NOL10, NOMO3, NPEPPS, NRD1, NREP, NRG1, NSUN4, NT5C2, NT5E, NTNG1, NUDT4, NUP153, NUP35, NUP50, NUPL1, NUSAP1, ODF2, OS9, OSBPL6, OSMR, P4HA1, P4HB, PABPC1, PAK4, PAPD4, PARD3, PARN, PARP14, PARP4, PARVB, PCBP2, PCBP4, PCDHGB3, PCGF3, PCM1, PCMTD2, PCNXL2, PCSK9, PDE4A, PDE7A, PDLIM7, PDXDC1, PEPD, PEX5, PFKP, PHF19, PHF8, PHRF1, PHTF2, PI4K2A, PIEZO1, PIGU, PIK3C2B, PITPNA, PITPNB, PITPNM1, PLAUI, PLEC, PLEKHB2, PLSCR3, PLXNB2, PLXNC1, PMS1, POLE3, POLR3D, POSTN, POU2F1, PPAPDC1A, PPARA, PPHLN1, PPIP5K1, PPP1R12A, PPP6R1, PPP6R2, PRKACB, PRKDC, PRMT1, PRNP, PRSS23, PSMA4, PSMC1, PSMD6, PTK2B, PTPN14, PUF60, PUS7, PVR, PXN, QKI, RAB23, RAB2B, RAB34, RAD1, RAD23B, RALB, RAP1A, RAP1GDS1, RARG, RASSF8, RBCK1, RBFOX2, RBM10, RCC1, RFTN1, RFWD2, RGS10, RGS3, RIF1, RNF14, RNF19A, RNF38, RNFT1, RPL10, RPS6KC1, RRBPI, RWDD4,

SAMD9, SAMD9L, SAR1A, SART3, SCAF4, SCAF8, SCD, SCLT1, SCO1, SDCBP, SEC14L1, SEC22A, SEC24B, SEC61A1, SEPT9, SERPINE2, SF1, SGOL2, SH3RF1, SKIL, SLC25A17, SLC39A3, SLC41A1, SLC4A4, SLC7A6, SLC7A8, SMARCA4, SMARCC2, SMC4, SMC6, SMCHD1, SMG1, SMN2, SMPD4, SMYD3, SMYD5, SNAP23, SNHG16, SNX14, SOCS2, SON, SOS2, SPATA20, SPATS2, SPG20, SPRED2, SQLE, SQRDL, SQSTM1, SRCAP, SREBF1, SREK1, SRSF3, STARD4, STAT1, STAT3, STAU1, STC2, STEAP2, STRIP1, STRN3, STX16, SUPT20H, SYNE1, SYNE2, SYT15, SYTL2, TACC1, TAF2, TANC2, TARBP1, TARS, TBC1D15, TBL2, TCF7L2, TENC1, TENM2, TEP1, TET3, TFCP2, TGFBI, TGFB1, TGFB1, THADA, THAP4, THRB, TIMP2, TJP2, TLE3, TLK1, TMEM154, TMEM47, TMEM63A, TNC, TNFAIP3, TNFRSF12A, TNIP1, TNKS1BP1, TNPO3, TNS1, TNS3, TOE1, TOMM40, TOMM5, TOPORS, TP53INP1, TRAF3, TRAK1, TRAPPC12, TRIB1, TRIM2, TRIM23, TRIM26, TRIM28, TRIM65, TRMT1L, TRPS1, TSC2, TSHZ1, TSPAN2, TTC7A, TUBB2C, TUBB3, TXNL1, TXNRD1, U2SURP, UBAP2L, UBE2G2, UBE2V1, UBQLN4, UCHL5, UHMK1, UHRF1BP1L, UNC5B, USP19, USP7, VANGL1, VARS2, VCL, VIPAS39, VPS13A, VPS29, VPS51, VWA8, WDR19, WDR37, WDR48, WIPF1, WNT5B, WSB1, WWTR1, XIAP, XRN2, YAP1, YES1, YPEL5, YTHDF3, Z24749, ZAK, ZBTB10, ZBTB24, ZBTB7A, ZC3H12C, ZC3H14, ZC3H18, ZCCHC11, ZEB1, ZEB2, ZFAND1, ZFAND5, ZHX3, ZMIZ1, ZMYM2, ZNF12, ZNF148, ZNF219, ZNF227, ZNF24, ZNF268, ZNF28, ZNF281, ZNF335, ZNF37A, ZNF37BP, ZNF395, ZNF583, ZNF621, ZNF652, ZNF655, ZNF674, ZNF74, ZNF764, ZNF778, ZNF780A, ZNF827, ZNF839 or ZNF91.

[00101] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCB8, ANKRD36, APLP2, ARHGAP12, ARMCX6, ASAP1, ATG5, AXIN1, BIRC6, C1orf86, CDC42BPA, CLTA, DYRK1A, ERGIC3, FBXL6, FOXM1, GGCT, KAT6B, KDM6A, KIF3A, KMT2D, LARP7, LYRM1, MADD, MAN2C1, MRPL55, MYCBP2, MYO9B, PNISR, RAP1A, RAPGEF1, SENP6, SH3YL1, SLC25A17, SMN2, SREK1, STRN3, TAF2, TMEM134, VPS29, ZFAND1 or ZNF431.

[00102] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCB8, ANKRD36, ARHGAP12, ARMCX6, ATG5, BIRC6, C1orf86, CLTA, DYRK1A, FBXL6,

KAT6B, KDM6A, KMT2D, LYRM1, MAN2C1, MRPL55, MYCBP2, PNISR, RAPGEF1, SENP6, SH3YL1, TMEM134 or ZNF431.

[00103] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCA10, ABCC1, ACTA2, ADAL, ADAM12, ADAMTS1, ADAMTS5, ADD1, ADGRG6, ADH6, ADHFE1, AFF2, AFF3, AGK, AGPS, AKAP3, ANK1, ANK2, ANK3, ANKRD33B, ANXA11, ANXA6, AP4B1-AS1, ARHGEF16, ARID5B, ARL9, ARMCX3, ASAP1, ASIC1, ATP2A3, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BIN3-IT1, BIRC3, BTG2, C10orf54, C11orf70, C11orf73, C11orf94, C12orf56, C19orf47, C3, C4orf27, C7orf31, C8orf34, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CCDC79, CCER2, CCNF, CDCA7, CDKAL1, CELSR1, CEMIP, CEP170, CFH, CIITA, CLDN23, CMAHP, CNGA4, CNTD1, COL11A1, COL12A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CRISPLD2, CRLF1, CRYL1, CUX1, CYB5B, CYB5R2, CYGB, CYP1B1, DCLK1, DCN, DDIT4L, DDX42, DDX50, DEGS1, DENND1A, DENND5A, DEPTOR, DFNB59, DGKA, DHFR, DIAPH3, DIRAS3, DIS3L, DLG5, DNAH8, DNAJC27, DOCK1, DOCK11, DYNC1I1, DZIP1L, EBF1, EFEMP1, EGR3, EIF2B3, ELN, ELP4, EMX2OS, ENPP1, ERCC8, ESM1, EVC2, F2R, FAM160A1, FAM198B, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXO9, FCHO1, FER, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALT, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GNAQ, GOLGB1, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HECTD2-AS1, HEPH, HEY1, HLTF, HMGN3-AS1, HMOX1, HOOK3, HSD17B12, HSPA1L, HTATIP2, HTT, IGDCC4, IGF2R, IGFBP3, IL16, INA, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1524, KIAA1715, KIAA1755, KIT, KLF17, KLRG1, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LRBA, LRP4, LRRC32, LRRC39, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN1A2, MAN2A1, MAPK13, MASP1, MB, MC4R, MEDAG, MEGF6, MEMO1, MIAT, MIR612, MLLT10, MMP10, MMP24, MMS19, MN1, MOXD1, MRV11, MSH4, MTERF3, MXRA5, MYO1D, NA, NAALADL2, NAE1, NAGS, NDNF, NEURL1B, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, NTNG1,

OCLN, OLR1, OSBPL10, OXCT2, PAIP2B, PAPD4, PBLD, PCM1, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PDXDC1, PEAR1, PEPD, PHACTR3, PI4K2B, PIK3R1, PIM2, PITPNB, PITPNM3, PLAUI, PLEK2, PLEKHA6, PLEKHH2, PLXNC1, PMS1, PODN, POLN, POLR1A, POSTN, PPM1E, PPP3CA, PRKCA, PRKDC, PRKG1, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, RAB30, RAB38, RAB44, RAD9B, RARS, RBBP8, RBKS, RCC1, RDX, RFWD2, RFX3-AS1, RGCC, RNFT1, ROR1, ROR2, RWDD4, SCARNA9, SCO1, SEC22A, SHROOM3, SIGLEC10, SLC24A3, SLC35F3, SLC39A10, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SMYD3, SNED1, SORBS2, SORCS2, SOX7, SPDYA, SPEF2, SQRDL, STAC2, STAT1, STAT4, STEAP2, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TARBP1, TEX21P, TGFA, TGFB2, TGFB3, TGM2, THADA, THBS2, THRB, TMEM102, TMEM119, TMEM256-PLSCR3, TMEM50B, TNC, TNFAIP8L3, TNFRSF14, TNRC18P1, TNS3, TNXB, TP53AIP1, TPRG1, TRAF3, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TXNIP, UNC5B, USP27X, UVRAG, VIM-AS1, VPS41, VSTM2L, VWA8, VWF, WDR91, WISP1, WNT10B, XRN2, YDJC, ZBTB26, ZCCHC5, ZFP82, ZMIZ1-AS1, ZNF212, ZNF350, ZNF660, ZNF79 or ZNF837.

[00104] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCA10, ACTA2, ADAL, ADAMTS1, ADAMTS5, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AKAP3, ANK1, ANK3, ANKRD33B, AP4B1-AS1, ARHGEF16, ARID5B, ARL9, ASIC1, ATP2A3, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BIN3-IT1, BIRC3, BTG2, C10orf54, C11orf70, C11orf94, C12orf56, C19orf47, C3, C7orf31, C8orf34, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CCDC79, CCER2, CCNF, CELSR1, CEMIP, CEP170, CFH, CIITA, CLDN23, CMAHP, CNGA4, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CRISPLD2, CRLF1, CRYL1, CYB5R2, CYGB, CYP1B1, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DNAH8, DNAJC27, DOCK11, DYNC11I1, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENPP1, ERCC8, ESM1, EVC2, F2R, FAM160A1, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXO9, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5,

HECTD2-AS1, HEPH, HEY1, HMGN3-AS1, HOOK3, HSPA1L, HTATIP2, IGDCC4, IGF2R, IGFBP3, IL16, INA, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LRBA, LRP4, LRRC32, LRRC39, LSAMP, LUM, LYPD1, MAFB, MAMDC2, MAN2A1, MAPK13, MASP1, MB, MC4R, MEGF6, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRVI1, MSH4, MTERF3, MXRA5, NA, NAALADL2, NAE1, NAGS, NDNF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PI4K2B, PIK3R1, PIM2, PITPNM3, PLEK2, PLEKHA6, PLEKHH2, PODN, POLN, POLR1A, PPM1E, PPP3CA, PRKCA, PRKG1, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, RAB30, RAB38, RAB44, RAD9B, RARS, RBBP8, RBKS, RDX, RFX3-AS1, RGCC, ROR1, ROR2, SCARNA9, SHROOM3, SIGLEC10, SLC24A3, SLC35F3, SLC39A10, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SORBS2, SORCS2, SOX7, SPDYA, SPEF2, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TEX21P, TGFA, TGFB2, TGFB3, TGM2, THBS2, TMEM102, TMEM119, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TXNIP, USP27X, UVRAG, VIM-AS1, VPS41, VSTM2L, VWF, WDR91, WISP1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZFP82, ZMIZ1-AS1, ZNF212, ZNF350, ZNF660, ZNF79 or ZNF837.

[00105] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APLP2, APLP2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, AXIN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DAGLB, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DLGAP4, DNAJC13, DNMBP, DOCK1,

DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERCC1, ERGIC3, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FAM198B, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GGCT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HAT1, HDX, HLTF, HMGA2, HNMT, HPS1, HSD17B12, HSD17B4, HTT, IFT57, INPP5K, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MADD, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPHLN1, PPIP5K2, PPP1R26, PRPF31, PRSS23, PRUNE2, PSMA4, PXX, RAF1, RAP1A, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RNFT1, RPA1, RPS10, RPS6KB2, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SKA2, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA18, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STRN3, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM189-UBE2V1, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TRIM65, TSPAN2, TTC7B, TUBE1, TYW5, UBAP2L, UBE2V1, URGCP, VAV2, VPS29, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232, ZNF37BP or ZNF680.

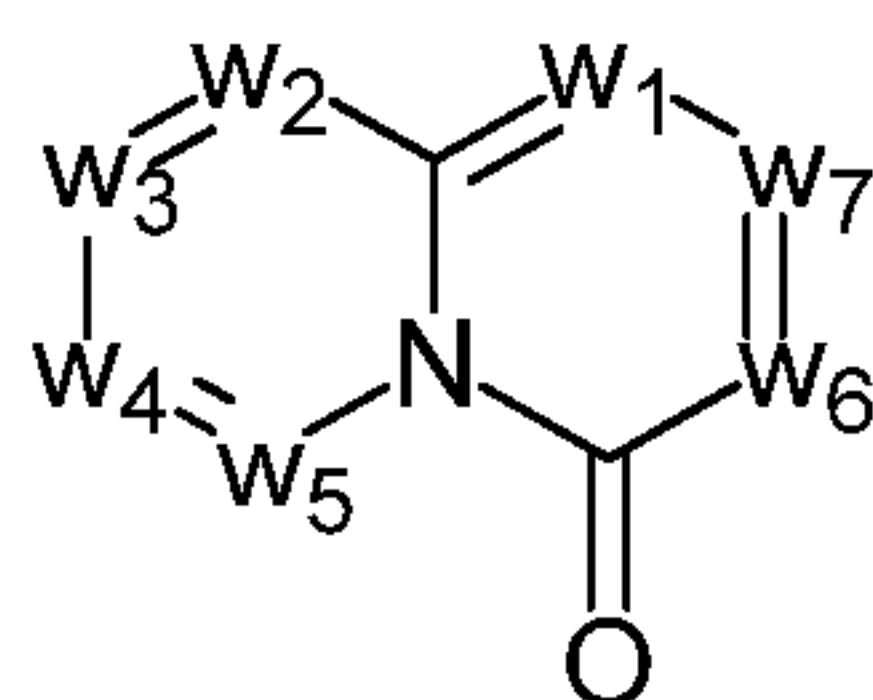
[00106] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HDX, HLTF, HMGA2, HNMT, HSD17B12, HSD17B4, HTT, IFT57, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45,

MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPIP5K2, PPP1R26, PRPF31, PRSS23, PSMA4, PXX, RAF1, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RPA1, RPS10, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TSPAN2, TTC7B, TYW5, UBAP2L, URGCP, VAV2, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232 or ZNF37BP.

[00107] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: APLP2, AXIN1, CECR7, DAGLB, DLGAP4, ERCC1, ERGIC3, FAM198B, GGCT, HAT1, HPS1, INPP5K, MADD, PPHLN1, PRUNE2, RAP1A, RNFT1, RPS6KB2, SH3YL1, SKA2, SPATA18, STRN3, TMEM189-UBE2V1, TRIM65, TUBE1, UBE2V1, VPS29 or ZNF680.

[00108] In another specific embodiment of the aspects and embodiments described herein, the gene is, or the RNA transcript is transcribed from a gene that is selected from: ABCB8, ABCC3, ADCY3, AGPAT4, ANKRA2, APIP, ARHGAP1, ARL15, ATXN1, BECN1, BHMT2, BTN3A1, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASP7, CCDC122, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DAGLB, DCAF17, DLGAP4, DNAJC13, DNMBP, DYRK1A, ENAH, EP300, ERCC1, ERLIN2, ERFFI1, EVC, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FBN2, GGACT, GLCE, GULP1, GXYLT1, HDX, HMGA2, HNMT, HPS1, IFT57, INPP5K, IVD, KDM6A, LETM2, LOC400927, LRRC42, LYRM1, MB21D2, MCM10, MED13L, MFN2, MRPL45, MRPS28, MTERF3, MYCBP2, NGF, OXCT1, PDS5B, PIGN, PIK3CD, PIK3R1, PIKFYVE, PLEKHA1, PLSCR1, POMT2, PPARG, PPIP5K2, PPP1R26, PRPF31, PRUNE2, PXX, RAF1, RAPGEF1, RARS2, RBKS, RERE, RPA1, RPS10, RPS6KB2, SAMD4A, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SKA2, SLC12A2, SLC44A2, SNX7, SPATA18, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STXBP6, TASP1, TCF12, TCF4, TIAM1, TMC3, TMEM189-UBE2V1, TMEM214, TNRC6A, TTC7B, TUBE1, TYW5, URGCP, VAV2, WDR27, WDR91, WNK1, ZCCHC8, ZFP82, ZNF138, ZNF232 or ZNF680.

[00109] In another aspect, provide herein is a method of modulating the amount and type of a protein produced by a cell containing the artificial gene construct as described above, the method comprising contacting the cell with a compound of Formula (I) or a form thereof, wherein Formula (I) is



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl,

aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or

heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino,

(C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00110] In a specific embodiment, in the context of DNA, the nucleotide sequence encoding the intronic REMS comprises a sequence selected from the group consisting of ANGAgtrngn (SEQ ID NO: 1829), CNGAgtrngn (SEQ ID NO: 1835), GNGAgtrngn (SEQ ID NO: 1841), TNGAgtrngn (SEQ ID NO: 1847), NAGAgtrngn (SEQ ID NO: 1830), NCGAgtrngn (SEQ ID NO: 1836), NGGAgtrngn (SEQ ID NO: 1842), NTGAgtrngn (SEQ ID NO: 1848), AAGAgtrngn (SEQ ID NO: 1831), ACGAgtrngn (SEQ ID NO: 1837), AGGAgtrngn (SEQ ID NO: 1843), ATGAgtrngn (SEQ ID NO: 1849), CAGAgtrngn (SEQ ID NO: 1832), CCGAgtrngn (SEQ ID NO: 1838), CGGAgtrngn (SEQ ID NO: 1844), CTGAgtrngn (SEQ ID NO: 1850), GAGAgtrngn (SEQ ID NO: 1833), GCGAgtrngn (SEQ ID NO: 1839), GGGAgtrngn (SEQ ID NO: 1845), GTGAgtrngn (SEQ ID NO: 1851), TAGAgtrngn (SEQ ID NO: 1834), TCGAgtrngn (SEQ ID NO: 1840), TGGAgtrngn (SEQ ID NO: 1846) and TTGAgtrngn (SEQ ID NO: 1852), wherein r is adenine or guanine and n or N is any nucleotide.

[00111] In a further specific embodiment, in the context of DNA, the nucleotide sequence encoding the intronic REMS comprises a sequence selected from the group consisting of ANGAgtragt (SEQ ID NO: 2237), CNGAgtragt (SEQ ID NO: 2243), GNGAgtragt (SEQ ID NO: 2249), TNGAgtragt (SEQ ID NO: 2255), NAGAgtragt (SEQ ID NO: 2238), NCGAgtragt (SEQ ID NO: 2244), NGGAgtragt (SEQ ID NO: 2250), NTGAgtragt (SEQ ID NO: 2256), AAGAgtragt (SEQ ID NO: 2239), ACGAgtragt (SEQ ID NO: 2245), AGGAgtragt (SEQ ID NO: 2251), ATGAgtragt (SEQ ID NO: 2257), CAGAgtragt (SEQ ID NO: 2240), CCGAgtragt (SEQ ID NO: 2246), CGGAgtragt (SEQ ID NO: 2252), CTGAgtragt (SEQ ID NO: 2258), GAGAgtragt (SEQ ID NO: 2241), GCGAgtragt (SEQ ID NO: 2247),

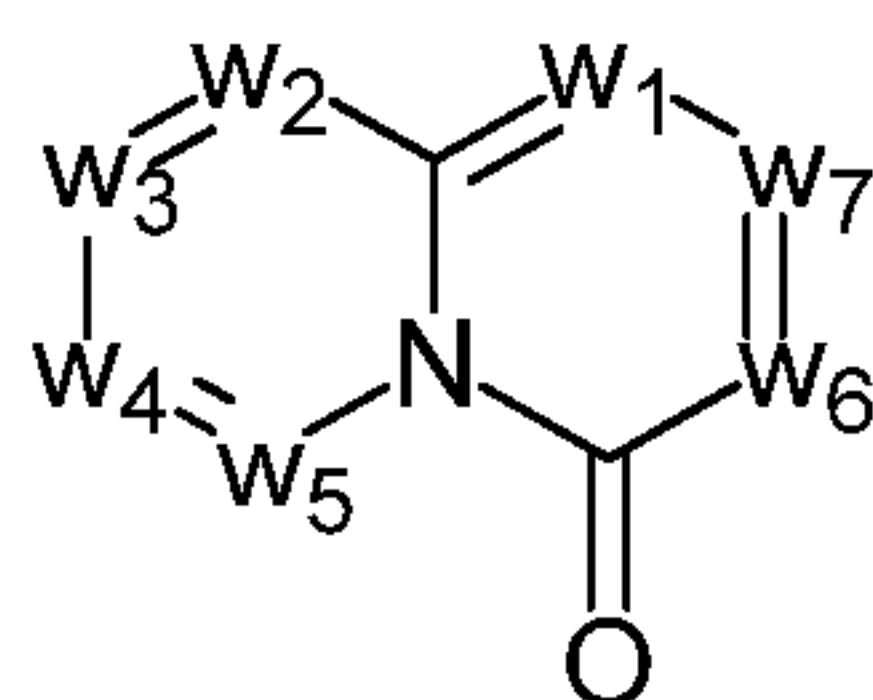
GGGAgtragt (SEQ ID NO: 2253), GTGAgtragt (SEQ ID NO: 2259), TAGAgtragt (SEQ ID NO: 2242), TCGAgtragt (SEQ ID NO: 2248), TGGAgtragt (SEQ ID NO: 2254) and TTGAgtragt (SEQ ID NO: 2260), wherein r is adenine or guanine and N is any nucleotide. In one or more embodiments provided herein, N is adenine or guanine.

[00112] In various specific embodiments, the nucleotide sequence encoding the intronic REMS is a nucleotide sequence encoding a non-endogenous intronic REMS, i.e., a precursor RNA transcript comprising the non-endogenous intronic REMS not naturally found in the DNA sequence of the artificial construct.

[00113] In one aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence comprising in 5' to 3' order: a branch point, a 3' splice site and an endogenous intronic recognition element for splicing modifier (iREMS), wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the RNA transcript is an RNA transcript of a gene that is selected from: ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARMCX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1,

FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27,

WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837; the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl,

aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or

heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

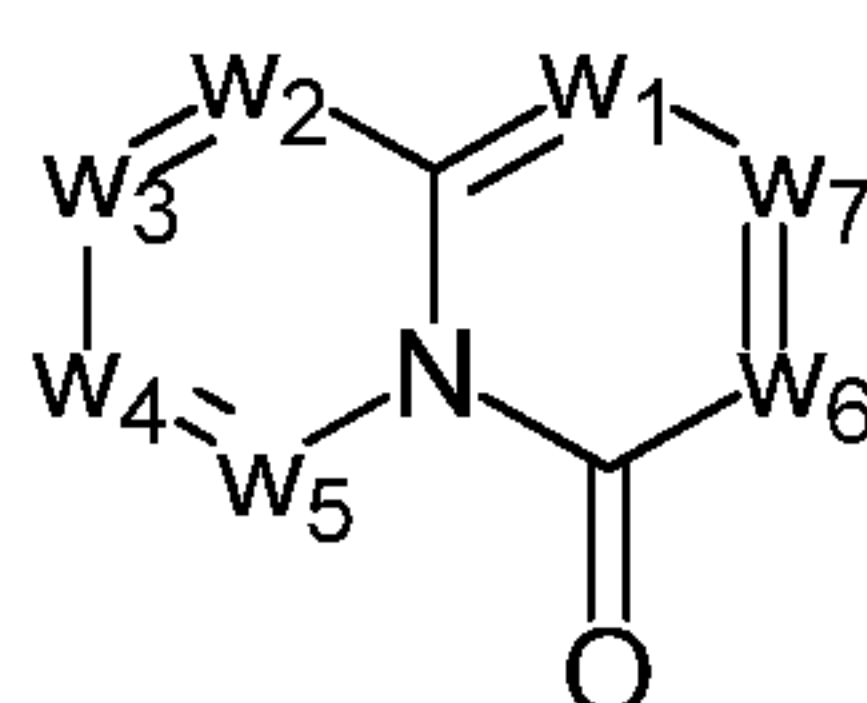
R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino,

(C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00114] In another aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence comprising in 5' to 3' order: a branch point, a 3' splice site and an endogenous intronic recognition element for splicing modifier (iREMS); wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the RNA transcript is an RNA transcript of a gene not disclosed in either International Publication No. WO 2015/105657, International Publication No. WO 2016/196386, or both; the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,

C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,
 (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,

(aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

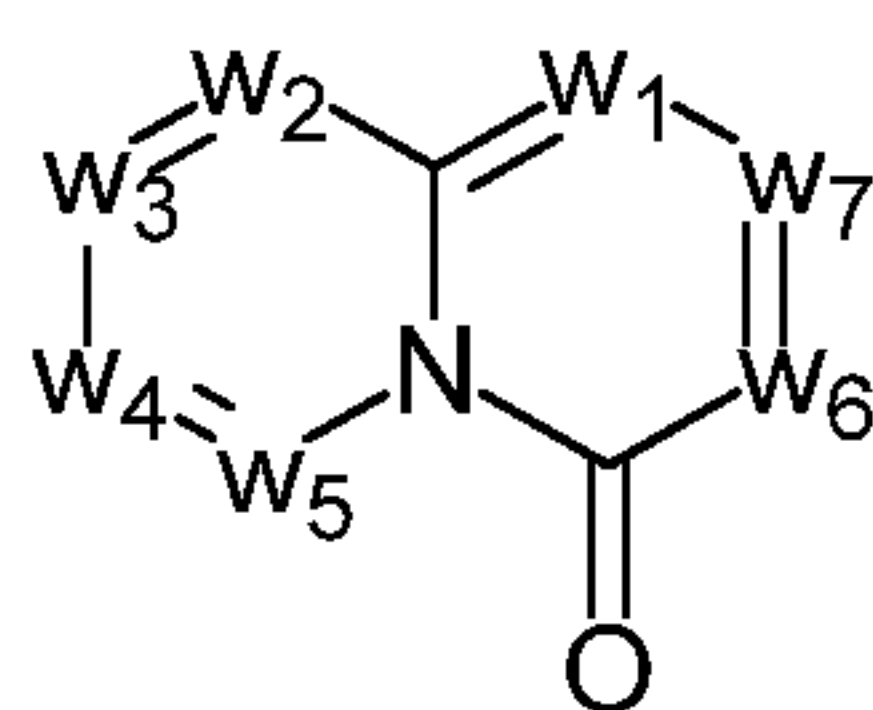
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00115] In another aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence comprising in 5' to 3' order: a branch point, a 3' splice site and a non-endogenous intronic recognition element for splicing modifier (iREMS),; wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,
 when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,
 wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;
 R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,
 (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,
 C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,
 (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,

heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

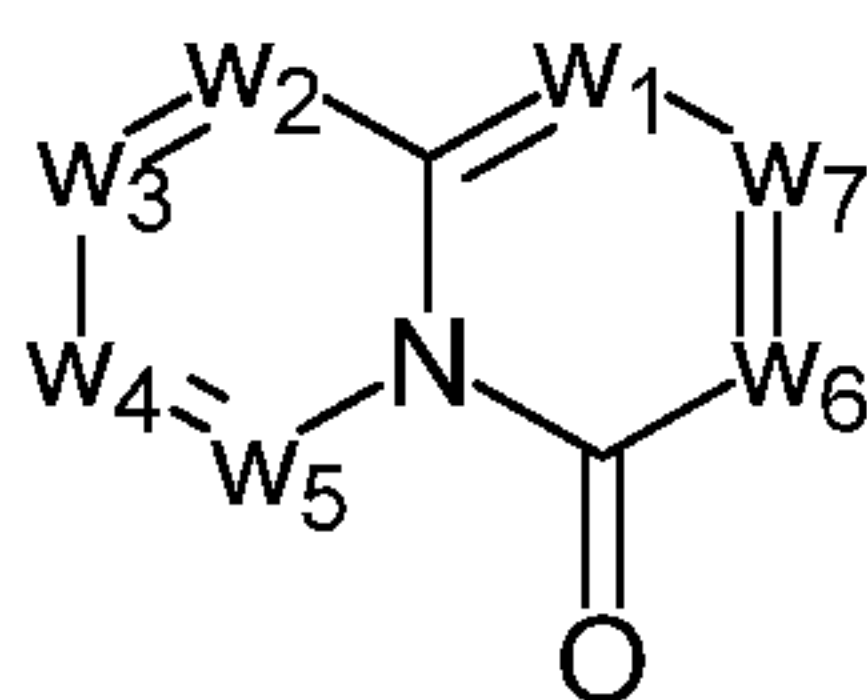
[00116] In certain embodiments, the iREMS comprises an RNA sequence

GAguragu (SEQ ID NO: 3866), wherein r is adenine or guanine and n is any nucleotide. In some embodiments, the iREMS comprises an RNA sequence NNGAgurngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide. In a specific embodiment, the RNA sequence NNGAgurngn (SEQ ID NO: 1) is selected from the group consisting of ANGAgurngn (SEQ ID NO: 29), CNGAgurngn (SEQ ID NO: 35), GNGAgurngn (SEQ ID NO: 41), UNGAgurngn (SEQ ID NO: 47), NAGAgurngn (SEQ ID NO: 30), NCGAgurngn (SEQ ID NO: 36), NGGAgurngn (SEQ ID NO: 42), NUGAgurngn (SEQ ID NO: 48), AAGAgurngn (SEQ ID NO: 31), ACGAgurngn (SEQ ID NO: 37), AGGAgurngn (SEQ ID NO: 43), AUGAgurngn (SEQ ID NO: 49), CAGAgurngn (SEQ ID NO: 32), CCGAgurngn (SEQ ID NO: 38), CGGAgurngn (SEQ ID NO: 44), CUGAgurngn (SEQ ID NO: 50), GAGAgurngn (SEQ ID NO: 33), GCGAgurngn (SEQ ID NO: 39), GGGAgurngn (SEQ ID NO: 45), GUGAgurngn (SEQ ID NO: 51), UAGAgurngn (SEQ ID NO: 34),

UCGAgurngn (SEQ ID NO: 40), UGGAgurngn (SEQ ID NO: 46) and UUGAgurngn (SEQ ID NO: 52), wherein r is adenine or guanine and n or N is any nucleotide. In certain embodiments, n is adenine or guanine.

[00117] In certain embodiments, the iREMS comprises an RNA sequence NNGAguragu (SEQ ID NO: 3862), wherein r is adenine or guanine and N is any nucleotide. In a specific embodiment, the RNA sequence NNGAguragu (SEQ ID NO: 3862) is selected from the group consisting of ANGAguragu (SEQ ID NO: 437), CNGAguragu (SEQ ID NO: 443), GNGAguragu (SEQ ID NO: 449), UNGAguragu (SEQ ID NO: 455), NAGAguragu (SEQ ID NO: 438), NCGAguragu (SEQ ID NO: 444), NGGAguragu (SEQ ID NO: 450), NUGAguragu (SEQ ID NO: 456), AAGAguragu (SEQ ID NO: 439), ACGAguragu (SEQ ID NO: 445), AGGAguragu (SEQ ID NO: 451), AUGAguragu (SEQ ID NO: 457), CAGAguragu (SEQ ID NO: 440), CCGAguragu (SEQ ID NO: 446), CGGAguragu (SEQ ID NO: 452), CUGAguragu (SEQ ID NO: 458), GAGAguragu (SEQ ID NO: 441), GCGAguragu (SEQ ID NO: 447), GGGAguragu (SEQ ID NO: 453), GUGAguragu (SEQ ID NO: 459), UAGAguragu (SEQ ID NO: 442), UCGAguragu (SEQ ID NO: 448), UGGAguragu (SEQ ID NO: 454) and UUGAguragu (SEQ ID NO: 460), wherein r is adenine or guanine, and N is any nucleotide. the iREMS comprises an RNA sequence presented in Table 13. In certain embodiments, n is adenine or guanine.

[00118] In another aspect, provided herein is a method for modulating the amount of an RNA transcript produced from a DNA sequence comprising a DNA nucleotide sequence encoding exons and one or more introns, comprising in 5' to 3' order: a branch point, a 3' splice site and an endogenous iREMS; wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂,
provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,
(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,
C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino; wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

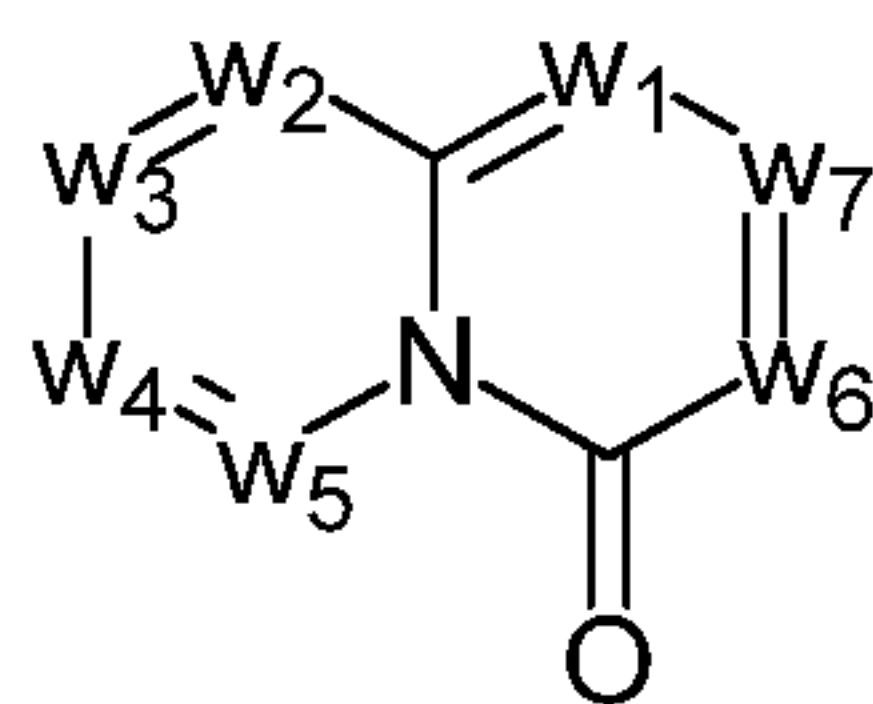
R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00119] In a specific embodiment, the DNA sequence is in a gene selected from: ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARM CX6, ASIC1,

ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG,

PIIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837. In another specific embodiment, the DNA sequence is a gene not disclosed in either International Publication No. WO 2015/105657, International Publication No. WO 2016/196386, or both.

[00120] In another aspect, provided herein is a method for modulating the amount of an RNA transcript produced from a DNA sequence comprising a DNA nucleotide sequence encoding exons and one or more introns, comprising in 5' to 3' order: a branch point, a 3' splice site and a non-endogenous iREMS; wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino, [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00121] In certain embodiments, the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide. In certain embodiments, n is adenine or guanine. In certain embodiments, the iREMS comprises a DNA sequence NNGAgtrngn (SEQ ID NO: 3), wherein r is adenine or guanine and n or N is any nucleotide. In a specific embodiment, the DNA sequence NNGAgtrngn (SEQ ID NO: 3) is selected from the group consisting of ANGAgtrngn (SEQ ID NO: 1829), CNGAgtrngn (SEQ ID NO: 1835), GNGAgtrngn (SEQ ID NO: 1841), TNGAgtrngn (SEQ ID NO: 1847),

NAGAgtrngn (SEQ ID NO: 1830), NCGAgtrngn (SEQ ID NO: 1836),
 NGGAgtrngn (SEQ ID NO: 1842), NTGAgtrngn (SEQ ID NO: 1848),
 AAGAgtrngn (SEQ ID NO: 1831), ACGAgtrngn (SEQ ID NO: 1837),
 AGGAgtrngn (SEQ ID NO: 1843), ATGAgtrngn (SEQ ID NO: 1849),
 CAGAgtrngn (SEQ ID NO: 1832), CCGAgtrngn (SEQ ID NO: 1838),
 CGGAgtrngn (SEQ ID NO: 1844), CTGAgtrngn (SEQ ID NO: 1850),
 GAGAgtrngn (SEQ ID NO: 1833), GCGAgtrngn (SEQ ID NO: 1839),
 GGGAgtrngn (SEQ ID NO: 1845), GTGAgtrngn (SEQ ID NO: 1851),
 TAGAgtrngn (SEQ ID NO: 1834), TCGAgtrngn (SEQ ID NO: 1840),
 TGGAgtrngn (SEQ ID NO: 1846) and TTGAgtrngn (SEQ ID NO: 1852). In certain
 embodiments, n is adenine or guanine.

[00122] In certain embodiments, the iREMS comprises a DNA sequence NNGAgtragt (SEQ ID NO: 3864), wherein r is adenine or guanine and N is any nucleotide. In a specific embodiment, the DNA sequence NNGAgtragt (SEQ ID NO: 3864) is selected from the group consisting of ANGAgtragt (SEQ ID NO: 2237), CNGAgtragt (SEQ ID NO: 2243), GNGAgtragt (SEQ ID NO: 2249), TNGAgtragt (SEQ ID NO: 2255), NAGAgtragt (SEQ ID NO: 2238), NCGAgtragt (SEQ ID NO: 2244), NGGAgtragt (SEQ ID NO: 2250), NTGAgtragt (SEQ ID NO: 2256), AAGAgtragt (SEQ ID NO: 2239), ACGAgtragt (SEQ ID NO: 2245), AGGAgtragt (SEQ ID NO: 2251), ATGAgtragt (SEQ ID NO: 2257), CAGAgtragt (SEQ ID NO: 2240), CCGAgtragt (SEQ ID NO: 2246), CGGAgtragt (SEQ ID NO: 2252), CTGAgtragt (SEQ ID NO: 2258), GAGAgtragt (SEQ ID NO: 2241), GCGAgtragt (SEQ ID NO: 2247), GGGAgtragt (SEQ ID NO: 2253), GTGAgtragt (SEQ ID NO: 2259), TAGAgtragt (SEQ ID NO: 2242), TCGAgtragt (SEQ ID NO: 2248), TGGAgtragt (SEQ ID NO: 2254) and TTGAgtragt (SEQ ID NO: 2260), wherein r is adenine or guanine, and N is any nucleotide. In a specific embodiment, the iREMS comprises a DNA sequence presented in Table 14. In certain embodiments, n is adenine or guanine. In certain embodiments of the aspects and embodiments described herein, n is adenine or guanine.

[00123] In certain embodiments of a method for modulating the amount of an RNA transcript described herein, modulation of the amount of the RNA transcript is modulation of the amount of

the RNA transcript in a cell or a lysate of the cell, the method comprising contacting the compound of Formula (I) or a form thereof with the cell or the cell lysate. In a specific embodiment of a method for modulating the amount of an RNA transcript described herein, modulation of the amount of the RNA transcript is modulation of the amount of the RNA transcript in a cell, the method comprising contacting the compound of Formula (I) or a form thereof with the cell. In certain embodiments of a method of modulating the amount of an RNA transcript described herein, the modulation modulates the amount and/or type of a protein translated from the RNA transcript and produced in the cell or lysate of the cell.

[00124] In certain embodiments of a method for modulating the amount of an RNA transcript described herein, modulation of the amount of the RNA transcript is modulation of the amount of the RNA transcript in a subject, the method comprising administering the compound of Formula (I) or a form thereof to the subject. In certain embodiments of a method for modulating the amount of an RNA transcript described herein, the modulation modulates the amount and/or type of a protein translated from the RNA transcript and produced in the subject. In a specific embodiment, the subject is a non-human subject. In another specific embodiment, the subject is a human subject.

[00125] In certain embodiments, the RNA transcript encodes a detectable reporter protein.

[00126] In another aspect, provided herein is an artificial gene construct comprising an RNA sequence comprising exons and one or more introns, wherein at least one intron comprises an iREMS that is downstream of a branch point and a 3' splice site and wherein the iREMS comprises the sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In certain embodiments, n is adenine or guanine. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are non-endogenous. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are endogenous.

[00127] In another aspect, provided herein is an artificial gene construct comprising a DNA sequence encoding exons and one or more introns, wherein the nucleotide sequence encoding at least one intron comprises an iREMS that is downstream of the nucleotide sequence encoding a branch point and the nucleotide sequence encoding a 3' splice site, and wherein the iREMS comprises the sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide. In certain embodiments, n is adenine or guanine. In certain embodiments, one, two,

or all of the iREMS, the branch point, and the 3' splice site are non-endogenous. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are endogenous.

[00128] In another aspect, provided herein is a cell comprising an RNA sequence comprising exons and one or more introns, wherein at least one intron comprises an iREMS that is downstream of a branch point and a 3' splice site and wherein the iREMS comprises the sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In certain embodiments, n is adenine or guanine. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are non-endogenous. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are endogenous.

[00129] In another aspect, provided herein is a cell comprising a DNA sequence encoding exons and one or more introns, wherein the nucleotide sequence encoding at least one intron comprises an iREMS that is downstream of the nucleotide sequence encoding a branch point and the nucleotide sequence encoding a 3' splice site, and wherein the iREMS comprises the sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are non-endogenous. In certain embodiments, one, two, or all of the iREMS, the branch point, and the 3' splice site are endogenous.

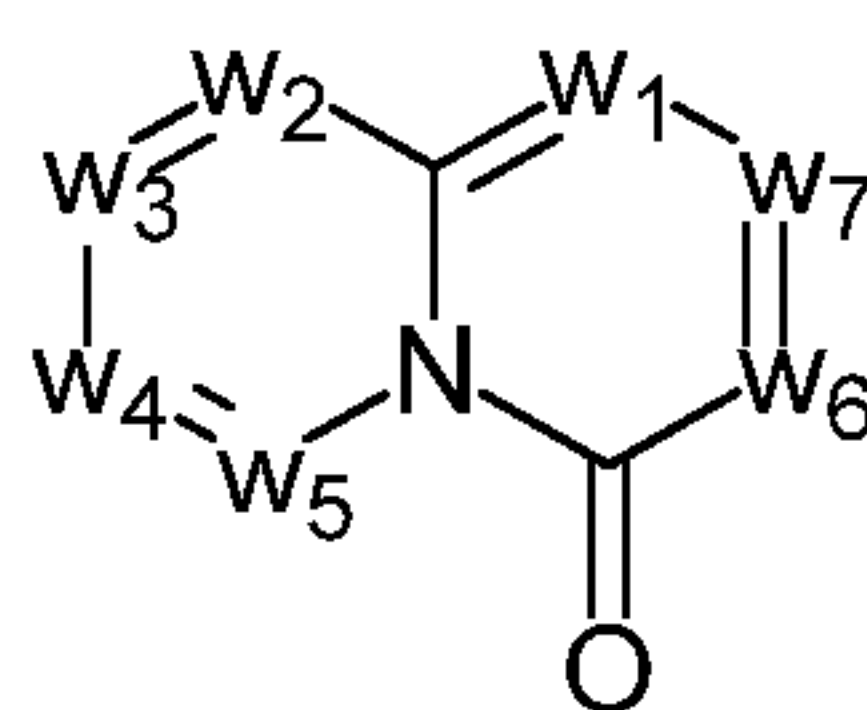
[00130] In another aspect, provided herein is a cell comprising an artificial gene construct described herein.

[00131] In another aspect, provided herein is a cell comprising a vector comprising an artificial gene construct described herein.

[00132] In another aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence comprising in 5' to 3' order: a branch point, a 3' splice site, and an endogenous intronic recognition element for splicing modifier (iREMS), wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the RNA transcript is an RNA transcript of a gene that is selected from ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARM CX6, ASIC1, ATG5, ATP2A3, ATXN1,

B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6,
 BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47,
 C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2,
 CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1,
 CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP,
 CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6,
 COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1,
 CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L,
 DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13,
 DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4,
 EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFF1, ESM1, EVC,
 EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A,
 FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1,
 FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE,
 GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1,
 HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1,
 HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4,
 IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA,
 IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT,
 KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2,
 LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678,
 LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1,
 LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1,
 MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10,
 MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1,
 MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA,
 NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM,
 NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD,
 PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1,
 PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR,
 PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA,

PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837; the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,
 when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,
 wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;
 R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,
 (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,
 C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,
 (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,

heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo,

C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

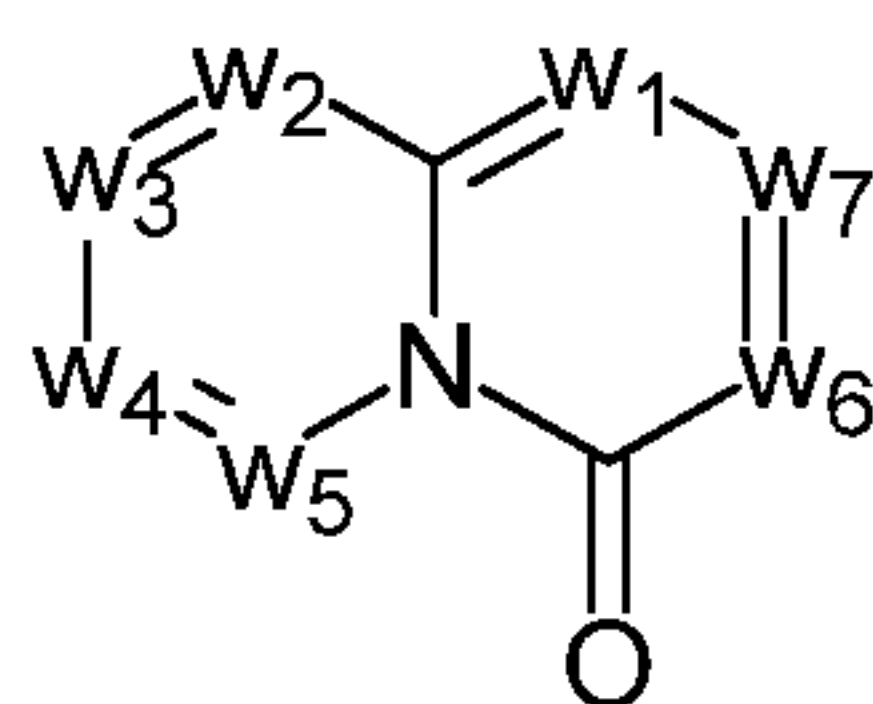
[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00133] In another aspect provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence comprising in 5' to 3' order: a branch point, a 3' splice site and an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS); wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂,
provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino,
(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl,
C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

(hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

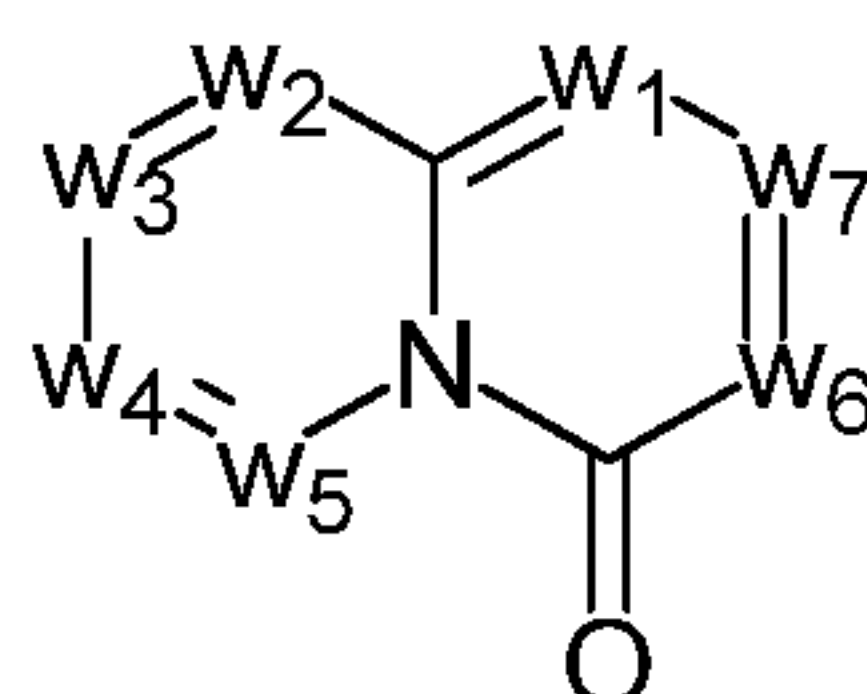
R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00134] In certain embodiments, the RNA transcript is an RNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APLP2, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, AXIN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DAGLB, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DLGAP4, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERCC1, ERGIC3, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FAM198B, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GGCT,

GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HAT1, HDX, HLTF, HMGA2, HNMT, HPS1, HSD17B12, HSD17B4, HTT, IFT57, INPP5K, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MADD, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPHLN1, PPIP5K2, PPP1R26, PRPF31, PRSS23, PRUNE2, PSMA4, PXX, RAF1, RAP1A, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RNFT1, RPA1, RPS10, RPS6KB2, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SKA2, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA18, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STRN3, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM189-UBE2V1, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TRIM65, TSPAN2, TTC7B, TUBE1, TYW5, UBAP2L, UBE2V1, URGCP, VAV2, VPS29, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232, ZNF37BP or ZNF680.

[00135] In another aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

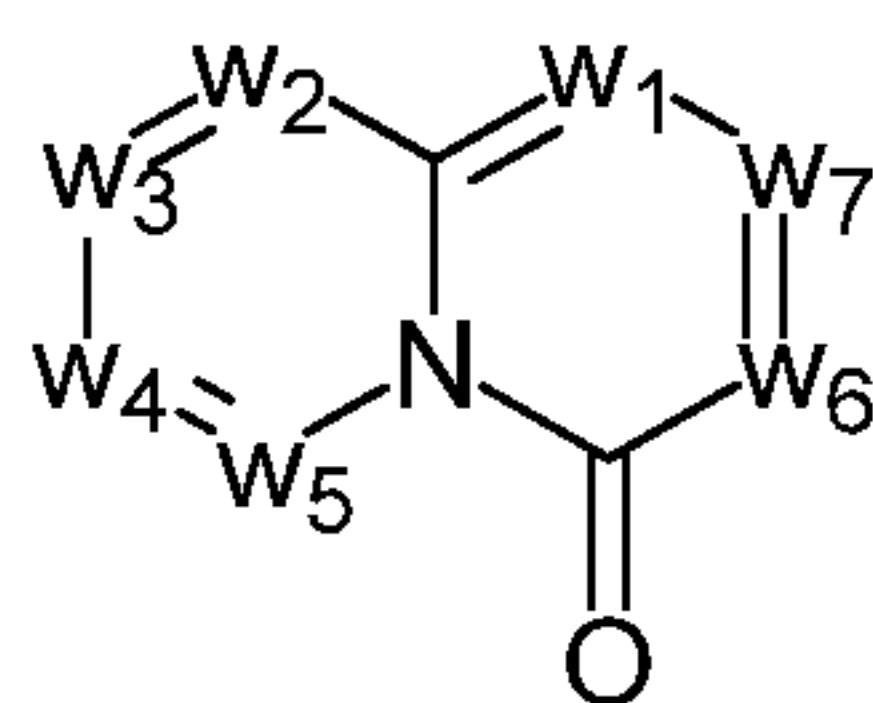
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00136] In another aspect, provided herein is a method for modulating the amount of an RNA transcript comprising a RNA nucleotide sequence, wherein the RNA nucleotide sequence comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: an iREMS, a first branch point and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n

is any nucleotide, the method comprising contacting the RNA transcript with a compound of Formula (I) or a form thereof, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally
 substituted with one, two or three R₃ substituents and optionally, with one additional R₄
 substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino; wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

[00137] In certain embodiments, the iREMS is an endogenous iREMS, and the RNA transcript is an RNA transcript of a gene that is selected from ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARMCX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFN59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10,

MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837.

[00138] In certain embodiments, the iREMS is an endogenous iREMS, and the RNA transcript is an RNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APLP2, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, AXIN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DAGLB, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DLGAP4, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERCC1, ERGIC3, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FAM198B, FBN2, FER, FHOD3,

FOCAD, GALC, GCFC2, GGACT, GGCT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HAT1, HDX, HLTF, HMGA2, HNMT, HPS1, HSD17B12, HSD17B4, HTT, IFT57, INPP5K, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MADD, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPHLN1, PPIP5K2, PPP1R26, PRPF31, PRSS23, PRUNE2, PSMA4, P XK, RAF1, RAP1A, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RNFT1, RPA1, RPS10, RPS6KB2, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SKA2, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA18, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STRN3, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM189-UBE2V1, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TRIM65, TSPAN2, TTC7B, TUBE1, TYW5, UBAP2L, UBE2V1, URGCP, VAV2, VPS29, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232, ZNF37BP or ZNF680.

[00139] In certain embodiments, the iREMS is a non-endogenous iREMS. In a specific embodiment, the iREMS is a non-endogenous iREMS and the RNA transcript is an RNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APLP2, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, AXIN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DAGLB, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DLGAP4, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERCC1, ERGIC3, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FAM198B, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GGCT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HAT1, HDX, HLTF, HMGA2, HNMT, HPS1, HSD17B12, HSD17B4, HTT, IFT57, INPP5K, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MADD, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19,

MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPHLN1, PPIP5K2, PPP1R26, PRPF31, PRSS23, PRUNE2, PSMA4, PPK, RAF1, RAP1A, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RNFT1, RPA1, RPS10, RPS6KB2, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SKA2, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA18, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STRN3, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM189-UBE2V1, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TRIM65, TSPAN2, TTC7B, TUBE1, TYW5, UBAP2L, UBE2V1, URGCP, VAV2, VPS29, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232, ZNF37BP or ZNF680.

[00140] In one aspect, provided herein is a method for producing a mature mRNA transcript comprising iExon from a pre-mRNA transcript, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In one embodiment, provided herein is a method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In another embodiment, provided herein is a method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a cell or cell lysate containing a pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form

thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In some embodiments, the pre-mRNA transcript is encoded by a gene disclosed herein (e.g., in a table herein).

[00141] In a particular embodiment, provided herein is a method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HDX, HLTF, HMGA2, HNMT, HSD17B12, HSD17B4, HTT, IFT57, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE,

PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPIP5K2, PPP1R26, PRPF31, PRSS23, PSMA4, PXX, RAF1, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RPA1, RPS10, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TSPAN2, TTC7B, TYW5, UBAP2L, URGCP, VAV2, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232 or ZNF37BP. In another particular embodiment, provided herein is a method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a cell or cell lysate containing a pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HDX, HLTF, HMGA2, HNMT, HSD17B12, HSD17B4, HTT, IFT57, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1,

PLSCR1, PMS1, POMT2, PPARG, PPIP5K2, PPP1R26, PRPF31, PRSS23, PSMA4, PXX, RAF1, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RPA1, RPS10, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TSPAN2, TTC7B, TYW5, UBAP2L, URGCP, VAV2, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232 or ZNF37BP.

[00142] In another aspect, provided herein is a method modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In one embodiment, provided herein is a method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting the pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In another embodiment, provided herein is a method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting a cell or cell lysate containing the pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous or non-endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence

GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide. In some embodiments, the intron further comprises a first 5' splice site, a second branch point, and a second 3' splice site upstream of the iREMS. In some embodiments, the pre-mRNA transcript is encoded by a gene disclosed herein (e.g., in a table herein).

[00143] In a particular embodiment, provided herein is a method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting the pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARM CX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFN B59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1,

GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-

AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837. In a particular embodiment, provided herein is a method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting a cell or cell lysate containing the pre-mRNA transcript with a compound described herein (e.g., a compound of Formula (I) or a form thereof), wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARMCX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3,

HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD, KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837. In some embodiments, the intron

further comprises a first 5' splice site, a second branch point, and a second 3' splice site upstream of the iREMS.

[00144] In one aspect, provided herein is a method for preventing, treating or preventing and treating a disease or disorder in which a change in the level of expression of one, two, three or more RNA isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, the method comprising administering a compound described herein to a subject in need thereof, wherein the one, two, three or more RNA isoforms are produced from a pre-mRNA transcript comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

[00145] In one aspect, provided herein is a method for preventing, treating or preventing and treating a disease or disorder in which a change in the level of expression of one, two, three or more RNA isoforms encoded by a gene is beneficial to the prevention and/or treatment of the disease, the method comprising administering a compound described herein to a subject in need thereof, wherein the one, two, three or more RNA isoforms are produced from a pre-mRNA transcript comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: an endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

[00146] In another aspect, provided herein is an artificial gene construct comprising an RNA sequence comprising exons and one or more introns, wherein at least one intron comprises an iREMS that is downstream of a branch point and a 3' splice site, and wherein the iREMS comprises the sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

[00147] In another aspect, provided herein is an artificial gene construct comprising an RNA sequence comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron

comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

[00148] In another aspect, provide herein is an artificial gene construct comprising an RNA sequence comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: an iREMS, a first branch point and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

[00149] In various embodiments of the aspects and embodiments described herein, the iREMS comprises an RNA sequence GAguragu, wherein r is adenine or guanine.

[00150] In various embodiments of the aspects and embodiments described herein, the iREMS comprises an RNA sequence NNGAgurngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide. In a specific embodiment, the RNA sequence NNGAgurngn (SEQ ID NO: 1) is selected from the group consisting of ANGAgurngn (SEQ ID NO: 29), CNGAgurngn (SEQ ID NO: 35), GNGAgurngn (SEQ ID NO: 41), UNGAgurngn (SEQ ID NO: 47), NAGAgurngn (SEQ ID NO: 30), NCGAgurngn (SEQ ID NO: 36), NGGAgurngn (SEQ ID NO: 42), NUGAgurngn (SEQ ID NO: 48), AAGAgurngn (SEQ ID NO: 31), ACGAgurngn (SEQ ID NO: 37), AGGAgurngn (SEQ ID NO: 43), AUGAgurngn (SEQ ID NO: 49), CAGAgurngn (SEQ ID NO: 32), CCGAgurngn (SEQ ID NO: 38), CGGAgurngn (SEQ ID NO: 44), CUGAgurngn (SEQ ID NO: 50), GAGAgurngn (SEQ ID NO: 33), GCGAgurngn (SEQ ID NO: 39), GGGAgurngn (SEQ ID NO: 45), GUGAgurngn (SEQ ID NO: 51), UAGAgurngn (SEQ ID NO: 34), UCGAgurngn (SEQ ID NO: 40), UGGAgurngn (SEQ ID NO: 46) and UUGAgurngn (SEQ ID NO: 52), wherein r is adenine or guanine and n or N is any nucleotide.

[00151] In various embodiments of the aspects and embodiments described herein, the iREMS comprises an RNA sequence NNGAguragu (SEQ ID NO: 3862), wherein r is adenine or guanine

and N is any nucleotide. In a specific embodiment, the RNA sequence NNGAguragu (SEQ ID NO: 3862) is selected from the group consisting of ANGAguragu (SEQ ID NO: 437), CNGAguragu (SEQ ID NO: 443), GNGAguragu (SEQ ID NO: 449), UNGAguragu (SEQ ID NO: 455), NAGAguragu (SEQ ID NO: 438), NCGAguragu (SEQ ID NO: 444), NGGAguragu (SEQ ID NO: 450), NUGAguragu (SEQ ID NO: 456), AAGAguragu (SEQ ID NO: 439), ACGAguragu (SEQ ID NO: 445), AGGAguragu (SEQ ID NO: 451), AUGAguragu (SEQ ID NO: 457), CAGAguragu (SEQ ID NO: 440), CCGAguragu (SEQ ID NO: 446), CGGAguragu (SEQ ID NO: 452), CUGAguragu (SEQ ID NO: 458), GAGAguragu (SEQ ID NO: 441), GCGAguragu (SEQ ID NO: 447), GGGAguragu (SEQ ID NO: 453), GUGAguragu (SEQ ID NO: 459), UAGAguragu (SEQ ID NO: 442), UCGAguragu (SEQ ID NO: 448), UGGAguragu (SEQ ID NO: 454) and UUGAguragu (SEQ ID NO: 460), wherein r is adenine or guanine, and N is any nucleotide.

[00152] In various embodiments of the method for modulating the amount of an RNA transcript described herein, modulation of the amount of the RNA transcript is modulation of the amount of the RNA transcript in a cell or a lysate of the cell, and the method comprises contacting the compound of Formula (I) or a form thereof with the cell or cell lysate. In a specific embodiment, modulation of the amount of the RNA transcript is modulation of the amount of the RNA transcript in a cell, and the method comprises contacting the compound of Formula (I) or a form thereof with the cell. In a specific embodiment, the modulation modulates the amount and/or type of a protein translated from the RNA transcript and produced in the cell or lysate of the cell.

[00153] In various embodiments of the method for modulating the amount of an RNA transcript described herein, the RNA transcript encodes a detectable reporter protein.

[00154] In another aspect, provided herein is an artificial gene construct comprising a DNA sequence encoding exons and one or more introns, wherein the nucleotide sequence encoding at least one intron comprises an iREMS that is downstream of the nucleotide sequence encoding a branch point and the nucleotide sequence encoding a 3' splice site, and wherein the iREMS

comprises the sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide.

[00155] In another aspect, provided herein is an artificial gene construct comprising a DNA sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the nucleotide sequence encoding the intron comprises in 5' to 3' order: the nucleotide sequence encoding a first 5' splice site, the nucleotide sequence encoding a first branch point, the nucleotide sequence encoding a first 3' splice site, an iREMS, the nucleotide sequence encoding a second branch point and the nucleotide sequence encoding a second 3' splice site, wherein the iREMS comprises a DNA sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide.

[00156] In another aspect, provide herein is an artificial gene construct comprising a DNA sequence encoding two exons and an intron, wherein the nucleotide sequence encoding one exon is upstream of the nucleotide sequence encoding the intron and the nucleotide sequence encoding the other exon is downstream of the nucleotide sequence encoding the intron, wherein the nucleotide sequence encoding the intron comprises in 5' to 3' order: an iREMS, the nucleotide sequence encoding a first branch point and the nucleotide sequence encoding a first 3' splice site, wherein the iREMS comprises an DNA sequence GAgtrngn (SEQ ID NO: 4), wherein r is adenine or guanine and n is any nucleotide.

[00157] In various embodiments of the aspects and embodiments described herein, the iREMS comprises a DNA sequence GAgtragt, wherein r is adenine or guanine.

[00158] In various embodiments of the aspects and embodiments described herein, the iREMS comprises a DNA sequence NNGAgtrngn (SEQ ID NO: 1), wherein r is adenine or guanine and n or N is any nucleotide. In a specific embodiment, the DNA sequence NNGAgtrngn (SEQ ID NO: 1) is selected from the group consisting of ANGAgtrngn (SEQ ID NO: 29), CNGAgtrngn (SEQ ID NO: 35), GNGAgtrngn (SEQ ID NO: 41), TNGAgtrngn (SEQ ID NO: 47), NAGAgtrngn (SEQ ID NO: 30), NCGAgtrngn (SEQ ID NO: 36), NGGAgtrngn (SEQ ID NO: 42), NTGAgtrngn (SEQ ID NO: 48), AAGAgtrngn (SEQ ID NO: 31), ACGAgtrngn (SEQ ID NO: 37),

AGGAgtrngn (SEQ ID NO: 43), ATGAgtrngn (SEQ ID NO: 49), CAGAgtrngn (SEQ ID NO: 32), CCGAgtrngn (SEQ ID NO: 38), CGGAgtrngn (SEQ ID NO: 44), CTGAgtrngn (SEQ ID NO: 50), GAGAgtrngn (SEQ ID NO: 33), GCGAgtrngn (SEQ ID NO: 39), GGGAgtrngn (SEQ ID NO: 45), GTGAgtrngn (SEQ ID NO: 51), TAGAgtrngn (SEQ ID NO: 34), TCGAgtrngn (SEQ ID NO: 40), TGGAgtrngn (SEQ ID NO: 46) and TTGAgtrngn (SEQ ID NO: 52), wherein r is adenine or guanine and n or N is any nucleotide.

[00159] In various embodiments of the aspects and embodiments described herein, the iREMS comprises a DNA sequence NNGAgtragt (SEQ ID NO: 3862), wherein r is adenine or guanine and N is any nucleotide. In a specific embodiment, the DNA sequence NNGAgtragt (SEQ ID NO: 3862) is selected from the group consisting of ANGAgtragt (SEQ ID NO: 437), CNGAgtragt (SEQ ID NO: 443), GNGAgtragt (SEQ ID NO: 449), TNGAgtragt (SEQ ID NO: 455), NAGAgtragt (SEQ ID NO: 438), NCGAgtragt (SEQ ID NO: 444), NGGAgtragt (SEQ ID NO: 450), NTGAgtragt (SEQ ID NO: 456), AAGAgtragt (SEQ ID NO: 439), ACGAgtragt (SEQ ID NO: 445), AGGAgtragt (SEQ ID NO: 451), ATGAgtragt (SEQ ID NO: 457), CAGAgtragt (SEQ ID NO: 440), CCGAgtragt (SEQ ID NO: 446), CGGAgtragt (SEQ ID NO: 452), CTGAgtragt (SEQ ID NO: 458), GAGAgtragt (SEQ ID NO: 441), GCGAgtragt (SEQ ID NO: 447), GGGAgtragt (SEQ ID NO: 453), GTGAgtragt (SEQ ID NO: 459), TAGAgtragt (SEQ ID NO: 442), TCGAgtragt (SEQ ID NO: 448), TGGAgtragt (SEQ ID NO: 454) and TTGAgtragt (SEQ ID NO: 460), wherein r is adenine or guanine, and N is any nucleotide.

BRIEF DESCRIPTION OF THE DRAWINGS

[00160] **Figures 1A-1C.** Representative schematics of intronic exon splicing mediated by an intronic REMS, where 5'ss represents a 5' splice site, 3'ss represents a 3' splice site and BP represents a splicing branch point. Exon 1e and Exon 2e represent extended exons. iExon 1a

represents an intronic exon. Splicing events mediated by an intronic REMS in the absence of a compound described herein are illustrated by solid lines, splicing events mediated by an intronic REMS in the presence of a compound described herein are illustrated by dashed lines.

[00161] Figures 2A-2D, 3, 4, 5, 6A. The dose dependent production of iExons for certain genes (as specified in the figures) in the presence of certain compounds or control (DMSO) are shown, each of which represent aspects of the operation of an intronic REMS and compounds as described herein. Compounds used in the experiments depicted in Figures 3, 4, 5, and 6A are described herein. Compound 774 was used for the experiments depicted in Figures 2A-2D.

[00162] Figures 6B and 6C. Figure 6B illustrates the production of exon isoforms with control (DMSO). Figure 6C illustrates the production of certain intronic Exon isoforms for ELMO2 in the presence of a compound described herein, each of which represent aspects of the interactions of an intronic REMS, one or more branch points, one or more 3' splice sites and compounds as described herein.

DETAILED DESCRIPTION

INTRONIC RECOGNITION ELEMENT FOR SPLICING MODIFIER (REMS)

[00163] In one aspect, provided herein is an intronic recognition element for splicing modifier (otherwise referred to as “iREMS”) recognized by a small molecule splicing modifier, whereby elements of the associated iREMS complex affect interactions with the spliceosome as further described herein. In a specific embodiment, the intronic REMS has the nucleotide sequence GAgurngn (SEQ ID NO: 2) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n is any nucleotide. In another specific embodiment, the intronic REMS has the nucleotide sequence GAguragu (SEQ ID NO: 3866) at the RNA level, wherein r is adenine or guanine. In one or more of such specific embodiments provided herein, n is adenine or guanine. In a more specific embodiment, the intronic REMS has the nucleotide sequence NNGAgurngn (SEQ ID NO: 1) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n or N is any nucleotide. In another more specific embodiment, the intronic REMS has the nucleotide sequence NNGAguragu (SEQ ID NO: 3862) at the RNA level, wherein r is adenine or guanine and N is any nucleotide. In one or more of such more specific embodiments provided herein, N is adenine or guanine.

[00164] In another specific embodiment, the intronic REMS is downstream of an intronic branch point and a functional intronic 3' splice site, wherein the intronic REMS comprises a nucleotide sequence selected from the group consisting of ANGAgurngn (SEQ ID NO: 29), CNGAgurngn (SEQ ID NO: 35), GNGAgurngn (SEQ ID NO: 41), UNGAgurngn (SEQ ID NO: 47), NAGAgurngn (SEQ ID NO: 30), NCGAgurngn (SEQ ID NO: 36), NGGAgurngn (SEQ ID NO: 42), NUGAgurngn (SEQ ID NO: 48), AAGAgurngn (SEQ ID NO: 31), ACGAgurngn (SEQ ID NO: 37), AGGAgurngn (SEQ ID NO: 43), AUGAgurngn (SEQ ID NO: 49), CAGAgurngn (SEQ ID NO: 32), CCGAgurngn (SEQ ID NO: 38), CGGAgurngn (SEQ ID NO: 44), CUGAgurngn (SEQ ID NO: 50), GAGAgurngn (SEQ ID NO: 33), GCGAgurngn (SEQ ID NO: 39), GGGAgurngn (SEQ ID NO: 45), GUGAgurngn (SEQ ID NO: 51), UAGAgurngn (SEQ ID NO: 34), UCGAgurngn (SEQ ID NO: 40), UGGAgurngn (SEQ ID NO: 46) and UUGAgurngn (SEQ ID NO: 52) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n or N is any nucleotide, by which the intronic REMS, in the presence of a compound described herein, functions as an intronic 5' splice site, causing the NNGA (SEQ ID NO: 3863) nucleotides of the REMS and the intronic nucleotide sequence between the intronic 3' splice site down to and including the NNGA (SEQ ID NO: 3863) nucleotides to be spliced into the mature RNA as an intronic exon to provide a non-wild-type, nonfunctional mRNA.

[00165] In a preferred embodiment, the REMS has a nucleotide sequence selected from the group consisting of ANGAguragu (SEQ ID NO: 437), CNGAguragu (SEQ ID NO: 443), GNGAguragu (SEQ ID NO: 449), UNGAguragu (SEQ ID NO: 455), NAGAguragu (SEQ ID NO: 438), NCGAguragu (SEQ ID NO: 444), NGGAguragu (SEQ ID NO: 450), NUGAguragu (SEQ ID NO: 456), AAGAguragu (SEQ ID NO: 439), ACGAguragu (SEQ ID NO: 445), AGGAguragu (SEQ ID NO: 451), AUGAguragu (SEQ ID NO: 457), CAGAguragu (SEQ ID NO: 440), CCGAguragu (SEQ ID NO: 446), CGGAguragu (SEQ ID NO: 452), CUGAguragu (SEQ ID NO: 458), GAGAguragu (SEQ ID NO: 441), GCGAguragu (SEQ ID NO: 447),

GGGAguragu (SEQ ID NO: 453), GUGAguragu (SEQ ID NO: 459), UAGAguragu (SEQ ID NO: 442), UCGAguragu (SEQ ID NO: 448), UGGAguragu (SEQ ID NO: 454) and UUGAguragu (SEQ ID NO: 460) at the RNA level, wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and N is any nucleotide. In one or more embodiments provided herein, N is A or G.

[00166] In the context of DNA, in a specific embodiment, the nucleotide sequence encoding an intronic REMS has the sequence GAgtrngn (SEQ ID NO: 4), wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n is any nucleotide. In another specific embodiment, in the context of DNA, the nucleotide sequence encoding an intronic REMS has the sequence GAgtragt (SEQ ID NO: 3865), wherein r is A or G. In a specific embodiment, in the context of DNA, the nucleotide sequence encoding an intronic REMS has the sequence NNGAgtrngn (SEQ ID NO: 3), wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n or N is any nucleotide. In another specific embodiment, in the context of DNA, the nucleotide sequence encoding an intronic REMS has the sequence NNGAgtragt (SEQ ID NO: 3864), wherein r is A or G and N is any nucleotide.

[00167] In a specific embodiment, in the context of DNA, the nucleotide sequence encoding an intronic REMS comprises a sequence selected from the group consisting of ANGAgtrngn (SEQ ID NO: 1829), CNGAgtrngn (SEQ ID NO: 1835), GNGAgtrngn (SEQ ID NO: 1841), TNGAgtrngn (SEQ ID NO: 1847), NAGAgtrngn (SEQ ID NO: 1830), NCGAgtrngn (SEQ ID NO: 1836), NGGAgtrngn (SEQ ID NO: 1842), NTGAgtrngn (SEQ ID NO: 1848), AAGAgtrngn (SEQ ID NO: 1831), ACGAgtrngn (SEQ ID NO: 1837), AGGAgtrngn (SEQ ID NO: 1843), ATGAgtrngn (SEQ ID NO: 1849), CAGAgtrngn (SEQ ID NO: 1832), CCGAgtrngn (SEQ ID NO: 1838), CGGAgtrngn (SEQ ID NO: 1844), CTGAgtrngn (SEQ ID NO: 1850), GAGAgtrngn (SEQ ID NO: 1833), GCGAgtrngn (SEQ ID NO: 1839), GGGAgtrngn (SEQ ID NO: 1845), GTGAgtrngn (SEQ ID NO: 1851), TAGAgtrngn (SEQ ID NO: 1834), TCGAgtrngn (SEQ ID NO: 1840), TGGAgtrngn (SEQ ID NO: 1846) and TTGAgtrngn (SEQ ID NO: 1852), wherein r is A or G (*i.e.*, a purine nucleotide adenine or guanine) and n or N is any nucleotide.

[00168] In a preferred embodiment, in the context of DNA, the nucleotide sequence encoding the intronic REMS comprises a sequence selected from the group consisting of ANGAgtragt (SEQ ID NO: 2237), CNGAgtragt (SEQ ID NO: 2243), GNGAgtragt (SEQ ID NO: 2249), TNGAgtragt (SEQ ID NO: 2255), NAGAgtragt (SEQ ID NO: 2238), NCGAgtragt (SEQ ID NO: 2244), NGGAgtragt (SEQ ID NO: 2250), NTGAgtragt (SEQ ID NO: 2256), AAGAgtragt (SEQ ID NO: 2239), ACGAgtragt (SEQ ID NO: 2245), AGGAgtragt (SEQ ID NO: 2251), ATGAgtragt (SEQ ID NO: 2257), CAGAgtragt (SEQ ID NO: 2240), CCGAgtragt (SEQ ID NO: 2246), CGGAgtragt (SEQ ID NO: 2252), CTGAgtragt (SEQ ID NO: 2258), GAGAgtragt (SEQ ID NO: 2241), GCGAgtragt (SEQ ID NO: 2247), GGGAgtragt (SEQ ID NO: 2253), GTGAgtragt (SEQ ID NO: 2259), TAGAgtragt (SEQ ID NO: 2242), TCGAgtragt (SEQ ID NO: 2248), TGGAgtragt (SEQ ID NO: 2254) and TTGAgtragt (SEQ ID NO: 2260), wherein r is A or G and N is any nucleotide. In one or more embodiments provided herein, N is A or G.

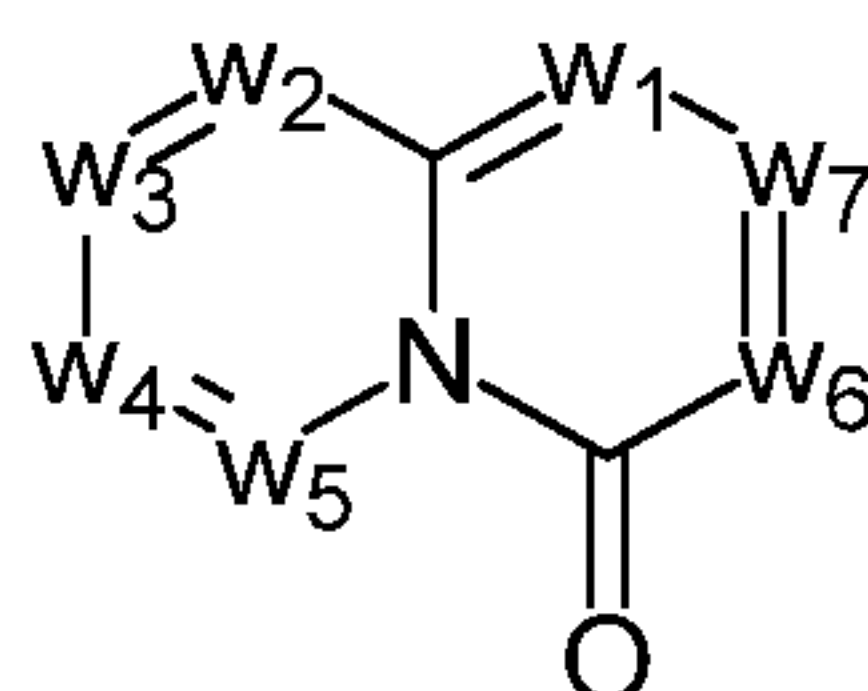
[00169] An intronic REMS can be part of an endogenous RNA or can be introduced into an RNA sequence that does not naturally contain the intronic REMS sequence (in which case, the introduced intronic REMS is a non-endogenous intronic REMS, i.e., an intronic REMS not naturally present in the corresponding RNA. A nucleotide sequence encoding an intronic REMS can also be part of an endogenous DNA sequence, or a nucleotide sequence encoding the intronic REMS can be introduced into a DNA sequence that does not naturally contain the nucleotide sequence encoding an intronic REMS.

[00170] In a specific embodiment, the intronic REMS is located in an intron which further comprises is downstream of a branch point and a functional 3' splice site which, in the presence of a small molecule splicing modifier, enables the REMS to function as a 5' splice site. In a specific embodiment, the intronic REMS is located in an intron and is downstream of a branch point and a functional 3' splice site which, in the presence of a small molecule splicing modifier, enables the REMS to function as a 5' splice site. Without being bound by any theory or mechanism, the small molecule compounds described herein have been shown to increase the affinity of the interaction between the U1 snRNP, as well as other components of the pre-mRNA splicing machinery, and the nucleotides NNGA (SEQ ID NO: 3863) of the REMS whereby, in

the presence of the compound, the intronic REMS functions as a U1 snRNP binding site, causing the intronic nucleotides to be spliced as an intronic exon.

COMPOUNDS

[00171] Provided herein are compounds of Formula (I) for use in the methods described herein:



(I)

[00172] or a form thereof, wherein:

[00173] w₁ and w₅ are independently C-R_a or N;

[00174] w₂ is C-R_b or N;

[00175] w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

[00176] w₆ is C-R₁, C-R₂, C-R_c or N;

[00177] wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00178] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00179] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00180] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00181] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

[00182] wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

[00183] R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl,

(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

amino-C₁₋₈alkyl-amino, (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy, C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 amino-C₂₋₈alkenyl, C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl,
 amino-C₂₋₈alkynyl, C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl,
 halo-C₁₋₈alkyl-amino, (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino,
 (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl,
 heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino,
 (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino,
 (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

[00184] wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

[00185] wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

[00186] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00187] wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

[00188] R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

[00189] R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

[00190] R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

[00191] R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

[00192] R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

[00193] R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

[00194] R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

- [00195] R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.
- [00196] In one embodiment of the use of a compound of Formula (I), w₁ is C-R_a.
- [00197] In another embodiment of the use of a compound of Formula (I), w₁ is N.
- [00198] In one embodiment of the use of a compound of Formula (I), w₂ is C-R_b.
- [00199] In another embodiment of the use of a compound of Formula (I), w₂ is N.
- [00200] In one embodiment of the use of a compound of Formula (I), w₃ is C-R_a.
- [00201] In another embodiment of the use of a compound of Formula (I), w₃ is N.
- [00202] In one embodiment of the use of a compound of Formula (I), w₄ is C-R_a.
- [00203] In another embodiment of the use of a compound of Formula (I), w₄ is N.
- [00204] In one embodiment of the use of a compound of Formula (I), w₅ is C-R_a.
- [00205] In another embodiment of the use of a compound of Formula (I), w₅ is N.
- [00206] In one embodiment of the use of a compound of Formula (I), w₆ is C-R_c.
- [00207] In another embodiment of the use of a compound of Formula (I), w₆ is N.
- [00208] In one embodiment of the use of a compound of Formula (I), w₇ is C-R_a.
- [00209] In another embodiment of the use of a compound of Formula (I), w₇ is N.
- [00210] In one embodiment of the use of a compound of Formula (I), w₃ is C-R₁ and w₆ is C-R₂.
- [00211] In another embodiment of the use of a compound of Formula (I), w₃ is C-R₂ and w₆ is C-R₁.
- [00212] In one embodiment of the use of a compound of Formula (I), w₄ is C-R₁ and w₇ is C-R₂.
- [00213] In another embodiment of the use of a compound of Formula (I), w₄ is C-R₂ and w₇ is C-R₁.
- [00214] In one embodiment of the use of a compound of Formula (I), w₃ is C-R₁, w₆ is C-R₂ and w₁, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.
- [00215] In another embodiment of the use of a compound of Formula (I), w₃ is C-R₂, w₆ is C-R₁ and w₁, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.
- [00216] In one embodiment of the use of a compound of Formula (I), w₄ is C-R₁, w₇ is C-R₂, w₁, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.
- [00217] In another embodiment of the use of a compound of Formula (I), w₄ is C-R₂, w₇ is C-R₁, w₁, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

- [00218] In one embodiment of the use of a compound of Formula (I), w_1 and w_2 are N.
- [00219] In one embodiment of the use of a compound of Formula (I), w_1 and w_3 are N.
- [00220] In one embodiment of the use of a compound of Formula (I), w_1 and w_4 are N.
- [00221] In one embodiment of the use of a compound of Formula (I), w_1 and w_5 are N.
- [00222] In one embodiment of the use of a compound of Formula (I), w_1 and w_6 are N.
- [00223] In one embodiment of the use of a compound of Formula (I), w_1 and w_7 are N.
- [00224] In one embodiment of the use of a compound of Formula (I),
- [00225] R_1 is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy, C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl, C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl, C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino, (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino, [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,

[(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00226] In another embodiment of the use of a compound of Formula (I),

[00227] R₁ is amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy, C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl, C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl, C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino, (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino, [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00228] In another embodiment of the use of a compound of Formula (I),

[00229] R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy, C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 amino-C₂₋₈alkenyl, C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl,
 amino-C₂₋₈alkynyl, C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl,
 halo-C₁₋₈alkyl-amino, (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino or
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino.

[00230] In another embodiment of the use of a compound of Formula (I),

[00231] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy,
 heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl,
 aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl,
 heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino,
 (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl,
 C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00232] In another embodiment of the use of a compound of Formula (I),

[00233] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl or heterocyclyl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00234] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl optionally substituted with R₃ and R₄ substituents.

[00235] In another embodiment of the use of a compound of Formula (I), R₁ is C₃₋₁₄cycloalkyl optionally substituted with R₃ and R₄ substituents.

[00236] In another embodiment of the use of a compound of Formula (I),

[00237] R₁ is aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of aryl is optionally substituted with R₃ and R₄ substituents.

[00238] In another embodiment of the use of a compound of Formula (I), R₁ is aryl-C₁₋₈alkyl-amino optionally substituted with R₃ and R₄ substituents.

[00239] In another embodiment of the use of a compound of Formula (I),

[00240] R₁ is heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00241] In another embodiment of the use of a compound of Formula (I), R₁ is heteroaryl optionally substituted with R₃ and R₄ substituents.

[00242] In one embodiment of the use of a compound of Formula (I),

[00243] R₁ is heterocyclyl selected from azetidiny, 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, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3*aR*,6*aR*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3*aR*,6*aS*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aR*,7*aR*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aS*,7*aS*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, 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 with R₃ and R₄ substituents.

[00244] In another embodiment of the use of a compound of Formula (I),

[00245] R₁ is heterocyclyl selected from azetidin-1-yl, tetrahydrofuran-3-yl, pyrrolidin-1-yl, piperidin-1-yl, piperidin-4-yl, piperazin-1-yl, 1,4-diazepan-1-yl, 1,2,5,6-tetrahydropyridin-5-yl, 1,2,3,6-tetrahydropyridin-4-yl, hexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl, (3*aR*,6*aR*)-hexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl, (3*aR*,6*aS*)-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, (4*aR*,7*aR*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl, (4*aS*,7*aS*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl, hexahydropyrrolo[1,2-*a*]pyrazin-6(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl, (7*R*,8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl, (8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl, (8*aR*)-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-2*H*-pyrido[1,2-*a*]pyrazin-2-yl, 3-azabicyclo[3.1.0]hex-3-yl, 8-azabicyclo[3.2.1]oct-3-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-3-yl, 8-azabicyclo[3.2.1]oct-2-en-3-yl, (1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-3-yl, 9-azabicyclo[3.3.1]non-3-yl, (1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl, 2,5-diazabicyclo[2.2.1]hept-2-yl, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]hept-2-yl, 2,5-diazabicyclo[2.2.2]oct-2-yl, 3,8-diazabicyclo[3.2.1]oct-3-yl, (1*R*,5*S*)-3,8-diazabicyclo[3.2.1]oct-3-yl, 1,4-diazabicyclo[3.2.2]non-4-yl, azaspiro[3.3]hept-2-yl, 2,6-diazaspiro[3.3]hept-2-yl, 2,7-diazaspiro[3.5]non-7-yl, 5,8-diazaspiro[3.5]non-8-yl, 2,7-diazaspiro[4.4]non-2-yl or 6,9-diazaspiro[4.5]dec-9-yl; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00246] In another embodiment of the use of a compound of Formula (I),

[00247] R₁ is substituted heterocyclyl selected from 4-methyl-1,4-diazepan-1-yl,

(3a*S*,6a*S*)-1-methylhexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,

(3a*S*,6a*S*)-5-methylhexahydropyrrolo[3,4-*b*]pyrrol-1(2*H*)-yl,

(3a*R*,6a*R*)-1-methylhexahydropyrrolo[3,4-*b*]pyrrol-5(1*H*)-yl,

(3a*R*,6a*S*)-5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,

(3a*R*,6a*S*)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,

(3a*R*,6a*S*)-5-(propan-2-yl)hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,

(3a*R*,6a*S*)-5-ethylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl,

(4a*R*,7a*R*)-1-methyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(4a*R*,7a*R*)-1-ethyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(4a*R*,7a*R*)-1-(2-hydroxyethyl)octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(4a*S*,7a*S*)-1-methyloctahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(4a*S*,7a*S*)-1-(2-hydroxyethyl)octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl,

(7*R*,8a*S*)-7-hydroxyhexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,

(8a*S*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,

(8a*R*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,

(1*R*,5*S*,6*s*)-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.

[00248] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkyl, wherein heterocyclyl is selected from morpholinyl, piperidinyl, piperazinyl, imidazolyl or pyrrolidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00249] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkyl selected from morpholin-4-yl-methyl, morpholin-4-yl-ethyl, morpholin-4-yl-propyl, piperidin-1-yl-methyl, piperazin-1-yl-methyl, piperazin-1-yl-ethyl, piperazin-1-yl-propyl, piperazin-1-yl-butyl, imidazol-1-yl-methyl, imidazol-1-yl-ethyl, imidazol-1-yl-propyl, imidazol-1-yl-butyl, pyrrolidin-1-yl-methyl, pyrrolidin-1-yl-ethyl, pyrrolidin-1-yl-propyl or pyrrolidin-1-yl-butyl; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00250] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkoxy, wherein heterocyclyl is selected from pyrrolidinyl, piperidinyl or morpholinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00251] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkoxy selected from pyrrolidin-2-yl-methoxy, pyrrolidin-2-yl-ethoxy, pyrrolidin-1-yl-methoxy, pyrrolidin-1-yl-ethoxy, piperidin-1-yl-methoxy, piperidin-1-yl-ethoxy, morpholin-4-yl-methoxy or morpholin-4-yl-ethoxy; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00252] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-amino, wherein heterocyclyl is selected from azetidiny, pyrrolidinyl, piperidinyl, 9-azabicyclo[3.3.1]nonyl or (1*R*,5*S*)-9-azabicyclo[3.3.1]nonyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00253] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-amino selected from azetidin-3-yl-amino, pyrrolidin-3-yl-amino, piperidin-4-yl-amino, 9-azabicyclo[3.3.1]non-3-yl-amino, (1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl-amino, 9-methyl-9-azabicyclo[3.3.1]non-3-yl-amino, (3-*exo*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl-amino or (1*R*,5*S*)-9-methyl-9-

azabicyclo[3.3.1]non-3-yl-amino; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00254] In one embodiment of the use of a compound of Formula (I), R₁ is (heterocyclyl)(C₁₋₈alkyl)amino, wherein heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00255] In another embodiment of the use of a compound of Formula (I), R₁ is (heterocyclyl)(C₁₋₈alkyl)amino selected from (pyrrolidin-3-yl)(methyl)amino or (piperidin-4-yl)(methyl)amino; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00256] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-amino-C₁₋₈alkyl, wherein heterocyclyl is selected from tetrahydrofuranyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00257] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-amino-C₁₋₈alkyl, selected from 3-(tetrahydrofuran-3-yl-amino)propyl; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00258] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, wherein heterocyclyl is selected from tetrahydrofuranyl, thienyl or pyridinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00259] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, selected from 3-[(tetrahydrofuran-2-ylmethyl)amino]propyl, 3-[(thienyl-3-ylmethyl)amino]propyl, 3-[(pyridin-2-ylmethyl)amino]propyl or 3-[(pyridin-4-ylmethyl)amino]propyl; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00260] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-oxy, wherein heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00261] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-oxy selected from pyrrolidin-3-yl-oxy or piperidin-4-yl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00262] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-carbonyl, wherein heterocyclyl is selected from piperazinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00263] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-carbonyl selected from piperazin-1-yl-carbonyl; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00264] In one embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-carbonyl-oxy, wherein heterocyclyl is selected from piperazinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00265] In another embodiment of the use of a compound of Formula (I), R₁ is heterocyclyl-carbonyl-oxy selected from piperazin-1-yl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents.

[00266] In one embodiment of the use of a compound of Formula (I), R₁ is C₃₋₁₄cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl or cycloheptyl; wherein, each instance of C₃₋₁₄cycloalkyl is optionally substituted with R₃ and R₄ substituents.

[00267] In another embodiment of the use of a compound of Formula (I), R₁ is C₃₋₈cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl or cycloheptyl; wherein, each instance of C₃₋₈cycloalkyl is optionally substituted with R₃ and R₄ substituents.

[00268] In one embodiment of the use of a compound of Formula (I), R₁ is aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R₃ and R₄ substituents.

[00269] In another embodiment of the use of a compound of Formula (I), R₁ is aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl selected from 3-(benzylamino)propyl; wherein, each instance of aryl is optionally substituted with R₃ and R₄ substituents.

[00270] In one embodiment of the use of a compound of Formula (I), R₁ is heteroaryl, wherein heteroaryl is selected from pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00271] In another embodiment of the use of a compound of Formula (I), R₁ is heteroaryl selected from pyridin-4-yl; wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00272] In one embodiment of the use of a compound of Formula (I), R₁ is heteroaryl-C₁₋₈alkyl, wherein heteroaryl is selected from 1*H*-imidazolyl; and, wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00273] In another embodiment of the use of a compound of Formula (I), R₁ is heteroaryl-C₁₋₈alkyl selected from 1*H*-imidazol-1-yl-methyl; wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00274] In one embodiment of the use of a compound of Formula (I), R₁ is (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, wherein heteroaryl is selected from pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00275] In another embodiment of the use of a compound of Formula (I), R₁ is (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino selected from (pyridin-3-ylmethyl)(methyl)amino; wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00276] In one embodiment of the use of a compound of Formula (I), R₁ is heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, wherein heteroaryl is selected from thienyl or pyridinyl; and, wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00277] In another embodiment of the use of a compound of Formula (I), R₁ is heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl selected from thien-3-yl-methyl-amino-propyl, pyridin-2-yl-methyl-amino-propyl, pyridin-3-yl-methyl-amino-propyl or pyridin-4-yl-methyl-amino-propyl; wherein, each instance of heteroaryl is optionally substituted with R₃ and R₄ substituents.

[00278] In one embodiment of the use of a compound of Formula (I), R₃ is selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino.

[00279] In another embodiment of the use of a compound of Formula (I), R₃ is selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl,

C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino.

[00280] In one embodiment of the use of a compound of Formula (I), R₃ is C₁₋₈alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

[00281] In another embodiment of the use of a compound of Formula (I), R₃ is C₁₋₈alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00282] In one embodiment of the use of a compound of Formula (I), R₃ is halo-C₁₋₈alkyl 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.

[00283] In another embodiment of the use of a compound of Formula (I), R₃ is halo-C₁₋₈alkyl 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.

[00284] In one embodiment of the use of a compound of Formula (I), R₃ is hydroxy-C₁₋₈alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00285] In another embodiment of the use of a compound of Formula (I), R₃ is hydroxy-C₁₋₈alkyl selected from hydroxy-methyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00286] In one embodiment of the use of compound of Formula (I), R₃ is C₁₋₈alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00287] In one embodiment of the use of a compound of Formula (I), R₃ is halo-C₁₋₈alkoxy 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.

[00288] In one embodiment of the use of a compound of Formula (I), R₃ is C₁₋₈alkoxy-carbonyl-amino selected from methoxy-carbonyl-amino, ethoxy-carbonyl-amino, propoxy-carbonyl-amino, isopropoxy-carbonyl-amino, tert-butoxy-carbonyl-amino.

[00289] In one embodiment of the use of a compound of Formula (I), R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl.

[00290] In one embodiment of the use of a compound of Formula (I), R_a is, in each instance, optionally and independently deuterium.

[00291] In one embodiment of the use of a compound of Formula (I), R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy.

[00292] In one embodiment of the use of a compound of Formula (I), R_c is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl.

[00293] In one embodiment of the use of a compound of Formula (I), R_c is, in each instance, optionally and independently deuterium.

[00294] In one embodiment of the use of a compound of Formula (I), R_b is deuterium.

[00295] In one embodiment of the use of a compound of Formula (I), R₄ is C₃₋₁₄cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; wherein, each instance of C₃₋₁₄cycloalkyl is optionally substituted with R₅ substituents.

[00296] In another embodiment of the use of a compound of Formula (I), R₄ is C₃₋₈cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; wherein, each instance of C₃₋₈cycloalkyl is optionally substituted with R₅ substituents.

[00297] In one embodiment of the use of a compound of Formula (I), R₄ is C₃₋₁₄cycloalkyl-C₁₋₈alkyl, wherein C₃₋₁₄cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C₃₋₁₄cycloalkyl is optionally substituted with R₅ substituents.

[00298] In another embodiment of the use of a compound of Formula (I), R₄ is C₃₋₈cycloalkyl-C₁₋₈alkyl, wherein C₃₋₈cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C₃₋₈cycloalkyl is optionally substituted with R₅ substituents.

[00299] In one embodiment of the use of a compound of Formula (I), R₄ is C₃₋₁₄cycloalkyl-amino, wherein C₃₋₁₄cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C₃₋₁₄cycloalkyl is optionally substituted with R₅ substituents.

[00300] In another embodiment of the use of a compound of Formula (I), R₄ is C₃₋₈cycloalkyl-amino, wherein C₃₋₈cycloalkyl is selected from cyclopropyl, cyclobutyl,

cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C₃₋₈cycloalkyl is optionally substituted with R₅ substituents.

[00301] In one embodiment of the use of a compound of Formula (I), R₄ is aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl or aryl-sulfonyloxy-C₁₋₈alkyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R₅ substituents.

[00302] In another embodiment of the use of a compound of Formula (I), R₄ is aryl-C₁₋₈alkyl or aryl-C₁₋₈alkoxy-carbonyl, wherein each instance of aryl is optionally substituted with R₅ substituents.

[00303] In one embodiment of the use of a compound of Formula (I), R₄ is heterocyclyl selected from oxetanyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,3-dioxanyl or morpholinyl, wherein each instance of heterocyclyl is optionally substituted with R₅ substituents.

[00304] In another embodiment of the use of a compound of Formula (I), R₄ is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1,3-dioxan-5-yl or morpholin-4-yl, wherein each instance of heterocyclyl is optionally substituted with R₅ substituents.

[00305] In one embodiment of the use of a compound of Formula (I), R₄ is heterocyclyl-C₁₋₈alkyl, wherein each instance of heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with R₅ substituents.

[00306] In another embodiment of the use of a compound of Formula (I), R₄ is heterocyclyl-C₁₋₈alkyl selected from pyrrolidin-1-yl-C₁₋₈alkyl or piperidin-1-yl-C₁₋₈alkyl, wherein each instance of heterocyclyl is optionally substituted with R₅ substituents.

[00307] In one embodiment of the use of a compound of Formula (I), R₅ is selected from halogen, hydroxy, cyano, nitro, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; wherein, halogen and halo is selected from fluoro, chloro, bromo or iodo.

[00308] In one embodiment of the use of a compound of Formula (I), R₅ is hydroxy.

[00309] In one embodiment of the use of a compound of Formula (I), R₅ is C₁₋₈alkyl selected from methyl, ethyl, propyl, isopropyl, n-butyl or tert-butyl.

[00310] In another embodiment of the use of a compound of Formula (I), R₅ is C₁₋₈alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00311] In one embodiment of the use of a compound of Formula (I), R₅ is halo-C₁₋₈alkyl 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.

[00312] In one embodiment of the use of a compound of Formula (I), R₅ is C₁₋₈alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00313] In one embodiment of the use of a compound of Formula (I), R₅ is halo-C₁₋₈alkoxy 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.

[00314] In one embodiment of the use of a compound of Formula (I), R₂ is aryl selected from phenyl optionally substituted with R₆ and R₇ substituents.

[00315] In one embodiment of the use of a compound of Formula (I), R₂ is aryl-amino, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R₆ and R₇ substituents.

[00316] In another embodiment of the use of a compound of Formula (I), R₂ is aryl-amino selected from phenyl-amino; wherein, each instance of aryl is optionally substituted with R₆ and R₇ substituents.

[00317] In one embodiment of the use of a compound of Formula (I), R₂ is aryl-amino-carbonyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with R₆ and R₇ substituents.

[00318] In another embodiment of the use of a compound of Formula (I), R₂ is aryl-amino-carbonyl selected from phenyl-amino-carbonyl; wherein, each instance of aryl is optionally substituted with R₆ and R₇ substituents.

[00319] In one embodiment of the use of a compound of Formula (I),

[00320] R₂ is heterocyclyl selected from 1,2,3,6-tetrahydropyridinyl, 1,3-benzodioxolyl or 2,3-dihydro-1,4-benzodioxinyl; wherein, each instance of heterocyclyl is optionally substituted with R₆ and R₇ substituents.

[00321] In another embodiment of the use of a compound of Formula (I),

[00322] R₂ is heterocyclyl selected from 1,2,3,6-tetrahydropyridin-4-yl, 1,3-benzodioxol-5-yl or 2,3-dihydro-1,4-benzodioxin-6-yl; wherein, each instance of heterocyclyl is optionally substituted with R₆ and R₇ substituents.

[00323] In one embodiment of the use of a compound of Formula (I),

[00324] R₂ is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indoliziny, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00325] In another embodiment of the use of a compound of Formula (I),

[00326] R₂ is heteroaryl selected from thien-2-yl, thien-3-yl, 1*H*-pyrazol-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1,3-thiazol-2-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-4-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl, 1*H*-indol-5-yl, 1*H*-indol-6-yl, 1*H*-indazol-5-yl, 2*H*-indazol-5-yl, indolizin-2-yl, benzofuran-2-yl, benzofuran-5-yl, benzothien-2-yl, benzothien-3-yl, 1*H*-benzimidazol-2-yl, 1*H*-benzimidazol-6-yl, 1,3-benzoxazol-2-yl, 1,3-benzoxazol-5-yl, 1,3-benzoxazol-6-yl, 1,3-benzothiazol-2-yl, 1,3-benzothiazol-5-yl, 1,3-benzothiazol-6-yl, 9*H*-purin-8-yl, furo[3,2-*b*]pyridin-2-yl, furo[3,2-*c*]pyridin-2-yl, furo[2,3-*c*]pyridin-2-yl, thieno[3,2-*c*]pyridin-2-yl, thieno[2,3-*d*]pyrimidin-6-yl, 1*H*-pyrrolo[2,3-*b*]pyridin-5-yl, 1*H*-pyrrolo[2,3-*c*]pyridin-4-yl, pyrrolo[1,2-*a*]pyrimidin-7-yl, pyrrolo[1,2-*a*]pyrazin-7-yl, pyrrolo[1,2-*b*]pyridazin-2-yl, pyrazolo[1,5-*a*]pyridin-2-yl, pyrazolo[1,5-*a*]pyrazin-2-yl, imidazo[1,2-*a*]pyridin-2-yl, imidazo[1,2-*a*]pyridin-6-yl, imidazo[1,2-*a*]pyrimidin-2-yl, imidazo[1,2-*a*]pyrimidin-6-yl, imidazo[1,2-*c*]pyrimidin-2-yl, imidazo[1,2-*b*]pyridazin-2-yl, imidazo[1,2-*a*]pyrazin-2-yl, imidazo[2,1-*b*][1,3]thiazol-6-yl,

imidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, [1,3]oxazolo[4,5-*b*]pyridin-2-yl or quinoxalin-2-yl; wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00327] In another embodiment of the use of a compound of Formula (I),

[00328] R₂ is substituted heteroaryl selected from 4-methylthien-2-yl, 1-methyl-1*H*-pyrazol-3-yl, 4-methyl-1*H*-pyrazol-3-yl, 1-phenyl-1*H*-pyrazol-3-yl, 1-phenyl-1*H*-imidazol-4-yl, 2-methyl-1-(pyridin-2-yl)-1*H*-imidazol-4-yl, 4-methyl-1,3-thiazol-2-yl, 4-(trifluoromethyl)-1,3-thiazol-2-yl, 4-phenyl-1,3-thiazol-2-yl, 5-phenyl-1,2,4-oxadiazol-3-yl, 3-fluoropyridin-4-yl, 6-fluoropyridin-2-yl, 2-chloropyridin-4-yl, 4-chloropyridin-3-yl, 5-chloropyridin-2-yl, 6-methylpyridin-3-yl, 2-(trifluoromethyl)pyridin-3-yl, 4-(trifluoromethyl)pyridin-2-yl, 6-(trifluoromethyl)pyridin-2-yl, 2-methoxypyridin-4-yl, 4-methoxypyridin-3-yl, 6-methoxypyridin-2-yl, 2-ethoxypyridin-3-yl, 6-ethoxypyridin-2-yl, 6-(propan-2-yloxy)pyridin-2-yl, 6-(dimethylamino)pyridin-3-yl, 6-(methylsulfanyl)pyridin-2-yl, 6-(cyclobutyloxy)pyridin-2-yl, 6-(pyrrolidin-1-yl)pyridin-2-yl, 2-methylpyrimidin-4-yl, 2-(propan-2-yl)pyrimidin-4-yl, 2-cyclopropylpyrimidin-4-yl, 1-methyl-1*H*-indol-3-yl, 2-methyl-2*H*-indazol-5-yl, 2-methyl-1-benzofuran-5-yl, 1-methyl-1*H*-benzimidazol-2-yl, 4-methyl-1*H*-benzimidazol-2-yl, 5-fluoro-1*H*-benzimidazol-2-yl, 4-fluoro-1,3-benzoxazol-2-yl, 5-fluoro-1,3-benzoxazol-2-yl, 4-chloro-1,3-benzoxazol-2-yl, 4-iodo-1,3-benzoxazol-2-yl, 2-methyl-1,3-benzoxazol-6-yl, 4-methyl-1,3-benzoxazol-2-yl, 4-(trifluoromethyl)-1,3-benzoxazol-2-yl, 7-(trifluoromethyl)-1,3-benzoxazol-2-yl, 2-methyl-1,3-benzothiazol-2-yl, 2-methyl-1,3-benzothiazol-5-yl, 2-methyl-1,3-benzothiazol-6-yl, 4-chloro-1,3-benzothiazol-2-yl, 7-chloro-1,3-benzothiazol-2-yl, 4-(trifluoromethyl)-1,3-benzothiazol-2-yl, 5-methylfuro[3,2-*b*]pyridin-2-yl, 4,6-dimethylfuro[3,2-*c*]pyridin-2-yl, 5,7-dimethylfuro[2,3-*c*]pyridin-2-yl, 4,6-dimethylthieno[3,2-*c*]pyridin-2-yl, 2,4-dimethylthieno[2,3-*d*]pyrimidin-6-yl, 1-methylpyrrolo[1,2-*a*]pyrazin-7-yl, 3-methylpyrrolo[1,2-*a*]pyrazin-7-yl, 1,3-dimethylpyrrolo[1,2-*a*]pyrazin-7-yl, 2-methylpyrrolo[1,2-*b*]pyridazin-2-yl, 4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl, 5-methylpyrazolo[1,5-*a*]pyridin-2-yl, 4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl, 2-chloroimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-methylimidazo[2,1-*b*][1,3]thiazol-6-yl, 3-methylimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-ethylimidazo[2,1-*b*][1,3]thiazol-6-yl, 2-methylimidazo[2,1-*b*][1,3,4]thiadiazol-6-yl, 6-cyanoimidazo[1,2-*a*]pyridin-2-yl (also referred to as 2-imidazo[1,2-*a*]pyridine-6-carbonitrile),

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

[00329] In another embodiment of the use of a compound of Formula (I),

[00330] R₂ is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl; wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00331] In another embodiment of the use of a compound of Formula (I),

[00332] R₂ is heteroaryl selected from furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00333] In one embodiment of the use of a compound of Formula (I), R₂ is heteroaryl-amino, wherein heteroaryl is selected from pyridinyl or pyrimidinyl; and, wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00334] In another embodiment of the use of a compound of Formula (I), R₂ is heteroaryl-amino selected from pyridin-2-yl-amino, pyridin-3-yl-amino or pyrimidin-2-yl-amino; wherein, each instance of heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00335] In one embodiment of the use of a compound of Formula (I), R₆ is selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; wherein, halogen and halo is selected from fluoro, chloro, bromo or iodo.

[00336] In one embodiment of the use of a compound of Formula (I), R₆ is C₁₋₈alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

[00337] In another embodiment of the use of a compound of Formula (I), R₆ is C₁₋₈alkyl selected from ethyl, propyl, isopropyl or tert-butyl.

[00338] In one embodiment of the use of a compound of Formula (I), R₆ is C₂₋₈alkenyl selected from ethenyl, allyl or buta-1,3-dienyl.

[00339] In another embodiment of the use of a compound of Formula (I), R₆ is C₂₋₈alkenyl selected from ethenyl or allyl.

[00340] In one embodiment of the use of a compound of Formula (I), R₆ is halo-C₁₋₈alkyl 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.

[00341] In one embodiment of the use of a compound of Formula (I), R₆ is hydroxy-C₁₋₈alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00342] In another embodiment of the use of a compound of Formula (I), R₆ is hydroxy-C₁₋₈alkyl selected from hydroxy-methyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

[00343] In one embodiment of the use of a compound of Formula (I), R₆ is C₁₋₈alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

[00344] In one embodiment of the use of a compound of Formula (I), R₆ is halo-C₁₋₈alkoxy 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.

[00345] In one embodiment of the use of a compound of Formula (I), R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl; wherein C₃₋₁₄cycloalkyl is selected from cyclopropyl or cyclobutoxy; wherein aryl is selected from phenyl; wherein heterocyclyl is selected from oxetanyl, pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl; and, wherein heteroaryl is selected from thienyl or pyridinyl.

[00346] In another embodiment of the use of a compound of Formula (I), R₇ is C₃₋₁₄cycloalkyl or C₃₋₁₄cycloalkyl-oxy, wherein each instance of C₃₋₁₄cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

[00347] In another embodiment of the use of a compound of Formula (I), R₇ is C₃₋₈cycloalkyl or C₃₋₈cycloalkyl-oxy, wherein each instance of C₃₋₈cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

[00348] In one embodiment of the use of a compound of Formula (I), R₇ is aryl selected from phenyl.

[00349] In one embodiment of the use of a compound of Formula (I), R₇ is heterocyclyl selected from oxetanyl, pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl.

[00350] In another embodiment of the use of a compound of Formula (I), R₇ is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl or 1,2,3,6-tetrahydropyridin-4-yl.

[00351] In one embodiment of the use of a compound of Formula (I), R₇ is heteroaryl selected from thienyl or pyridinyl.

[00352] In another embodiment of the use of a compound of Formula (I), R₇ is heteroaryl selected from pyridinyl.

[00353] In one embodiment of the use of a compound of Formula (I), R₇ is heteroaryl selected from thien-2-yl or pyridin-2-yl.

[00354] In another embodiment of the use of a compound of Formula (I), R₇ is heteroaryl selected from pyridin-2-yl.

[00355] In one embodiment of the use of a compound of Formula (I), R_c is hydrogen or C₁₋₈alkyl.

[00356] In another embodiment of the use of a compound of Formula (I),

[00357] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents; and,

[00358] wherein, heterocyclyl is selected from azetidiny, 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, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3*aR*,6*aR*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3*aR*,6*aS*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl,

octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aR*,7*aR*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aS*,7*aS*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, 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.

[00359] In another embodiment of the use of a compound of Formula (I),

[00360] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00361] wherein, aryl is phenyl;

[00362] wherein, heterocyclyl is selected from 1,2,3,6-tetrahydropyridinyl, 1,3-benzodioxolyl or 2,3-dihydro-1,4-benzodioxinyl;

[00363] wherein, heteroaryl is selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxalinyl; and, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00364] In another embodiment of the use of a compound of Formula (I),

[00365] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

[00366] wherein, heterocyclyl is selected from azetidiny, 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, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3*aR*,6*aR*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3*aS*,6*aS*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3*aR*,6*aS*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aR*,7*aR*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4*aS*,7*aS*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aS*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8*aR*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, 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; and, wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents; and

[00367] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

[00368] wherein, heterocyclyl is selected from 1,2,3,6-tetrahydropyridin-4-yl, 1,3-benzodioxol-5-yl or 2,3-dihydro-1,4-benzodioxin-6-yl;

[00369] wherein, heteroaryl is selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indoliziny, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, pyrrolo[1,2-*a*]pyrimidinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl or quinoxaliny; and, wherein, each instance of heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00370] In another embodiment of the use of a compound of Formula (I),

[00371] R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy, C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl, C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl, C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino, (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino, [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino or [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino; and

[00372] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00373] In another embodiment of the use of a compound of Formula (I),

[00374] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or

(heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents; and

[00375] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00376] In another embodiment of the use of a compound of Formula (I),

[00377] R₁ is heterocyclyl, heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino, (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy, heterocyclyl-carbonyl or heterocyclyl-carbonyl-oxy; wherein, each instance of heterocyclyl is optionally substituted with R₃ and R₄ substituents; and

[00378] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00379] In another embodiment of the use of a compound of Formula (I),

[00380] R₁ is heterocyclyl optionally substituted with R₃ and R₄ substituents; and

[00381] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00382] In another embodiment of the use of a compound of Formula (I),

[00383] R₁ is C₃₋₁₄cycloalkyl optionally substituted with R₃ and R₄ substituents; and

[00384] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00385] In another embodiment of the use of a compound of Formula (I),

[00386] R₁ is aryl-C₁₋₈alkyl-amino, (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of aryl is optionally substituted with R₃ and R₄ substituents; and

[00387] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00388] In another embodiment of the use of a compound of Formula (I),

[00389] R₁ is aryl-C₁₋₈alkyl-amino optionally substituted with R₃ and R₄ substituents; and

[00390] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00391] In another embodiment of the use of a compound of Formula (I),

[00392] R₁ is heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl; wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with R₃ and R₄ substituents; and

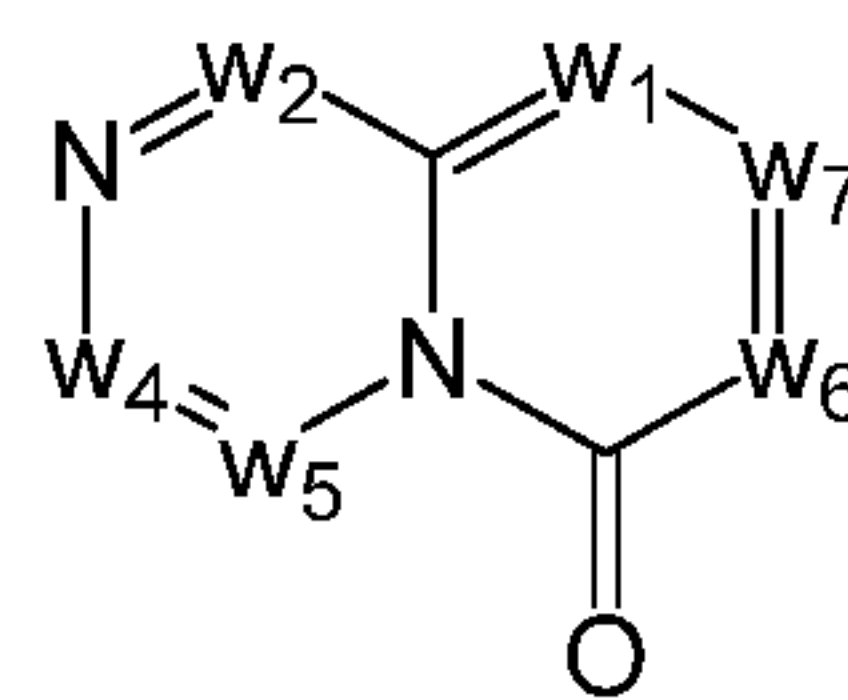
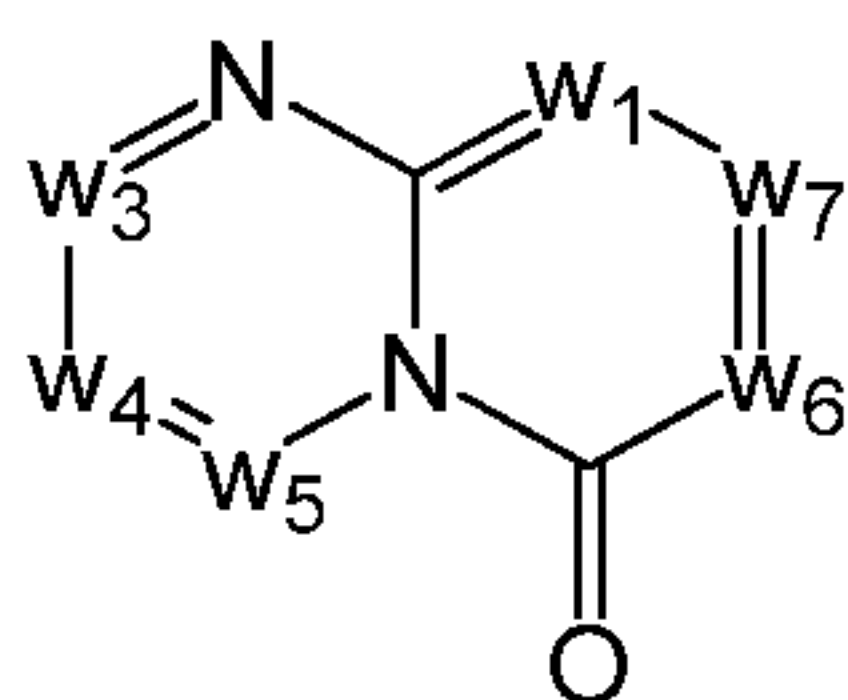
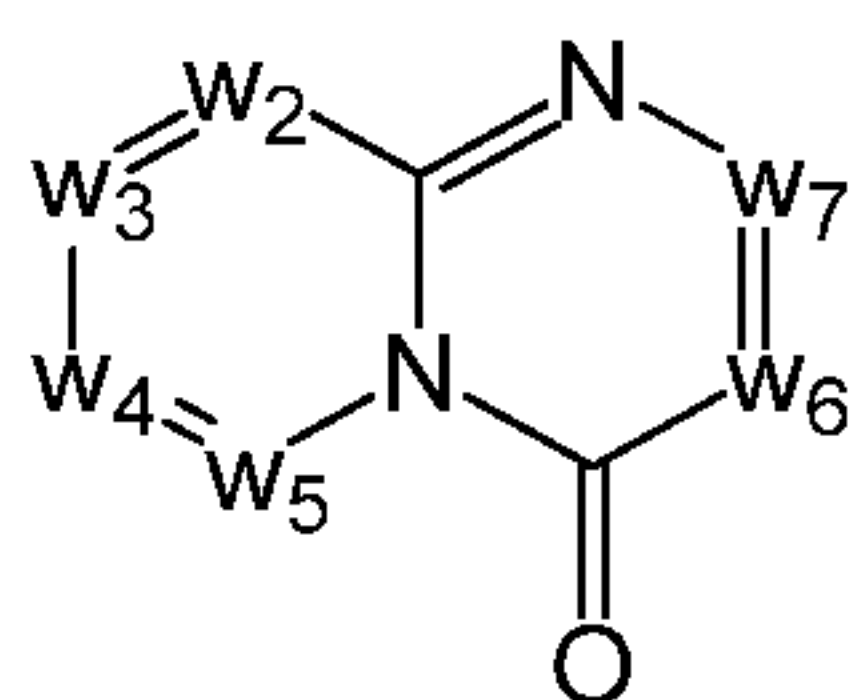
[00393] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

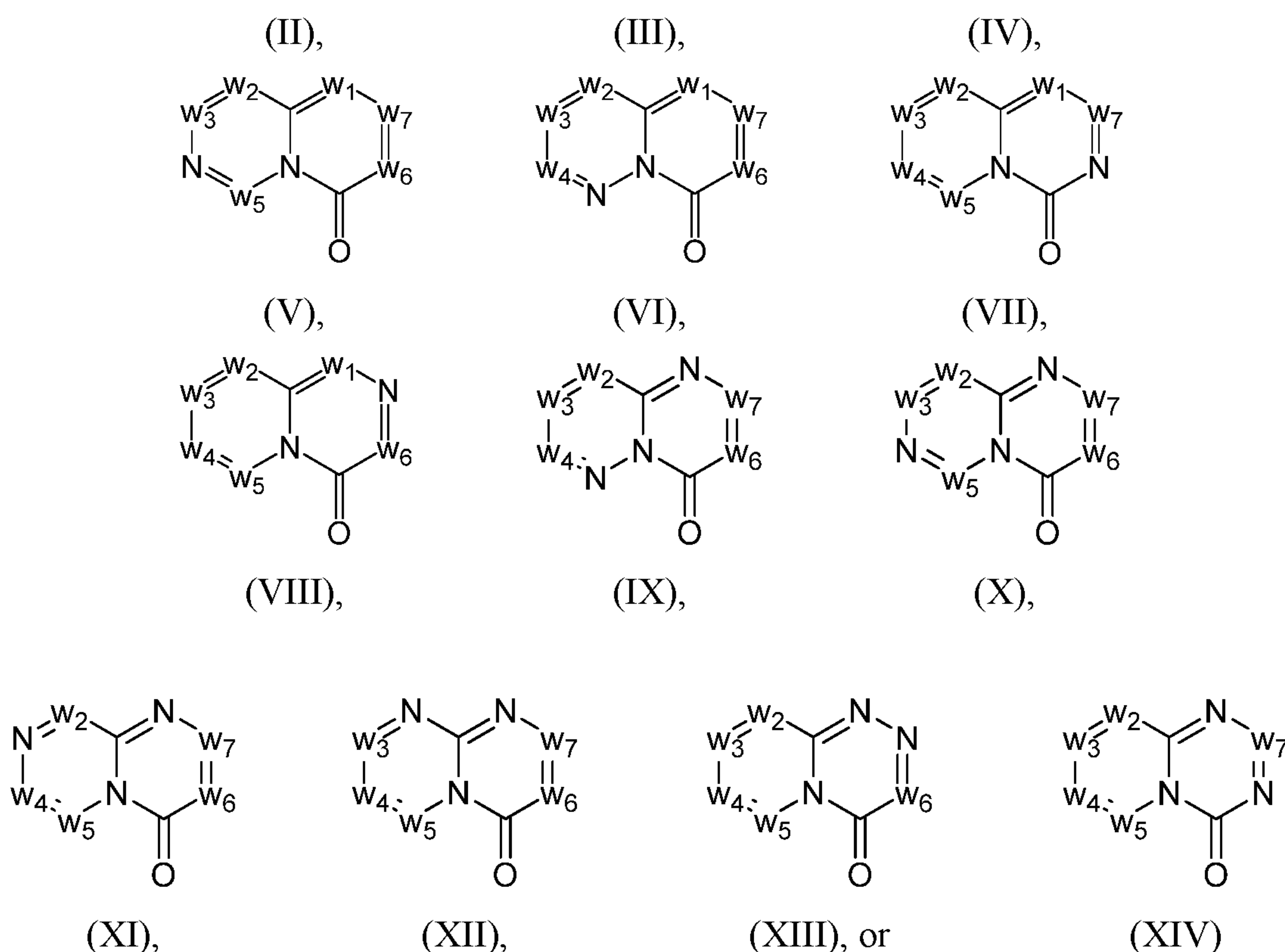
[00394] In another embodiment of the use of a compound of Formula (I),

[00395] R₁ is heteroaryl optionally substituted with R₃ and R₄ substituents; and

[00396] R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino, wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with R₆ and R₇ substituents.

[00397] In one embodiment, the compound of Formula (I), used in a method disclosed herein, is a compound selected from Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV):





[00398] or a form thereof.

[00399] In an embodiment of the use of the compound of Formula (I), w₃ is C-R₁, w₆ is C-R₂, w₁, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00400] In another embodiment of the use of the compound of Formula (I), w₃ is C-R₂, w₆ is C-R₁, w₁, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00401] In another embodiment of the use of the compound of Formula (I), w₄ is C-R₁, w₇ is C-R₂, w₁, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00402] In another embodiment of the use of the compound of Formula (I), w₄ is C-R₂, w₇ is C-R₁, w₁, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00403] In an embodiment of the use of the compound of Formula (II), w₃ is C-R₁, w₆ is C-R₂, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00404] In another embodiment of the use of the compound of Formula (II), w₃ is C-R₂, w₆ is C-R₁, w₄, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00405] In another embodiment of the use of the compound of Formula (II), w₄ is C-R₁, w₇ is C-R₂, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00406] In another embodiment of the use of the compound of Formula (II), w₄ is C-R₂, w₇ is C-R₁, w₃ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00407] In an embodiment of the use of the compound of Formula (III), w₃ is C-R₁, w₆ is C-R₂ and w₁, w₄, w₅ and w₇ are independently C-R_a or N.

[00408] In another embodiment of the use of the compound of Formula (III), w₃ is C-R₂, w₆ is C-R₁ and w₁, w₄, w₅ and w₇ are independently C-R_a or N.

[00409] In another embodiment of the use of the compound of Formula (III), w₄ is C-R₁, w₇ is C-R₂, w₁, w₃ and w₅ are independently C-R_a or N and w₆ is C-R_c or N.

[00410] In another embodiment of the use of the compound of Formula (III), w₄ is C-R₂, w₇ is C-R₁, w₁, w₃ and w₅ are independently C-R_a or N and w₆ is C-R_c or N.

[00411] In an embodiment of the use of the compound of Formula (IV), w₄ is C-R₁, w₇ is C-R₂, w₁ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00412] In another embodiment of the use of the compound of Formula (IV), w₄ is C-R₂, w₇ is C-R₁, w₁ and w₅ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00413] In an embodiment of the use of the compound of Formula (V), w₃ is C-R₁, w₆ is C-R₂, w₁, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00414] In another embodiment of the use of the compound of Formula (V), w₃ is C-R₂, w₆ is C-R₁, w₁, w₅ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00415] In an embodiment of the use of the compound of Formula (VI), w₃ is C-R₁, w₆ is C-R₂, w₁, w₄ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00416] In another embodiment of the use of the compound of Formula (VI), w₃ is C-R₂, w₆ is C-R₁, w₁, w₄ and w₇ are independently C-R_a or N and w₂ is C-R_b or N.

[00417] In another embodiment of the use of the compound of Formula (VI), w₄ is C-R₁, w₇ is C-R₂, w₁ and w₃ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00418] In another embodiment of the use of the compound of Formula (VI), w₄ is C-R₂, w₇ is C-R₁, w₁ and w₃ are independently C-R_a or N, w₂ is C-R_b or N and w₆ is C-R_c or N.

[00419] In another embodiment of the use of the compound of Formula (VII), w₄ is C-R₁, w₇ is C-R₂, w₁, w₃ and w₅ are C-R_a or N and w₂ is C-R_b or N.

[00420] In another embodiment of the use of the compound of Formula (VII), w₄ is C-R₂, w₇ is C-R₁, w₁, w₃ and w₅ are C-R_a or N and w₂ is C-R_b or N.

[00421] In another embodiment of the use of the compound of Formula (VIII), w_3 is C-R₁, w_6 is C-R₂, w_1 , w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00422] In another embodiment of the use of the compound of Formula (VIII), w_3 is C-R₂, w_6 is C-R₁, w_1 , w_4 and w_5 are C-R_a or N and w_2 is C-R_b or N.

[00423] In an embodiment of the use of the compound of Formula (IX), w_3 is C-R₁, w_6 is C-R₂, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00424] In another embodiment of the use of the compound of Formula (IX), w_3 is C-R₂, w_6 is C-R₁, w_4 and w_7 are independently C-R_a or N and w_2 is C-R_b or N.

[00425] In another embodiment of the use of the compound of Formula (IX), w_4 is C-R₁, w_7 is C-R₂, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00426] In another embodiment of the use of the compound of Formula (IX), w_4 is C-R₂, w_7 is C-R₁, w_2 is C-R_b or N, w_3 is C-R_a or N and w_6 is C-R_c or N.

[00427] In an embodiment of the use of the compound of Formula (X), w_3 is C-R₁, w_6 is C-R₂, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00428] In another embodiment of the use of the compound of Formula (X), w_3 is C-R₂, w_6 is C-R₁, w_2 is C-R_b or N and w_5 and w_7 are independently C-R_a or N.

[00429] In an embodiment of the use of the compound of Formula (XI), w_4 is C-R₁, w_7 is C-R₂, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00430] In another embodiment of the use of the compound of Formula (XI), w_4 is C-R₂, w_7 is C-R₁, w_2 is C-R_b or N, w_5 is C-R_a or N and w_6 is C-R_c or N.

[00431] In an embodiment of the use of the compound of Formula (XII), w_3 is C-R₁, w_6 is C-R₂ and w_4 , w_5 and w_7 are independently C-R_a or N.

[00432] In another embodiment of the use of the compound of Formula (XII), w_3 is C-R₂, w_6 is C-R₁ and w_4 , w_5 and w_7 are independently C-R_a or N.

[00433] In another embodiment of the use of the compound of Formula (XII), w_4 is C-R₁, w_7 is C-R₂, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

[00434] In another embodiment of the use of the compound of Formula (XII), w_4 is C-R₂, w_7 is C-R₁, w_3 and w_5 are independently C-R_a or N and w_6 is C-R_c or N.

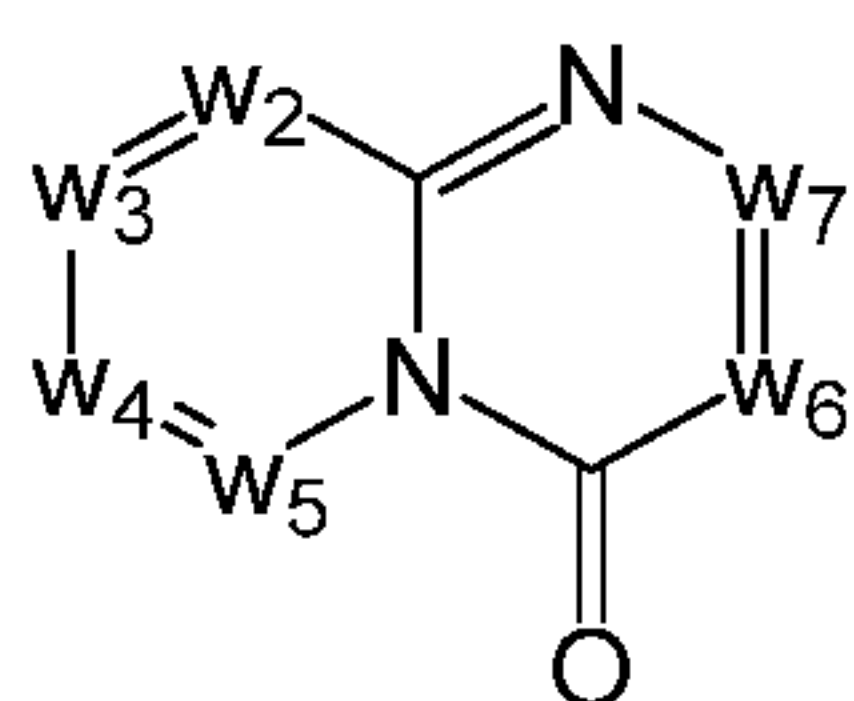
[00435] In an embodiment of the use of the compound of Formula (XIII), w_3 is C-R₁, w_6 is C-R₂, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

[00436] In another embodiment of the use of the compound of Formula (XIII), w_3 is C-R₂, w_6 is C-R₁, w_2 is C-R_b or N and w_4 and w_5 are independently C-R_a or N.

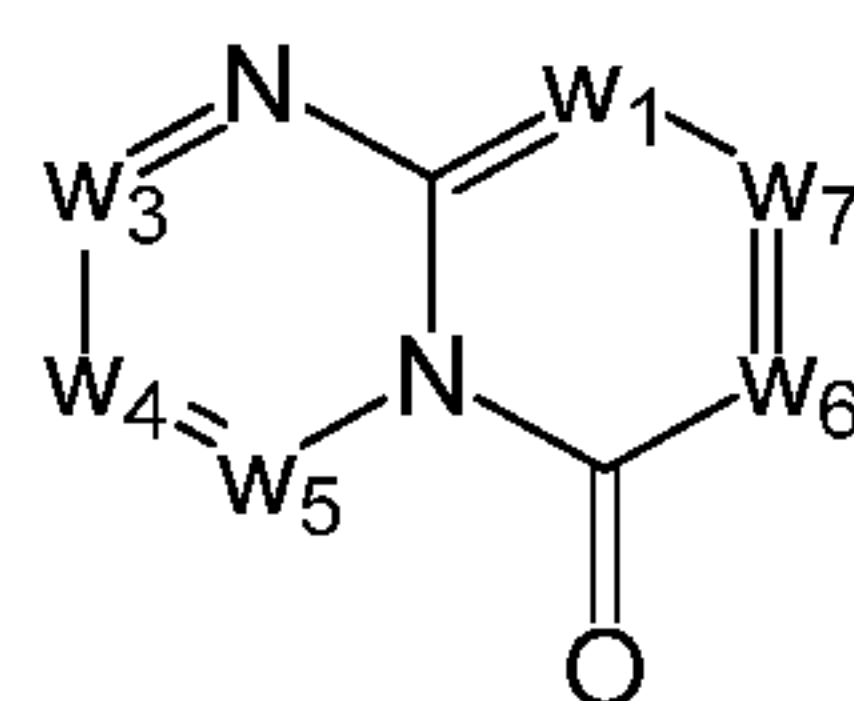
[00437] In an embodiment of the use of the compound of Formula (XIV), w_4 is C-R₁, w_7 is C-R₂, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

[00438] In another embodiment of the use of the compound of Formula (XIV), w_4 is C-R₂, w_7 is C-R₁, w_2 is C-R_b or N and w_3 and w_5 are independently C-R_a or N.

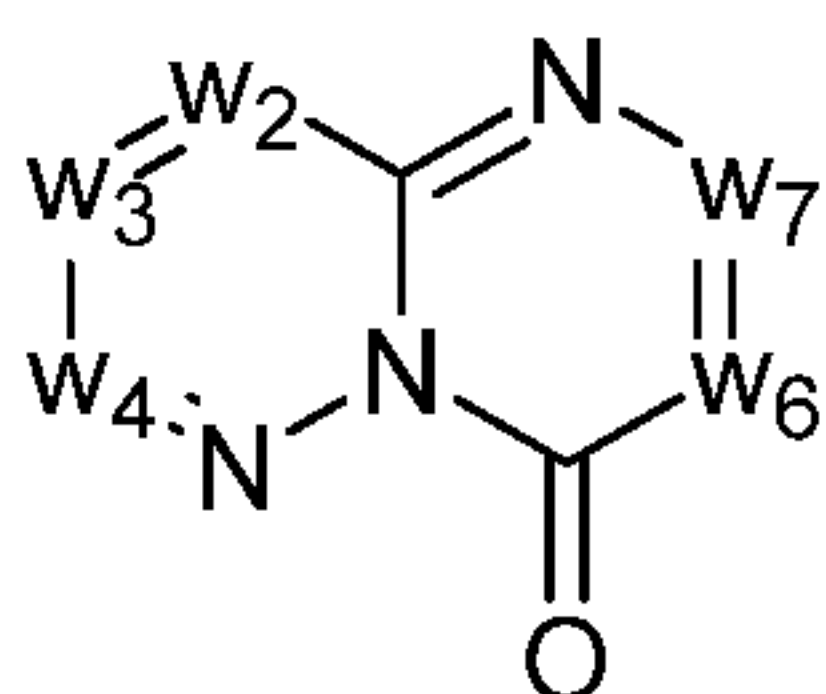
[00439] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound selected from Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII):



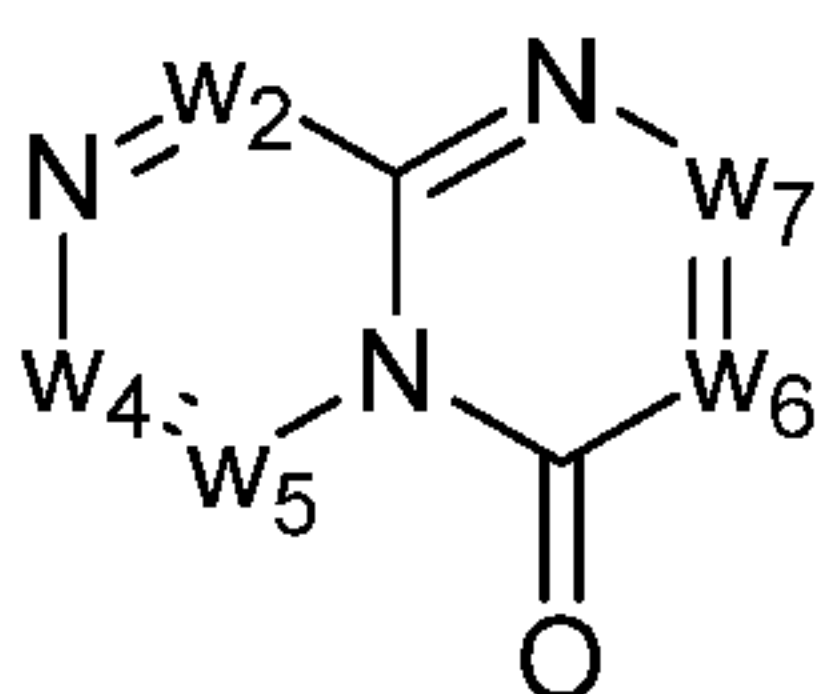
(II),



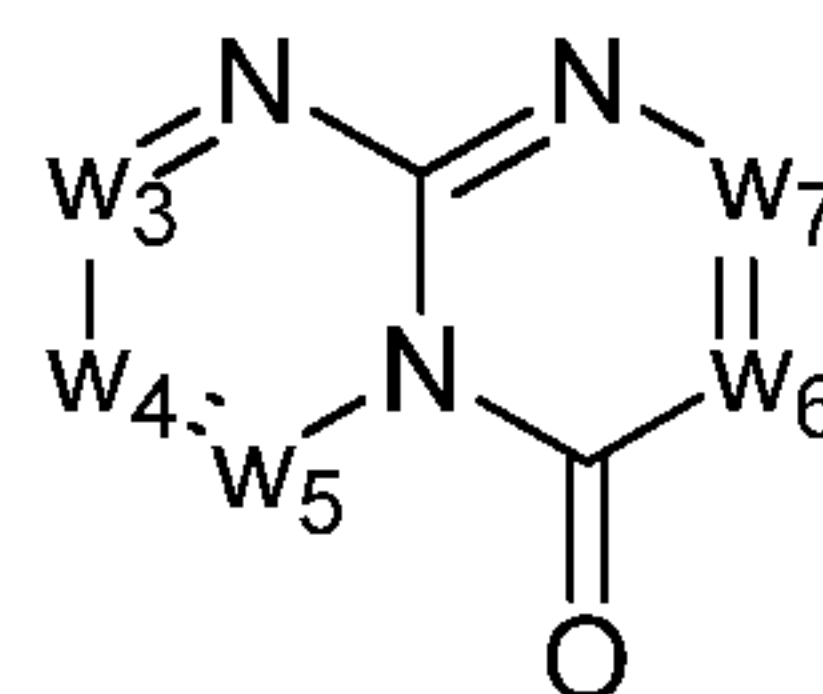
(III),



(IX),



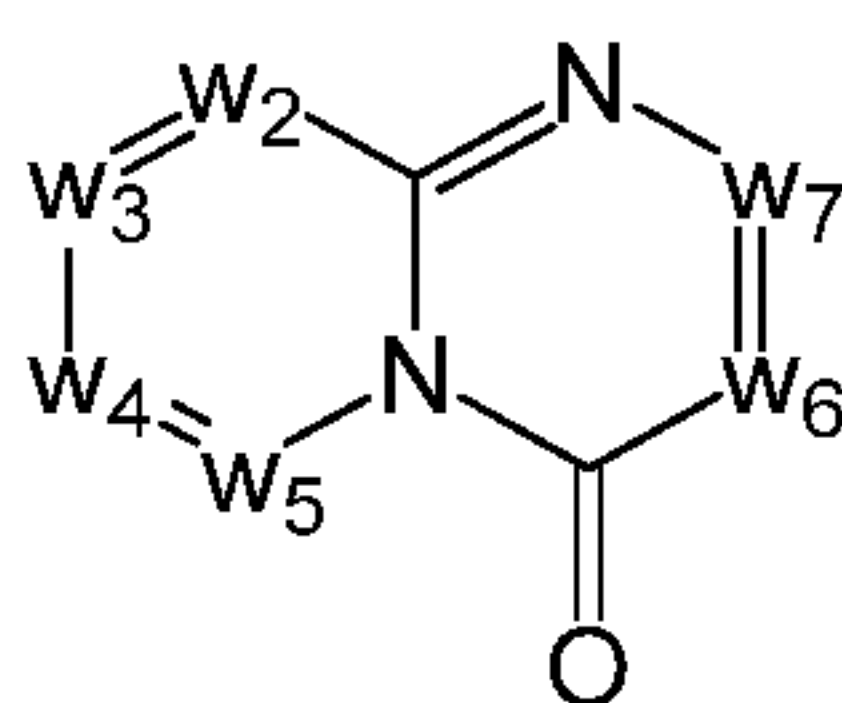
(XI), or



(XII)

[00440] or a form thereof.

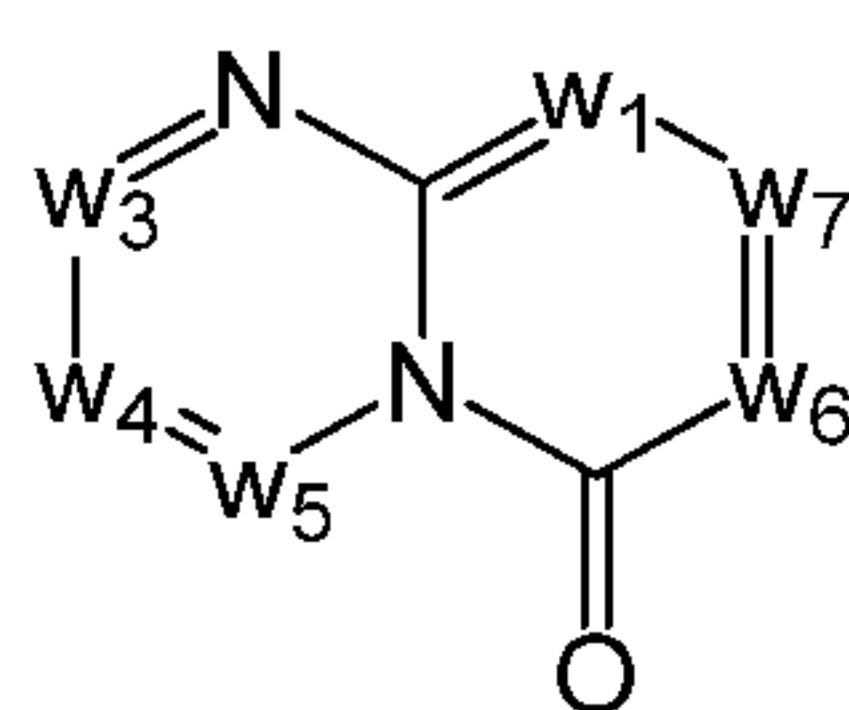
[00441] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (II):



(II)

[00442] or a form thereof.

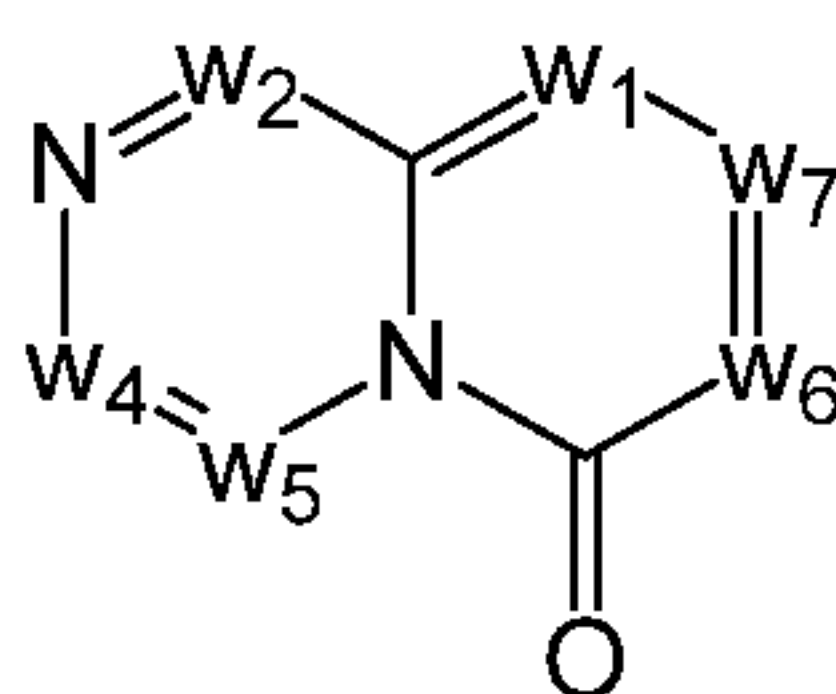
[00443] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (III):



(III)

[00444] or a form thereof.

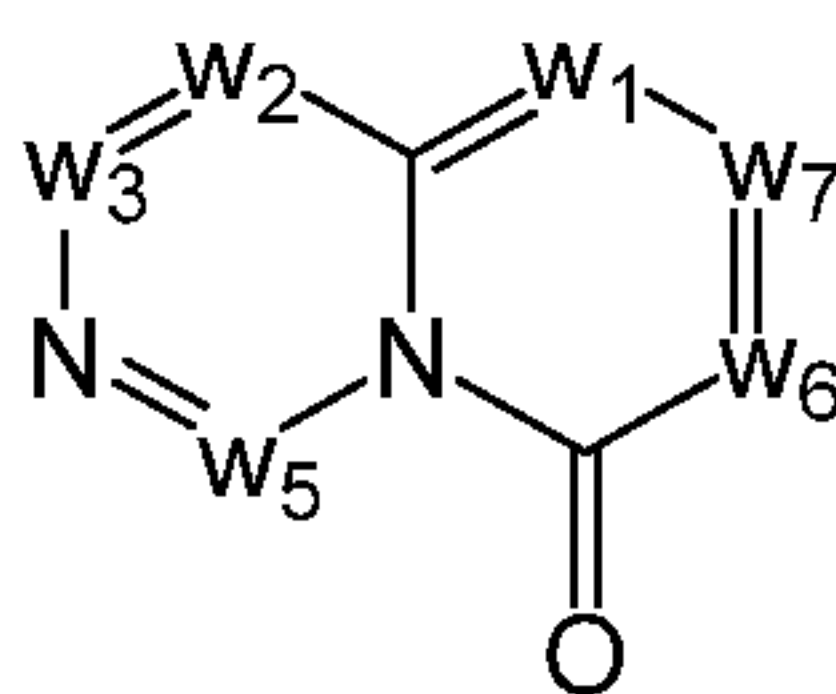
[00445] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (IV):



(IV)

[00446] or a form thereof.

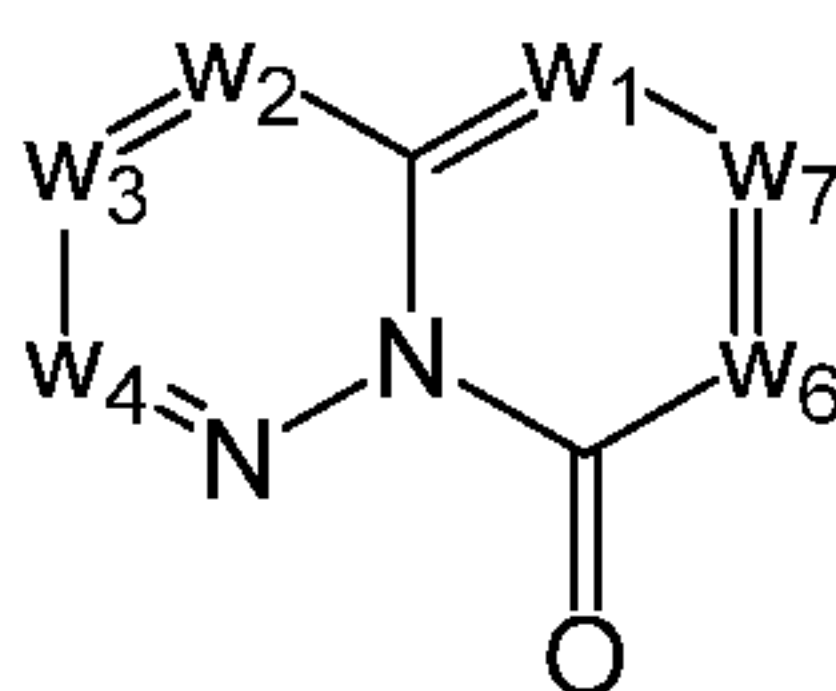
[00447] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (V):



(V)

[00448] or a form thereof.

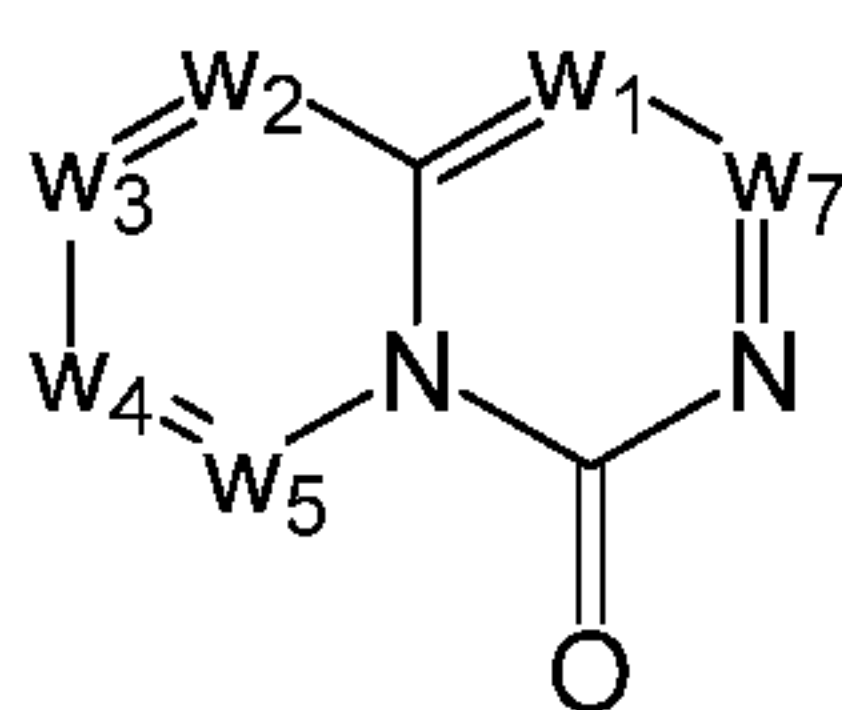
[00449] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (VI):



(VI)

[00450] or a form thereof.

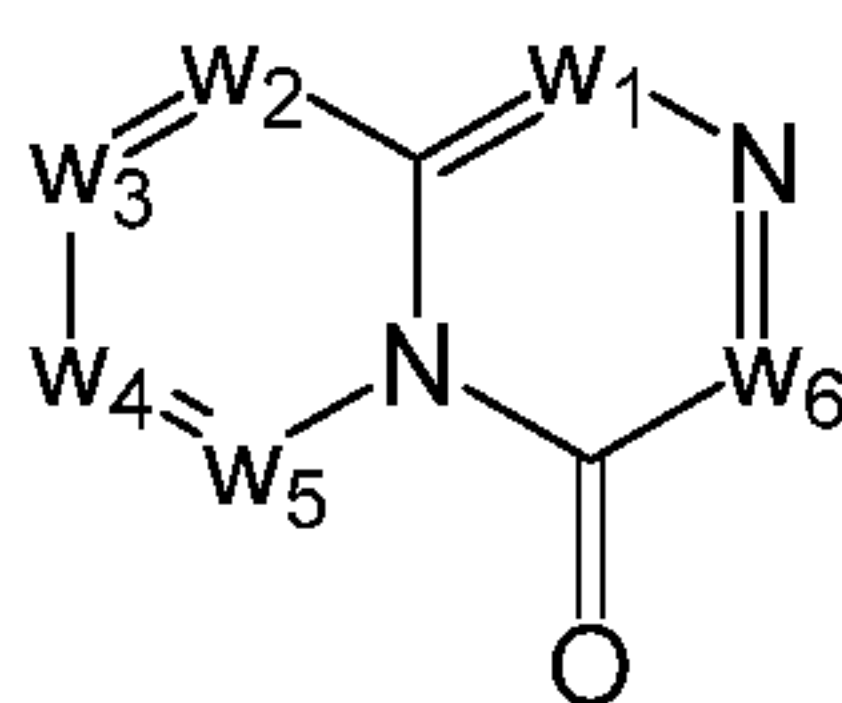
[00451] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (VII):



(VII)

[00452] or a form thereof.

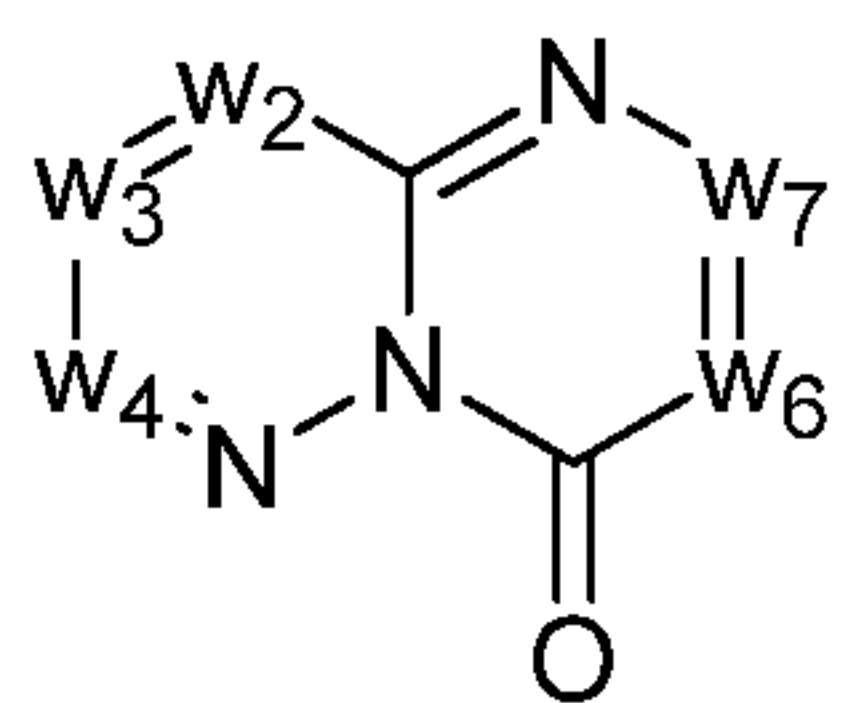
[00453] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (VIII):



(VIII)

[00454] or a form thereof.

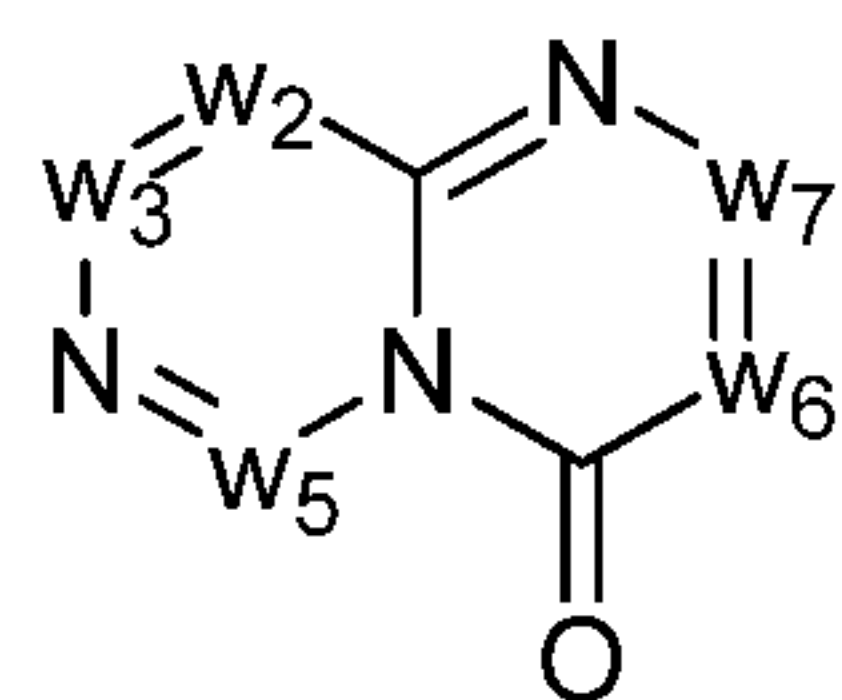
[00455] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (IX):



(IX)

[00456] or a form thereof.

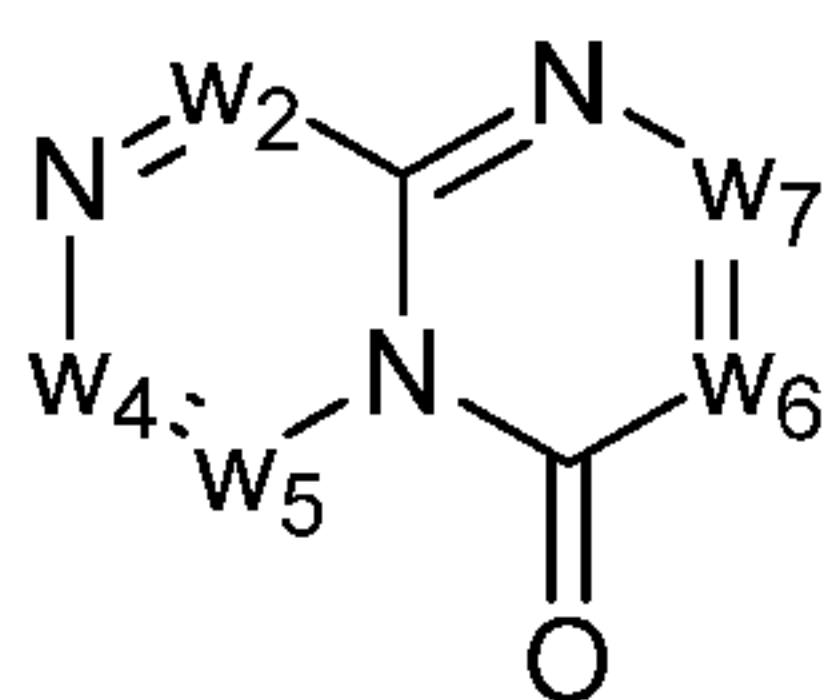
[00457] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (X):



(X)

[00458] or a form thereof.

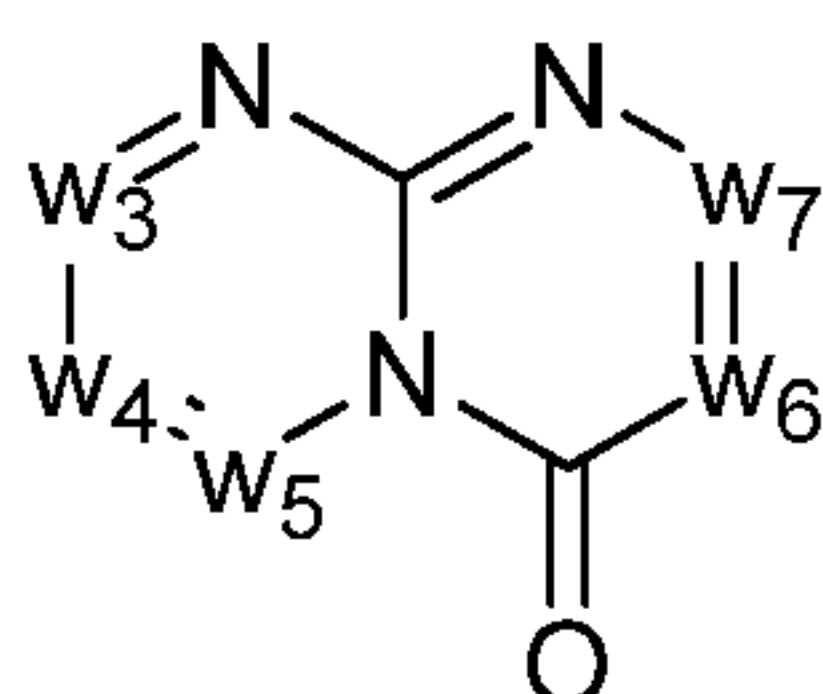
[00459] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (XI):



(XI)

[00460] or a form thereof.

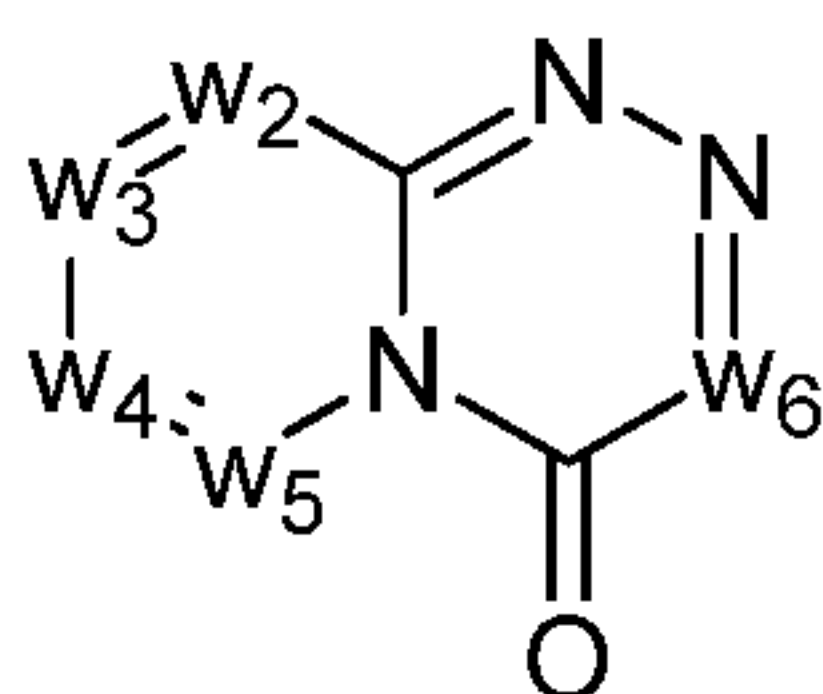
[00461] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (XII):



(XII)

[00462] or a form thereof.

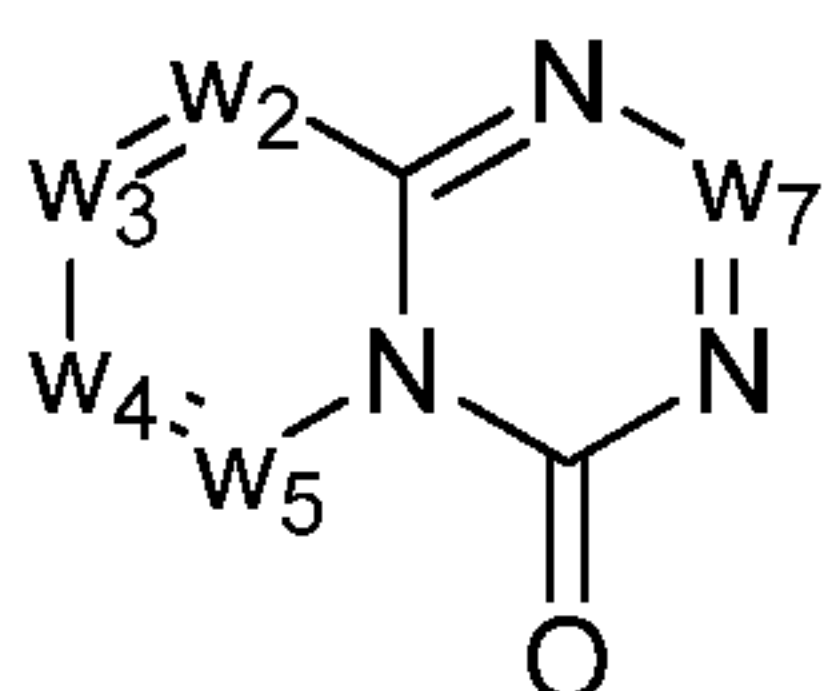
[00463] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (XIII):



(XIII)

[00464] or a form thereof.

[00465] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (XIV):

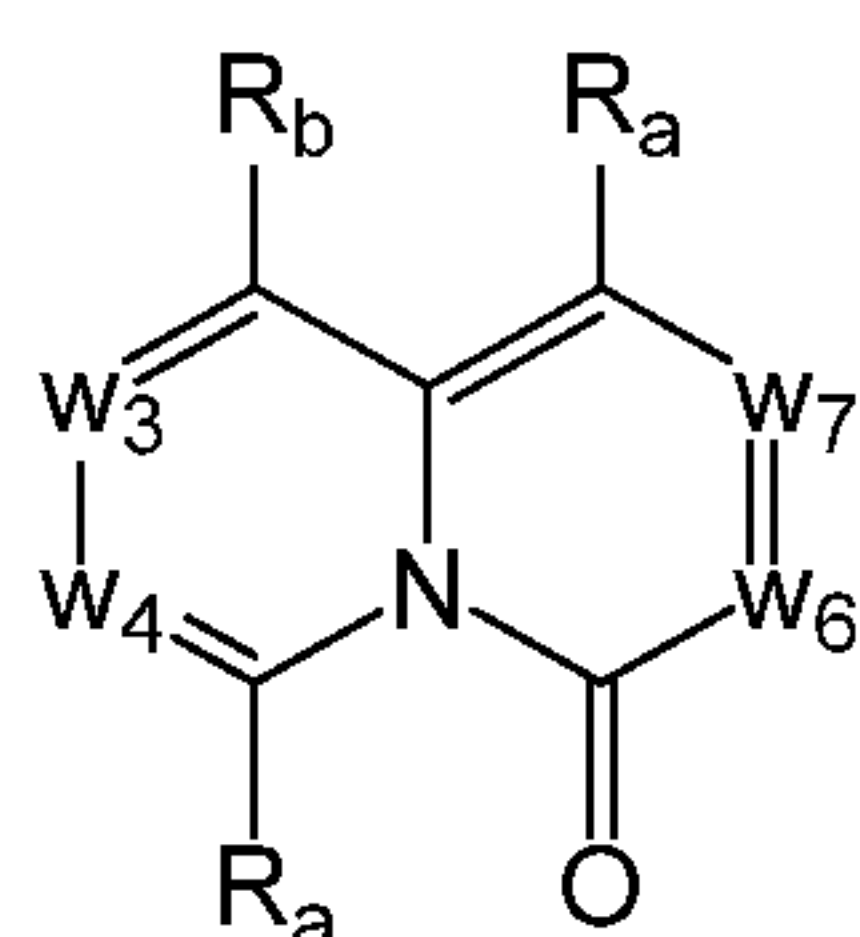


(XIV)

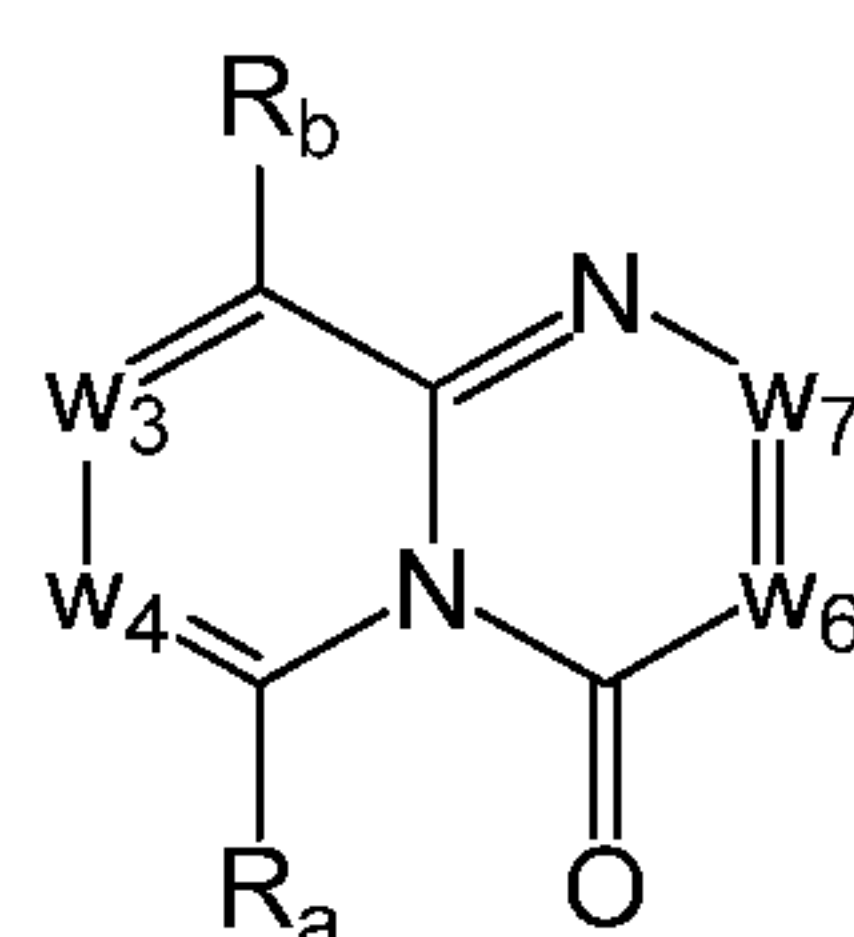
[00466] or a form thereof.

[00467] In one embodiment, the compound of Formula (I), Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII) or Formula (XIV) used in a method disclosed herein is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa),

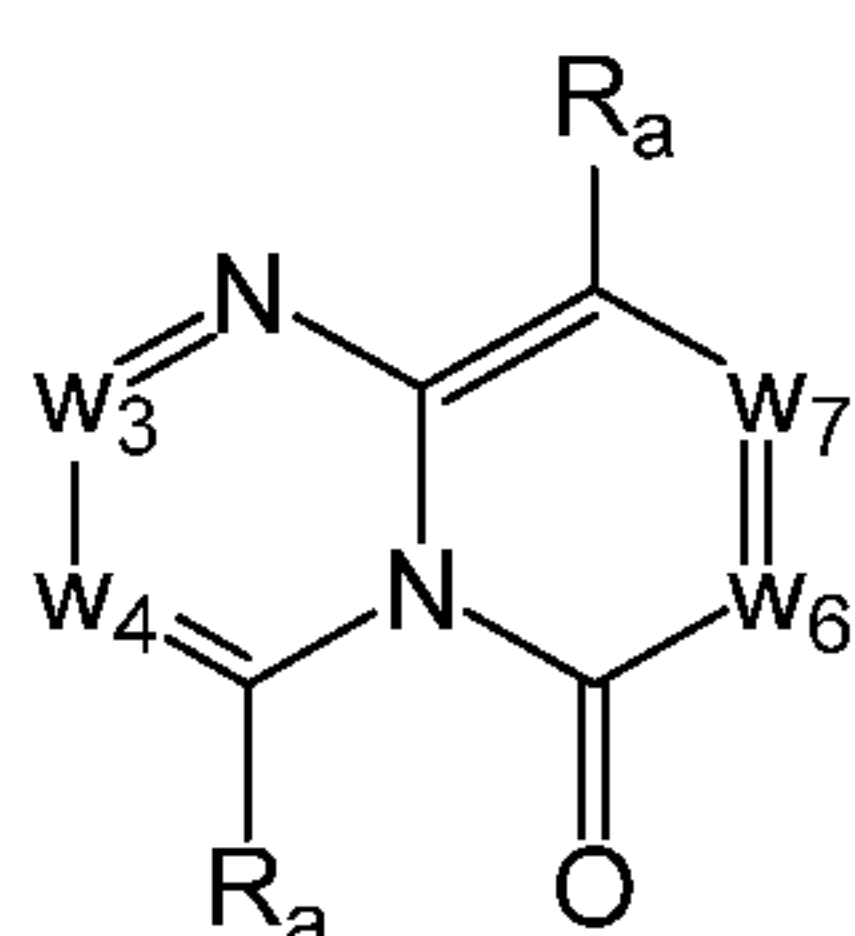
Formula (IVa), Formula (Va), Formula (VIa), Formula (VIIa), Formula (VIIIa), Formula (IXa), Formula (Xa), Formula (XIa), Formula (XIIa), Formula (XIIIa) or Formula (XIVa), respectively:



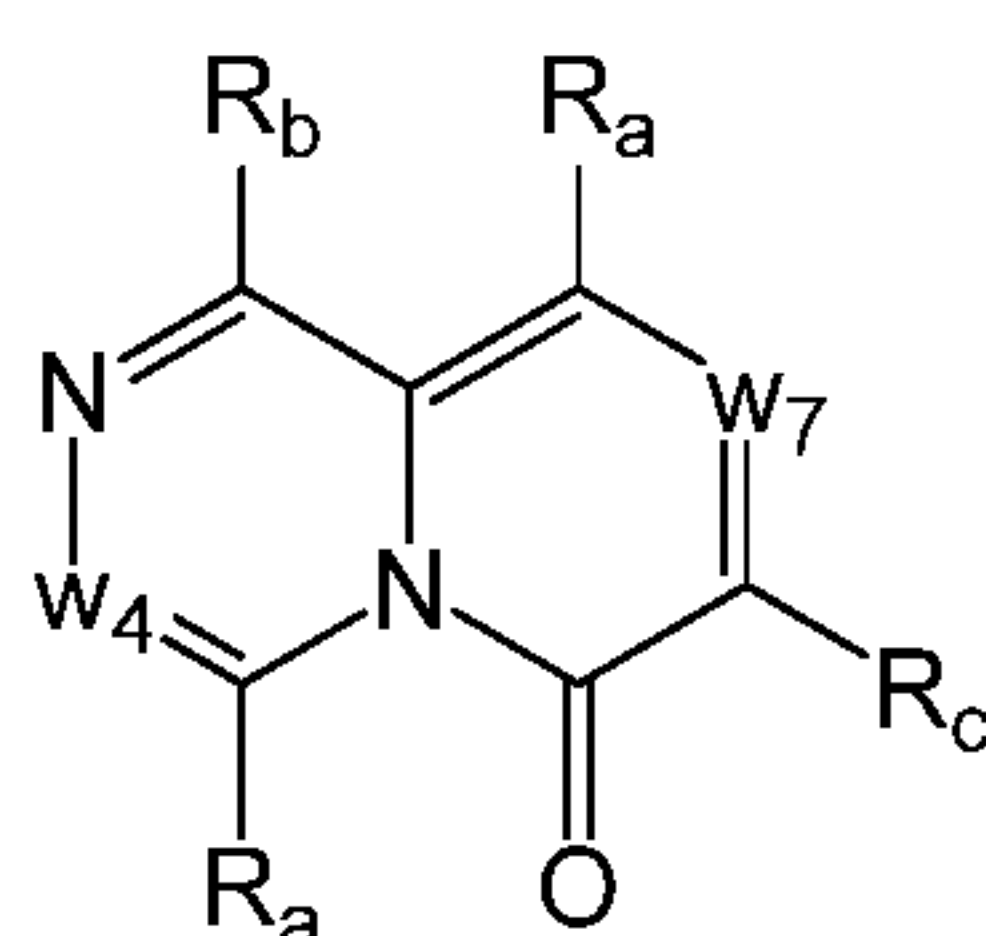
(Ia),



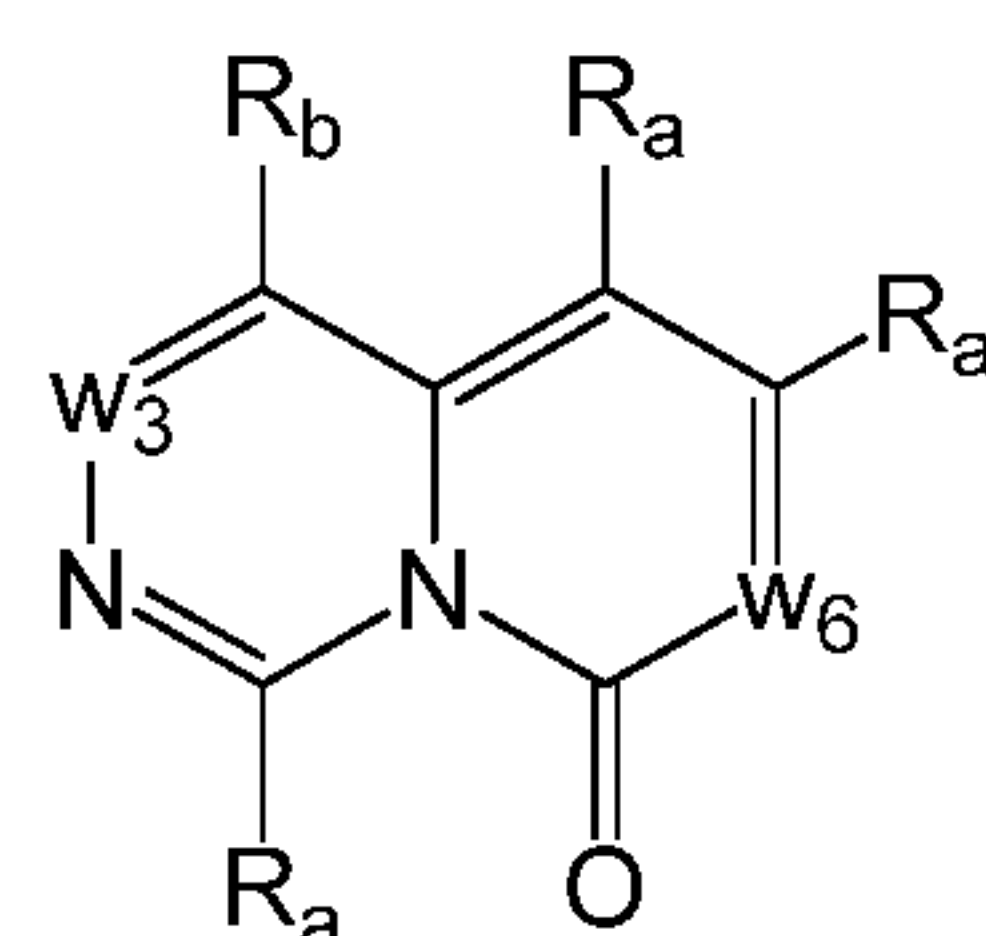
(IIa),



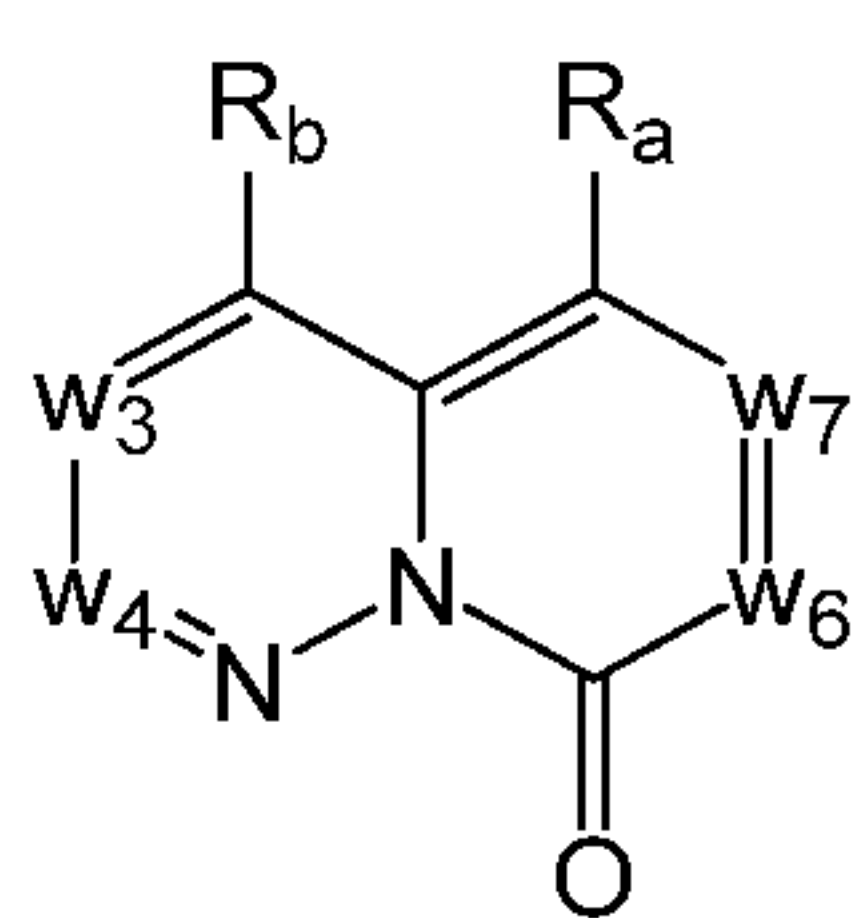
(IIIa),



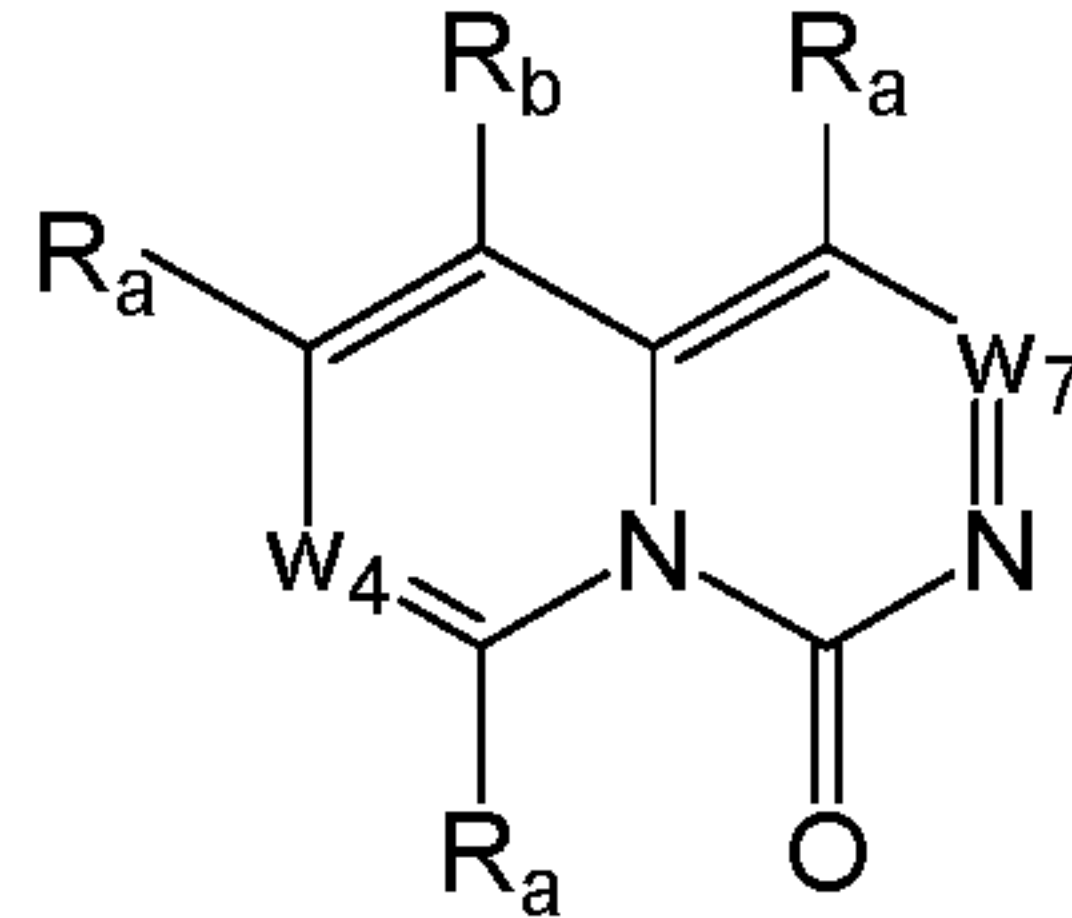
(IVa),



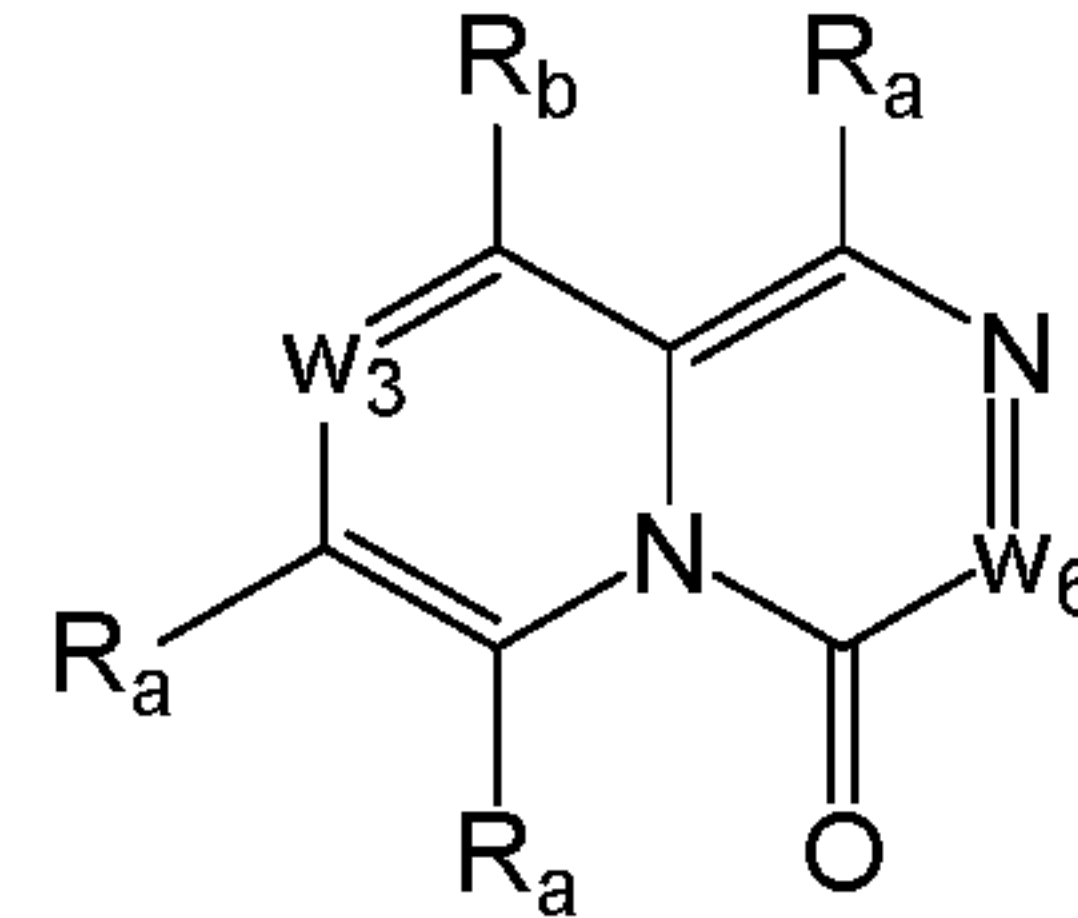
(Va),



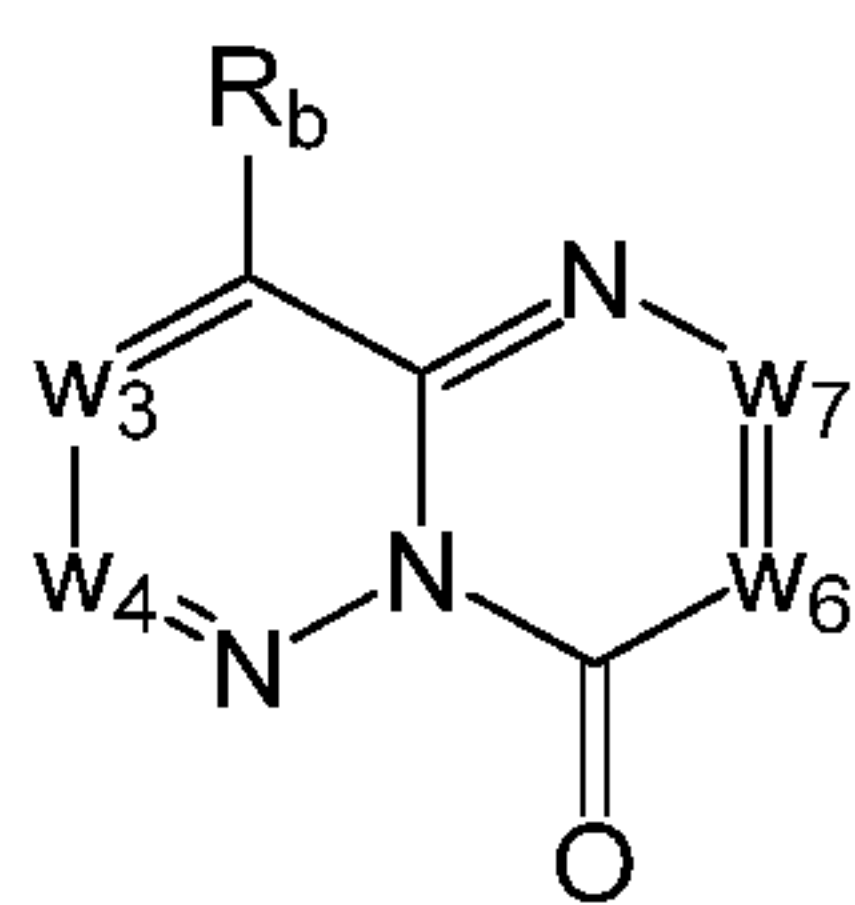
(VIa),



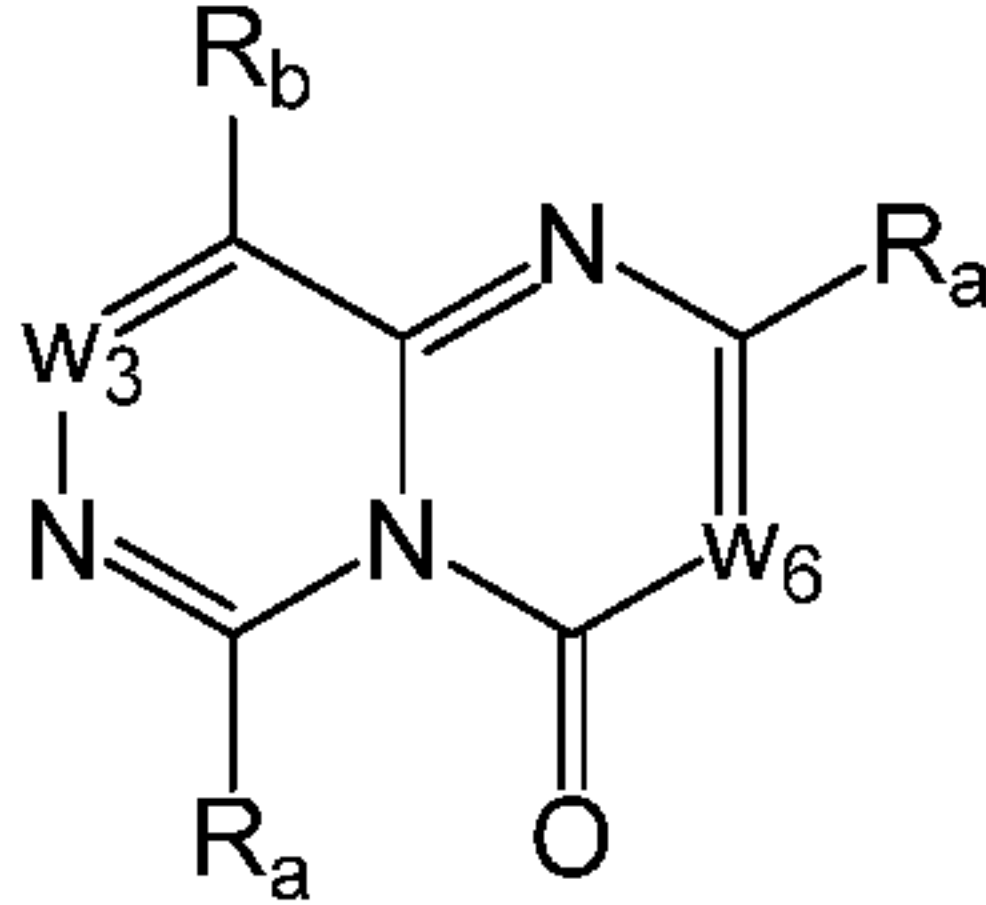
(VIIa),



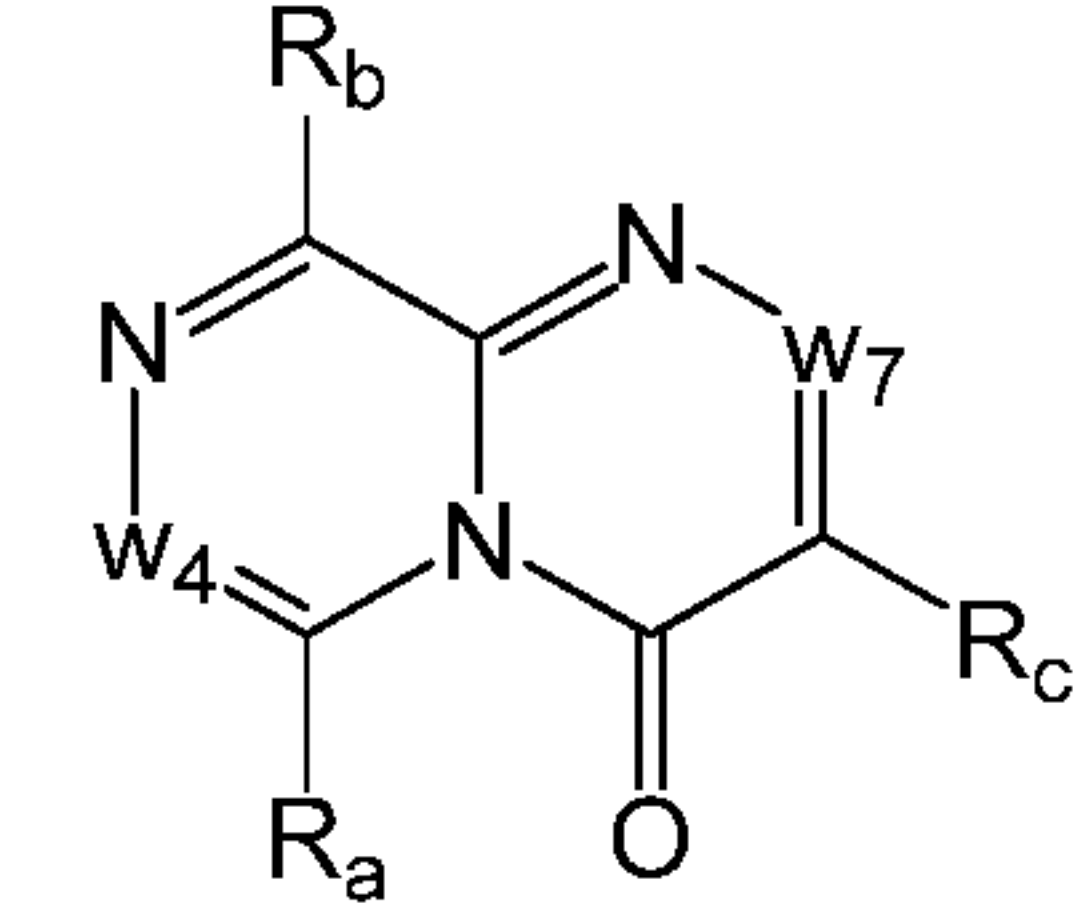
(VIIIa),



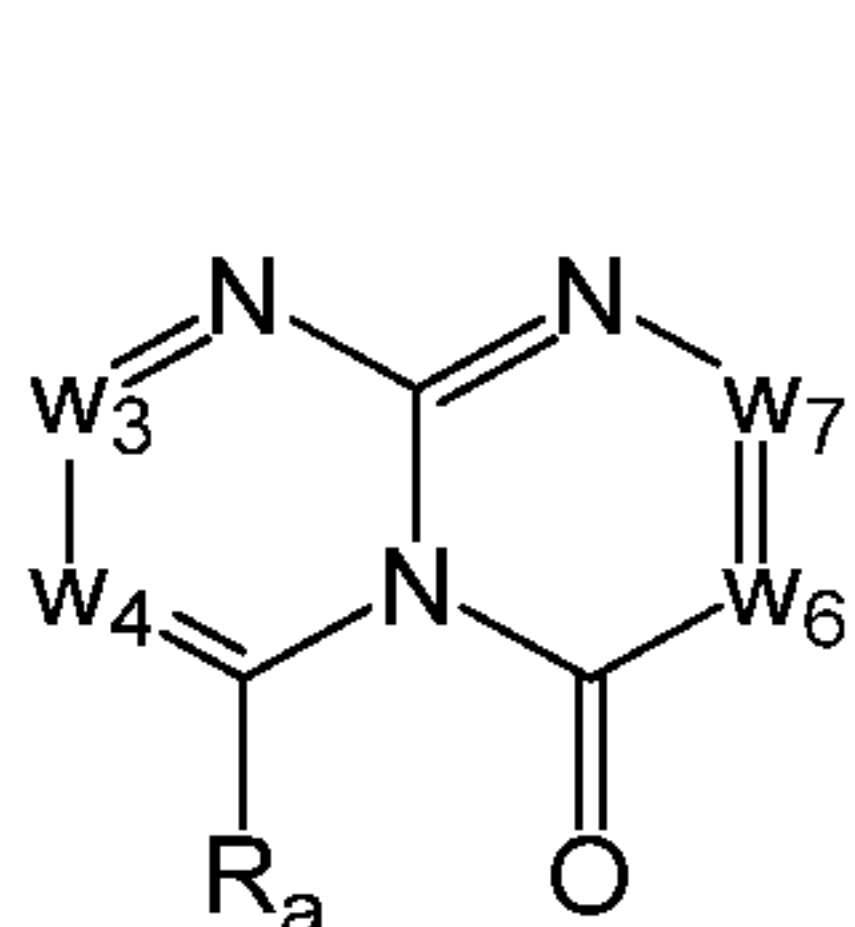
(IXa),



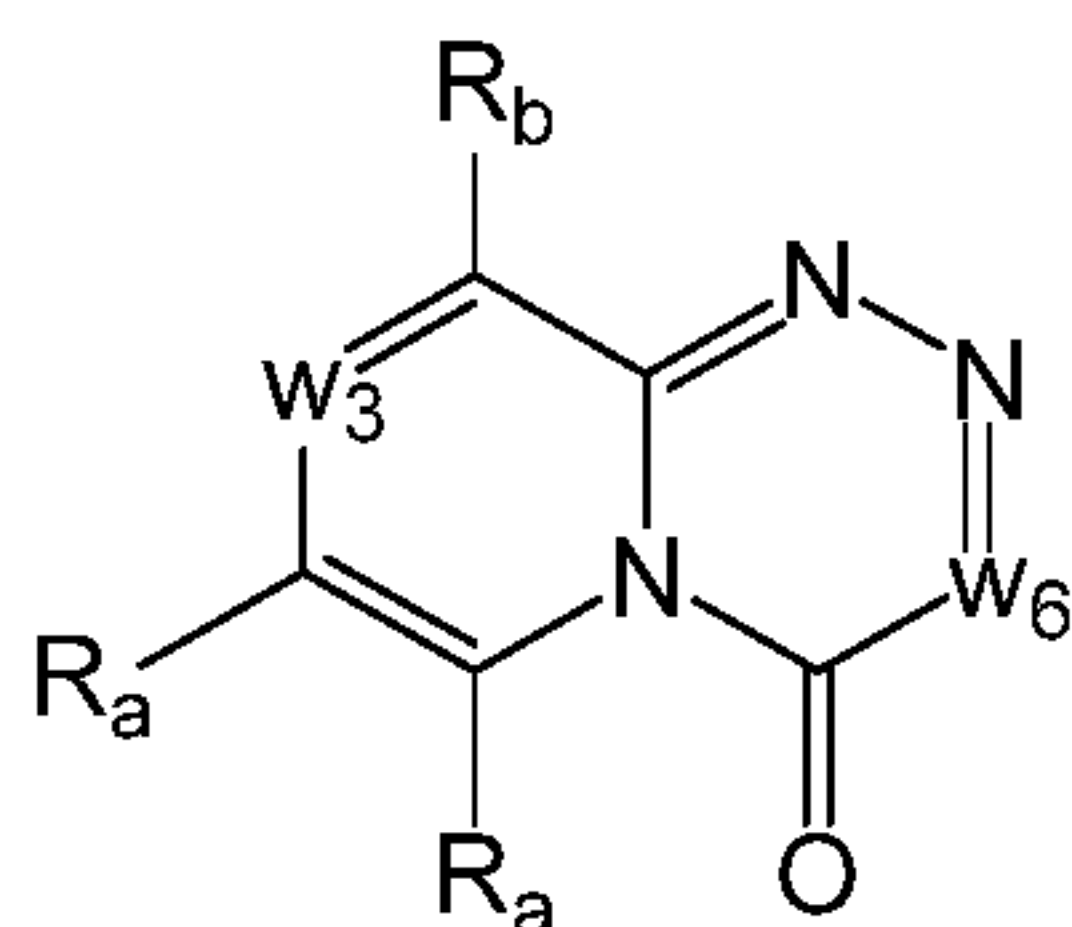
(Xa),



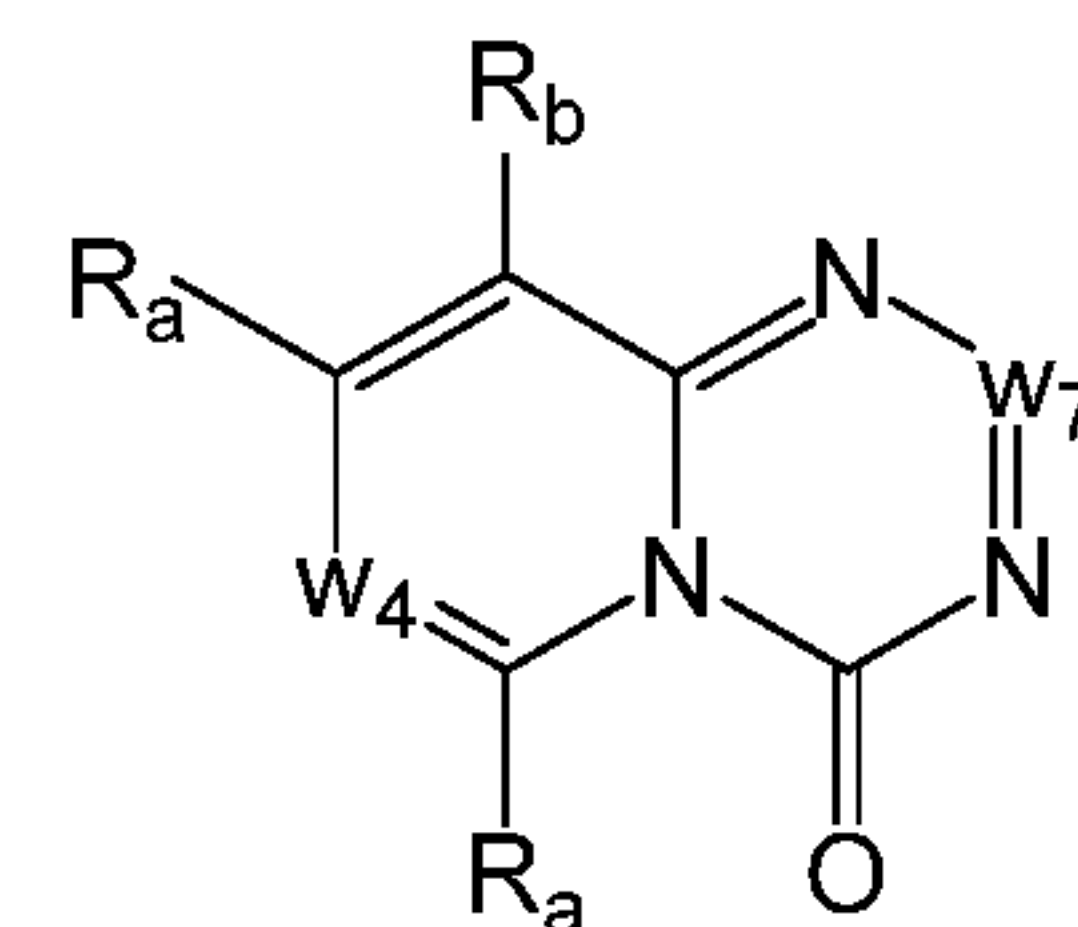
(XIa),



(XIIa),



(XIIIa), or



(XIVa)

[00468] or a form thereof.

[00469] In an embodiment of the use of the compound of Formula (Ia), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00470] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00471] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00472] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00473] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

[00474] In an embodiment of the use of the compound of Formula (IIa), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00475] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00476] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00477] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00478] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

[00479] In an embodiment of the use of the compound of Formula (IIIa), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00480] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00481] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00482] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00483] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

[00484] In an embodiment of the use of the compound of Formula (IVa), one of w₄ and w₇ is C-R₁ and the other is C-R₂, provided that, when w₄ is C-R₁, then w₇ is C-R₂; or, when w₄ is C-R₂, then w₇ is C-R₁.

[00485] In an embodiment of the use of the compound of Formula (Va), one of w₃ and w₆ is C-R₁ and the other is C-R₂, provided that, when w₃ is C-R₁, then w₆ is C-R₂; or, when w₃ is C-R₂, then w₆ is C-R₁.

[00486] In an embodiment of the use of the compound of Formula (VIa), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00487] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00488] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00489] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00490] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

[00491] In an embodiment of the use of the compound of Formula (VIIa), one of w₄ and w₇ is C-R₁ and the other is C-R₂, provided that, when w₄ is C-R₁, then w₇ is C-R₂; or, when w₄ is C-R₂, then w₇ is C-R₁.

[00492] In an embodiment of the use of the compound of Formula (VIIIa), one of w₃ and w₆ is C-R₁ and the other is C-R₂, provided that, when w₃ is C-R₁, then w₆ is C-R₂; or, when w₃ is C-R₂, then w₆ is C-R₁.

[00493] In an embodiment of the use of the compound of Formula (IXa), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00494] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00495] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

[00496] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00497] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

[00498] In an embodiment of the use of the compound of Formula (Xa), one of w₃ and w₆ is C-R₁ and the other is C-R₂, provided that, when w₃ is C-R₁, then w₆ is C-R₂; or, when w₃ is C-R₂, then w₆ is C-R₁.

[00499] In an embodiment of the use of the compound of Formula (XIa), one of w₄ and w₇ is C-R₁ and the other is C-R₂, provided that, when w₄ is C-R₁, then w₇ is C-R₂; or, when w₄ is C-R₂, then w₇ is C-R₁.

[00500] In an embodiment of the use of the compound of Formula (XIIa), one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

[00501] when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

[00502] when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

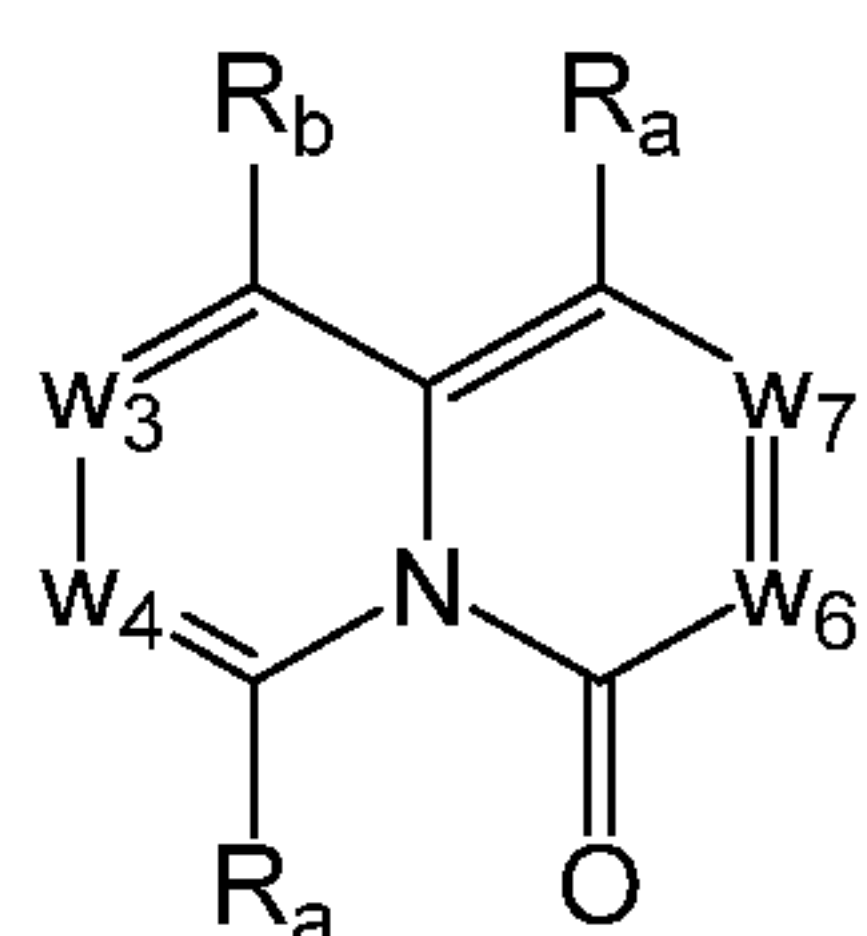
[00503] when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

[00504] when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N.

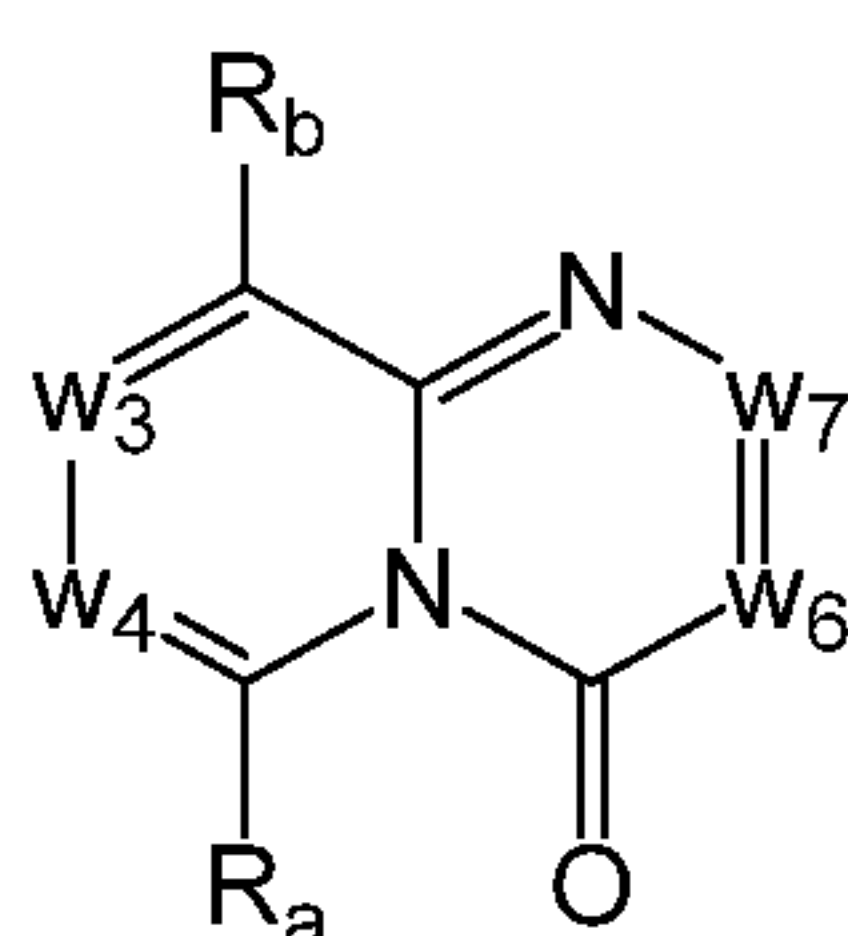
[00505] In an embodiment of the use of the compound of Formula (XIIIa), one of w₃ and w₆ is C-R₁ and the other is C-R₂, provided that, when w₃ is C-R₁, then w₆ is C-R₂; or, when w₃ is C-R₂, then w₆ is C-R₁.

[00506] In an embodiment of the use of the compound of Formula (XIVa), one of w₄ and w₇ is C-R₁ and the other is C-R₂, provided that, when w₄ is C-R₁, then w₇ is C-R₂; or, when w₄ is C-R₂, then w₇ is C-R₁.

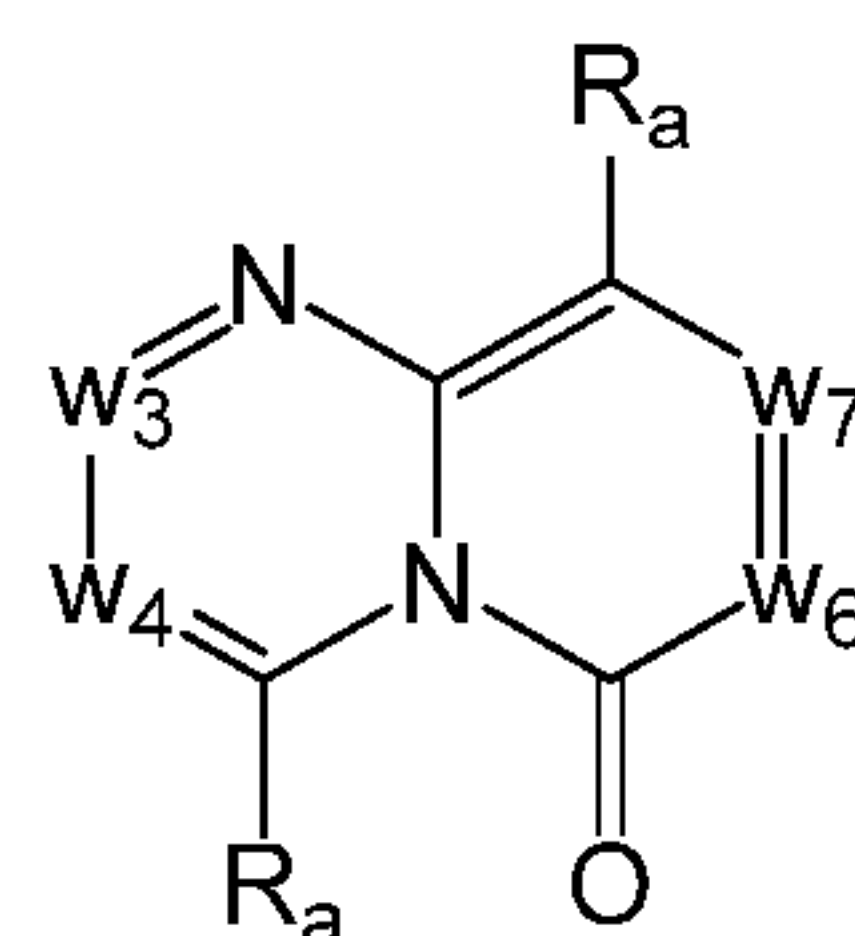
[00507] In another embodiment, the compound of Formula (I), Formula (II), Formula (III), Formula (IX), Formula (XI) or Formula (XII), used in a method disclosed herein, is a compound selected from Formula (Ia), Formula (IIa), Formula (IIIa), Formula (IXa), Formula (XIa) or Formula (XIIa), respectively:



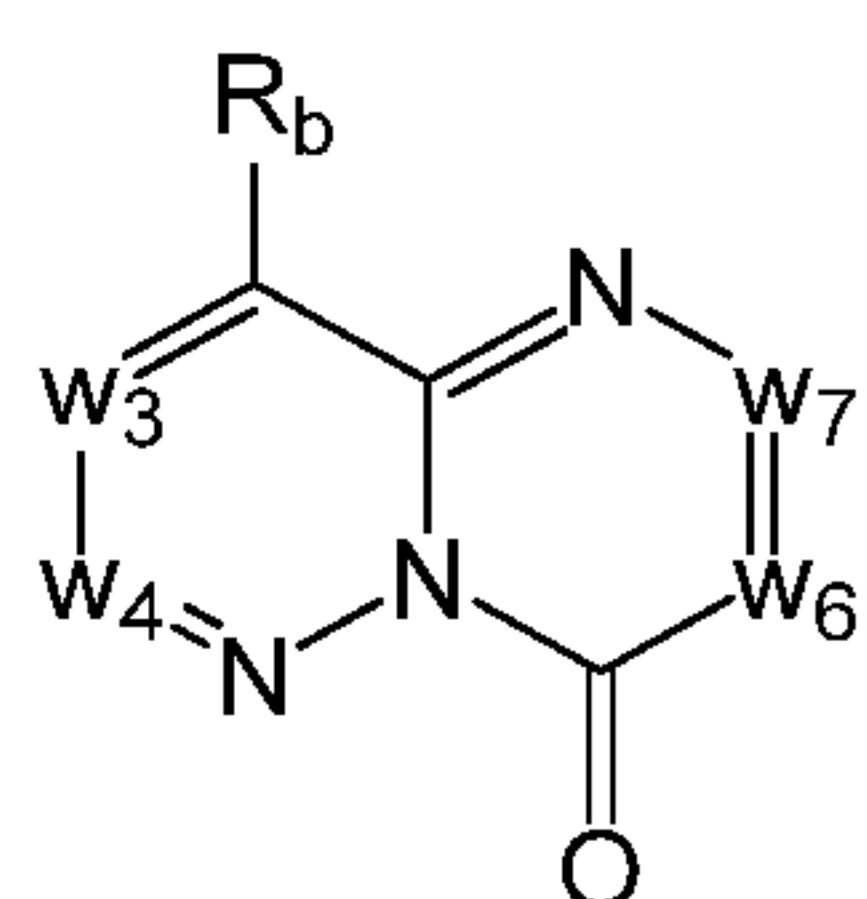
(Ia),



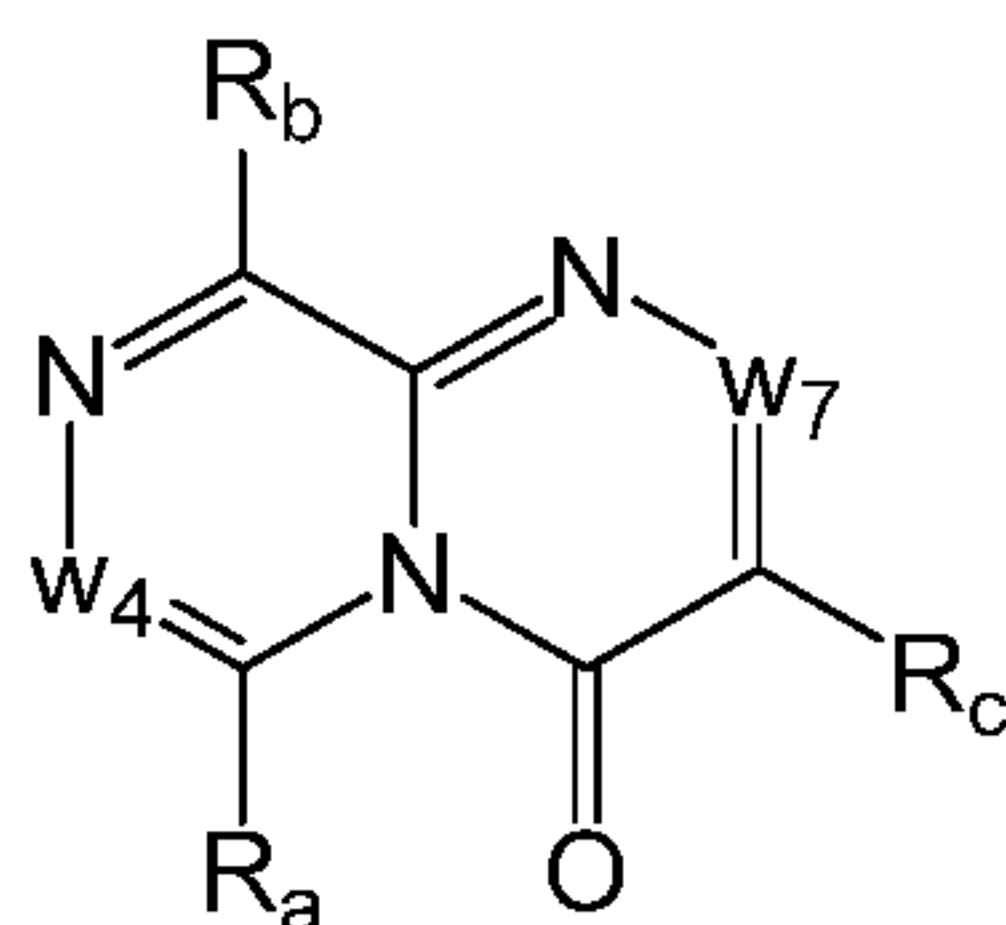
(IIa),



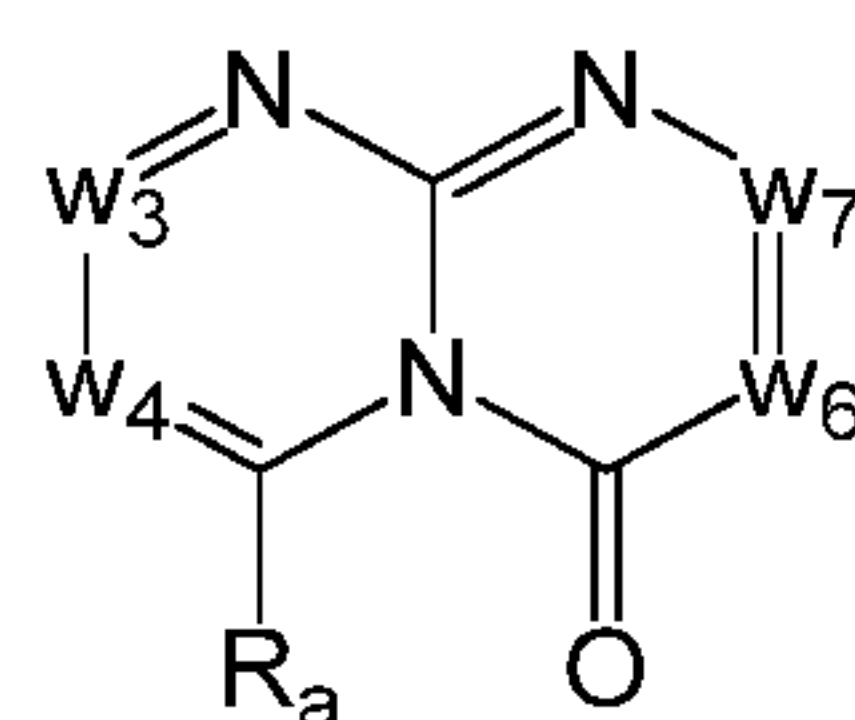
(IIIa),



(IXa),



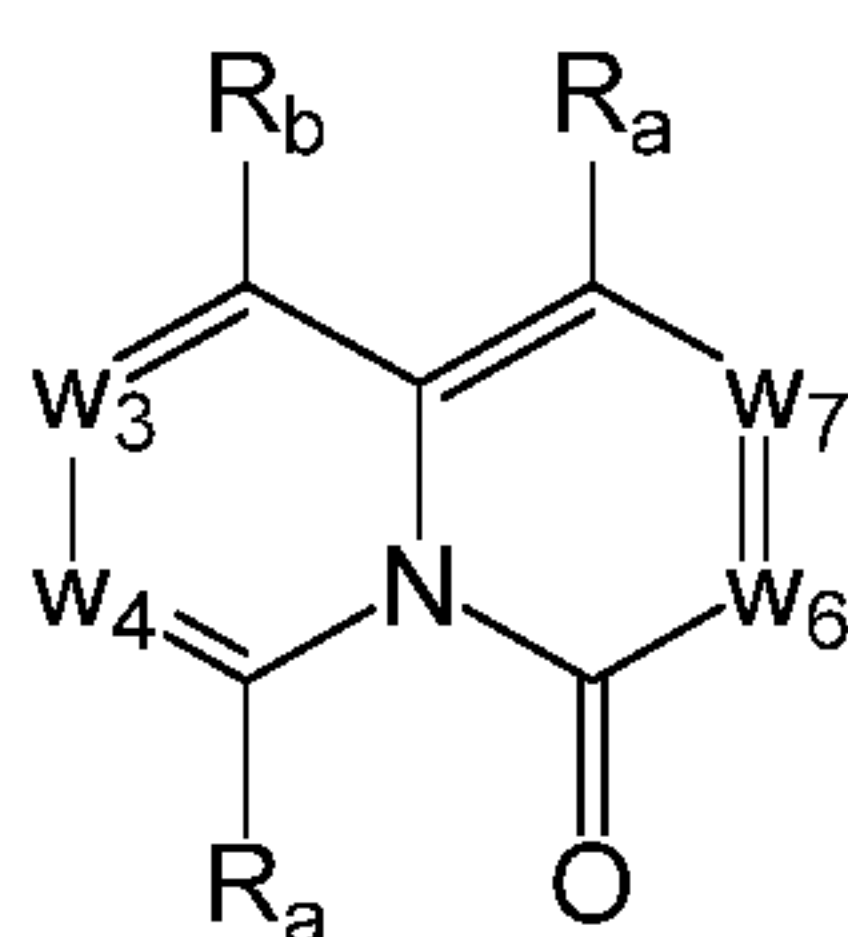
(XIa), or



(XIIa)

[00508] or a form thereof.

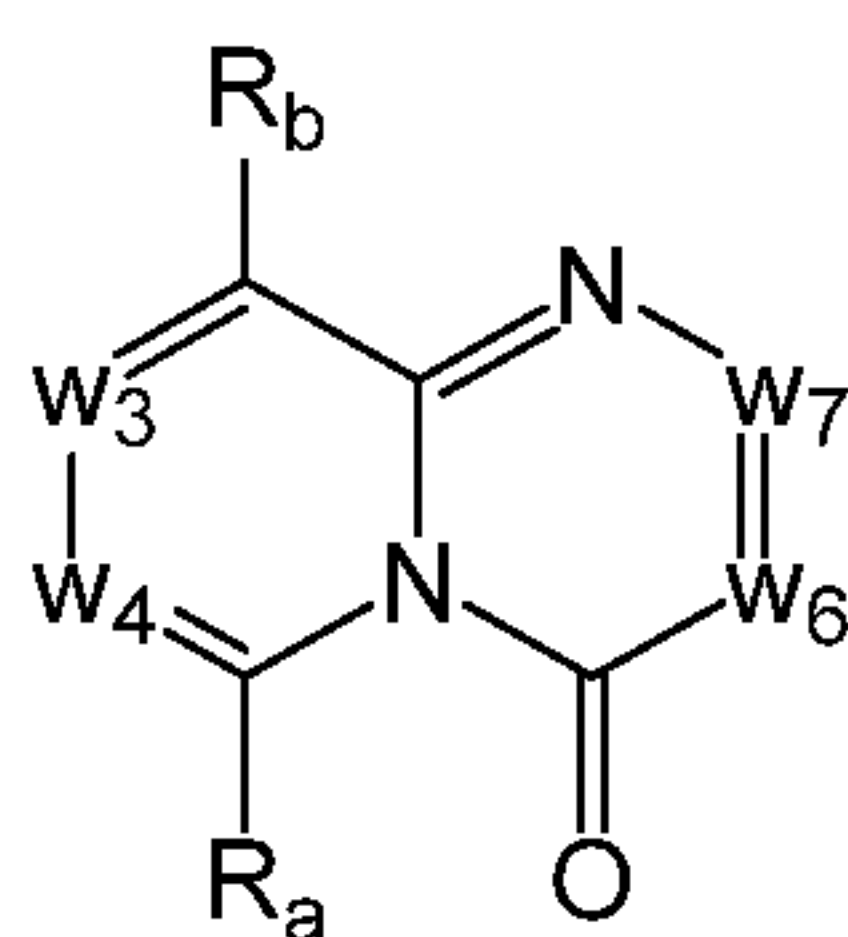
[00509] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound of Formula (Ia):



(Ia)

[00510] or a form thereof.

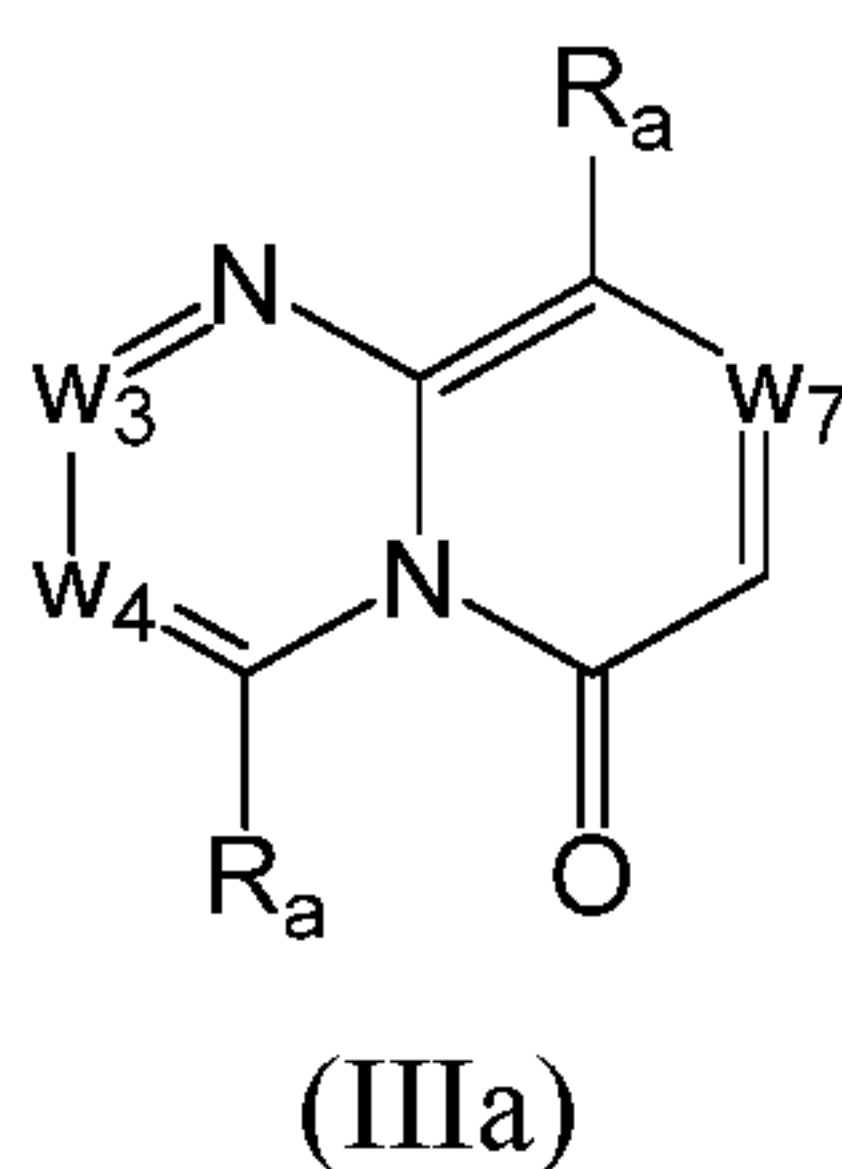
[00511] In another embodiment, the compound of Formula (II) used in a method disclosed herein is a compound of Formula (IIa):



(IIa)

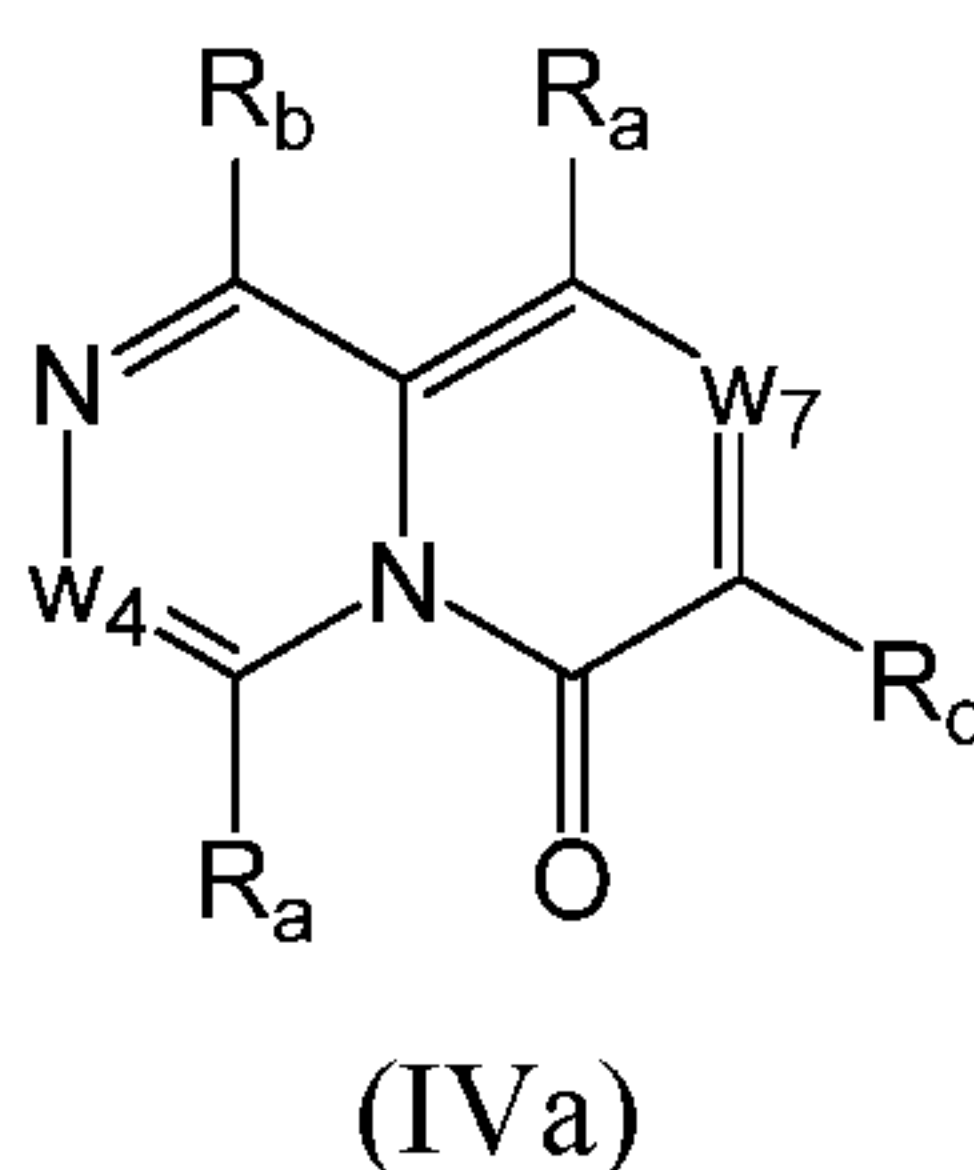
[00512] or a form thereof.

[00513] In another embodiment, the compound of Formula (III) used in a method disclosed herein is a compound of Formula (IIIa):



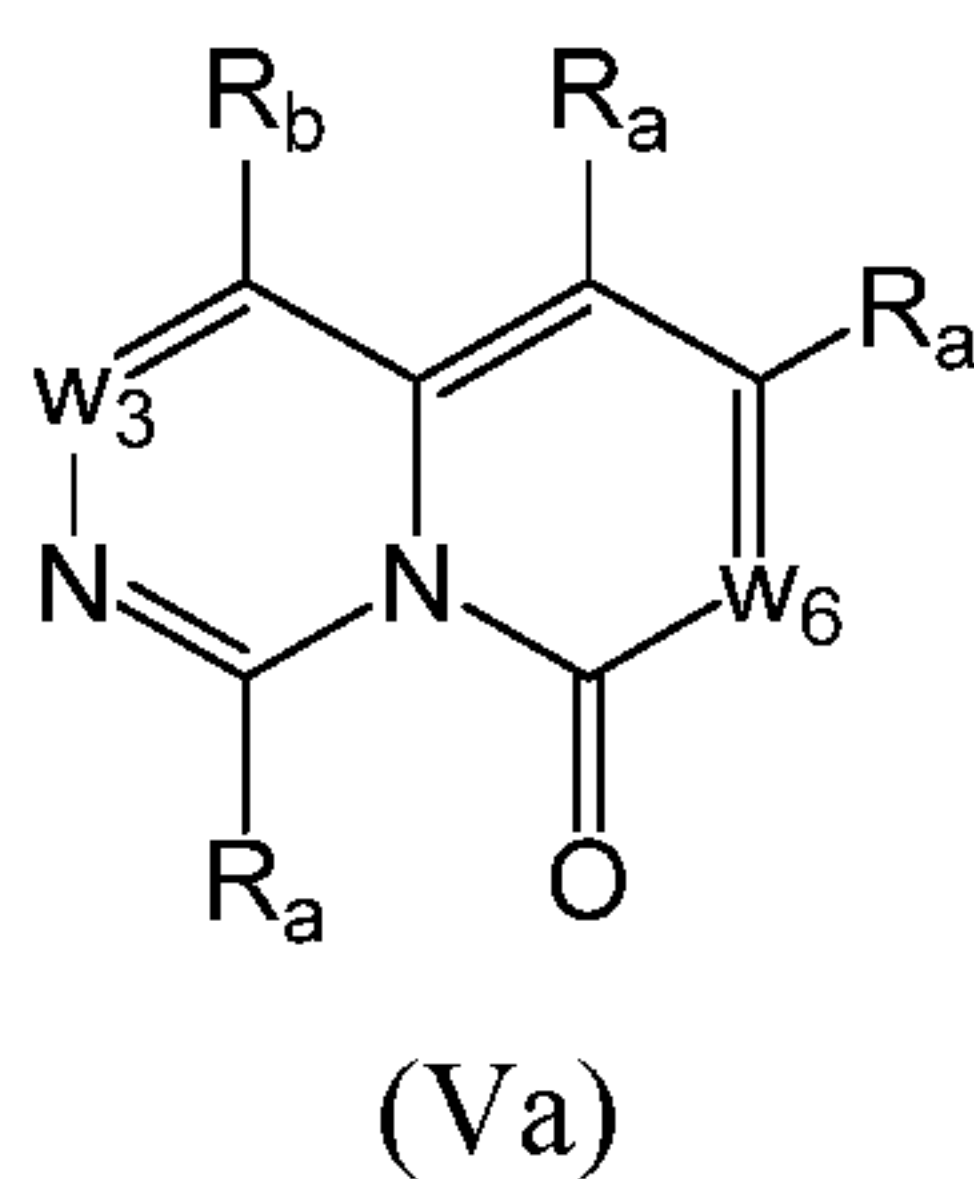
[00514] or a form thereof.

[00515] In another embodiment, the compound of Formula (IV) used in a method disclosed herein is a compound of Formula (IVa):



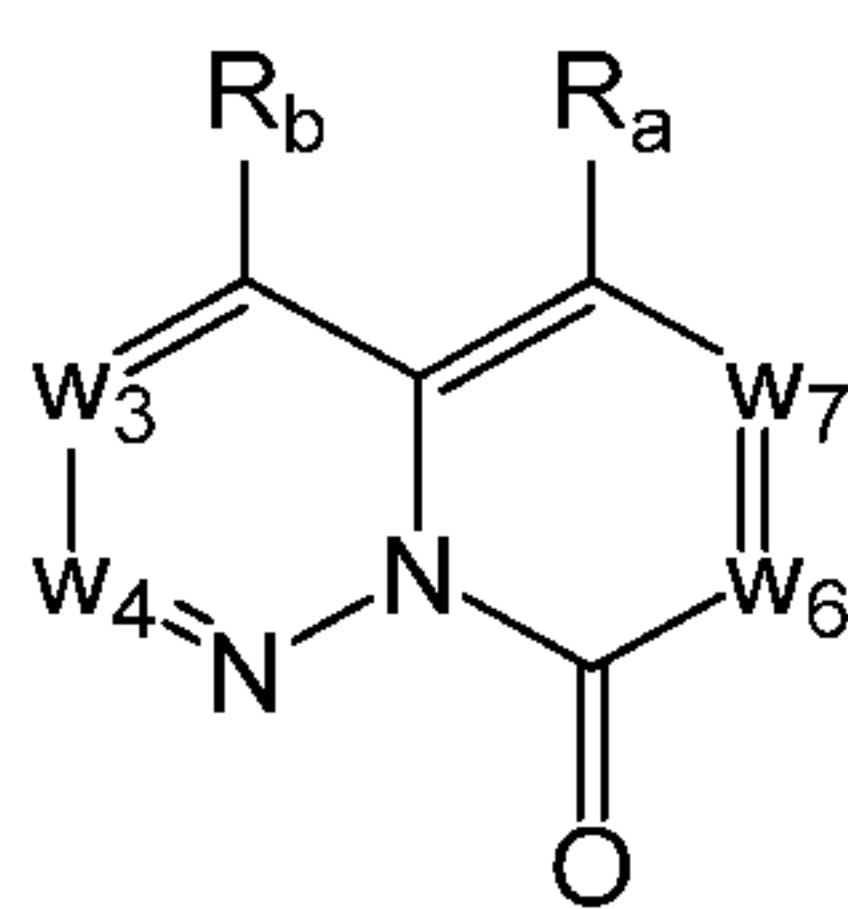
[00516] or a form thereof.

[00517] In another embodiment, the compound of Formula (V) used in a method disclosed herein is a compound of Formula (Va):



[00518] or a form thereof.

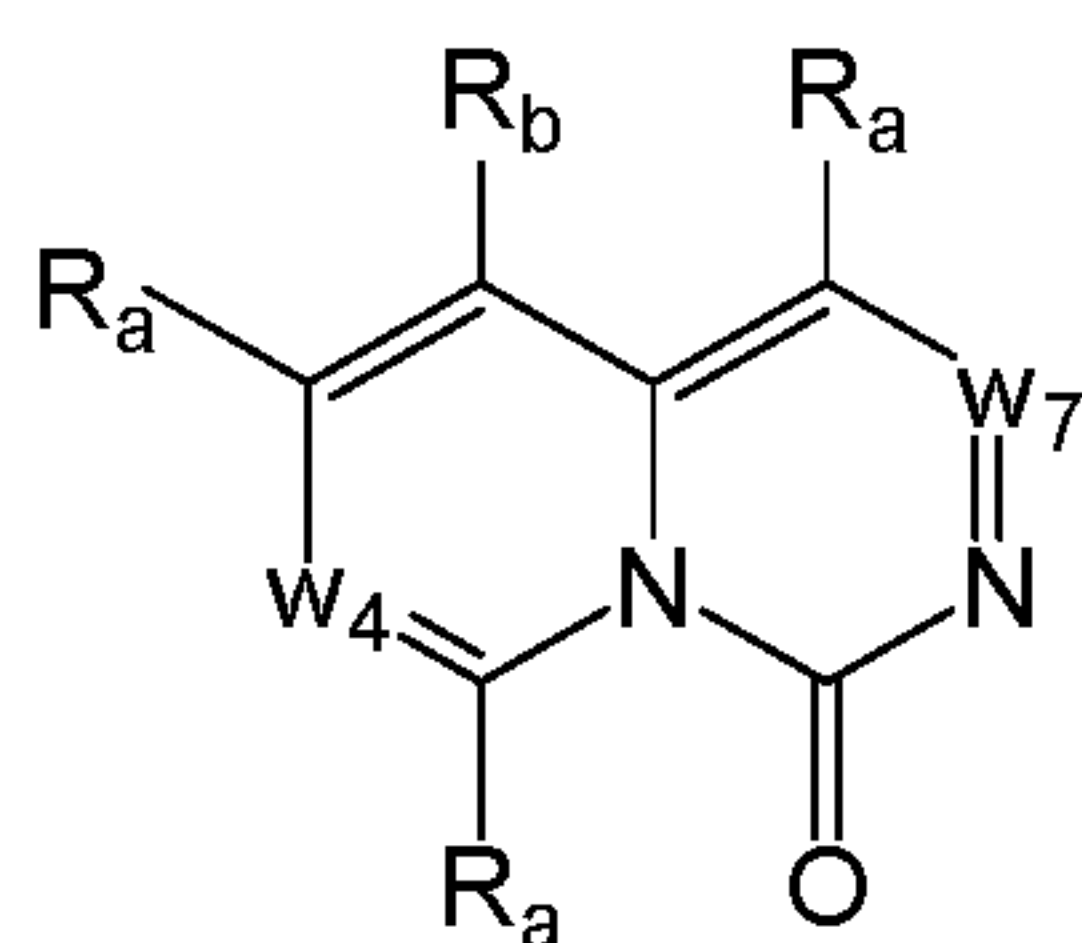
[00519] In another embodiment, the compound of Formula (VI) used in a method disclosed herein is a compound of Formula (VIa):



(VIa)

[00520] or a form thereof.

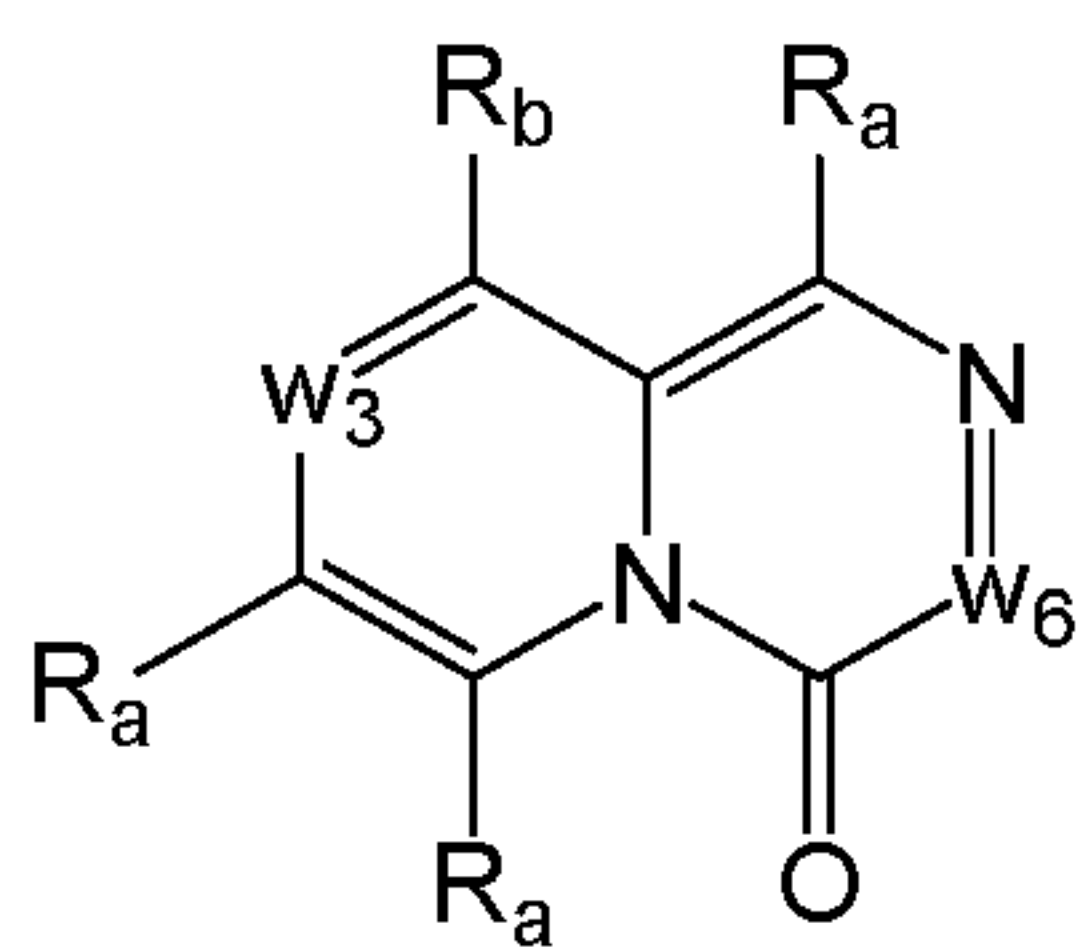
[00521] In another embodiment, the compound of Formula (VII) used in a method disclosed herein is a compound of Formula (VIIa):



(VIIa)

[00522] or a form thereof.

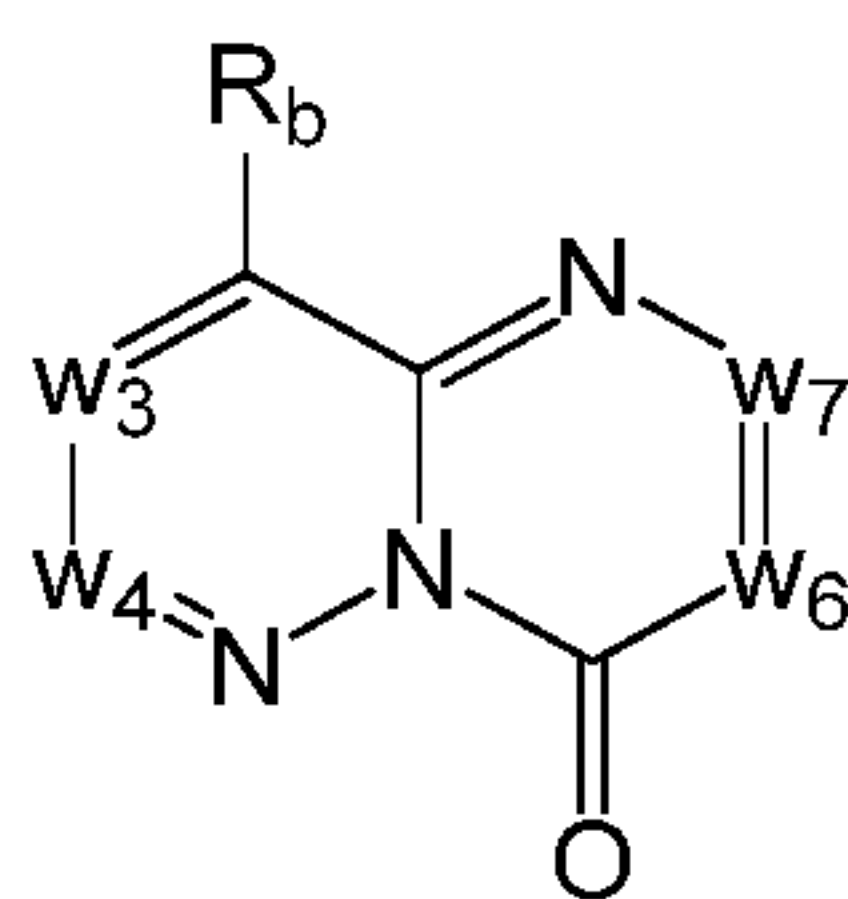
[00523] In another embodiment, the compound of Formula (VIII) used in a method disclosed herein is a compound of Formula (VIIIa):



(VIIIa)

[00524] or a form thereof.

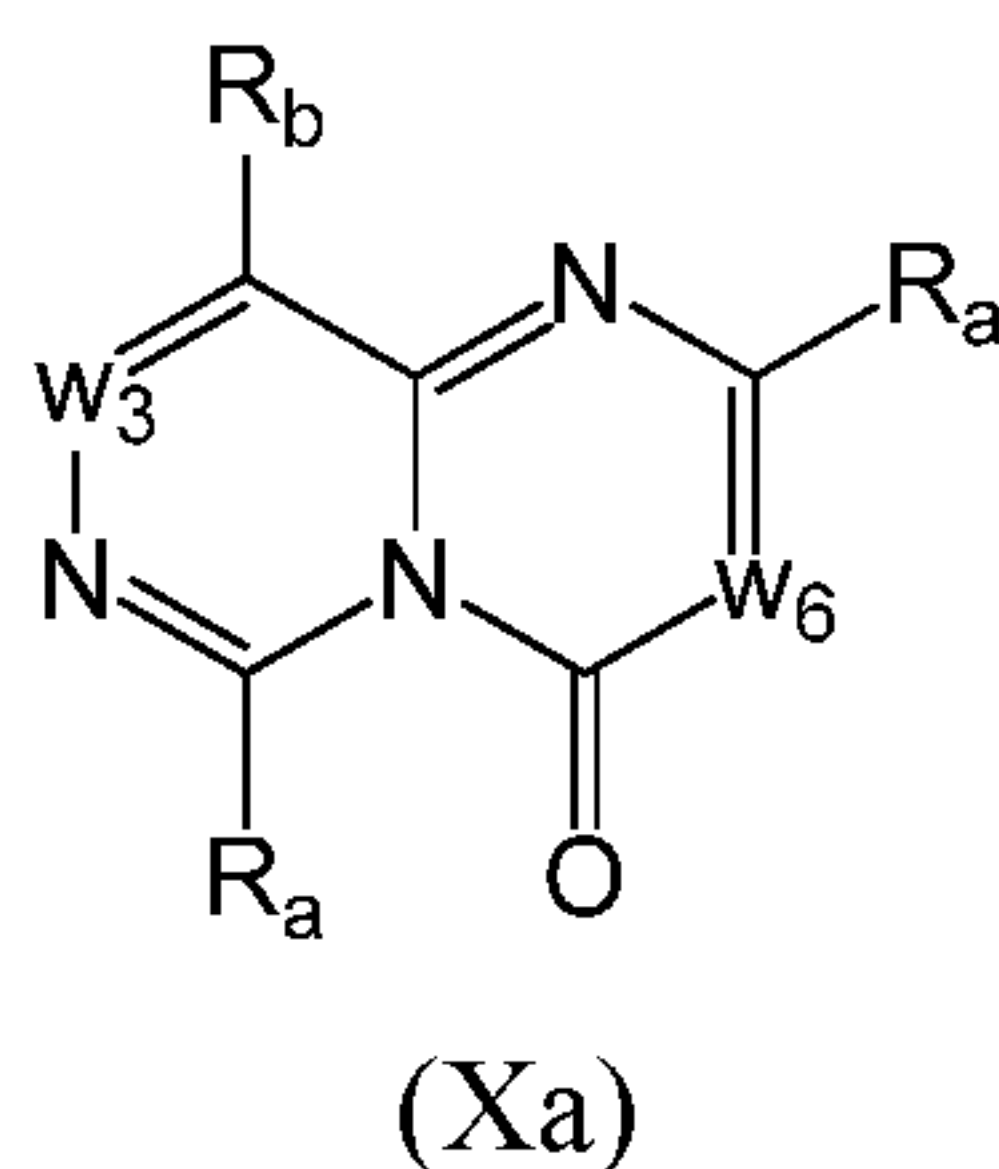
[00525] In another embodiment, the compound of Formula (IX) used in a method disclosed herein is a compound of Formula (IXa):



(IXa)

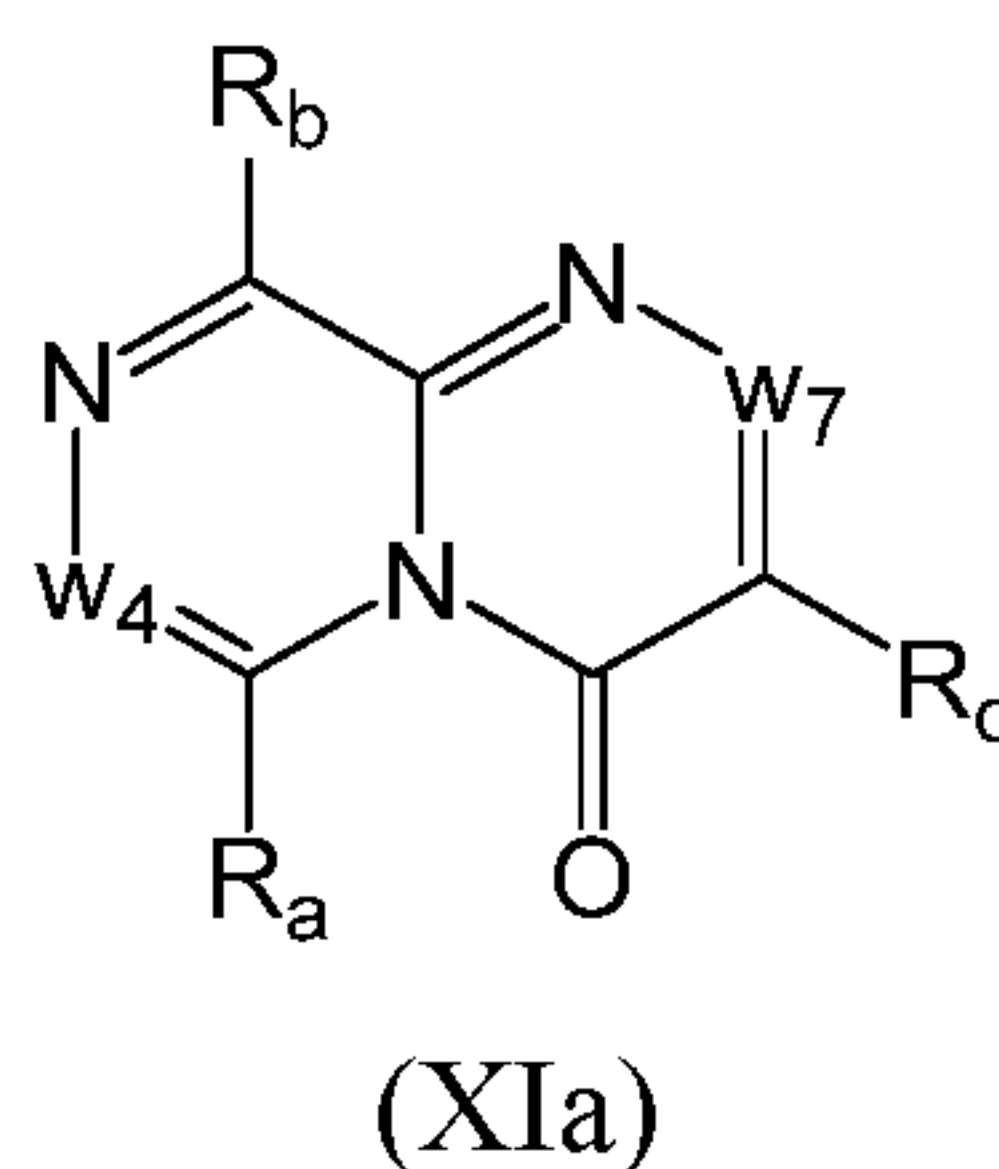
[00526] or a form thereof.

[00527] In another embodiment, the compound of Formula (X) used in a method disclosed herein is a compound of Formula (Xa):



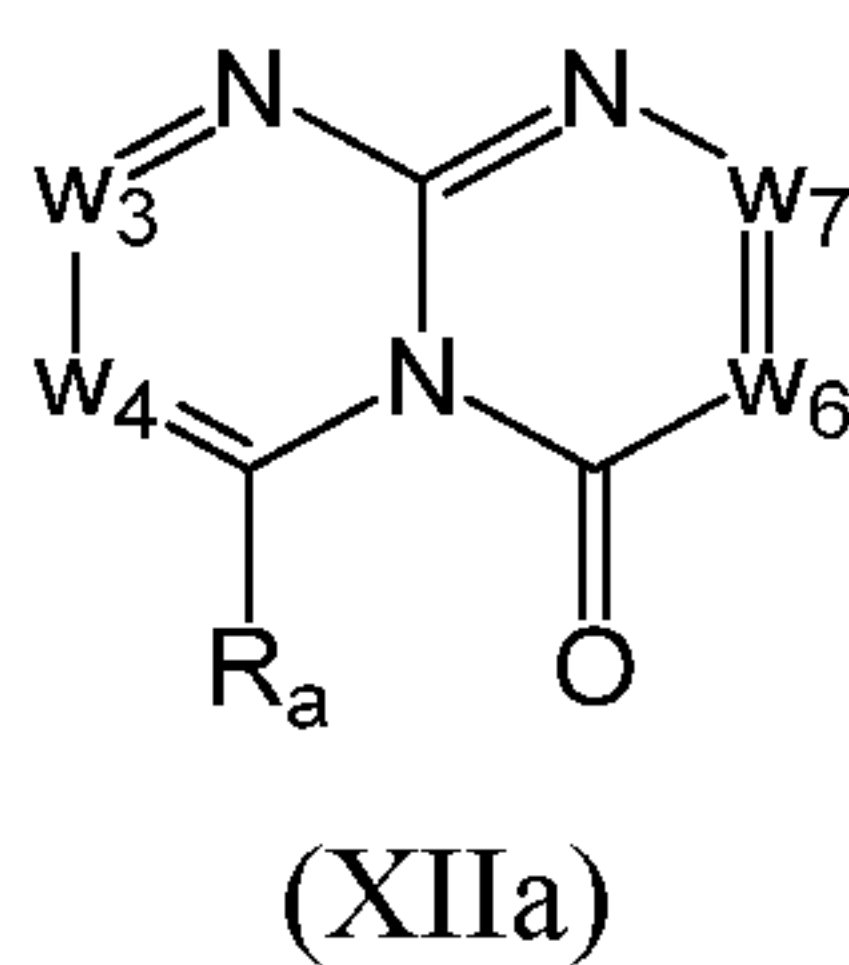
[00528] or a form thereof.

[00529] In another embodiment, the compound of Formula (XI) used in a method disclosed herein is a compound of Formula (XIa):



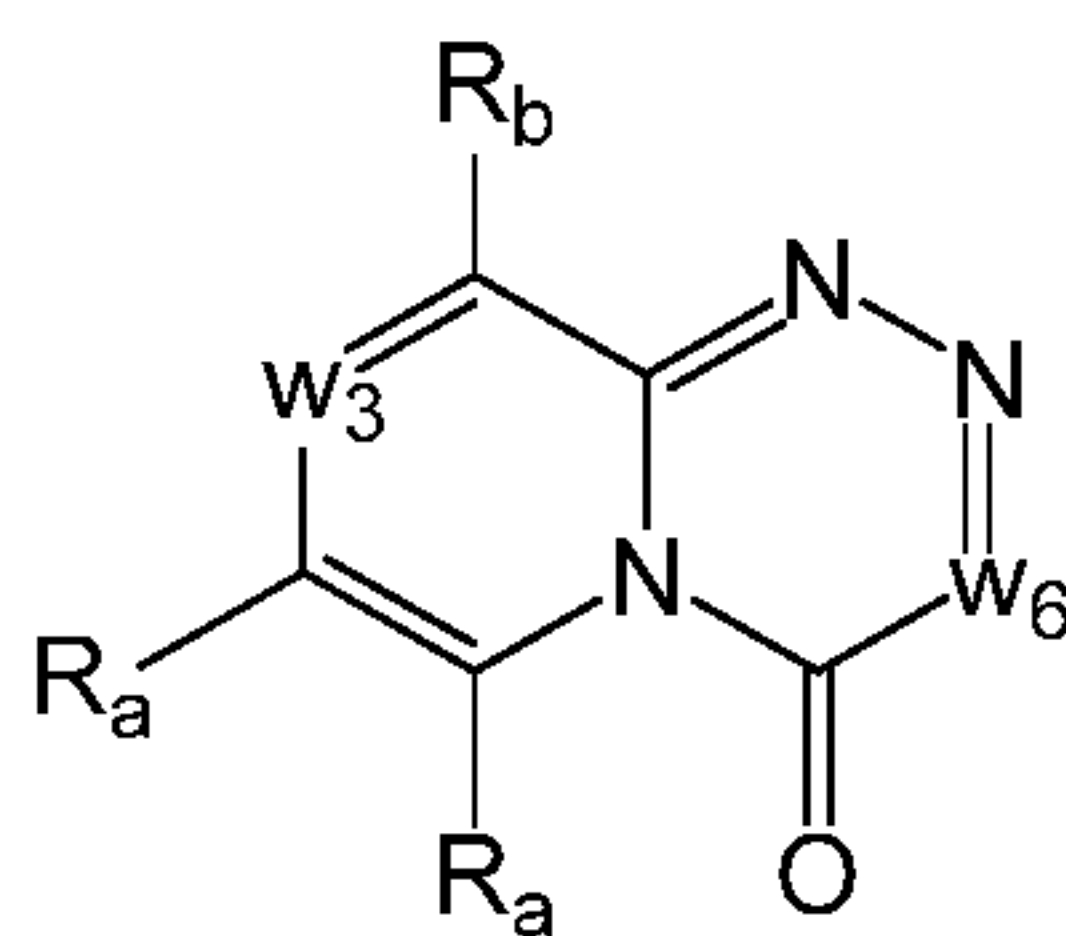
[00530] or a form thereof.

[00531] In another embodiment, the compound of Formula (XII) used in a method disclosed herein is a compound of Formula (XIIa):



[00532] or a form thereof.

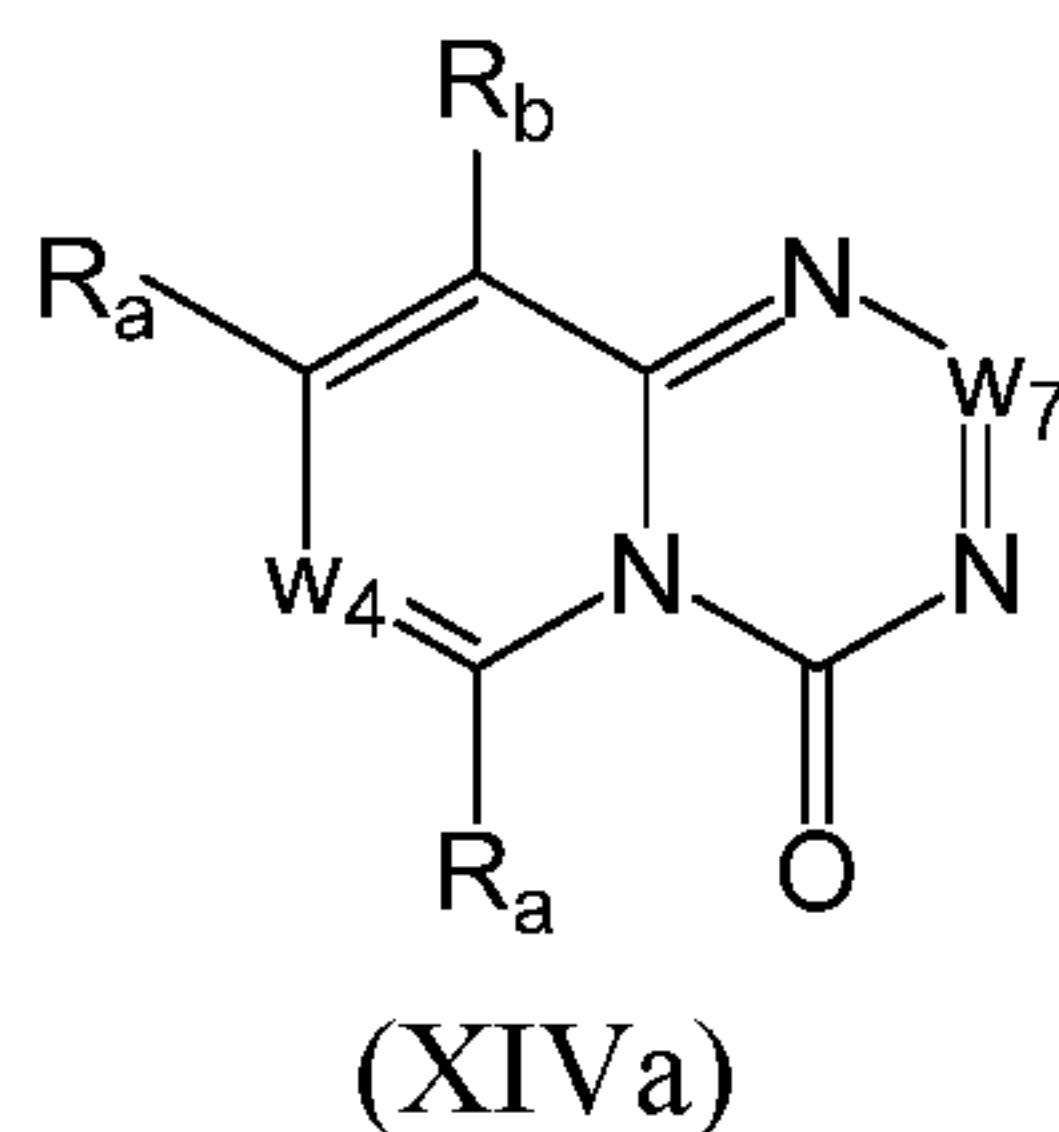
[00533] In another embodiment, the compound of Formula (XIII) used in a method disclosed herein is a compound of Formula (XIIIa):



(XIIIa)

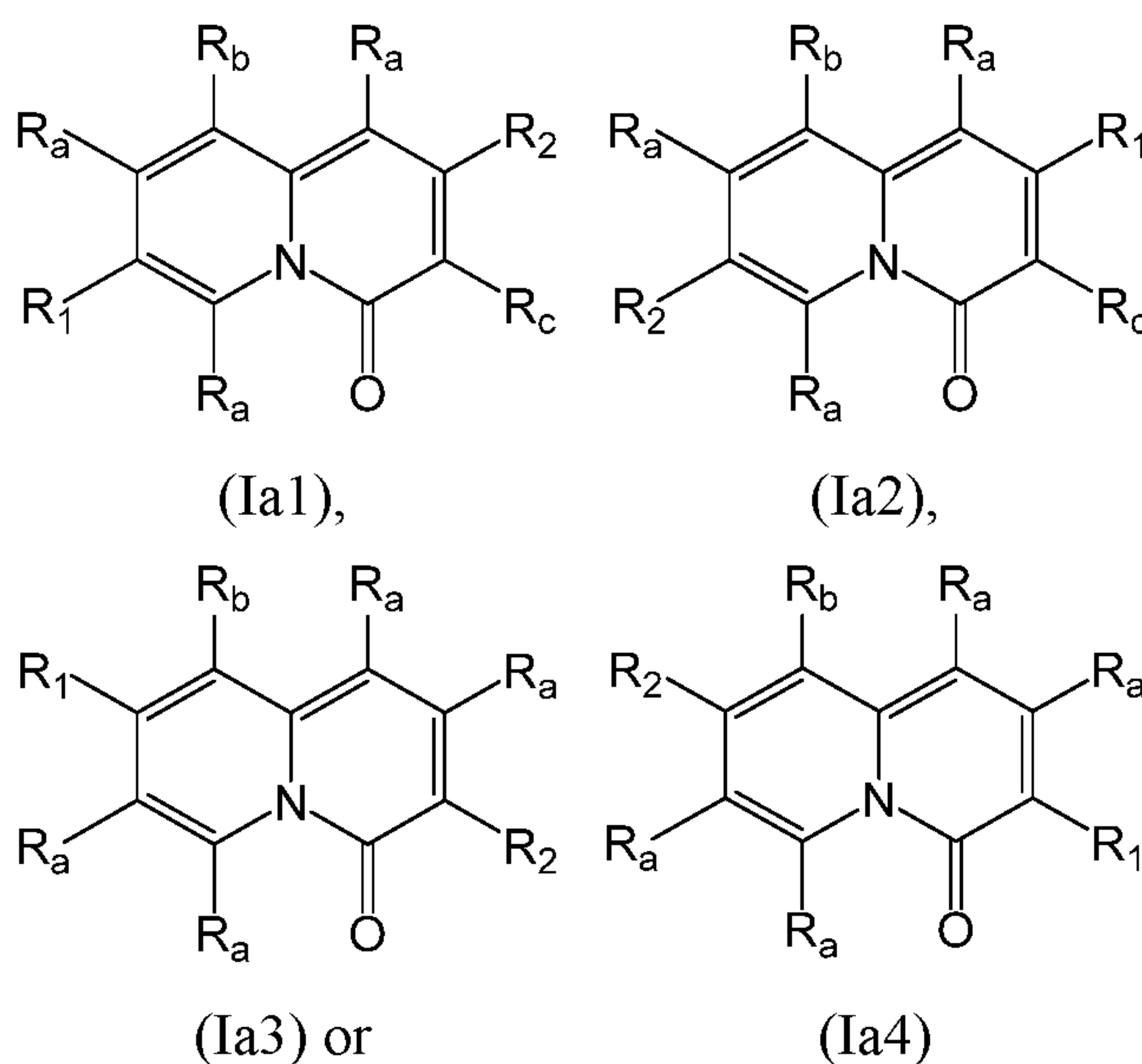
[00534] or a form thereof.

[00535] In another embodiment, the compound of Formula (XIV) used in a method disclosed herein is a compound of Formula (XIVa):



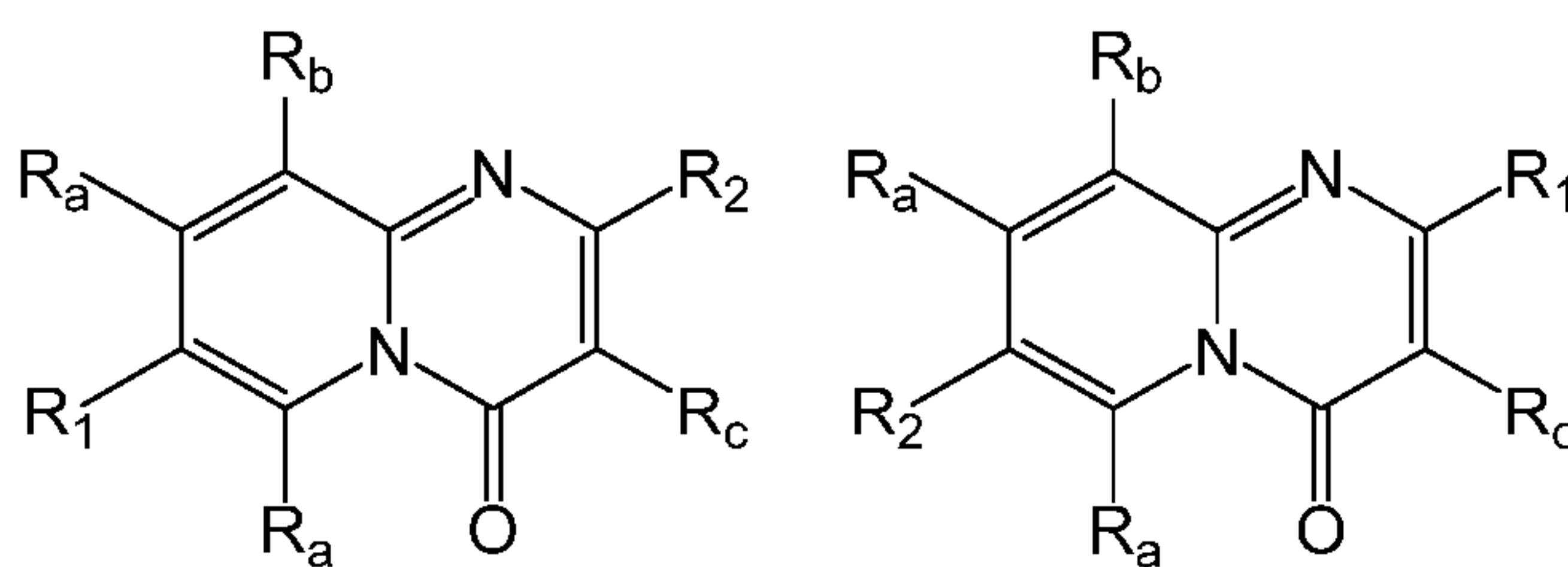
[00536] or a form thereof.

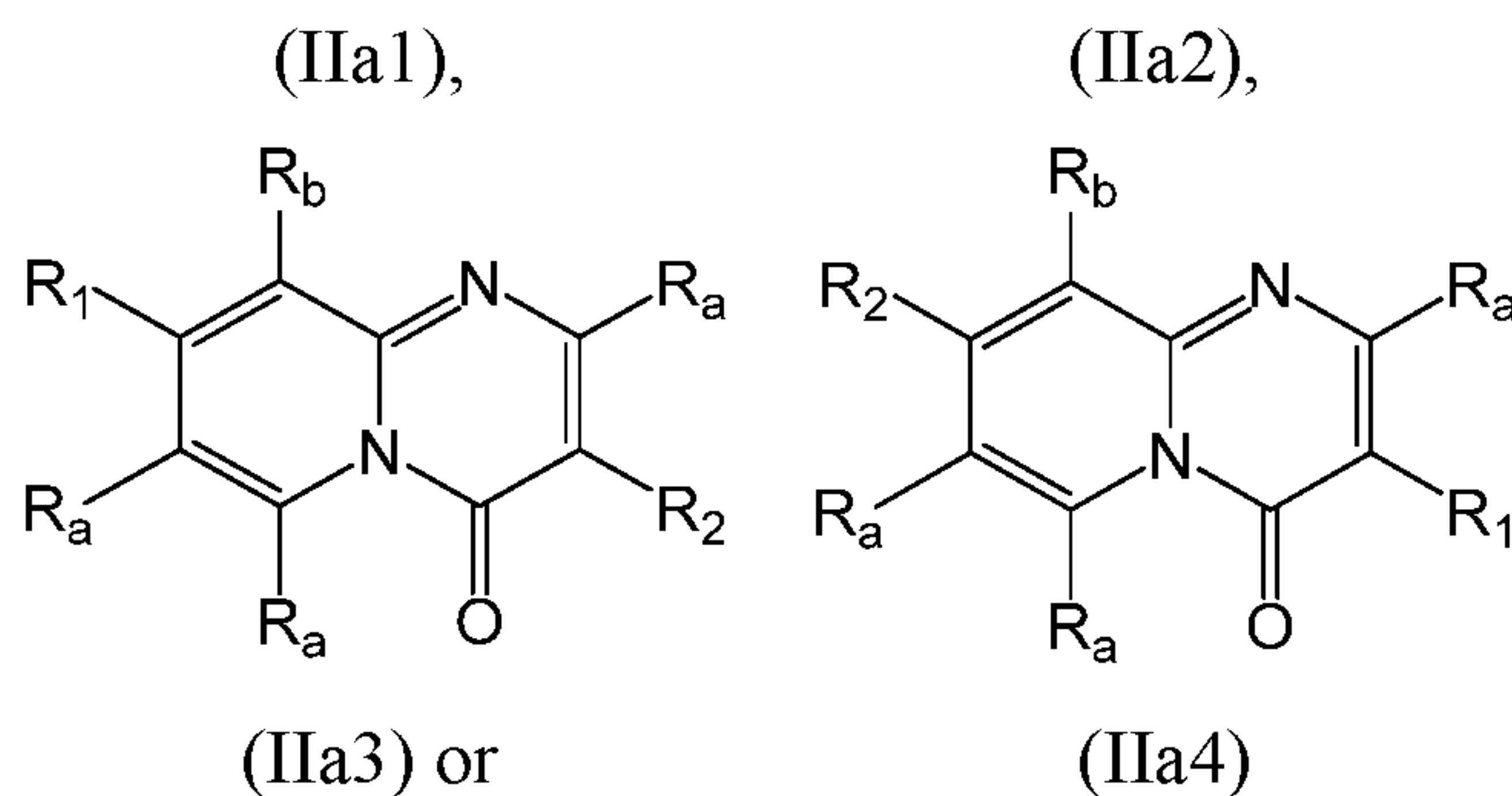
[00537] In one embodiment, the compound of Formula (Ia) used in a method disclosed herein is a compound of Formula (Ia1), Formula (Ia2), Formula (Ia3) or Formula (Ia4):



[00538] or a form thereof.

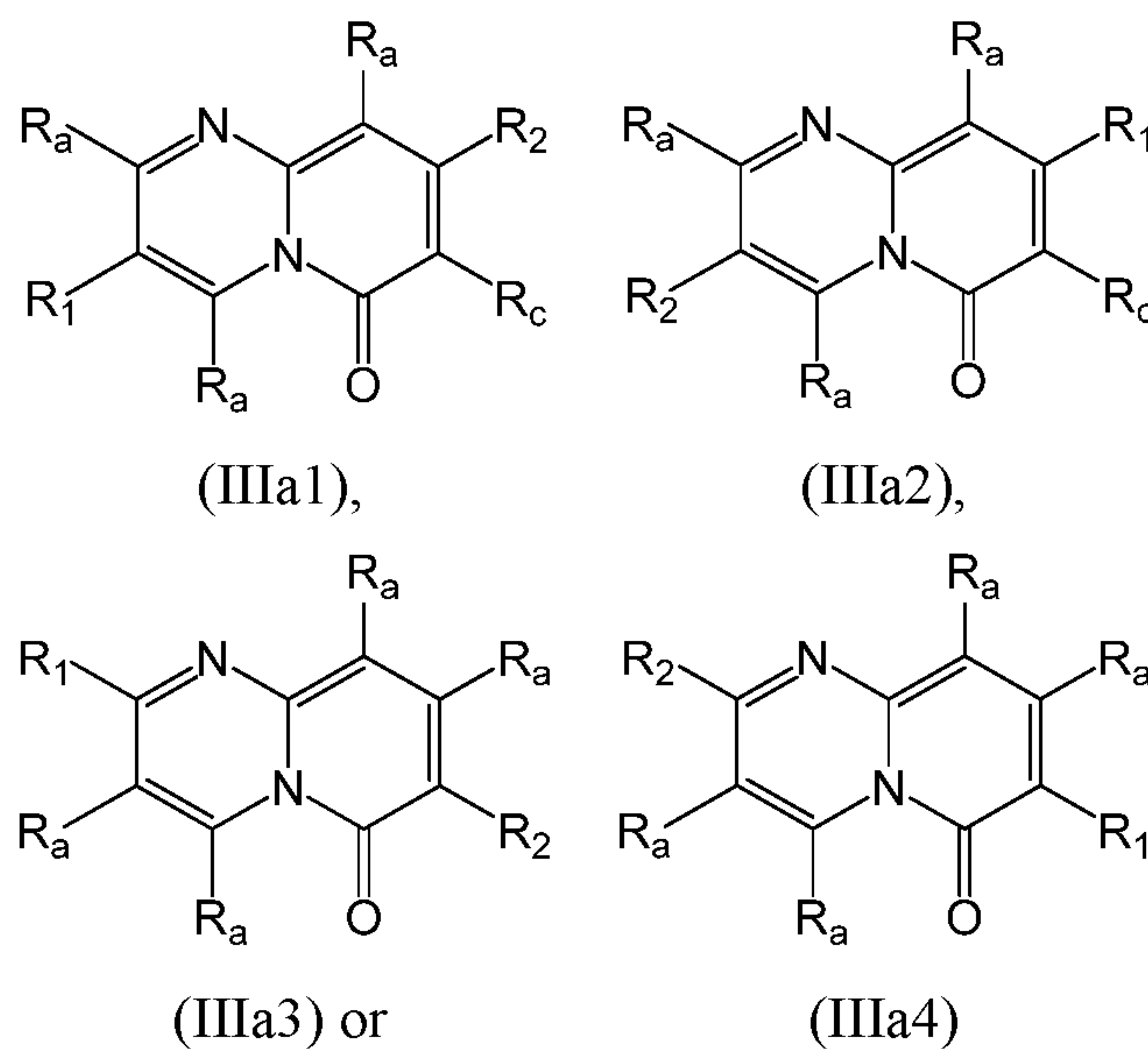
[00539] In one embodiment, the compound of Formula (IIa) used in a method disclosed herein is a compound of Formula (IIa1), Formula (IIa2), Formula (IIa3) or Formula (IIa4):





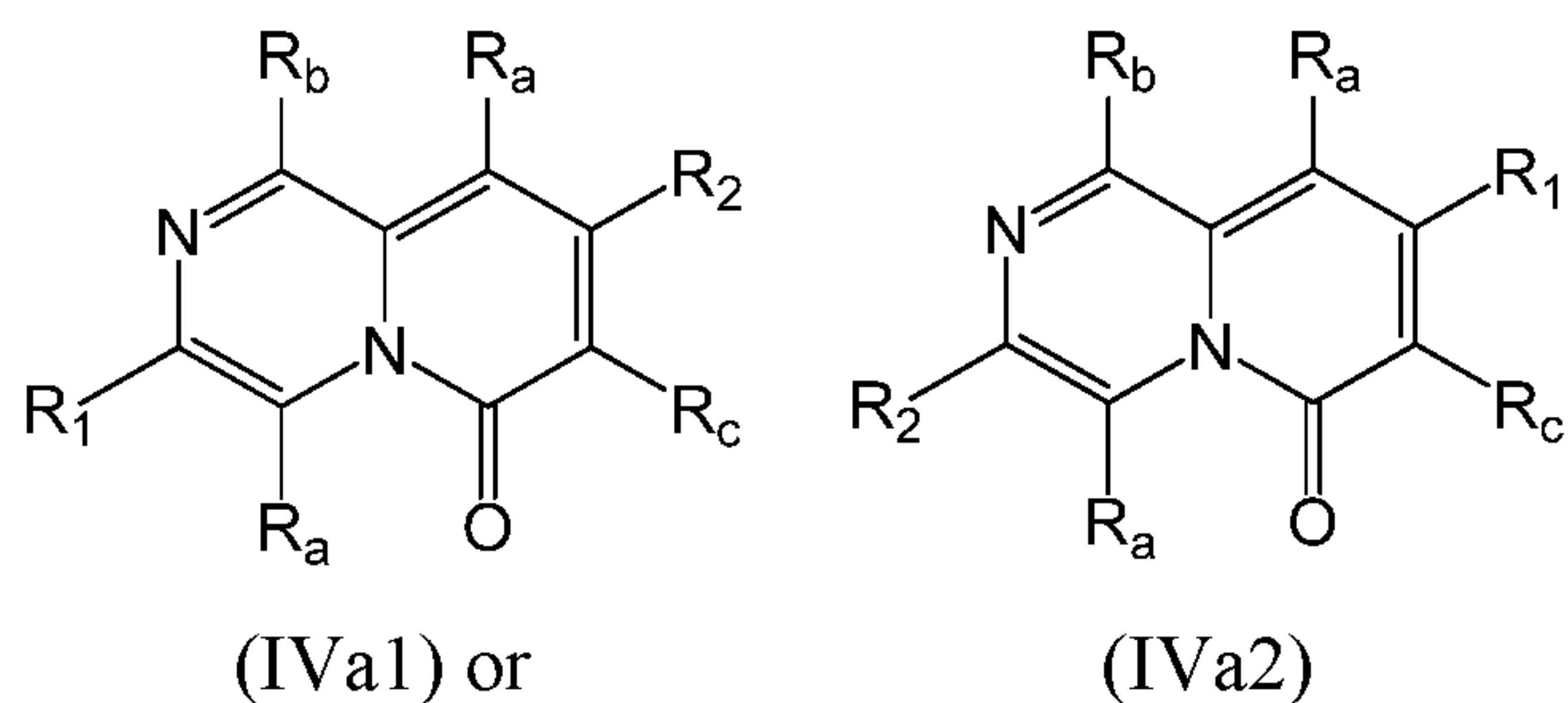
[00540] or a form thereof.

[00541] In one embodiment, the compound of Formula (IIIa) used in a method disclosed herein is a compound of Formula (IIIa1), Formula (IIIa2), Formula (IIIa3) or Formula (IIIa4):



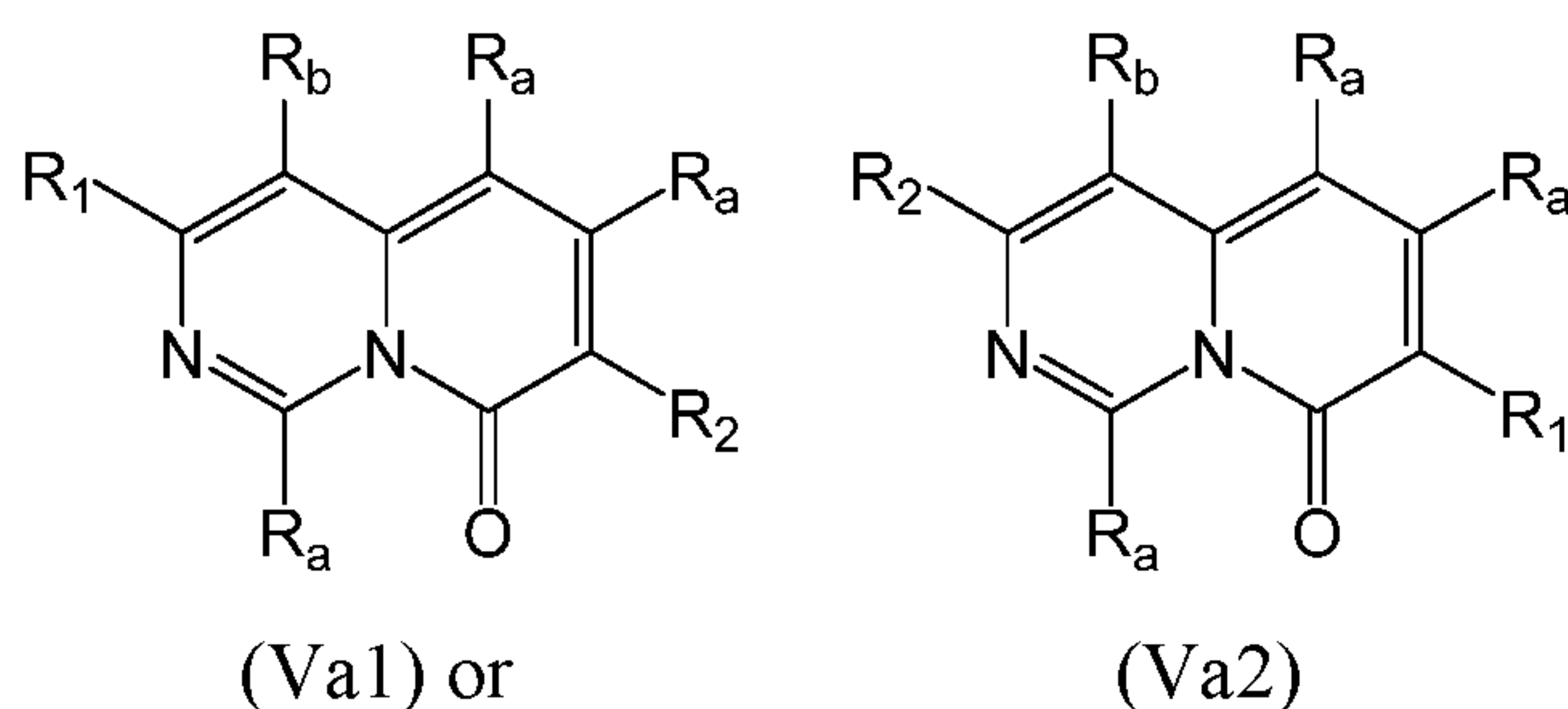
[00542] or a form thereof.

[00543] In one embodiment, the compound of Formula (IVa) used in a method disclosed herein is a compound of Formula (IVa1) or Formula (IVa2):



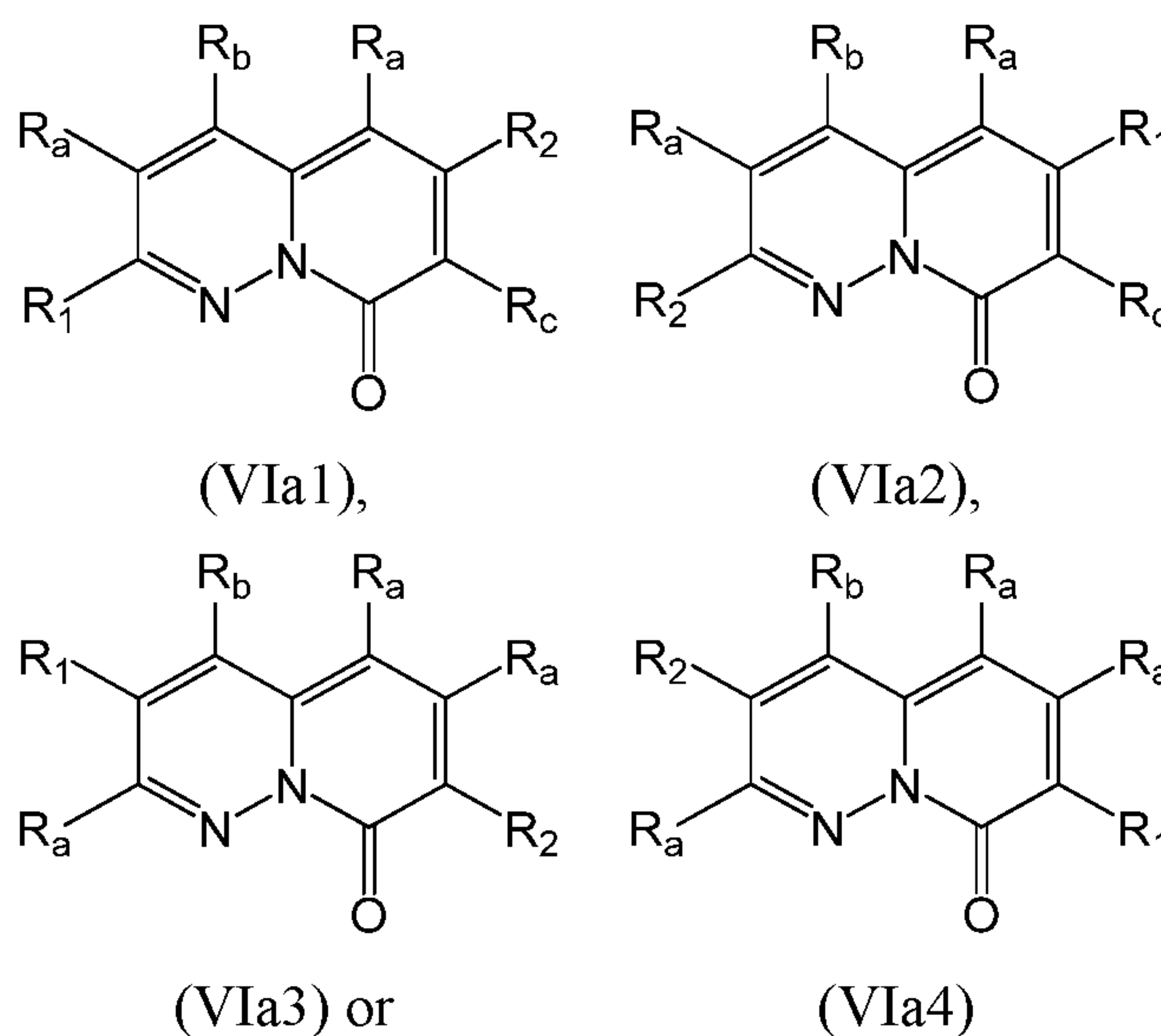
[00393] or a form thereof.

[00394] In one embodiment, the compound of Formula (Va) used in a method disclosed herein is a compound of Formula (Va1) or Formula (Va2):



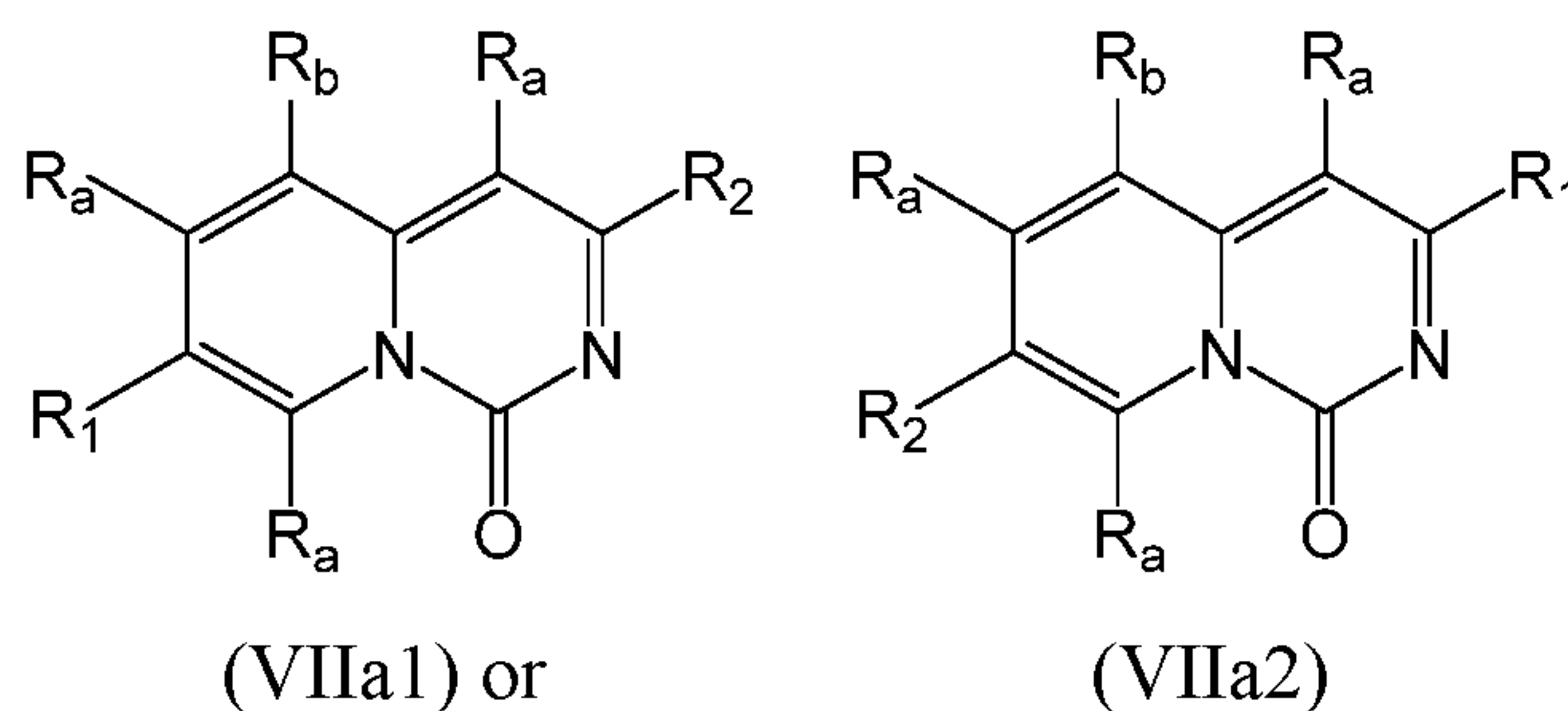
[00544] or a form thereof.

[00545] In one embodiment, the compound of Formula (VIa) used in a method disclosed herein is a compound of Formula (VIa1), Formula (VIa2), Formula (VIa3) or Formula (VIa4):



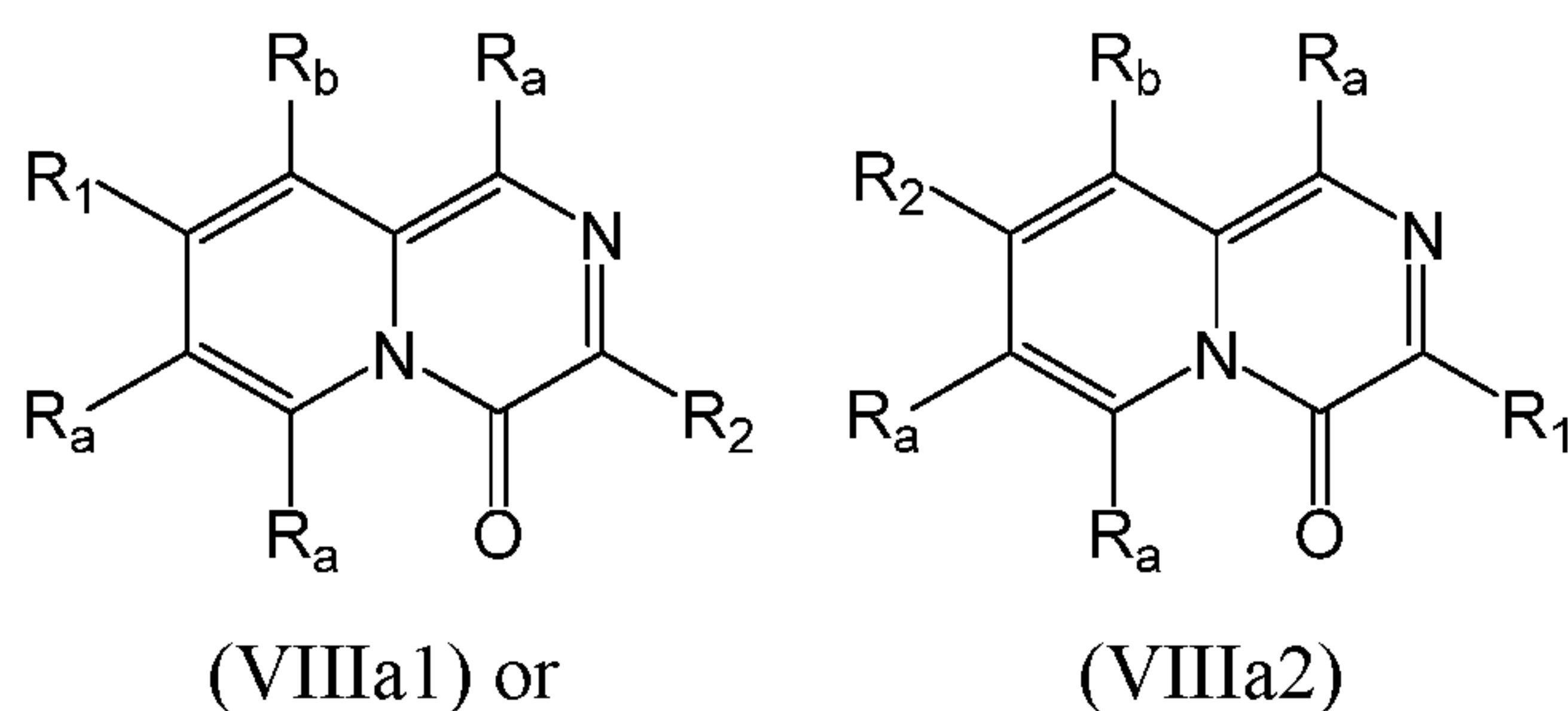
[00546] or a form thereof.

[00547] In one embodiment, the compound of Formula (VIIa) used in a method disclosed herein is a compound of Formula (VIIa1) or Formula (VIIa2):



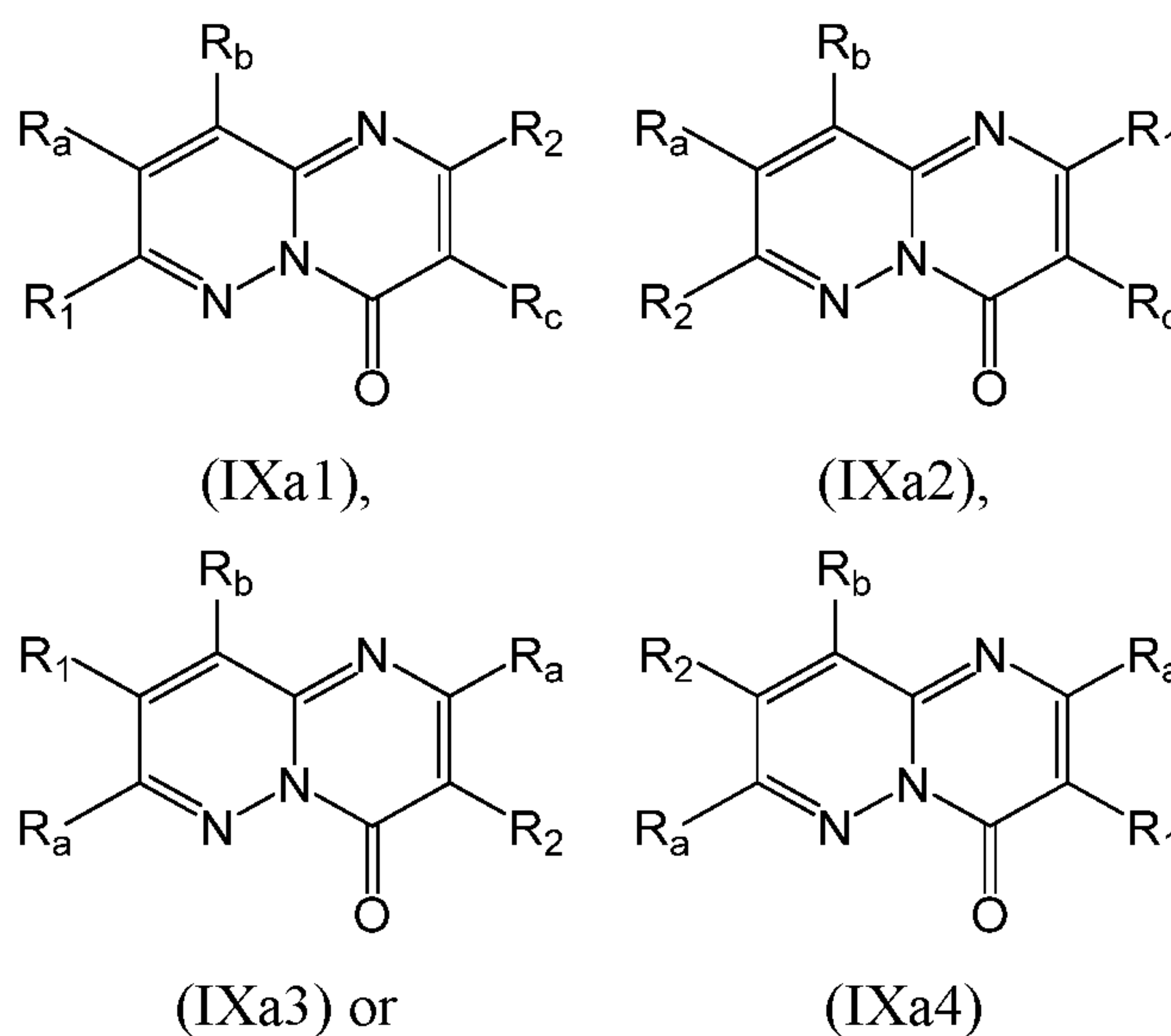
[00548] or a form thereof.

[00549] In one embodiment, the compound of Formula (VIIIa) used in a method disclosed herein is a compound of Formula (VIIIa1) or Formula (VIIIa2):



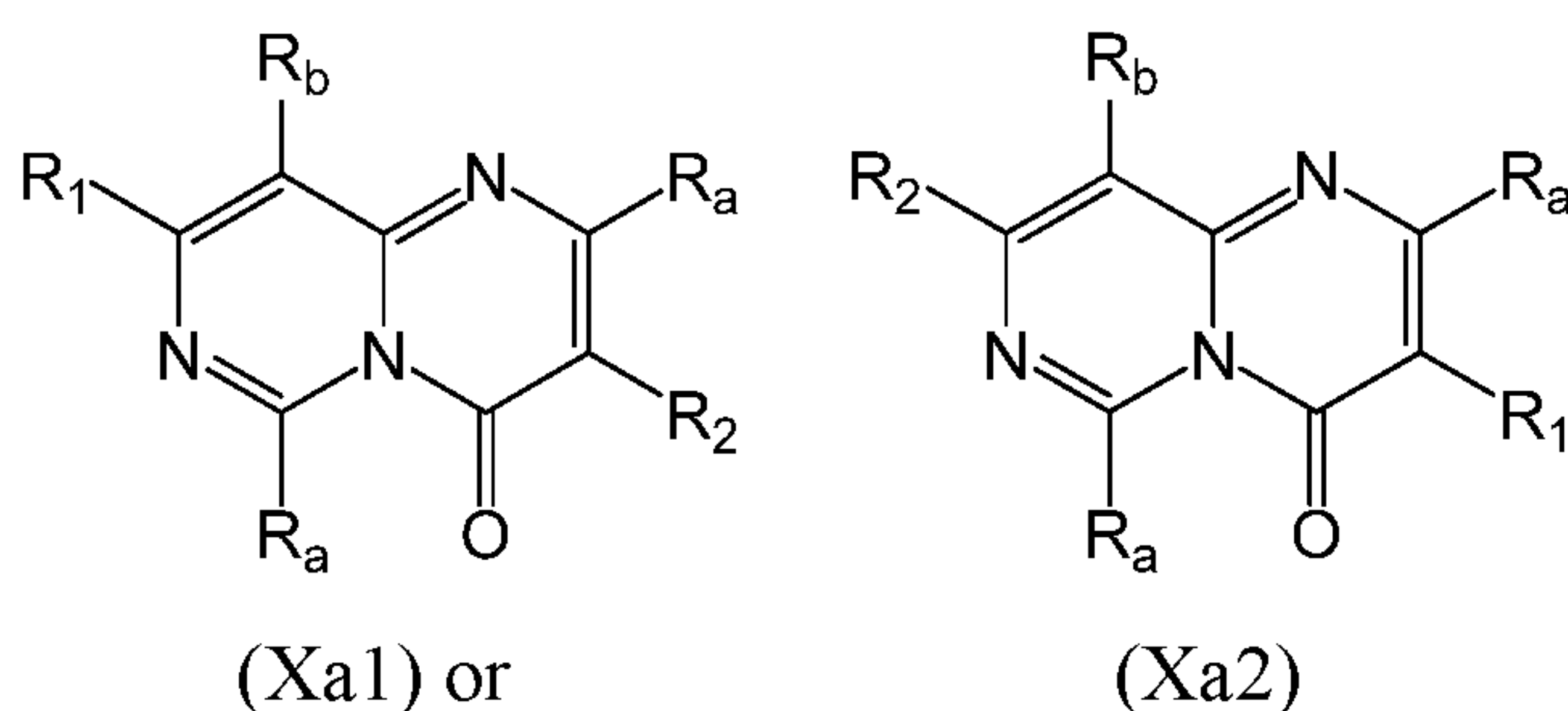
[00550] or a form thereof.

[00551] In one embodiment, the compound of Formula (IXa) used in a method disclosed herein is a compound of Formula (IXa1), Formula (IXa2), Formula (IXa3) or Formula (IXa4):



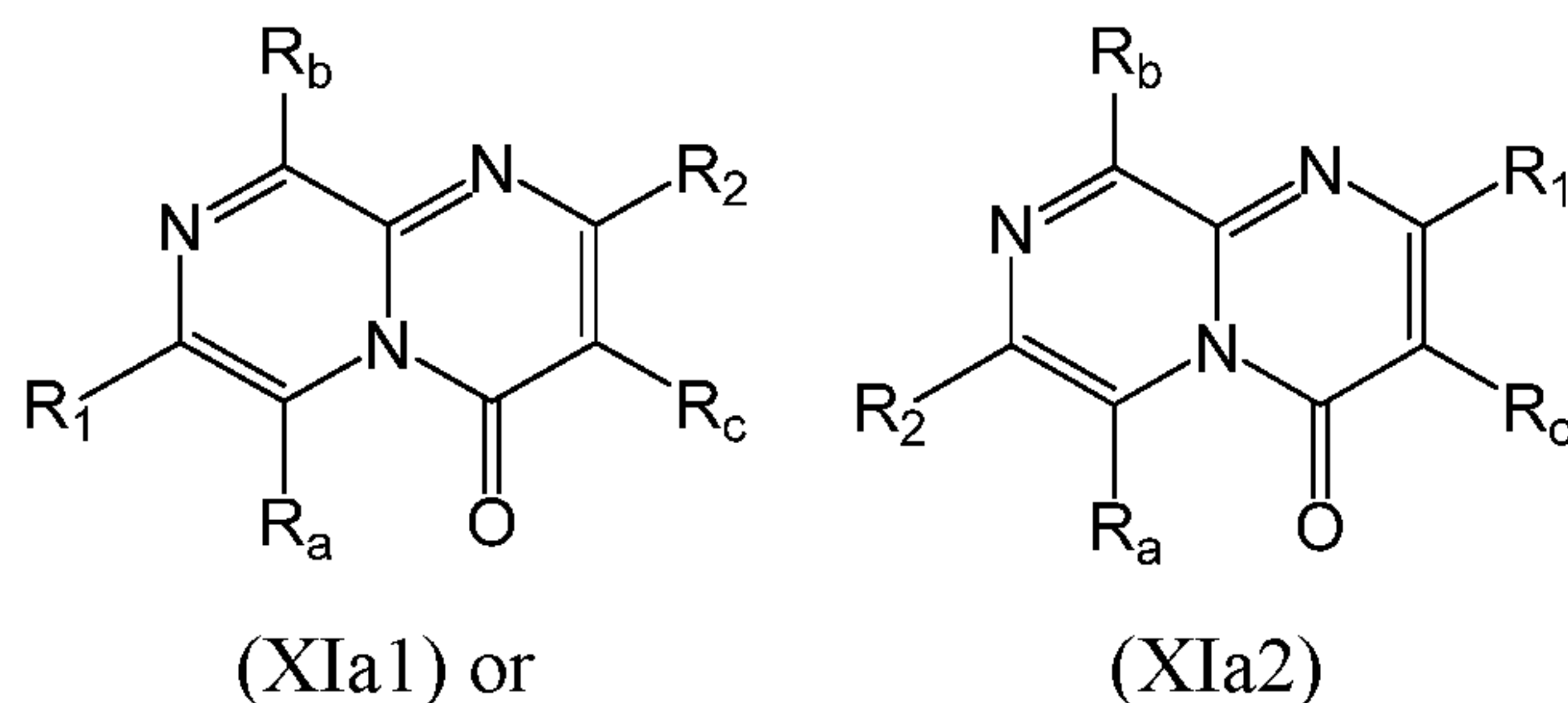
[00552] or a form thereof.

[00553] In one embodiment, the compound of Formula (Xa) used in a method disclosed herein is a compound of Formula (Xa1) or Formula (Xa2):



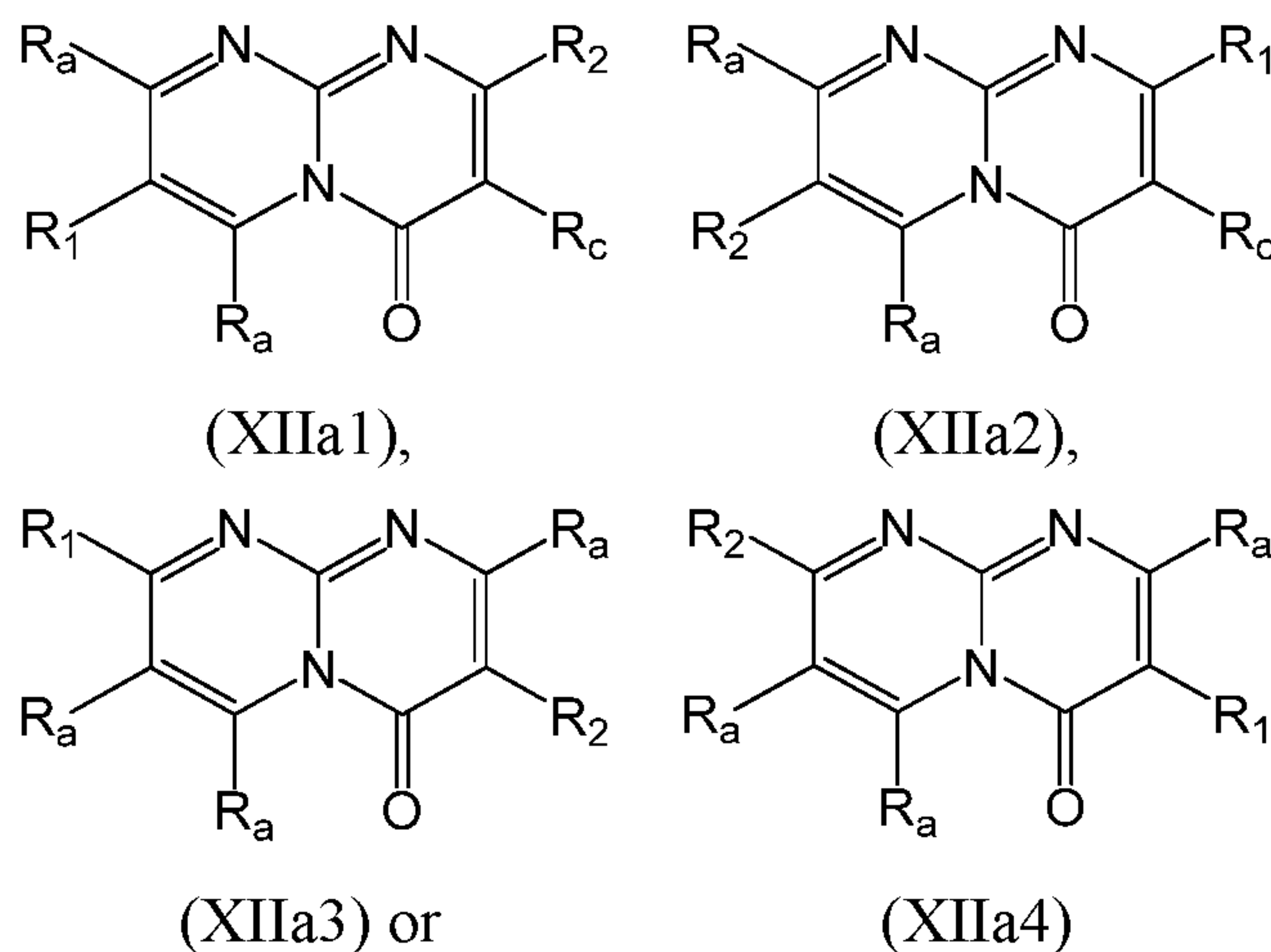
[00554] or a form thereof.

[00555] In one embodiment, the compound of Formula (XIa) used in a method disclosed herein is a compound of Formula (XIa1) or Formula (XIa2):



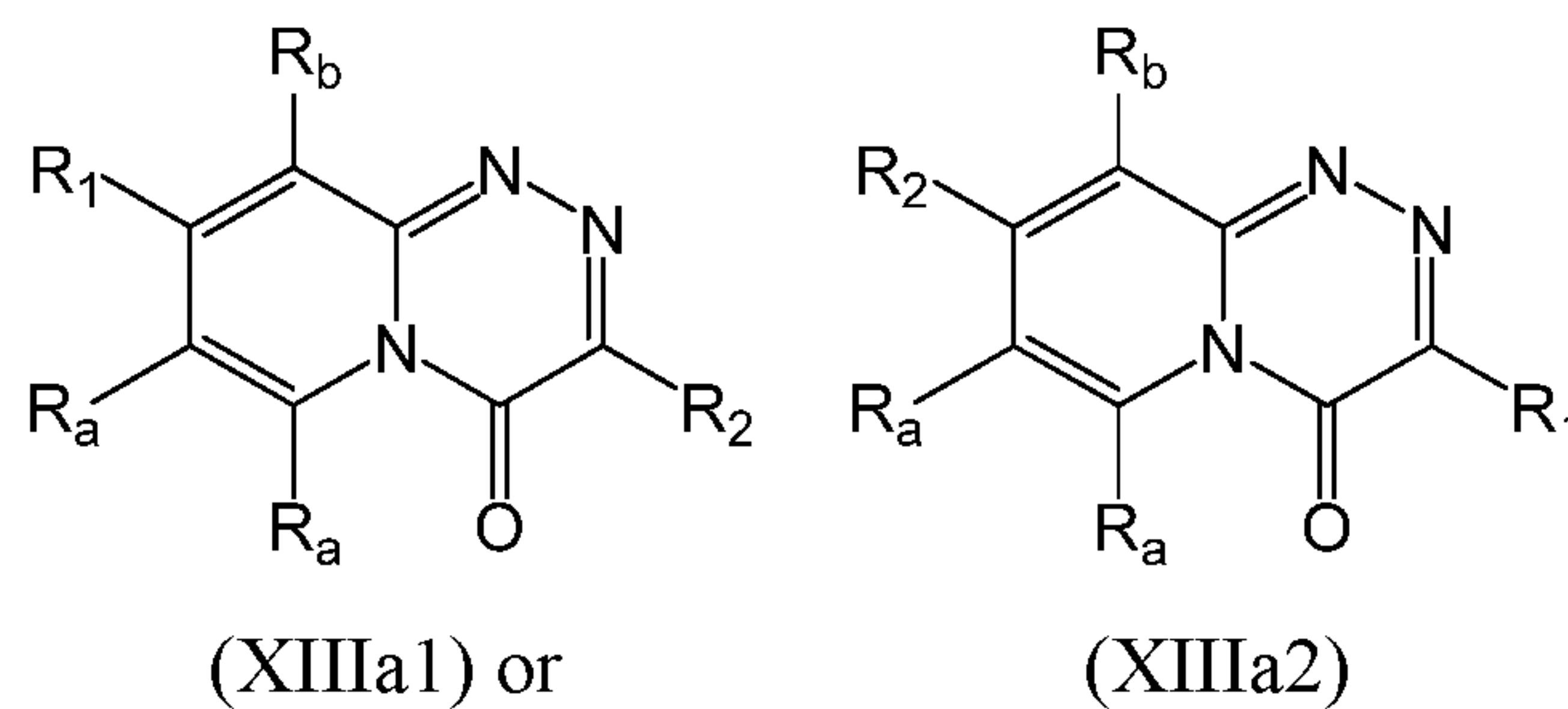
[00556] or a form thereof.

[00557] In one embodiment, the compound of Formula (XIIa) used in a method disclosed herein is a compound of Formula (XIIa1), Formula (XIIa2), Formula (XIIa3) or Formula (XIIa4):



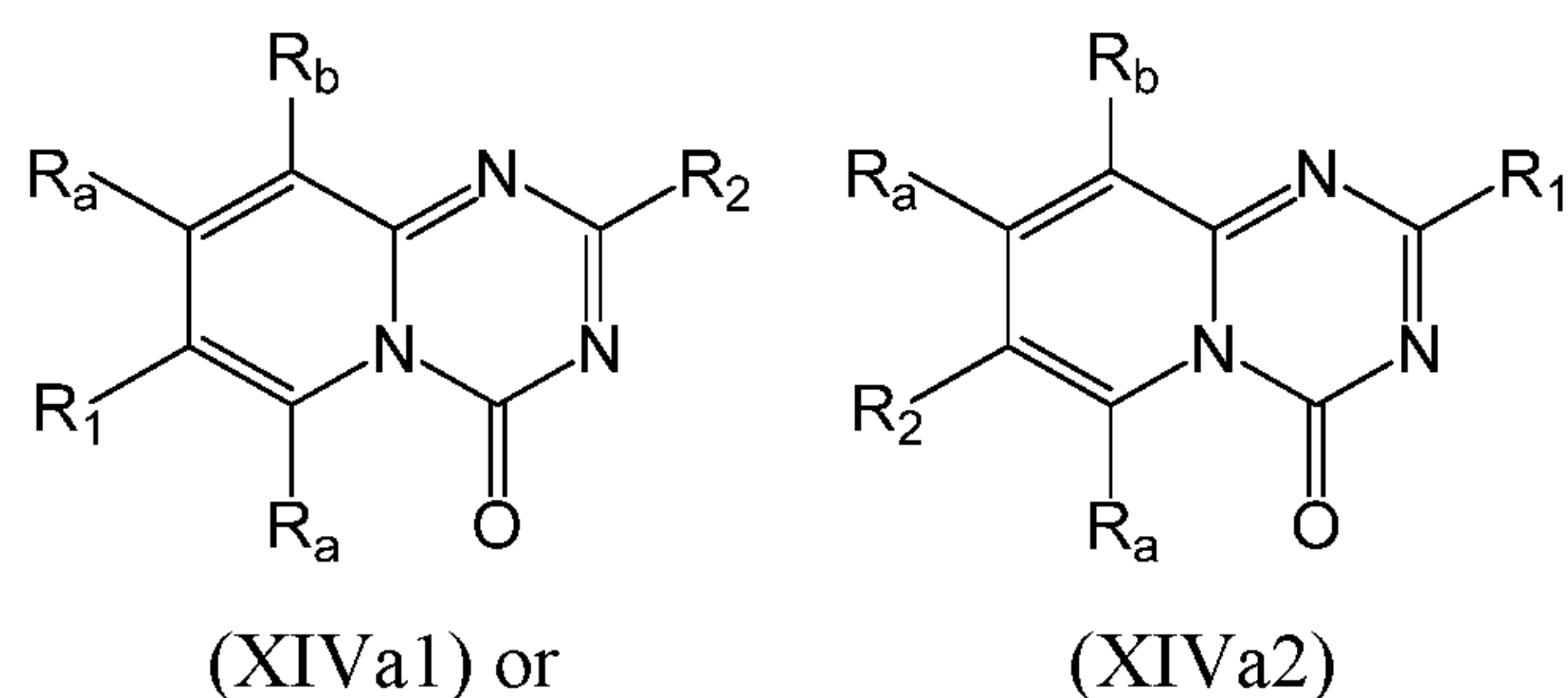
[00558] or a form thereof.

[00559] In one embodiment, the compound of Formula (XIIIa) used in a method disclosed herein is a compound of Formula (XIIIa1) or Formula (XIIIa2):



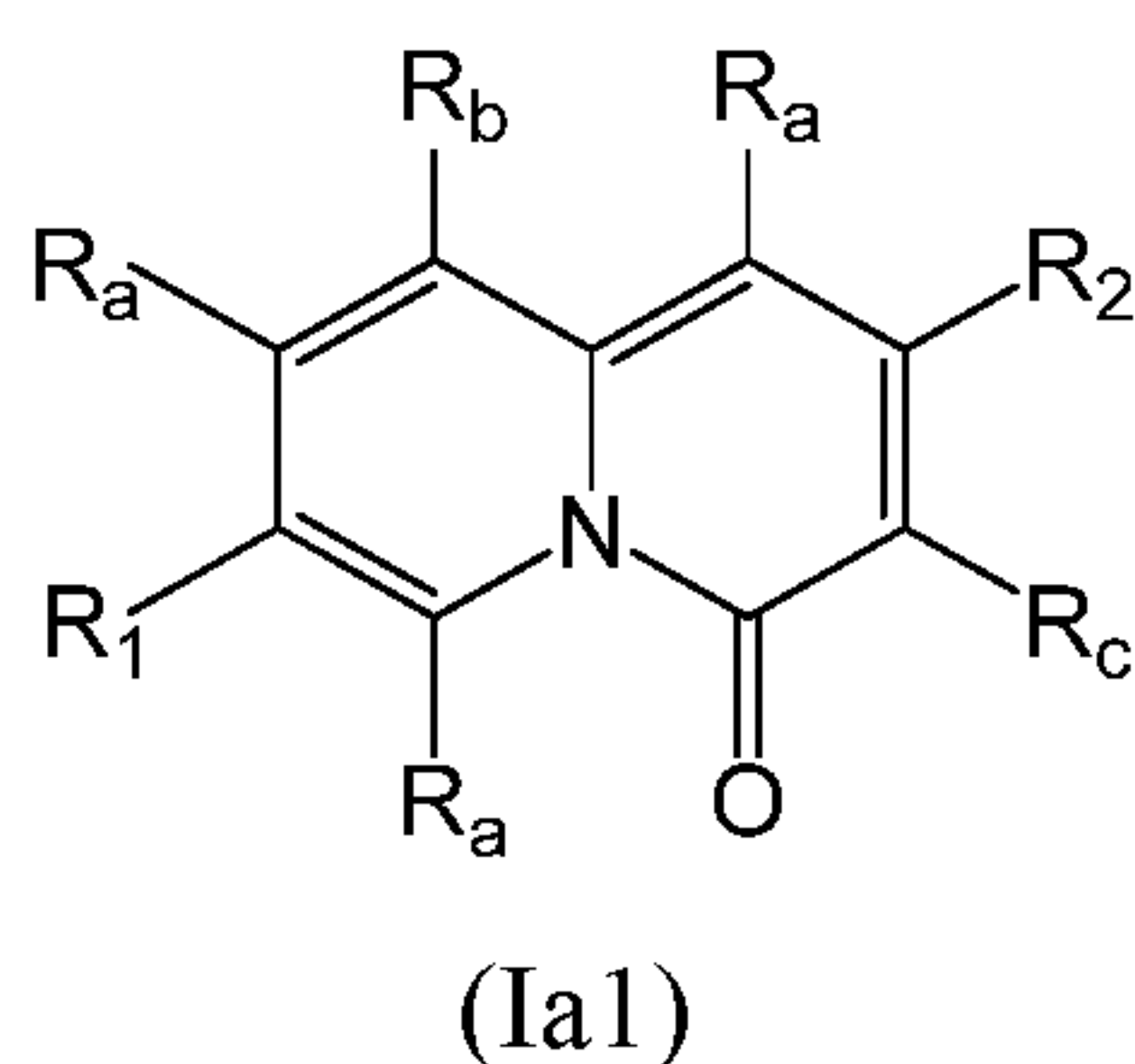
[00560] or a form thereof.

[00561] In one embodiment, the compound of Formula (XIVa) used in a method disclosed herein is a compound of Formula (XIVa1) or Formula (XIVa2):



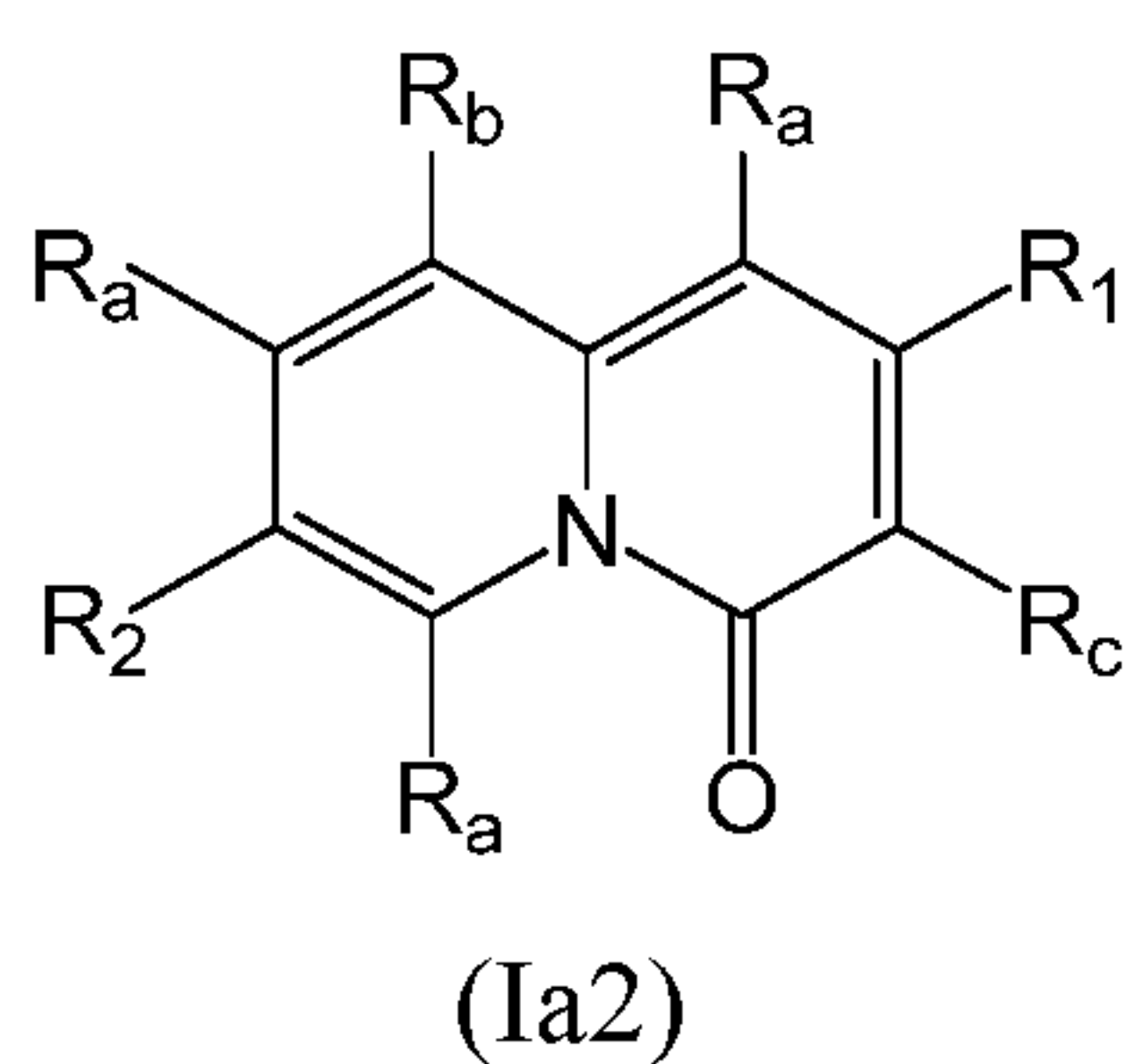
[00562] or a form thereof.

[00563] In one embodiment, the compound of Formula (Ia) used in a method disclosed herein is a compound of Formula (Ia1):



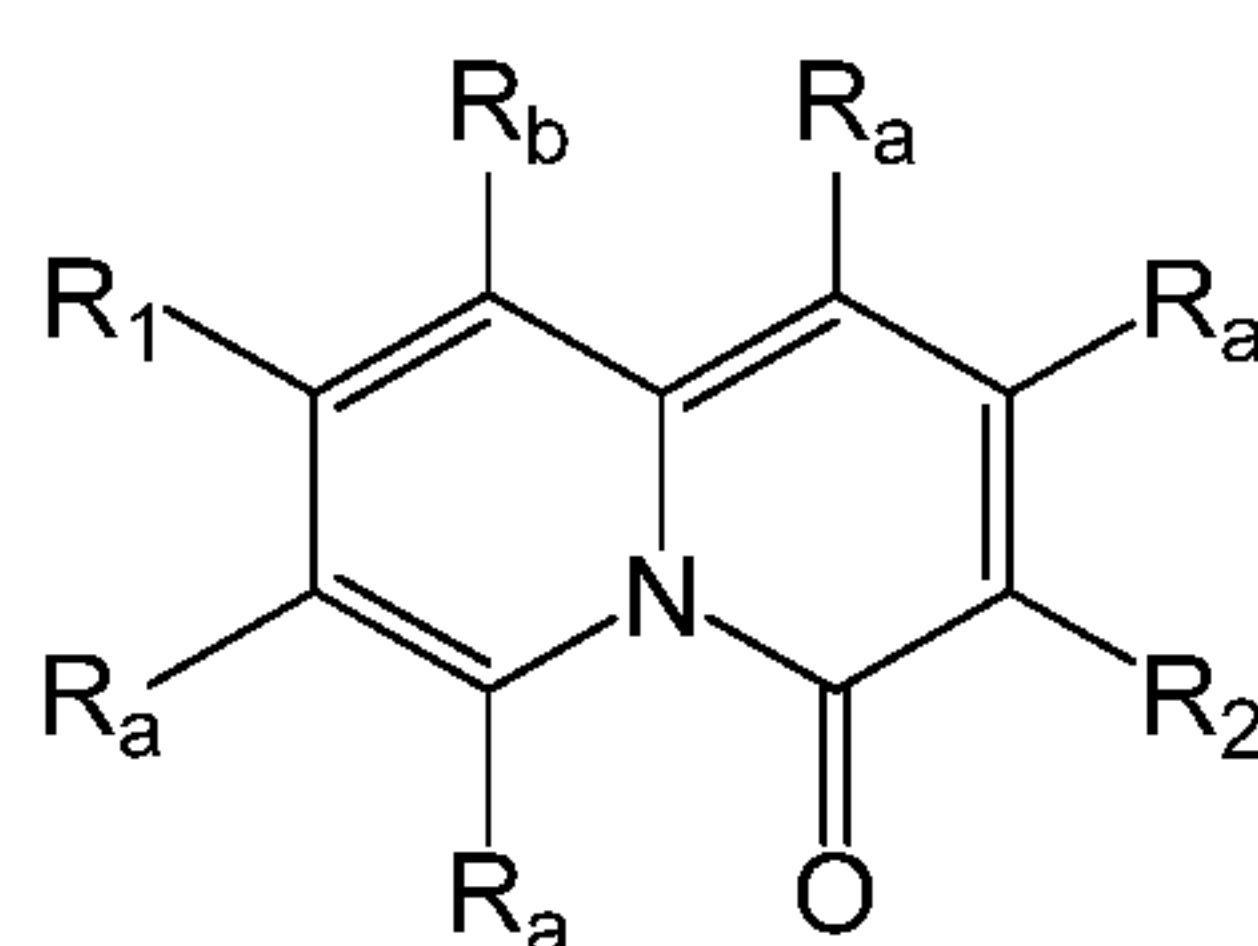
[00564] or a form thereof.

[00565] In one embodiment, the compound of Formula (Ia) used in a method disclosed herein is a compound of Formula (Ia2):



[00566] or a form thereof.

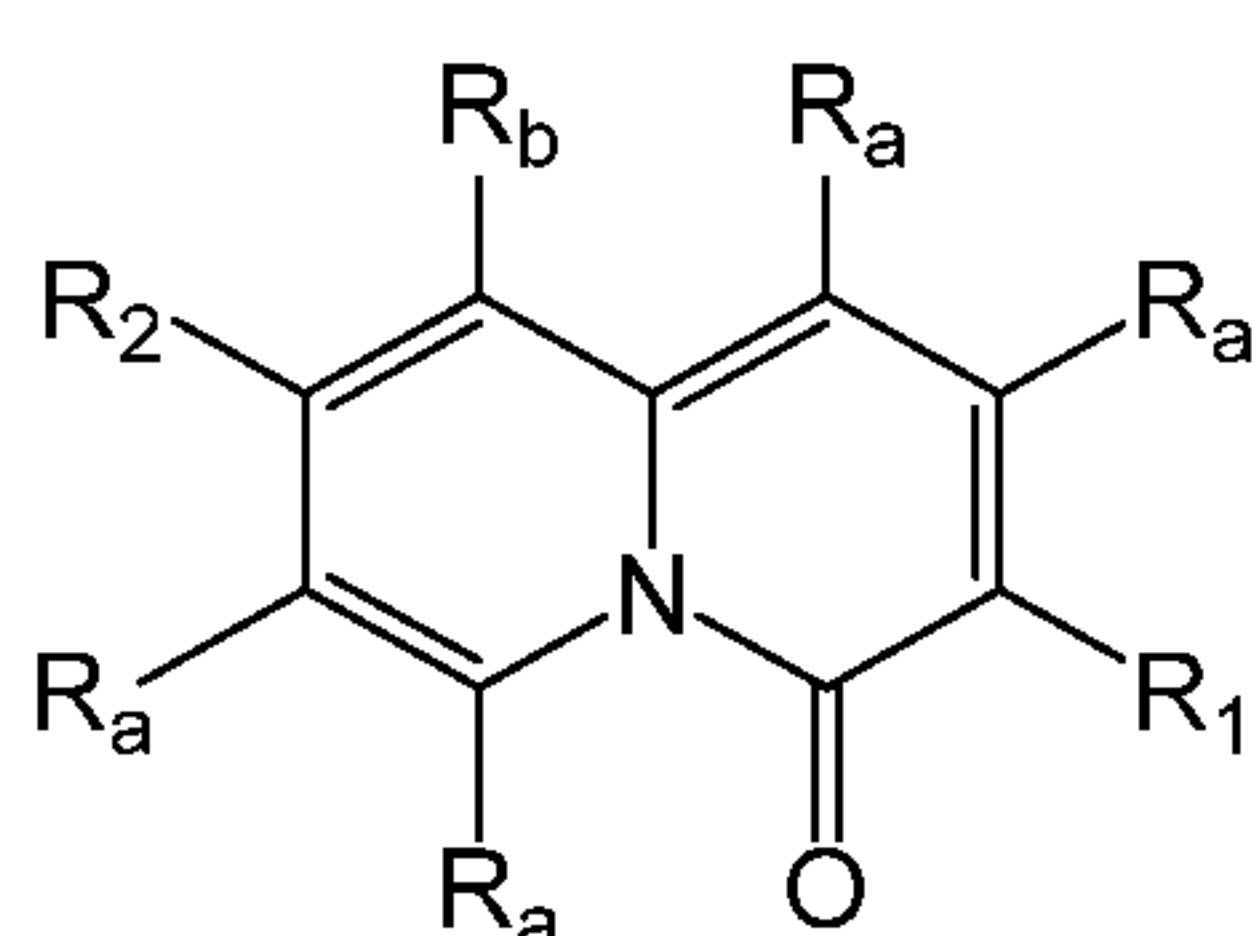
[00567] In one embodiment, the compound of Formula (Ia) used in a method disclosed herein is a compound of Formula (Ia3):



(Ia3)

[00568] or a form thereof.

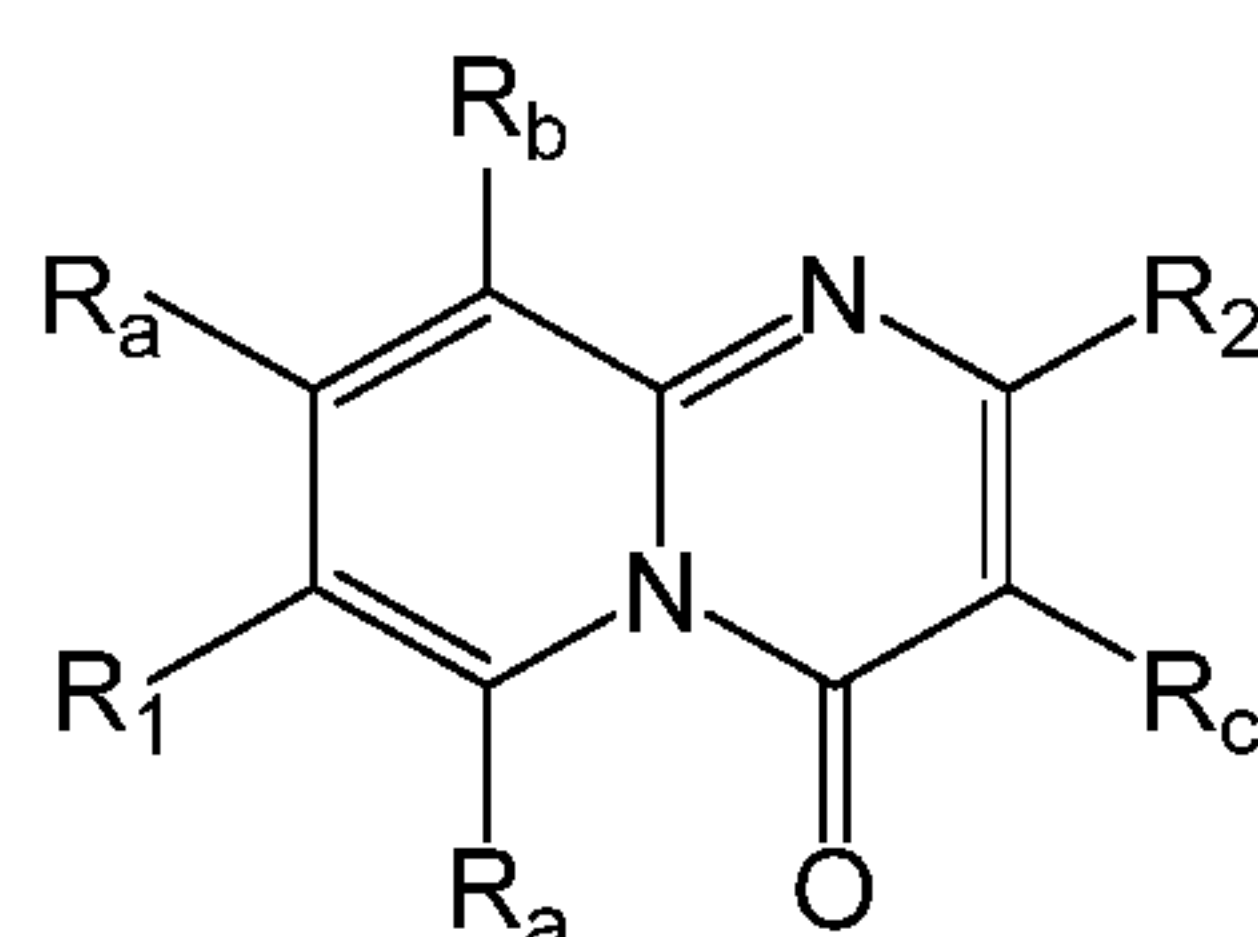
[00569] In one embodiment, the compound of Formula (Ia) used in a method disclosed herein is a compound of Formula (Ia4):



(Ia4)

[00570] or a form thereof.

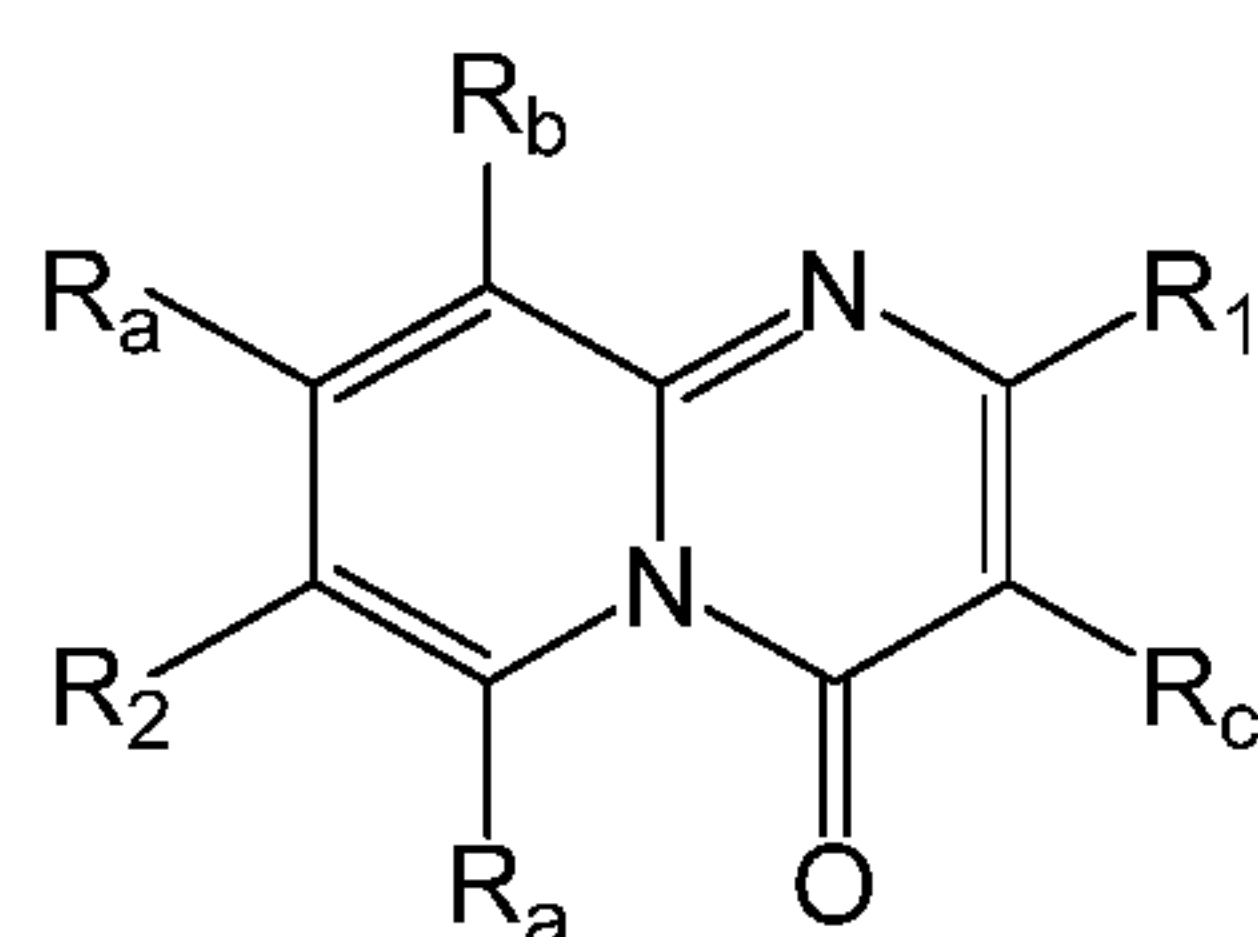
[00571] In one embodiment, the compound of Formula (IIa) used in a method disclosed herein is a compound of Formula (IIa1):



(IIa1)

[00572] or a form thereof.

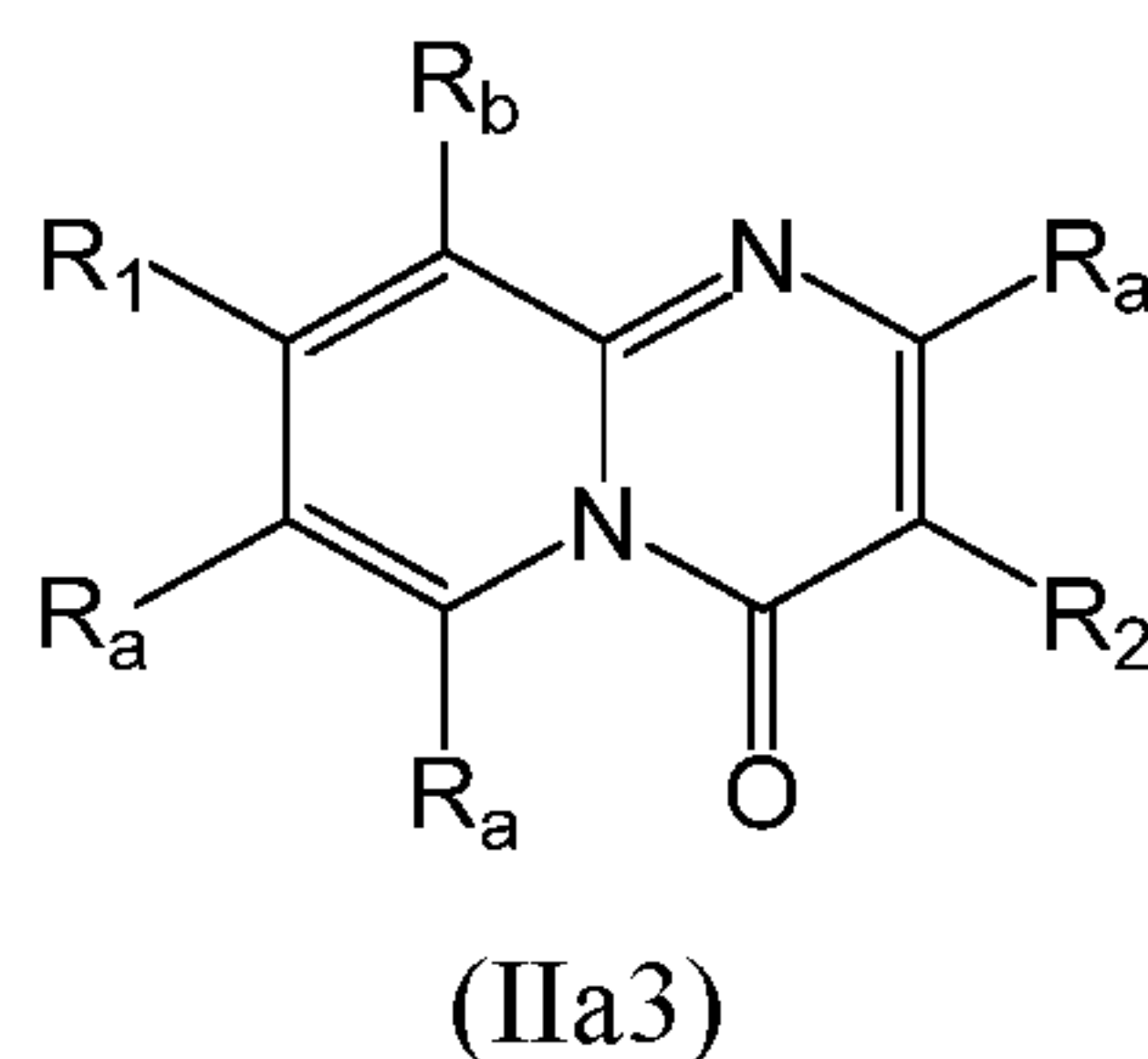
[00573] In one embodiment, the compound of Formula (IIa) used in a method disclosed herein is a compound of Formula (IIa2):



(IIa2)

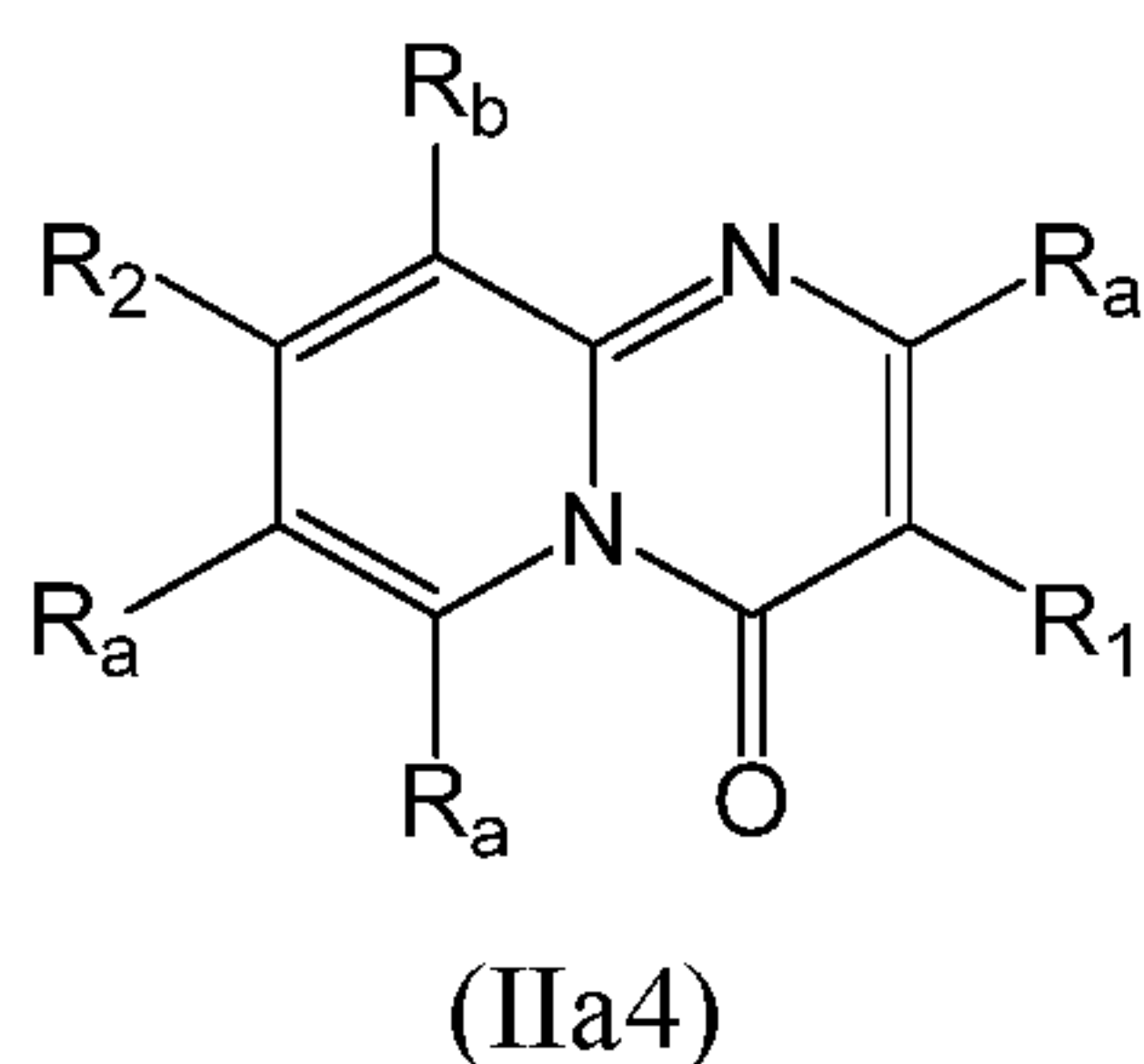
[00574] or a form thereof.

[00575] In one embodiment, the compound of Formula (IIa) used in a method disclosed herein is a compound of Formula (IIa3):



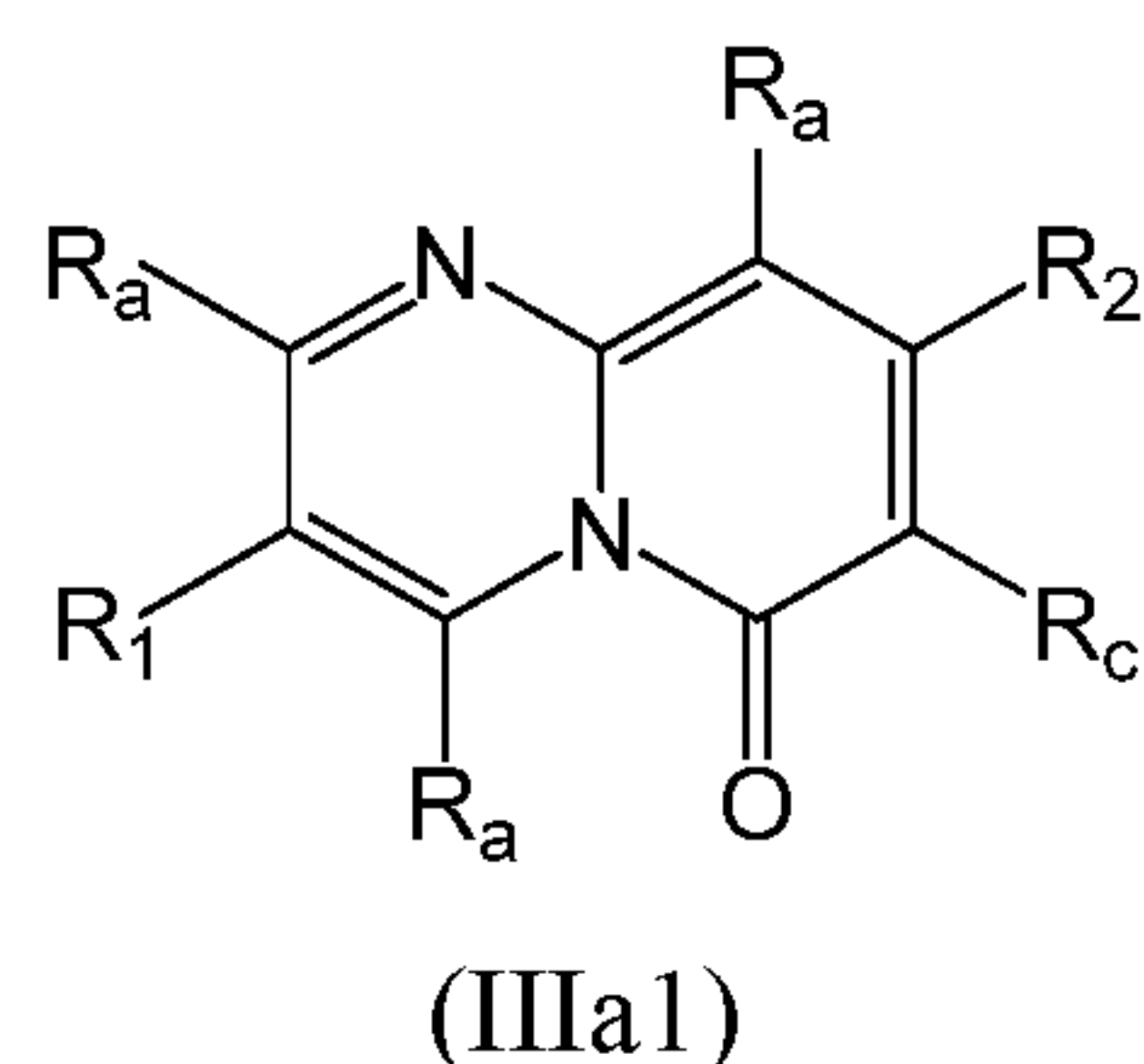
[00576] or a form thereof.

[00577] In one embodiment, the compound of Formula (IIa) used in a method disclosed herein is a compound of Formula (IIa4):



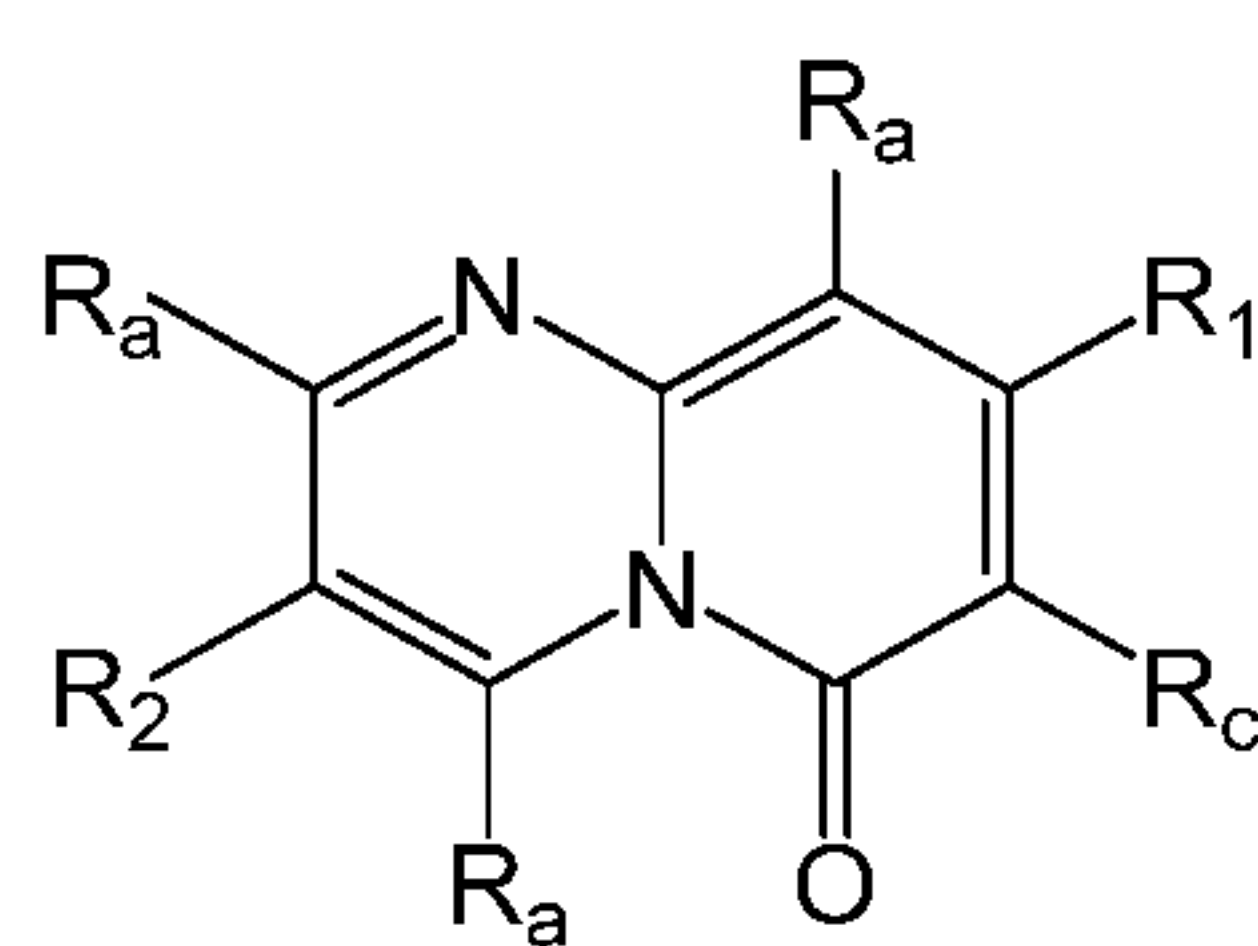
[00578] or a form thereof.

[00579] In one embodiment, the compound of Formula (IIIa) used in a method disclosed herein is a compound of Formula (IIIa1):



[00580] or a form thereof.

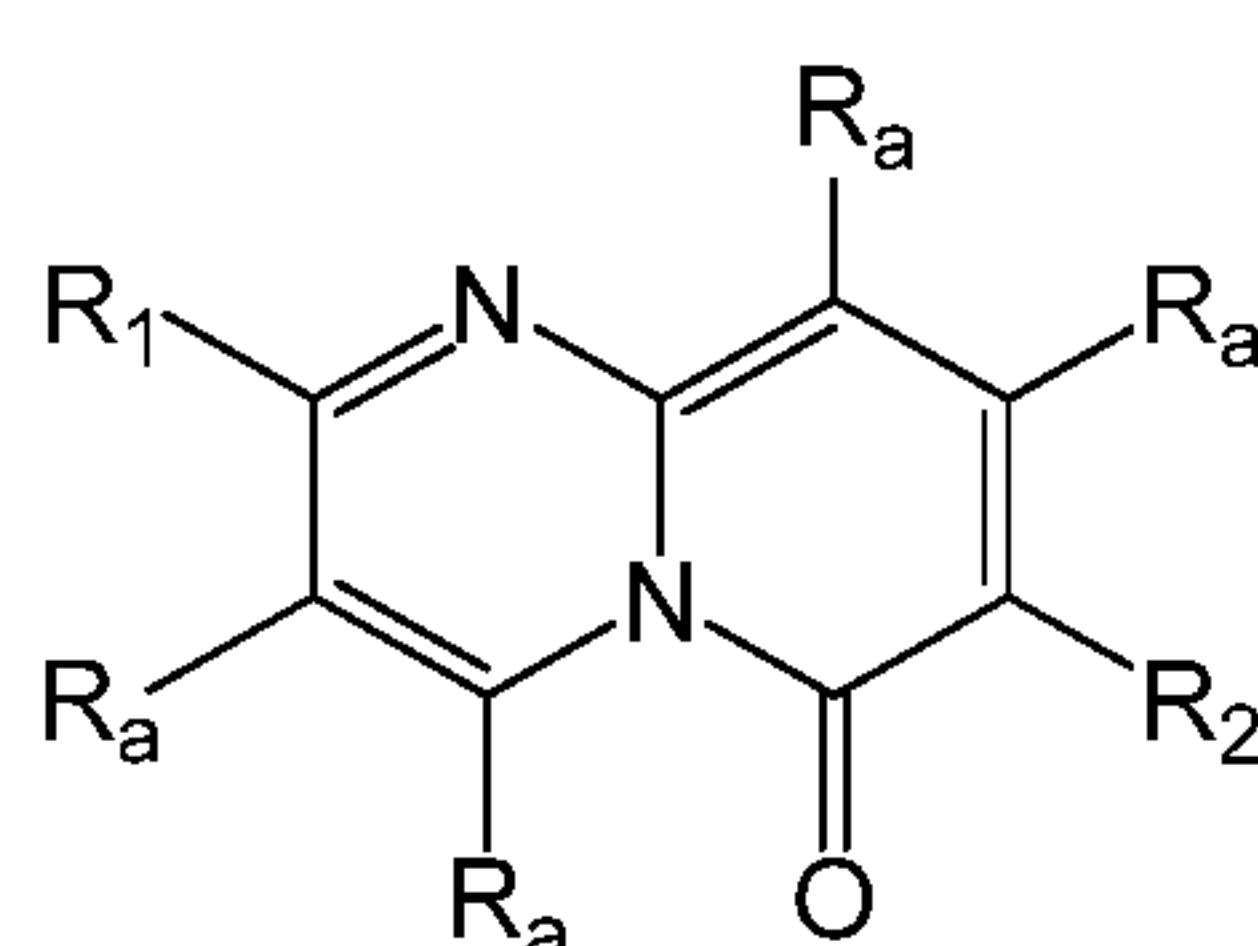
[00581] In one embodiment, the compound of Formula (IIIa) used in a method disclosed herein is a compound of Formula (IIIa2):



(IIIa2)

[00582] or a form thereof.

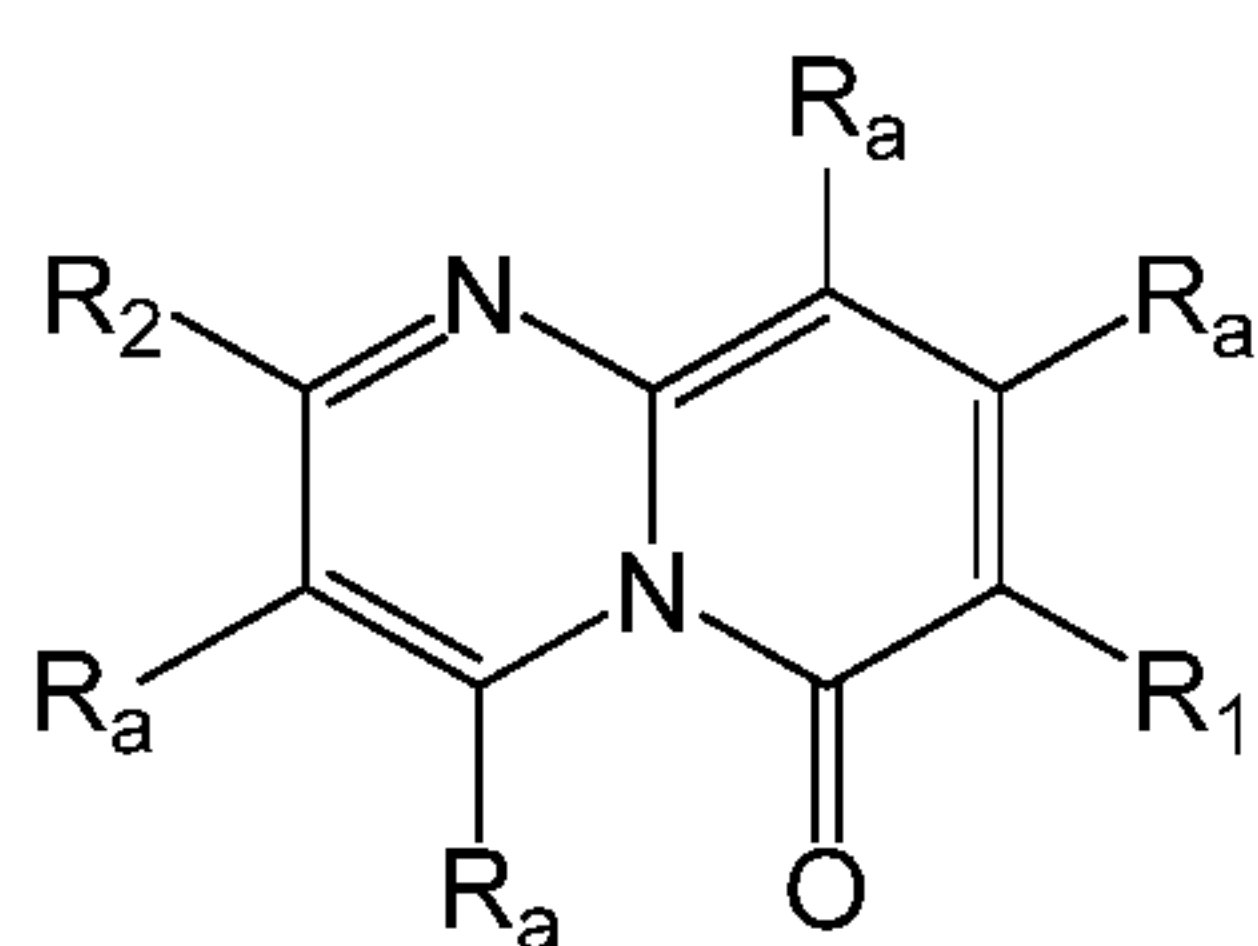
[00583] In one embodiment, the compound of Formula (IIIa) used in a method disclosed herein is a compound of Formula (IIIa3):



(IIIa3)

[00584] or a form thereof.

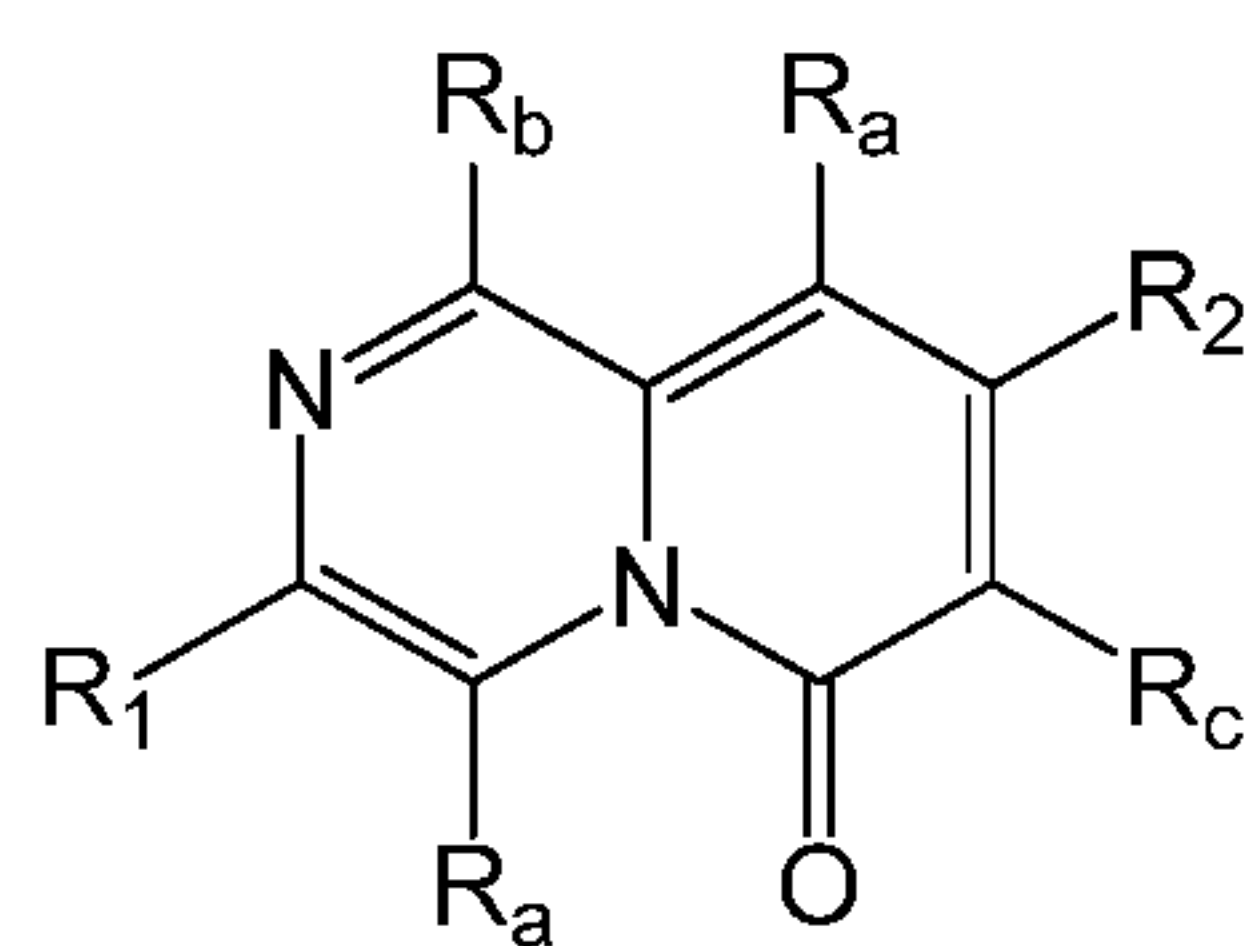
[00585] In one embodiment, the compound of Formula (IIIa) used in a method disclosed herein is a compound of Formula (IIIa4):



(IIIa4)

[00586] or a form thereof.

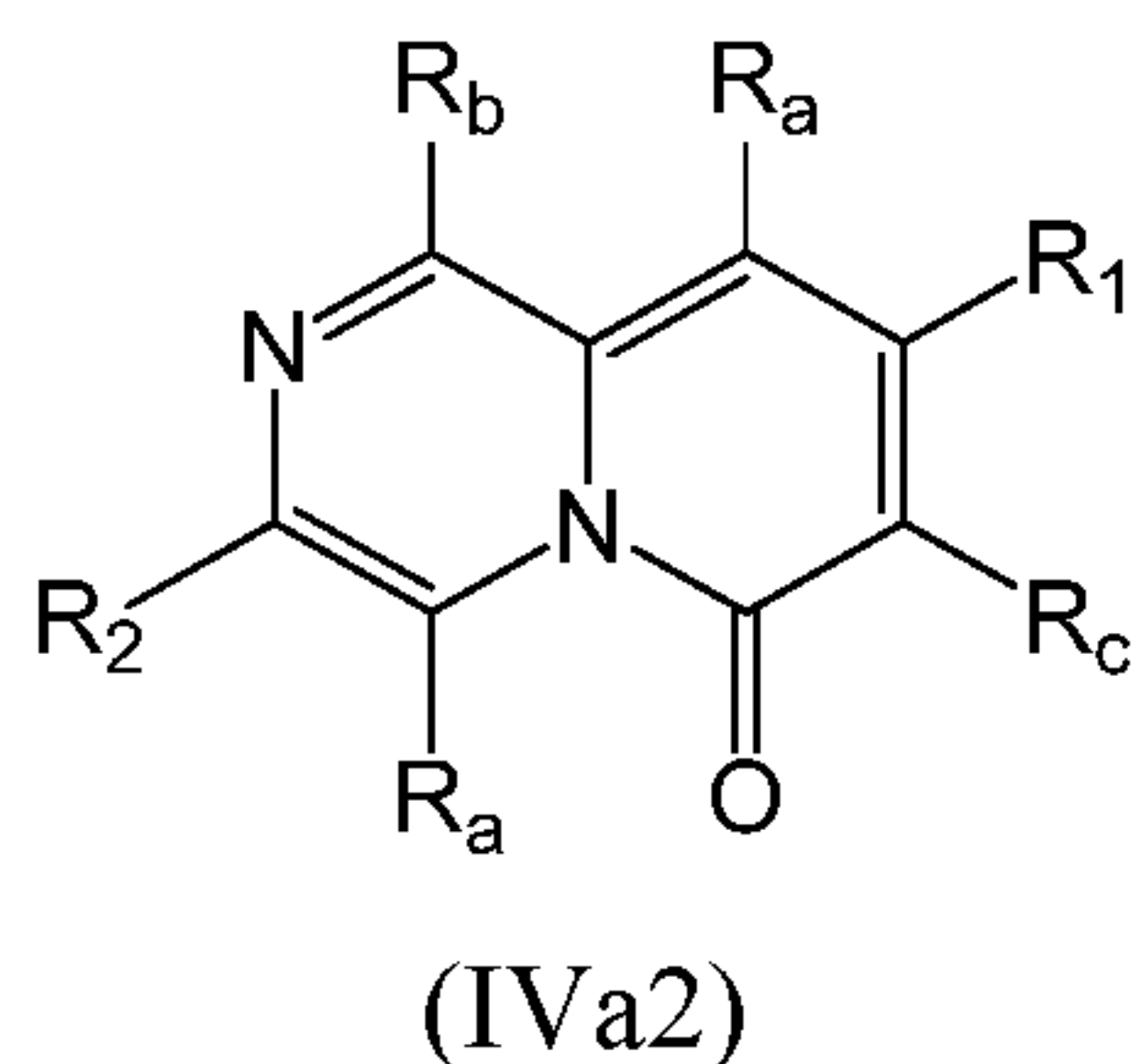
[00587] In one embodiment, the compound of Formula (IVa) used in a method disclosed herein is a compound of Formula (IVa1):



(IVa1)

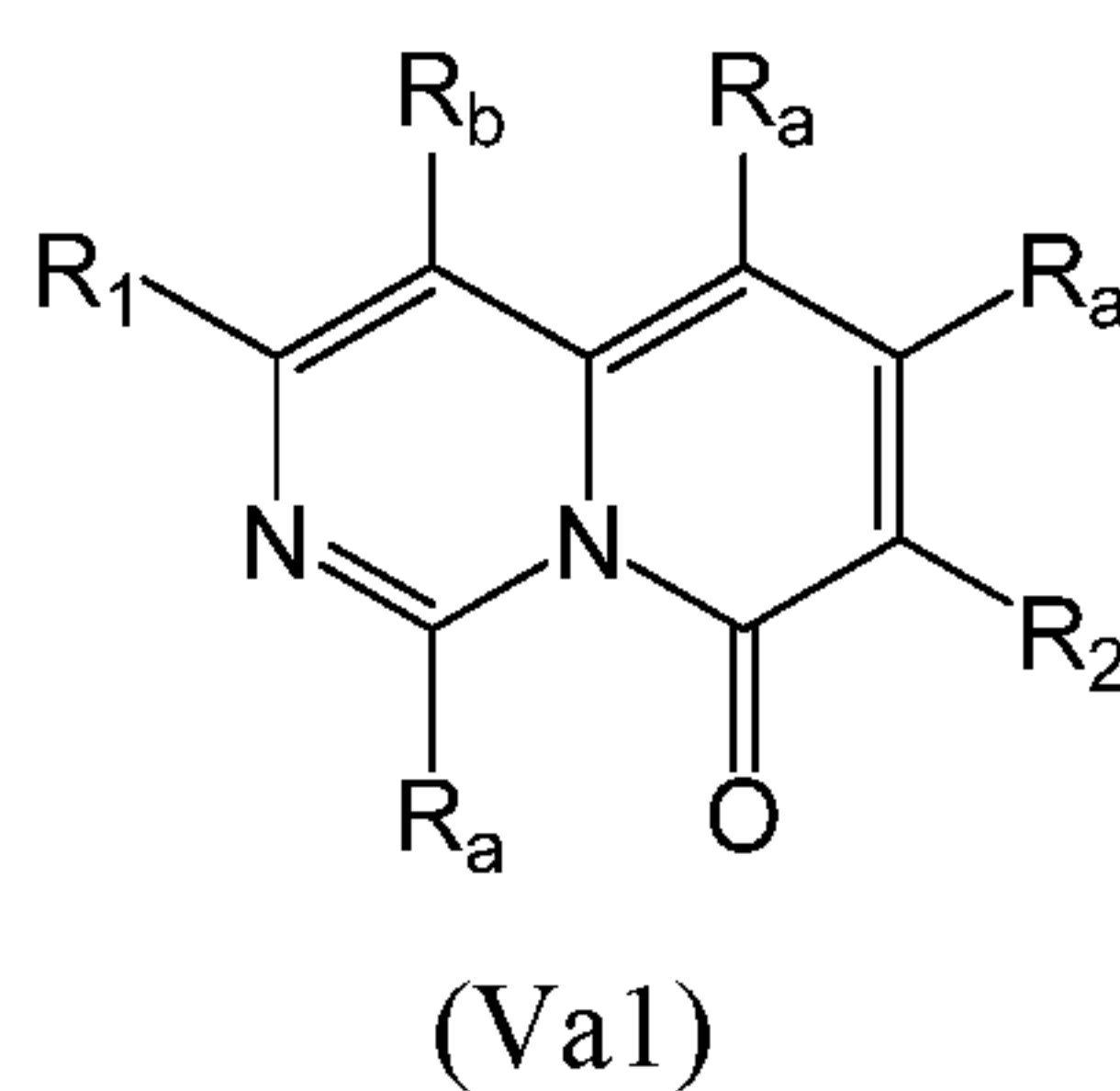
[00588] or a form thereof.

[00589] In one embodiment, the compound of Formula (IVa) used in a method disclosed herein is a compound of Formula (IVa2):



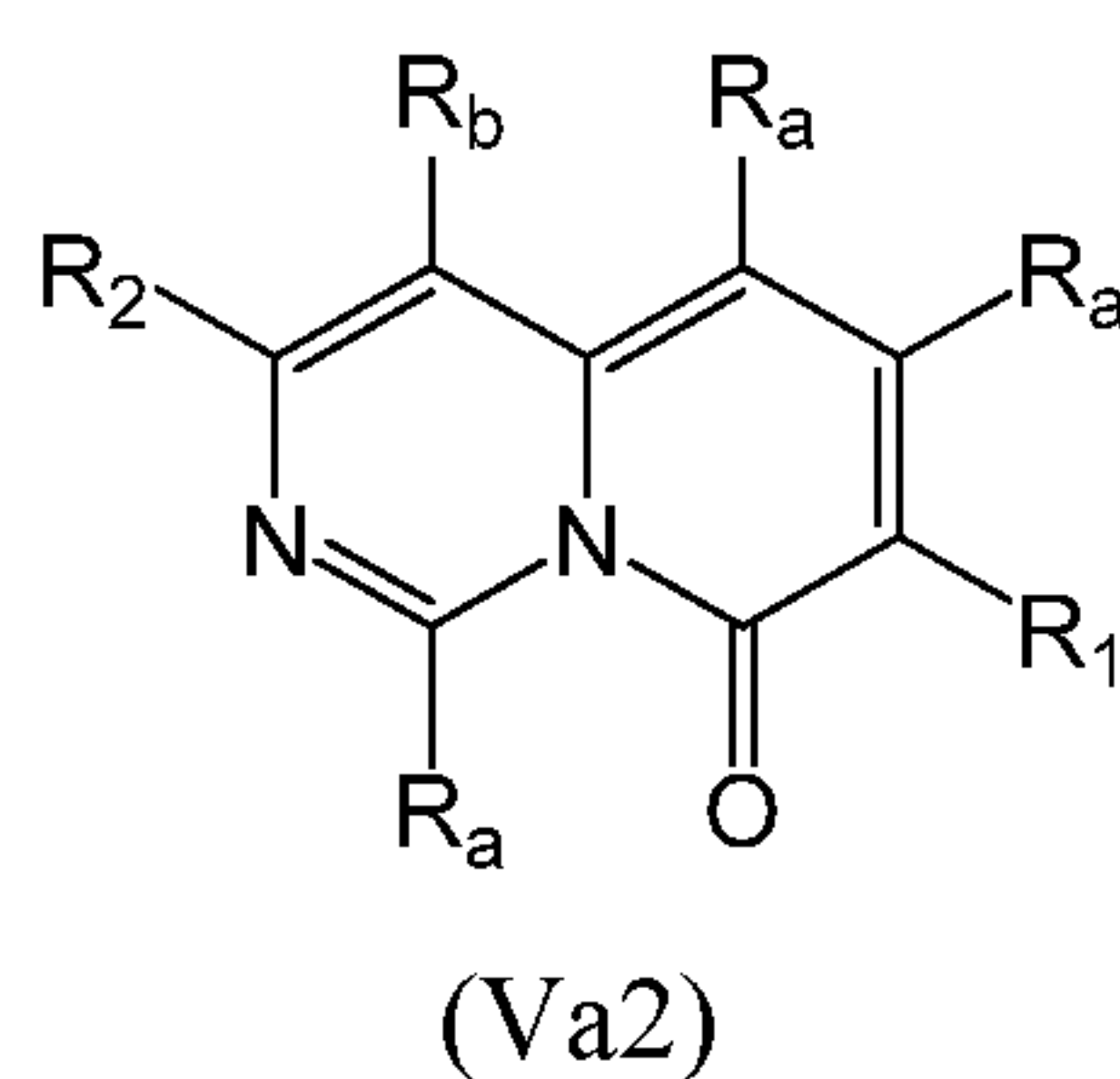
[00590] or a form thereof.

[00591] In one embodiment, the compound of Formula (Va) used in a method disclosed herein is a compound of Formula (Va1):



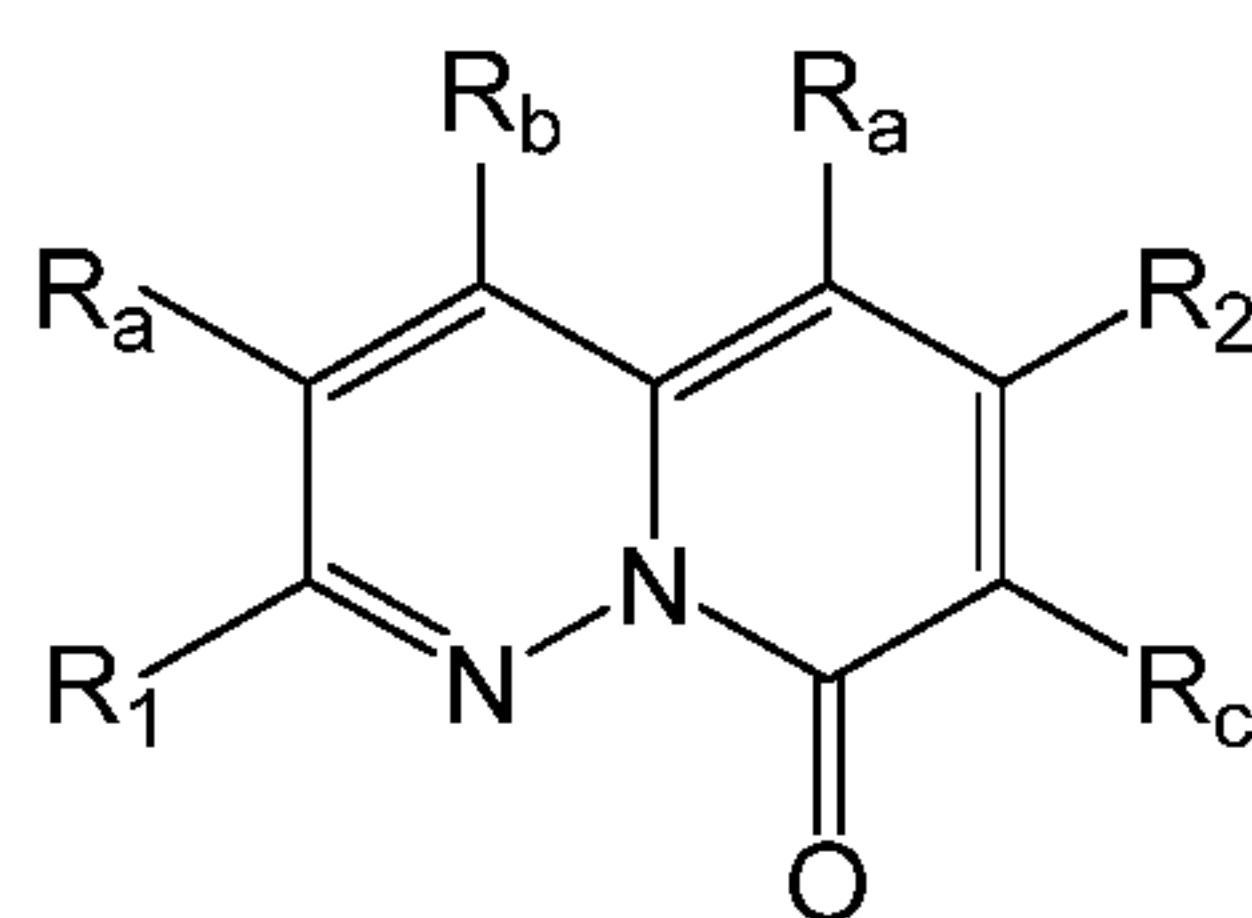
[00592] or a form thereof.

[00593] In one embodiment, the compound of Formula (Va) used in a method disclosed herein is a compound of Formula (Va2):



[00594] or a form thereof.

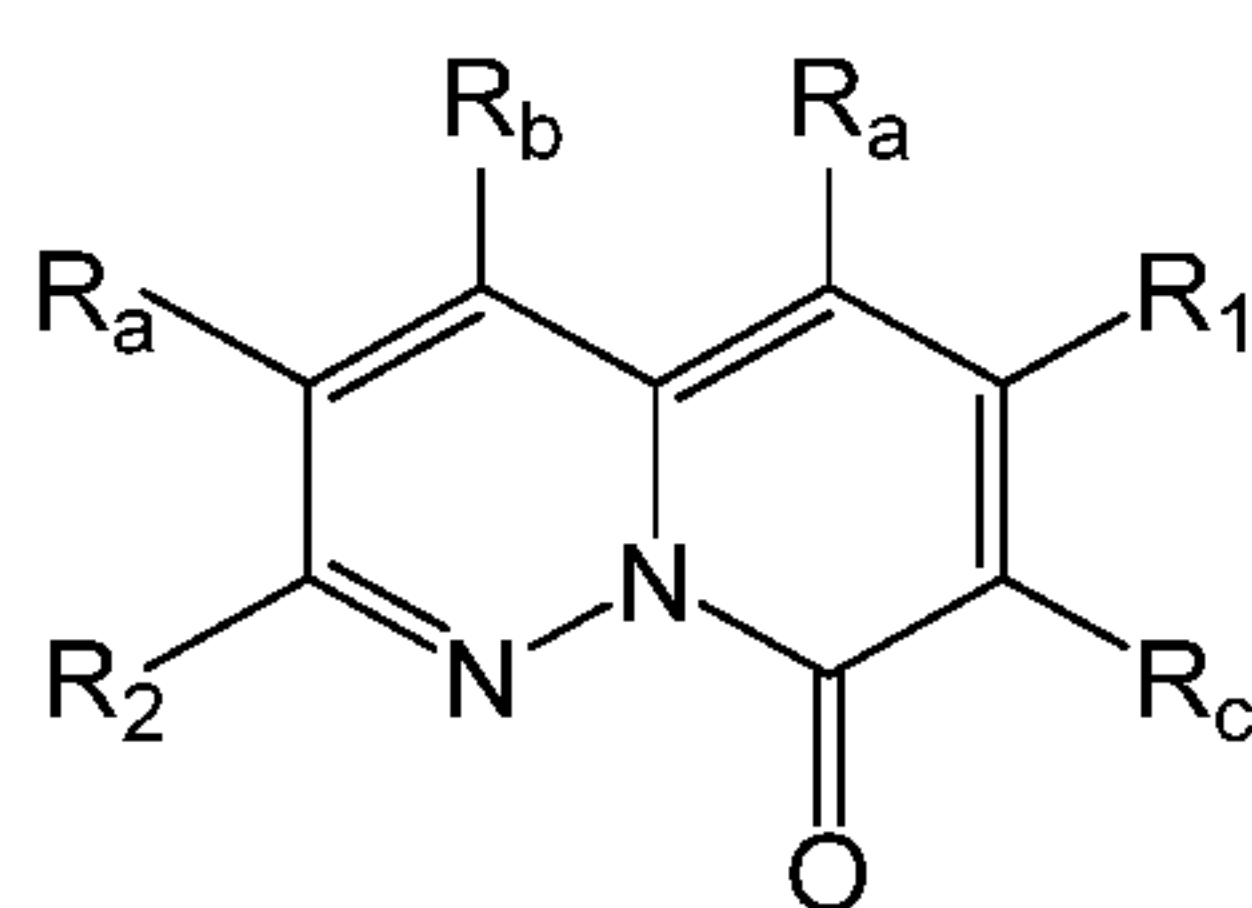
[00595] In one embodiment, the compound of Formula (VIa) used in a method disclosed herein is a compound of Formula (VIa1):



(VIa1)

[00596] or a form thereof.

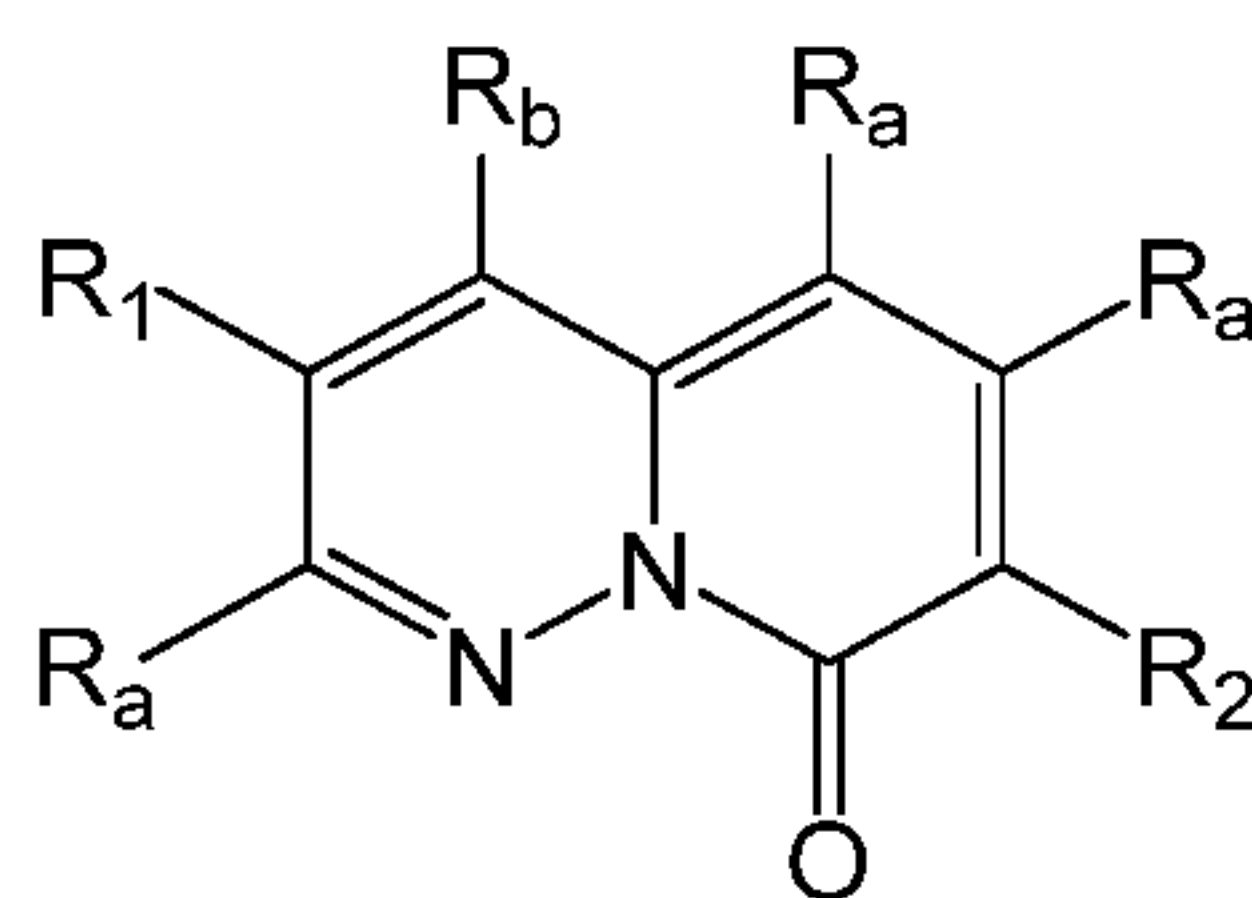
[00597] In one embodiment, the compound of Formula (VIa) used in a method disclosed herein is a compound of Formula (VIa2):



(VIa2)

[00598] or a form thereof.

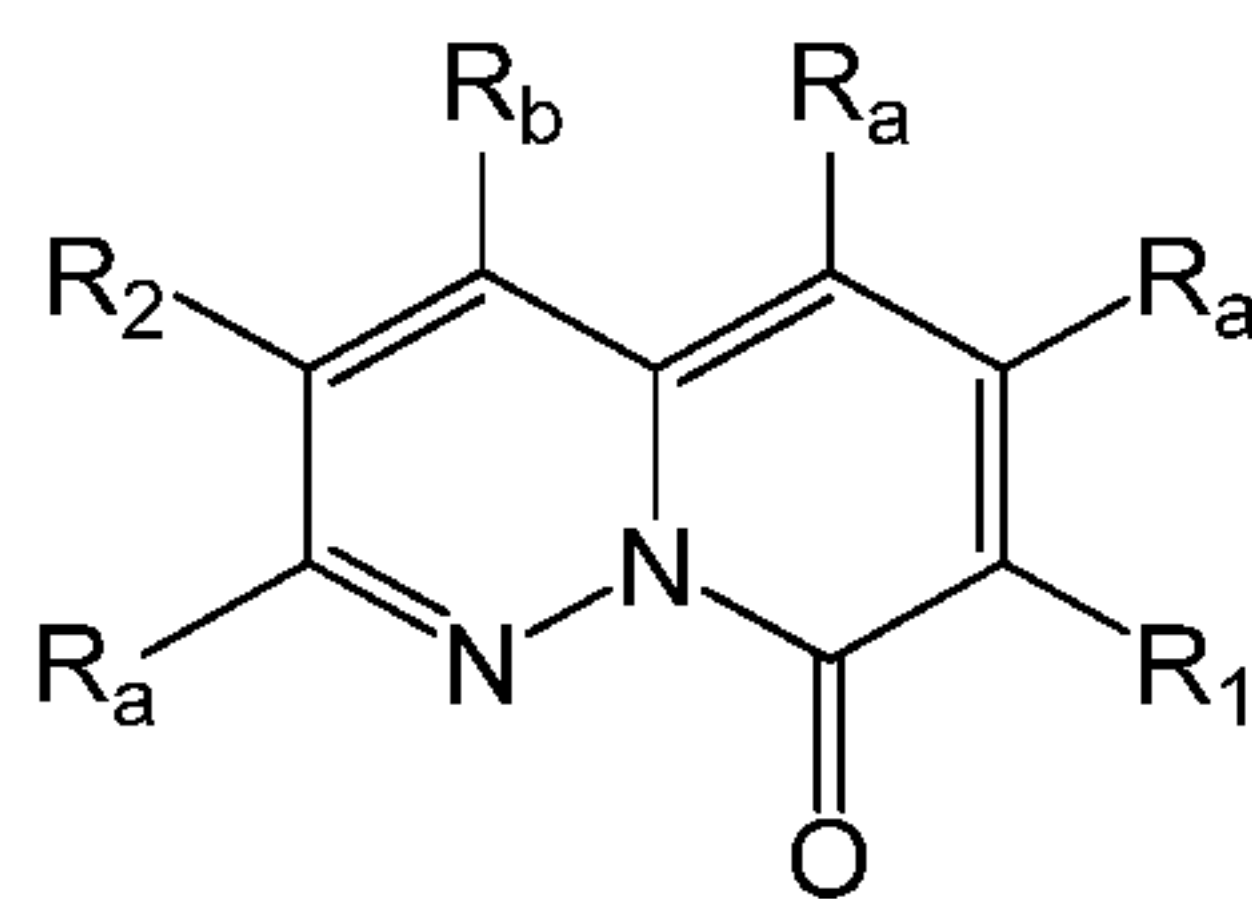
[00599] In one embodiment, the compound of Formula (VIa) used in a method disclosed herein is a compound of Formula (VIa3):



(VIa3)

[00600] or a form thereof.

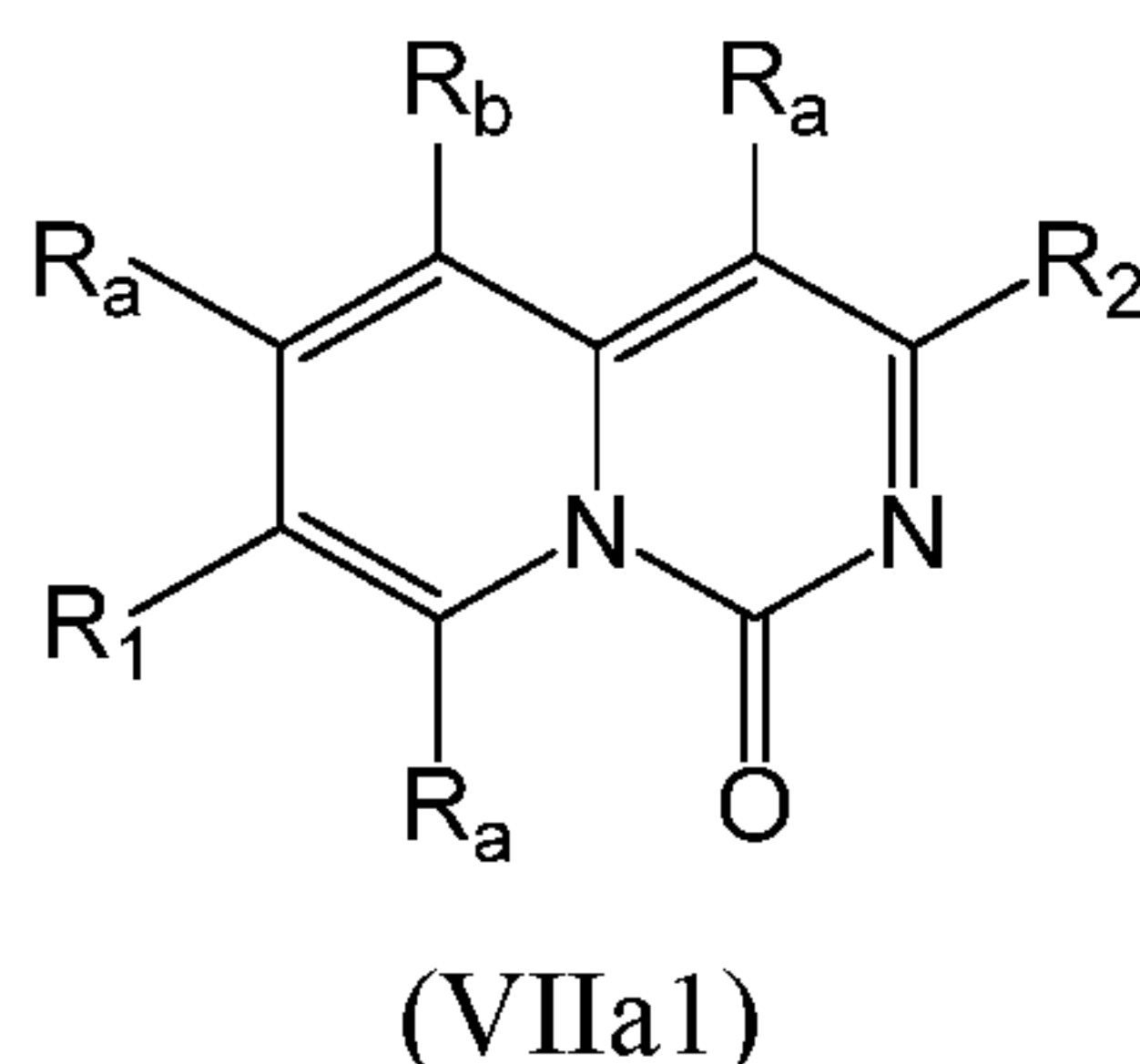
[00601] In one embodiment, the compound of Formula (VIa) used in a method disclosed herein is a compound of Formula (VIa4):



(VIa4)

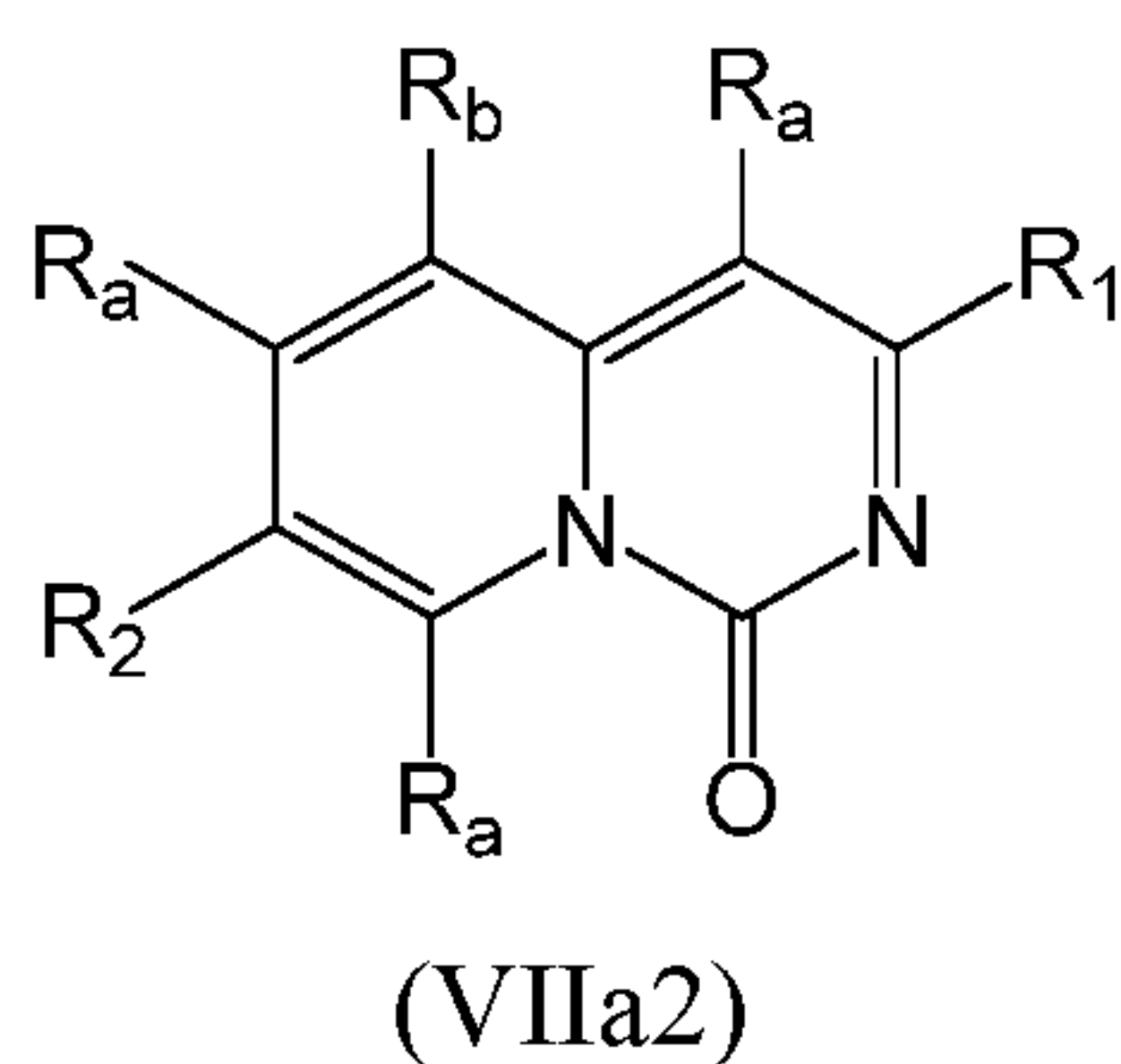
[00602] or a form thereof.

[00603] In one embodiment, the compound of Formula (VIIa) used in a method disclosed herein is a compound of Formula (VIIa1):



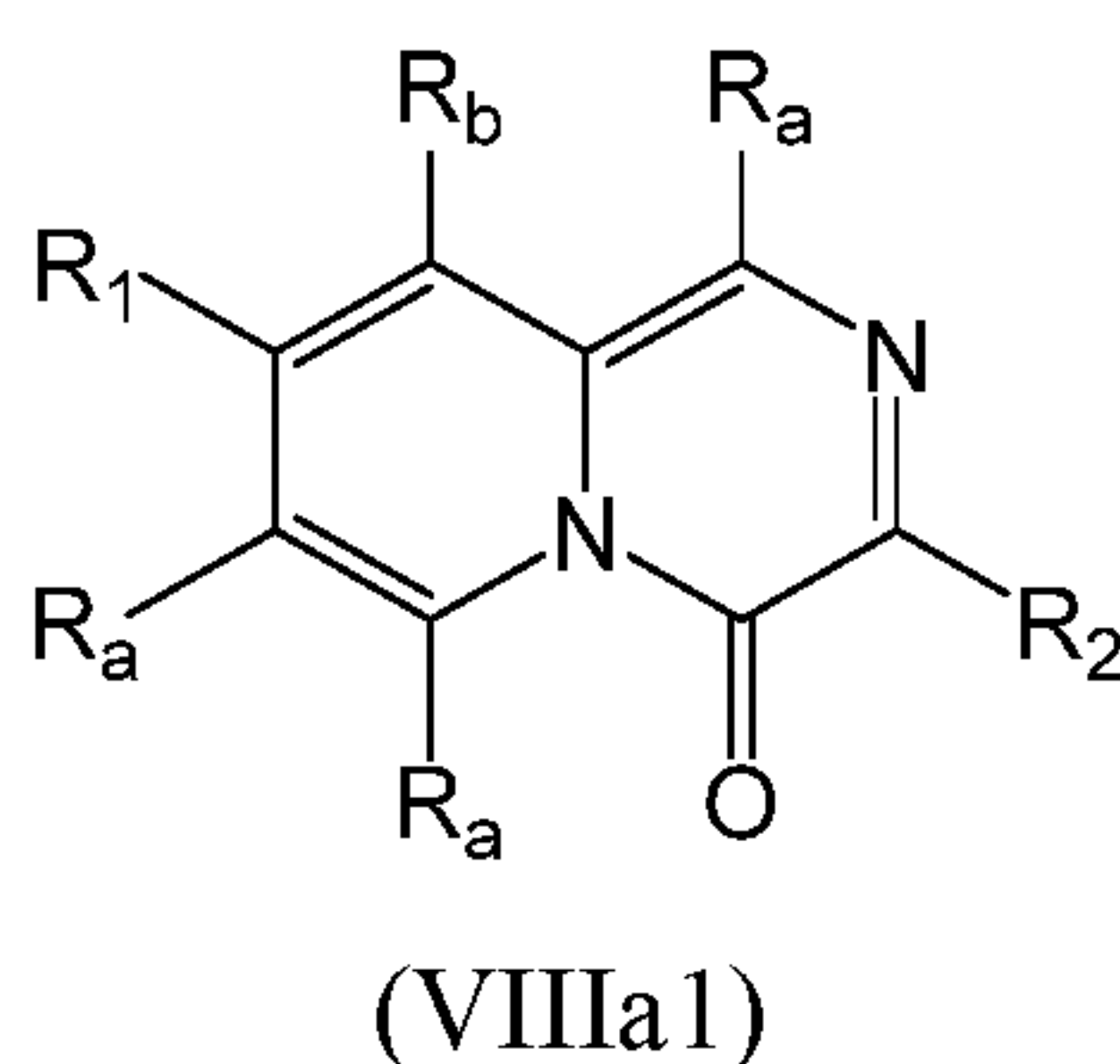
[00604] or a form thereof.

[00605] In one embodiment, the compound of Formula (VIIa) used in a method disclosed herein is a compound of Formula (VIIa2):



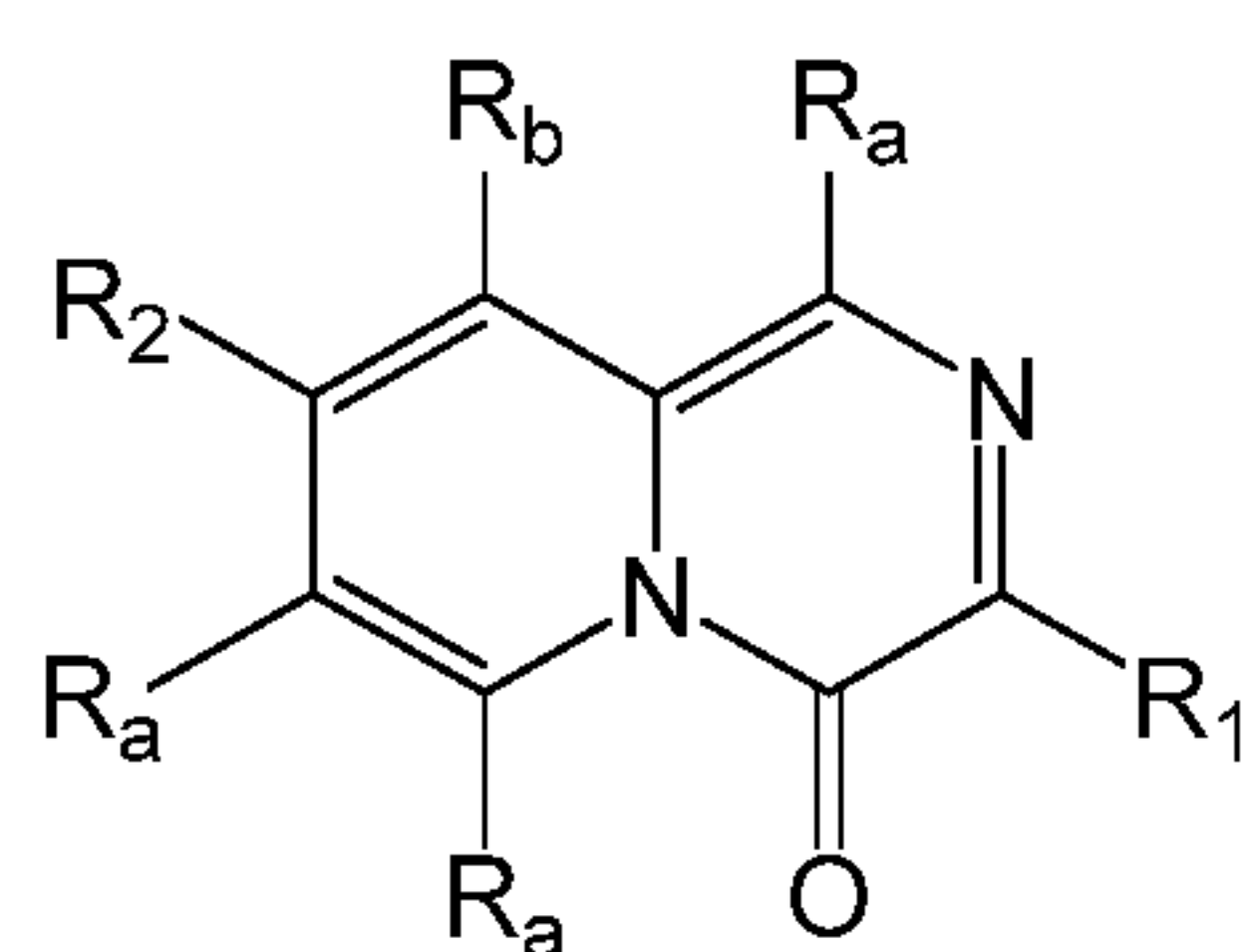
[00606] or a form thereof.

[00607] In one embodiment, the compound of Formula (VIIIa) used in a method disclosed herein is a compound of Formula (VIIIa1):



[00608] or a form thereof.

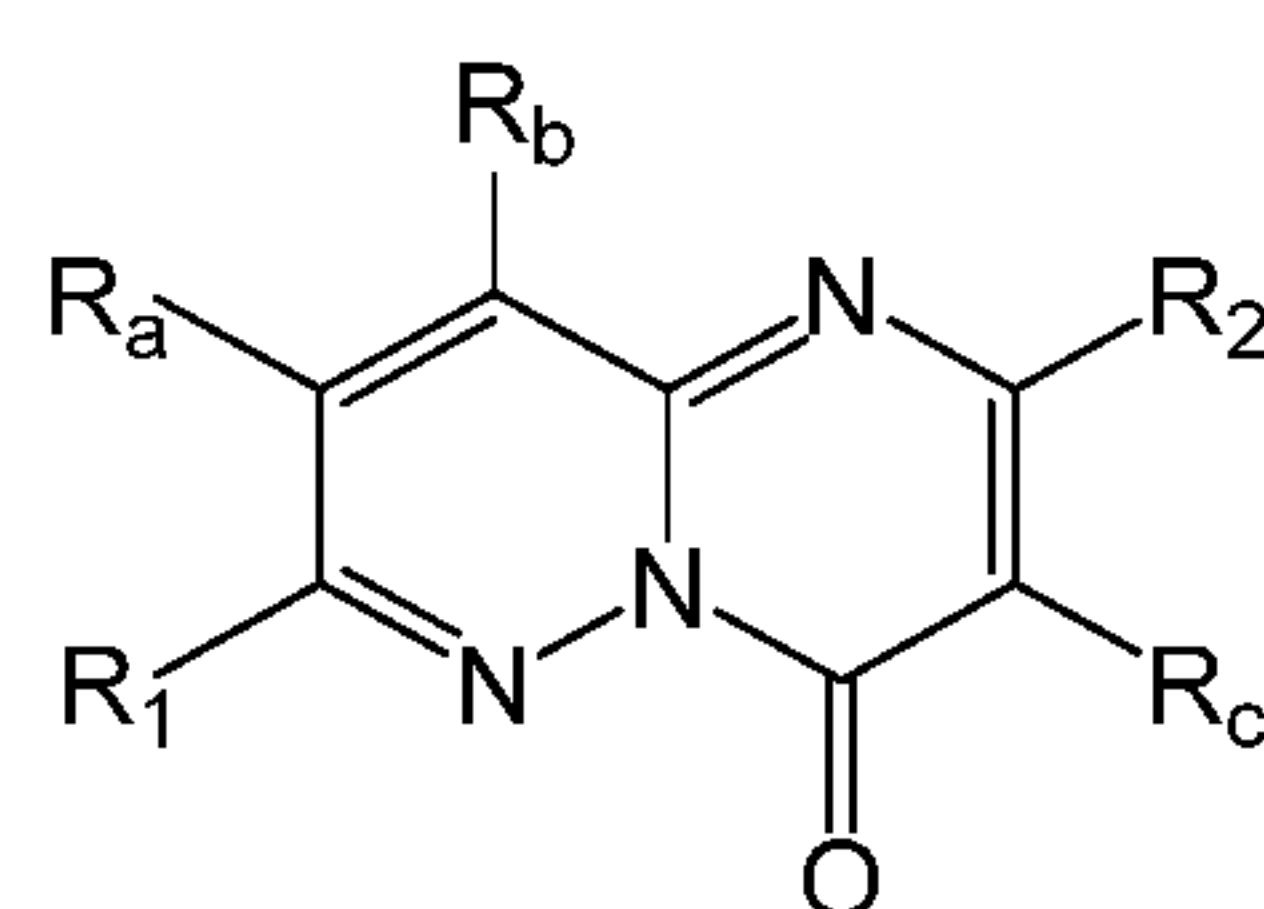
[00609] In one embodiment, the compound of Formula (VIIIa) used in a method disclosed herein is a compound of Formula (VIIIa2):



(VIIIa2)

[00610] or a form thereof.

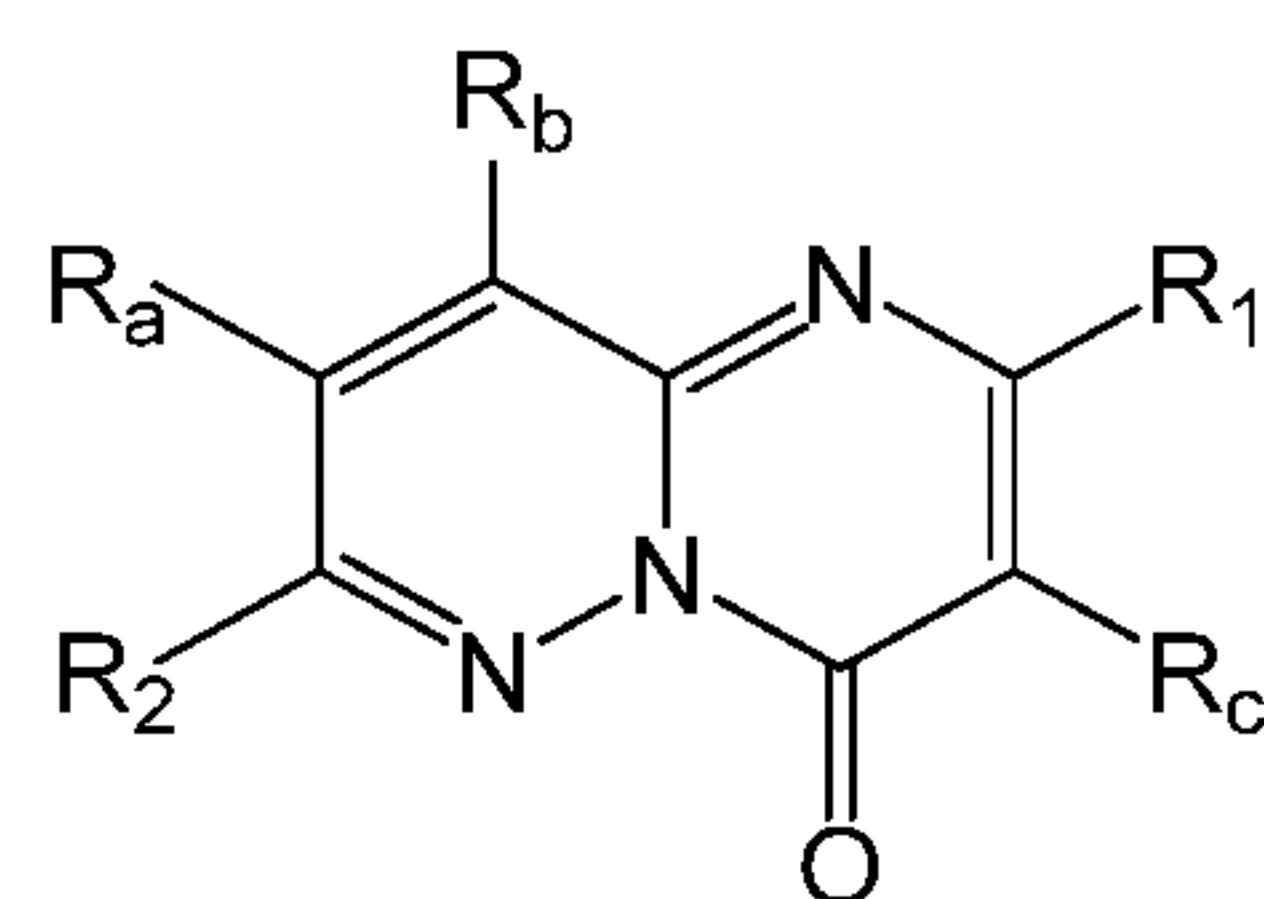
[00611] In one embodiment, the compound of Formula (IXa) used in a method disclosed herein is a compound of Formula (IXa1):



(IXa1)

[00612] or a form thereof.

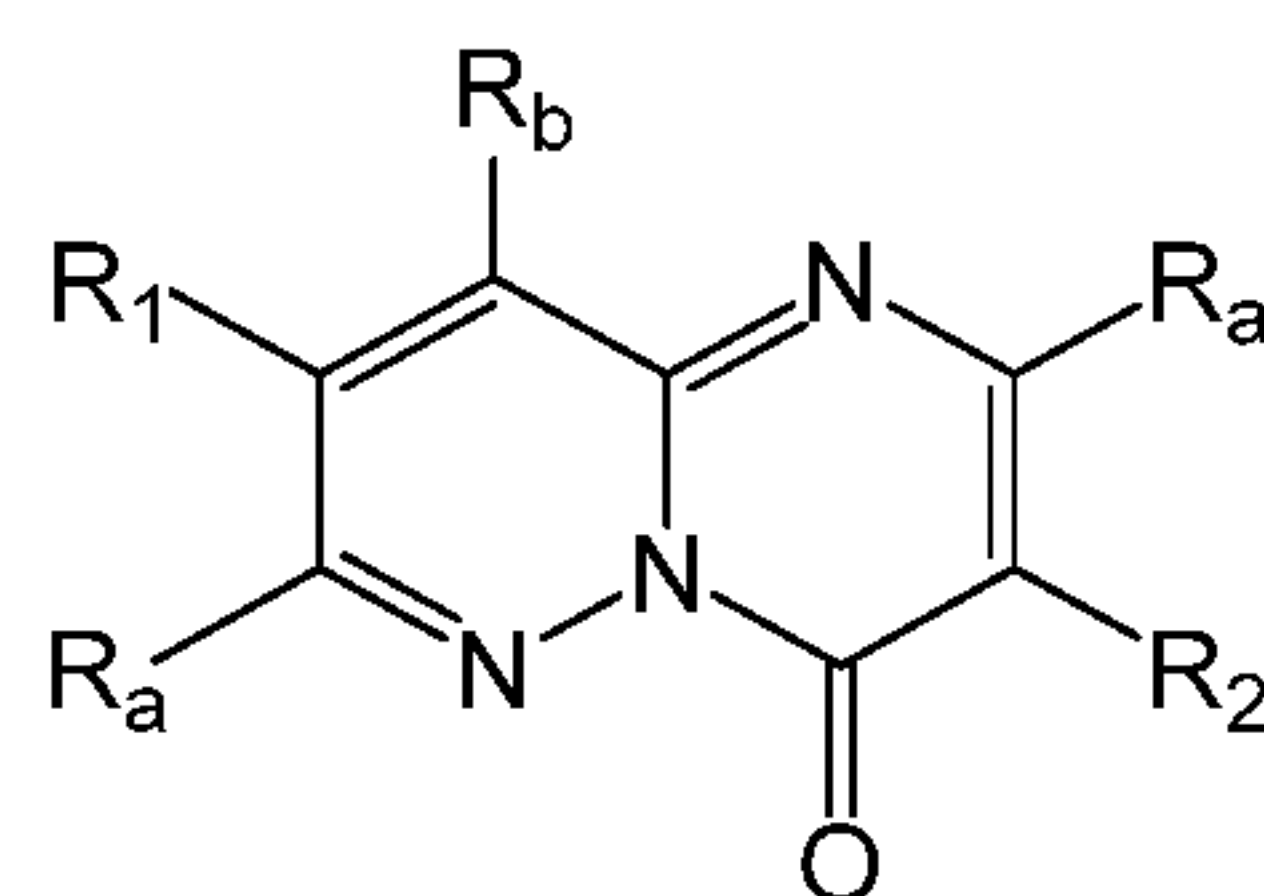
[00613] In one embodiment, the compound of Formula (IXa) used in a method disclosed herein is a compound of Formula (IXa2):



(IXa2)

[00614] or a form thereof.

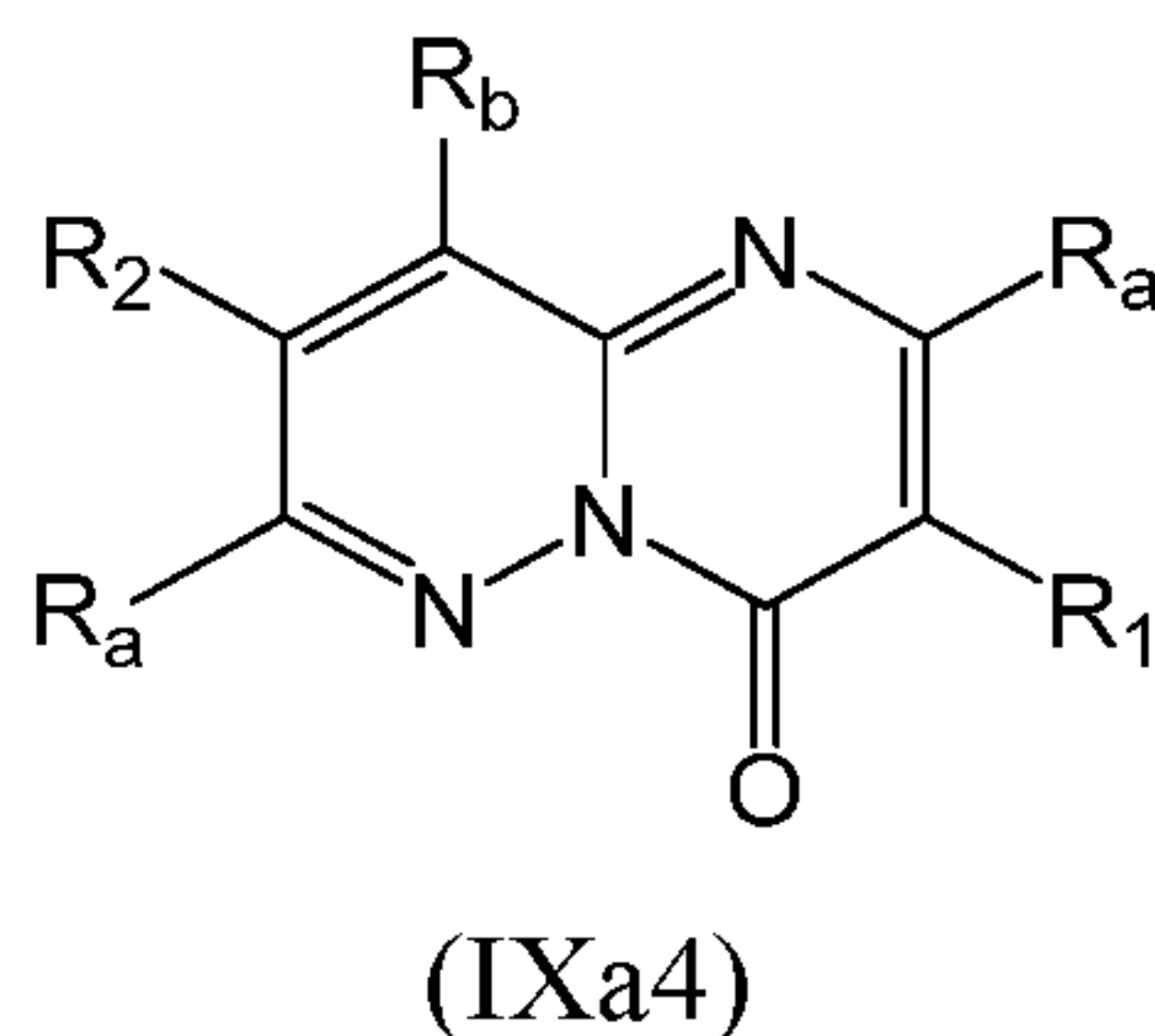
[00615] In one embodiment, the compound of Formula (IXa) used in a method disclosed herein is a compound of Formula (IXa3):



(IXa3)

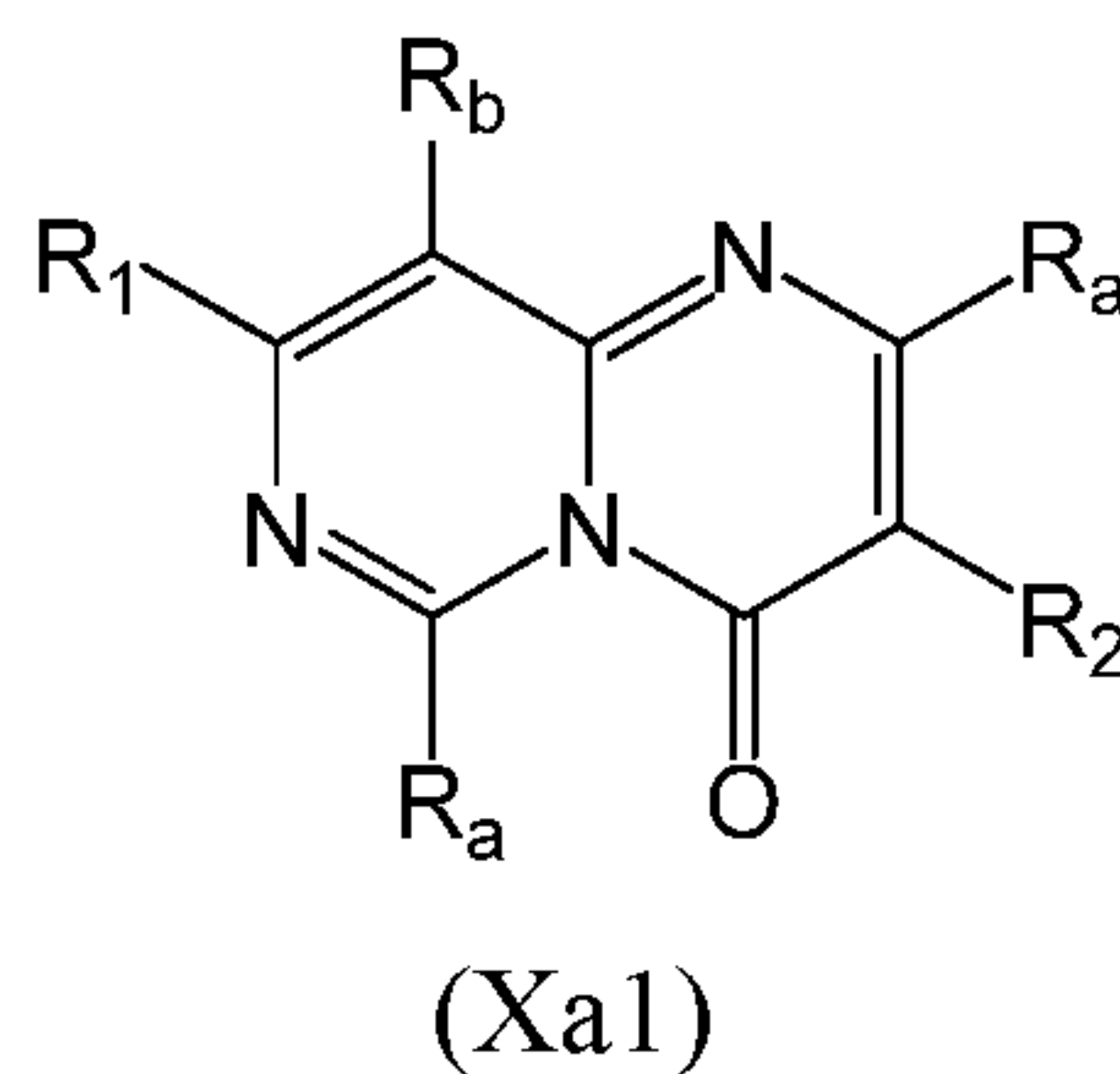
[00616] or a form thereof.

[00617] In one embodiment, the compound of Formula (IXa) used in a method disclosed herein is a compound of Formula (IXa4):



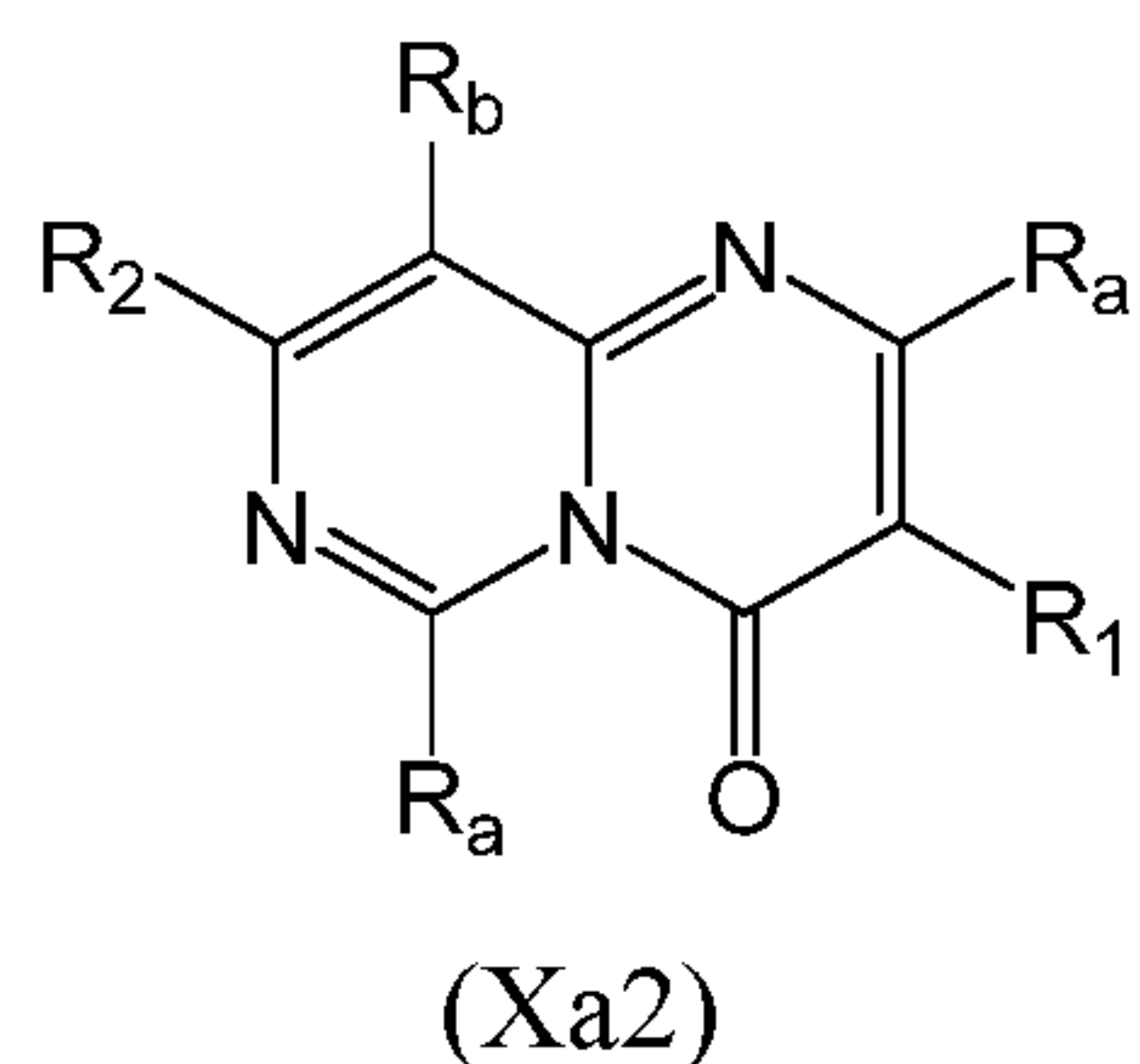
[00618] or a form thereof.

[00619] In one embodiment, the compound of Formula (Xa) used in a method disclosed herein is a compound of Formula (Xa1):



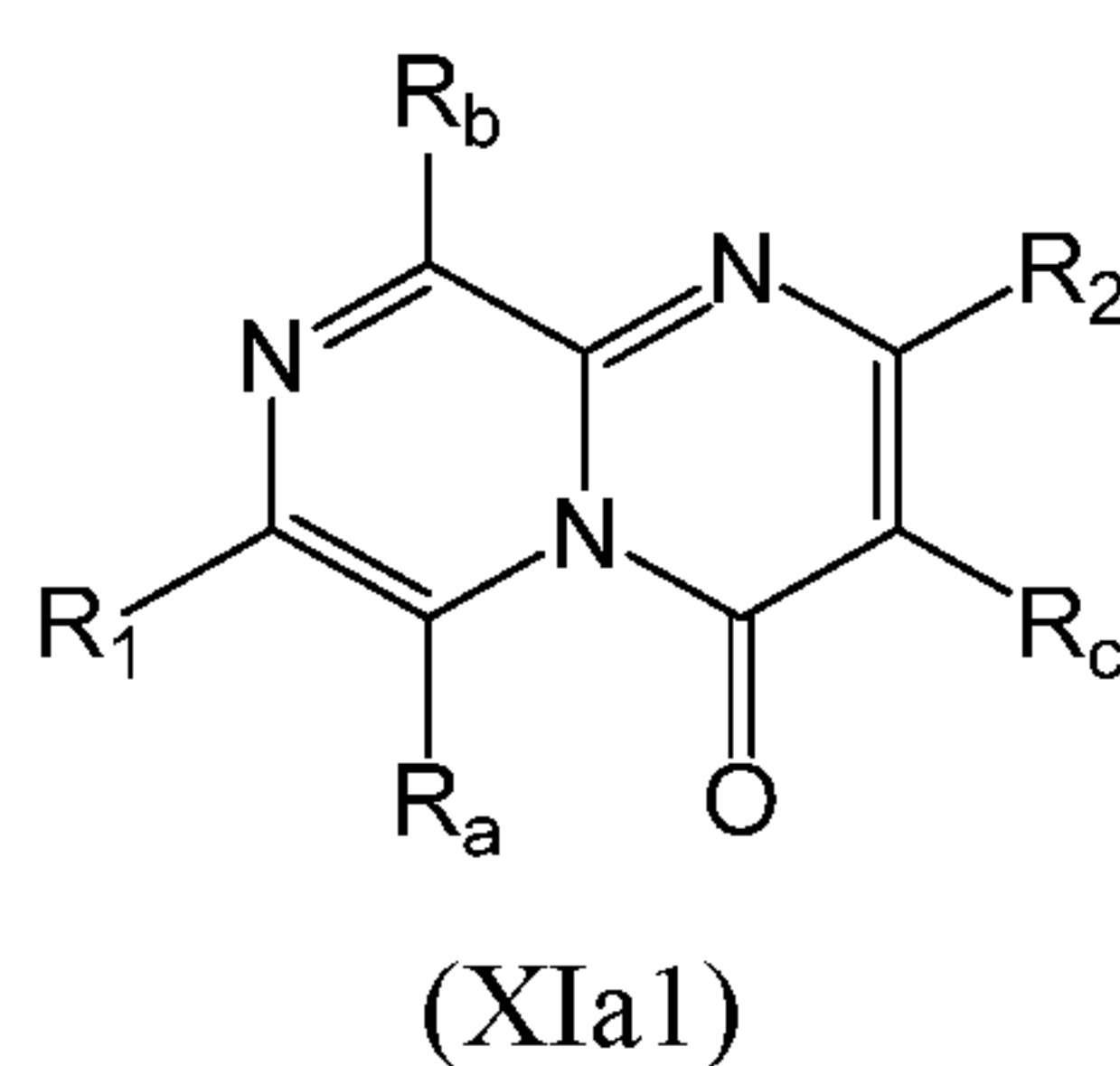
[00471] or a form thereof.

[00472] In one embodiment, the compound of Formula (Xa) used in a method disclosed herein is a compound of Formula (Xa2):



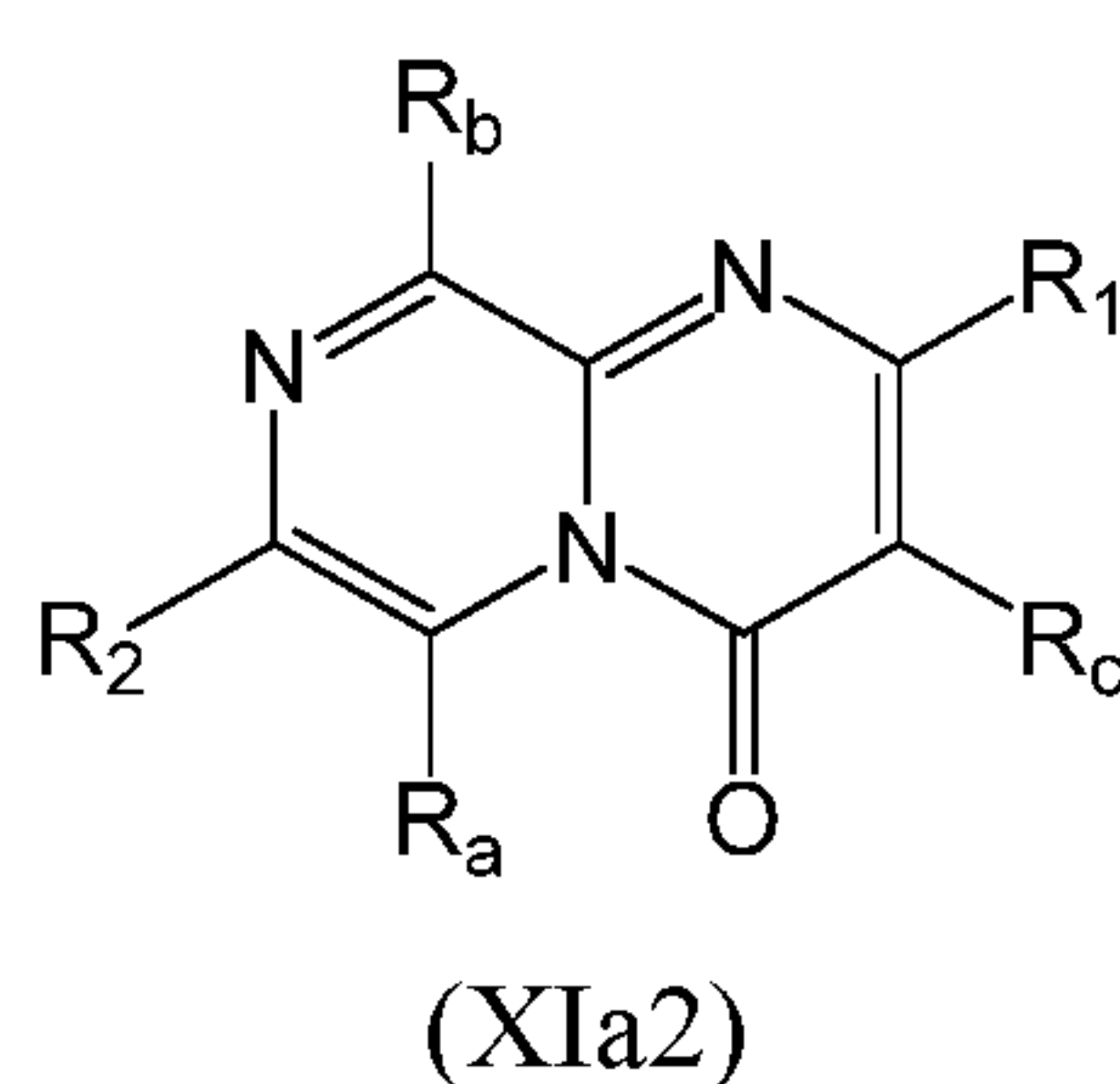
[00620] or a form thereof.

[00621] In one embodiment, the compound of Formula (XIa) used in a method disclosed herein is a compound of Formula (XIa1):



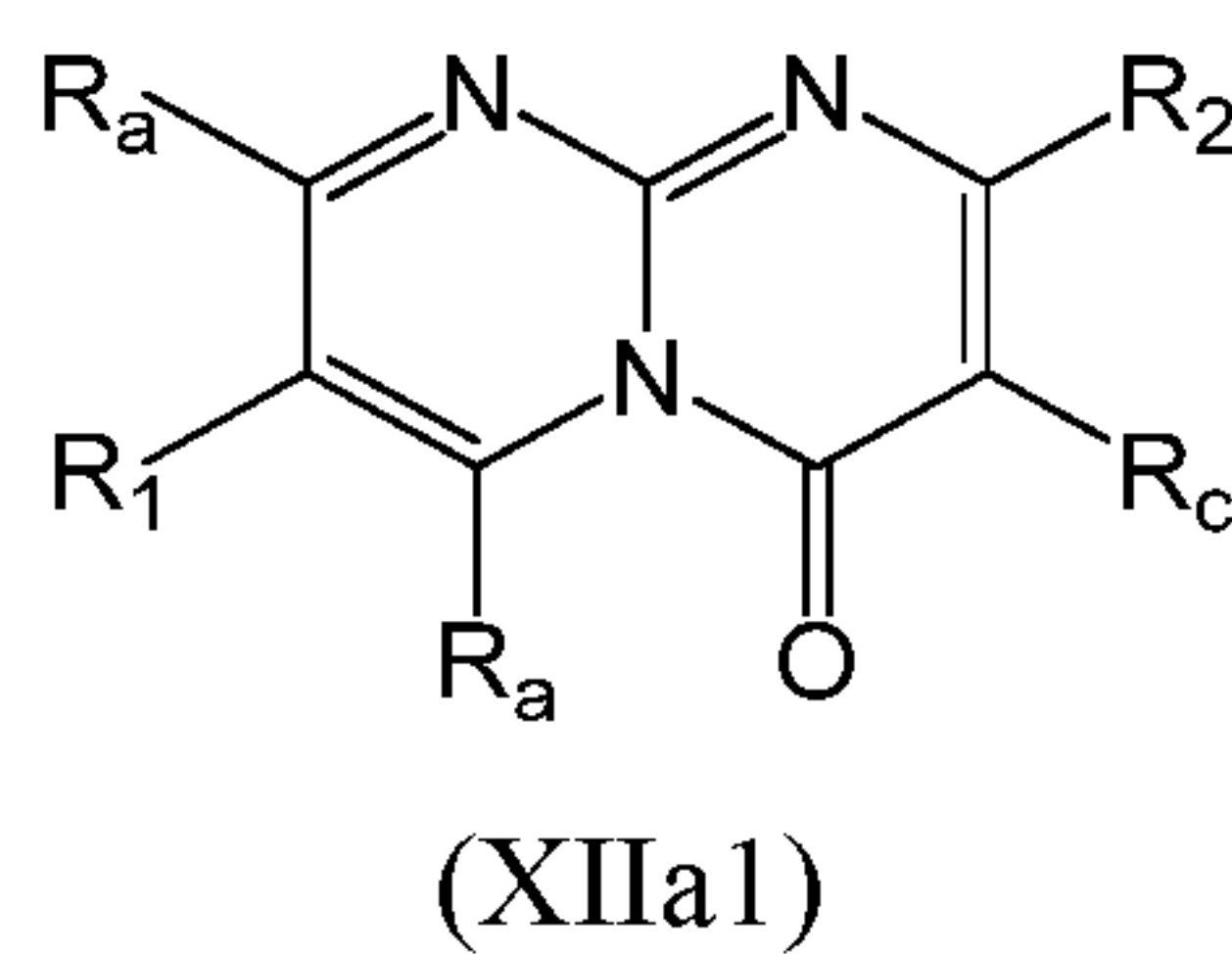
[00622] or a form thereof.

[00623] In one embodiment, the compound of Formula (XIa) used in a method disclosed herein is a compound of Formula (XIa2):



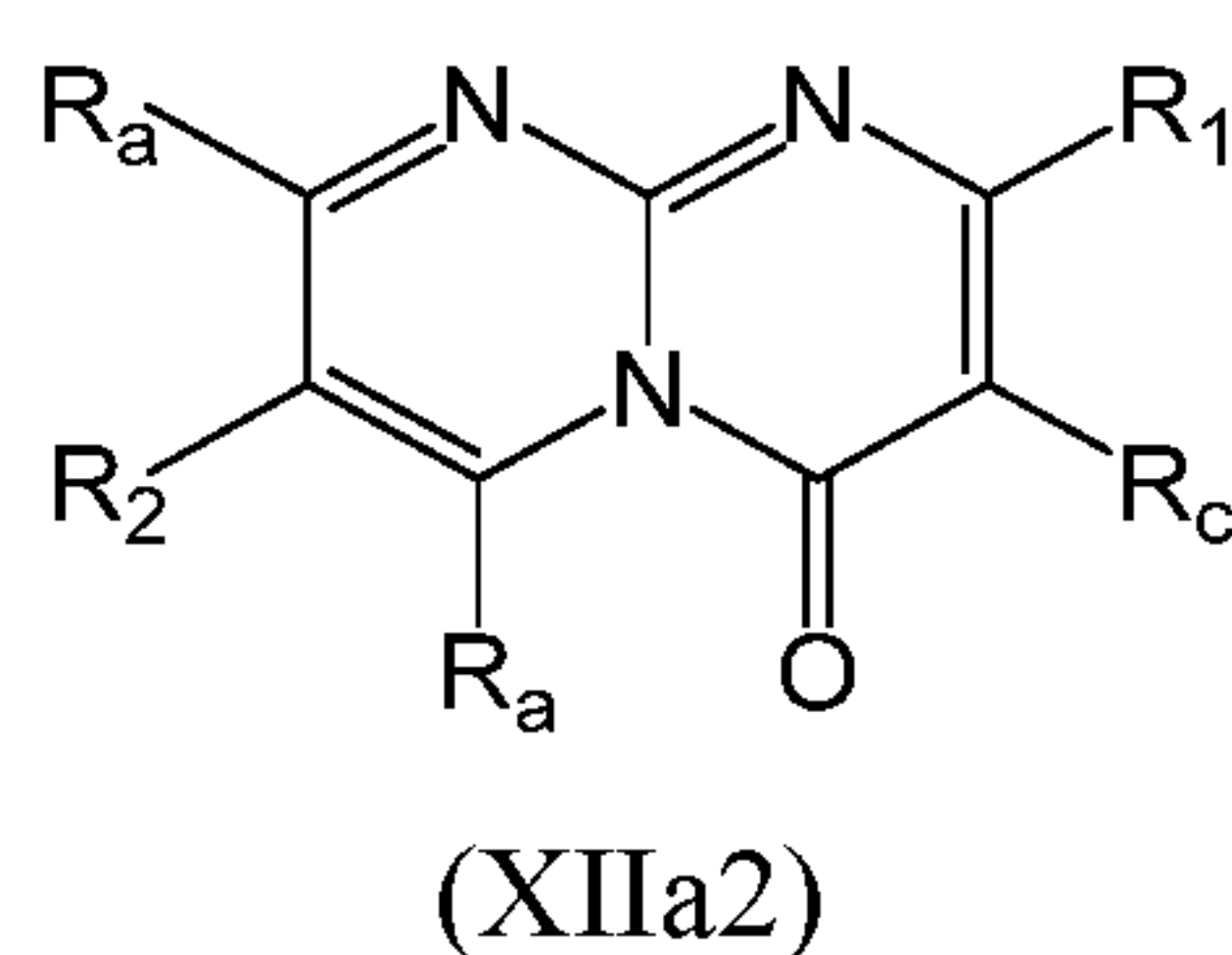
[00624] or a form thereof.

[00625] In one embodiment, the compound of Formula (XIIa) used in a method disclosed herein is a compound of Formula (XIIa1):



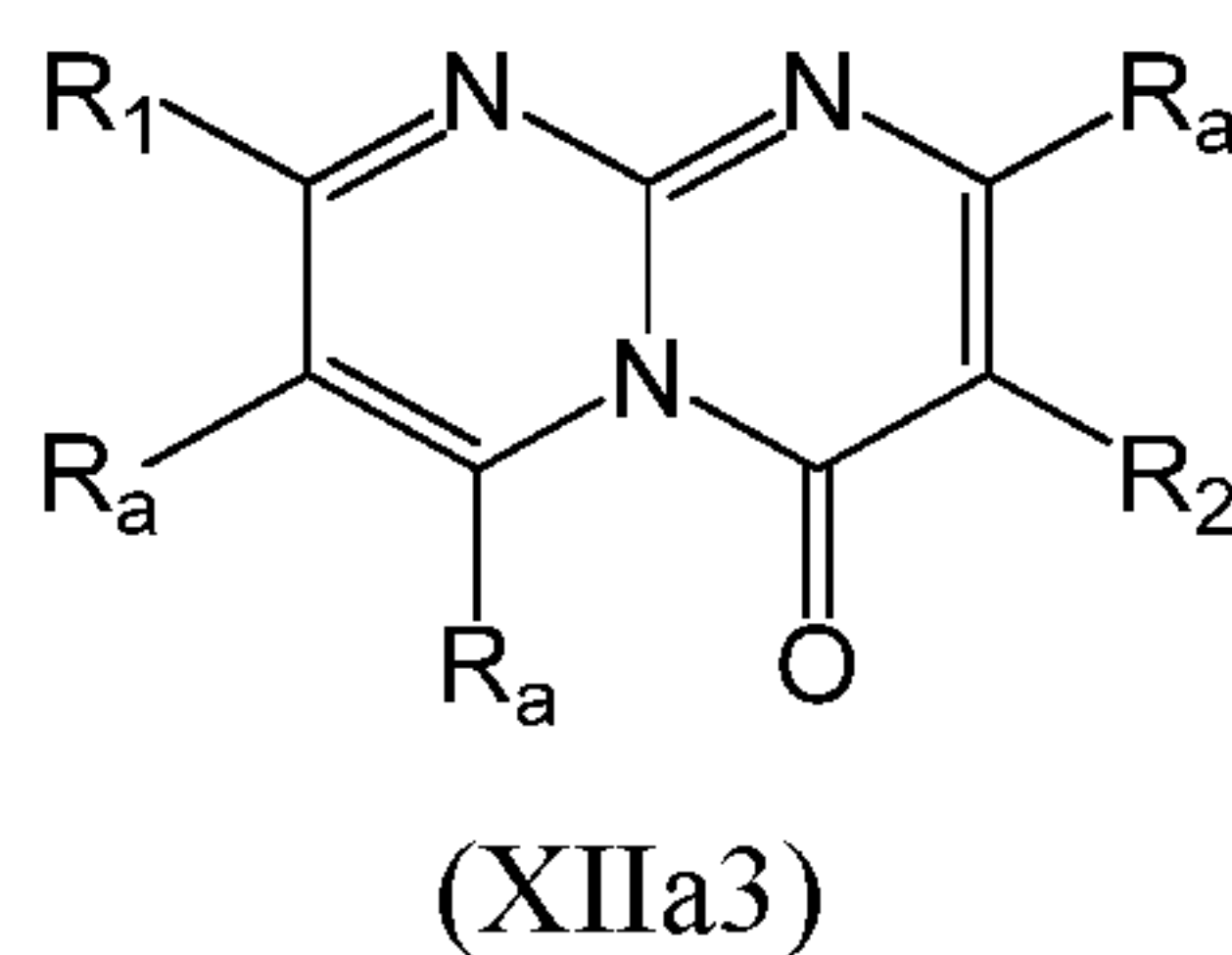
[00626] or a form thereof.

[00627] In one embodiment, the compound of Formula (XIIa) used in a method disclosed herein is a compound of Formula (XIIa2):



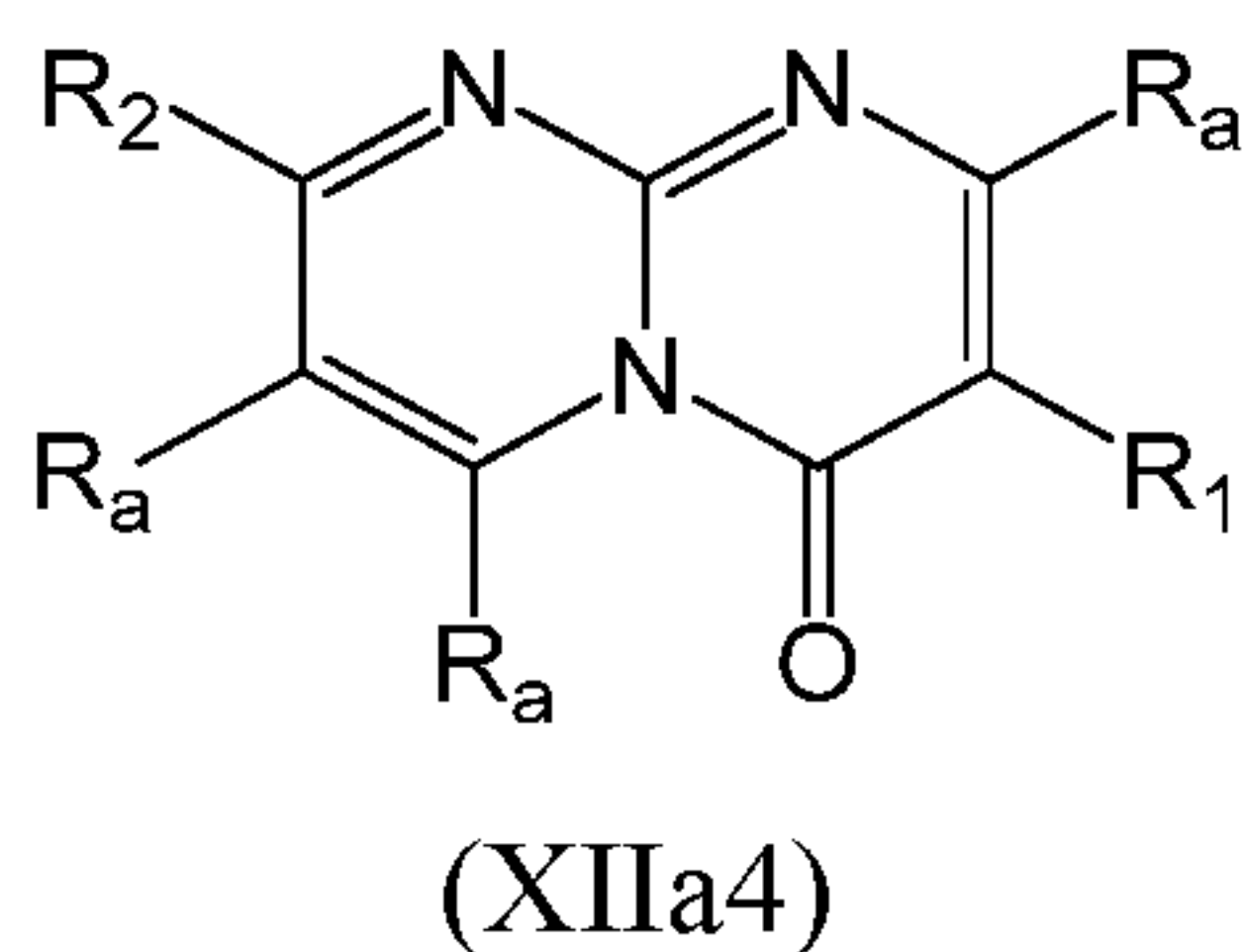
[00628] or a form thereof.

[00629] In one embodiment, the compound of Formula (XIIa) used in a method disclosed herein is a compound of Formula (XIIa3):



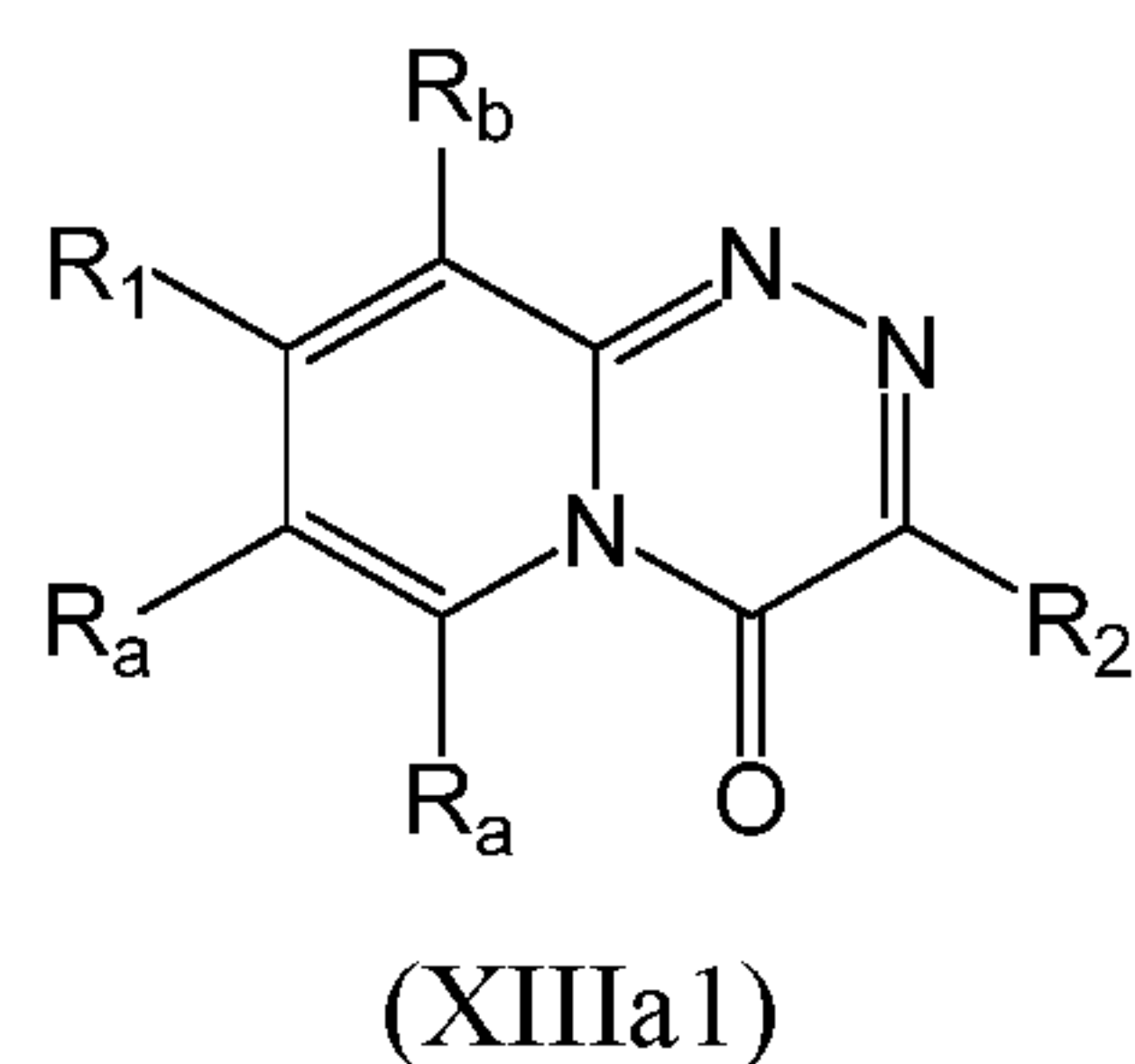
[00630] or a form thereof.

[00631] In one embodiment, the compound of Formula (XIIa) used in a method disclosed herein is a compound of Formula (XIIa4):



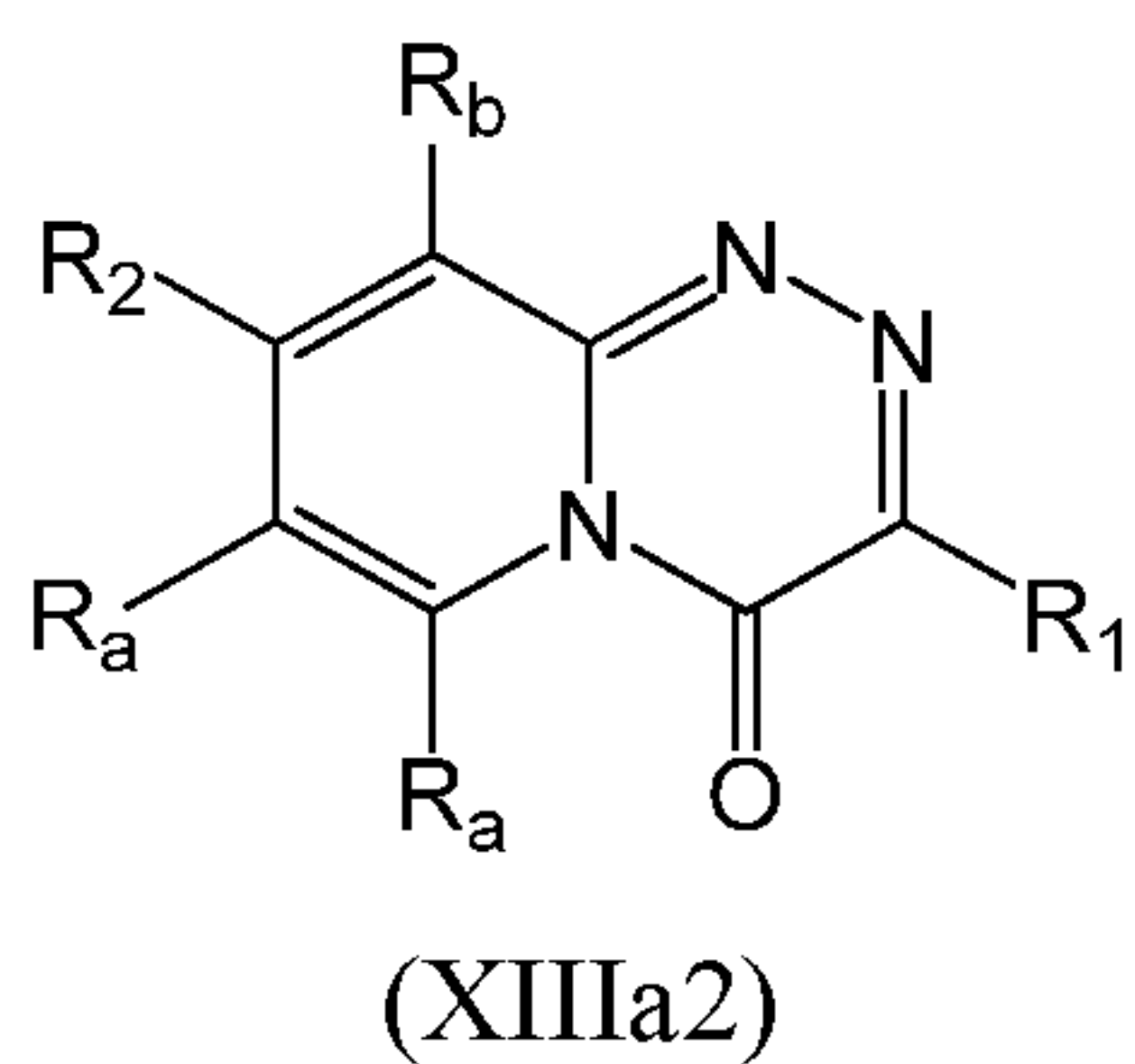
[00632] or a form thereof.

[00633] In one embodiment, the compound of Formula (XIIIa) used in a method disclosed herein is a compound of Formula (XIIIa1):



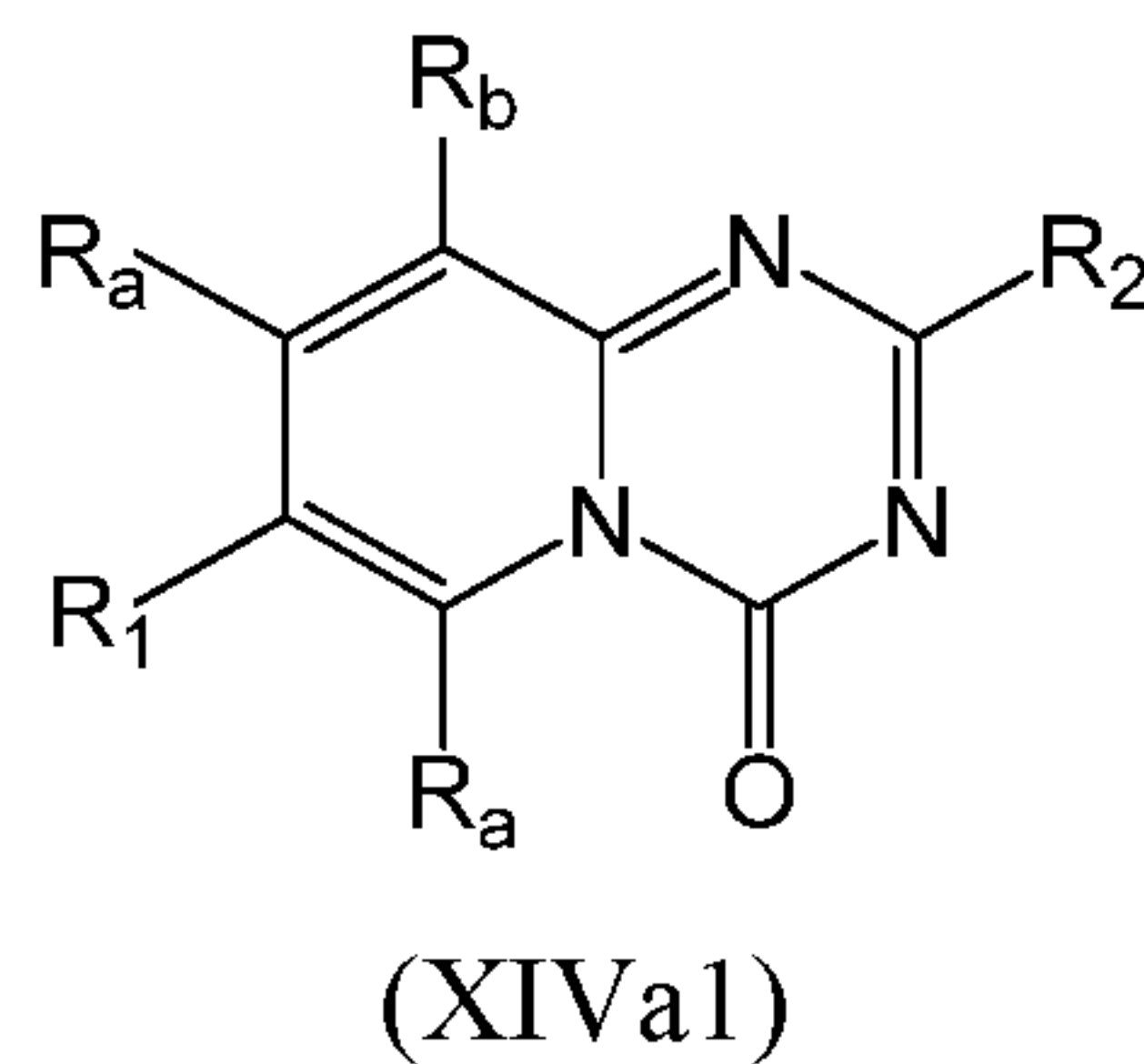
[00634] or a form thereof.

[00635] In one embodiment, the compound of Formula (XIIIa) used in a method disclosed herein is a compound of Formula (XIIIa2):



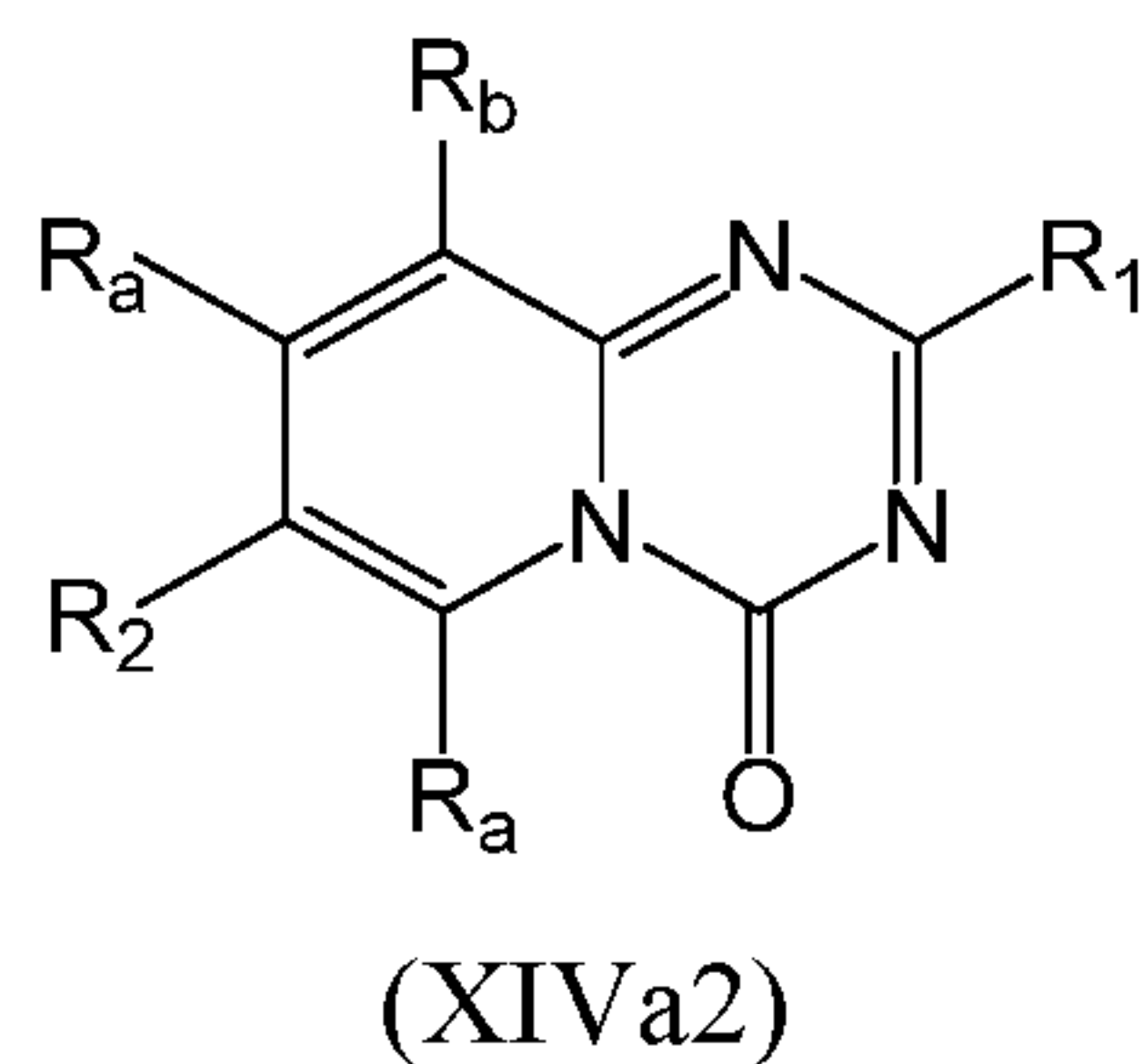
[00636] or a form thereof.

[00637] In one embodiment, the compound of Formula (XIVa) used in a method disclosed herein is a compound of Formula (XIVa1):



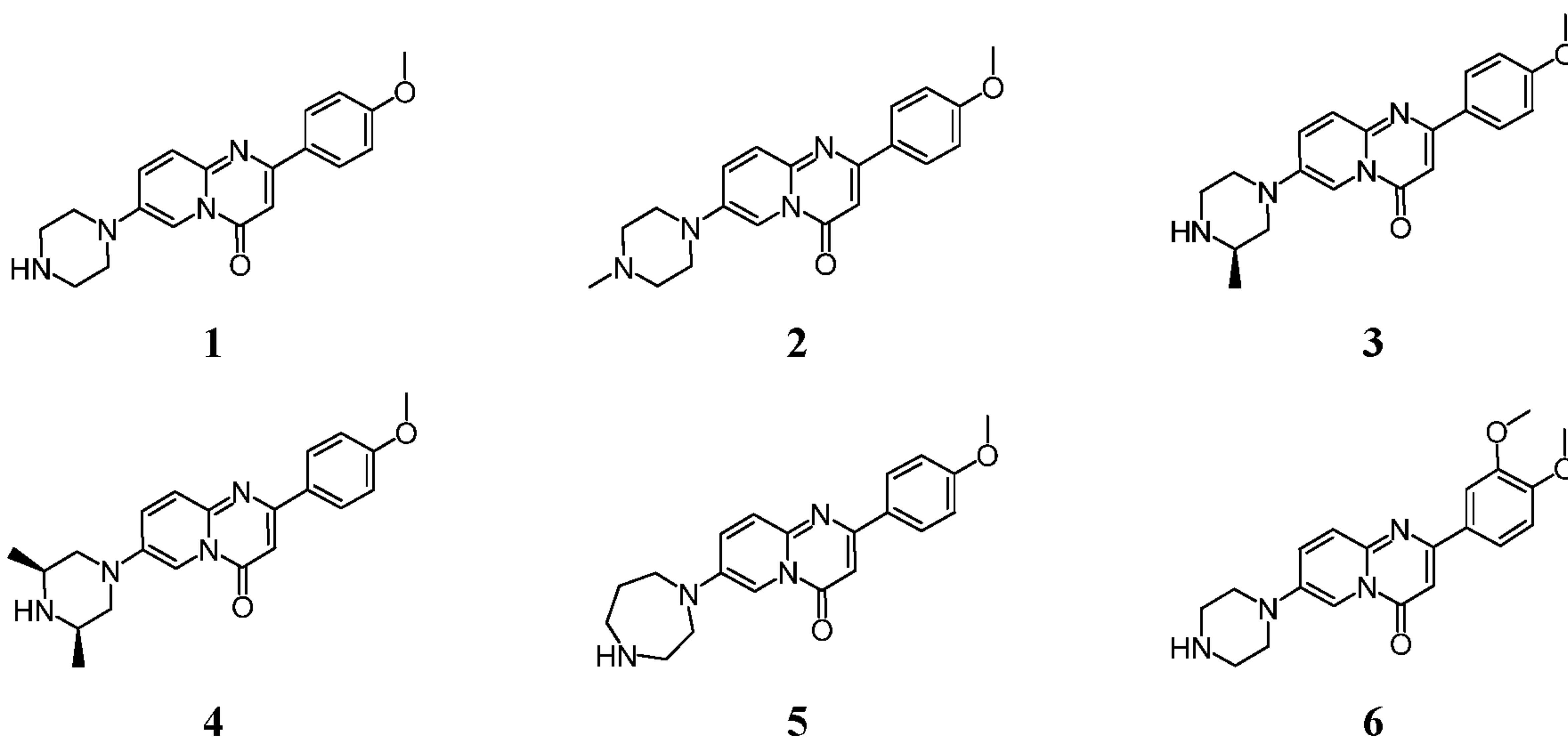
[00638] or a form thereof.

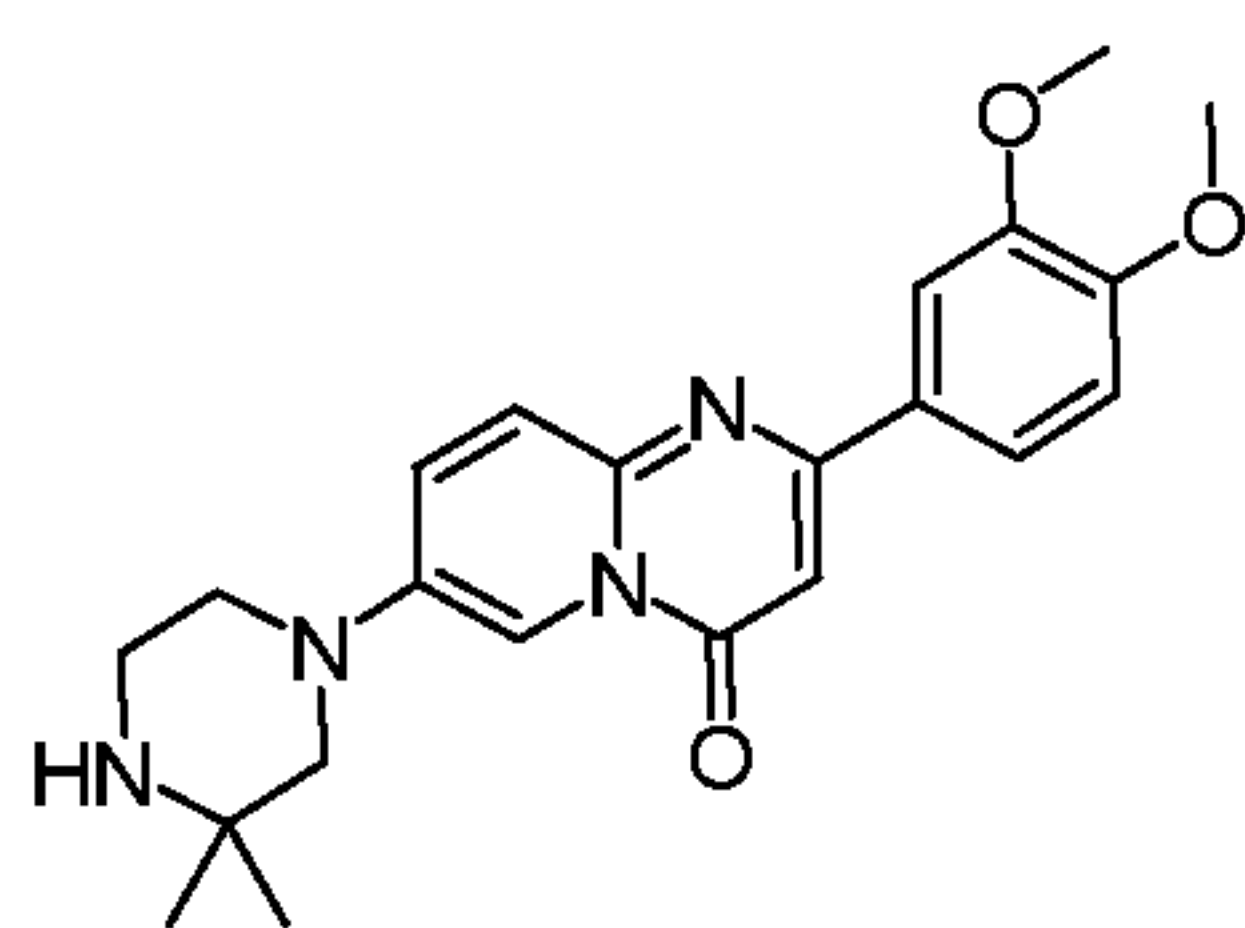
[00639] In one embodiment, the compound of Formula (XIVa) used in a method disclosed herein is a compound of Formula (XIVa2):



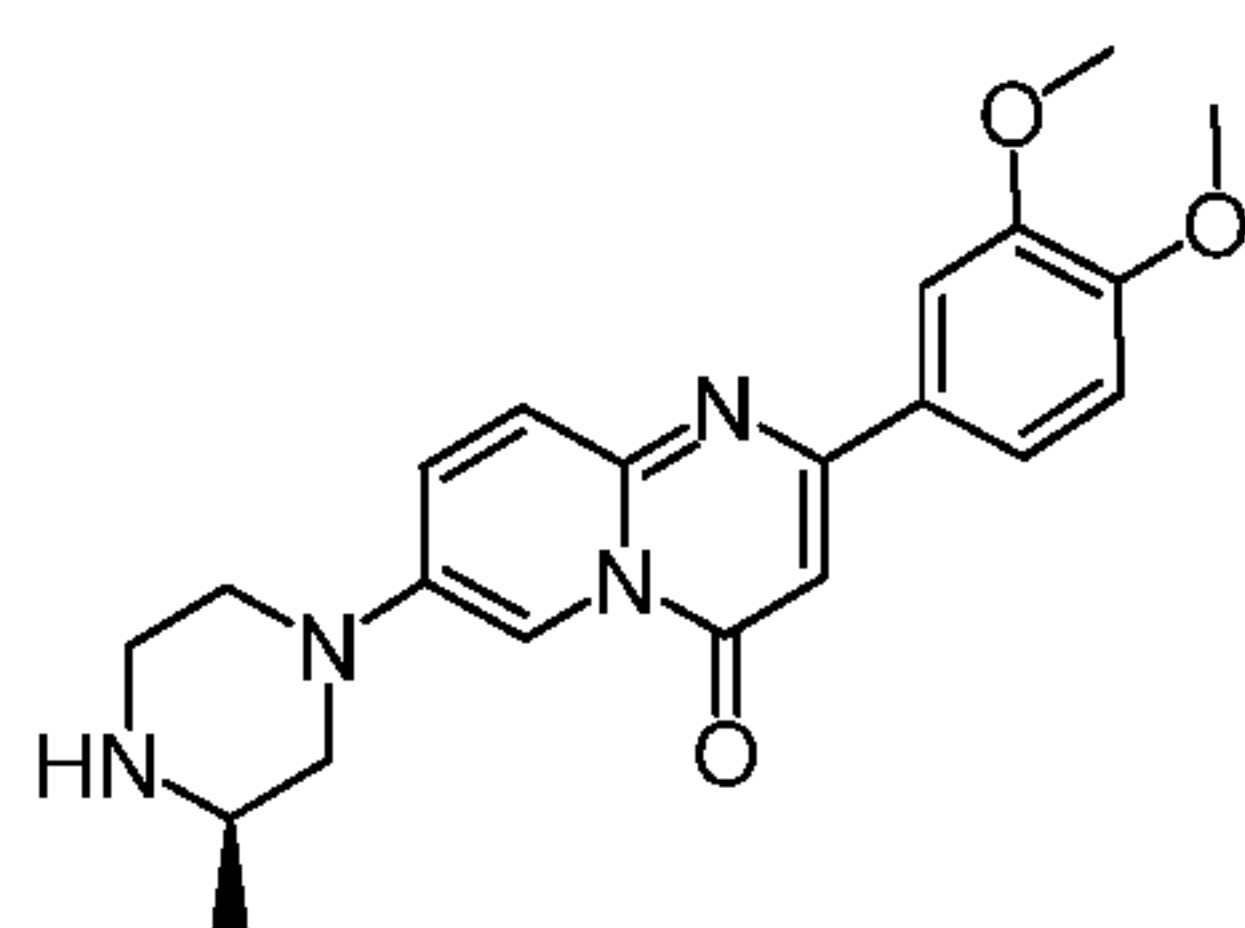
[00640] or a form thereof.

[00641] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound selected from the group consisting of:

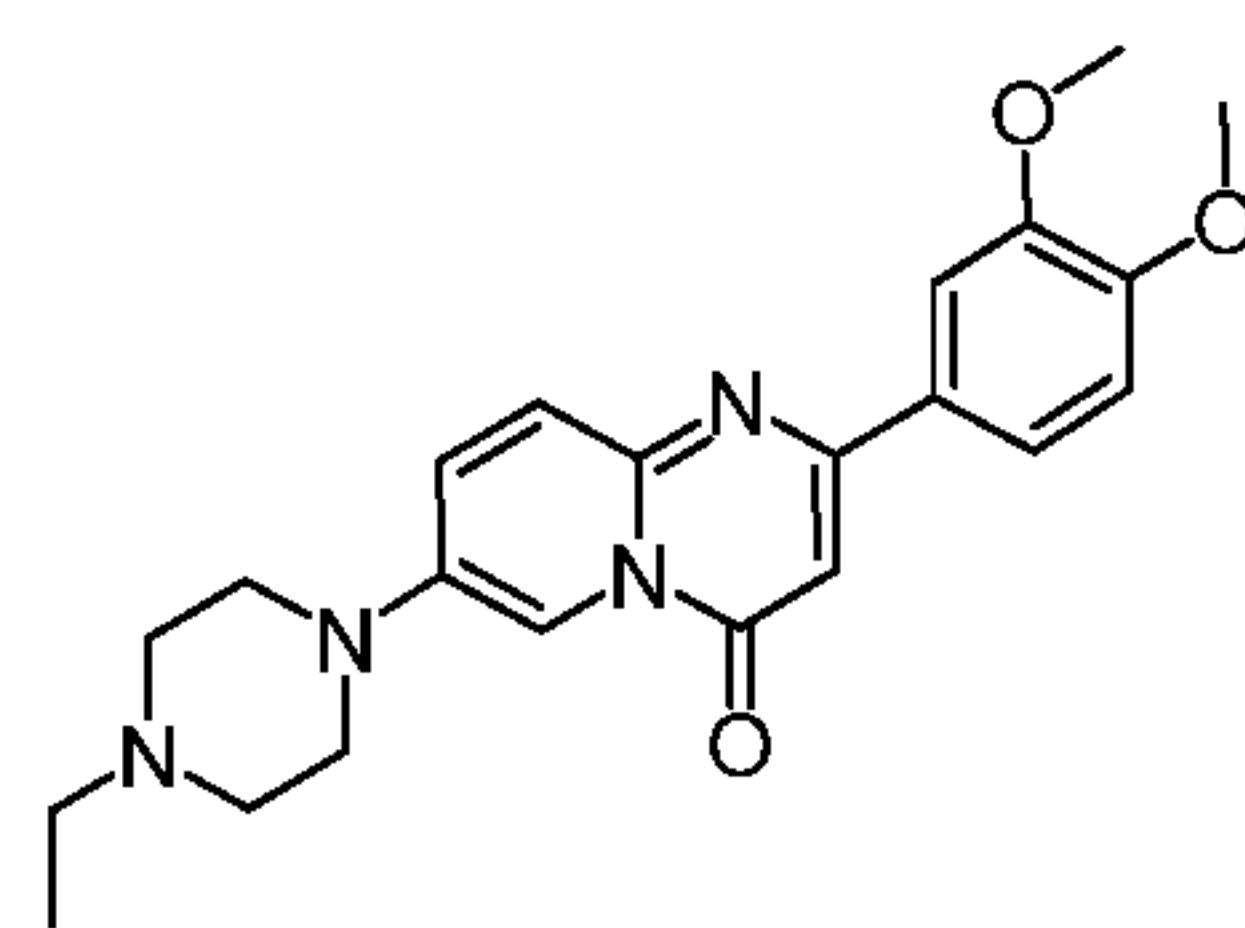




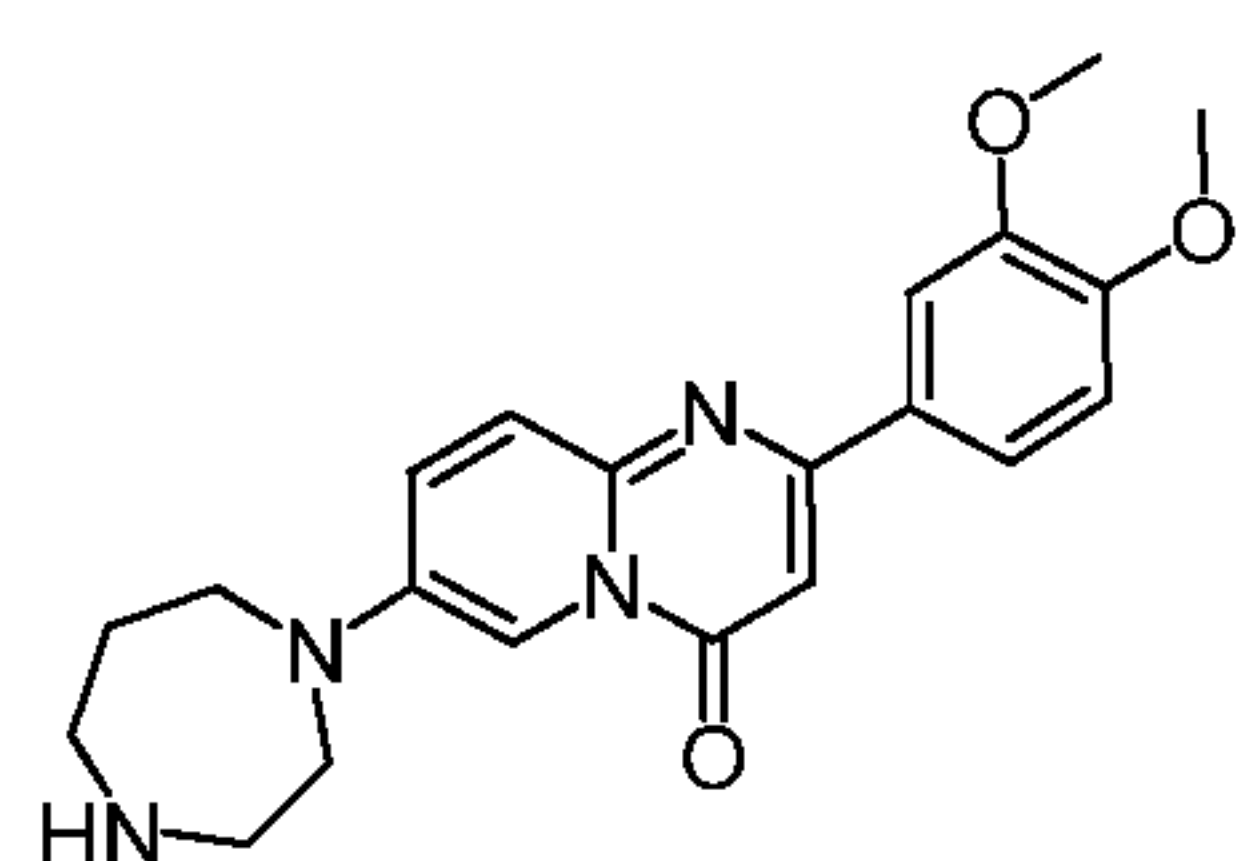
7



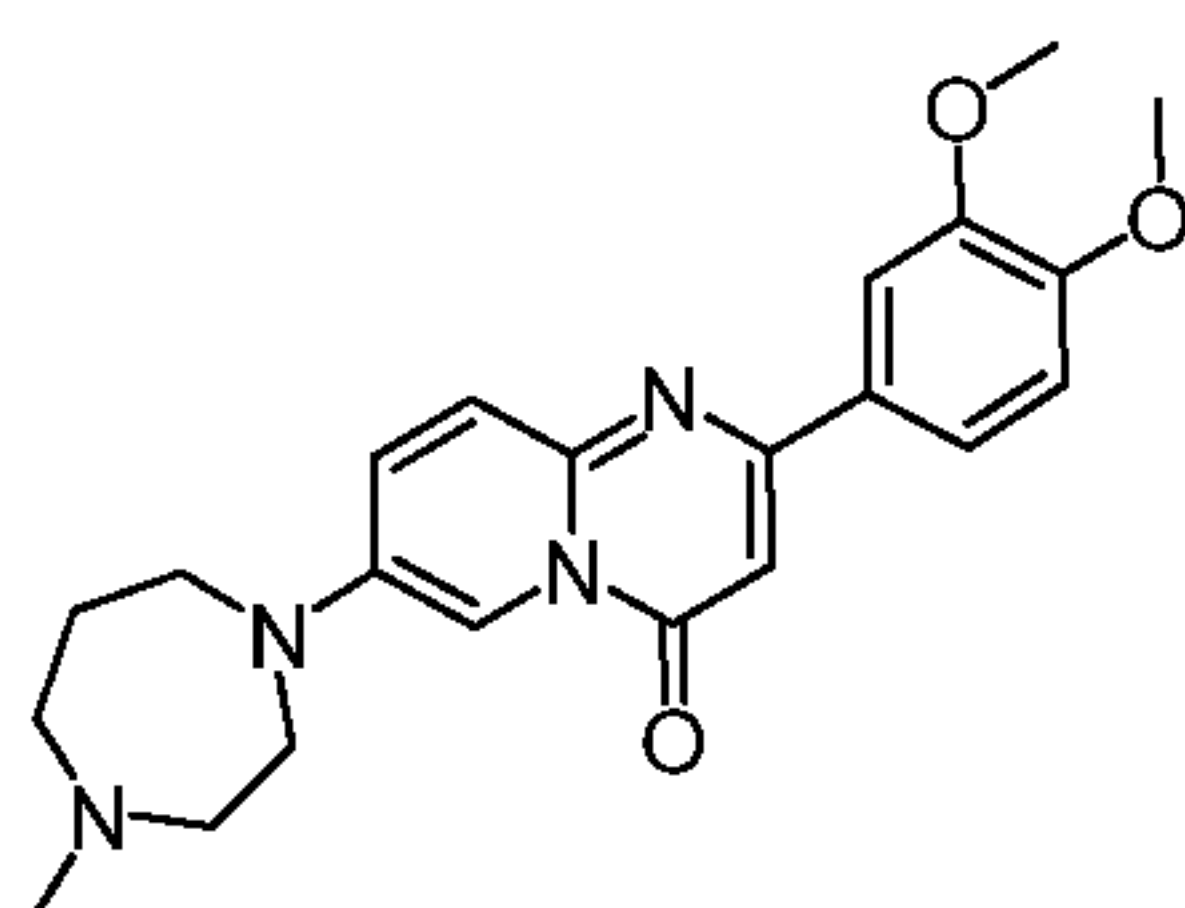
8



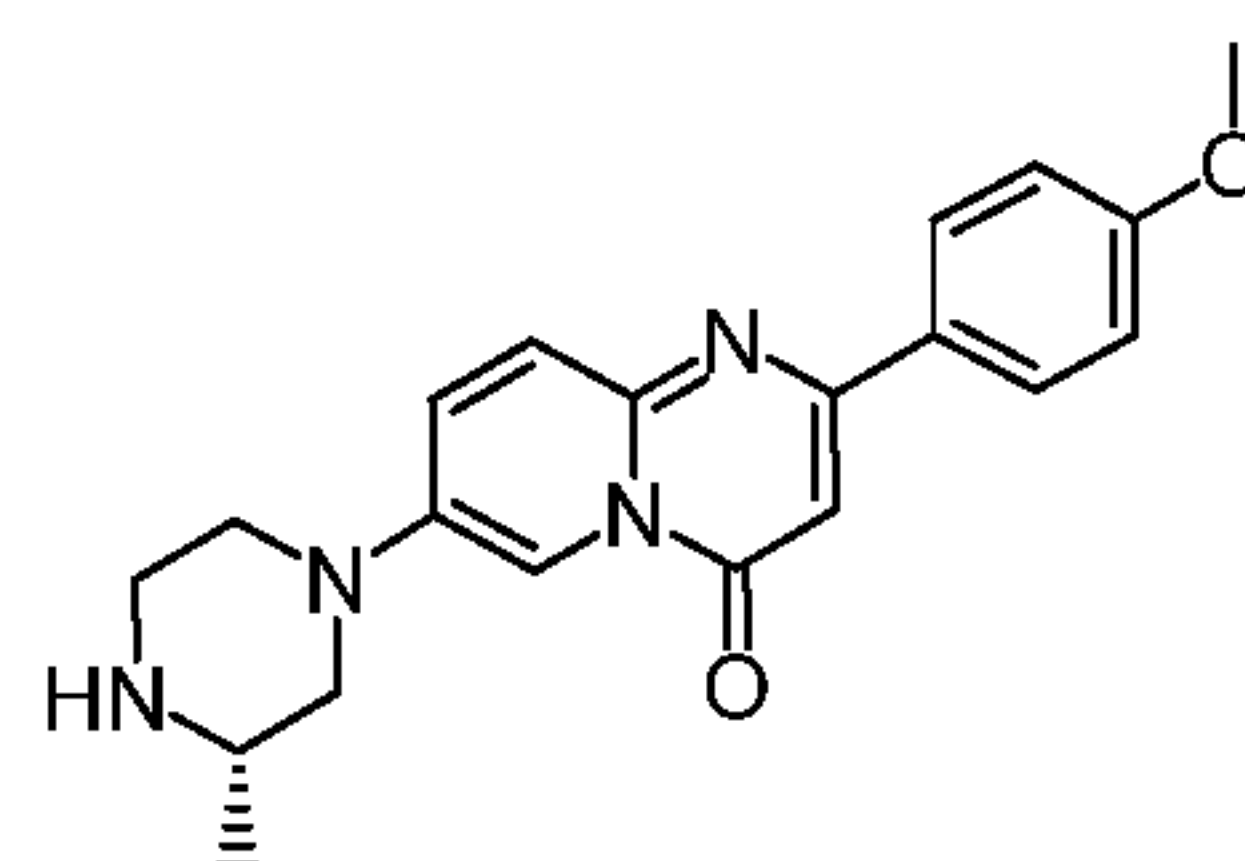
9



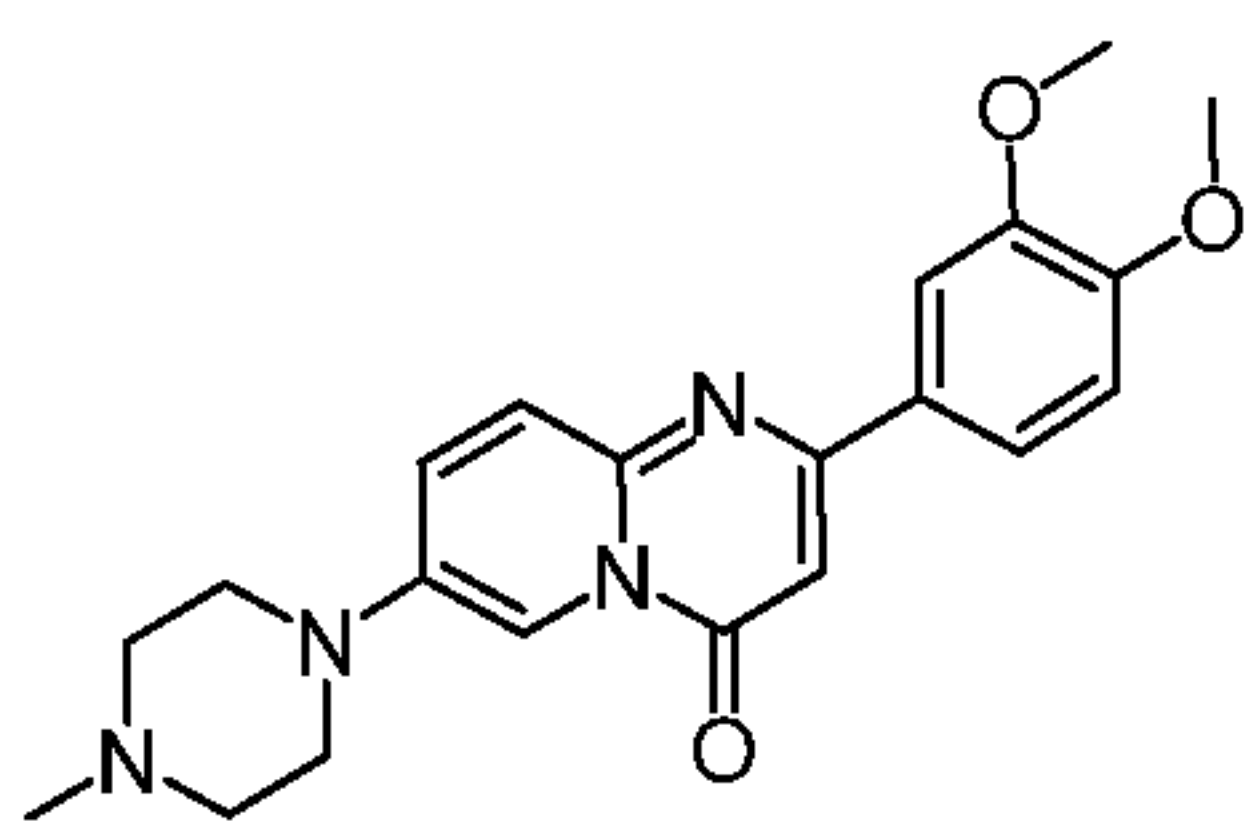
10



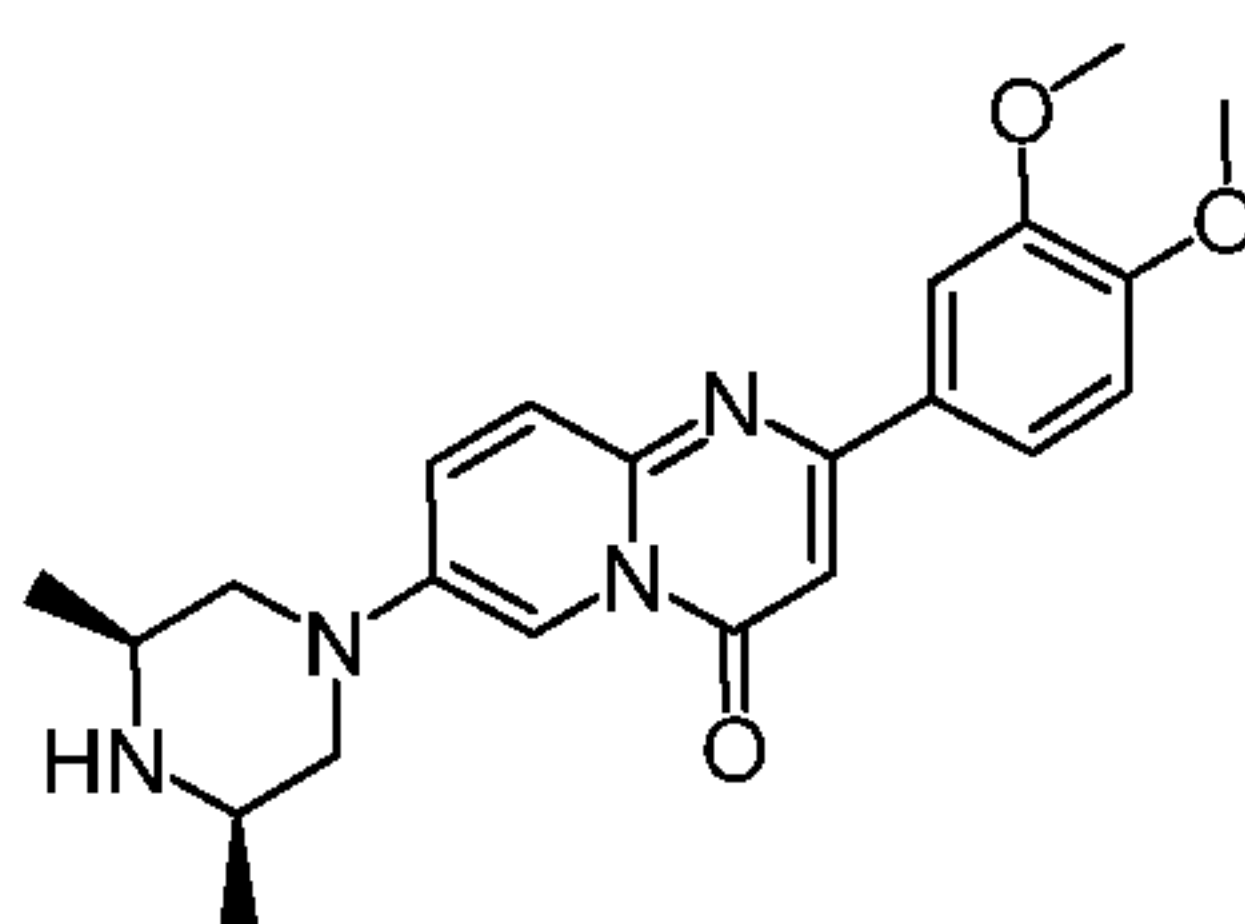
11



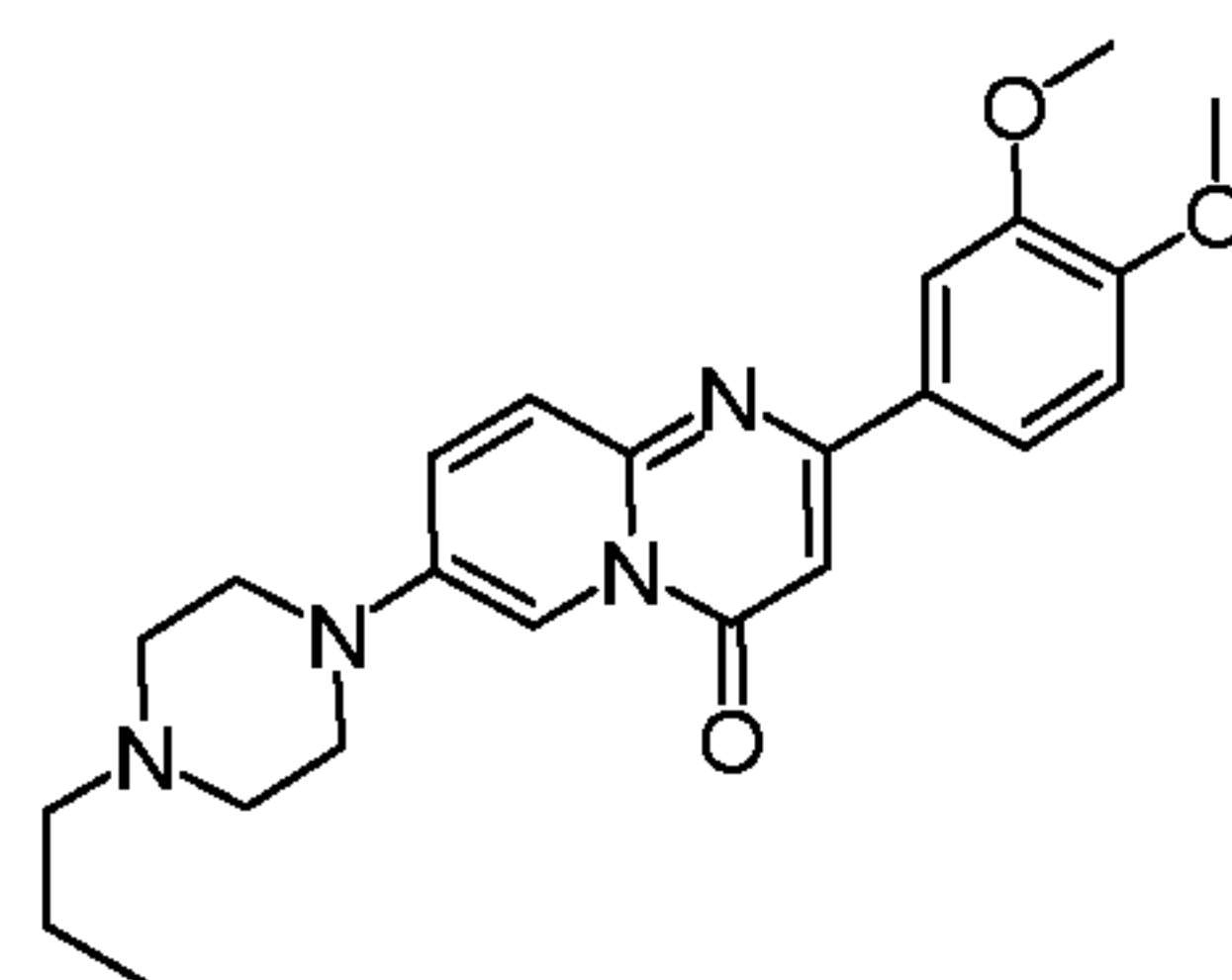
12



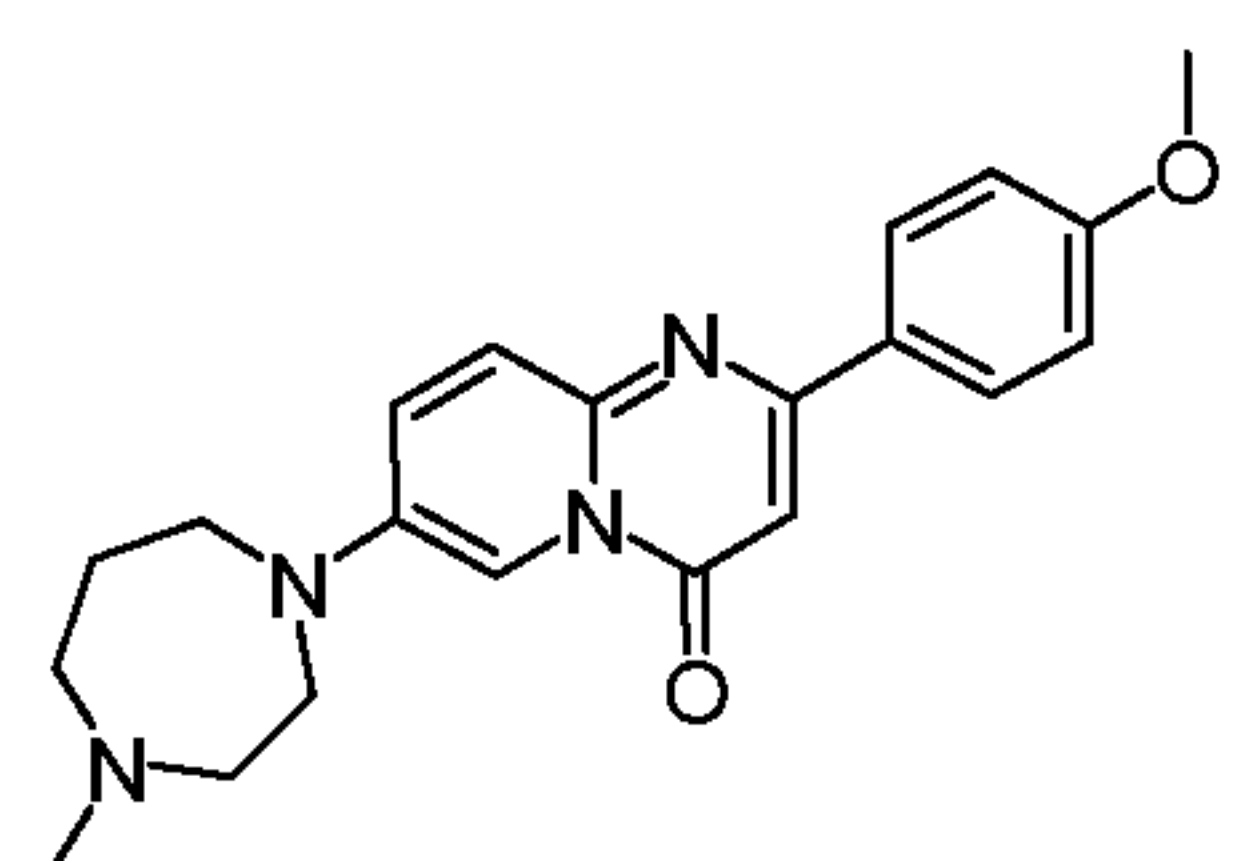
13



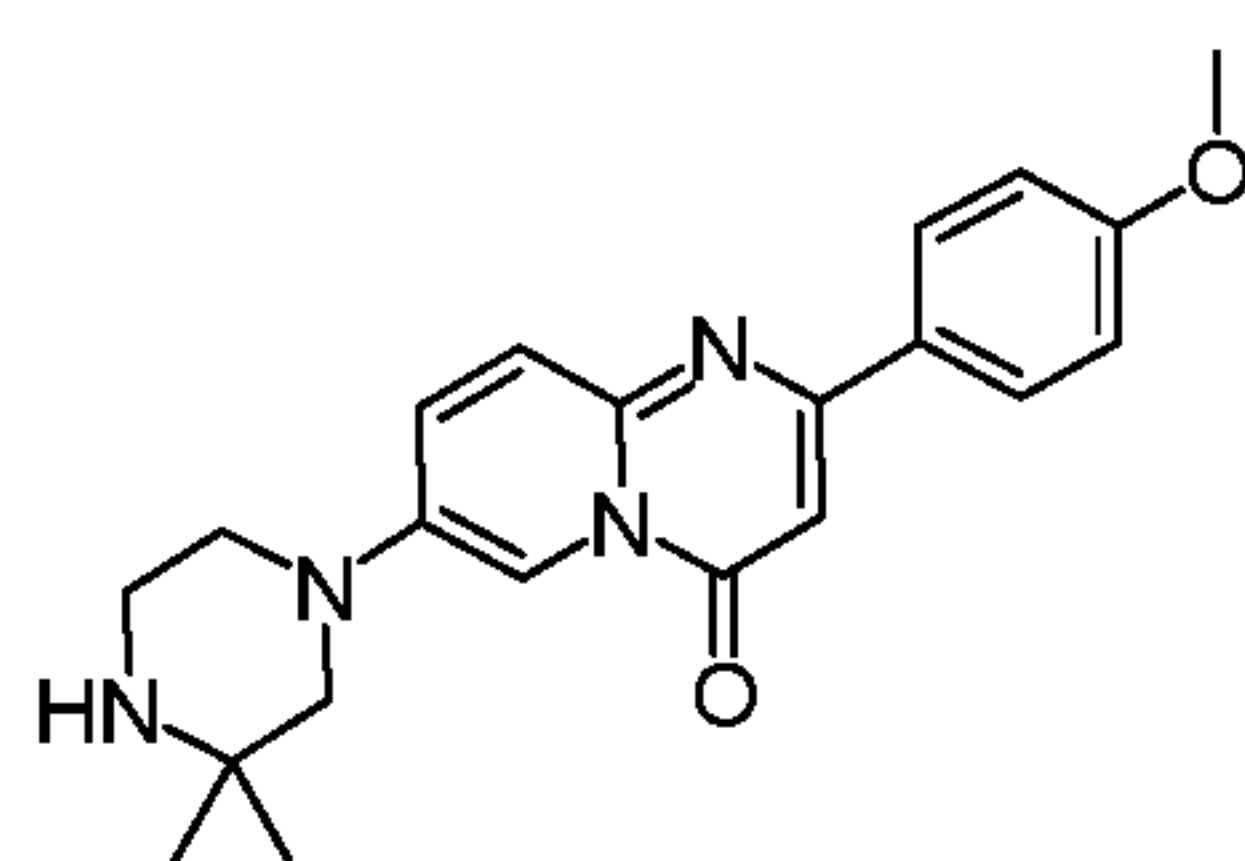
14



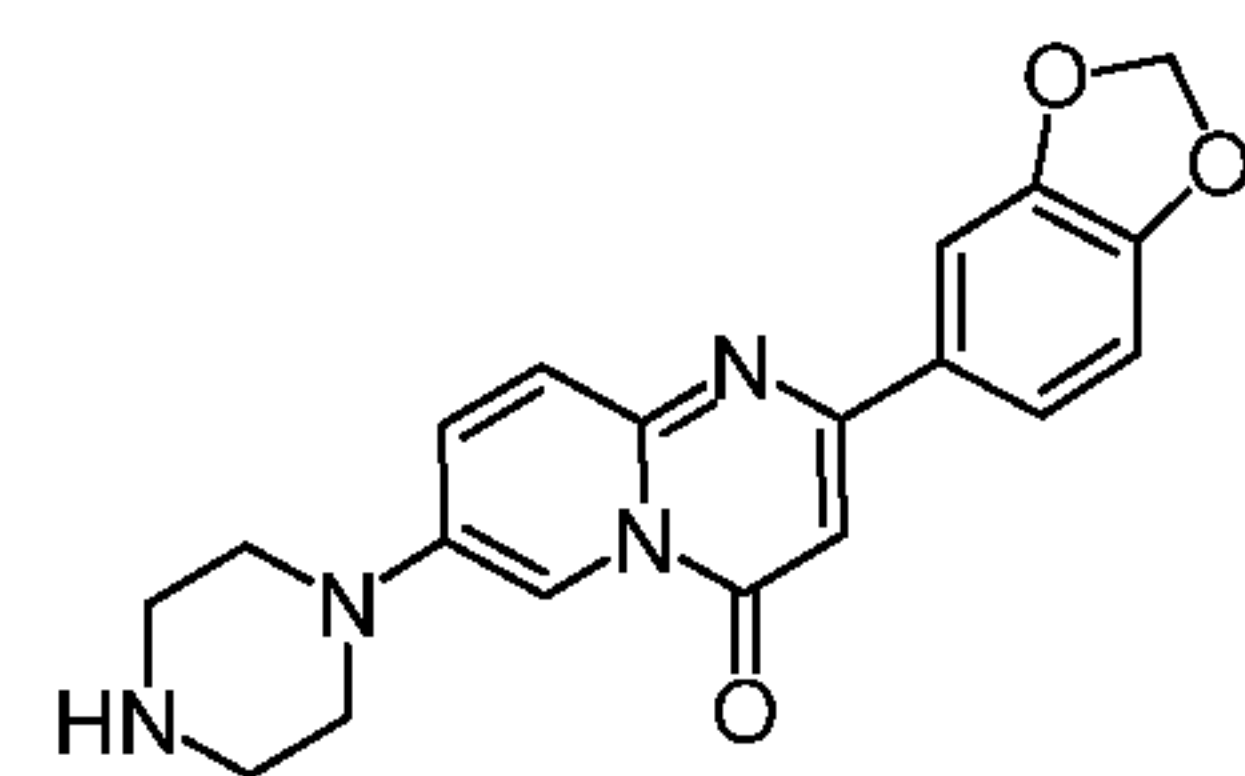
15



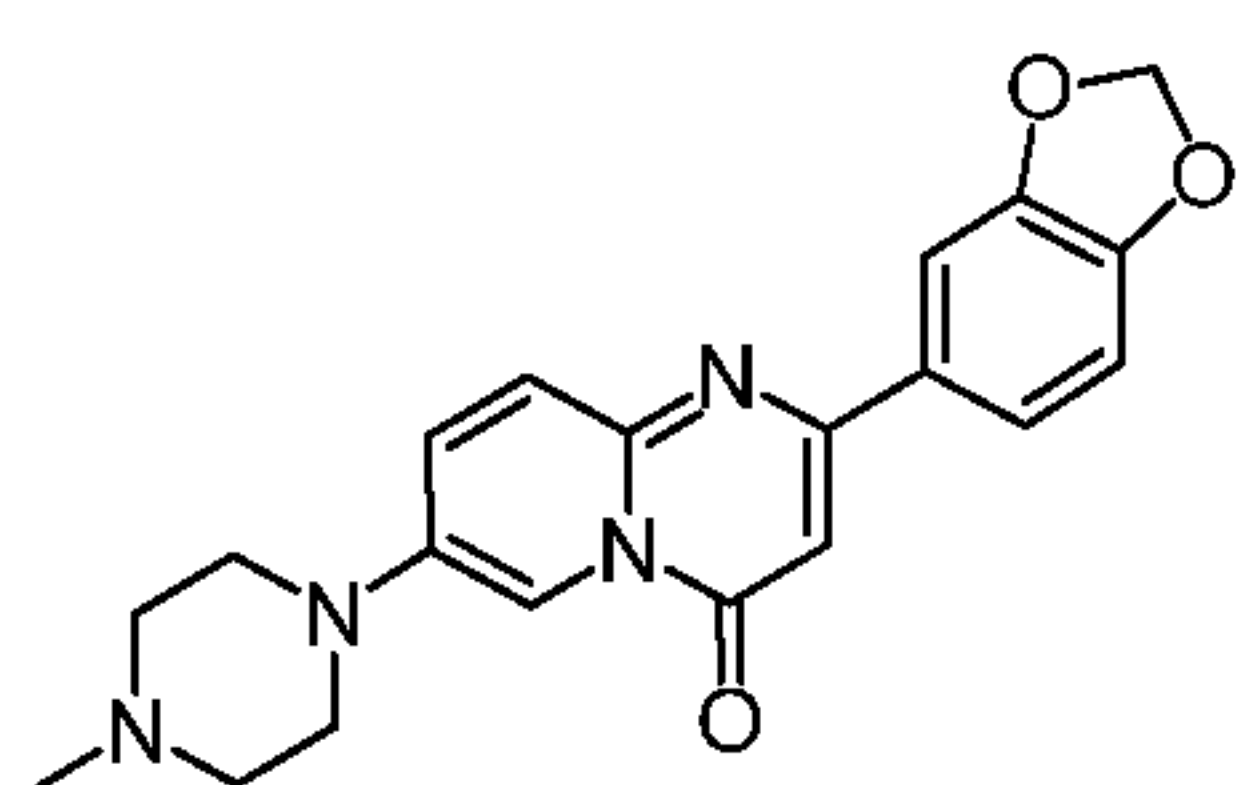
16



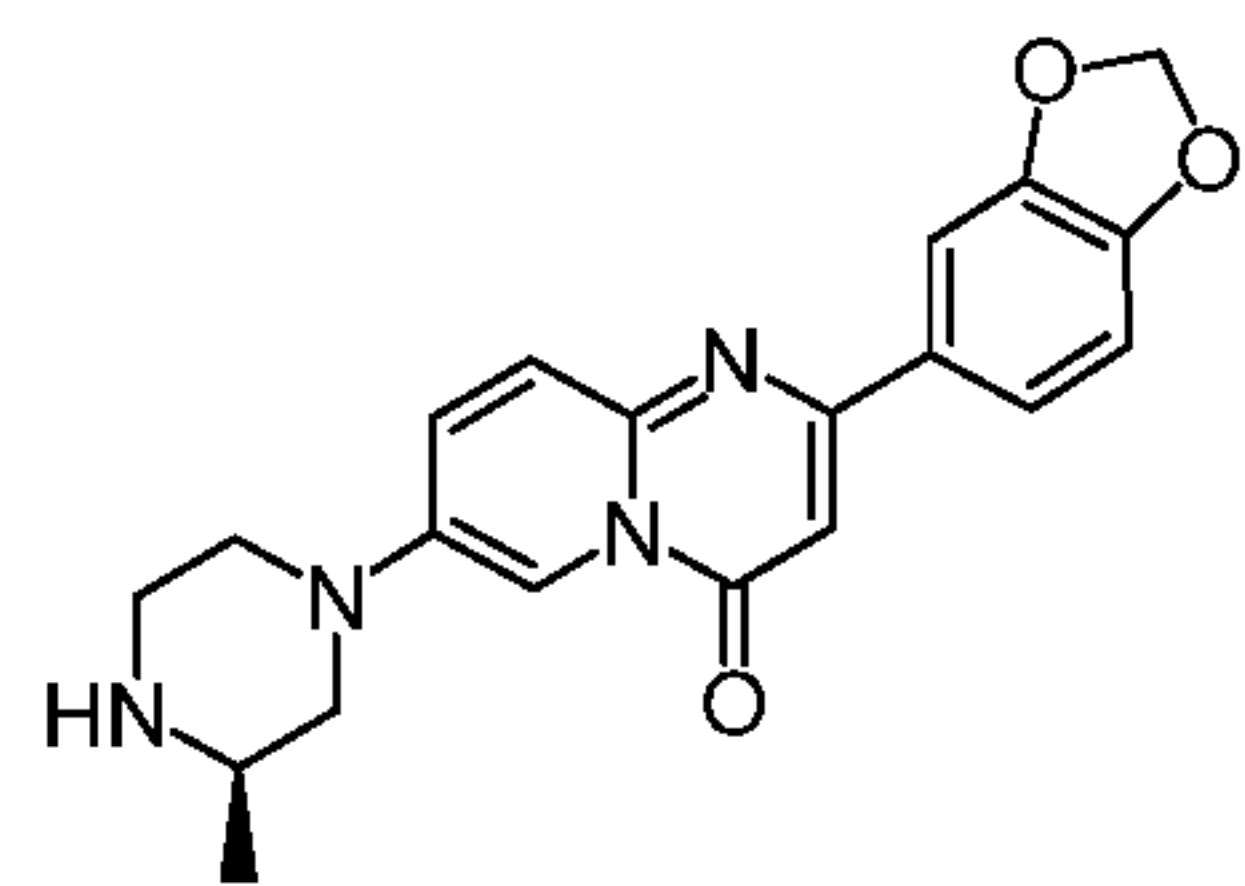
17



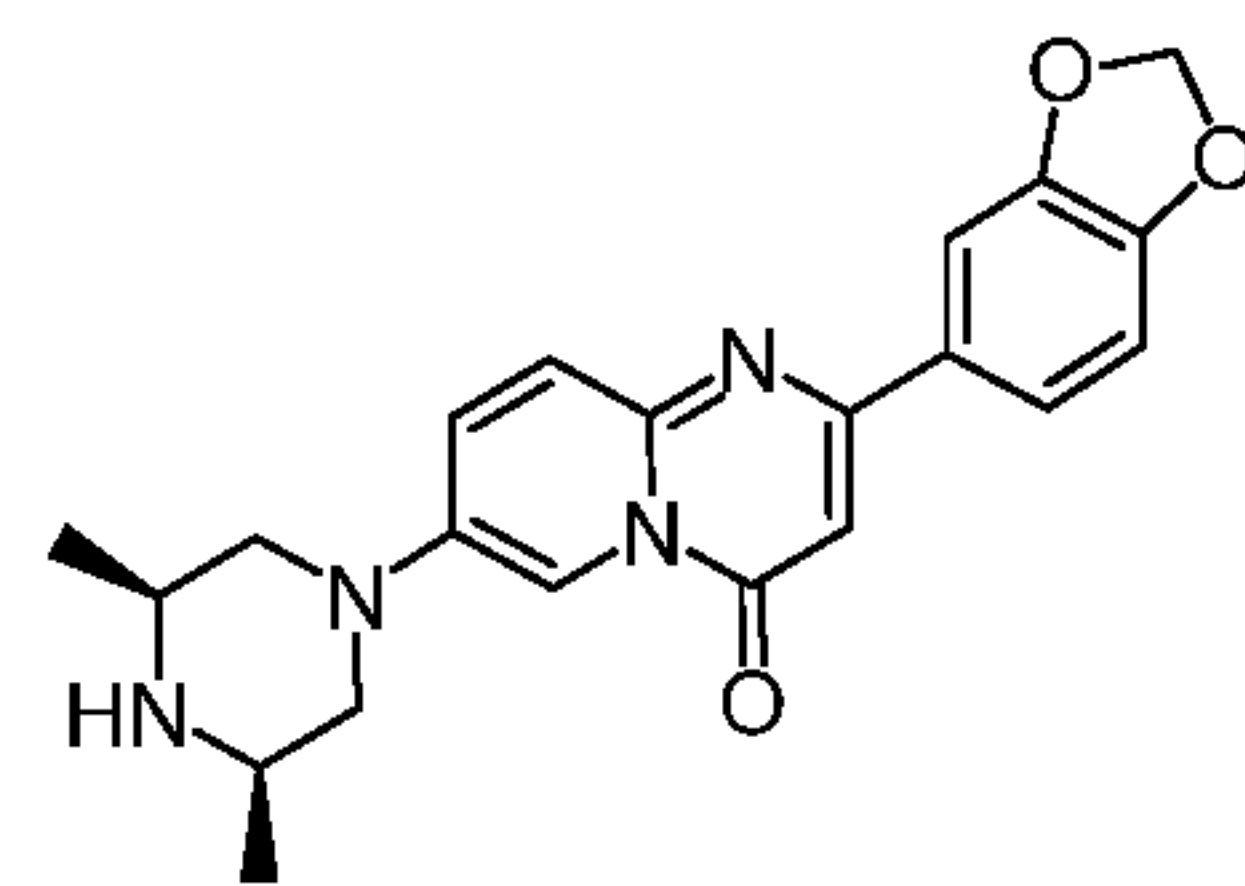
18



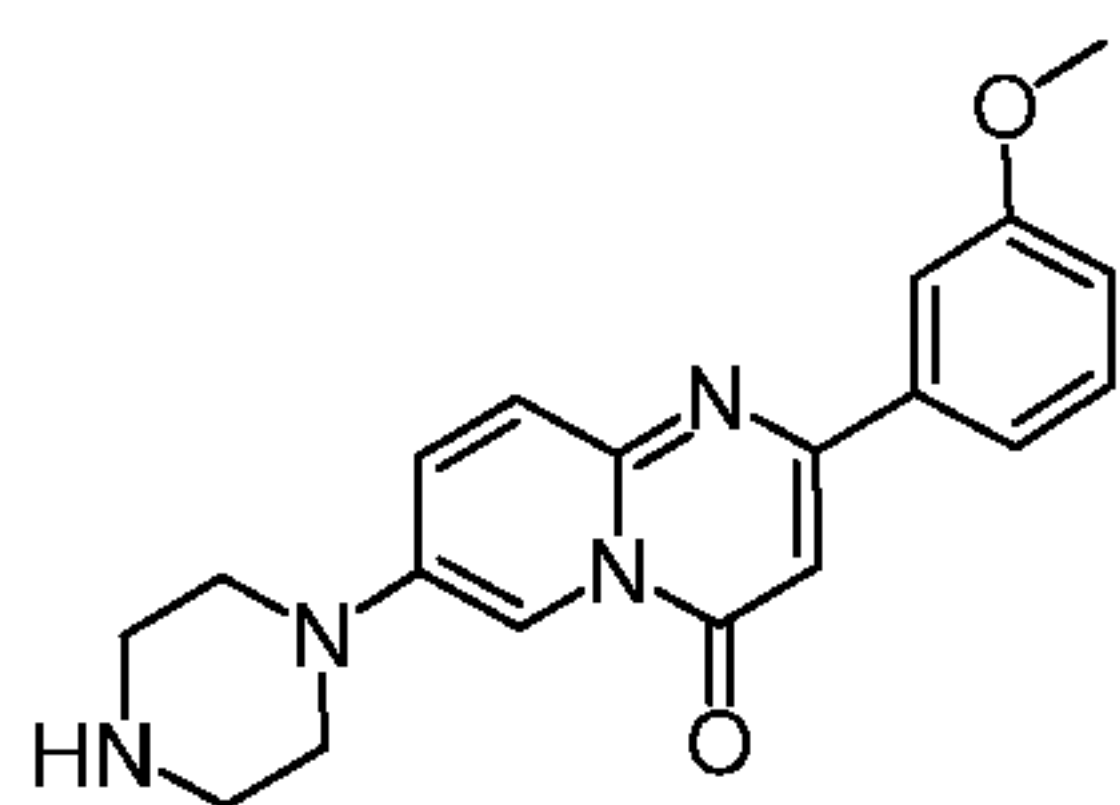
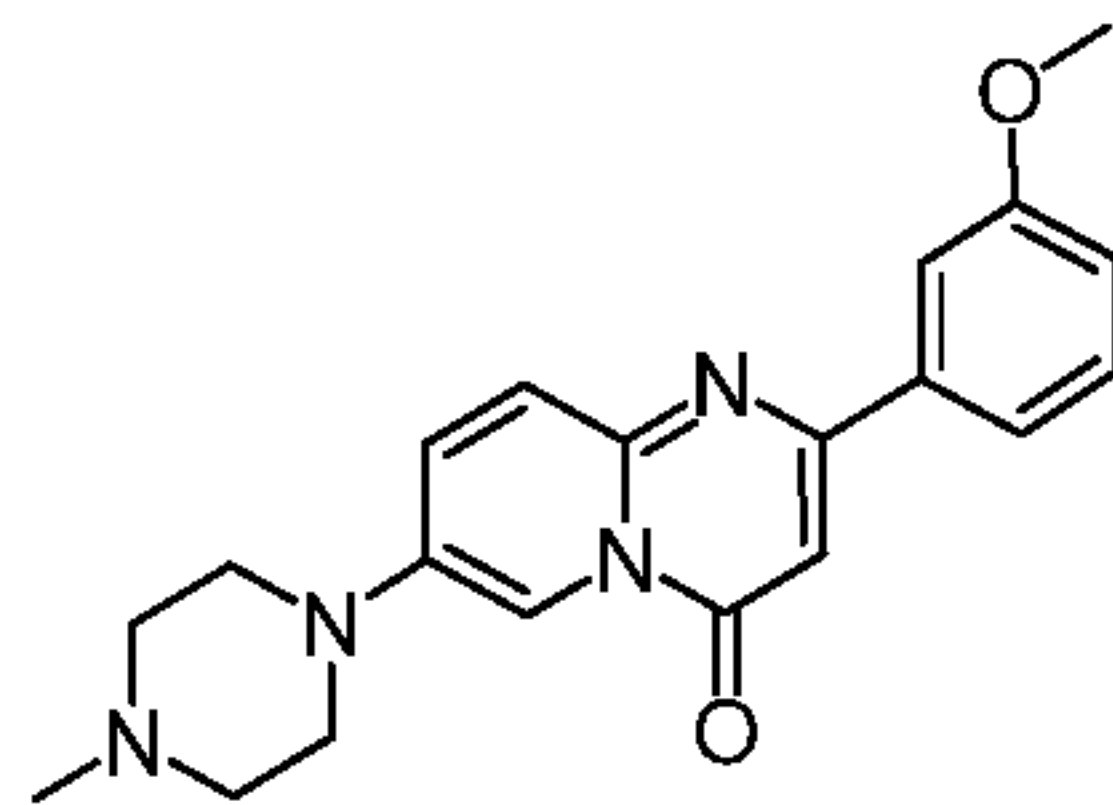
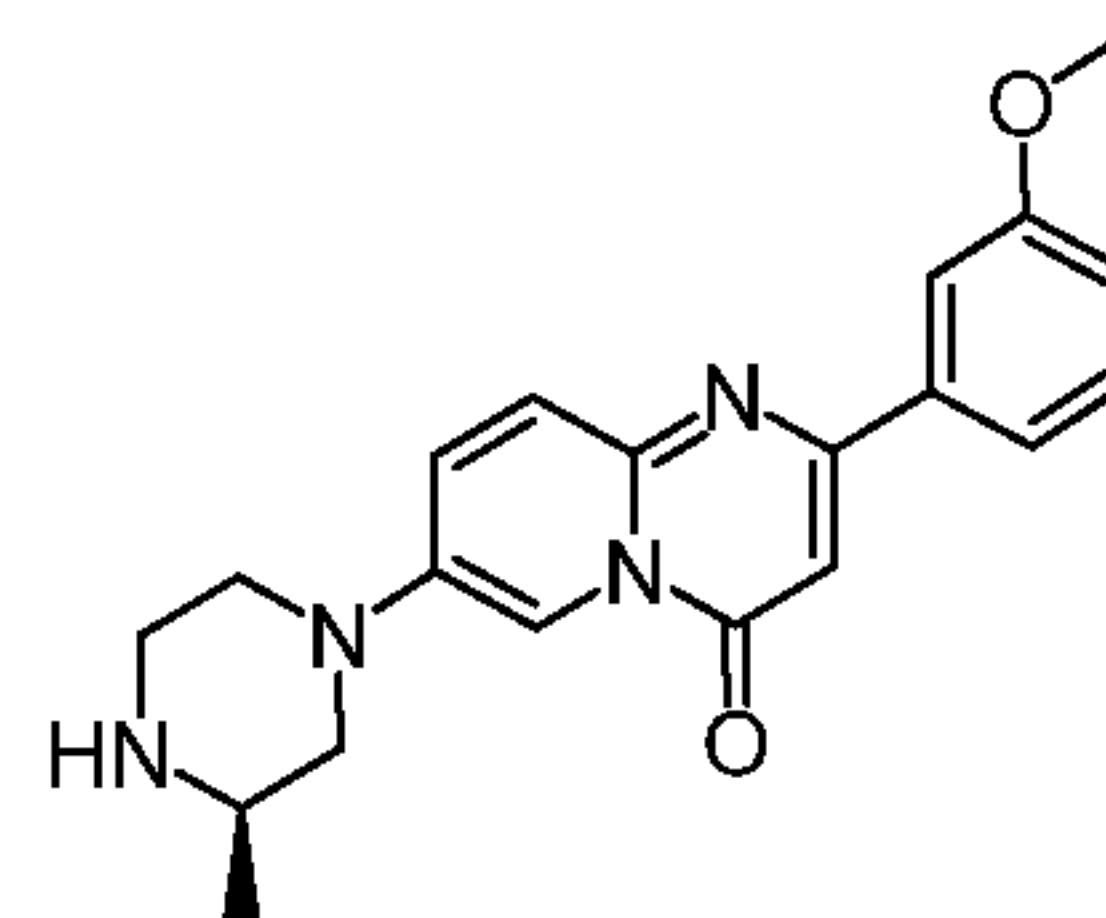
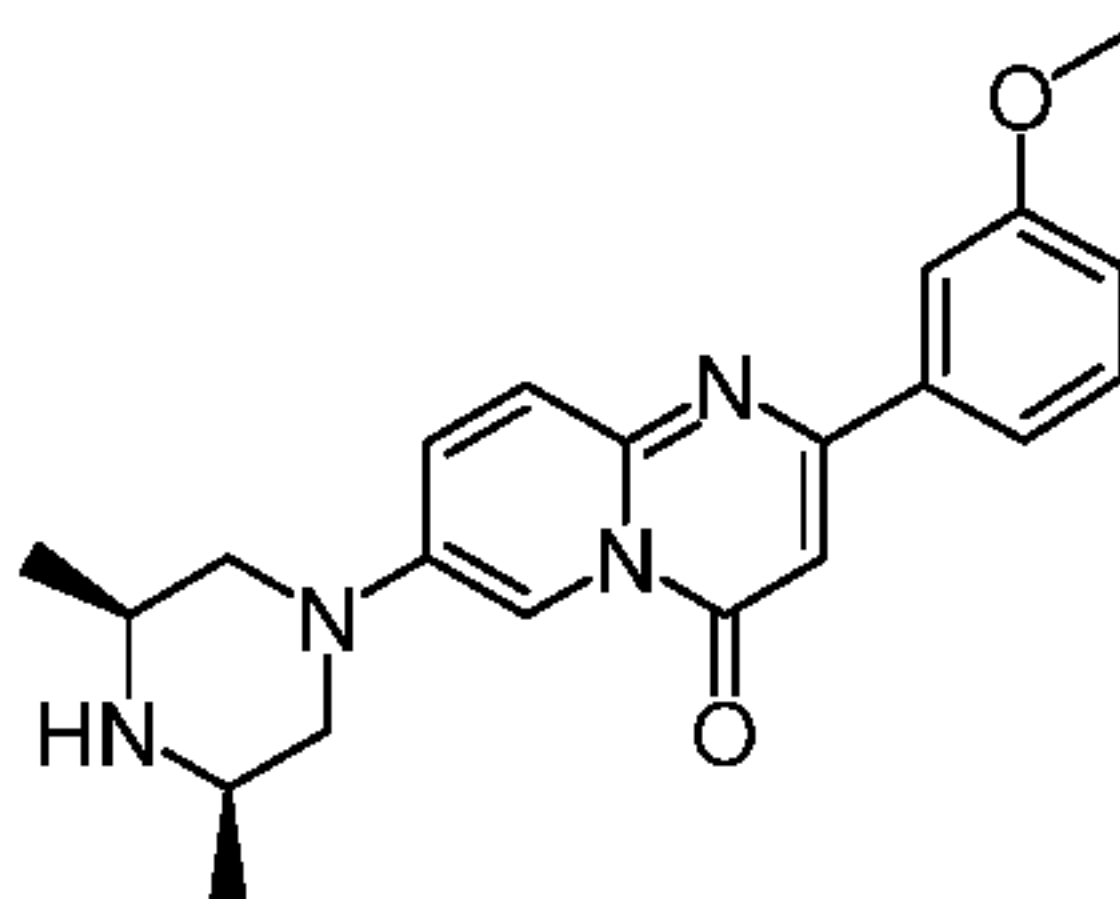
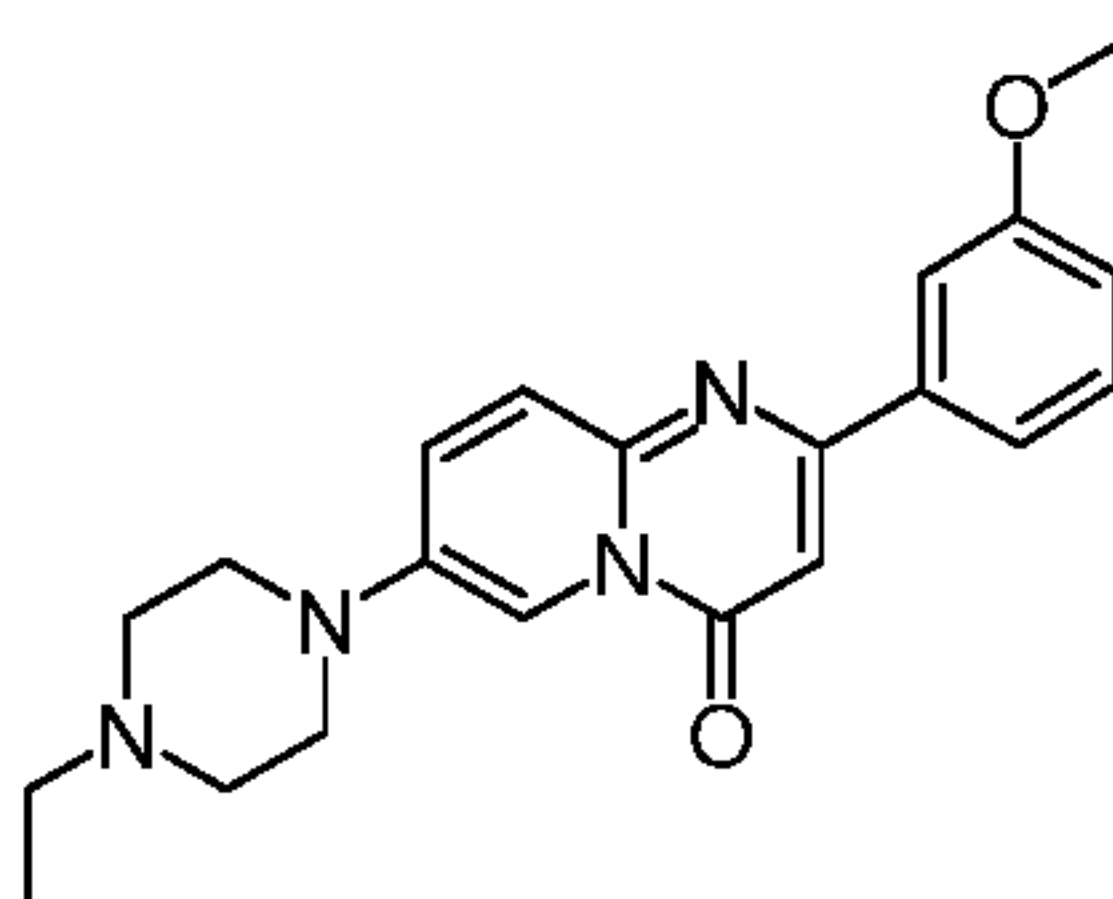
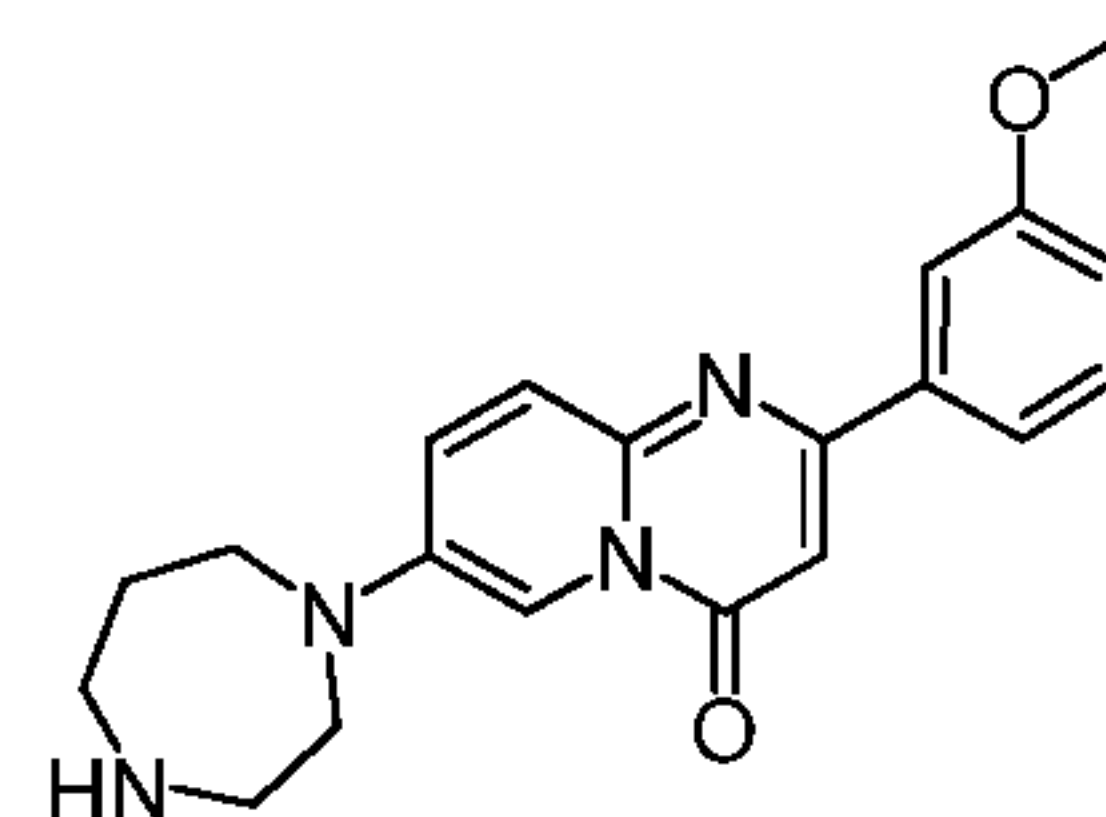
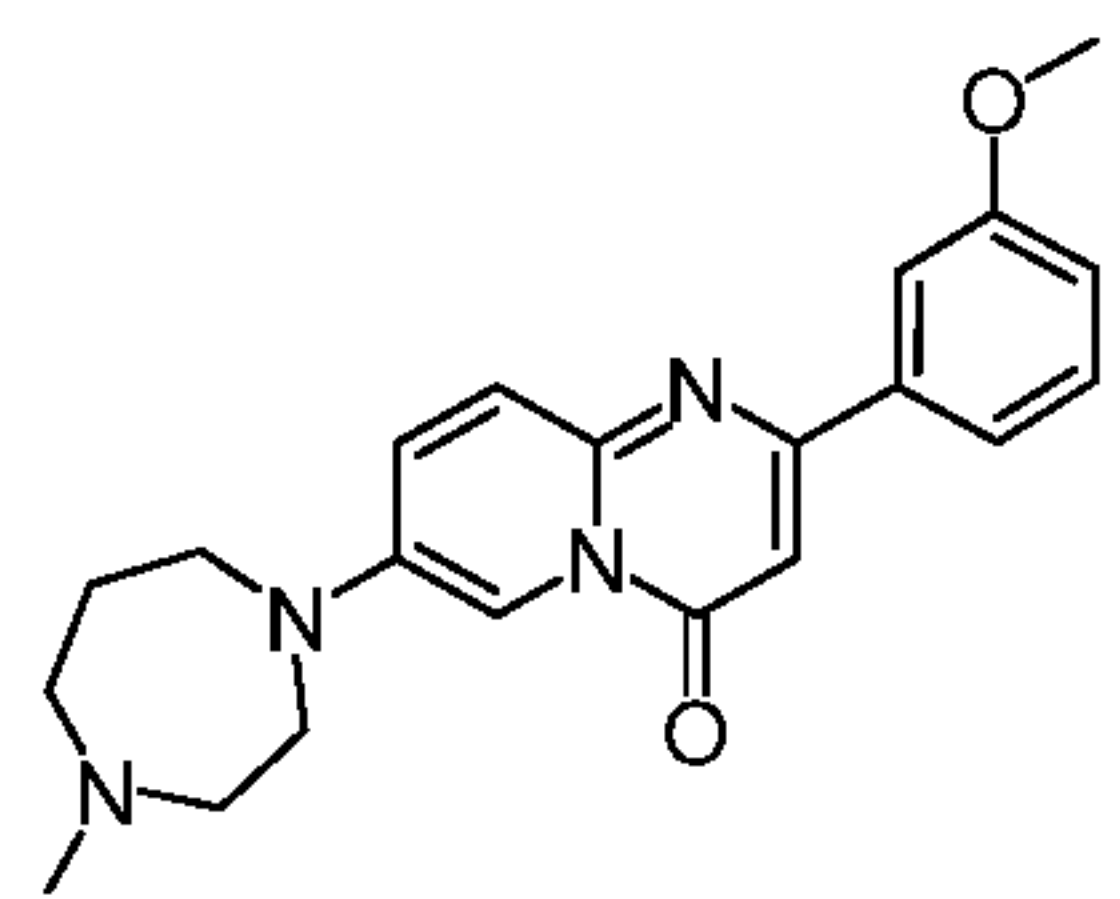
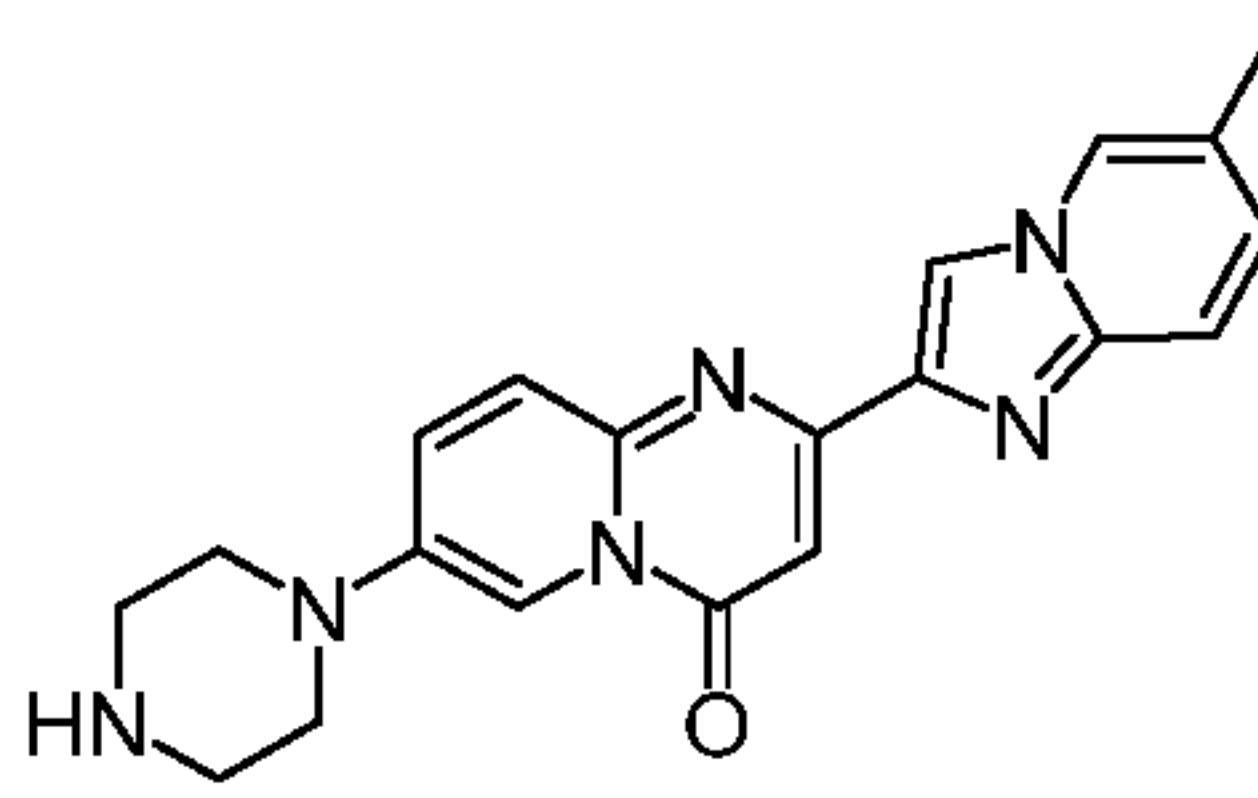
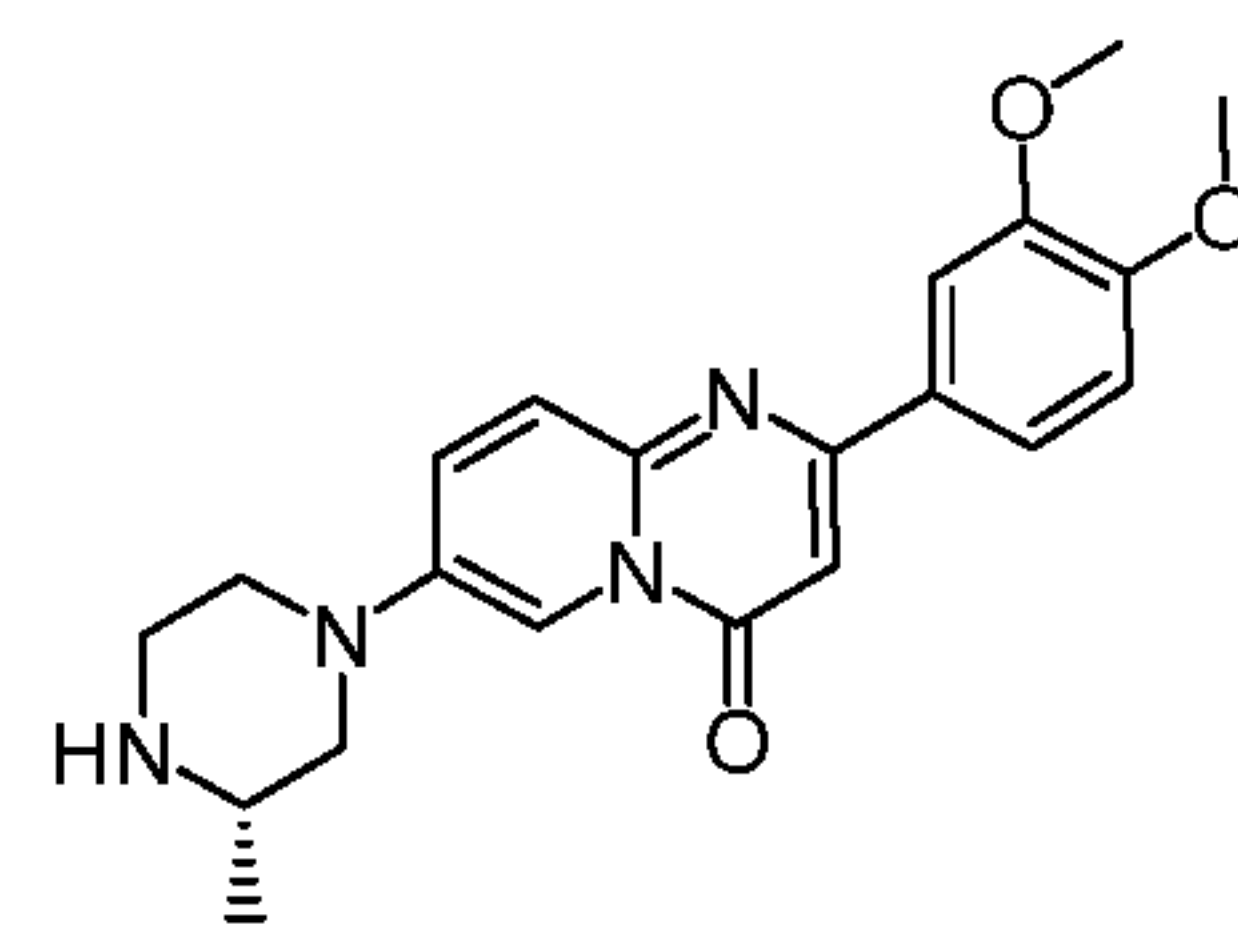
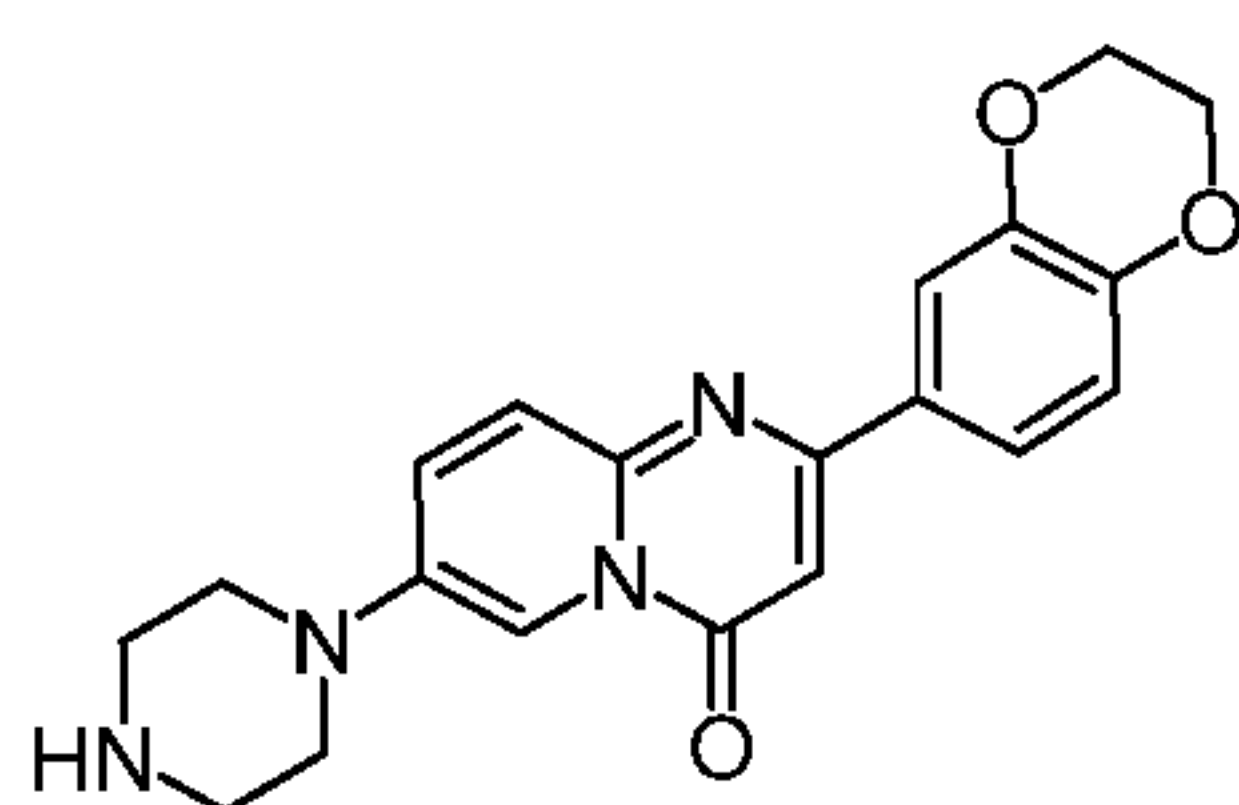
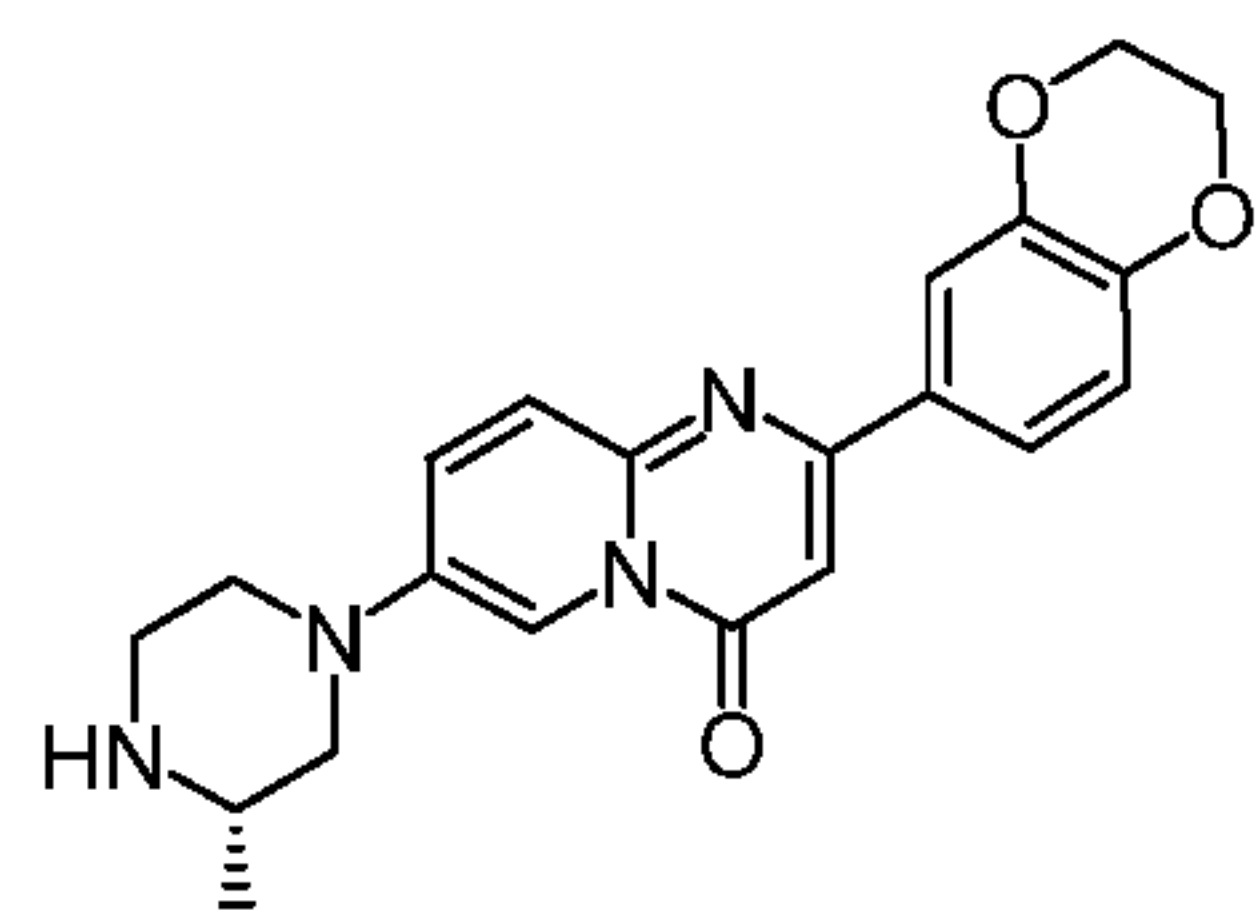
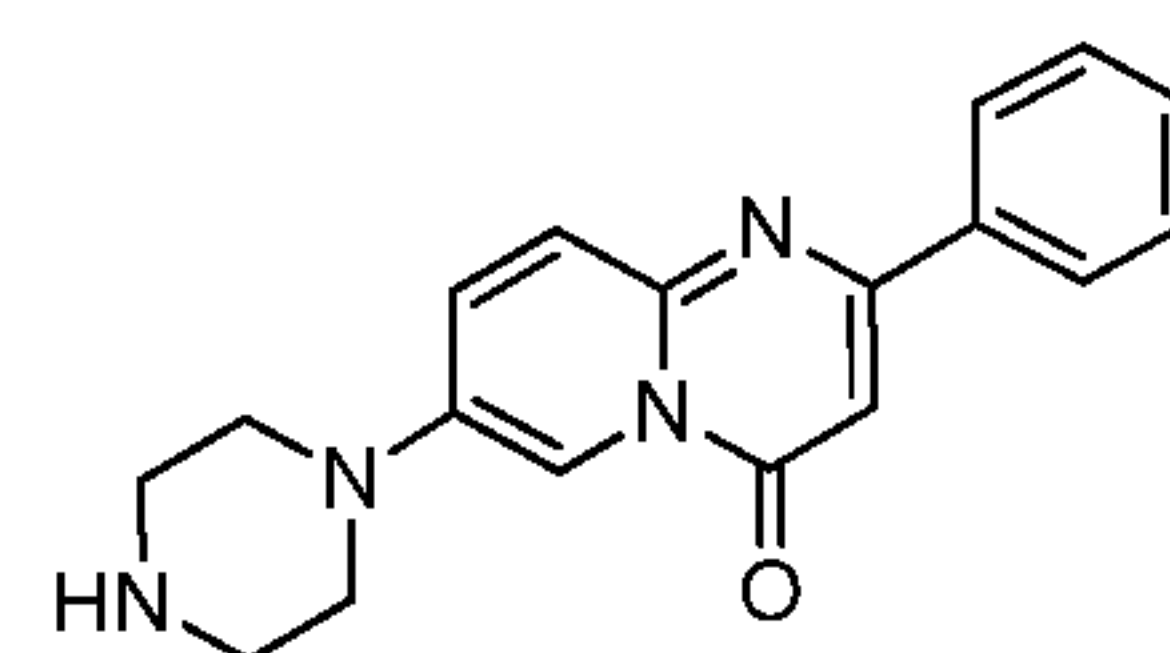
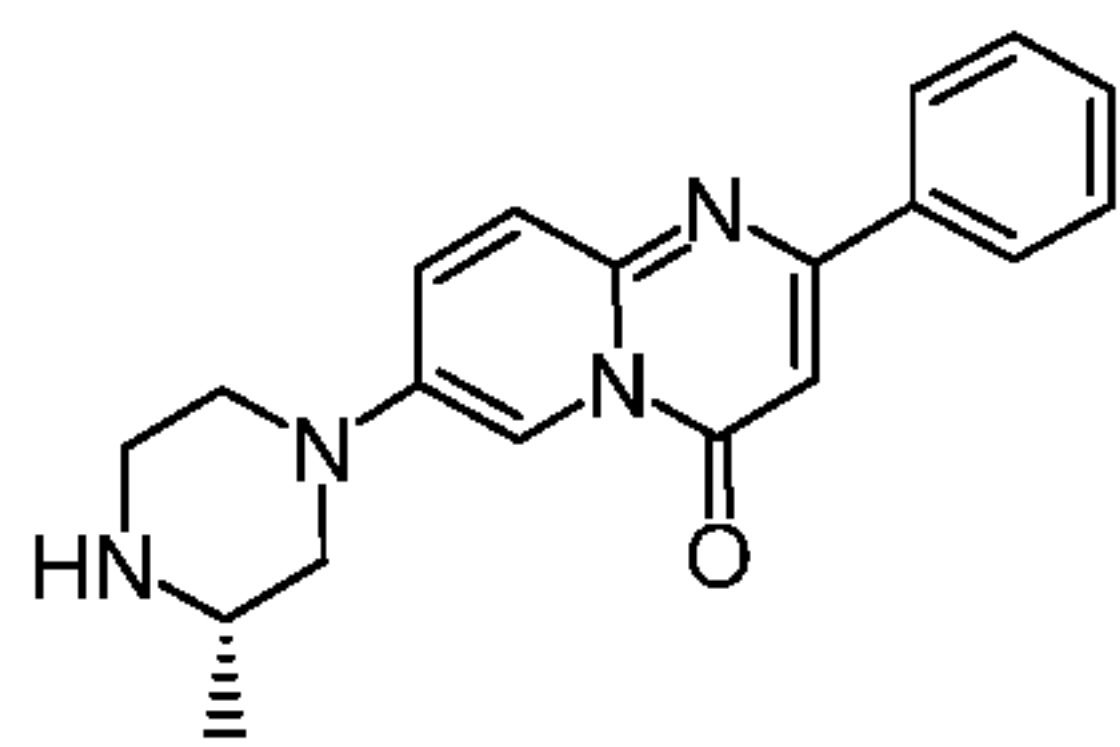
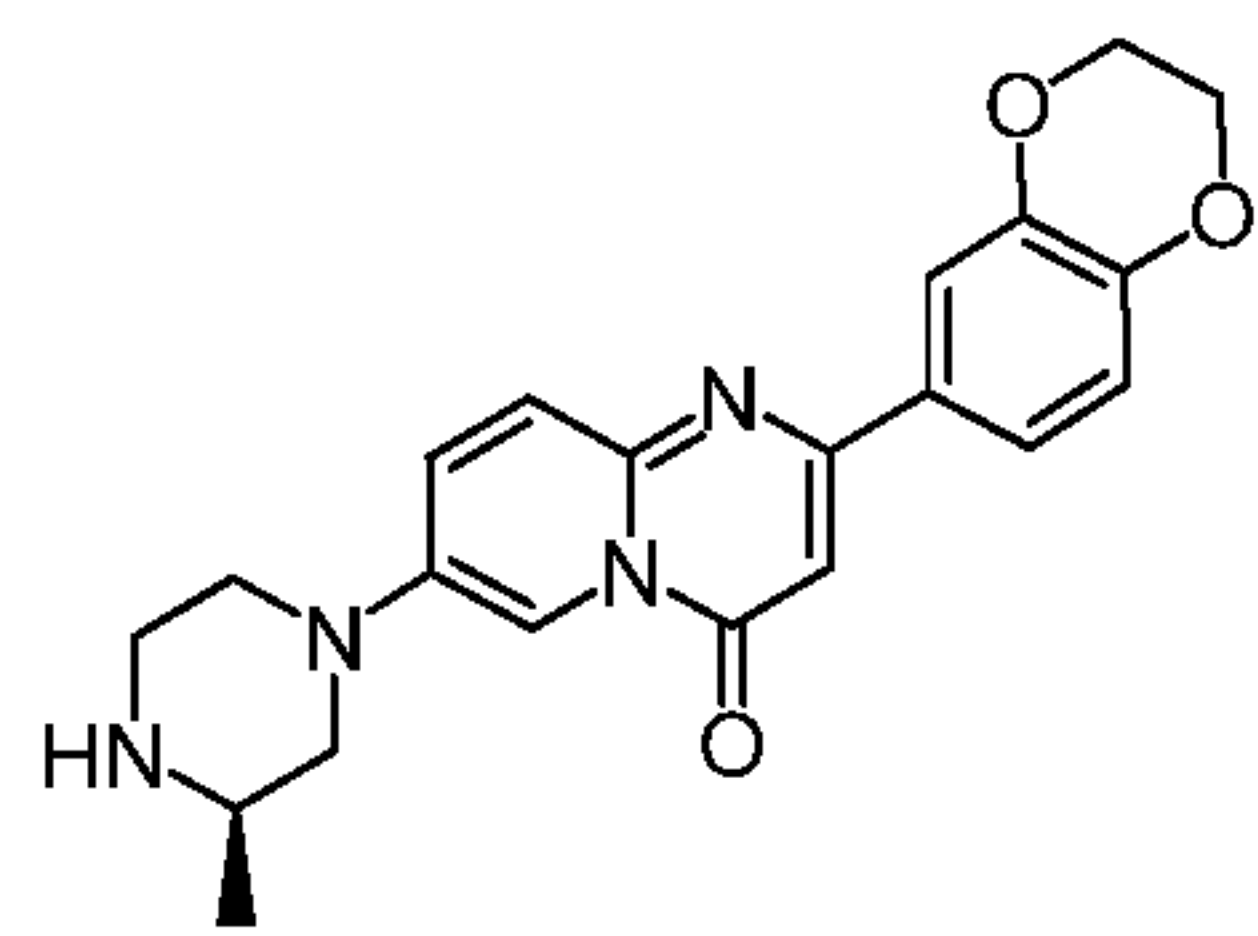
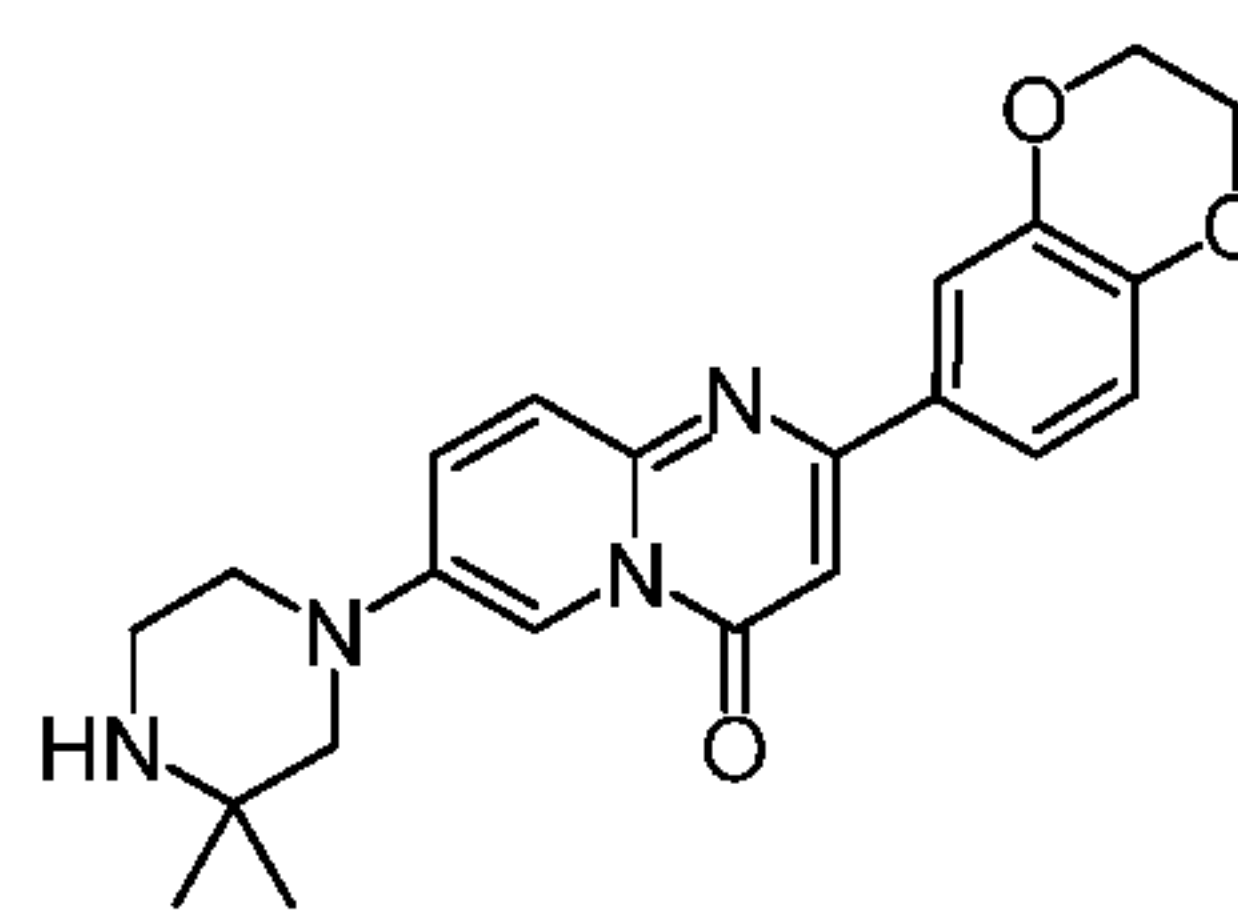
19

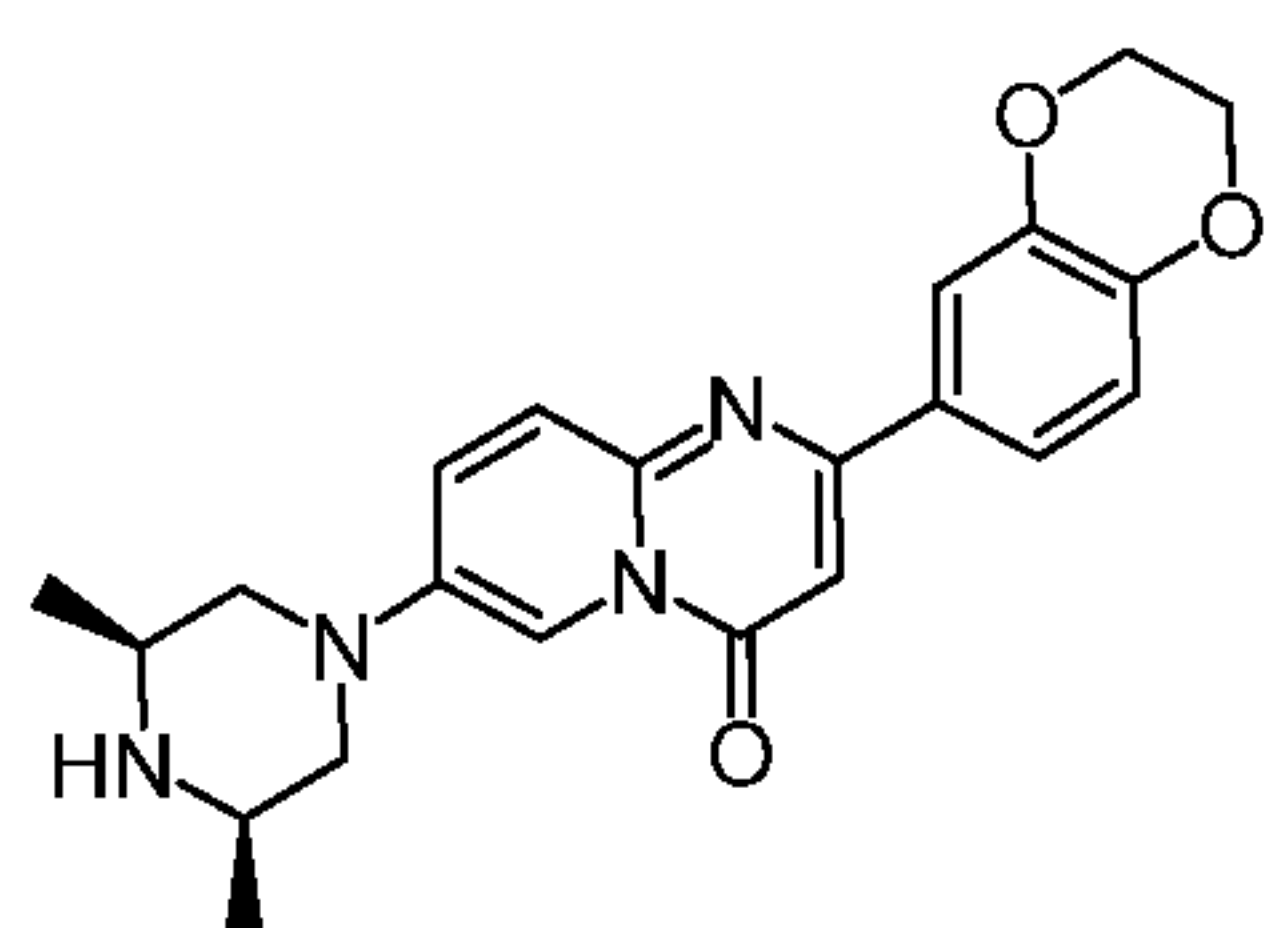


20

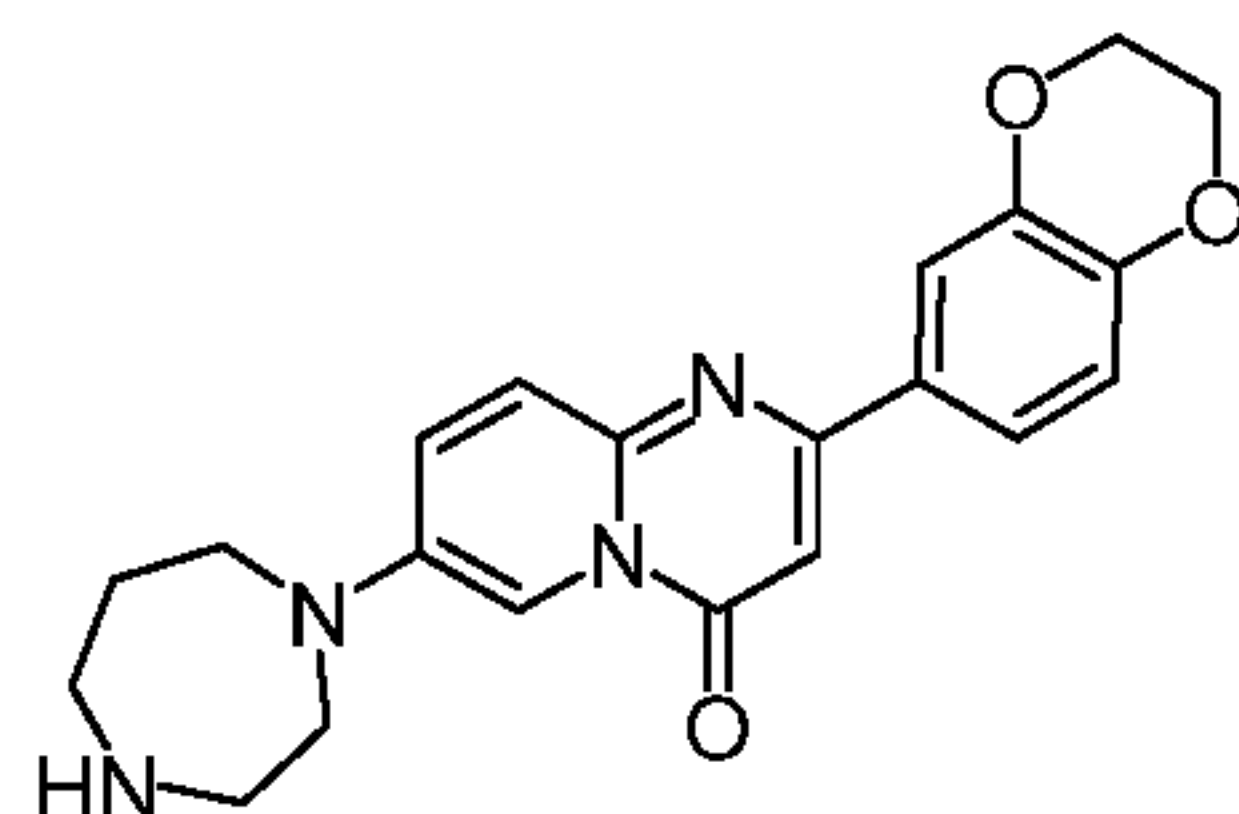


21

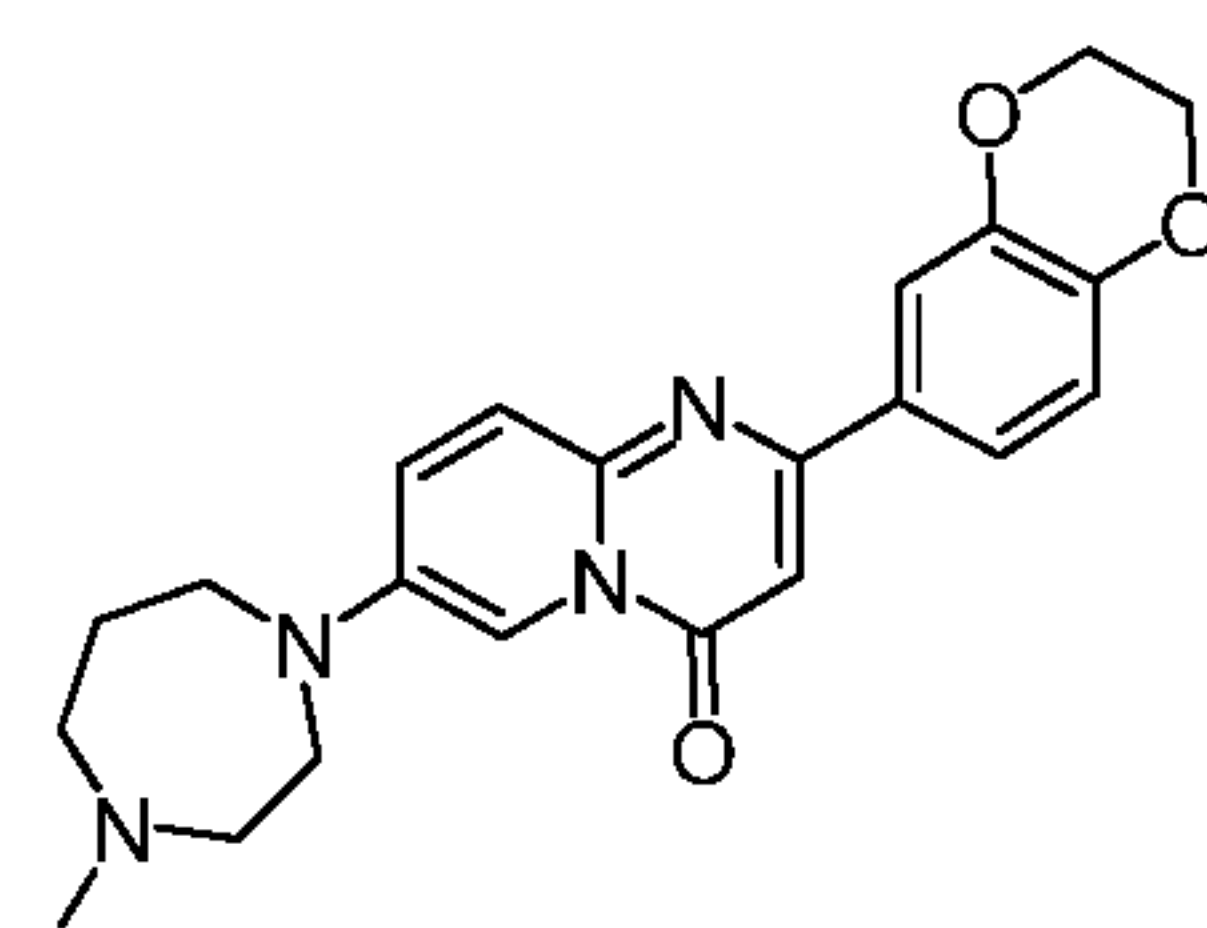
**22****23****24****25****26****27****28****29****30****31****32****33****34****35****36**



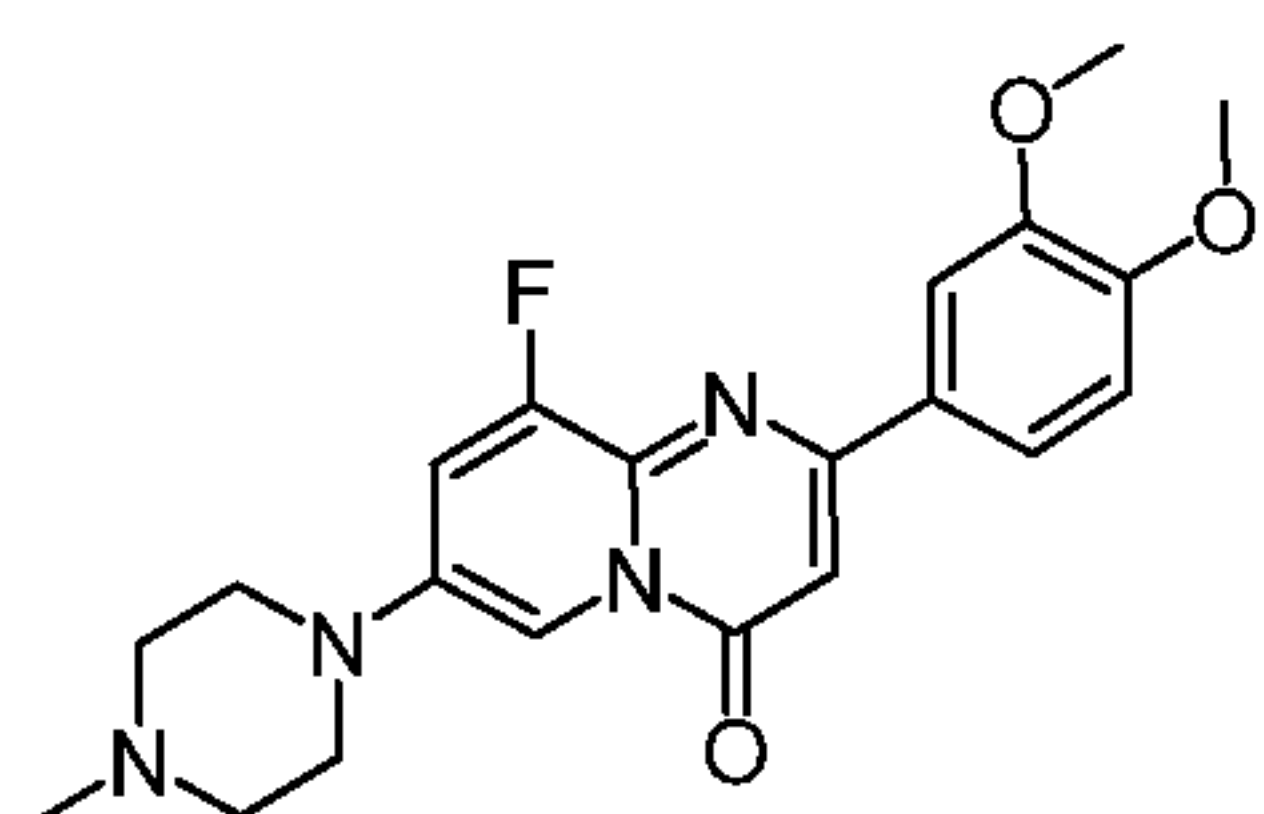
37



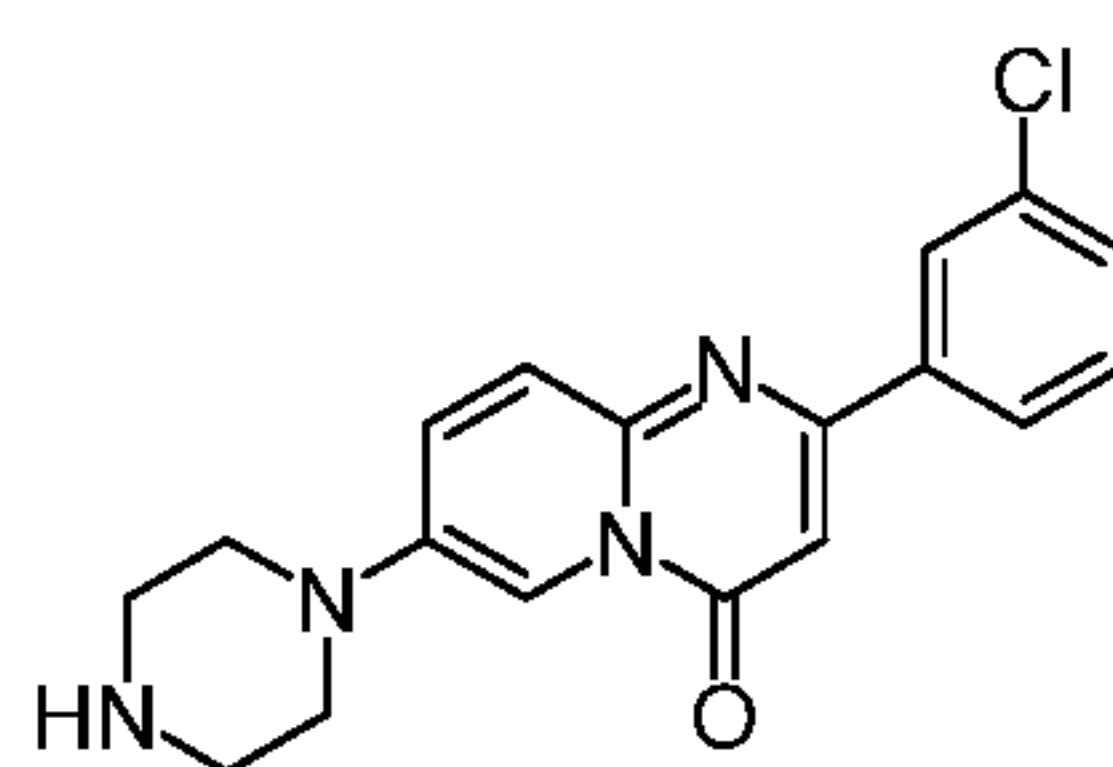
38



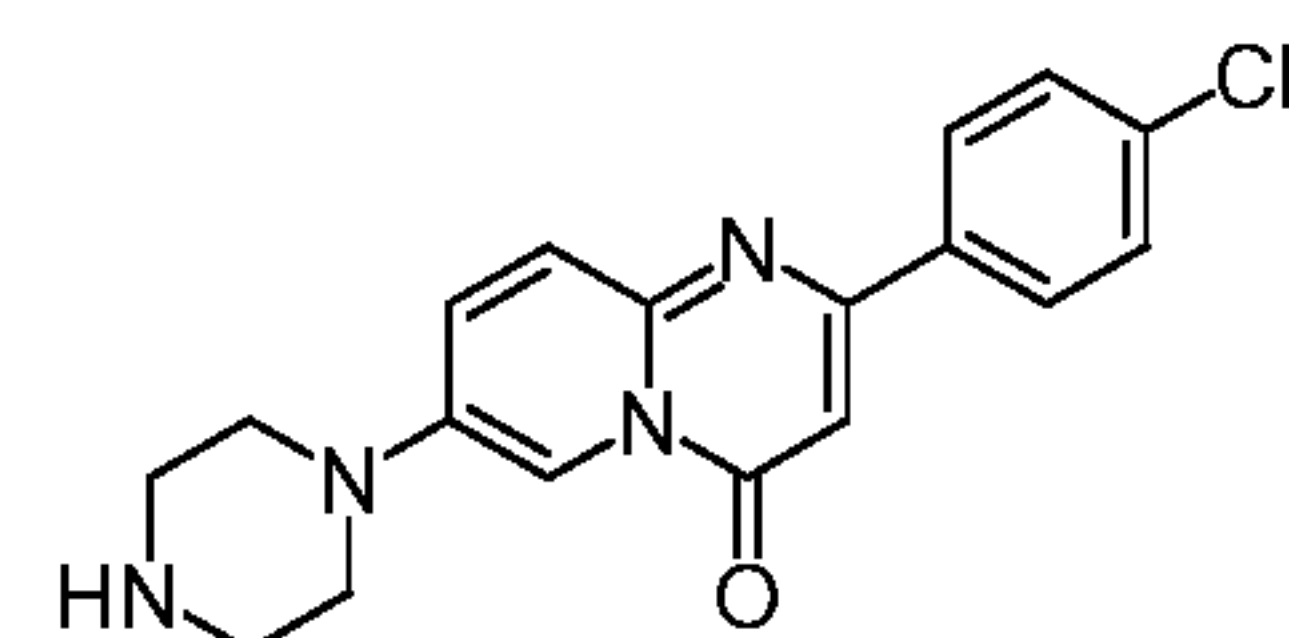
39



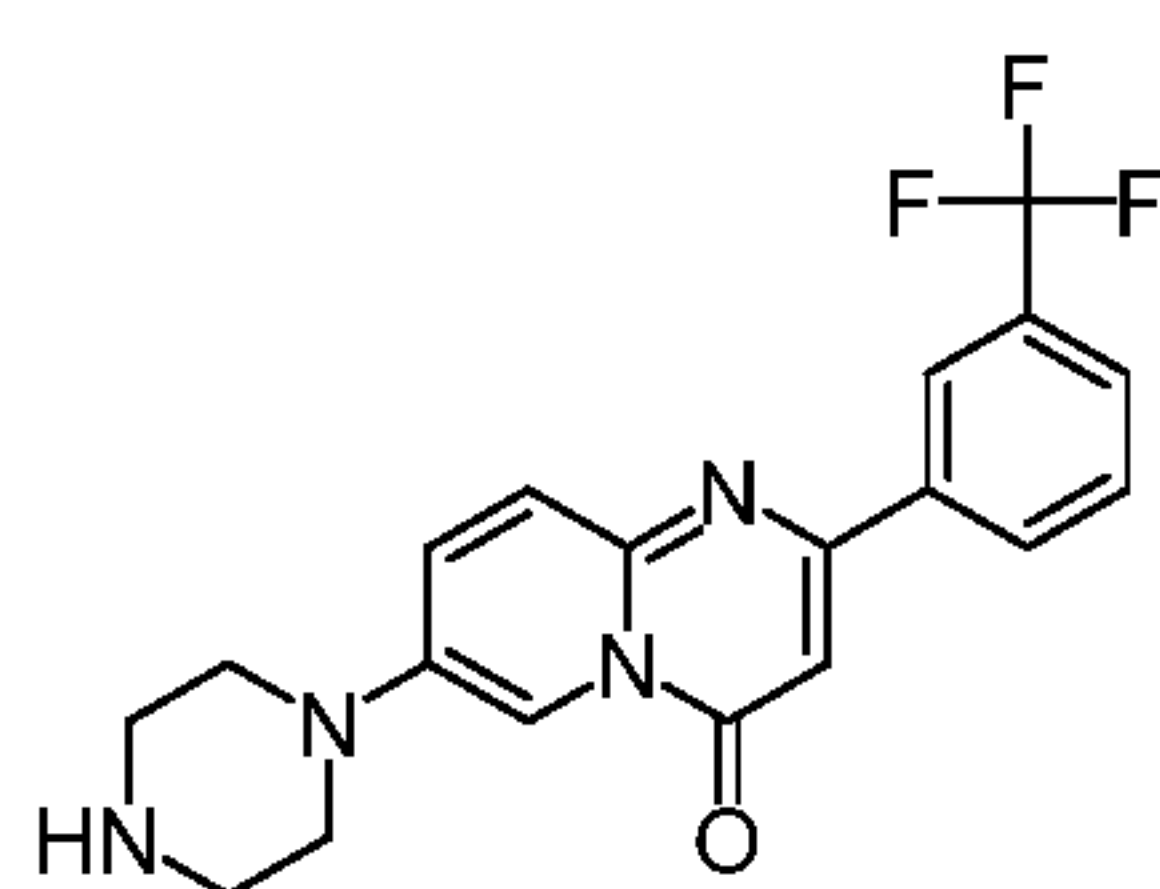
40



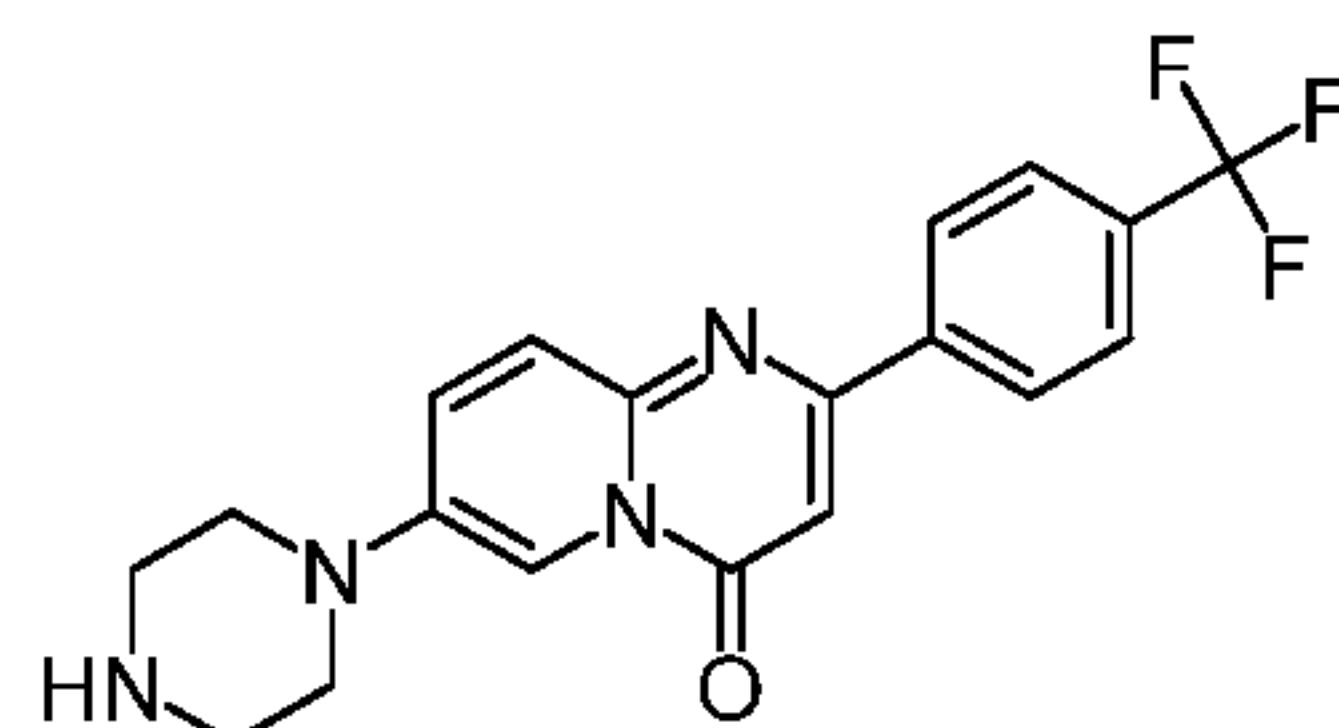
41



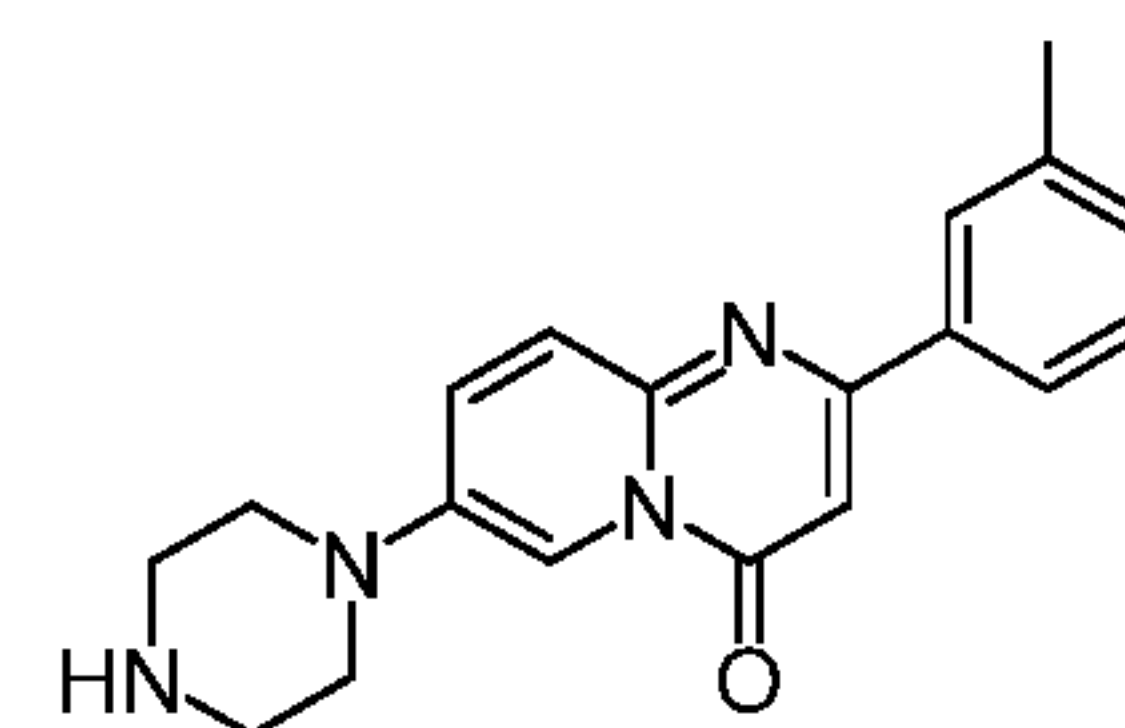
42



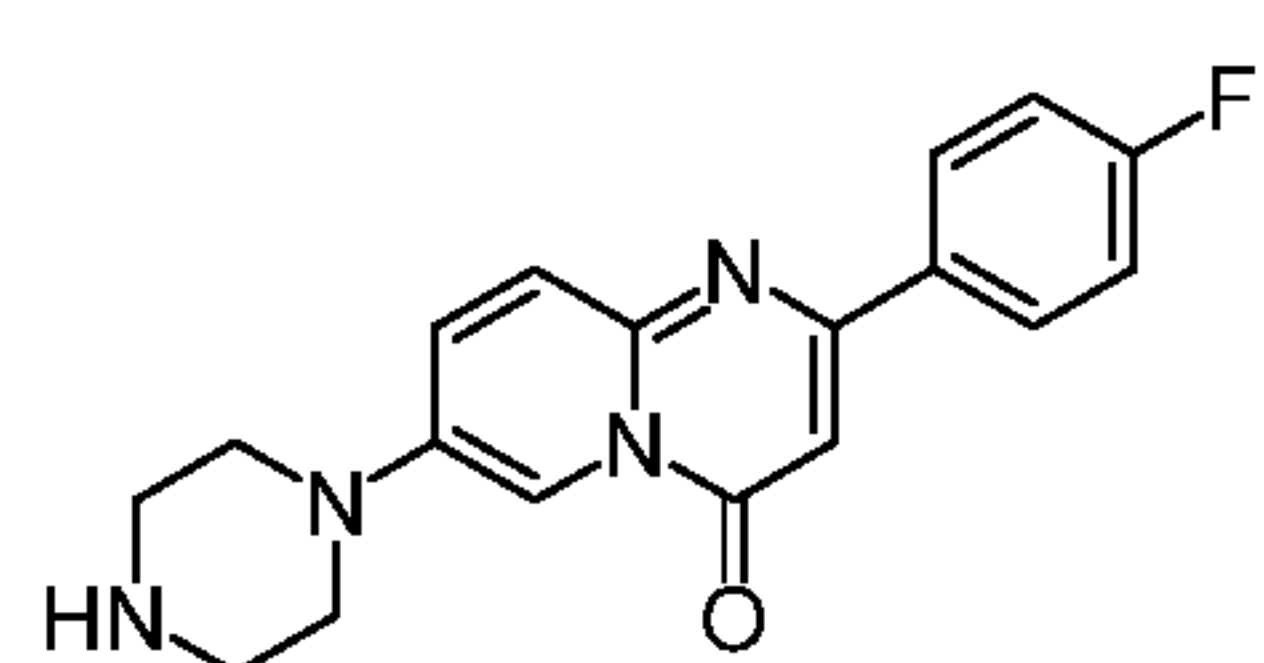
43



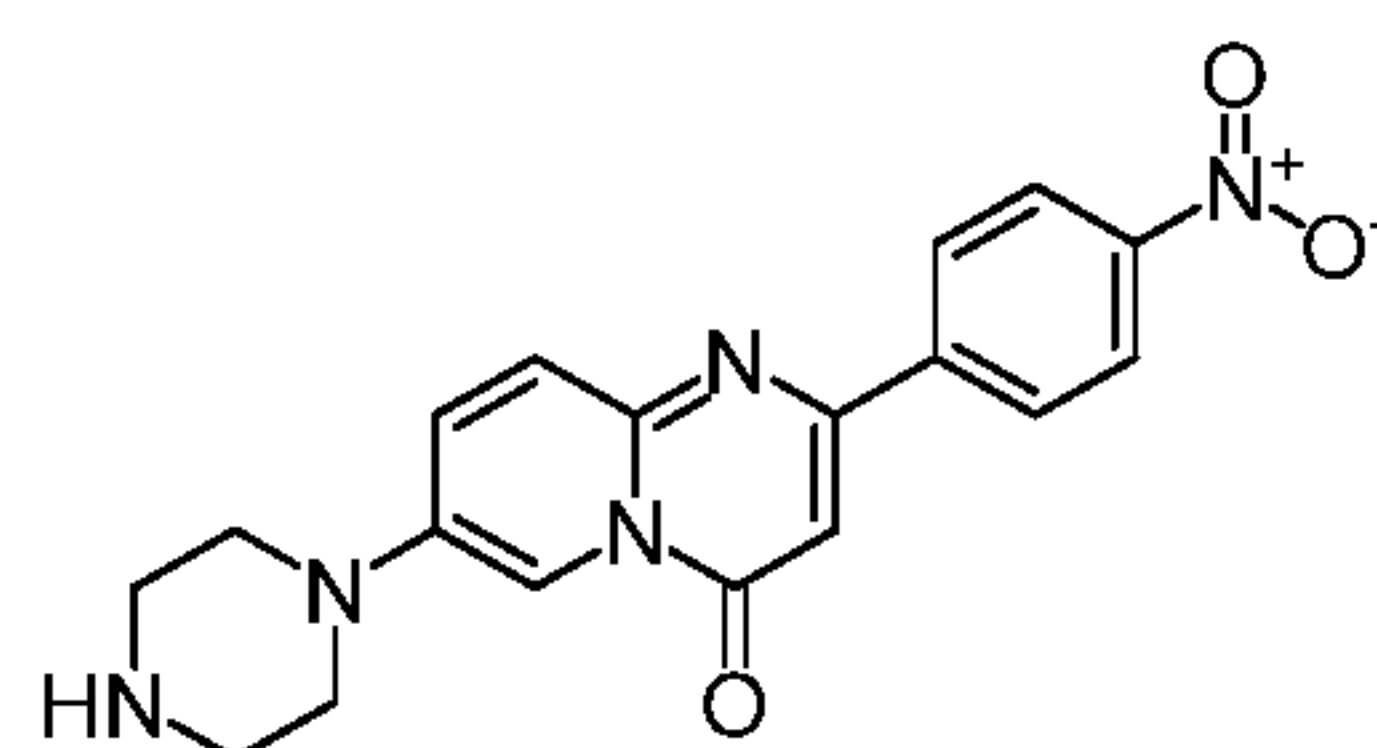
44



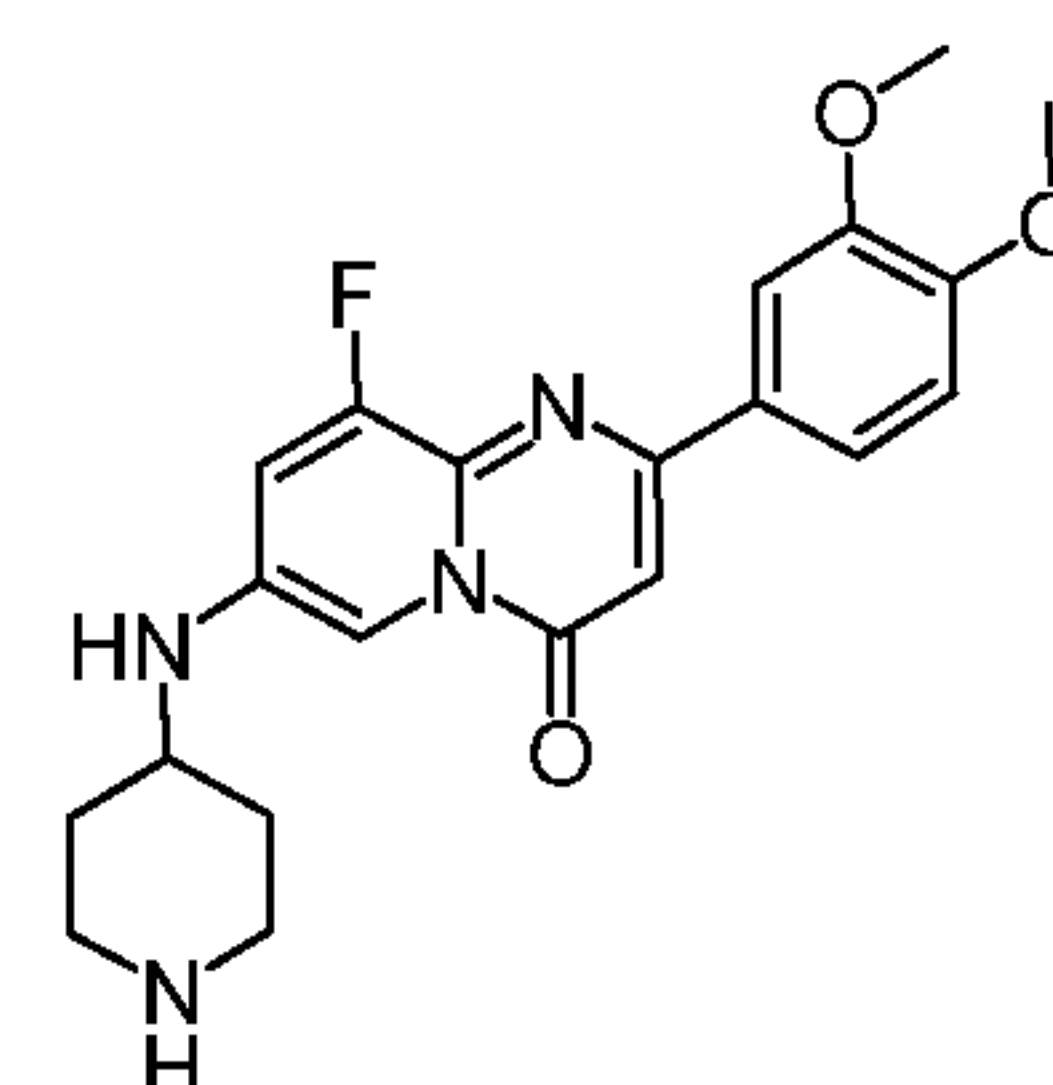
45



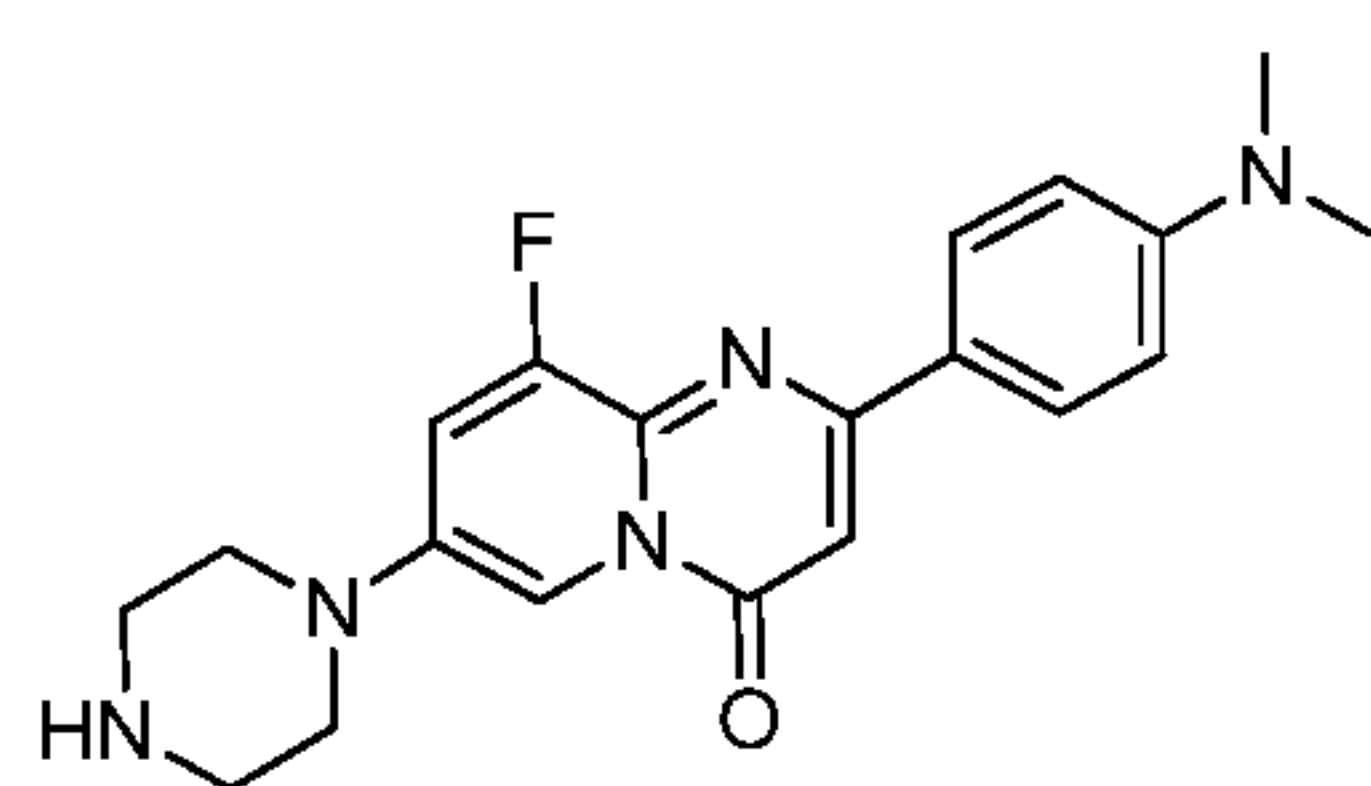
46



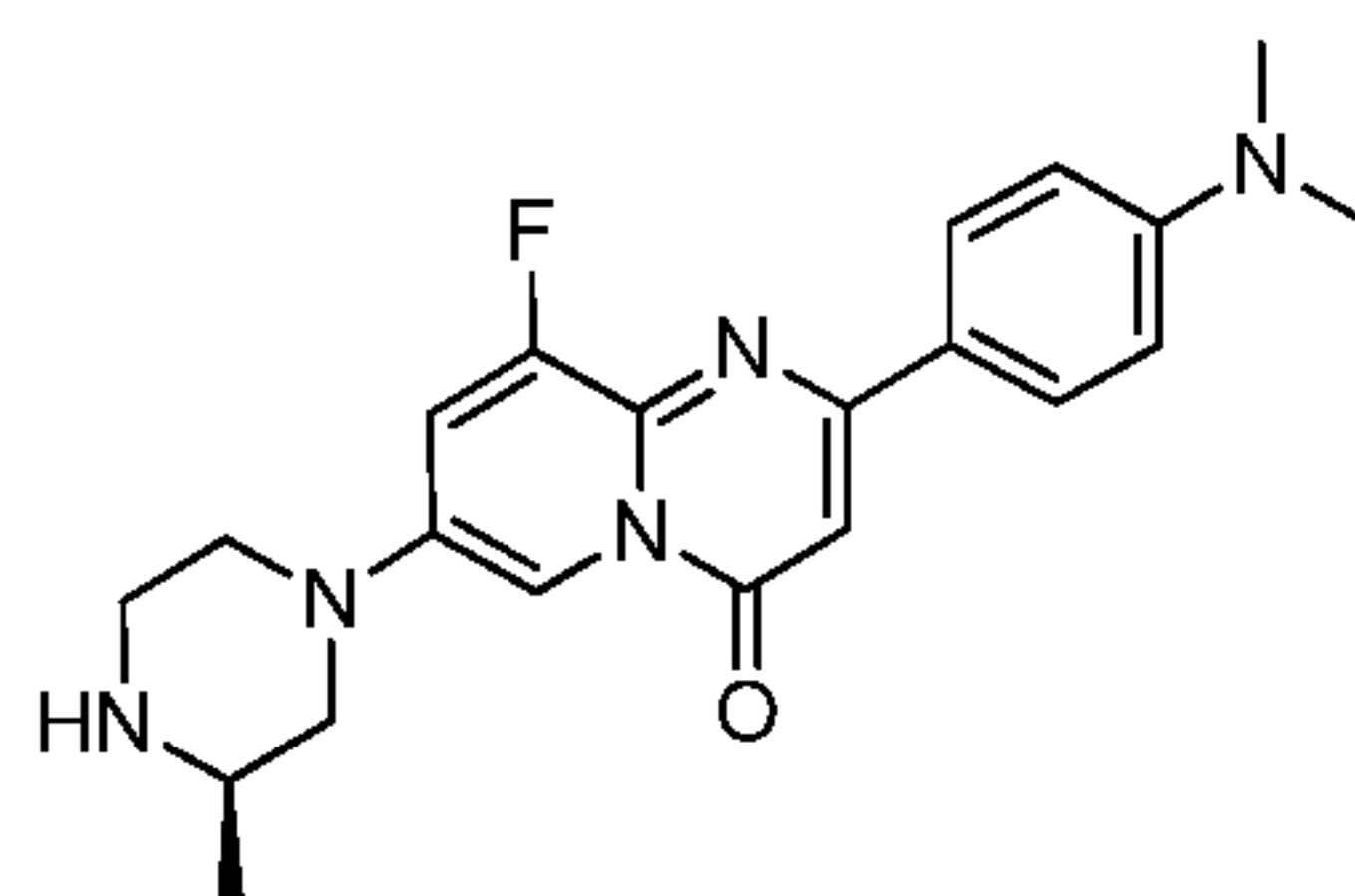
47



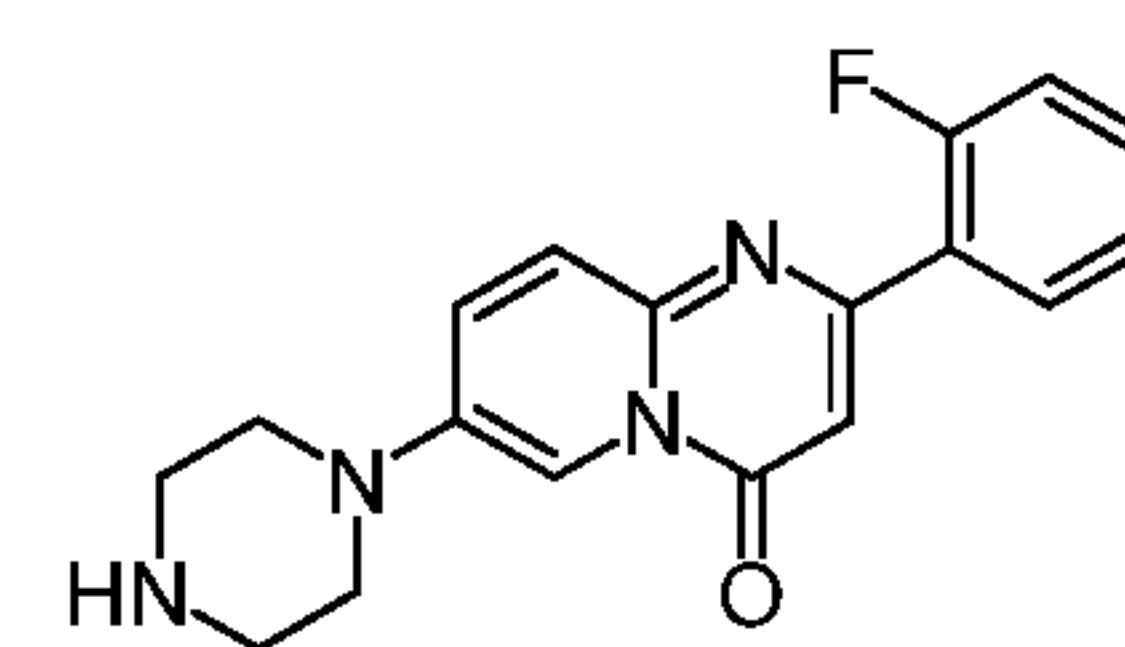
48



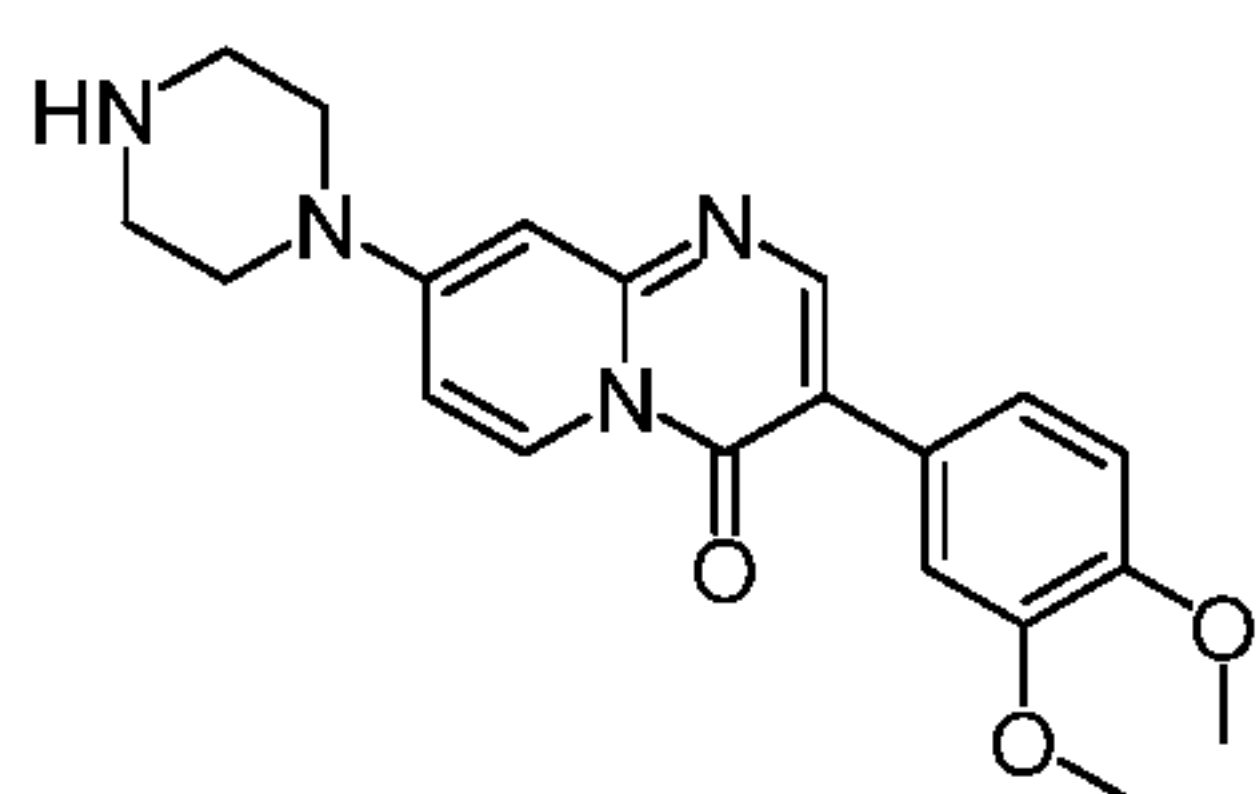
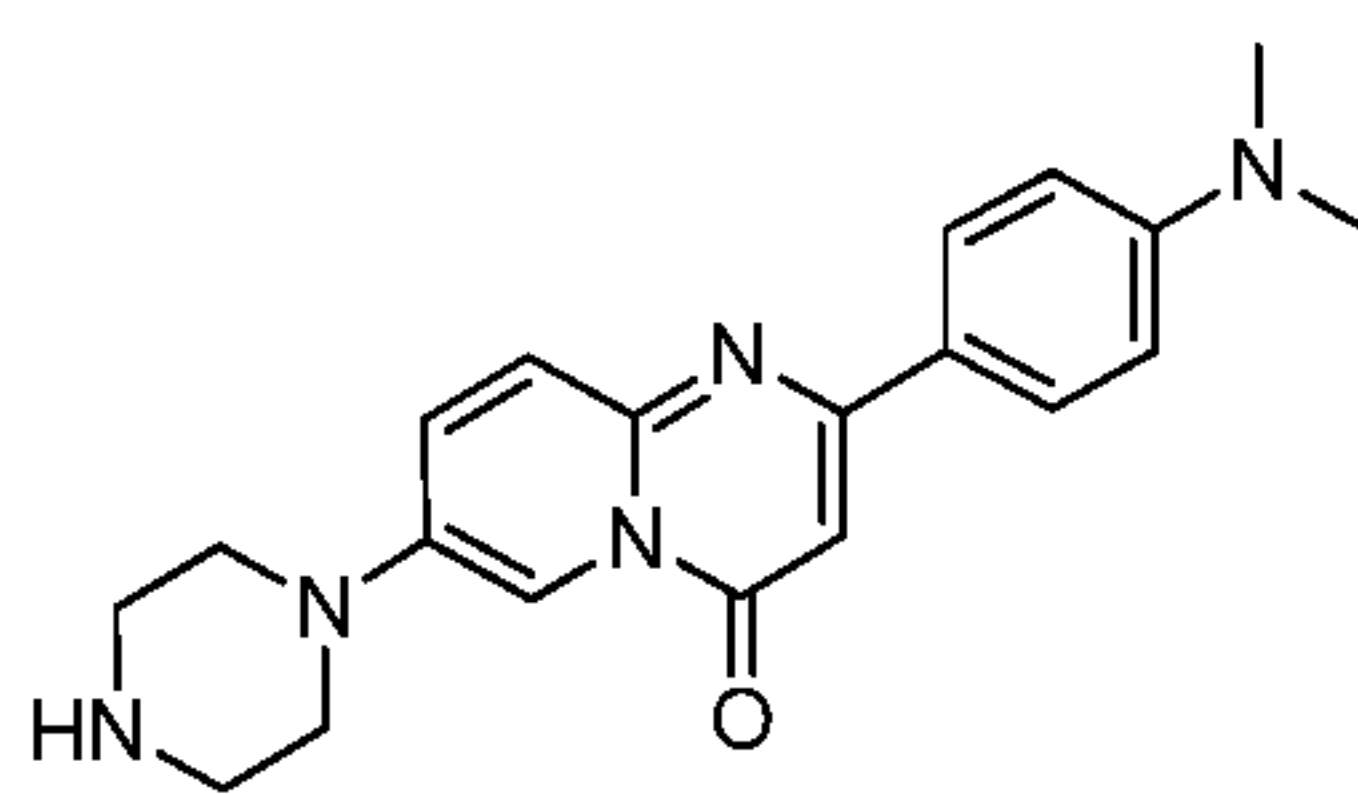
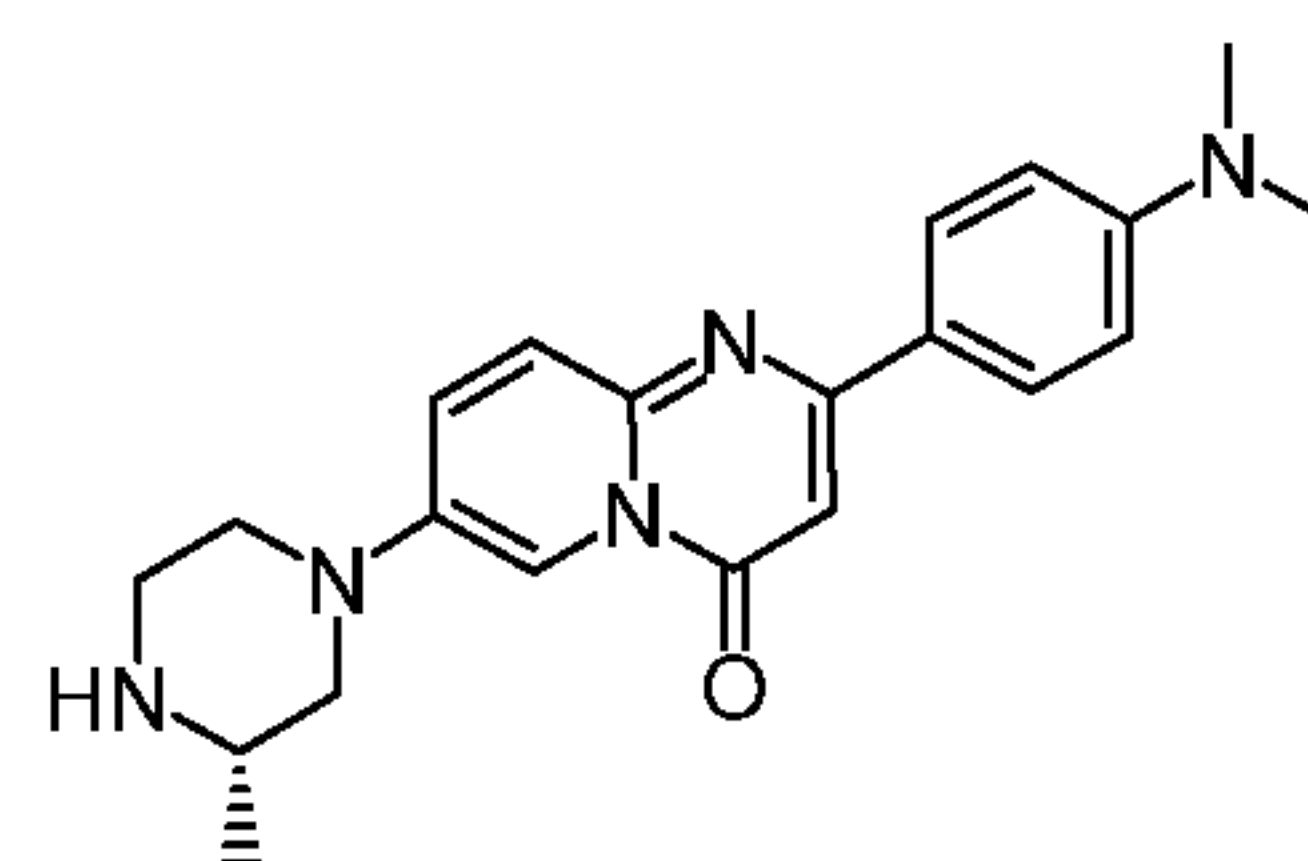
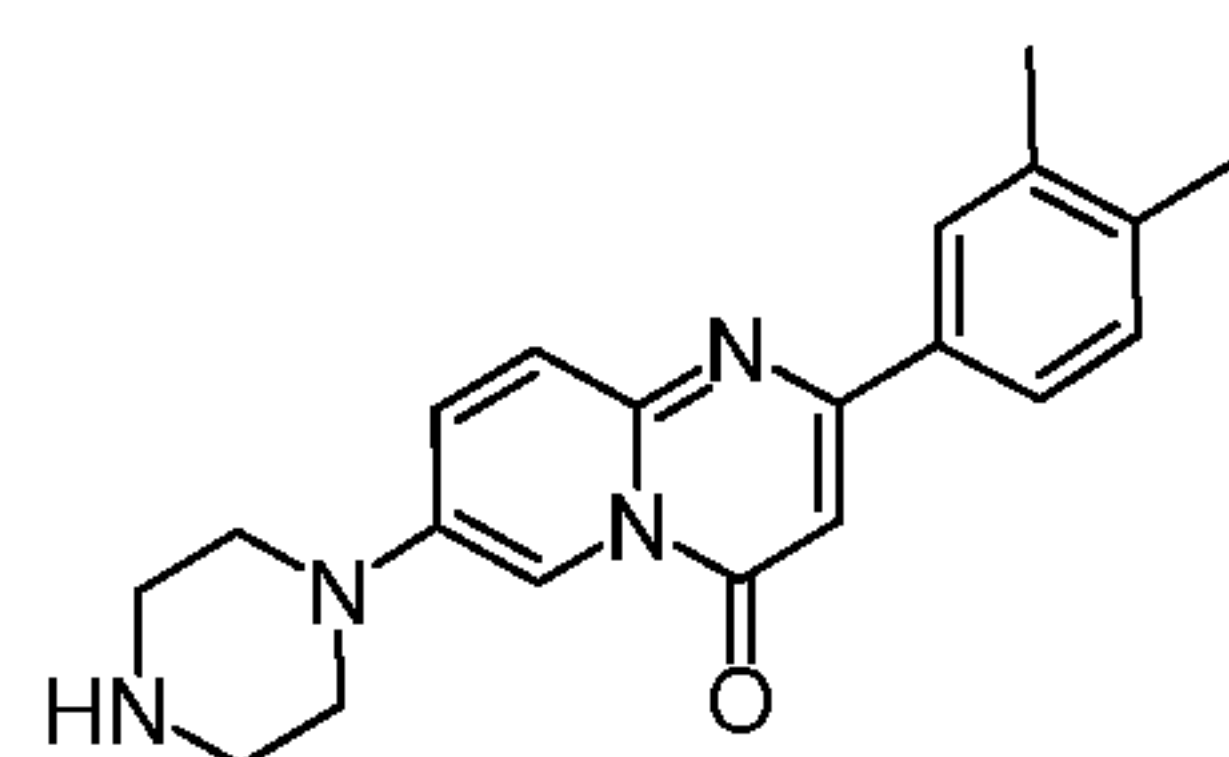
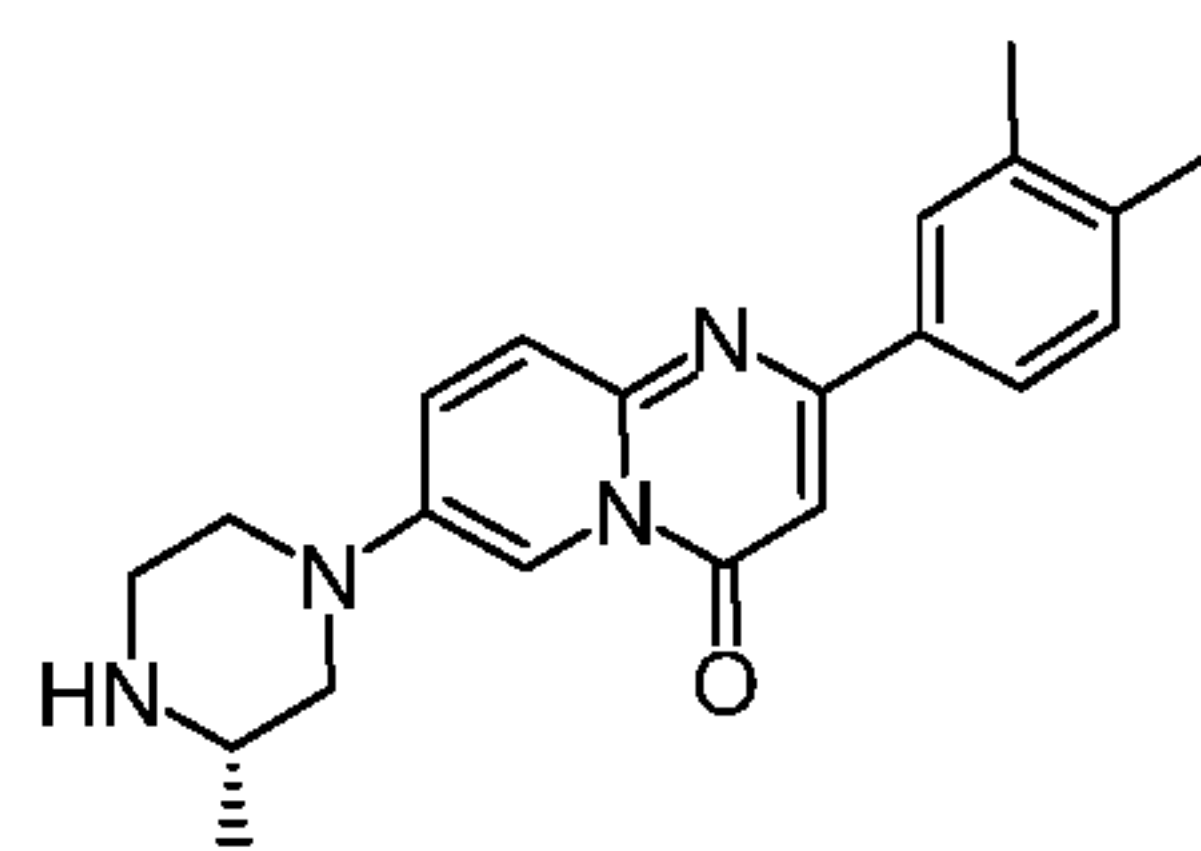
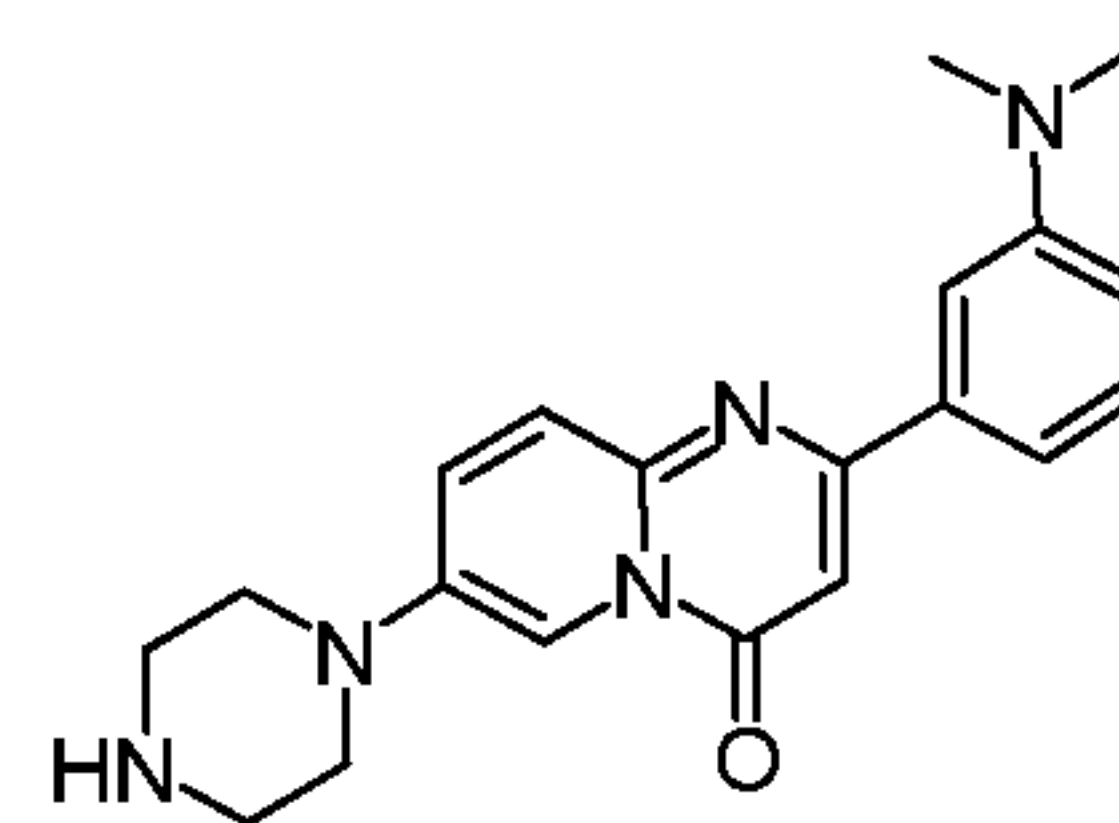
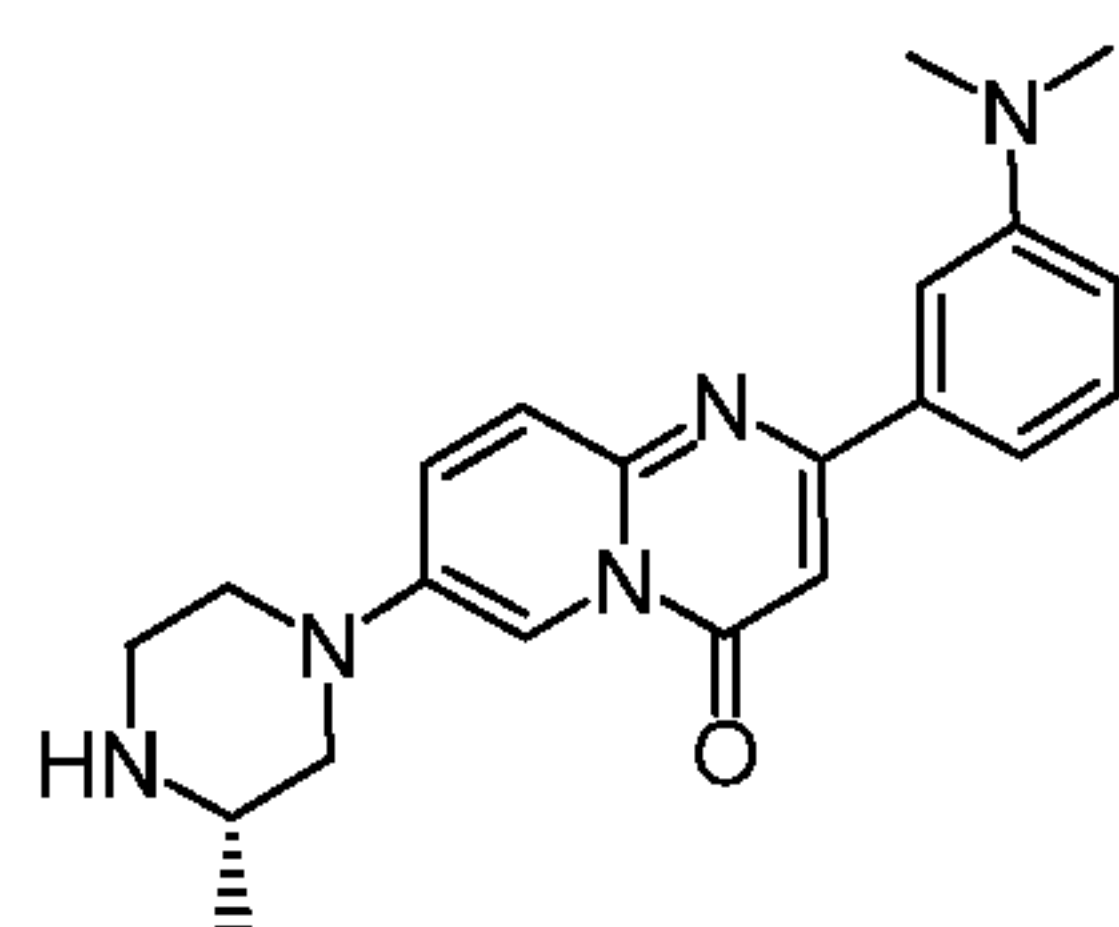
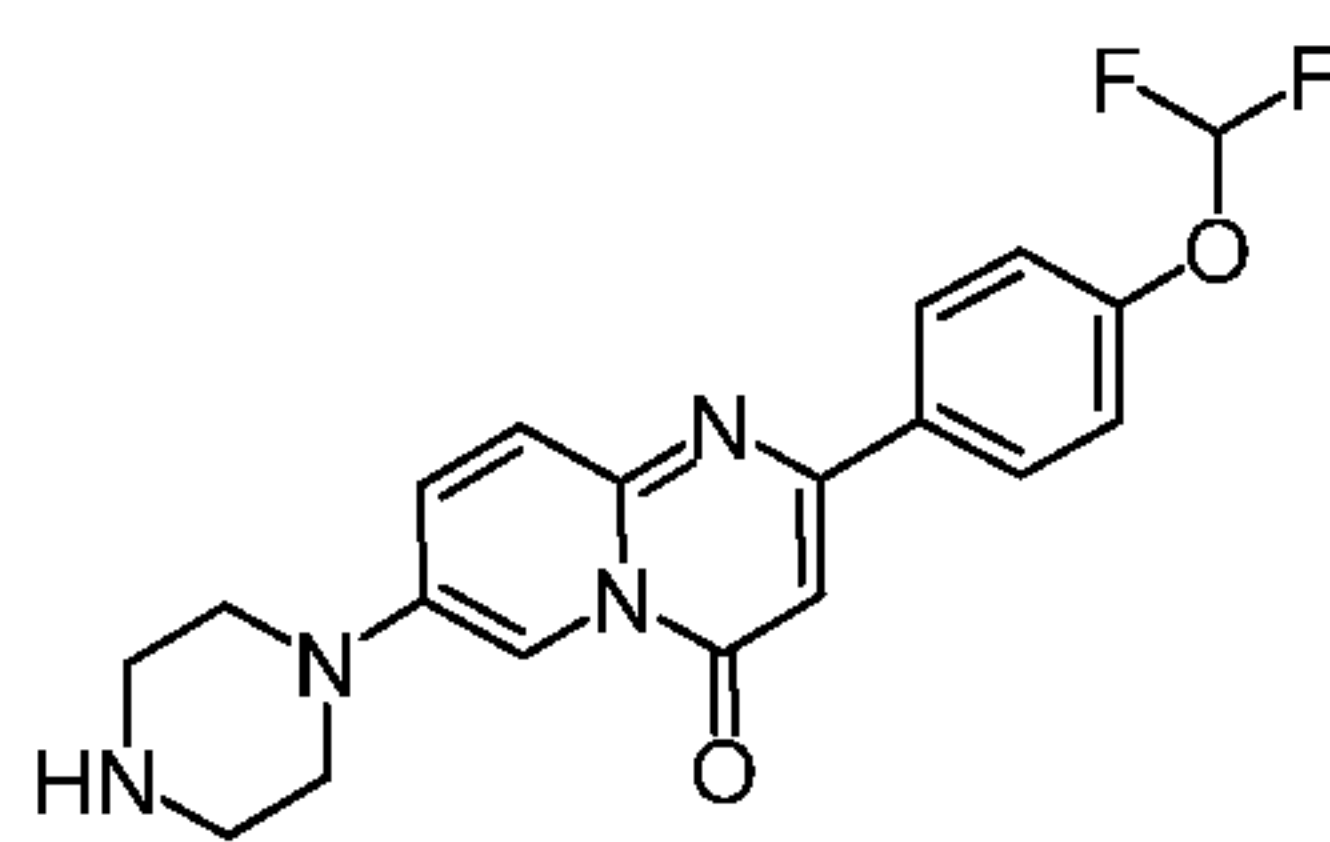
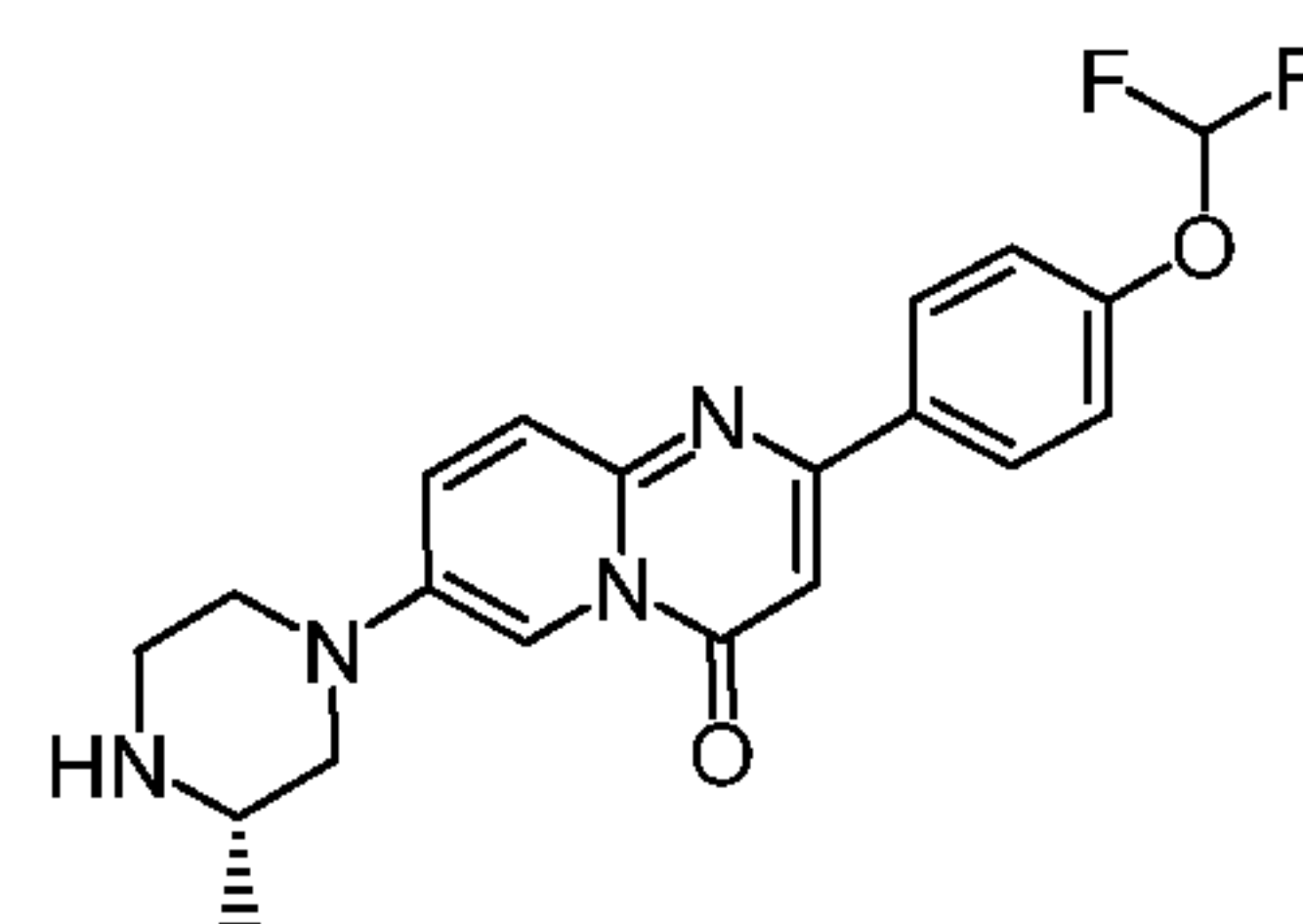
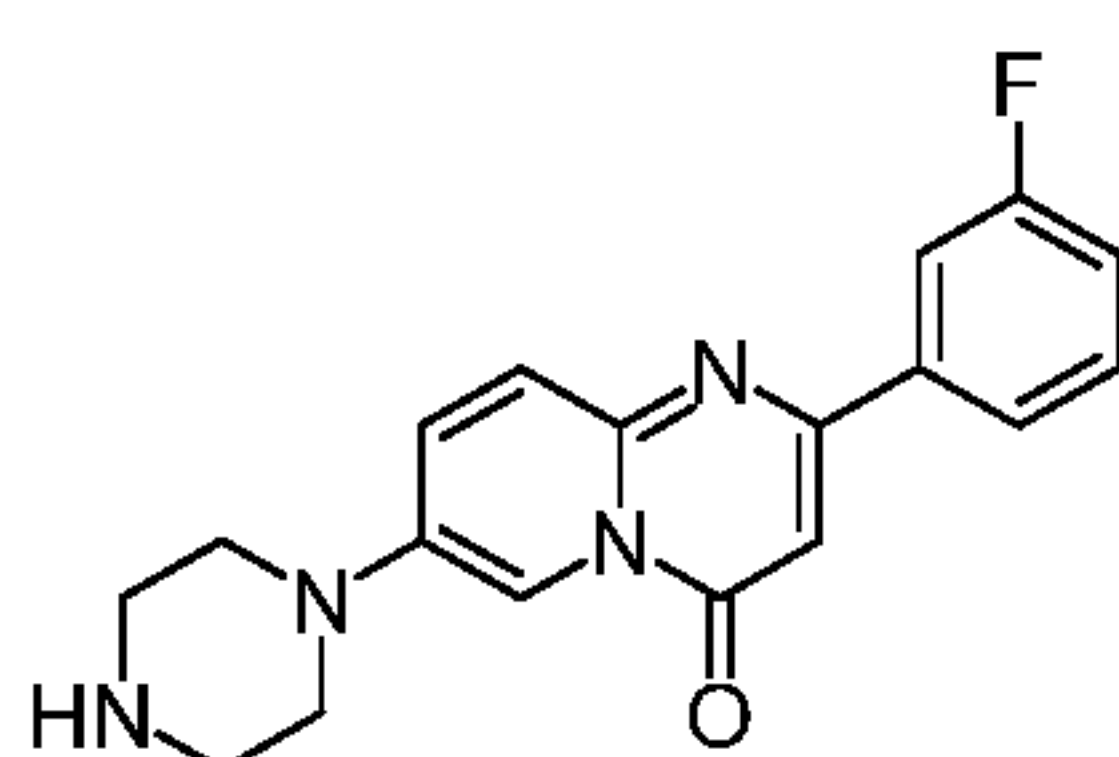
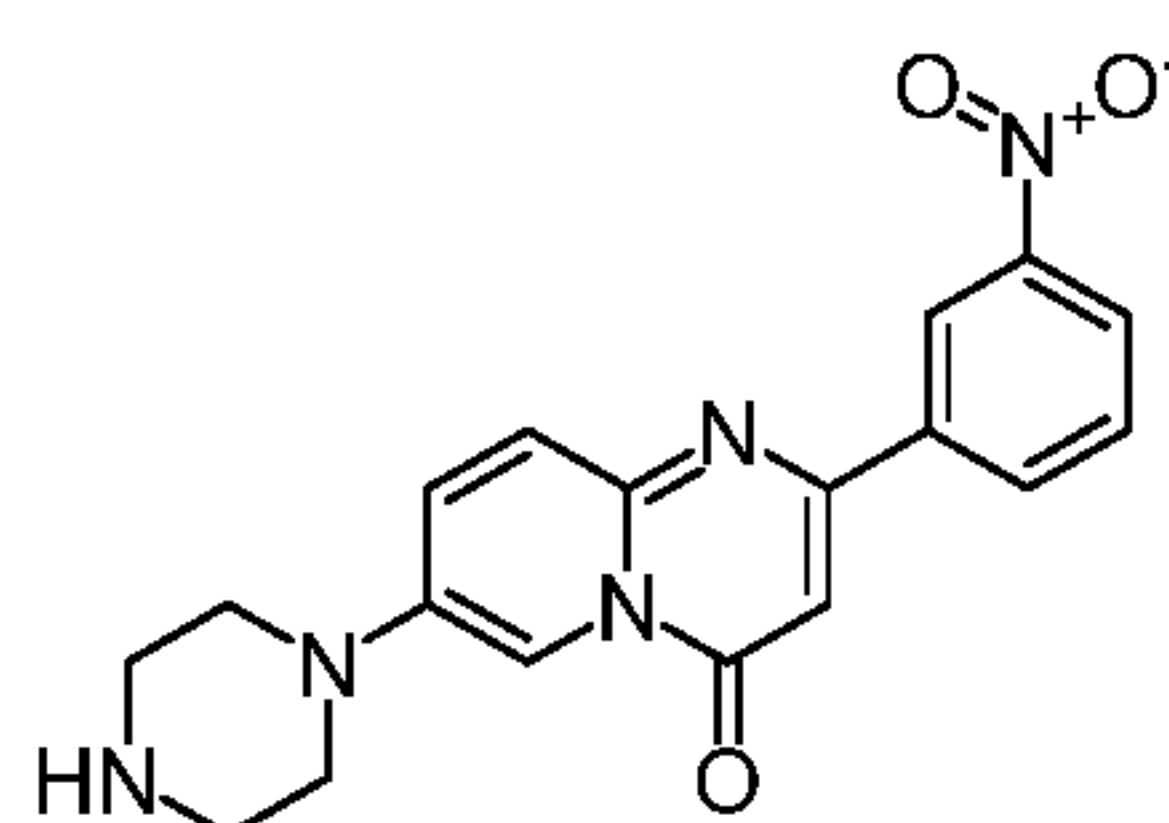
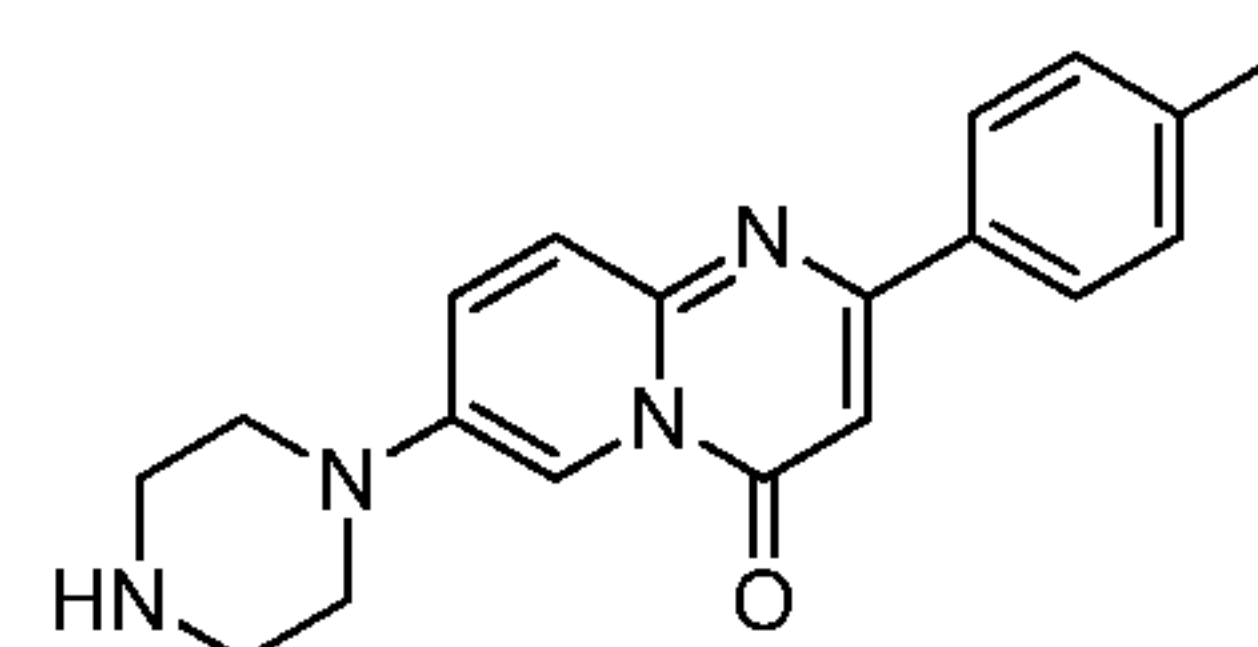
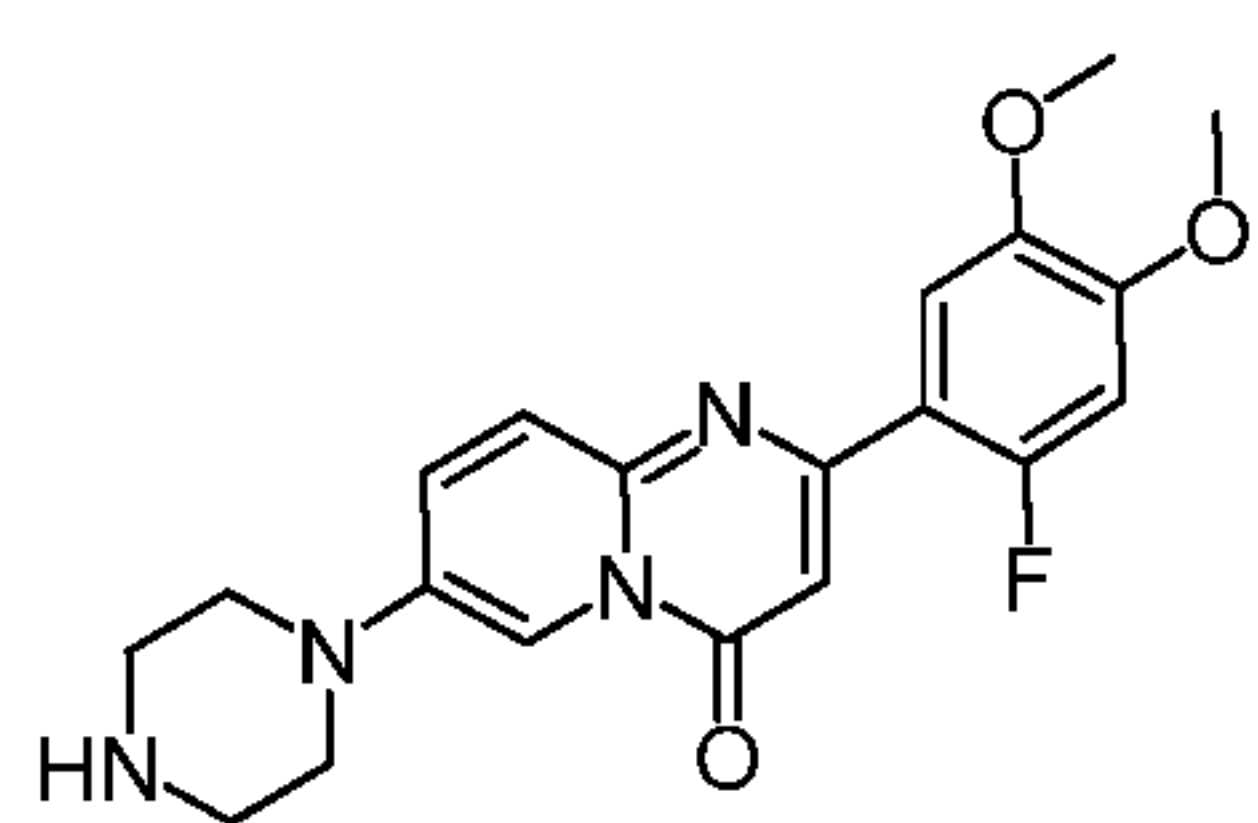
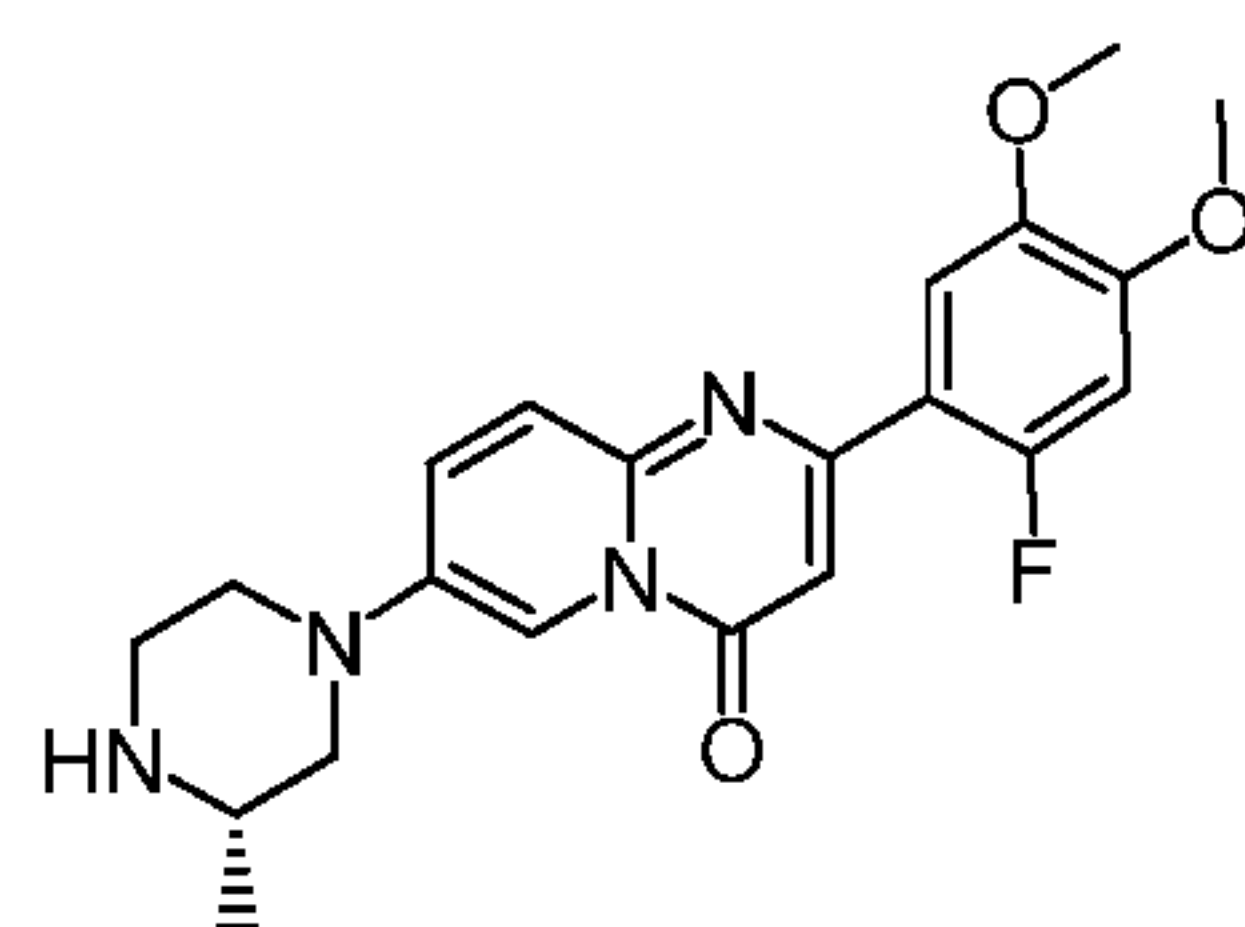
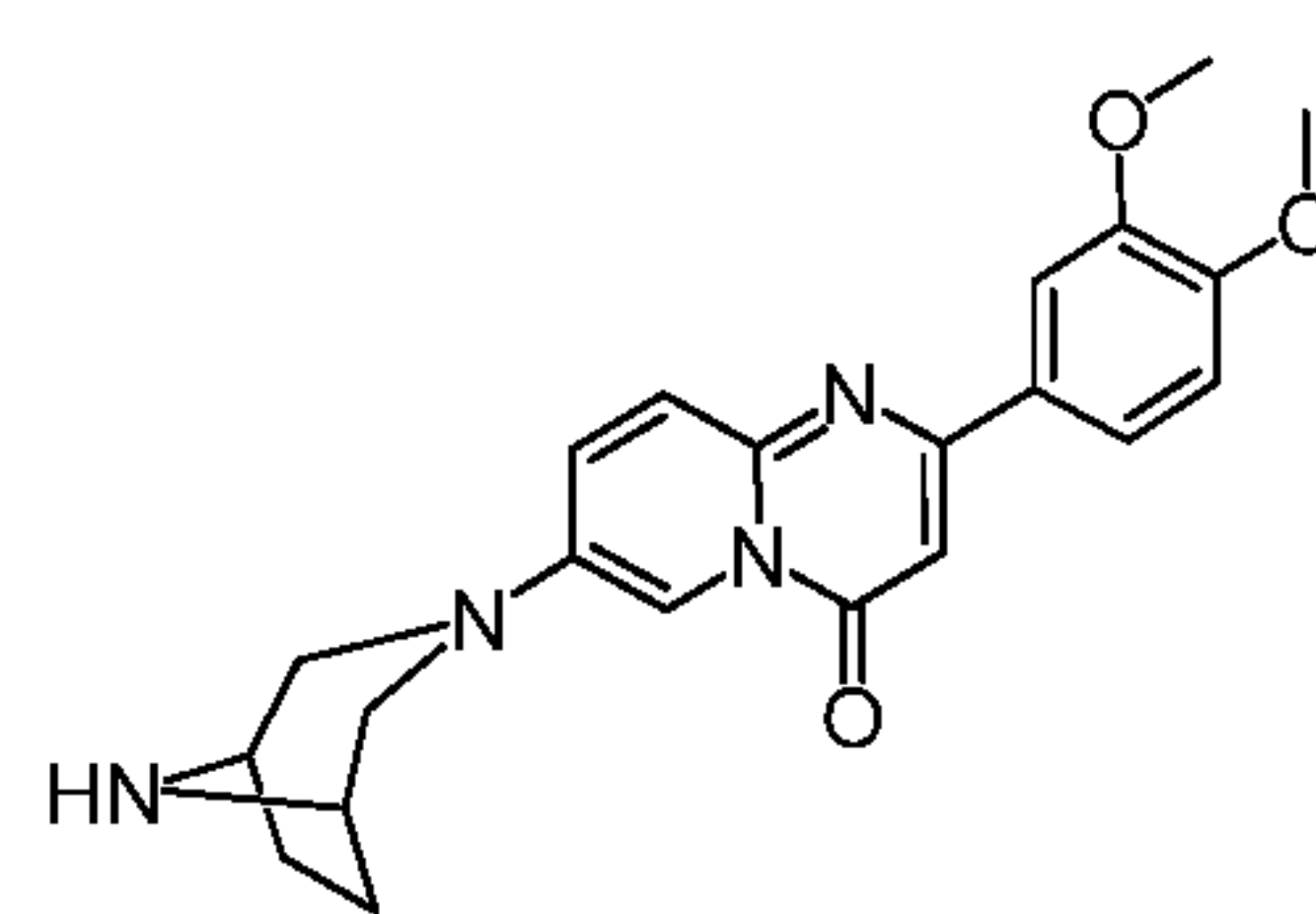
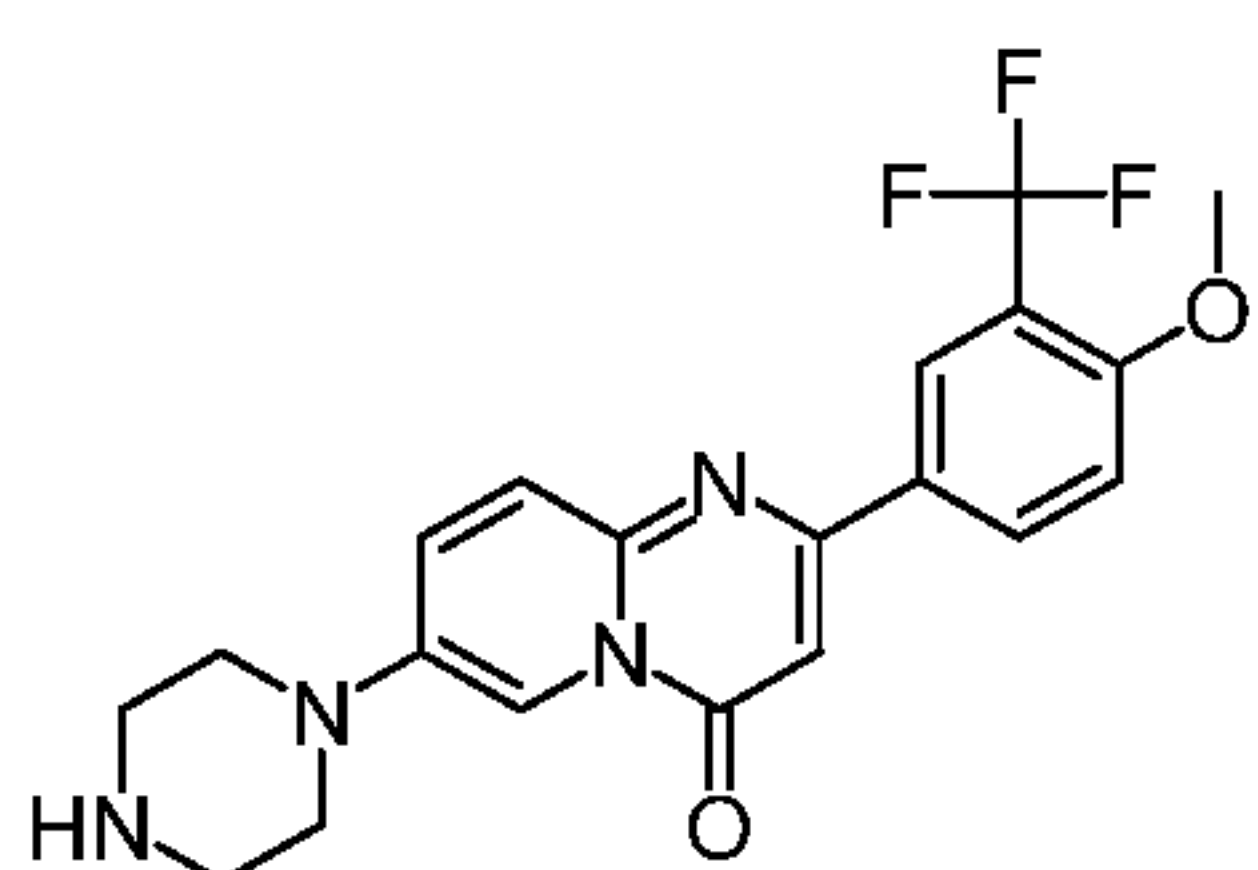
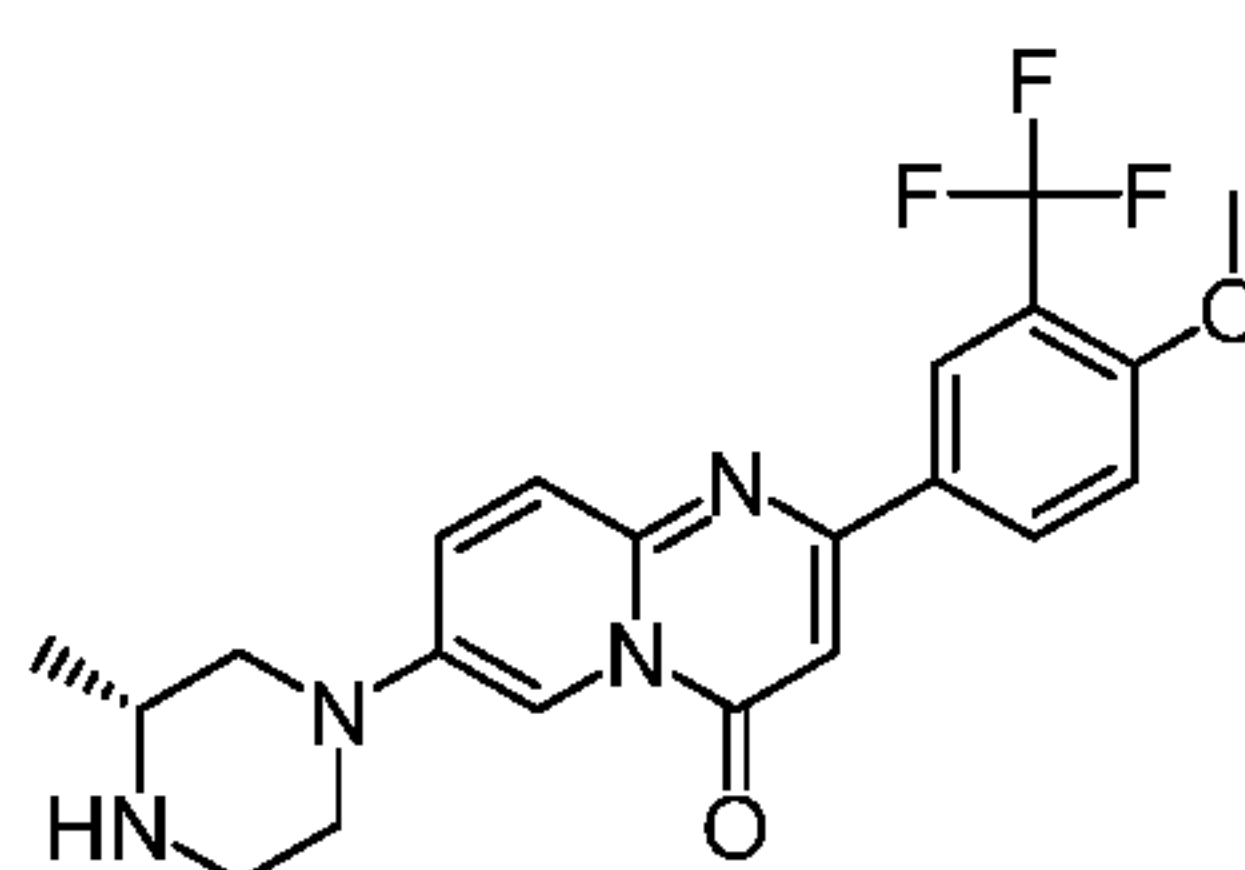
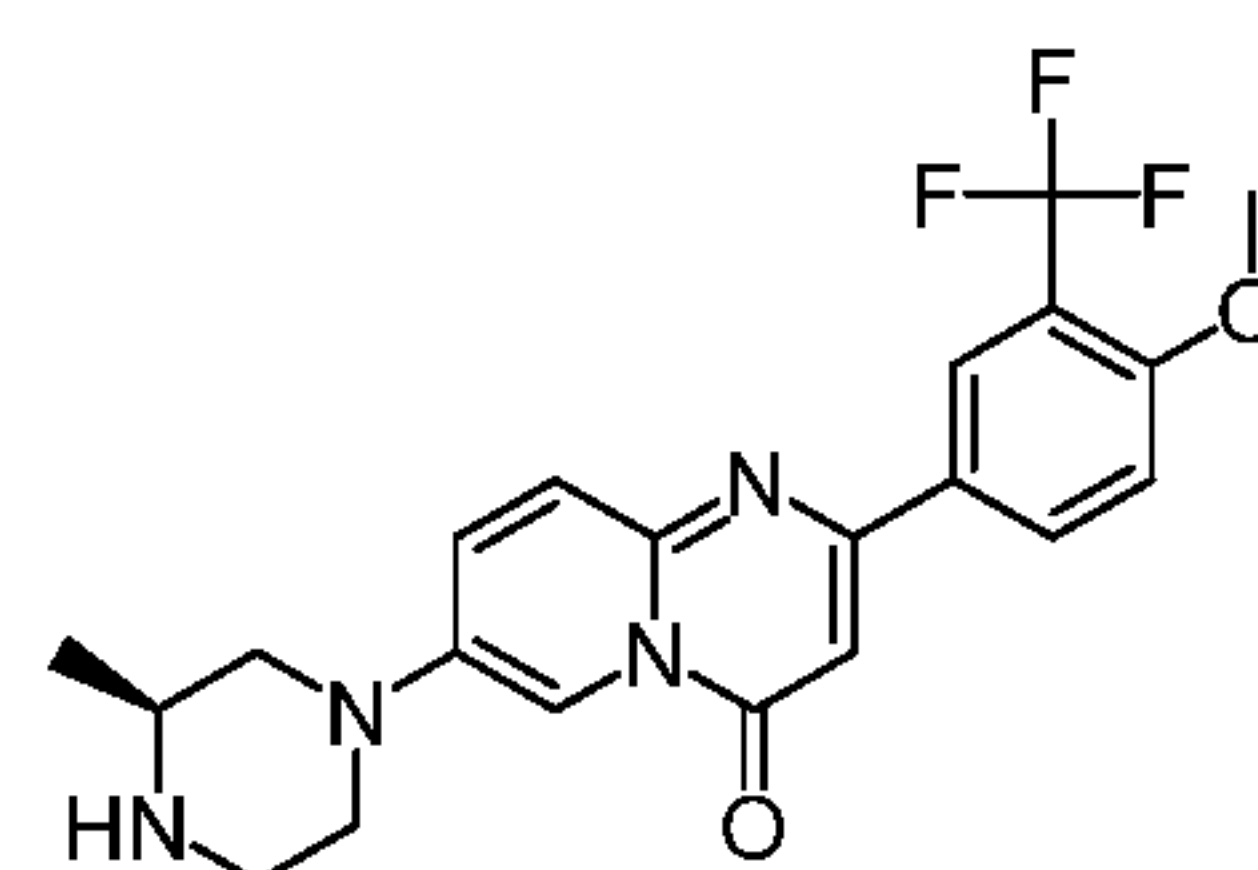
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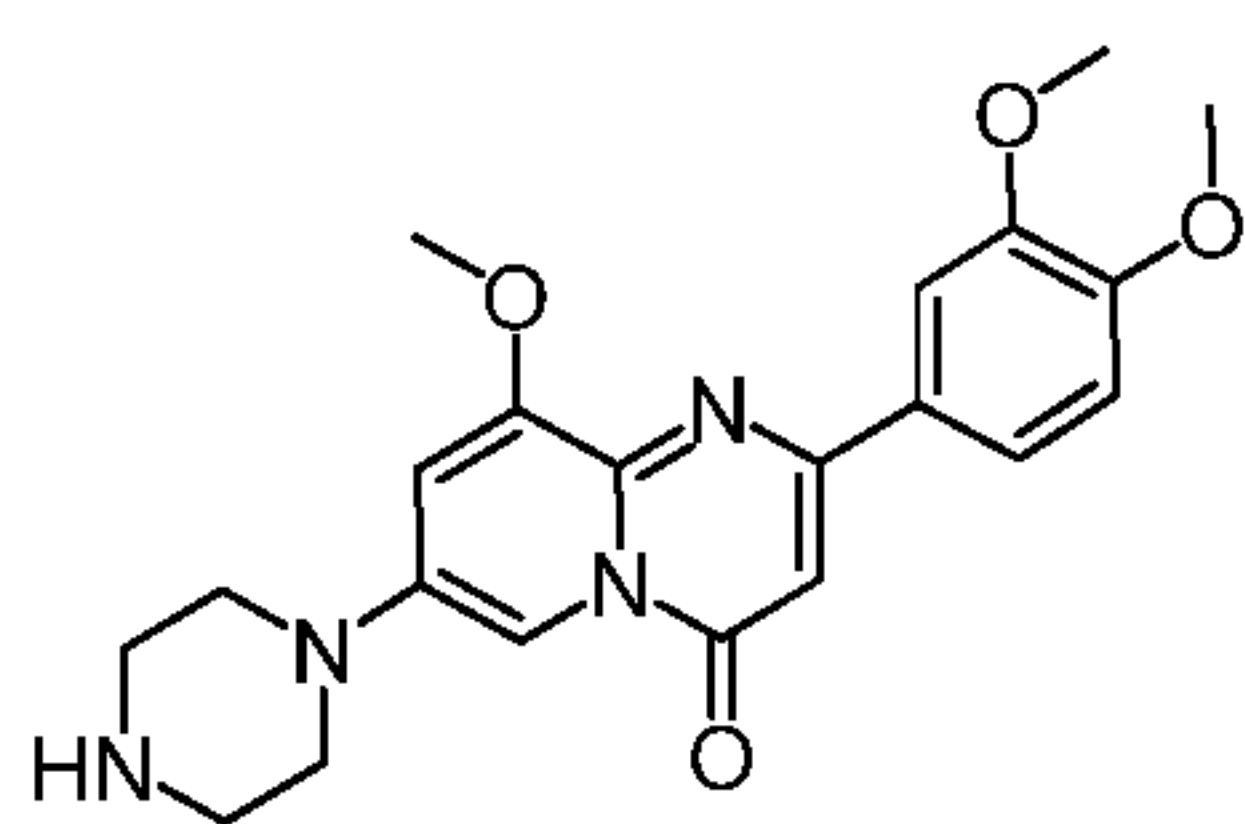
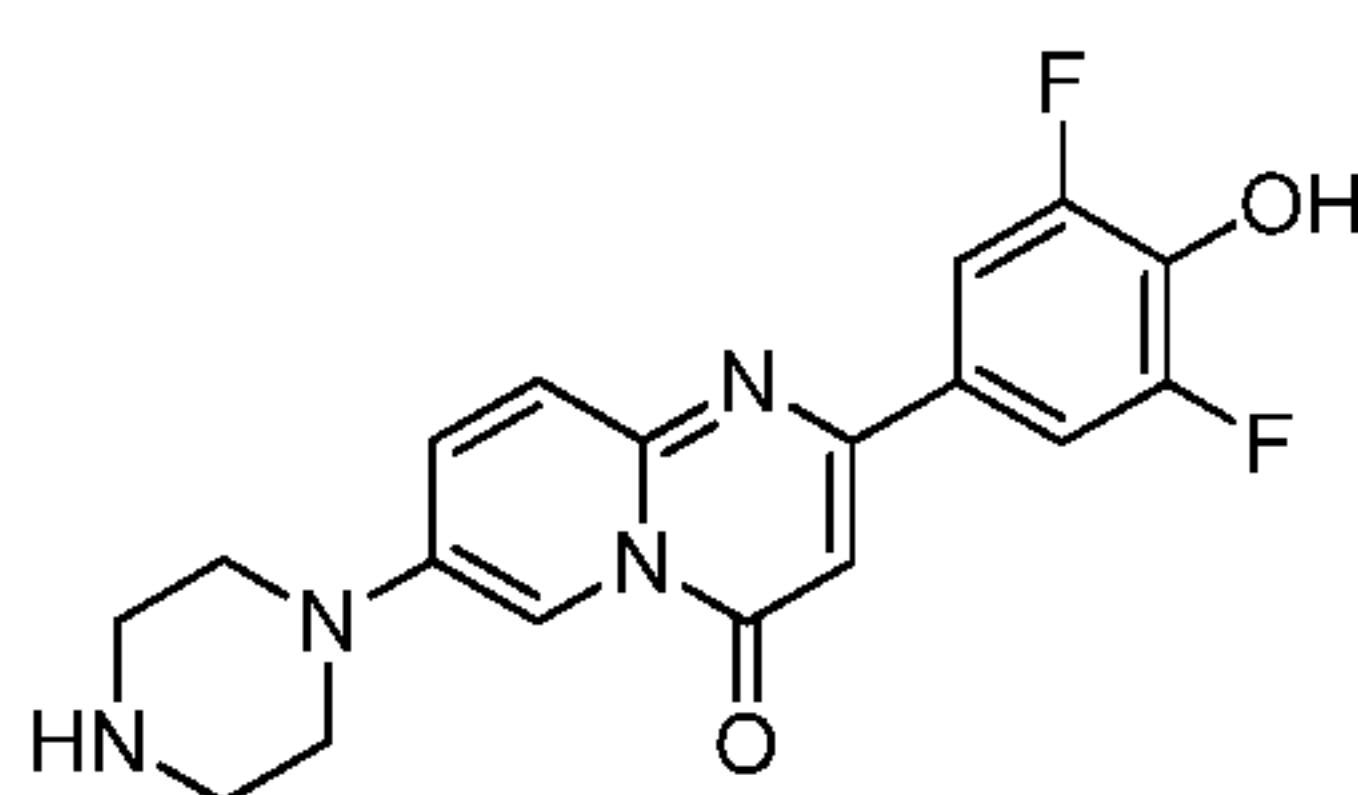
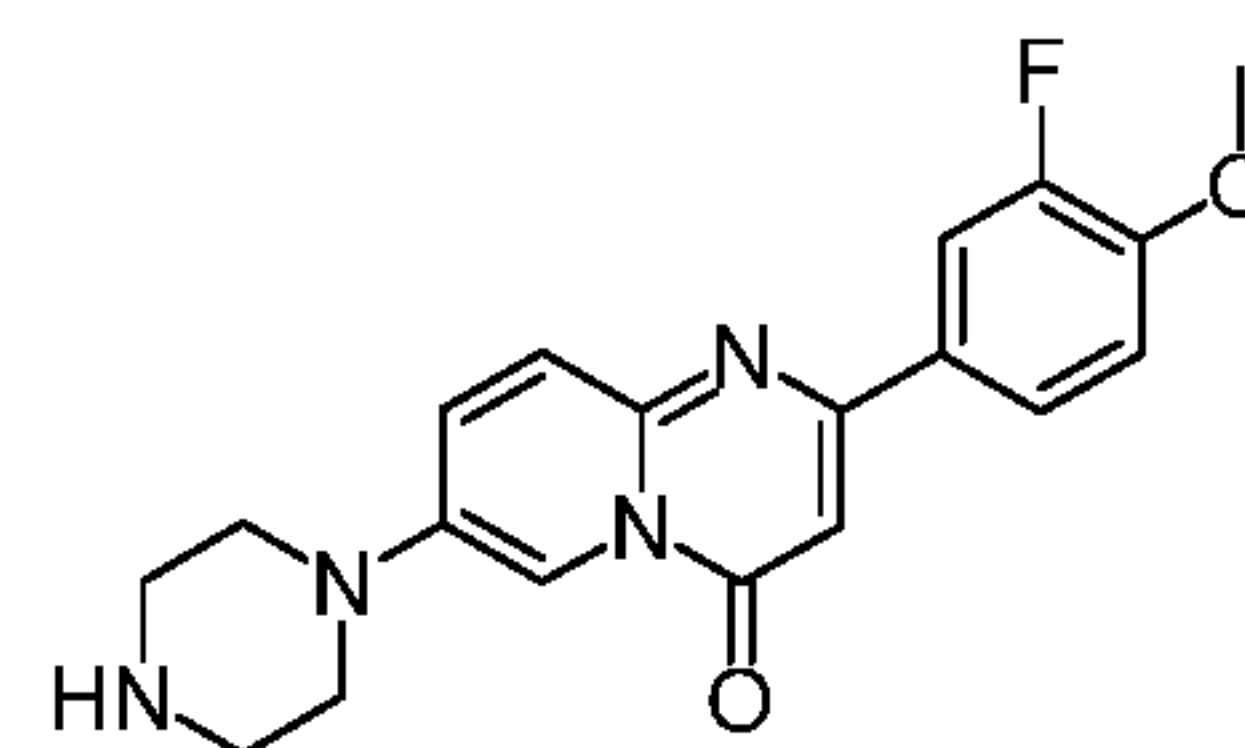
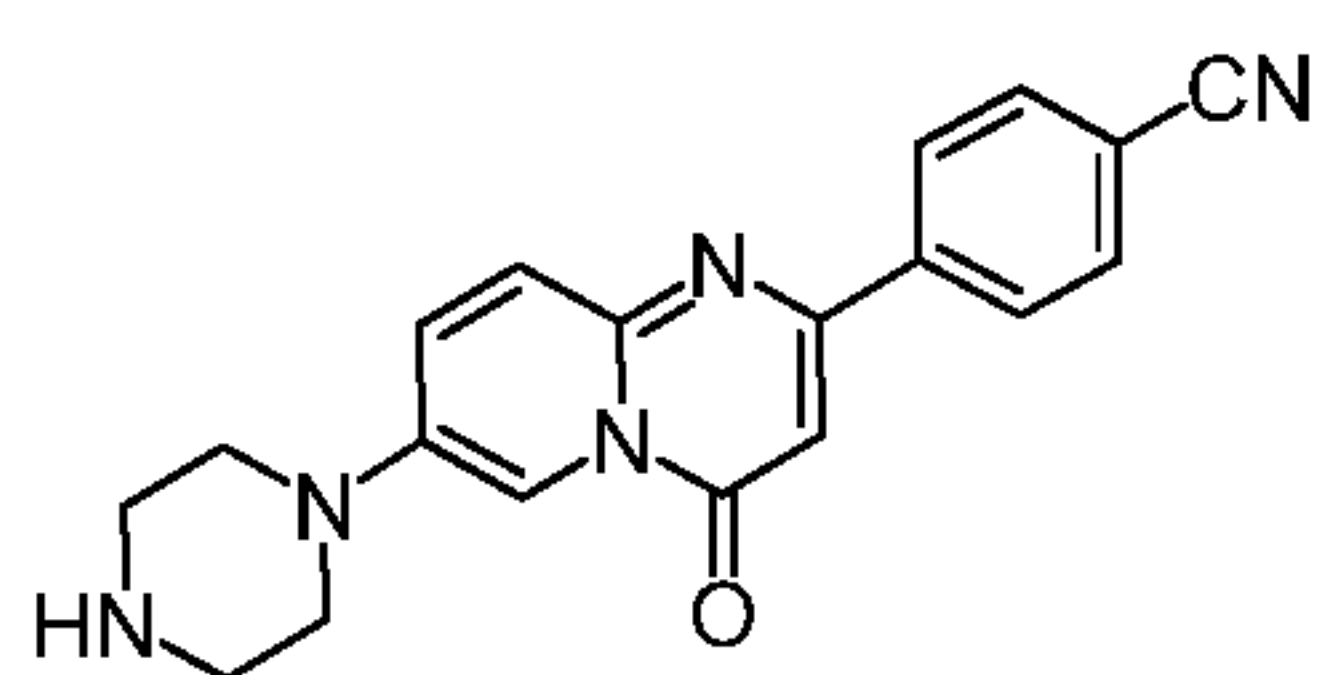
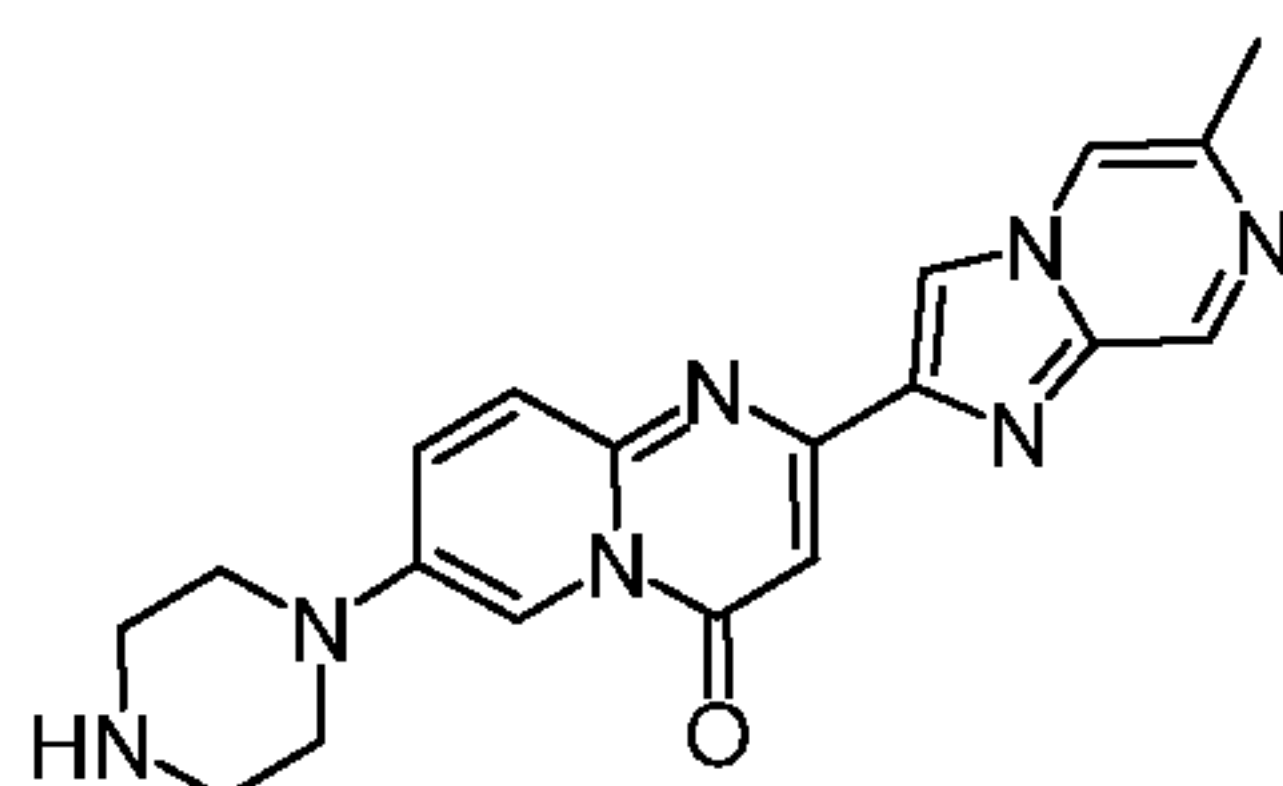
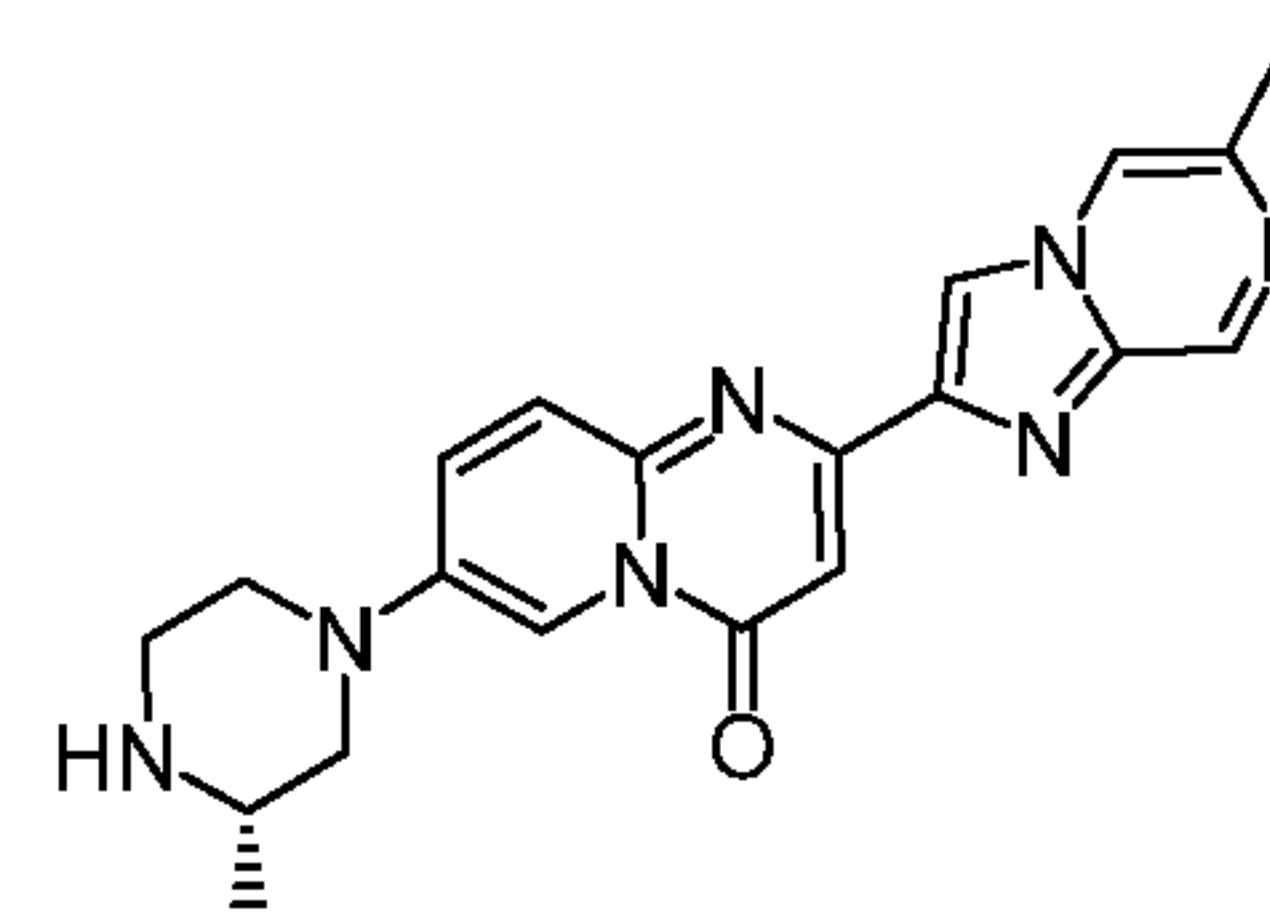
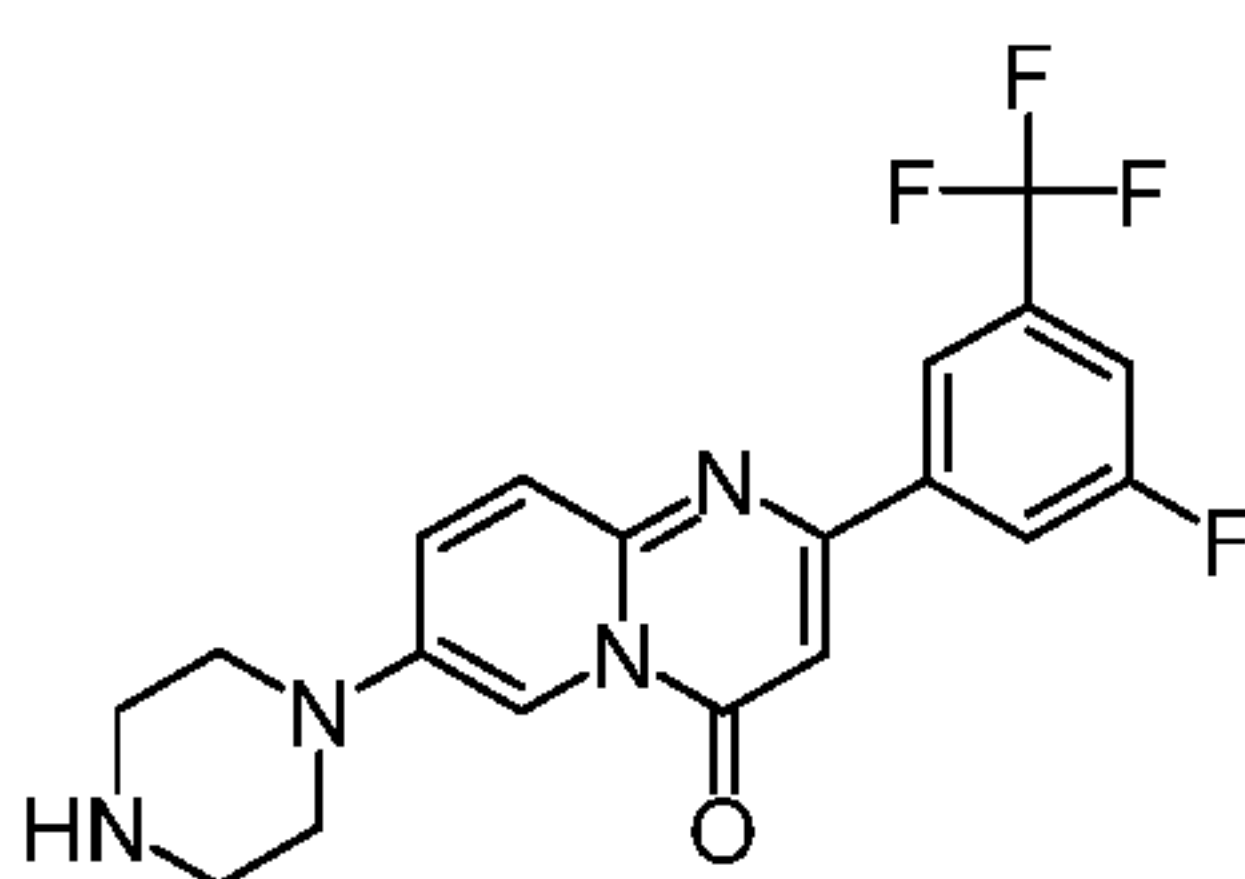
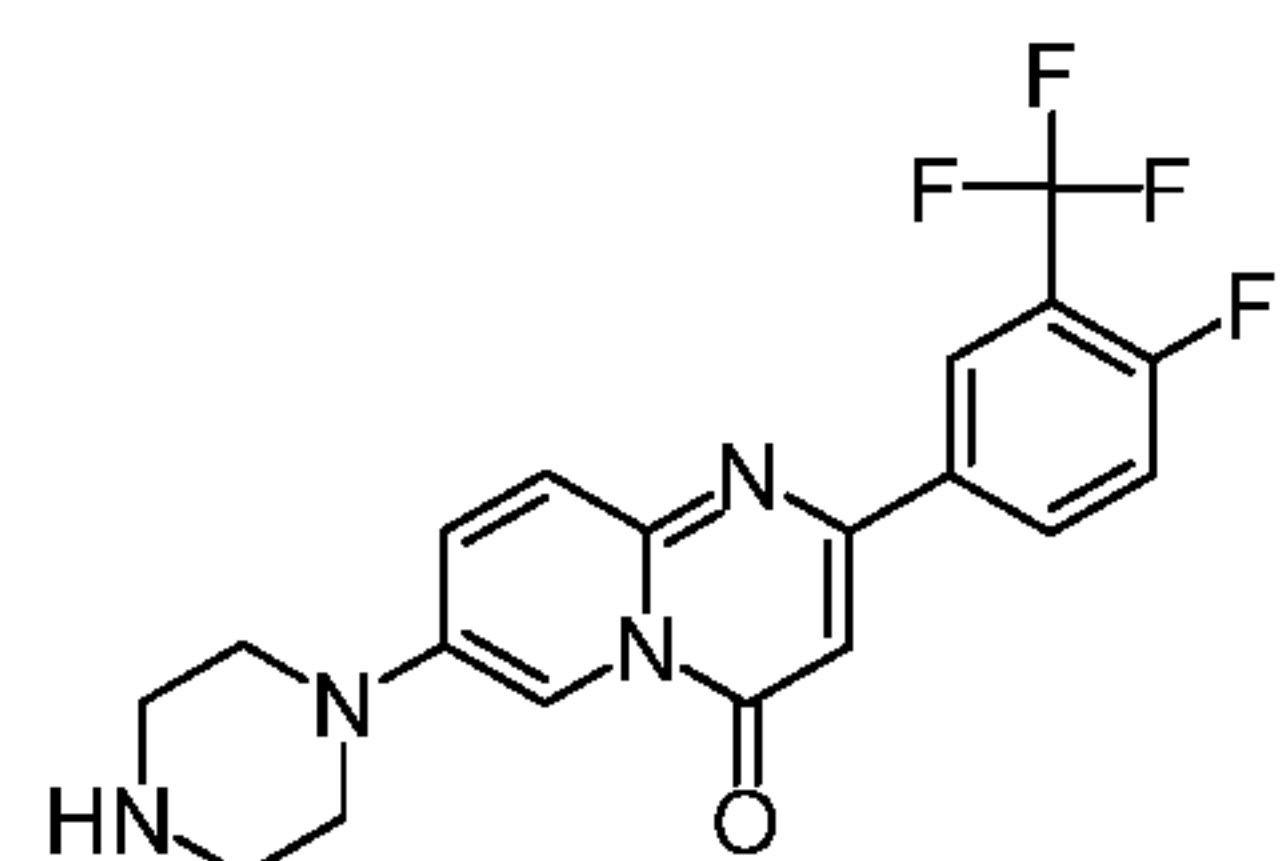
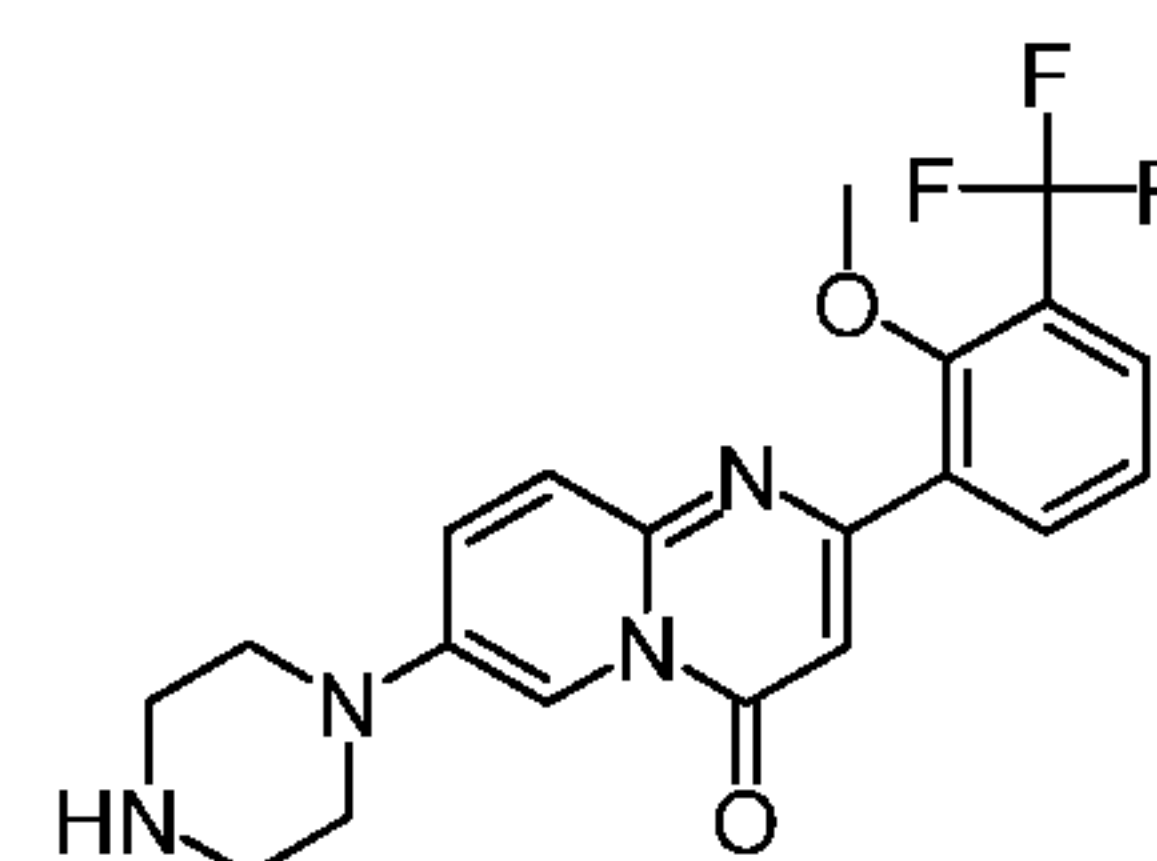
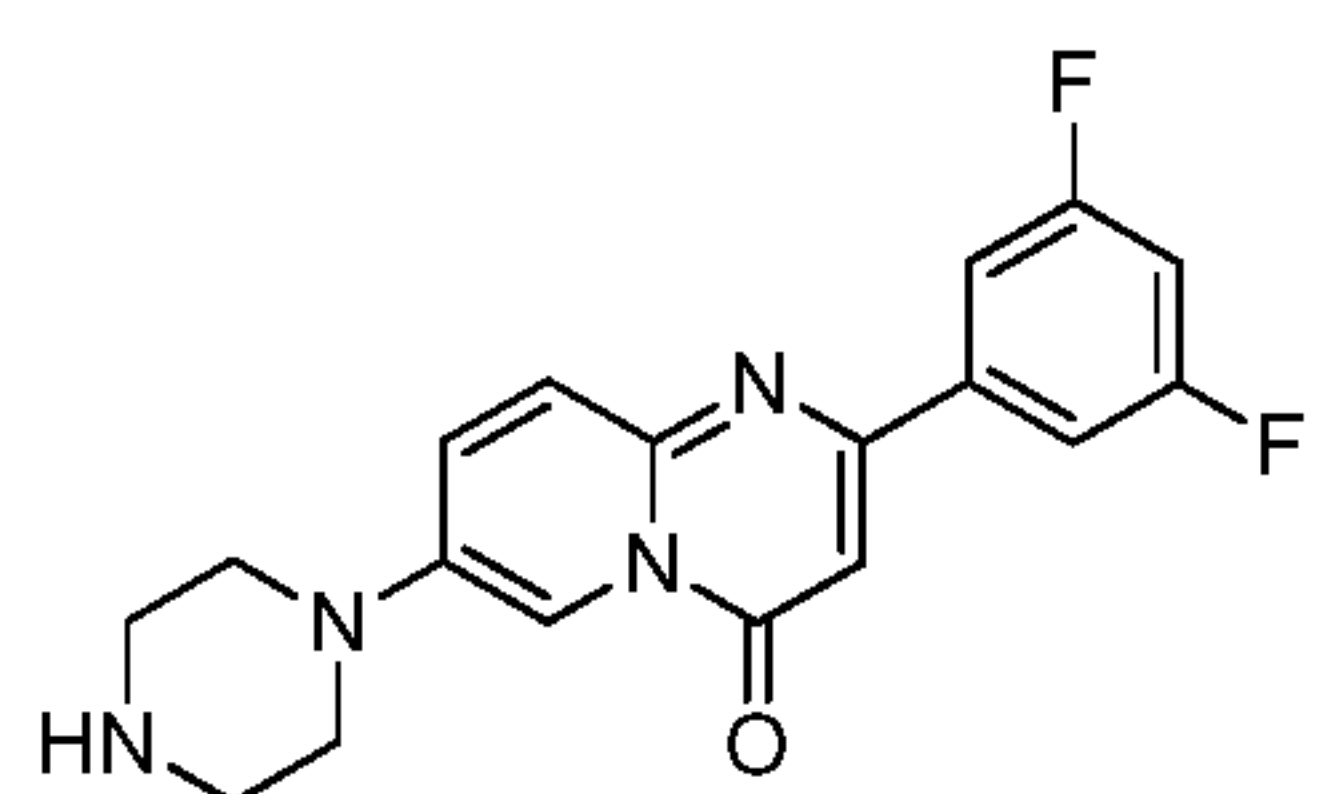
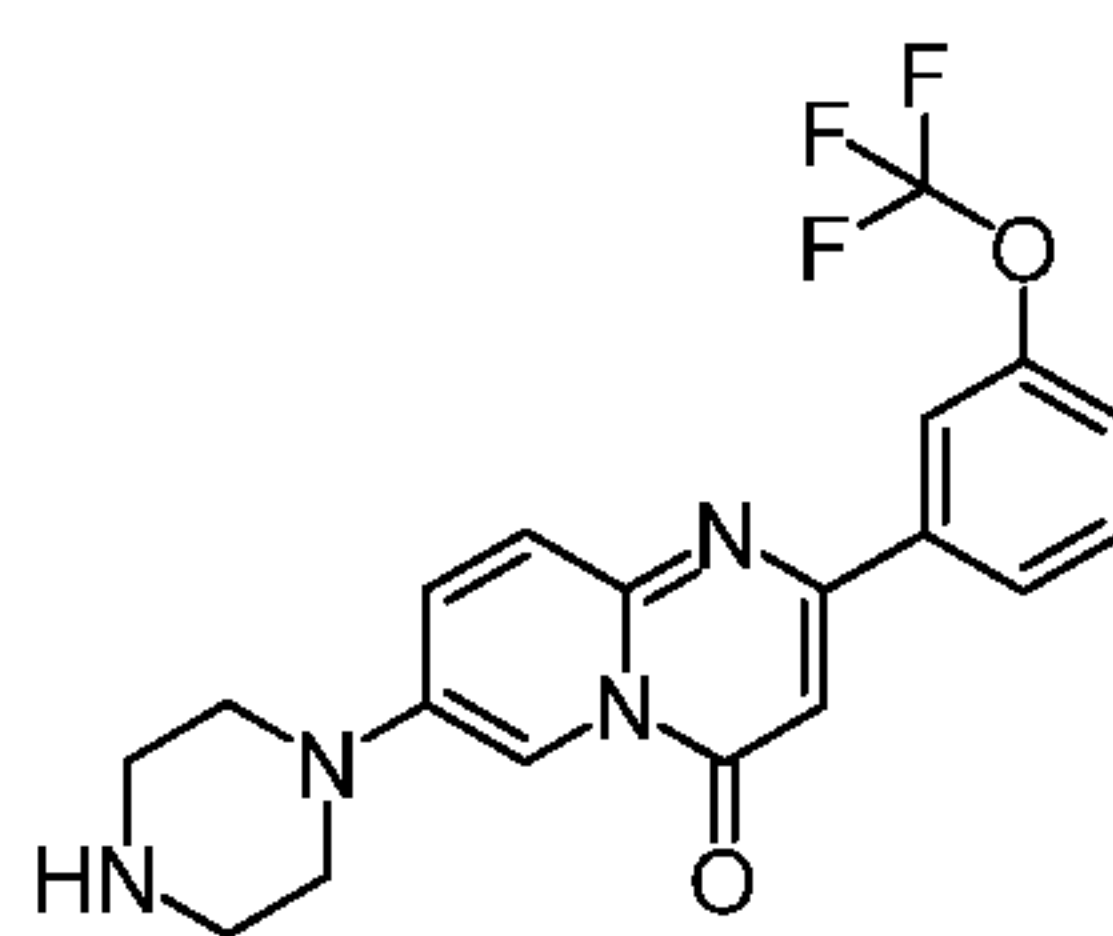
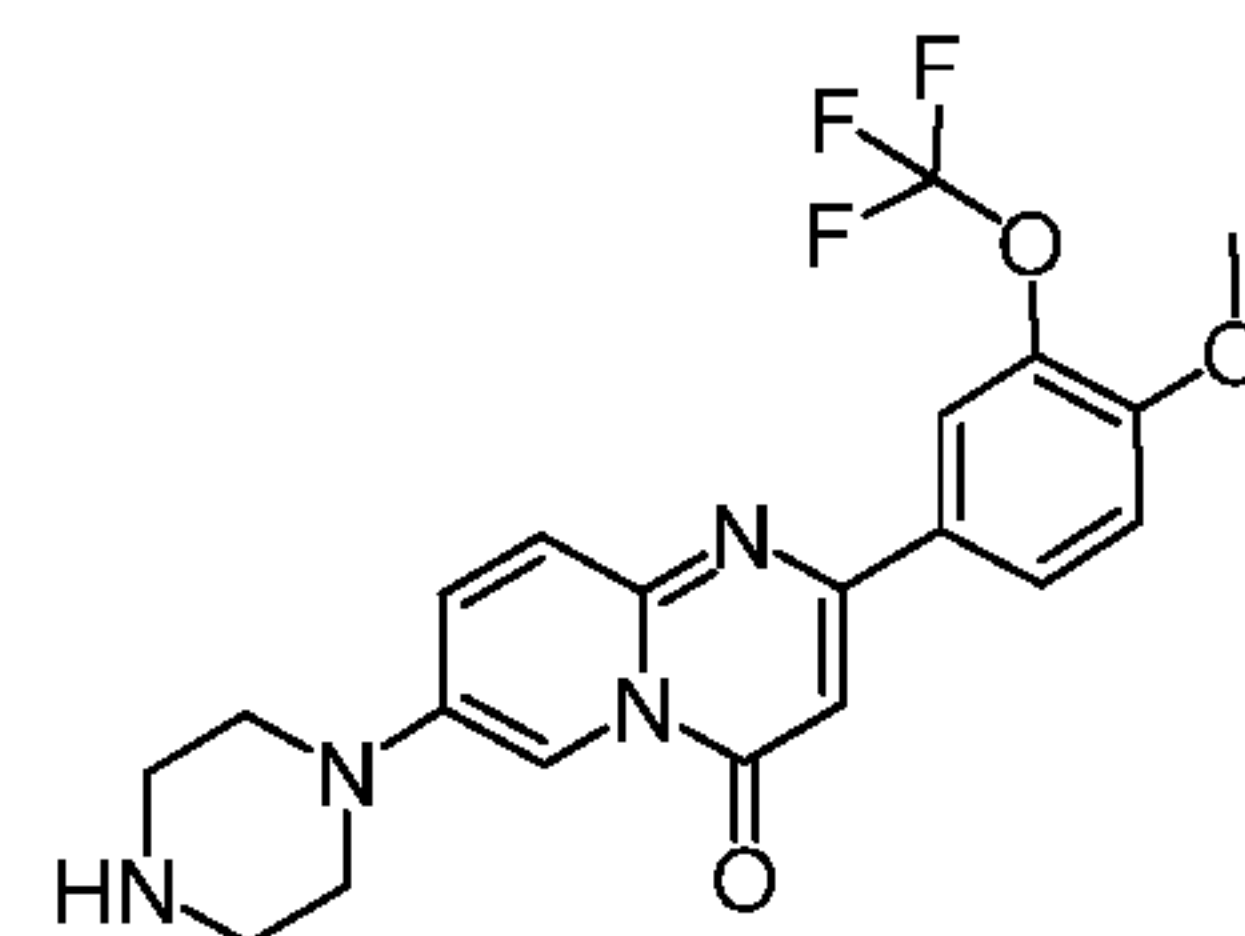
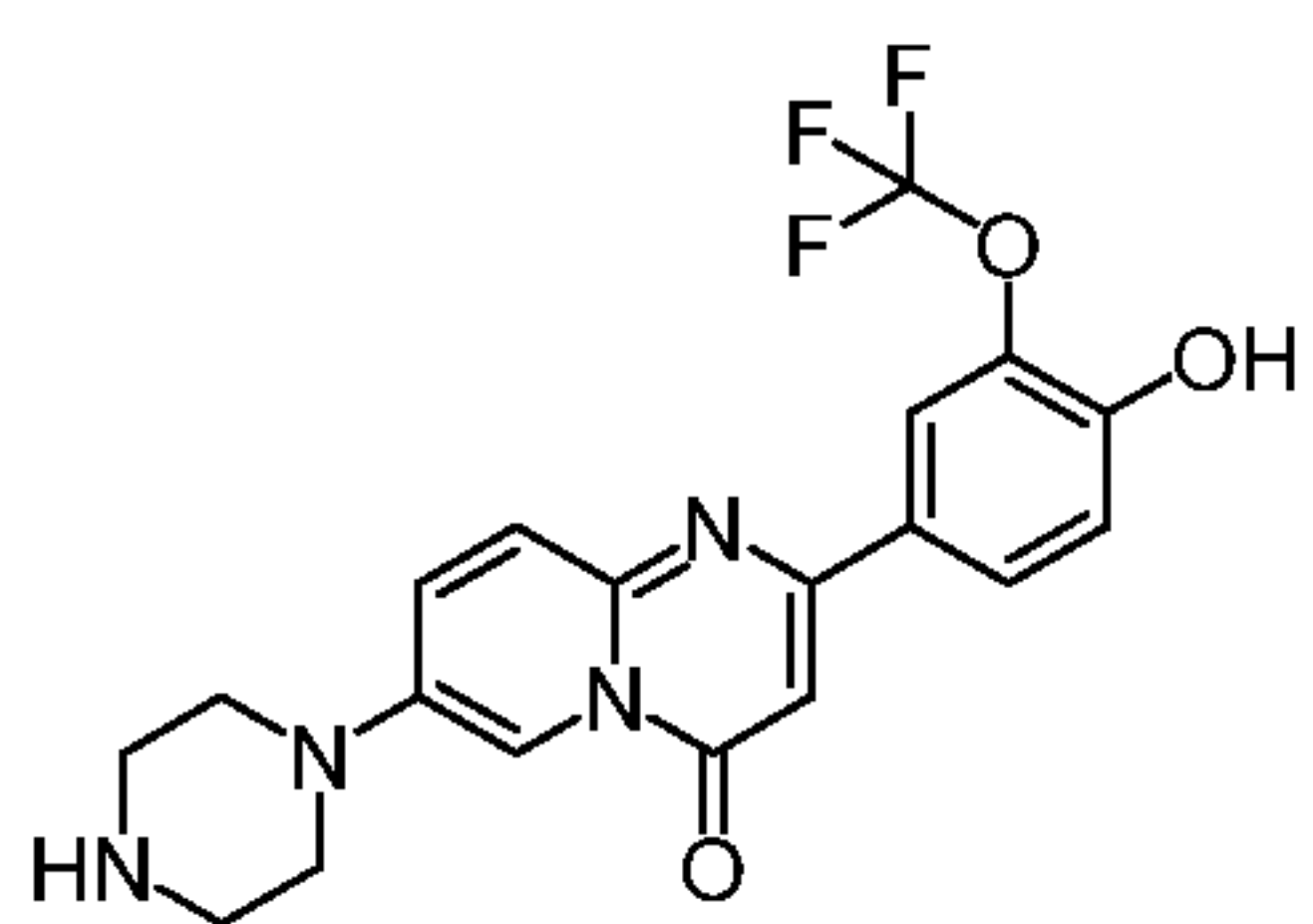
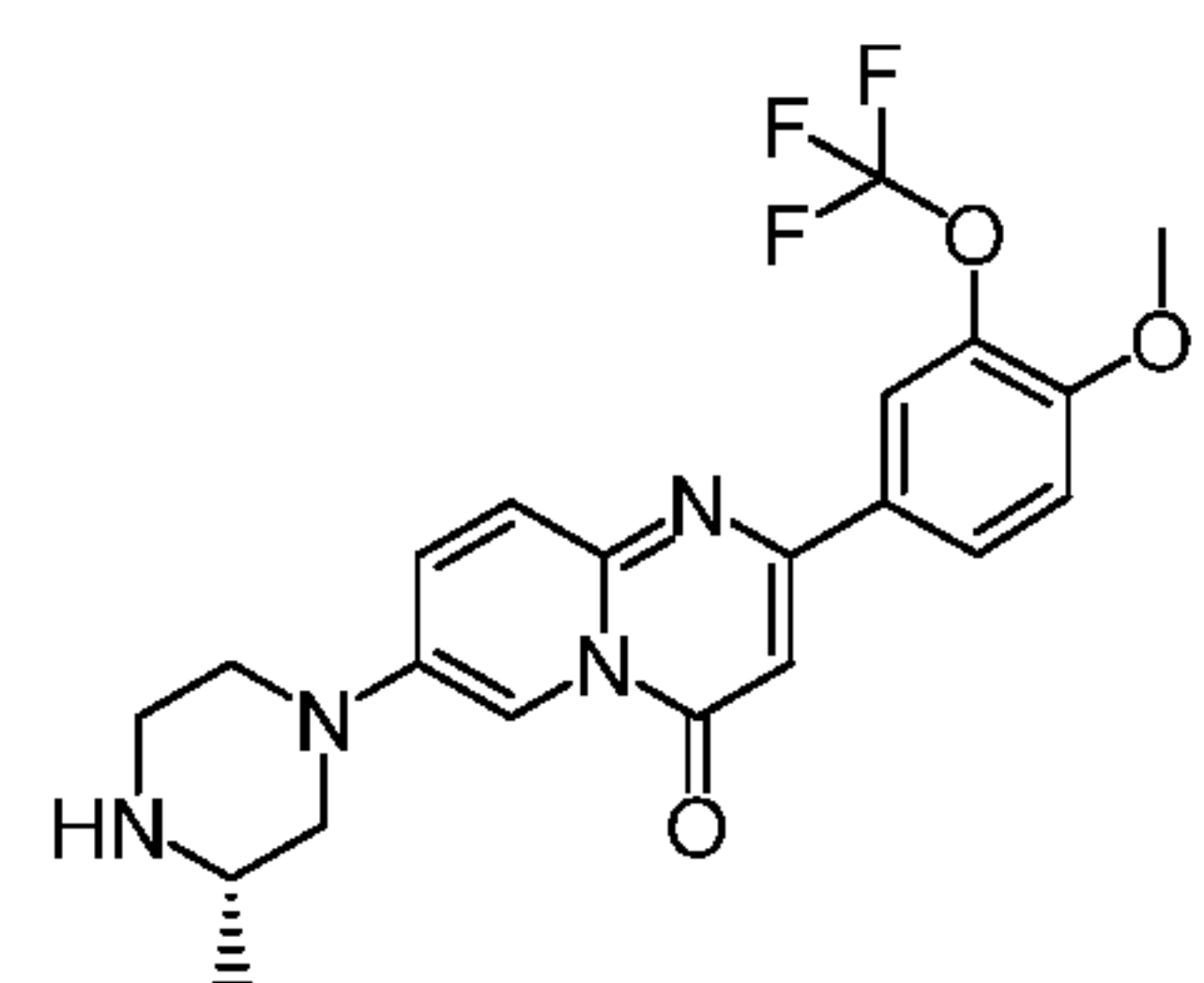
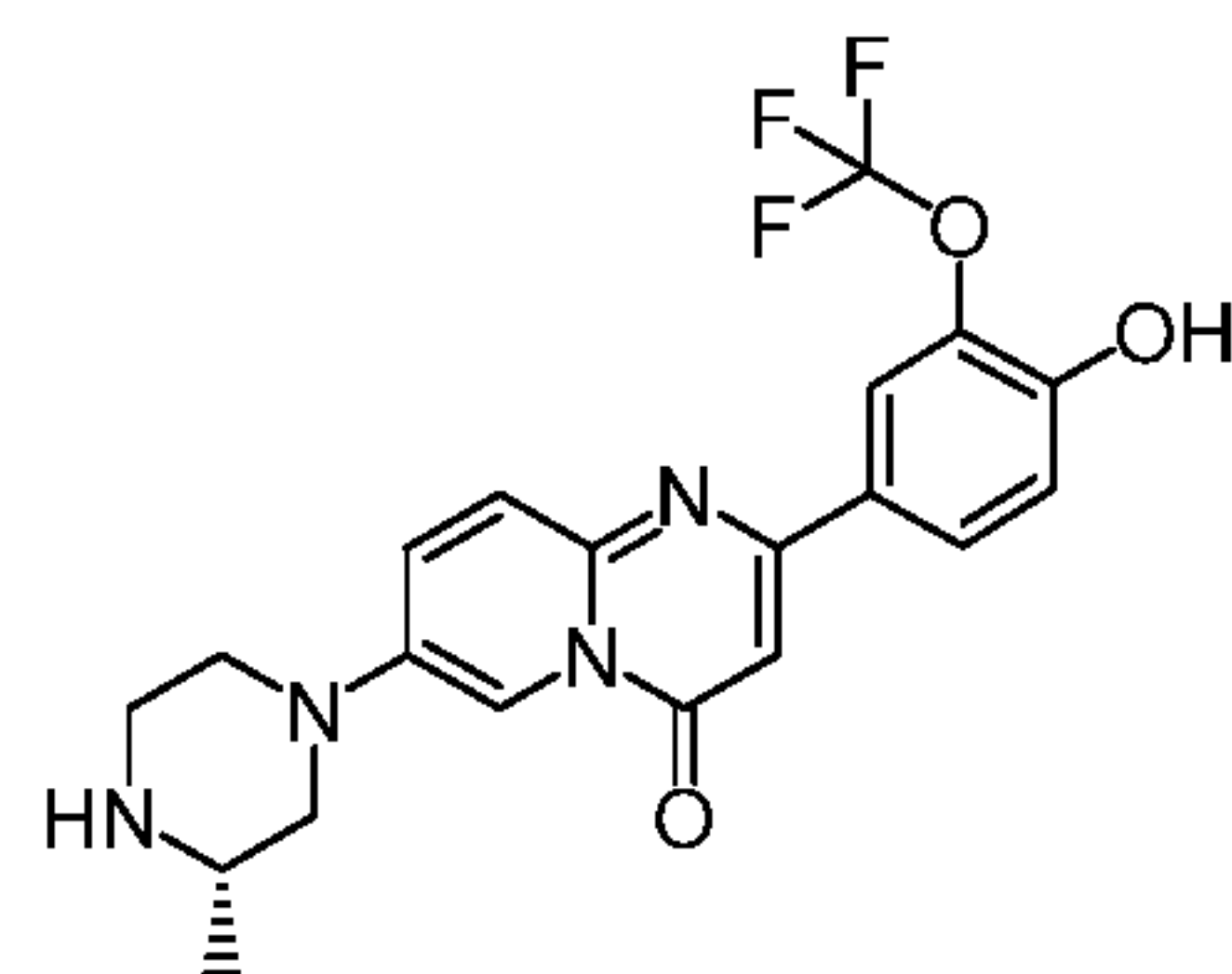
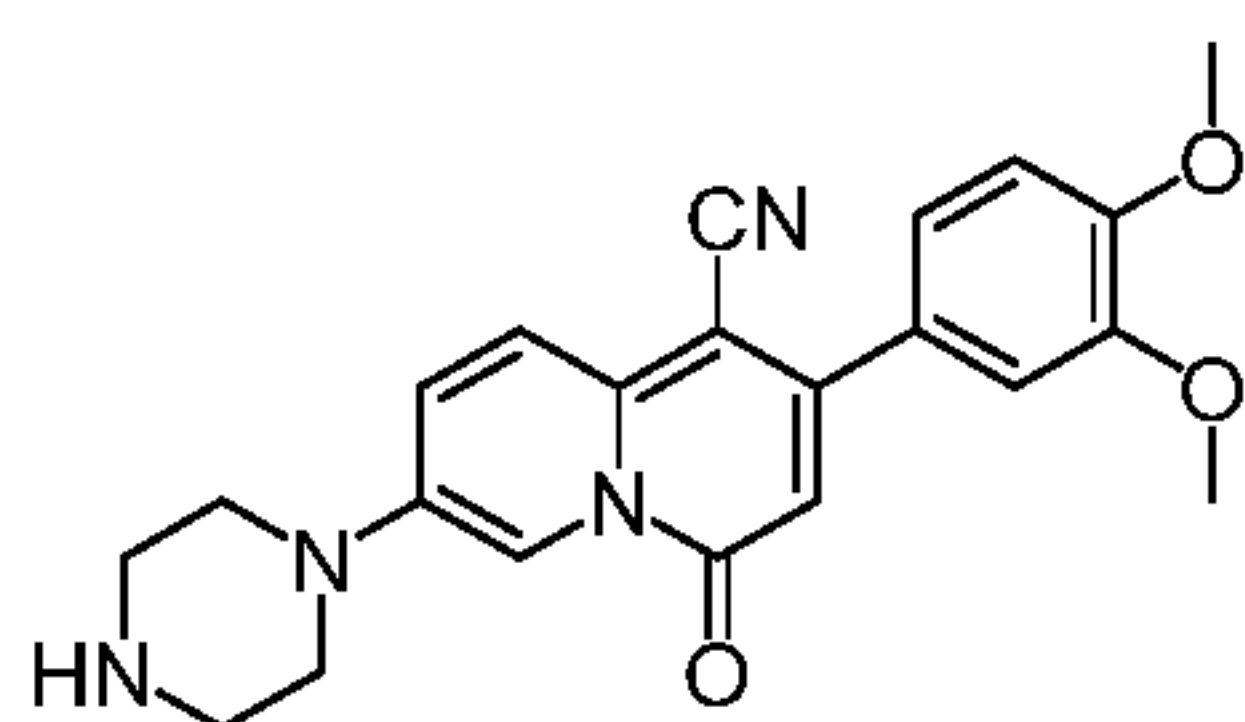
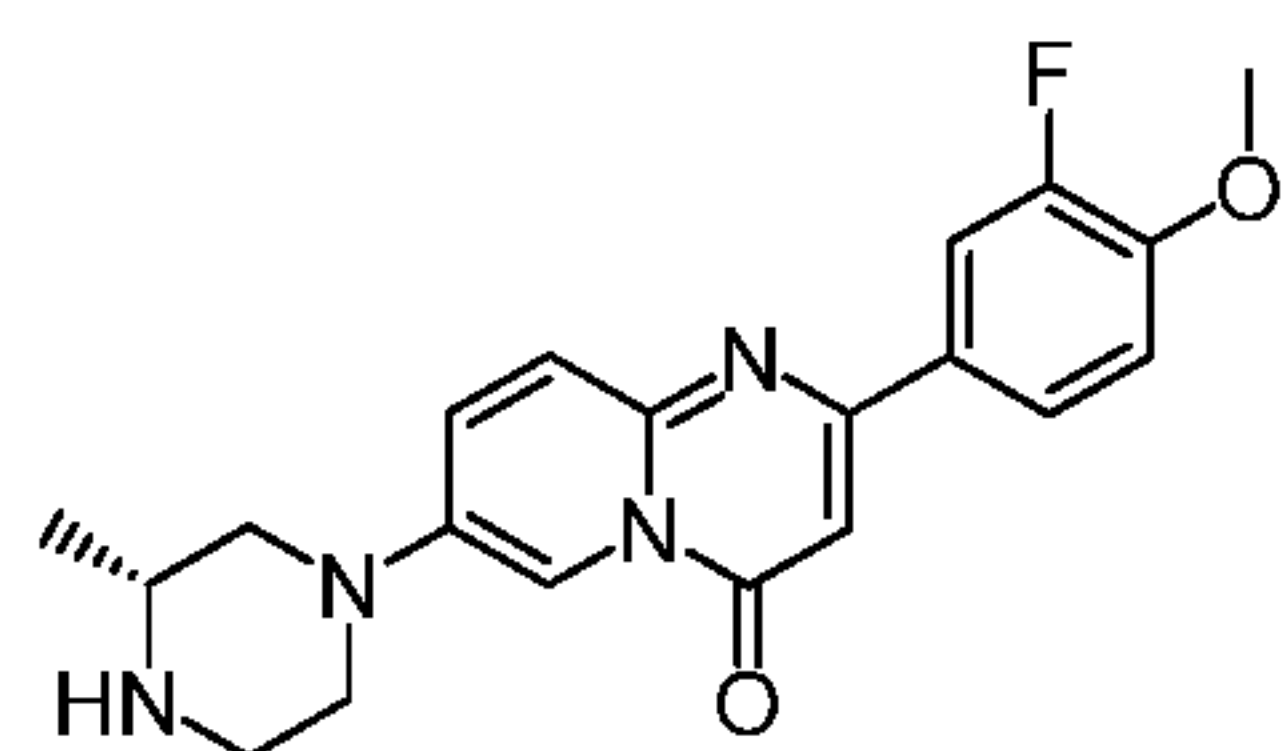
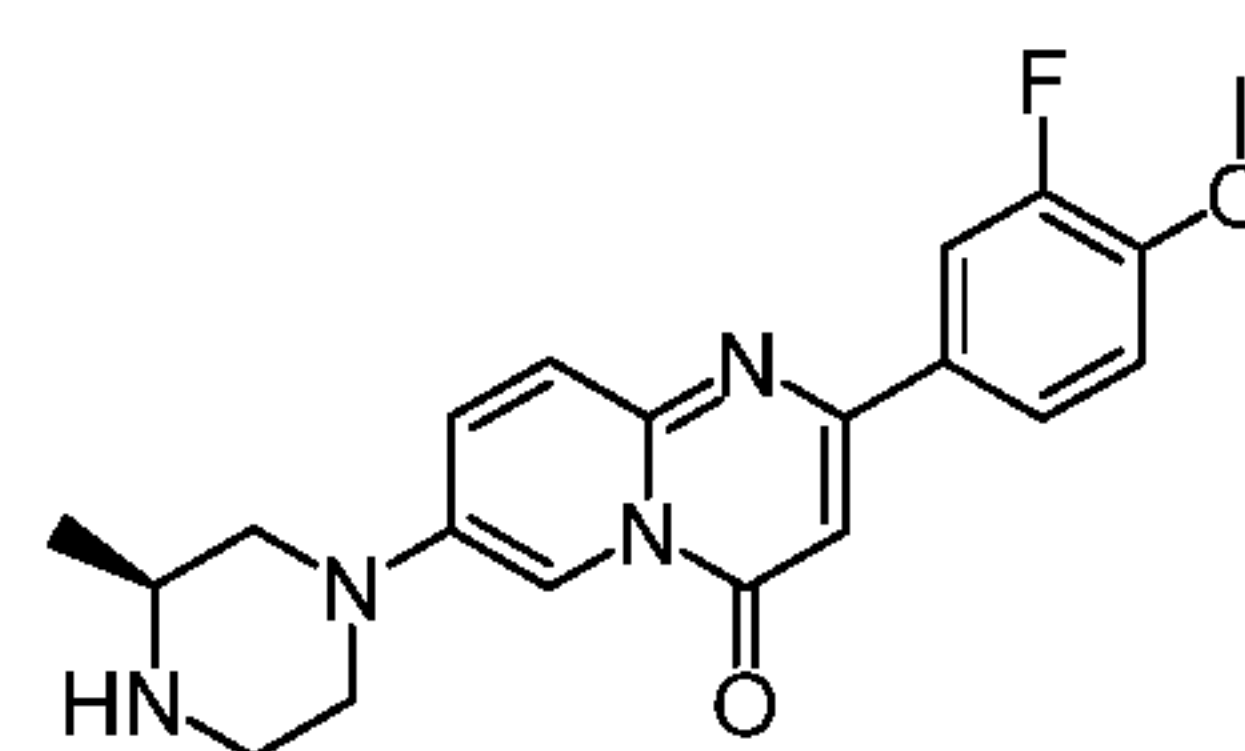


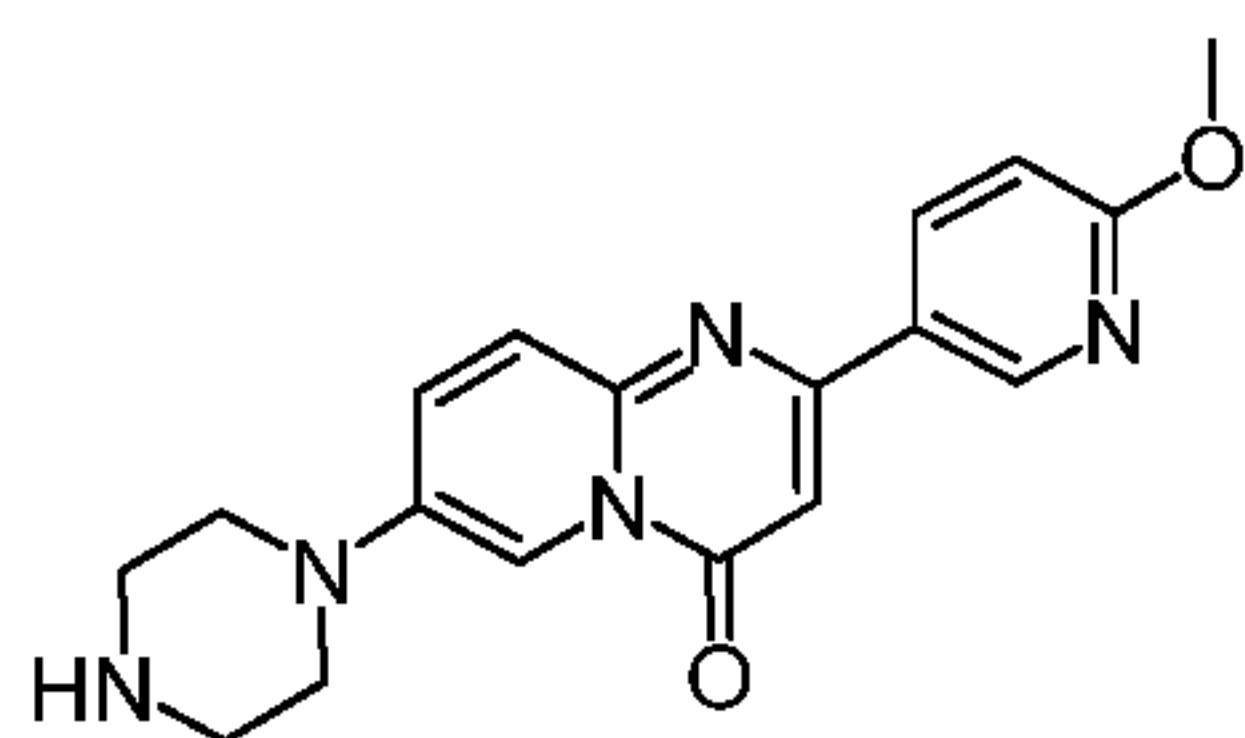
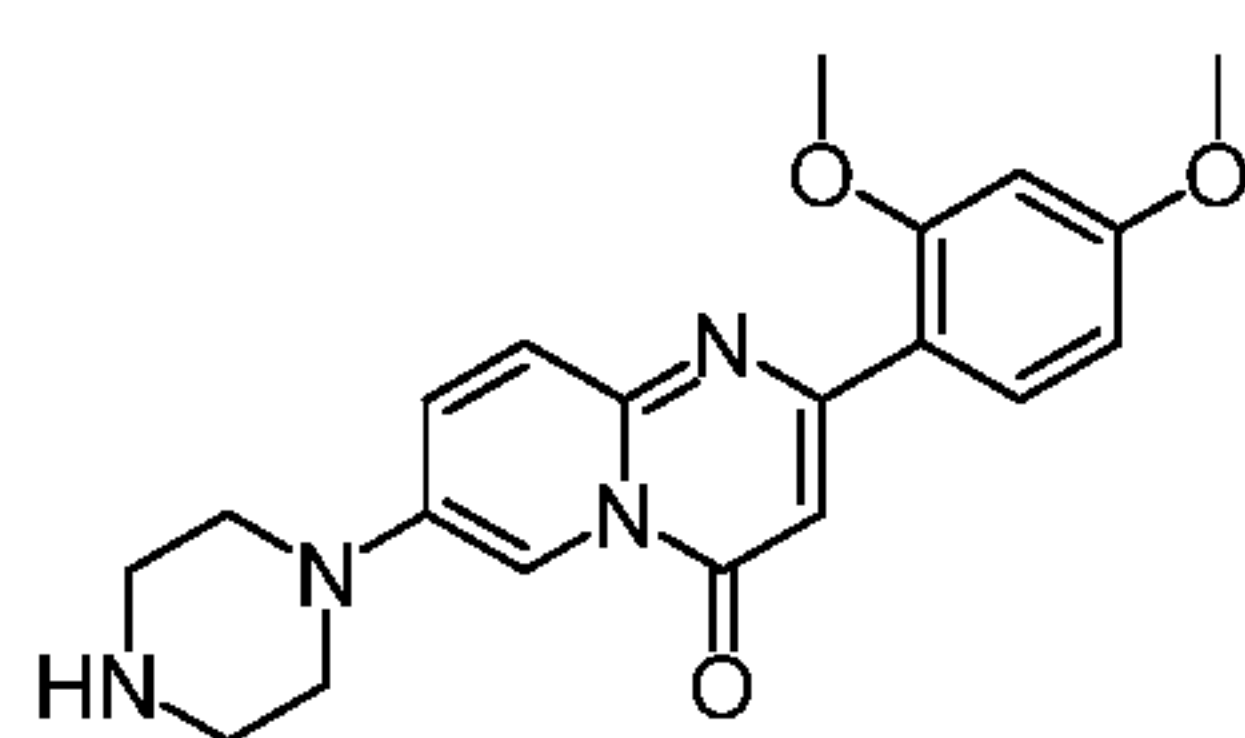
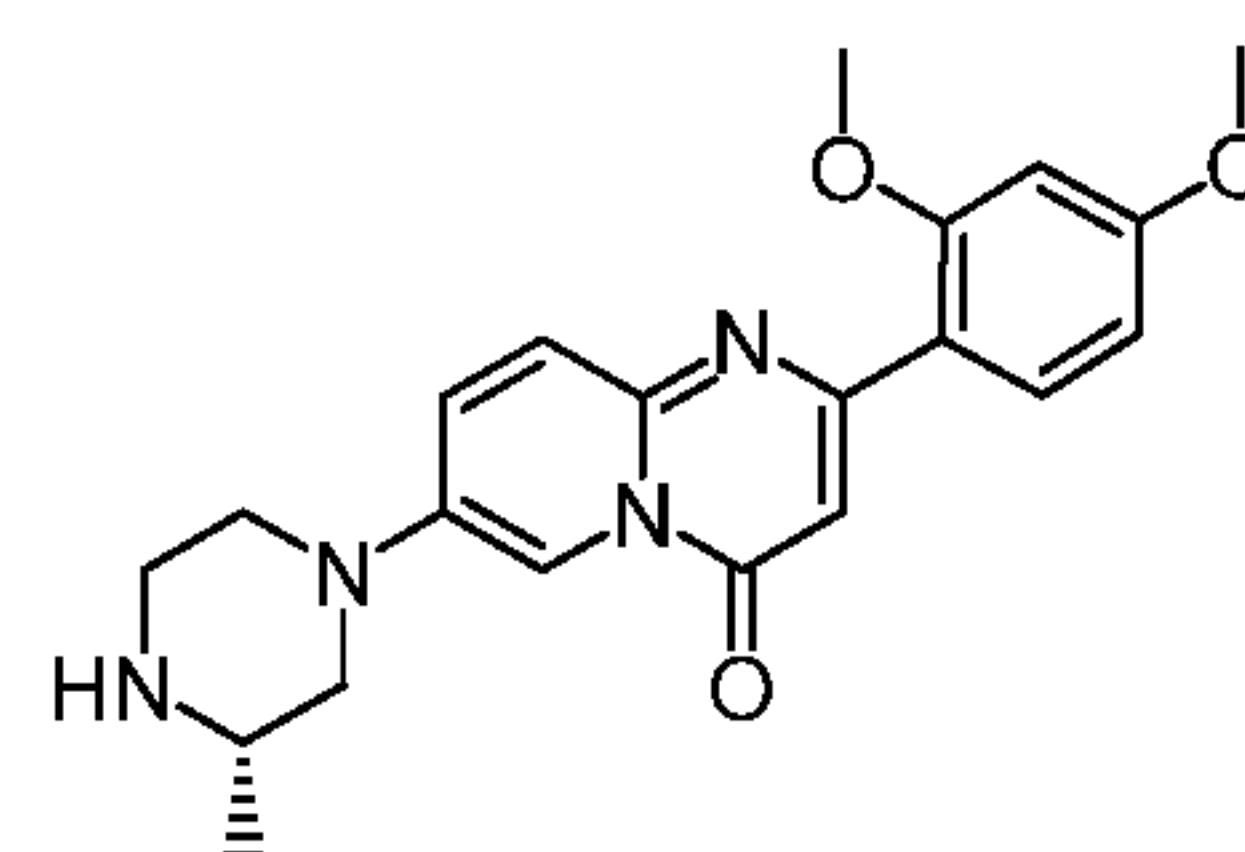
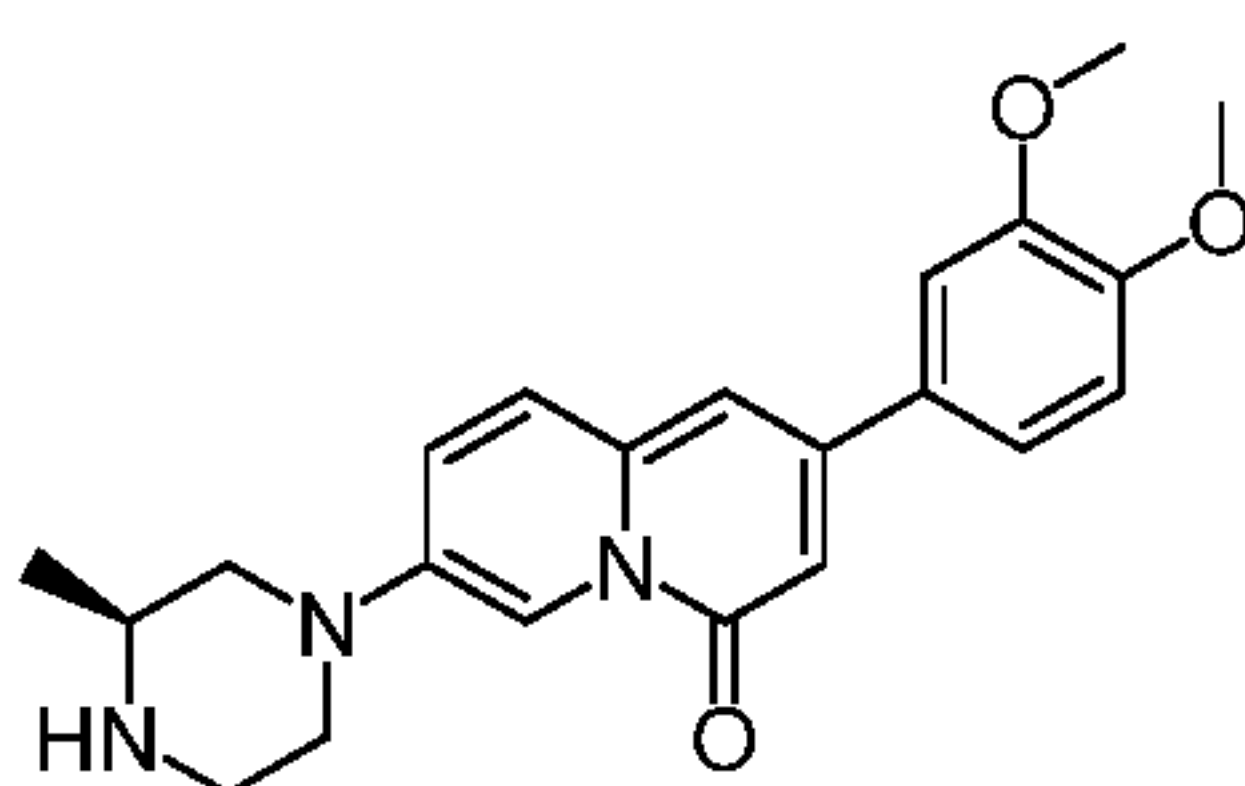
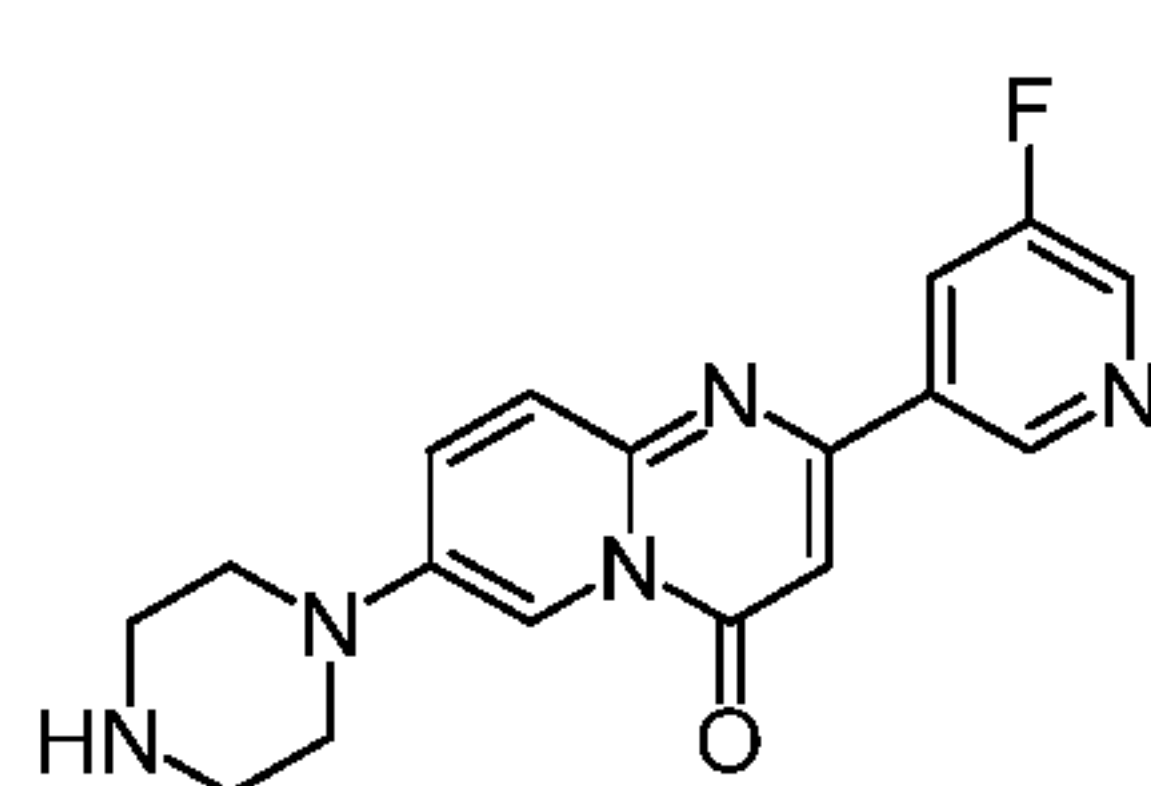
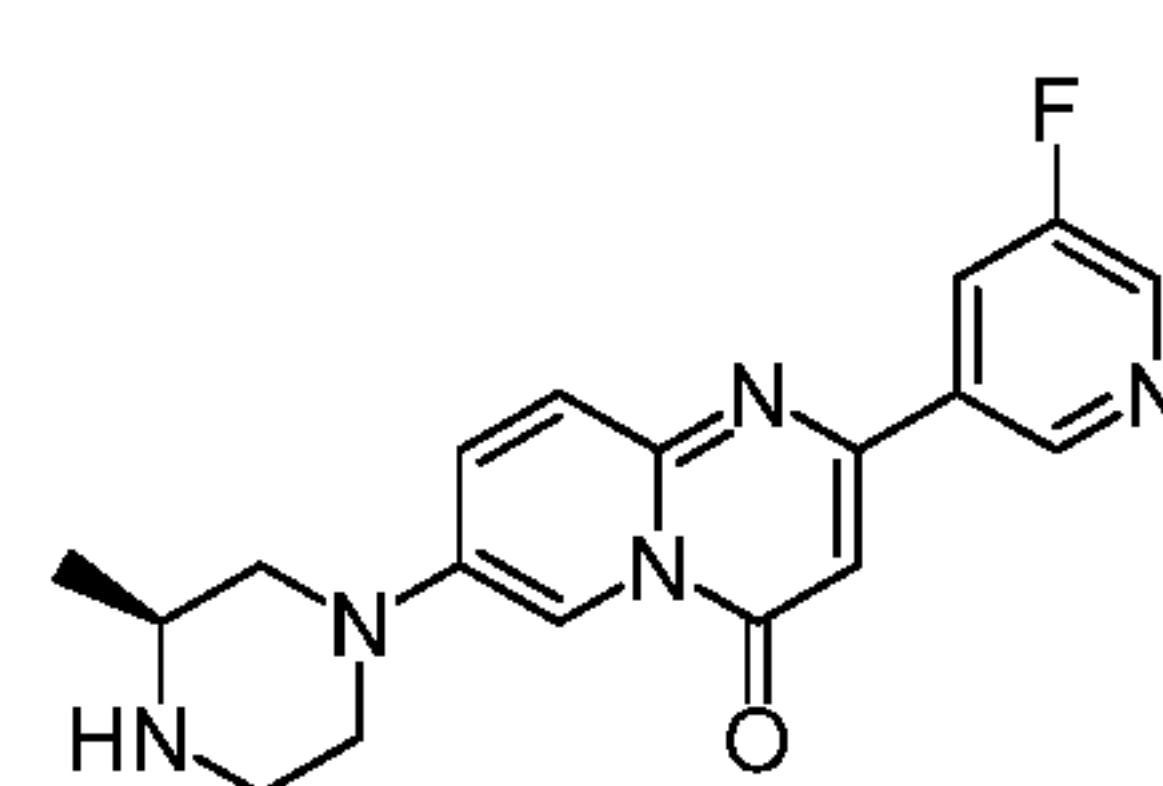
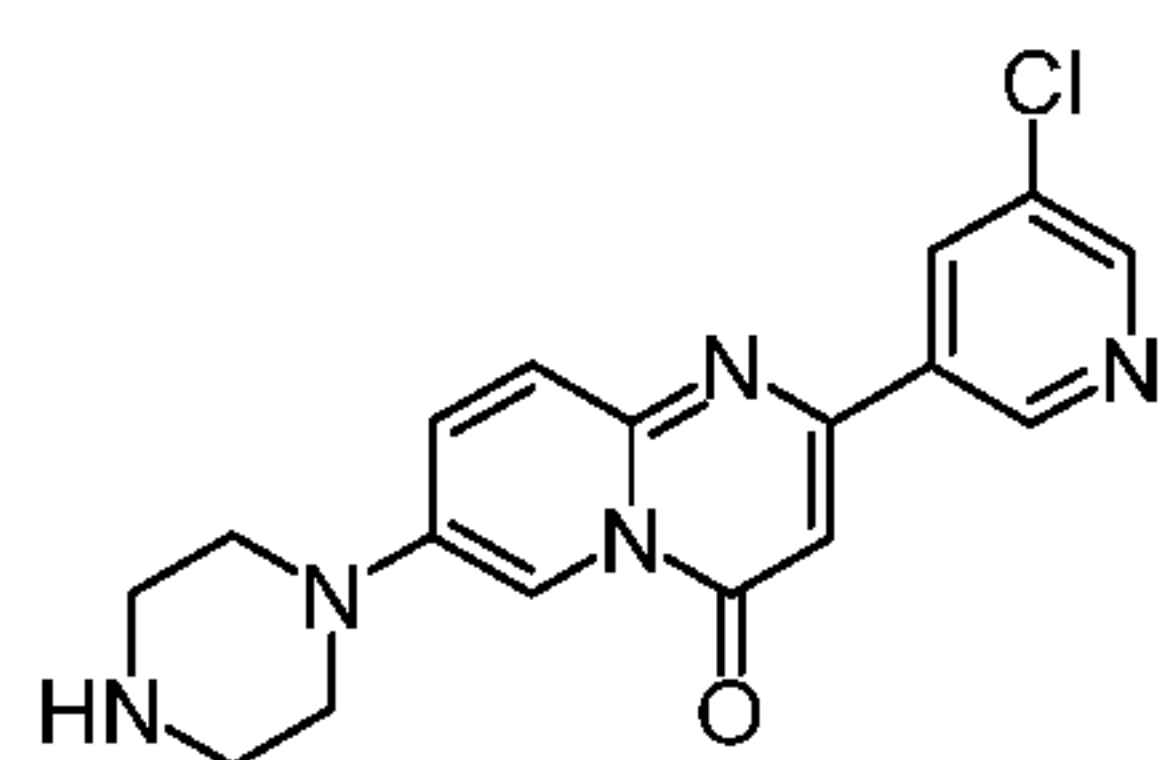
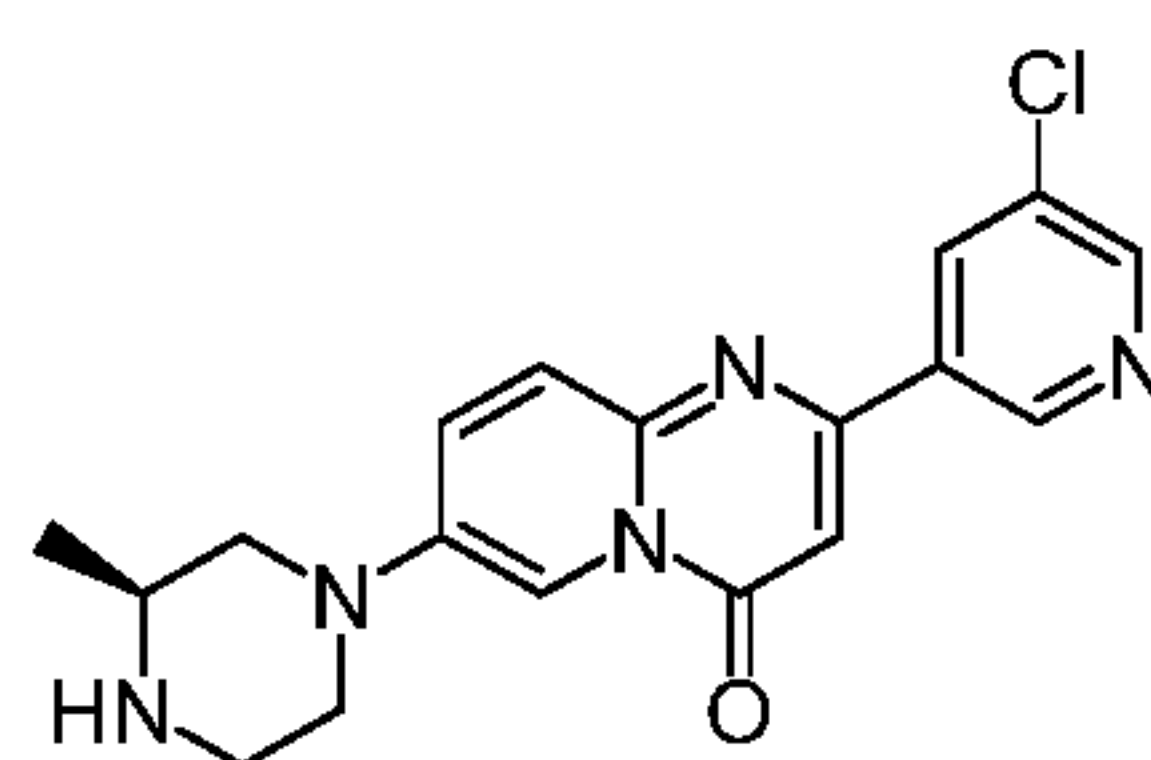
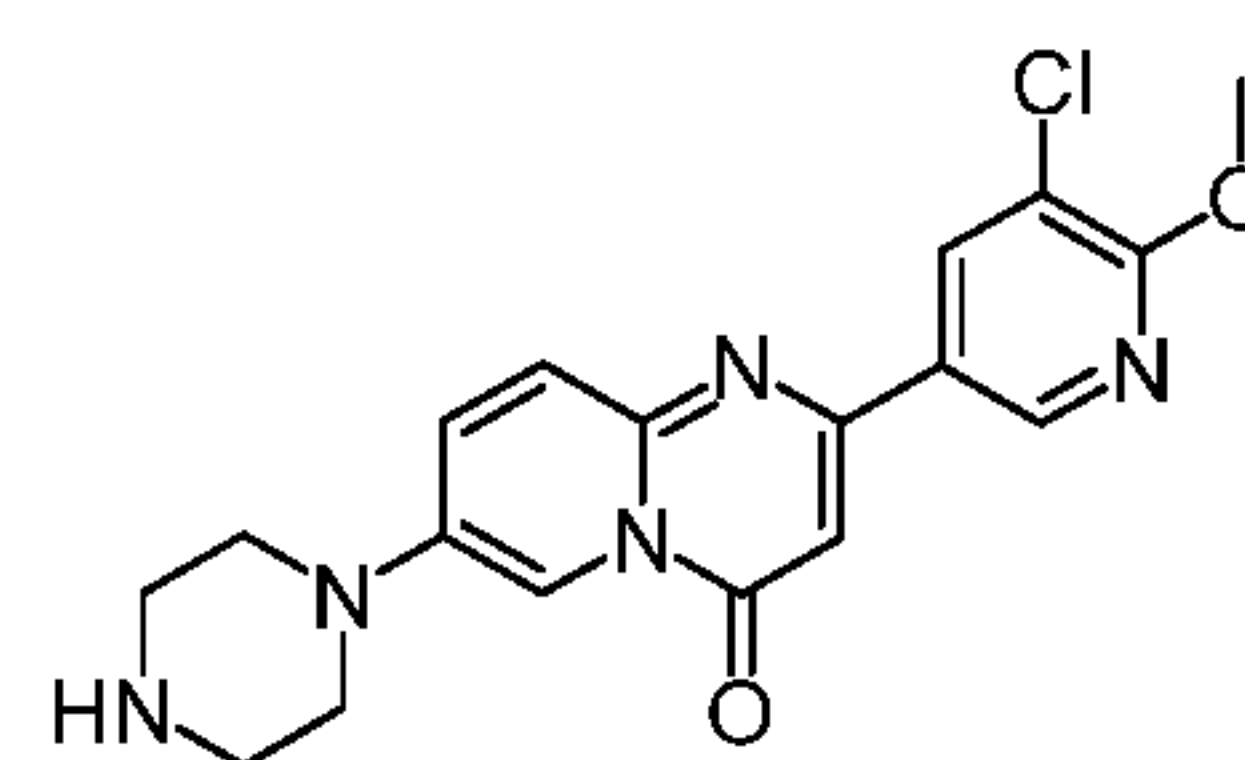
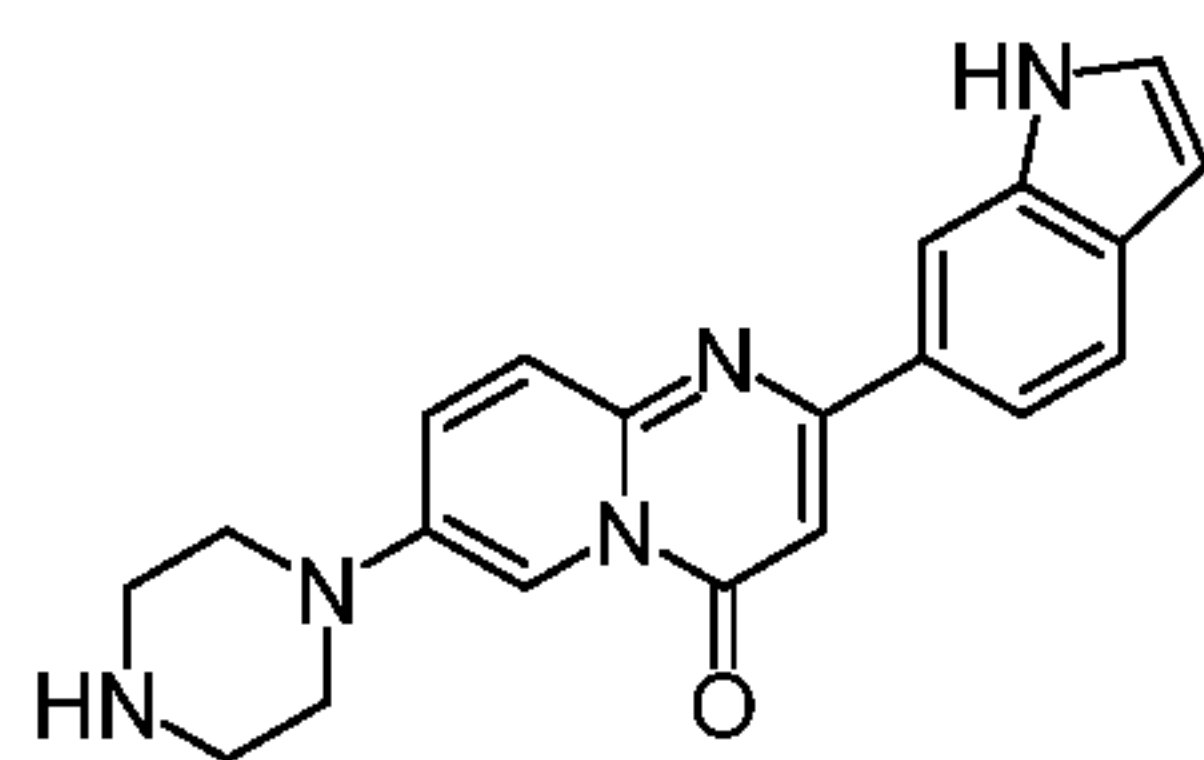
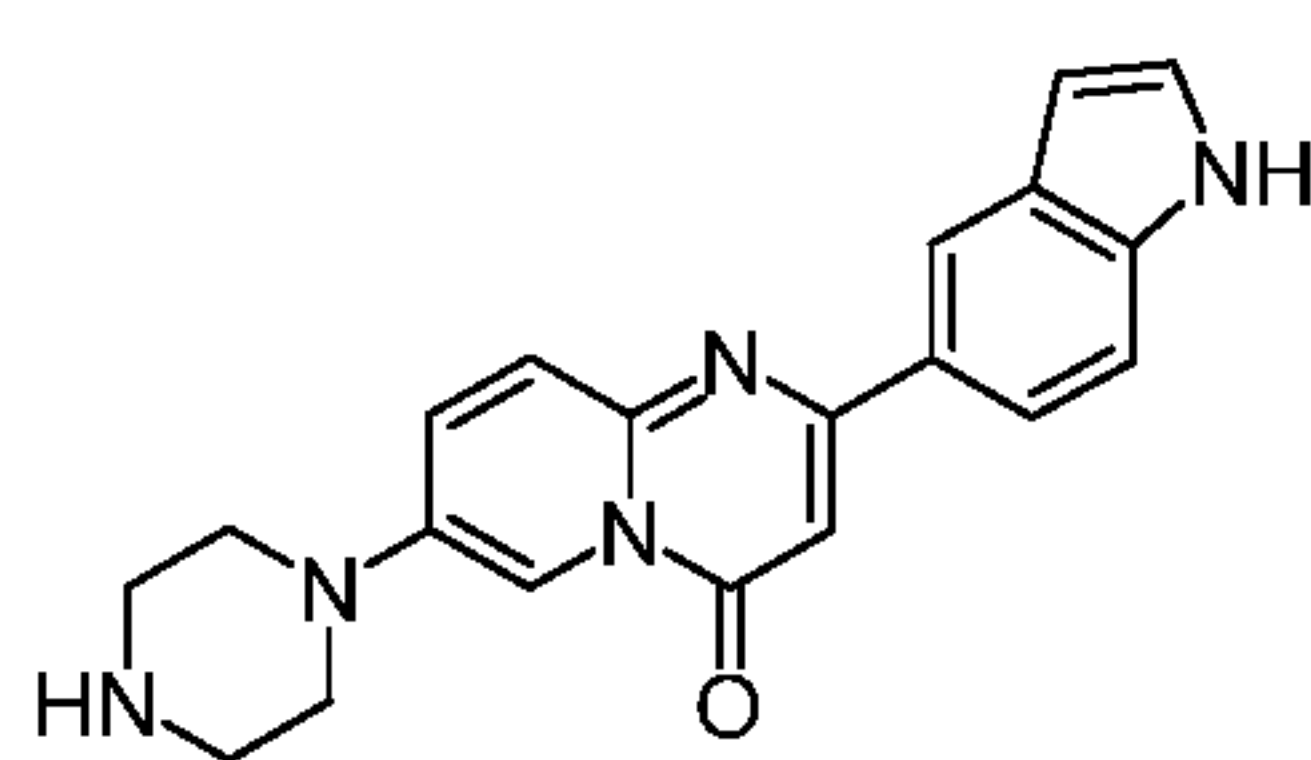
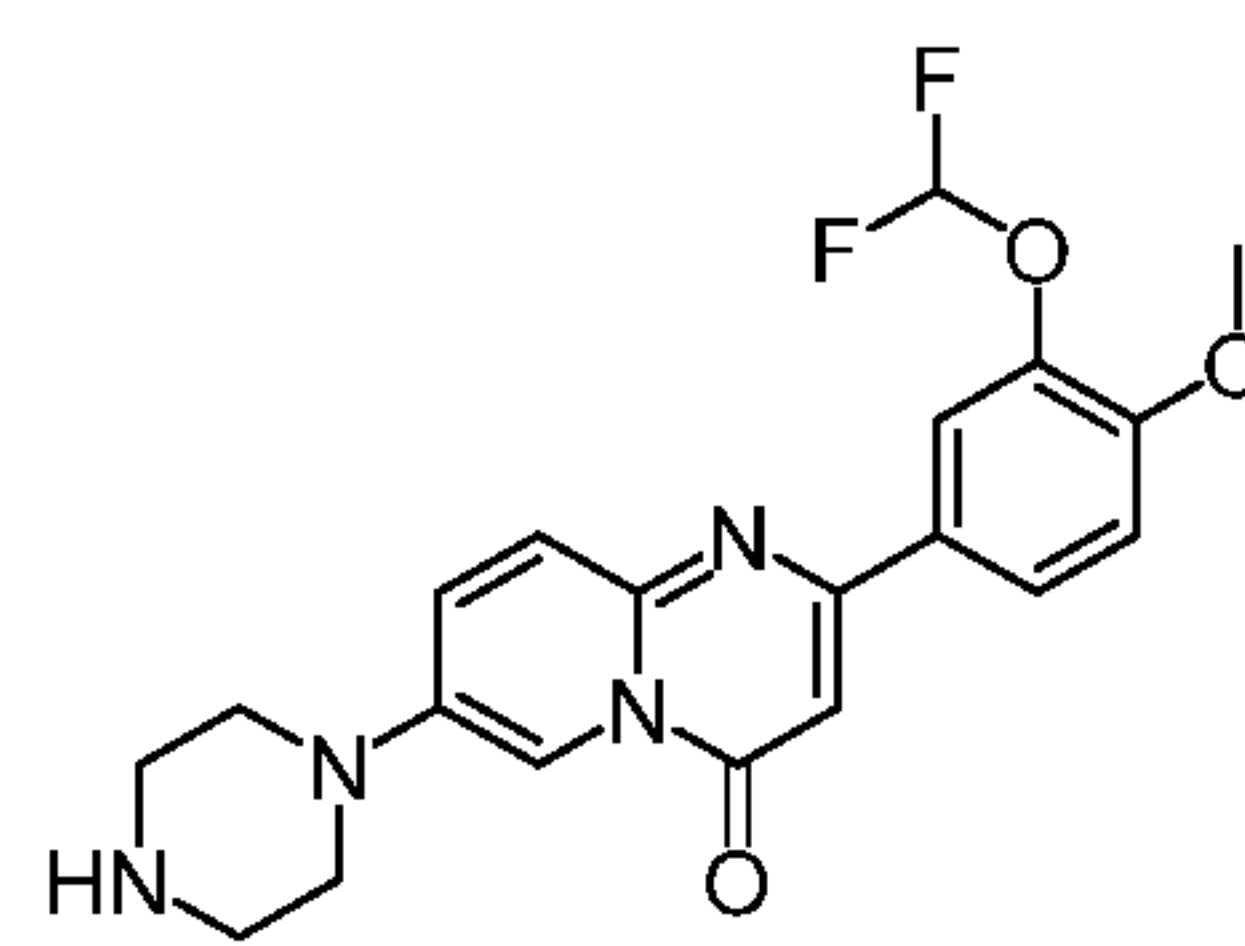
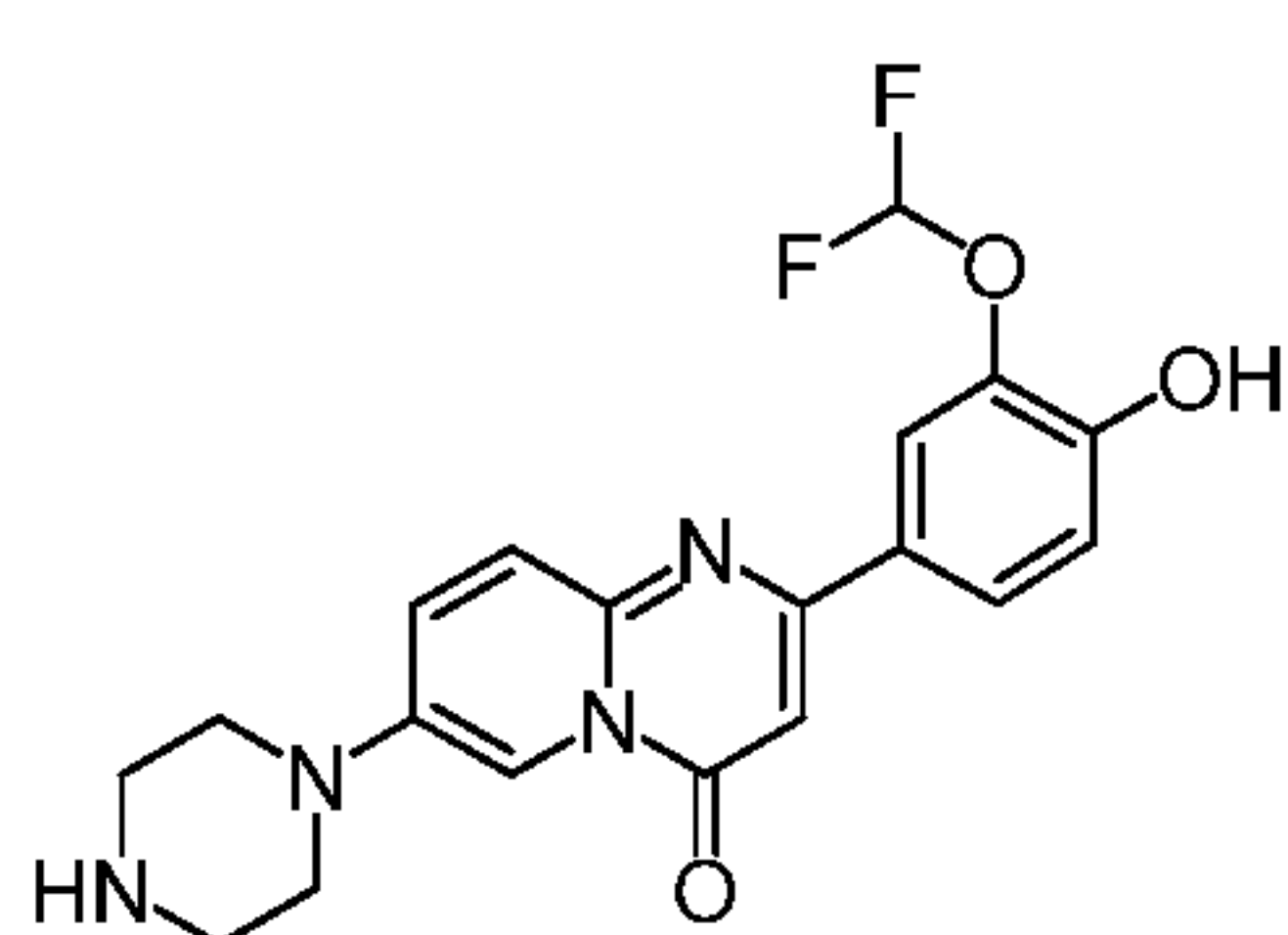
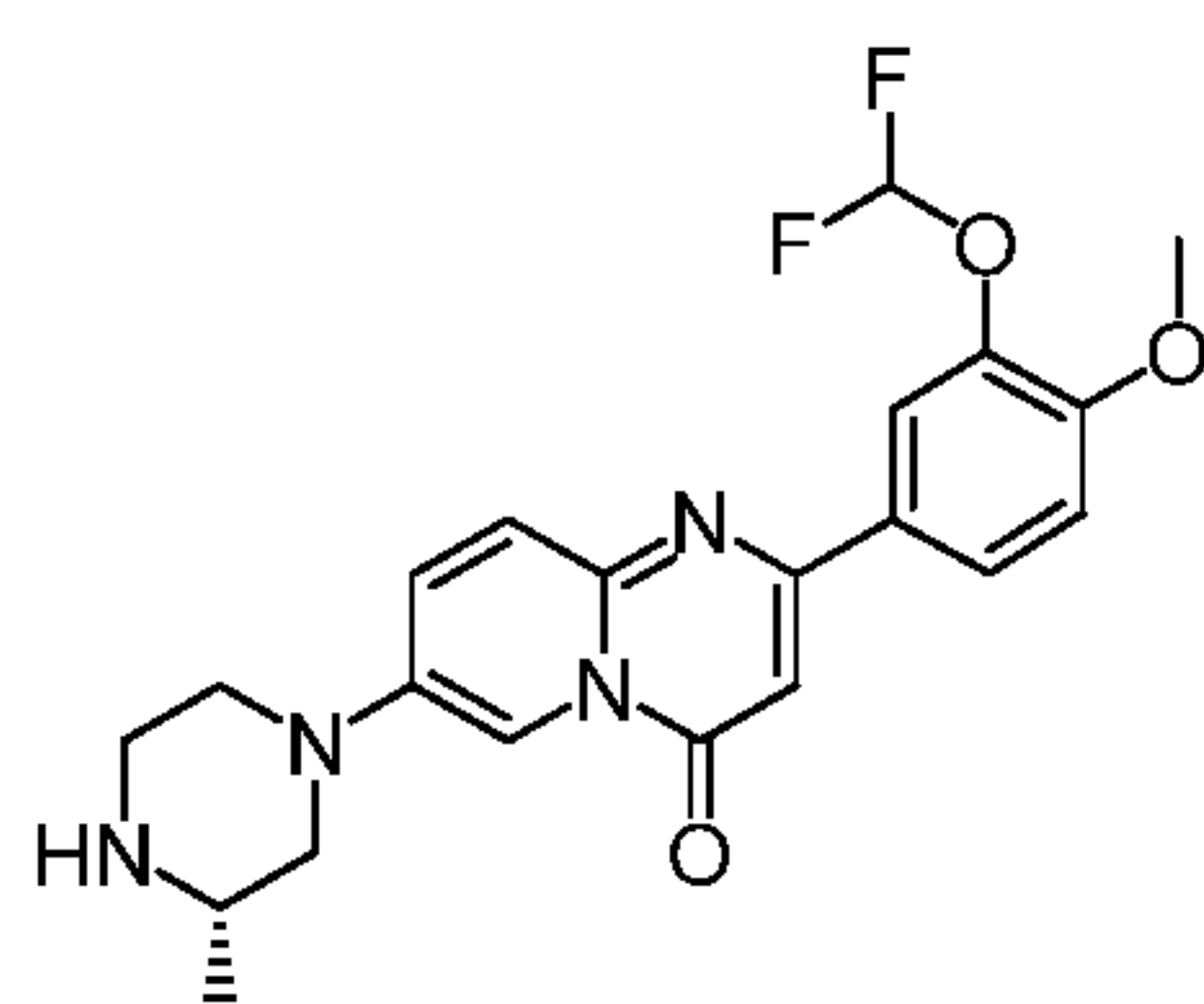
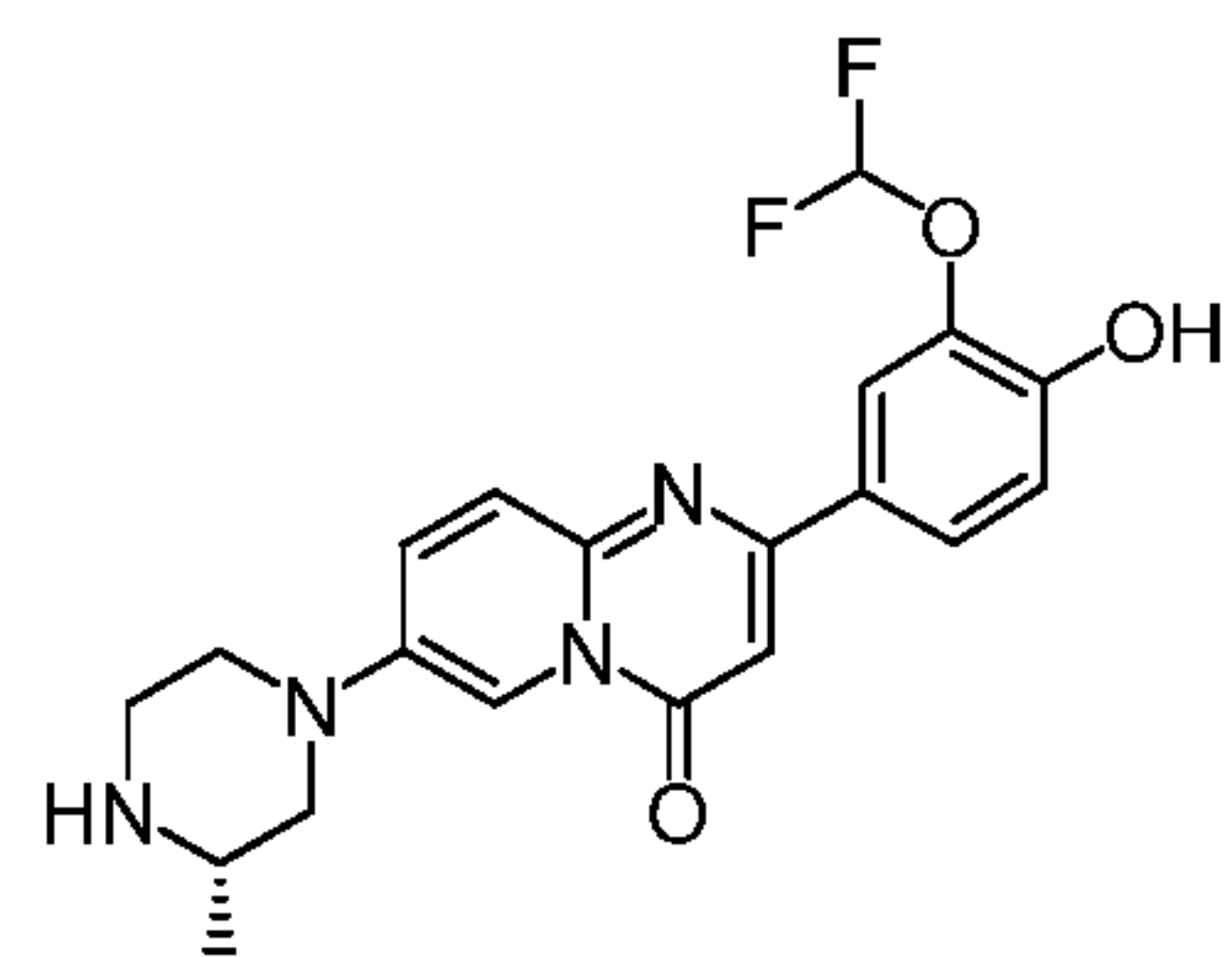
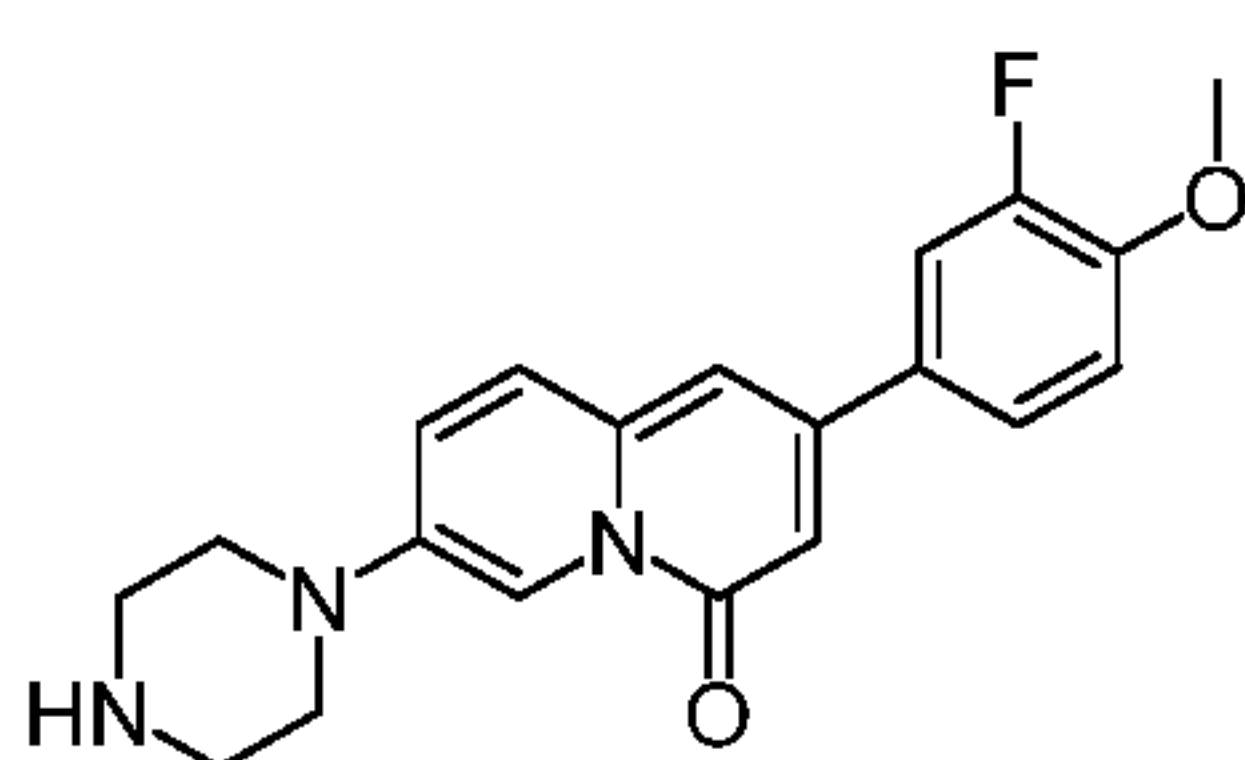
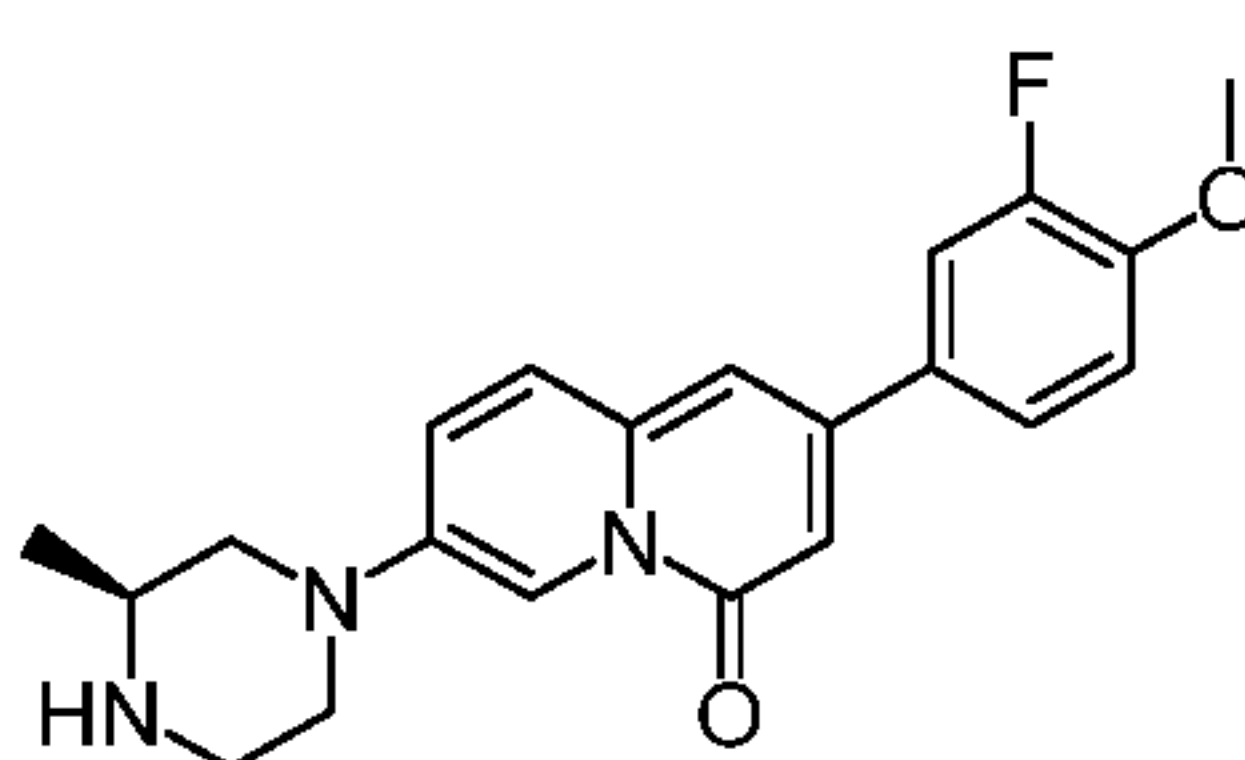
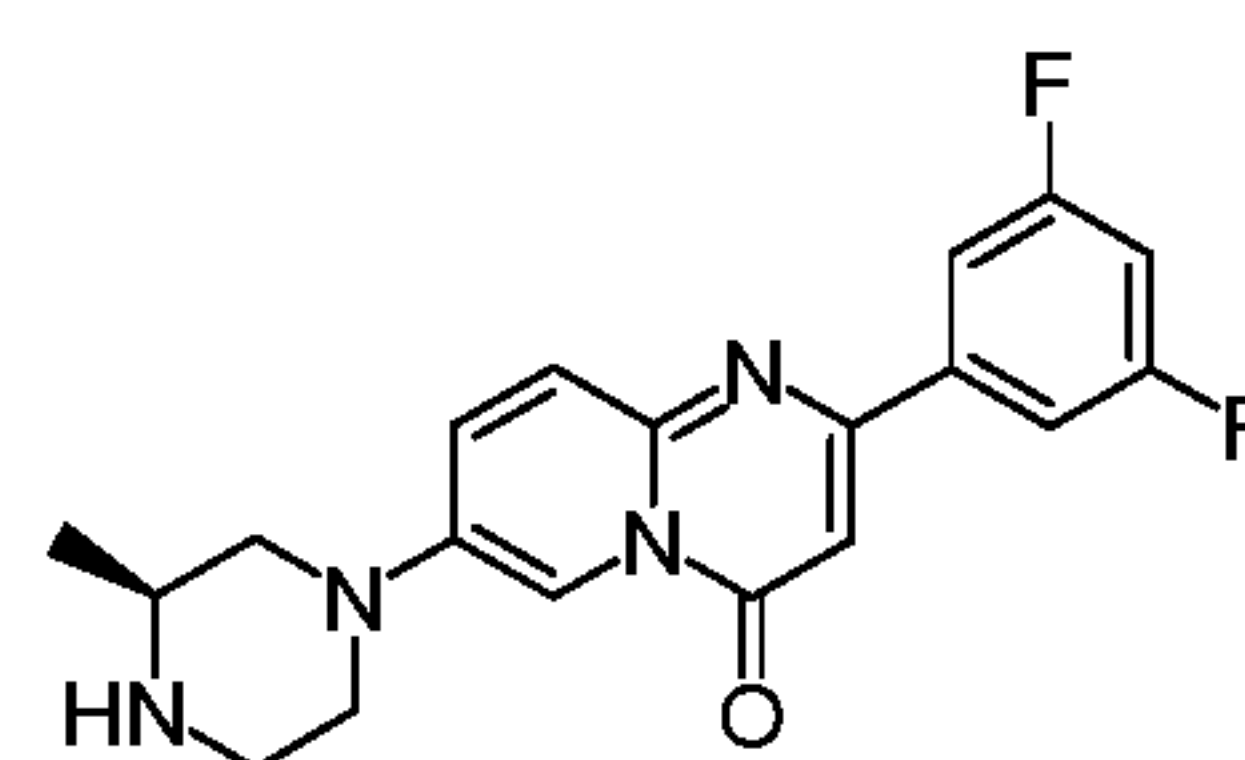
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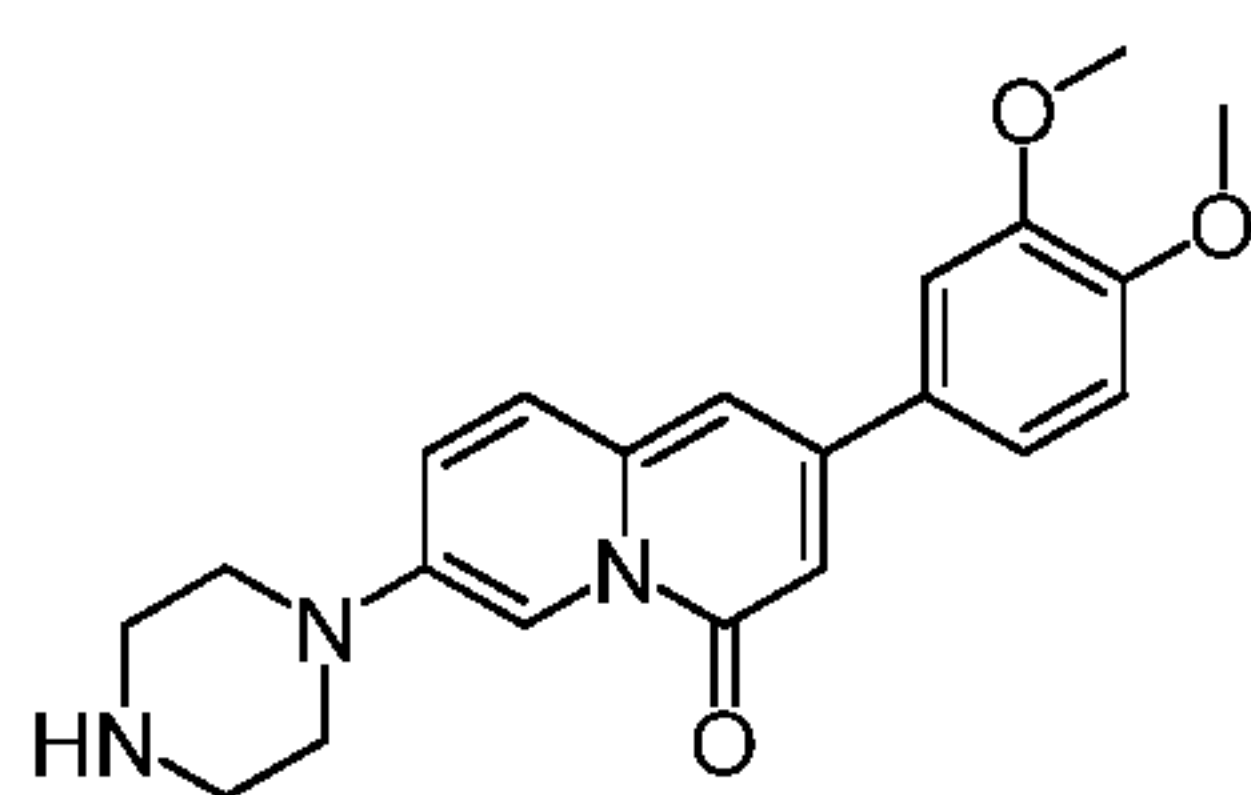
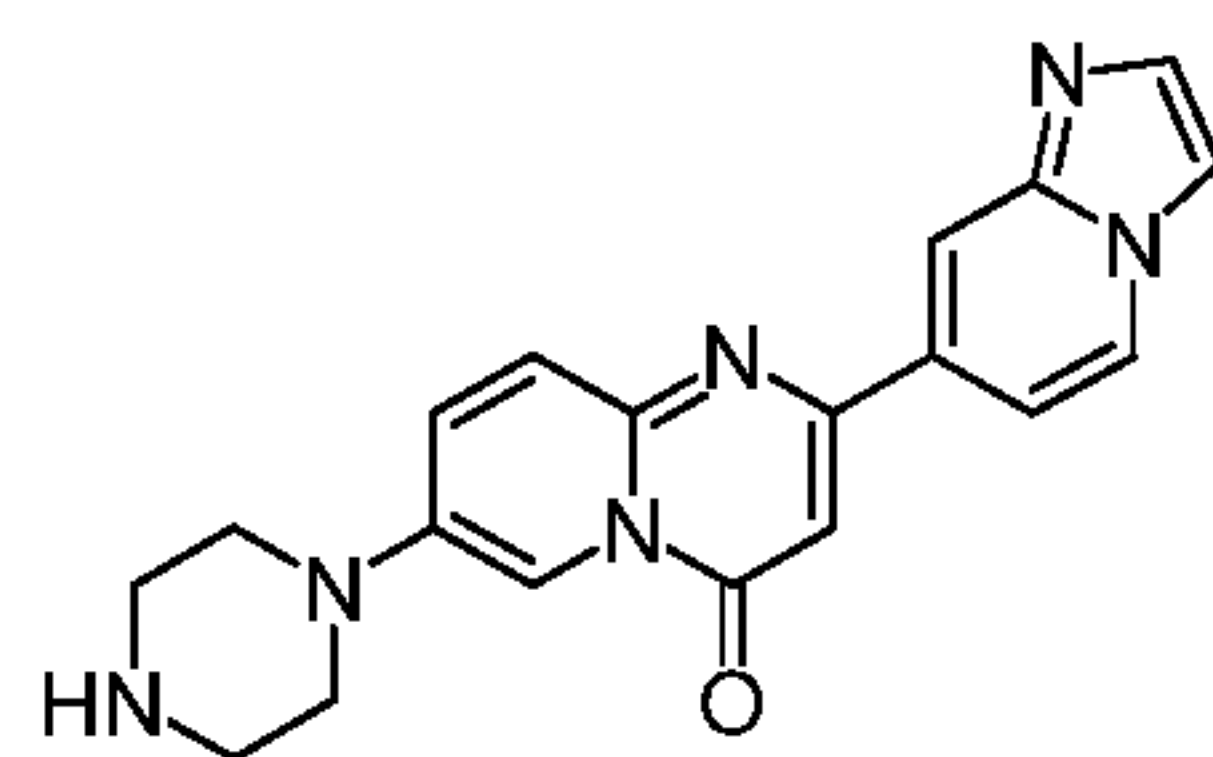
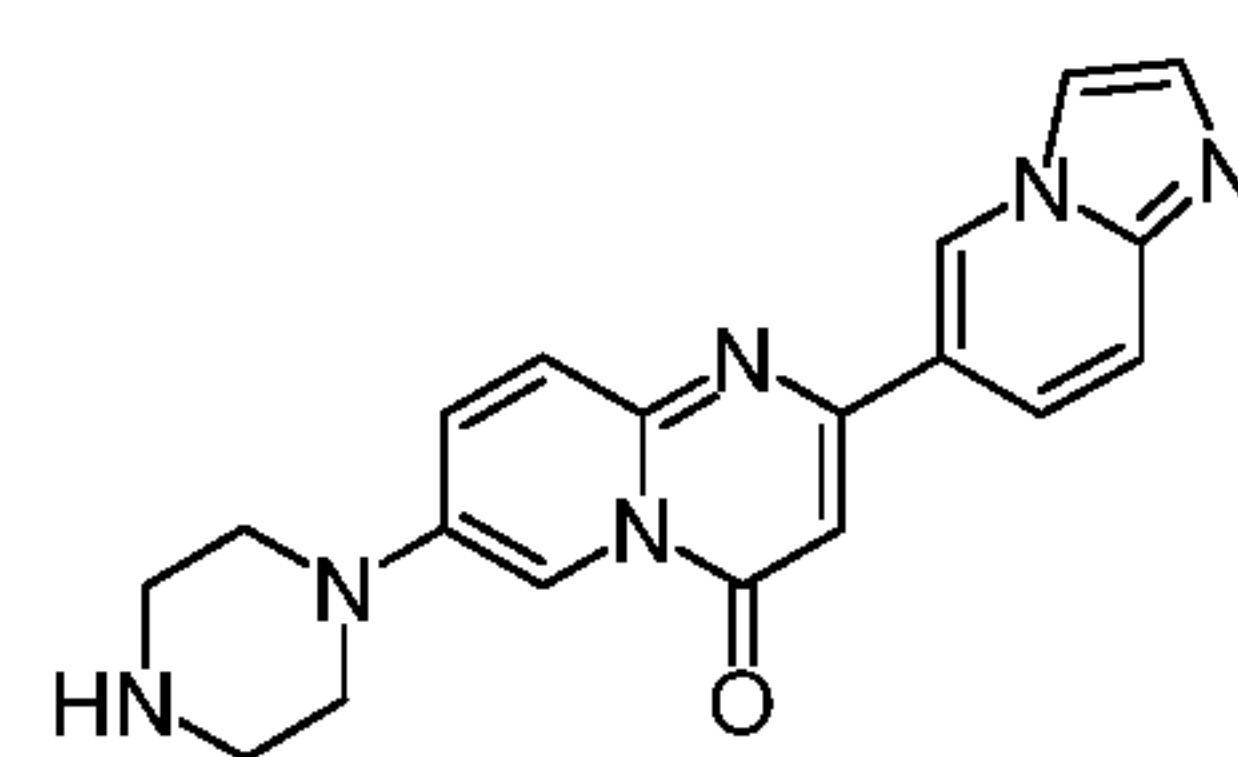
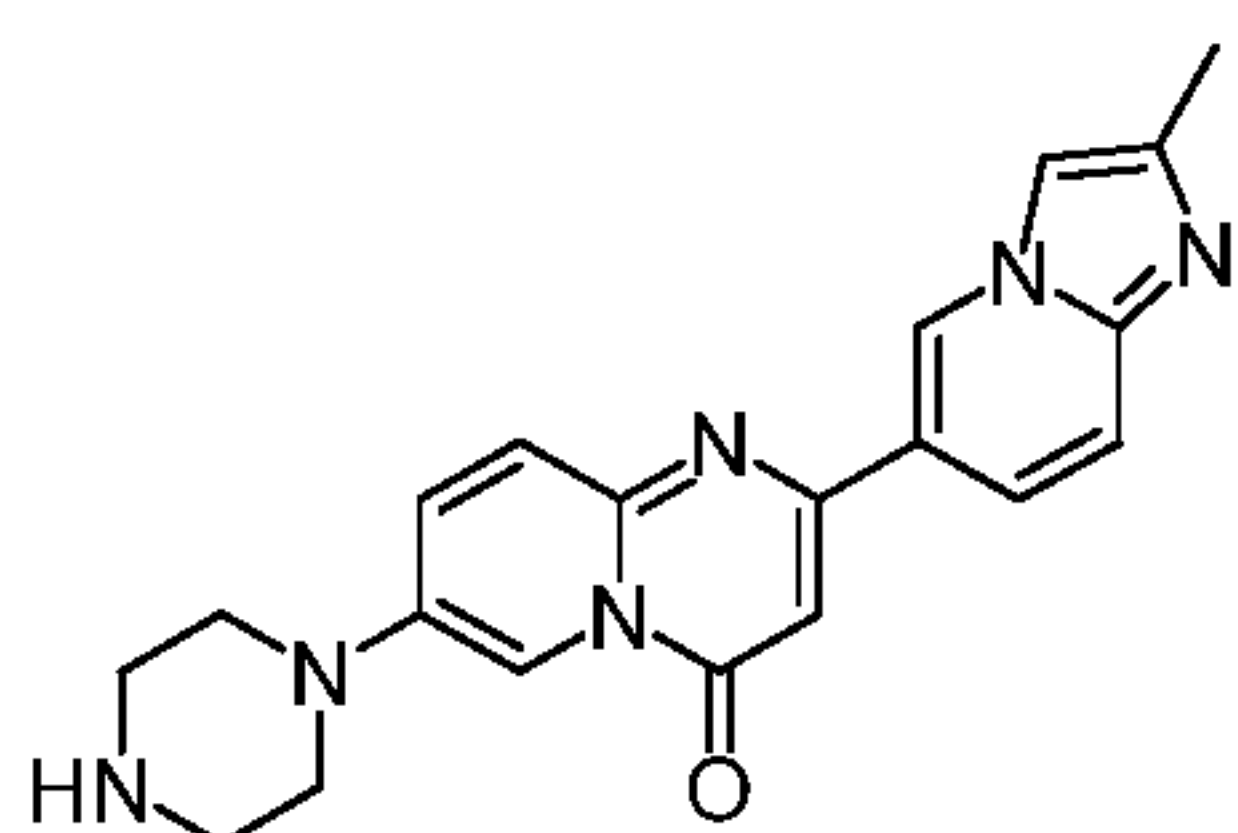
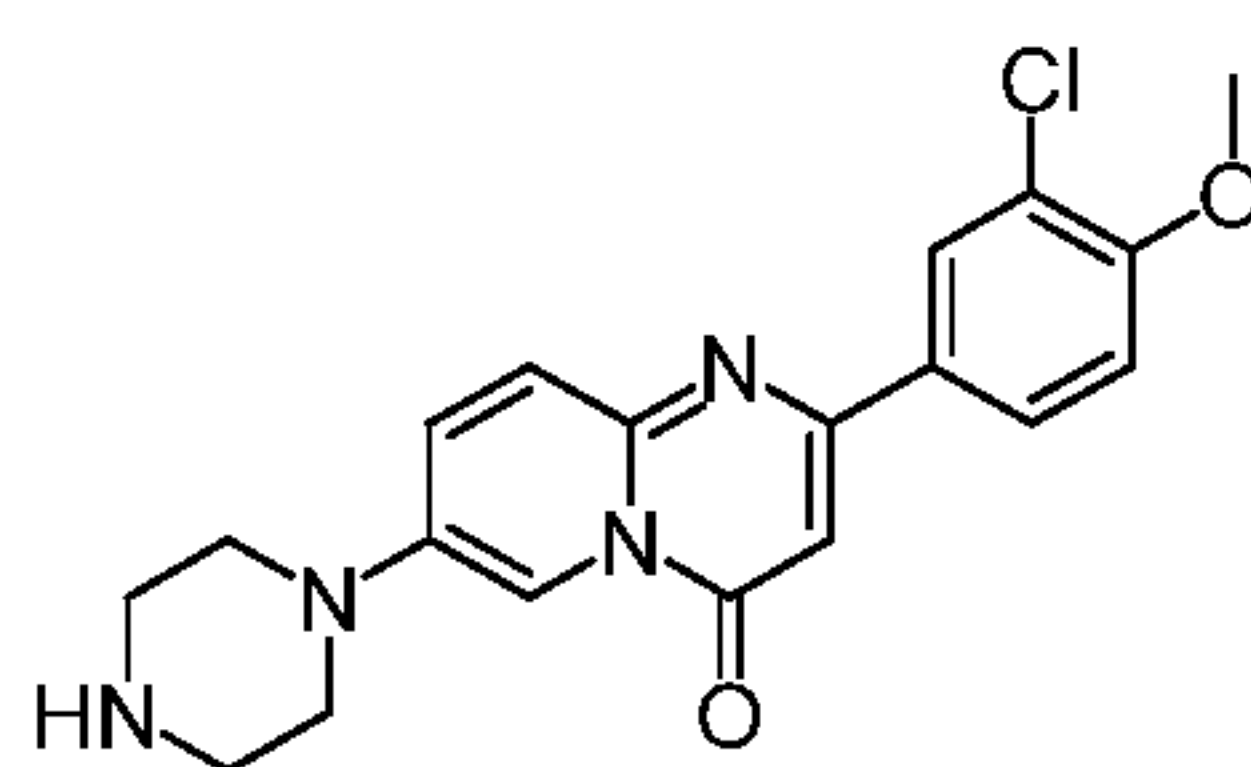
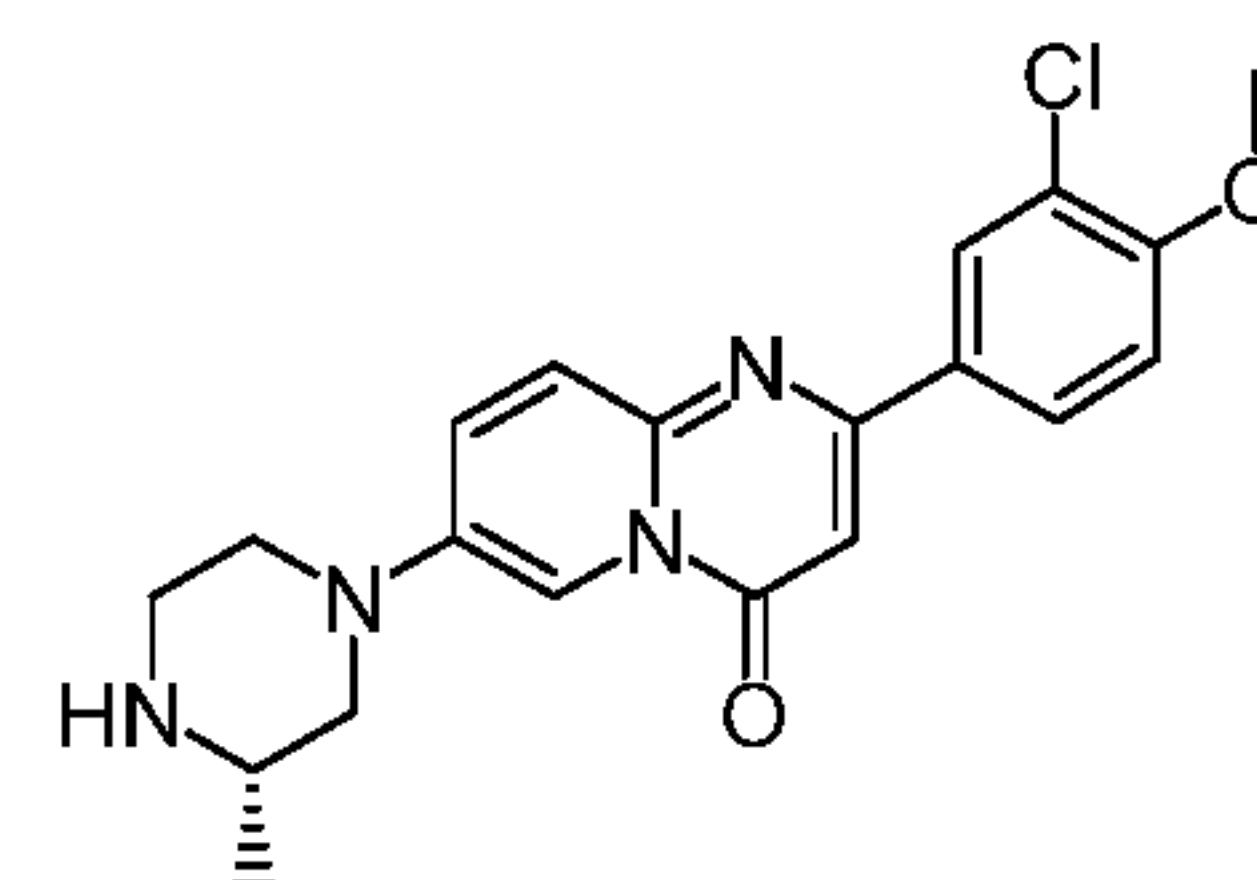
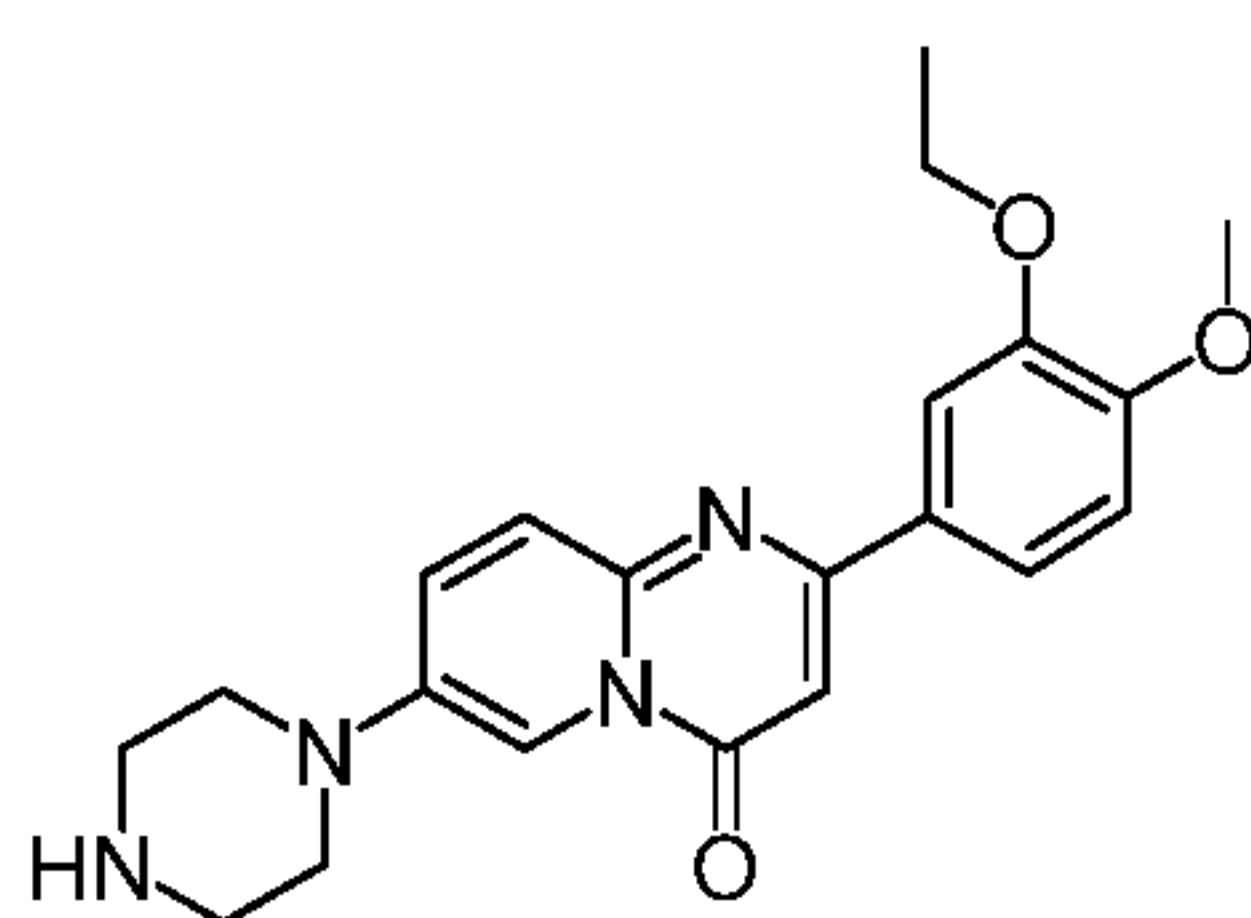
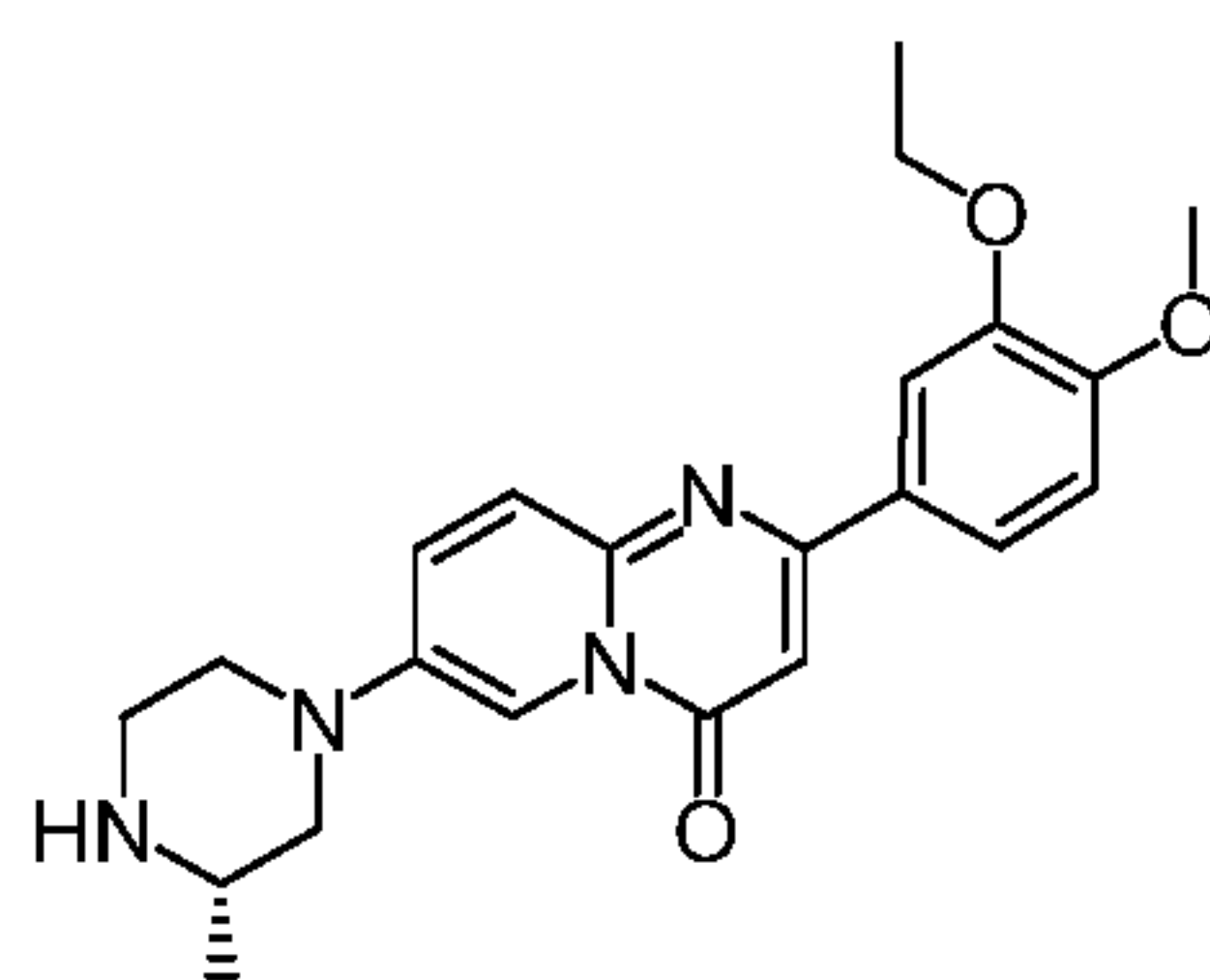
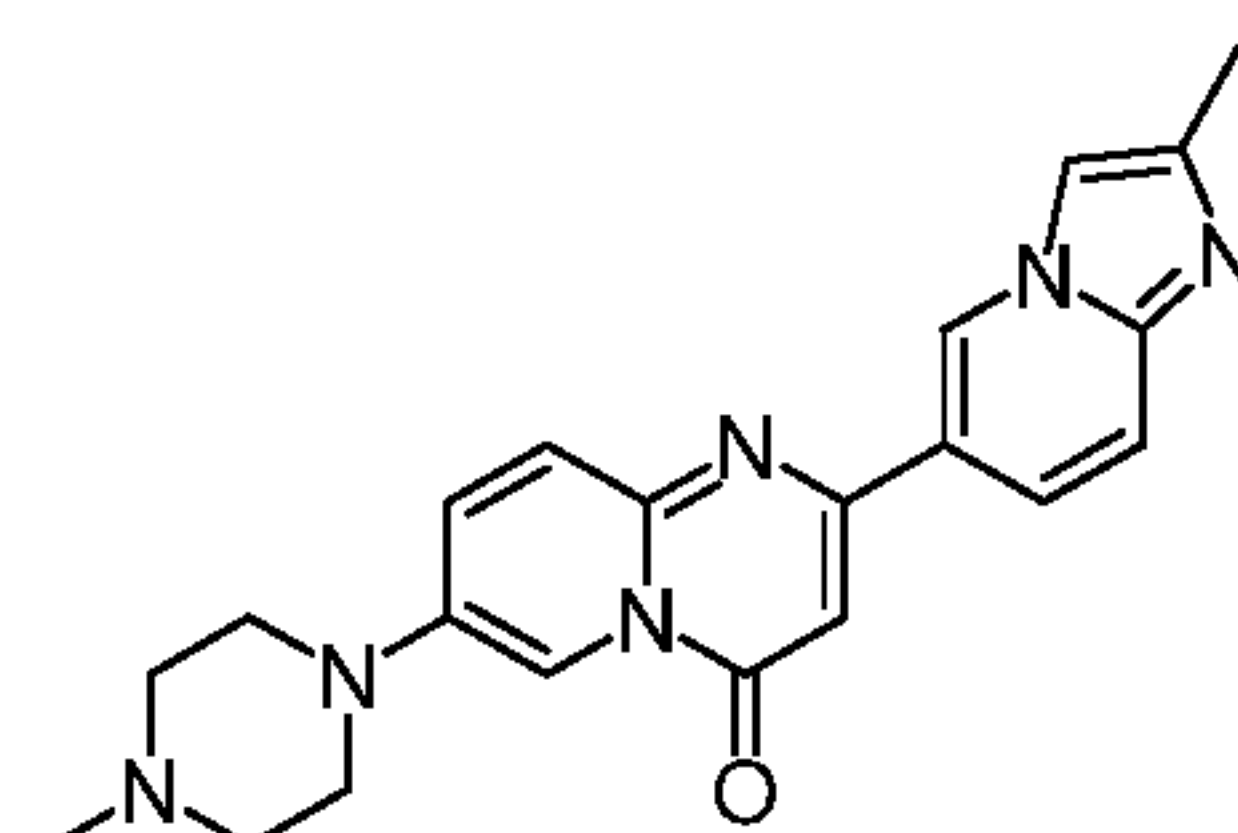
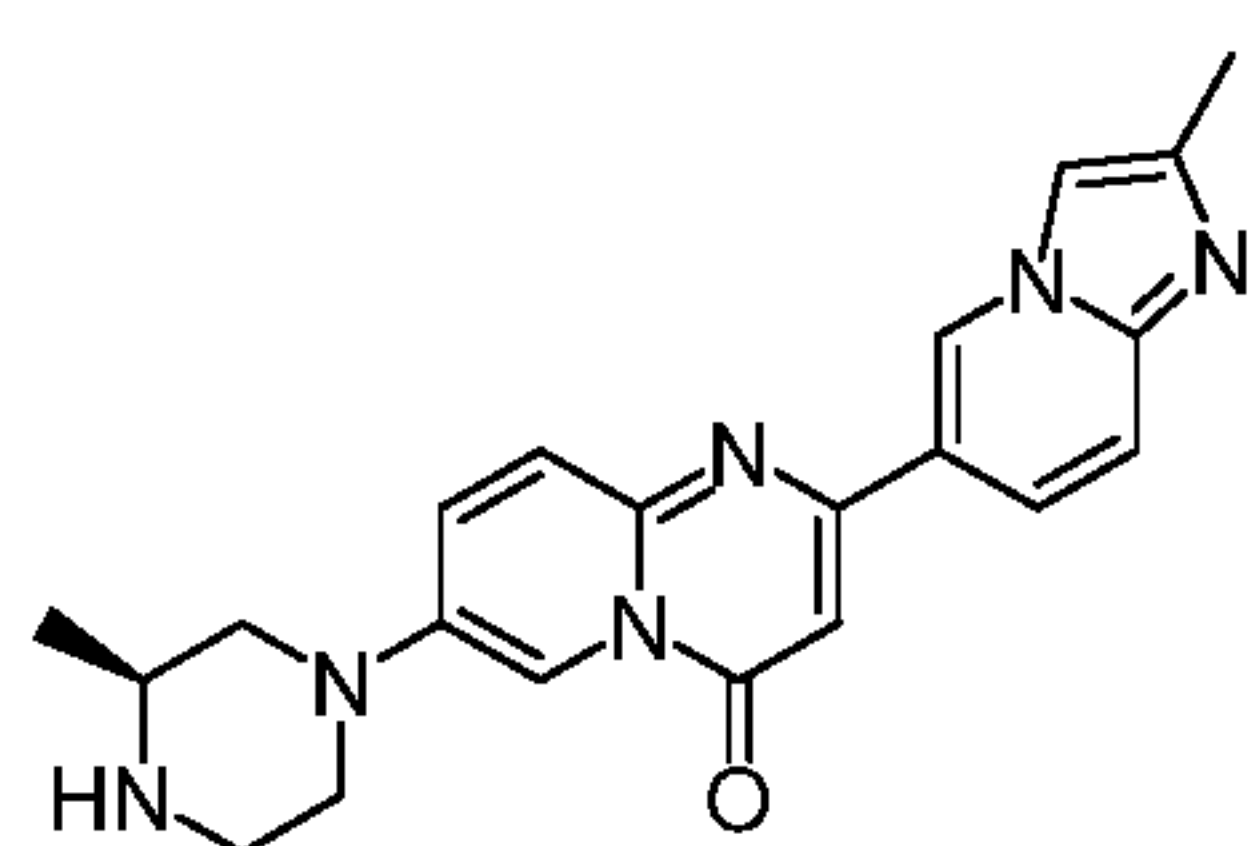
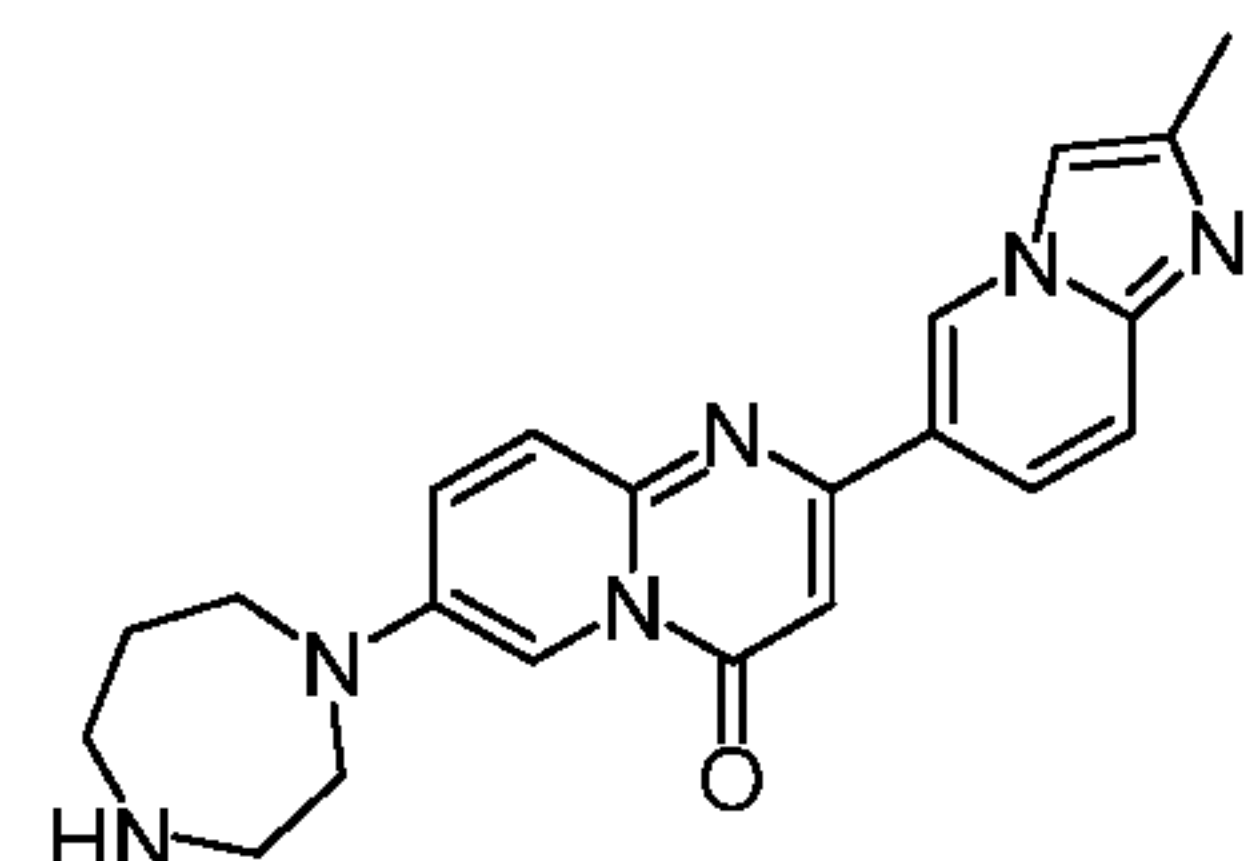
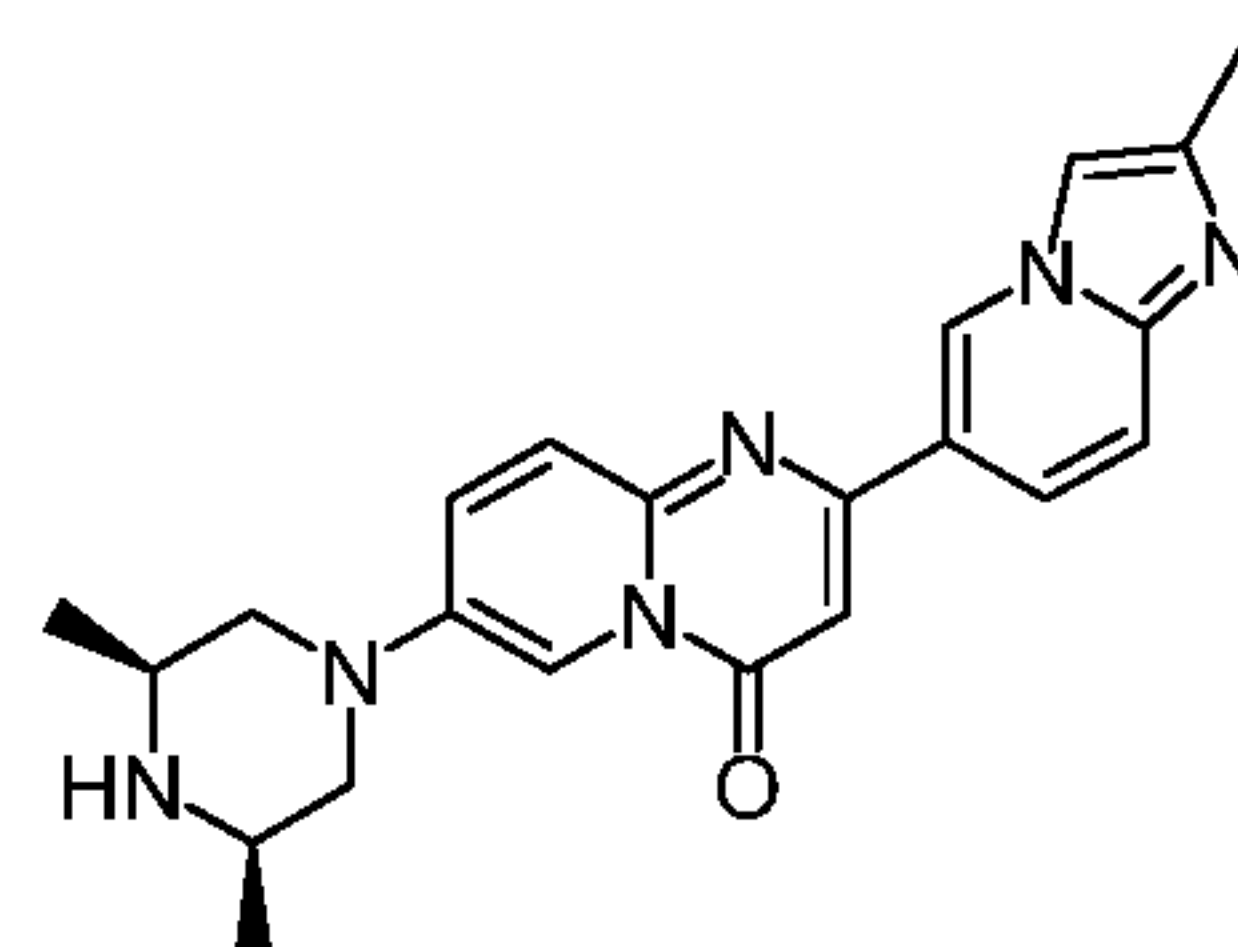
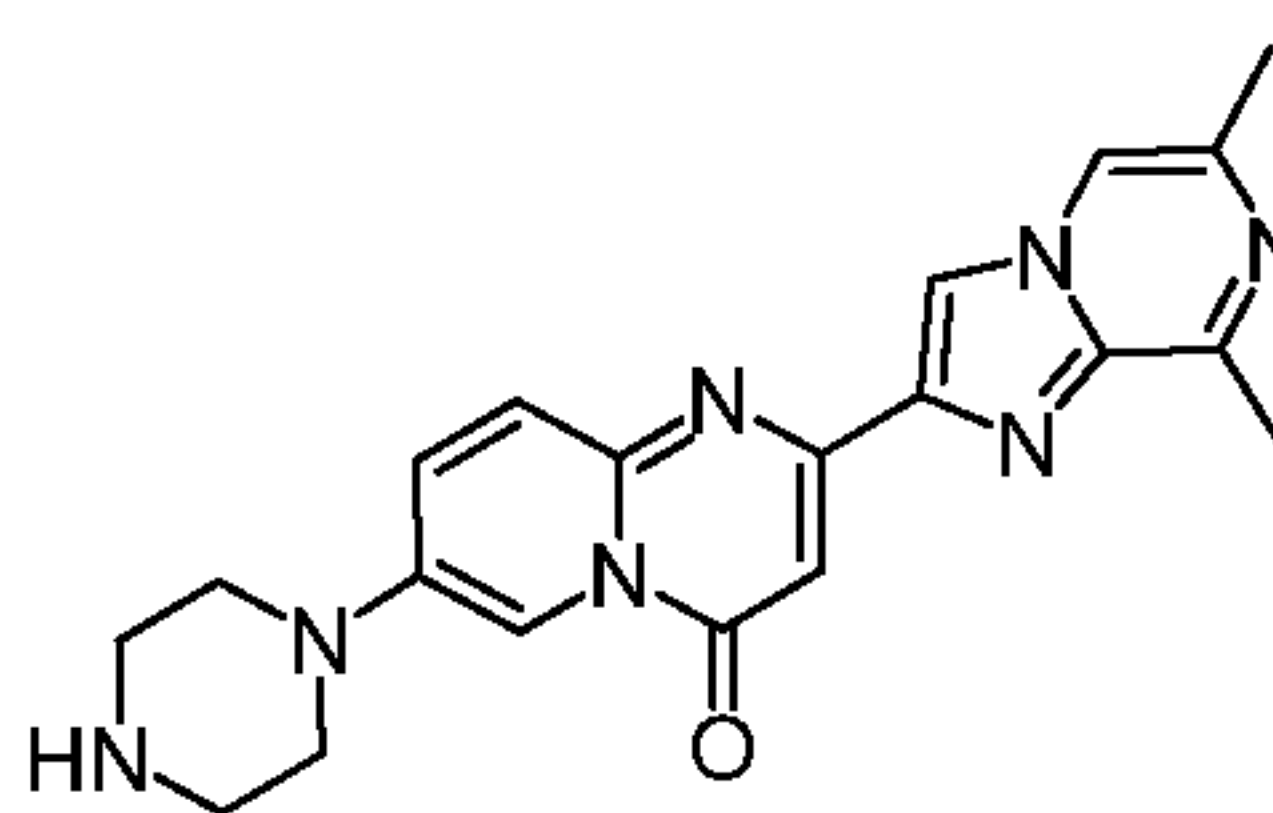
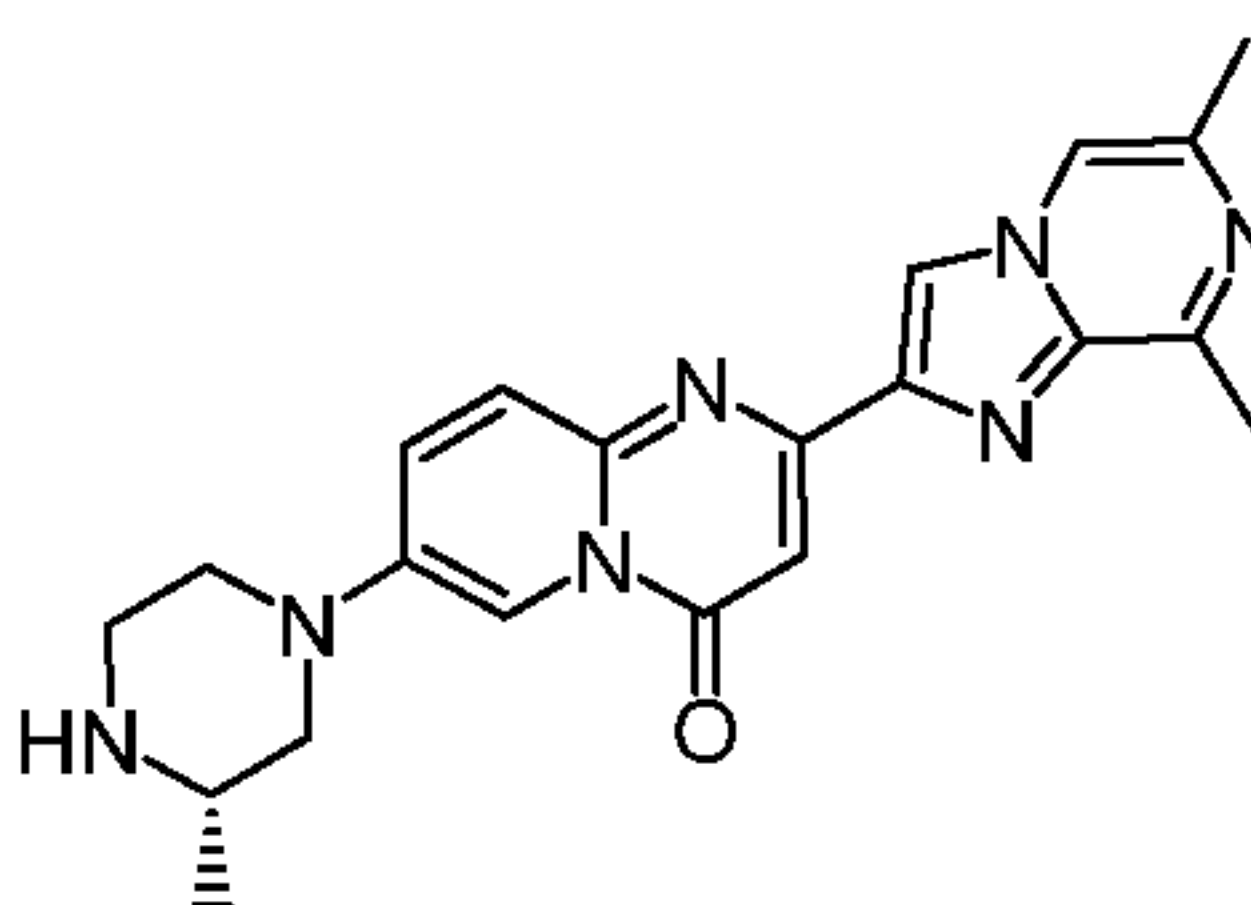
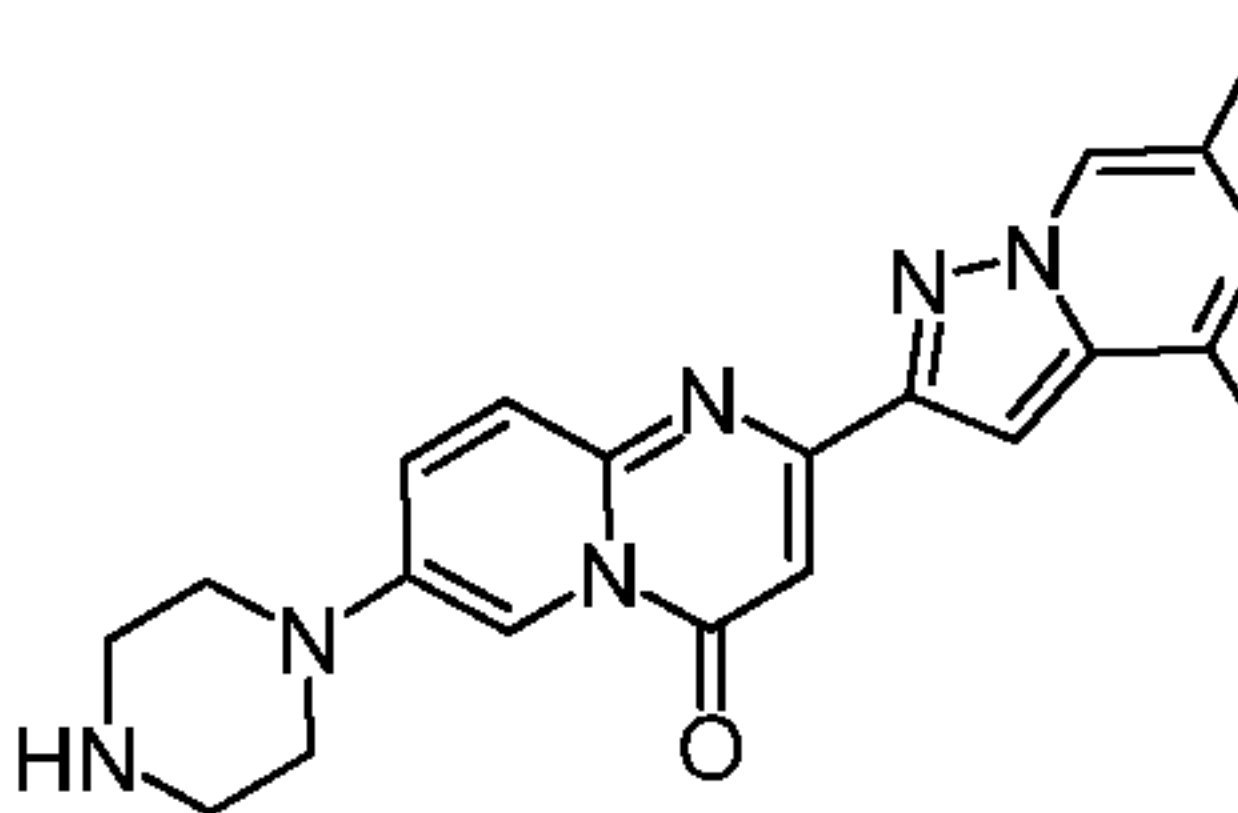


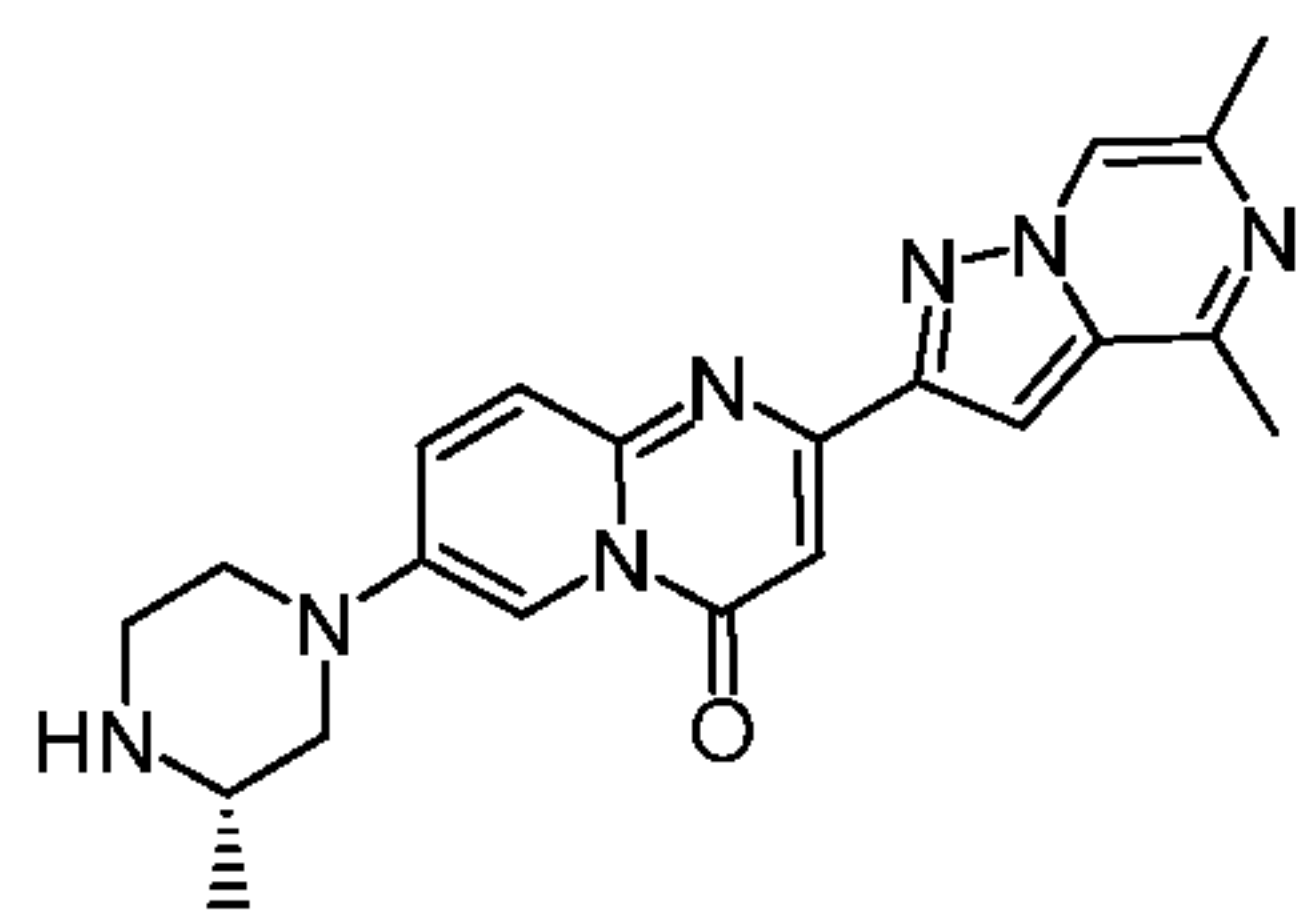
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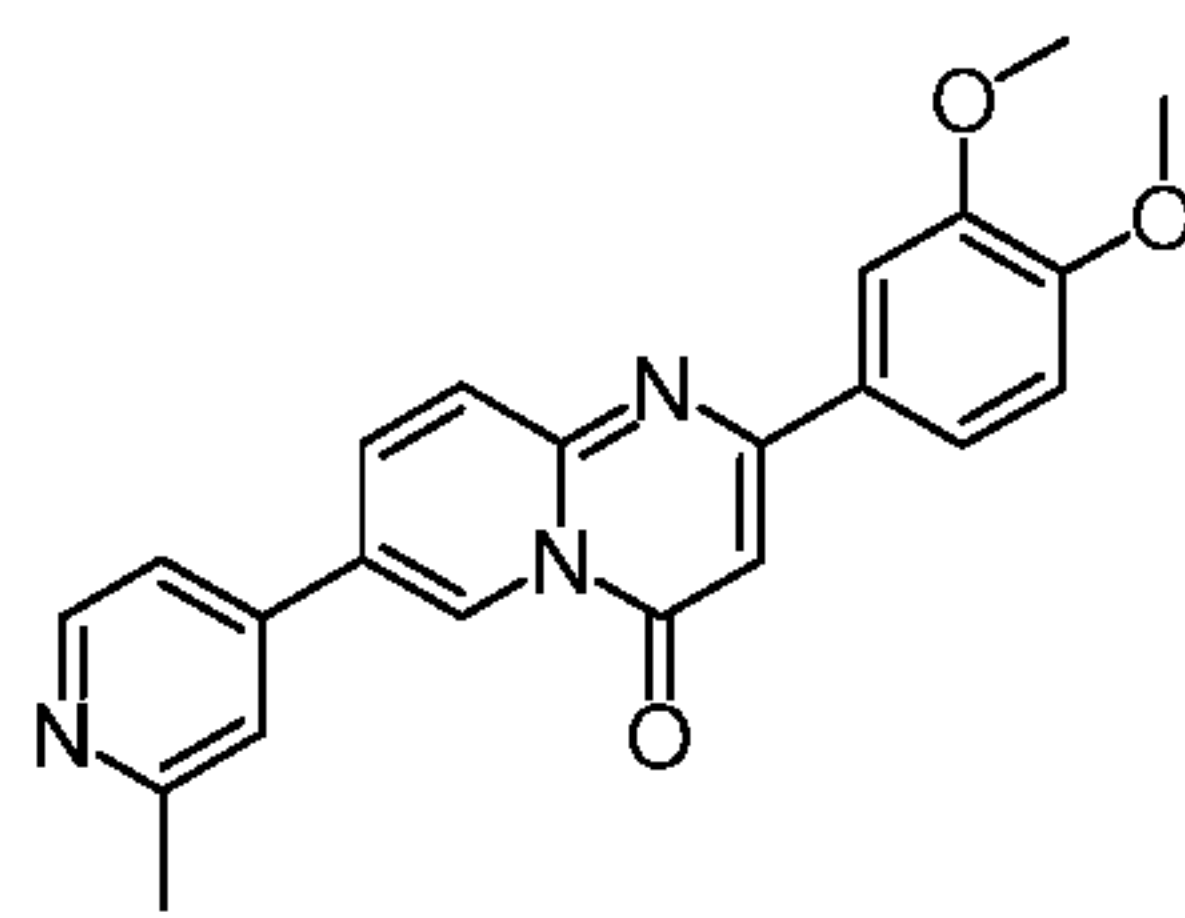
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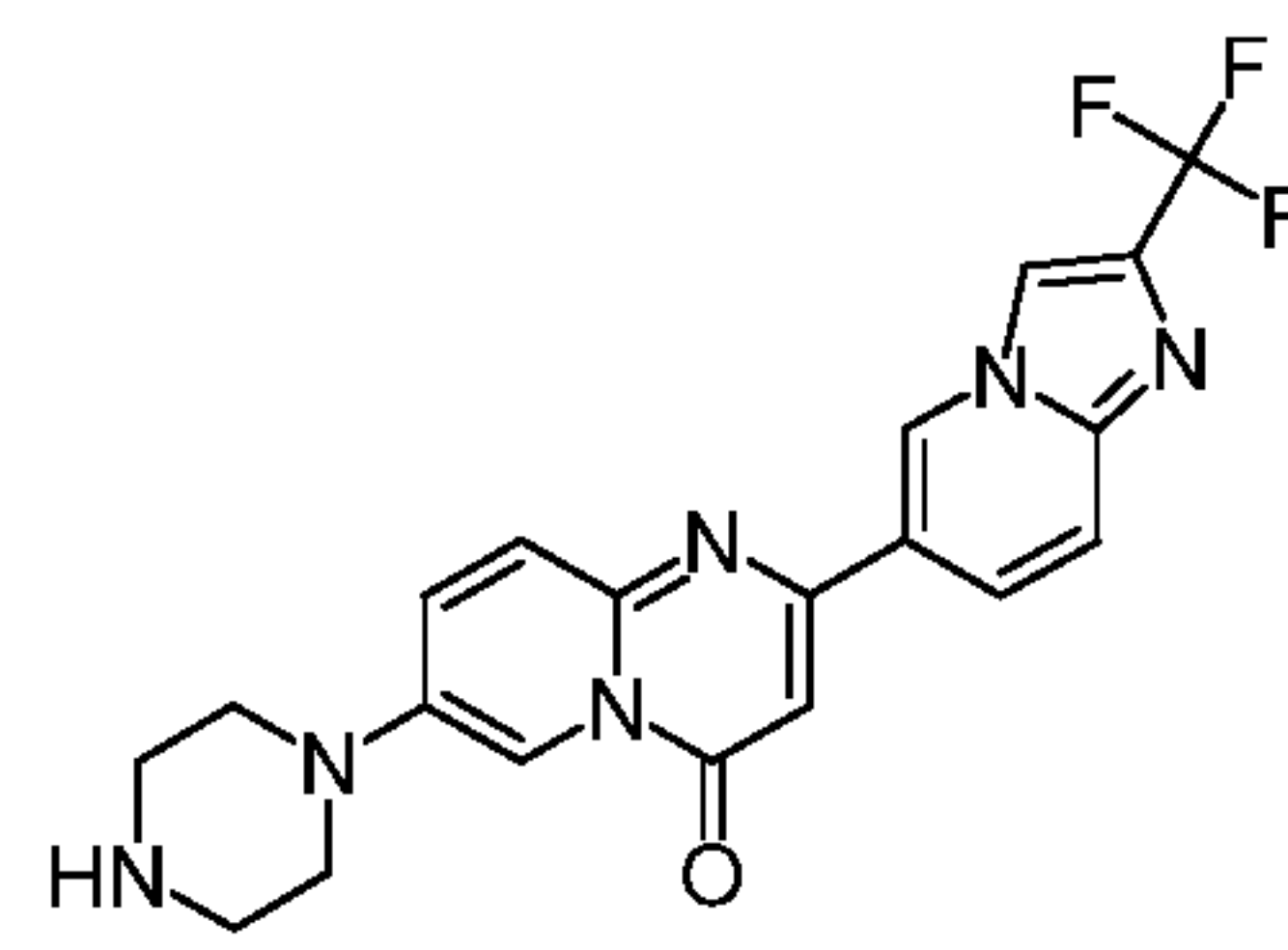
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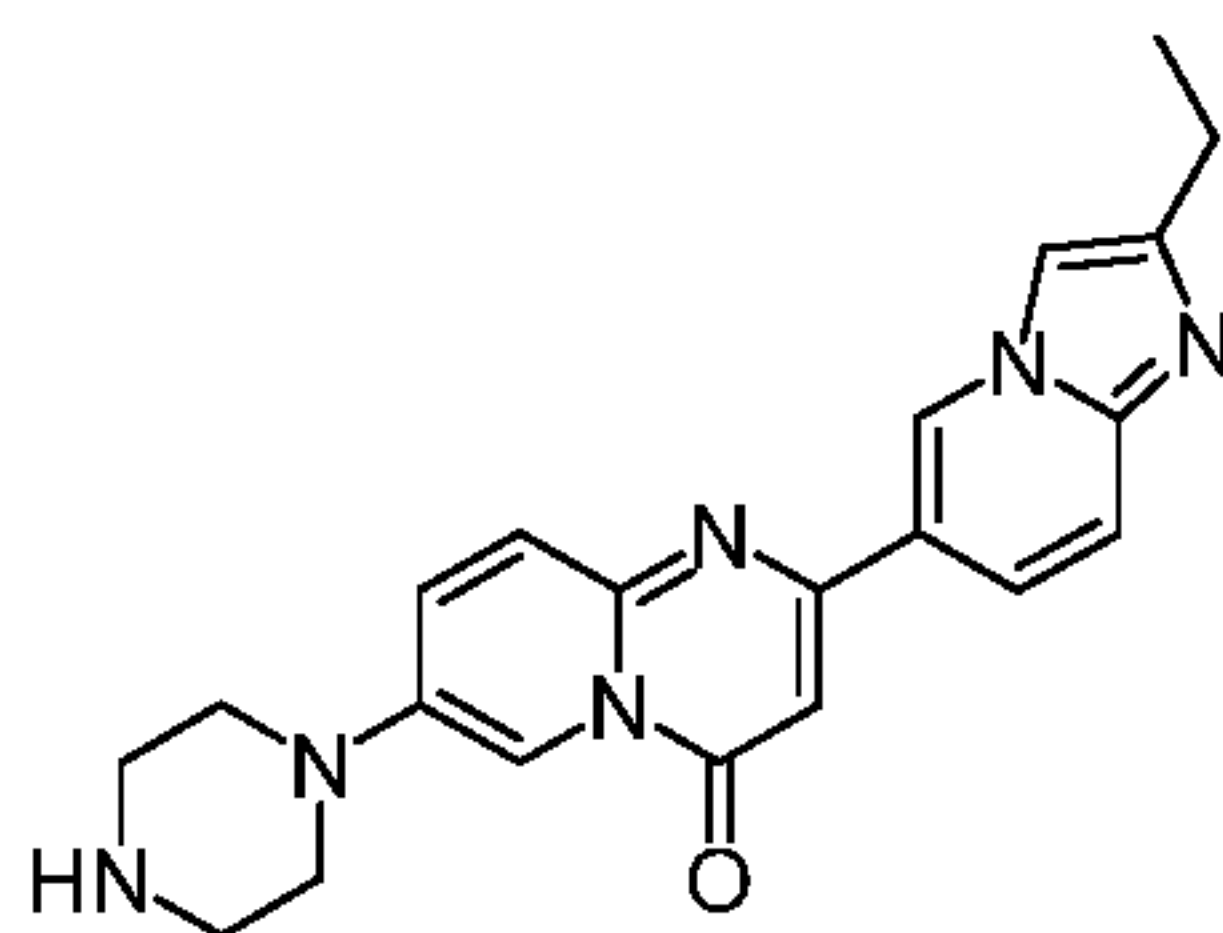
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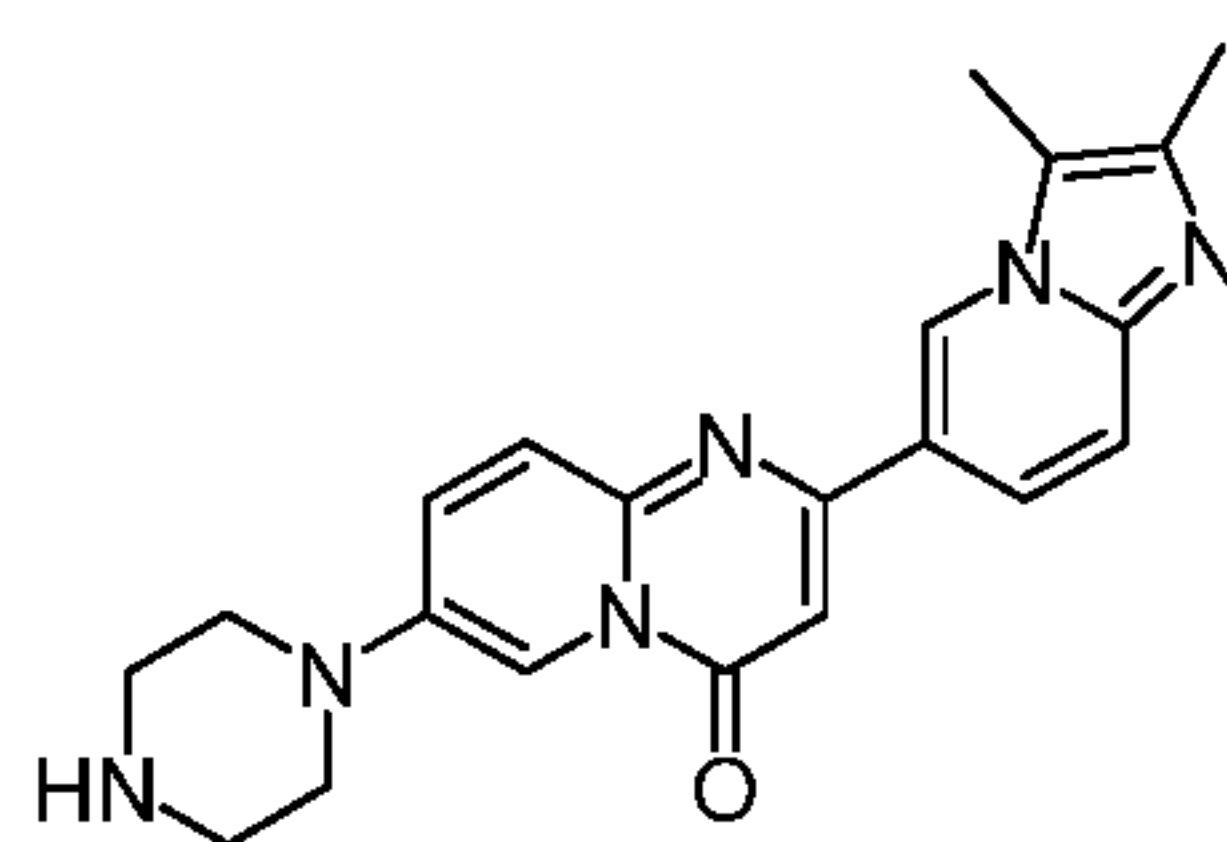
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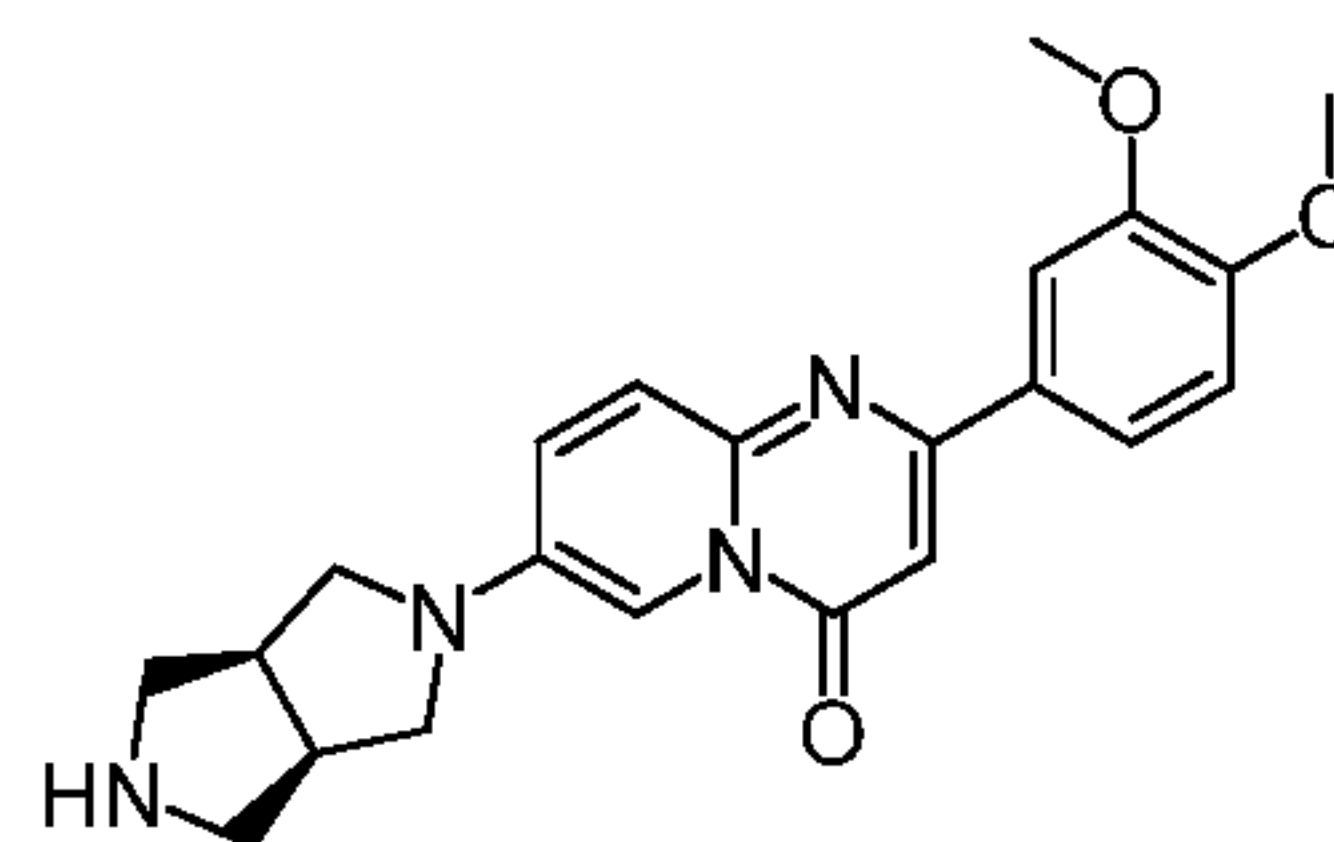
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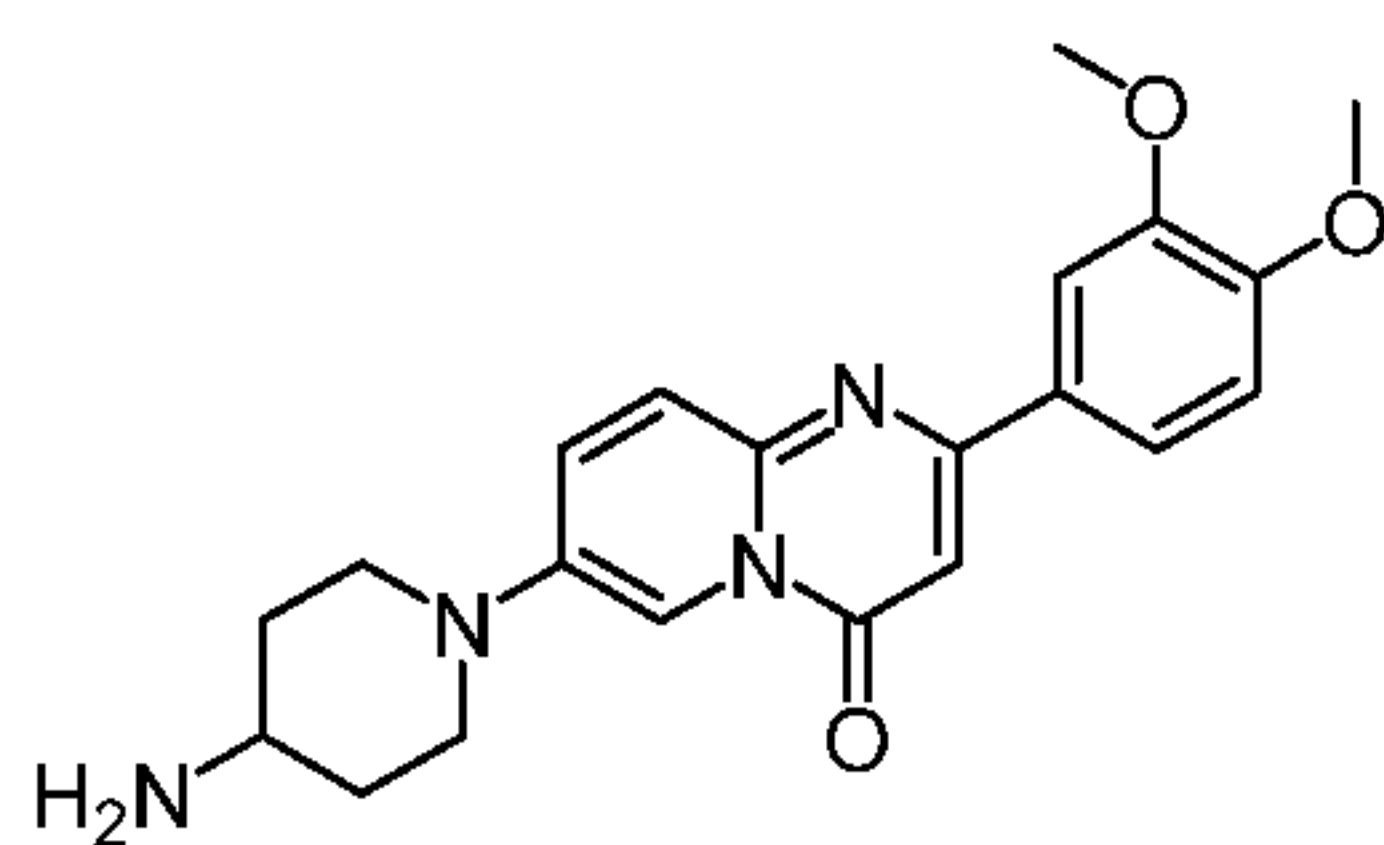
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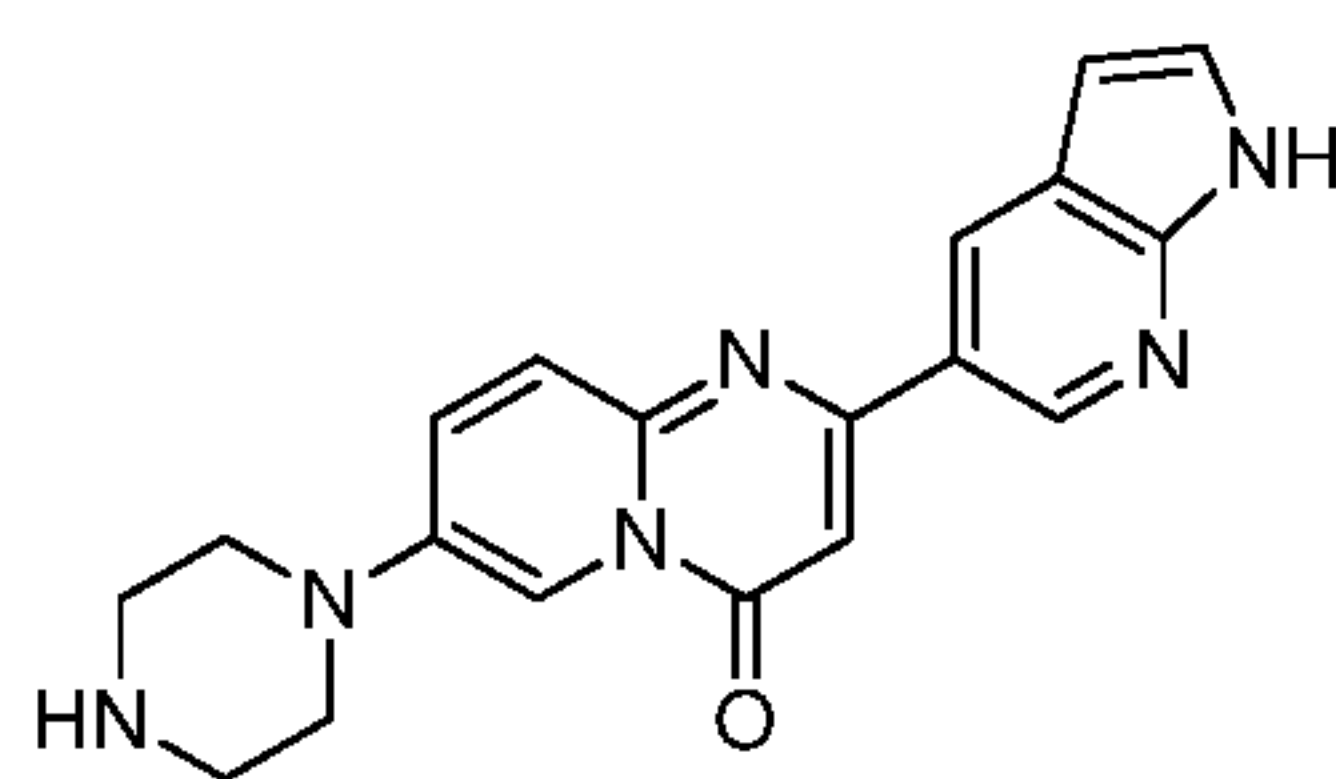
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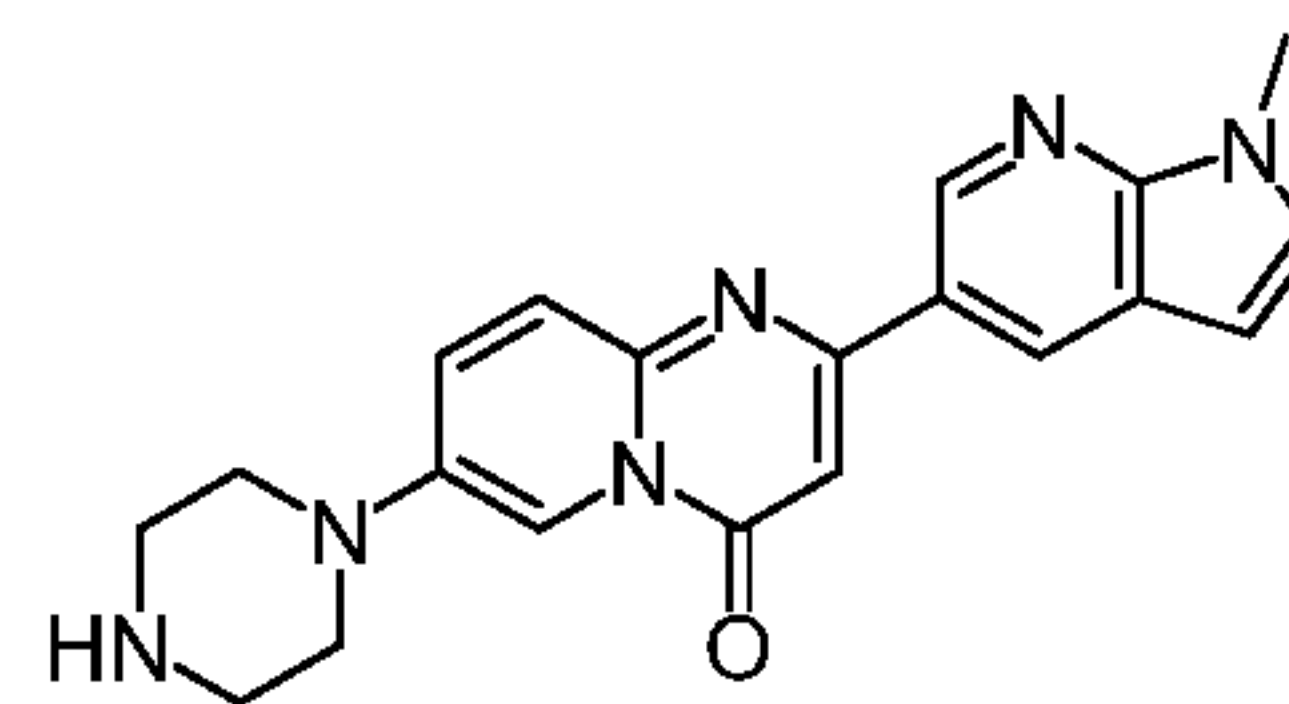
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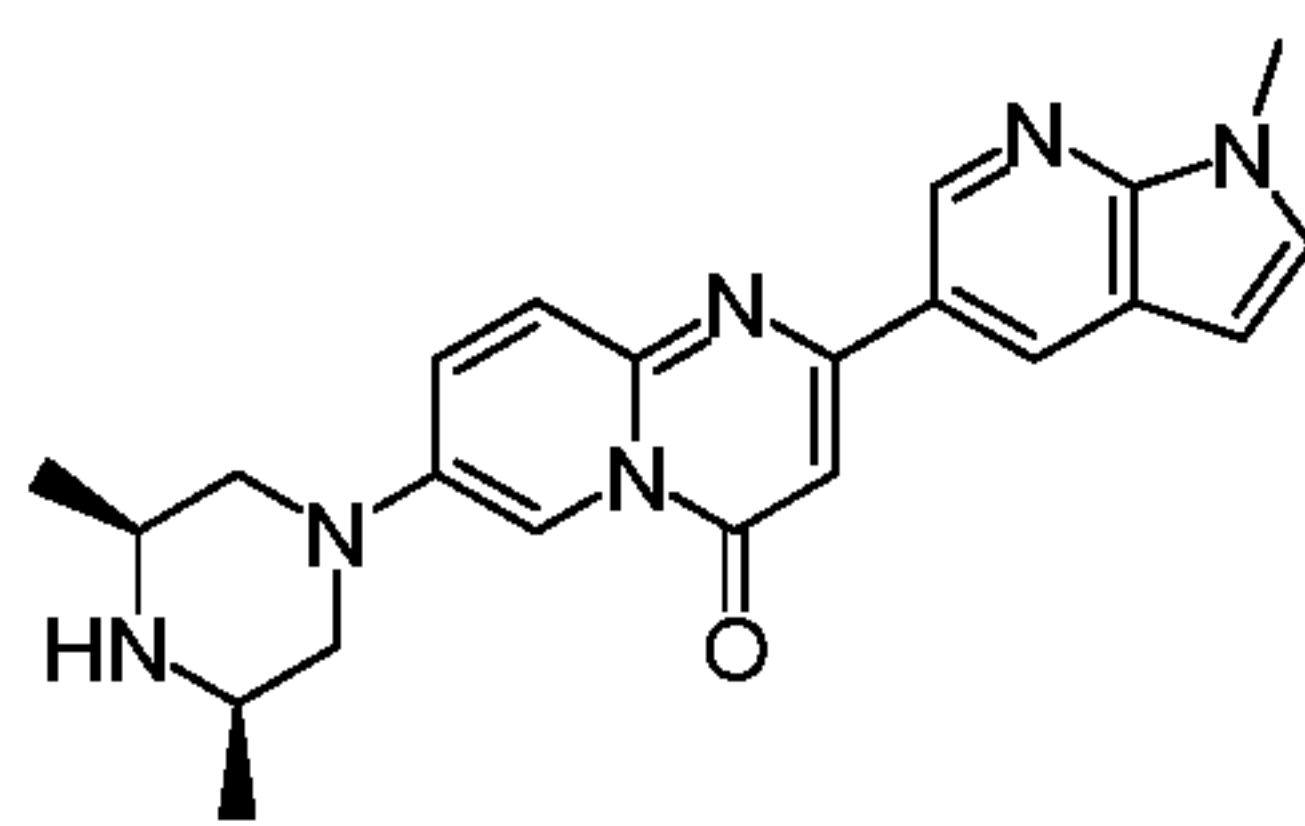
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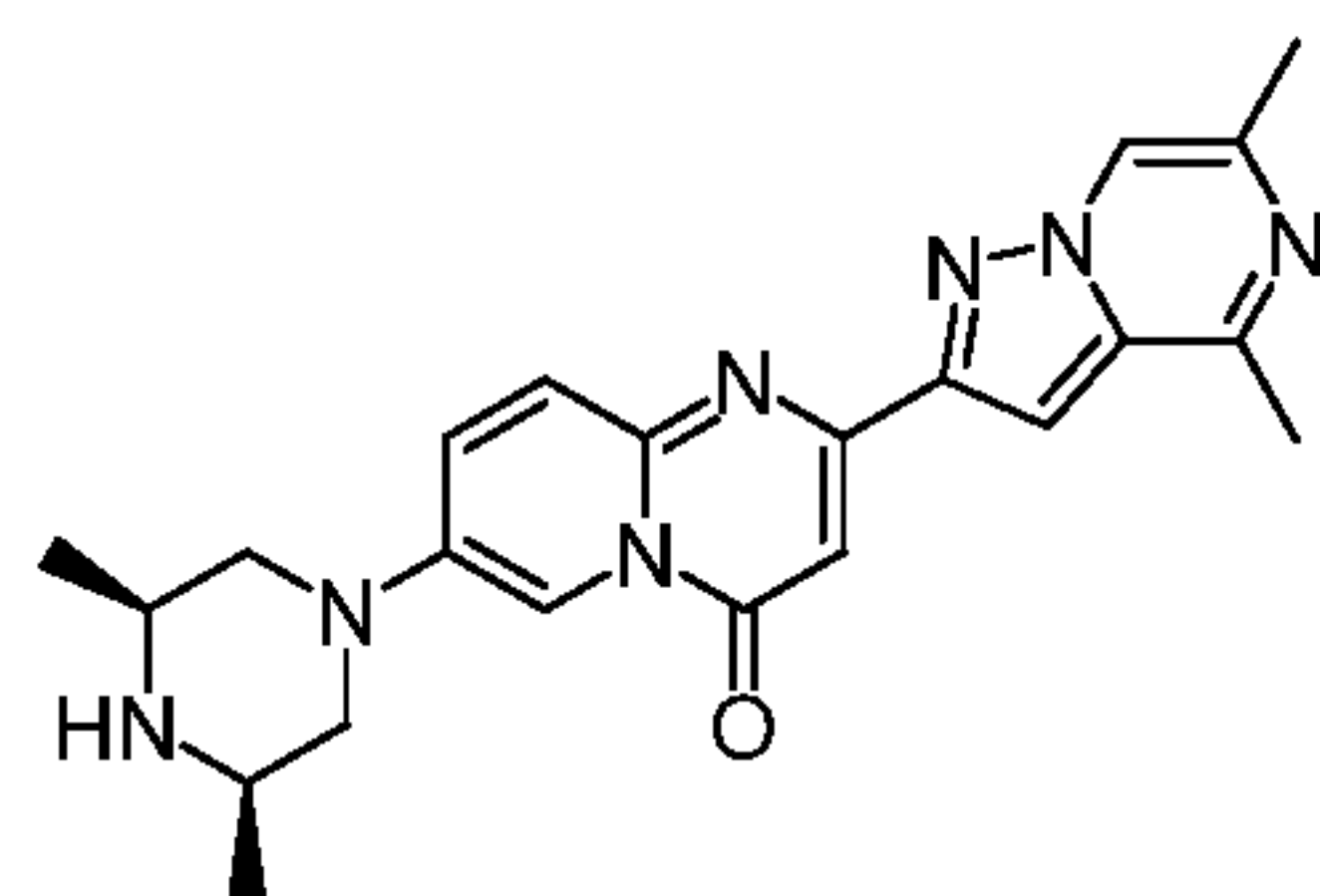
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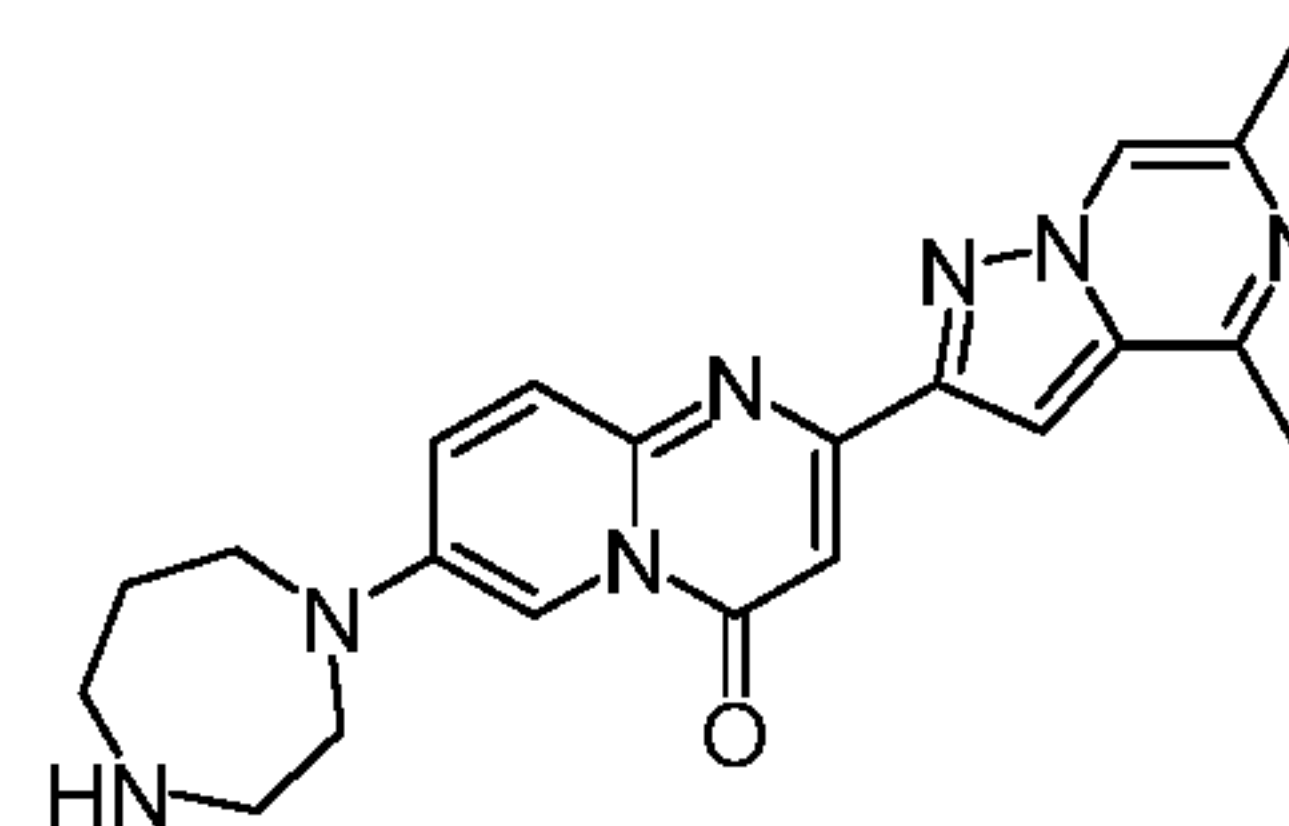
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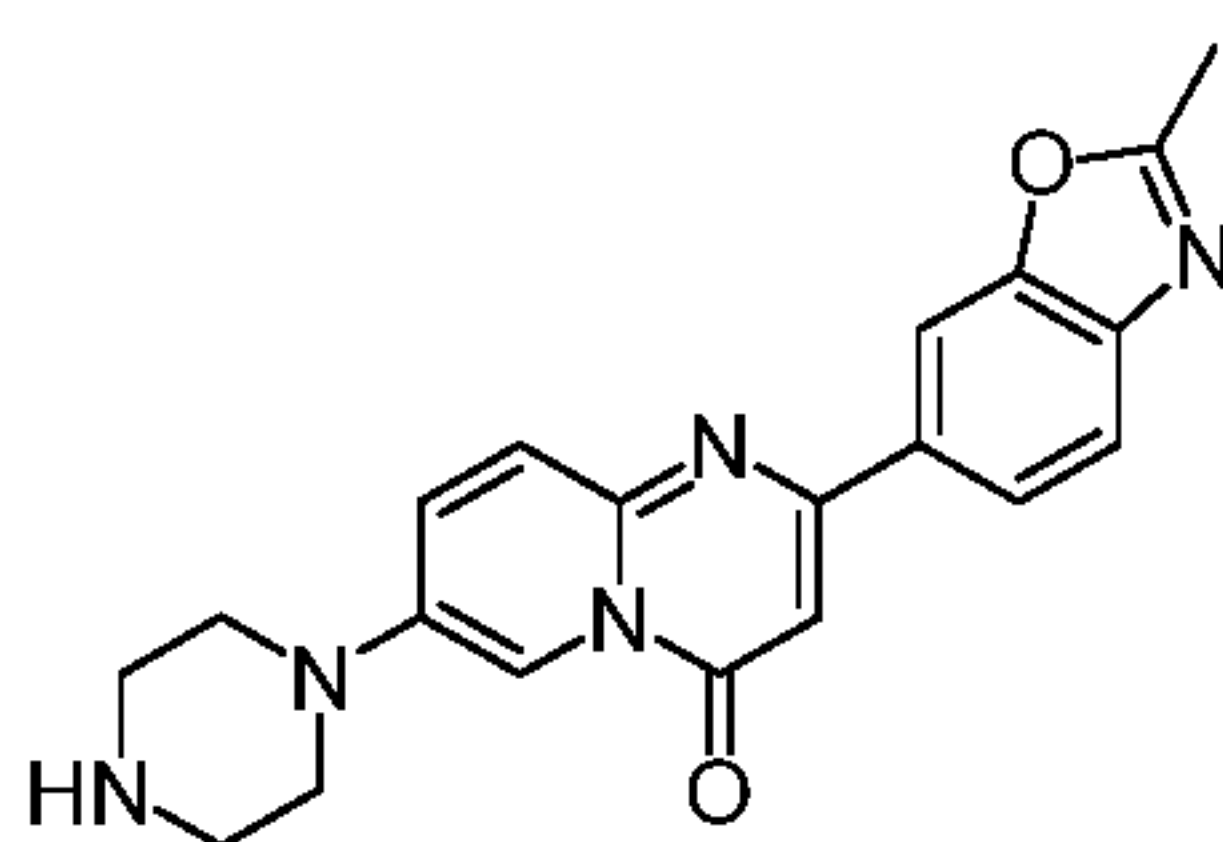
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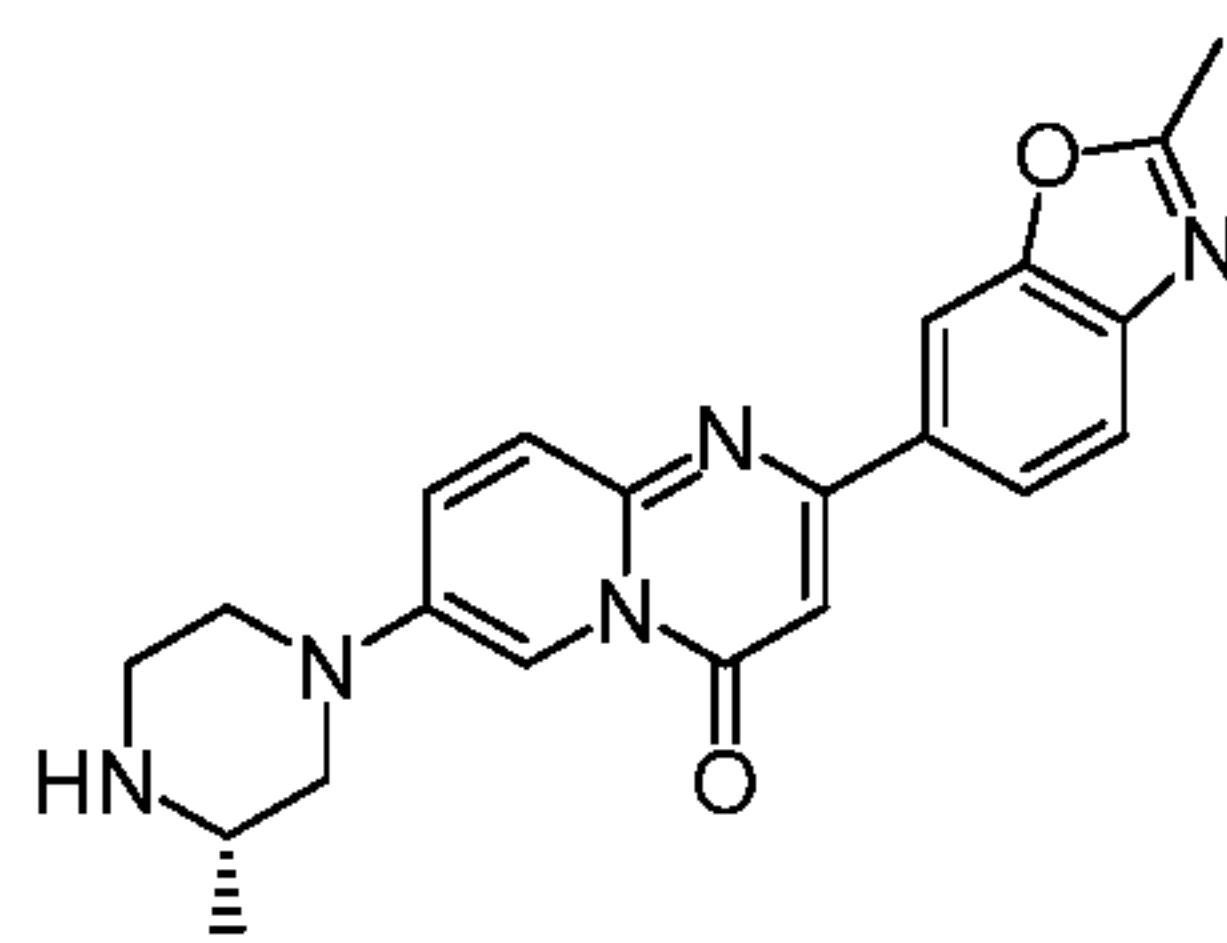
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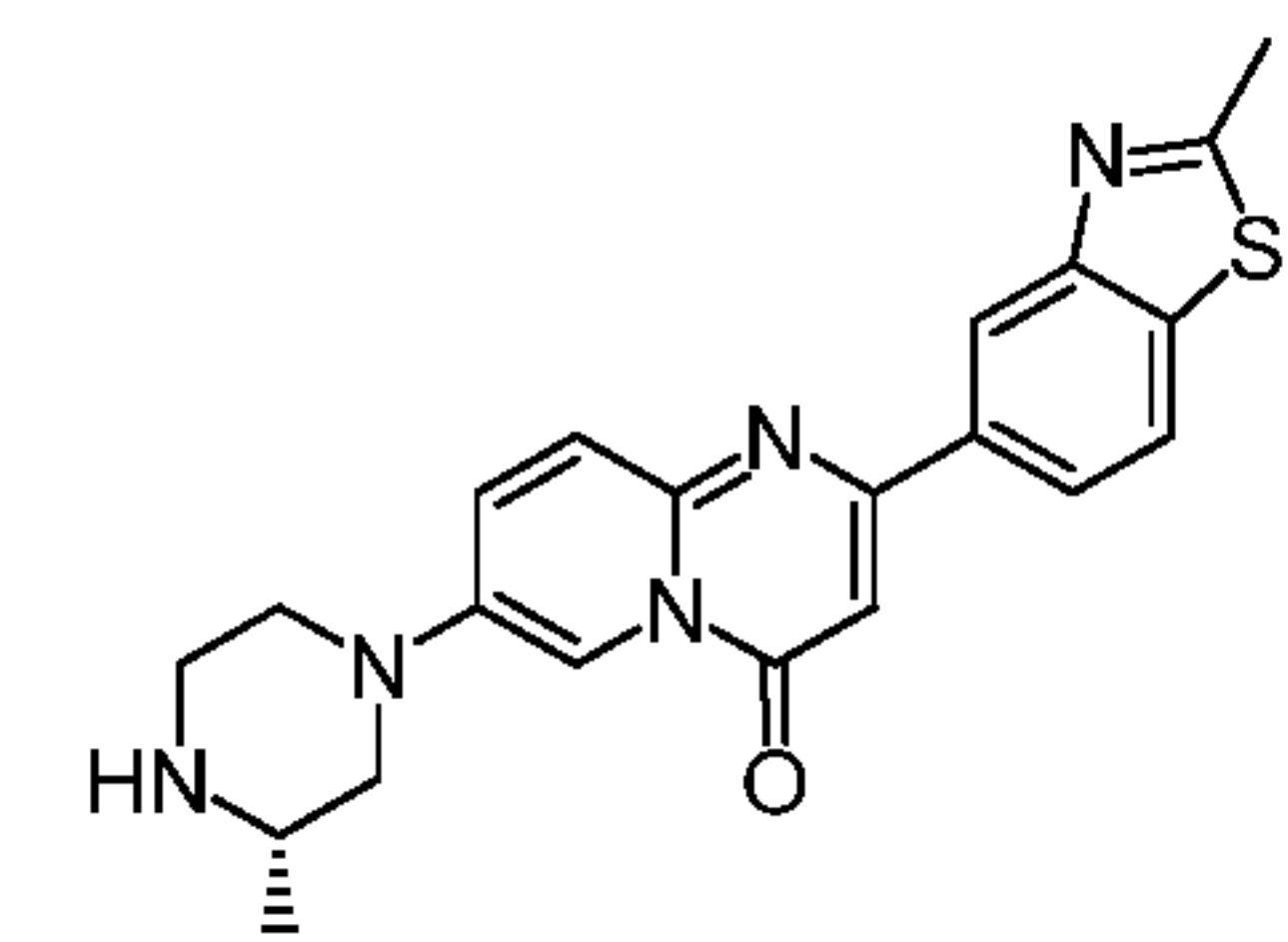
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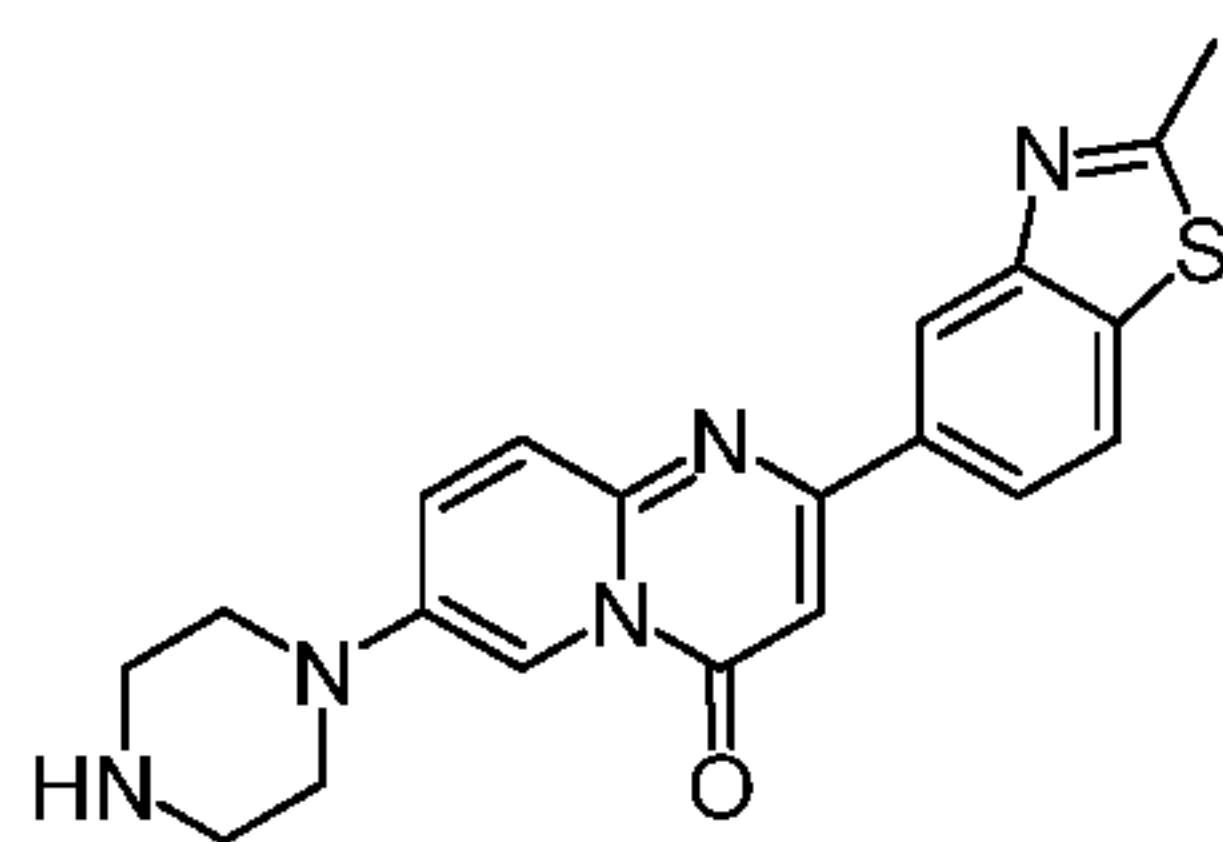
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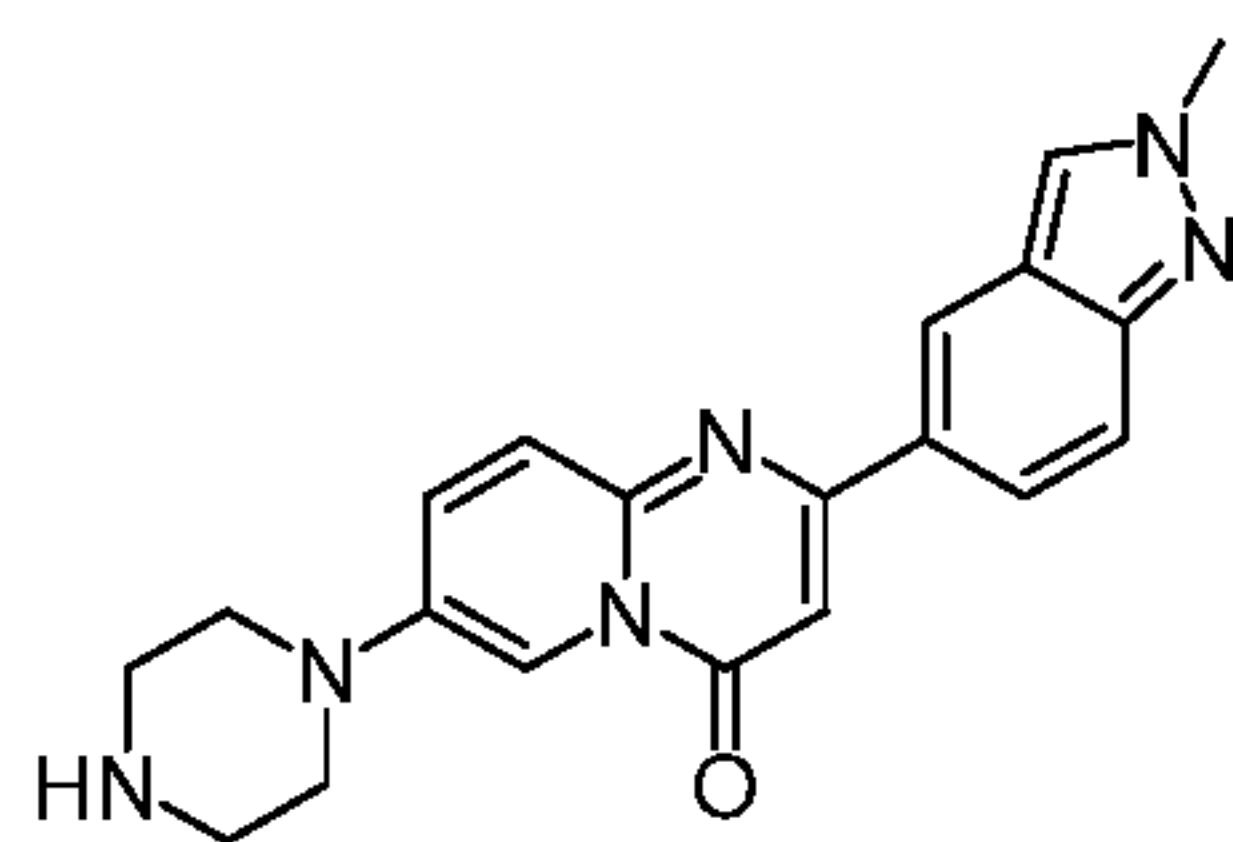
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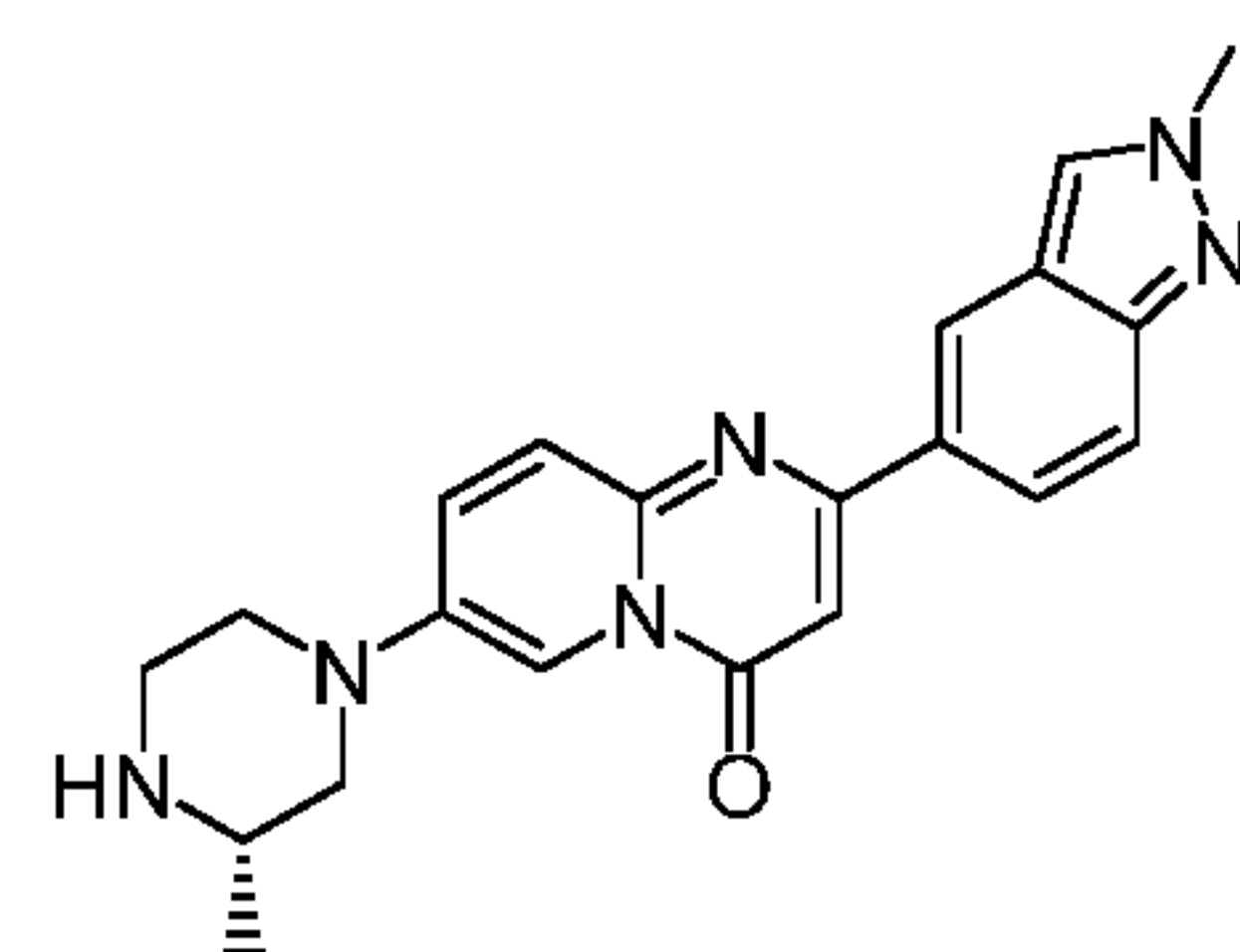
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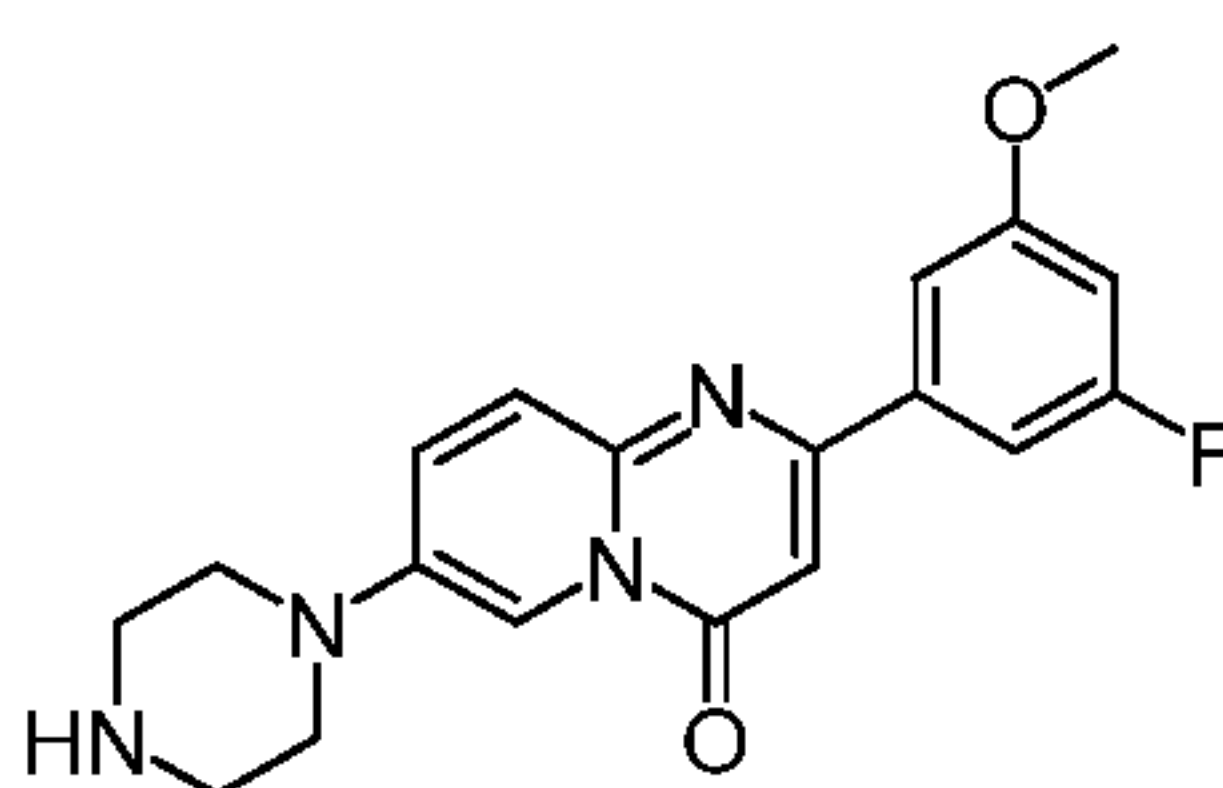
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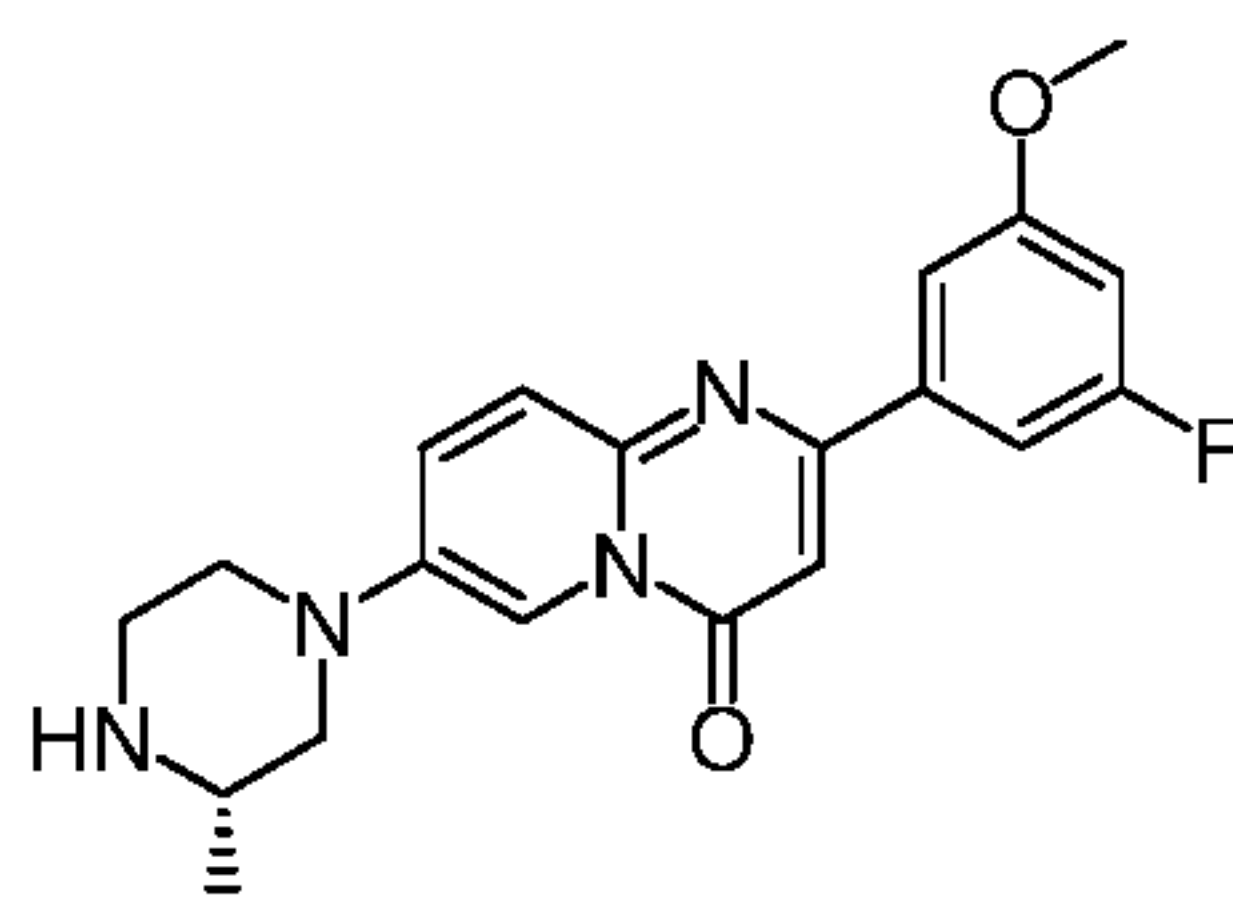
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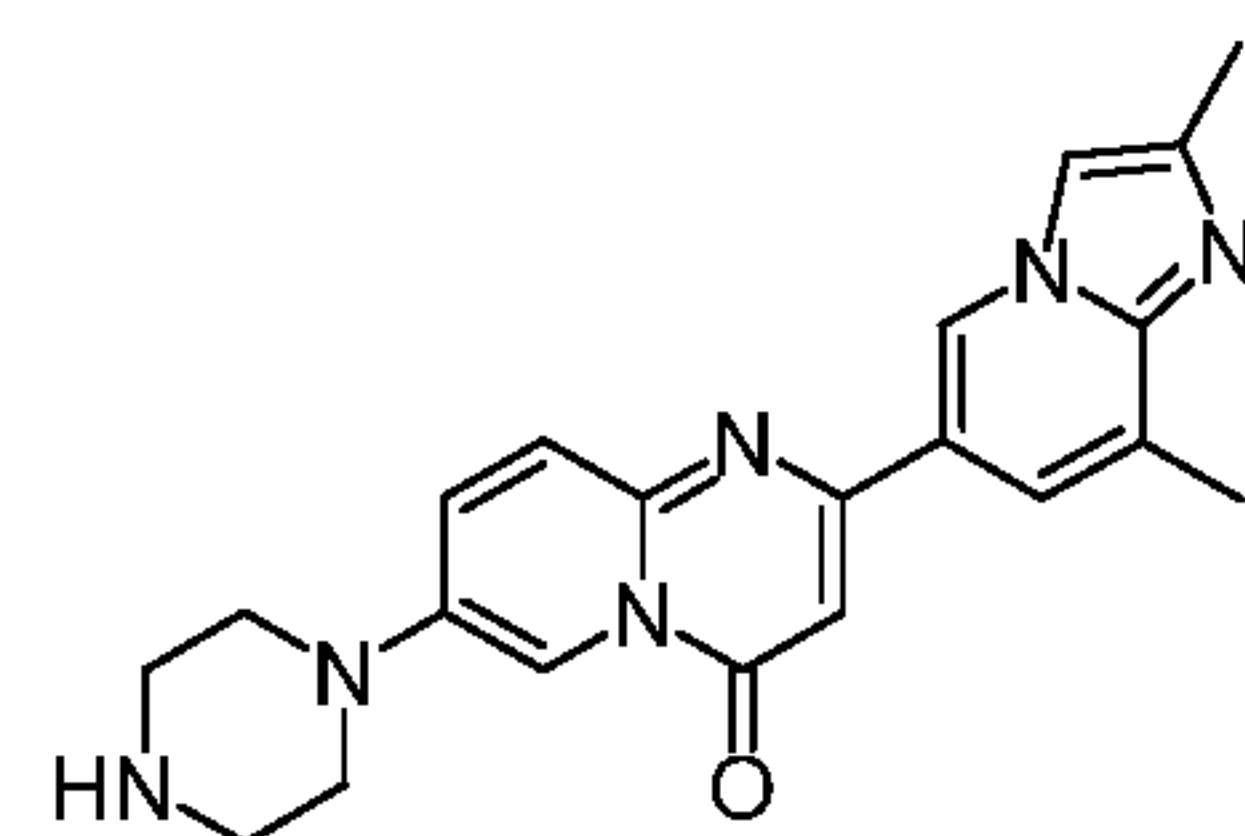
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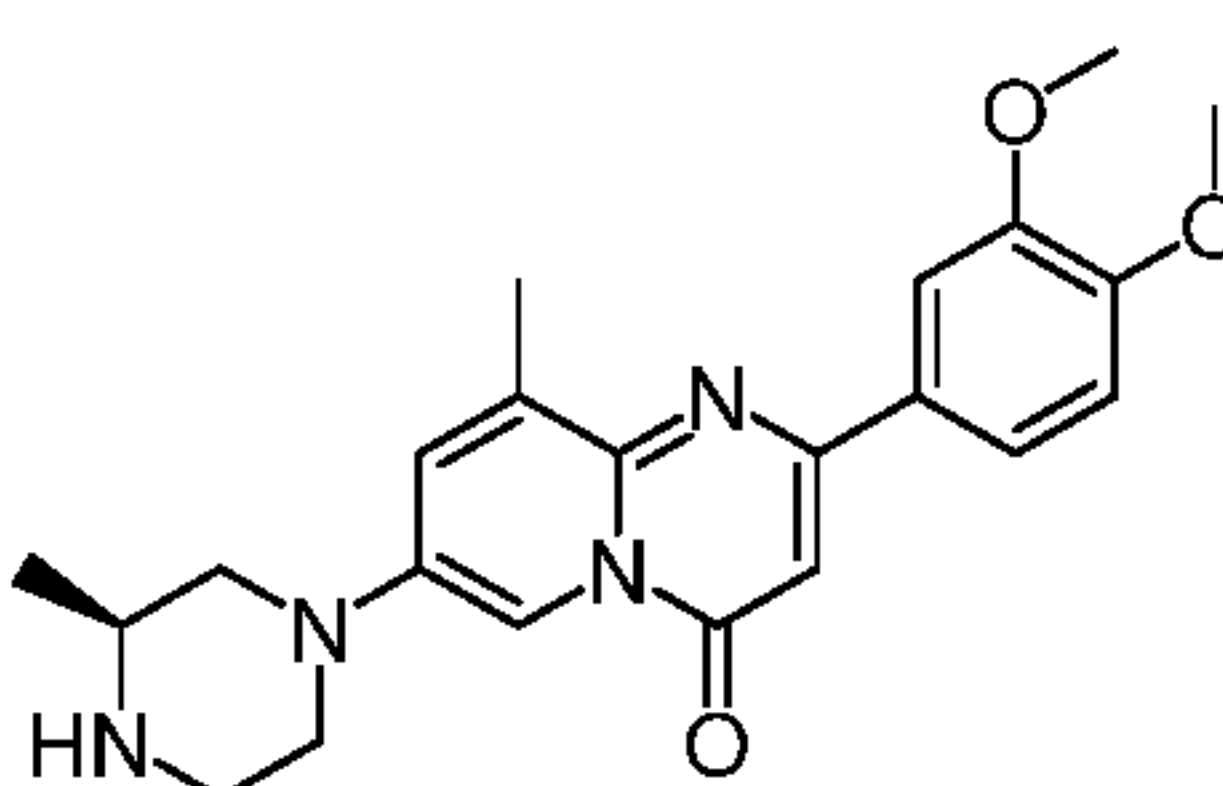
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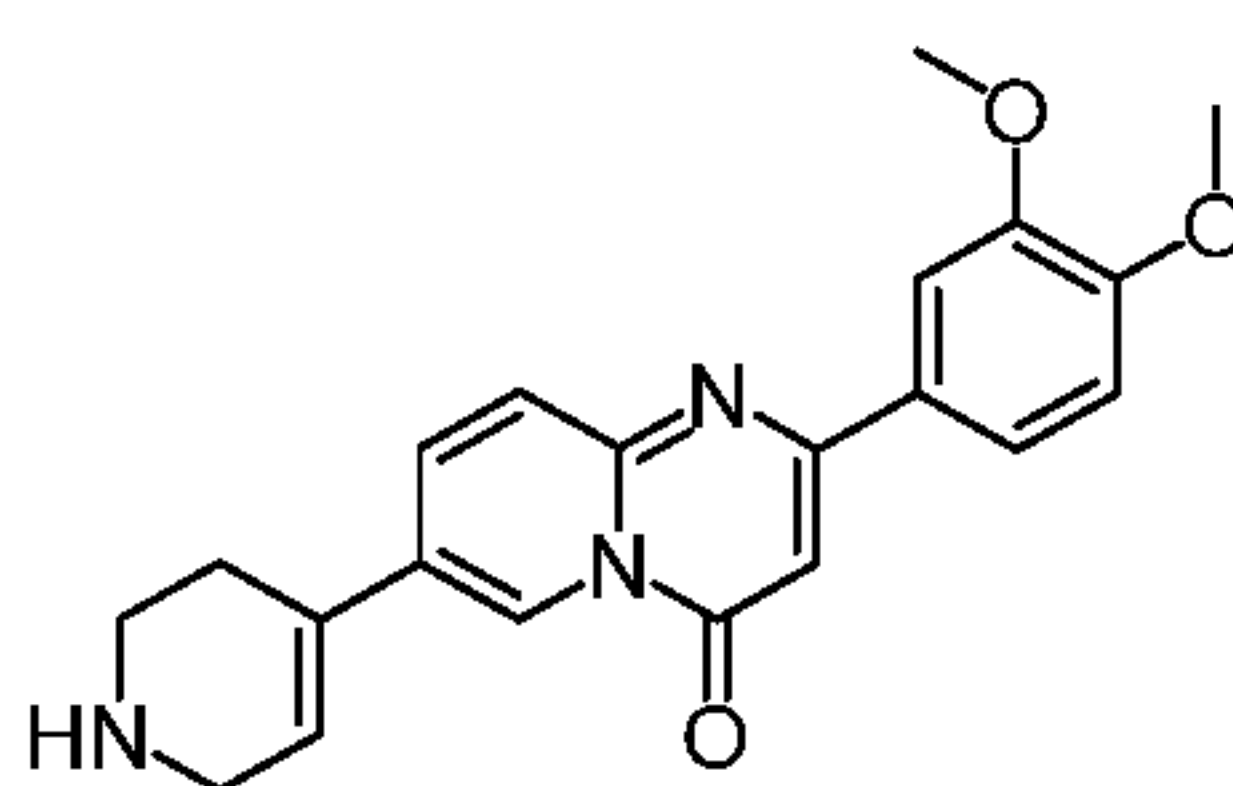
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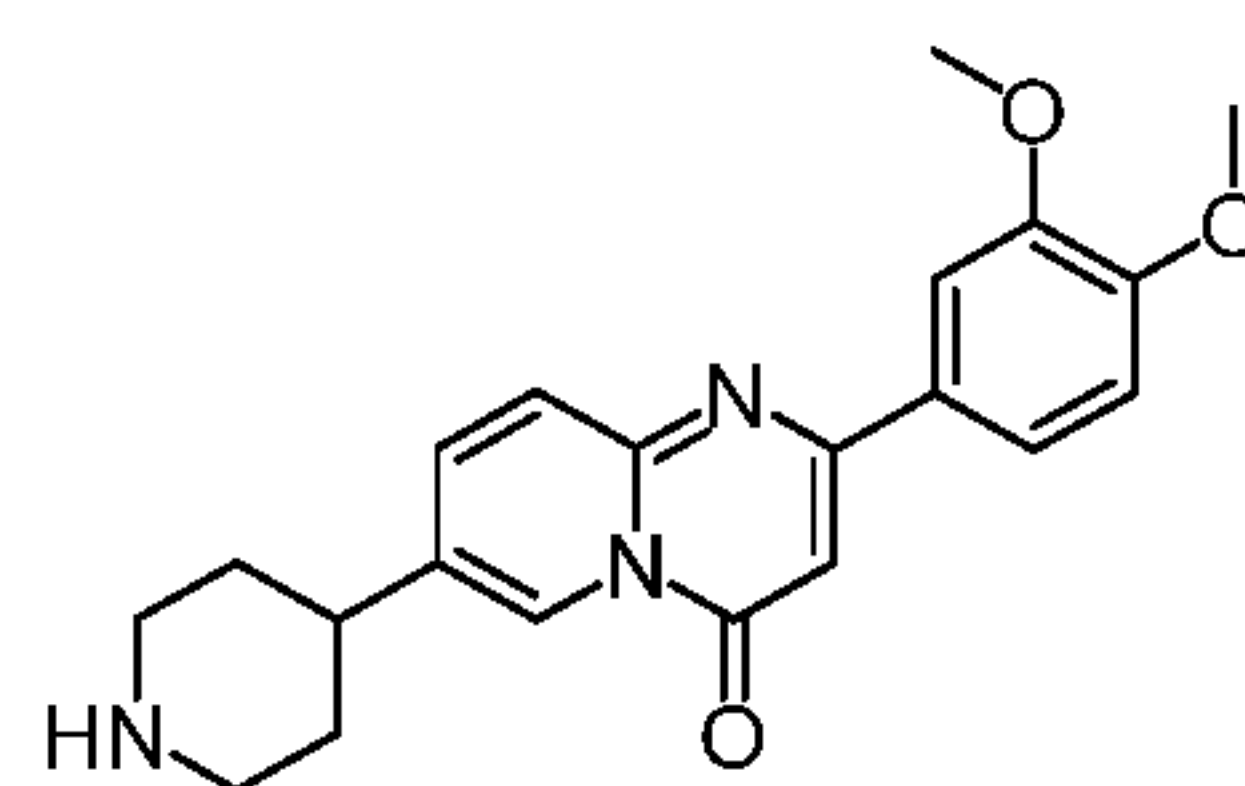
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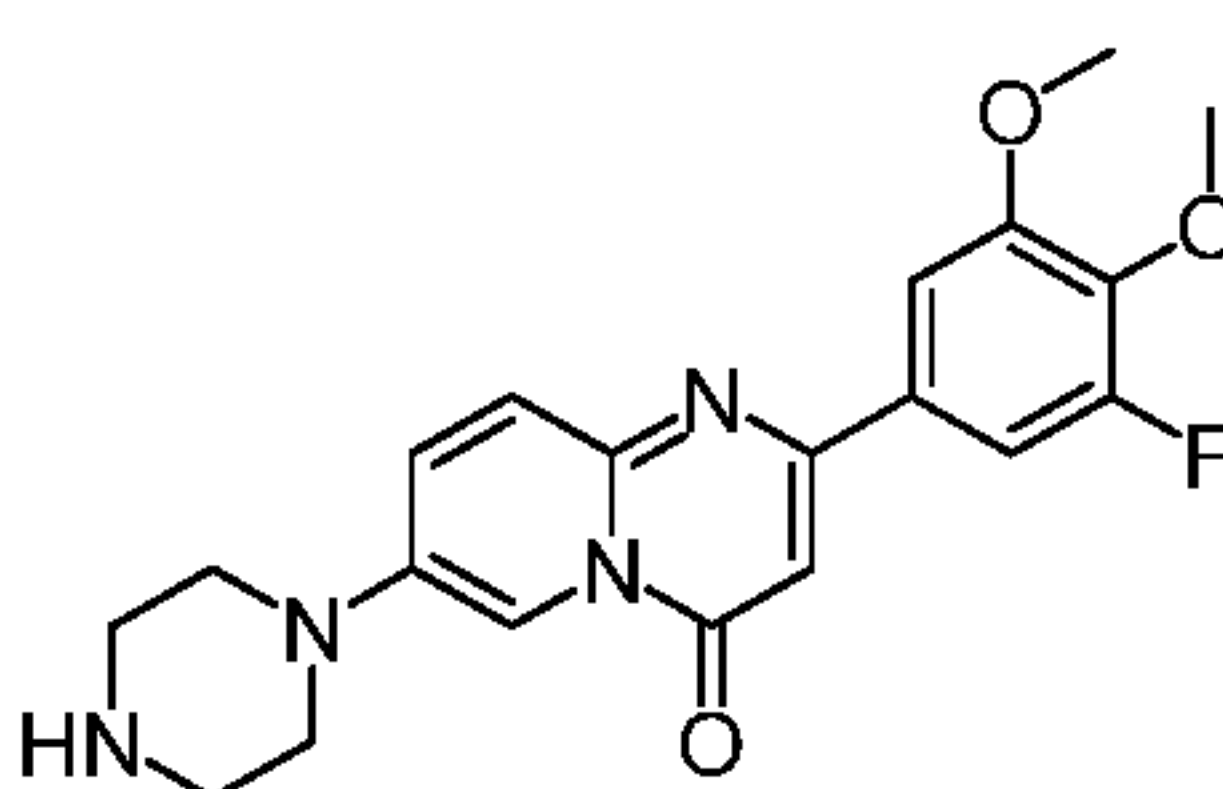
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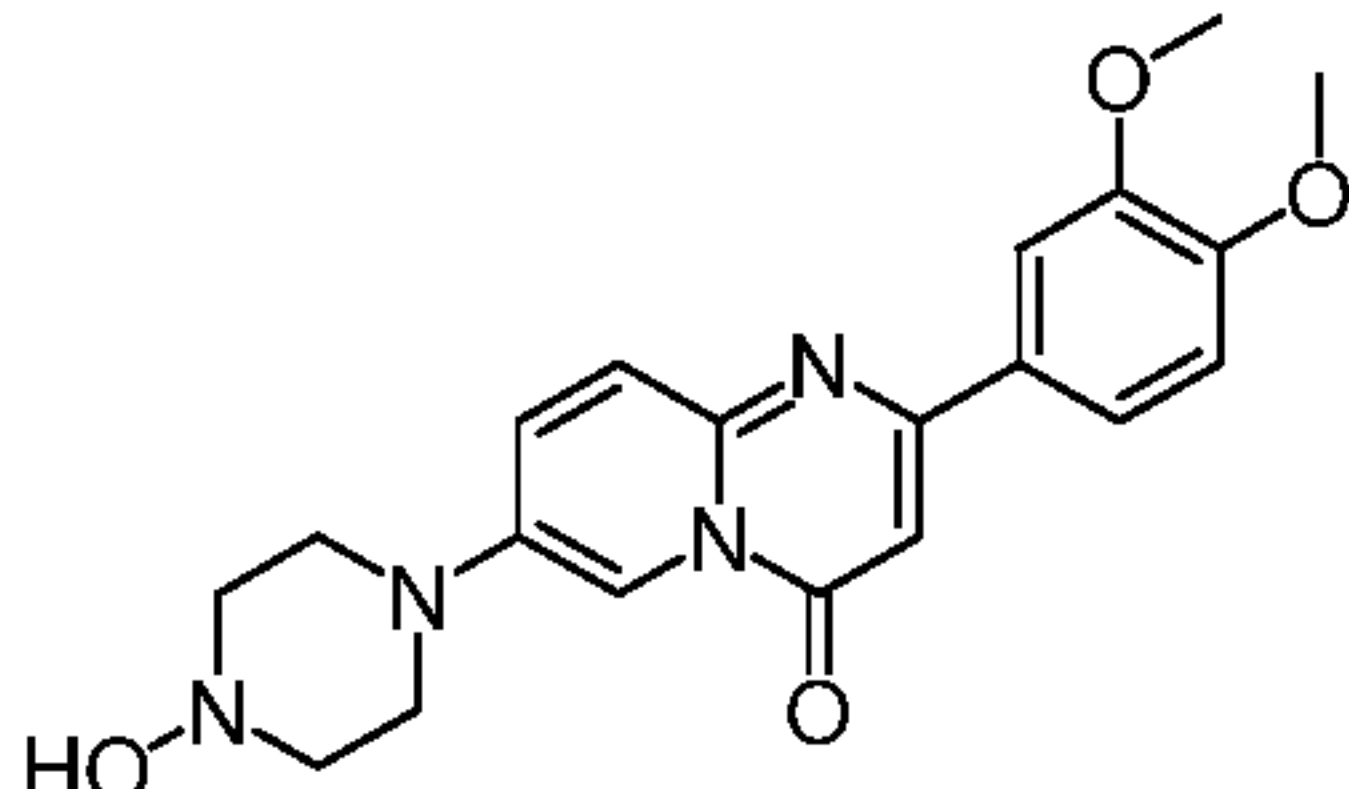
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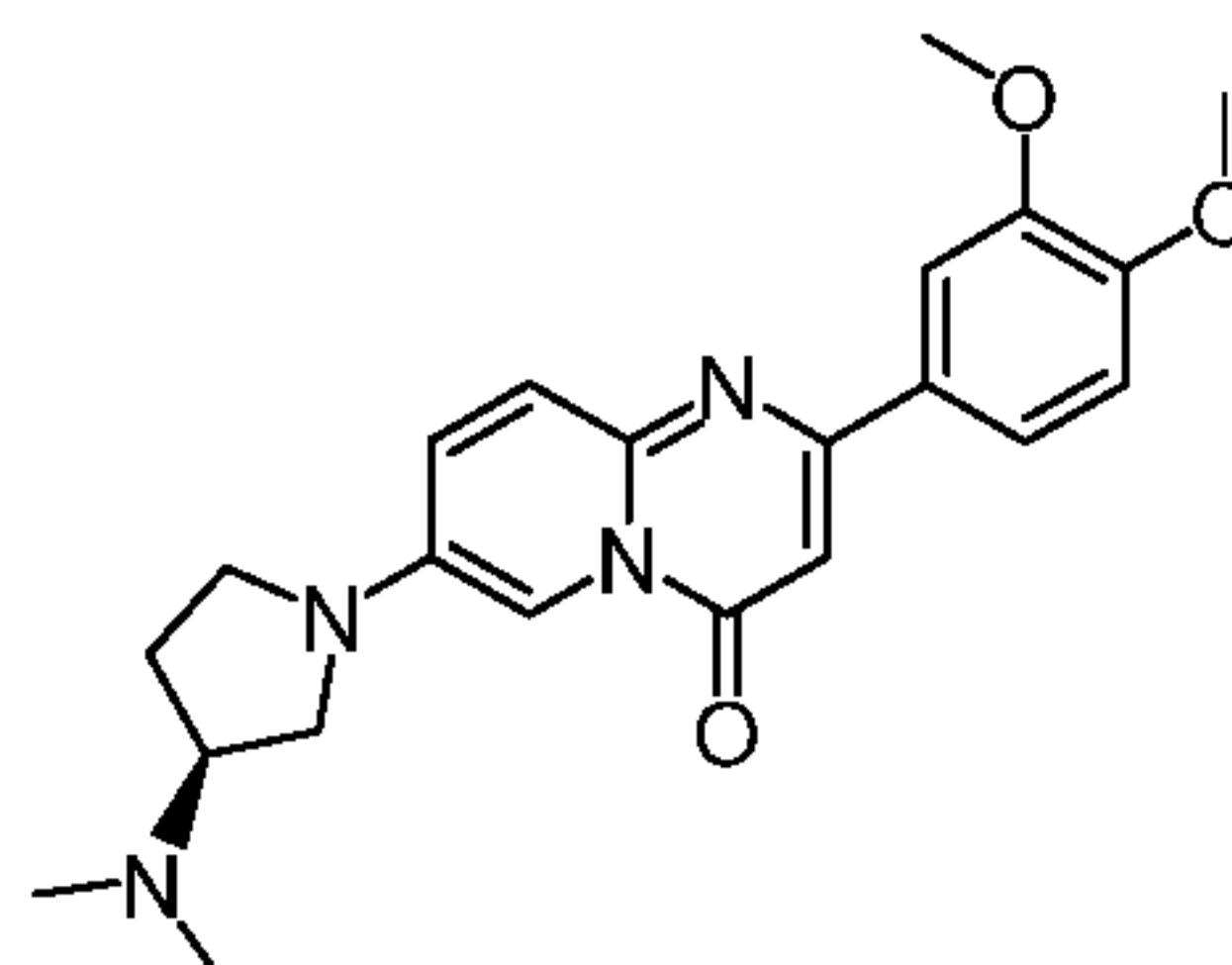
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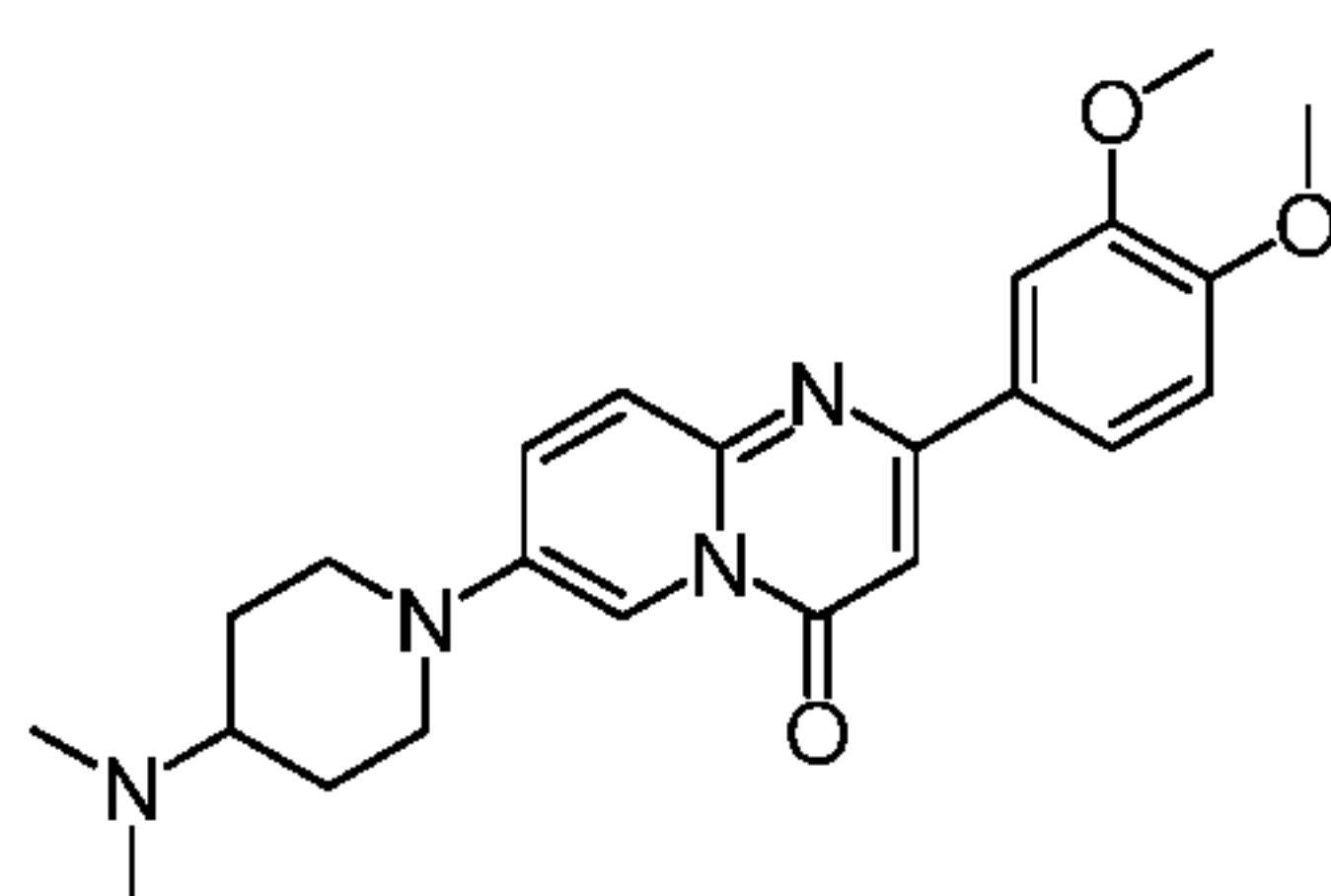
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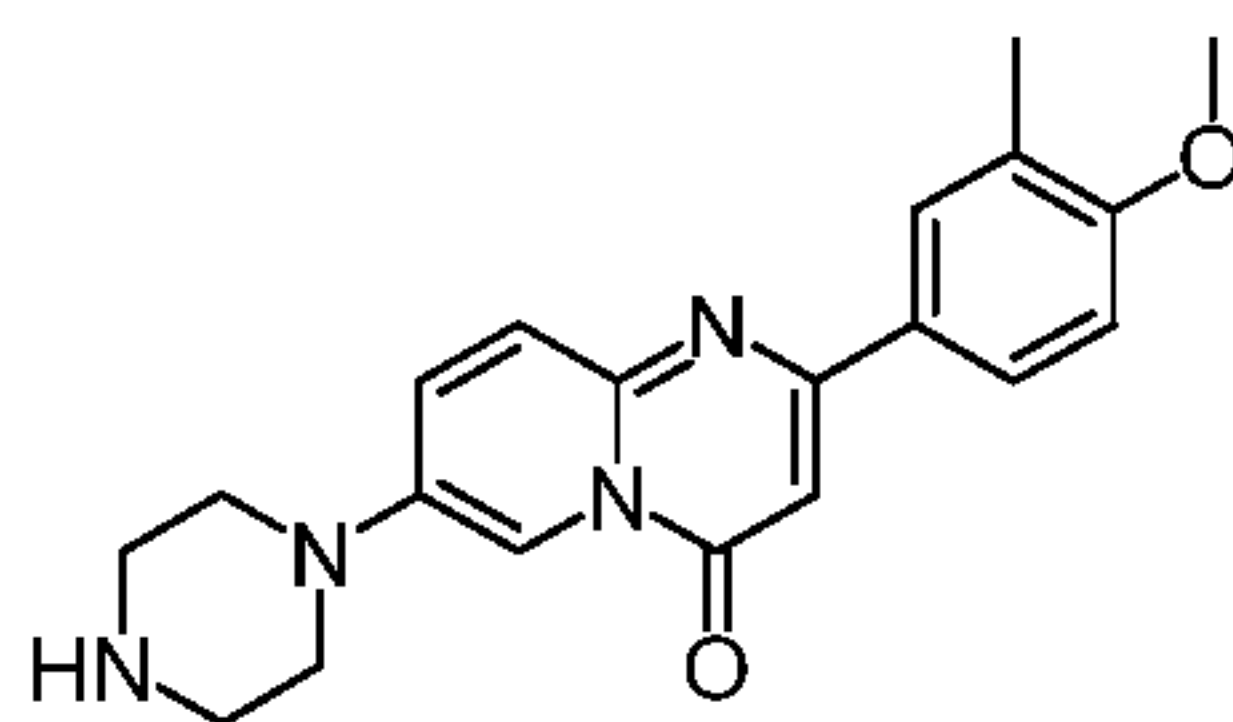
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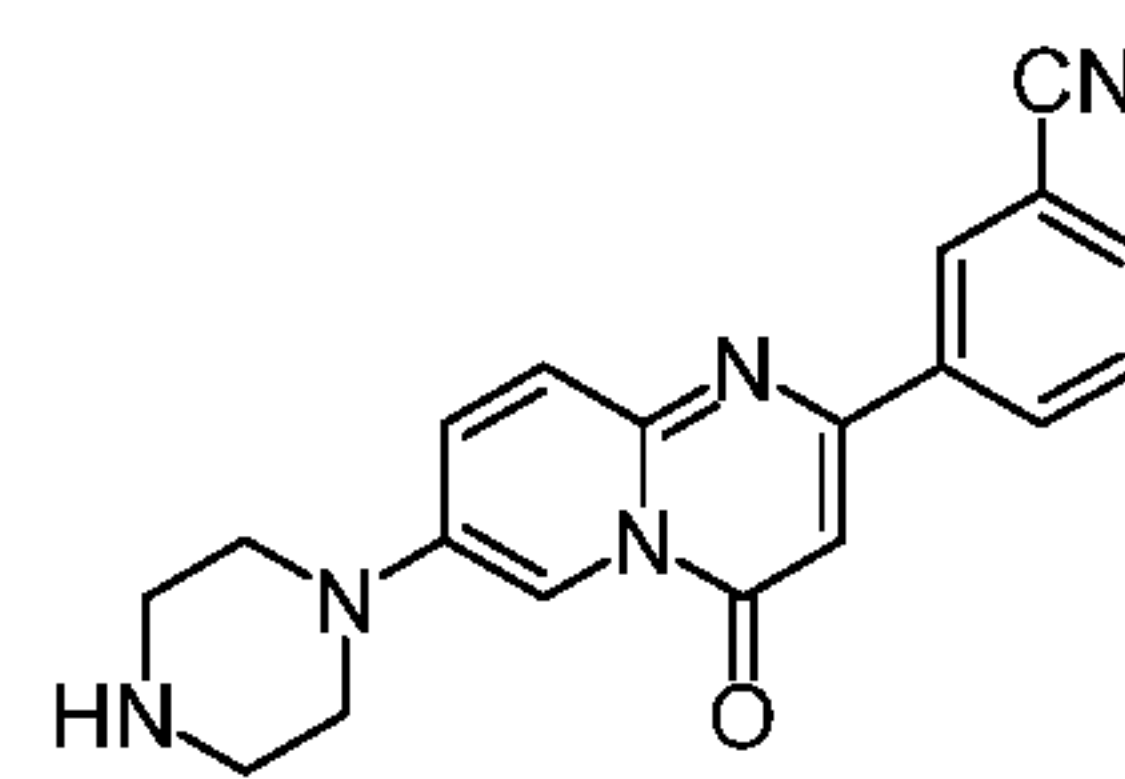
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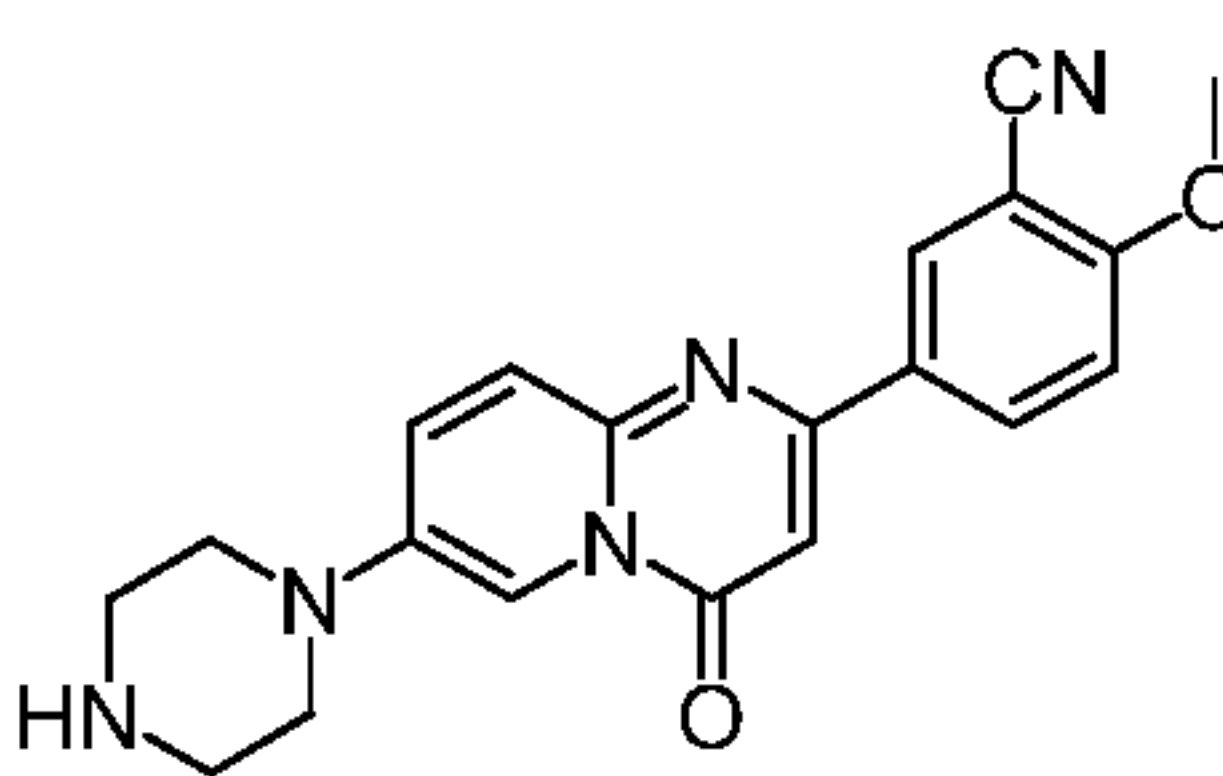
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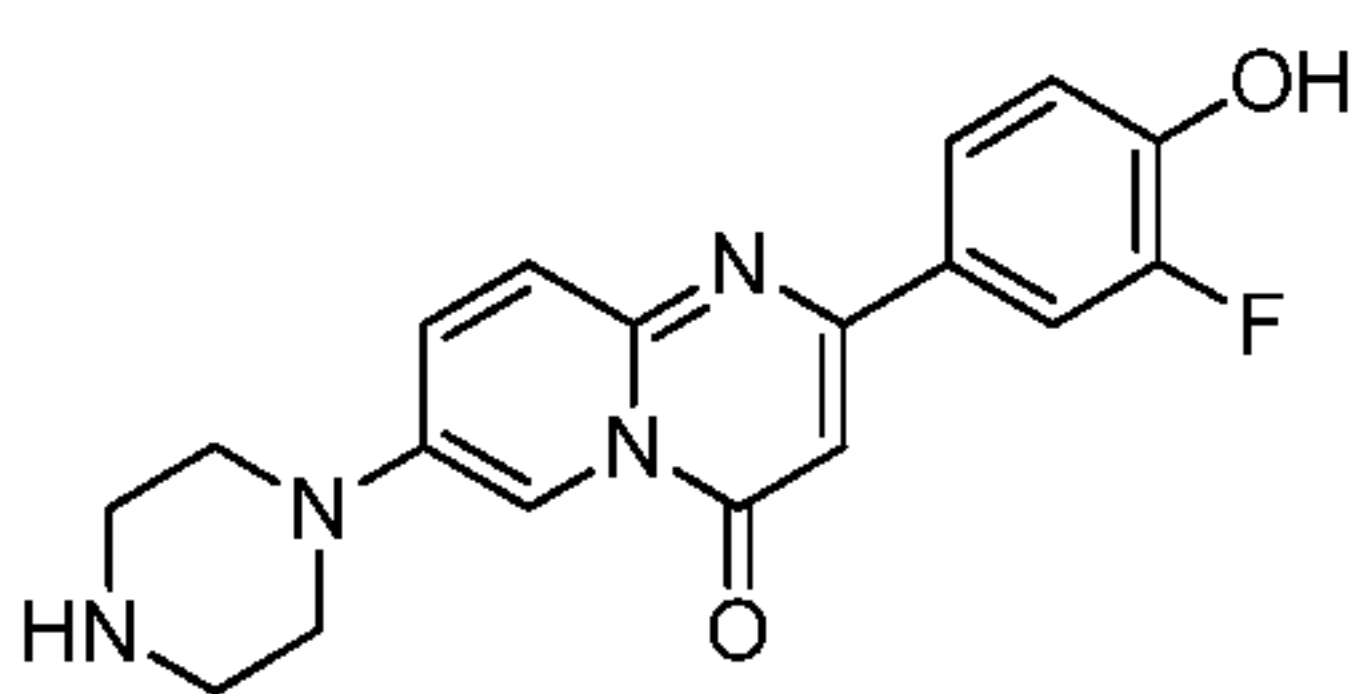
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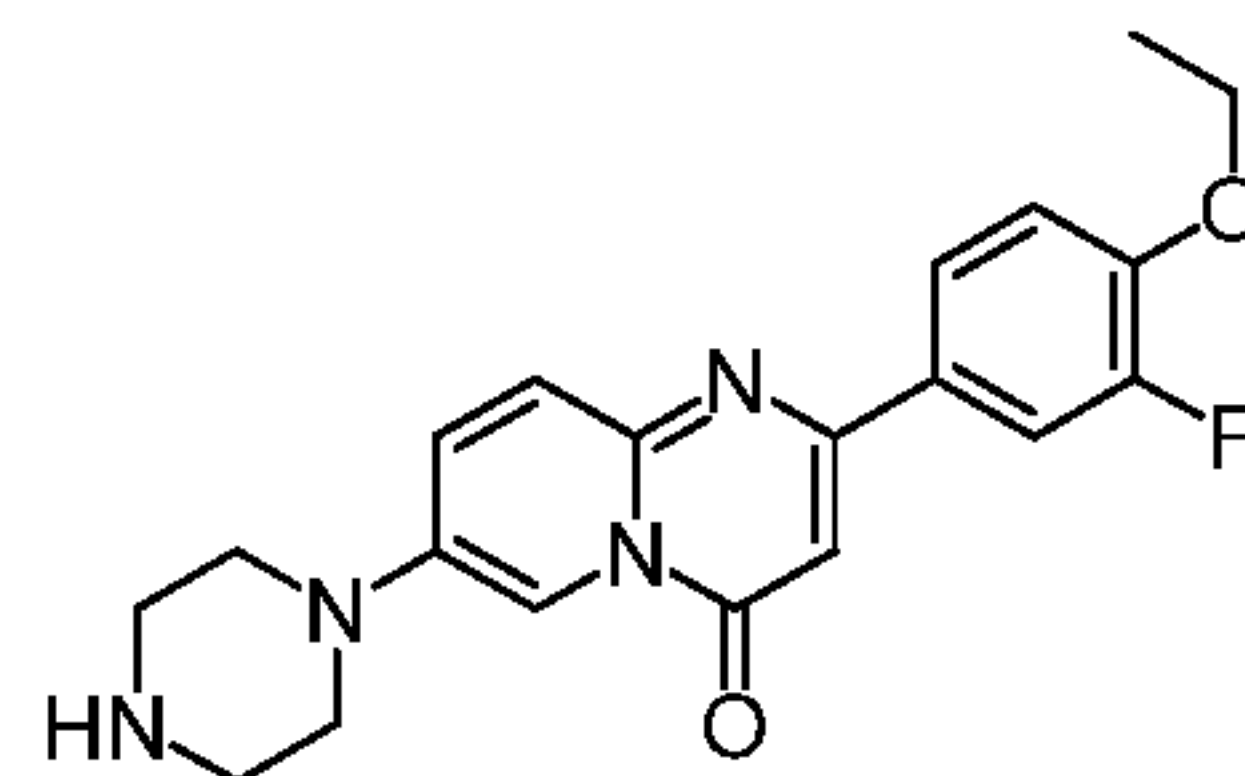
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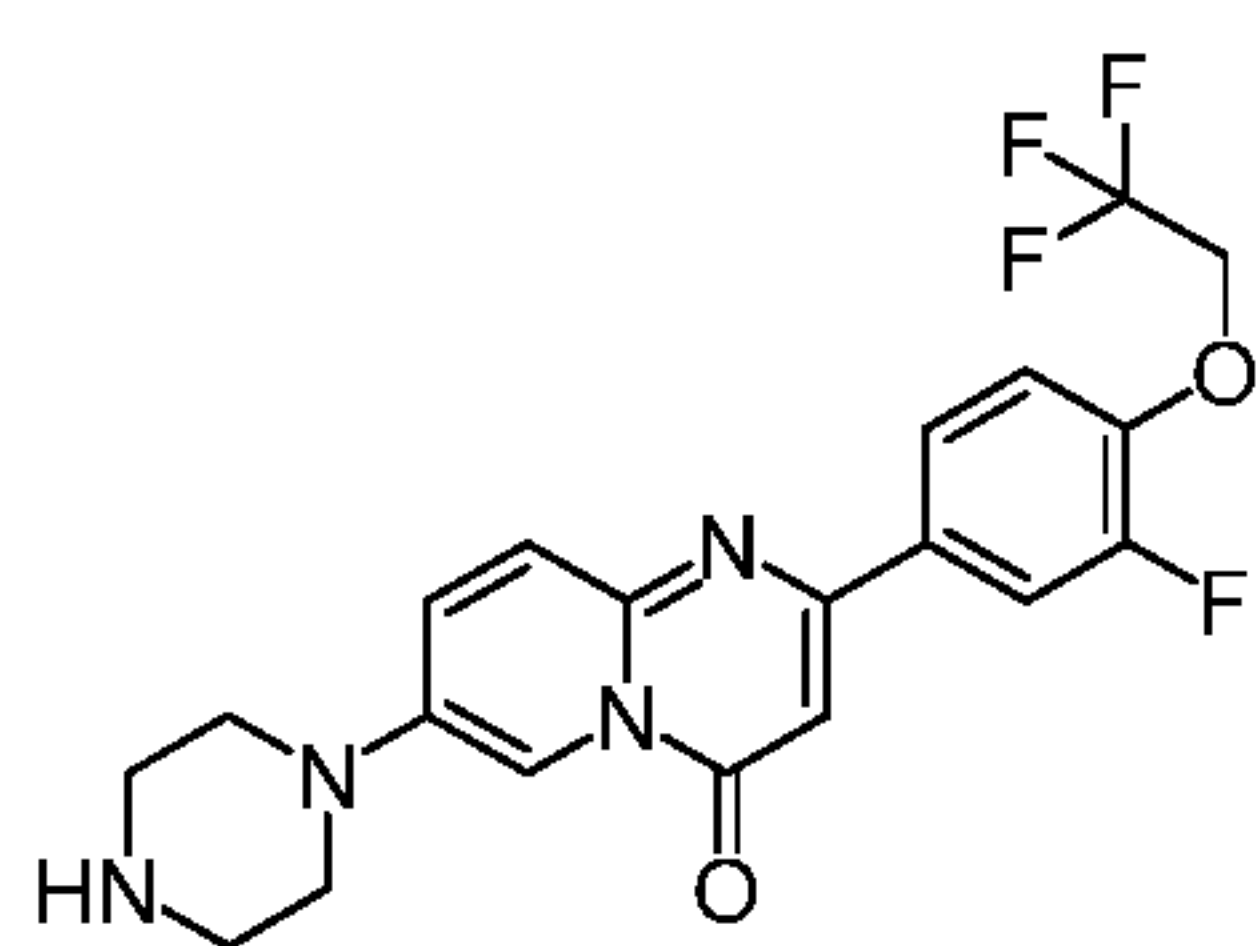
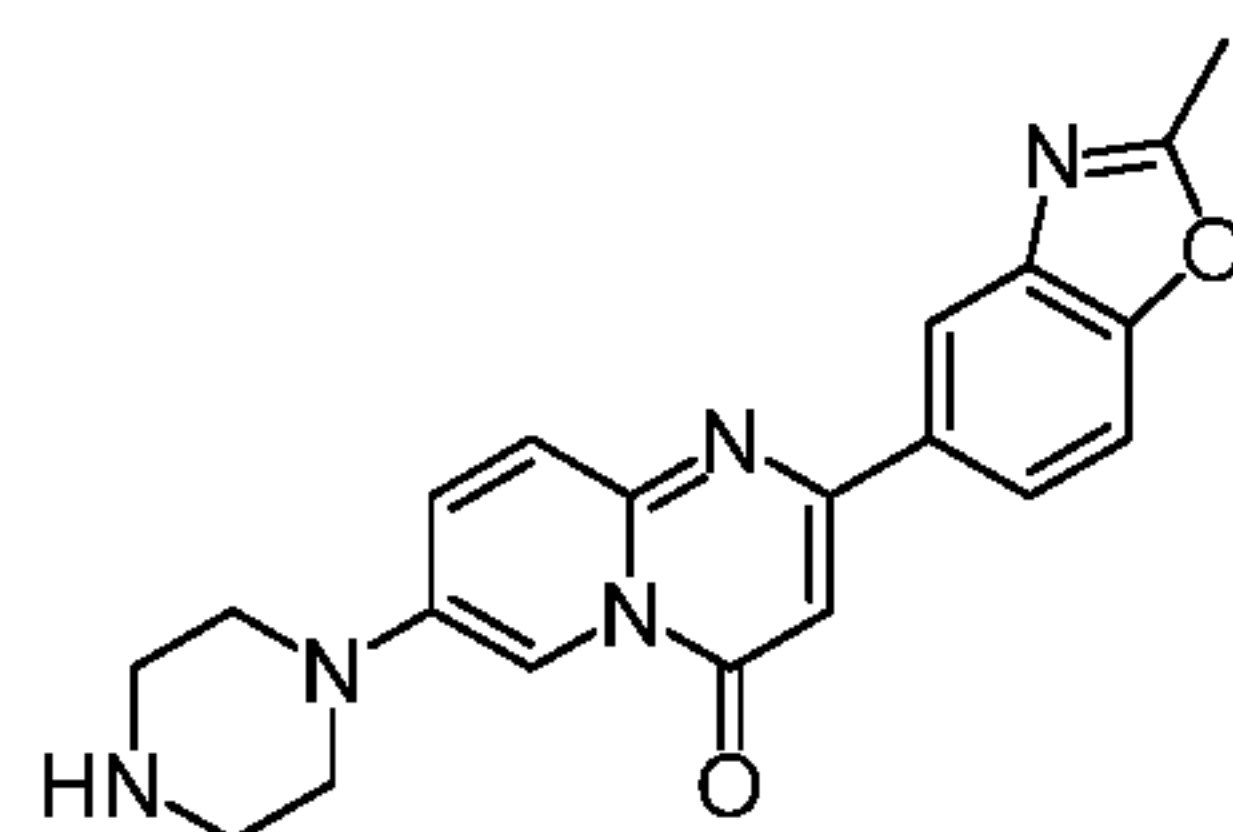
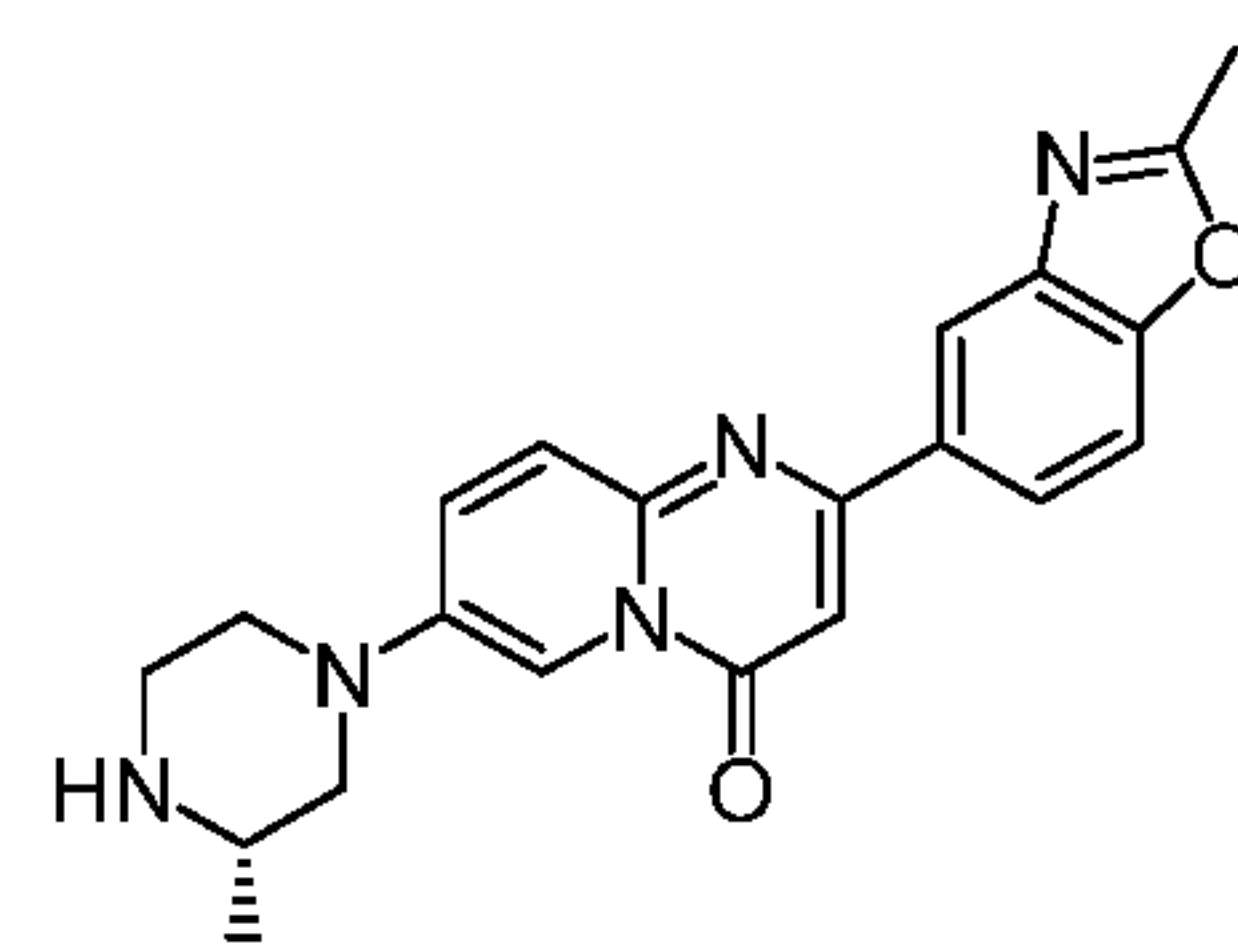
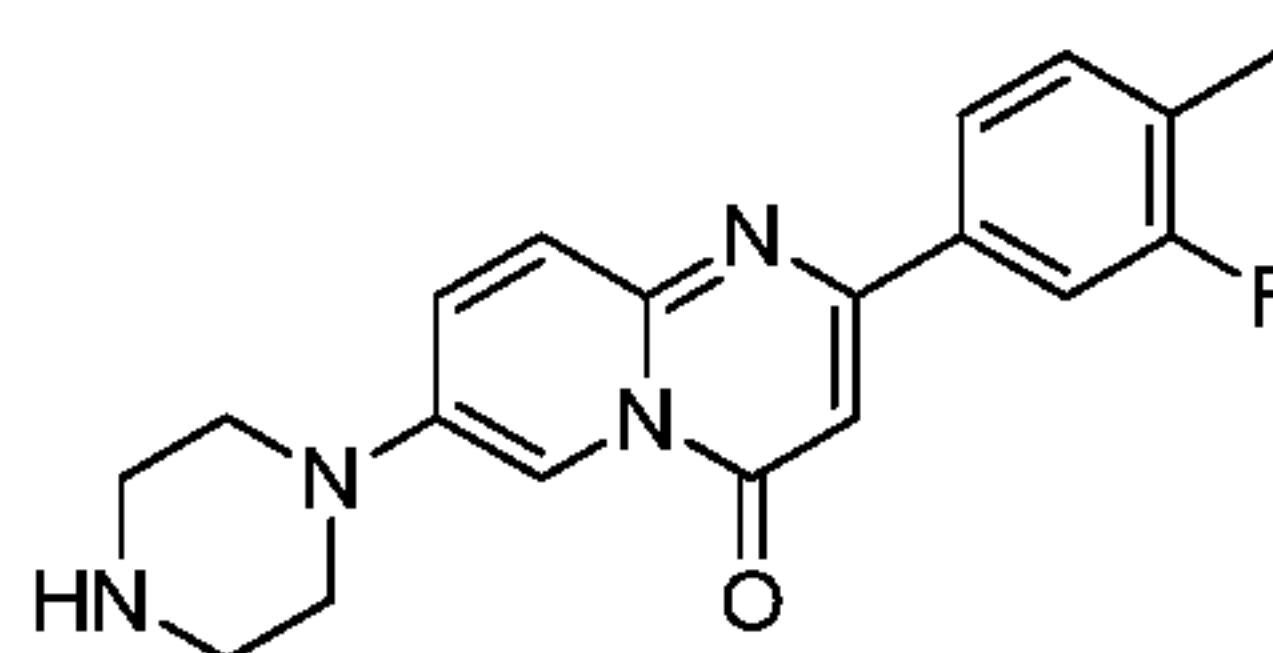
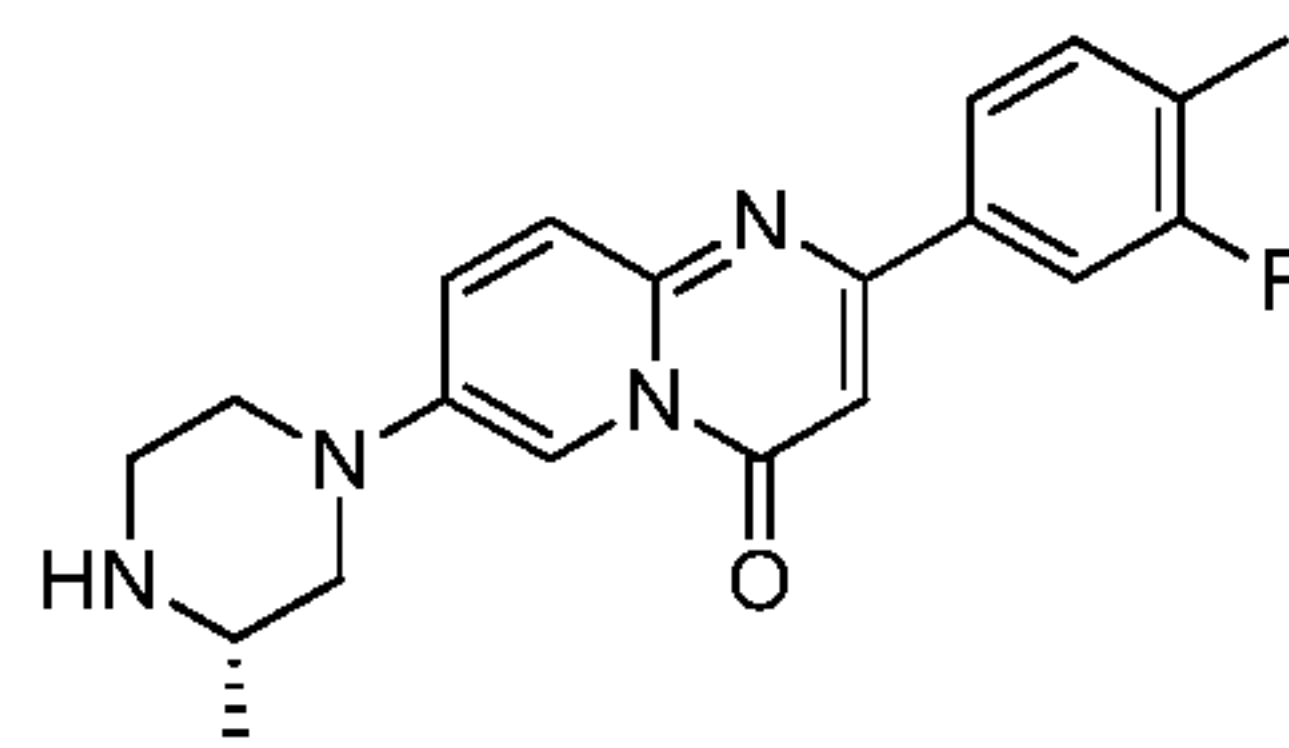
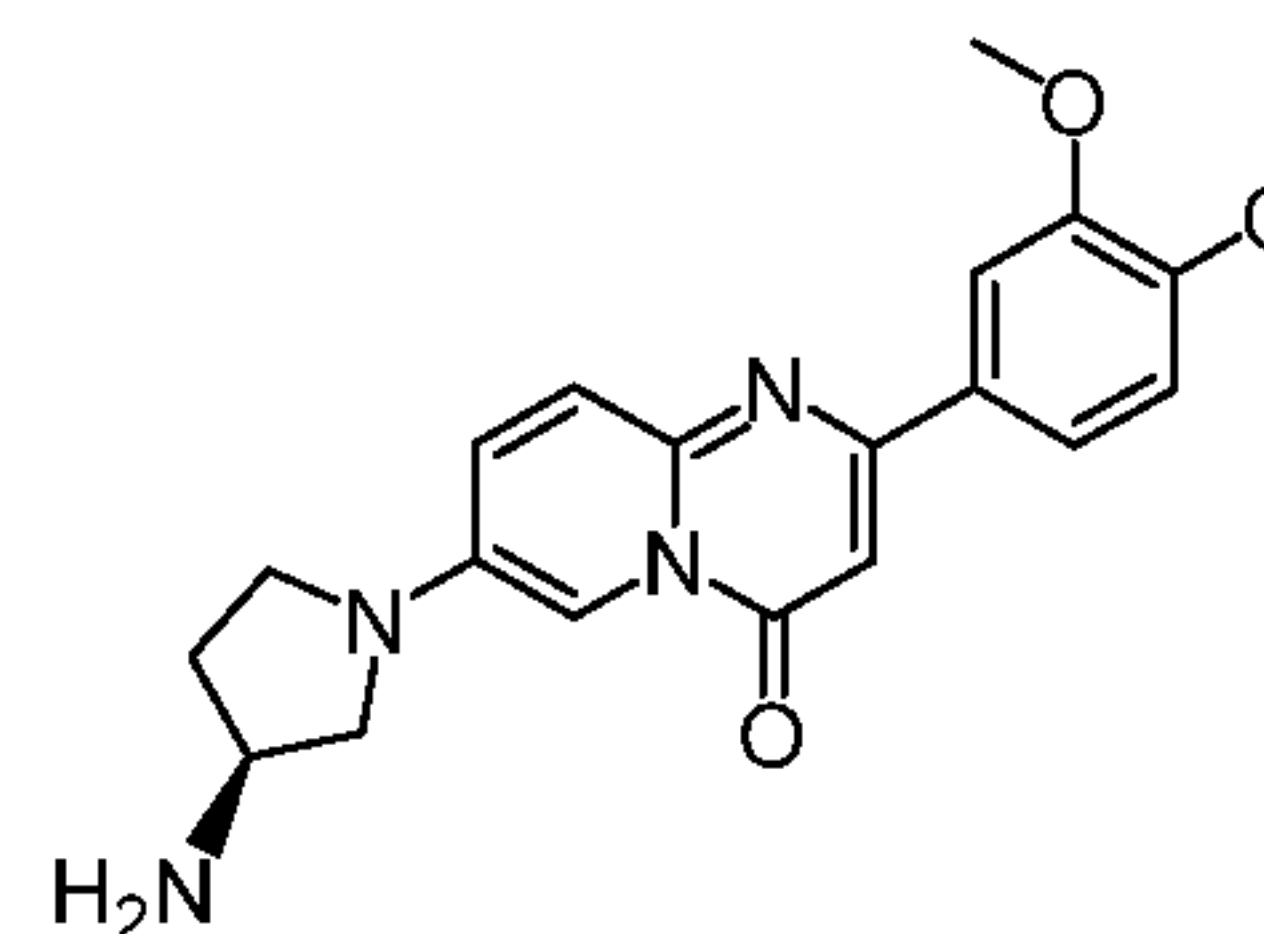
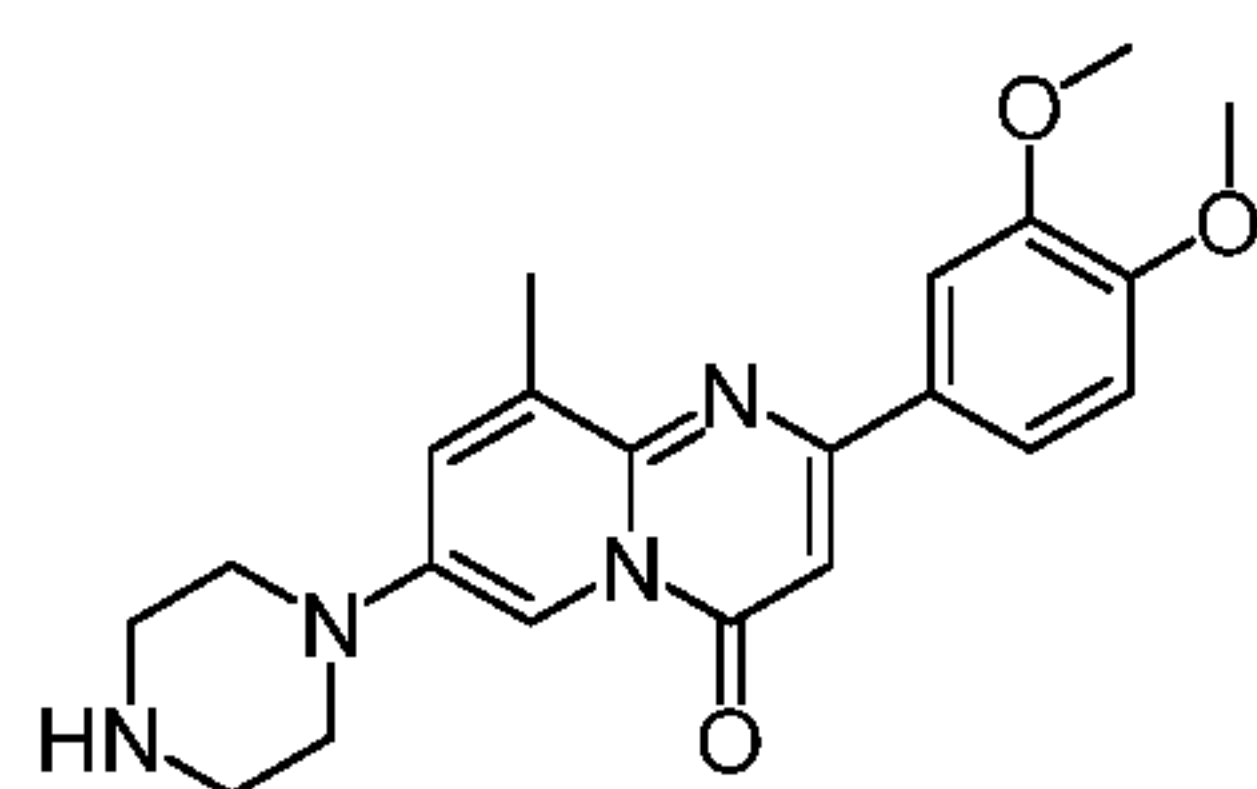
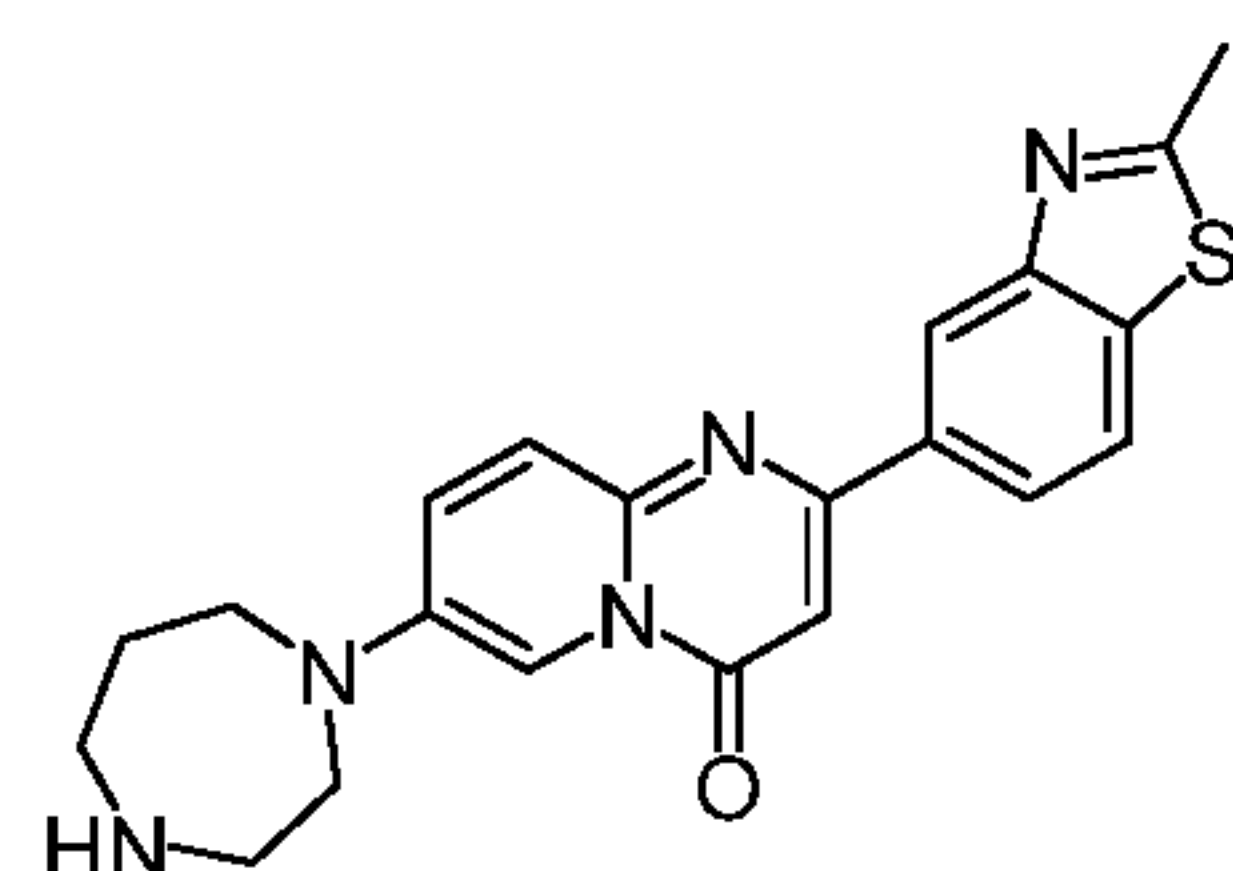
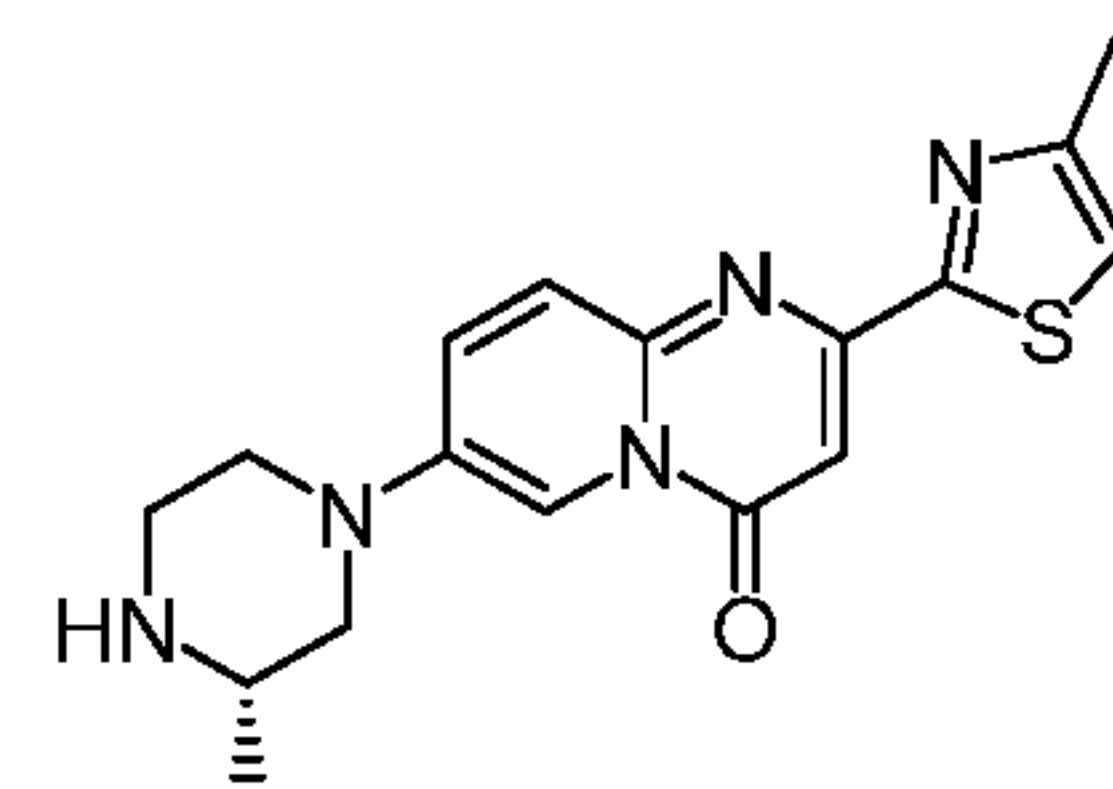
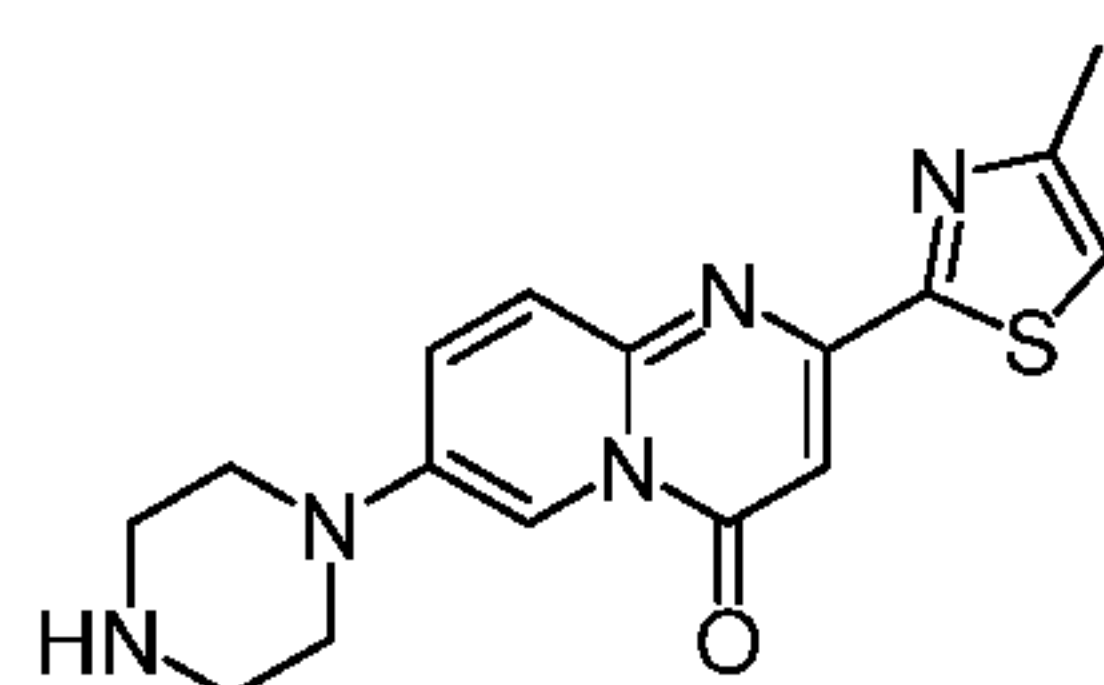
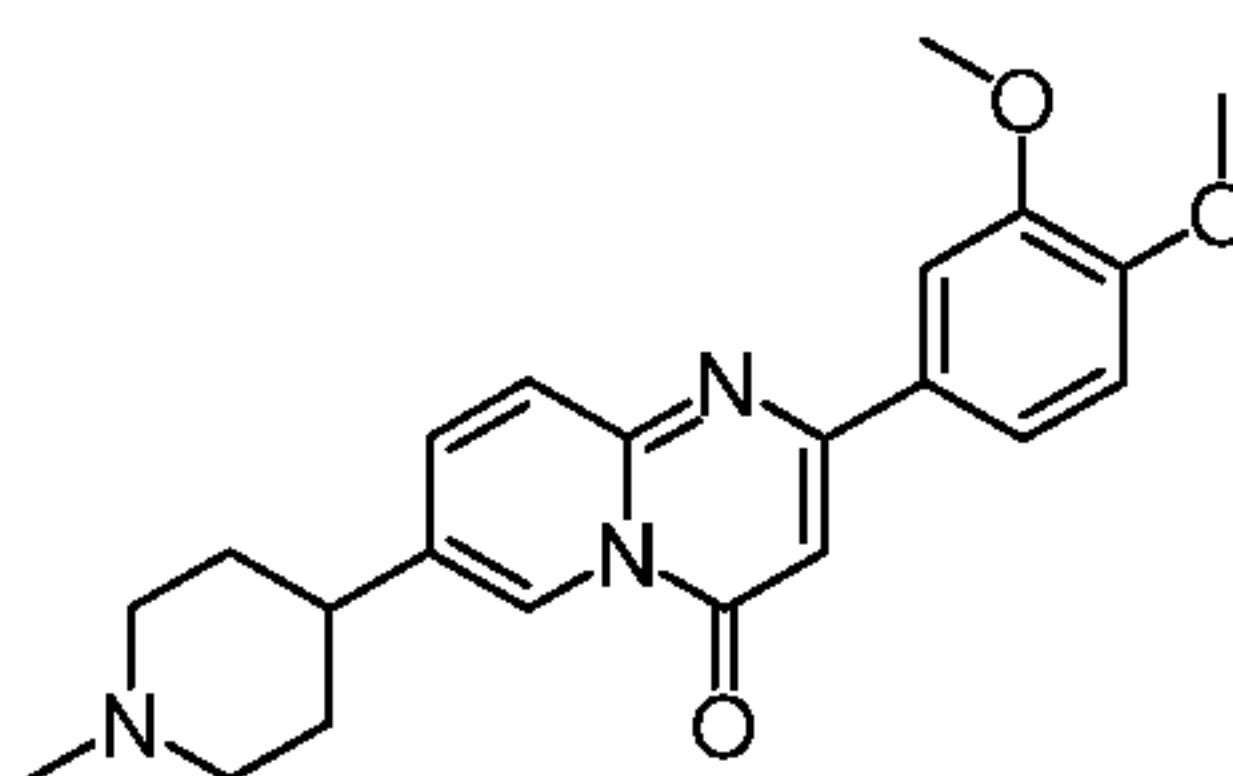
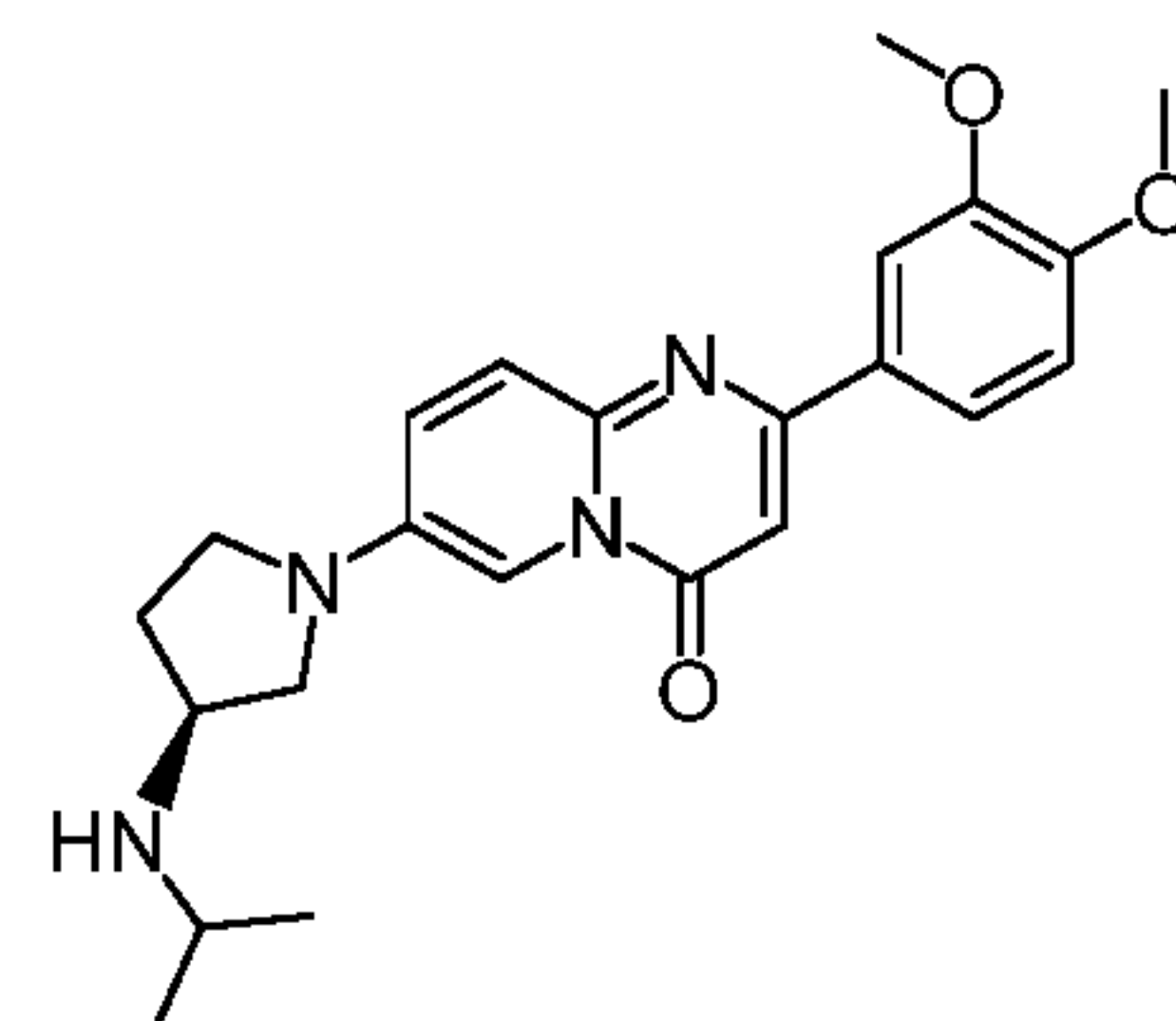
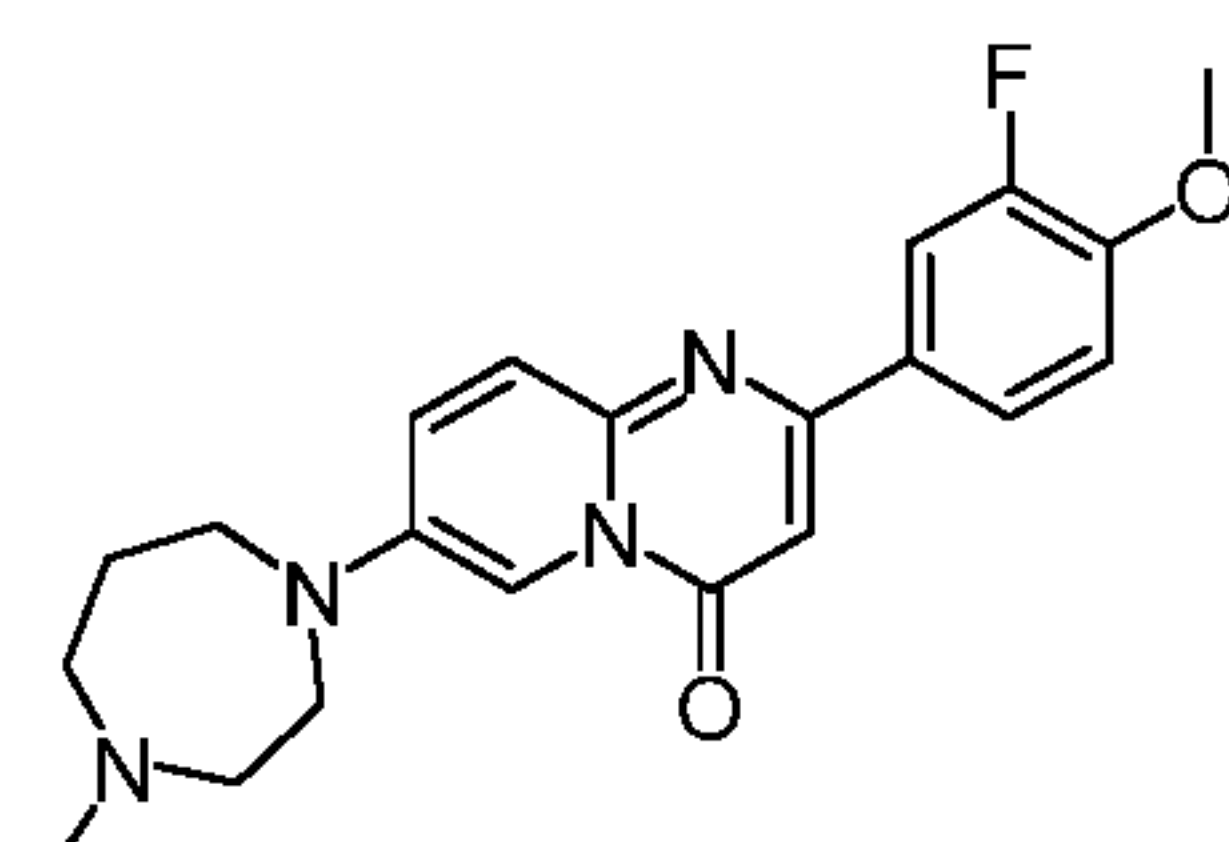
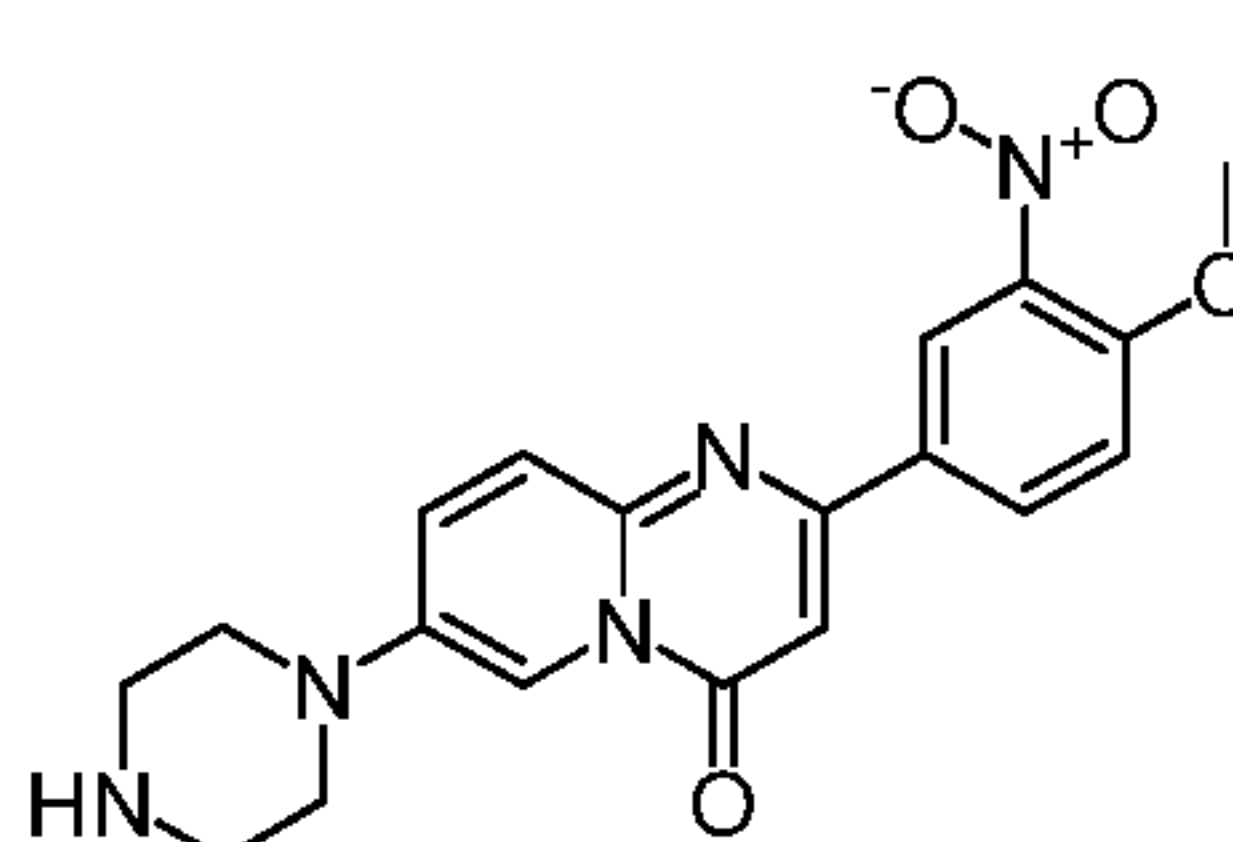
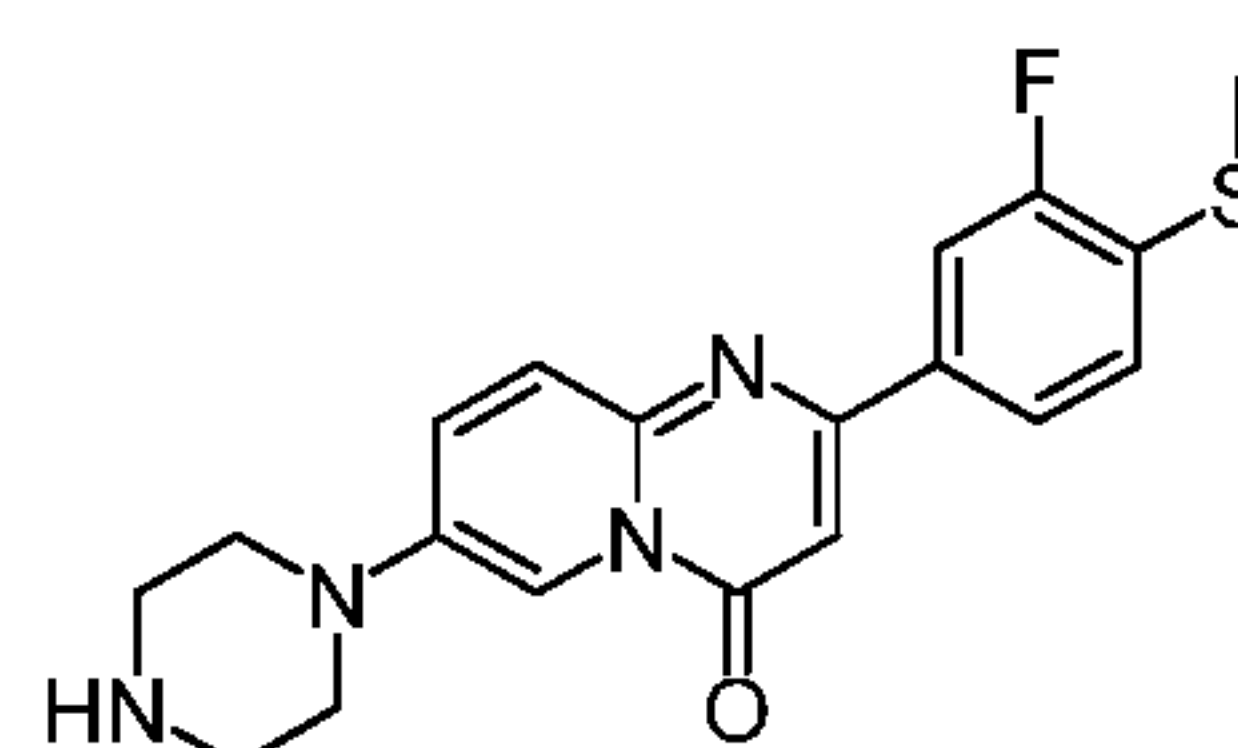
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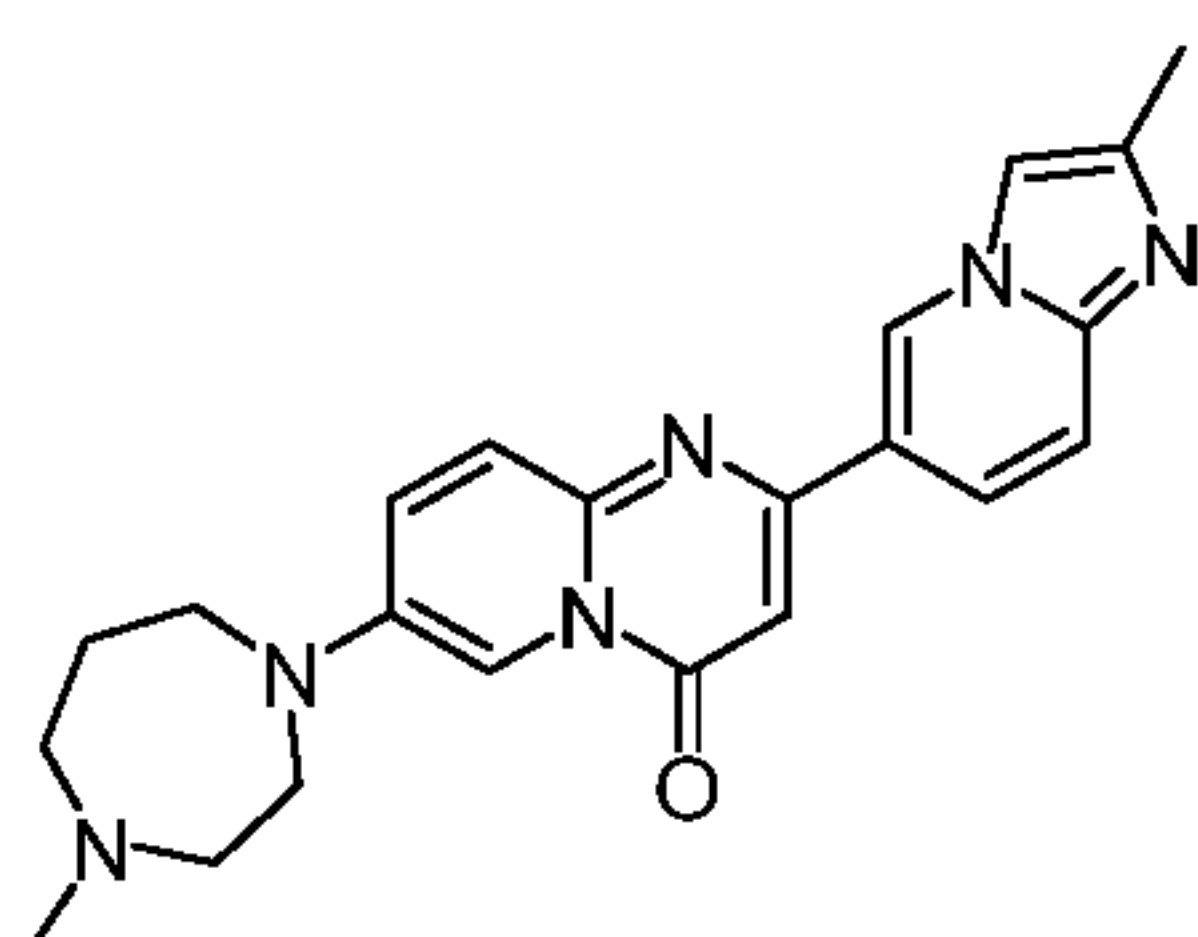


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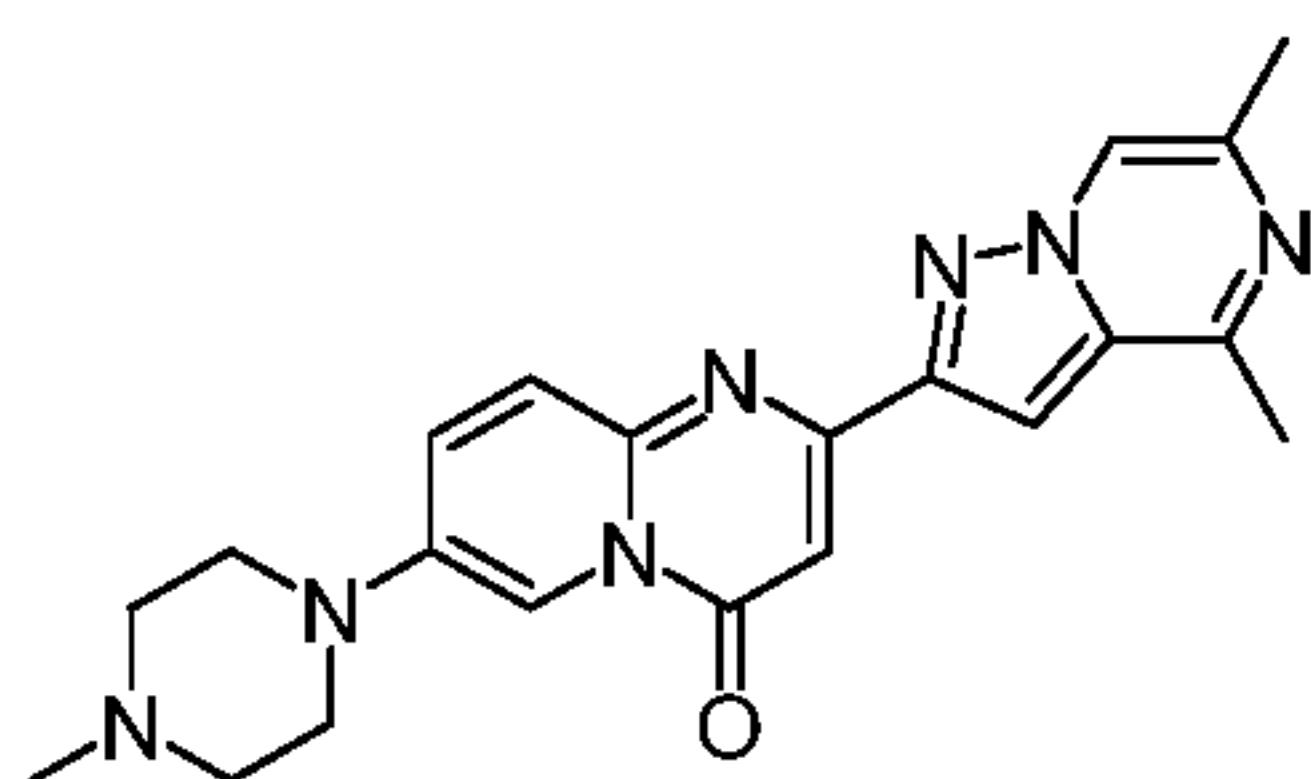


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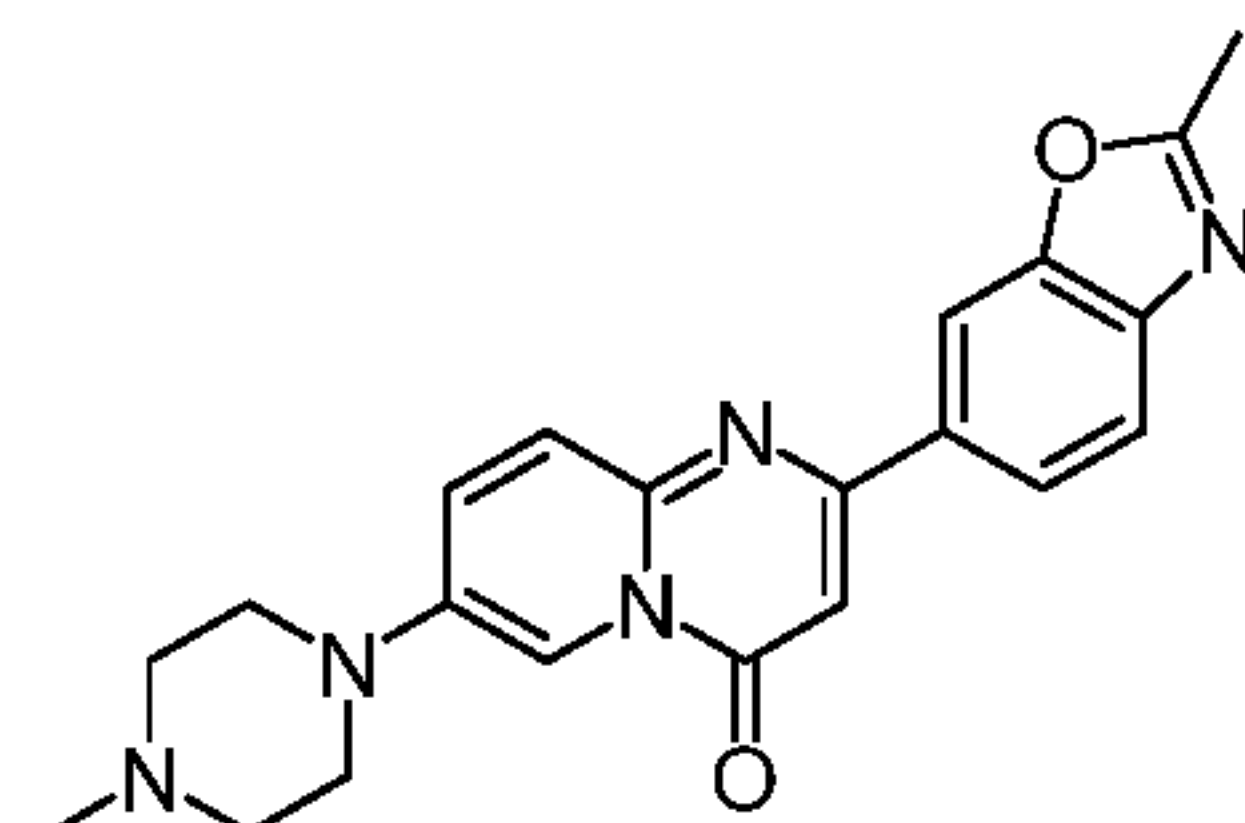
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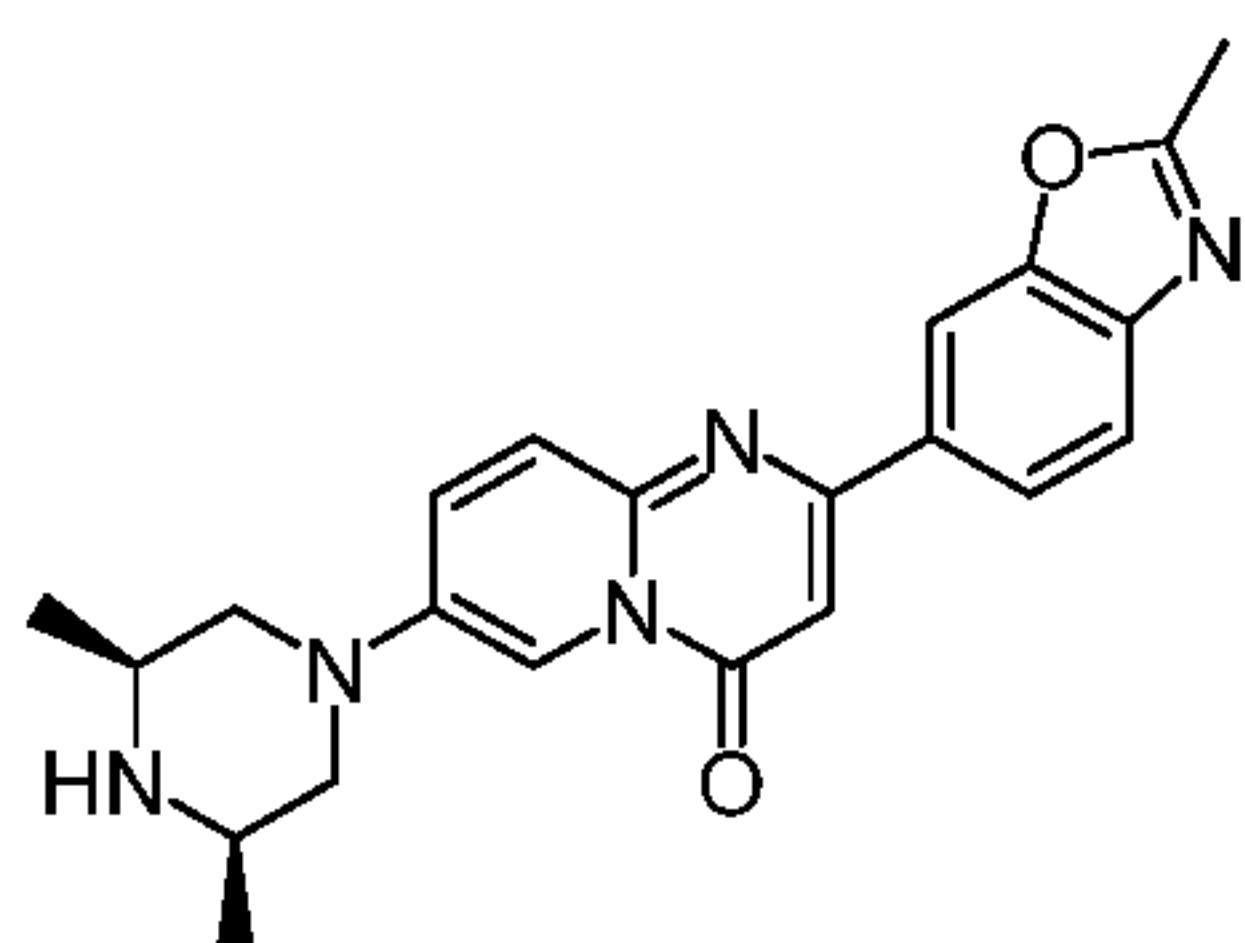
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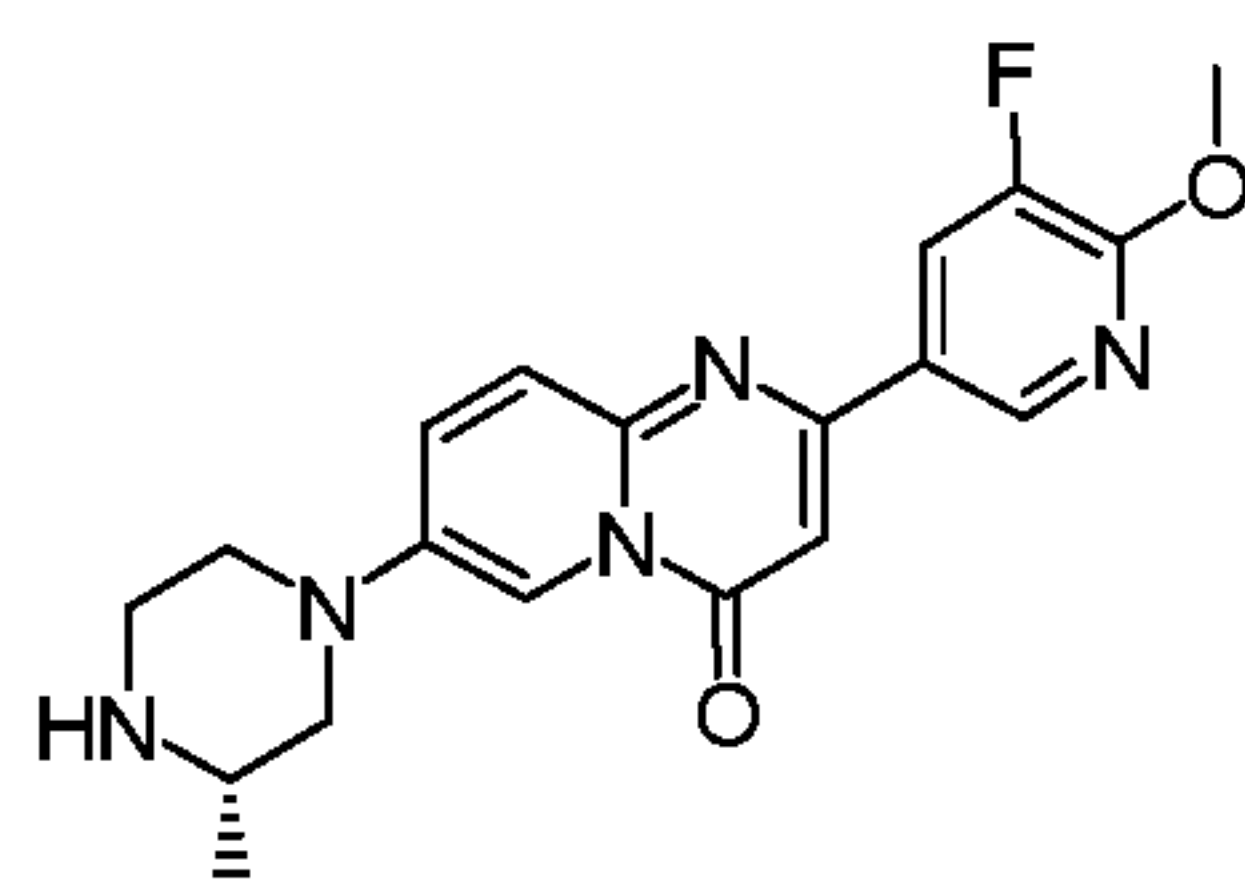
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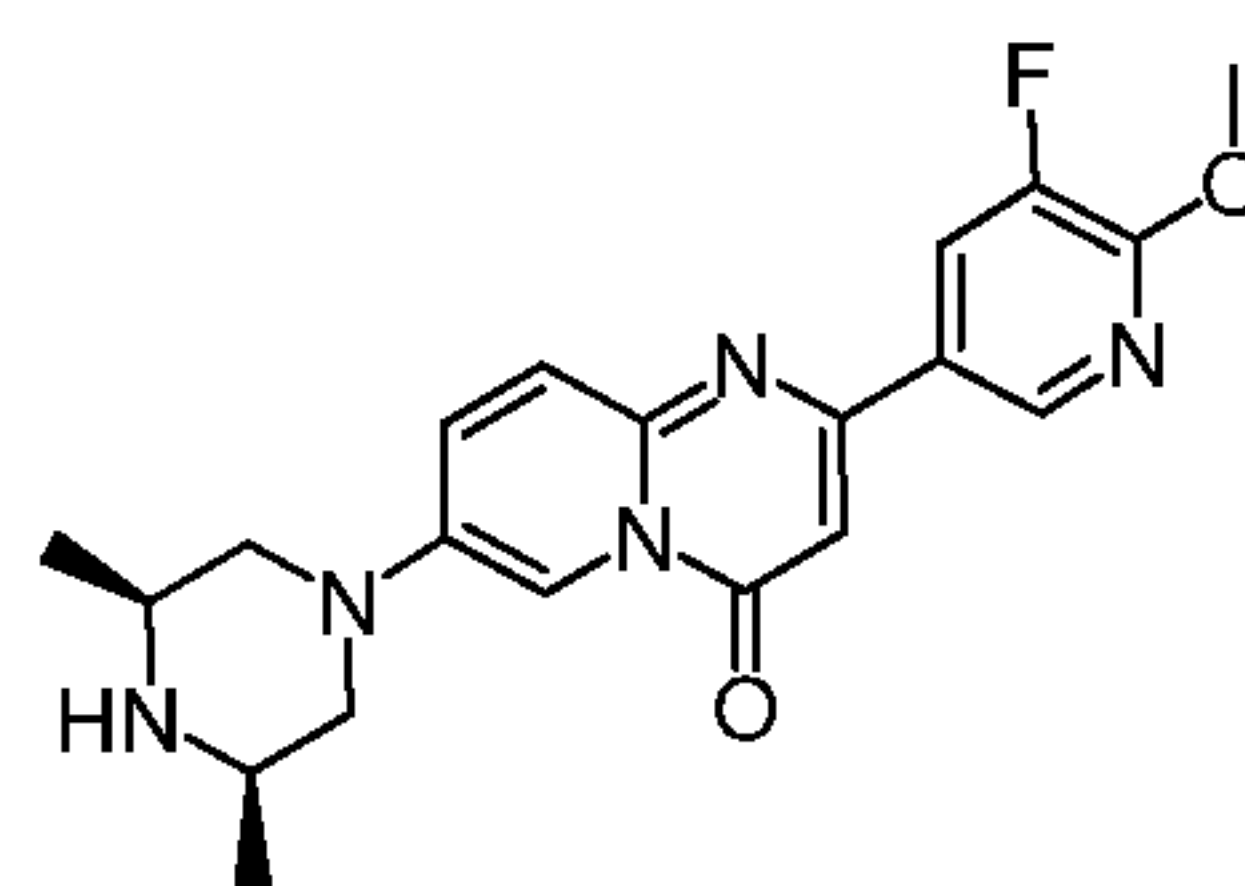
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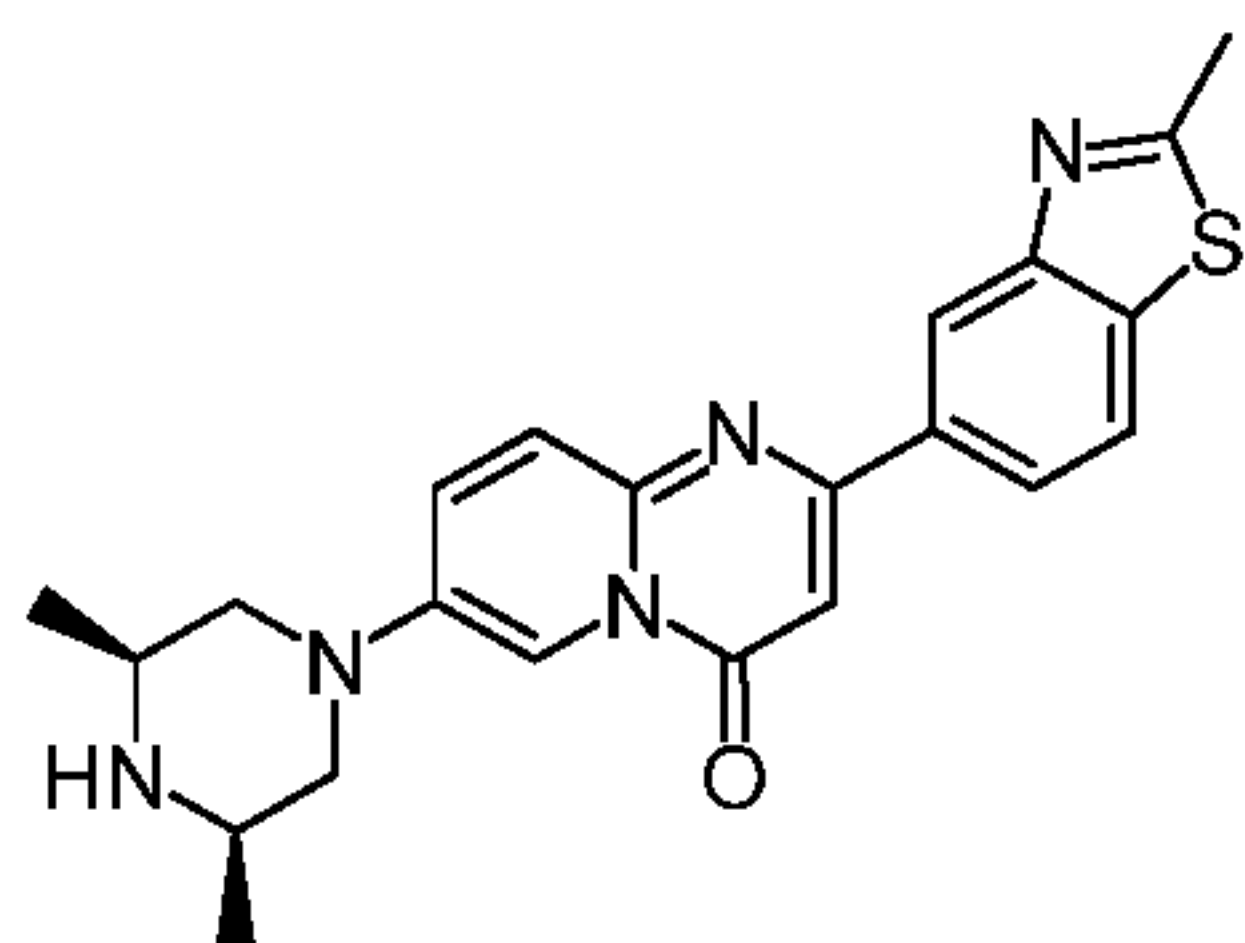
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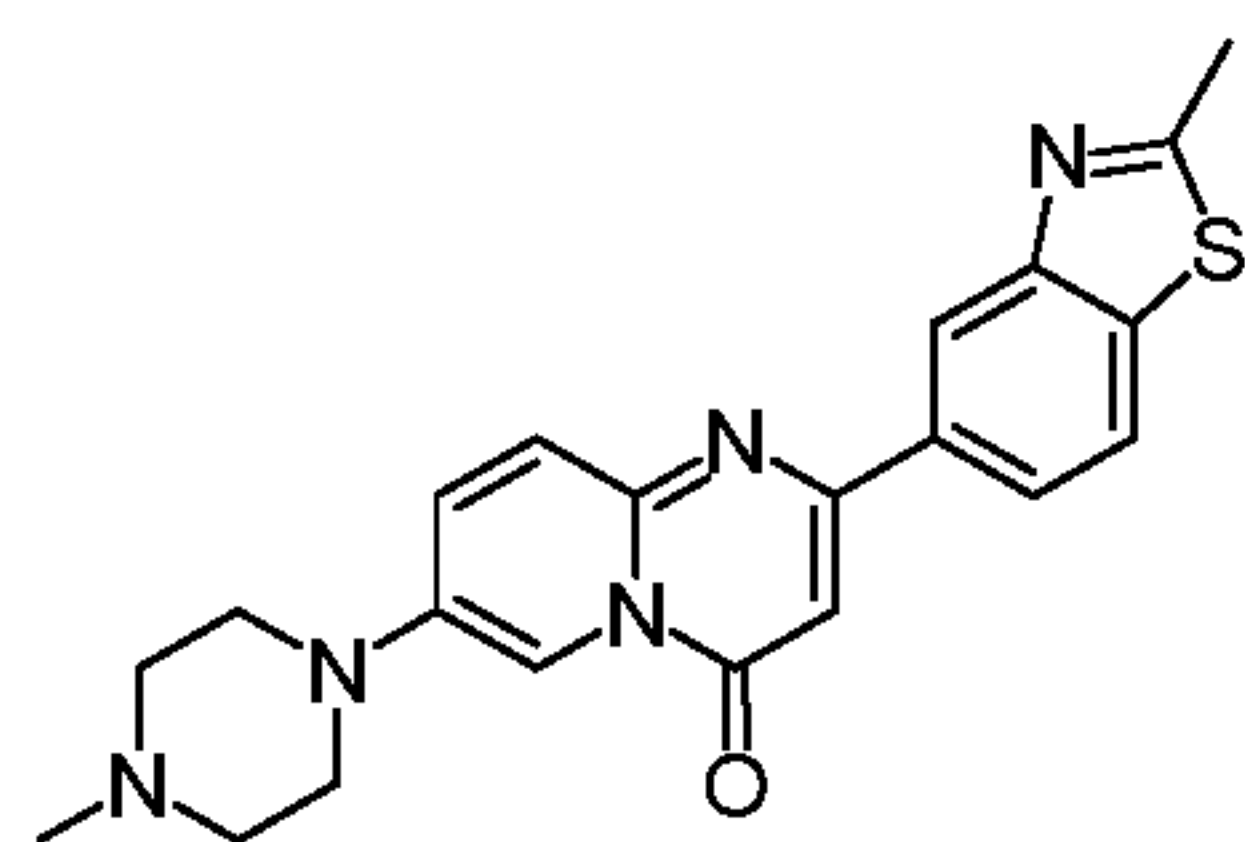
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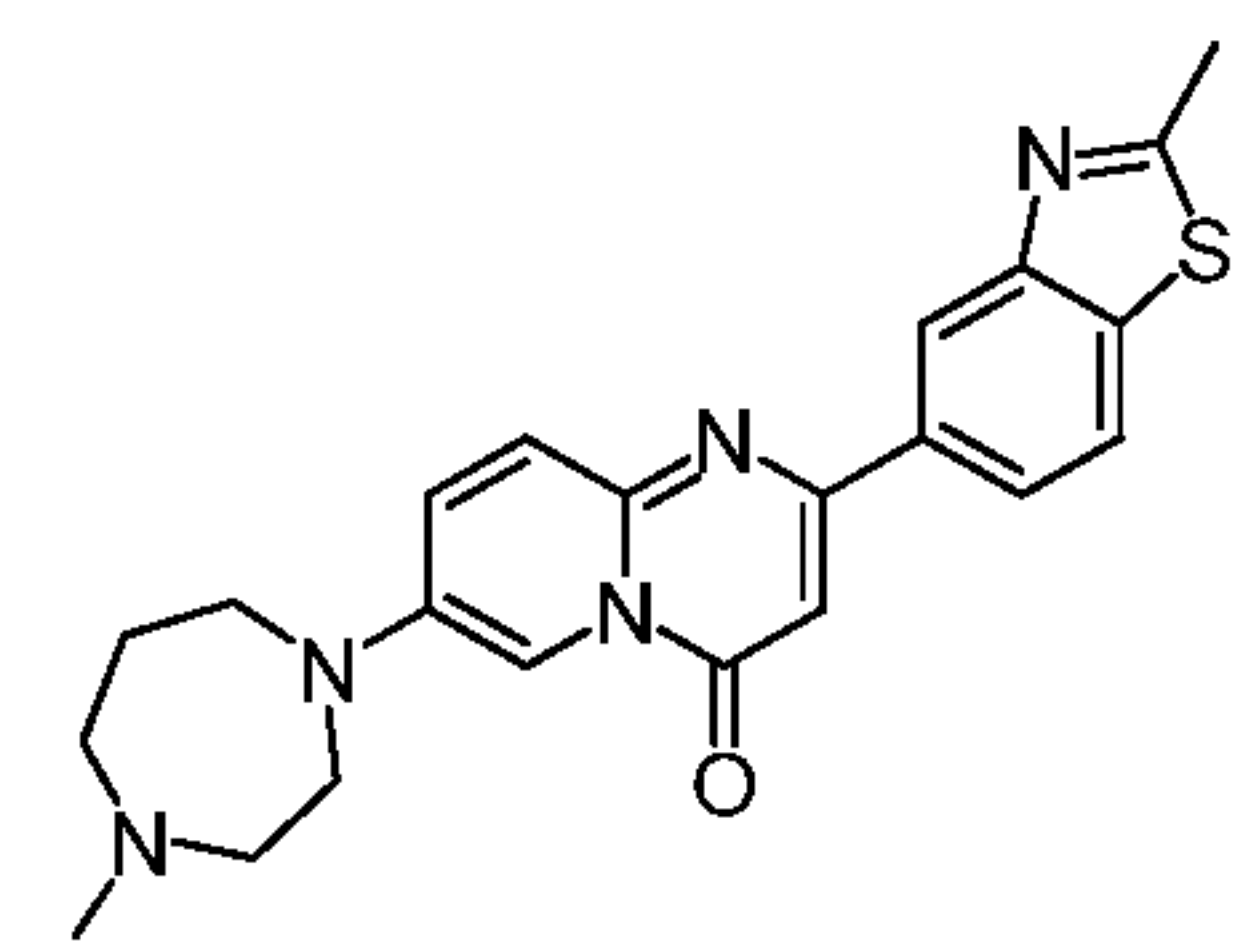
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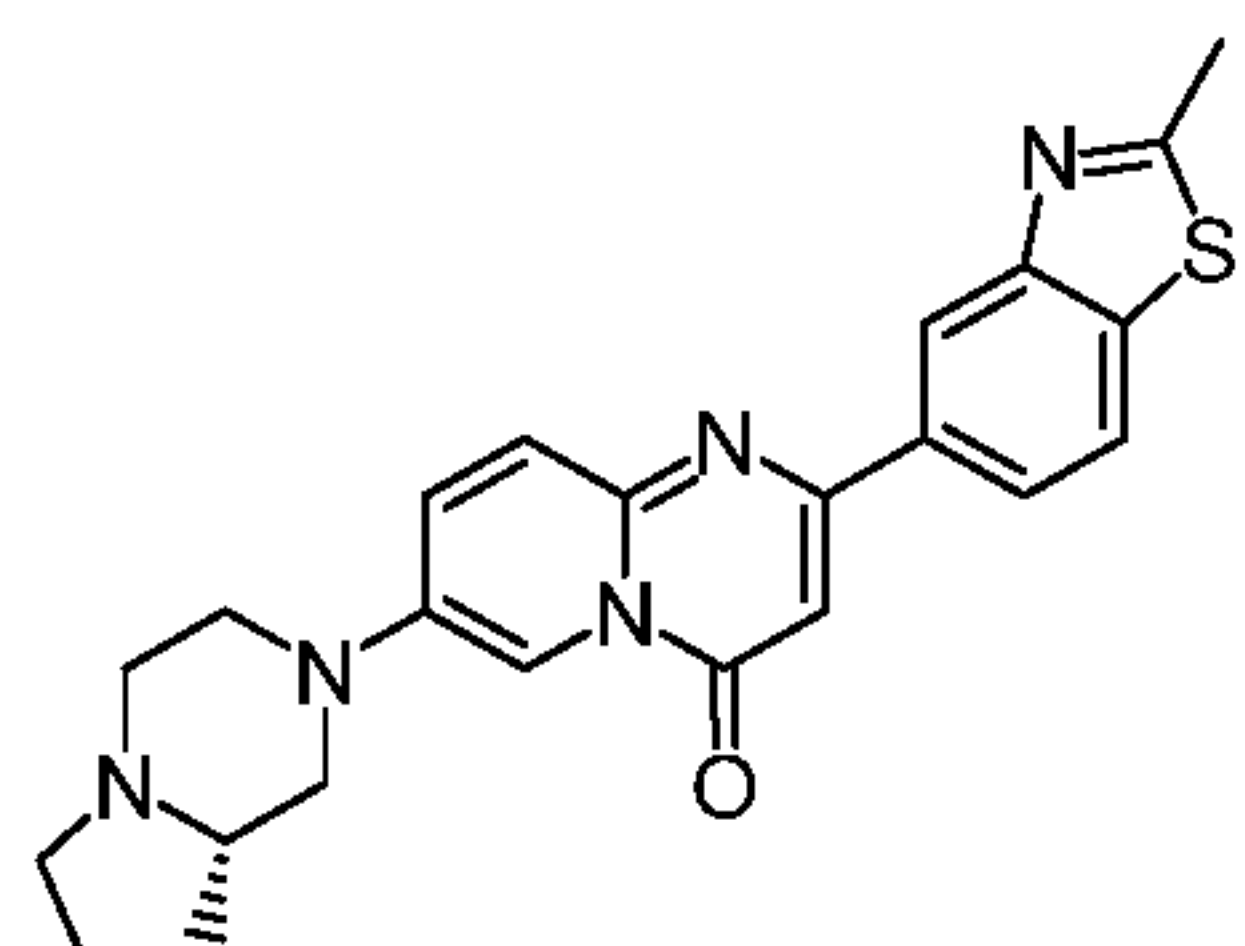
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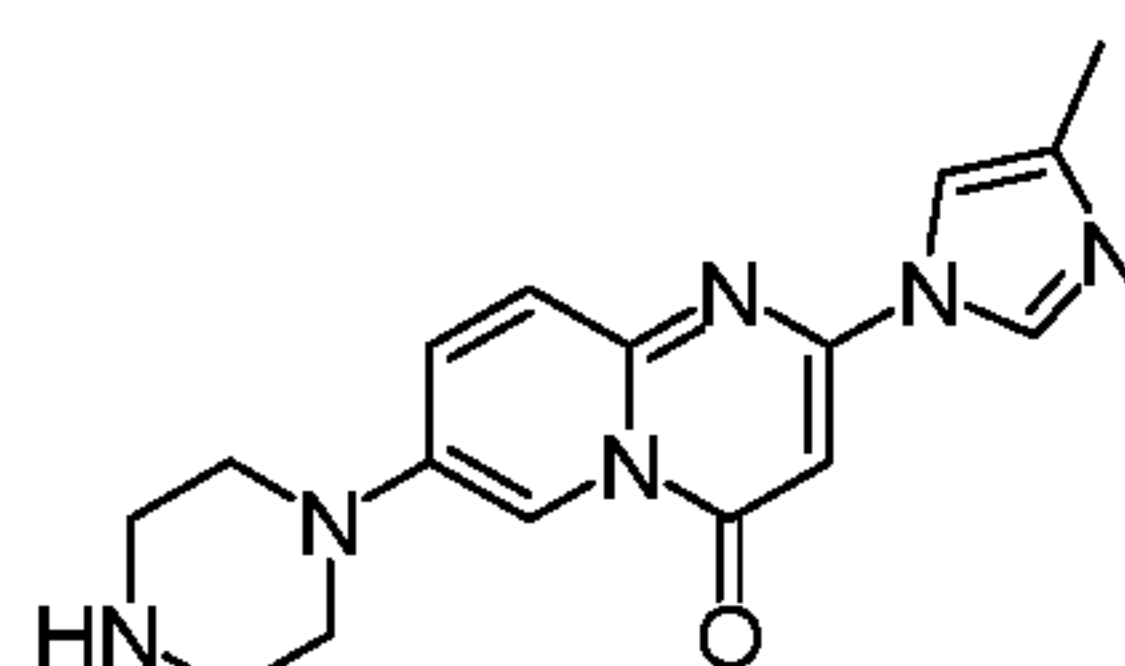
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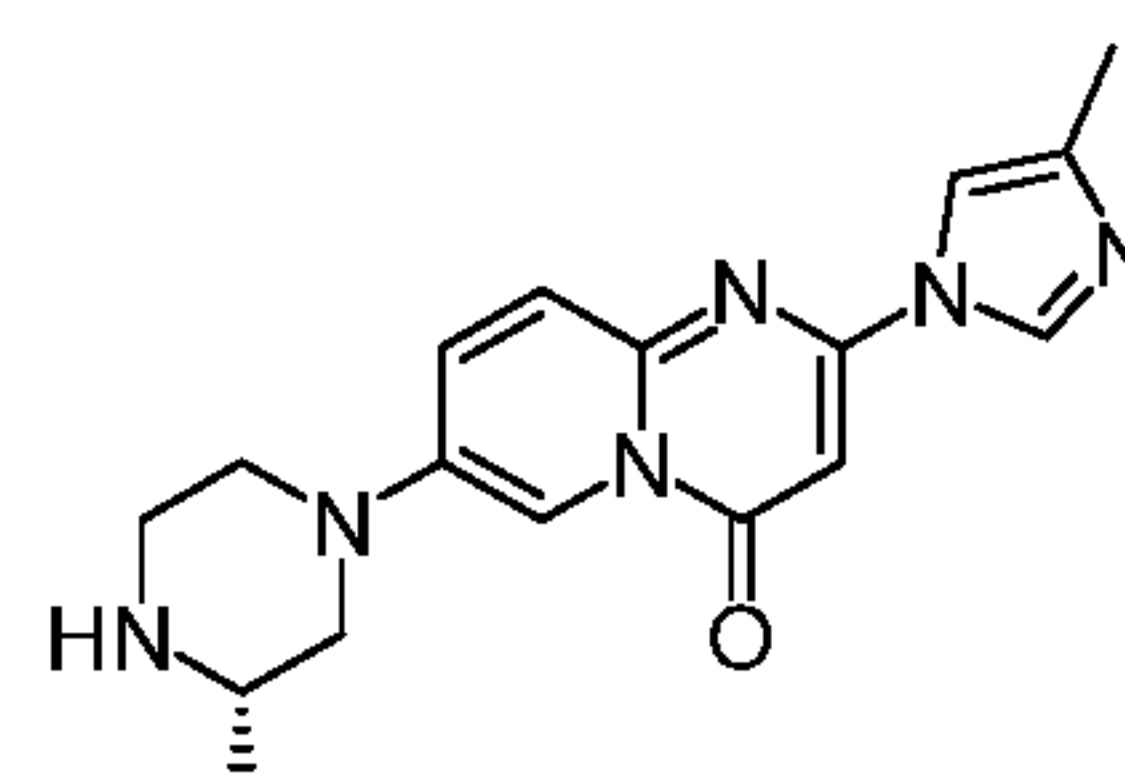
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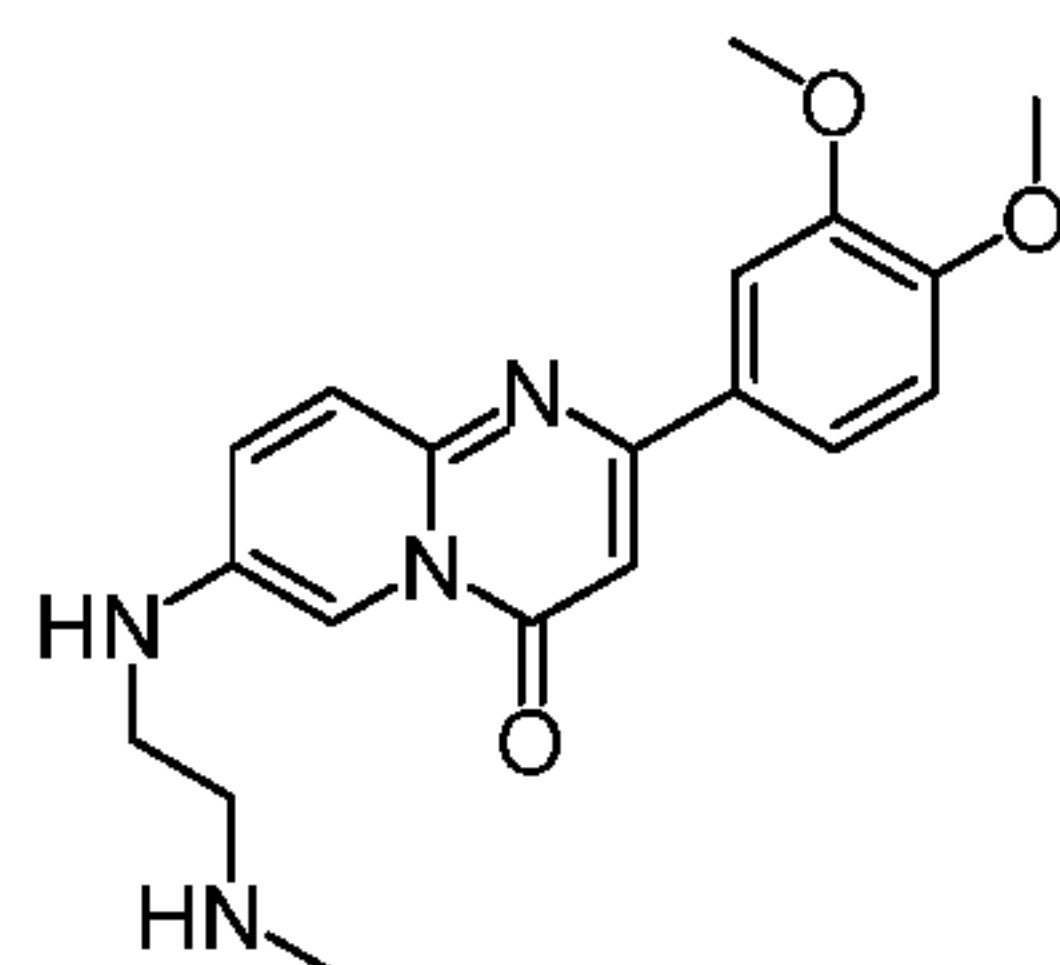
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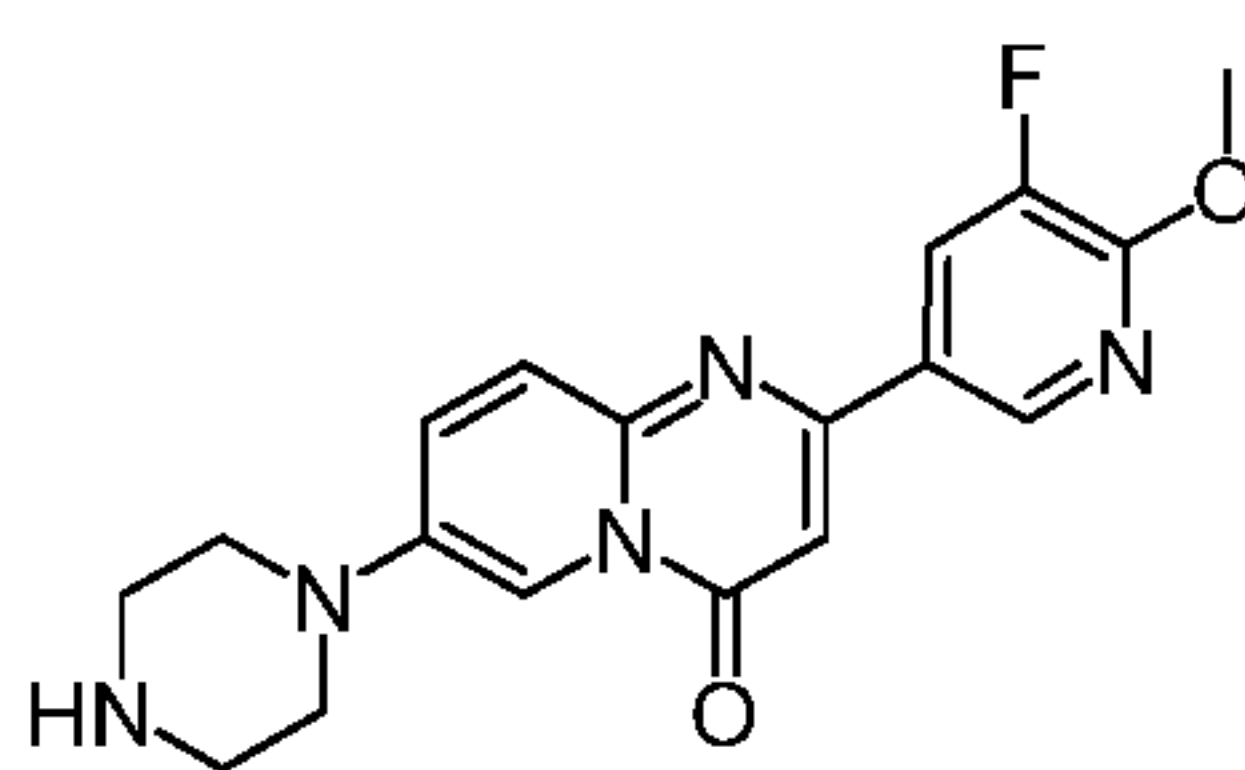
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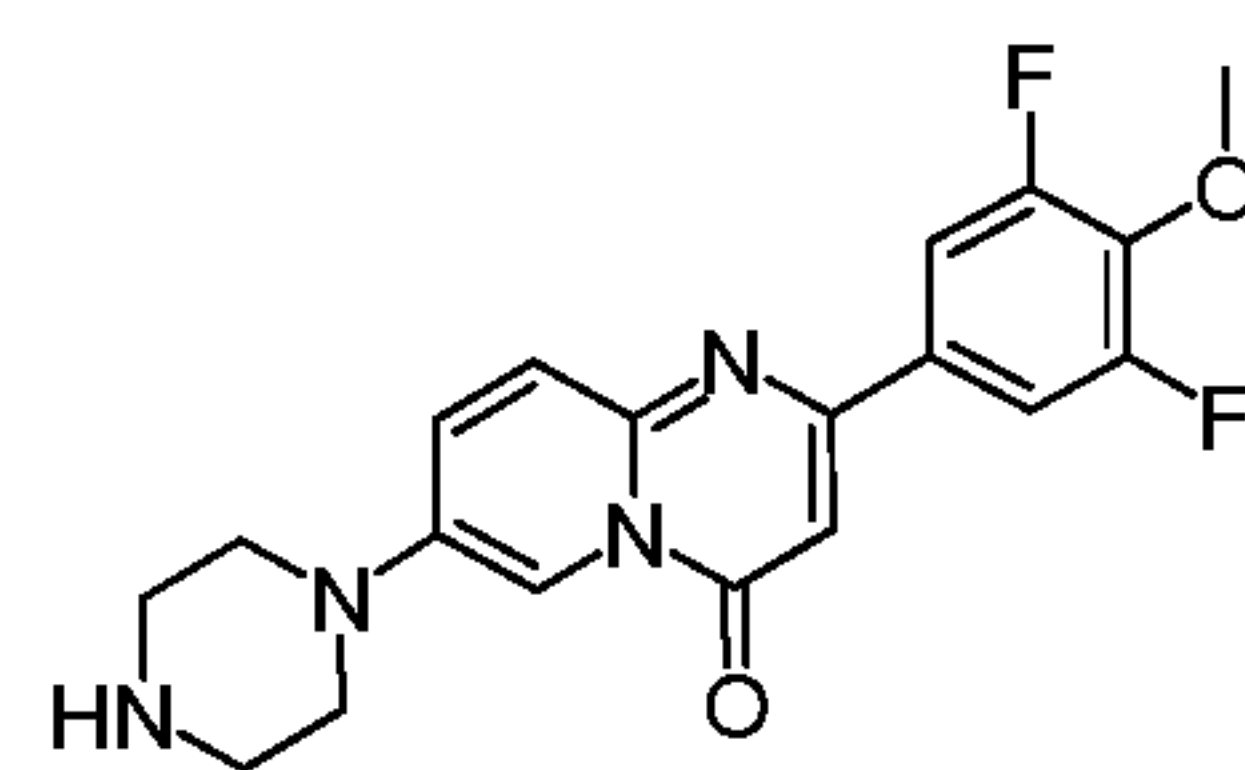
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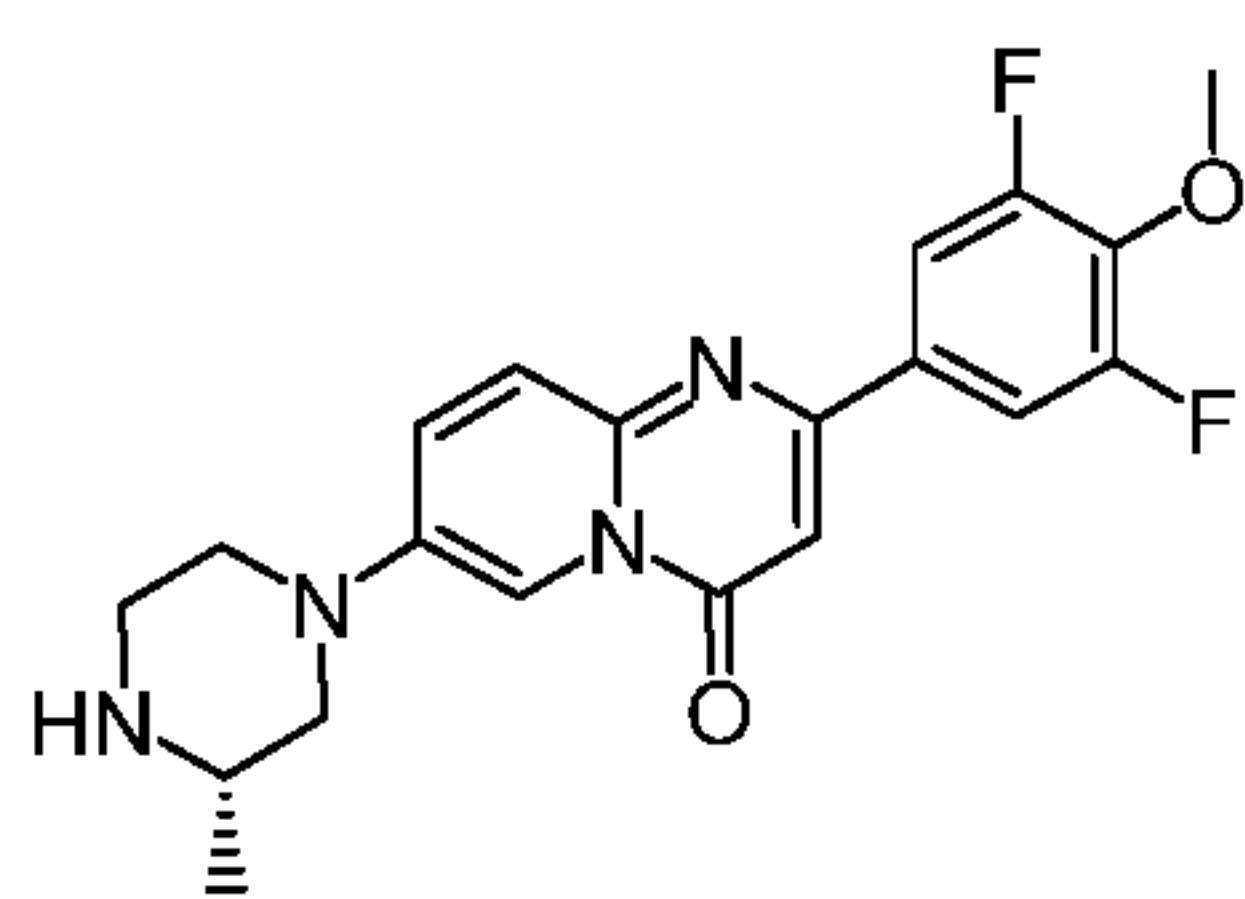
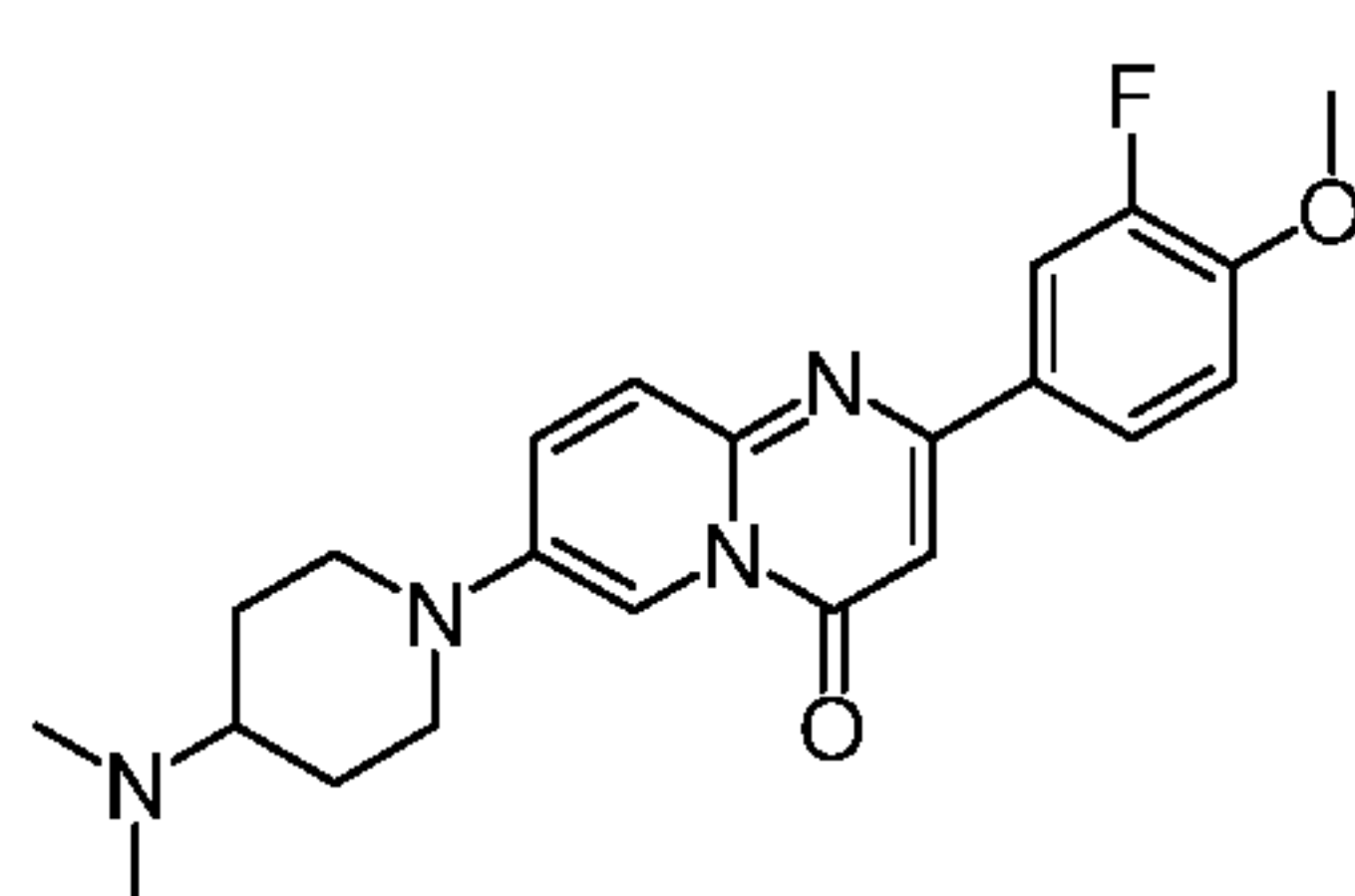
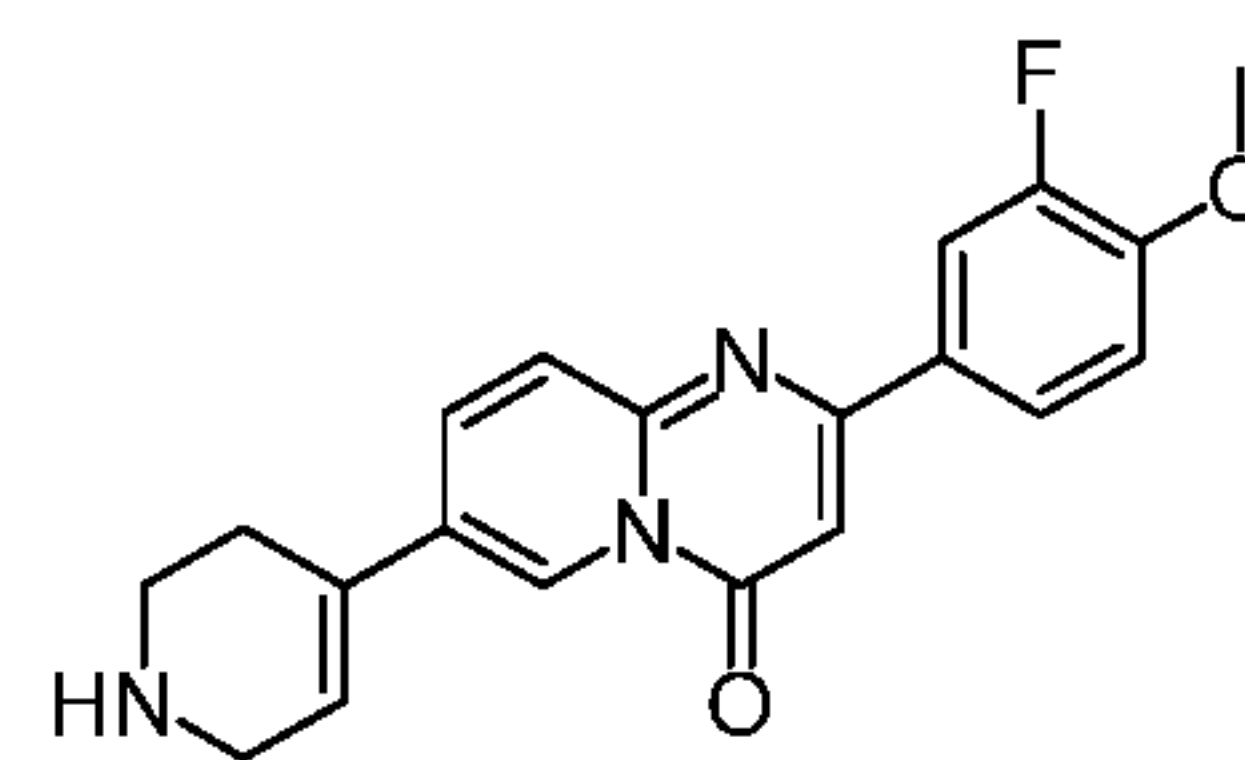
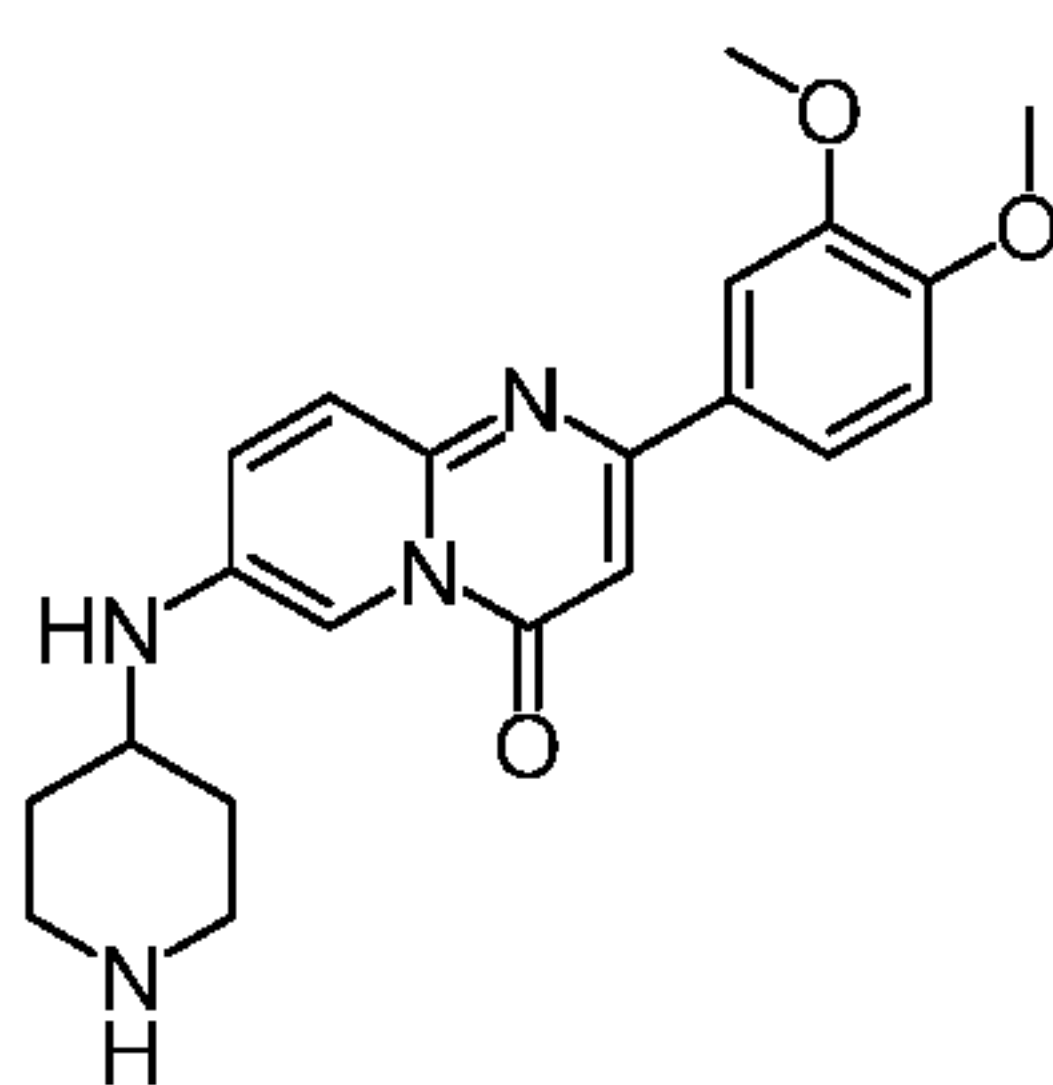
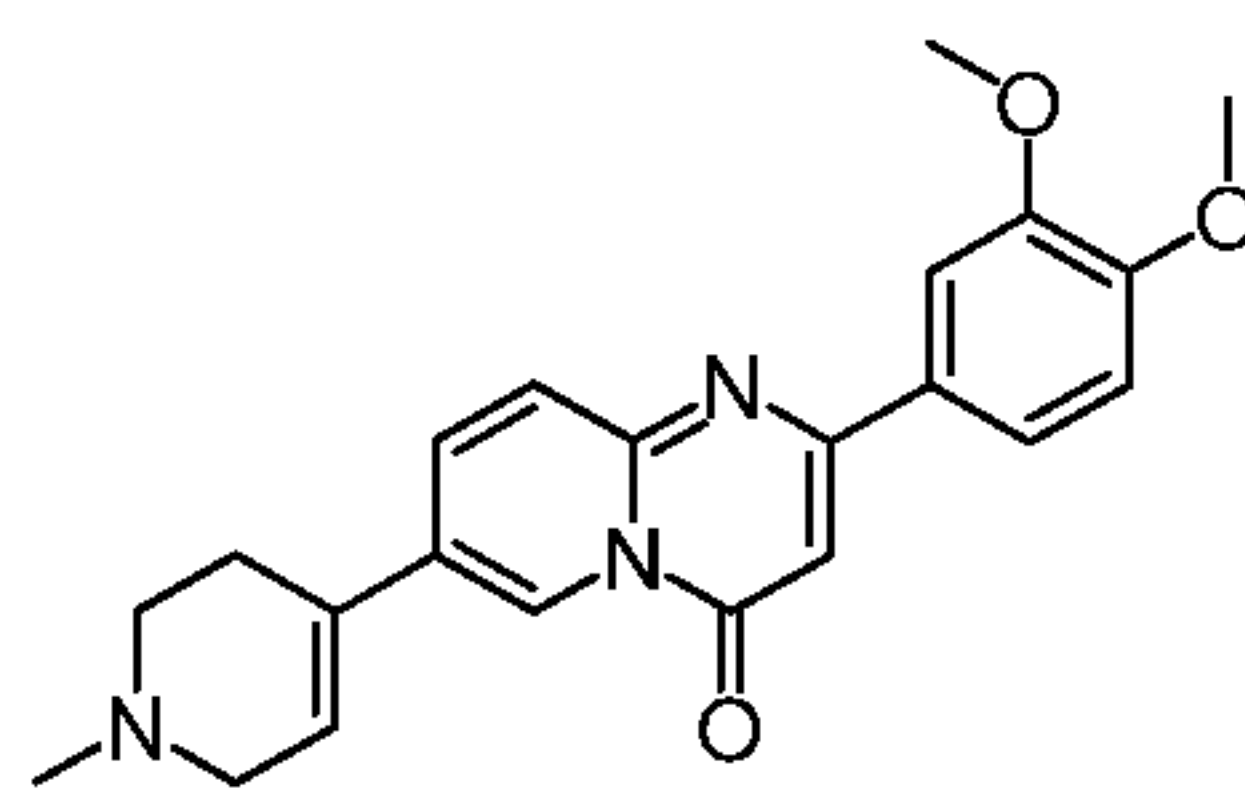
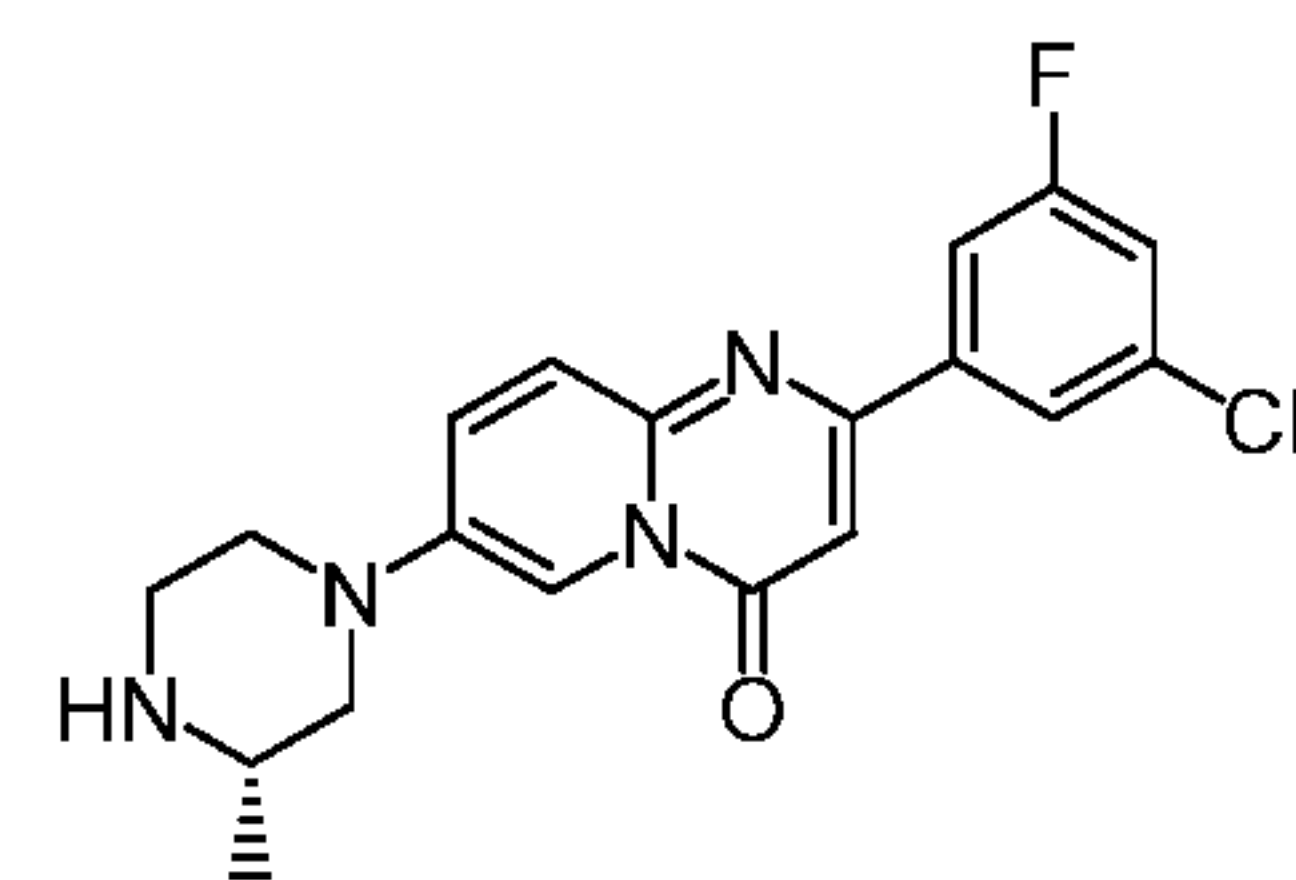
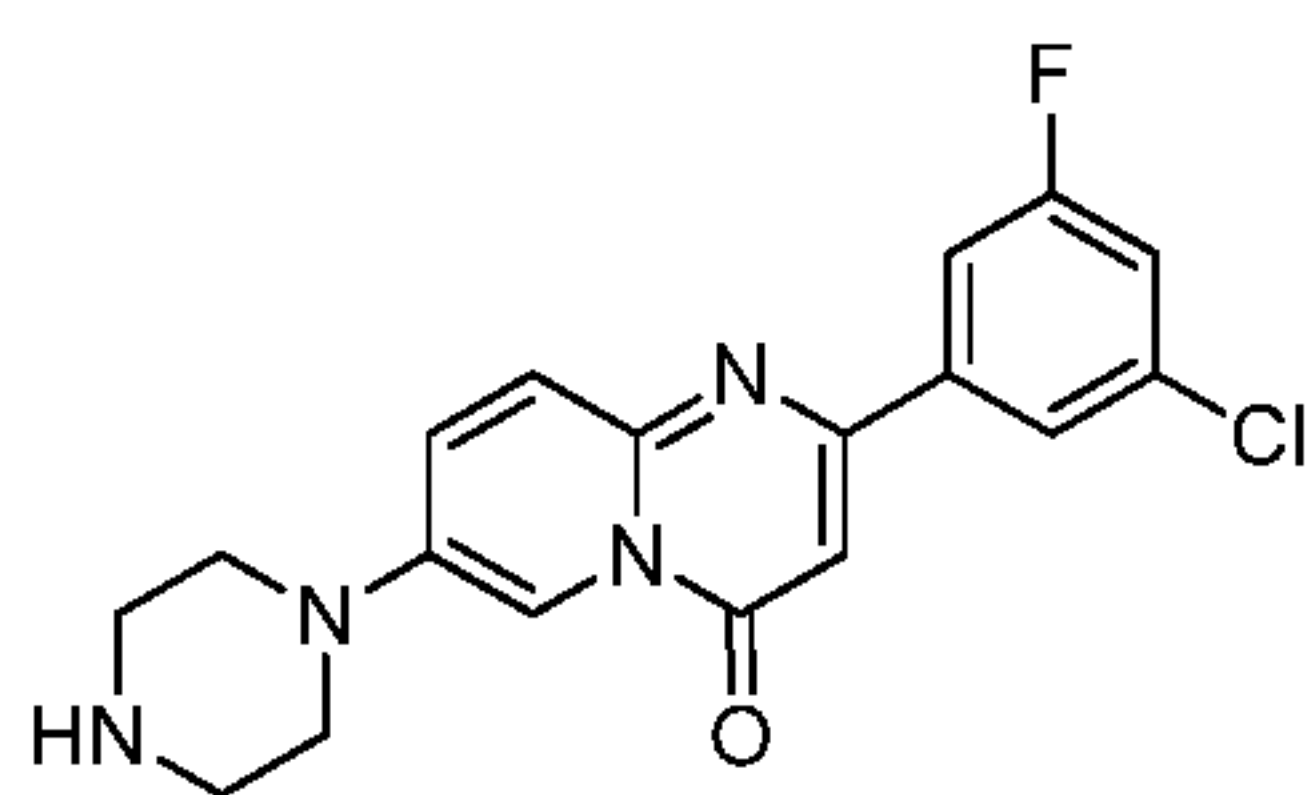
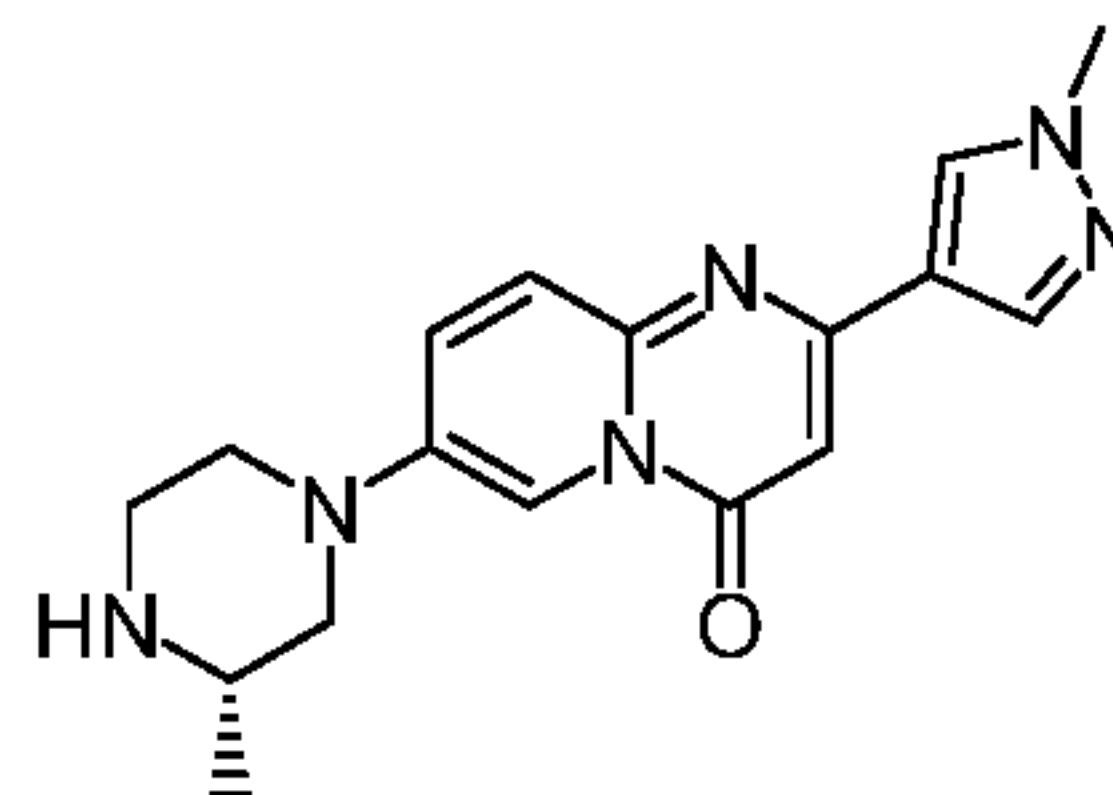
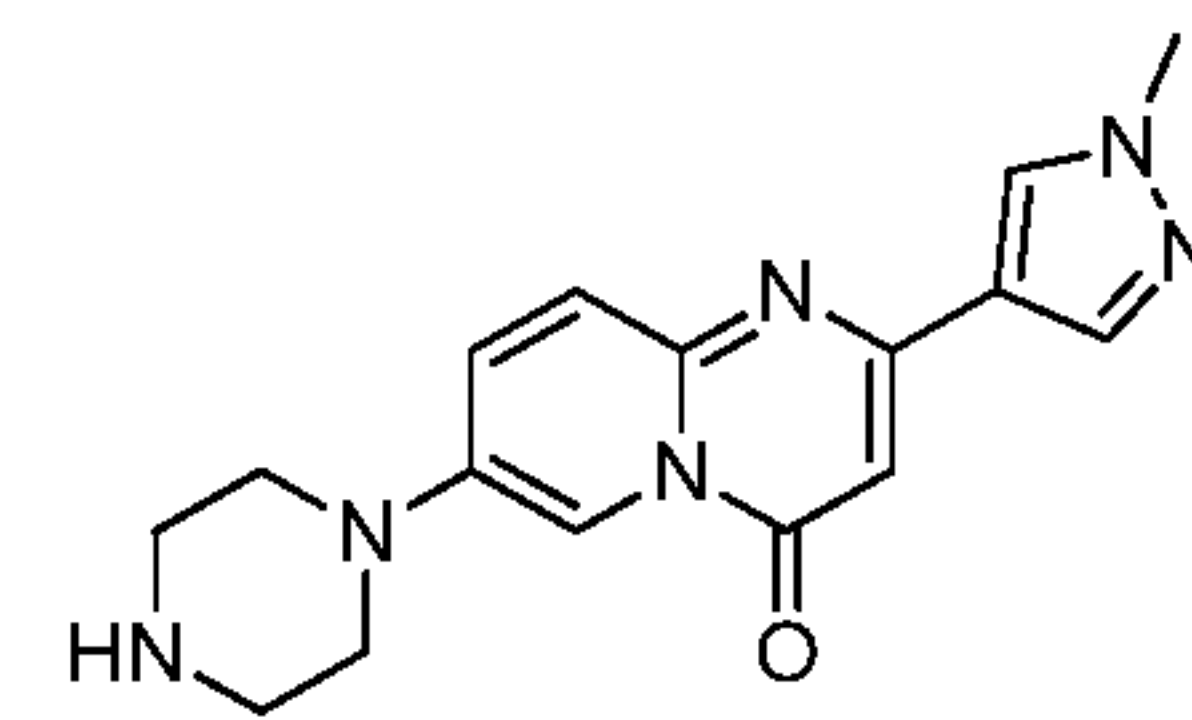
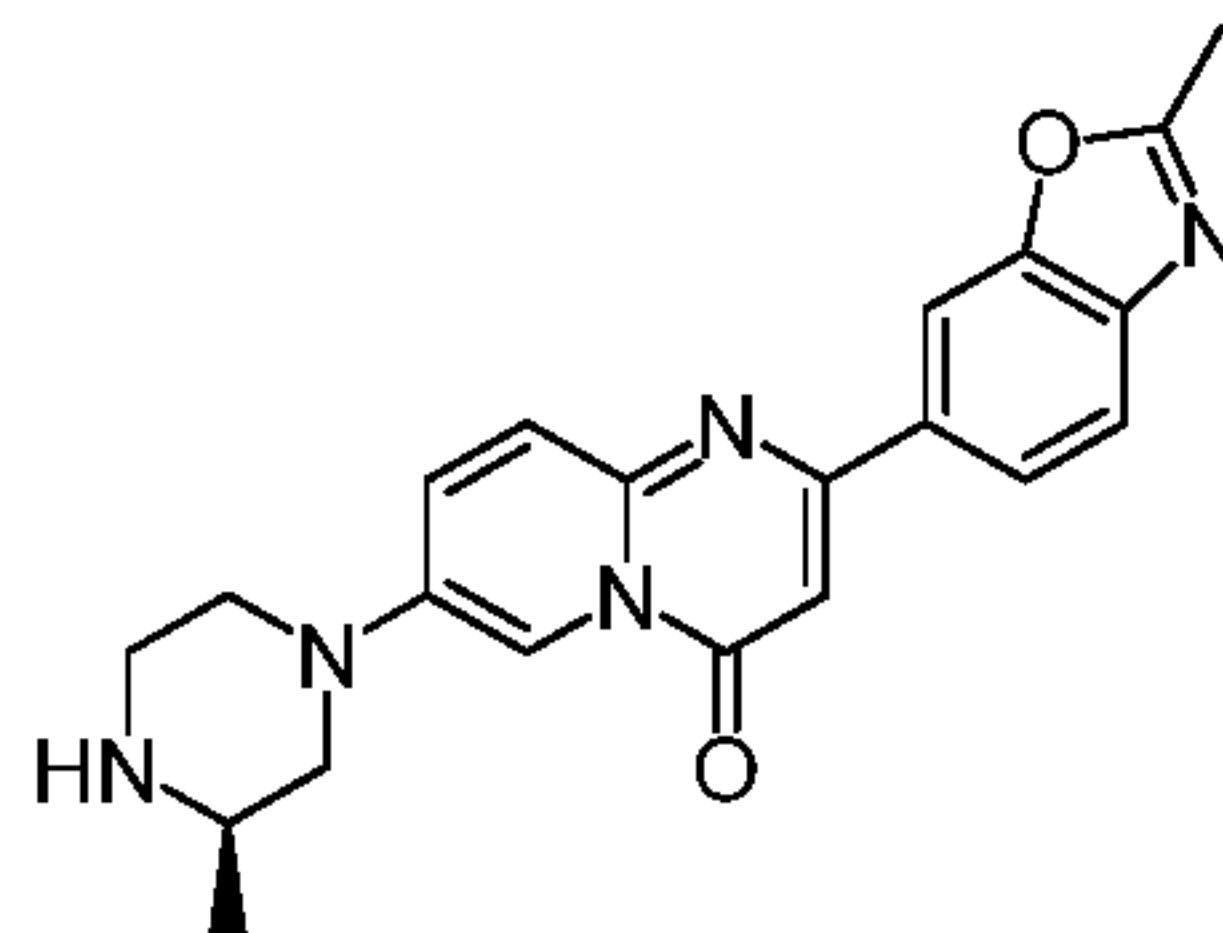
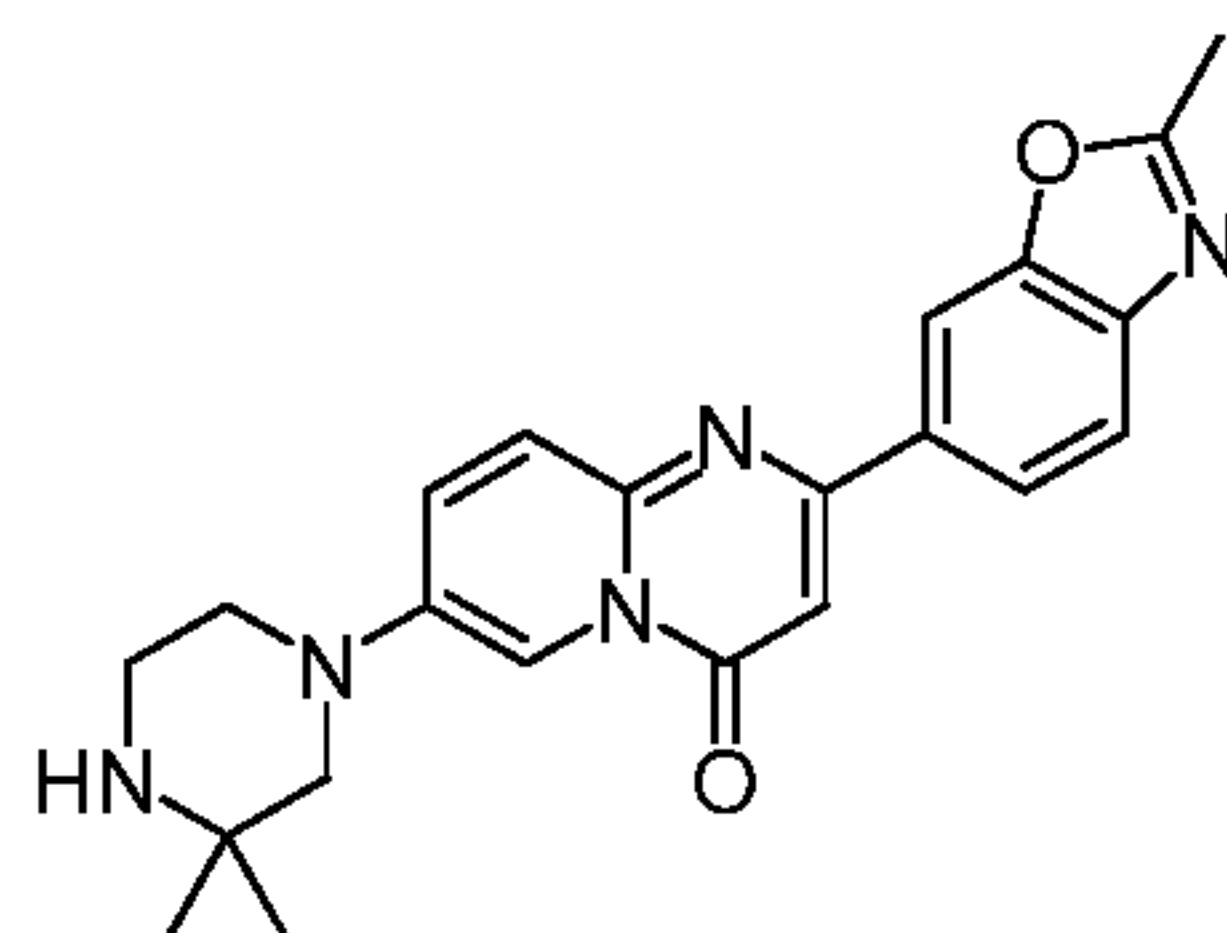
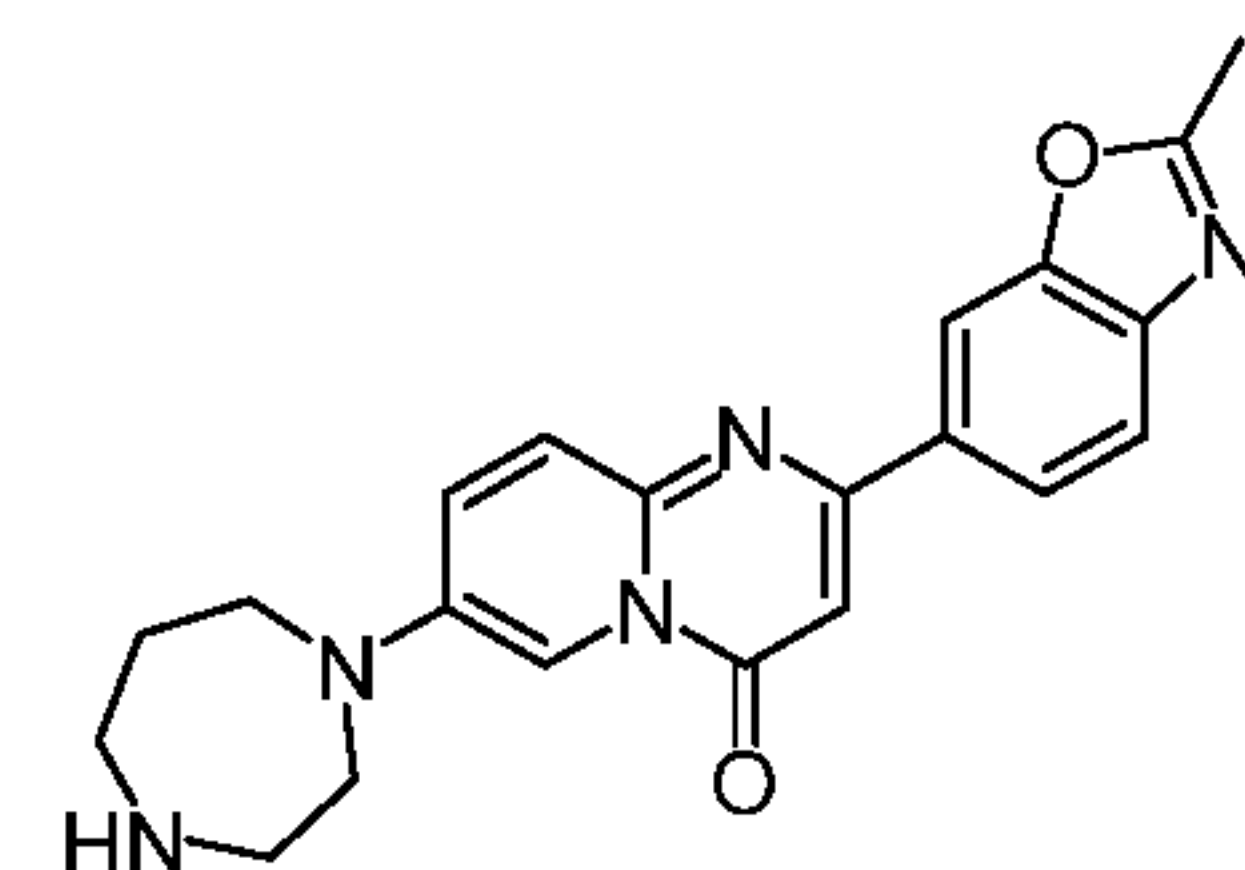
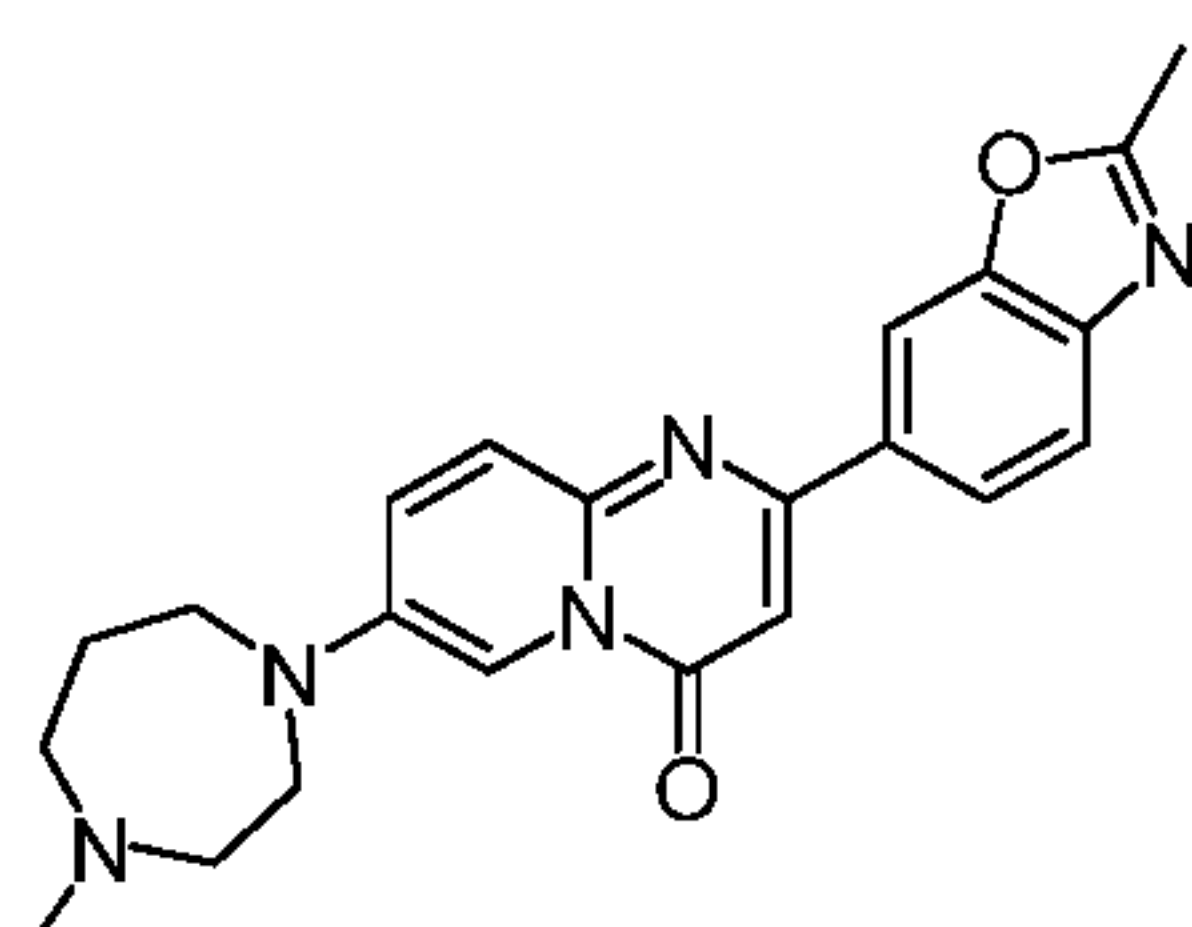
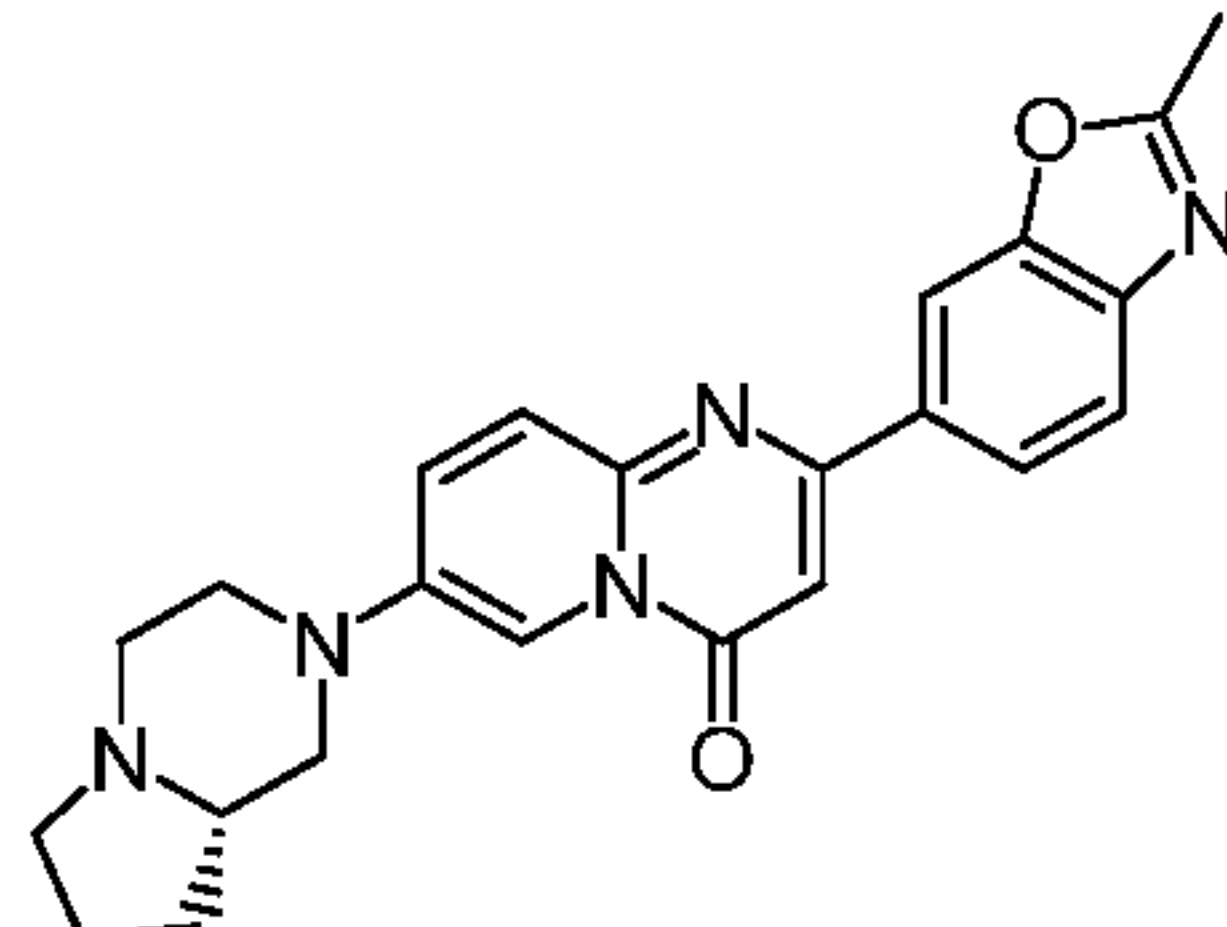
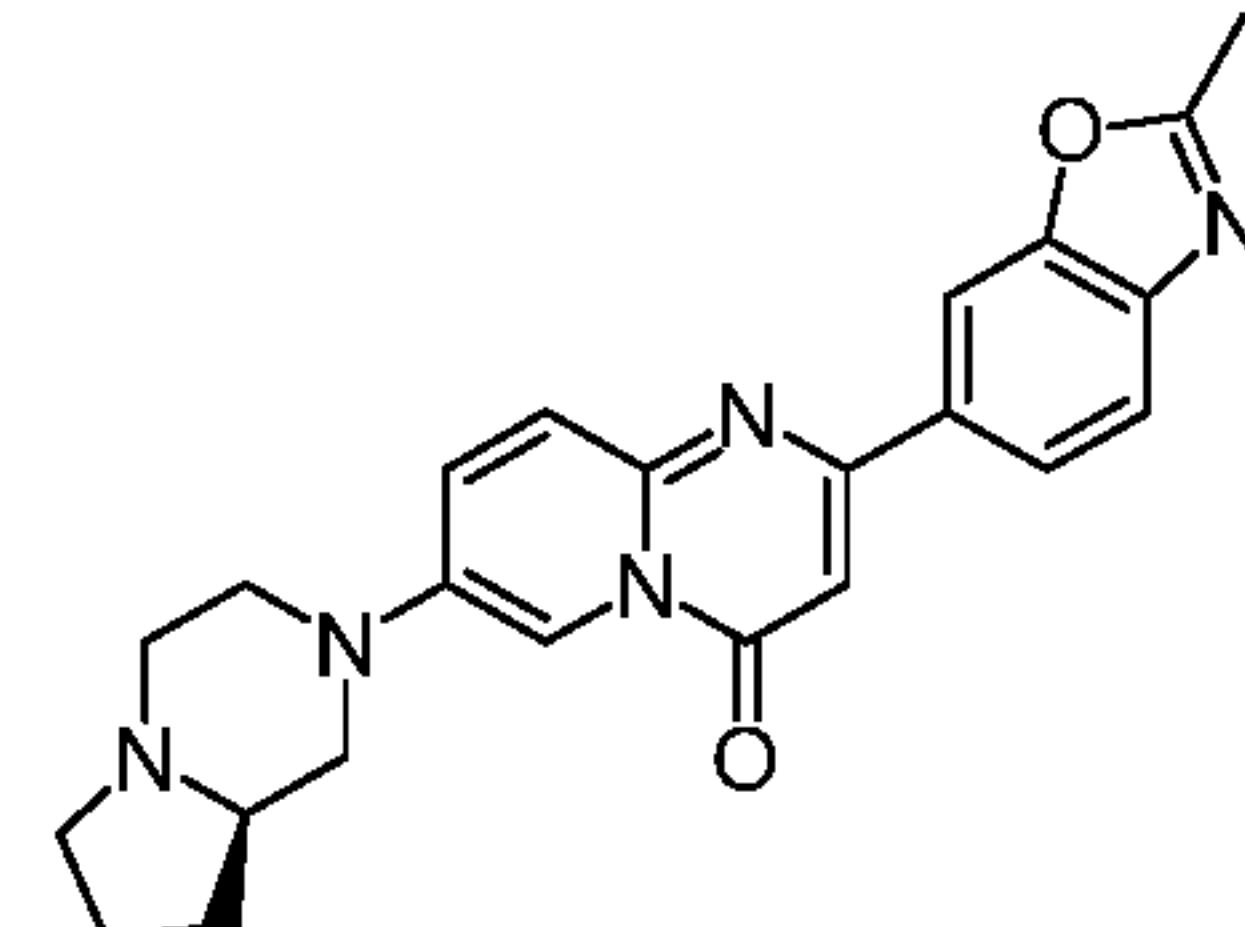
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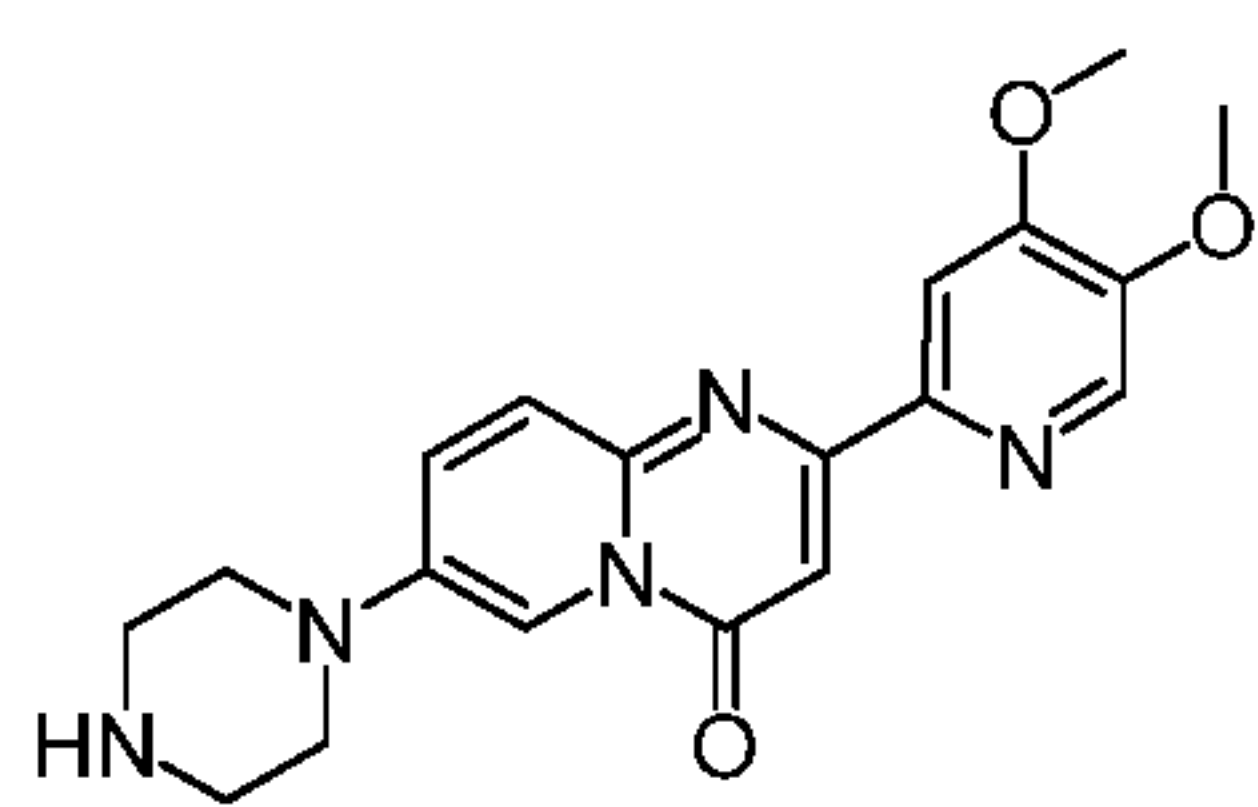


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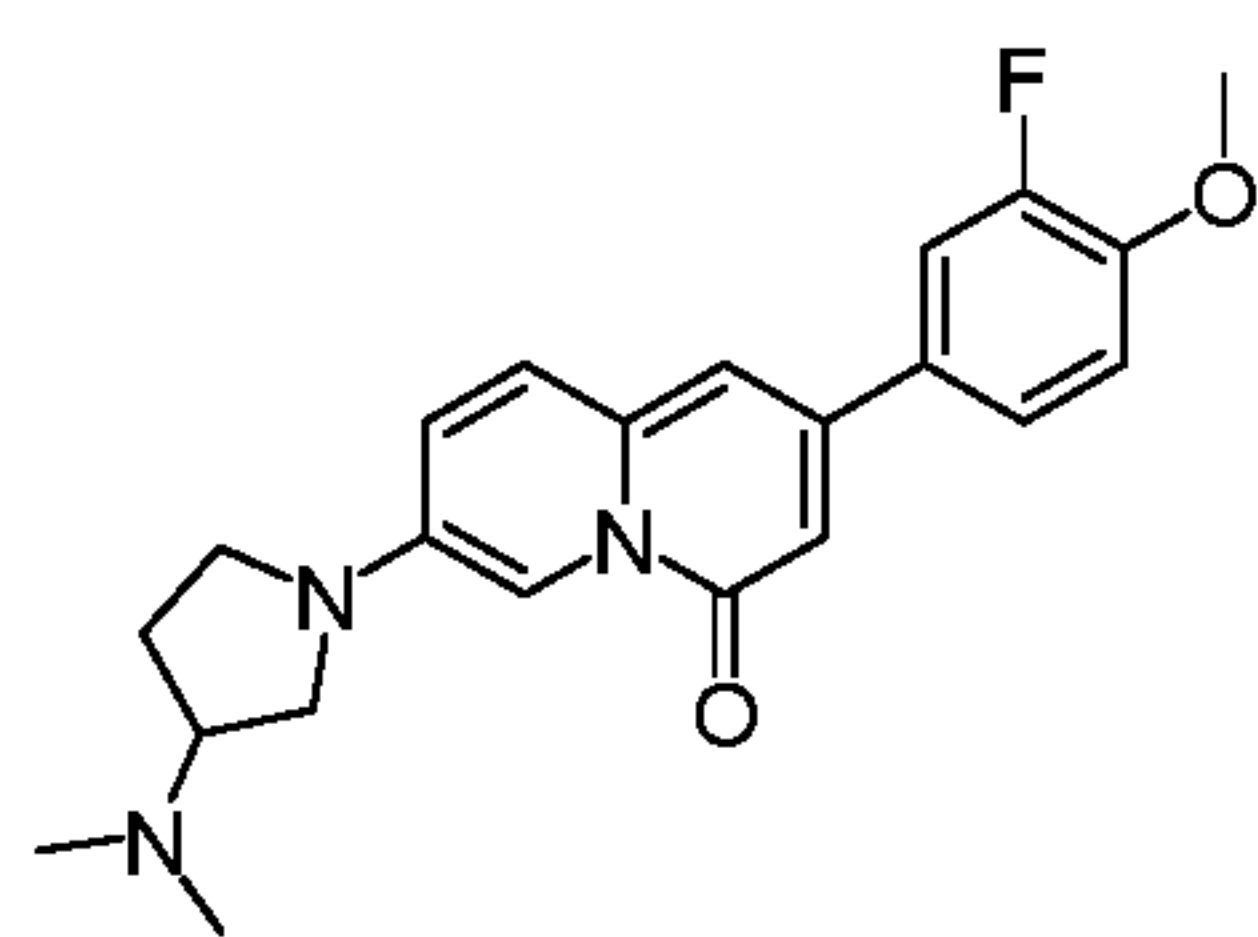


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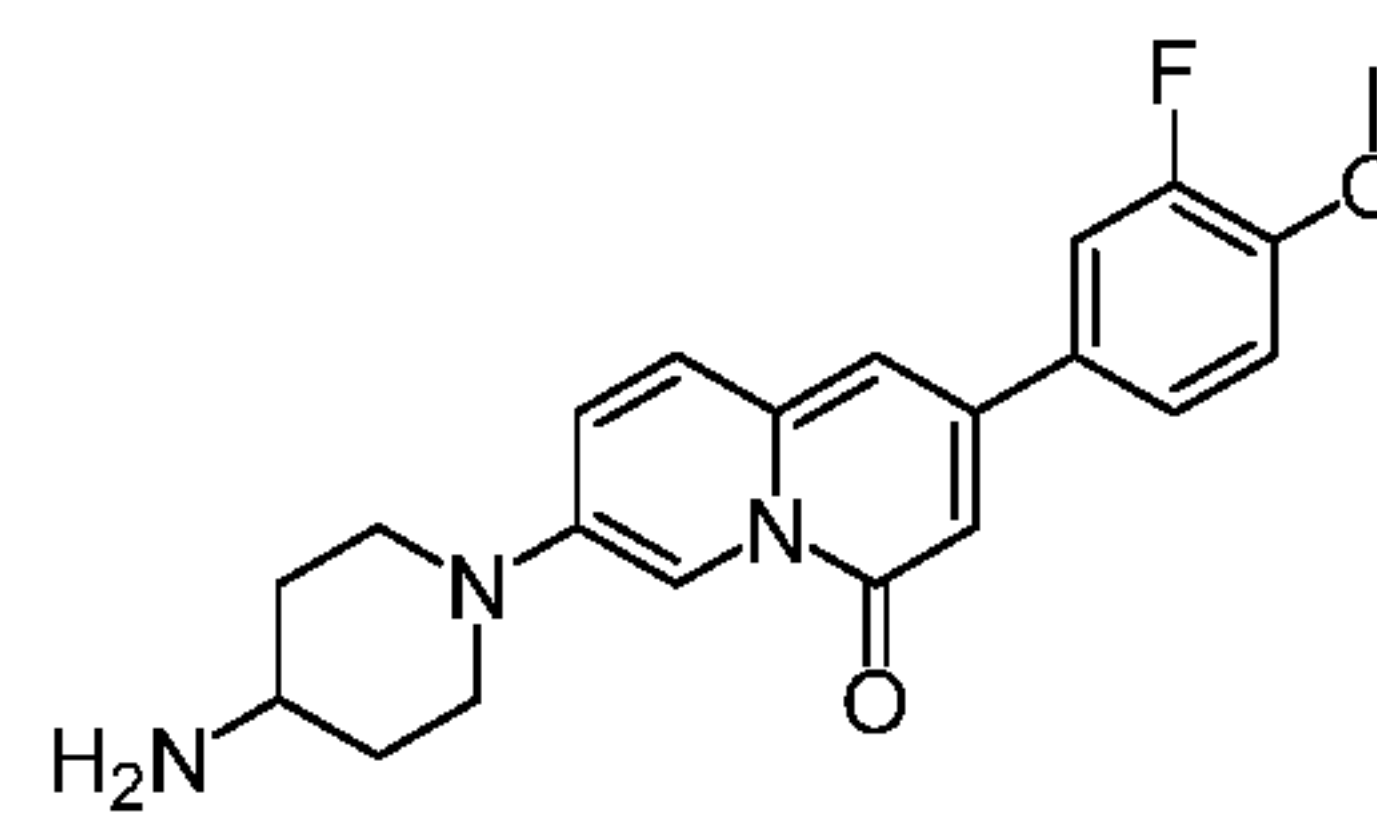
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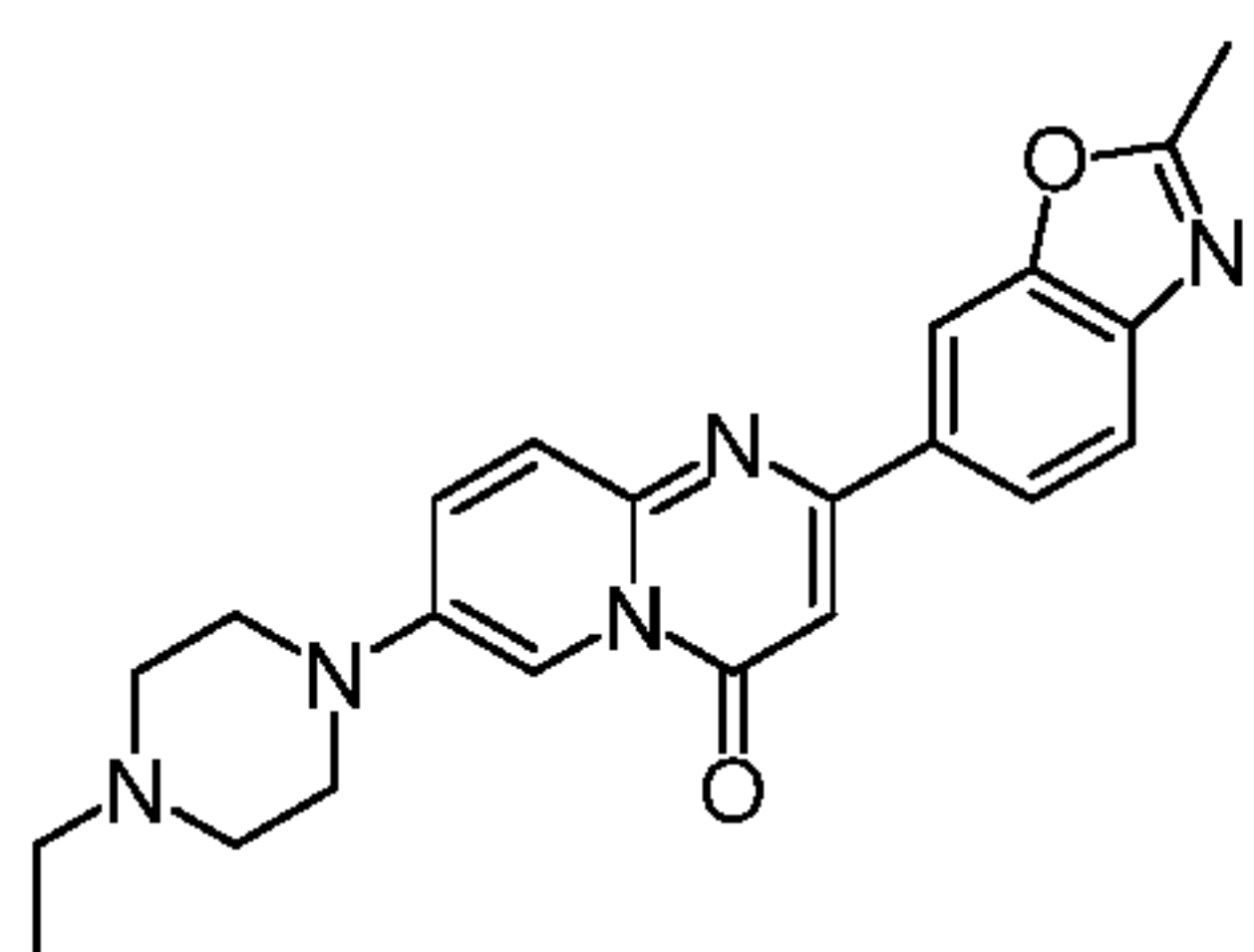
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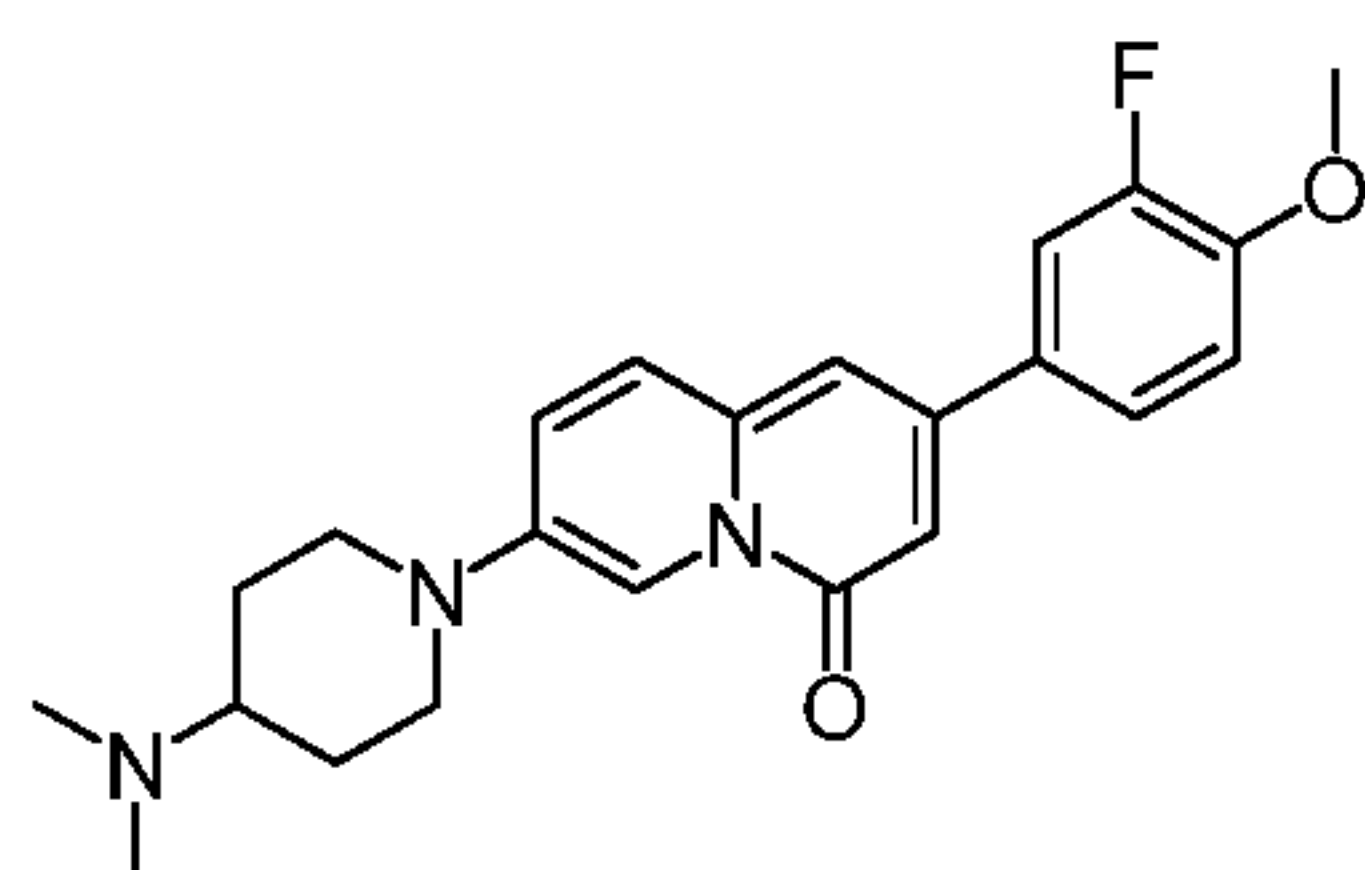
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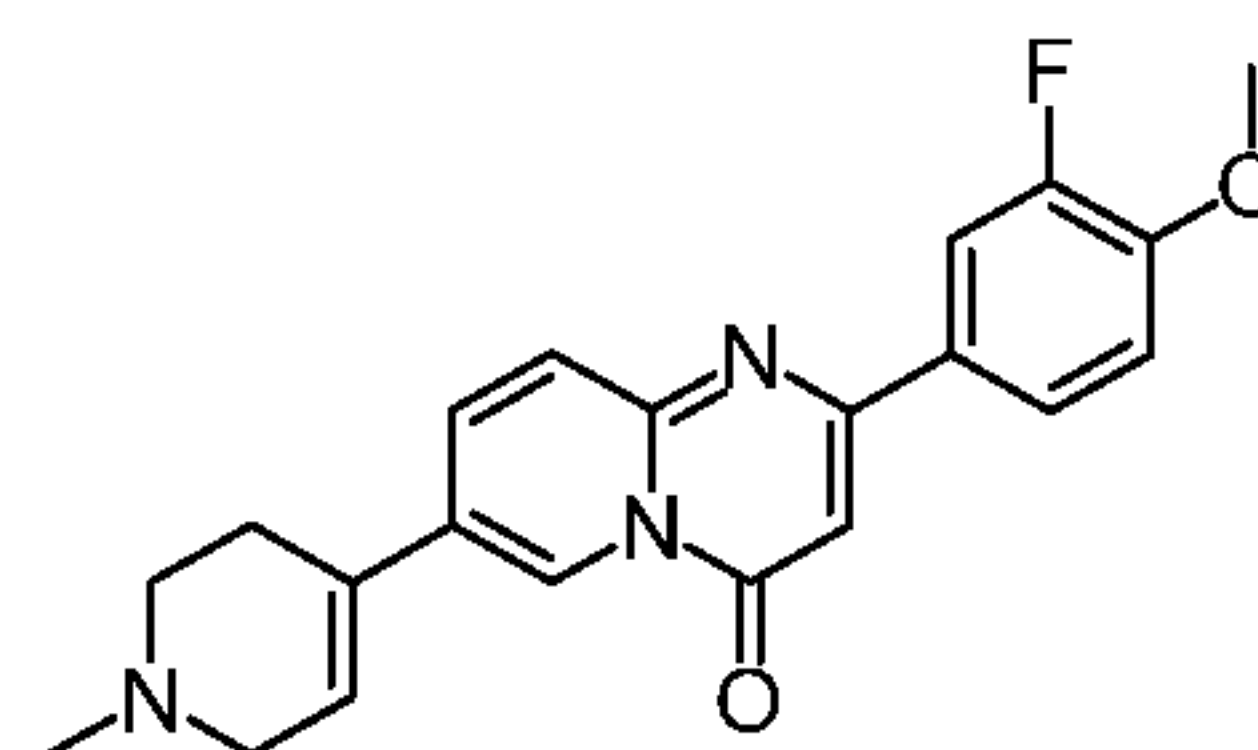
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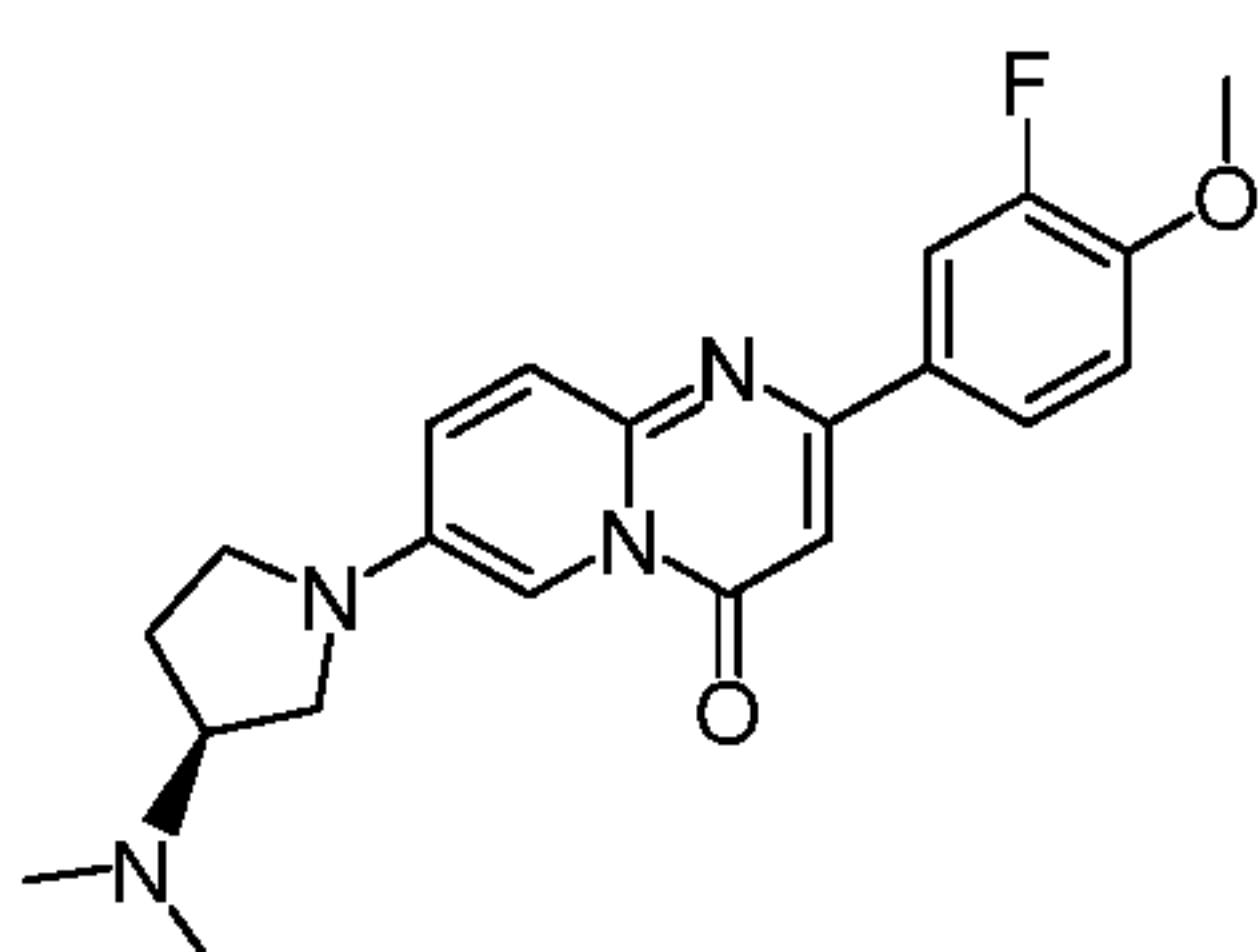
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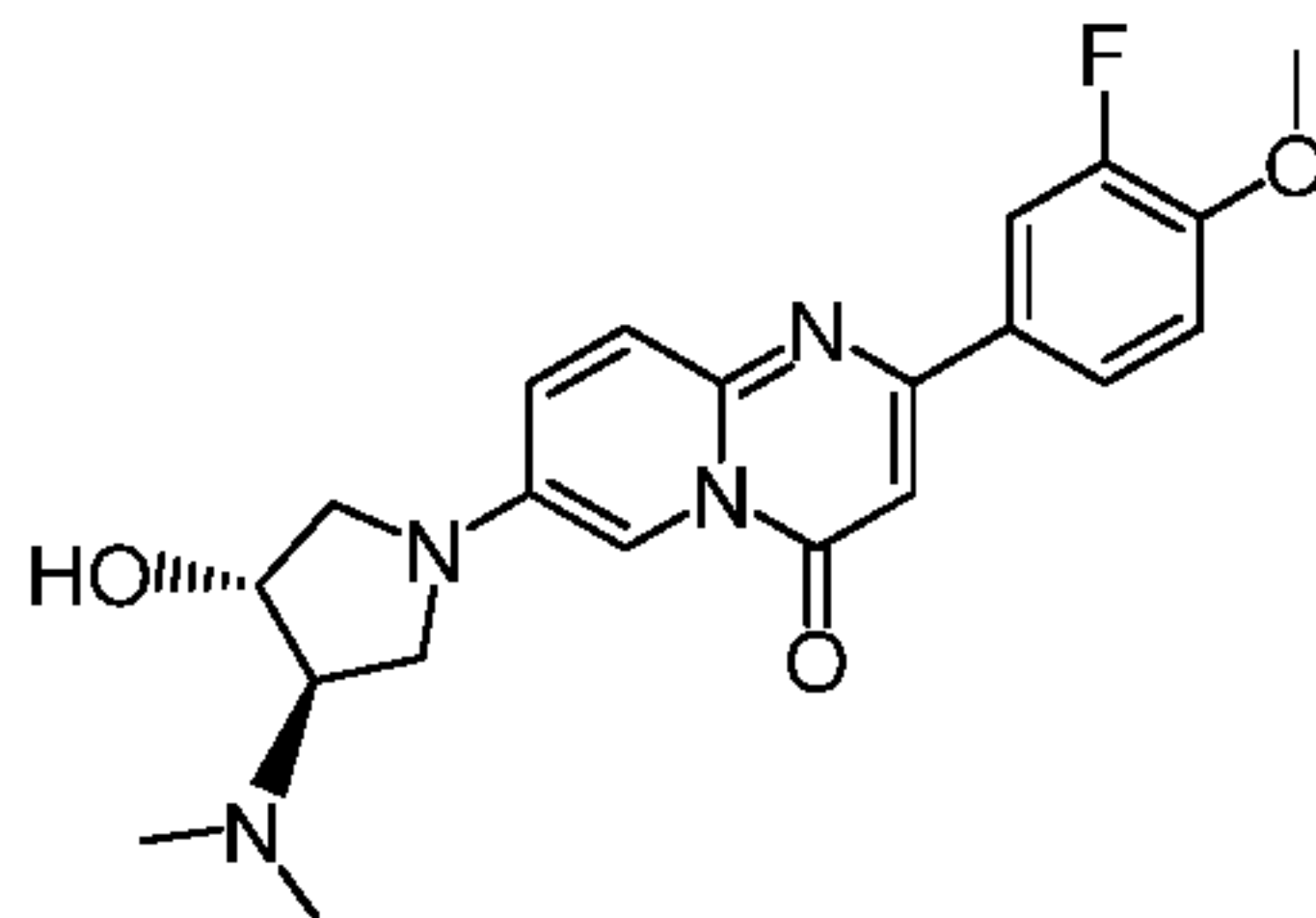
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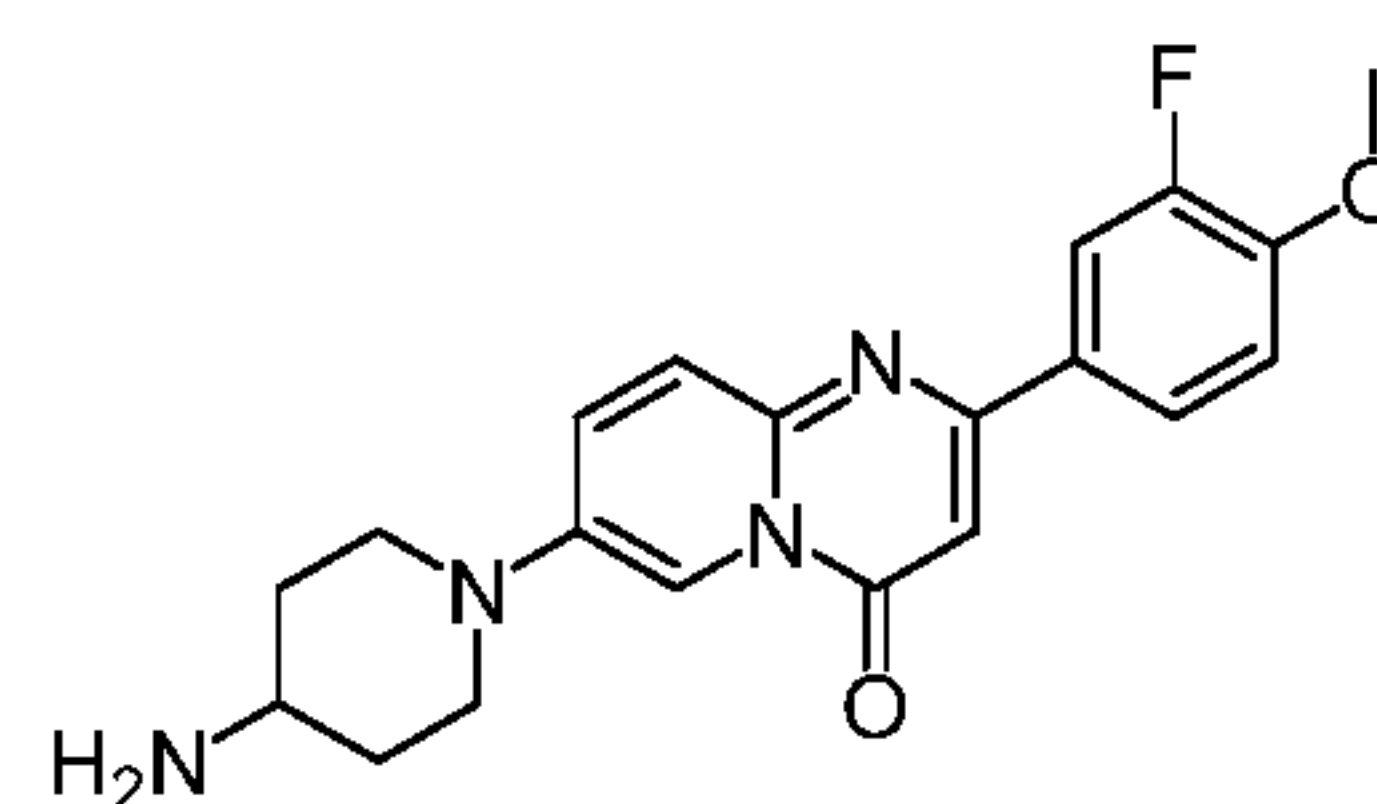
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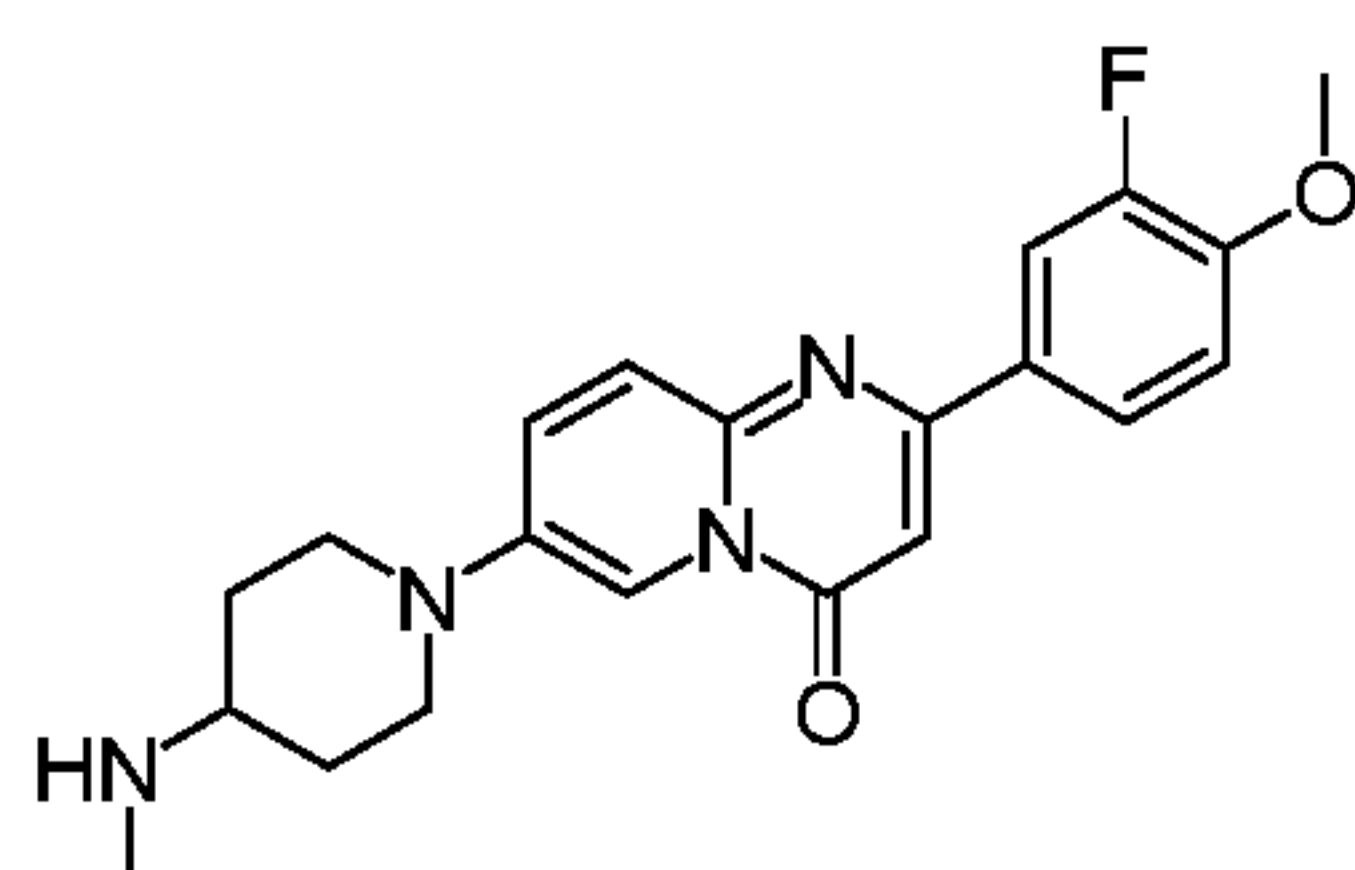
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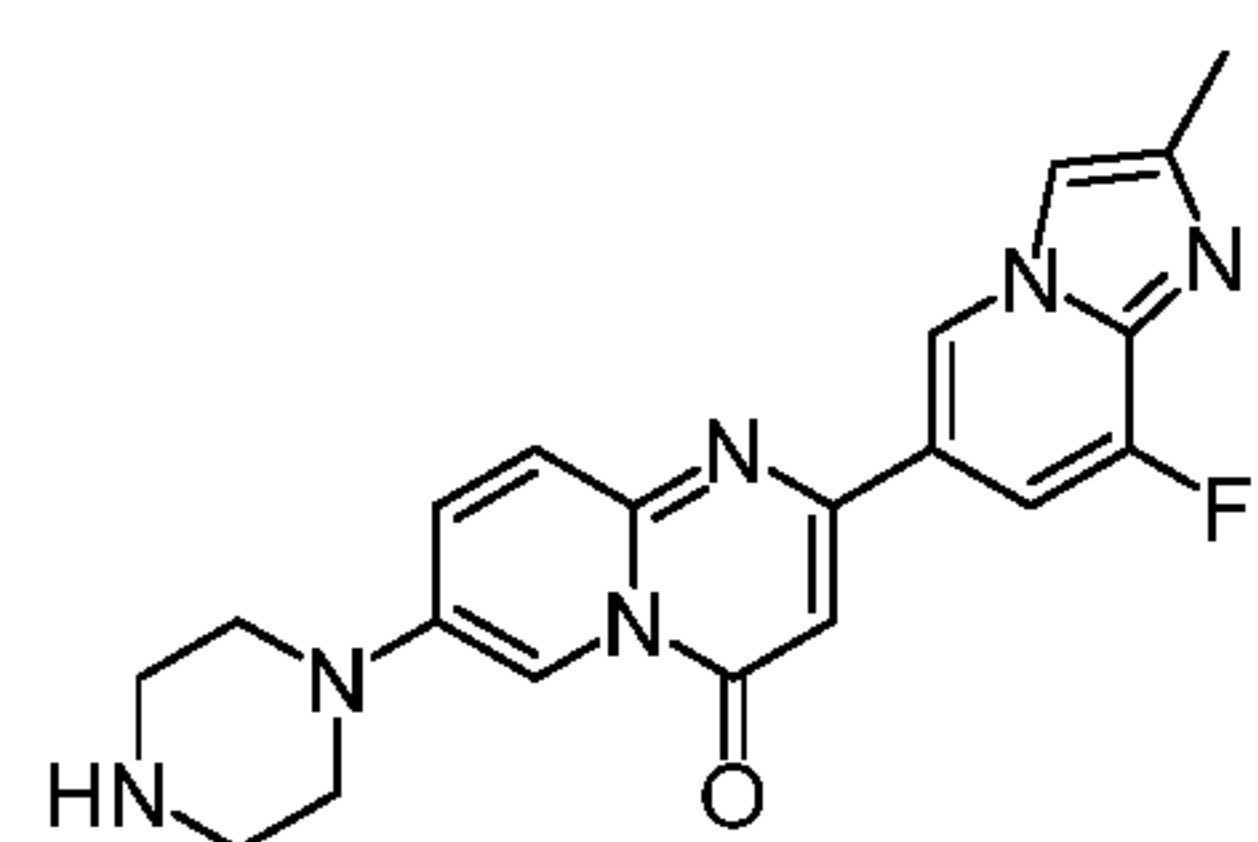
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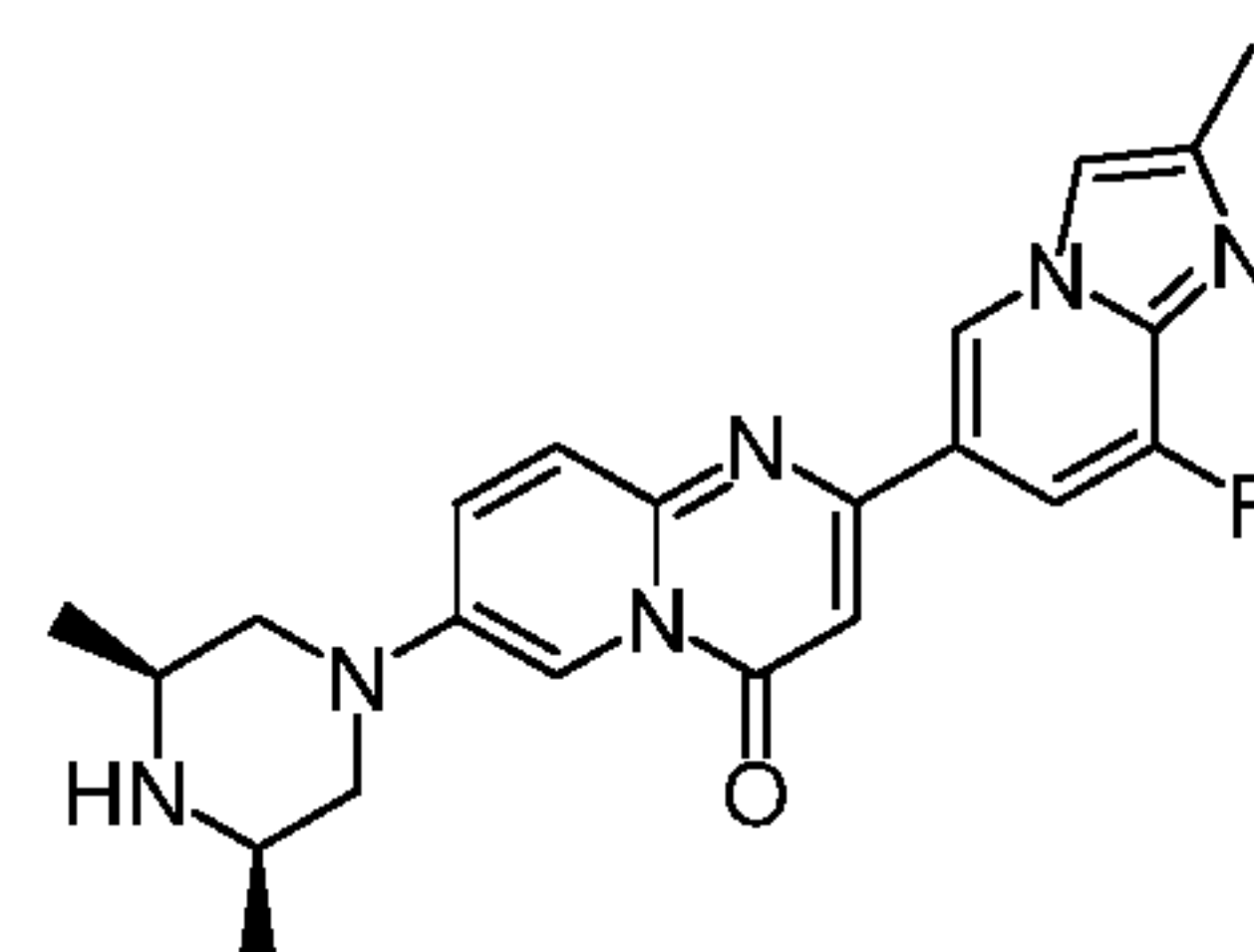
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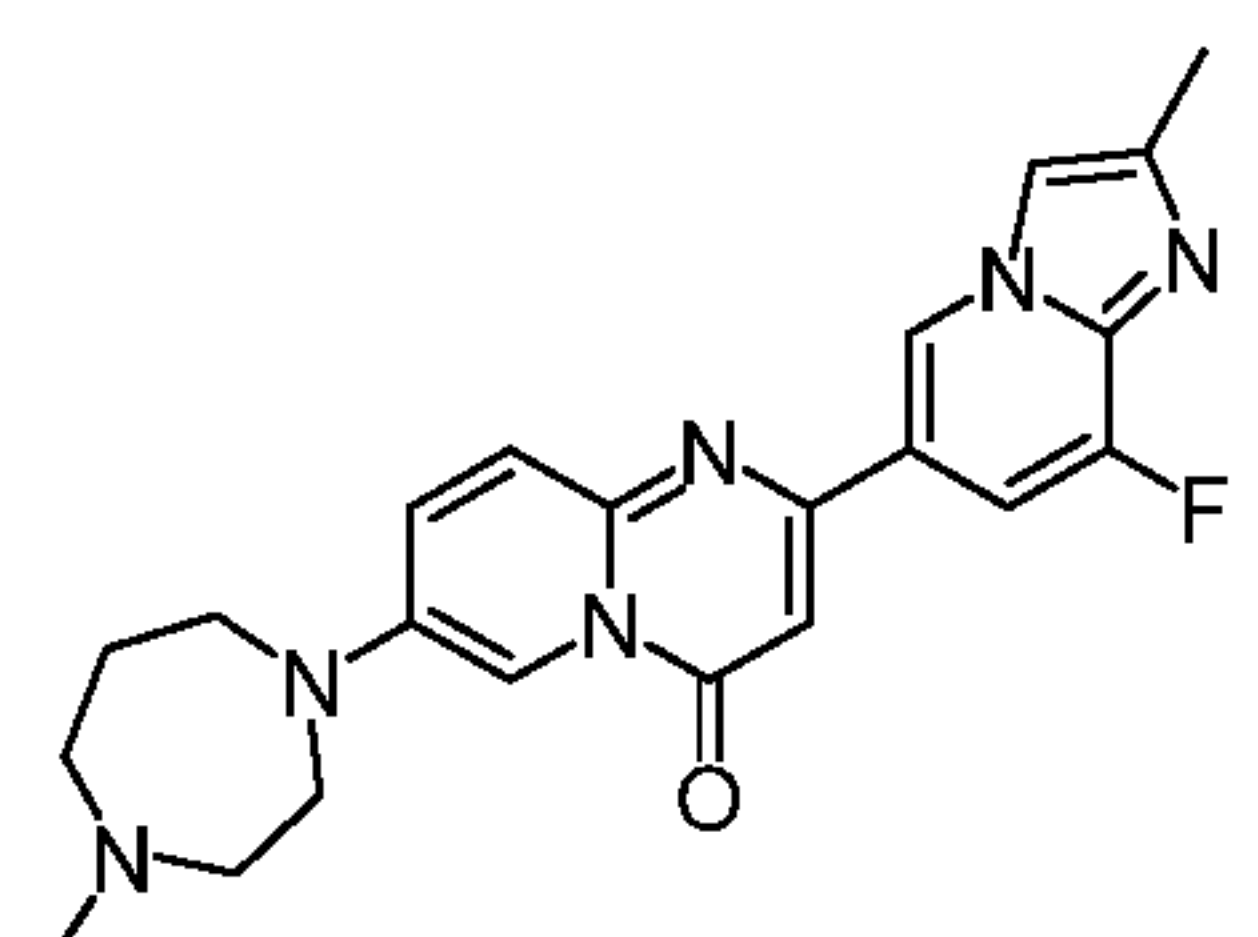
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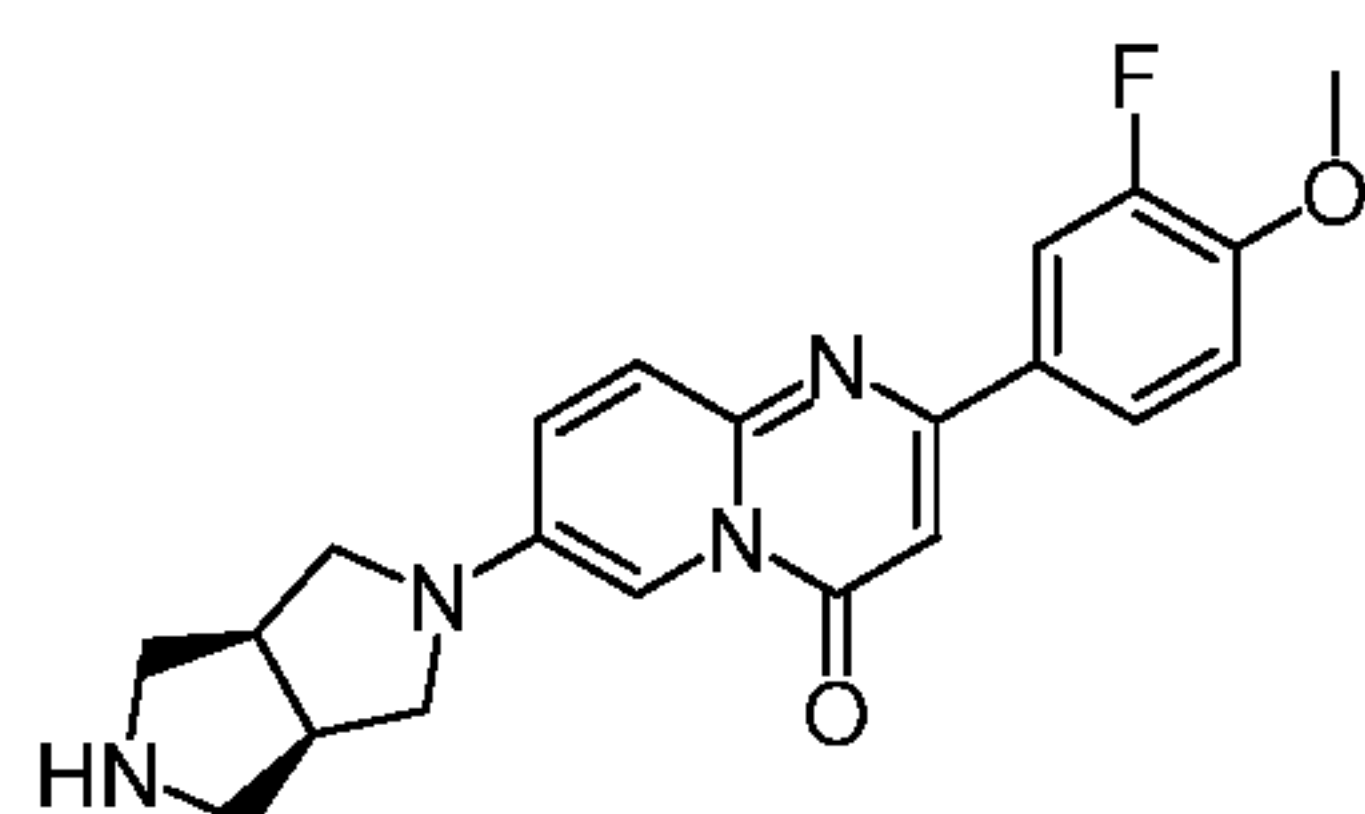
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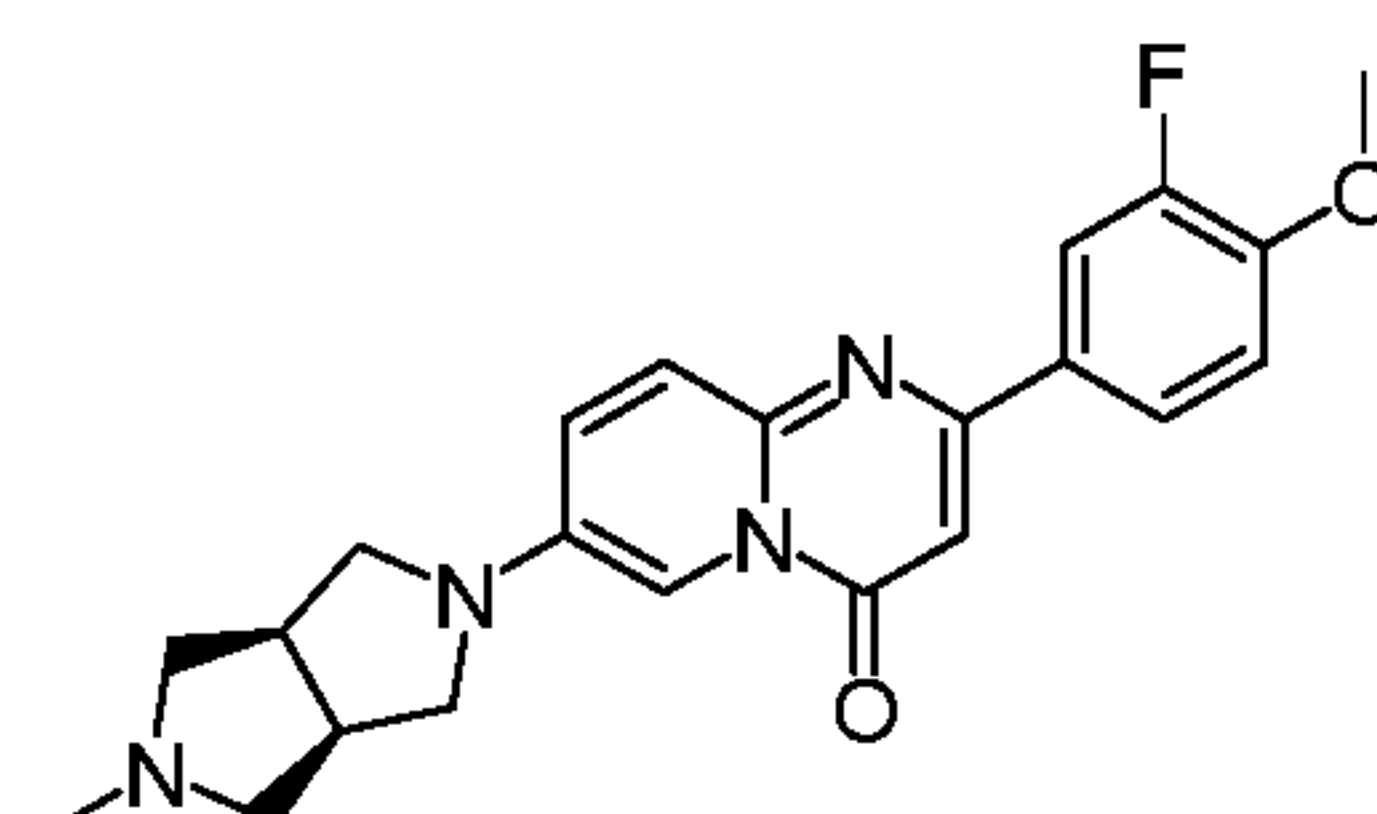
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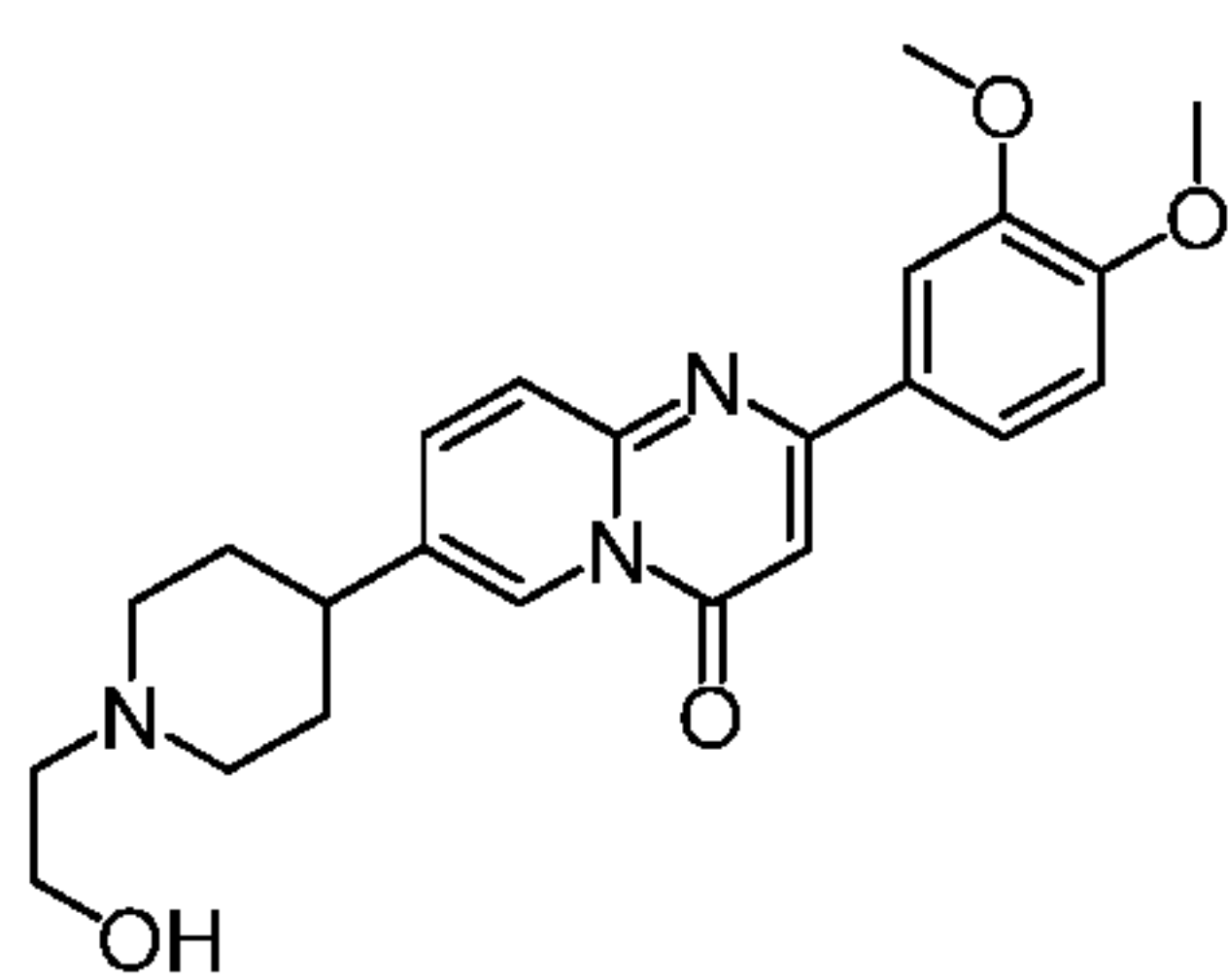
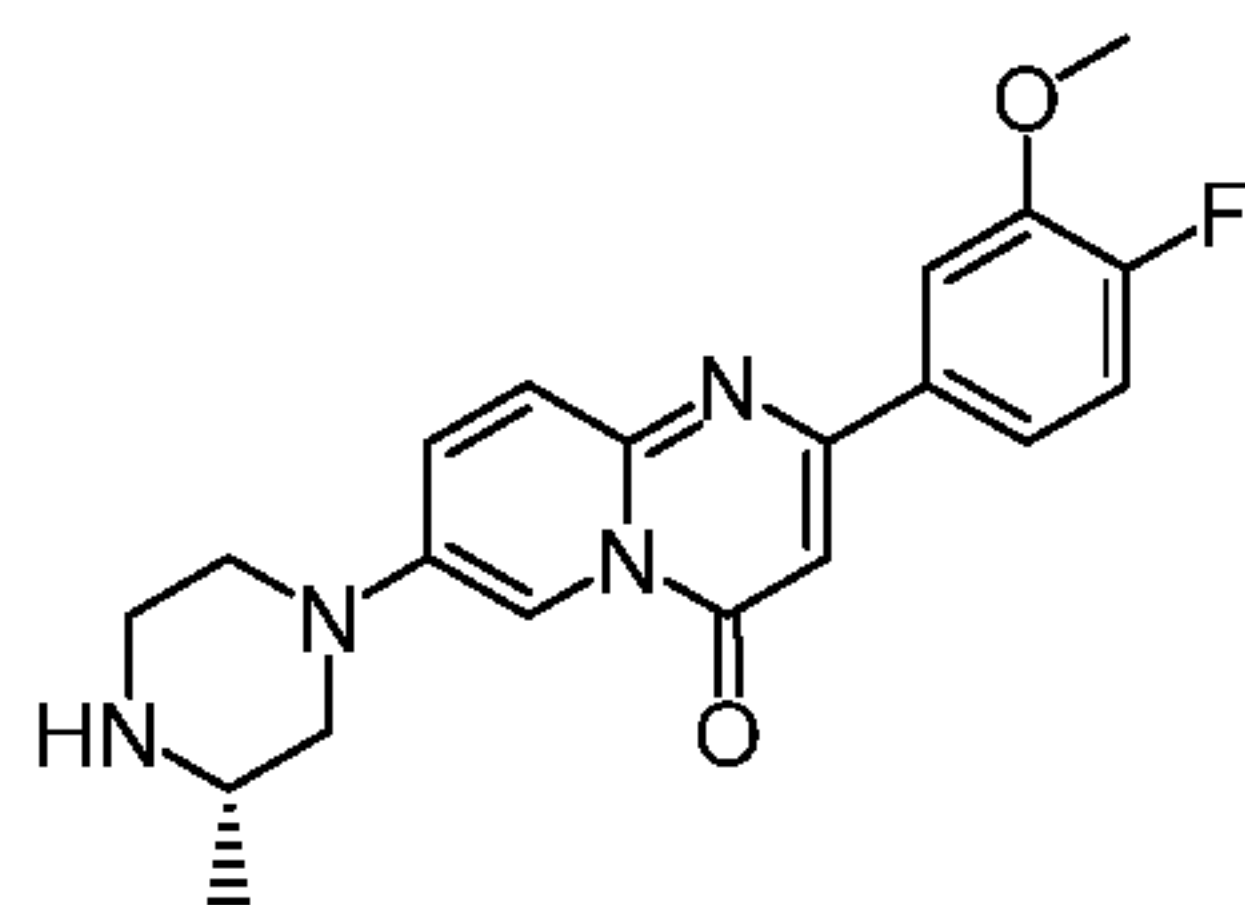
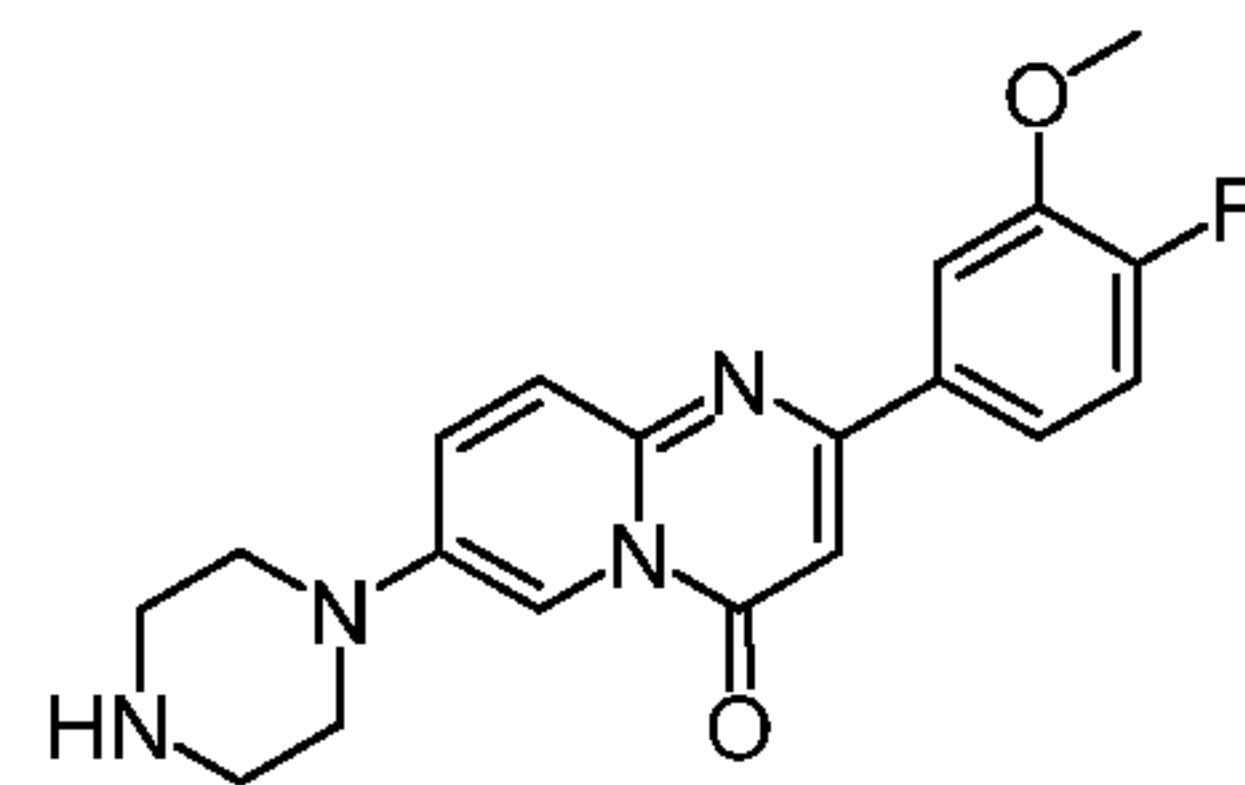
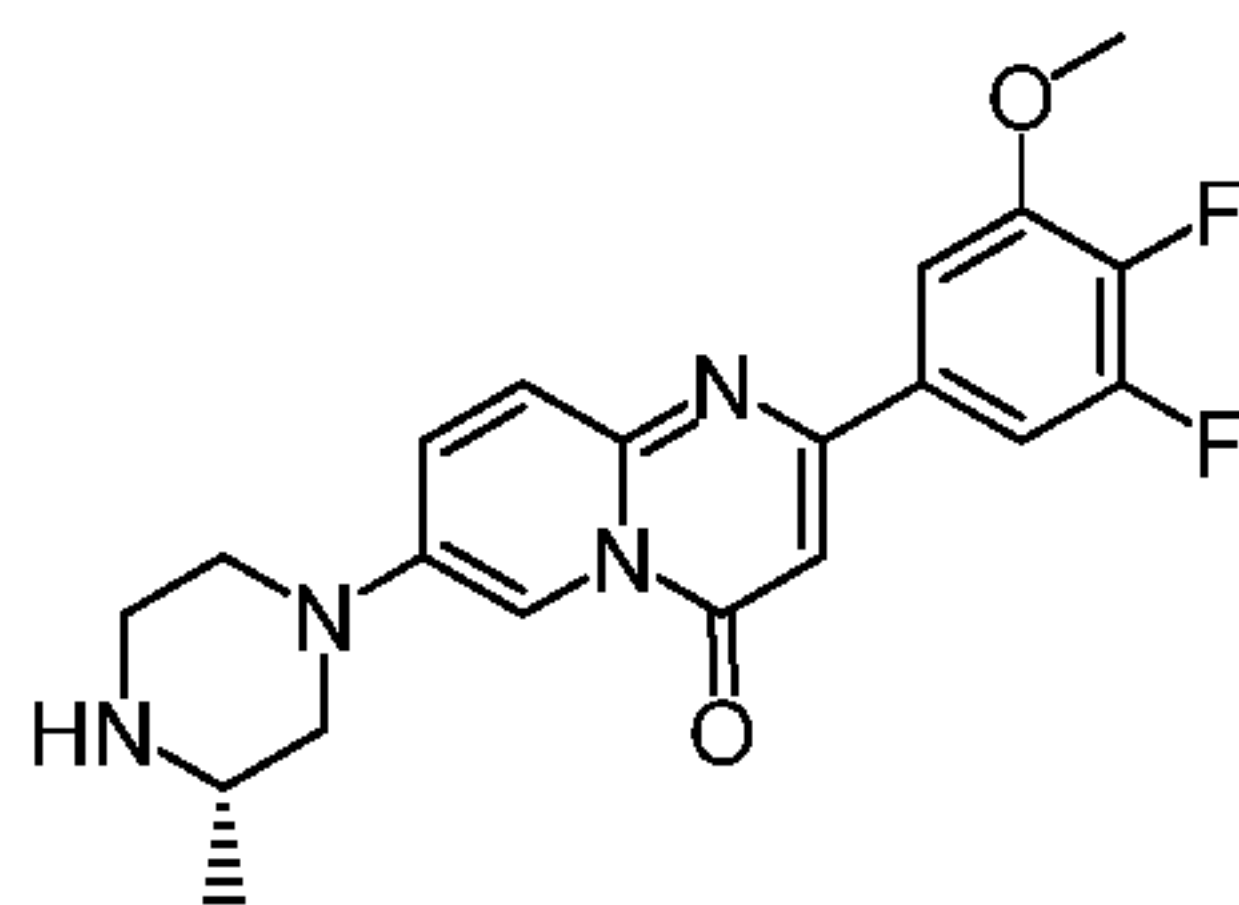
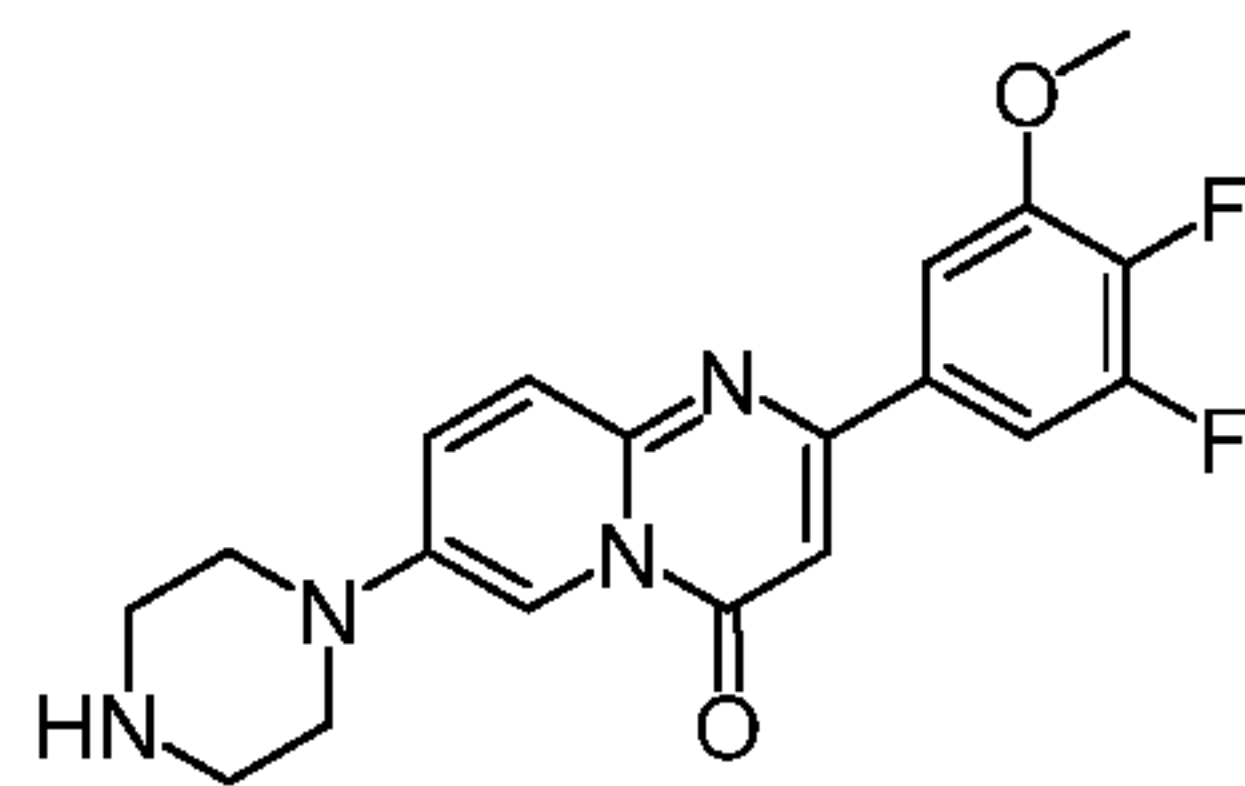
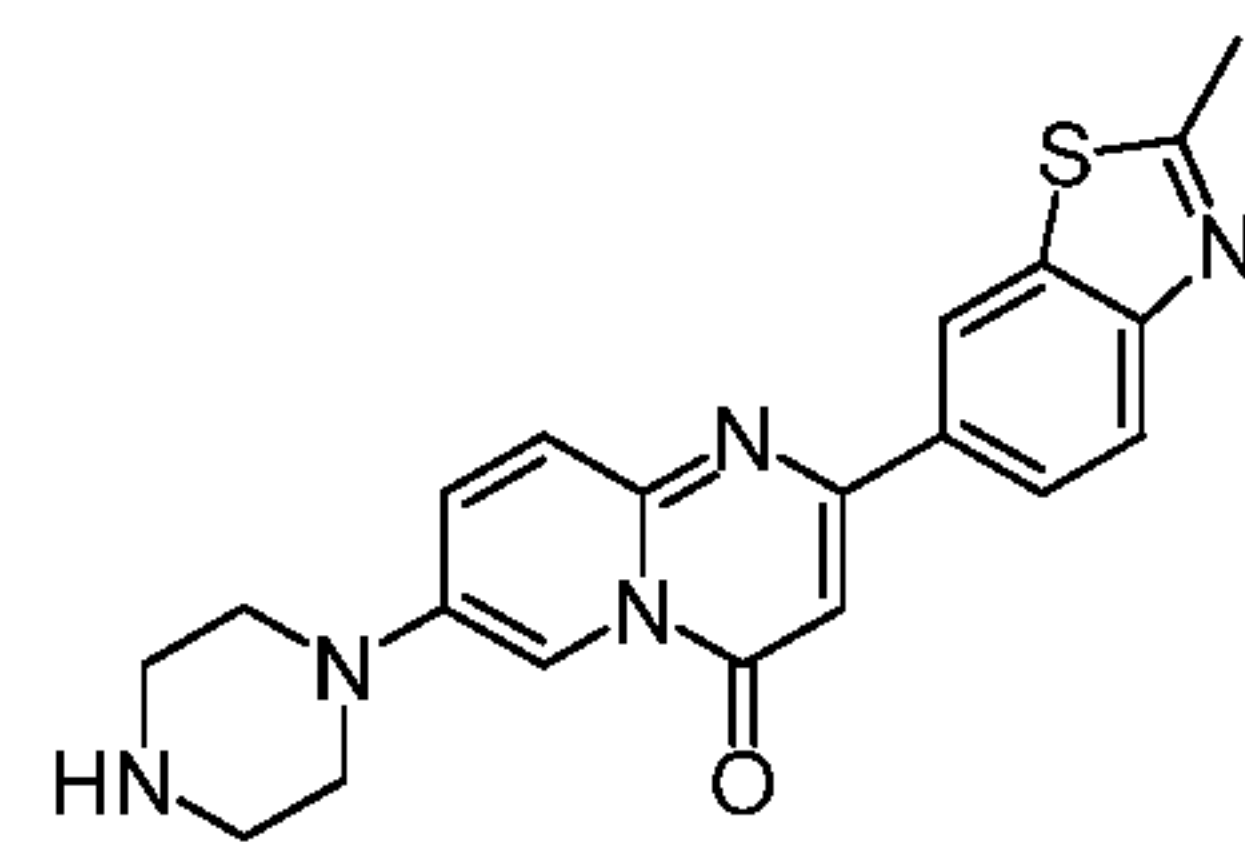
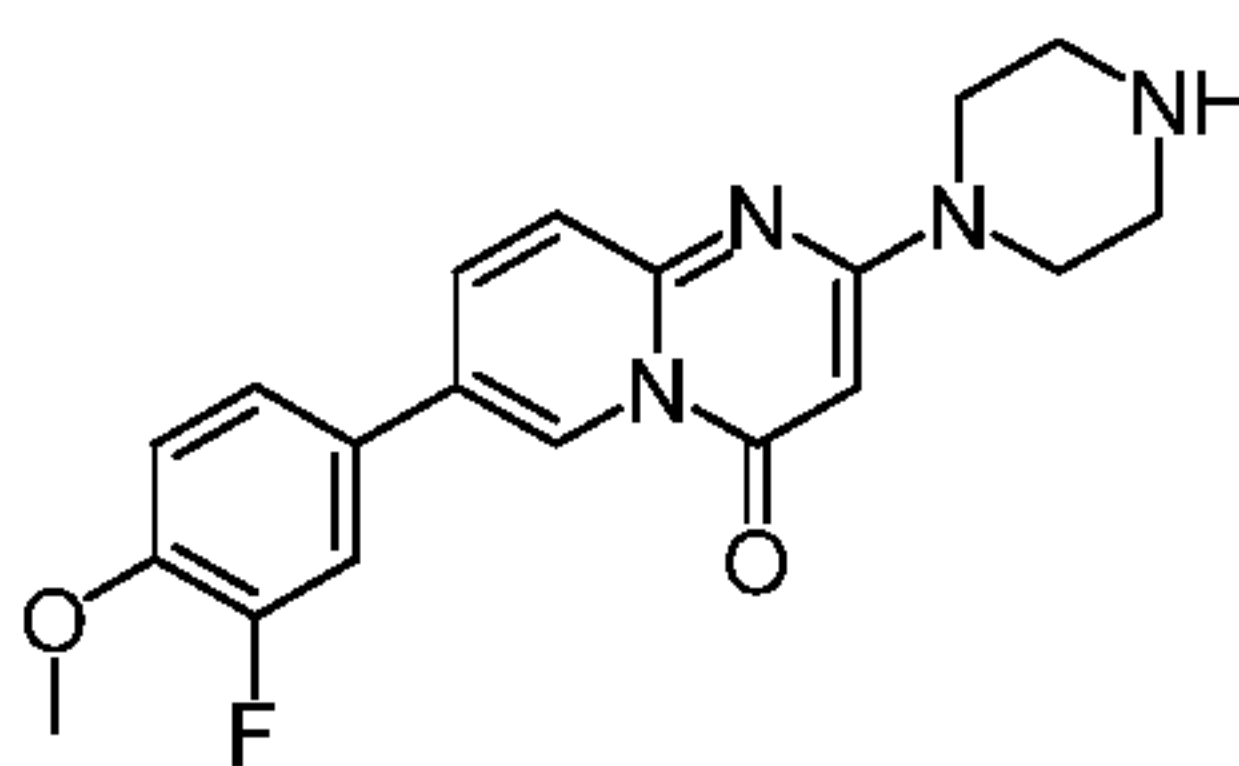
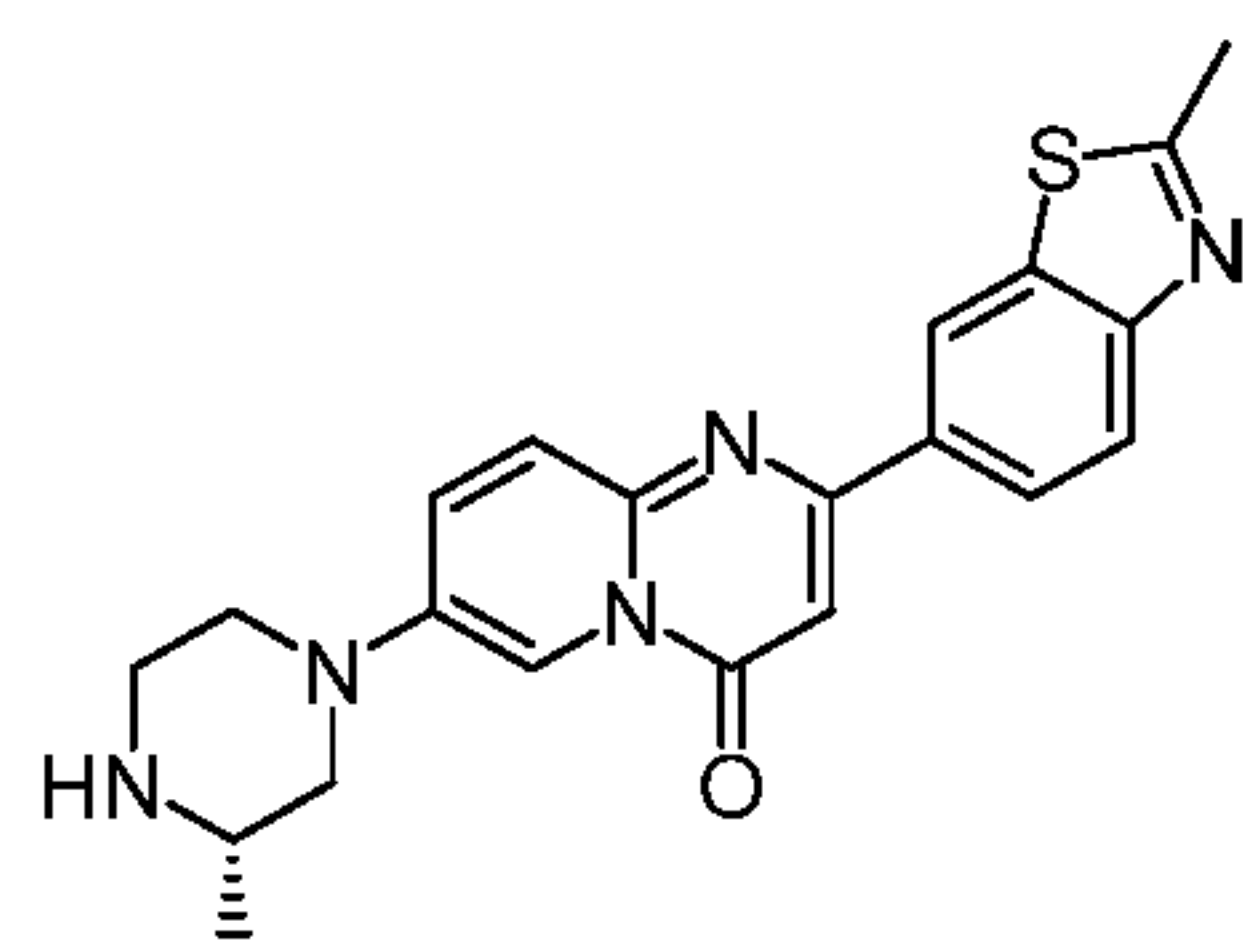
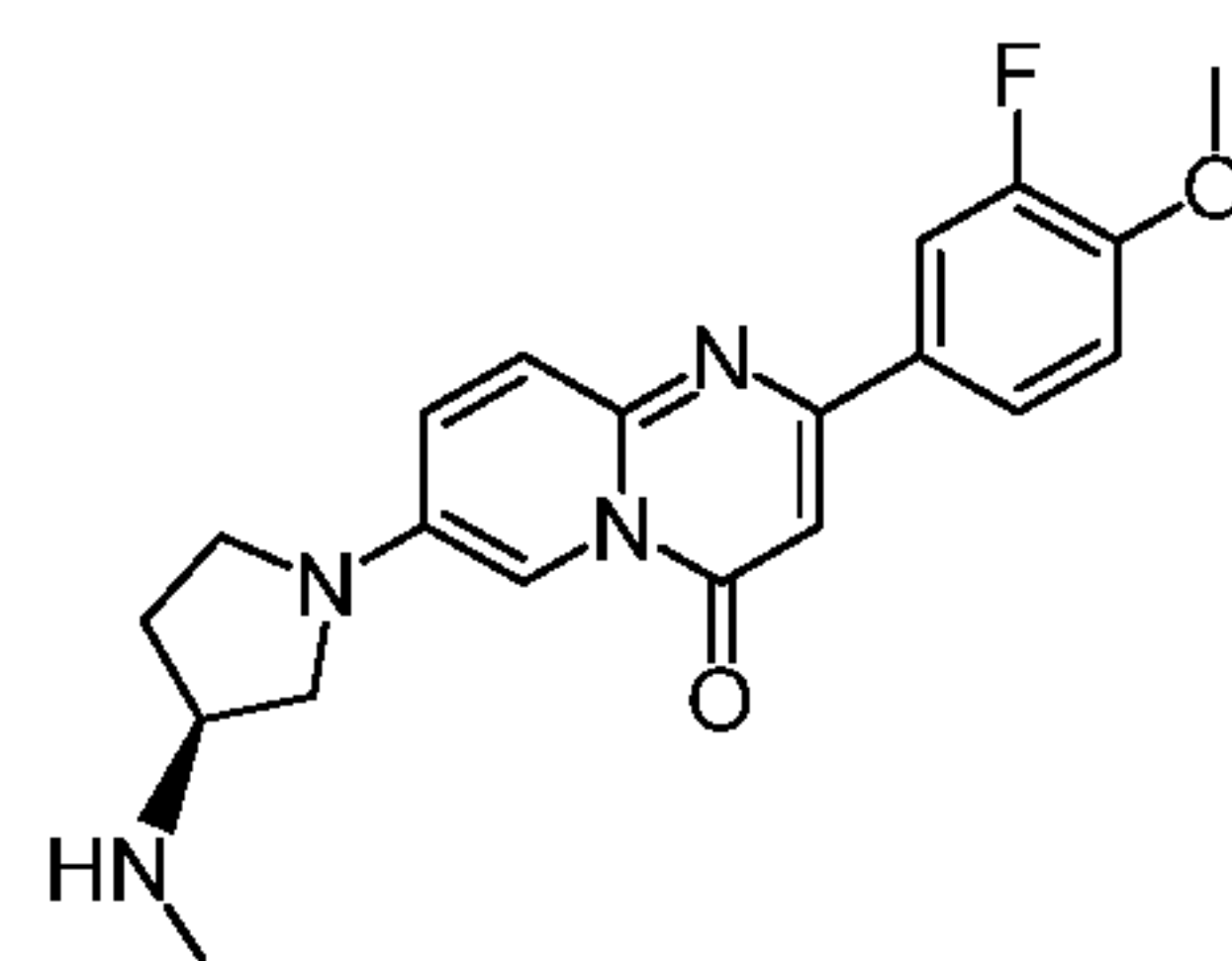
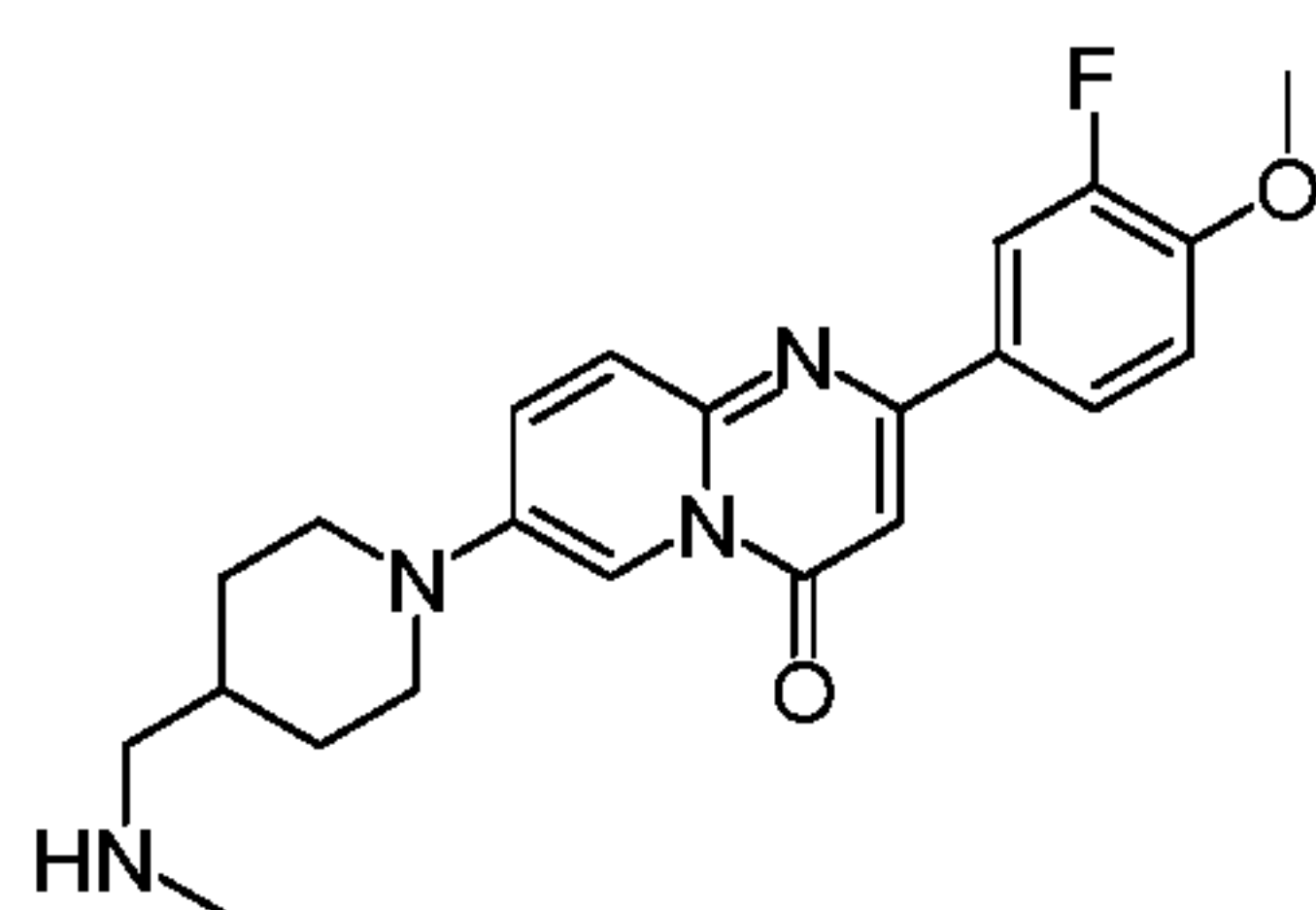
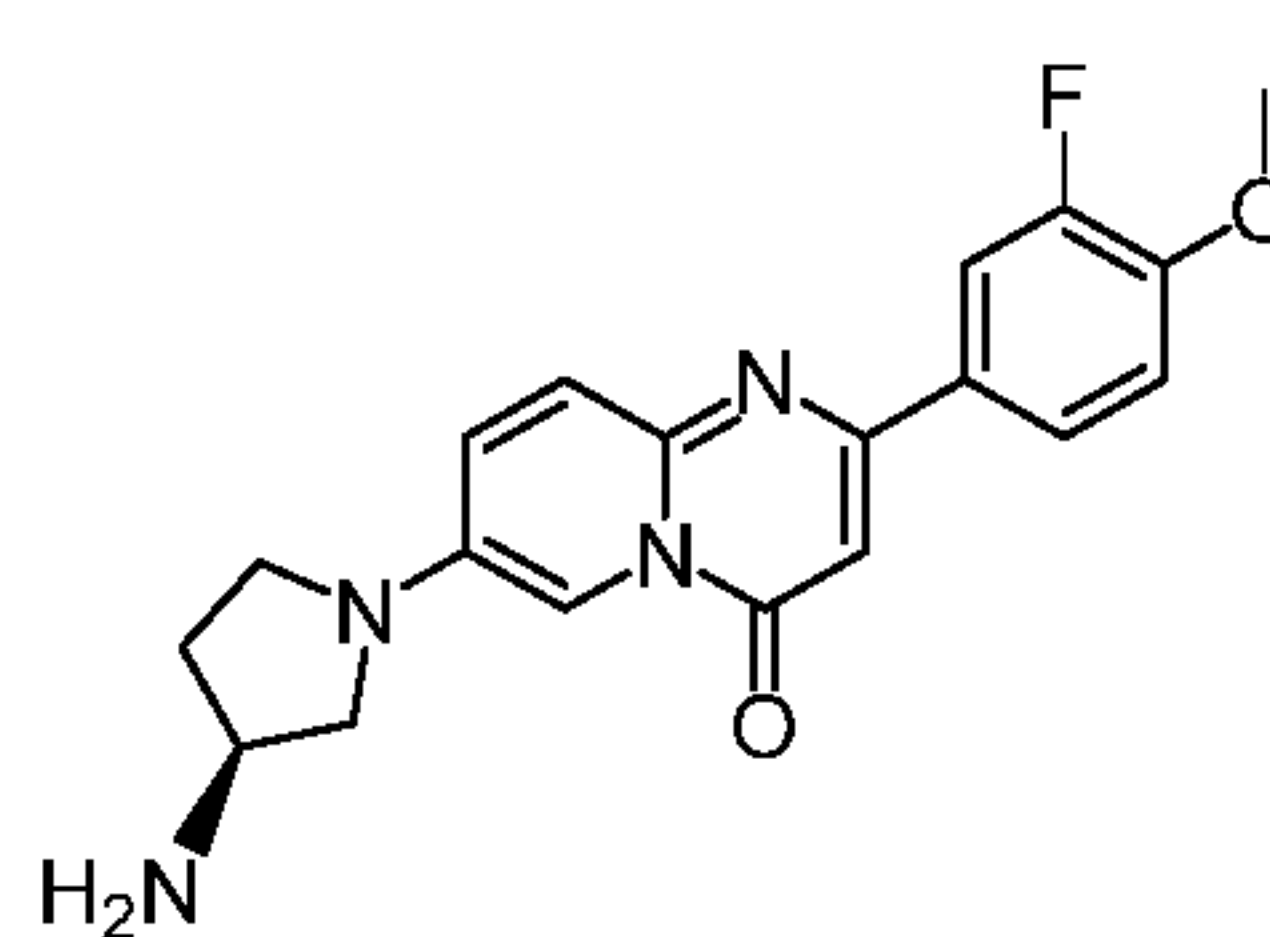
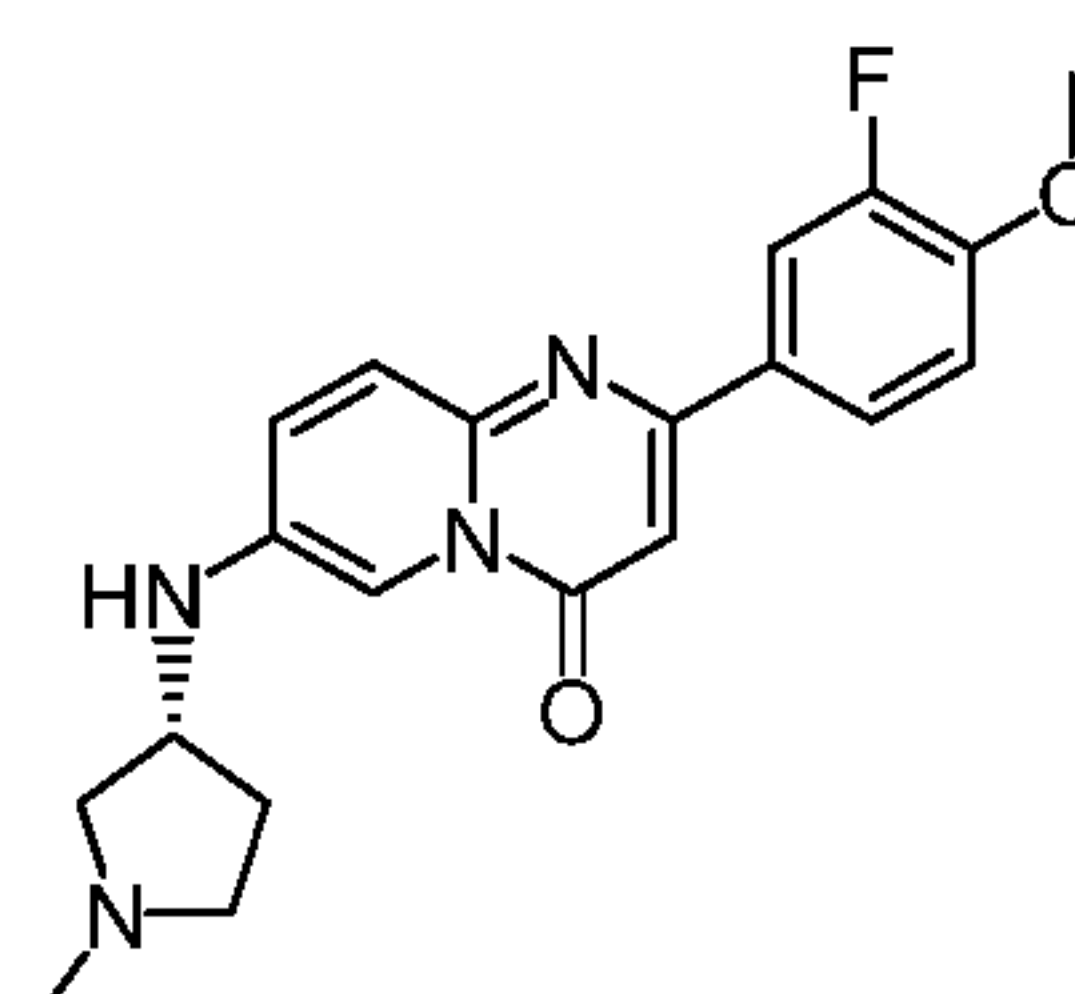
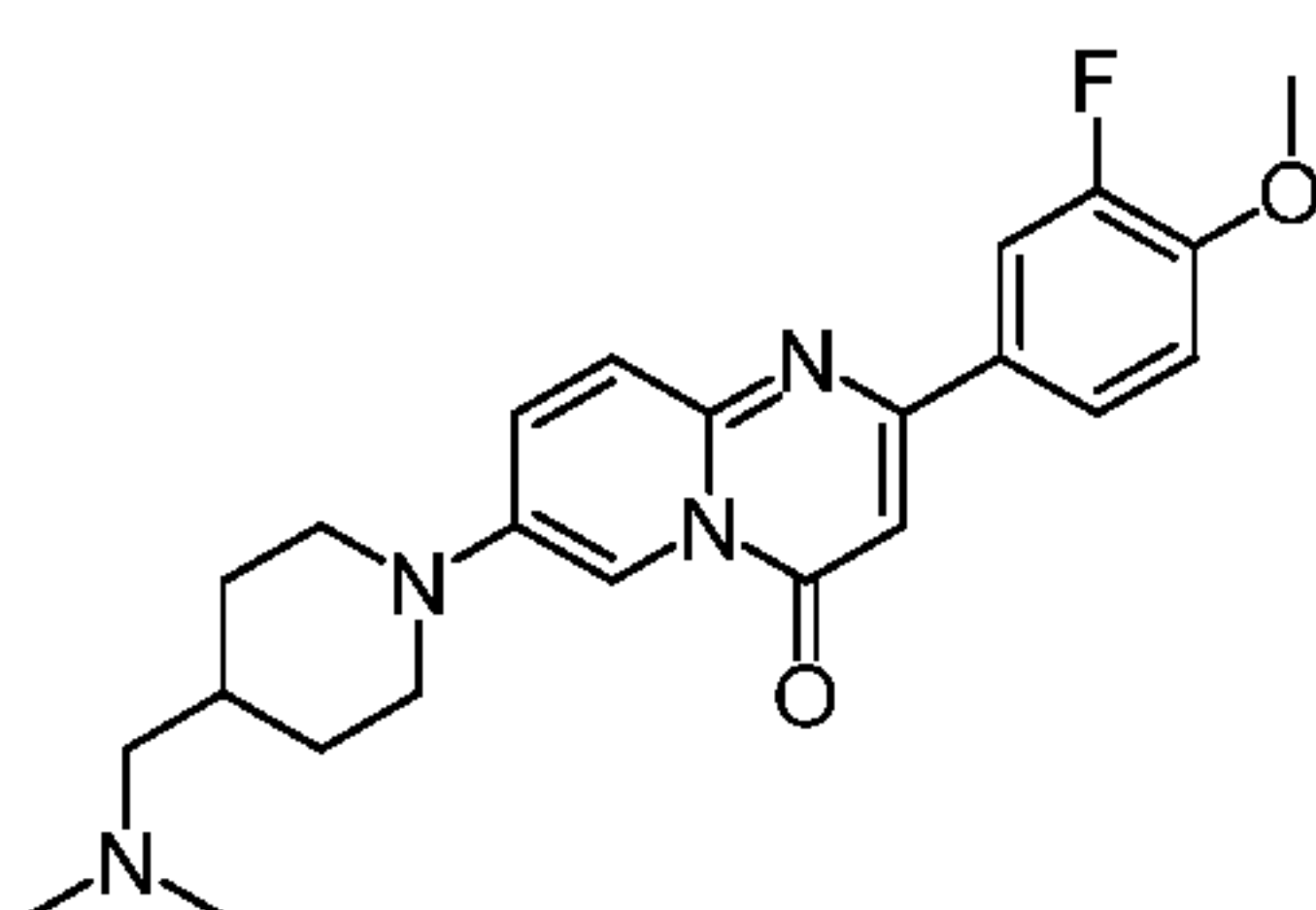
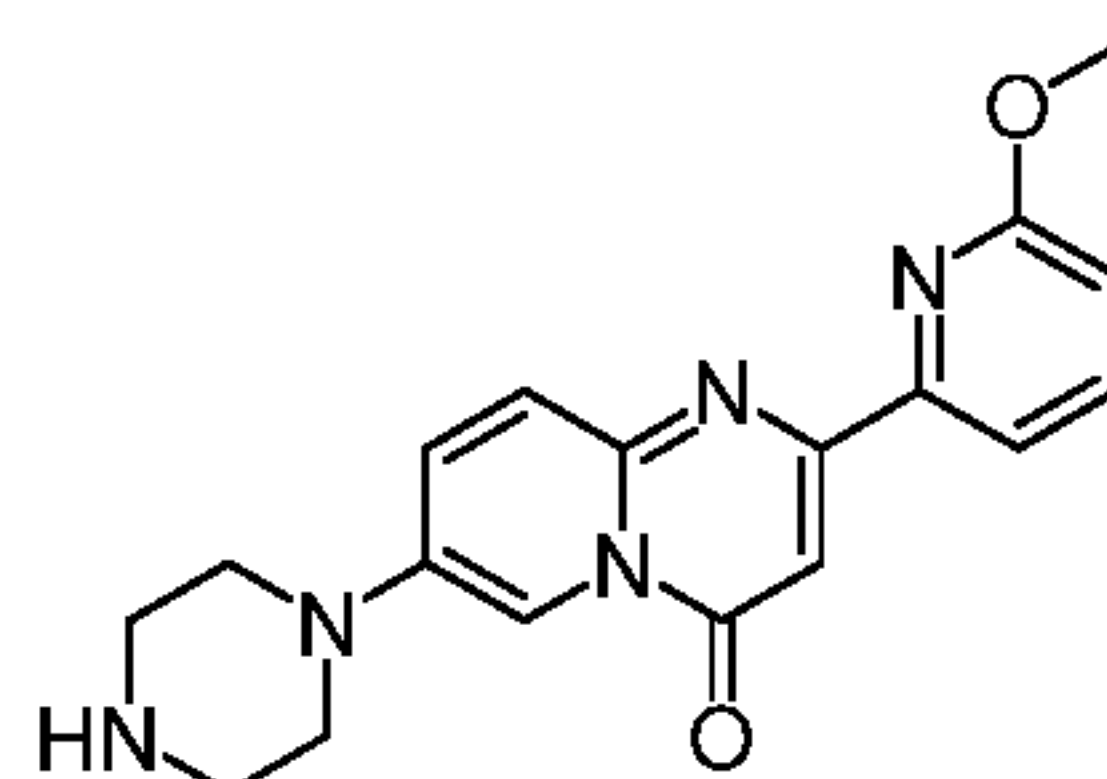
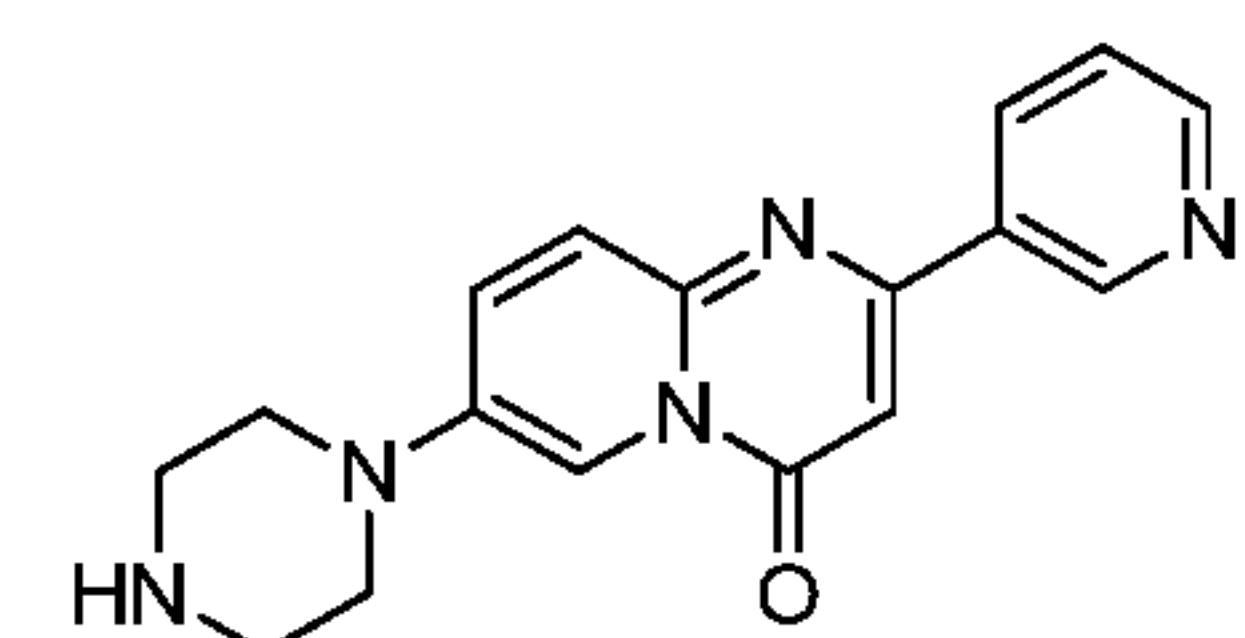
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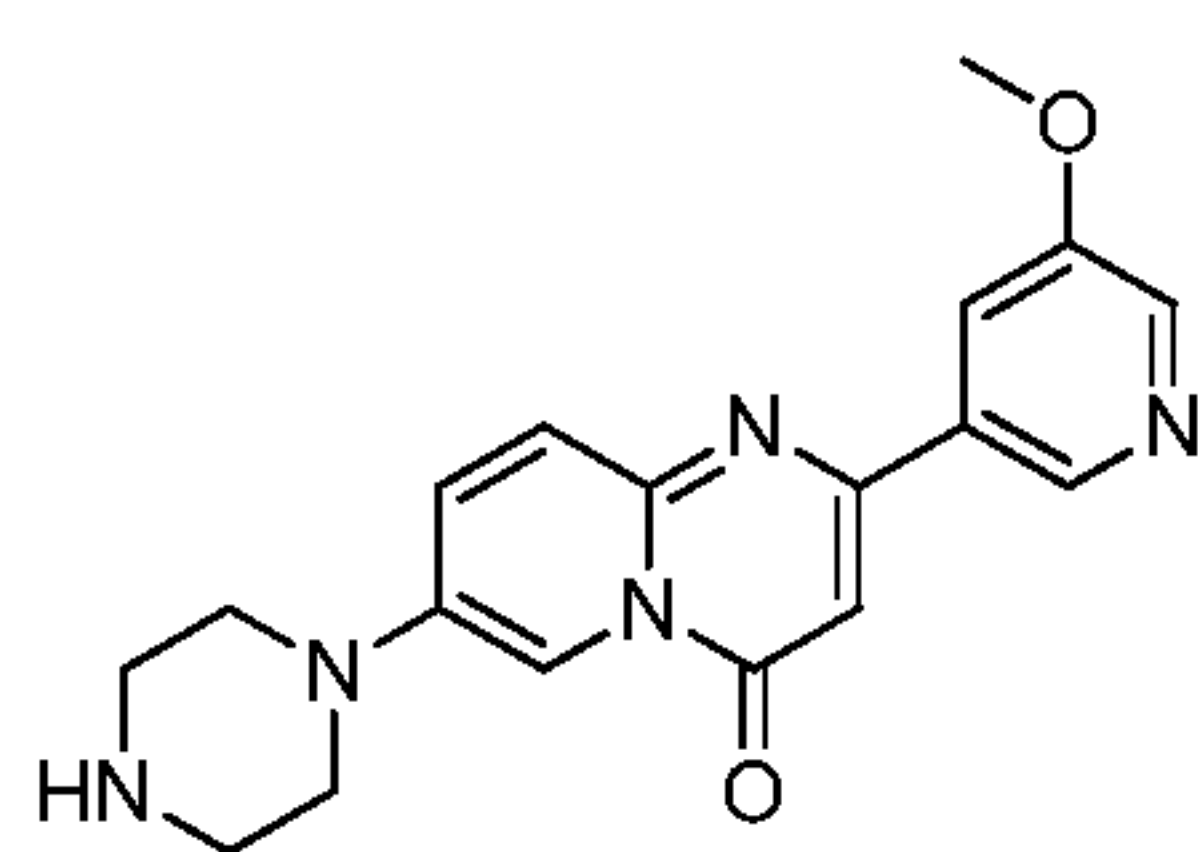
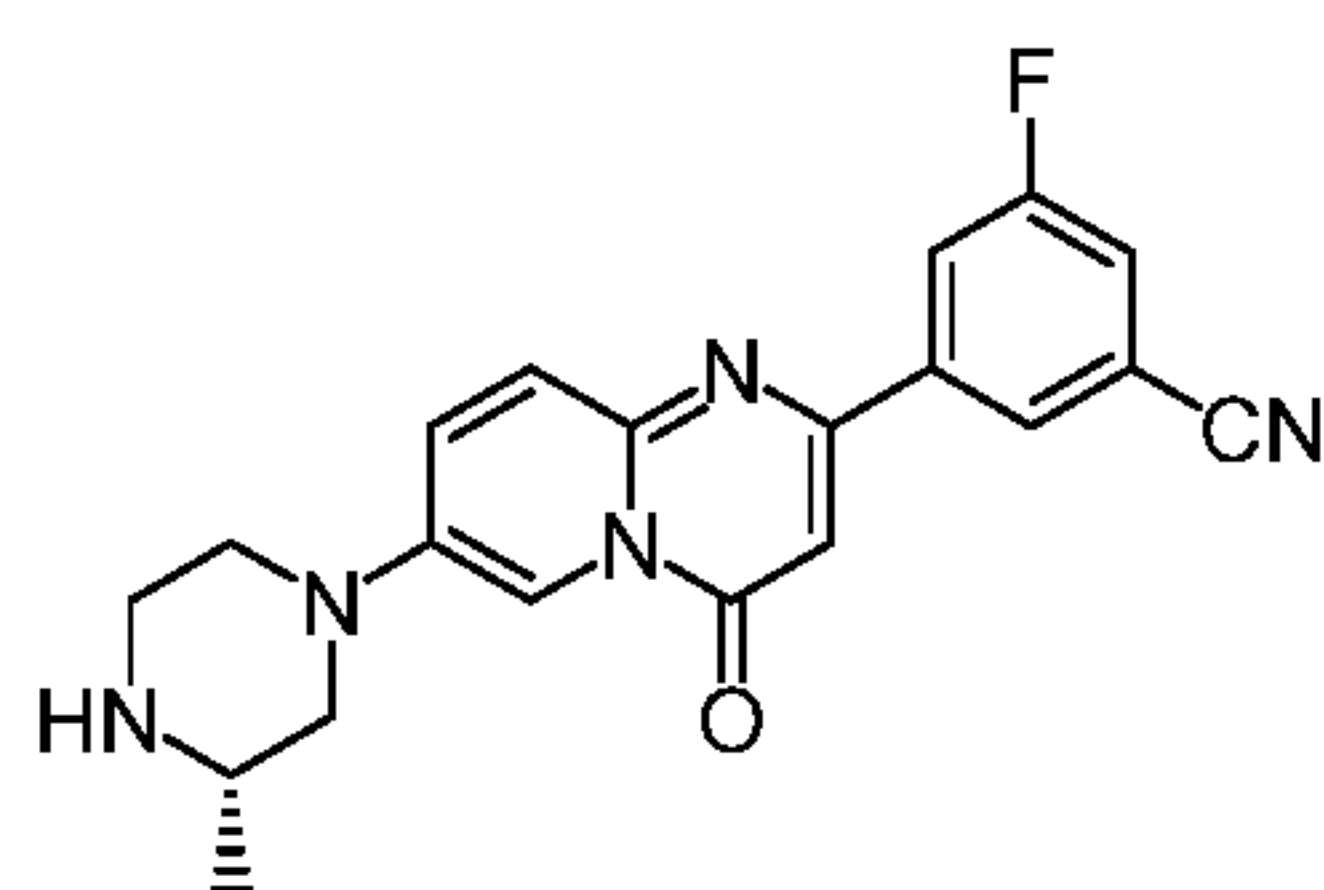
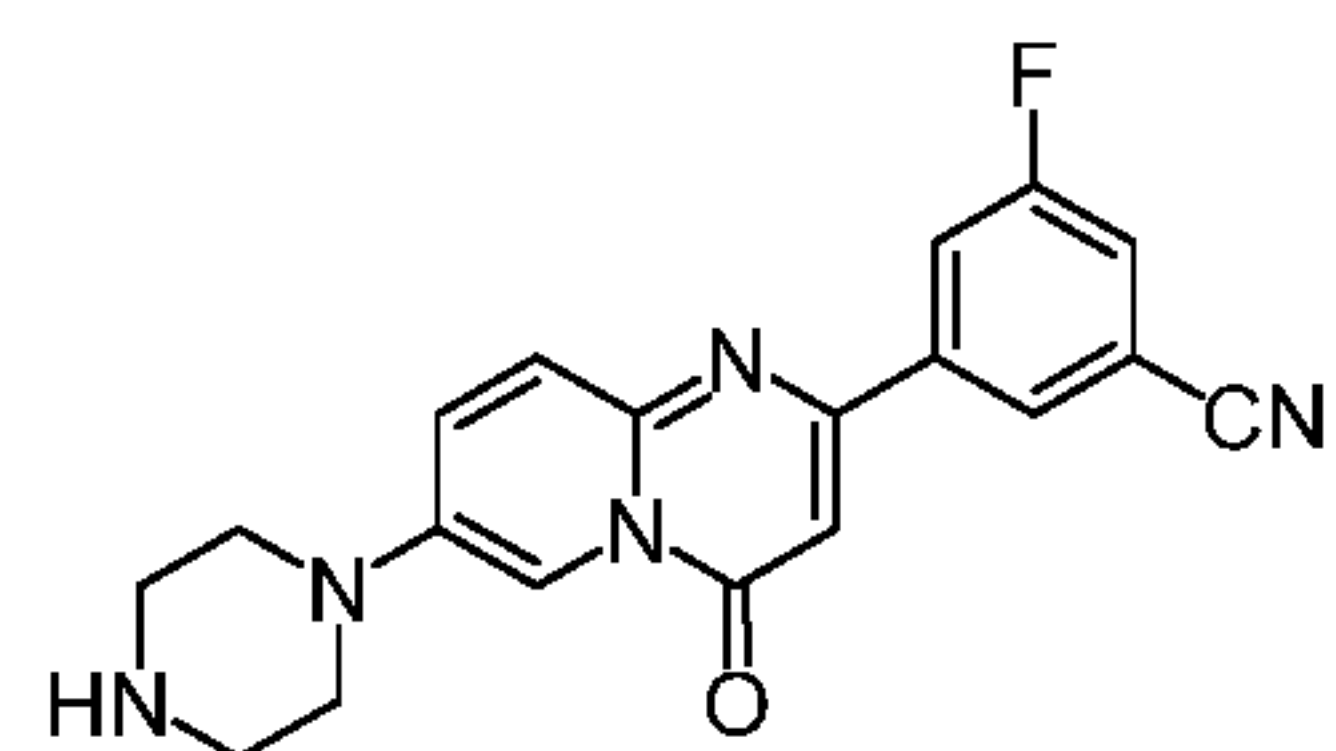
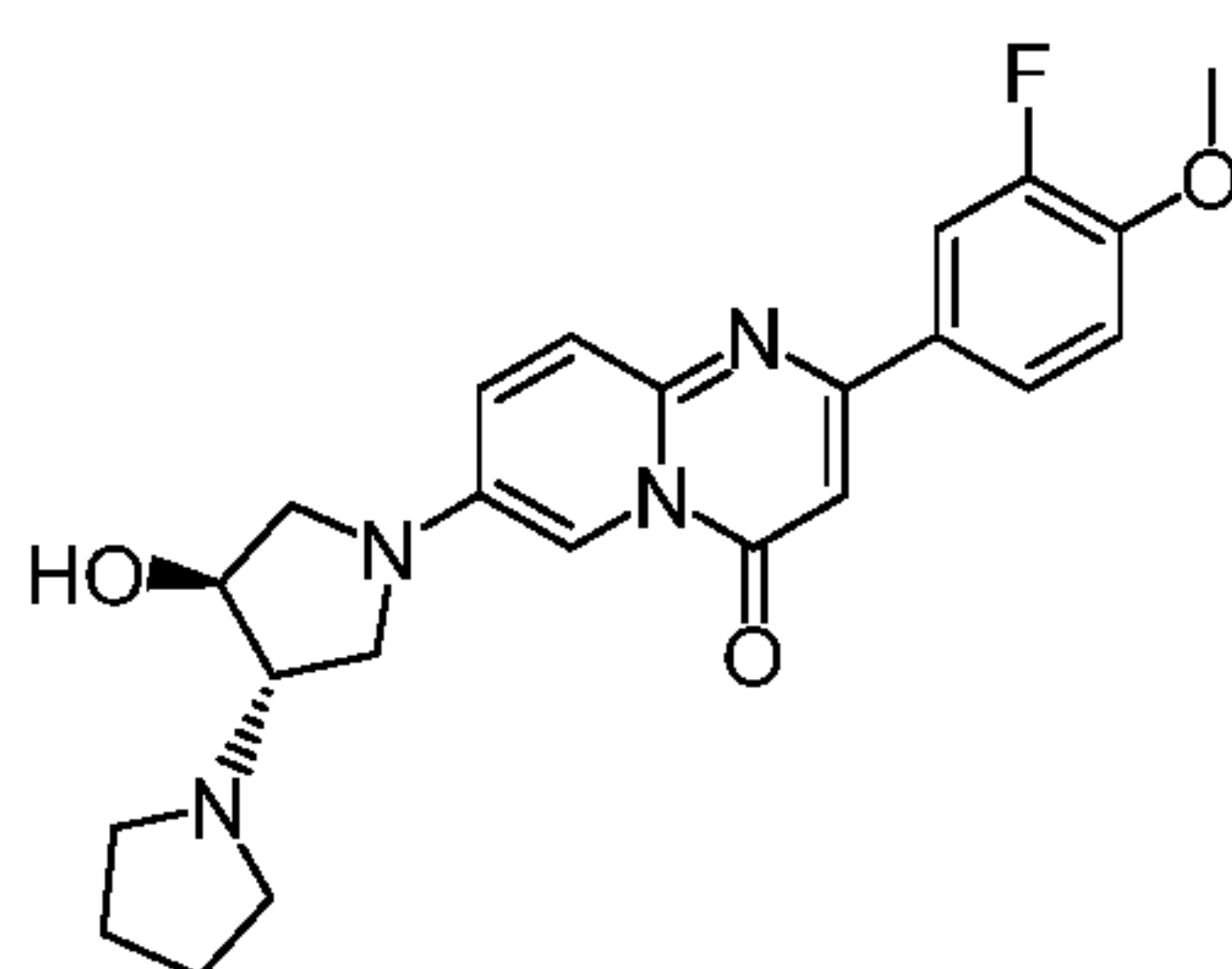
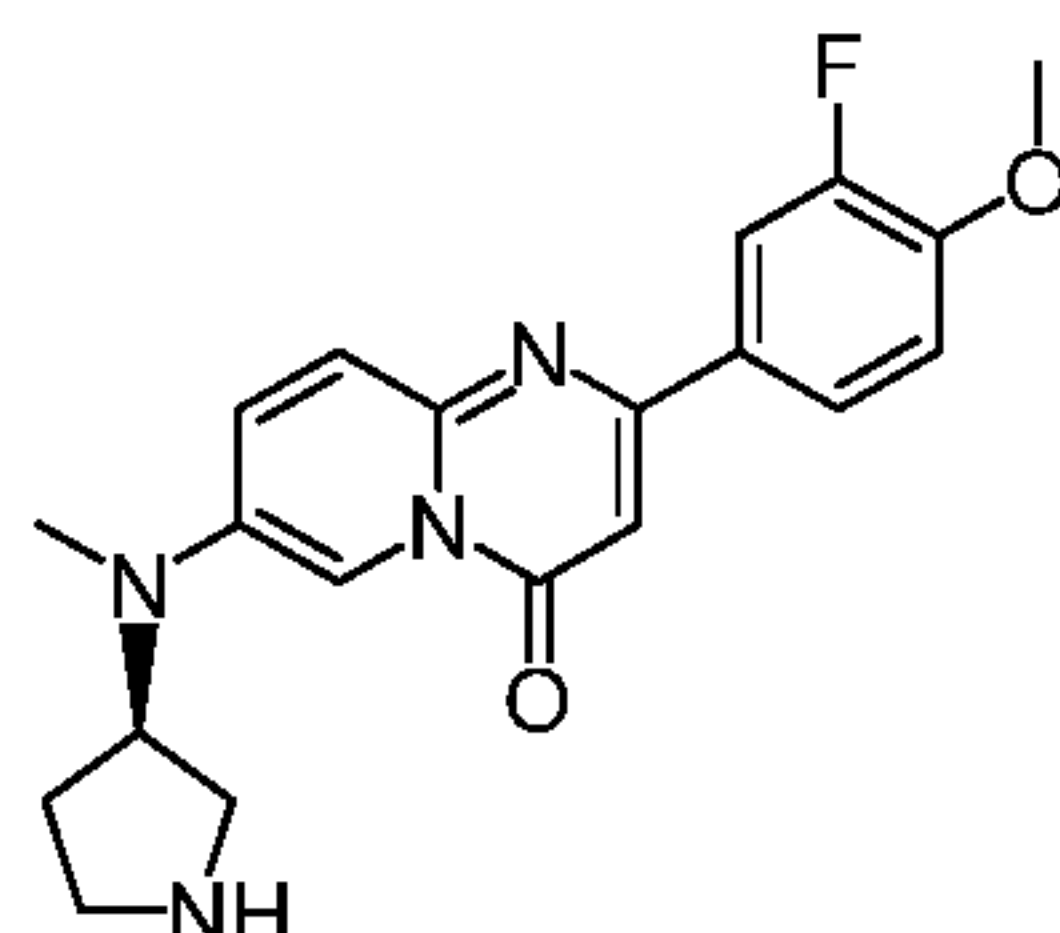
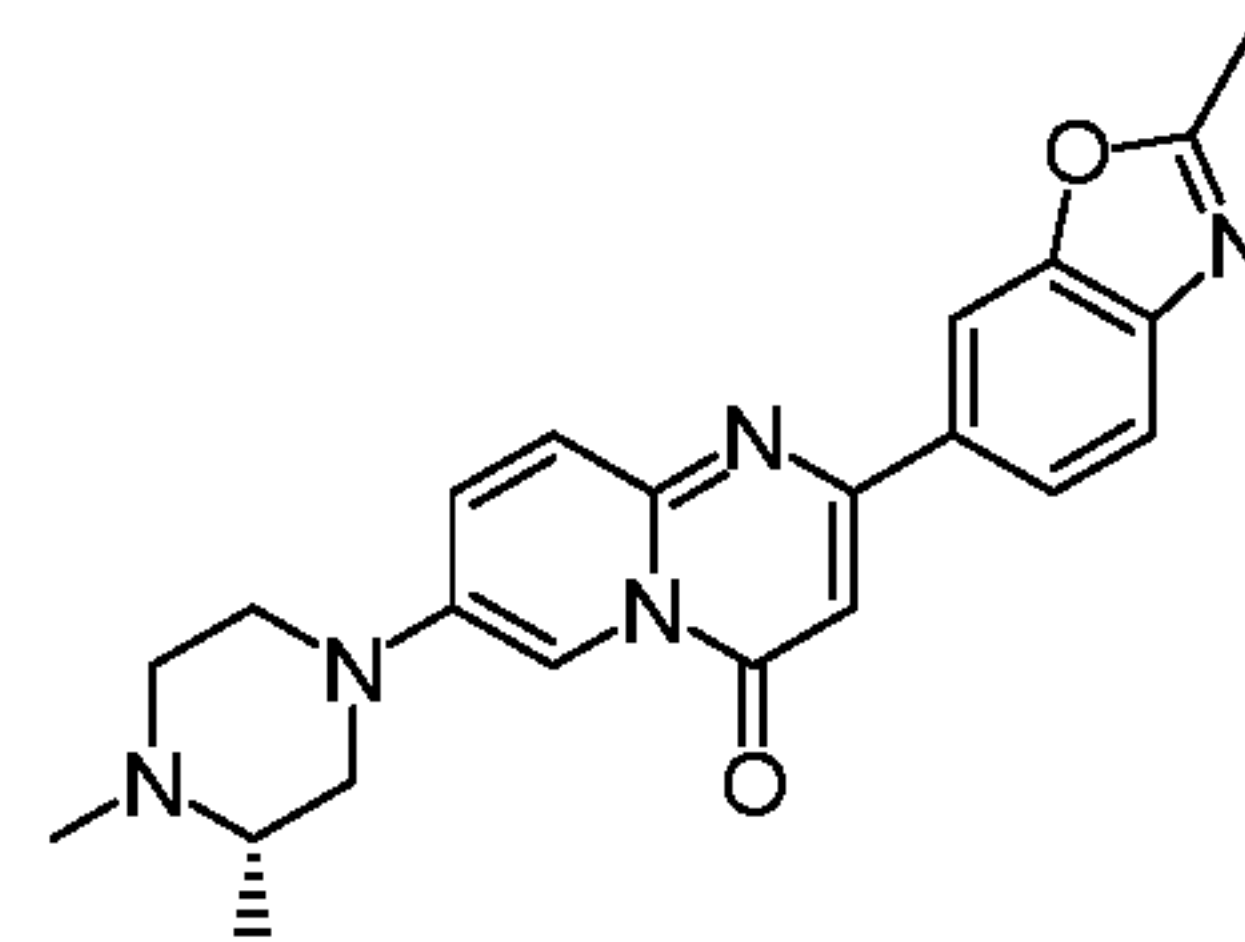
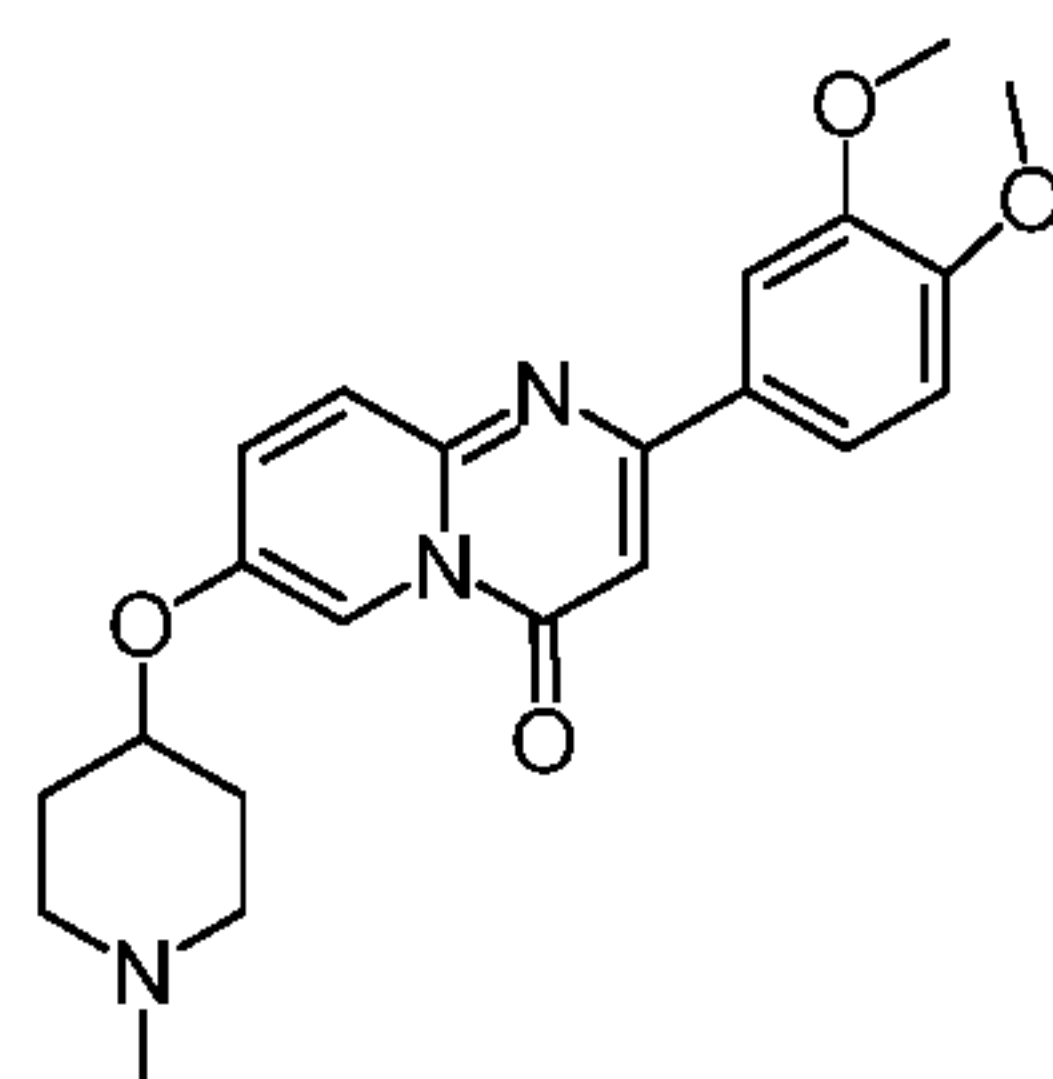
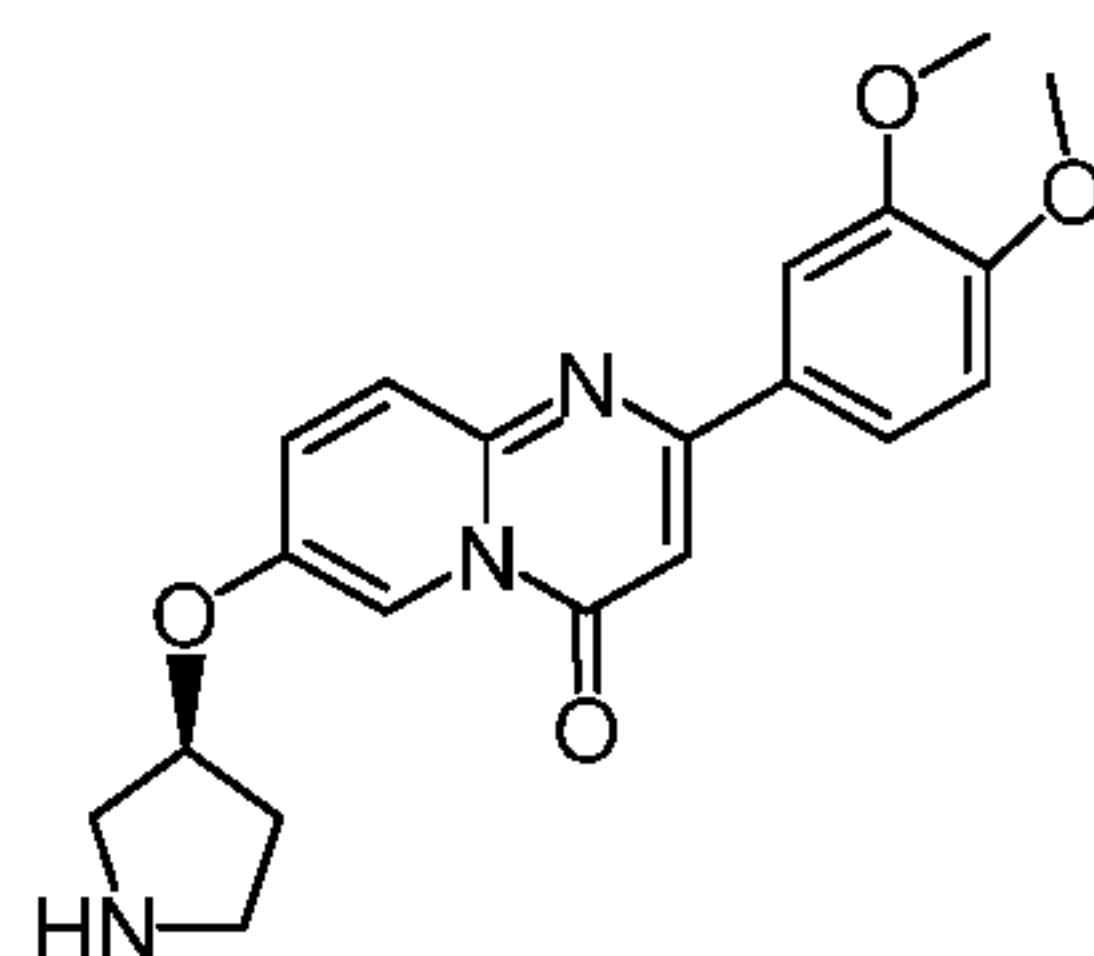
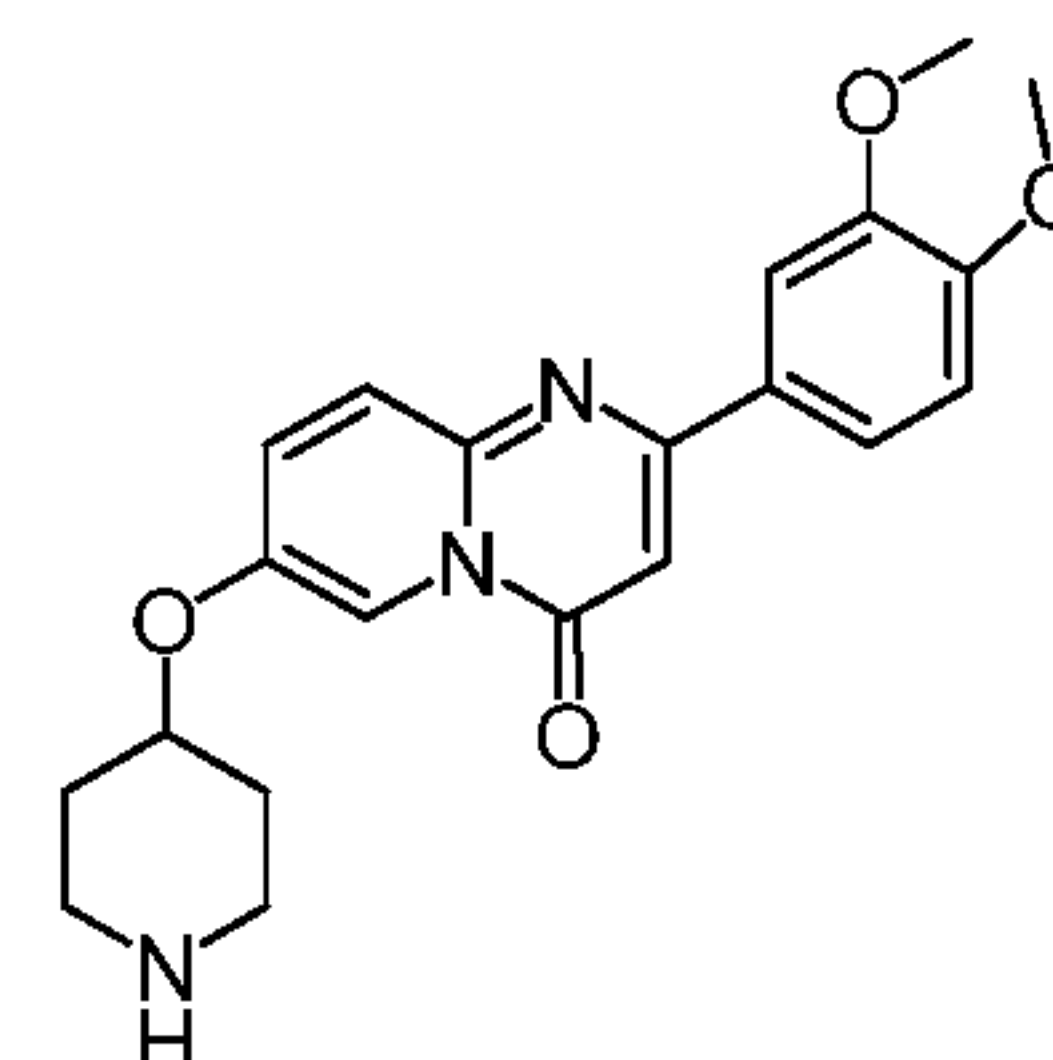
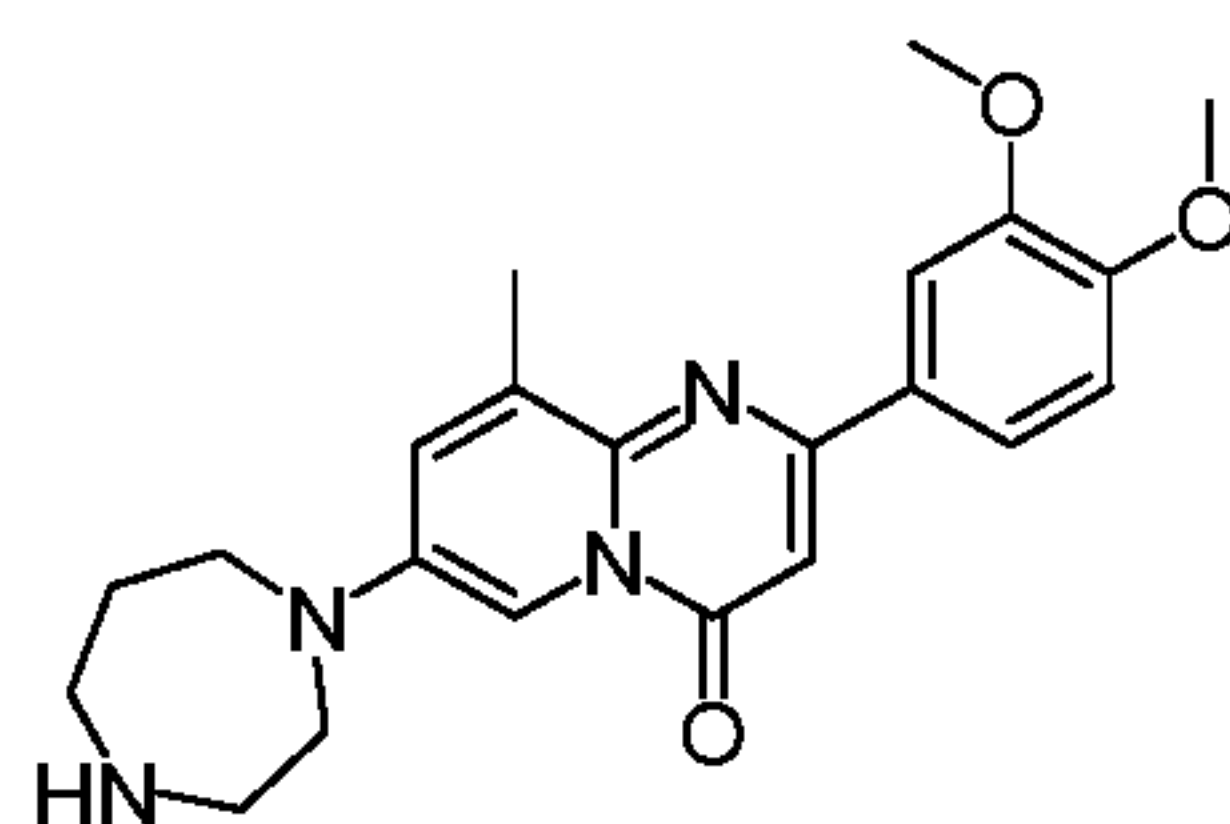
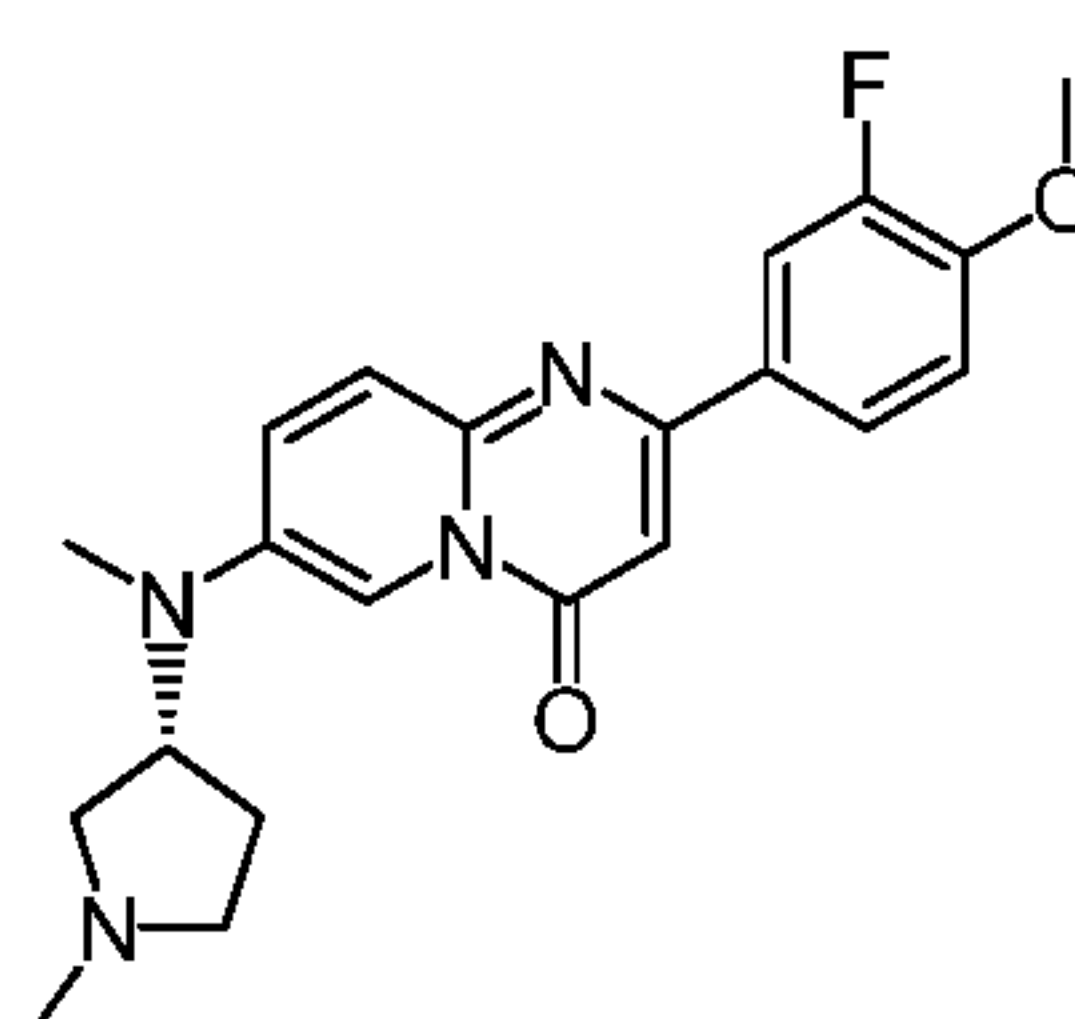
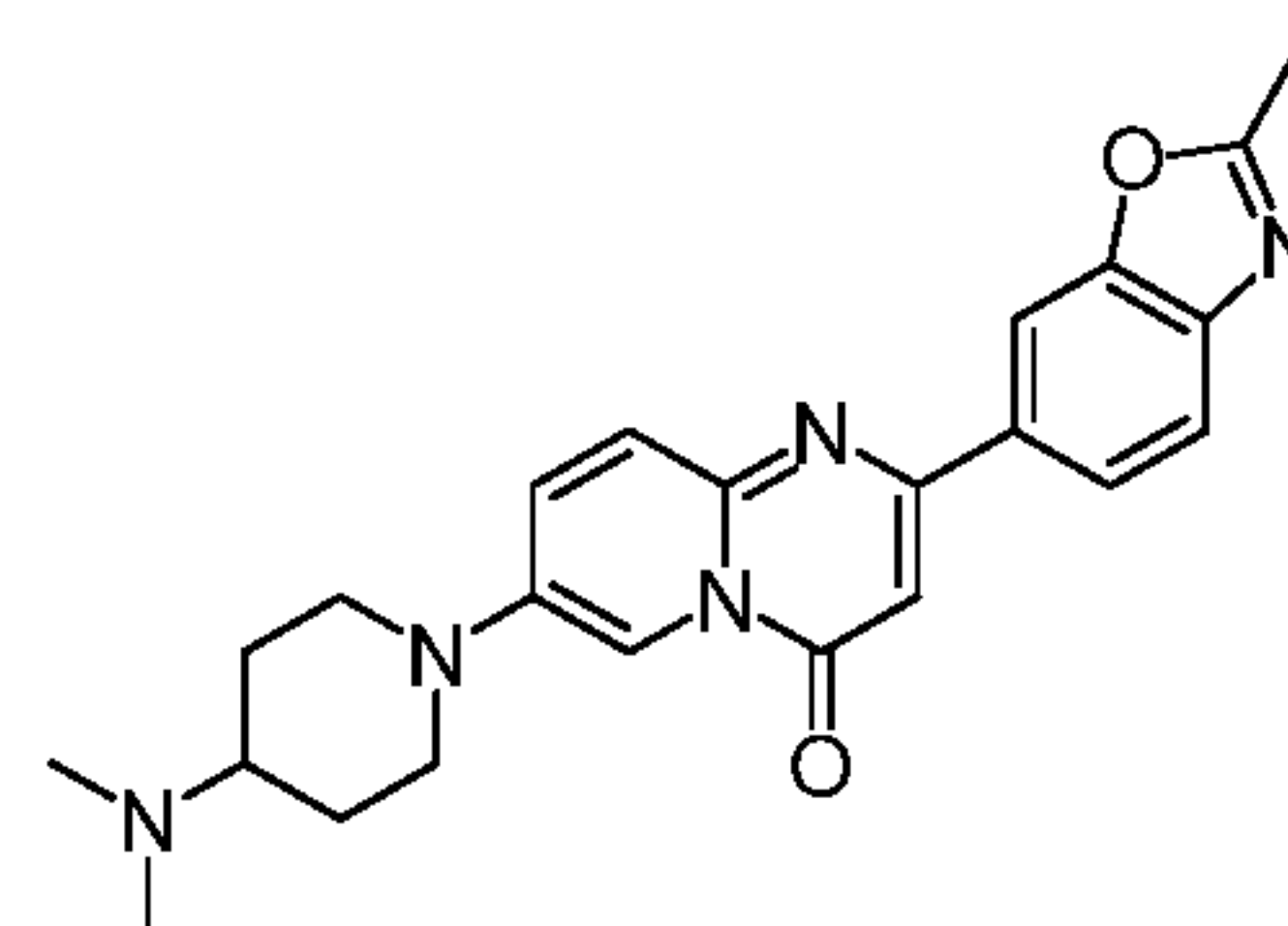
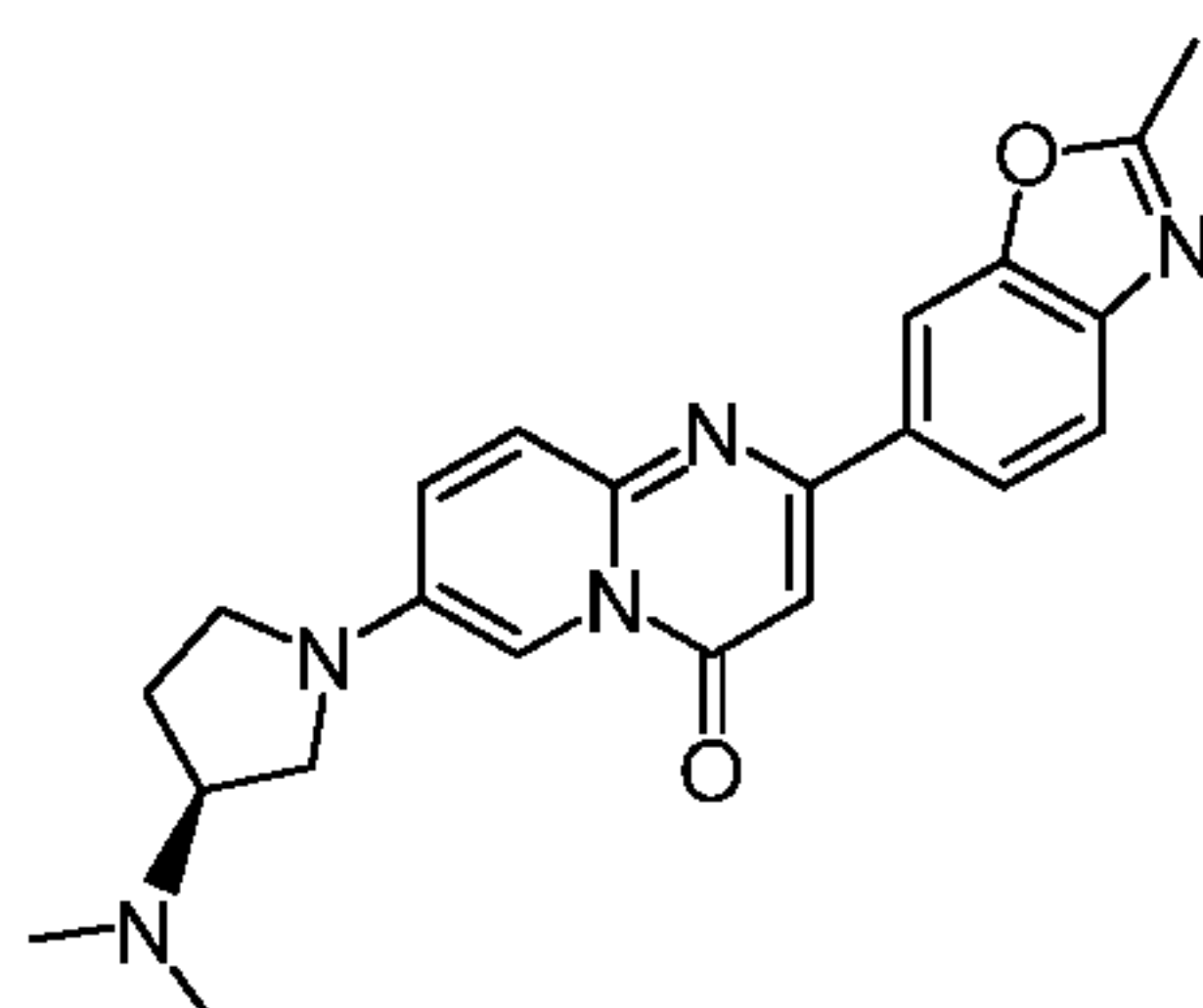
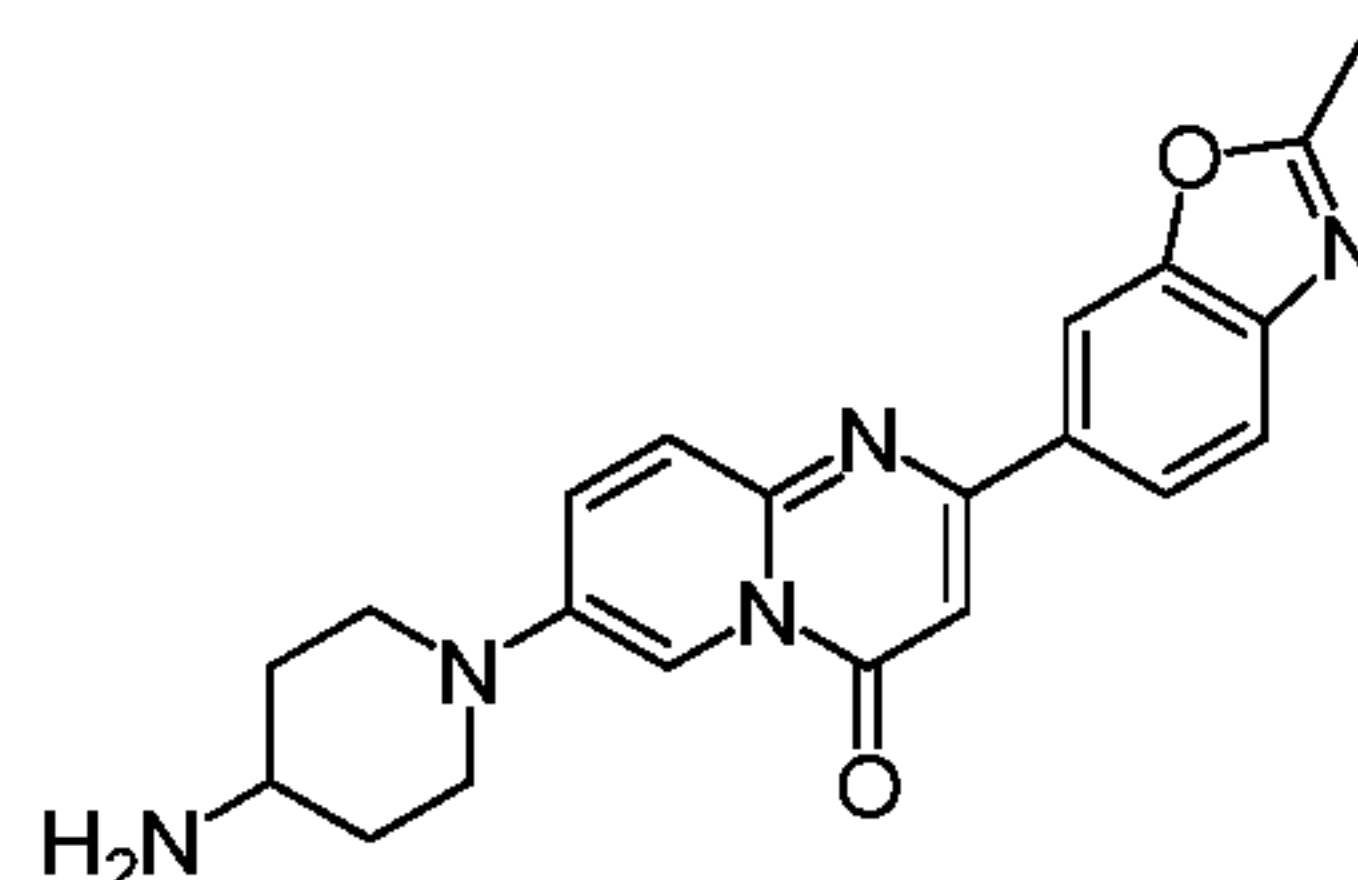
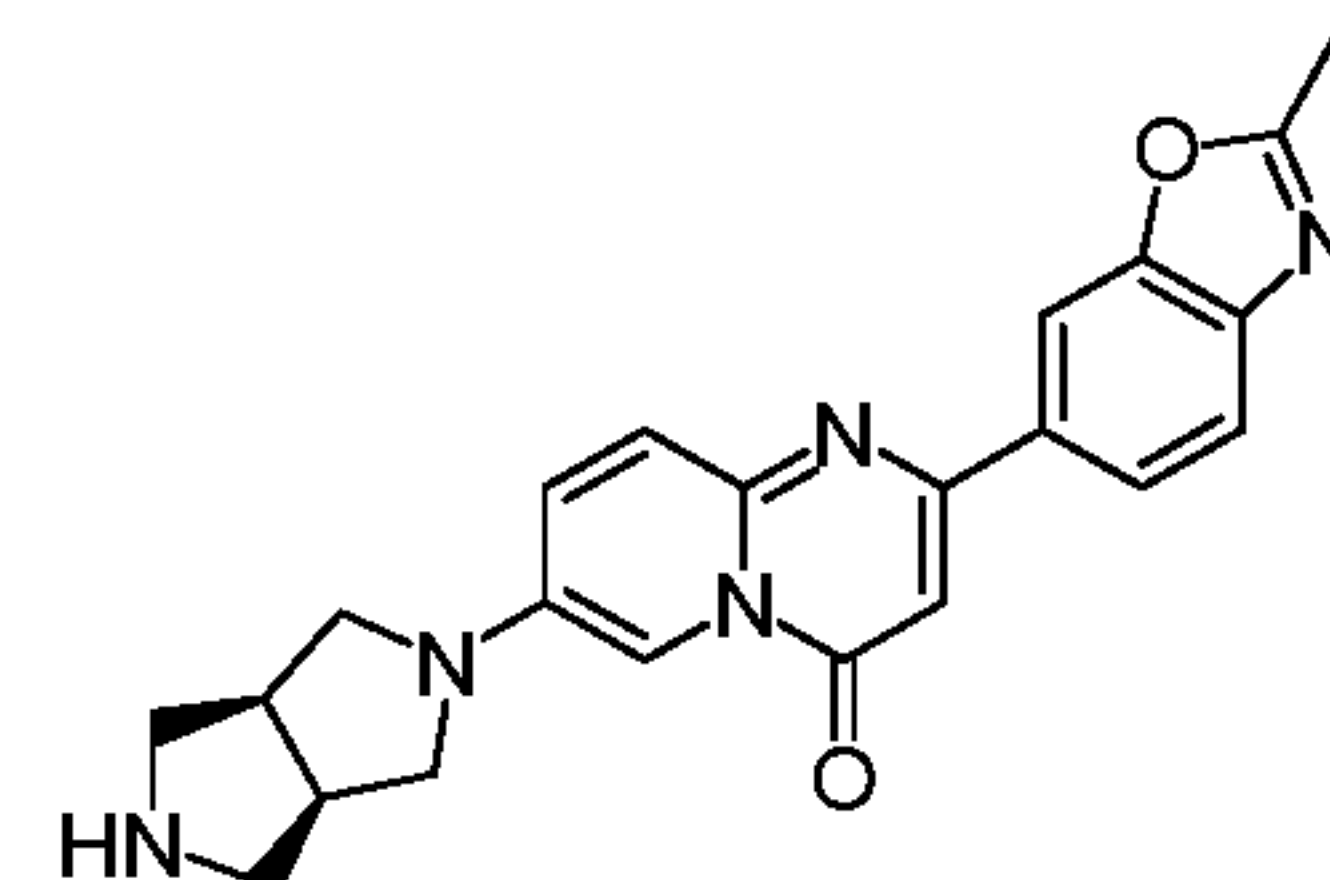


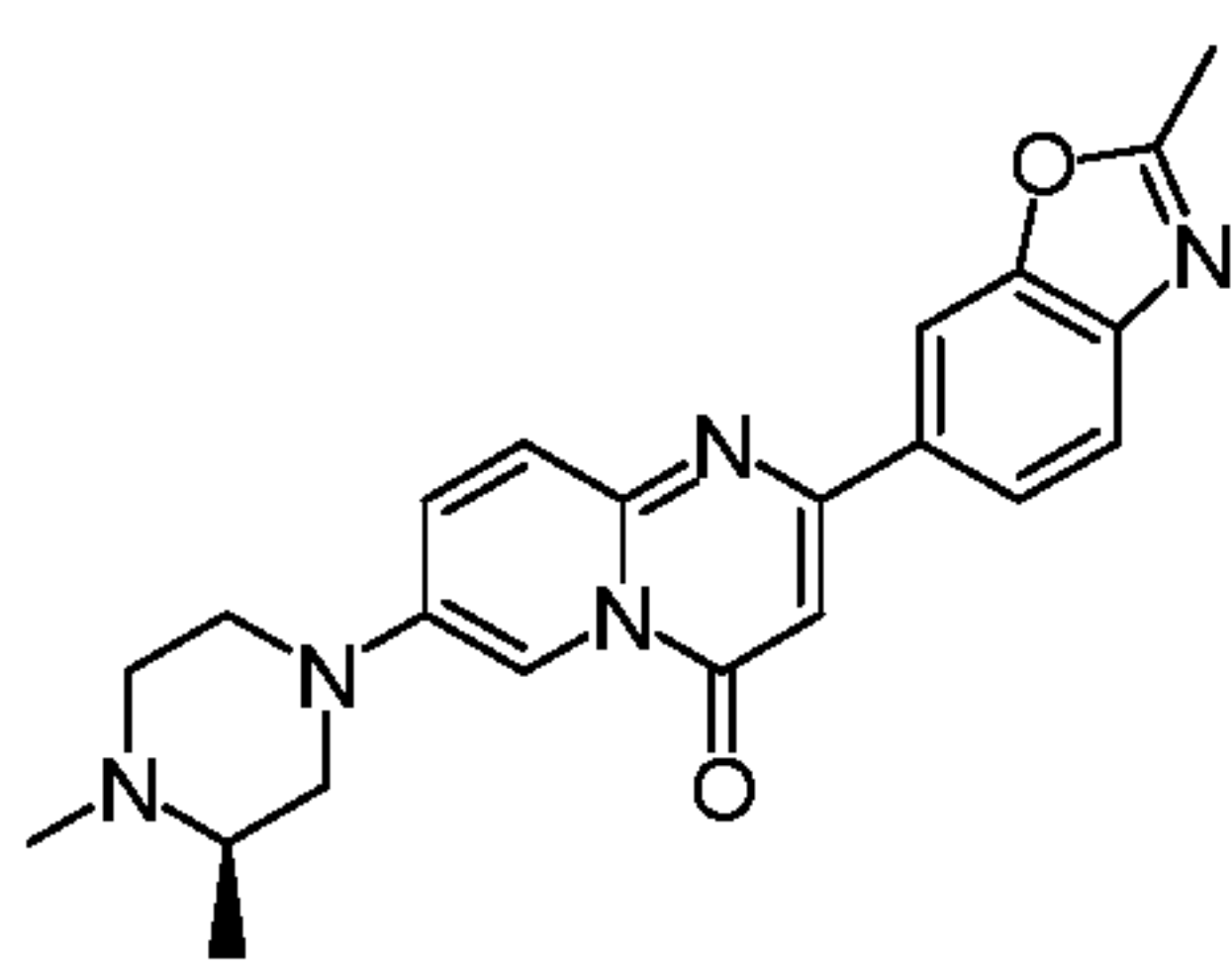
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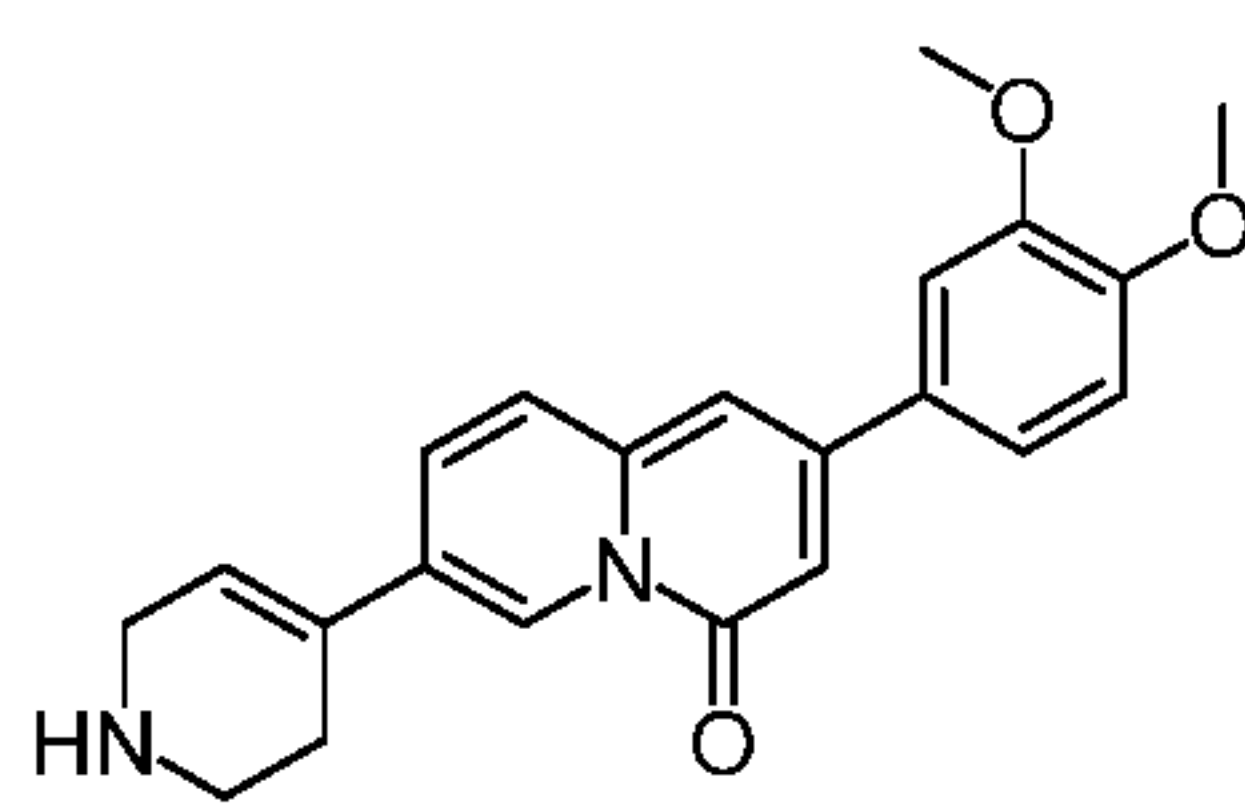
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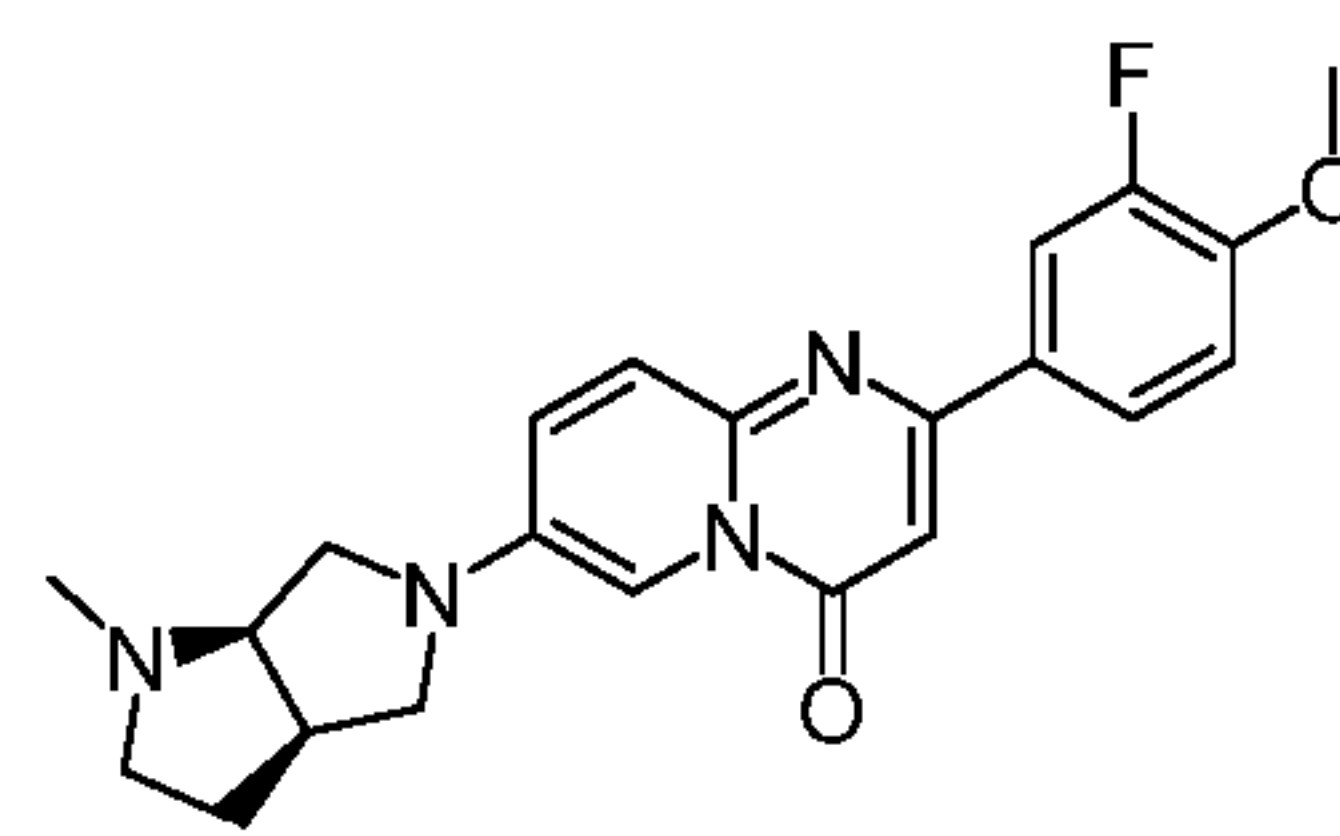
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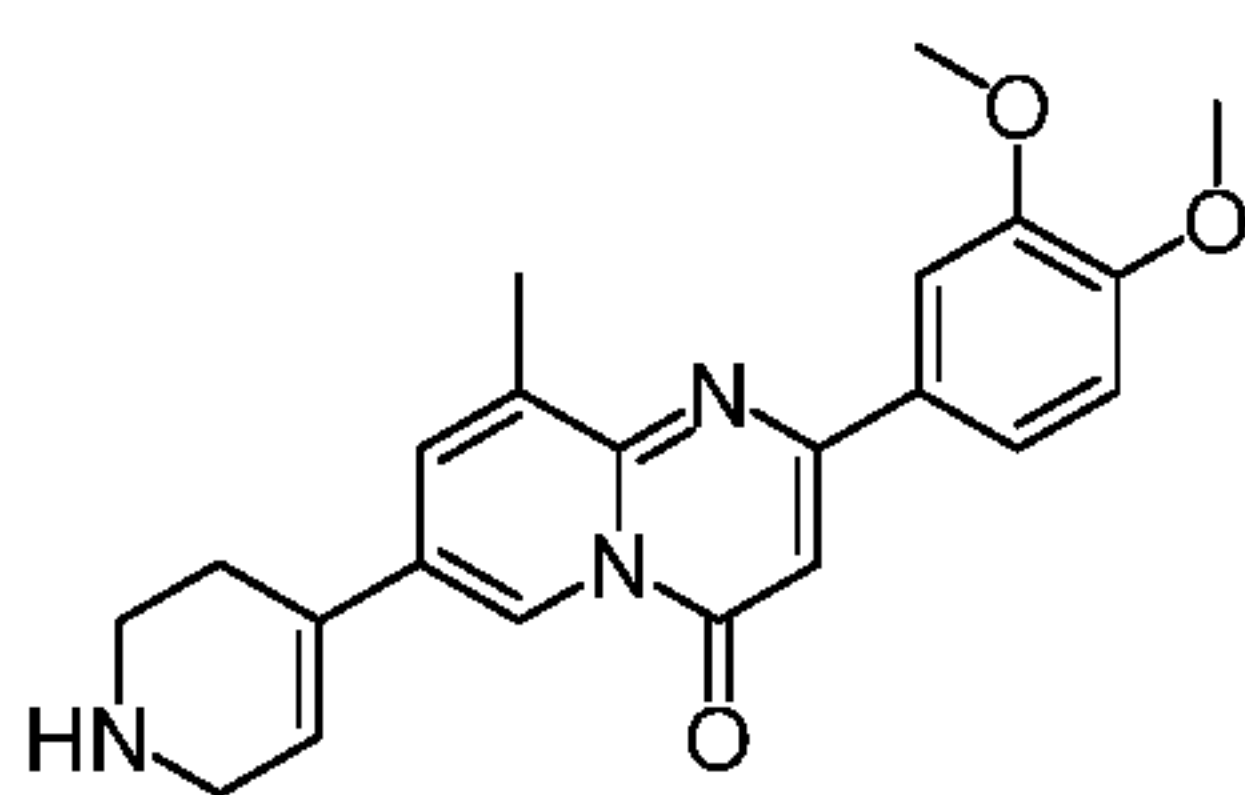
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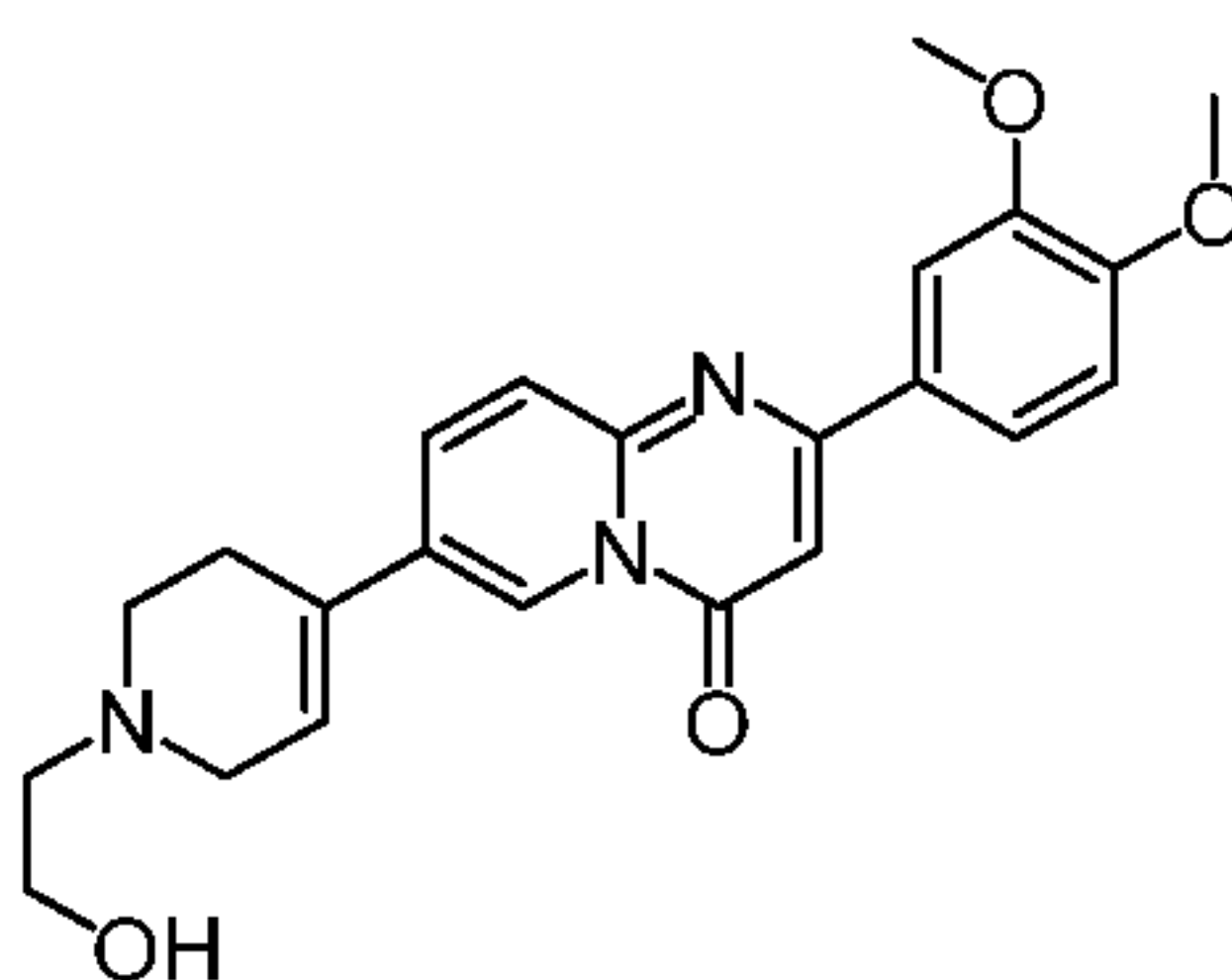
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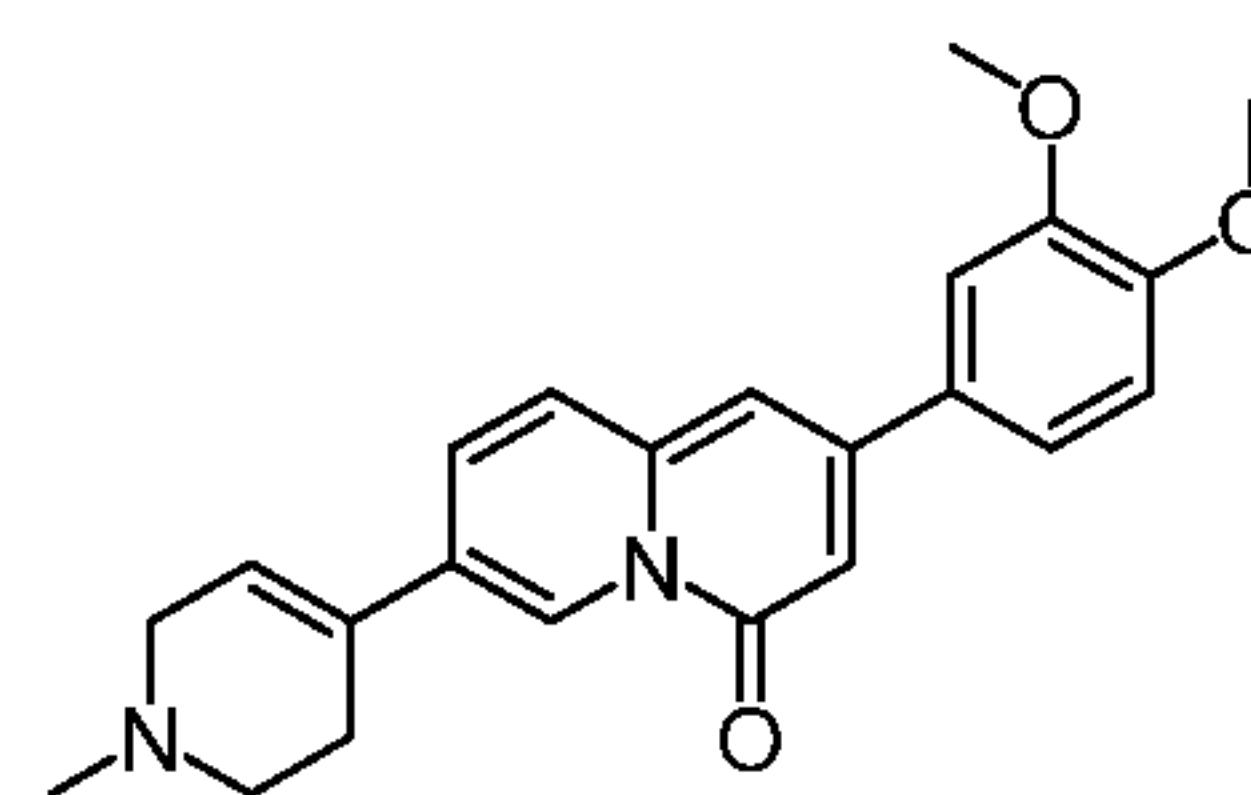
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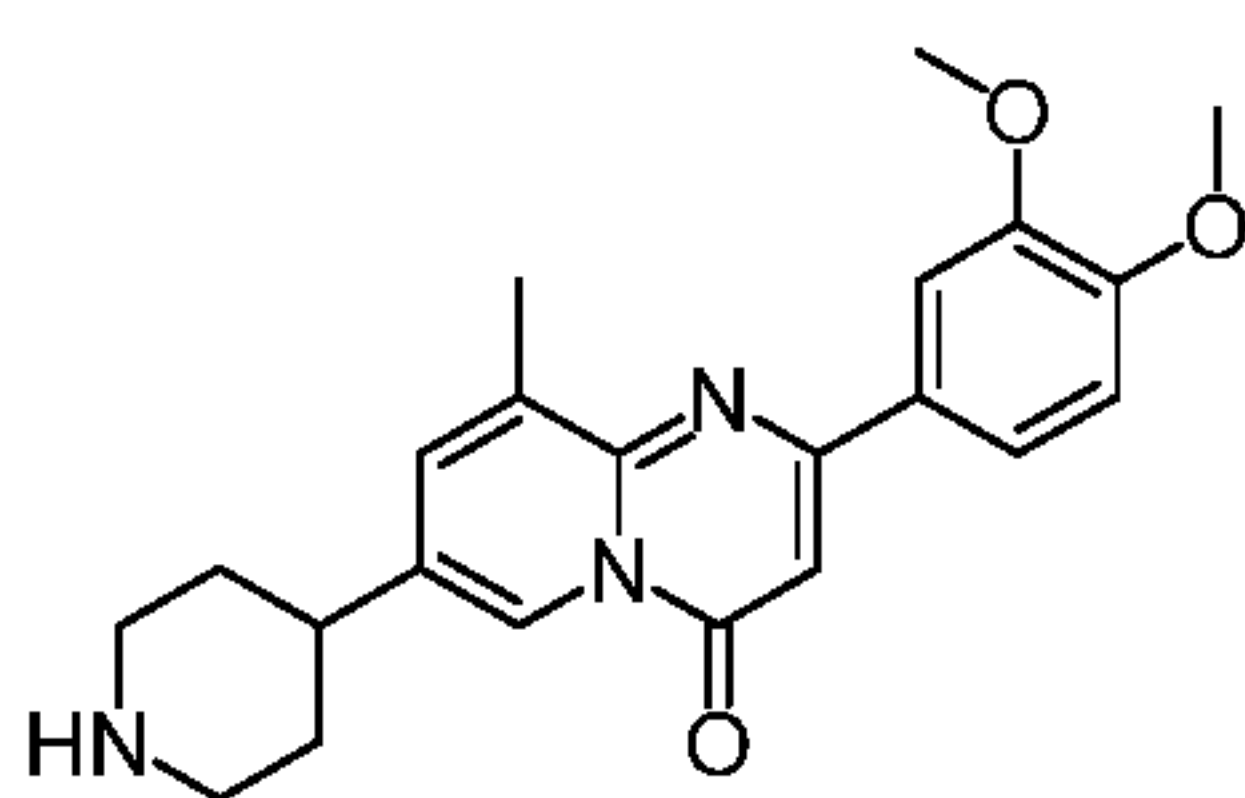
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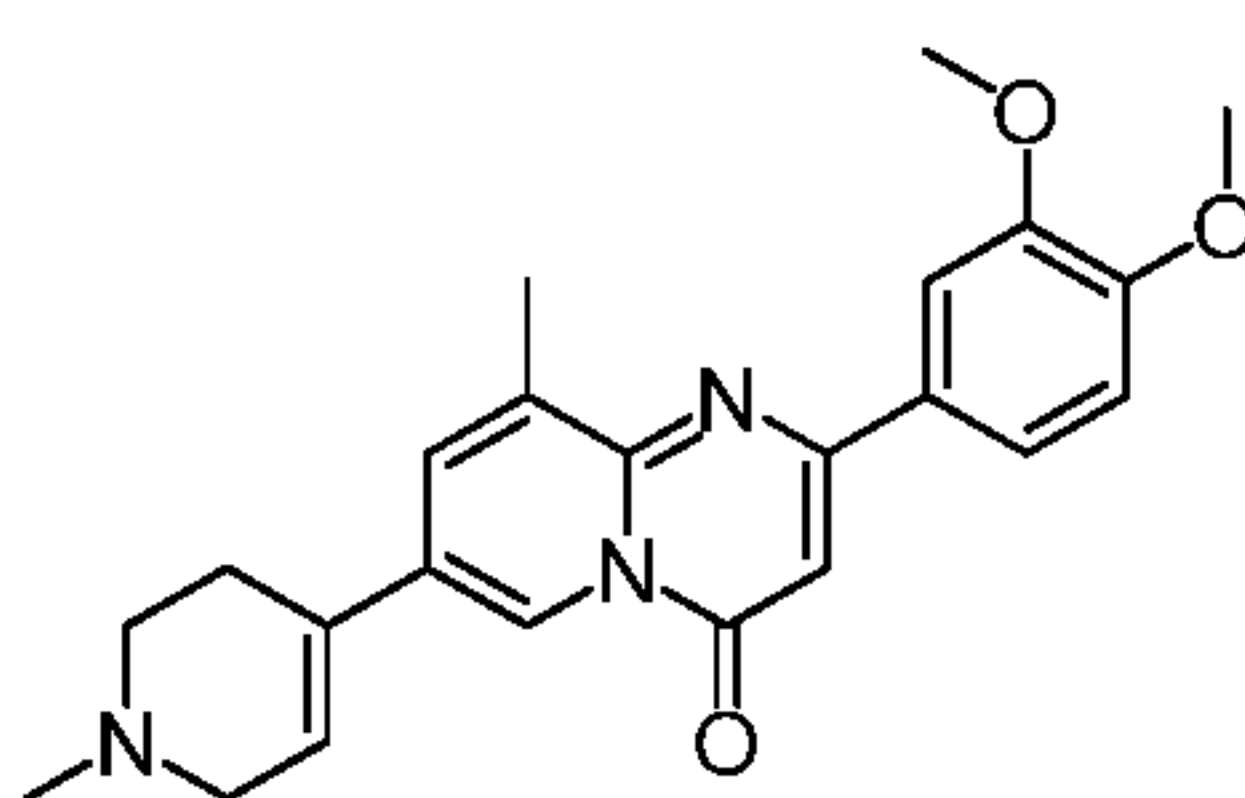
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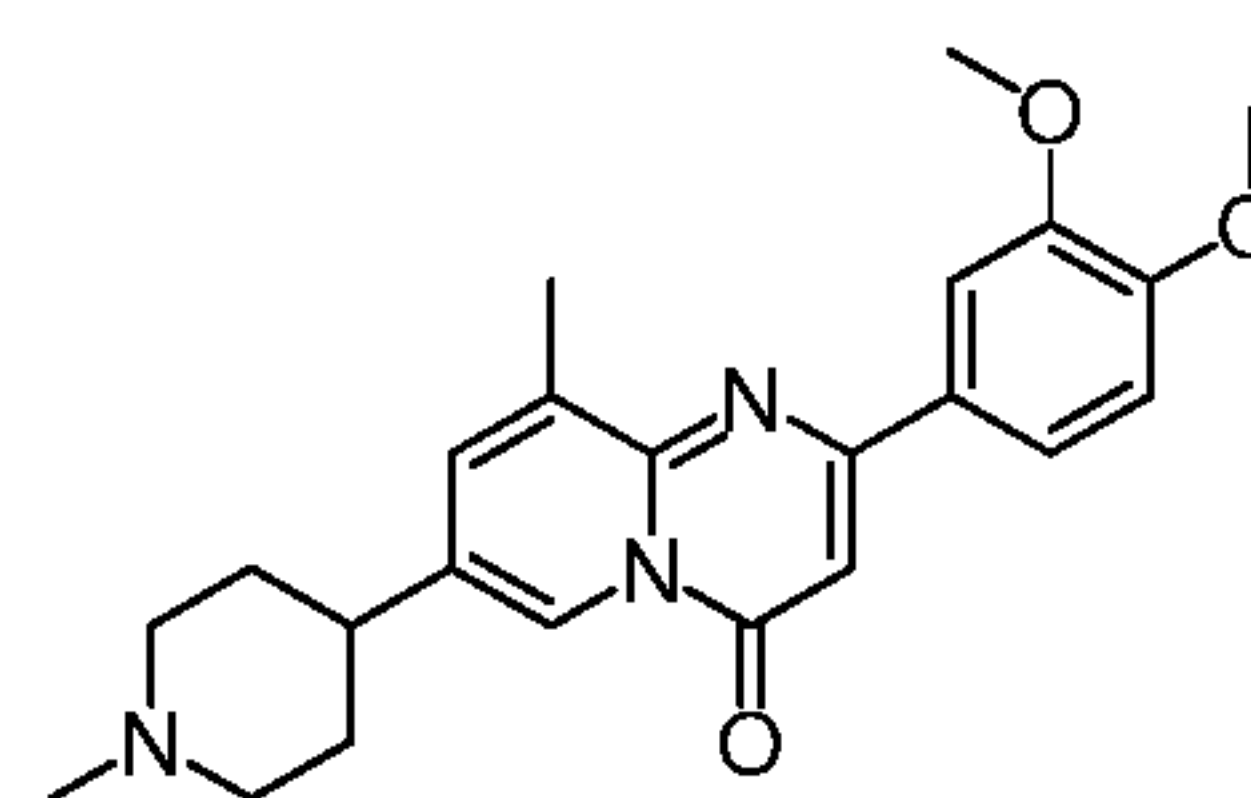
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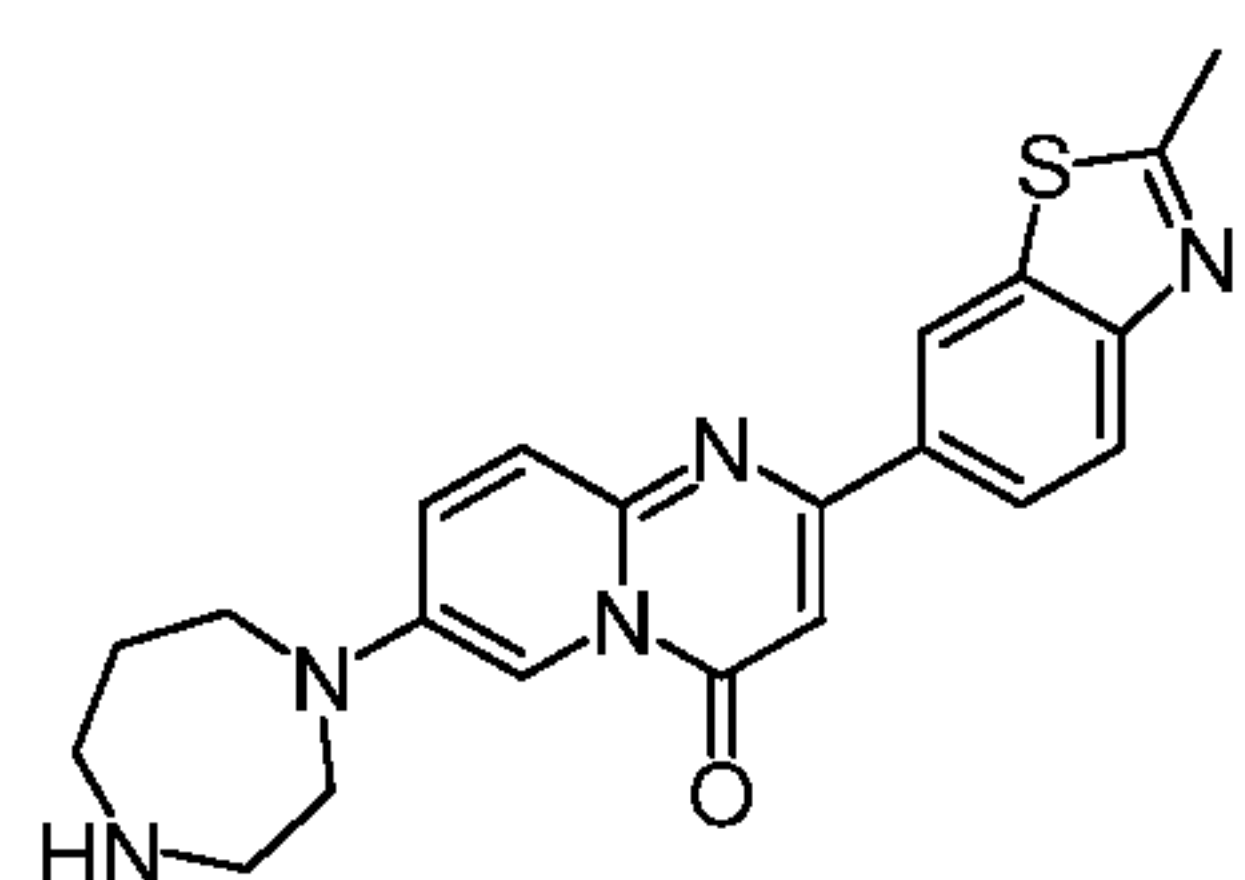
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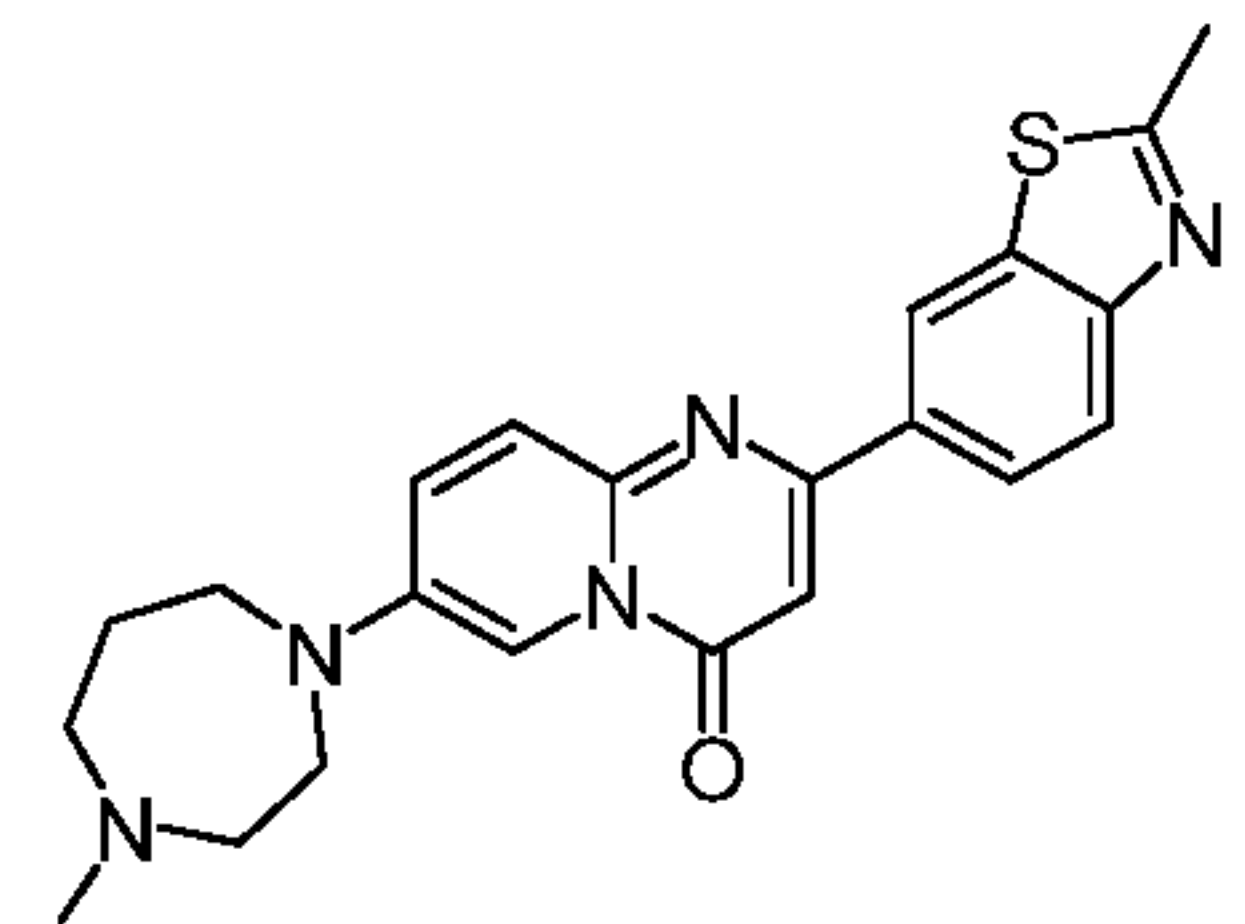
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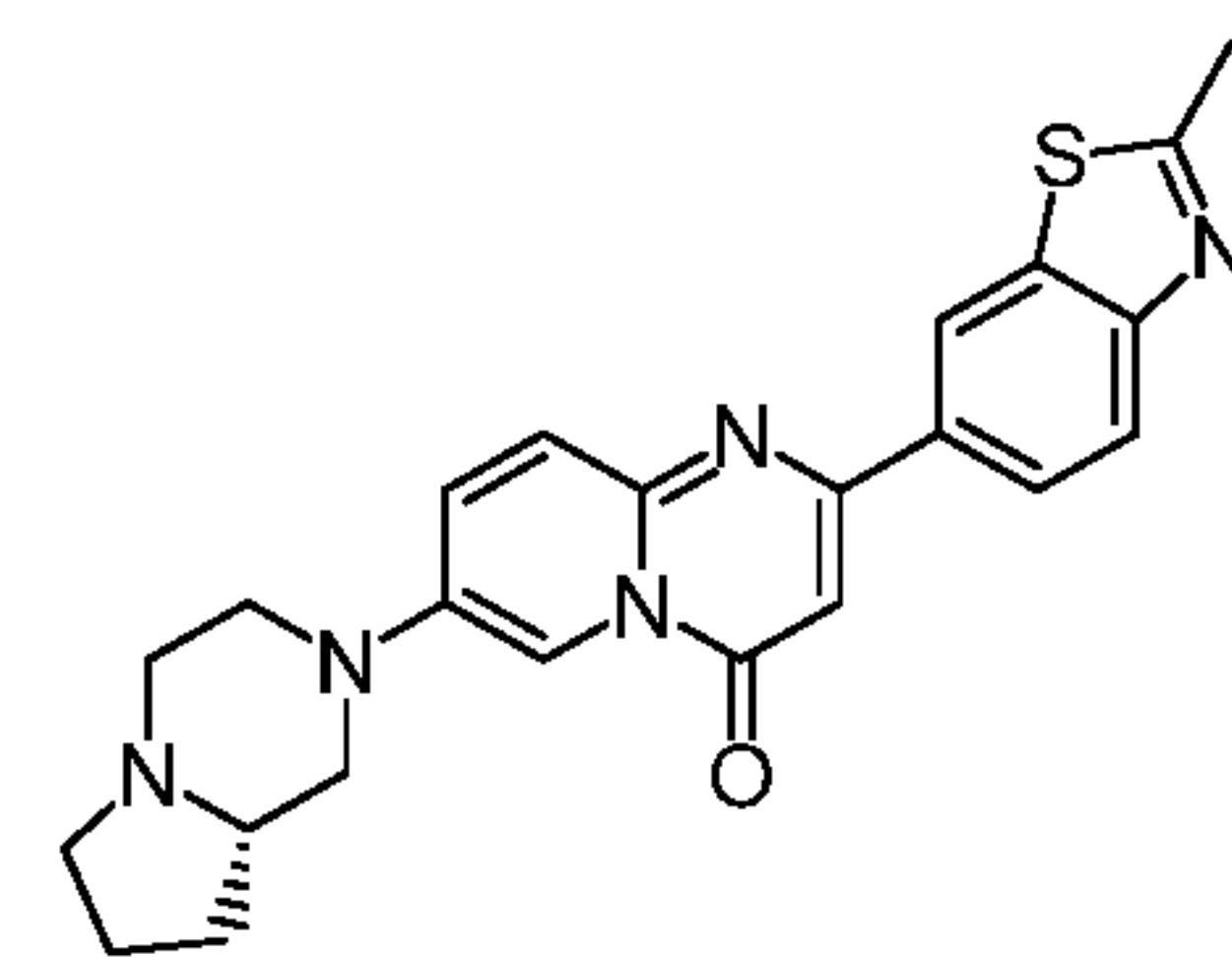
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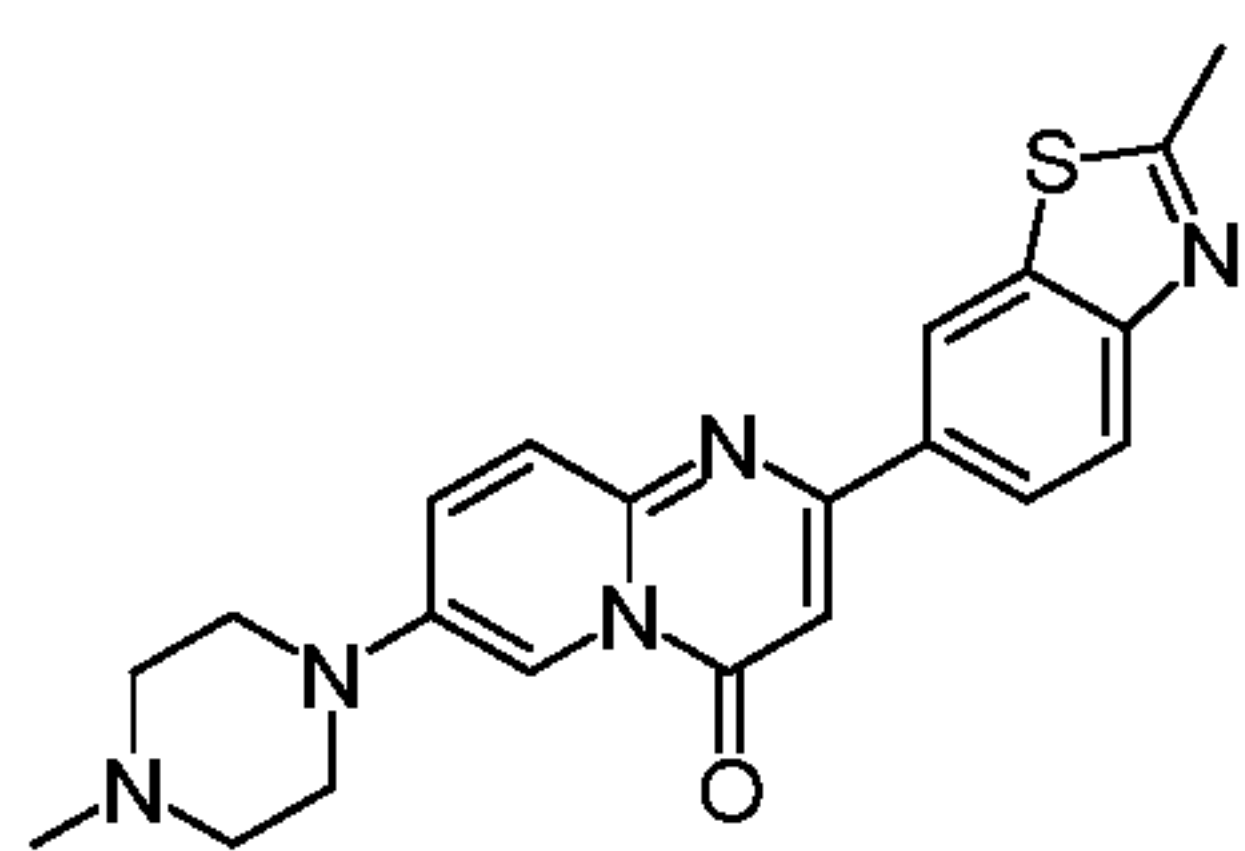
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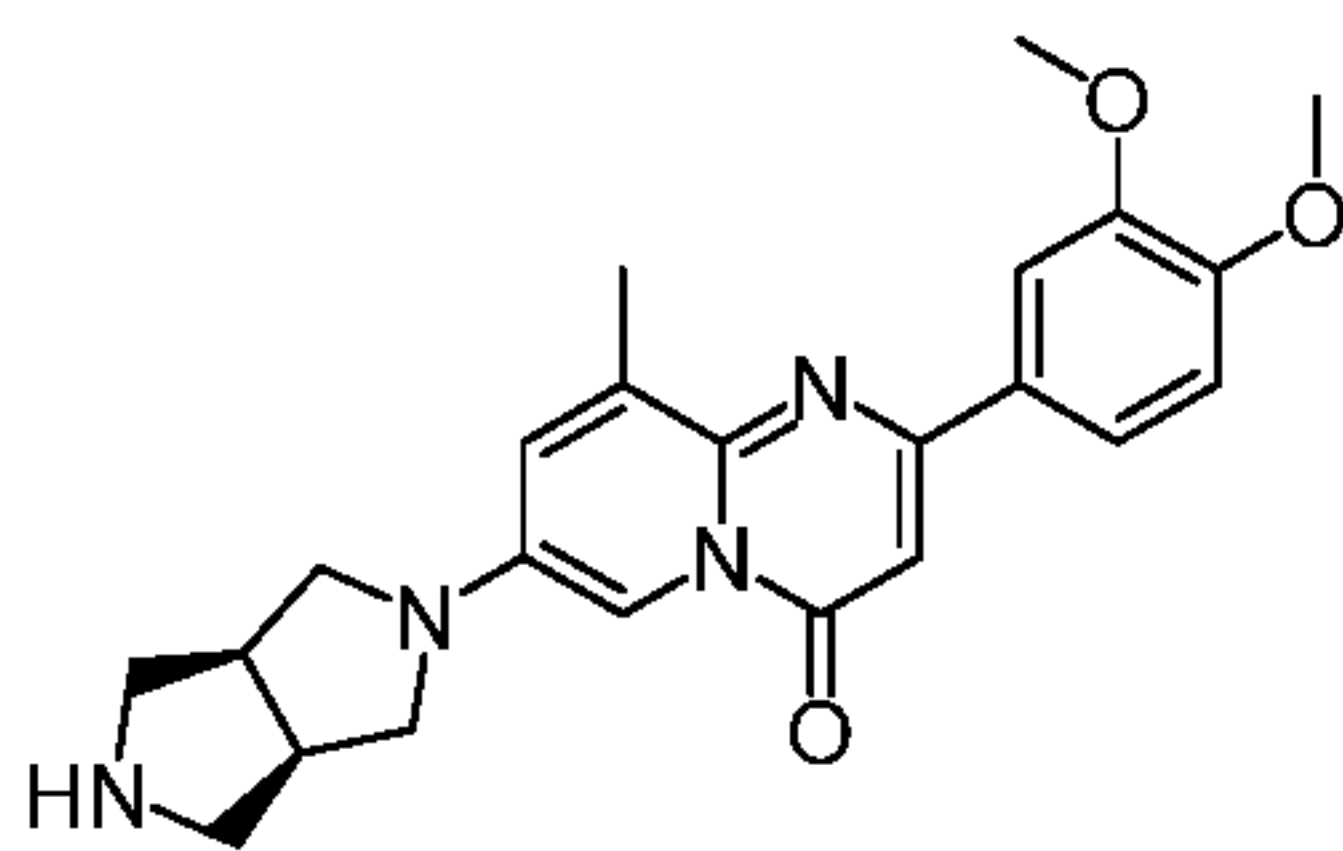
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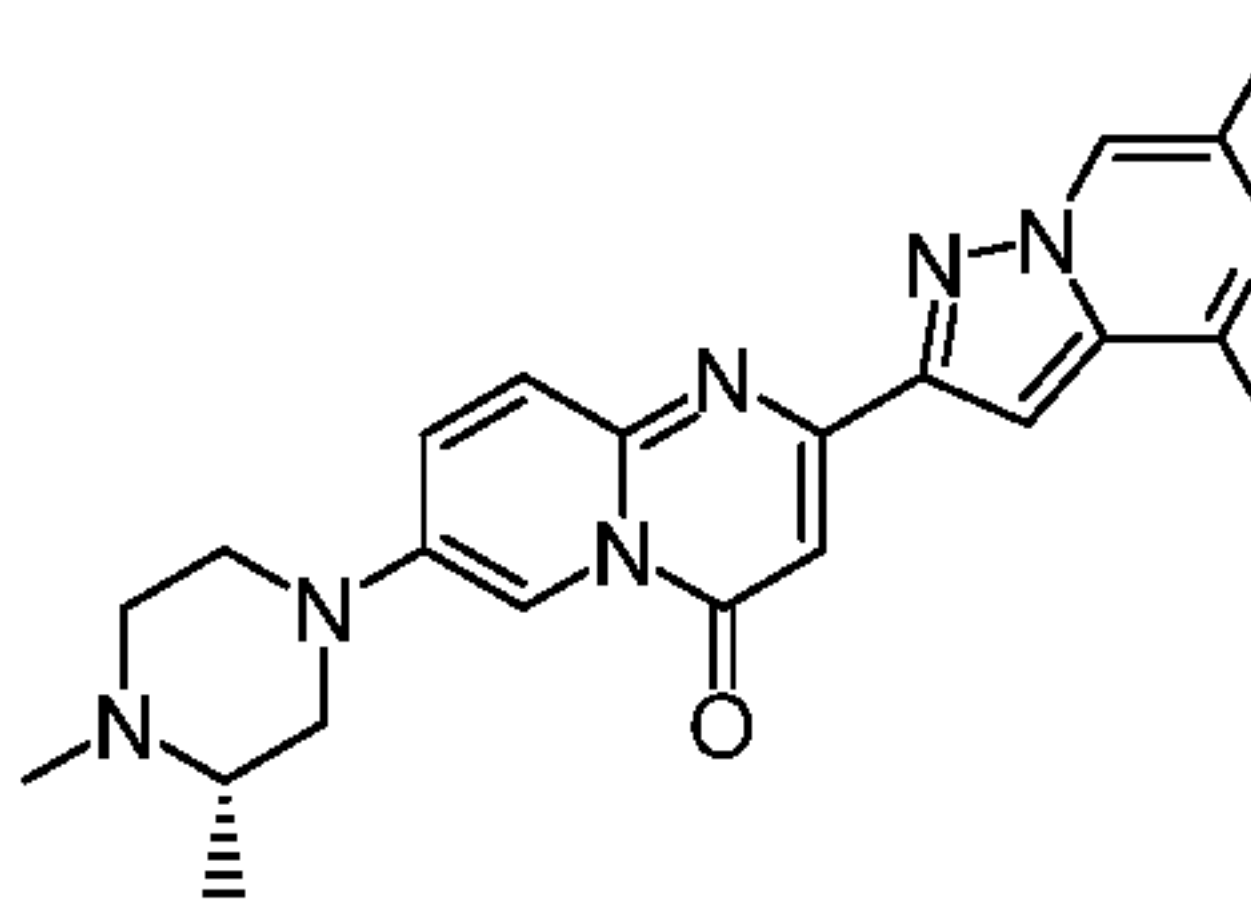
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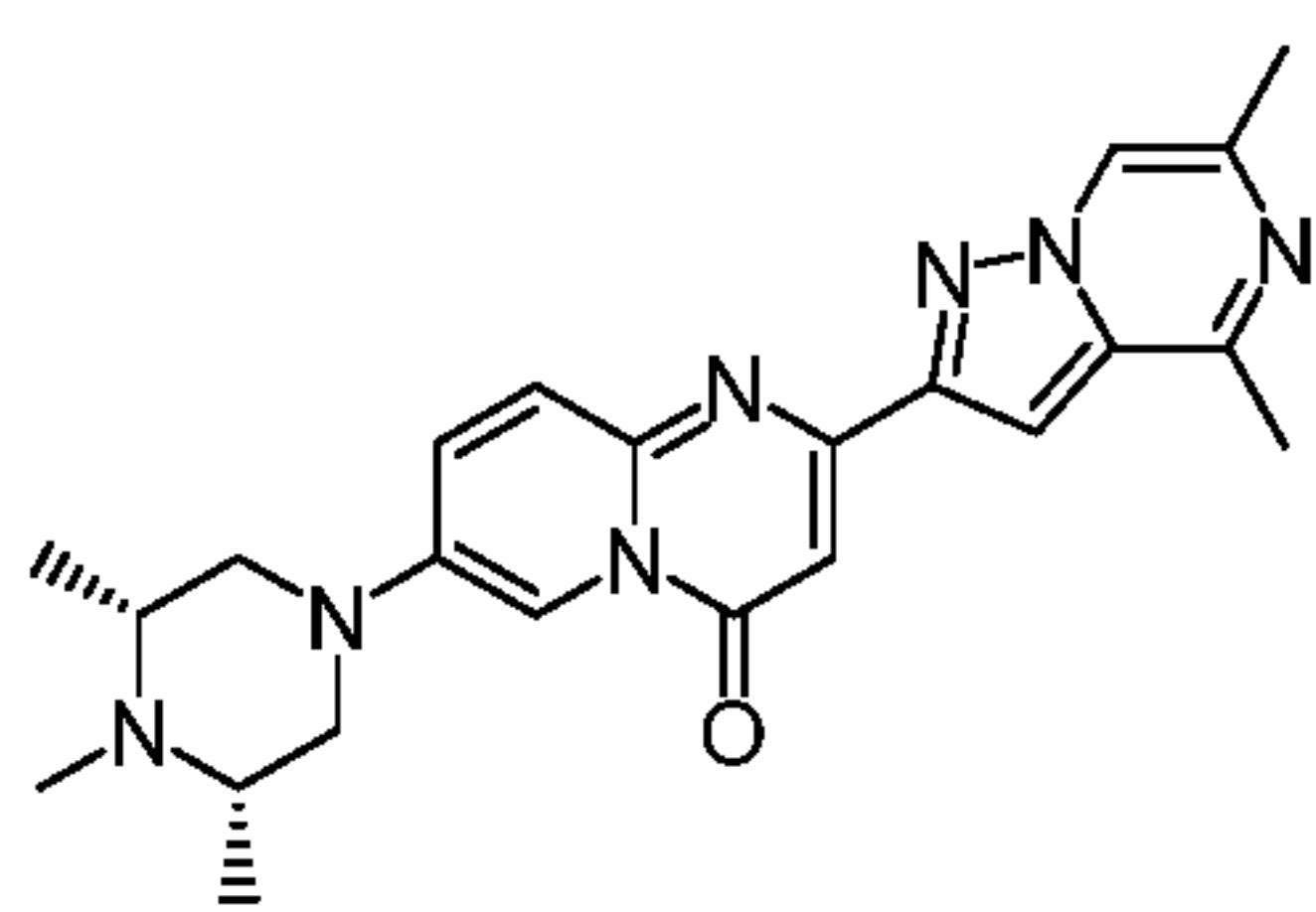
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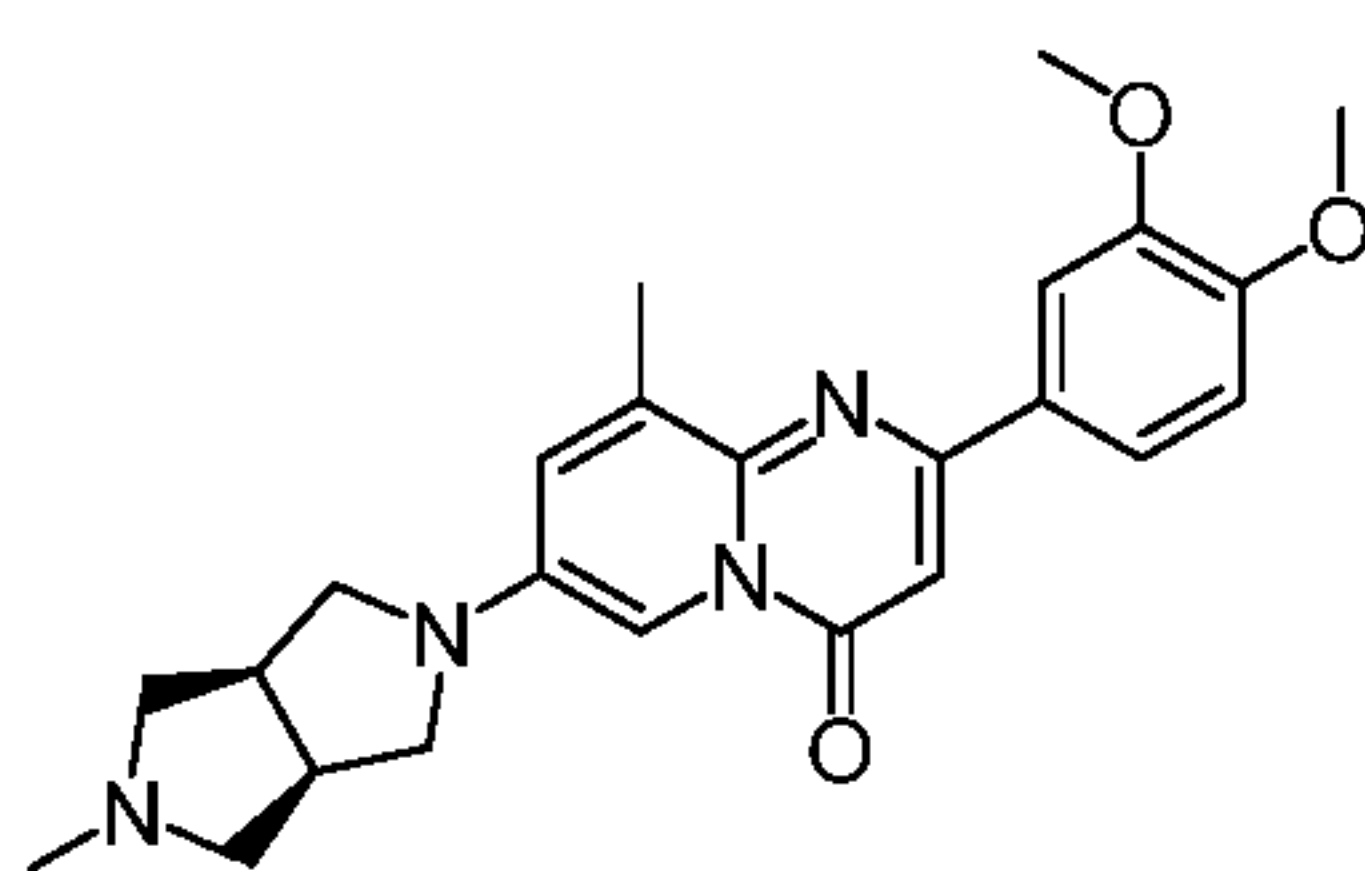
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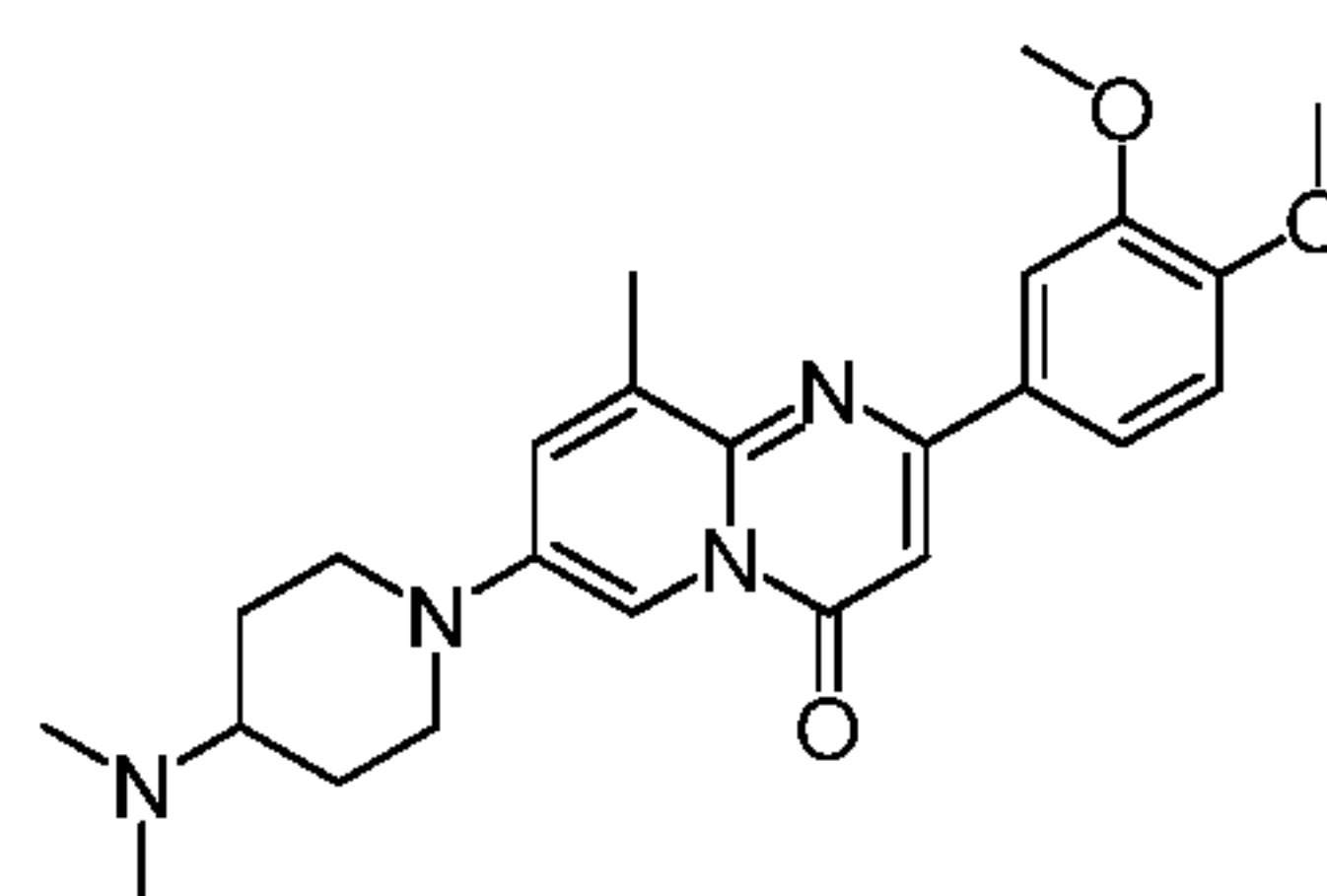
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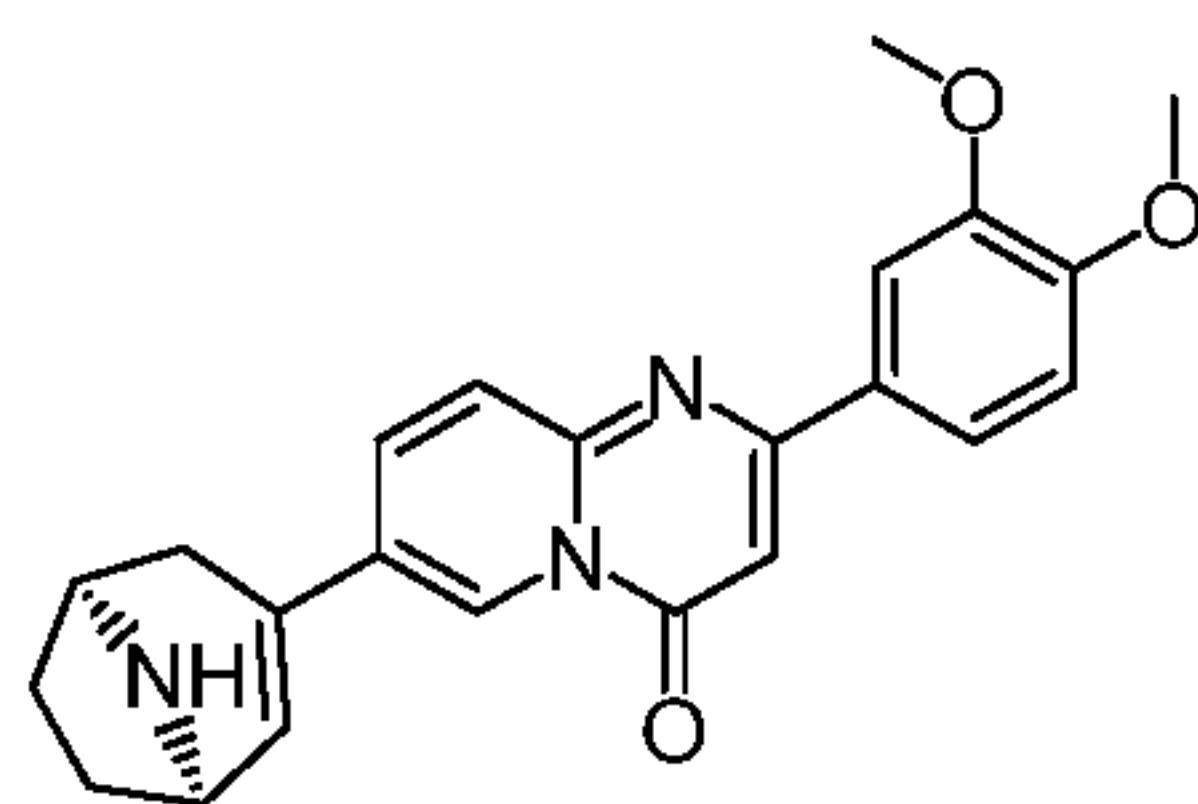
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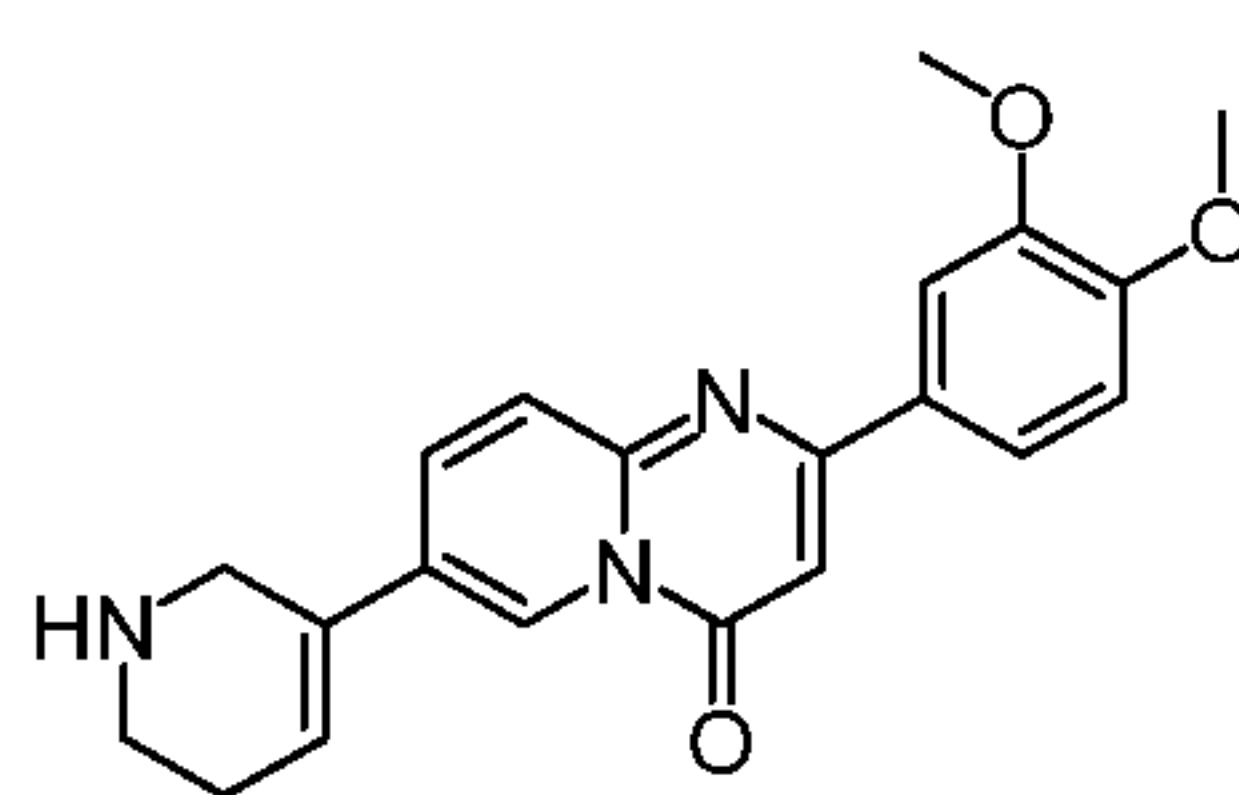
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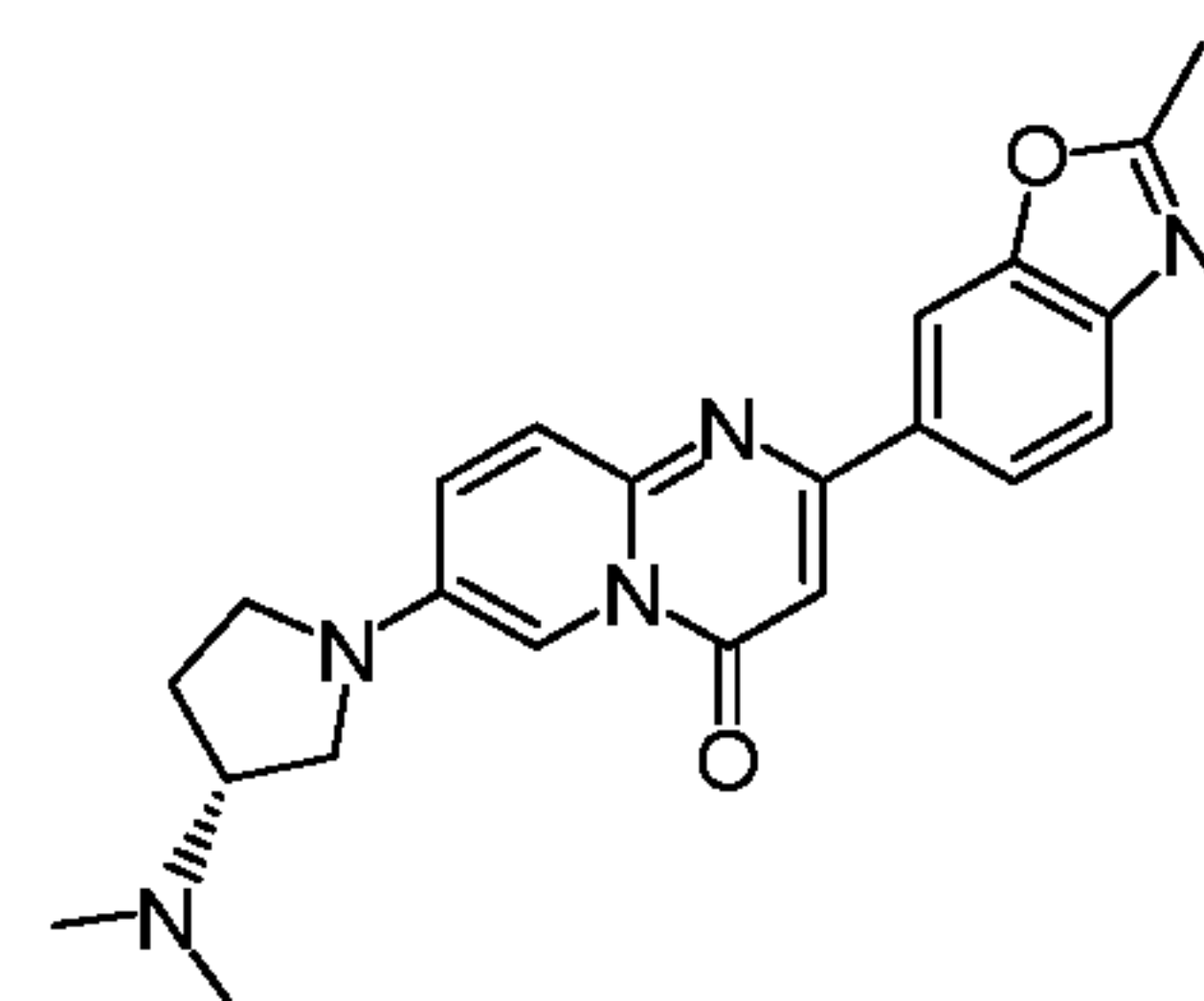
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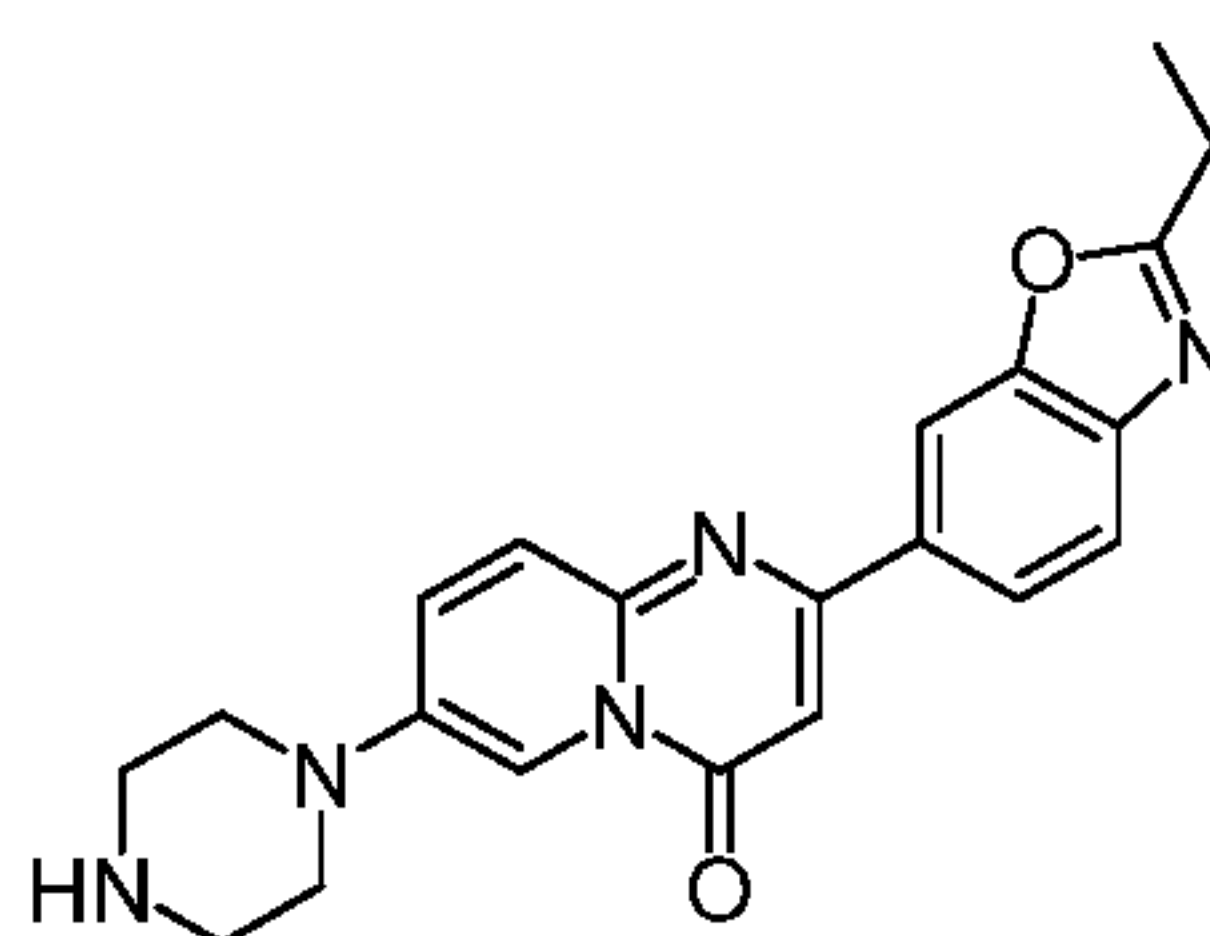
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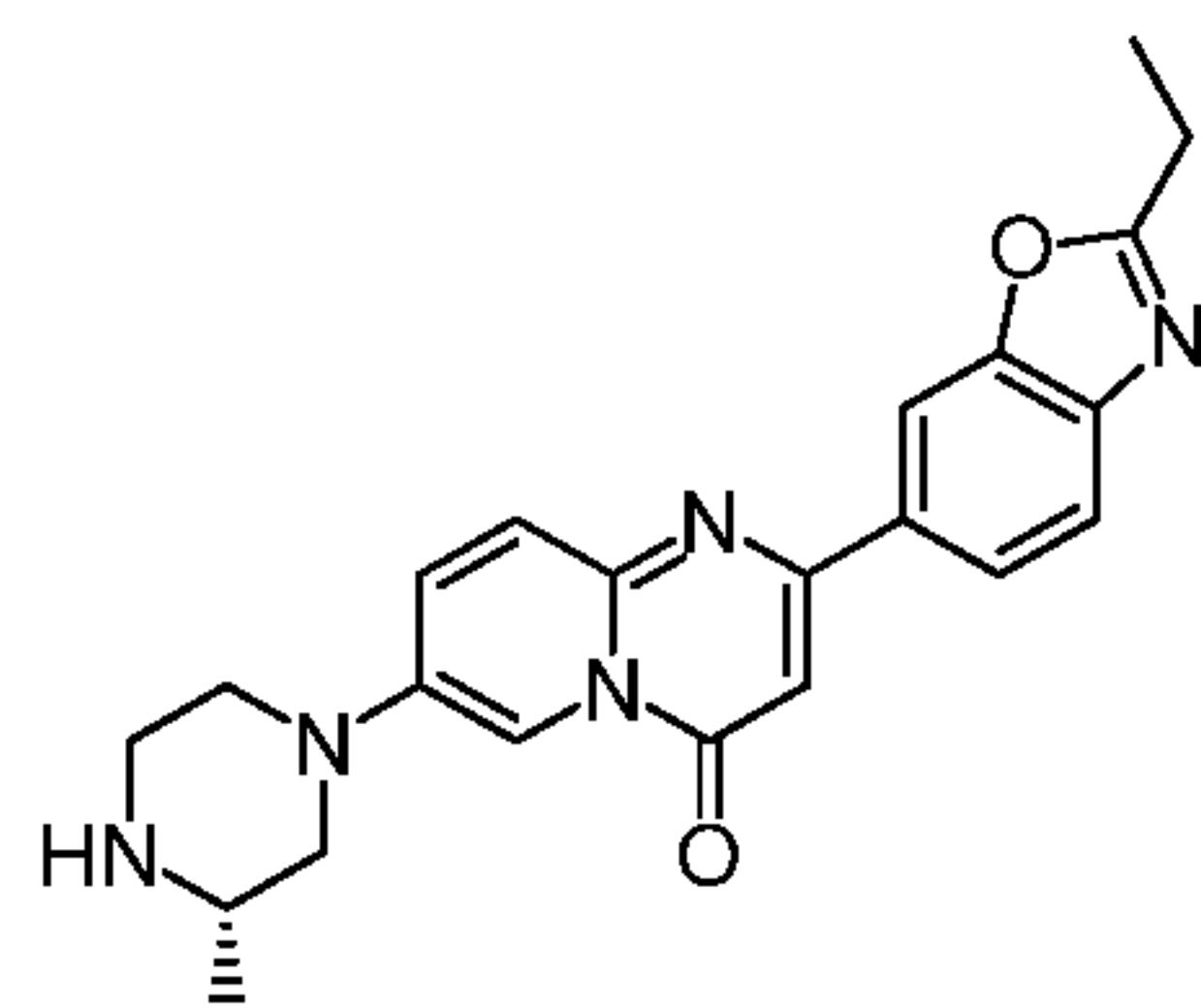
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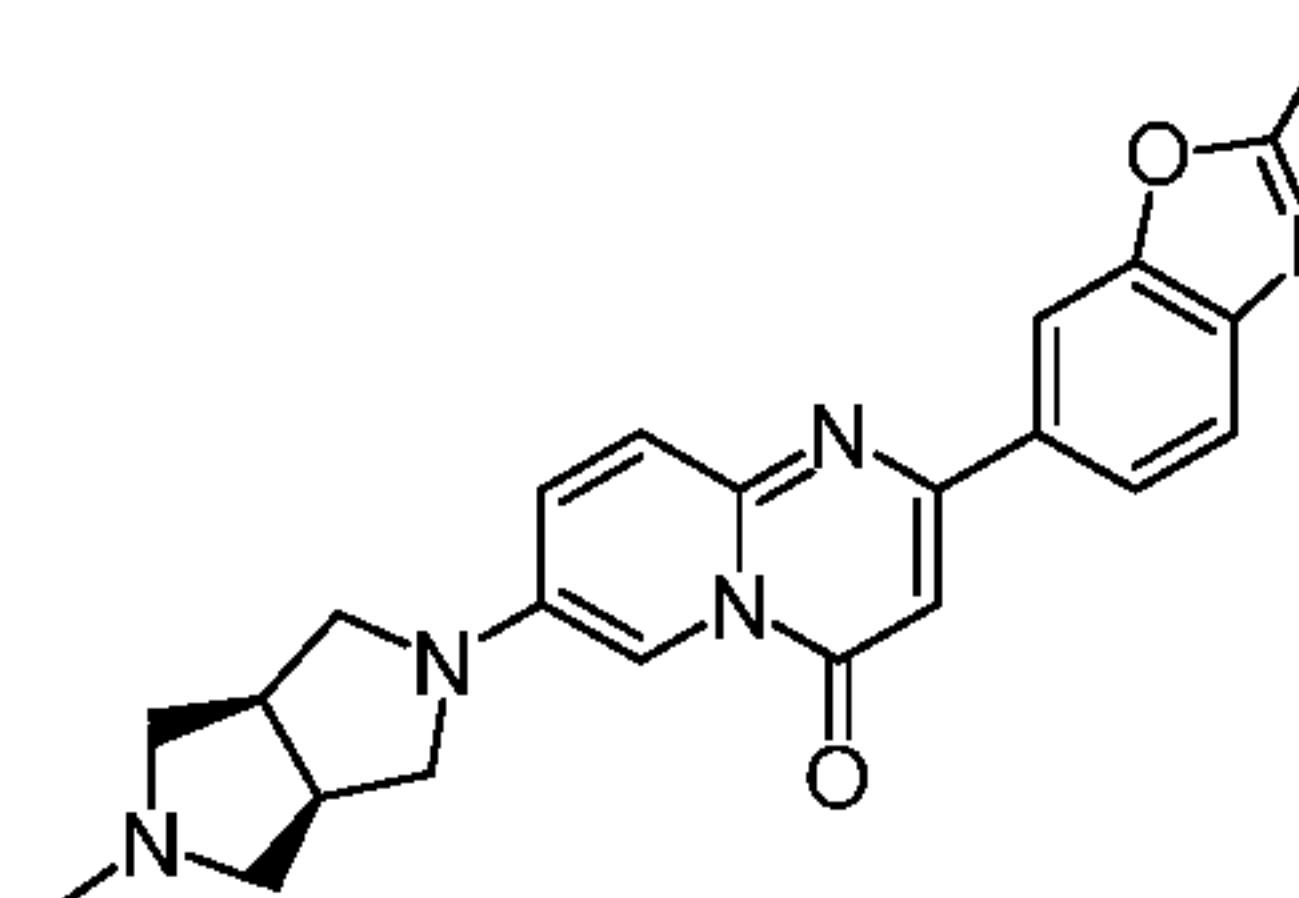
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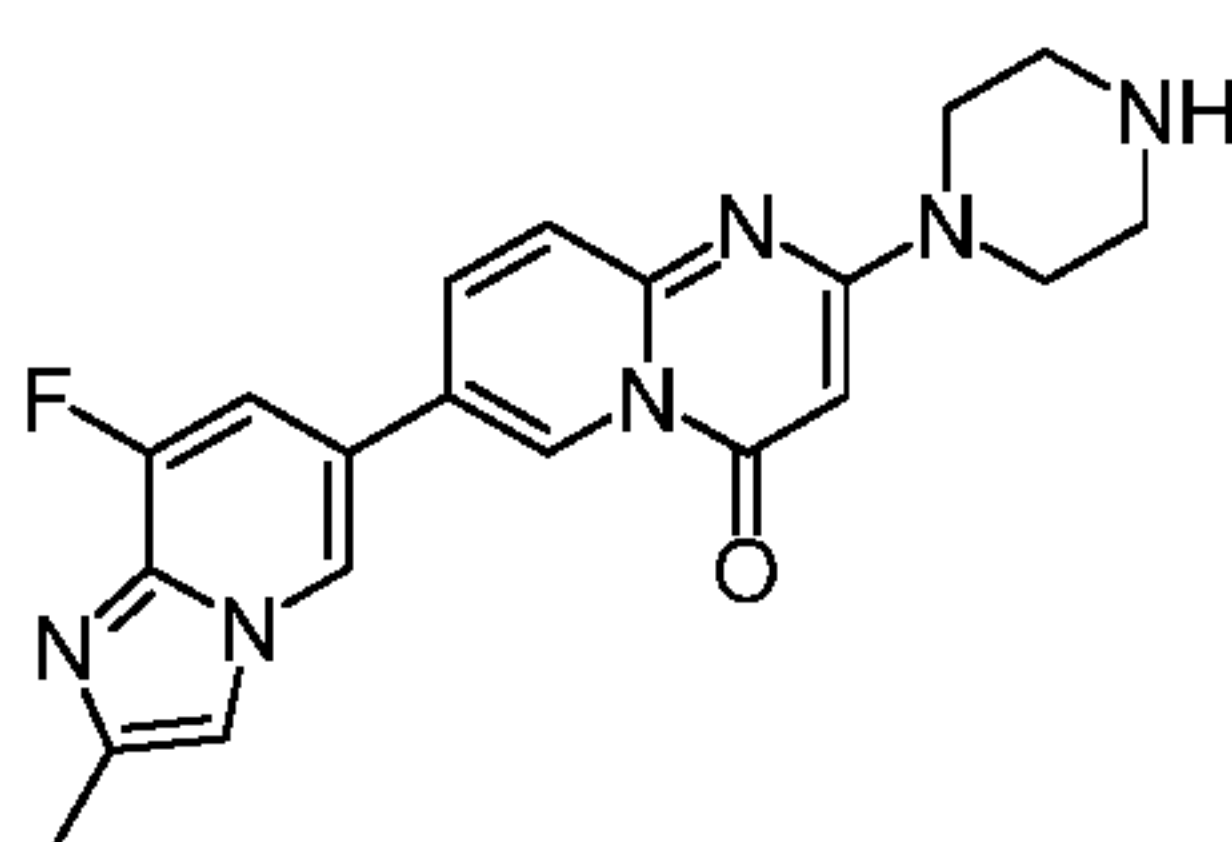
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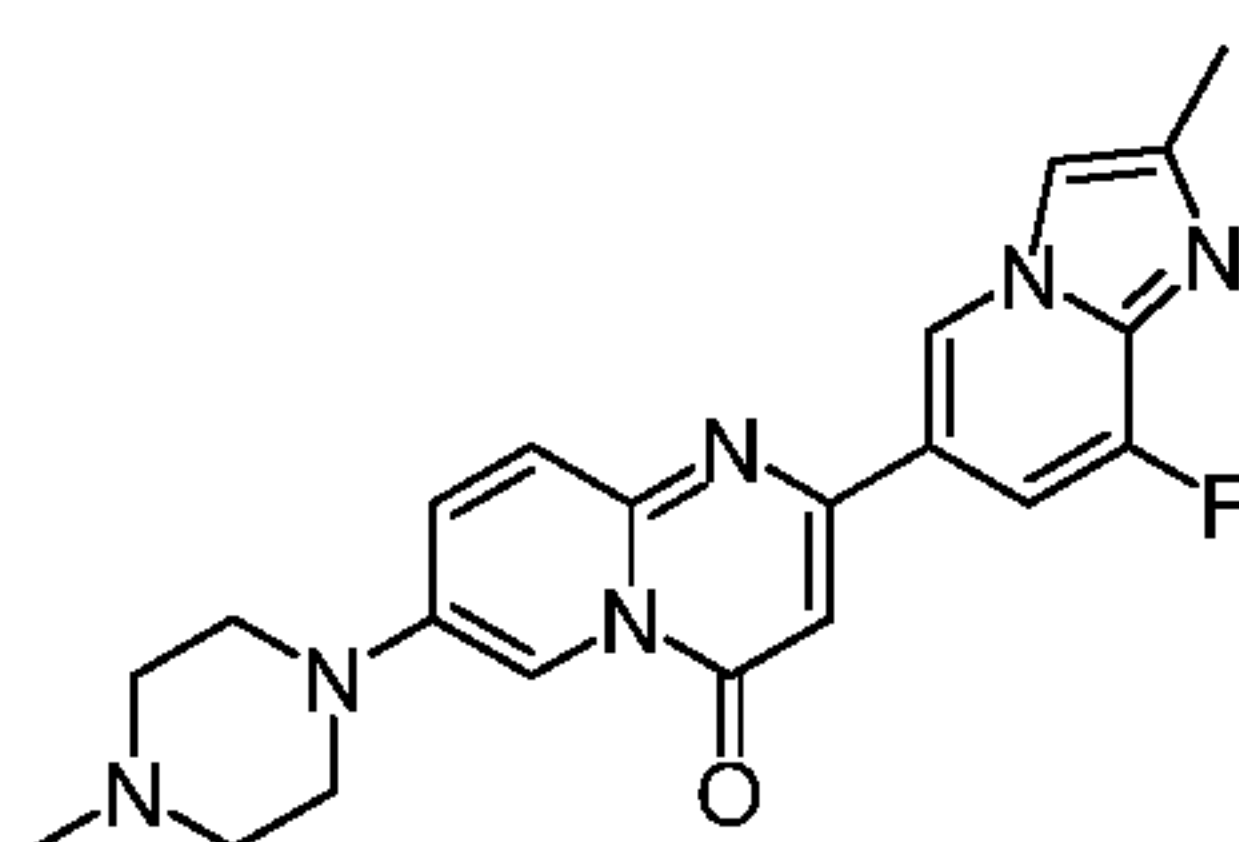
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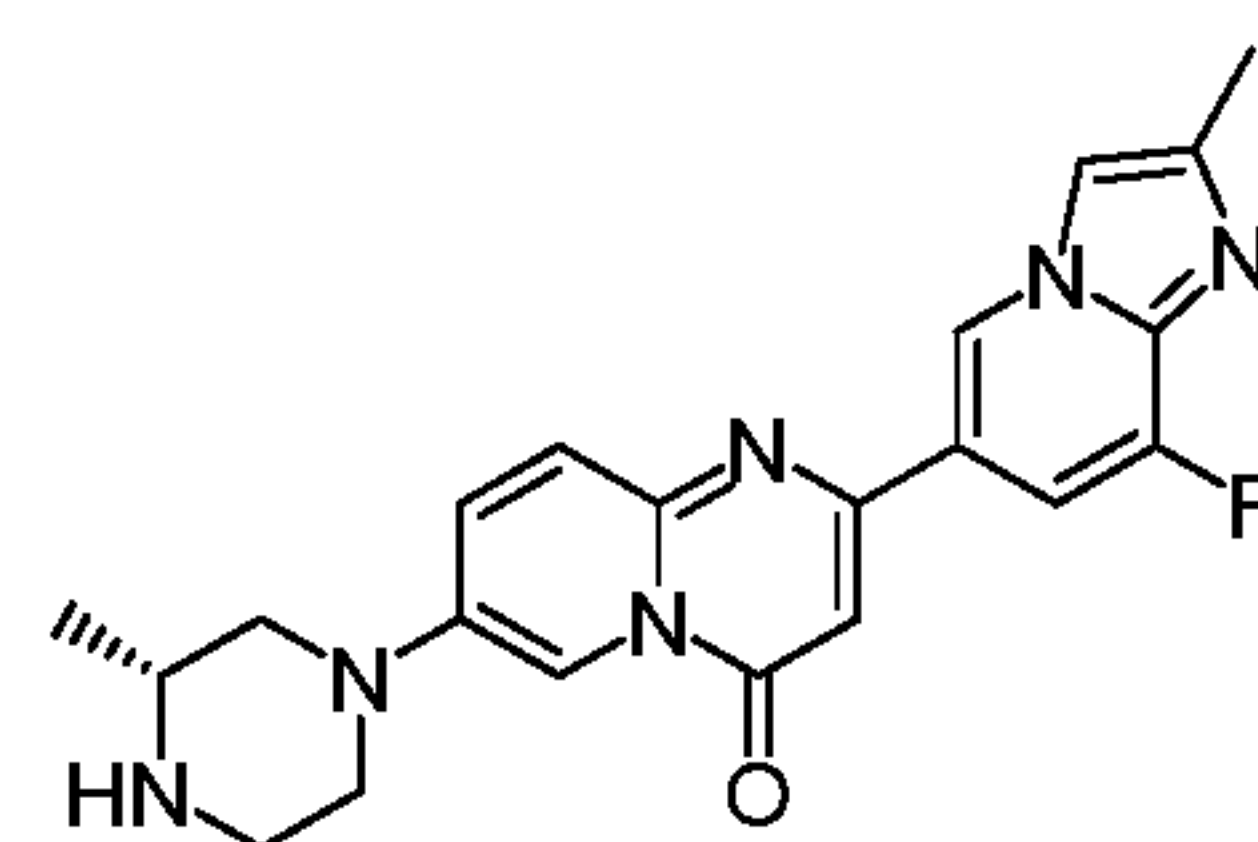
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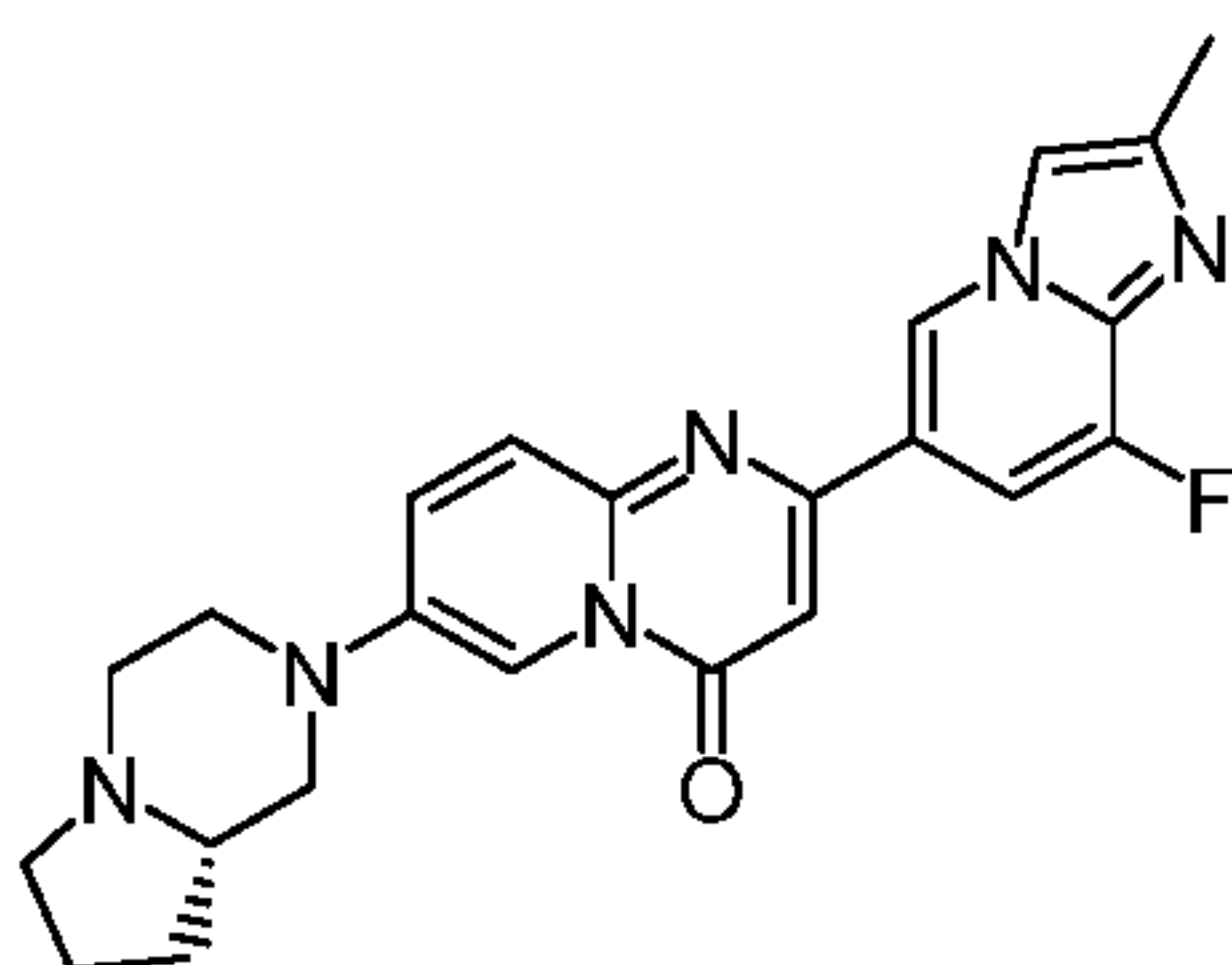
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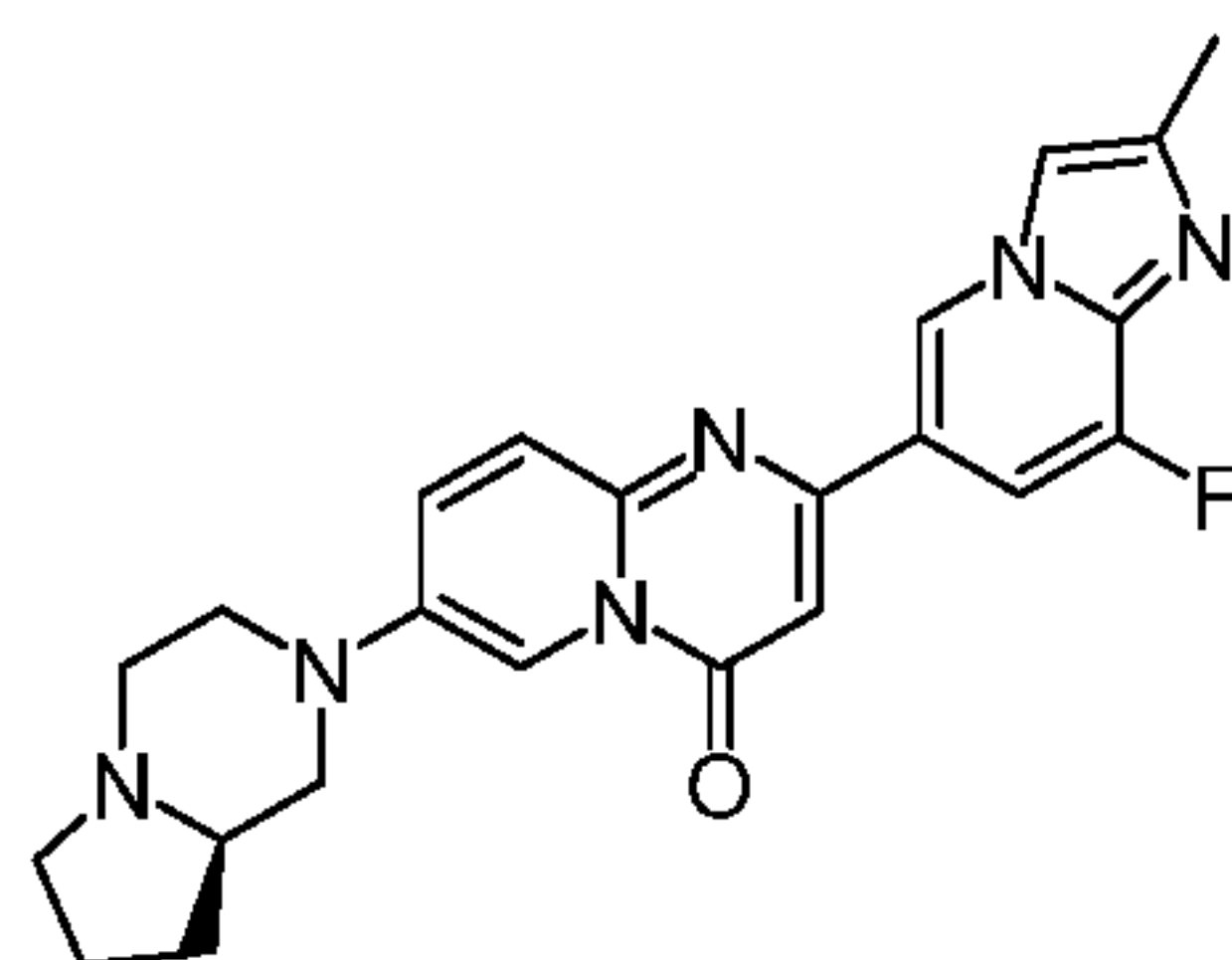
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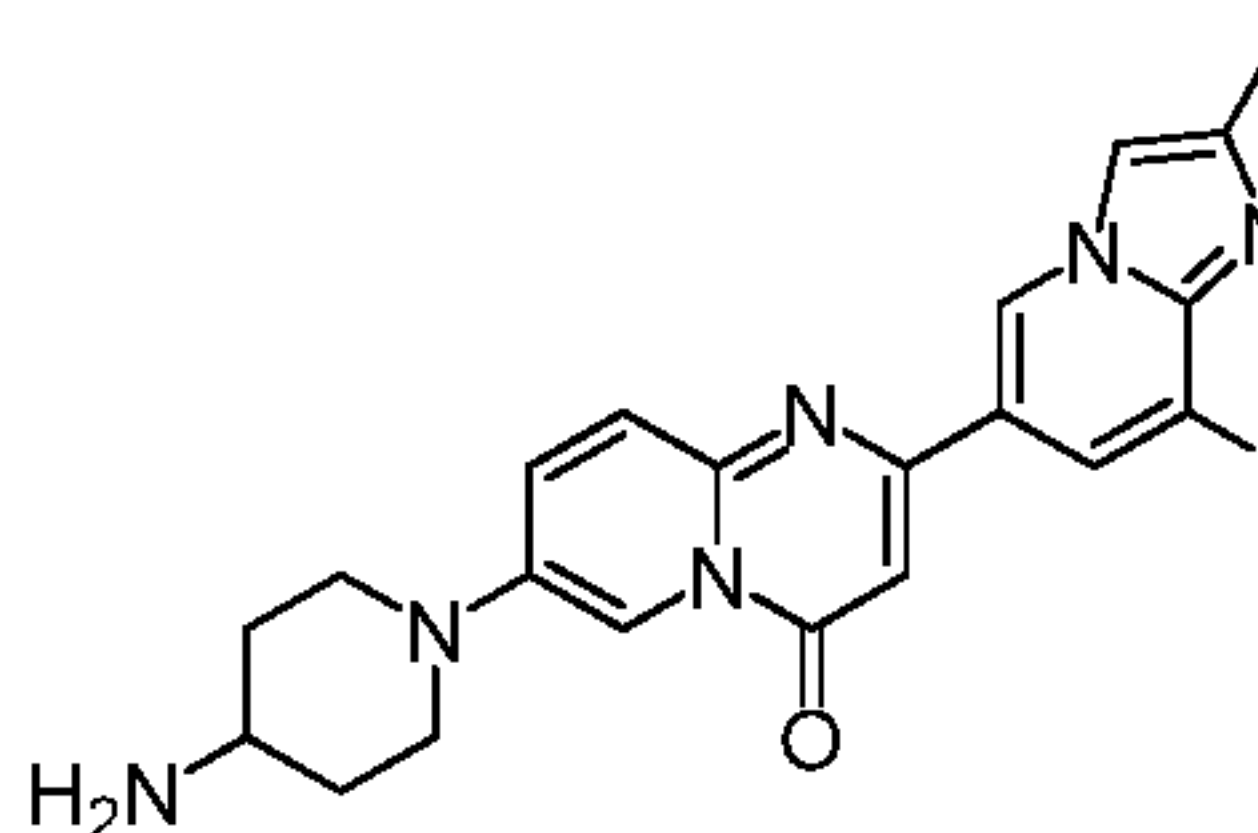
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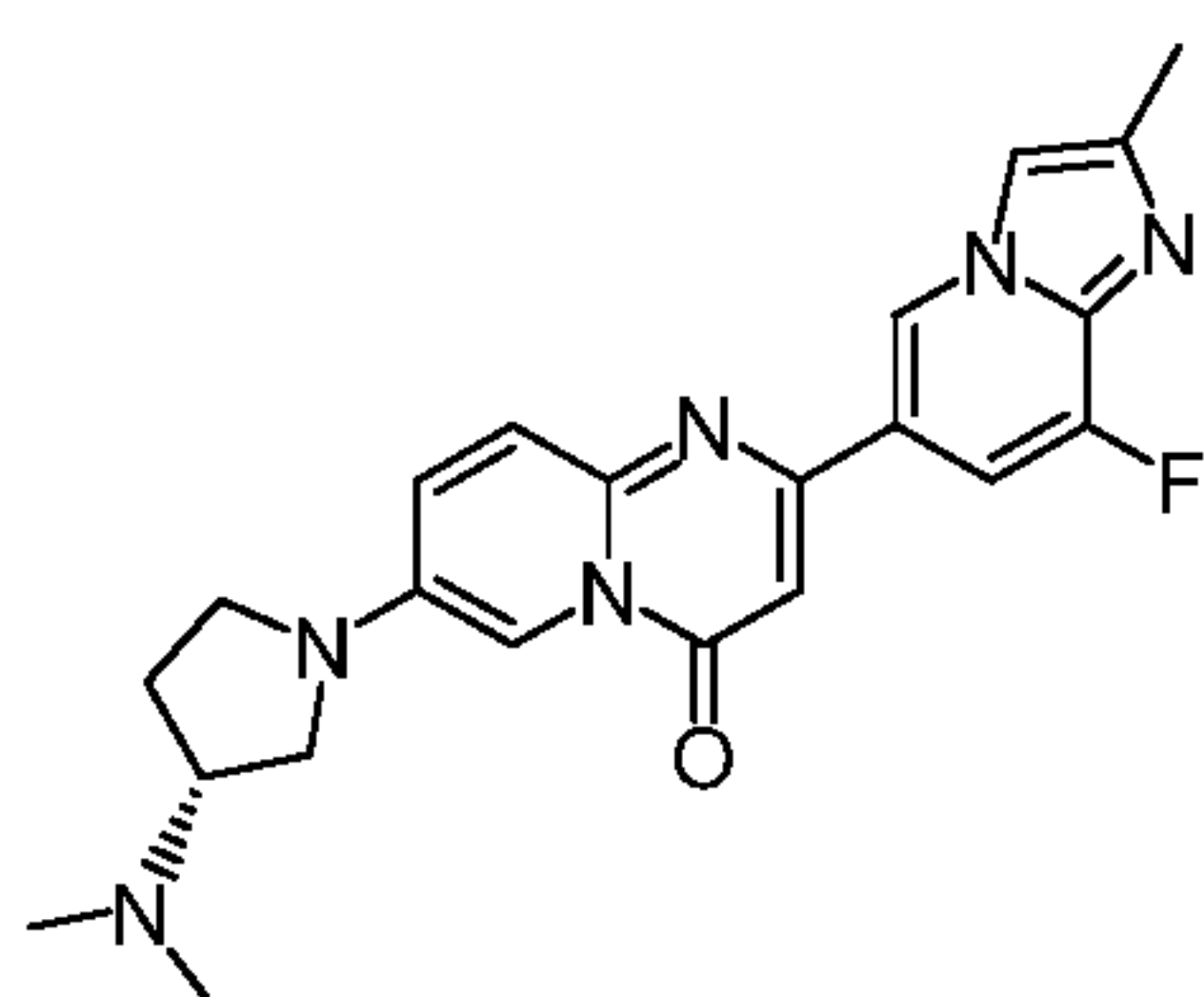
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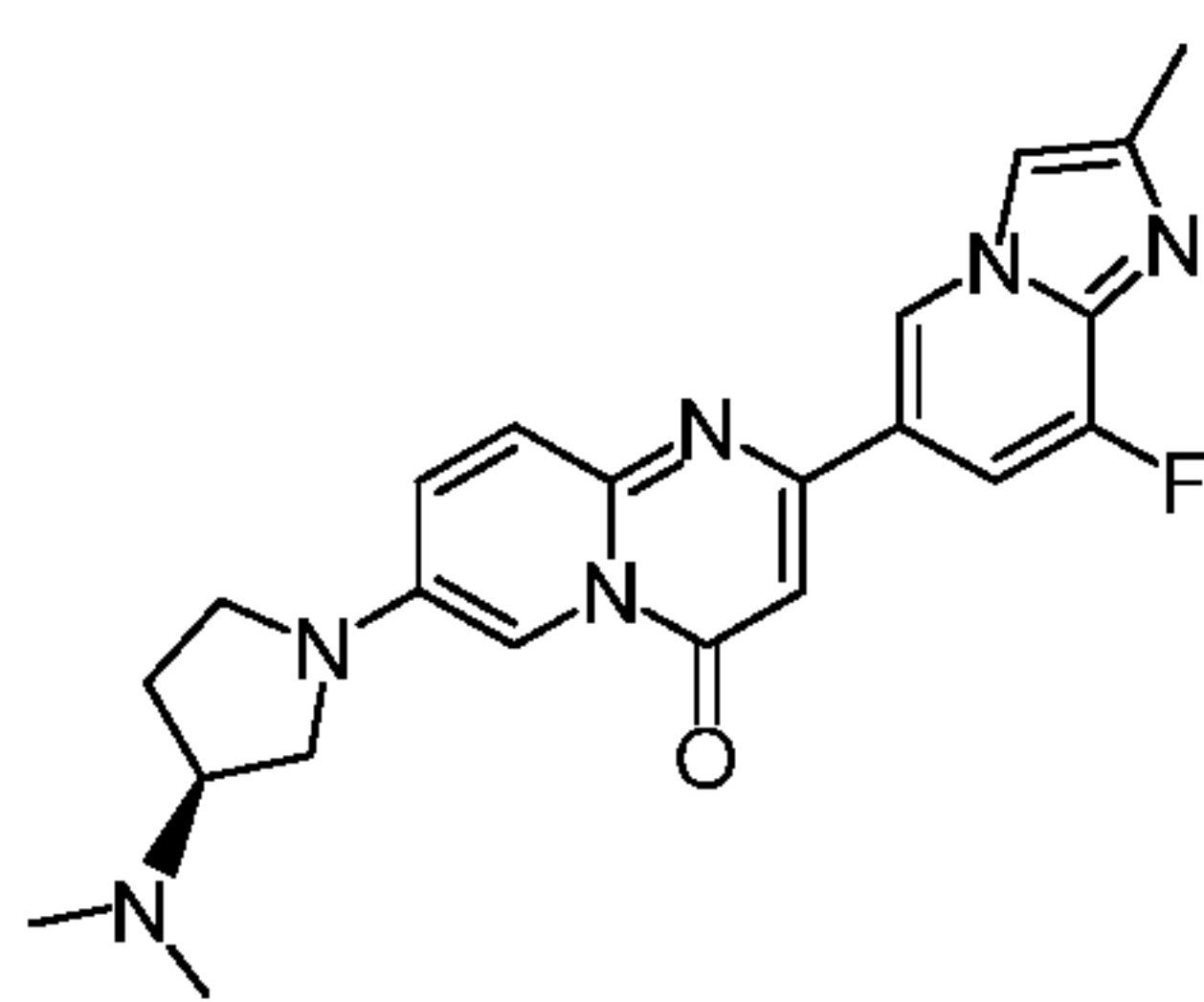
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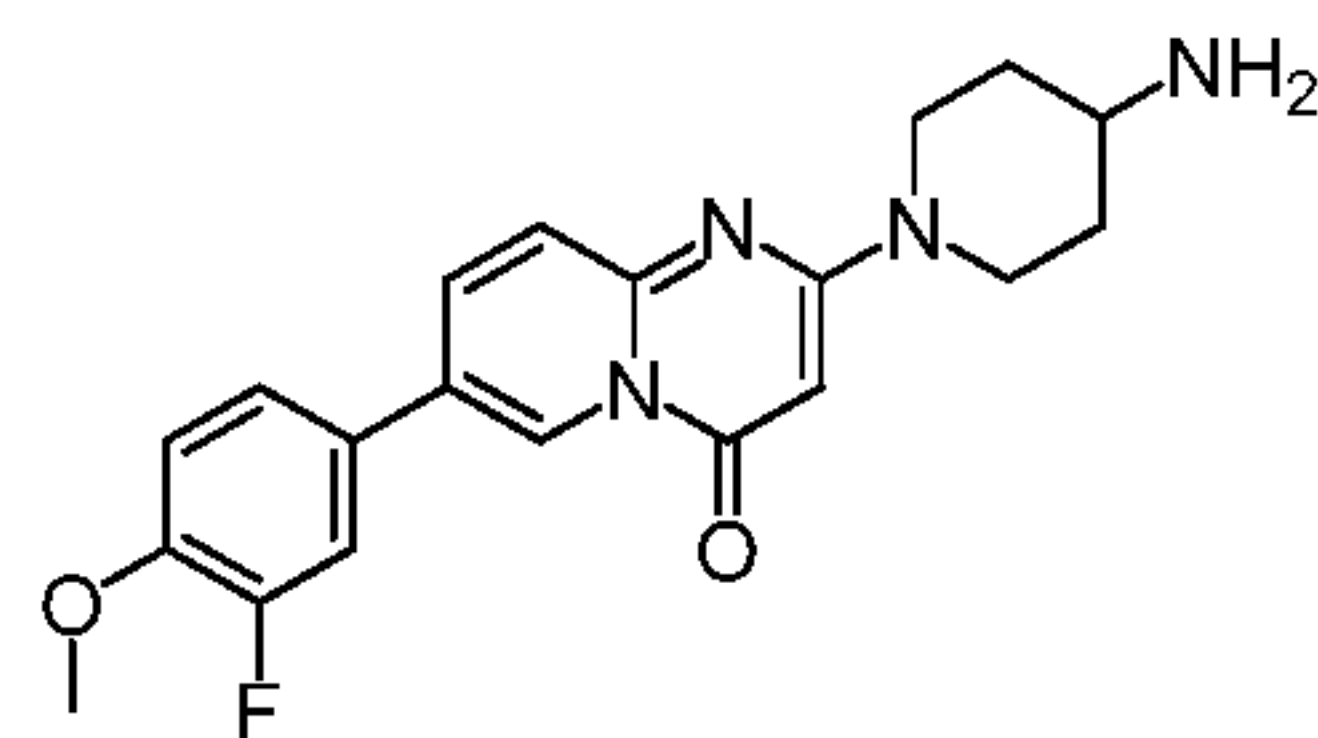
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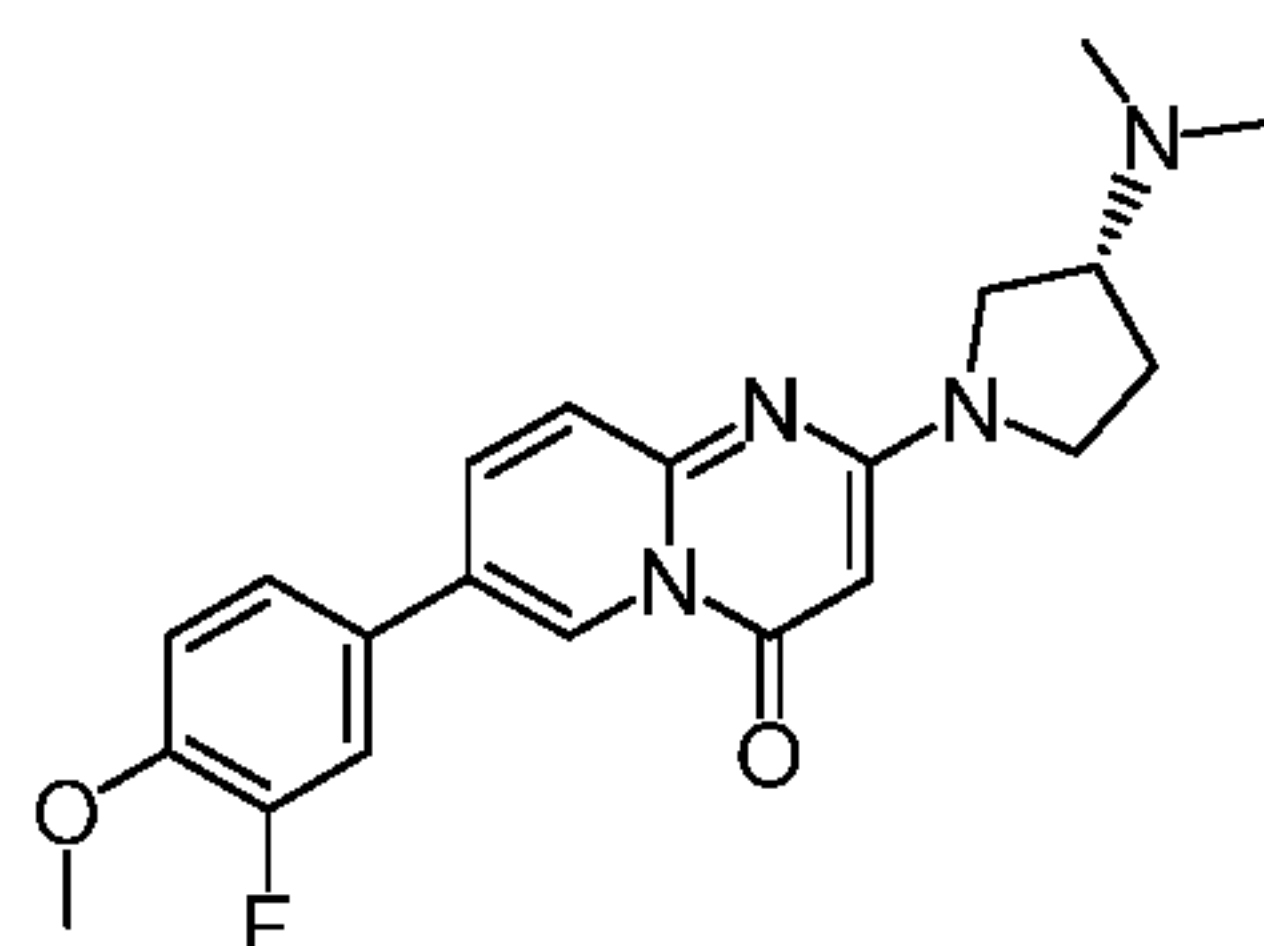
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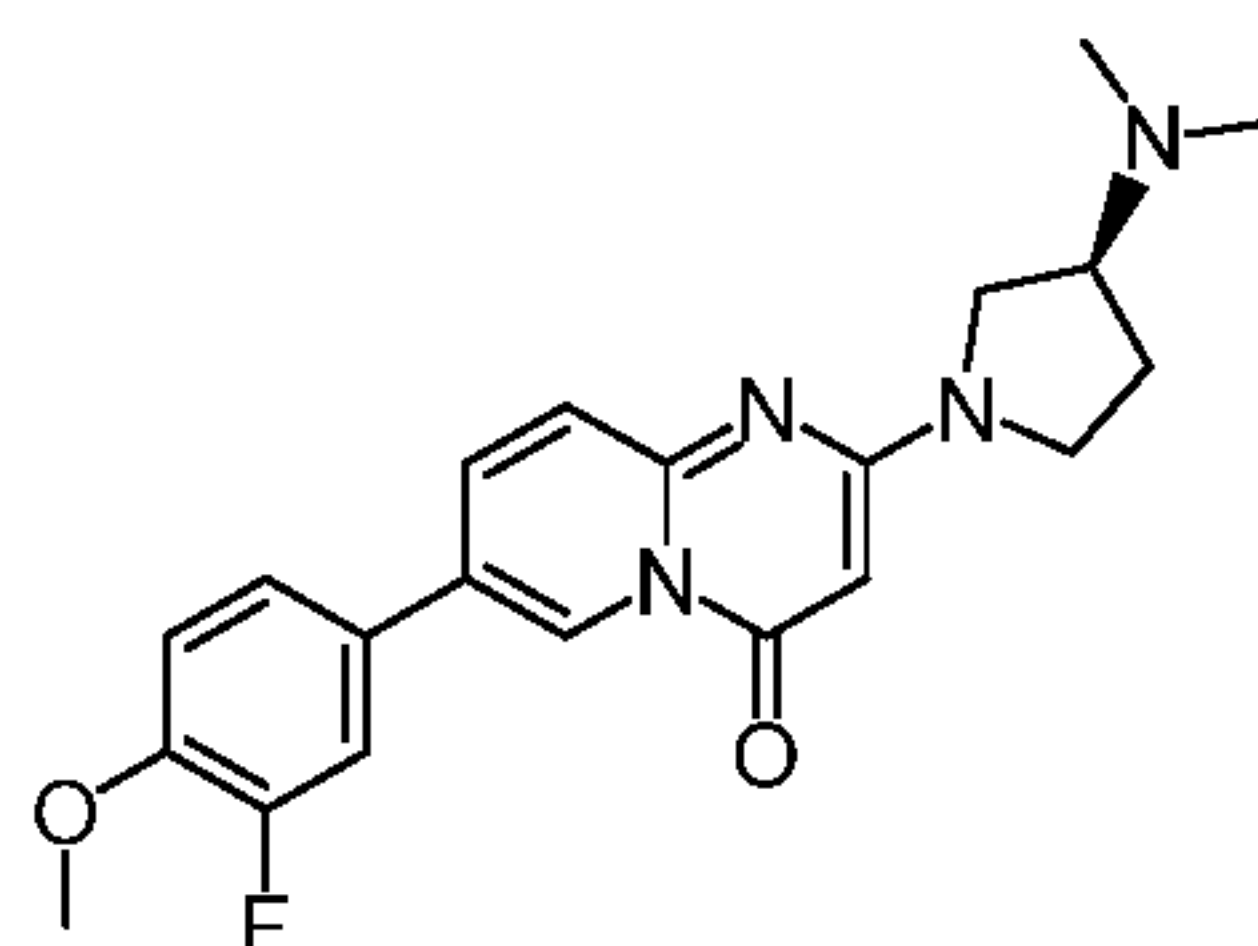
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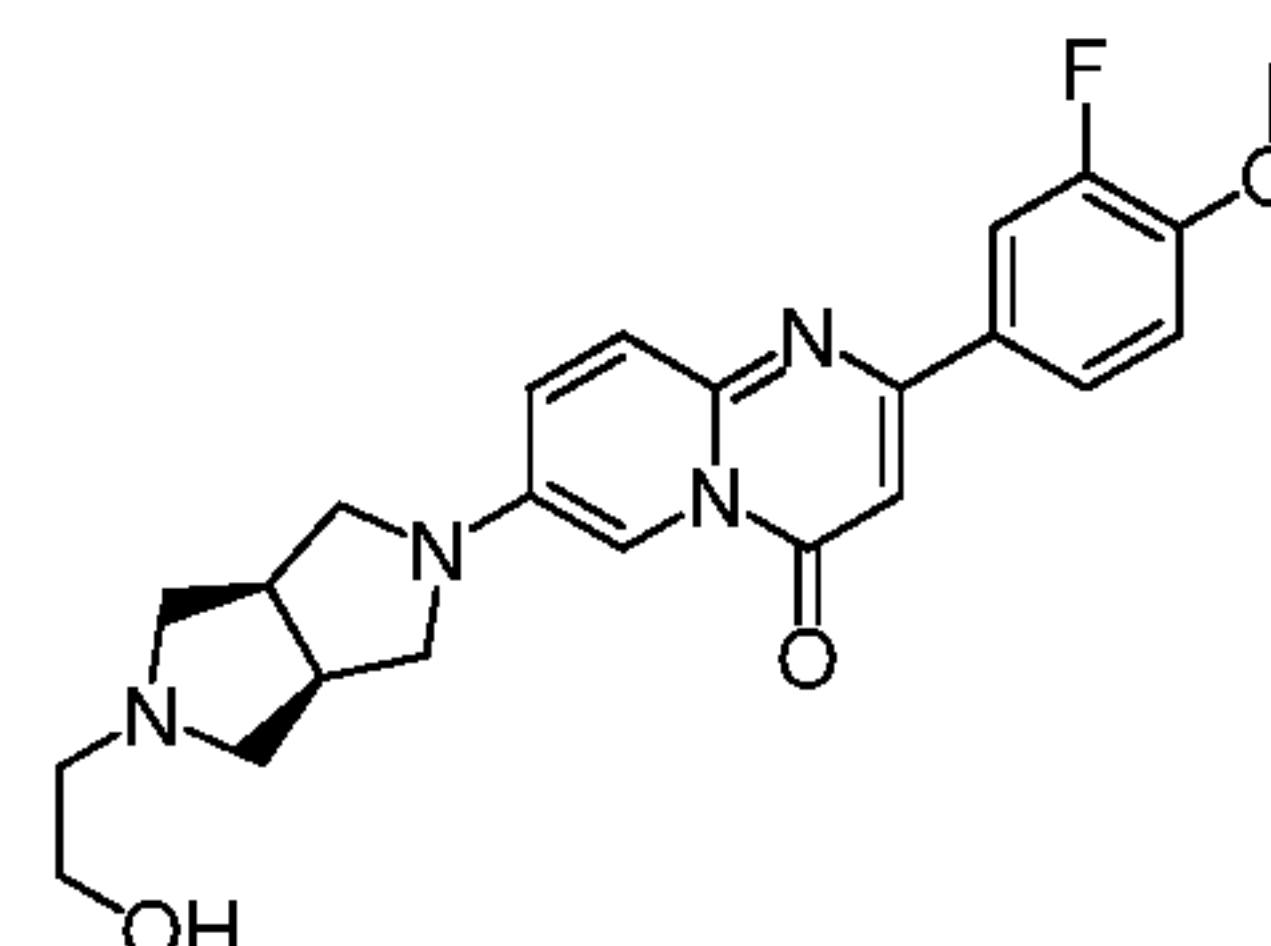
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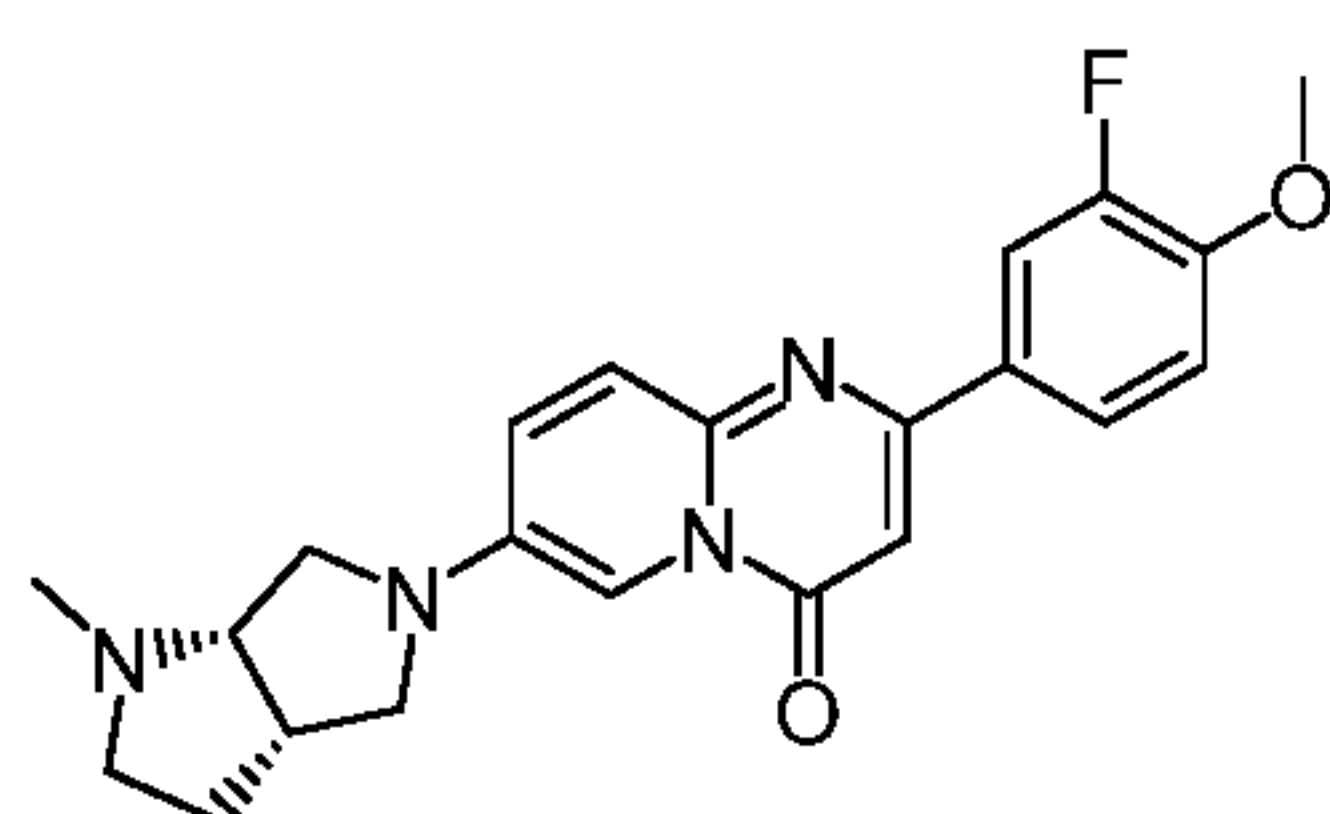
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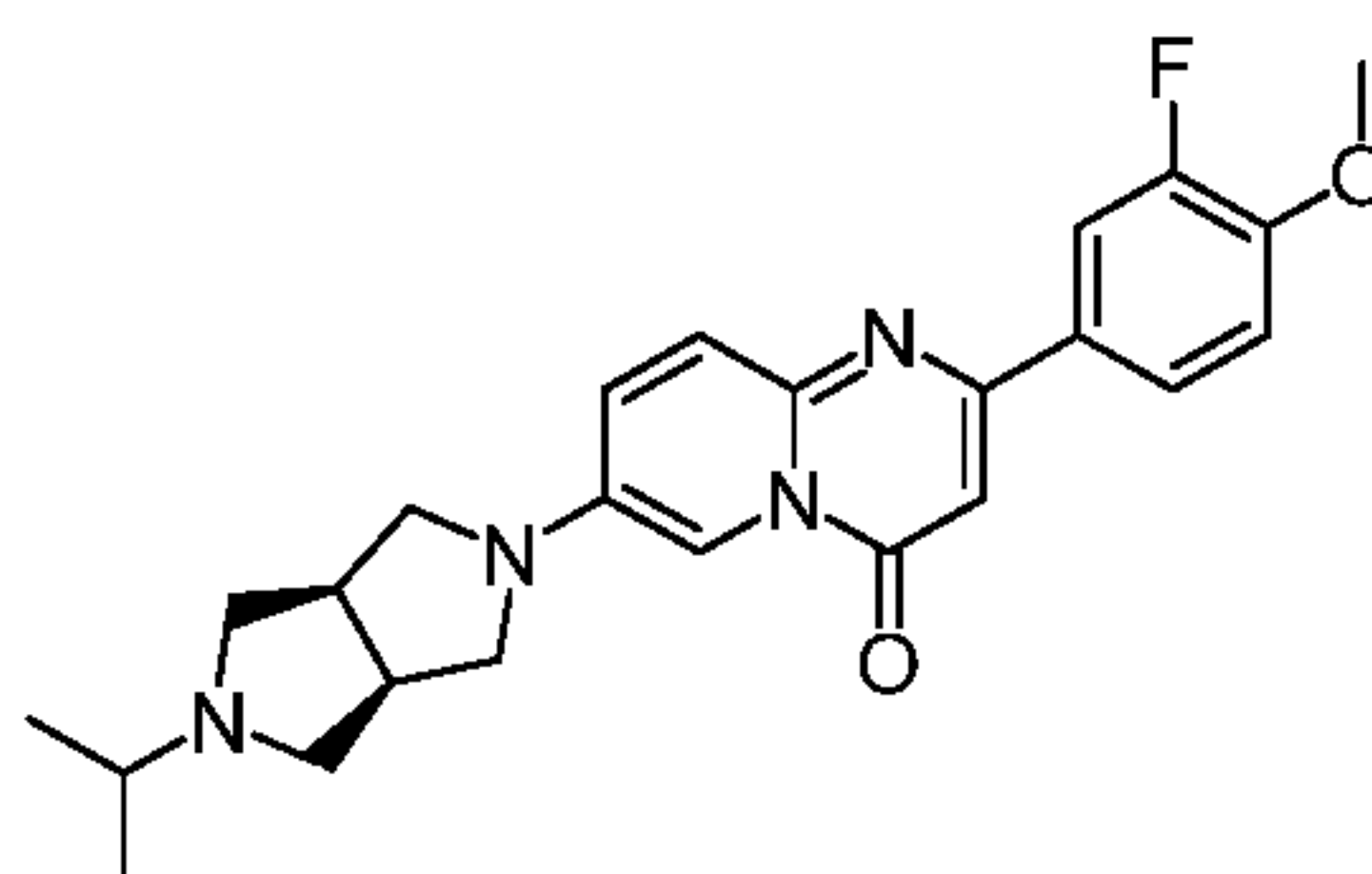
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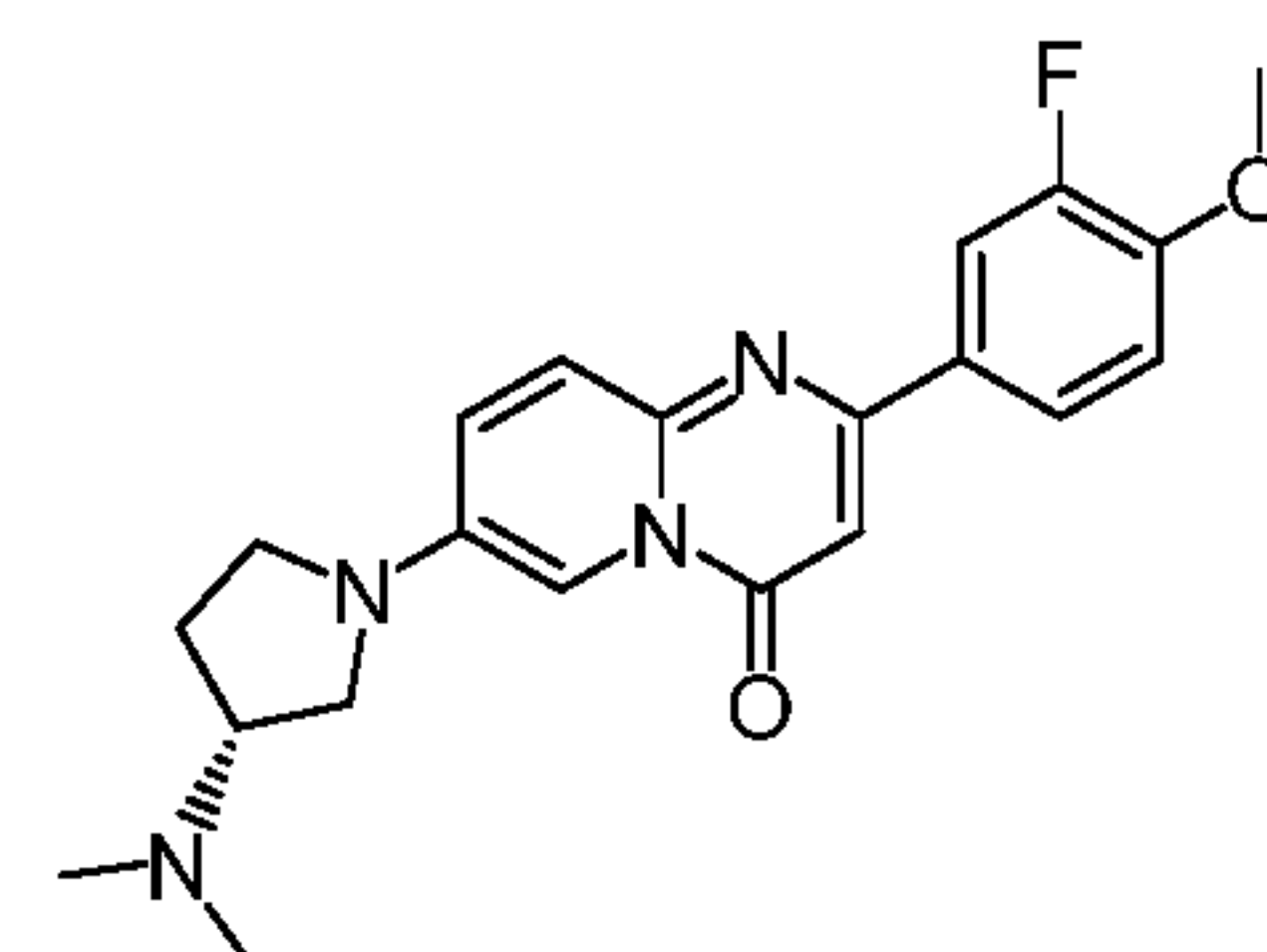
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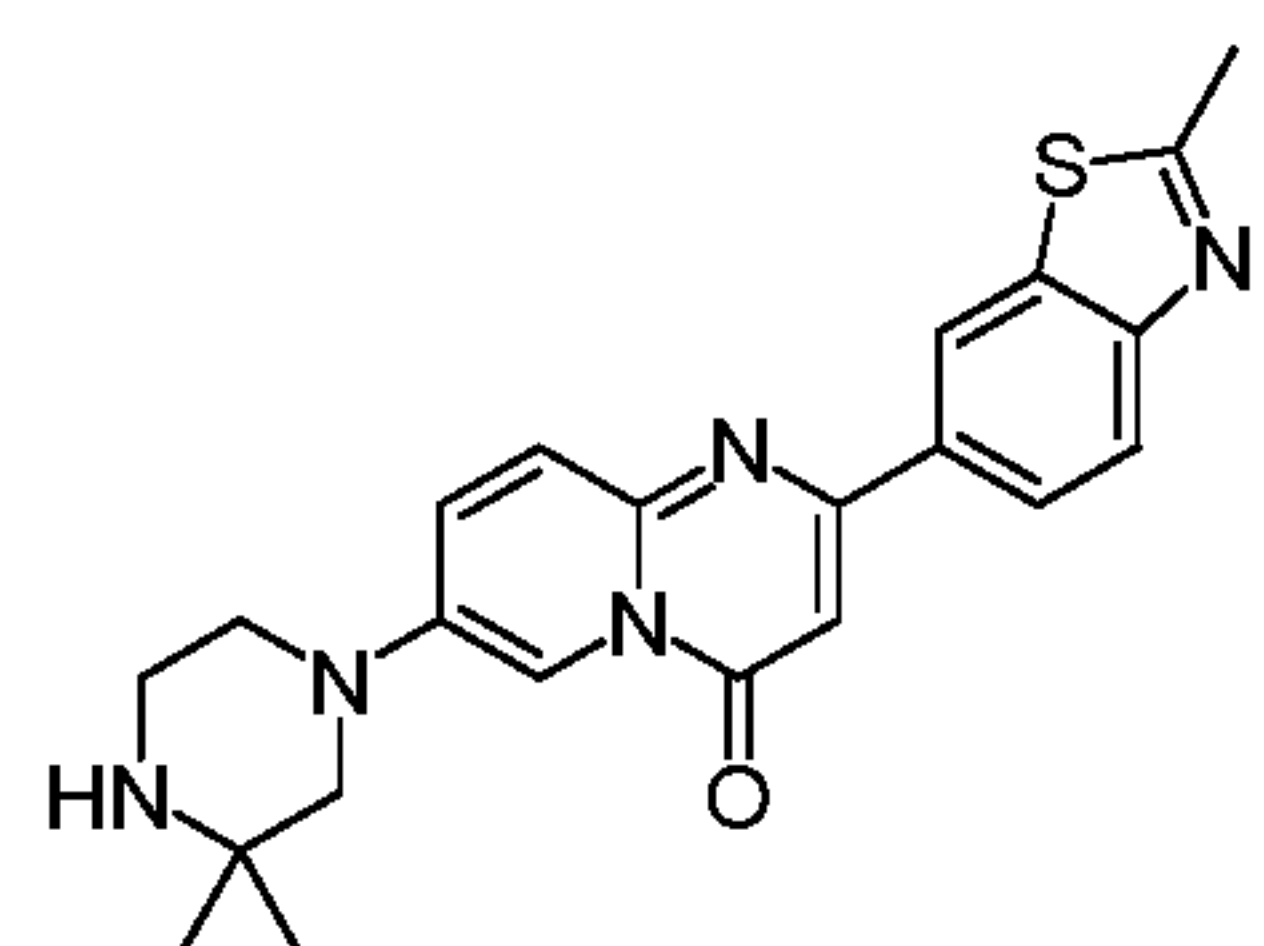
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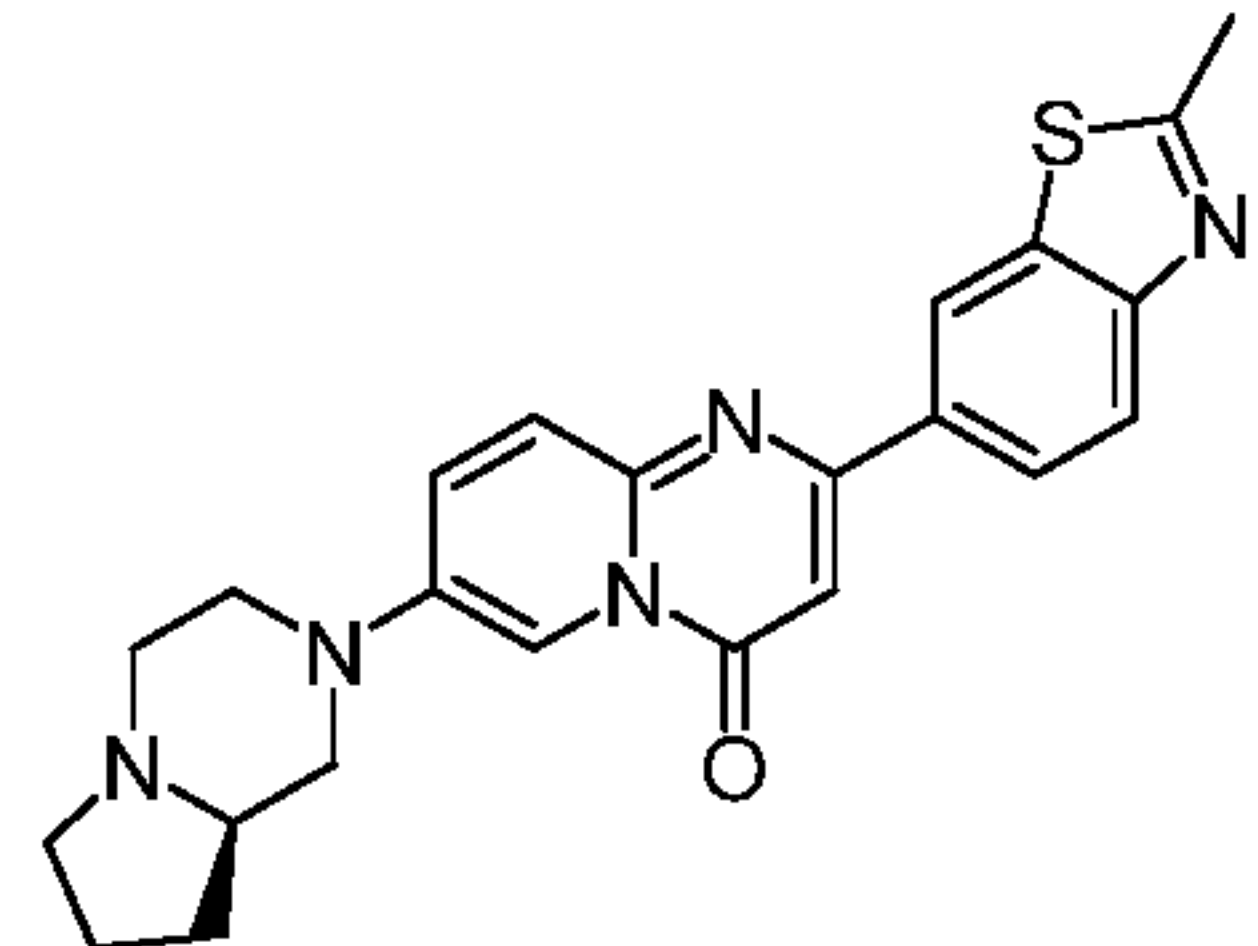
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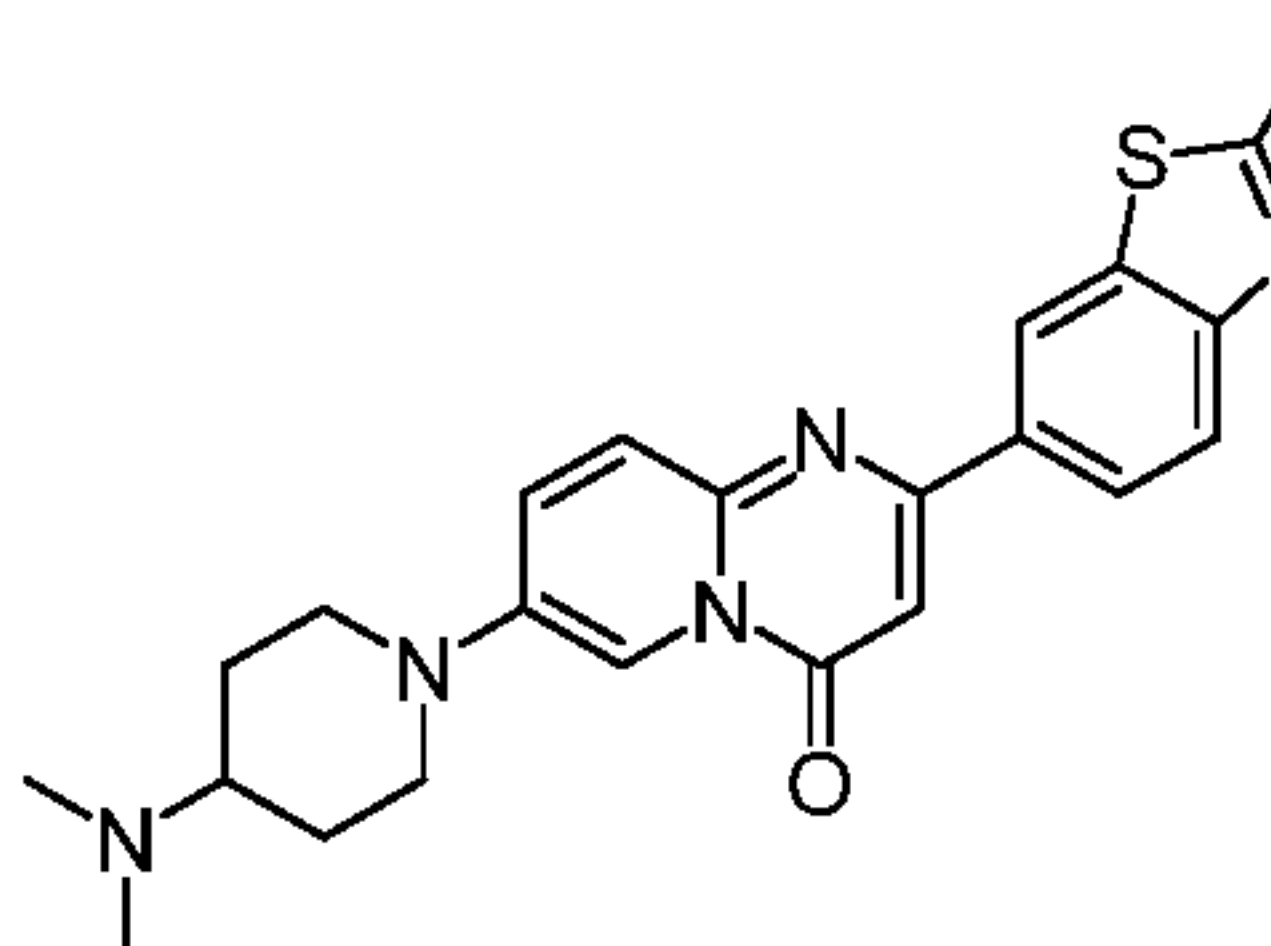
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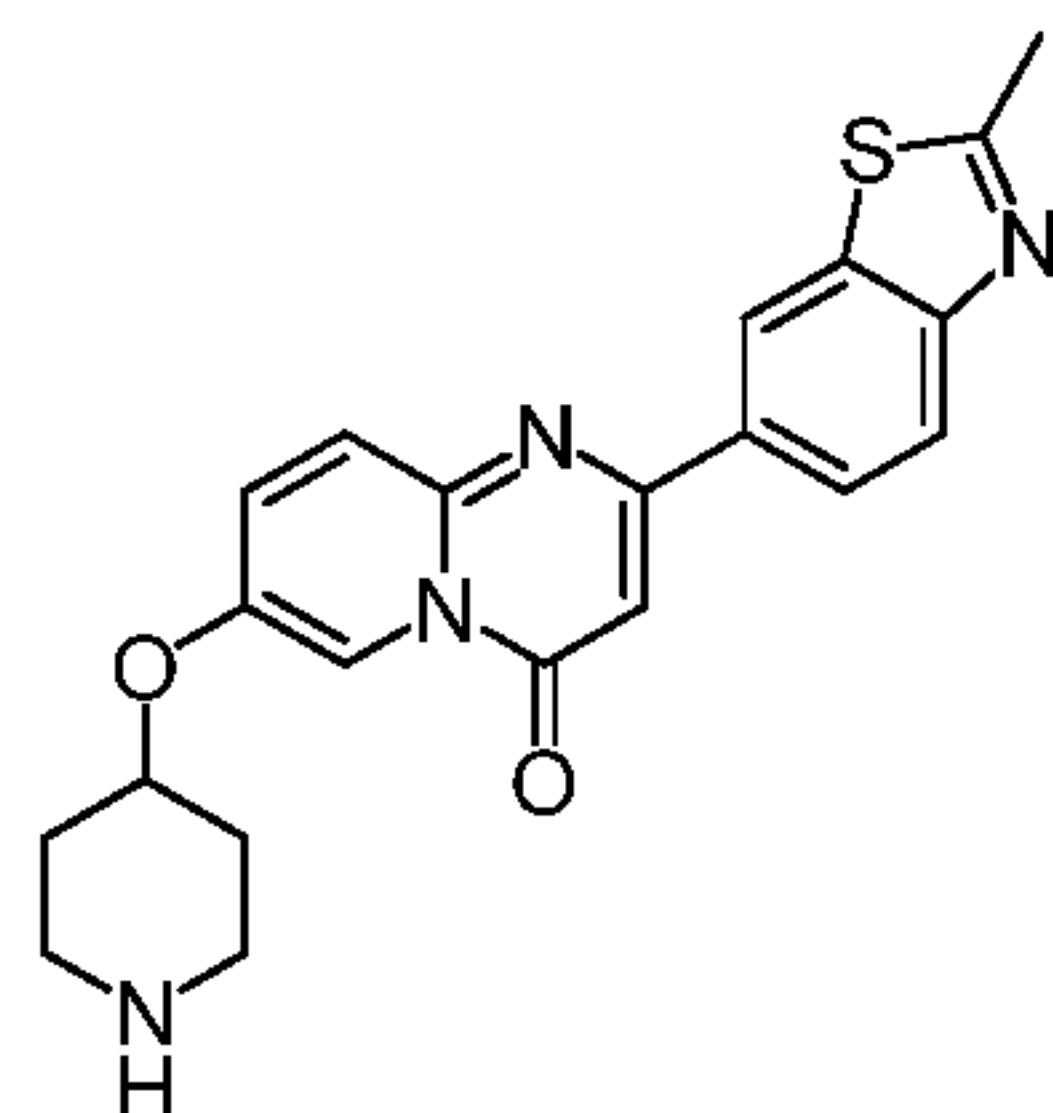
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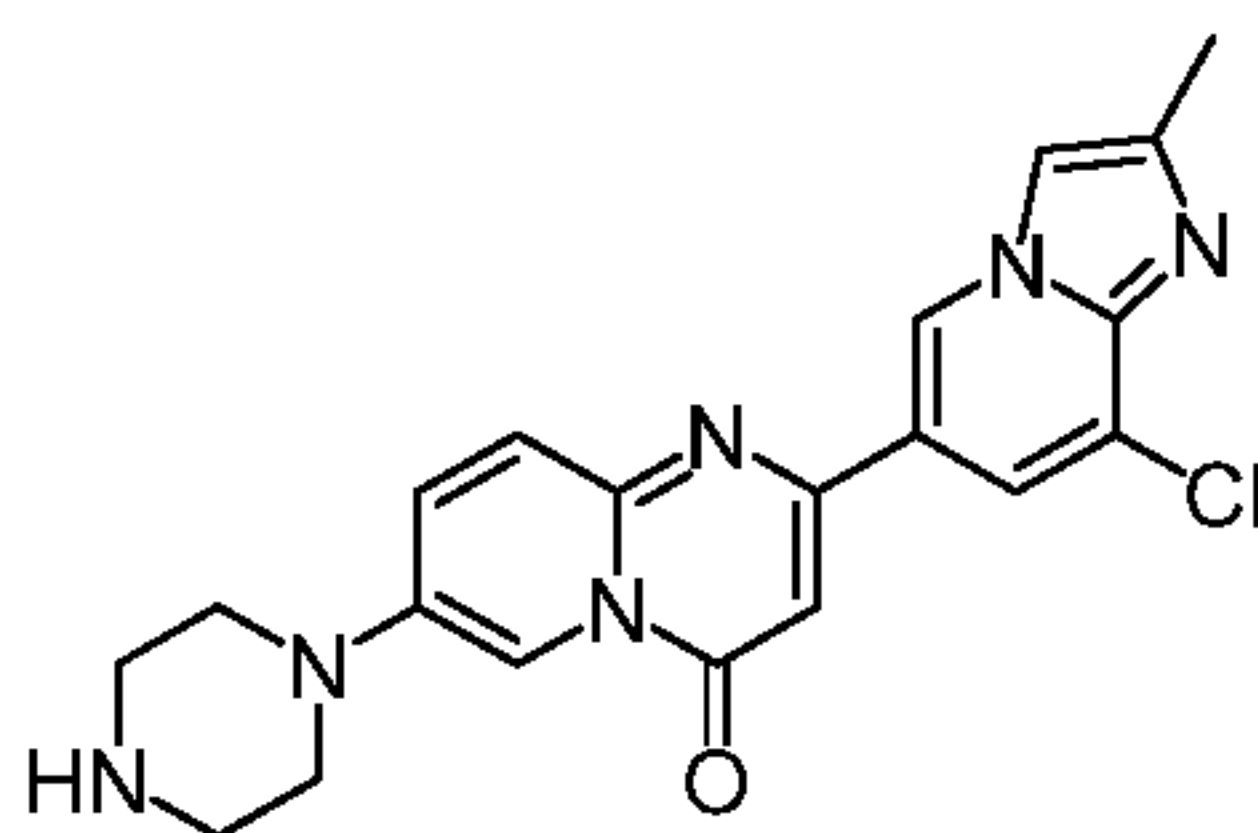
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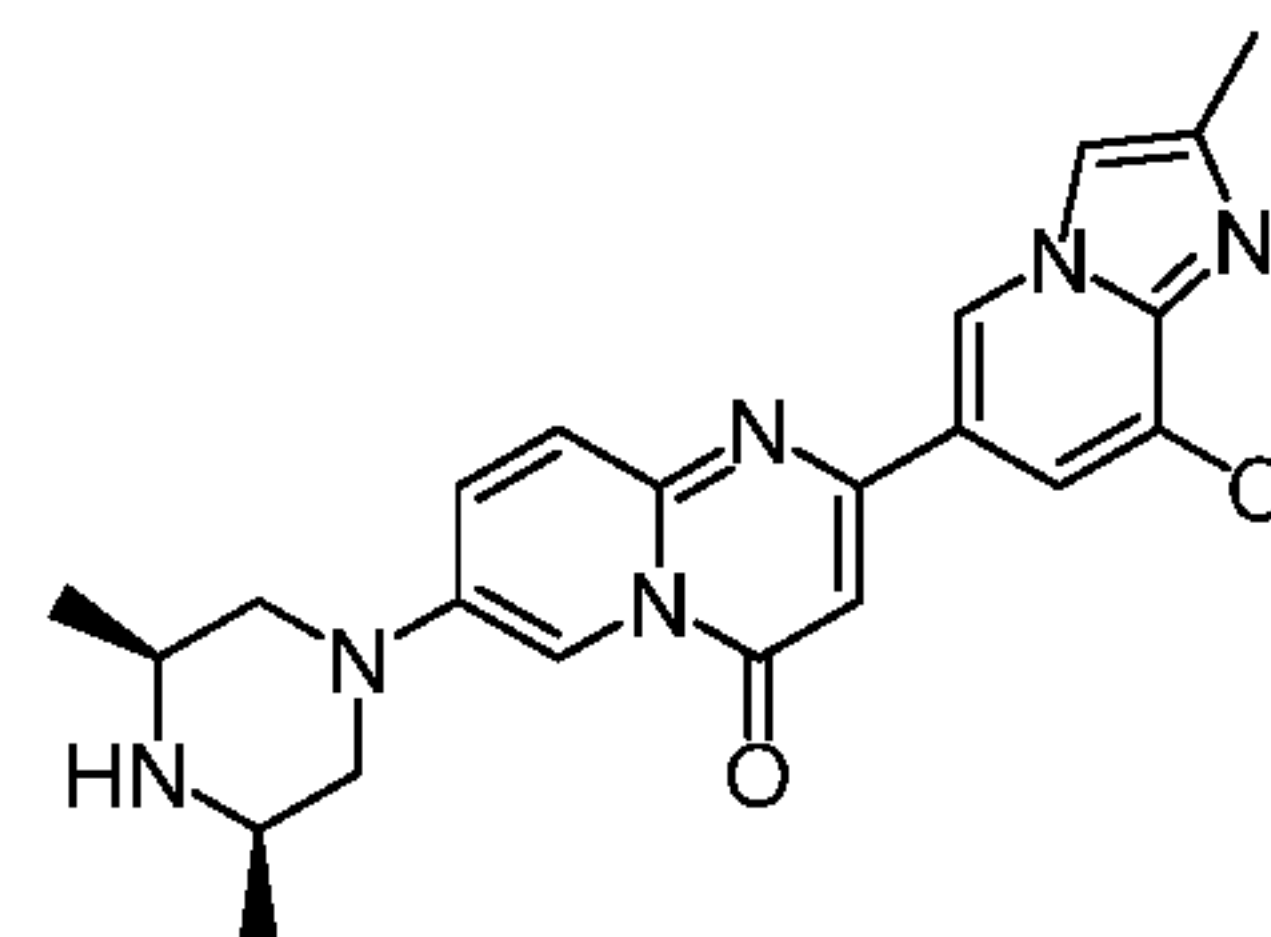
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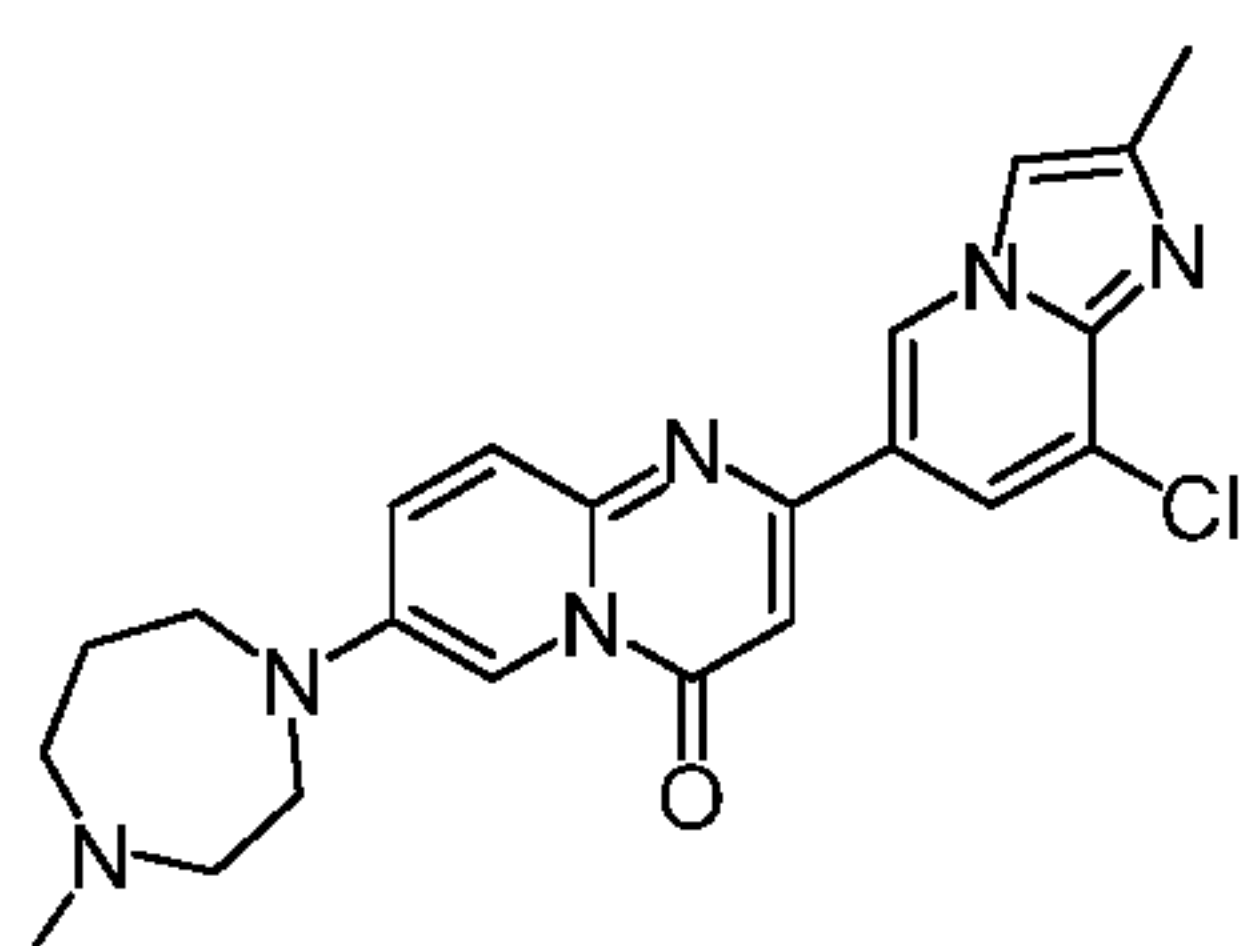
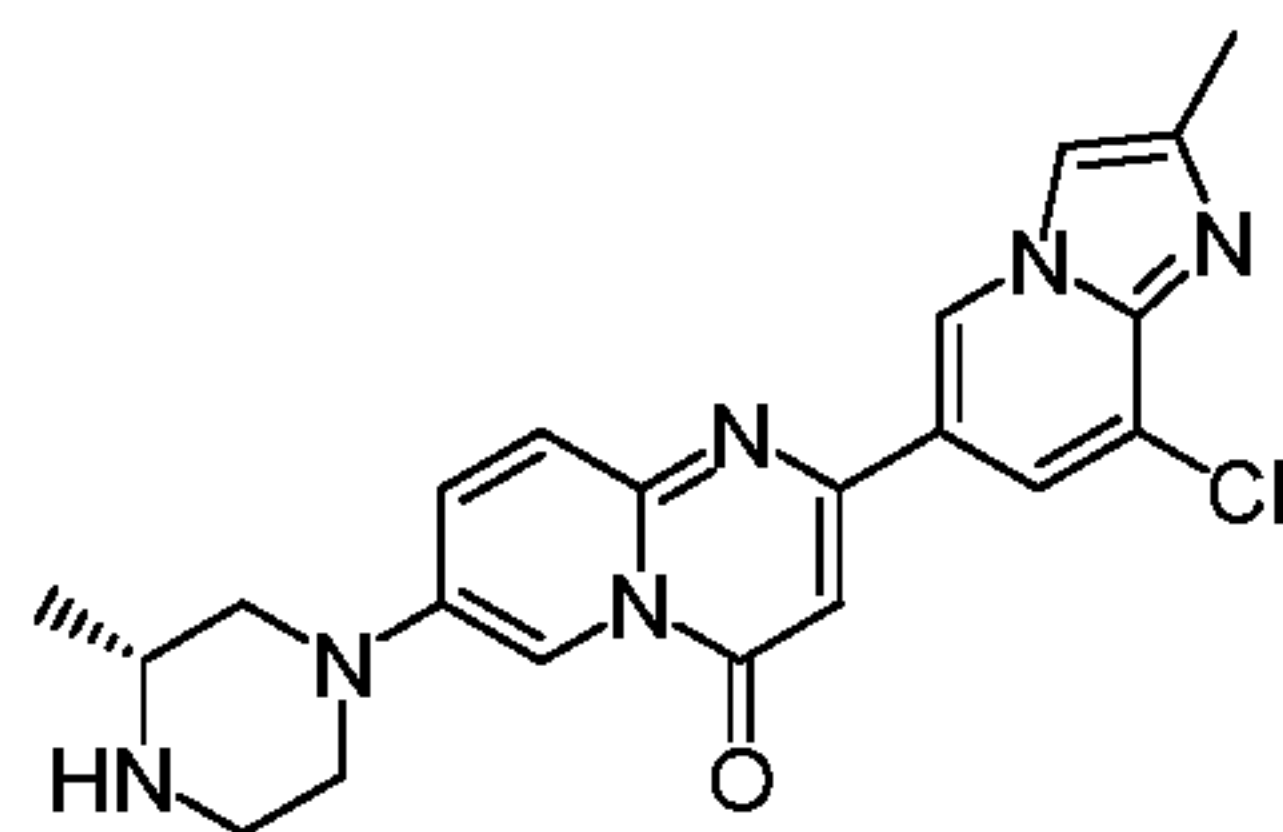
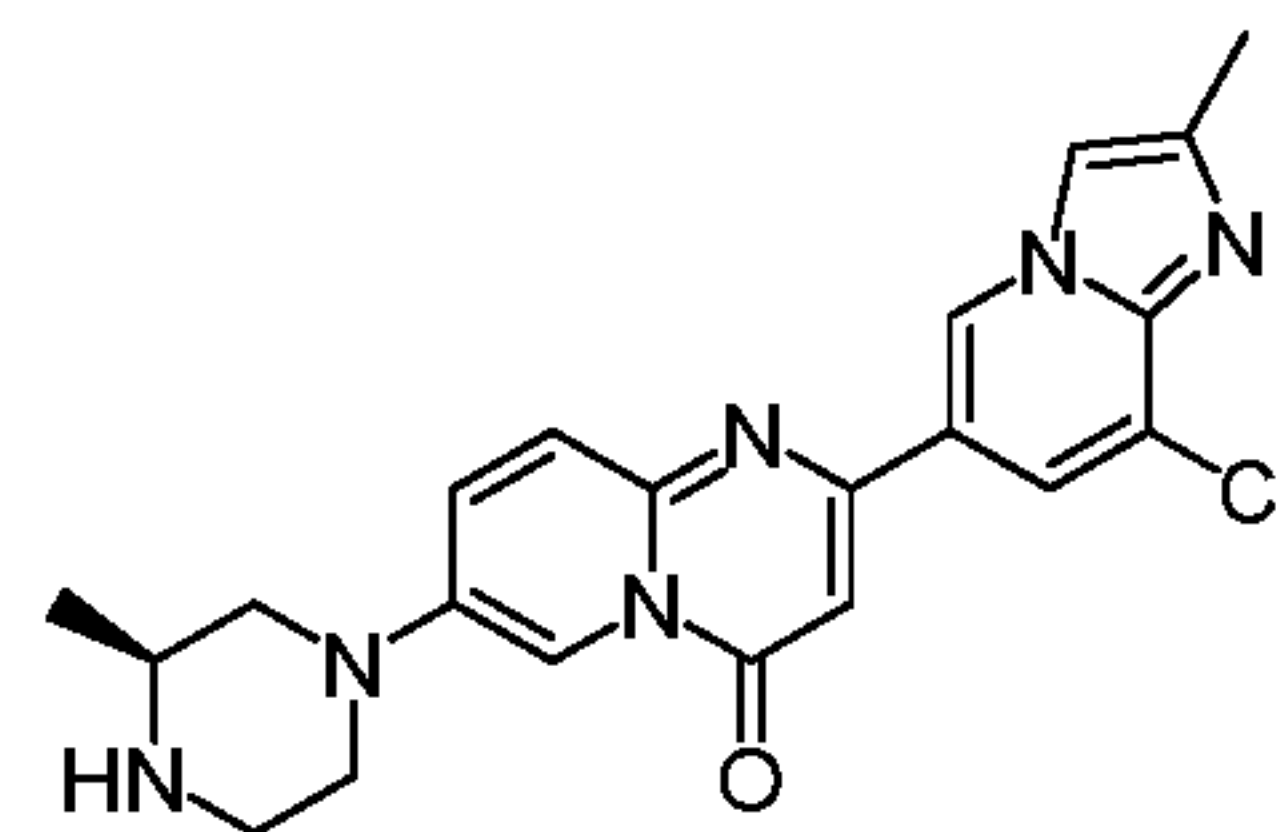
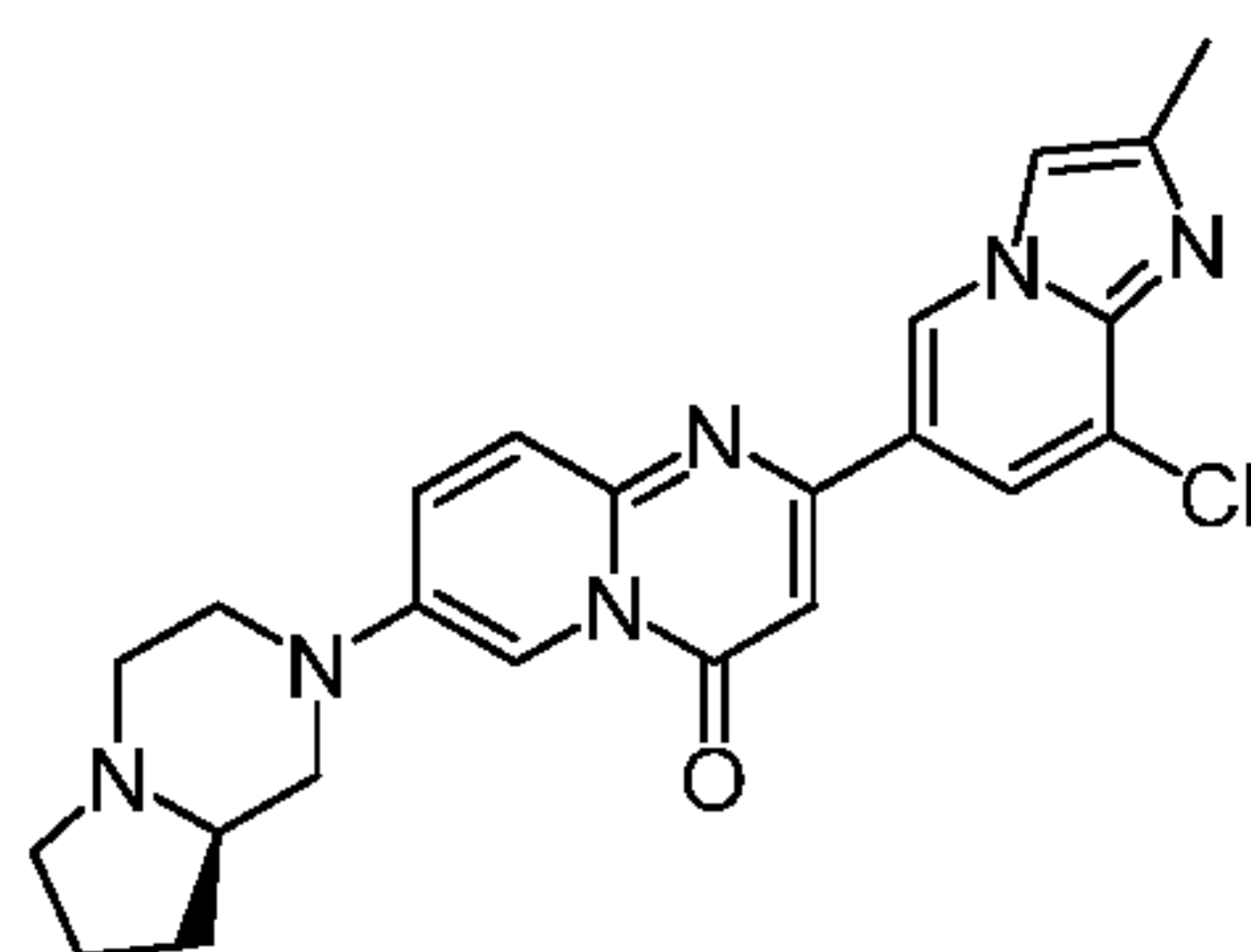
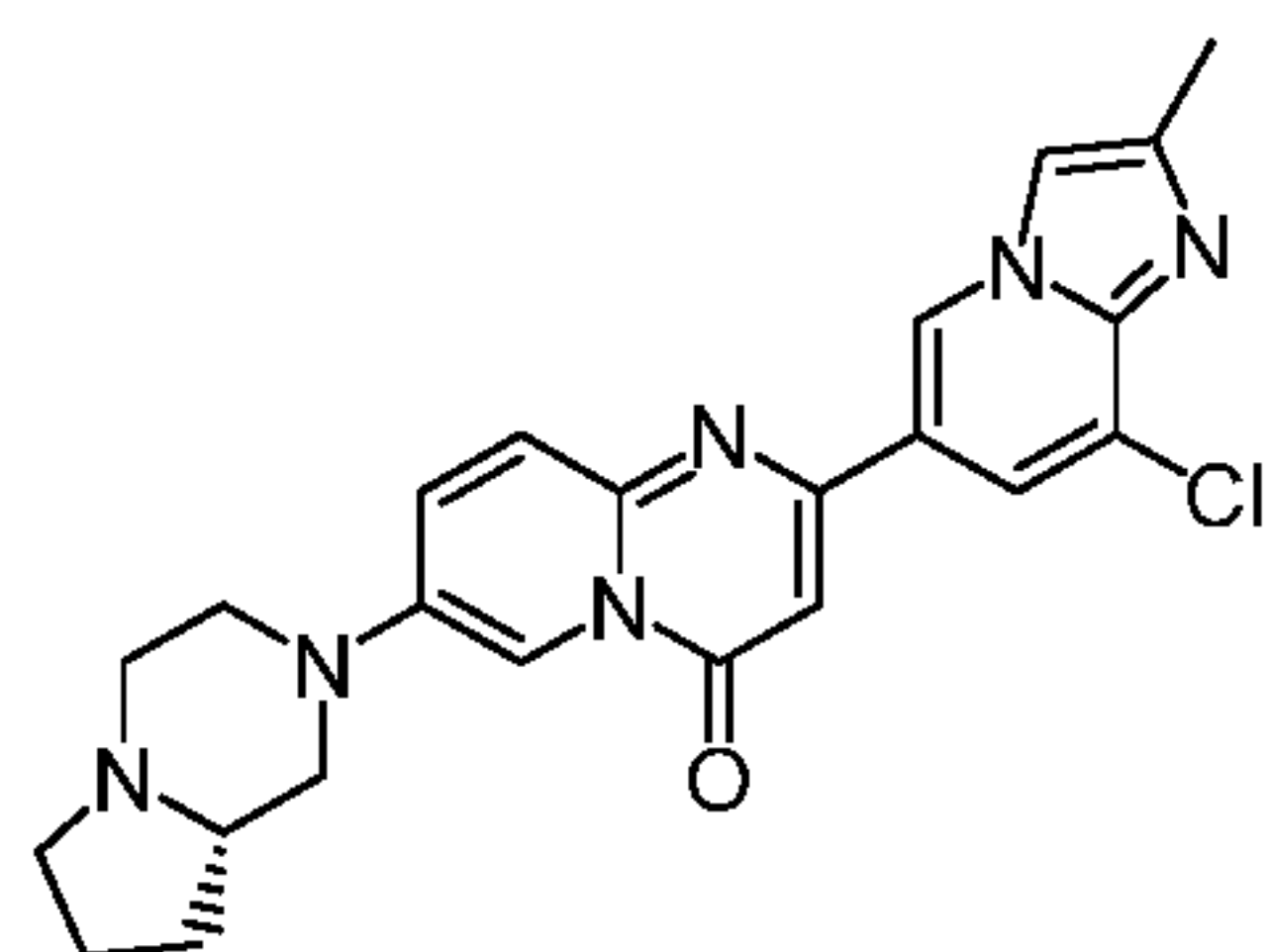
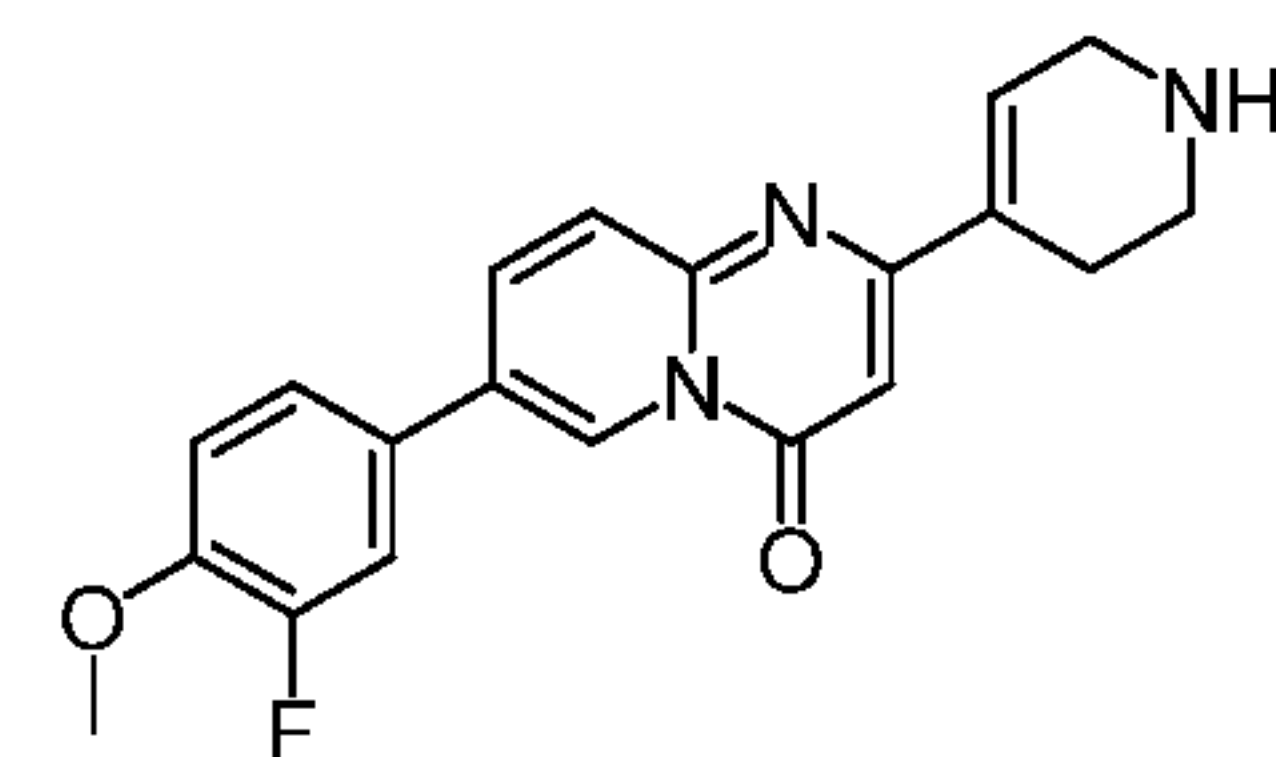
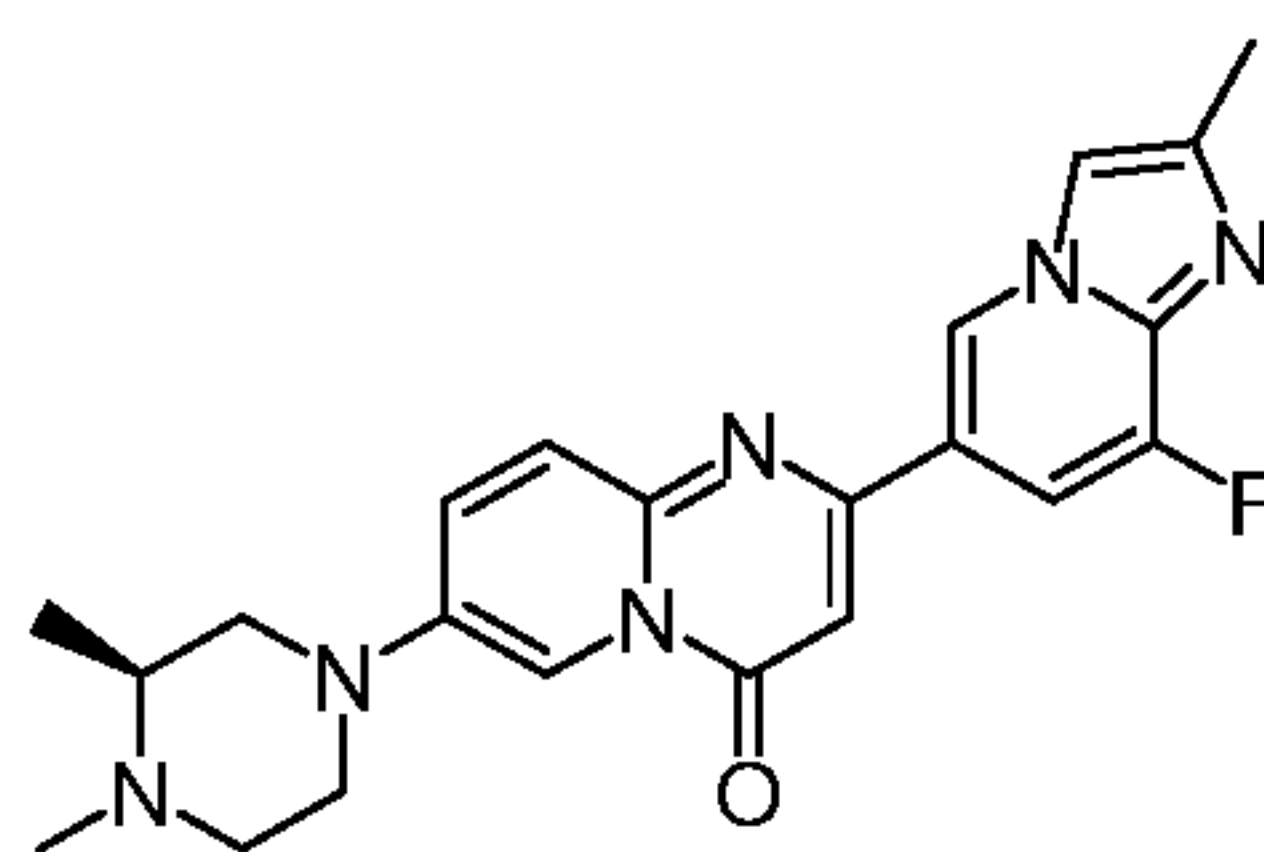
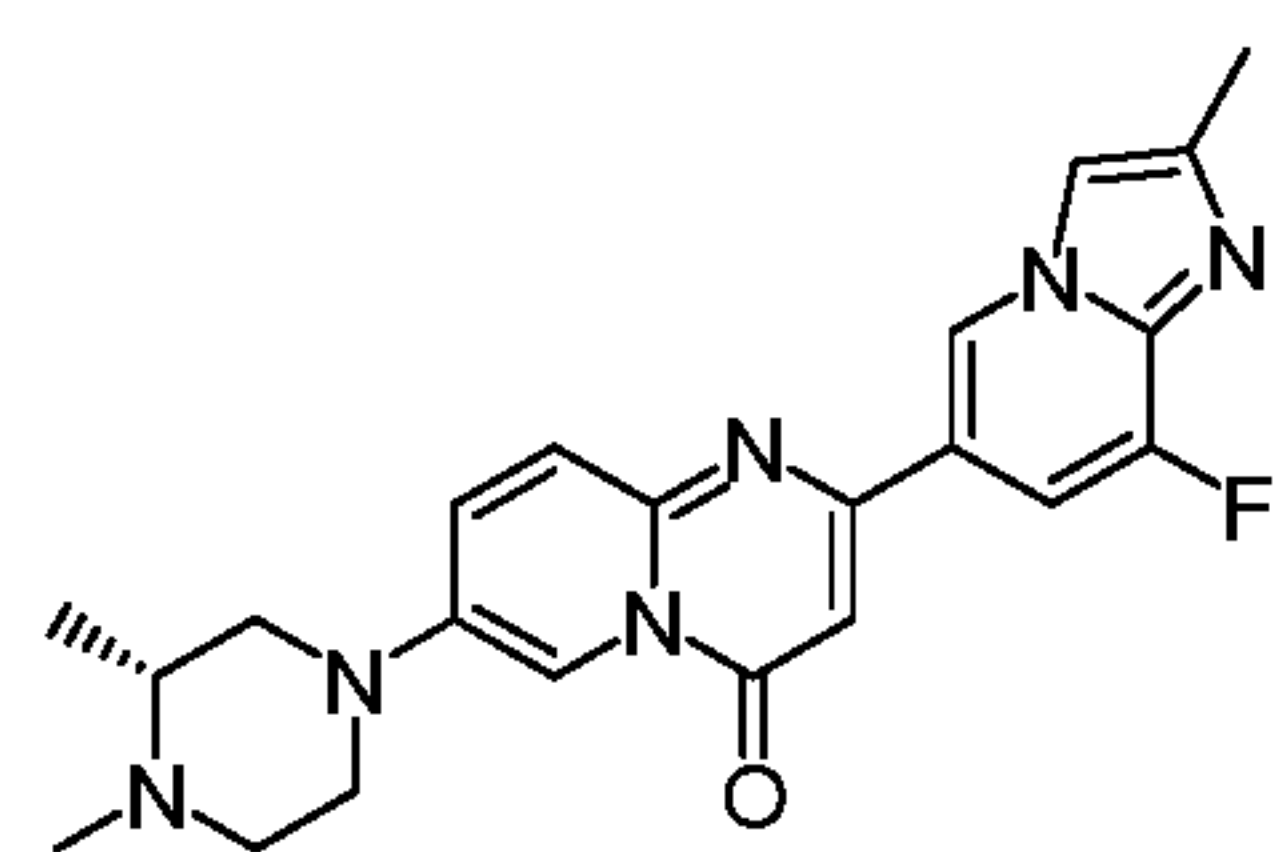
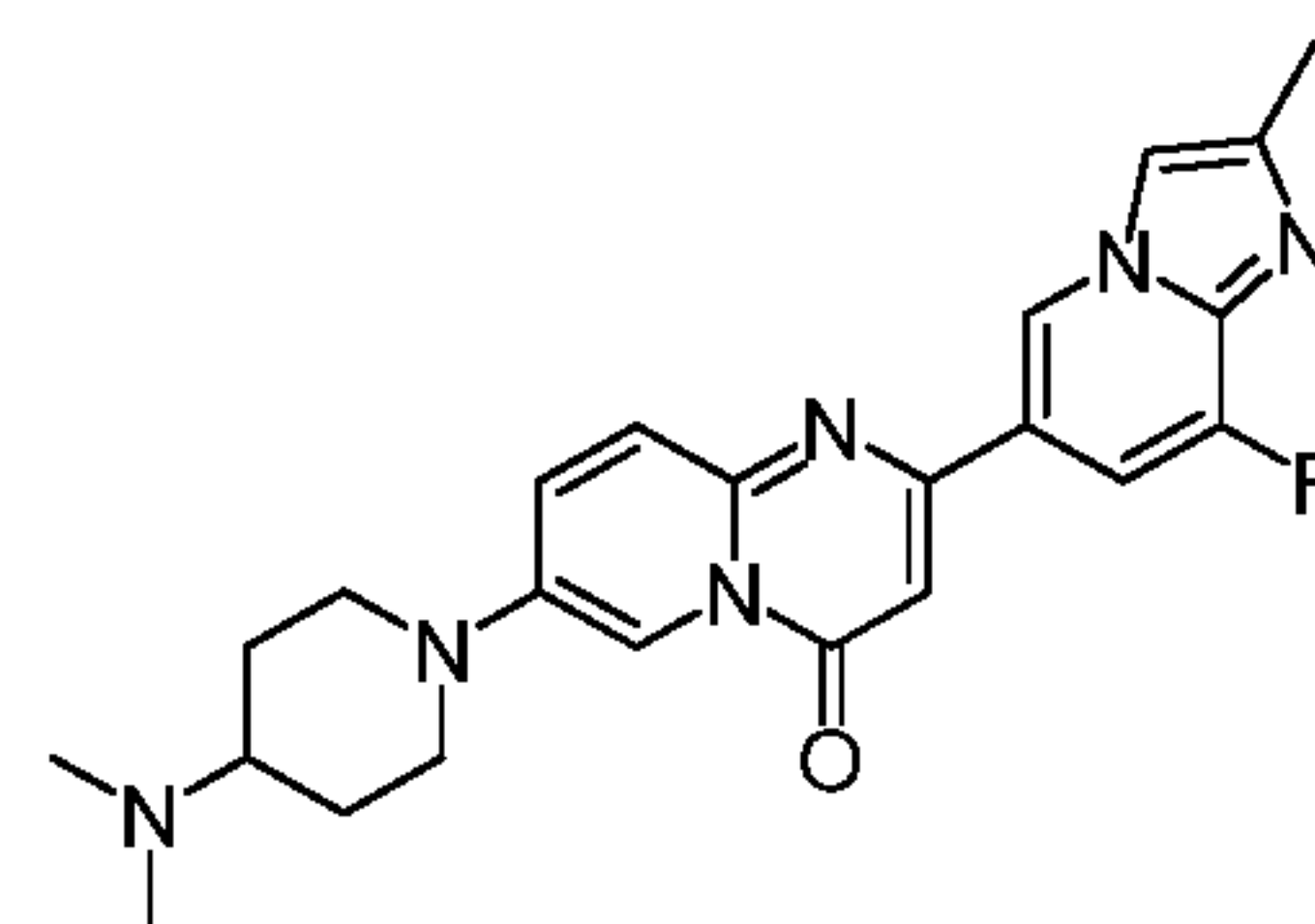
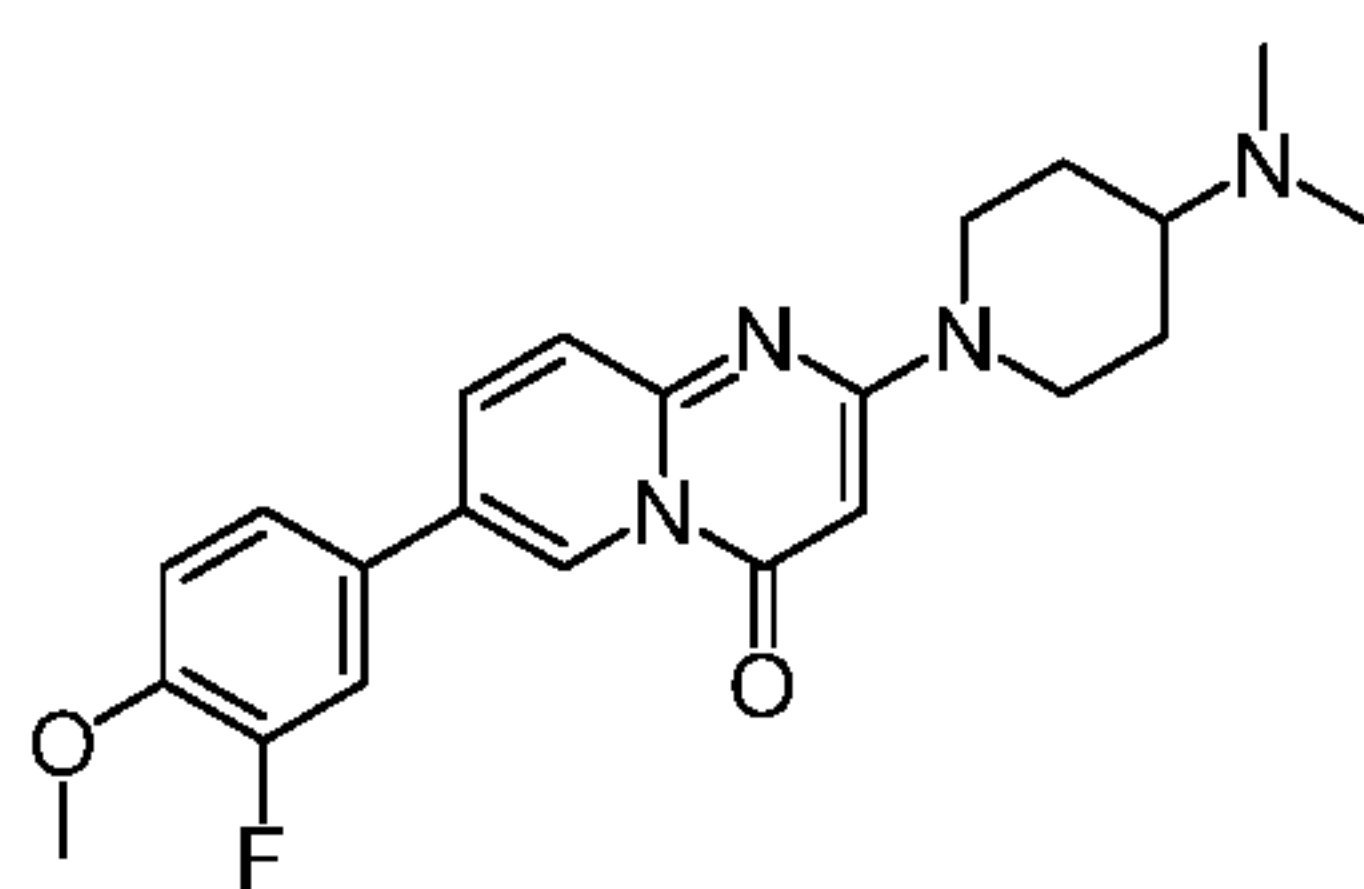
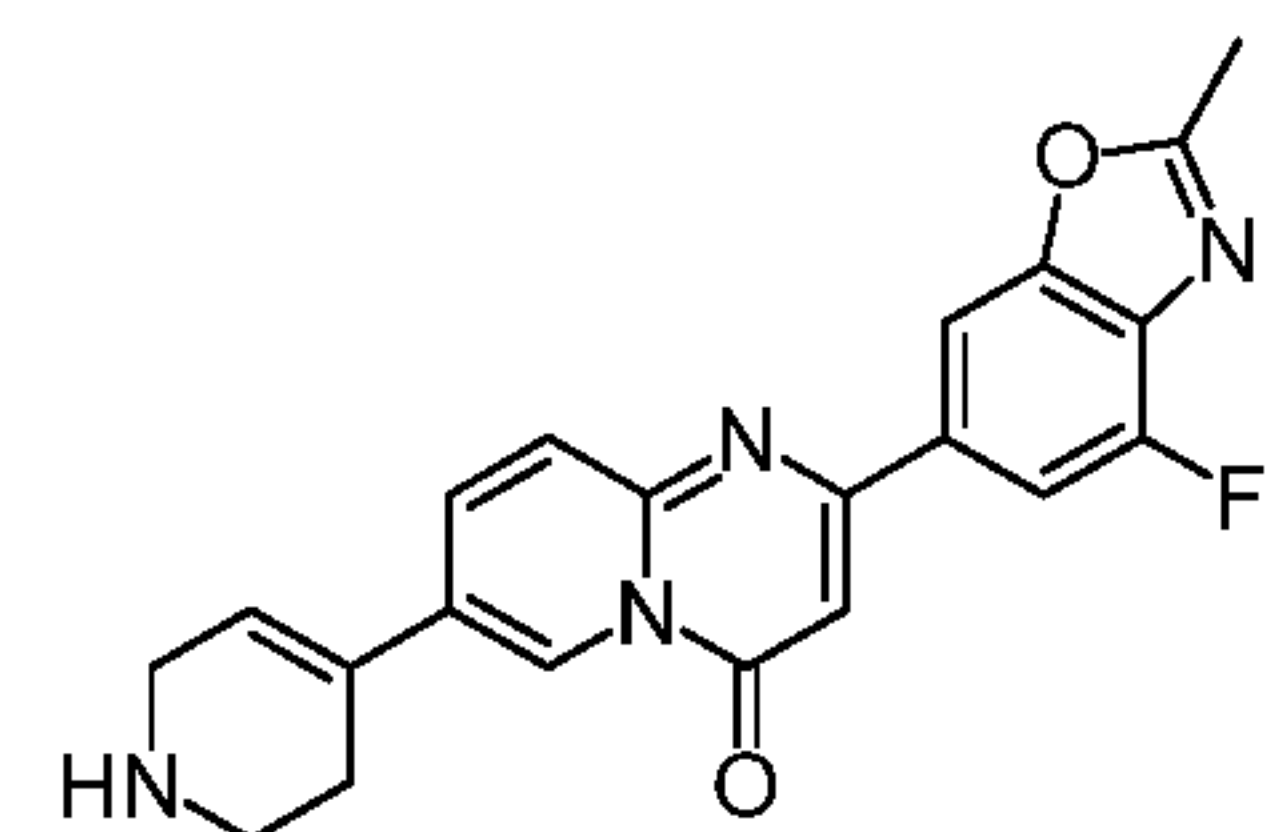
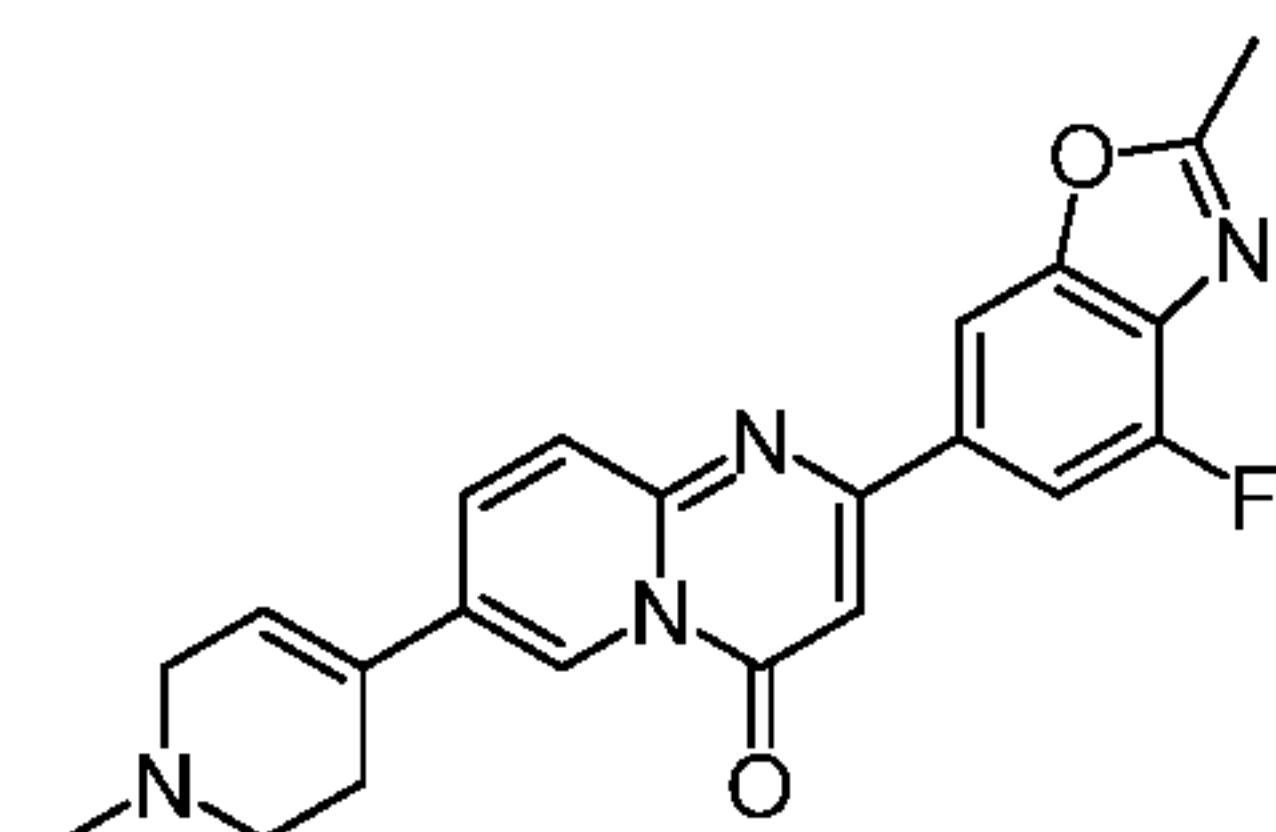
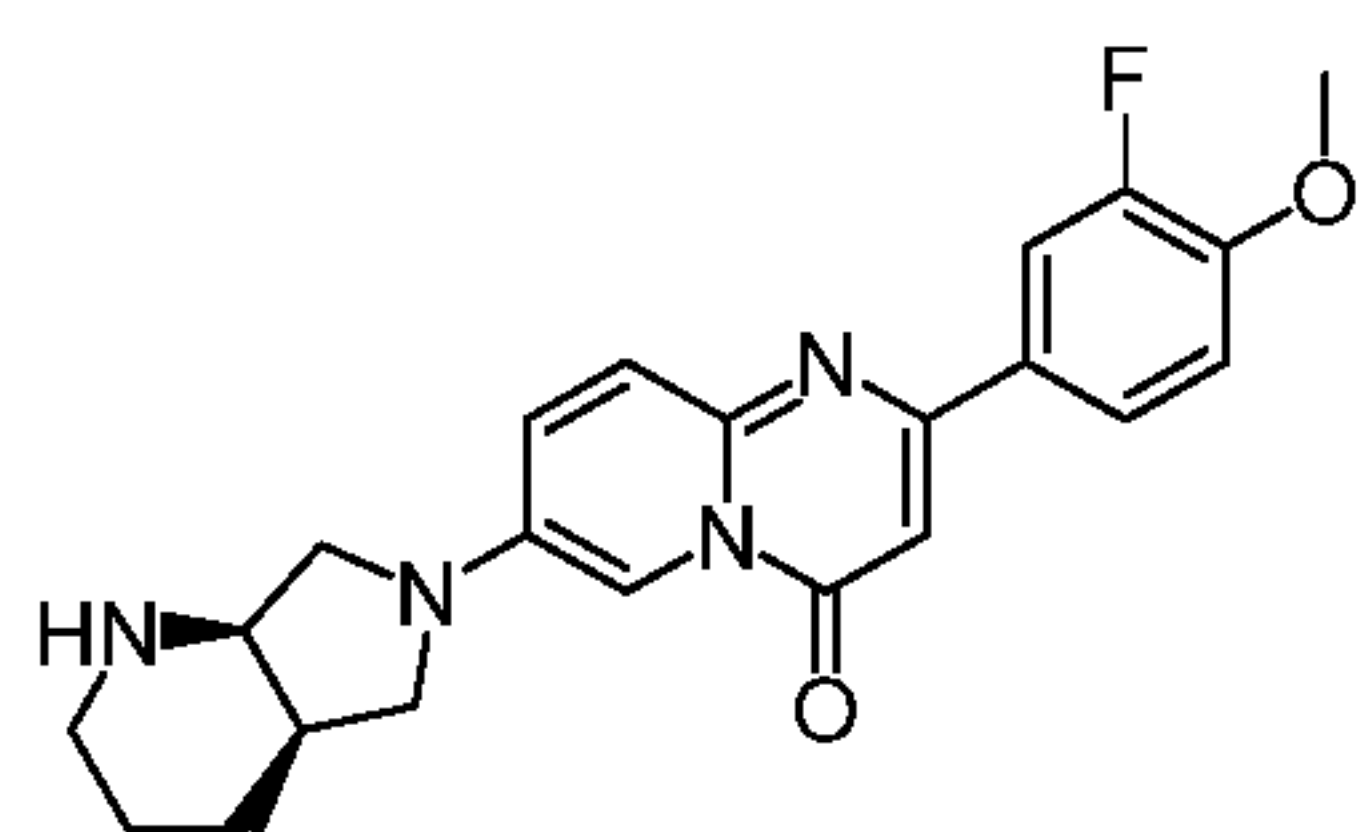
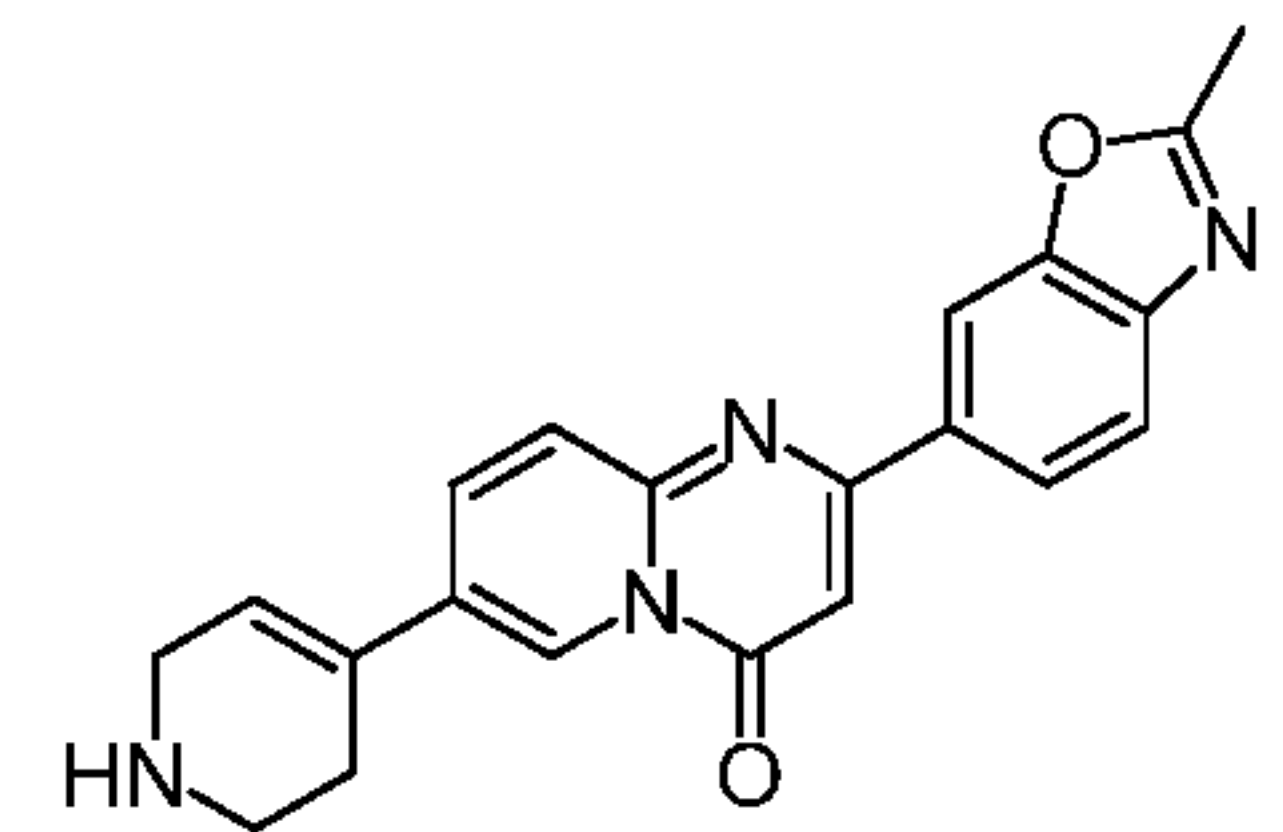
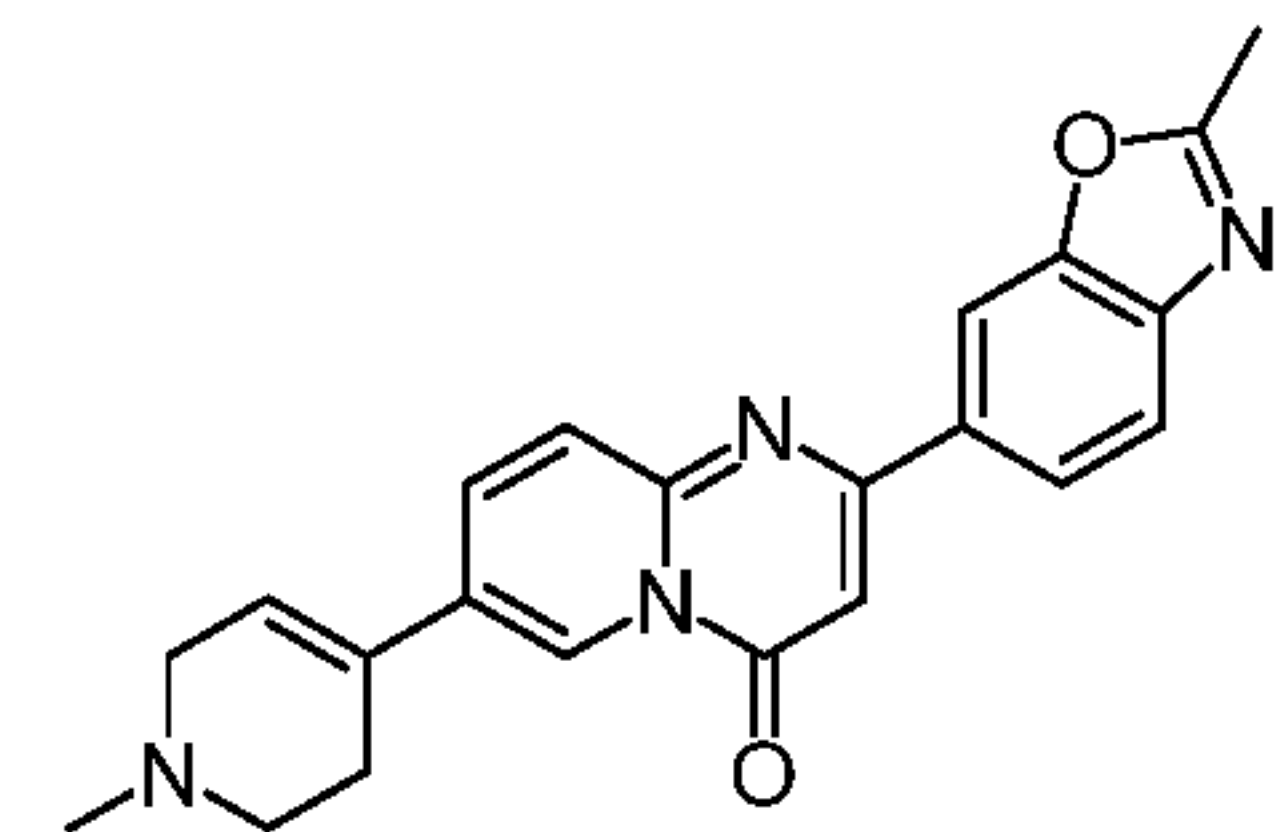
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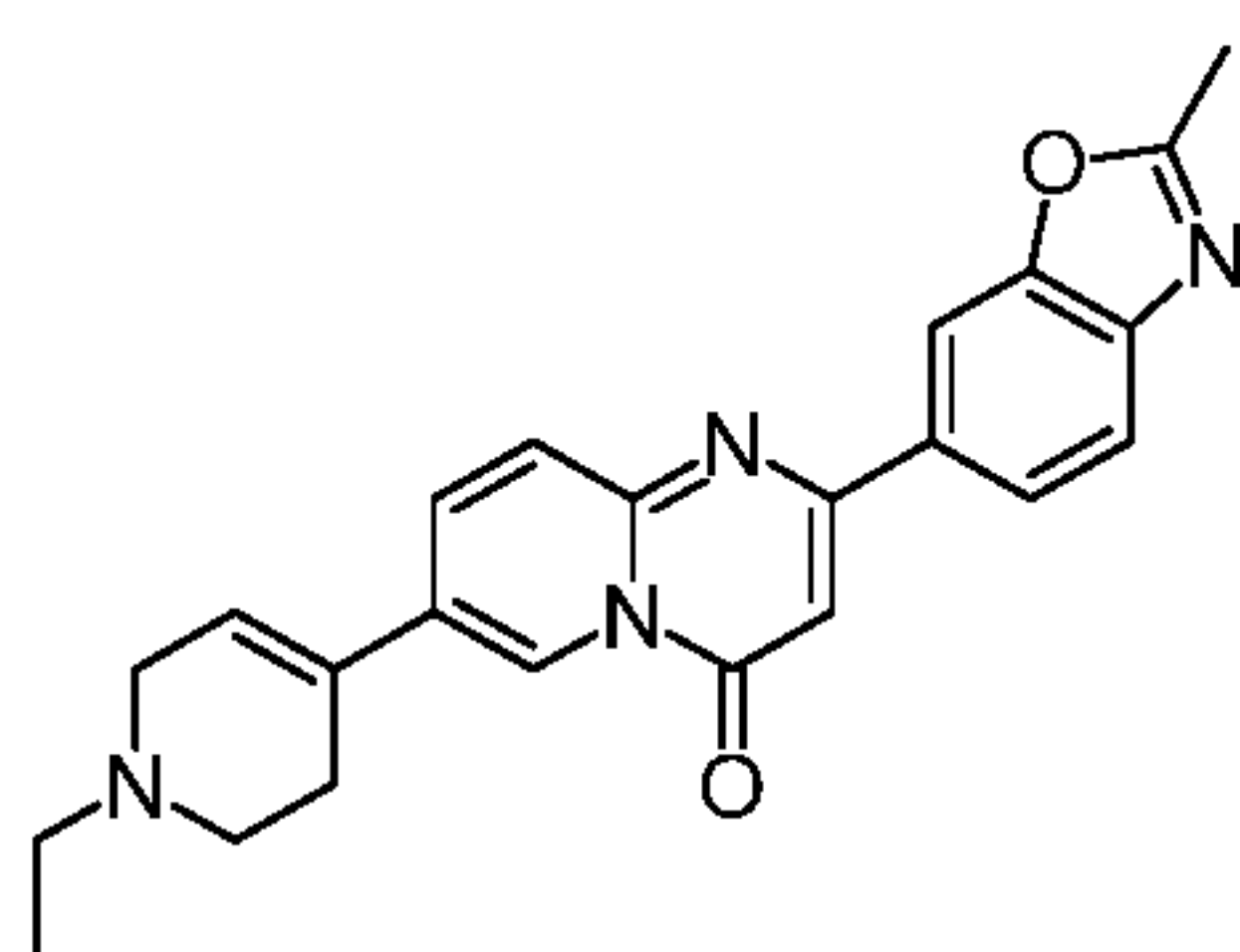
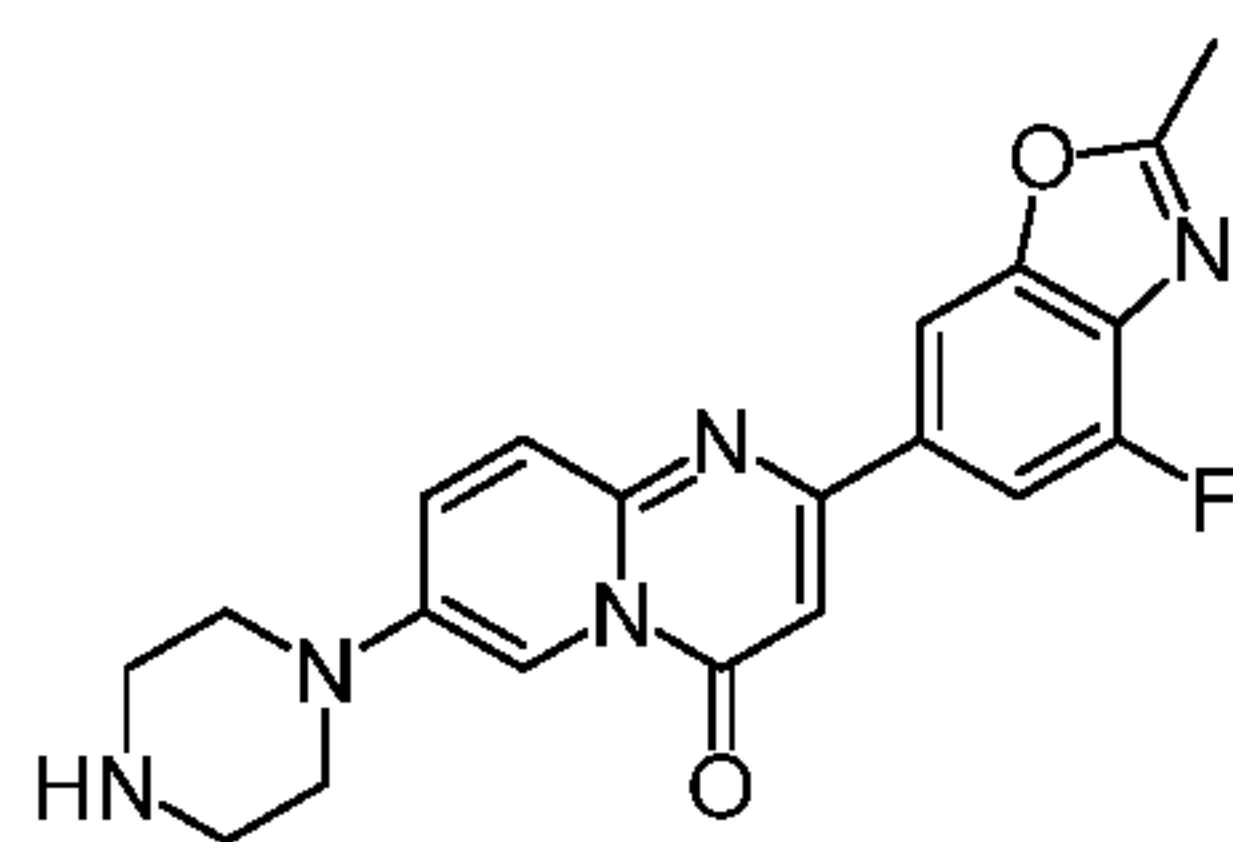
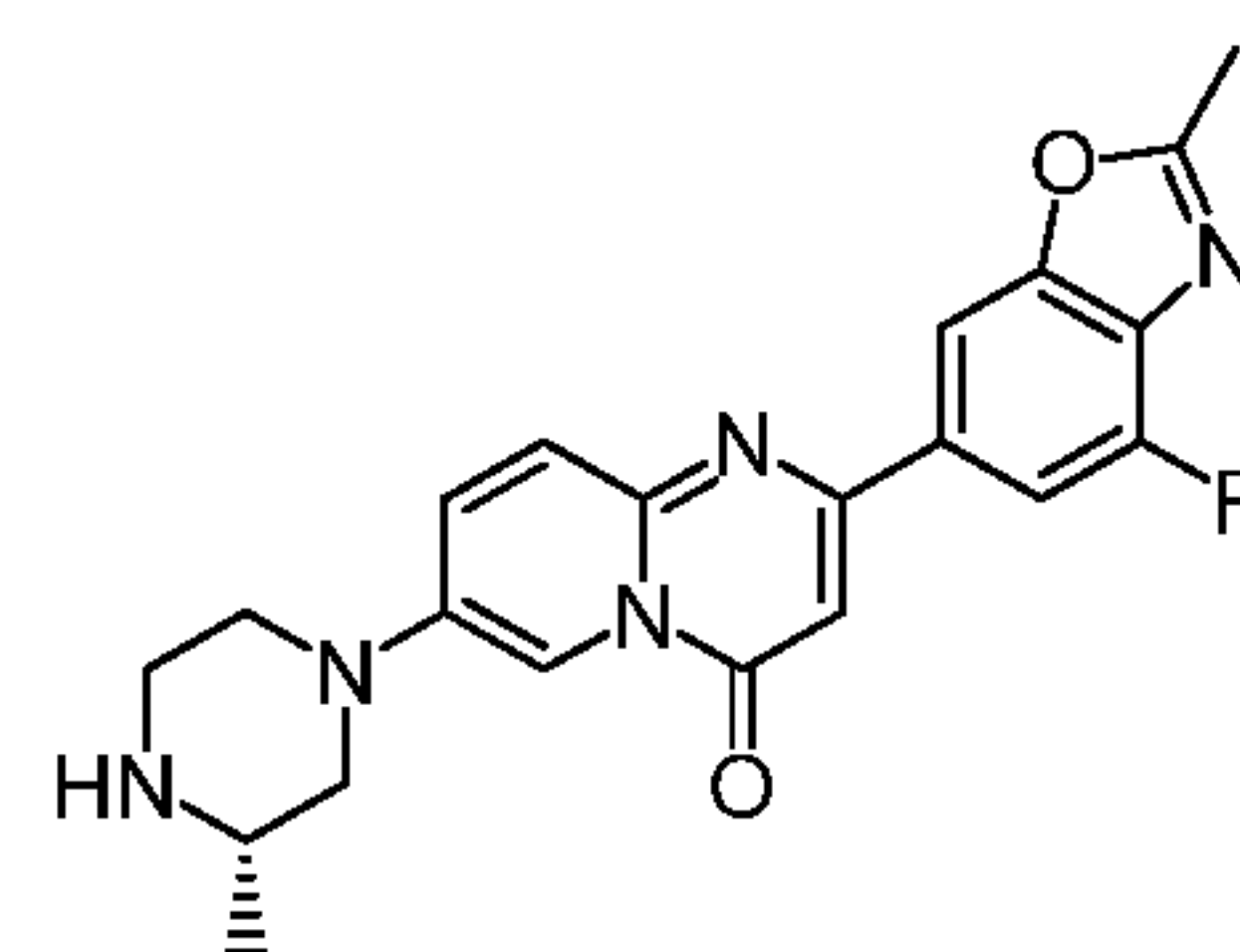
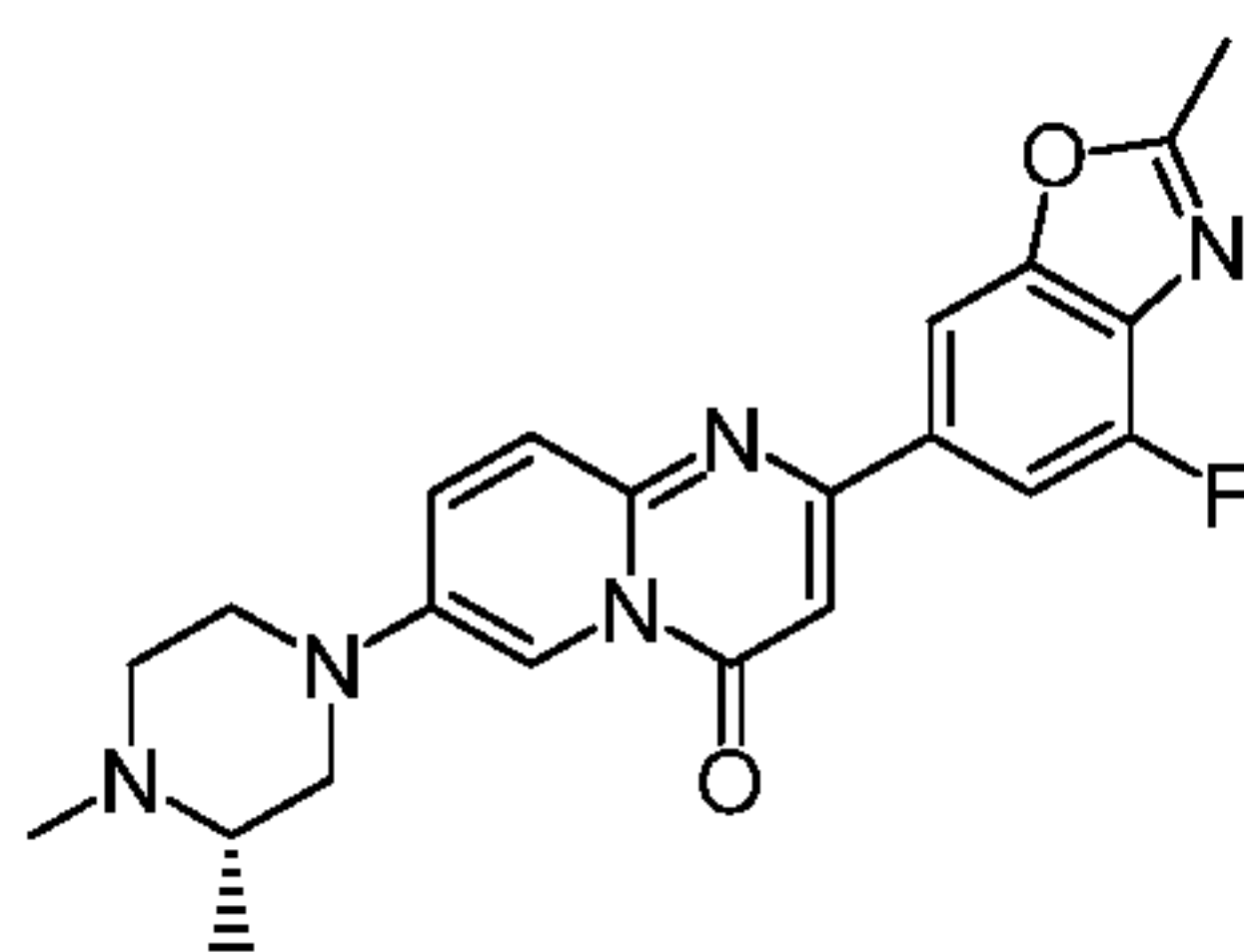
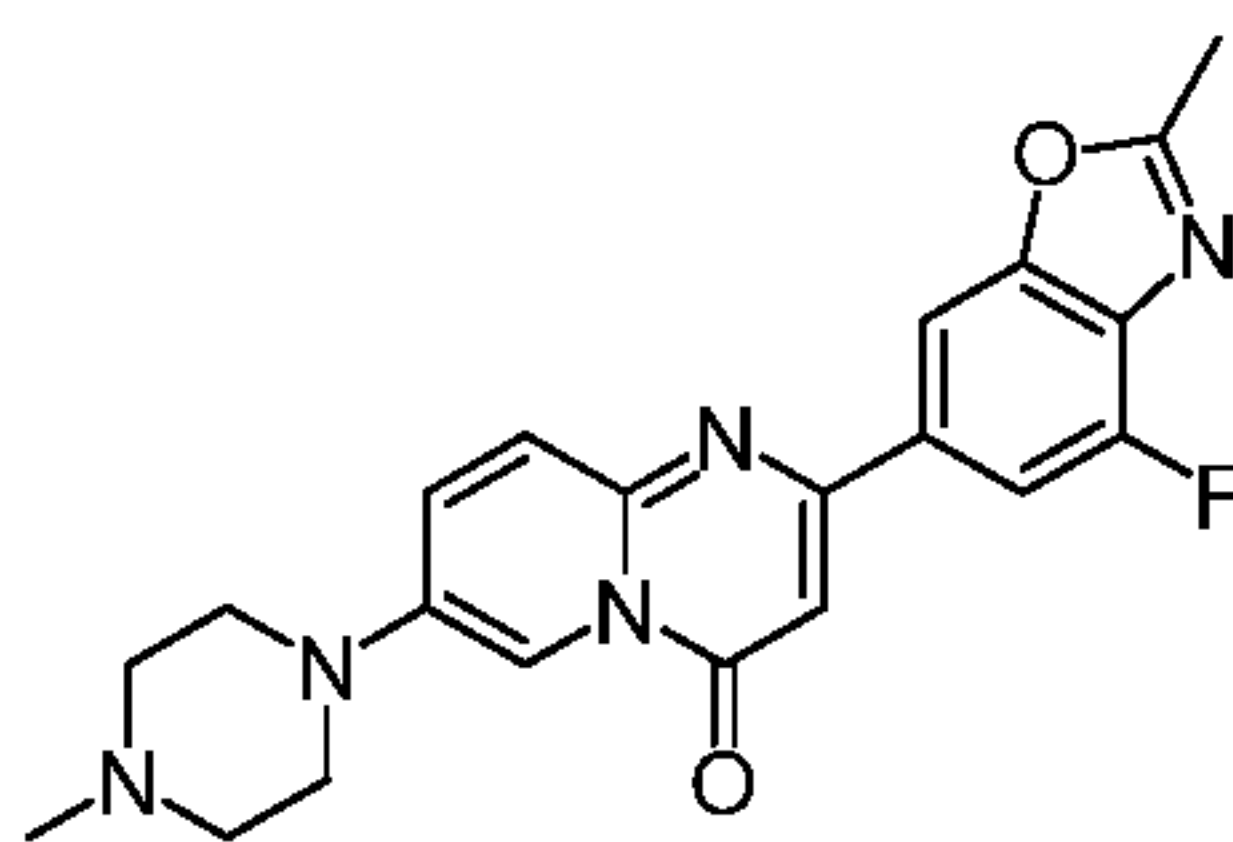
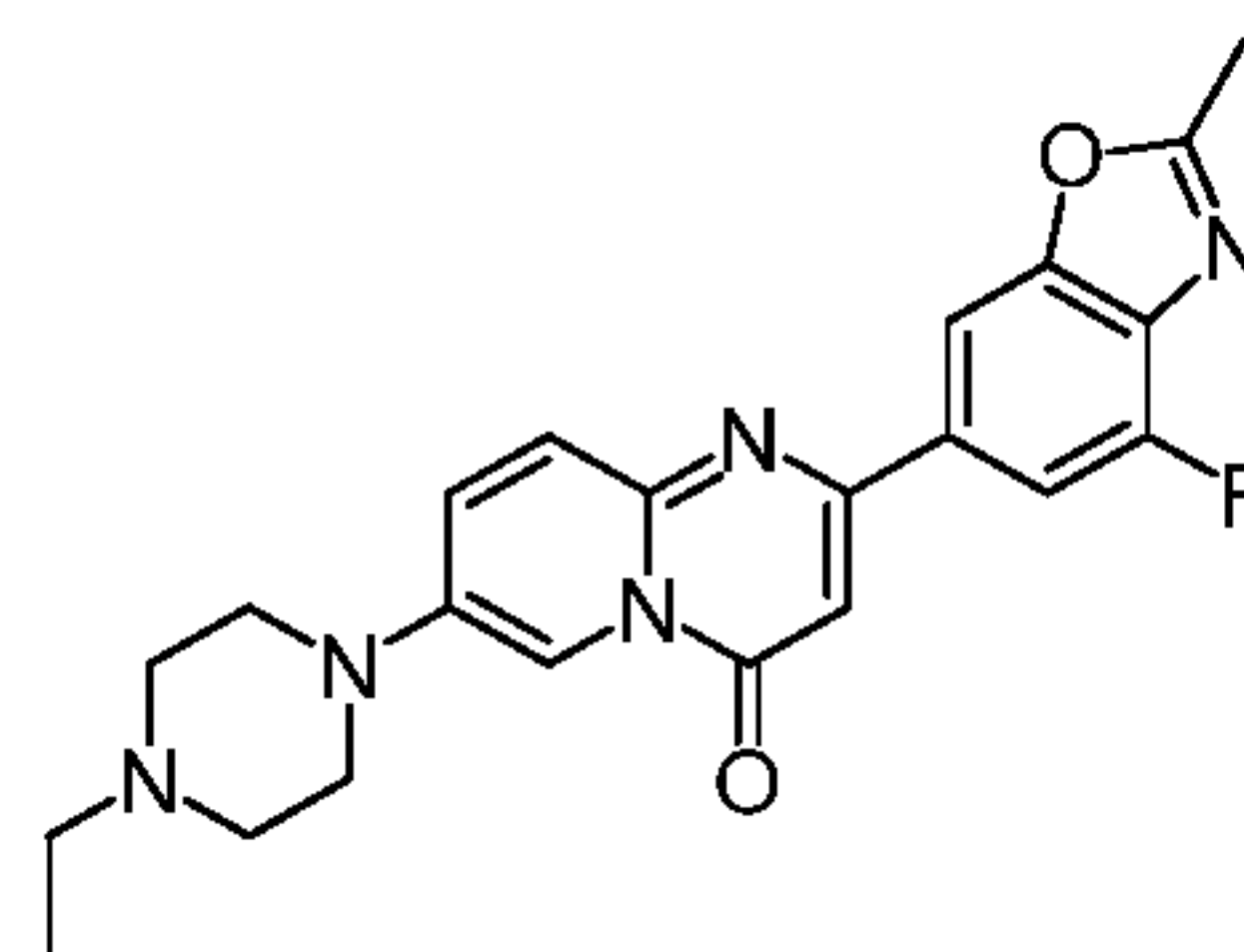
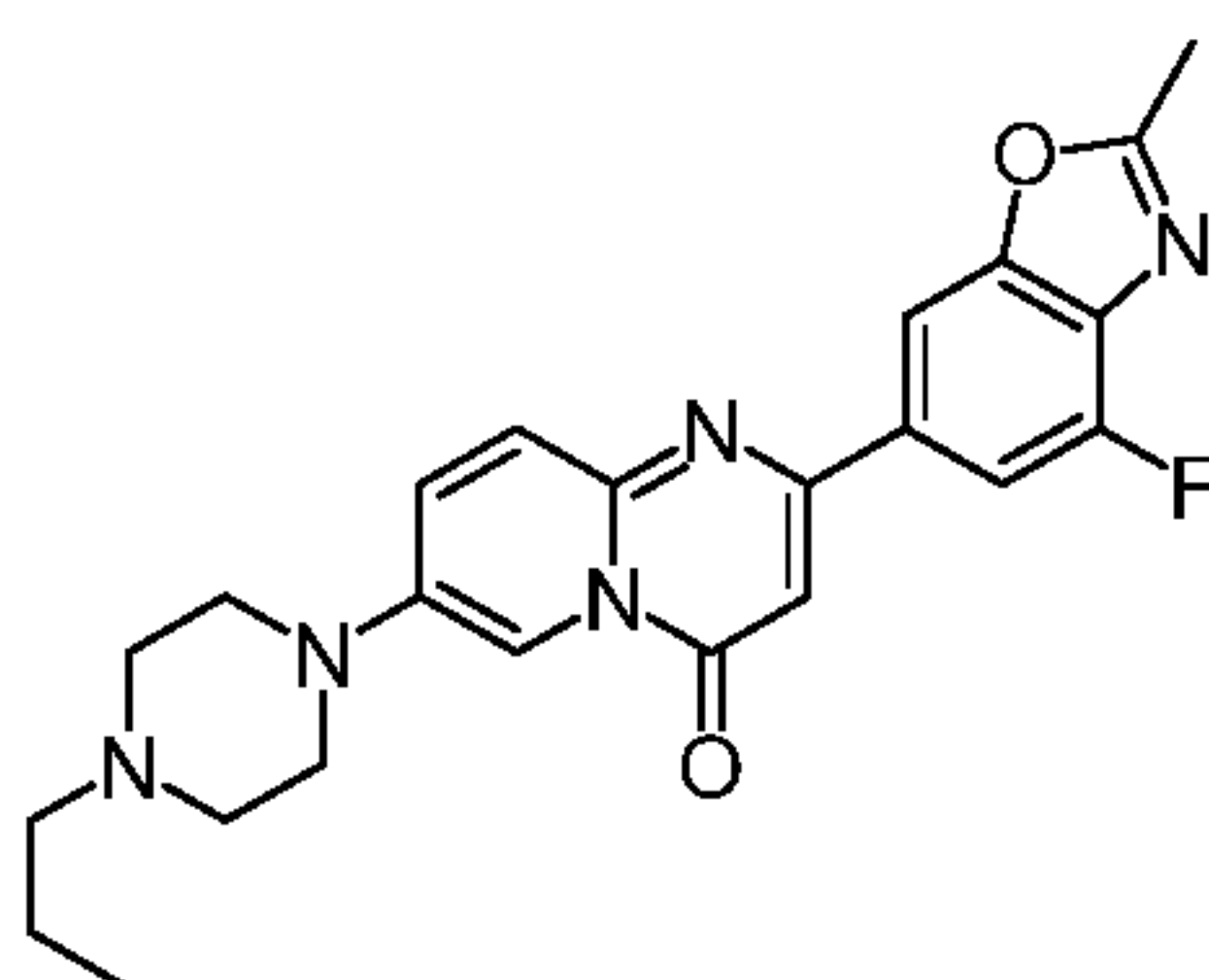
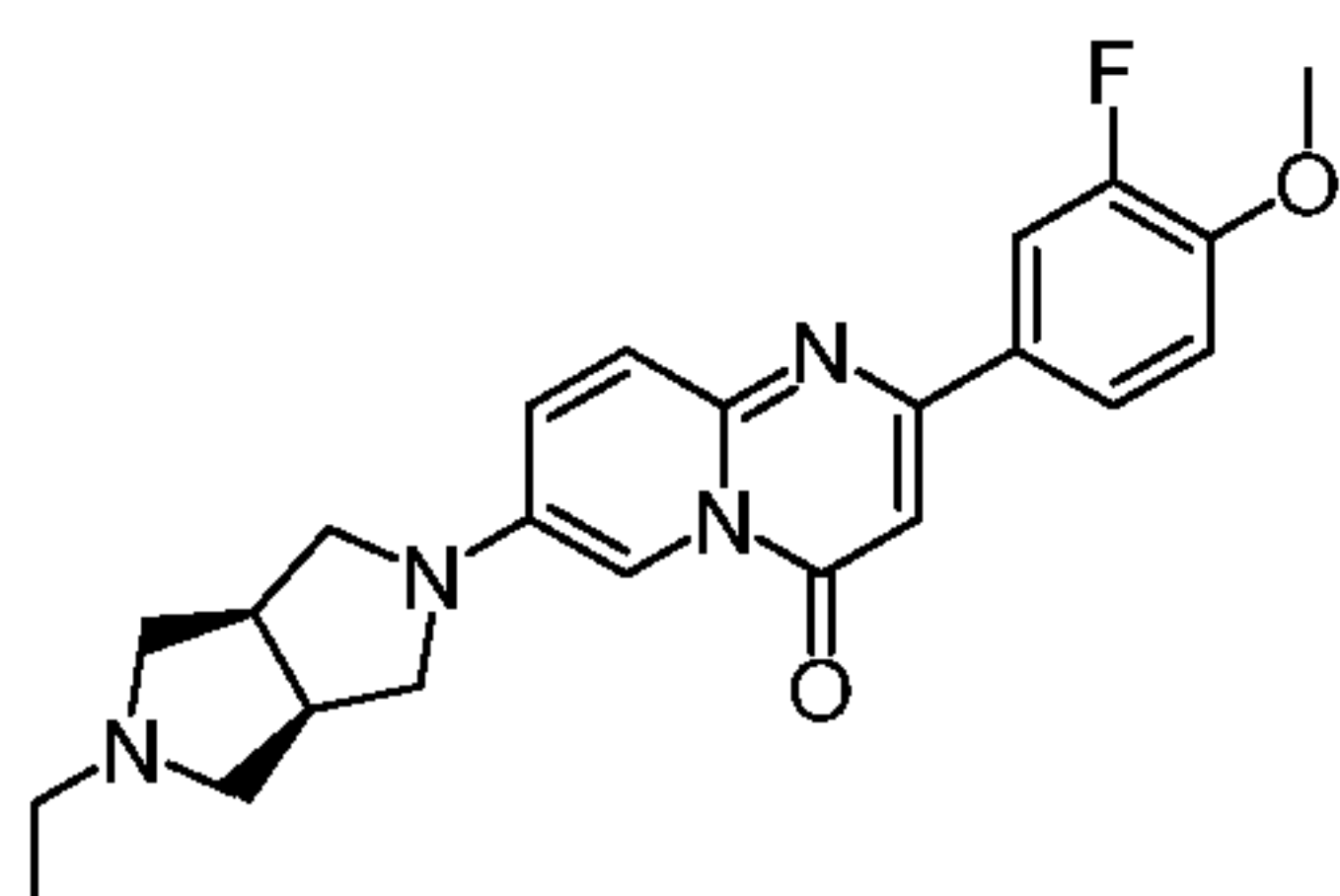
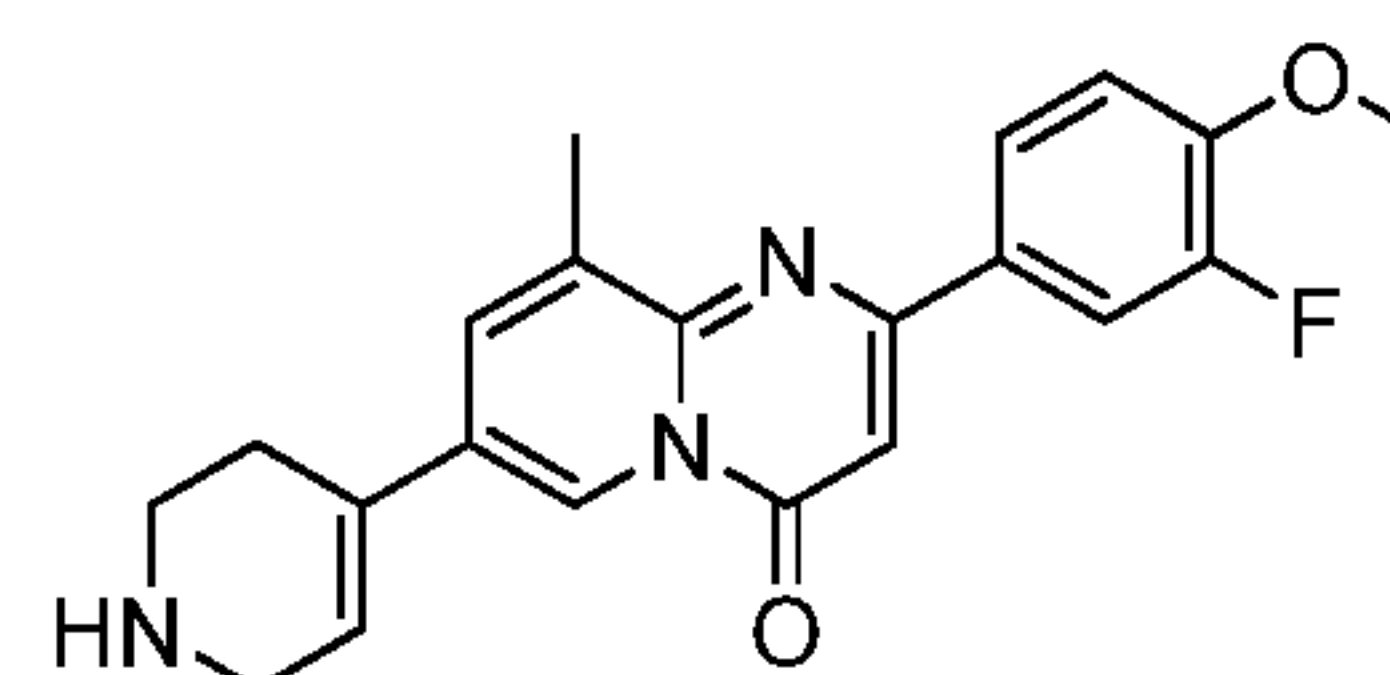
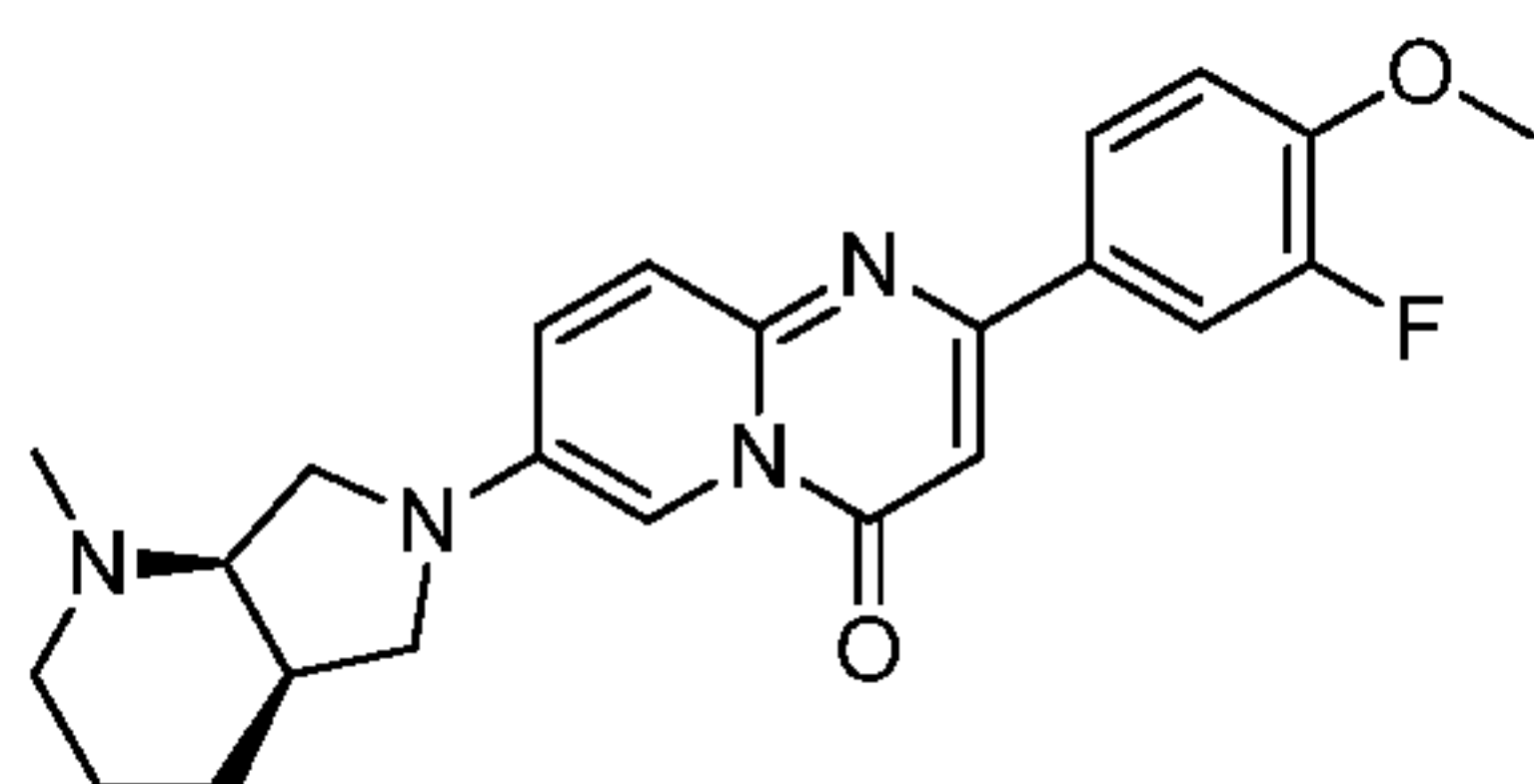
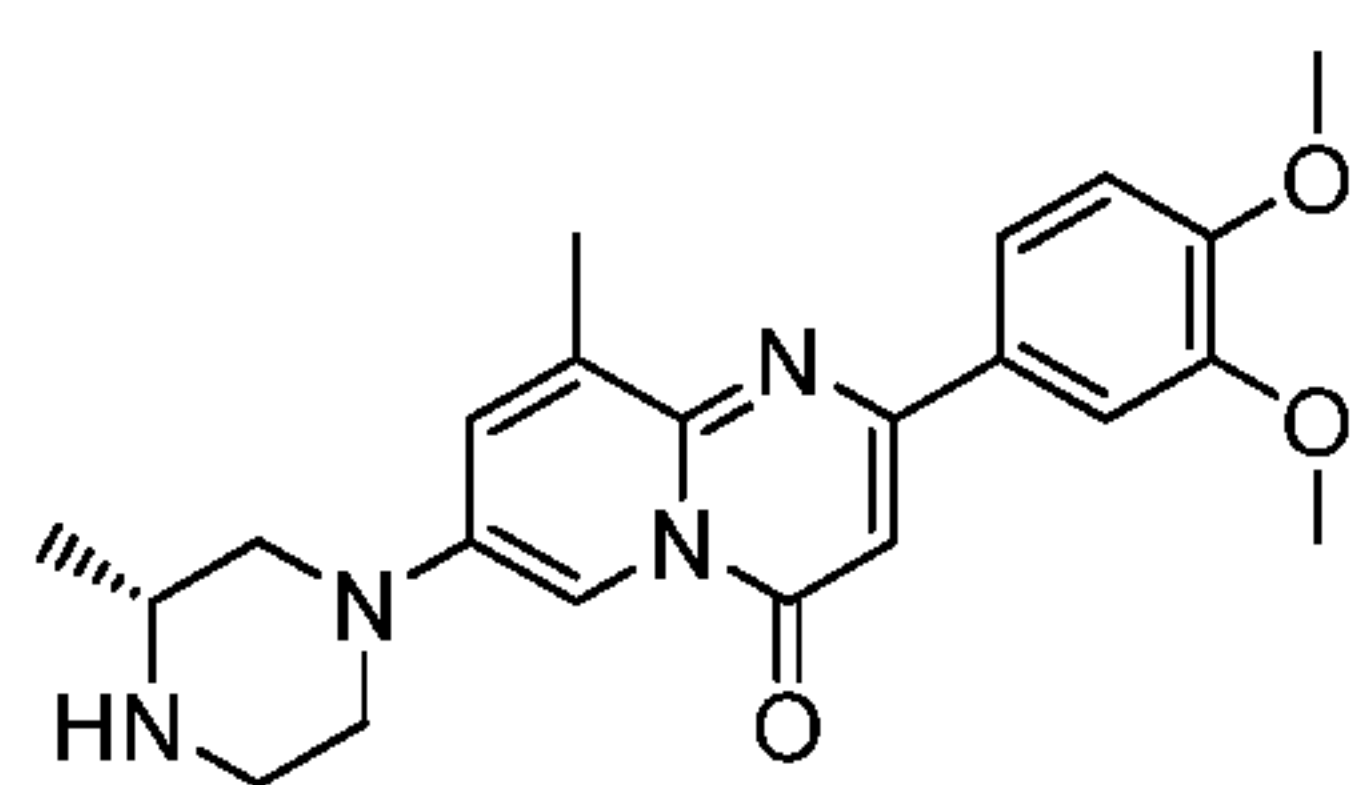
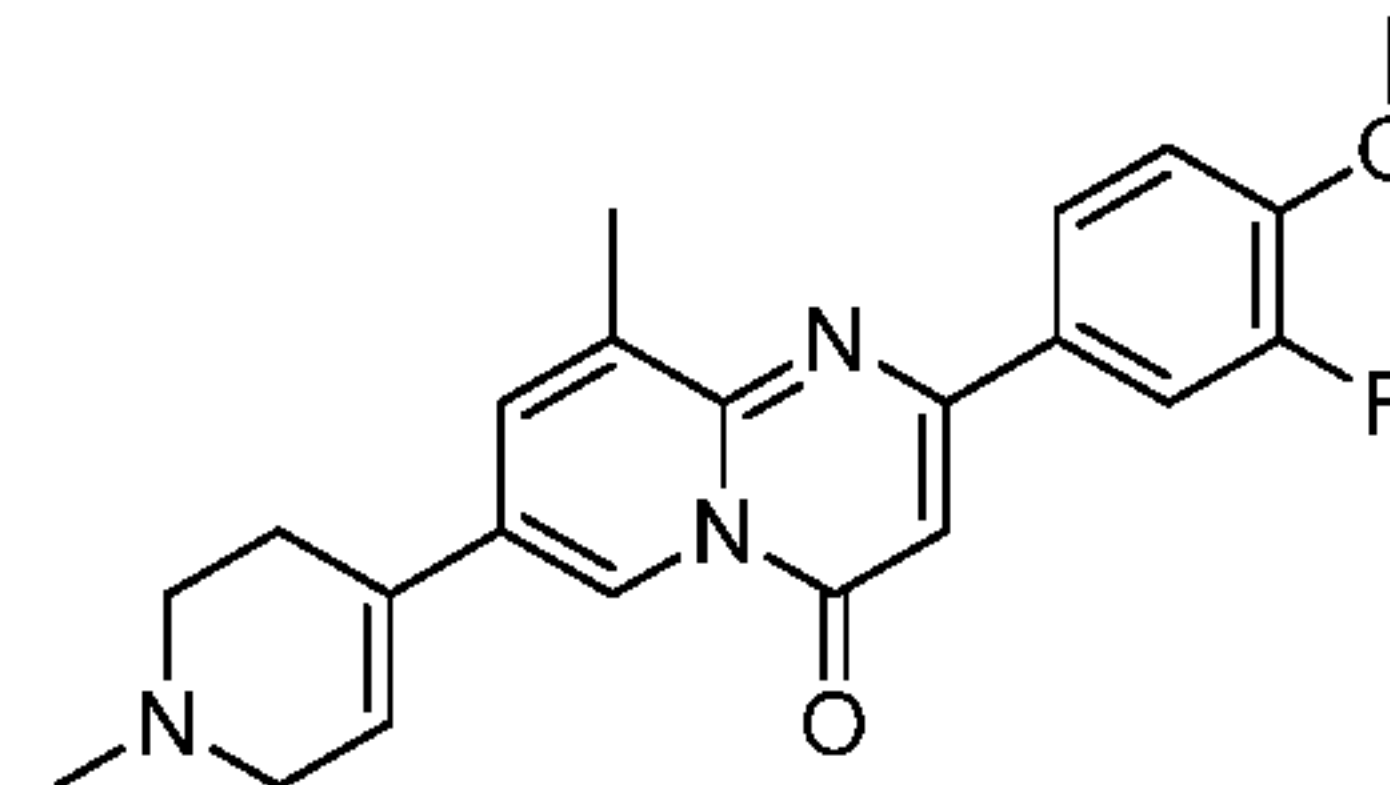
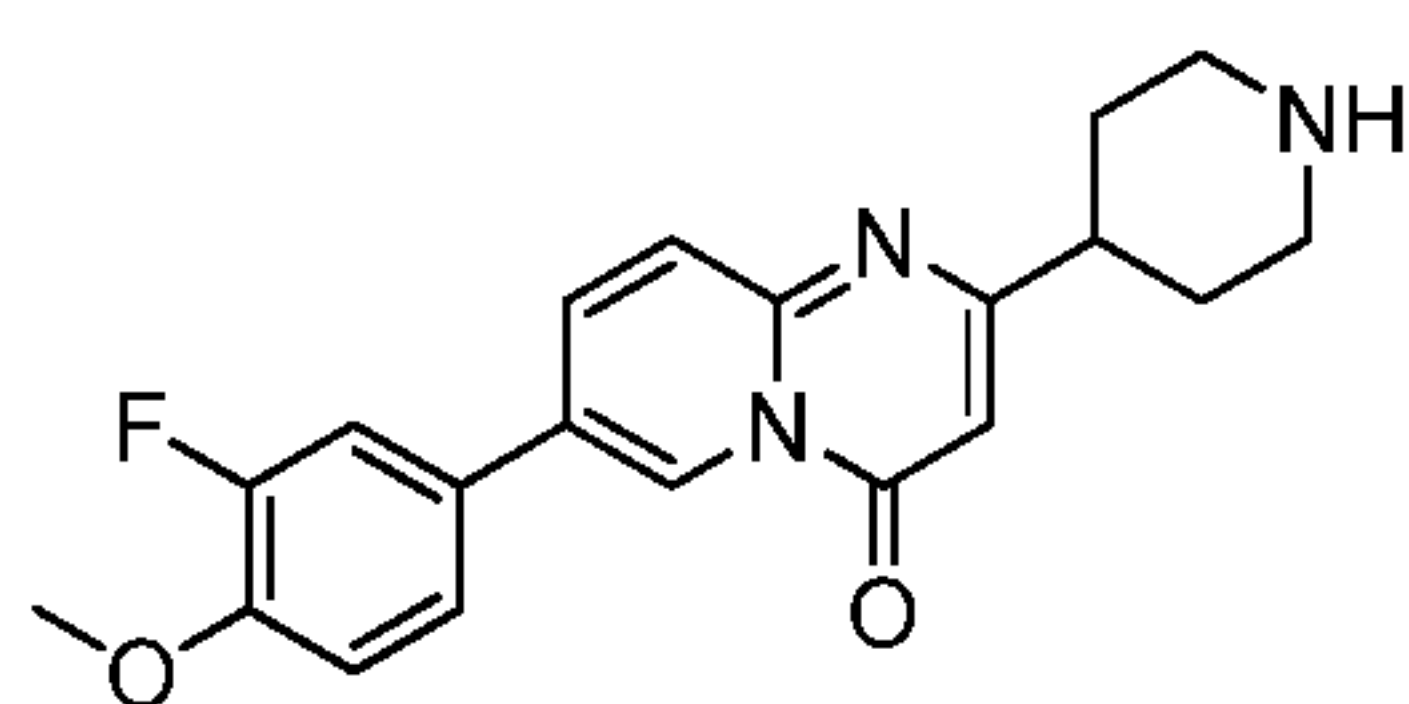
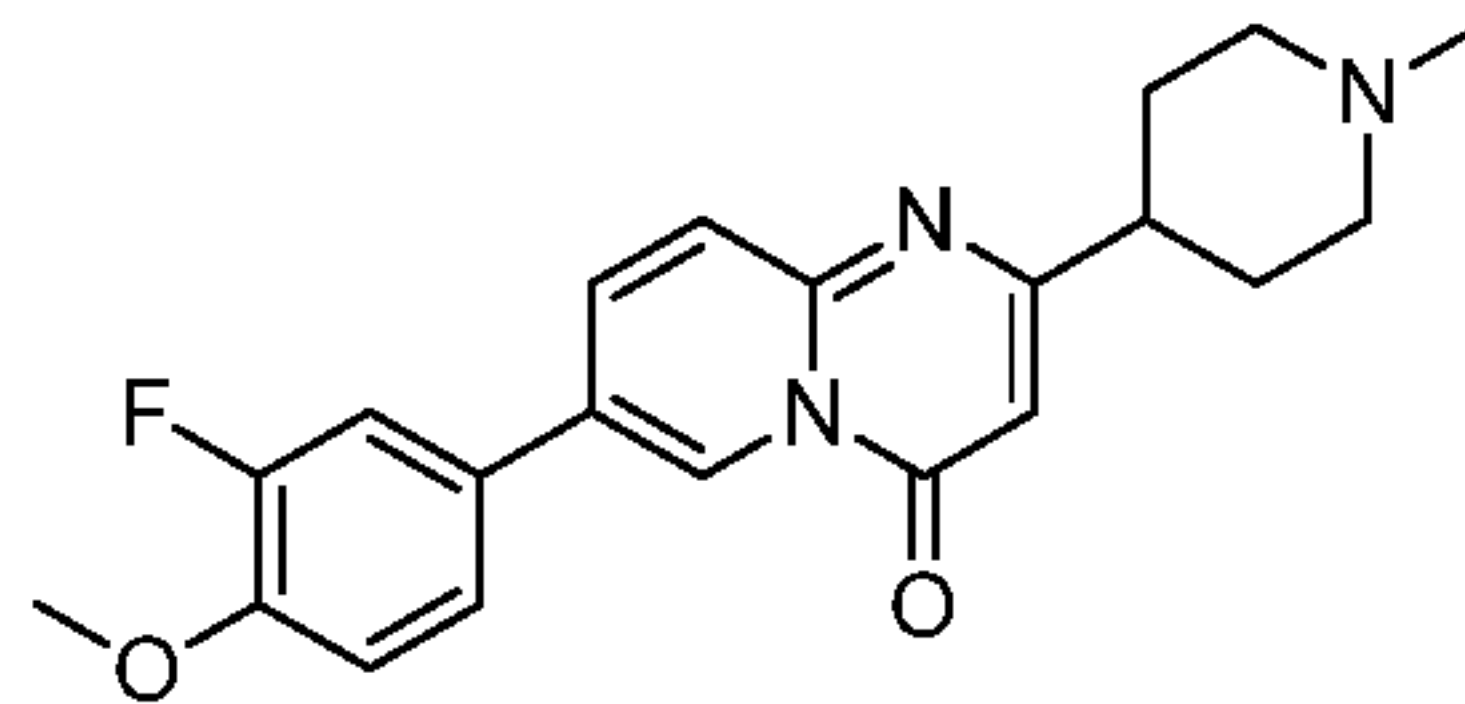
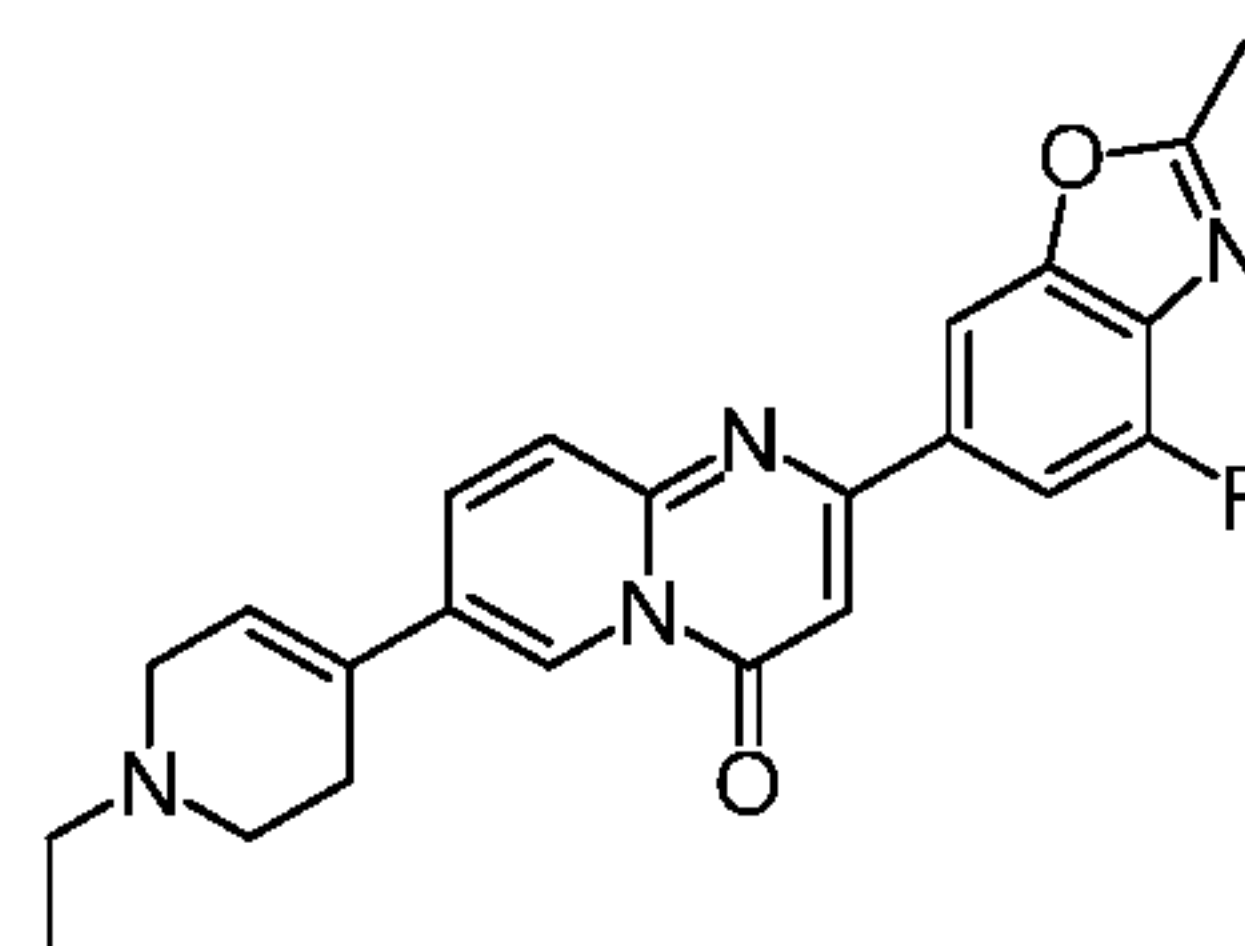


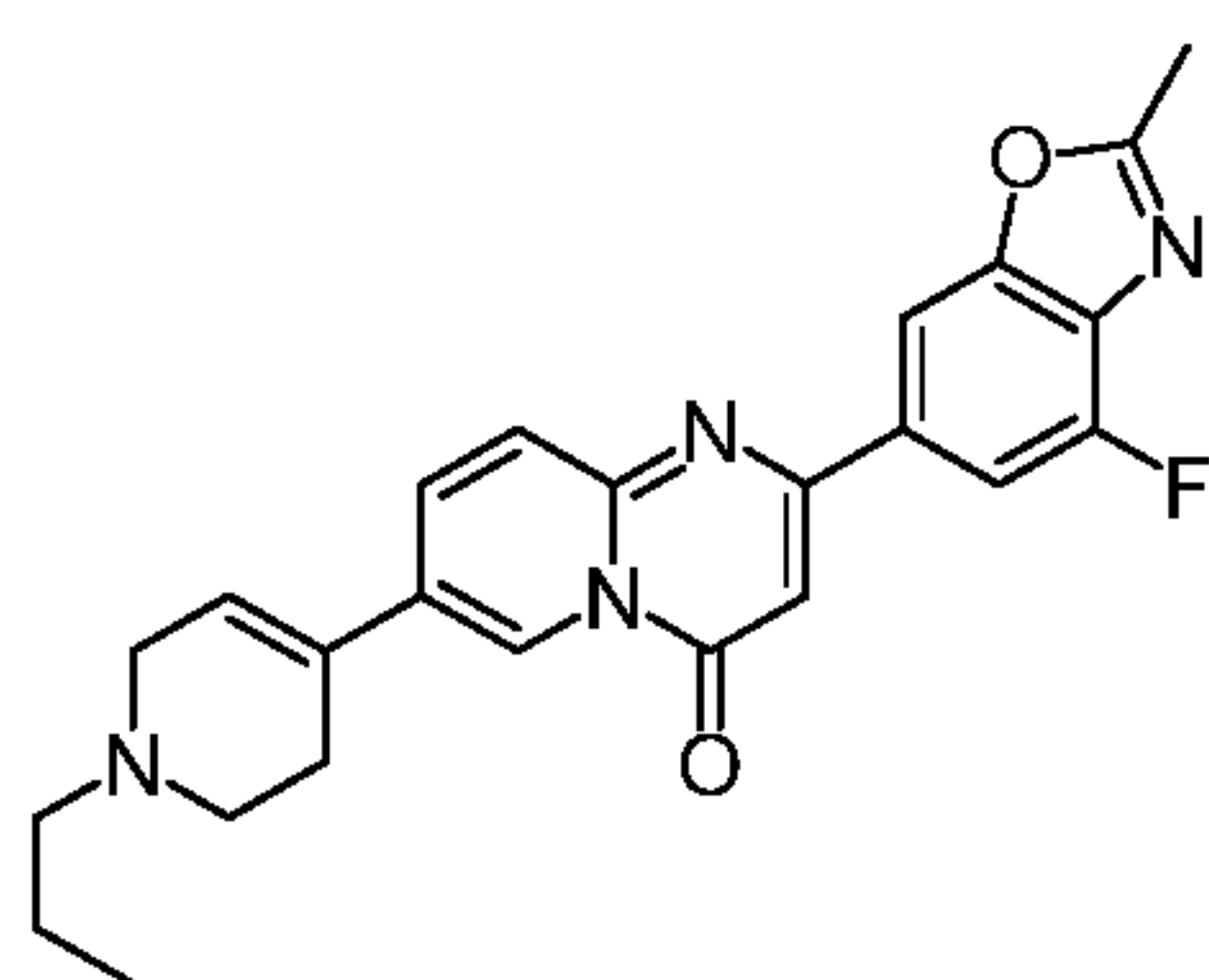
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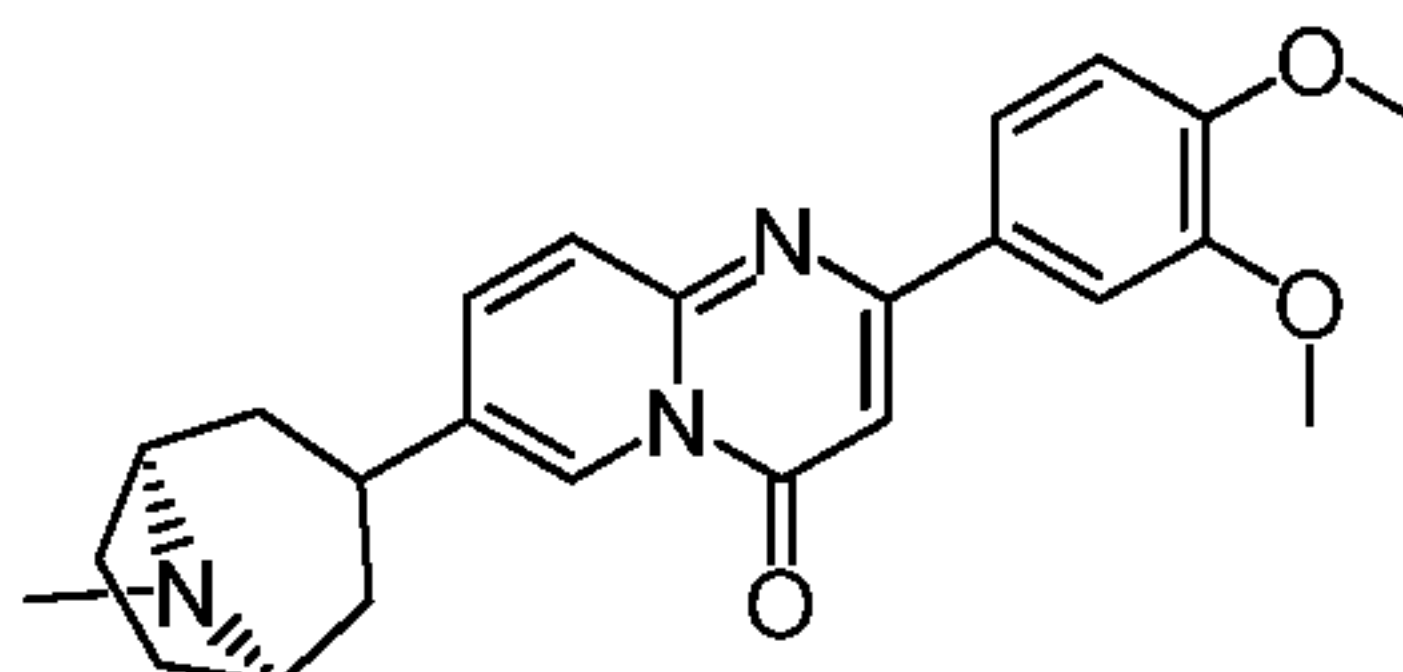
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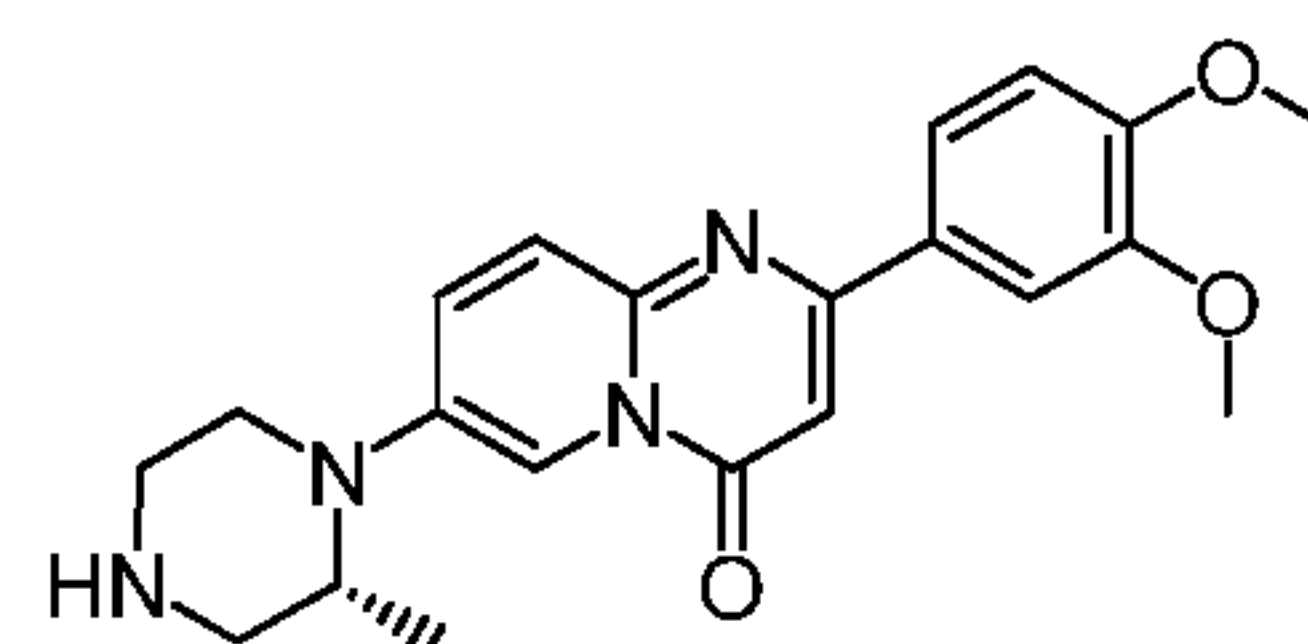
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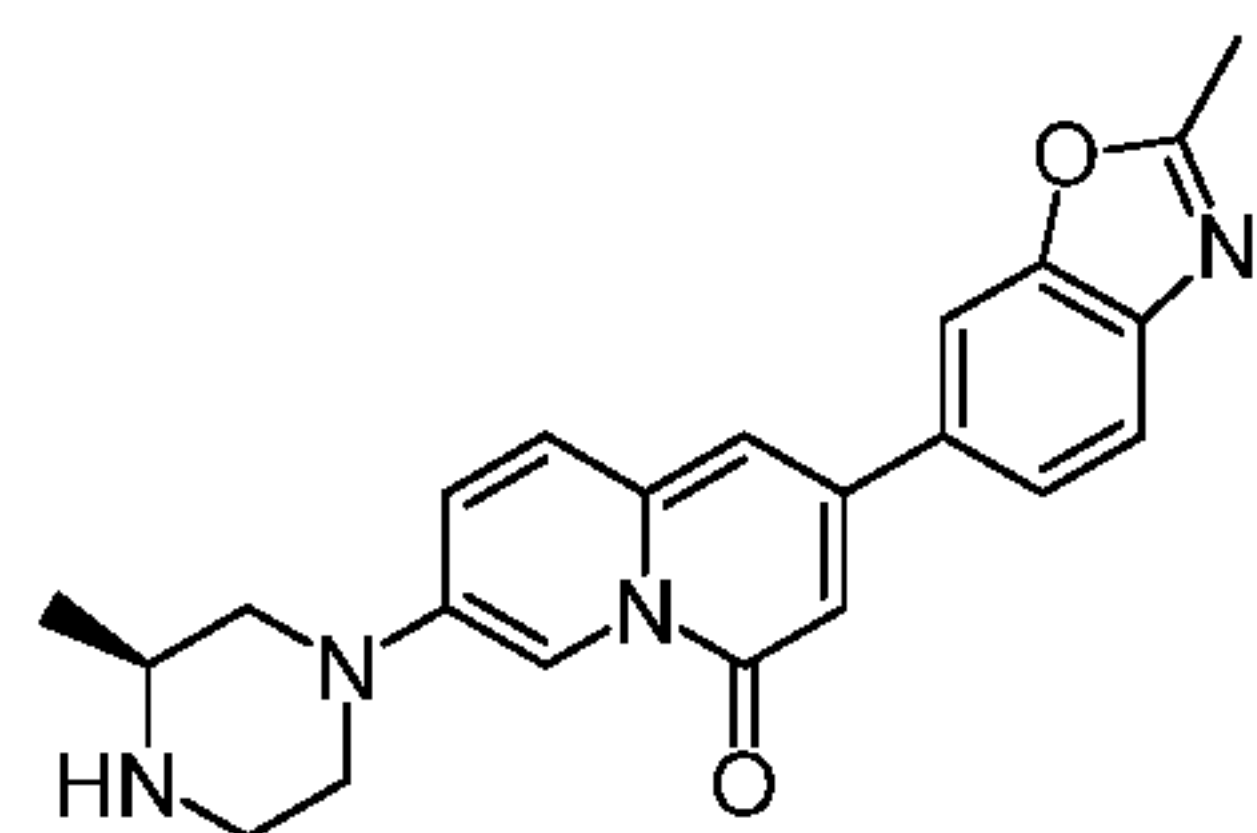
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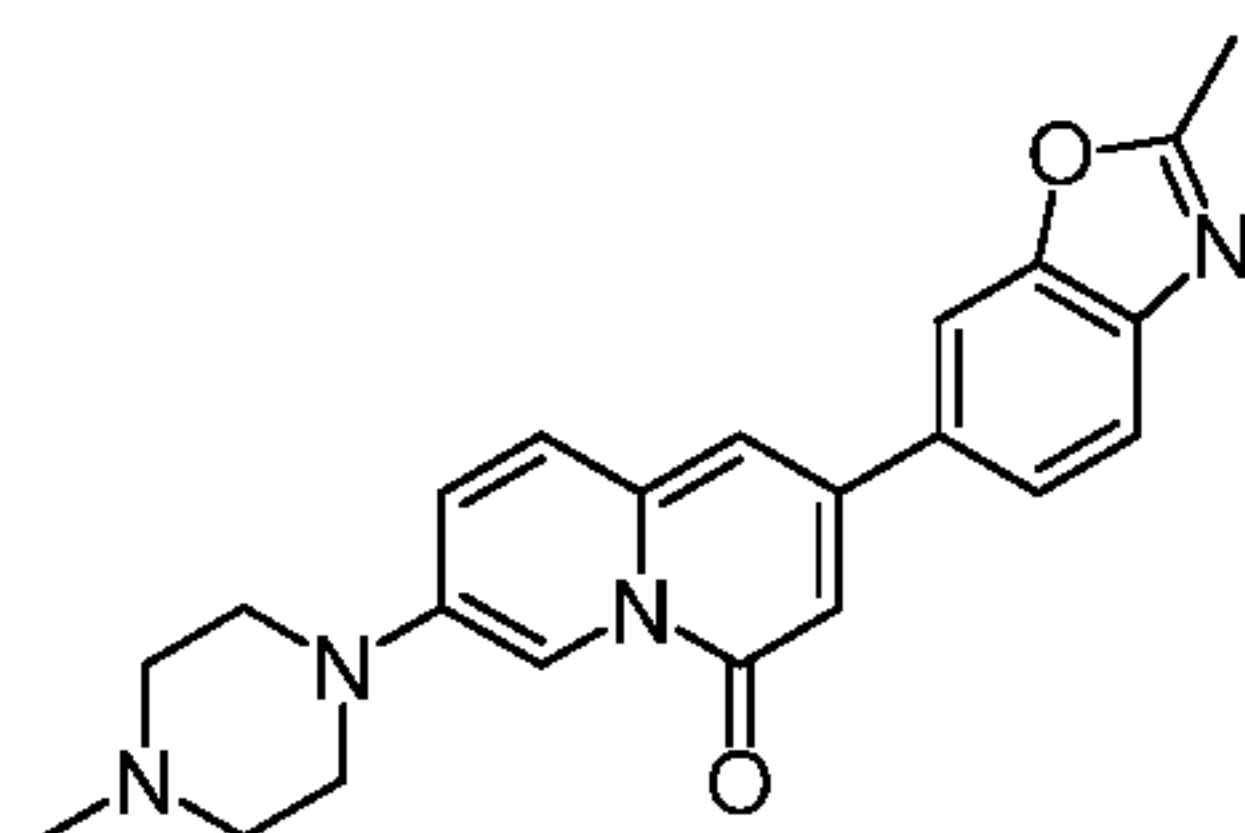
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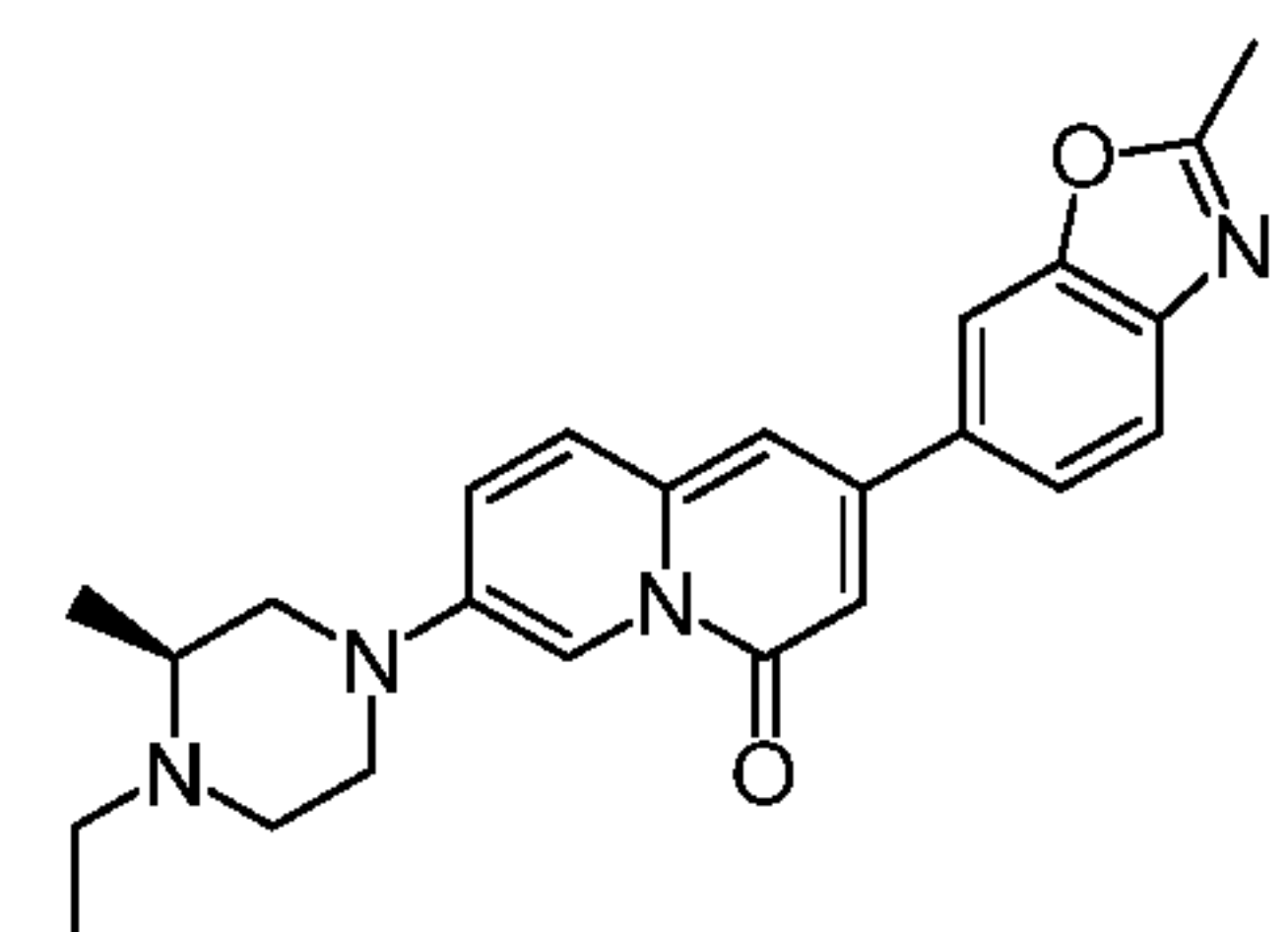
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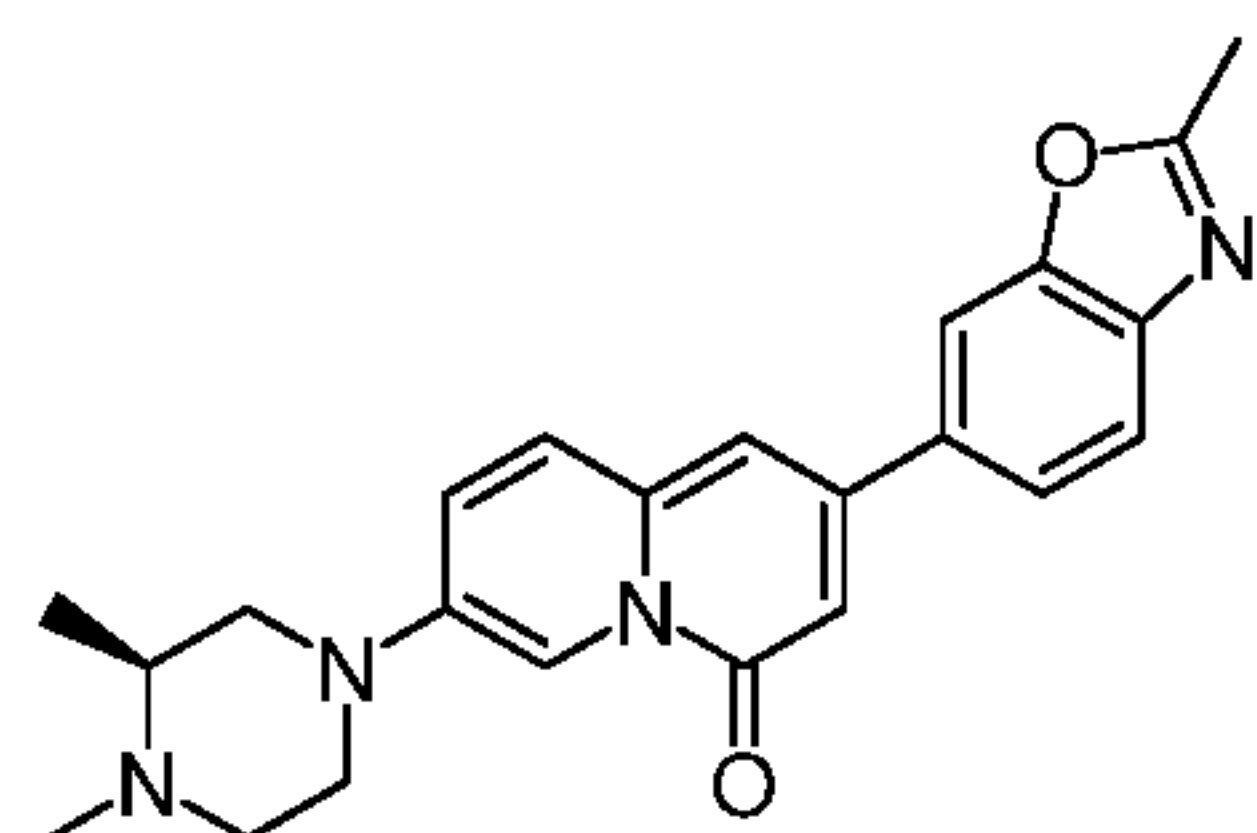
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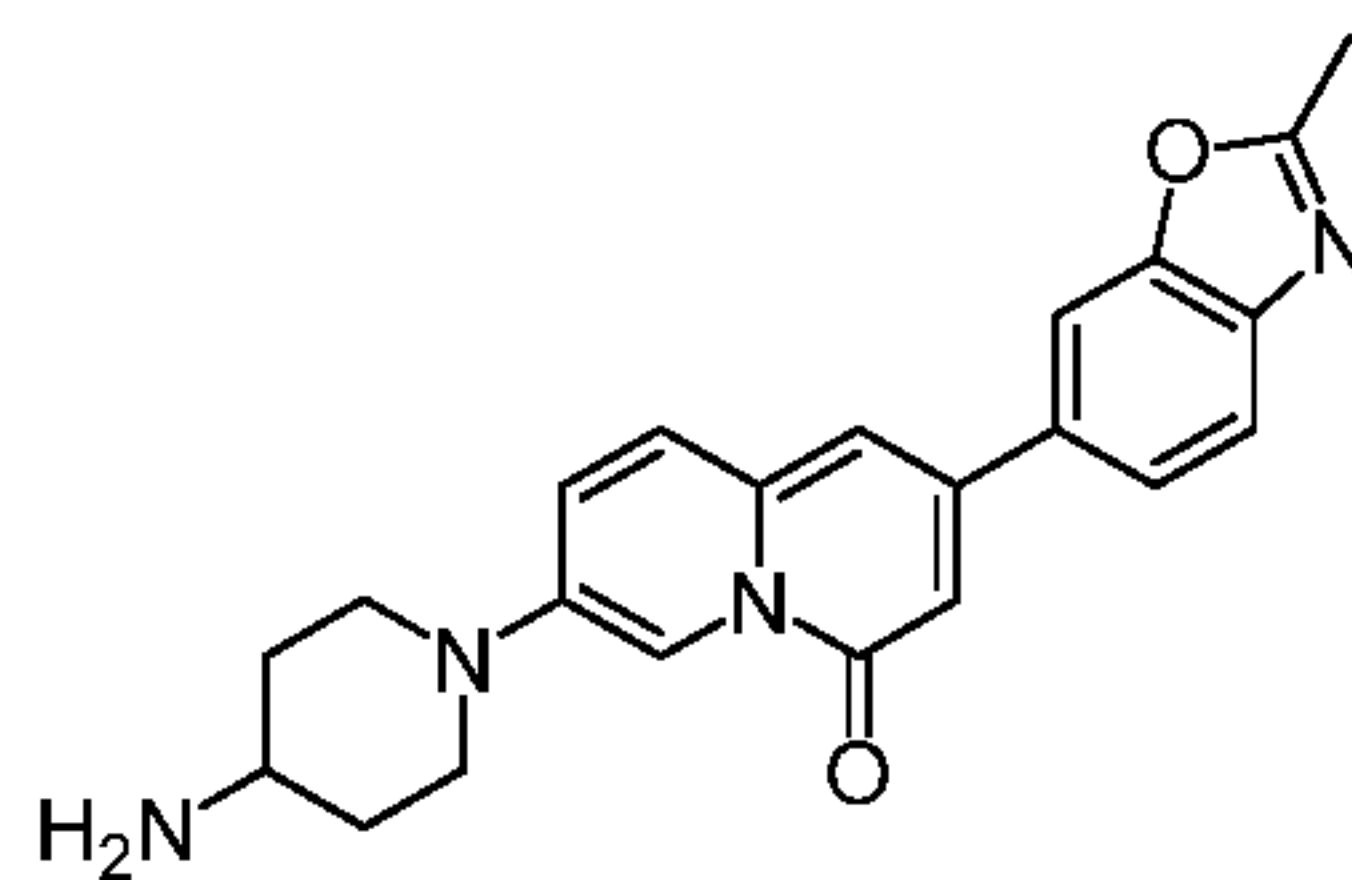
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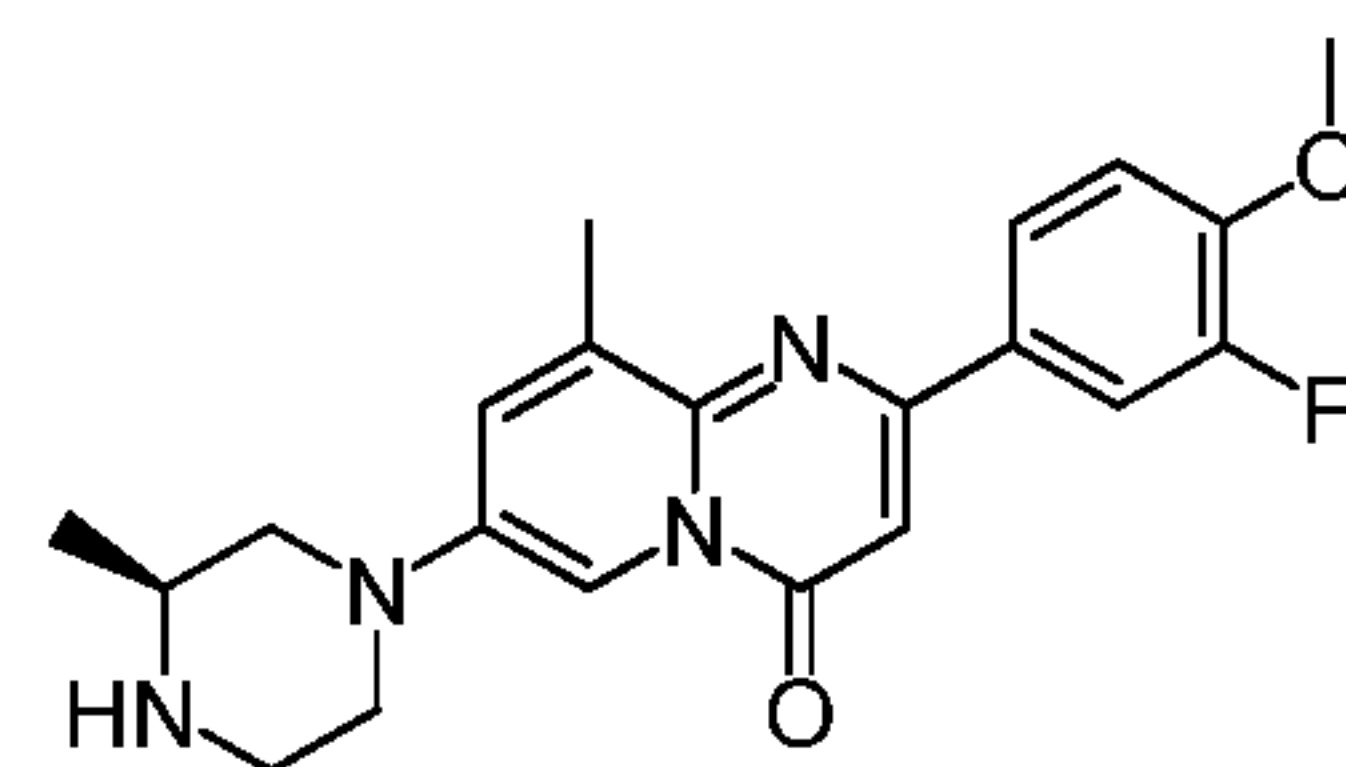
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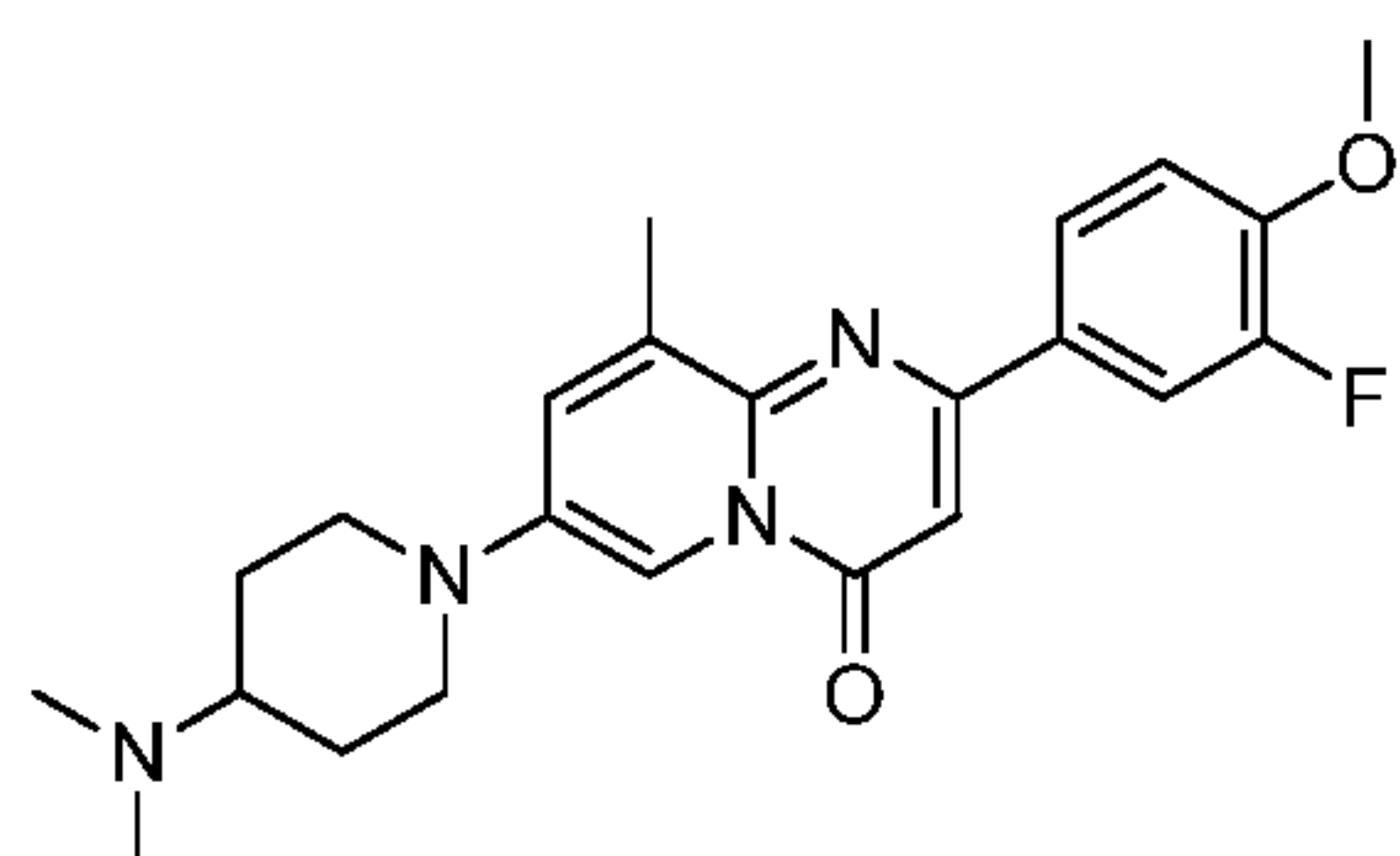
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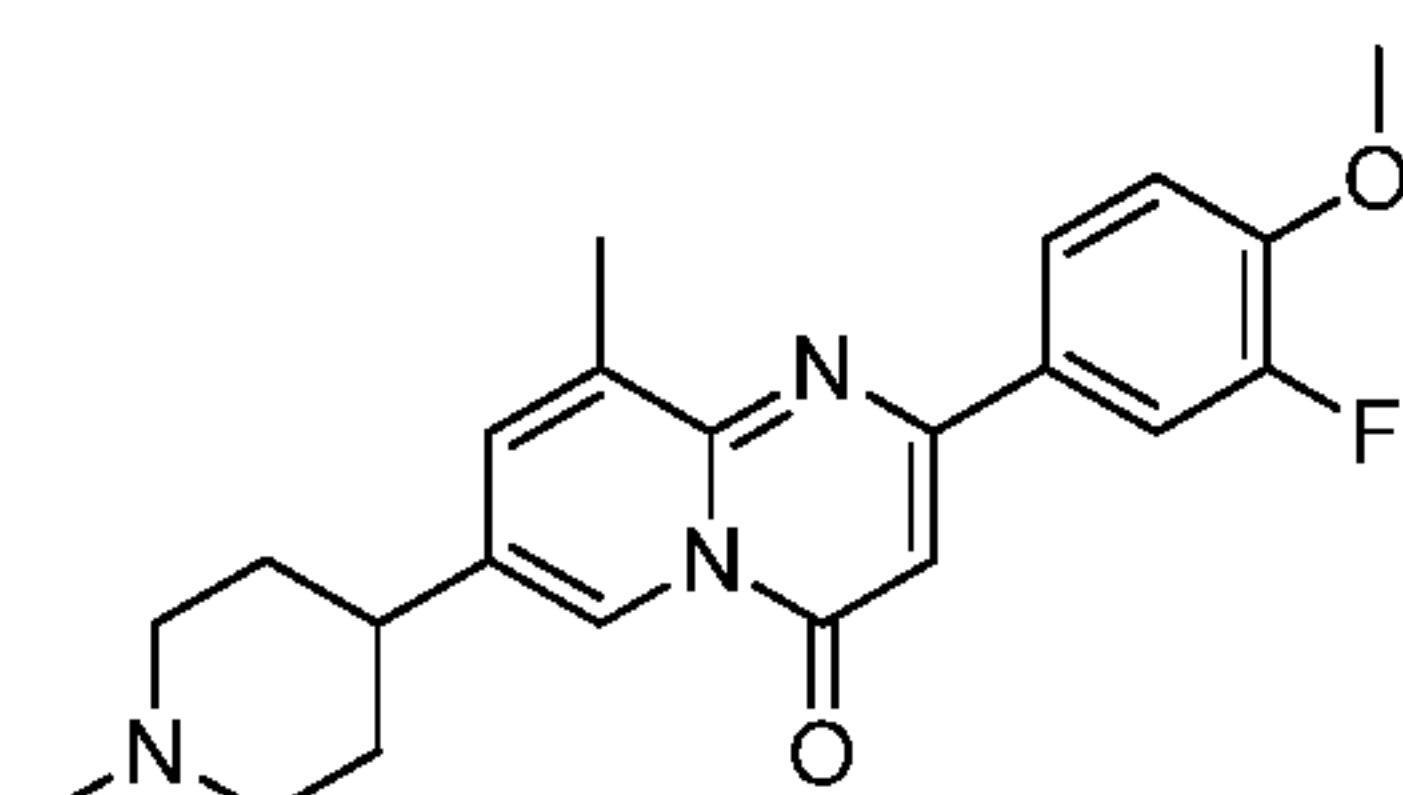
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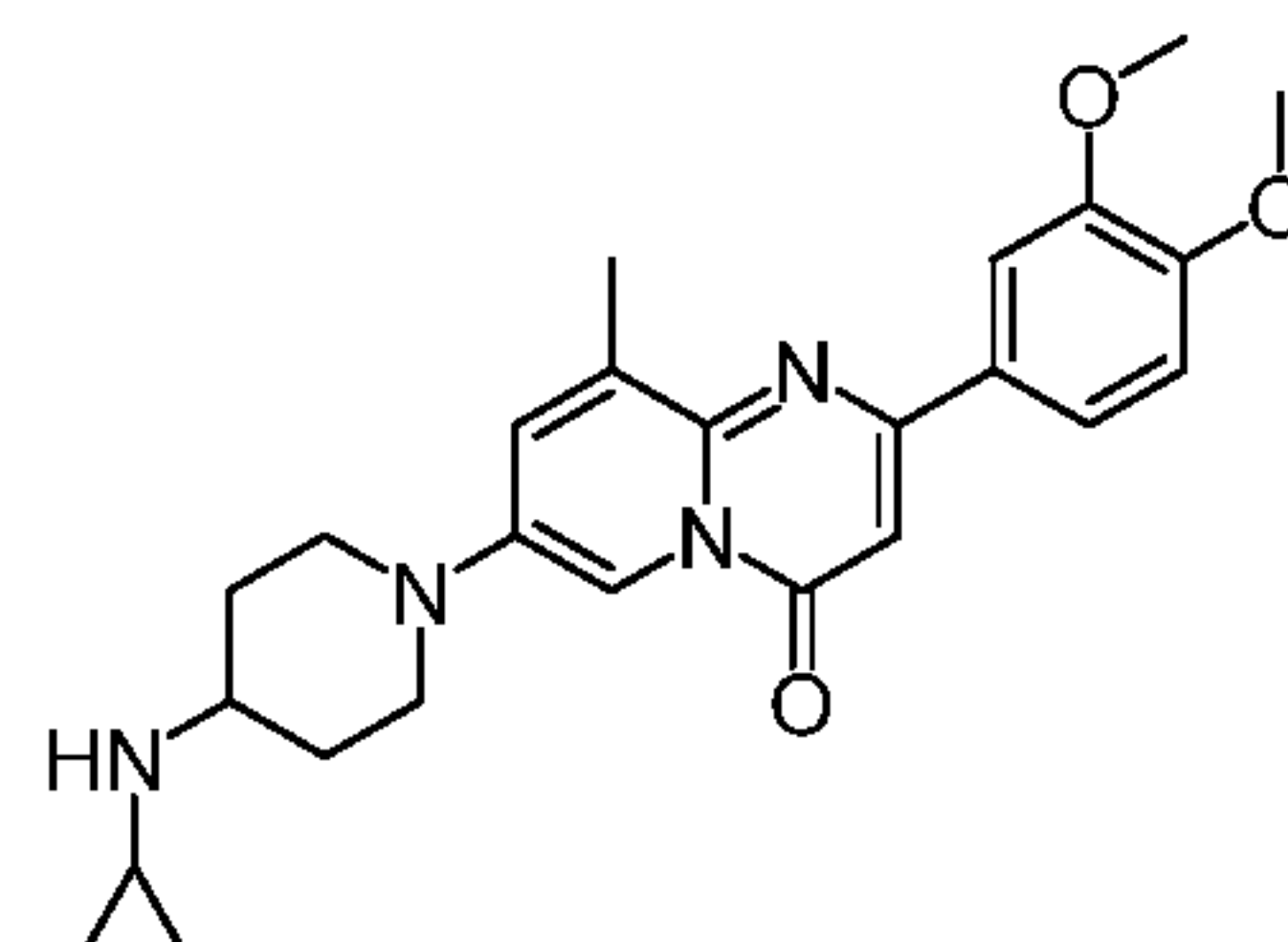
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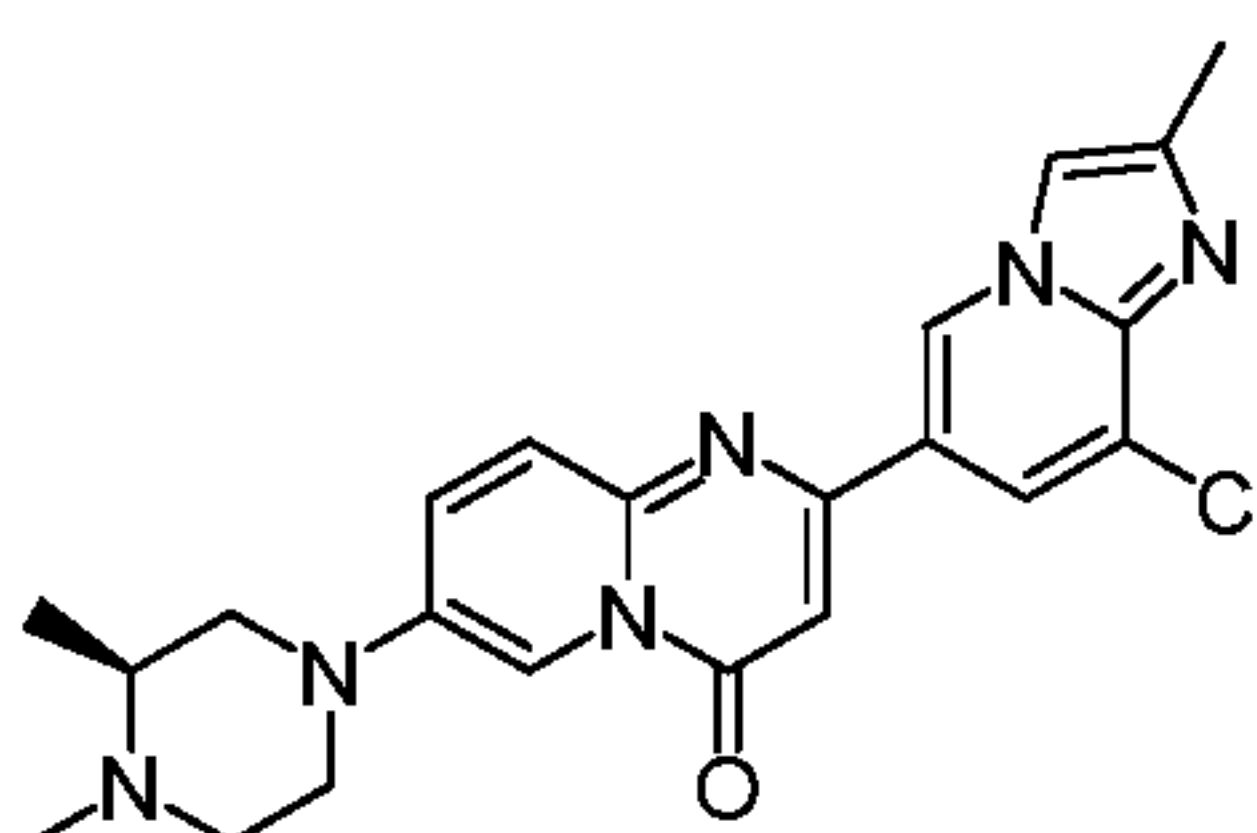
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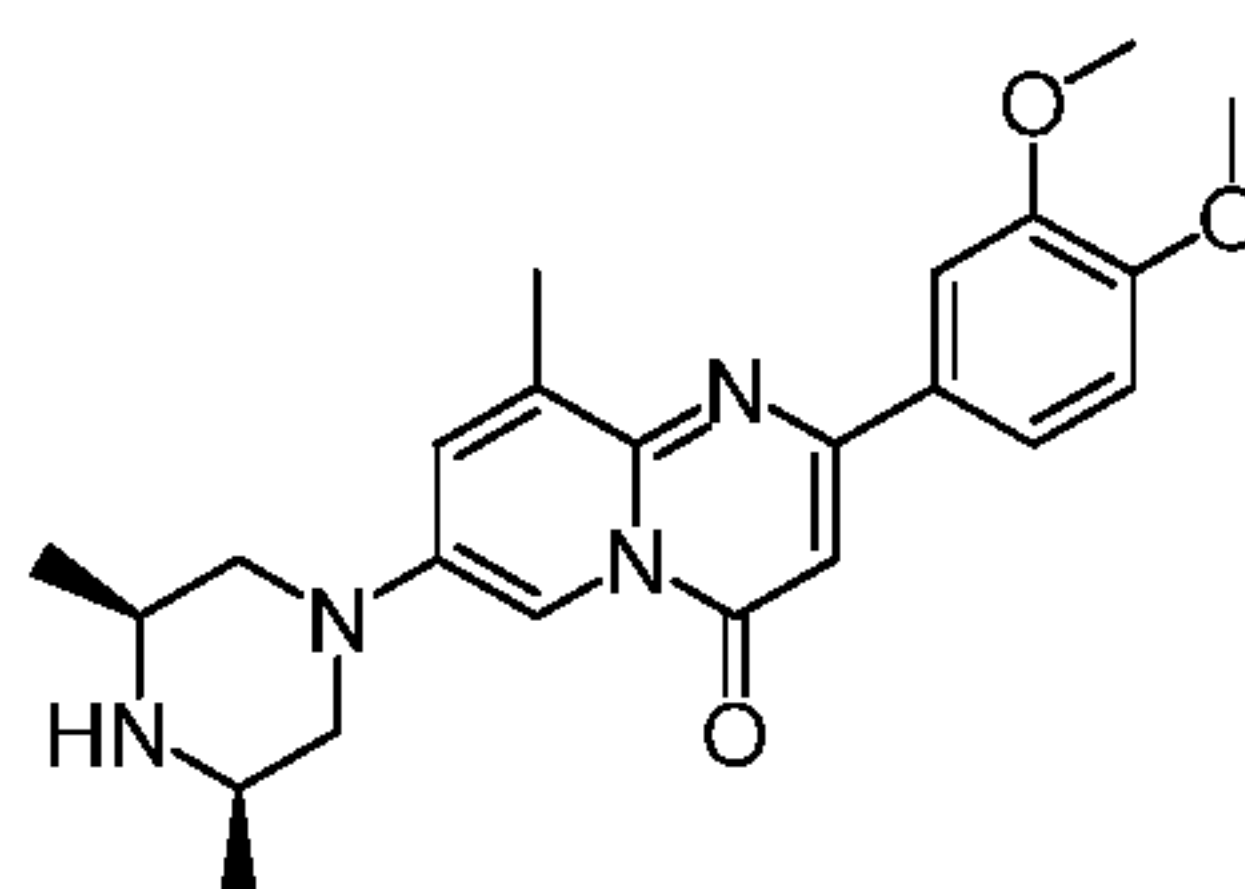
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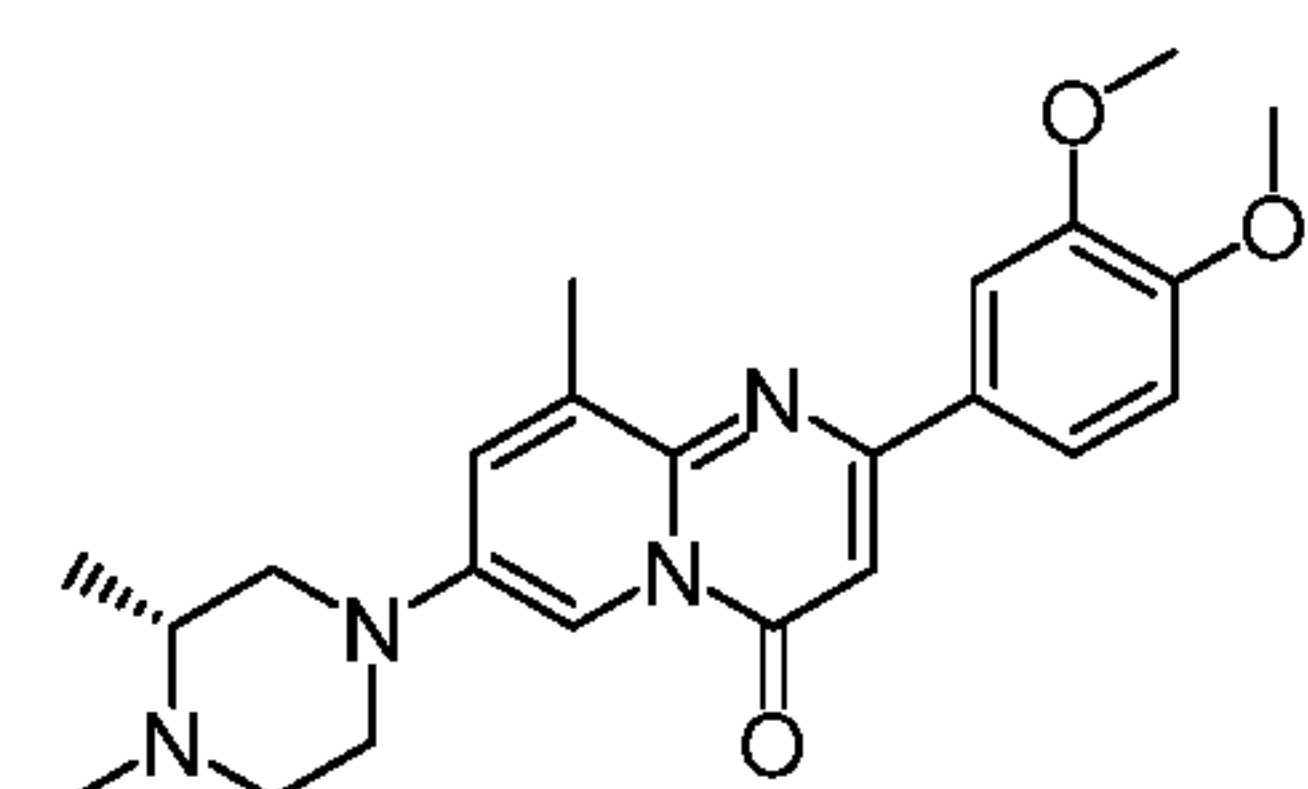
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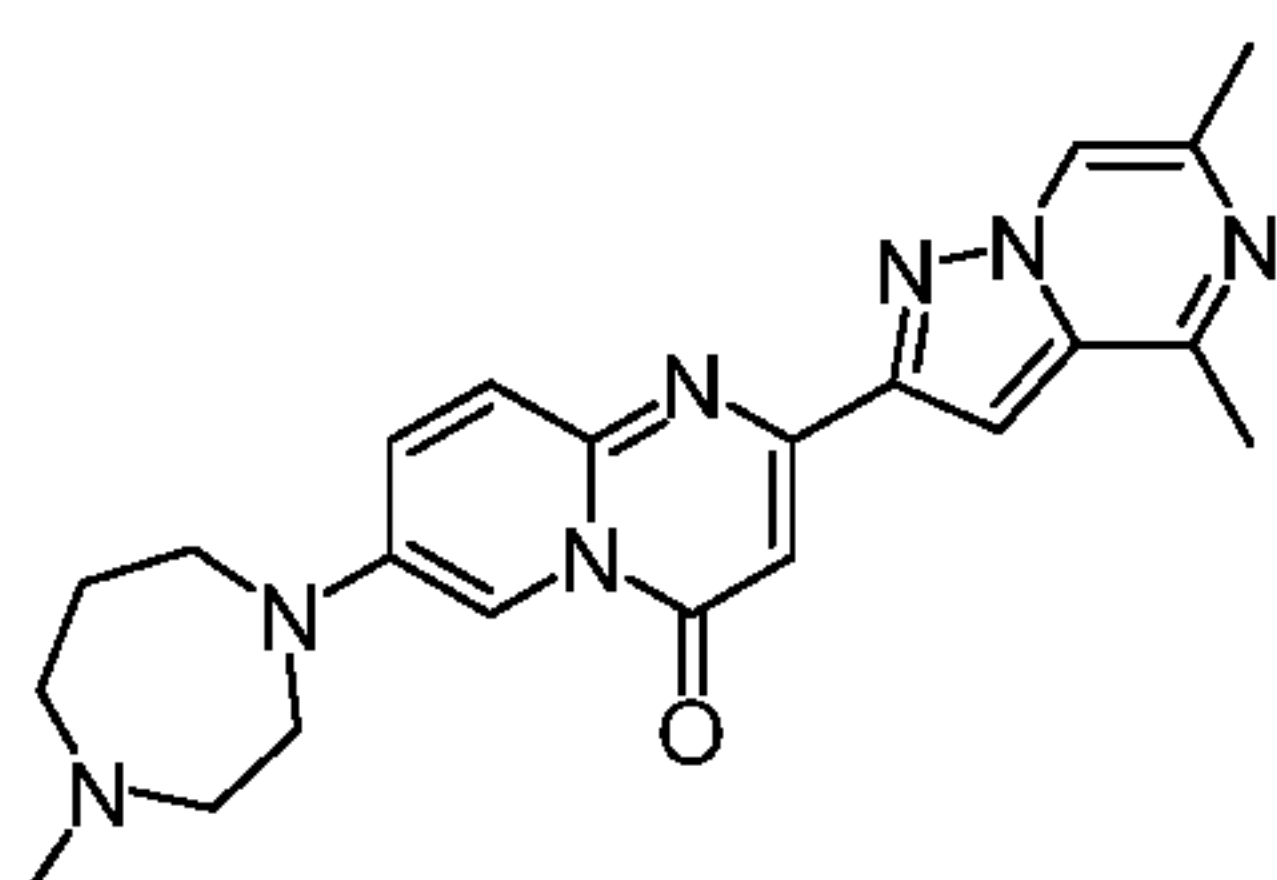
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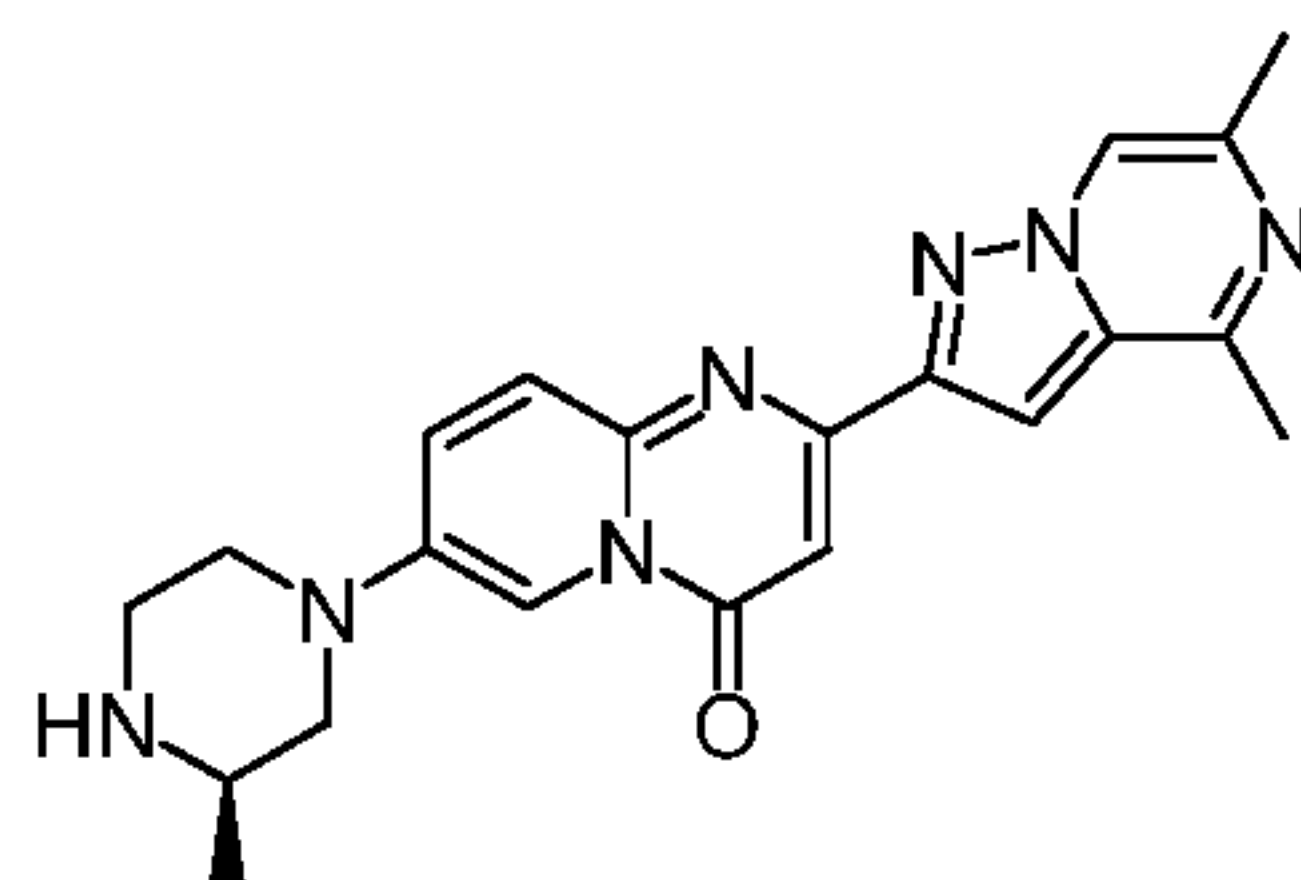
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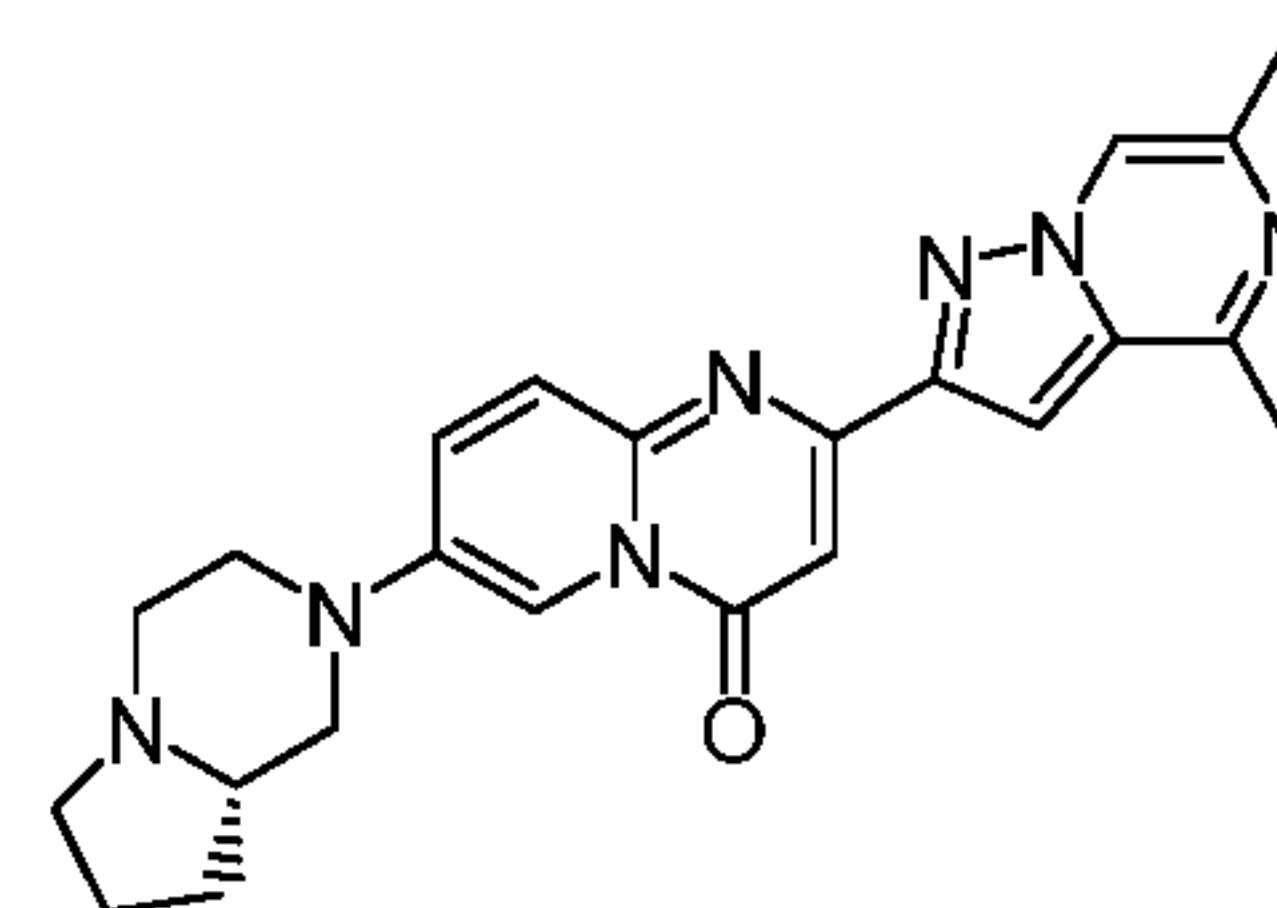
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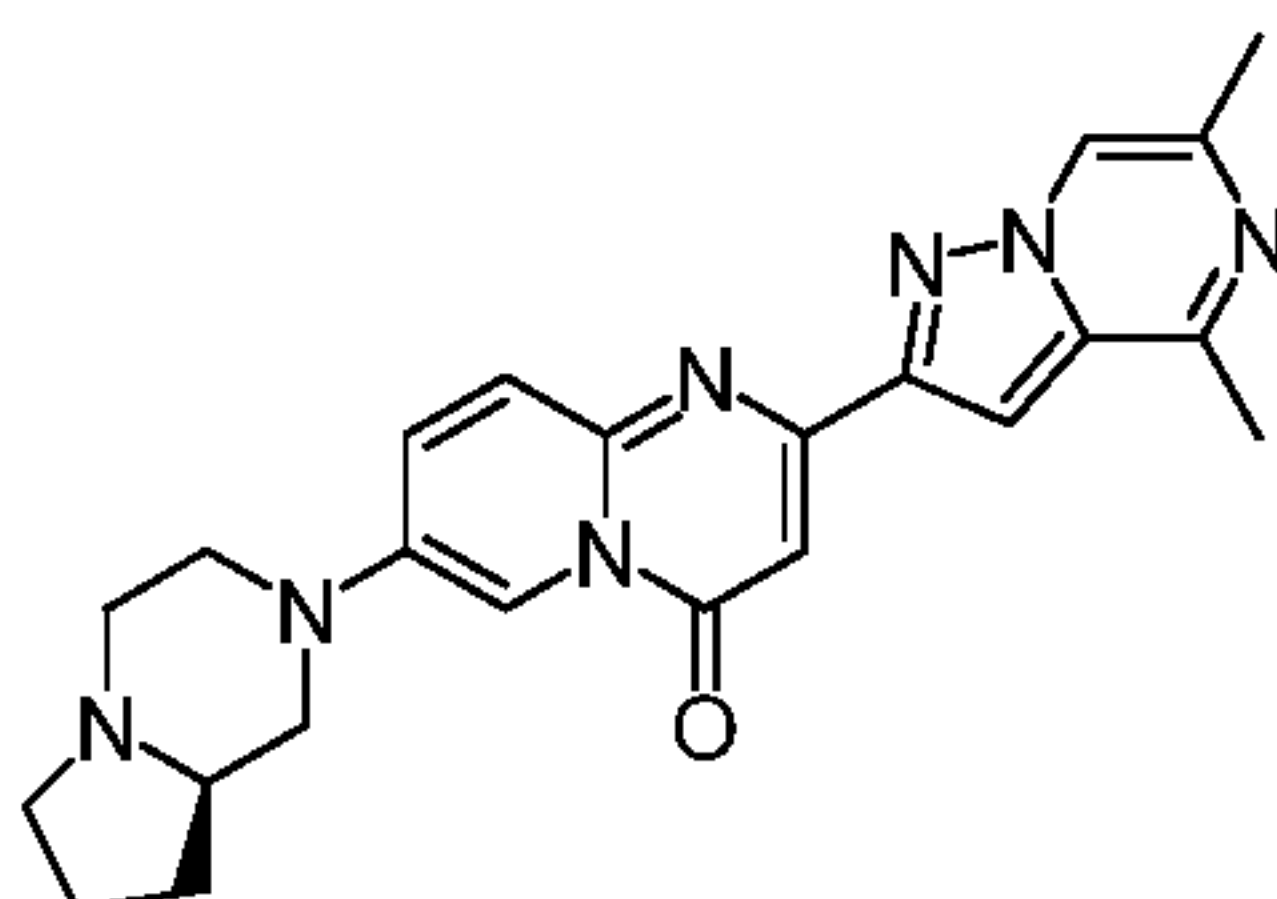
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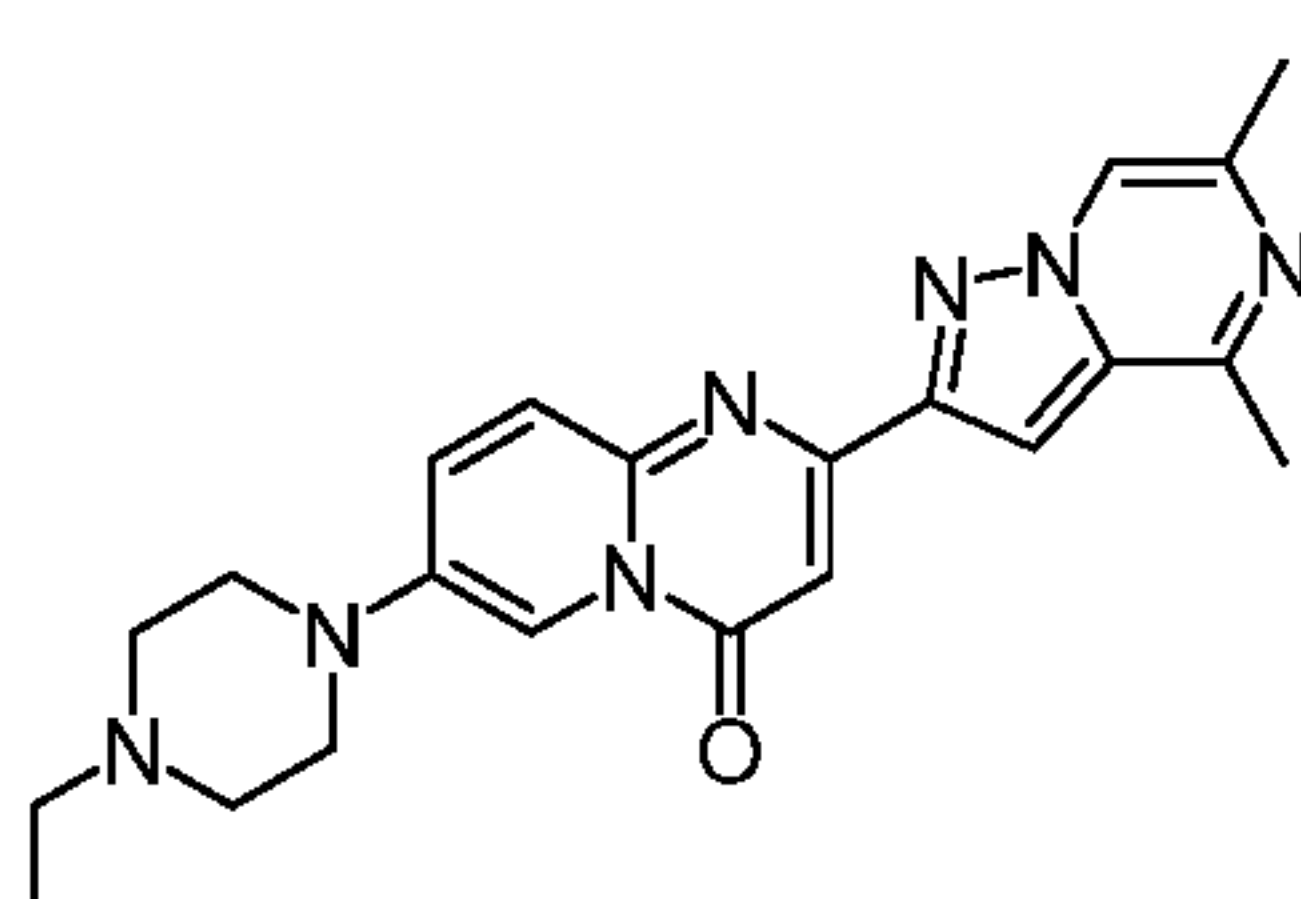
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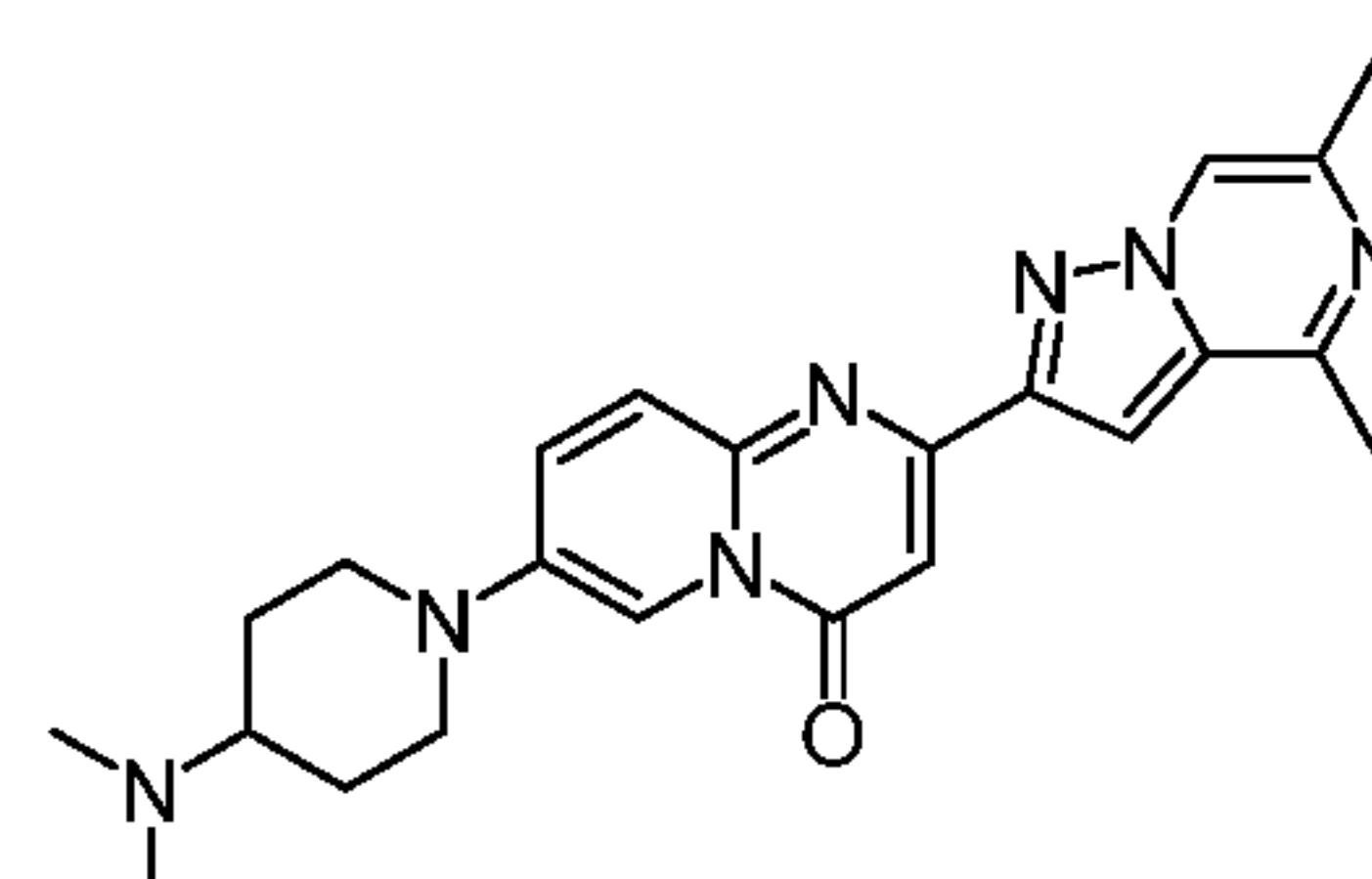
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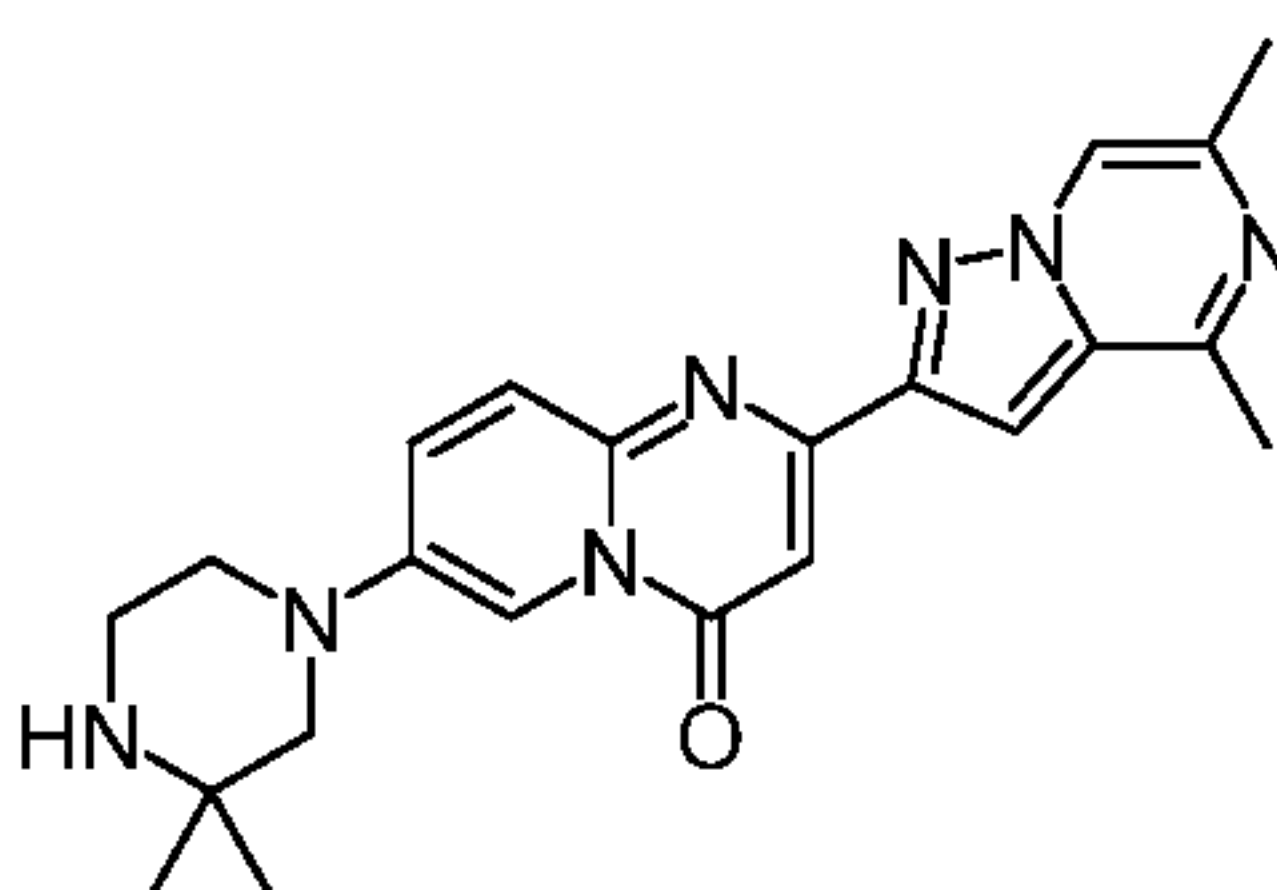
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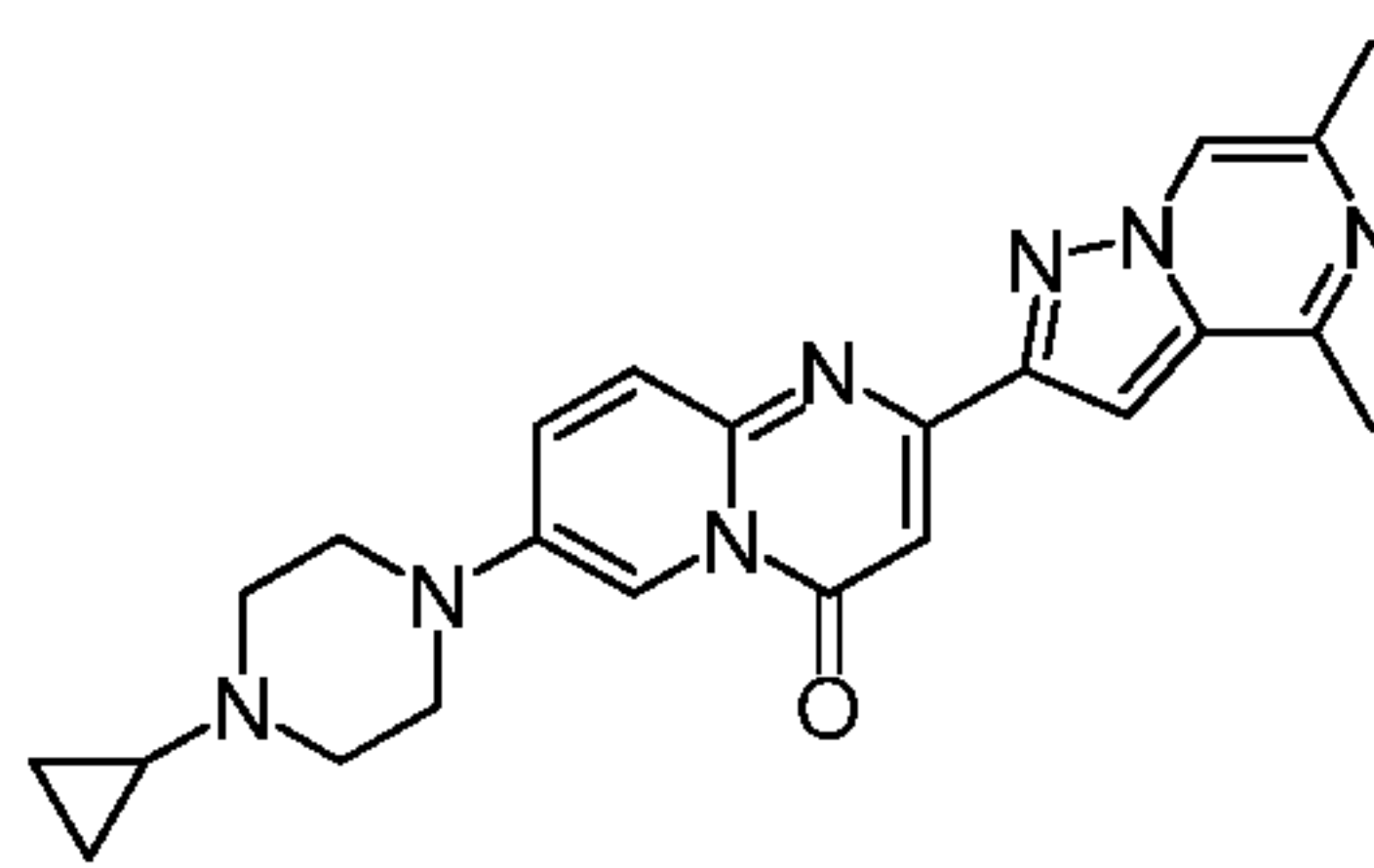
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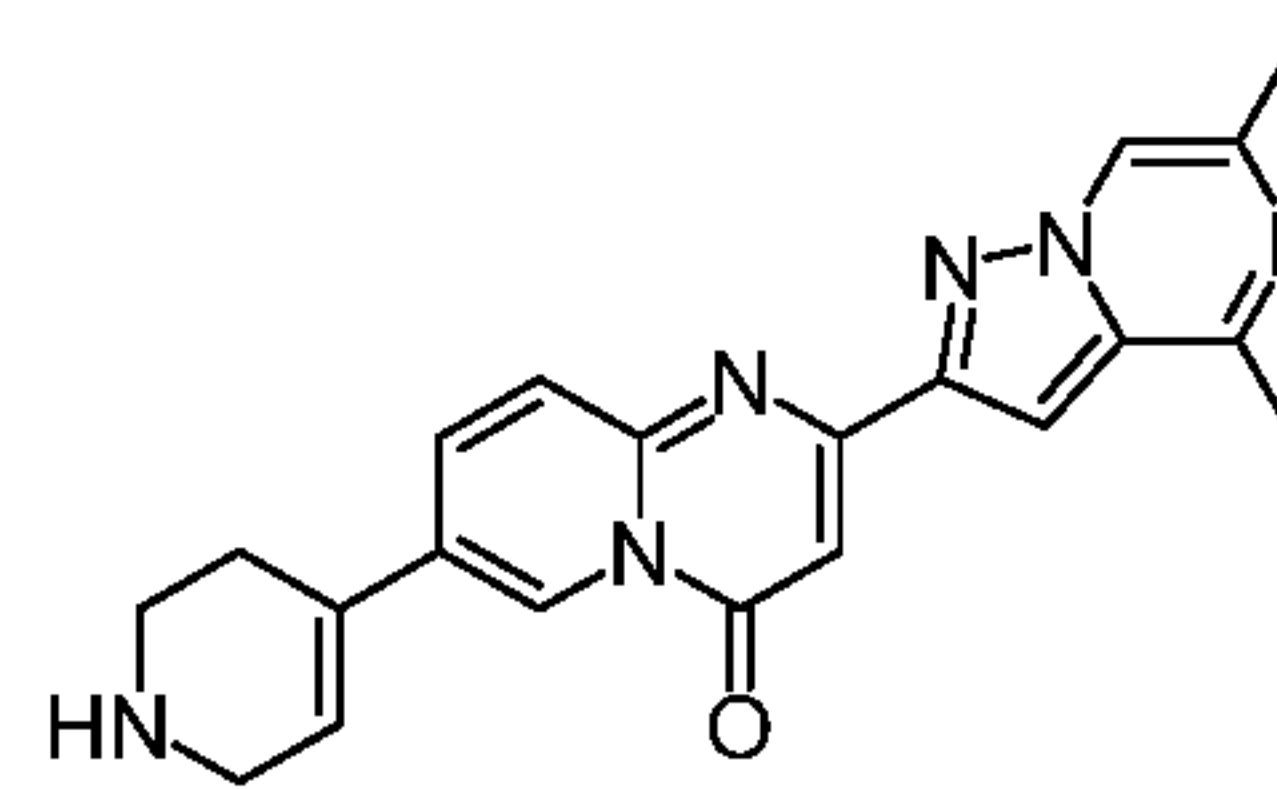
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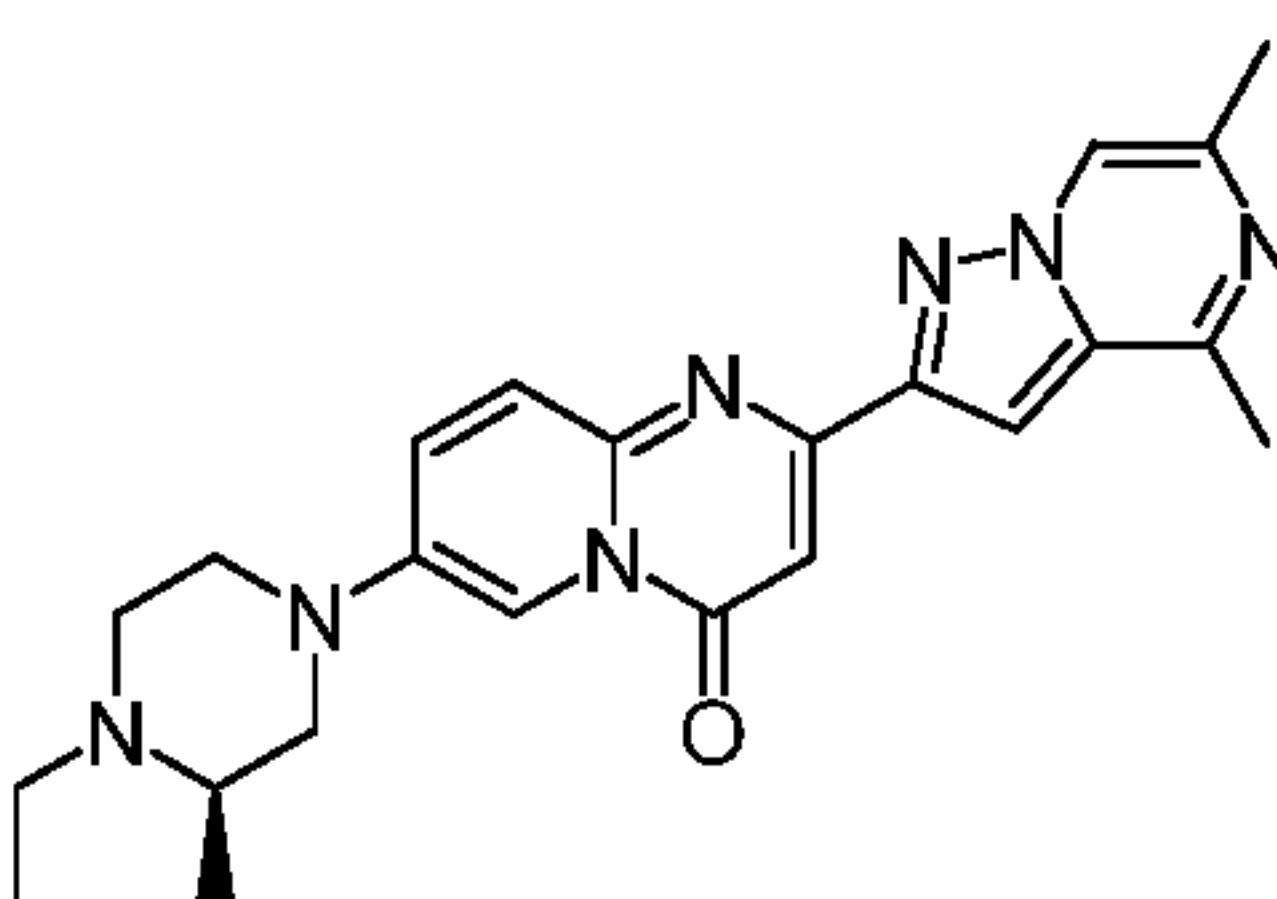
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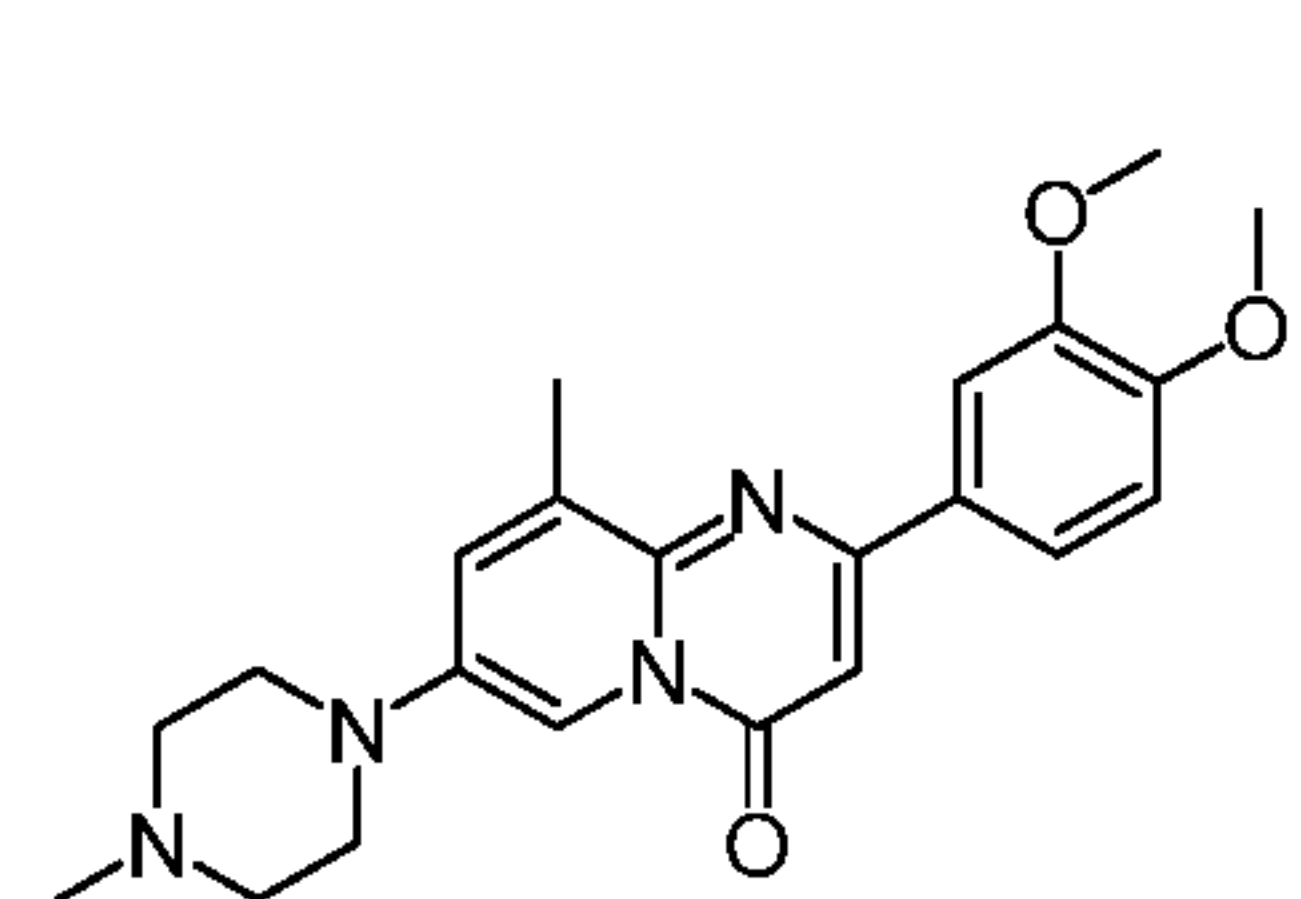
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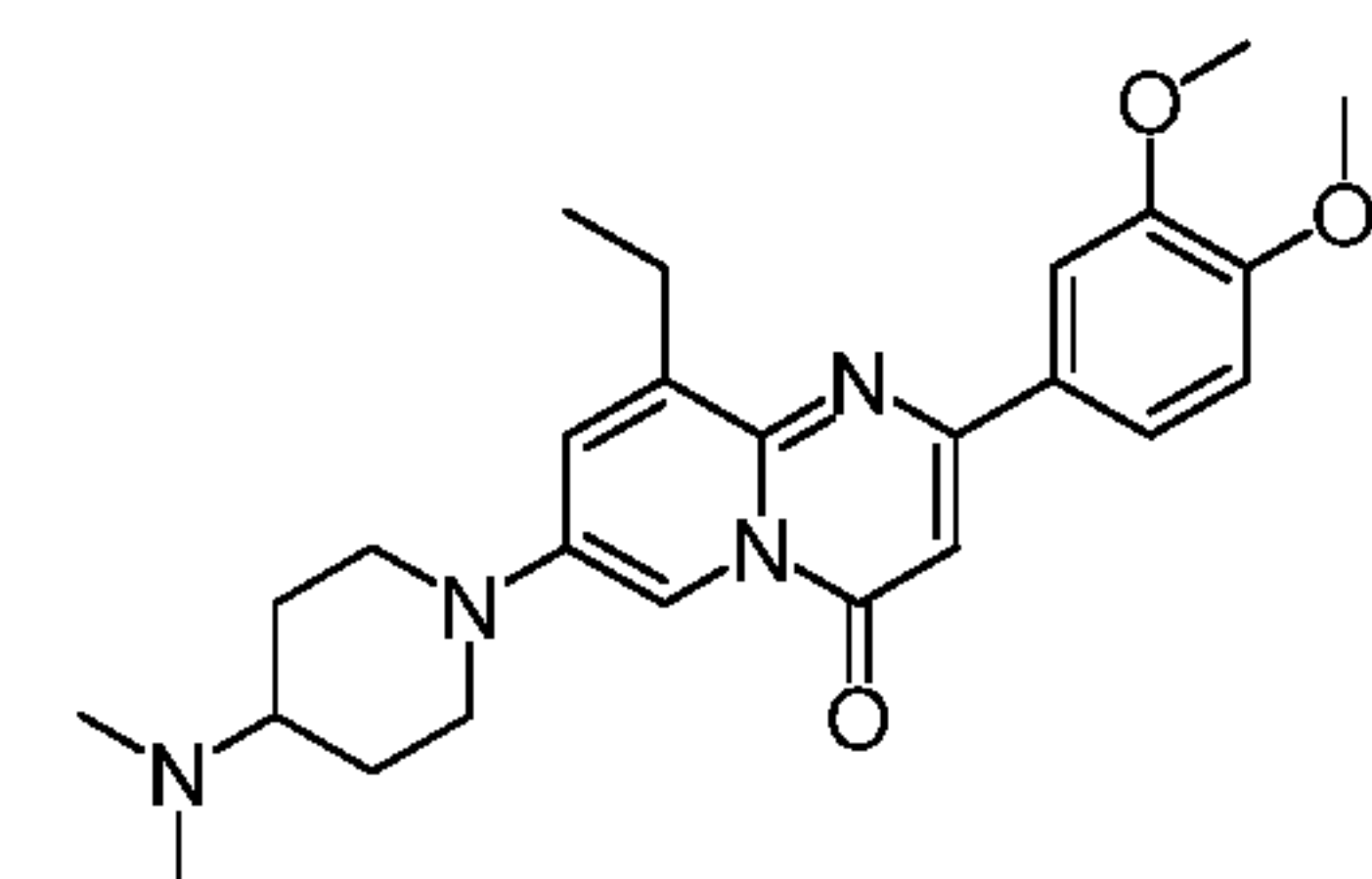
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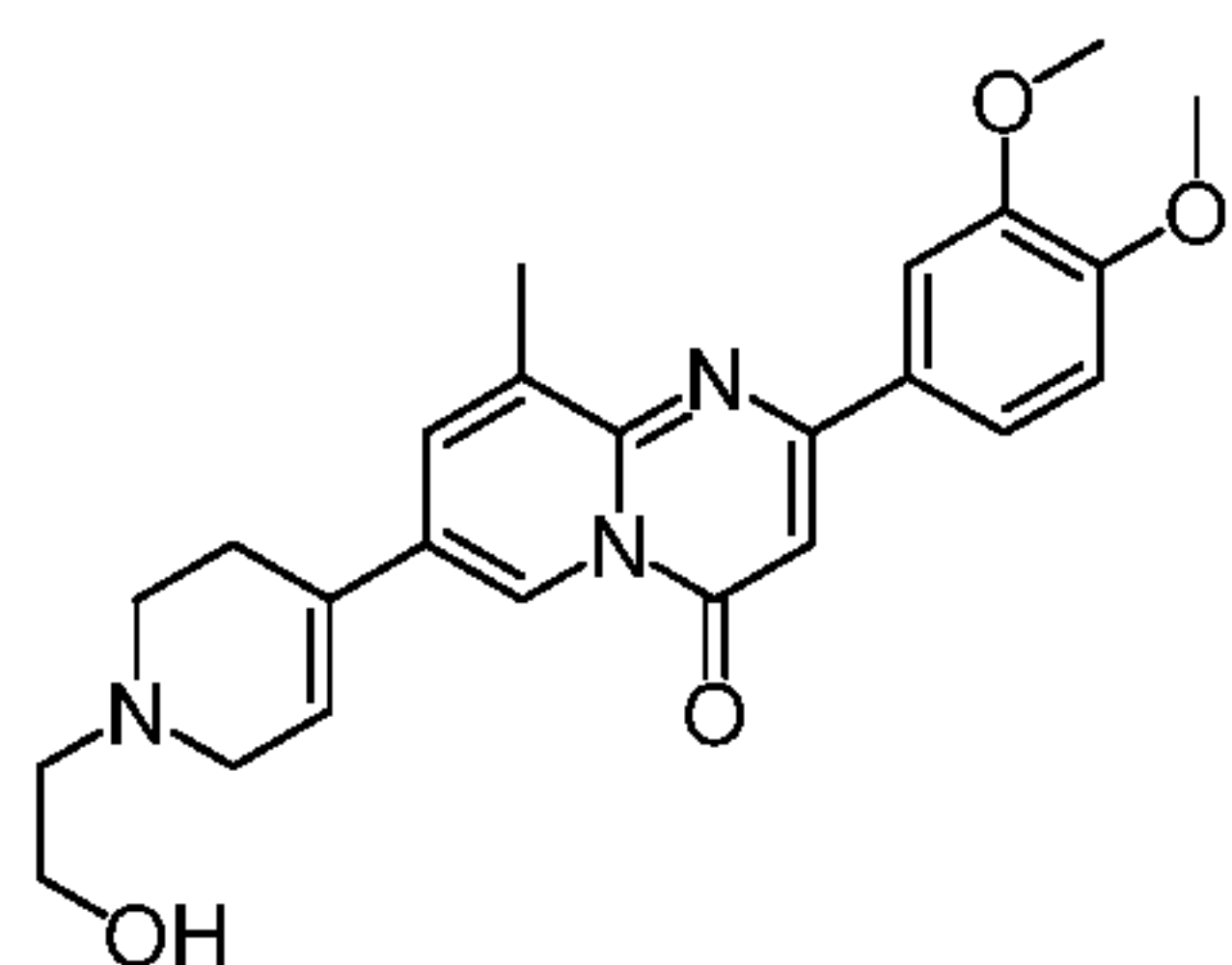
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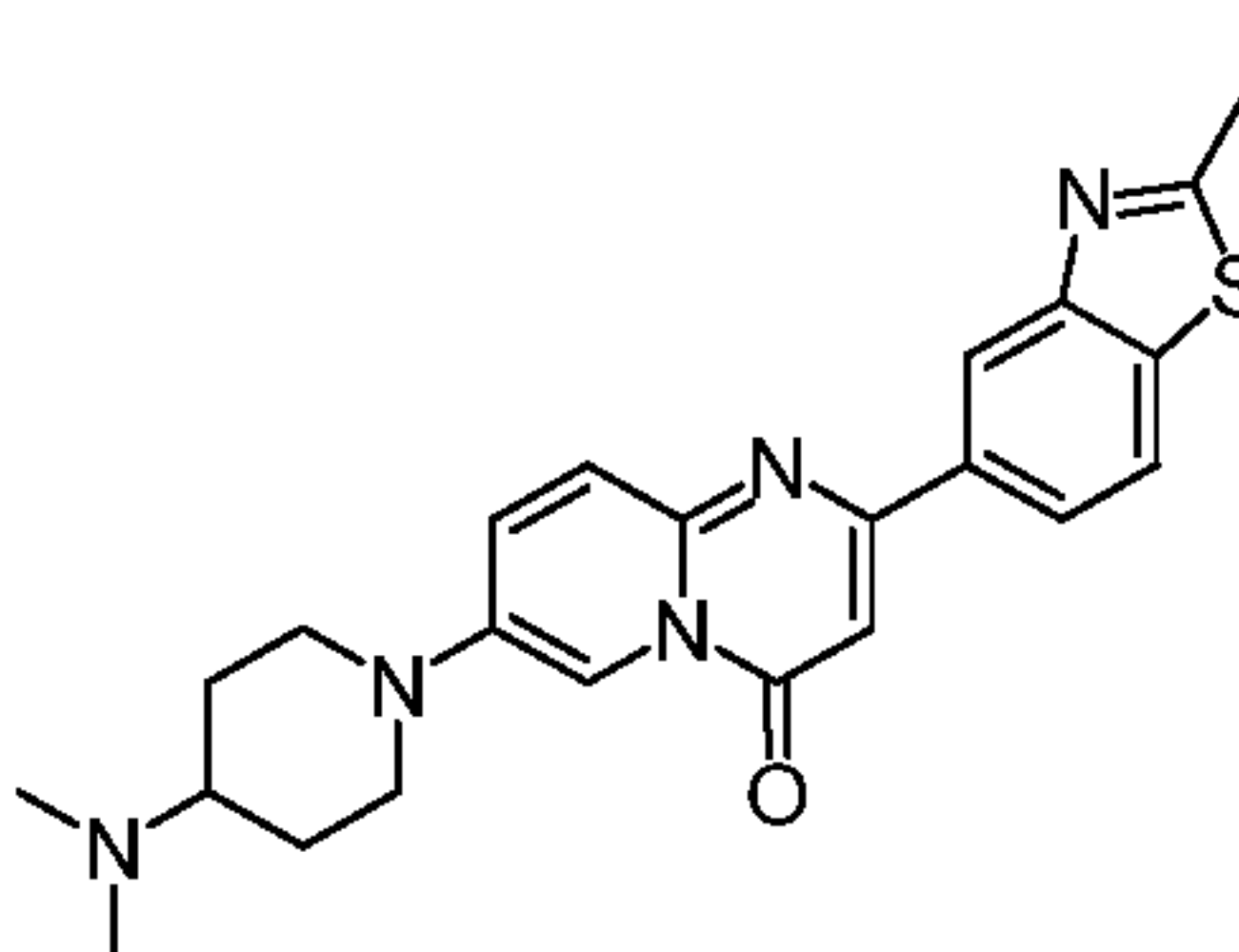
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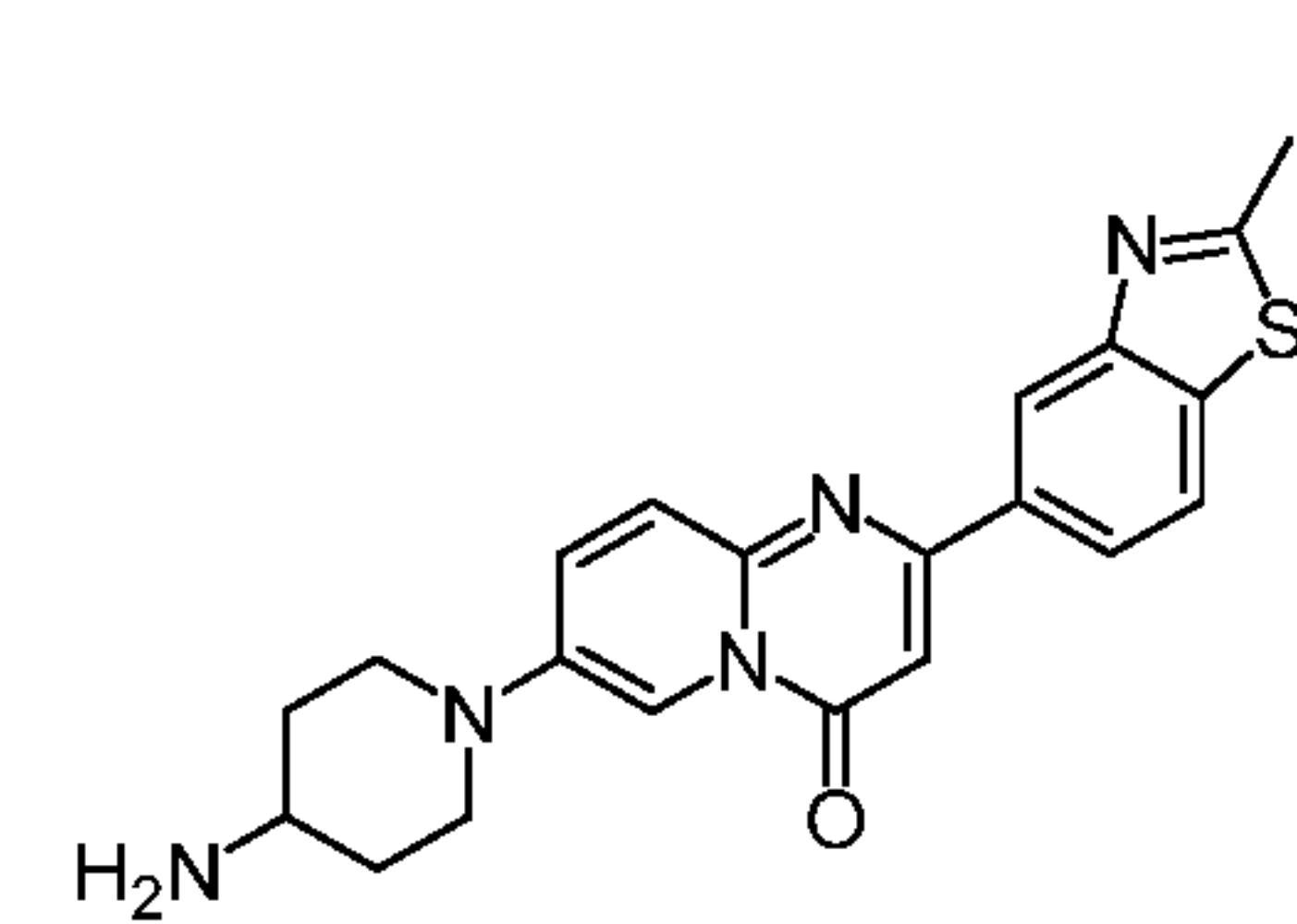
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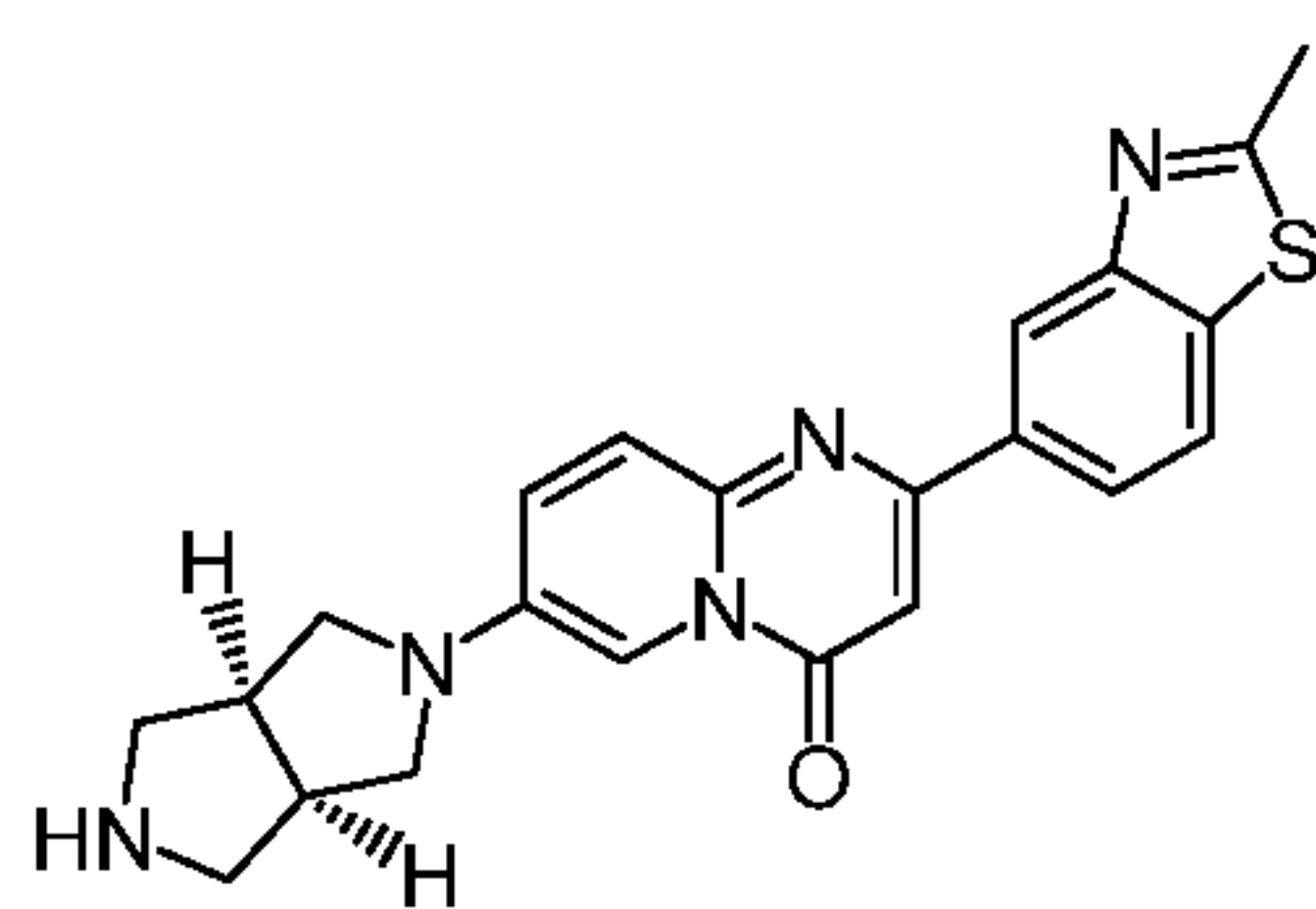
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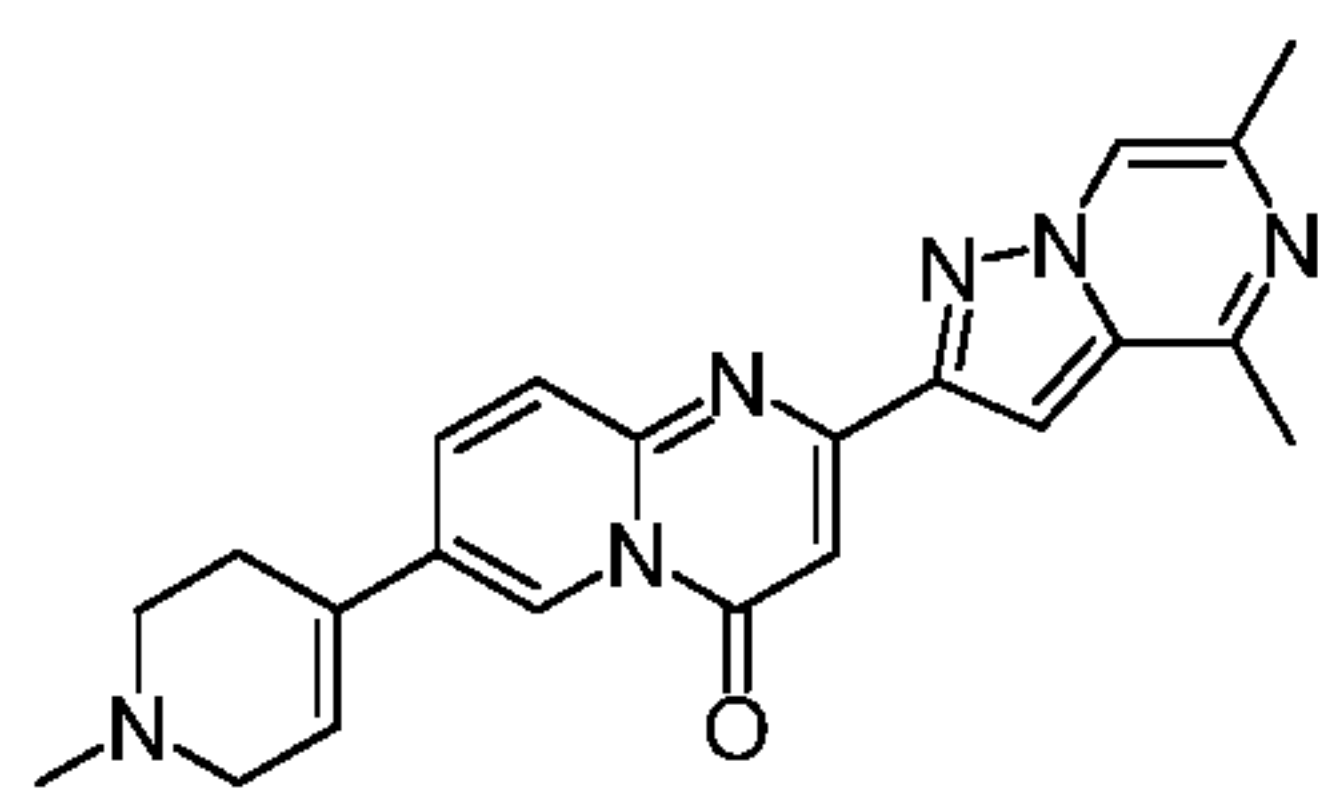
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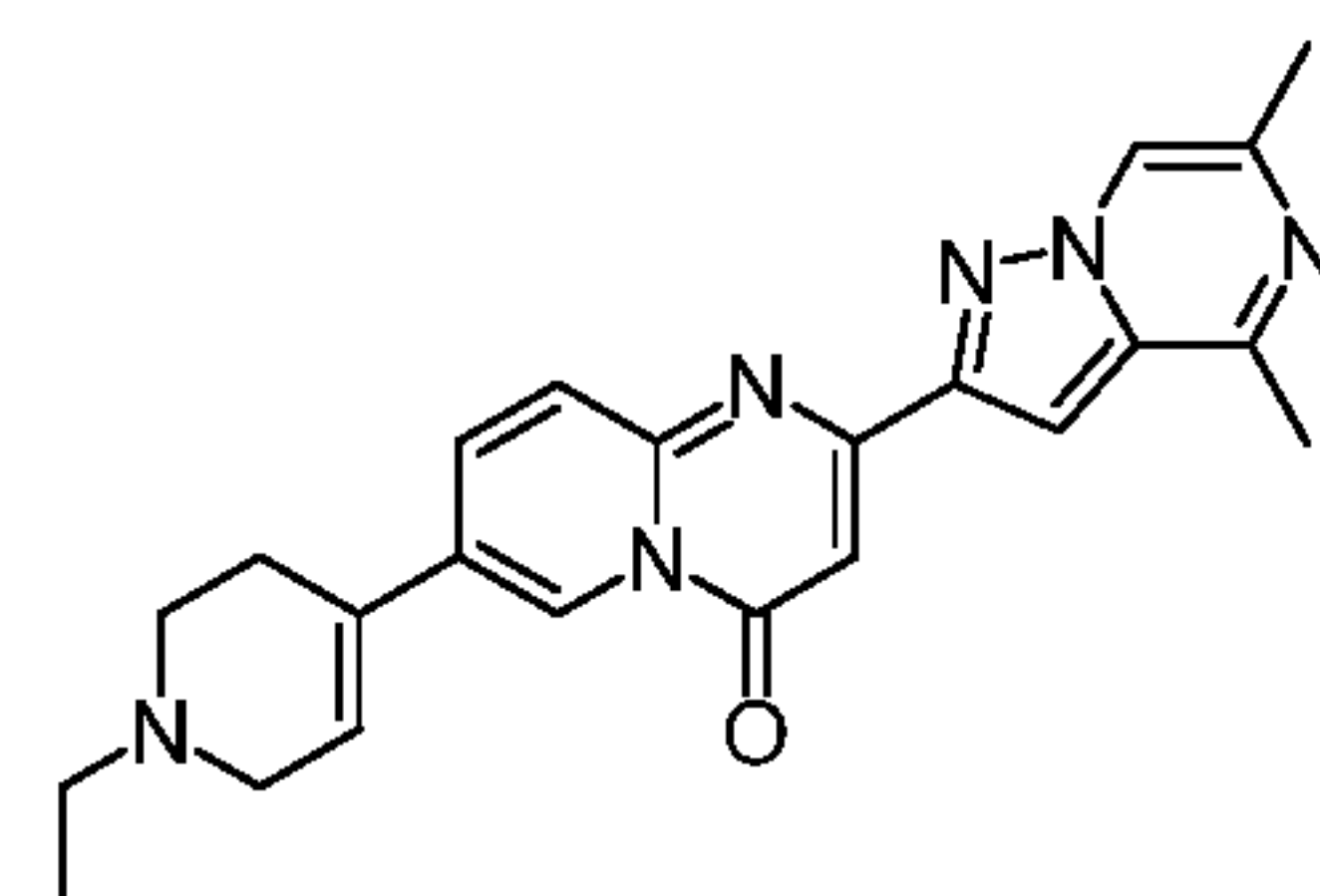
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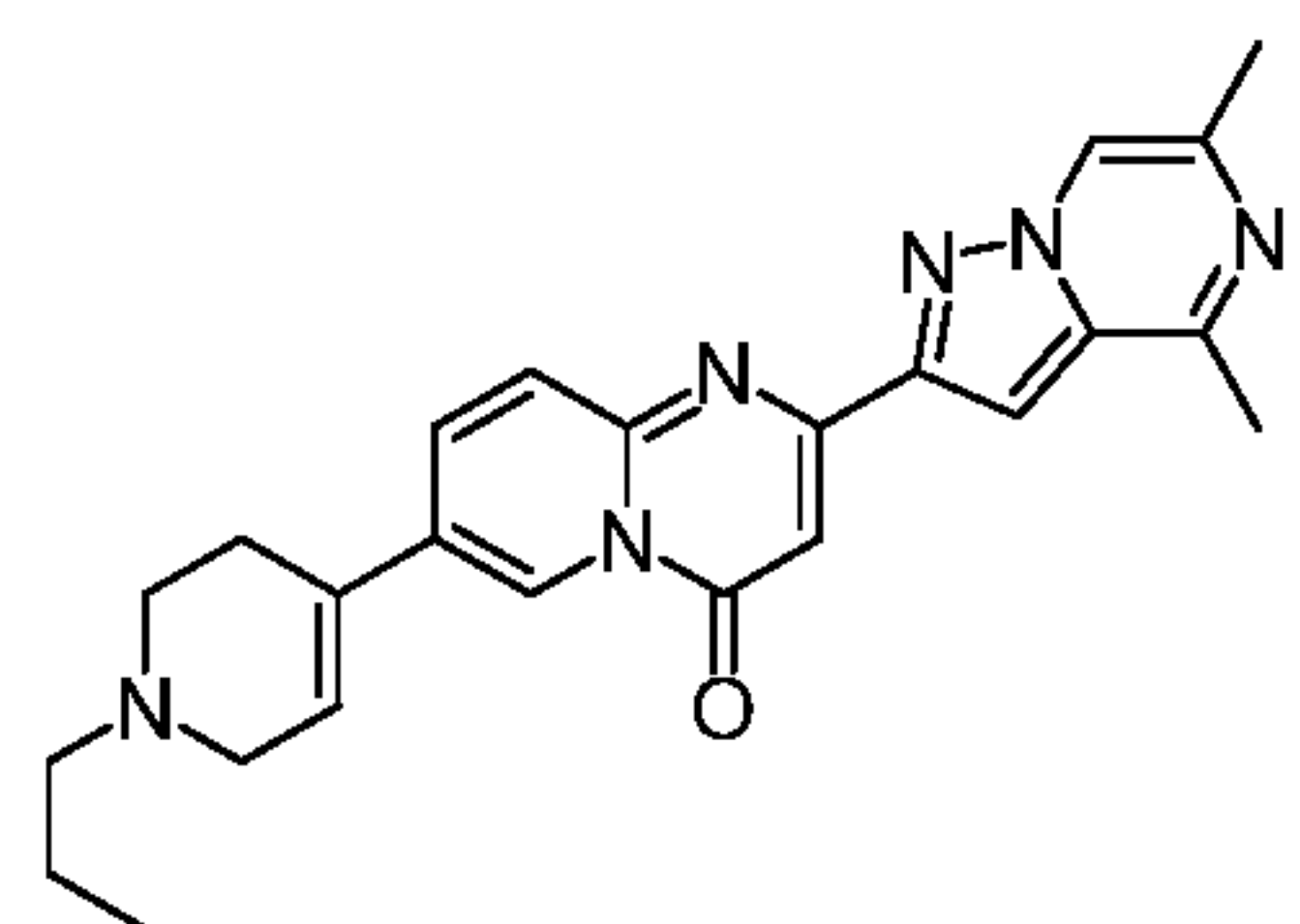
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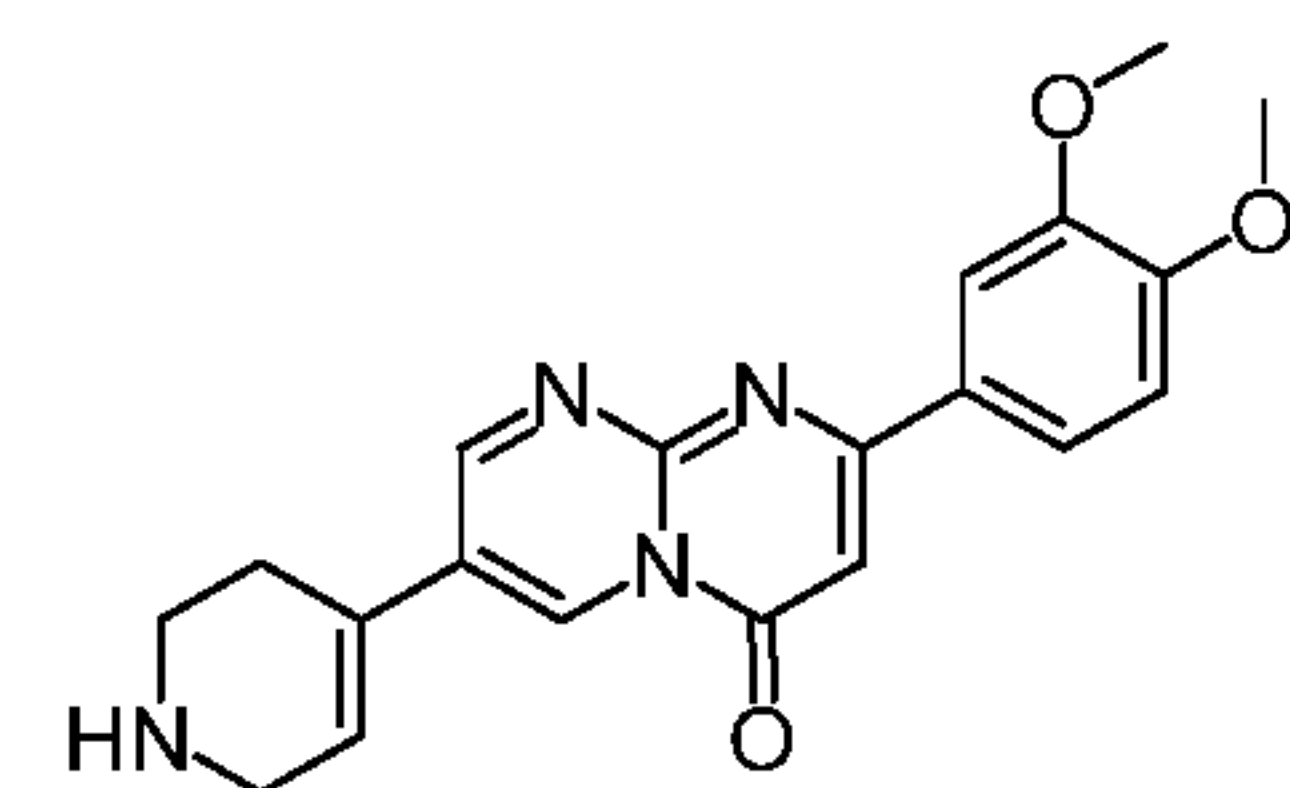
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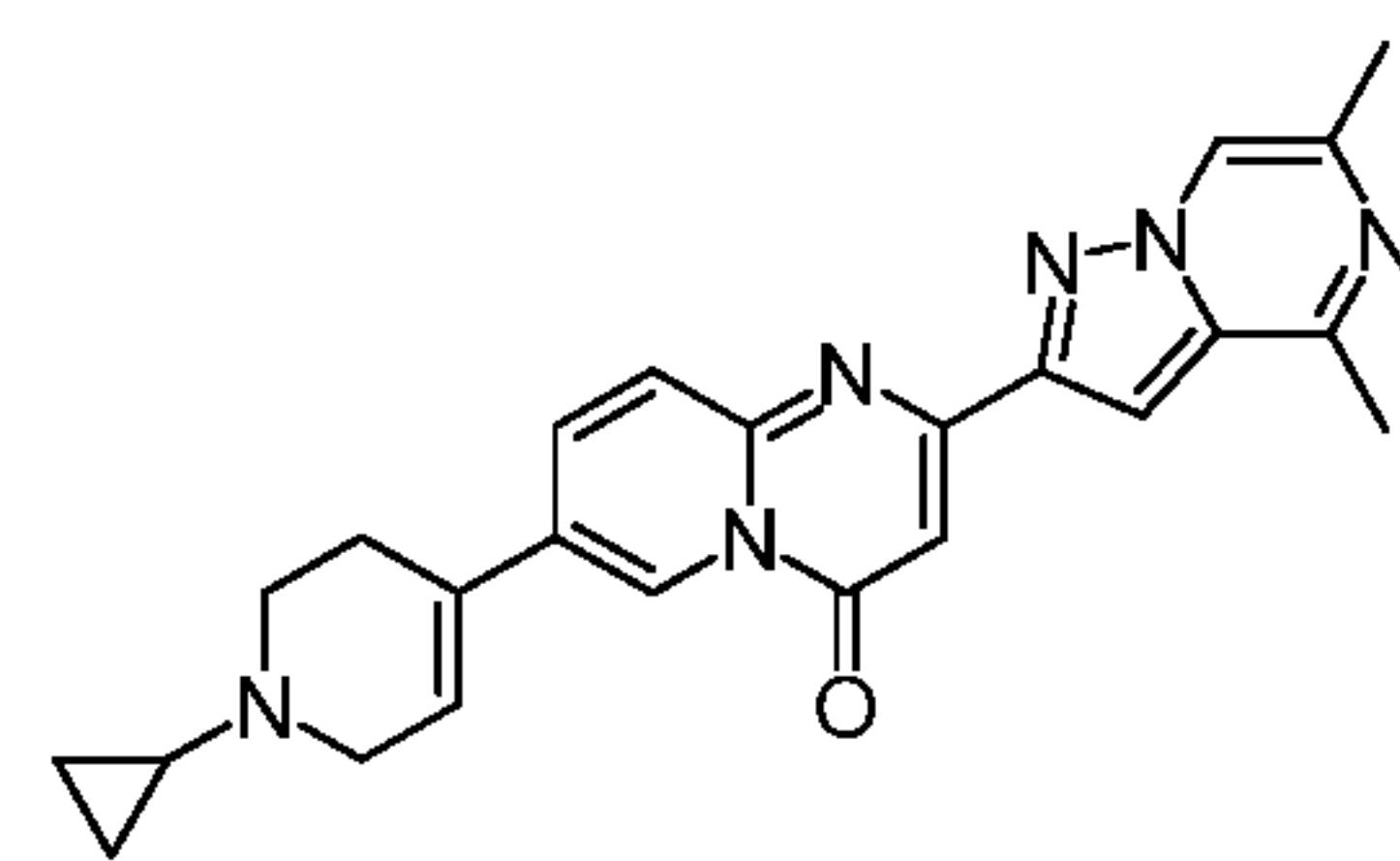
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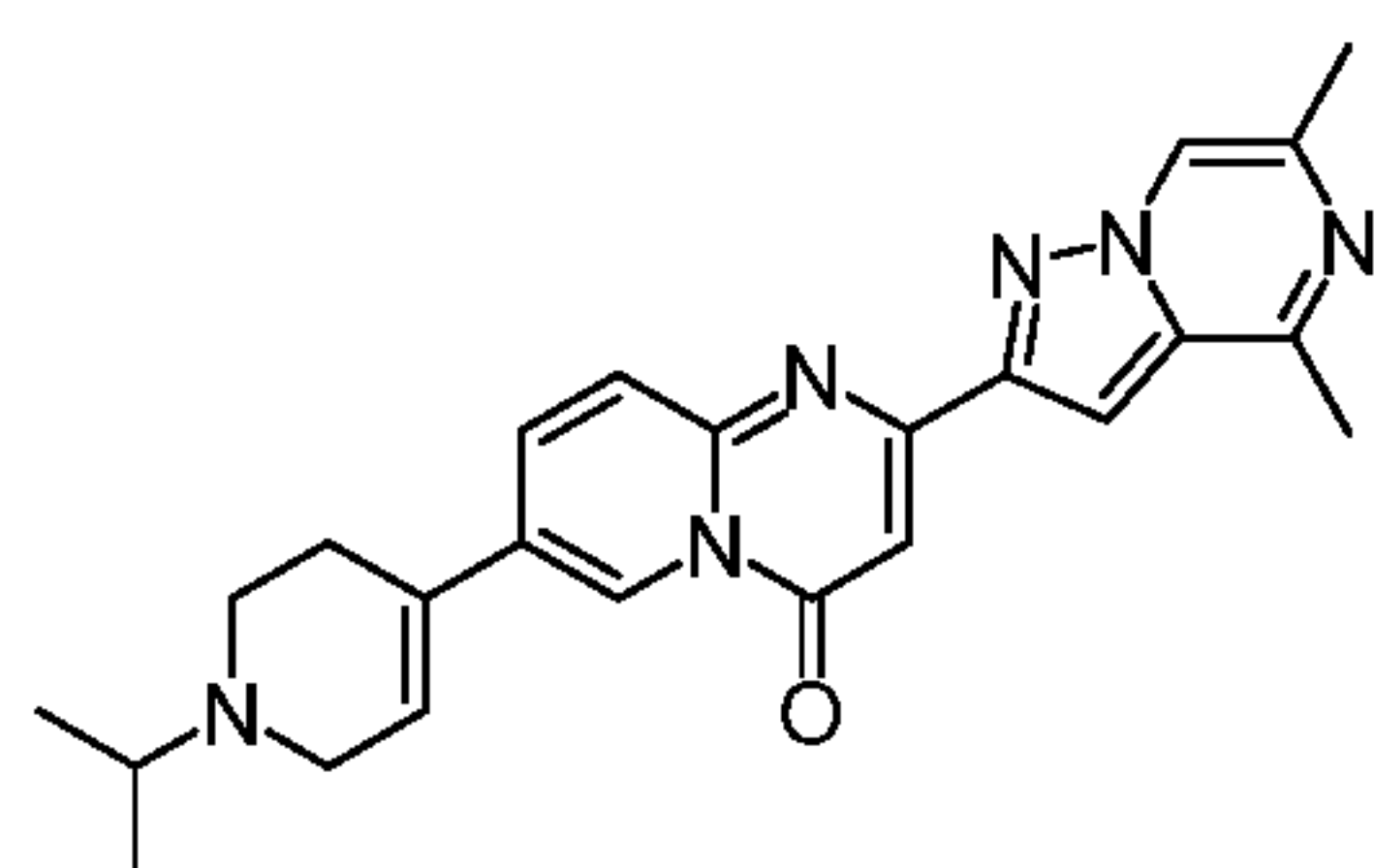
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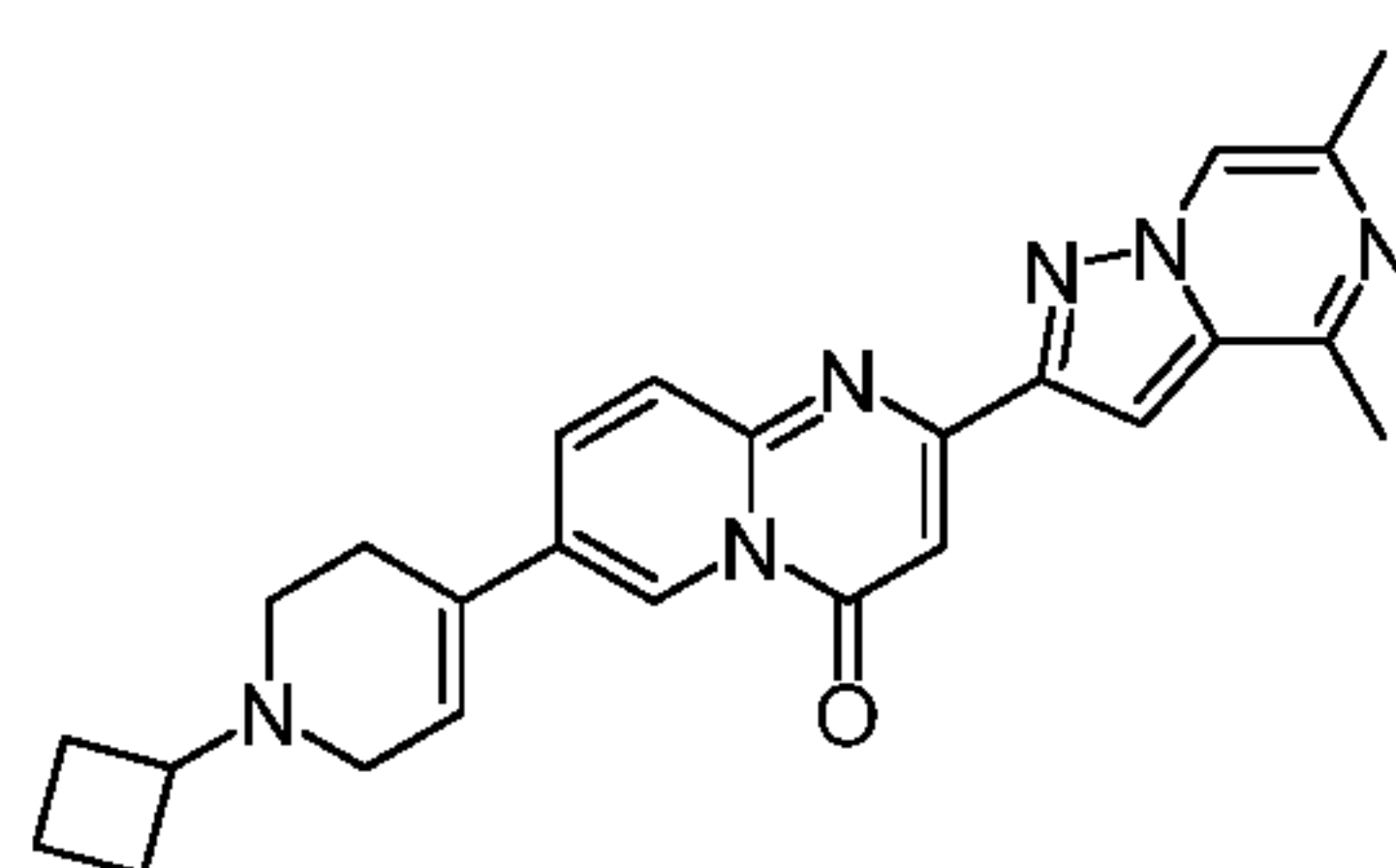
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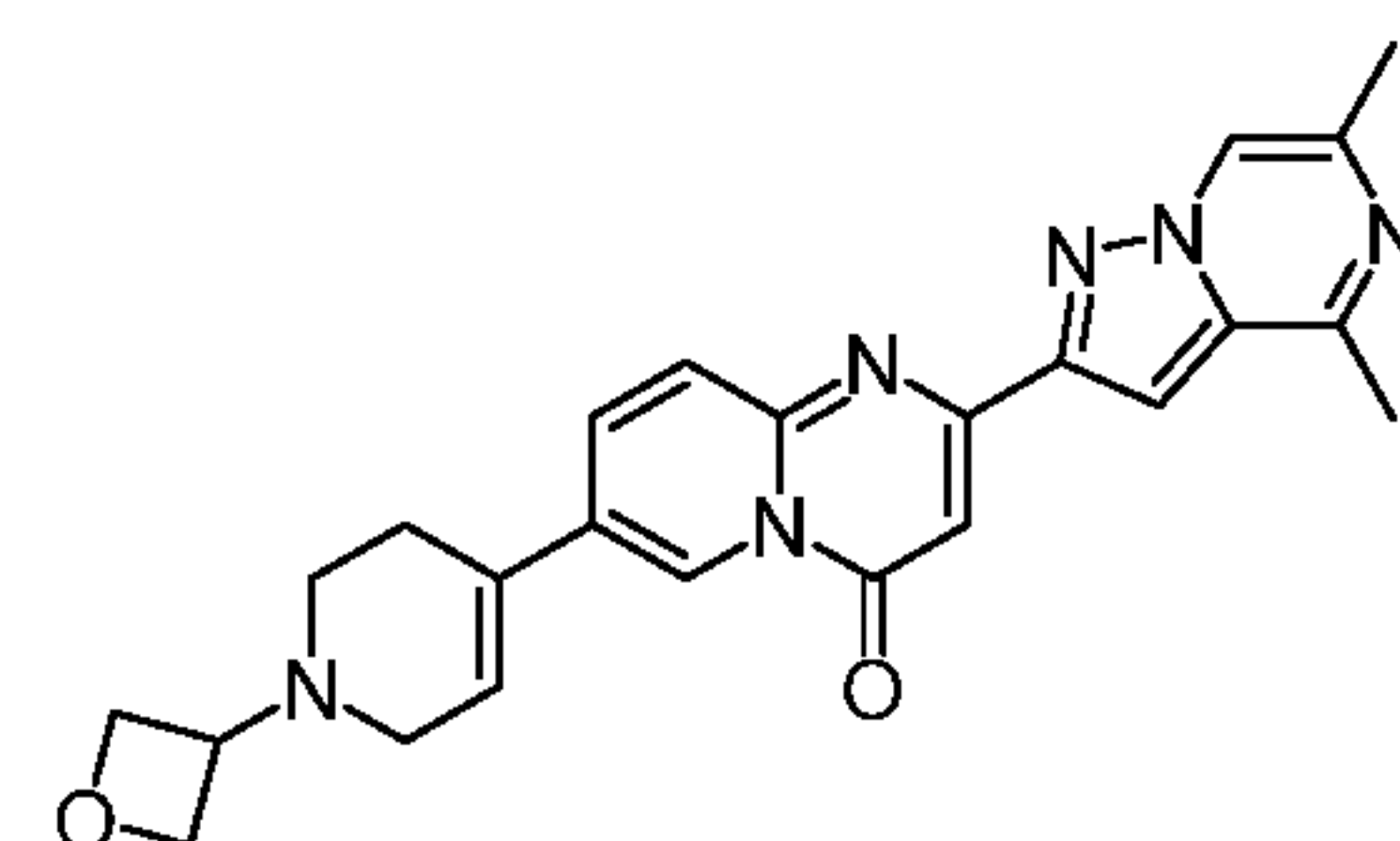
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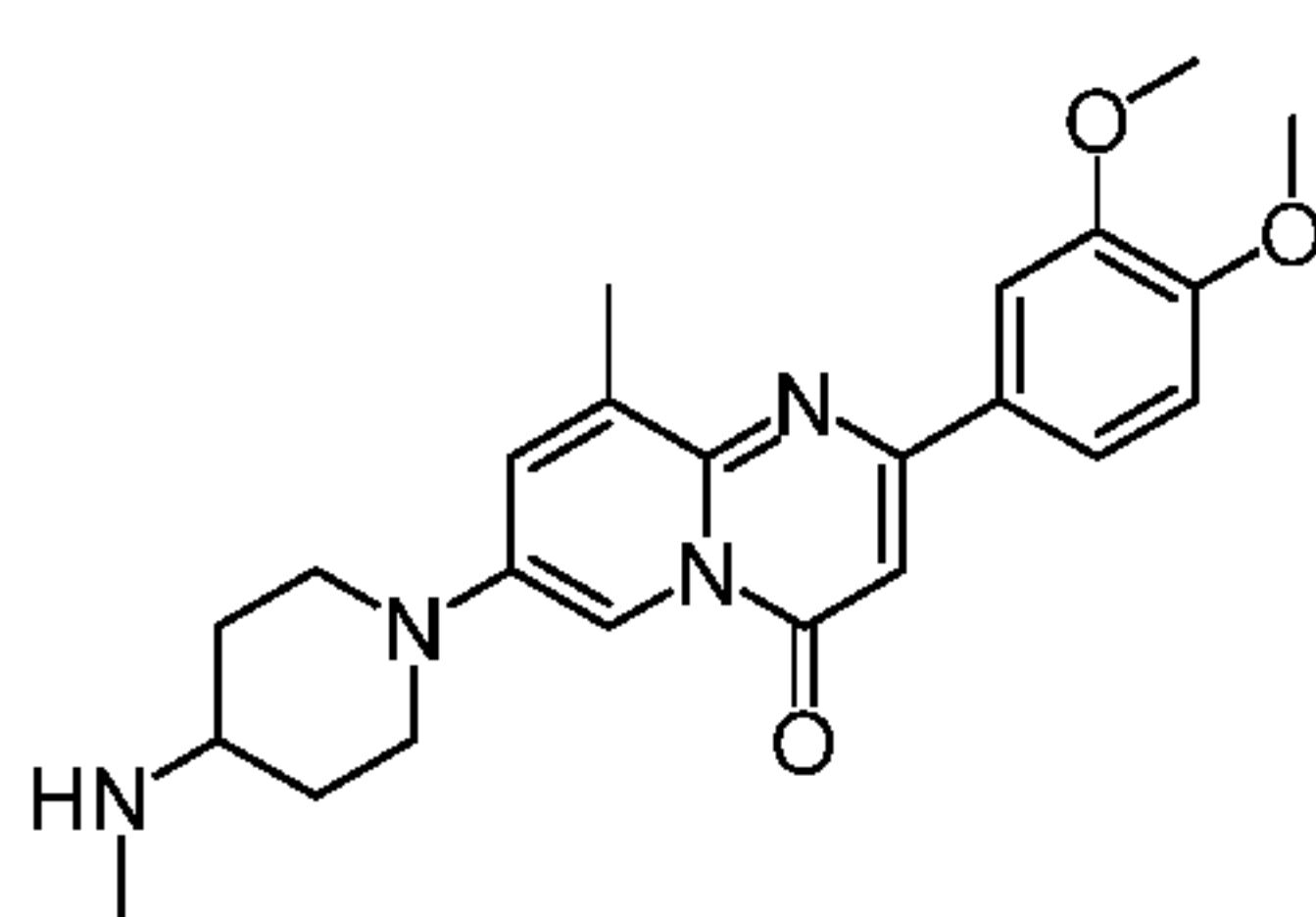
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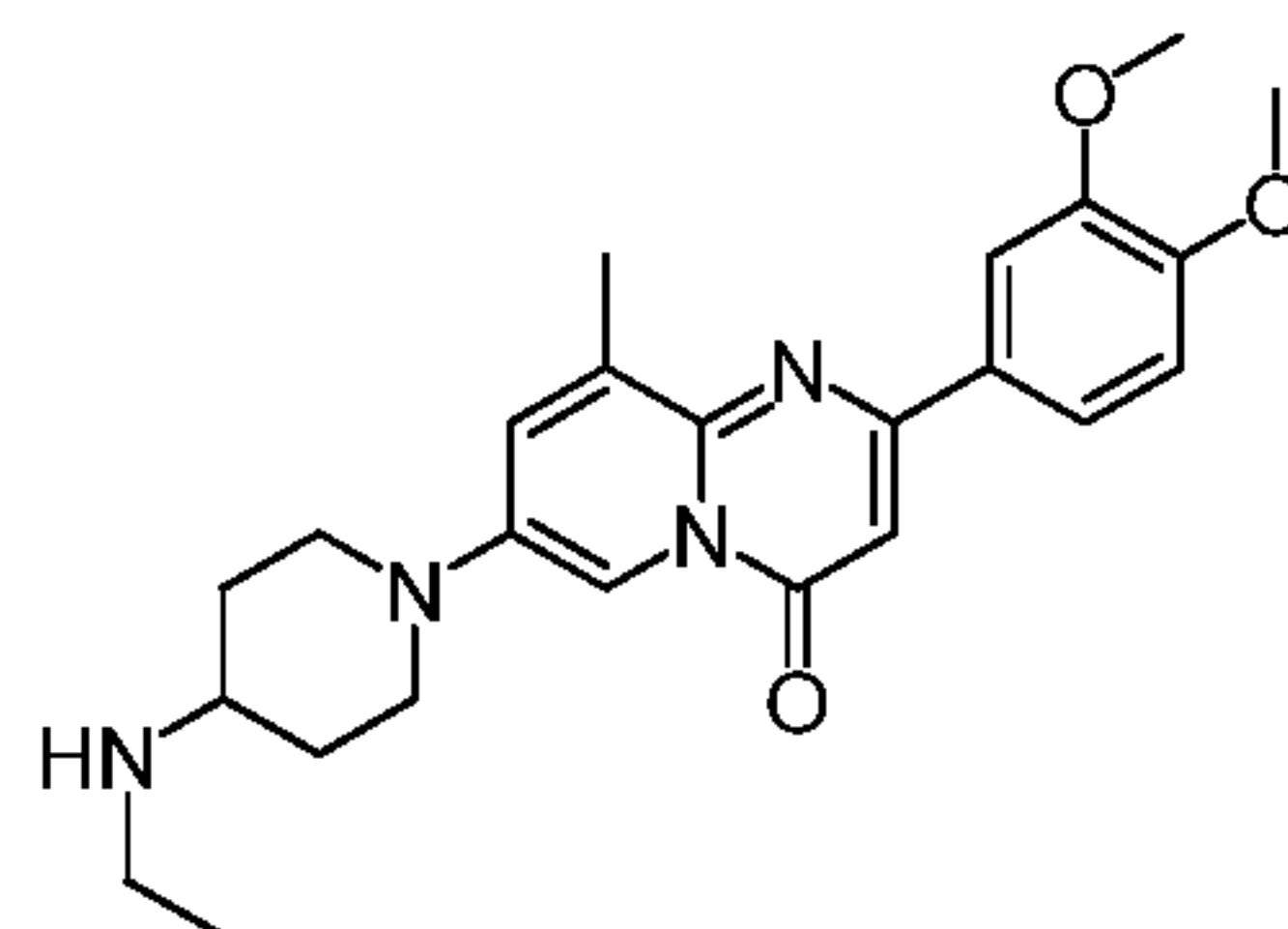
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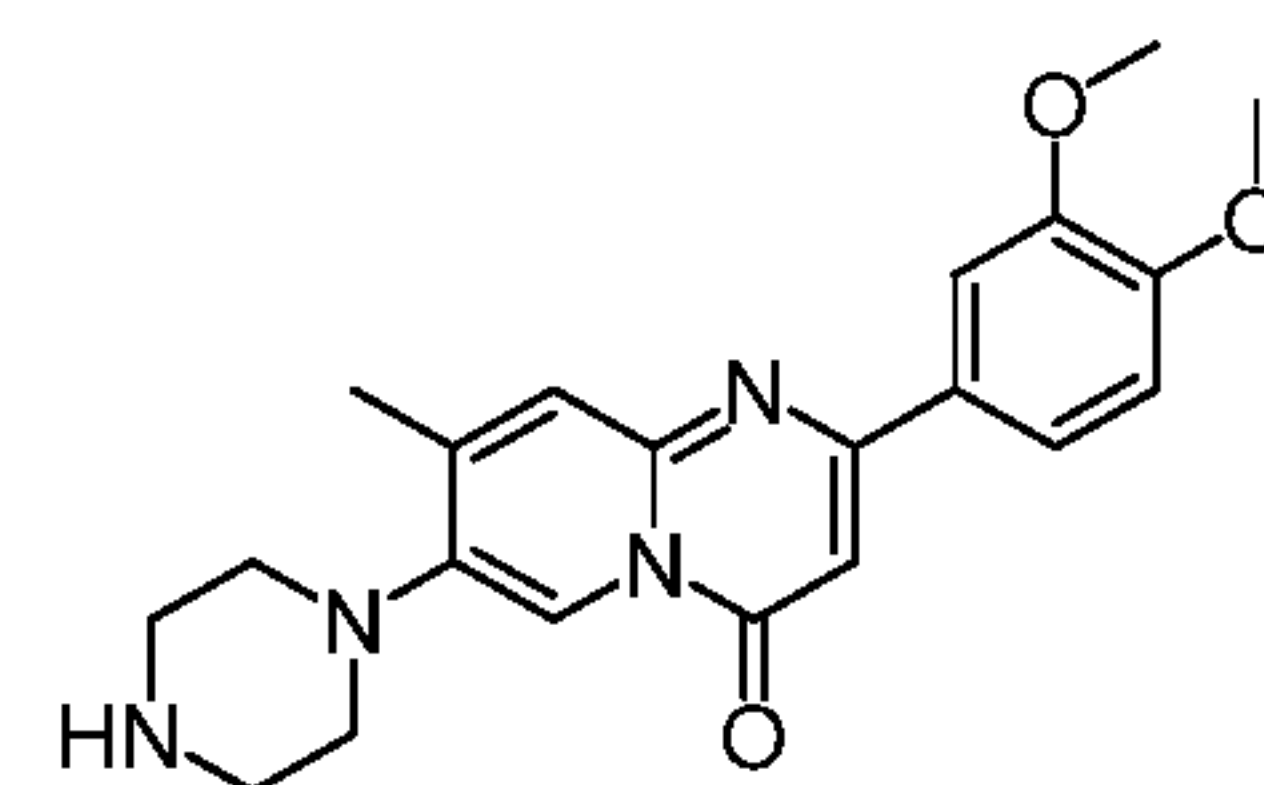
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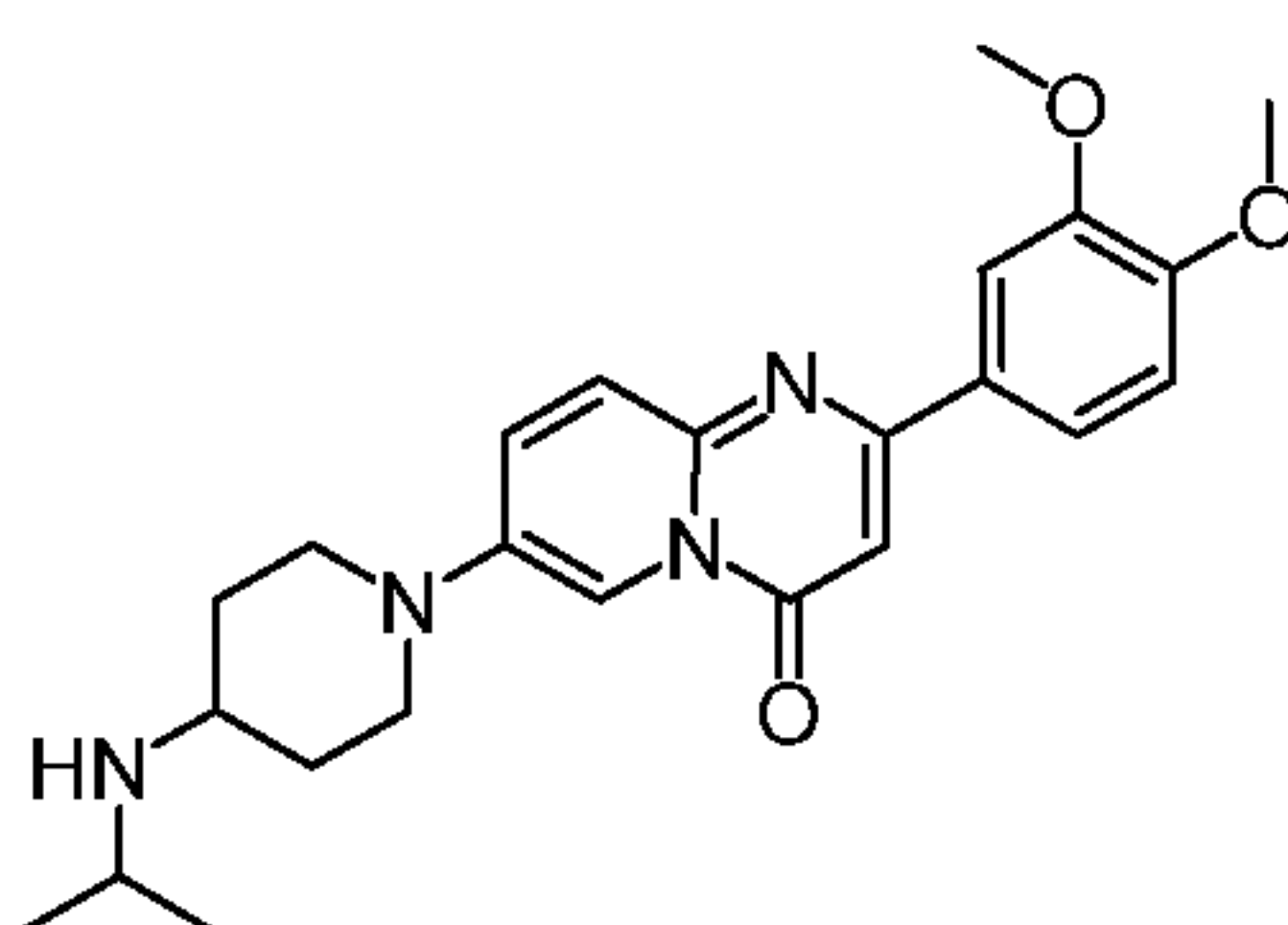
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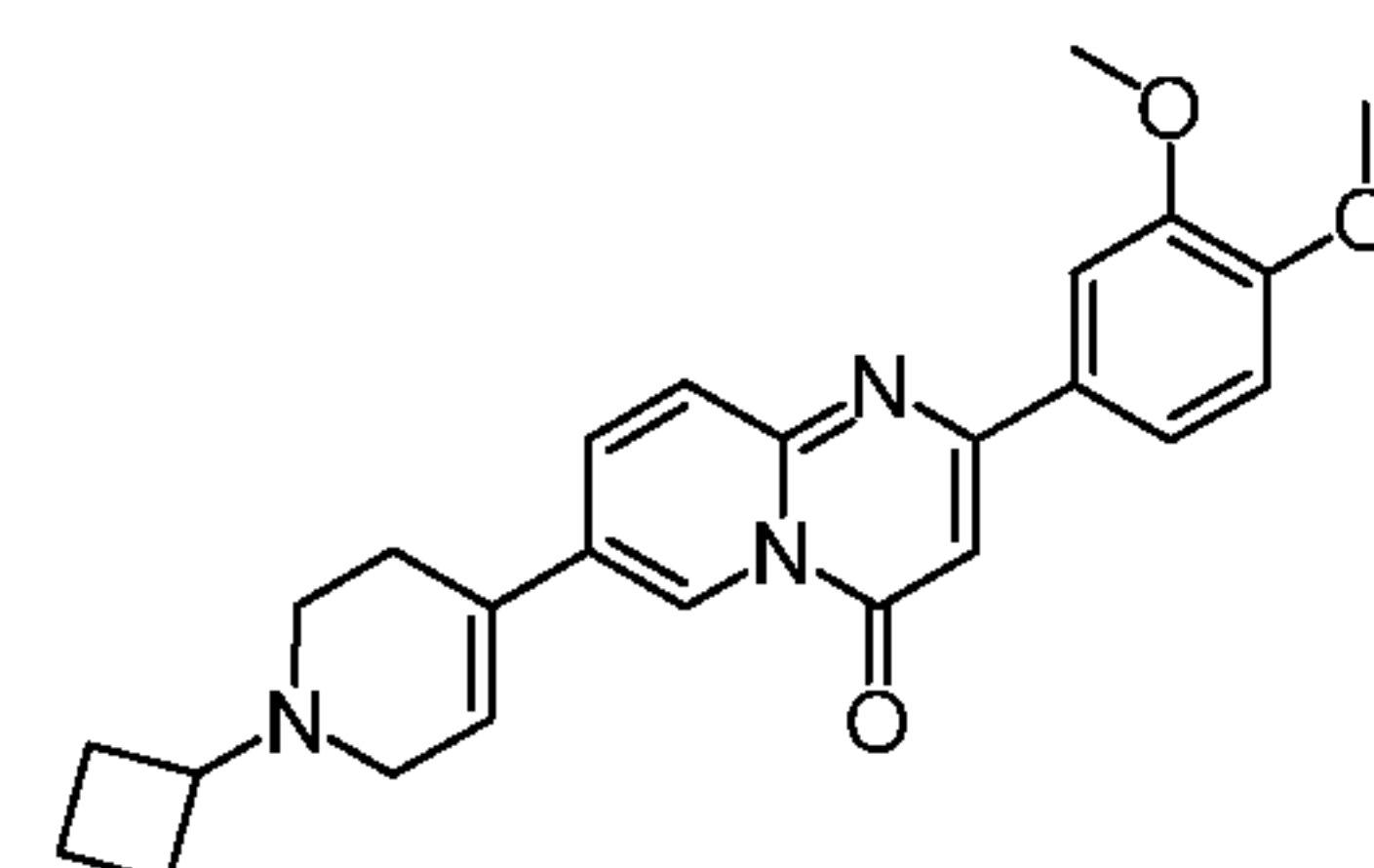
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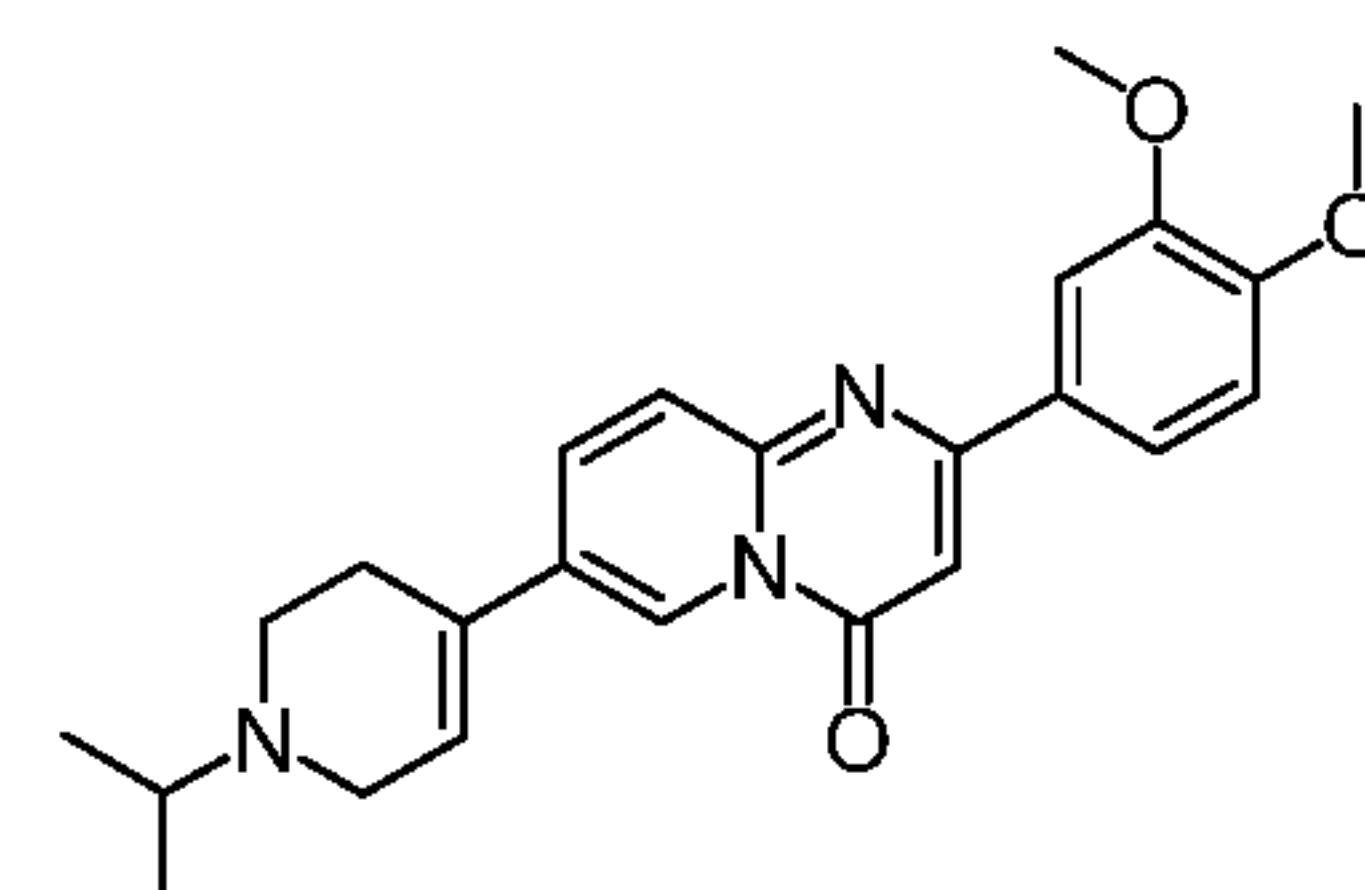
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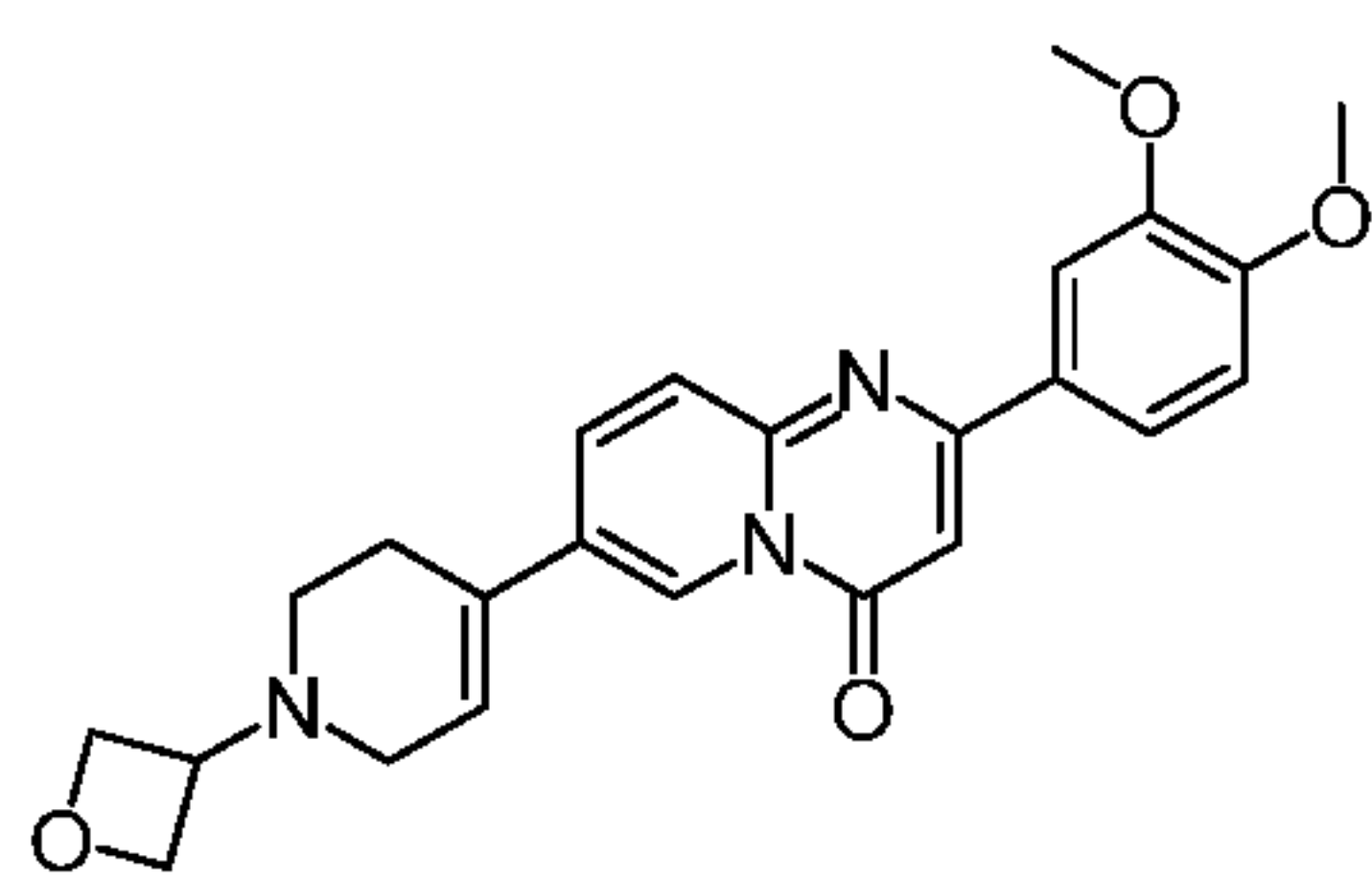
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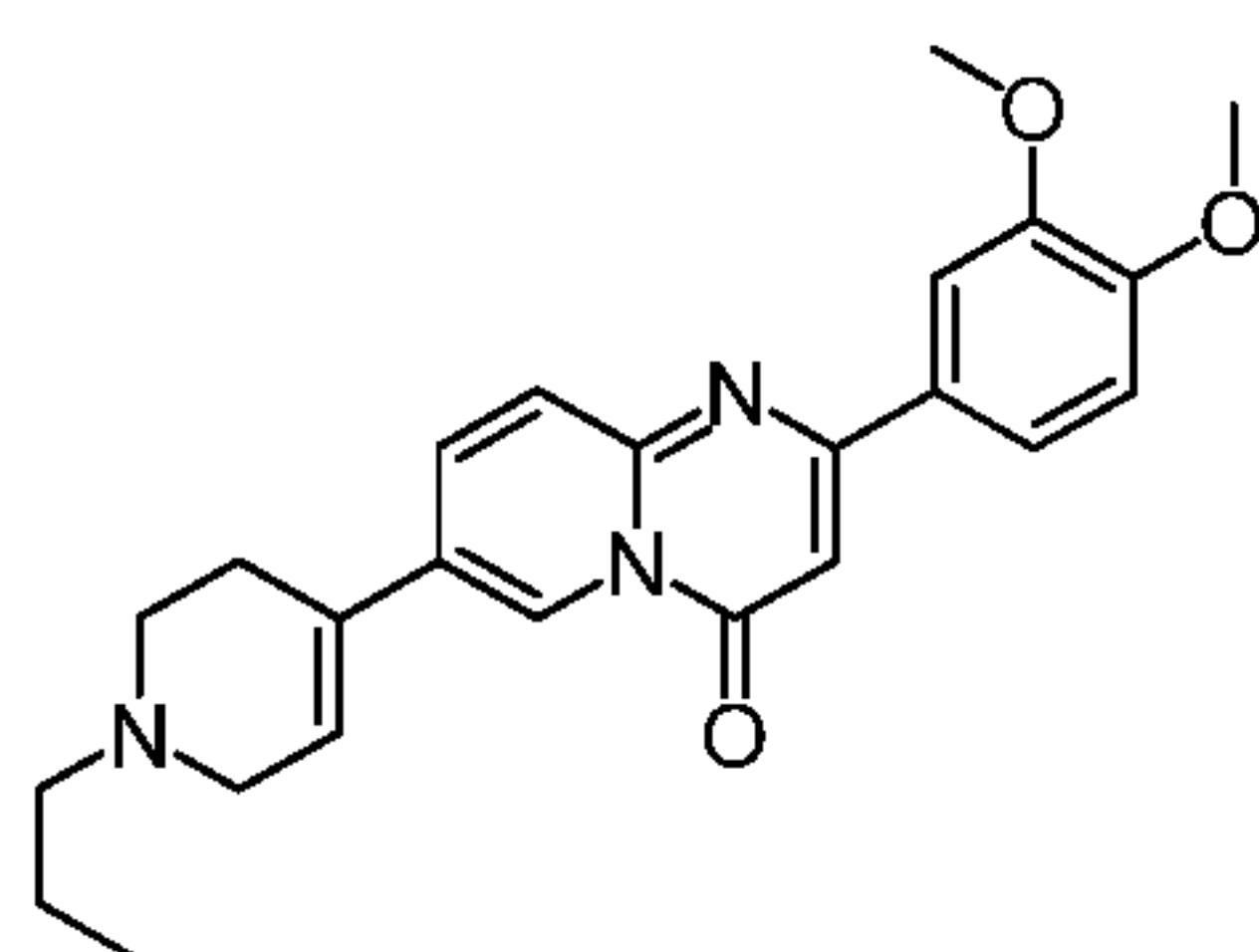
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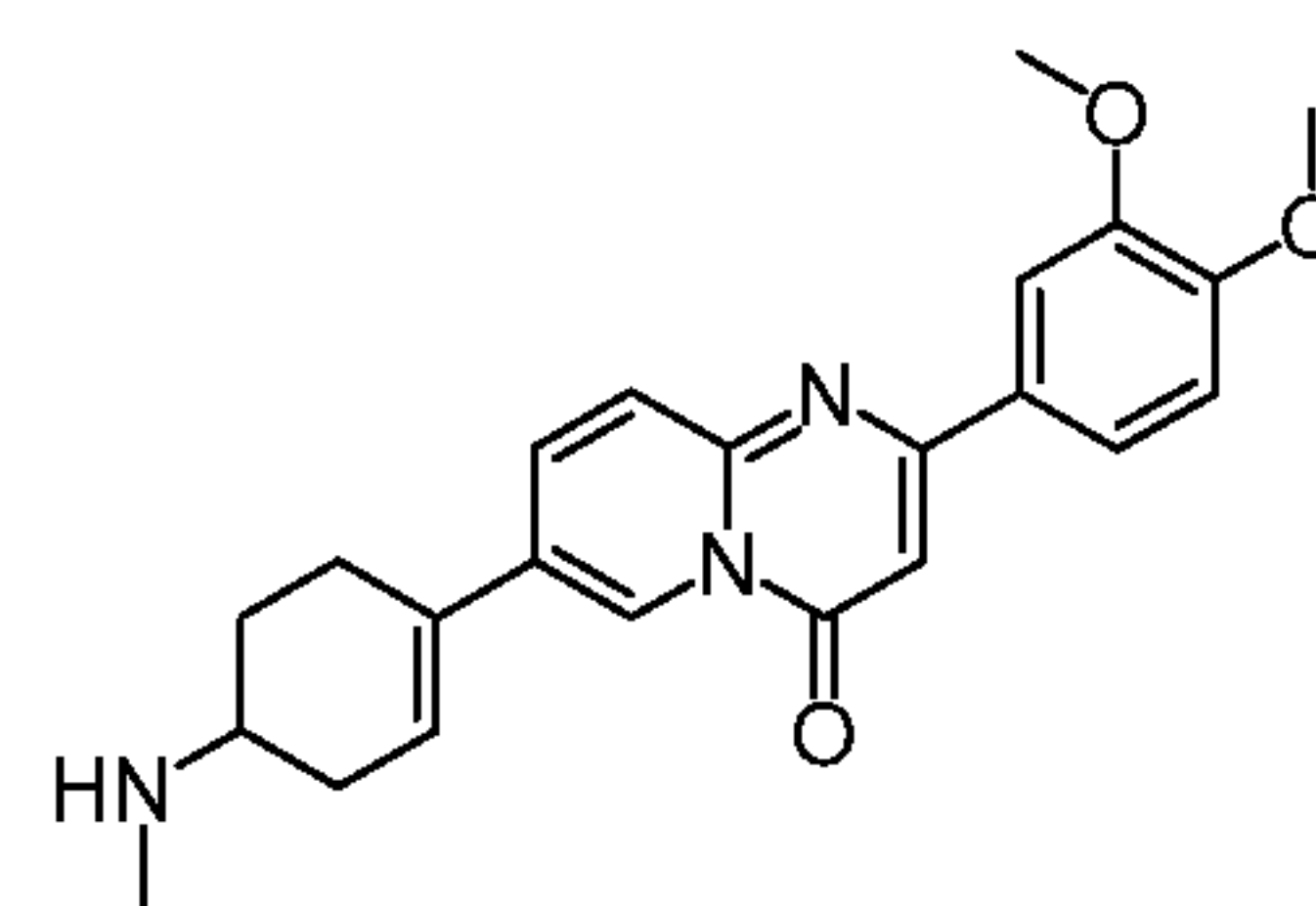
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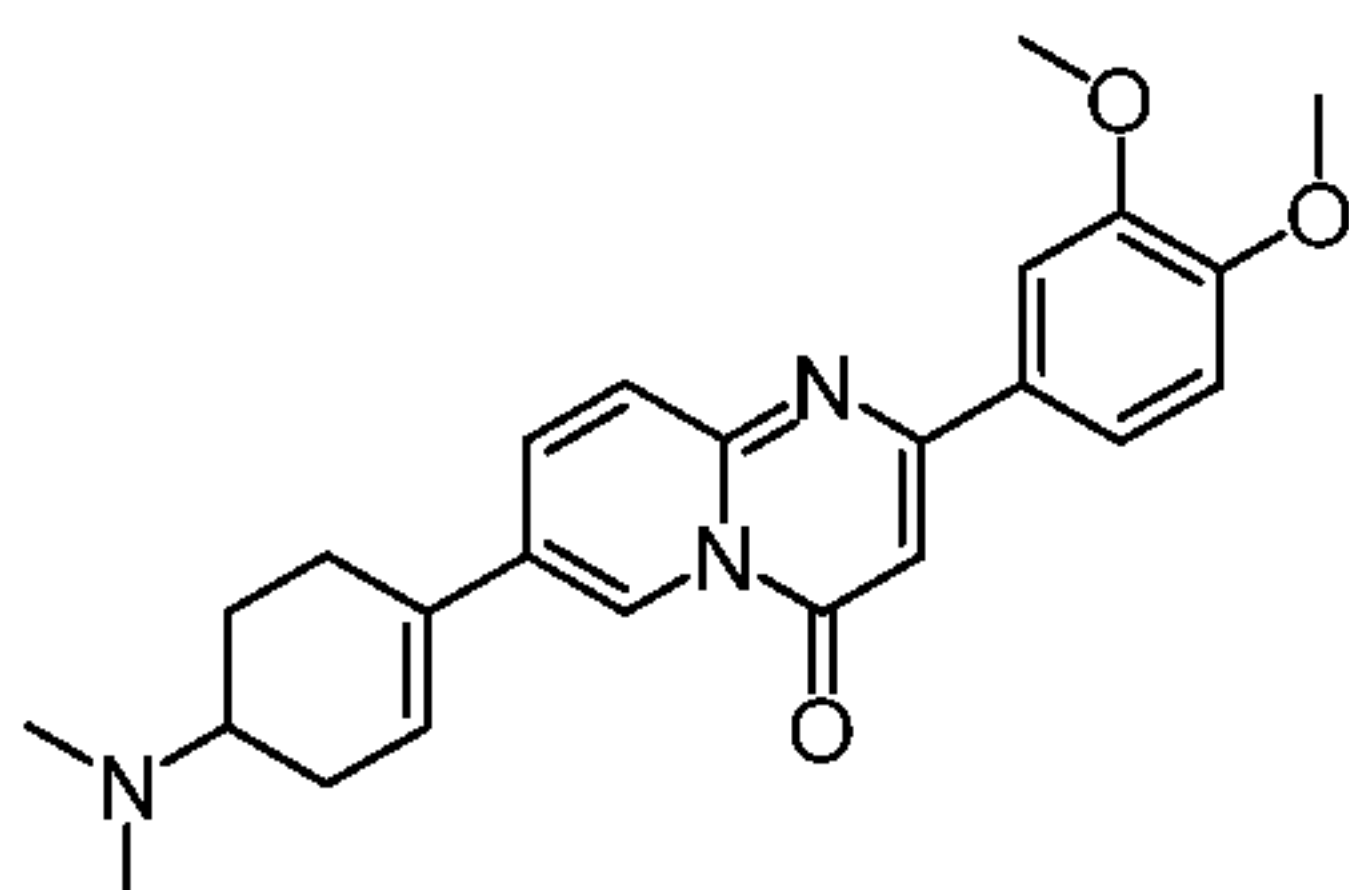
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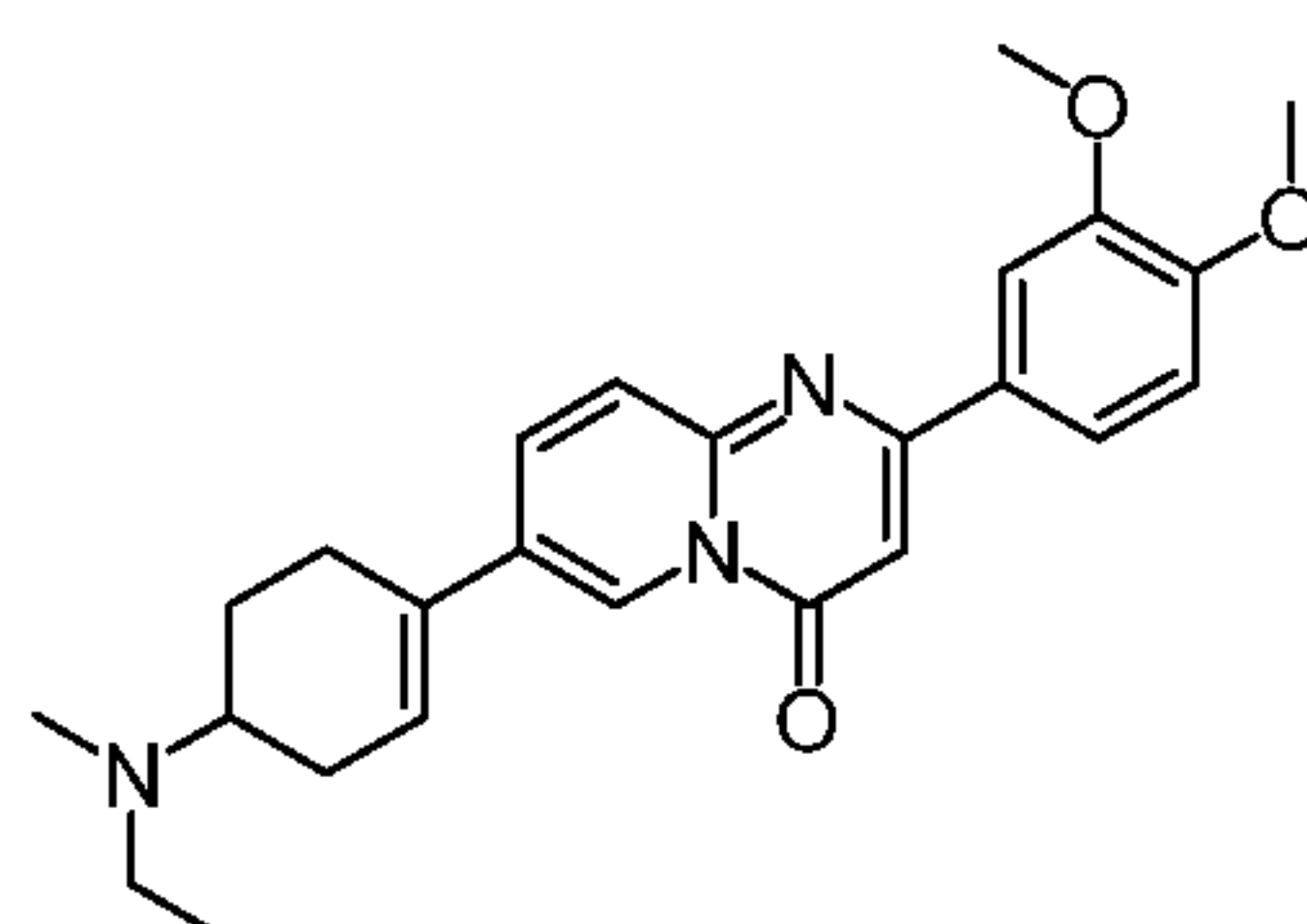
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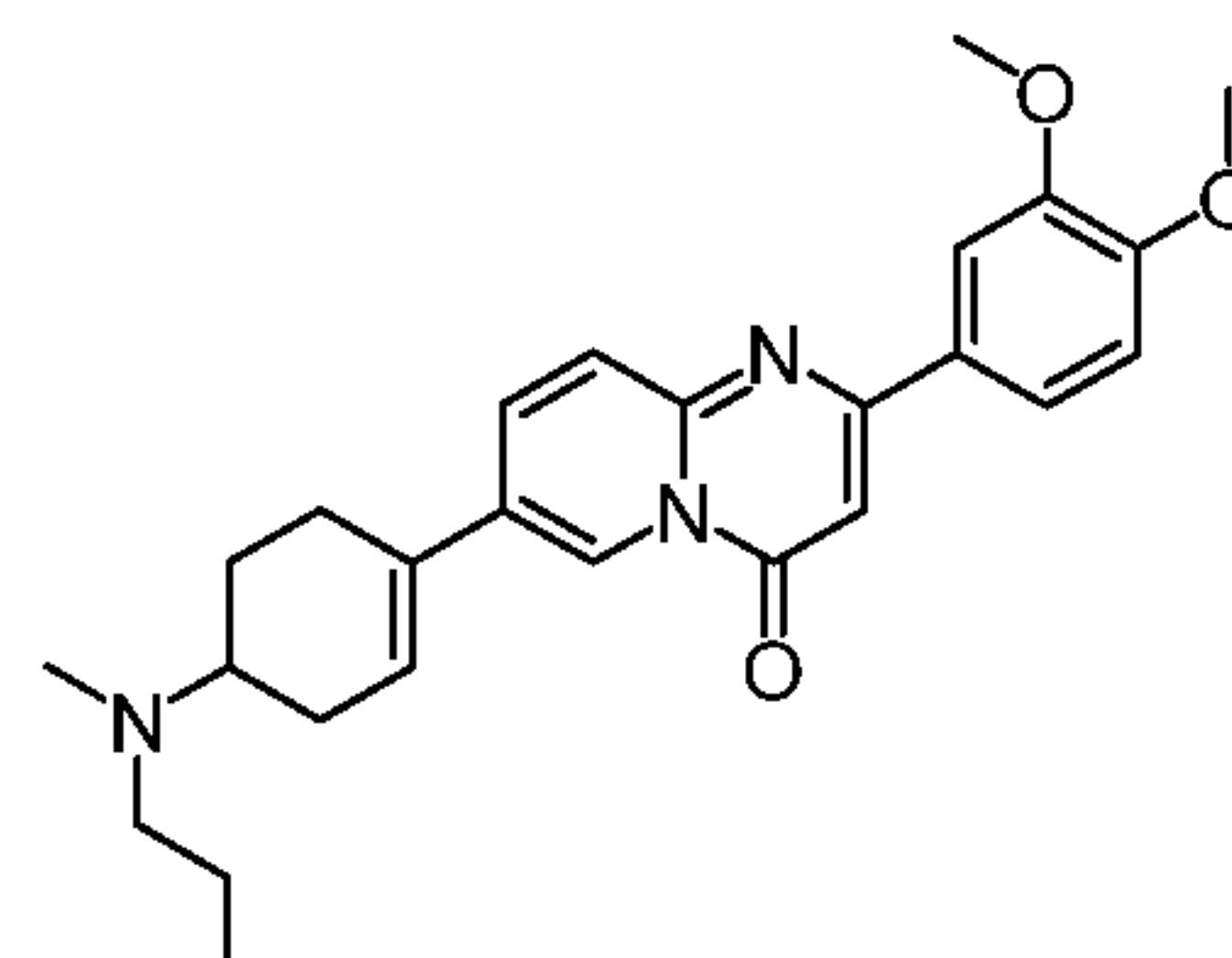
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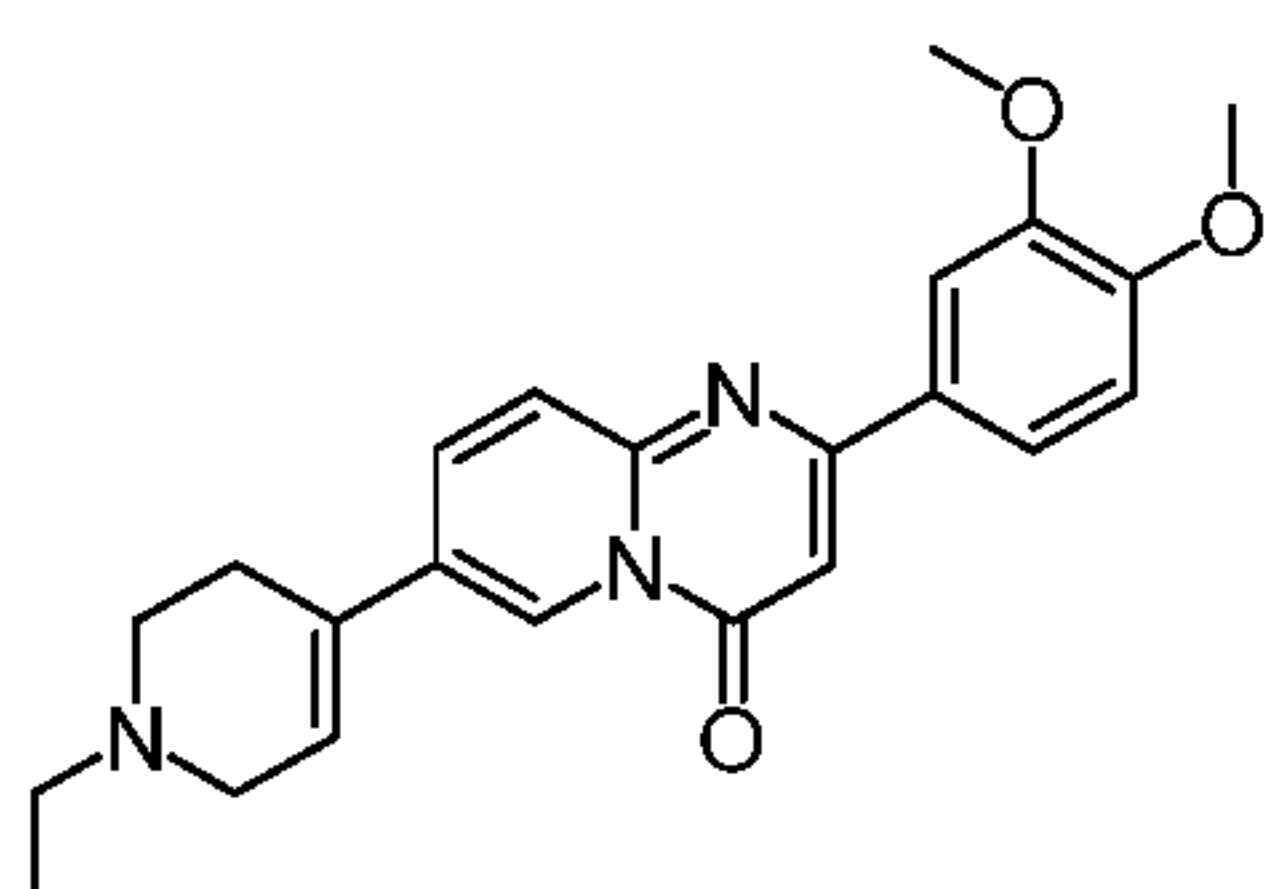
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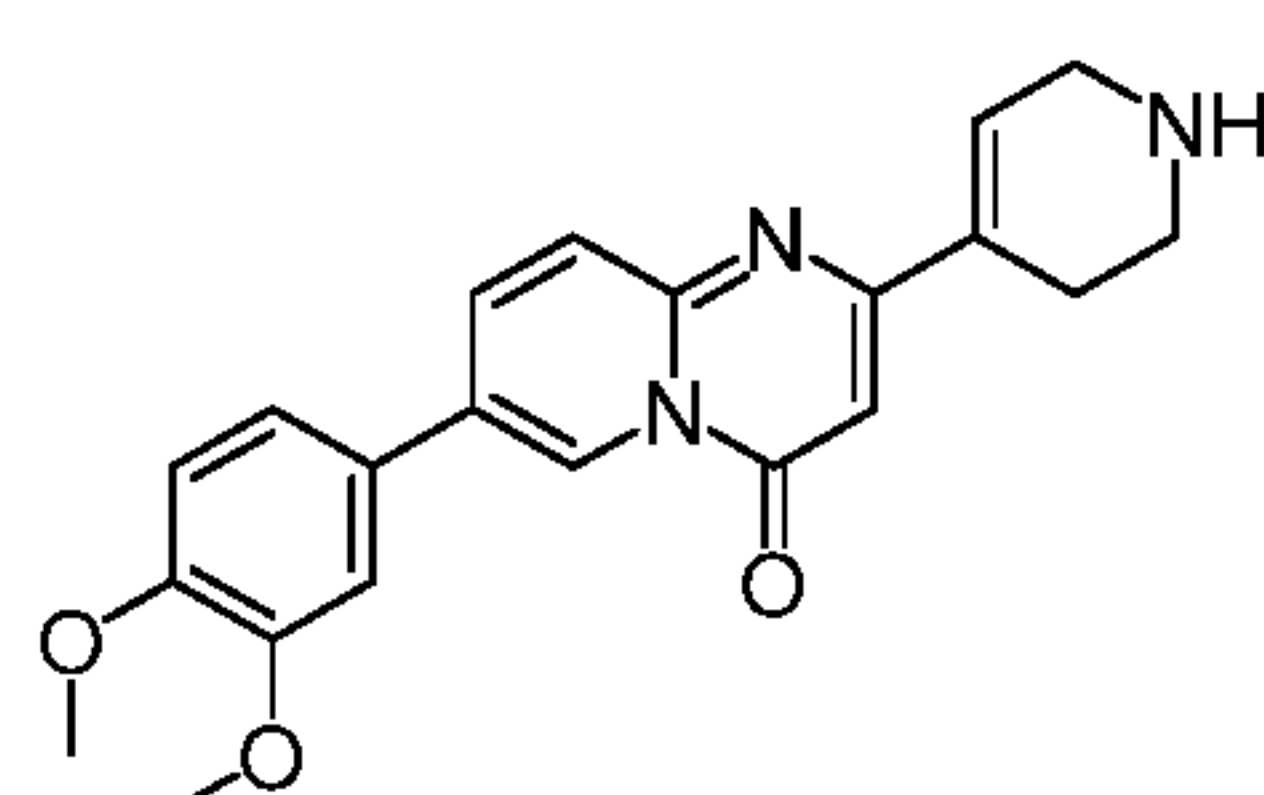
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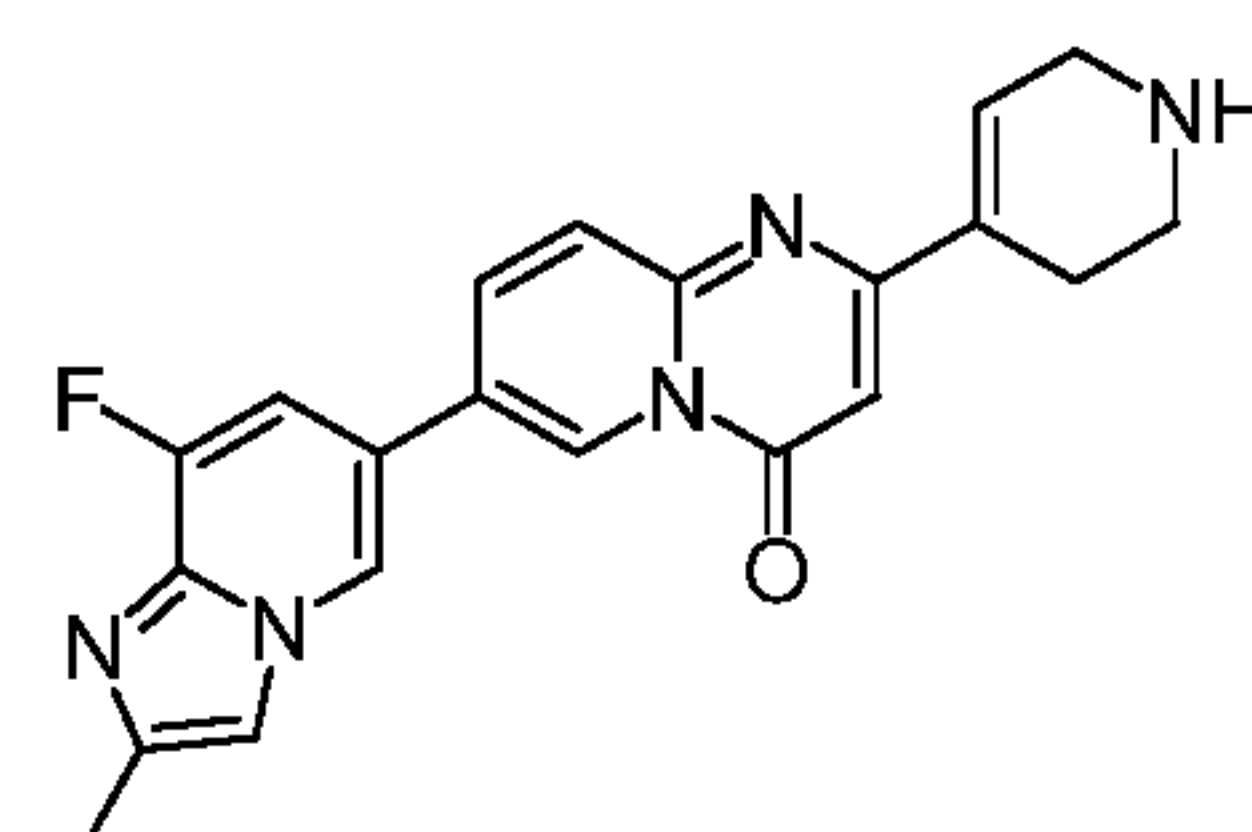
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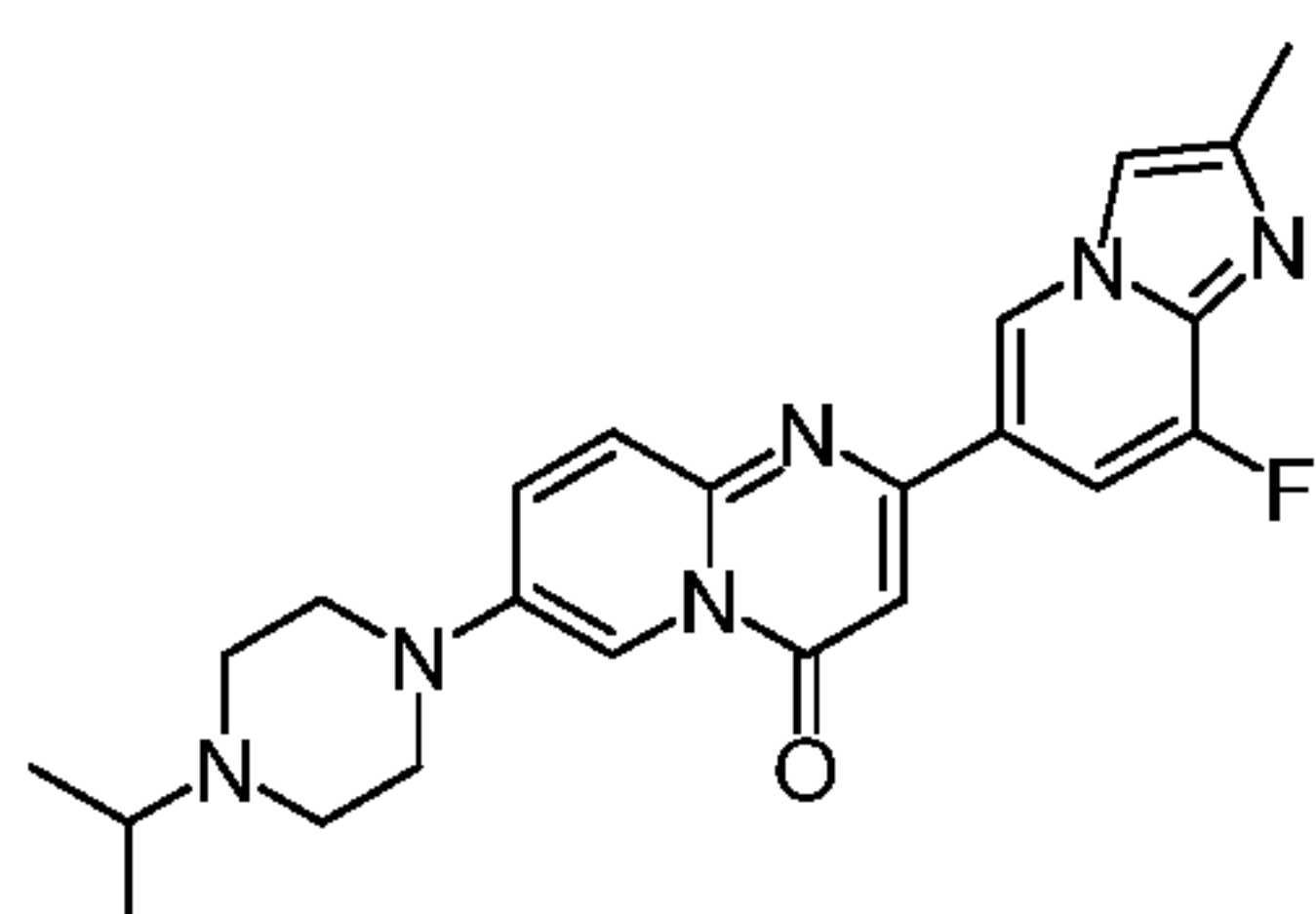
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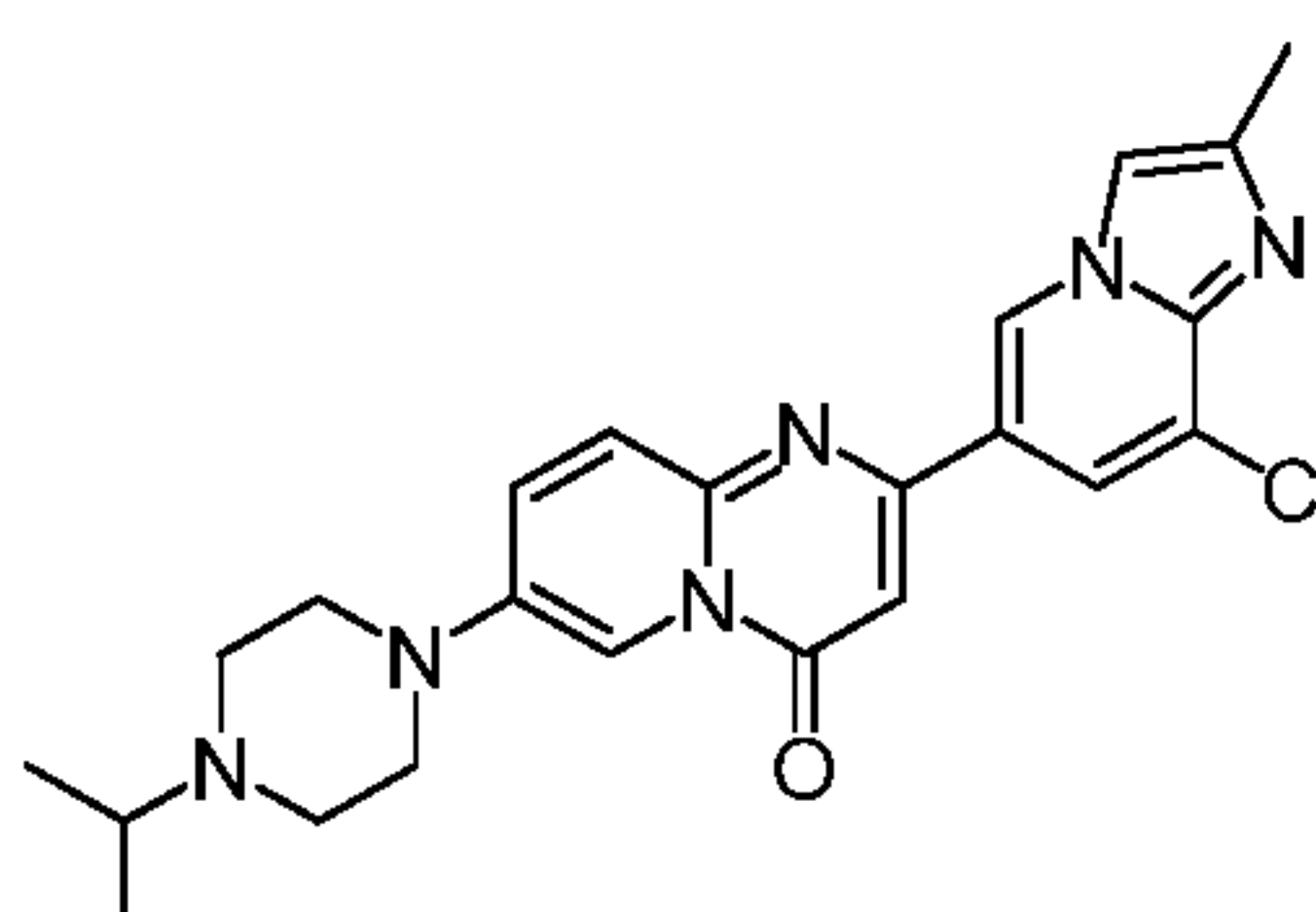
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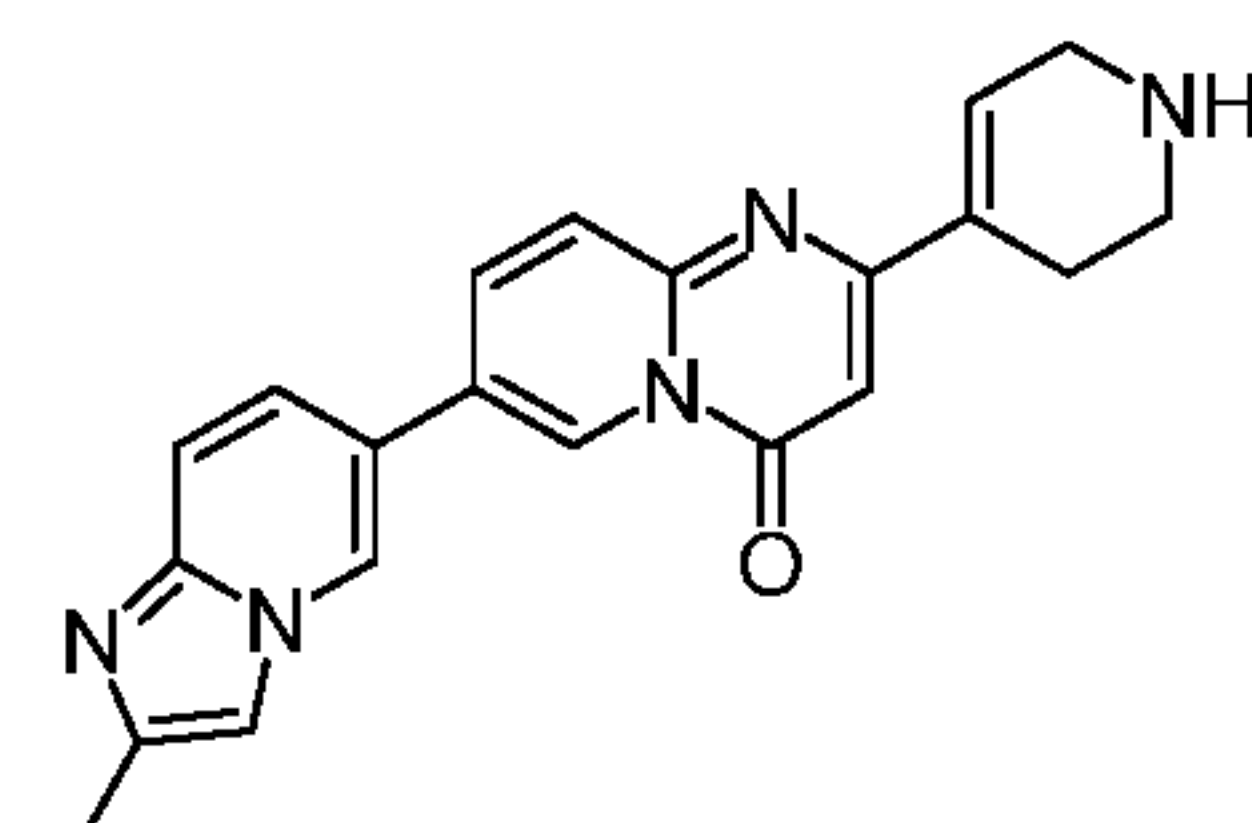
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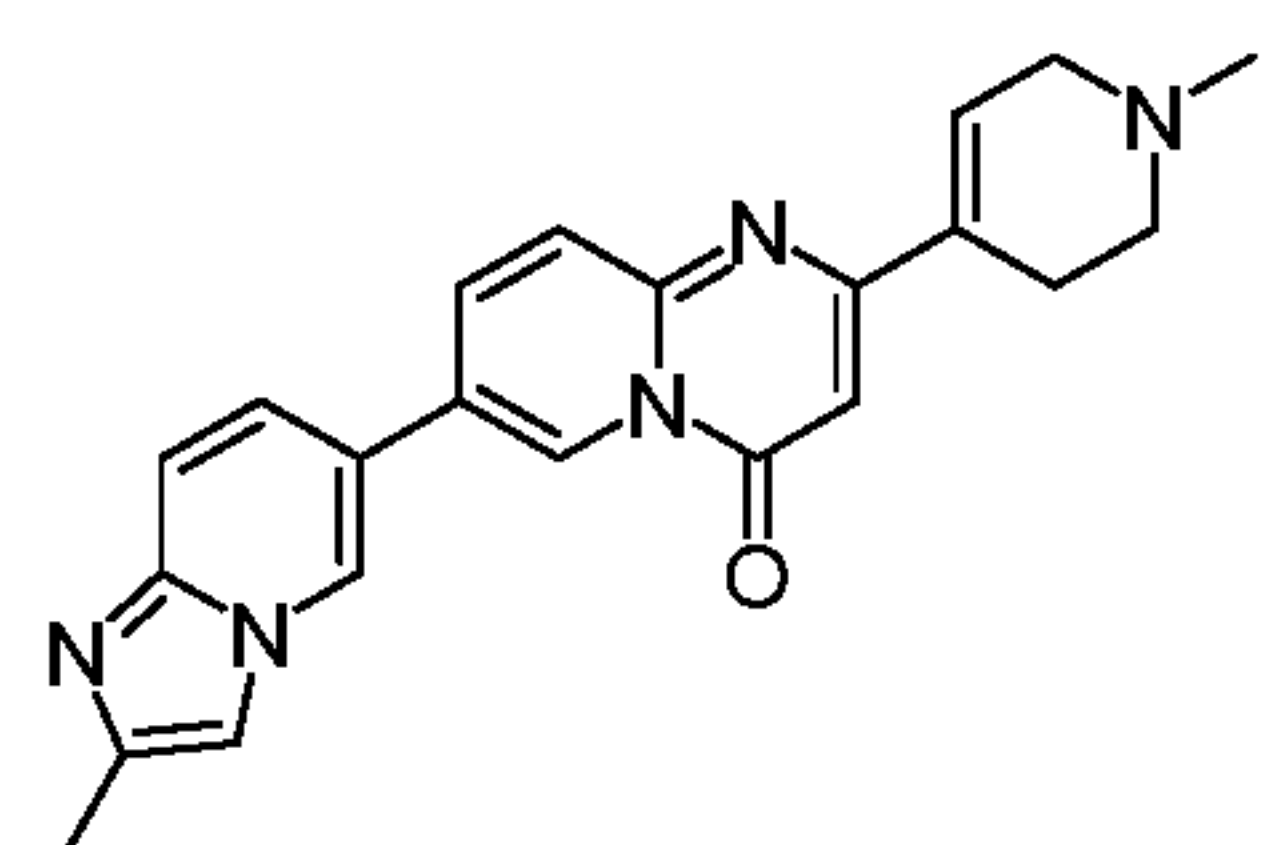
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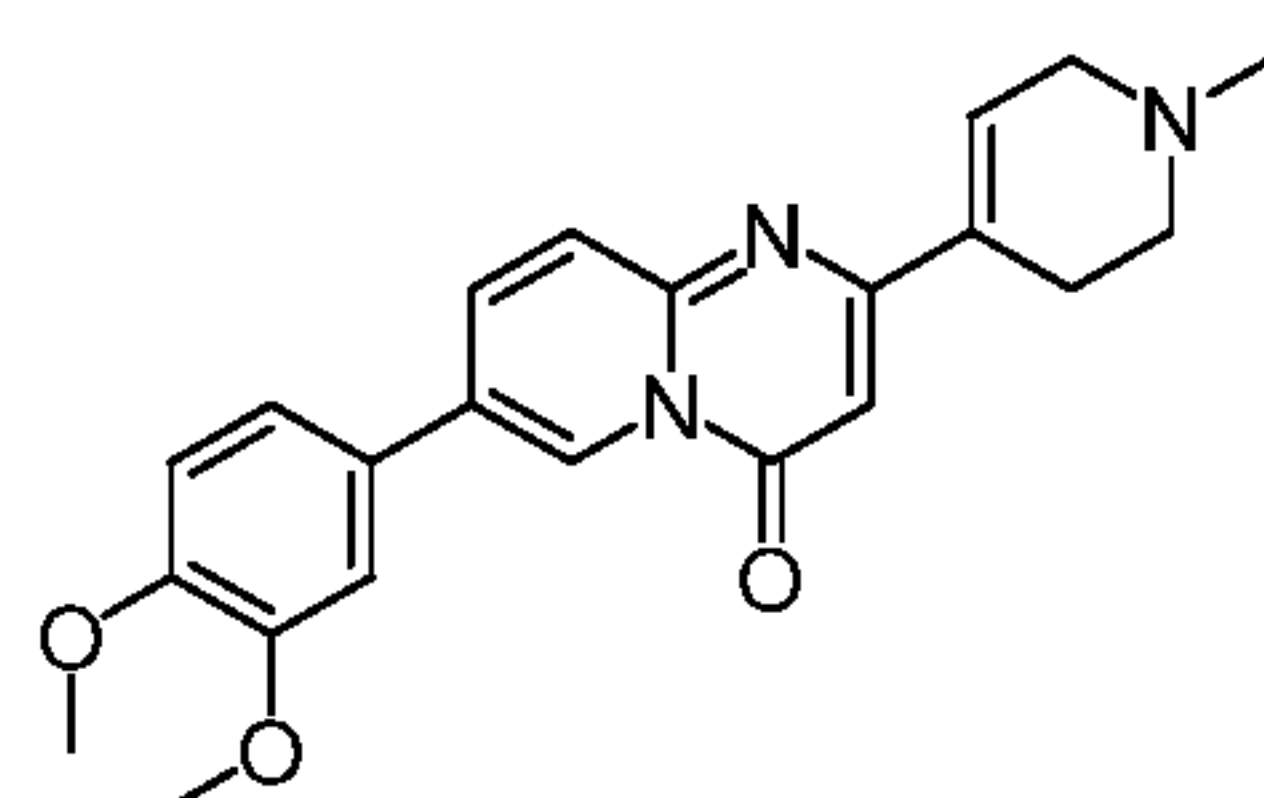
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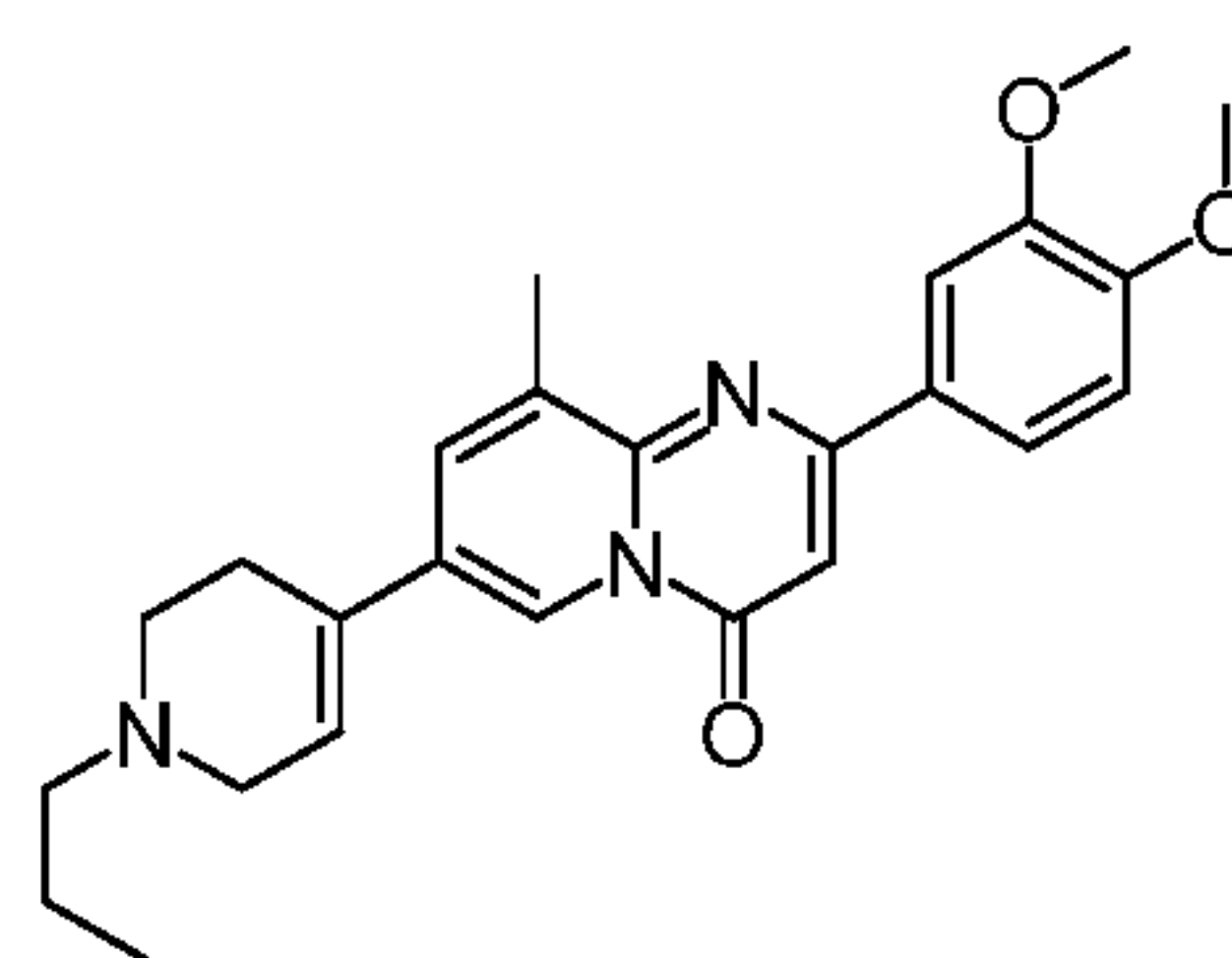
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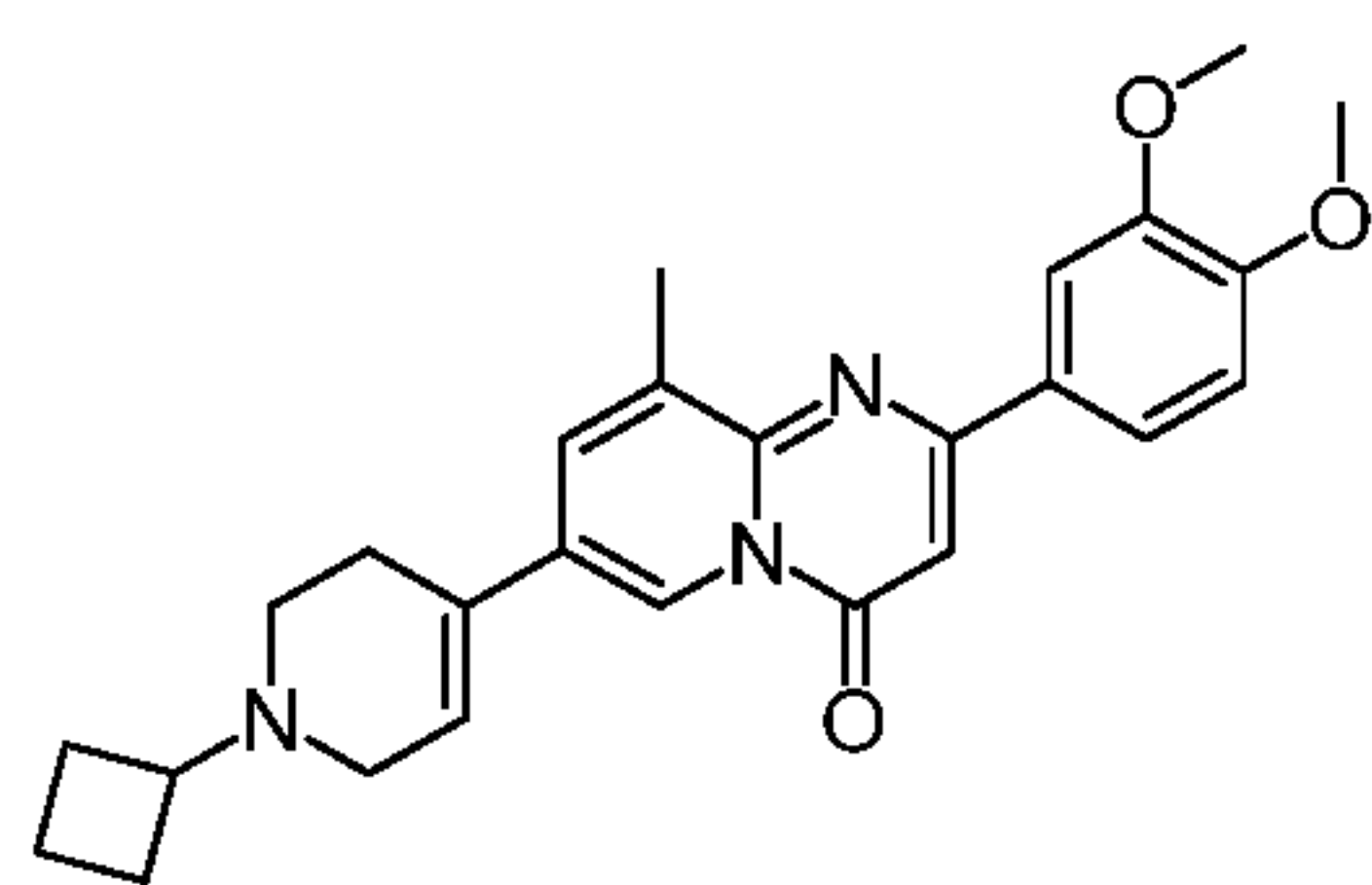
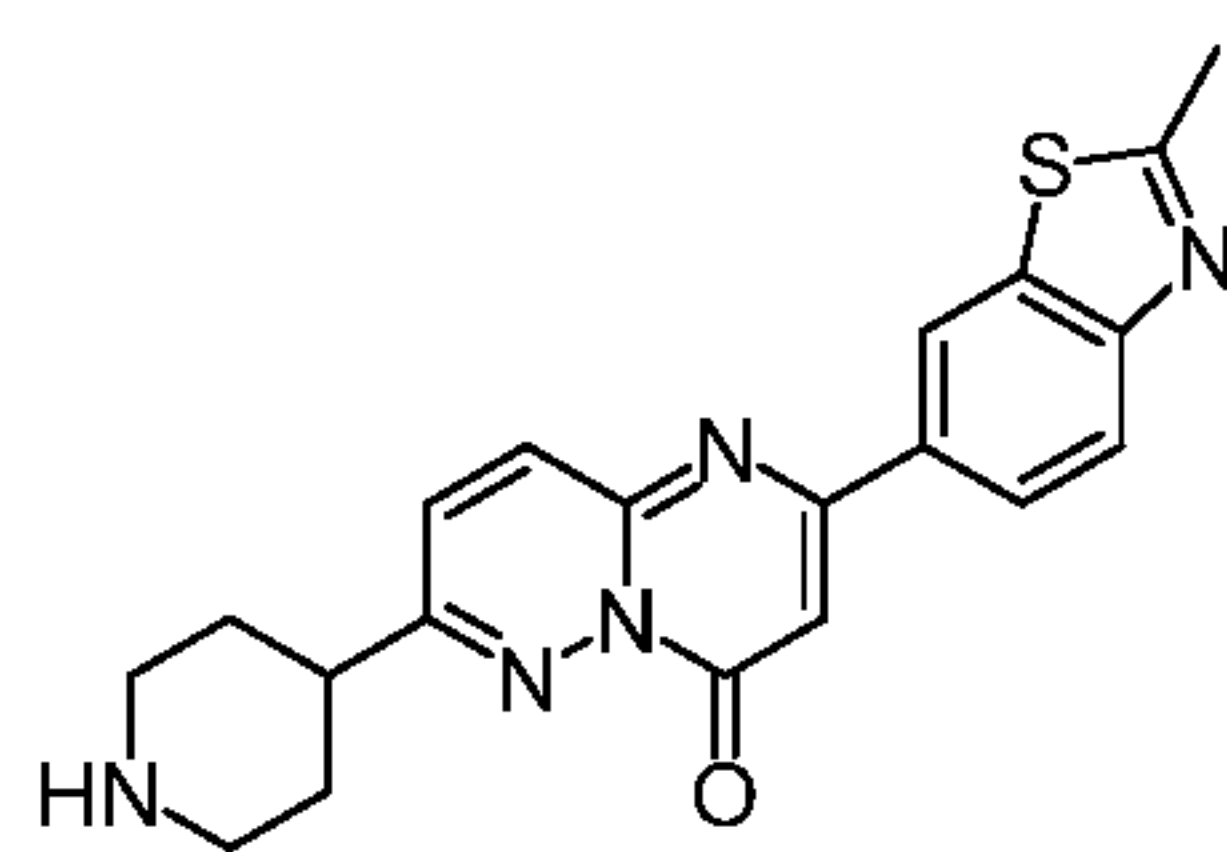
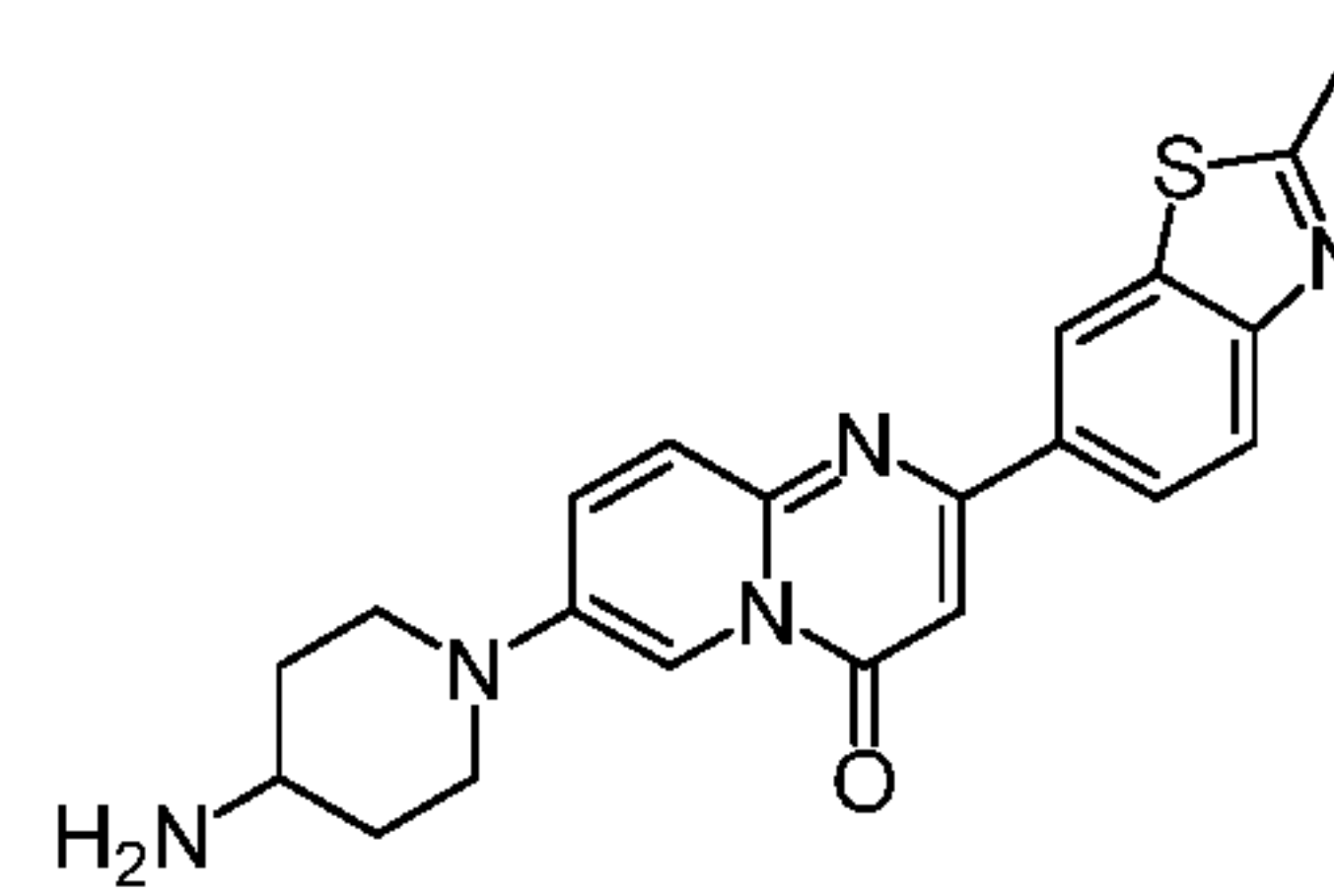
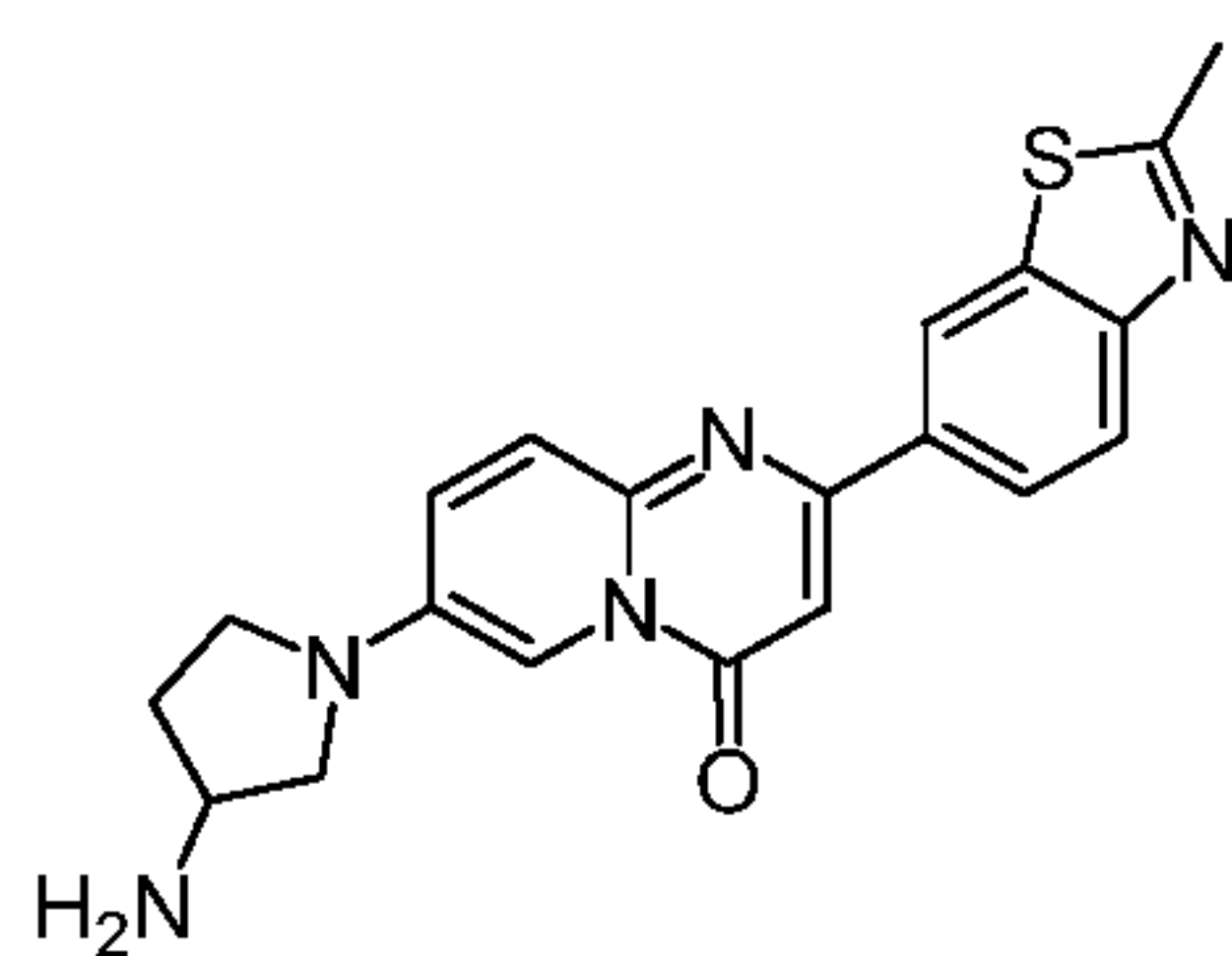
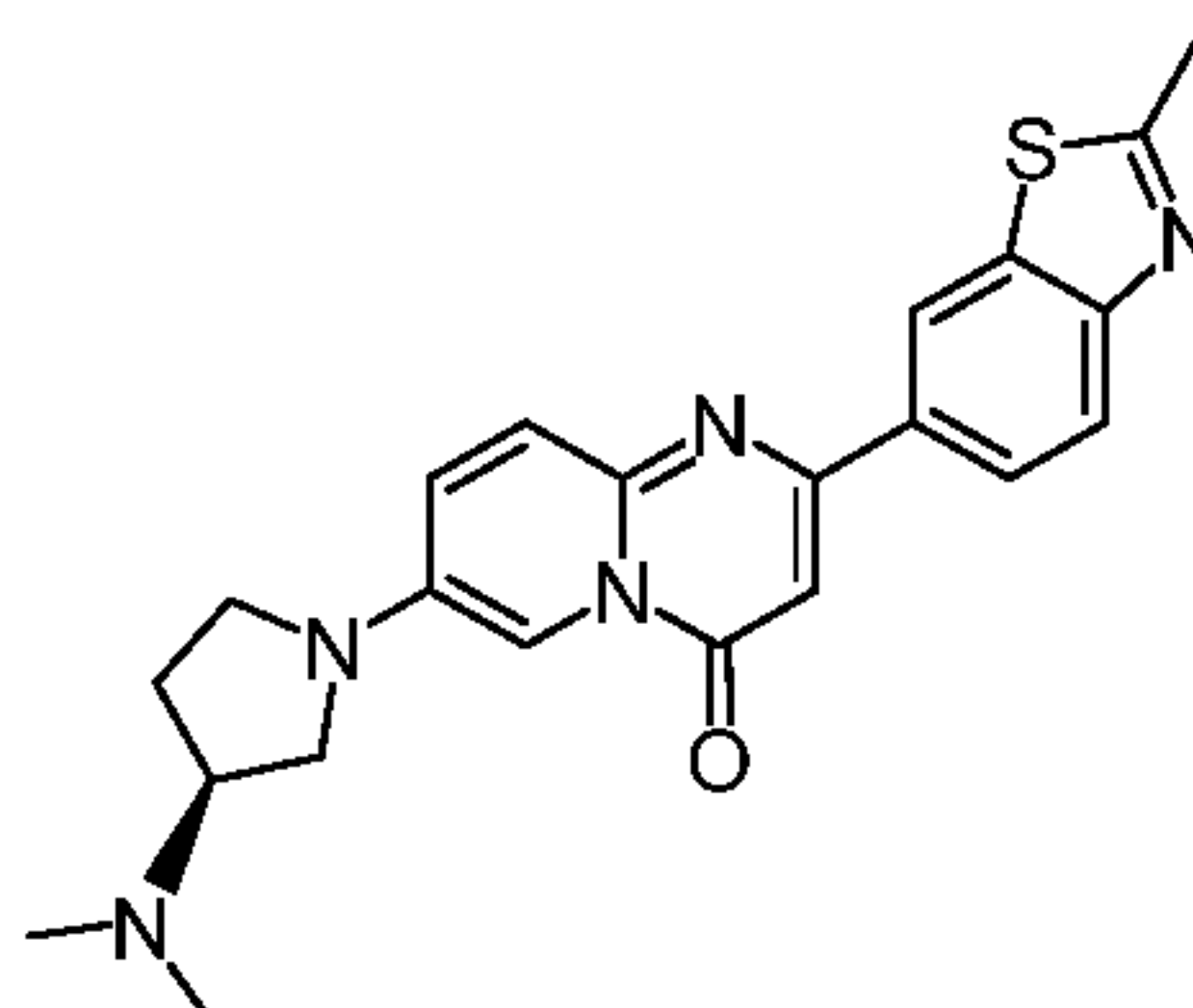
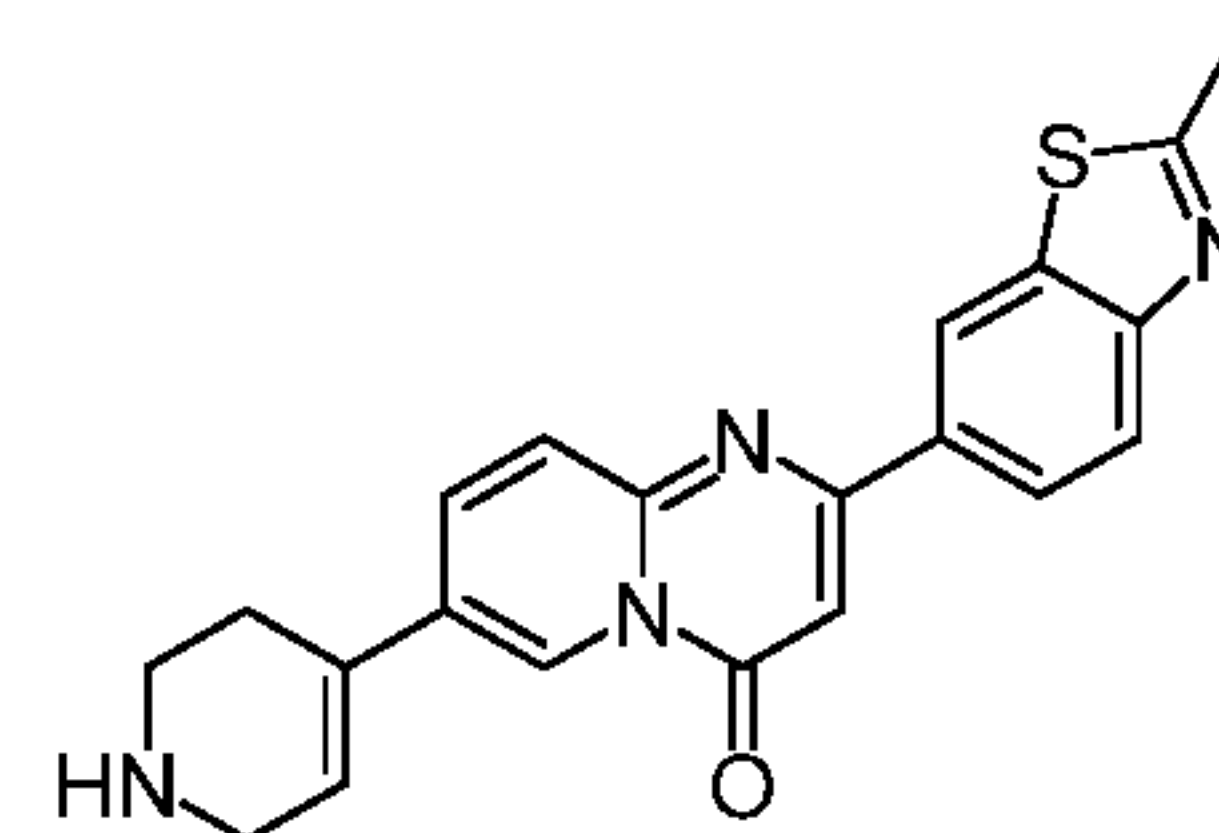
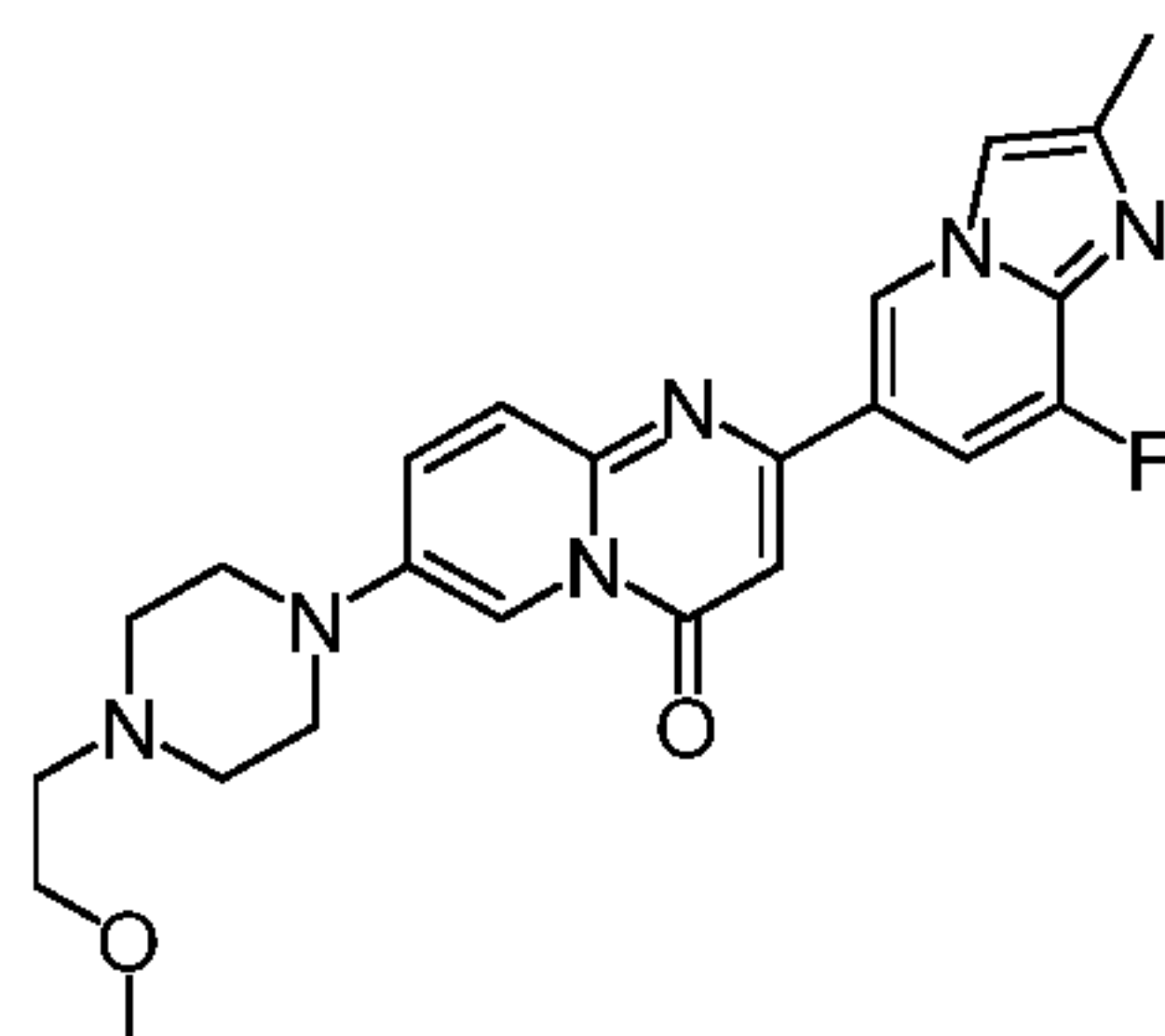
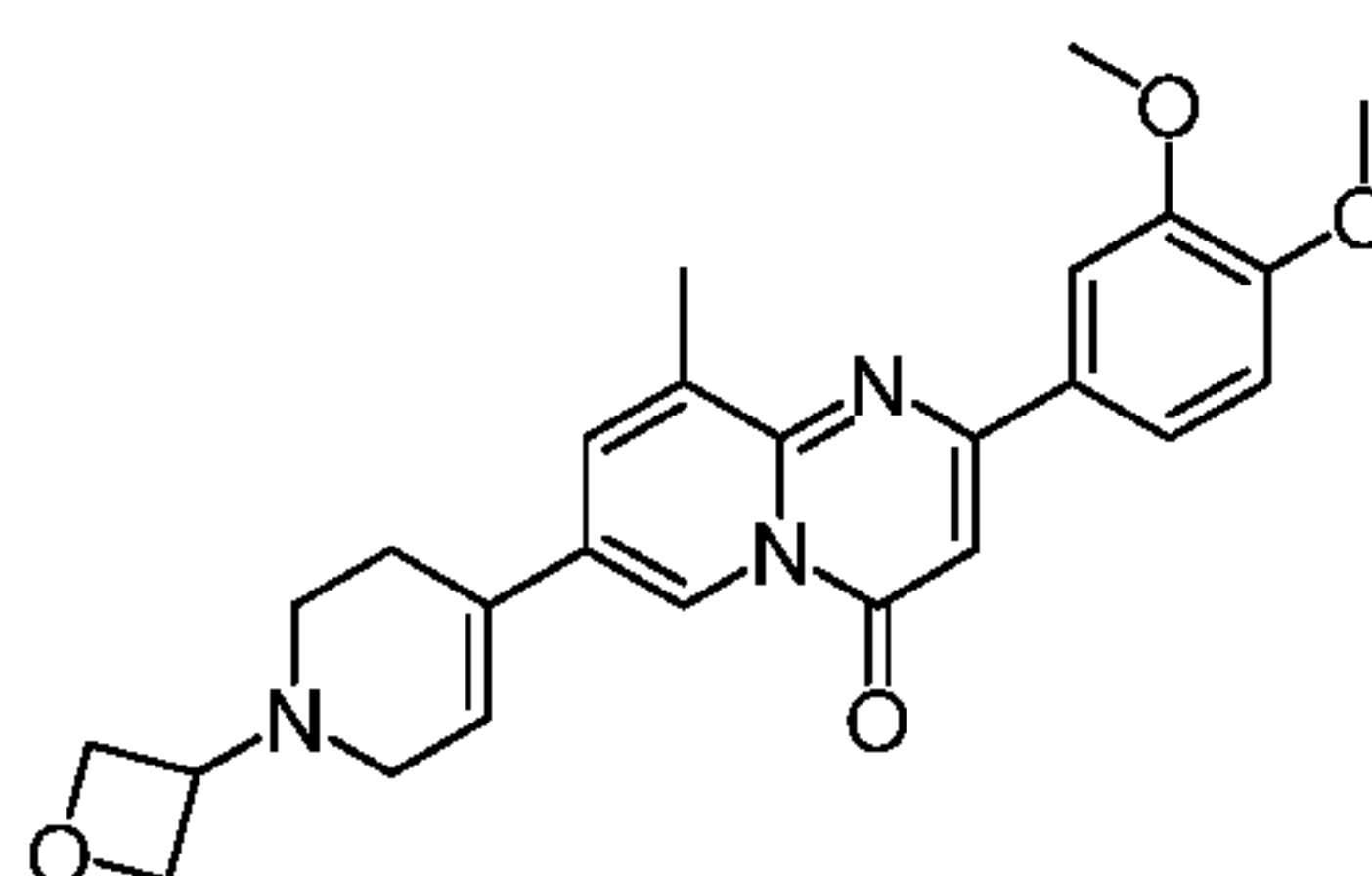
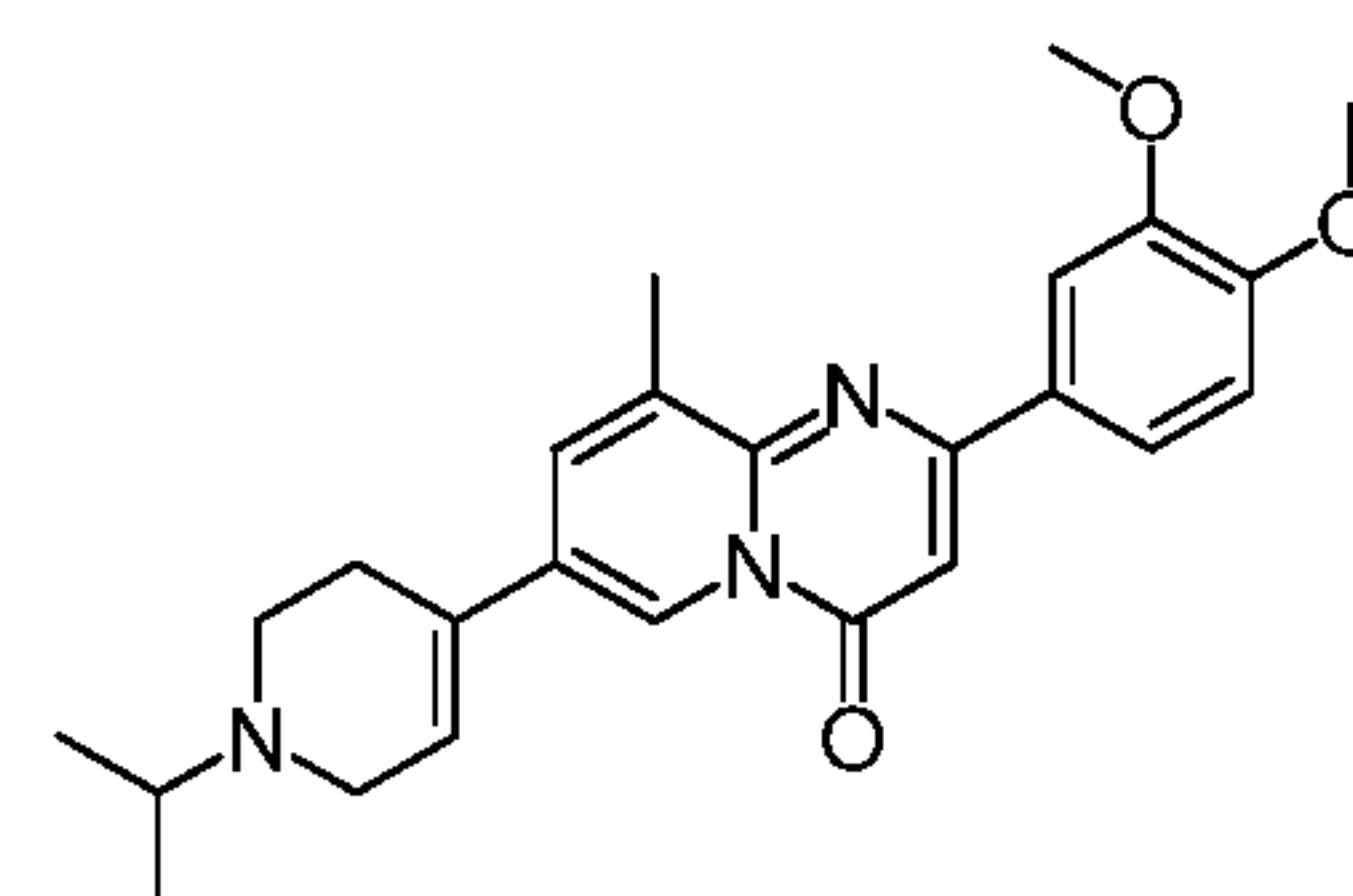
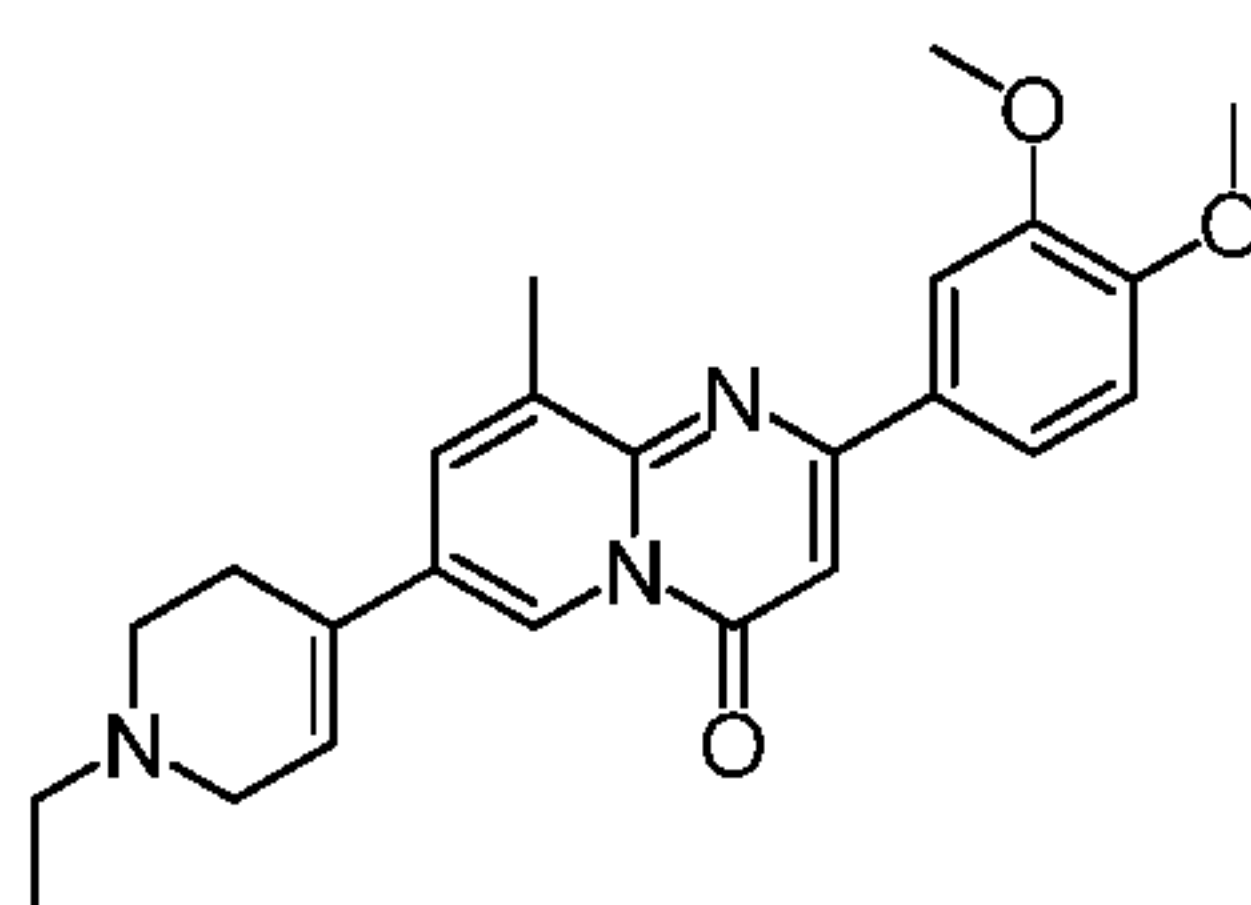
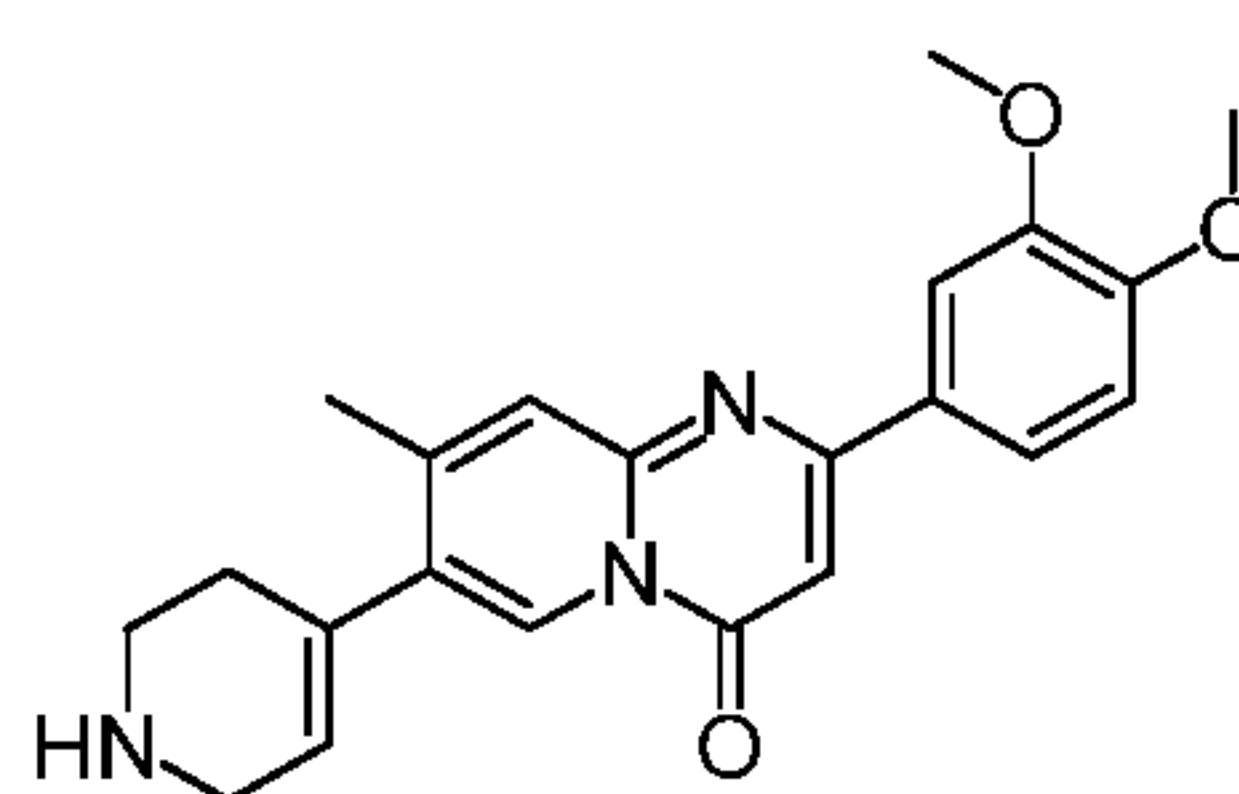
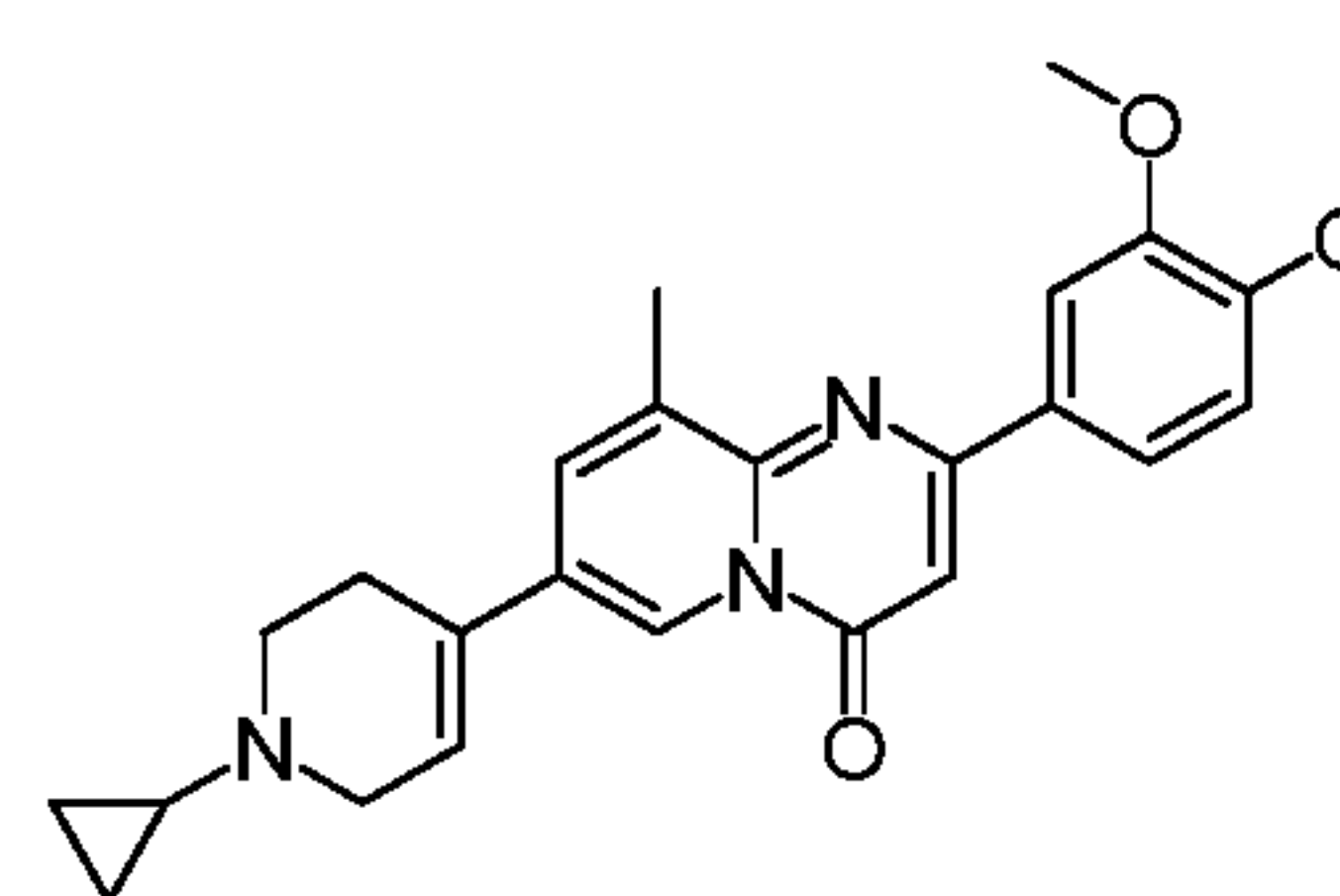
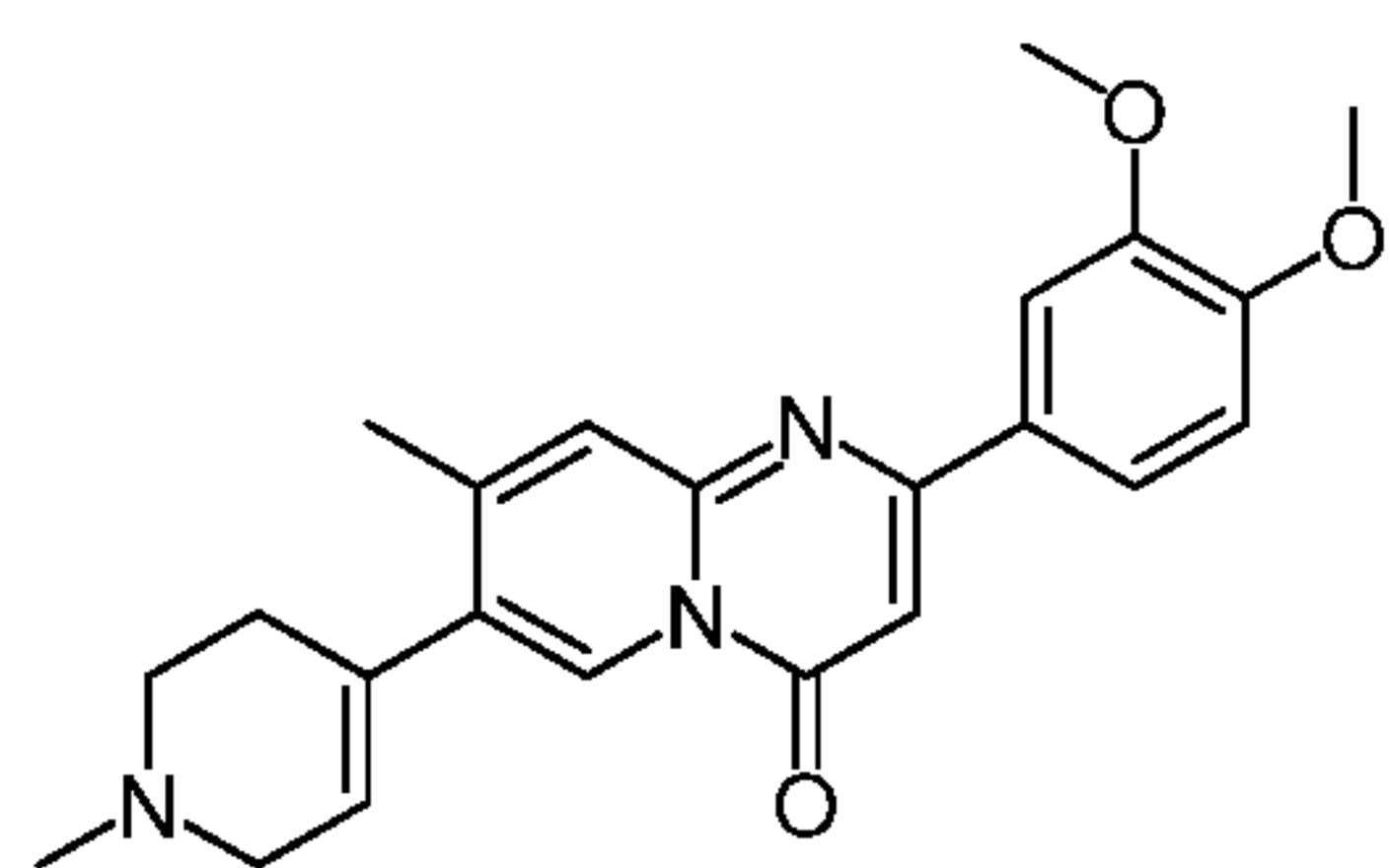
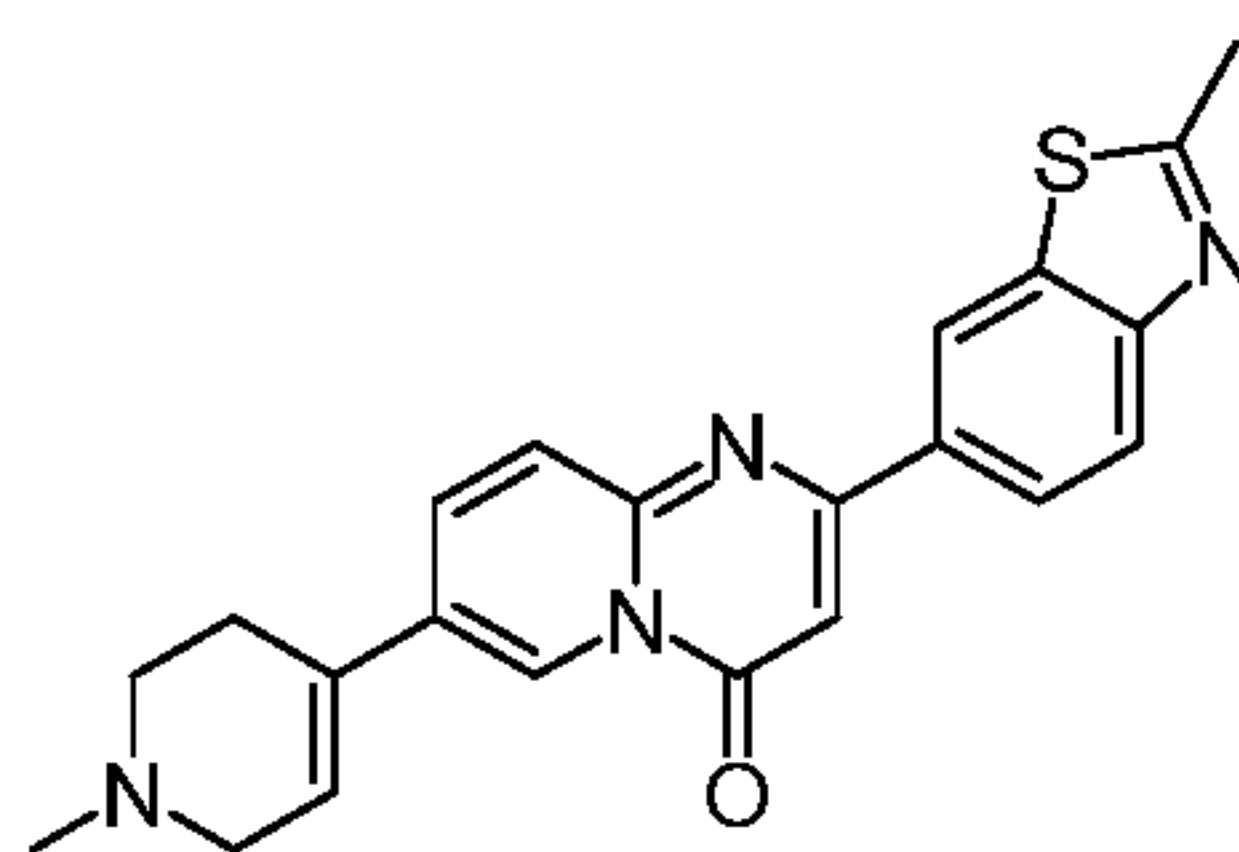
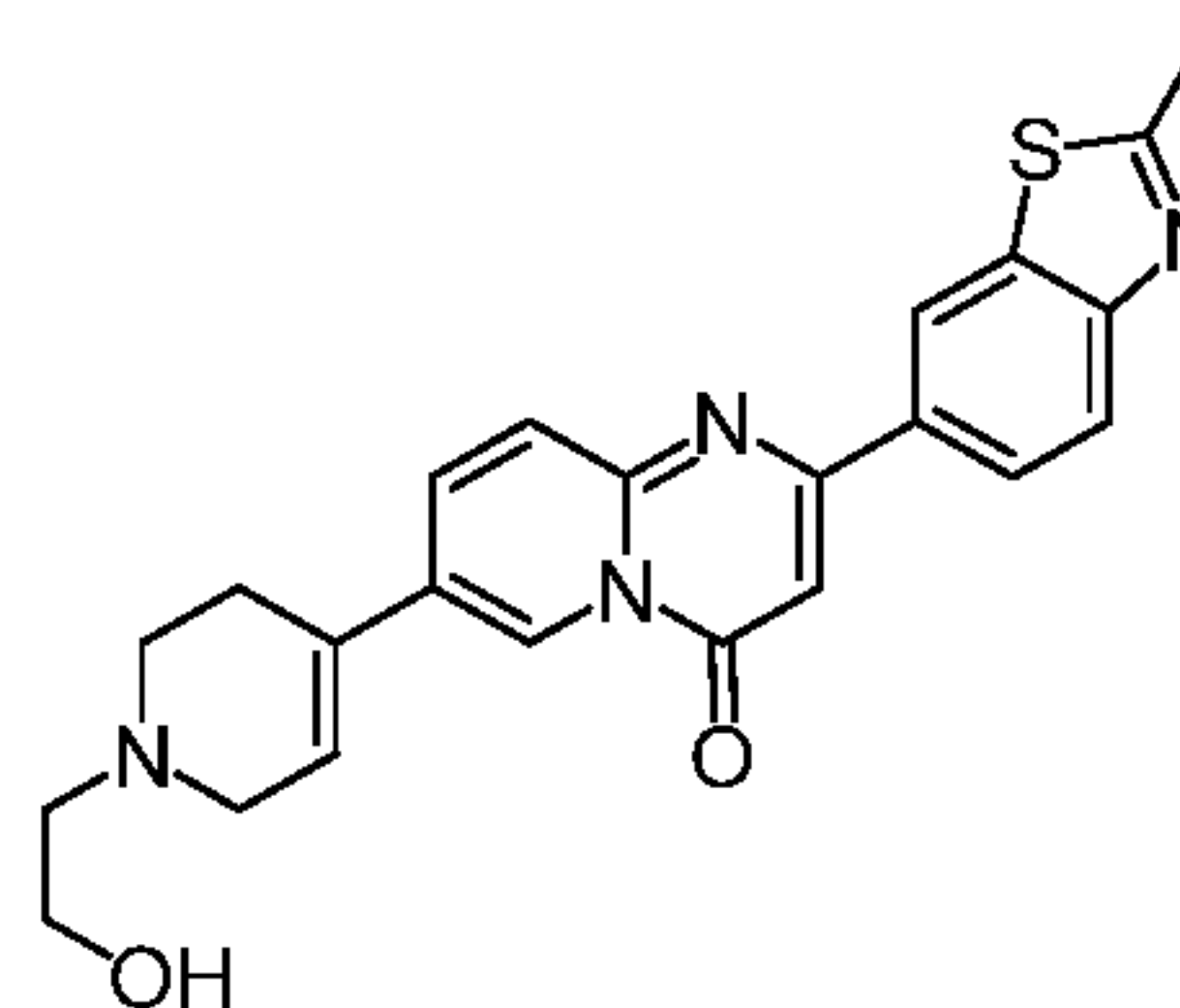
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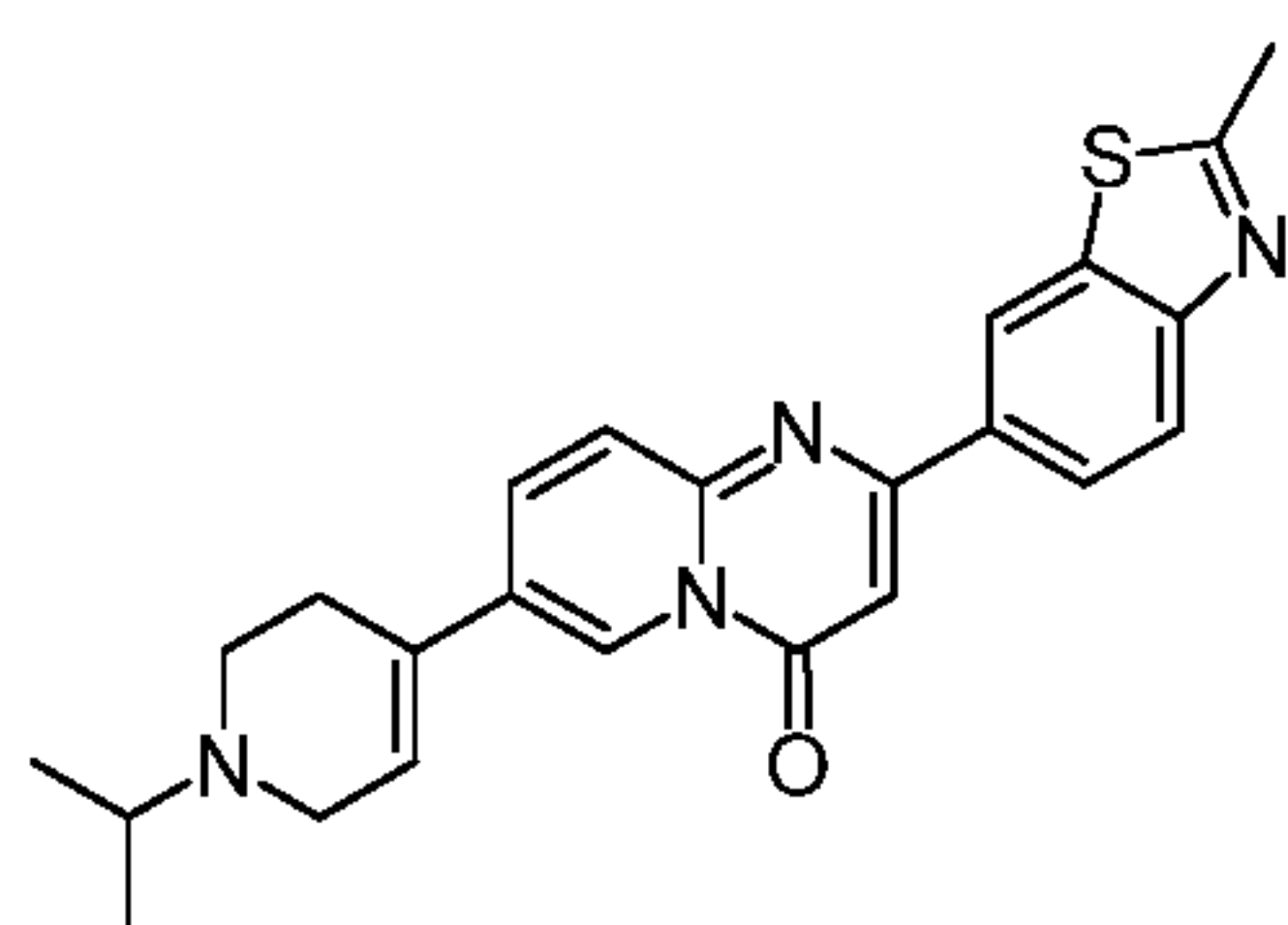
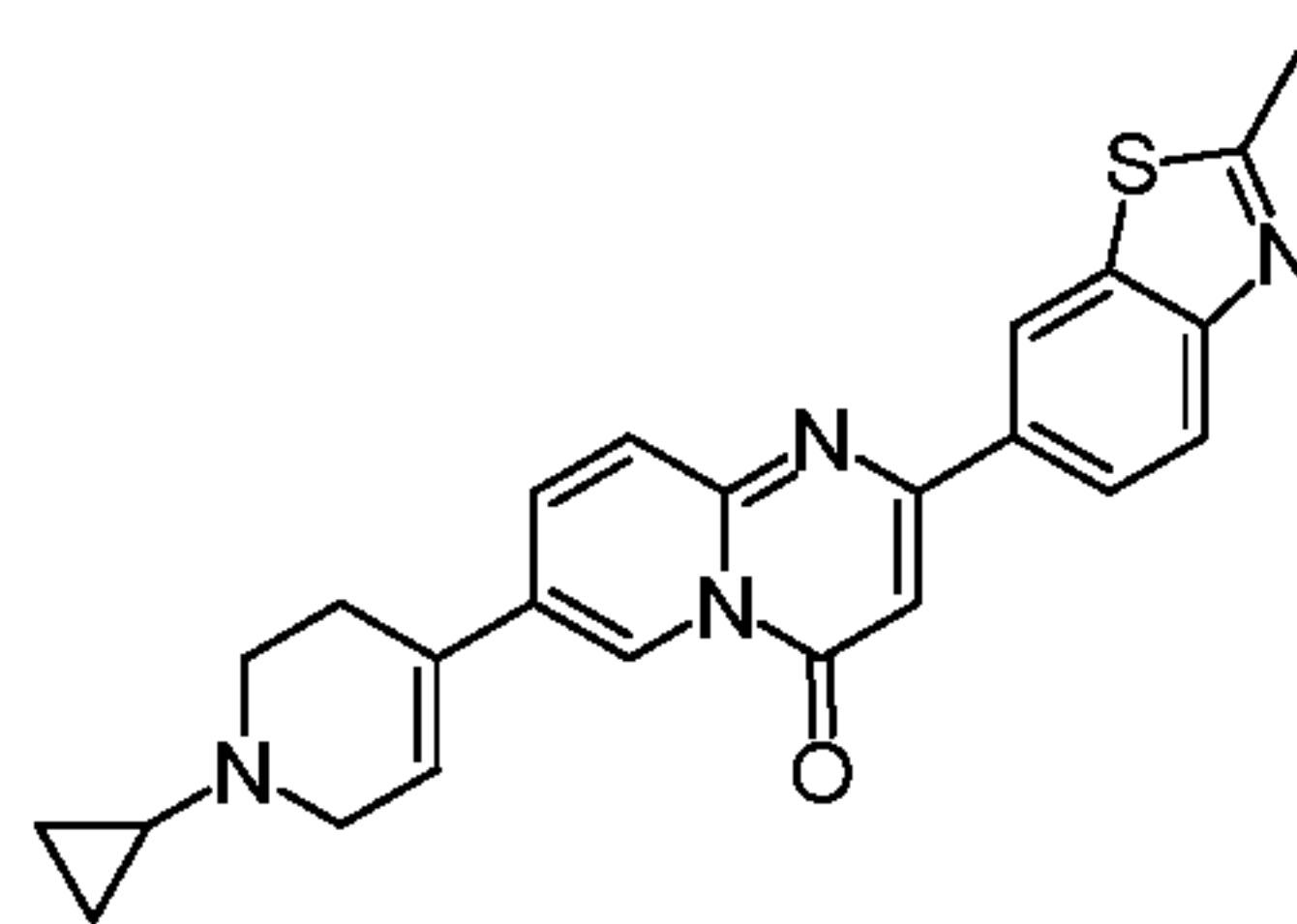
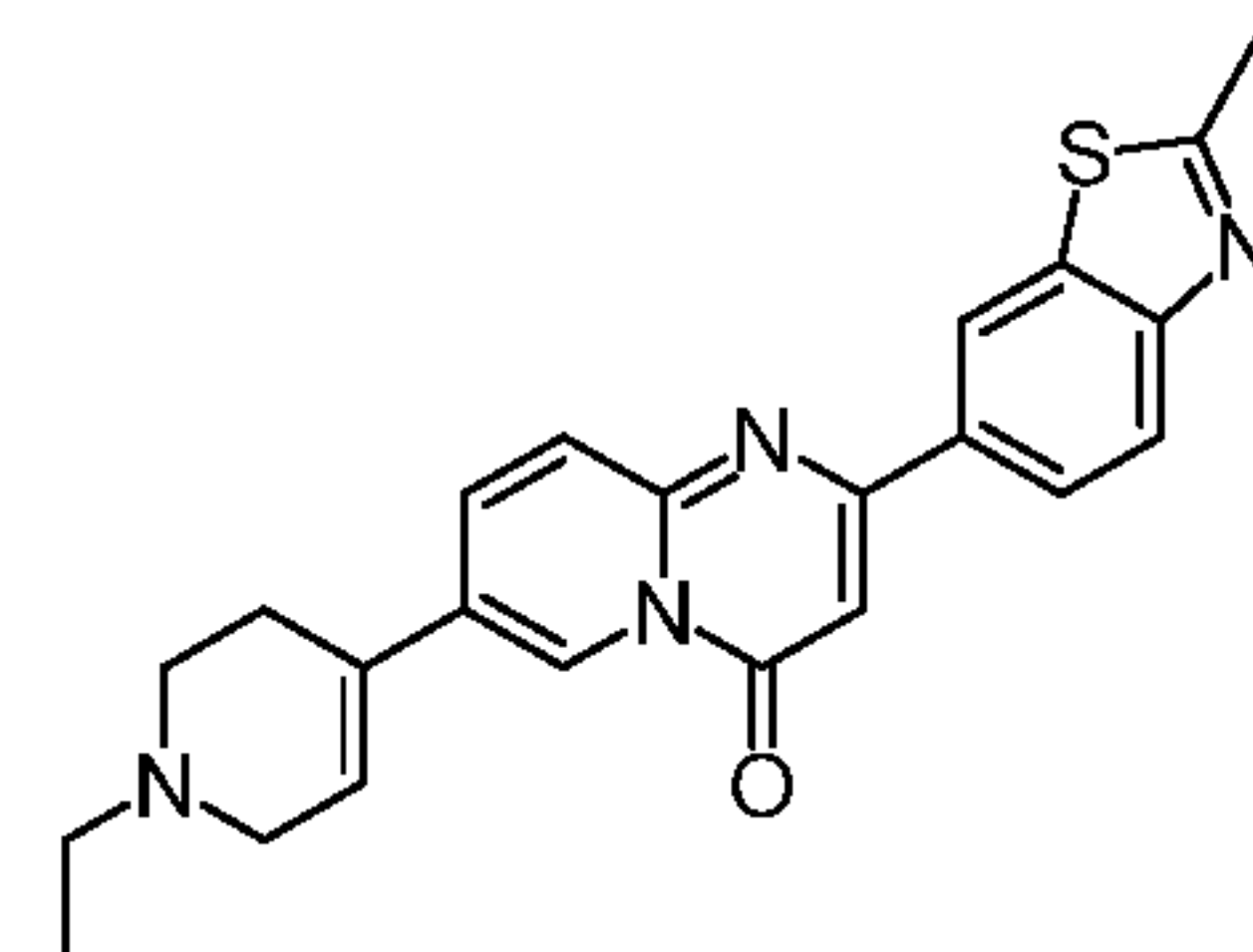
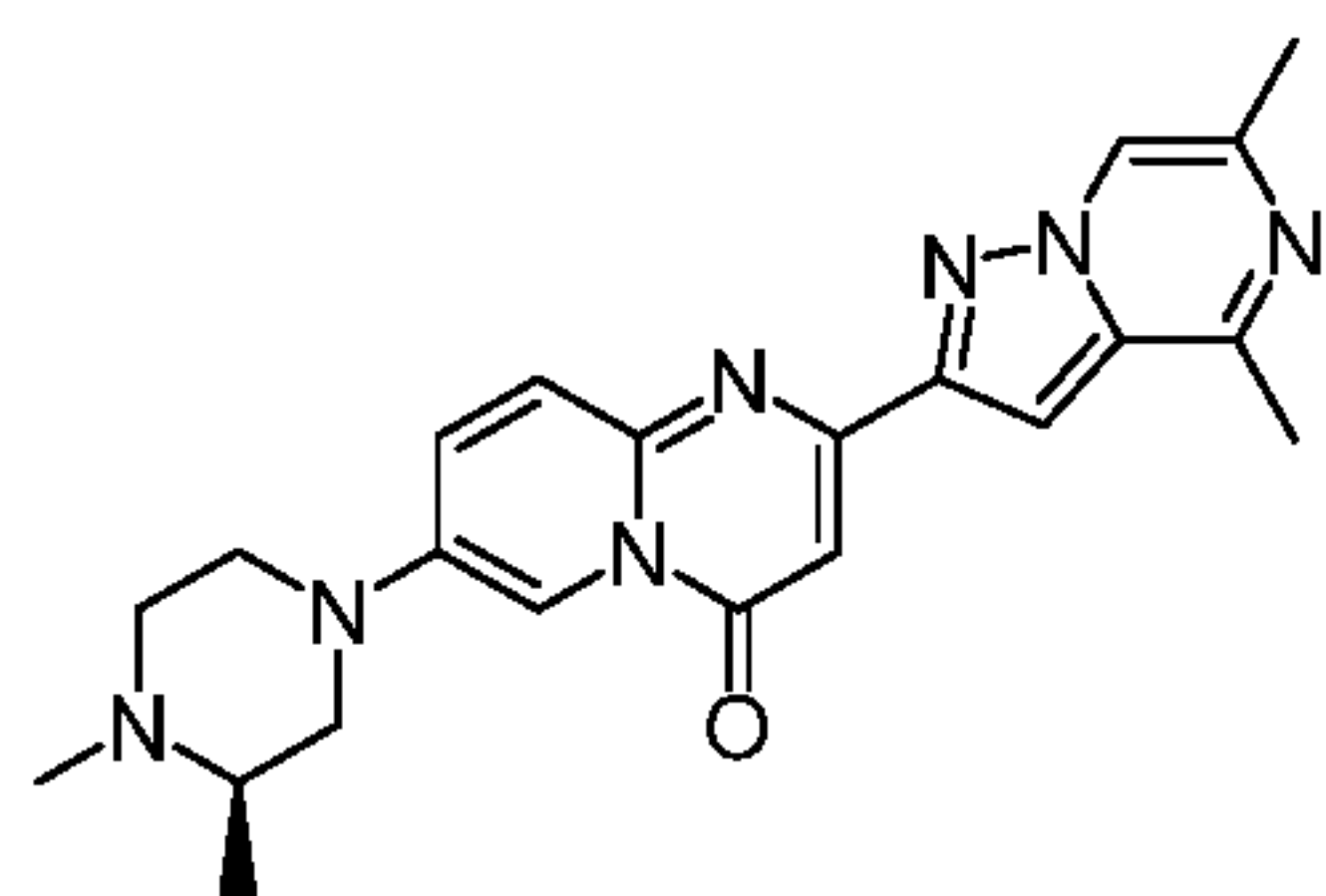
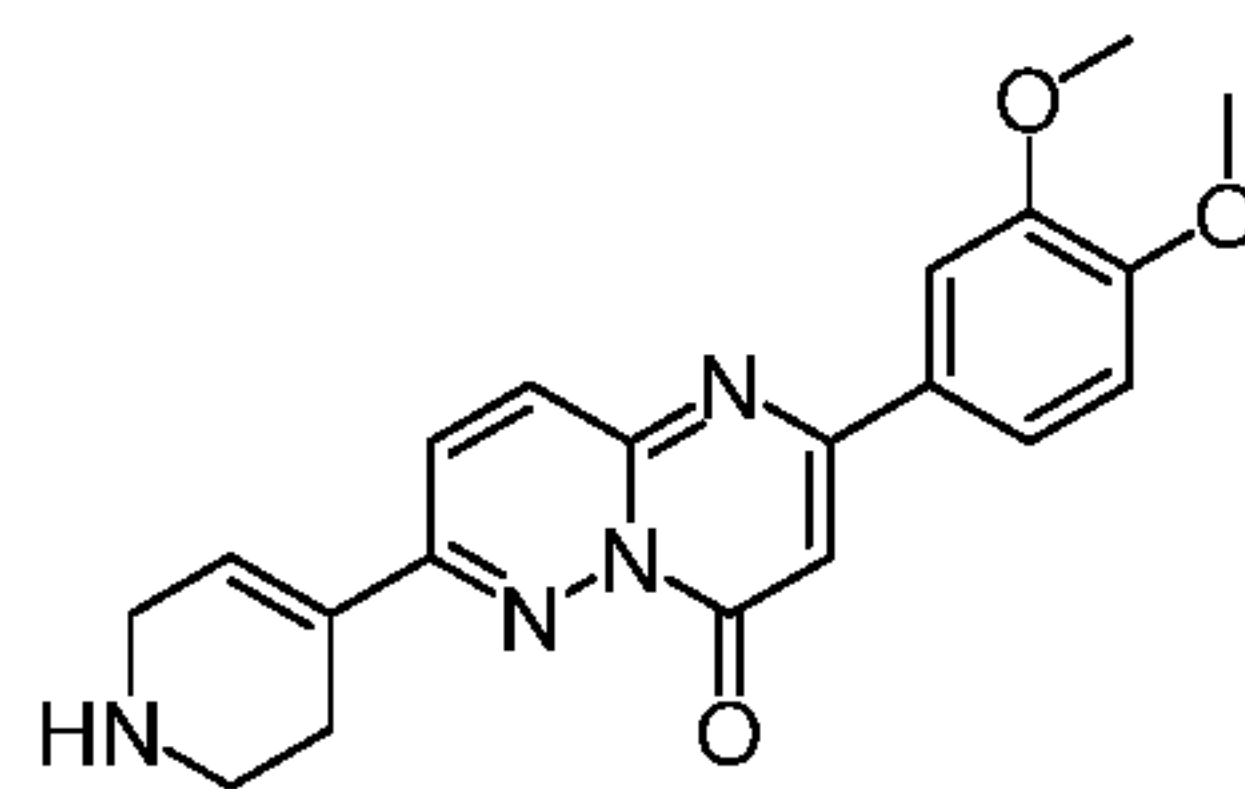
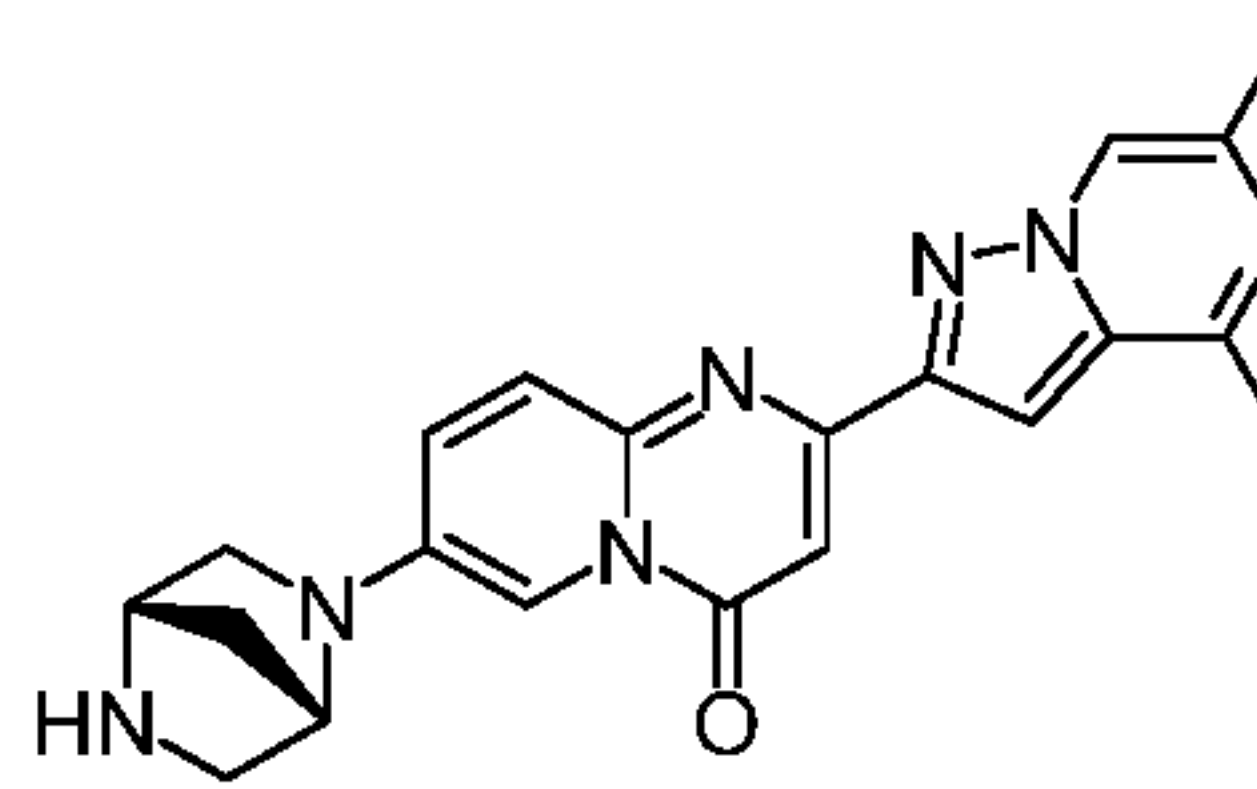
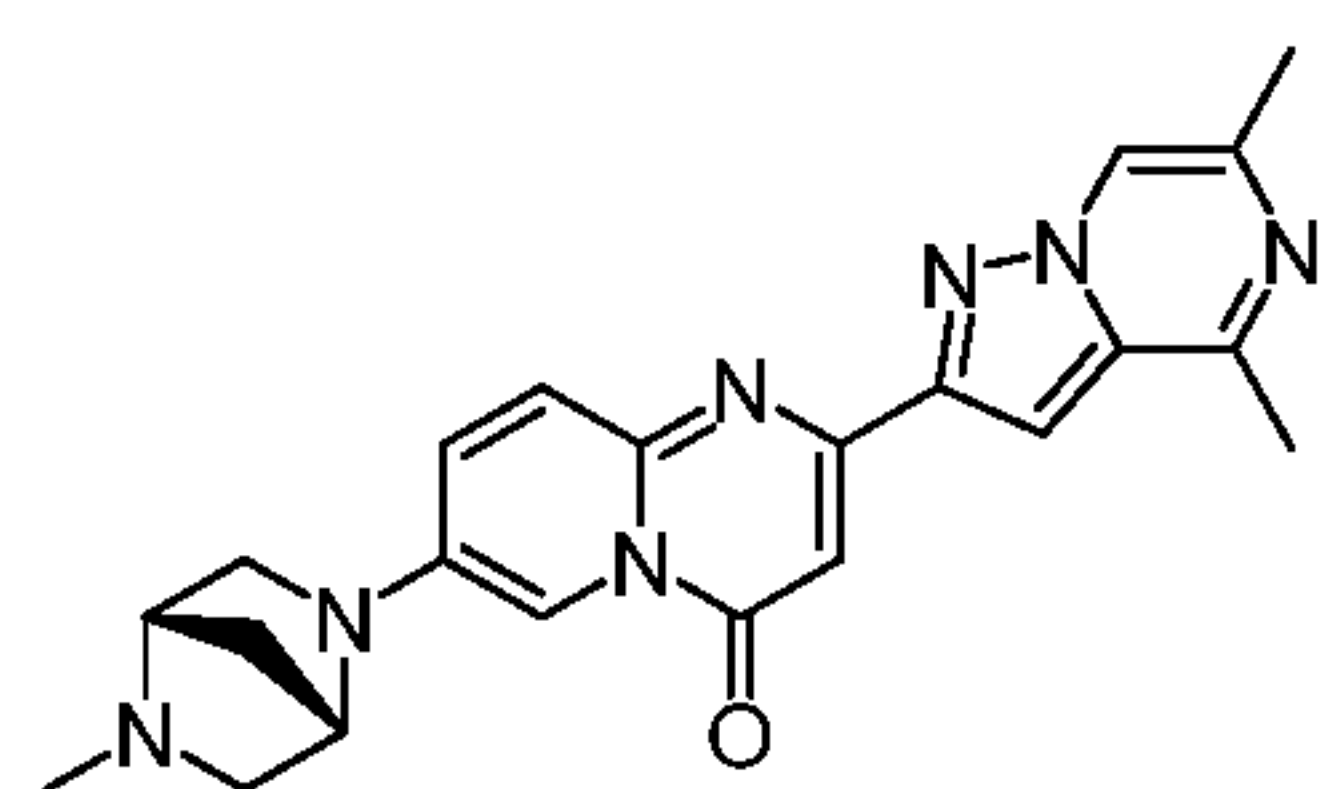
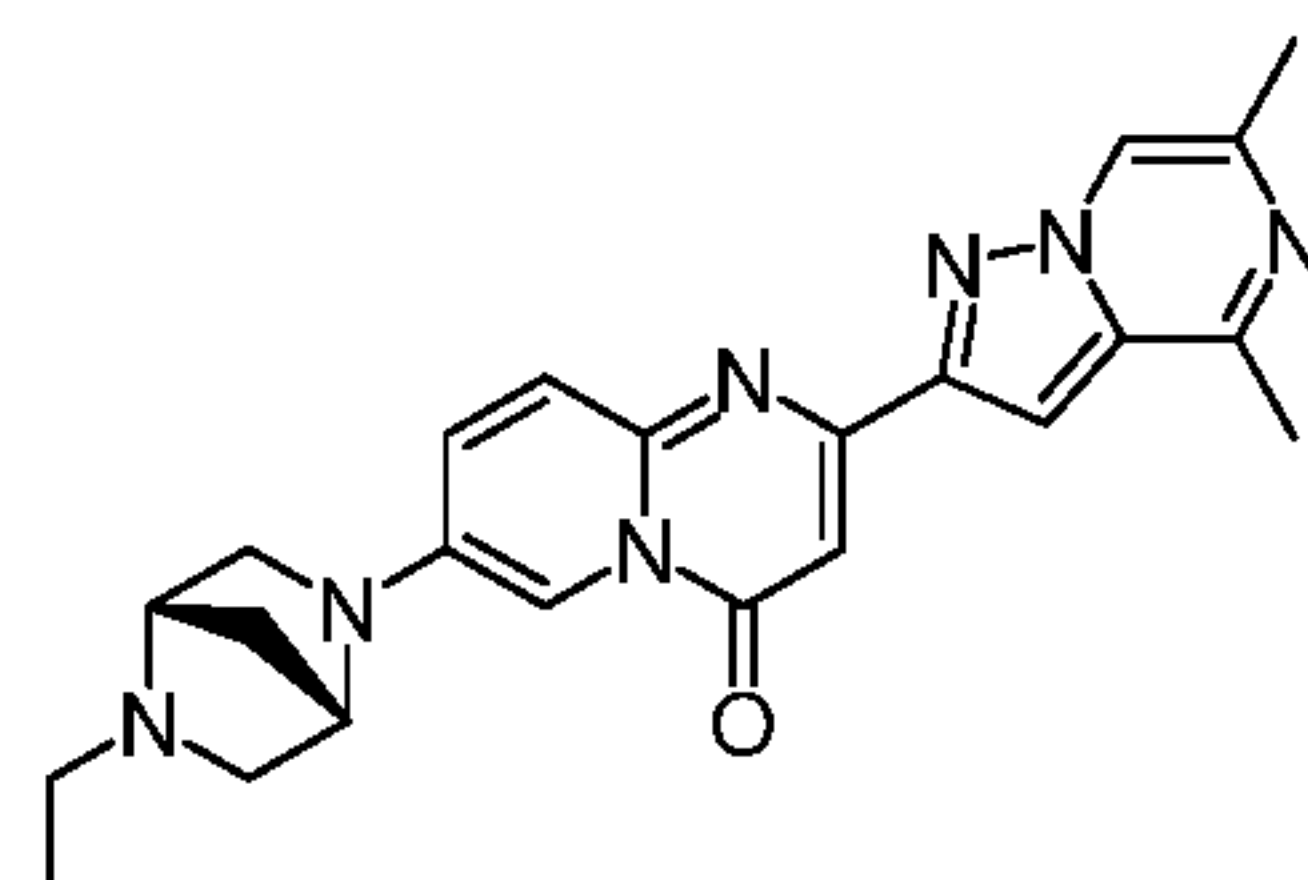
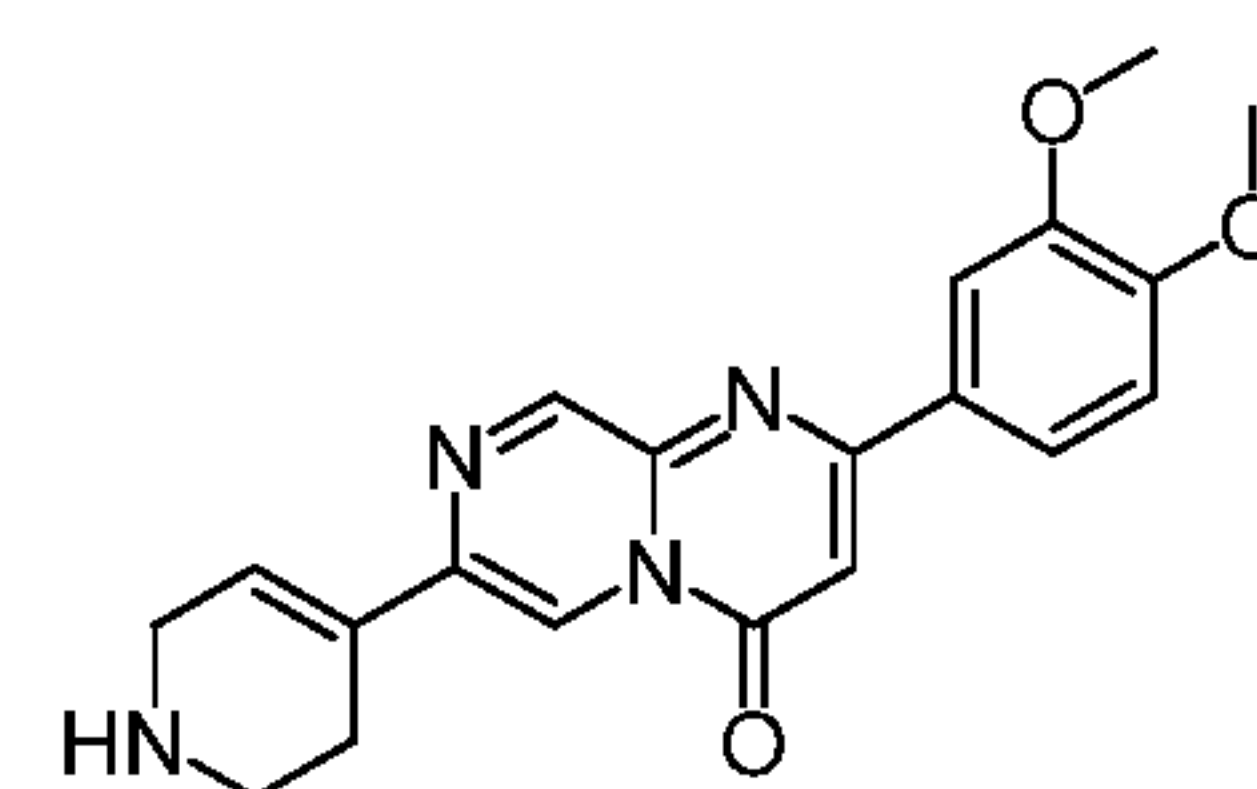
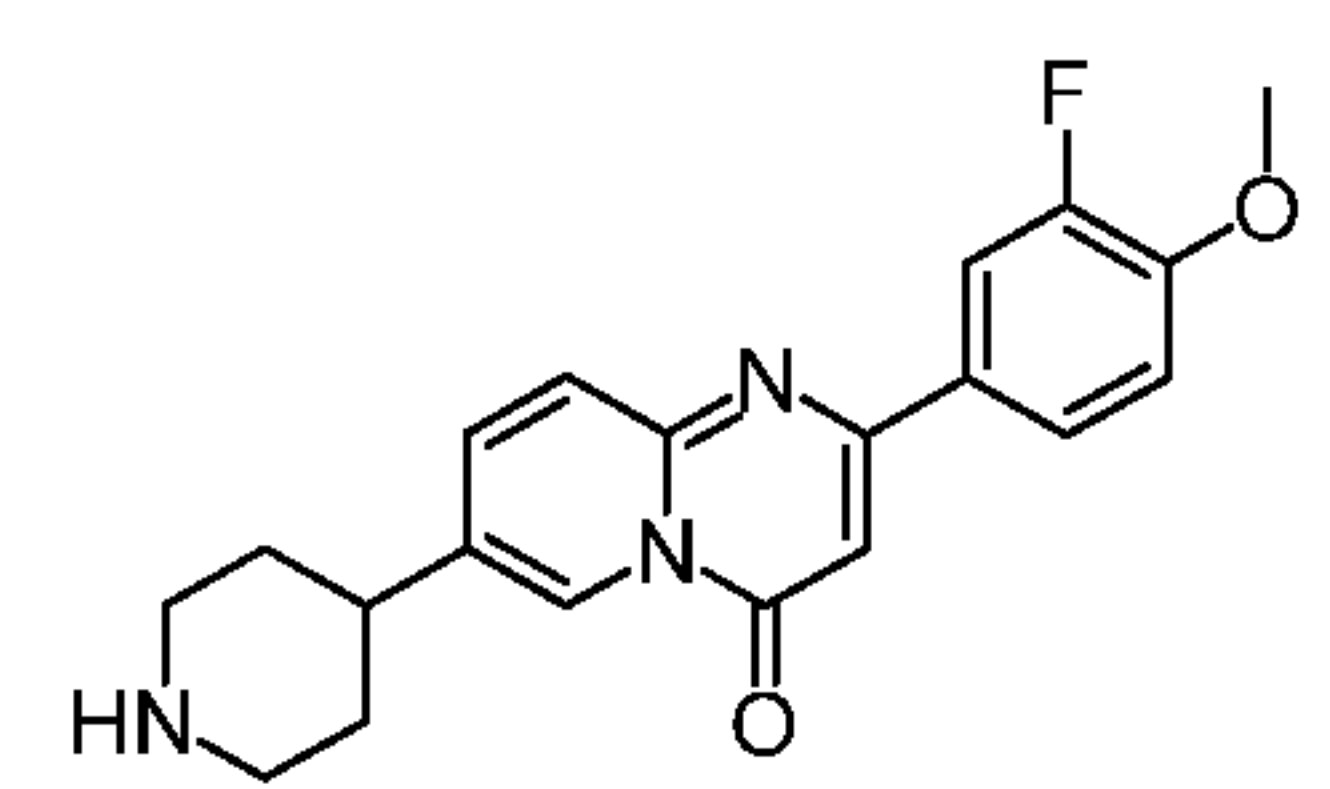
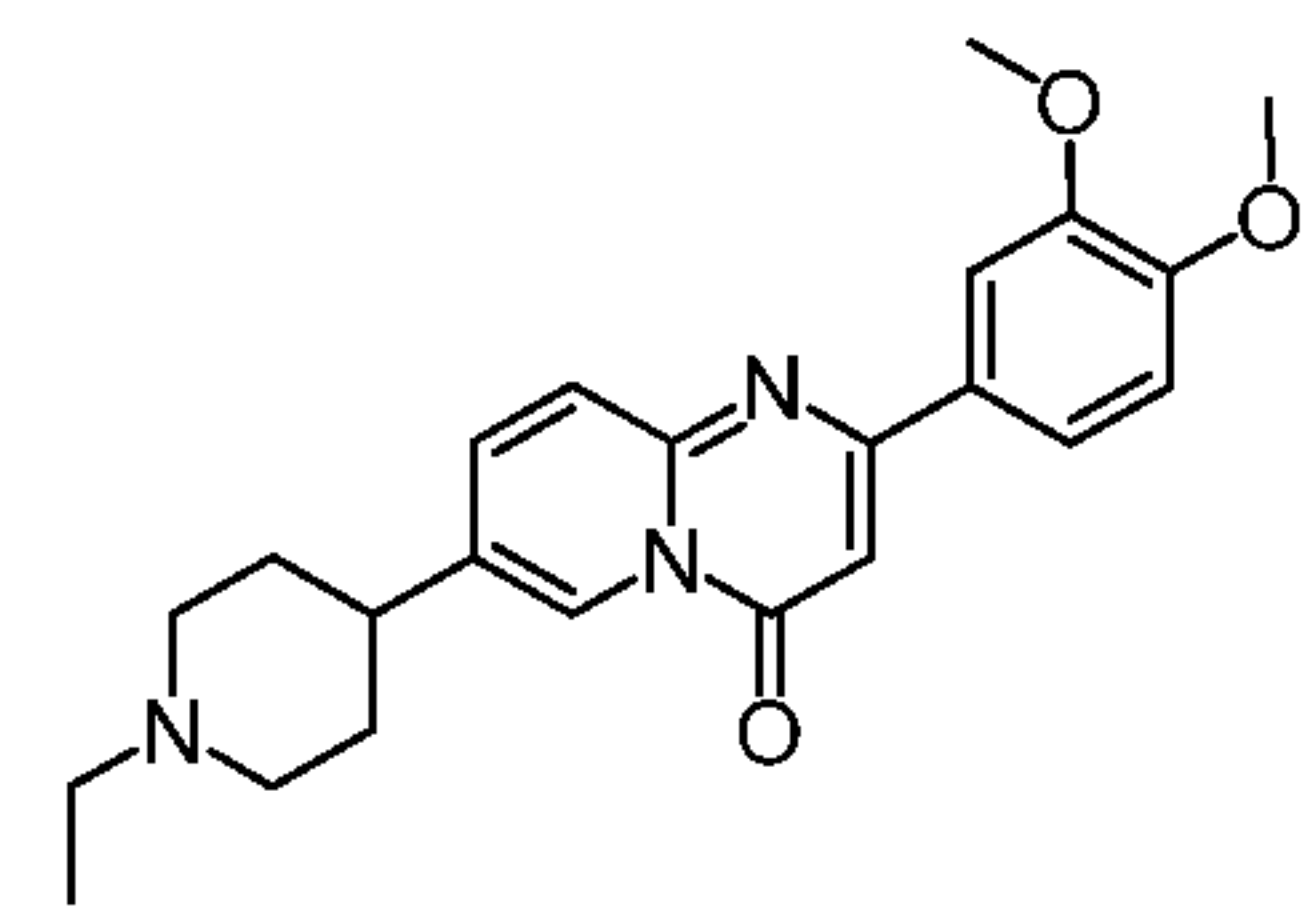
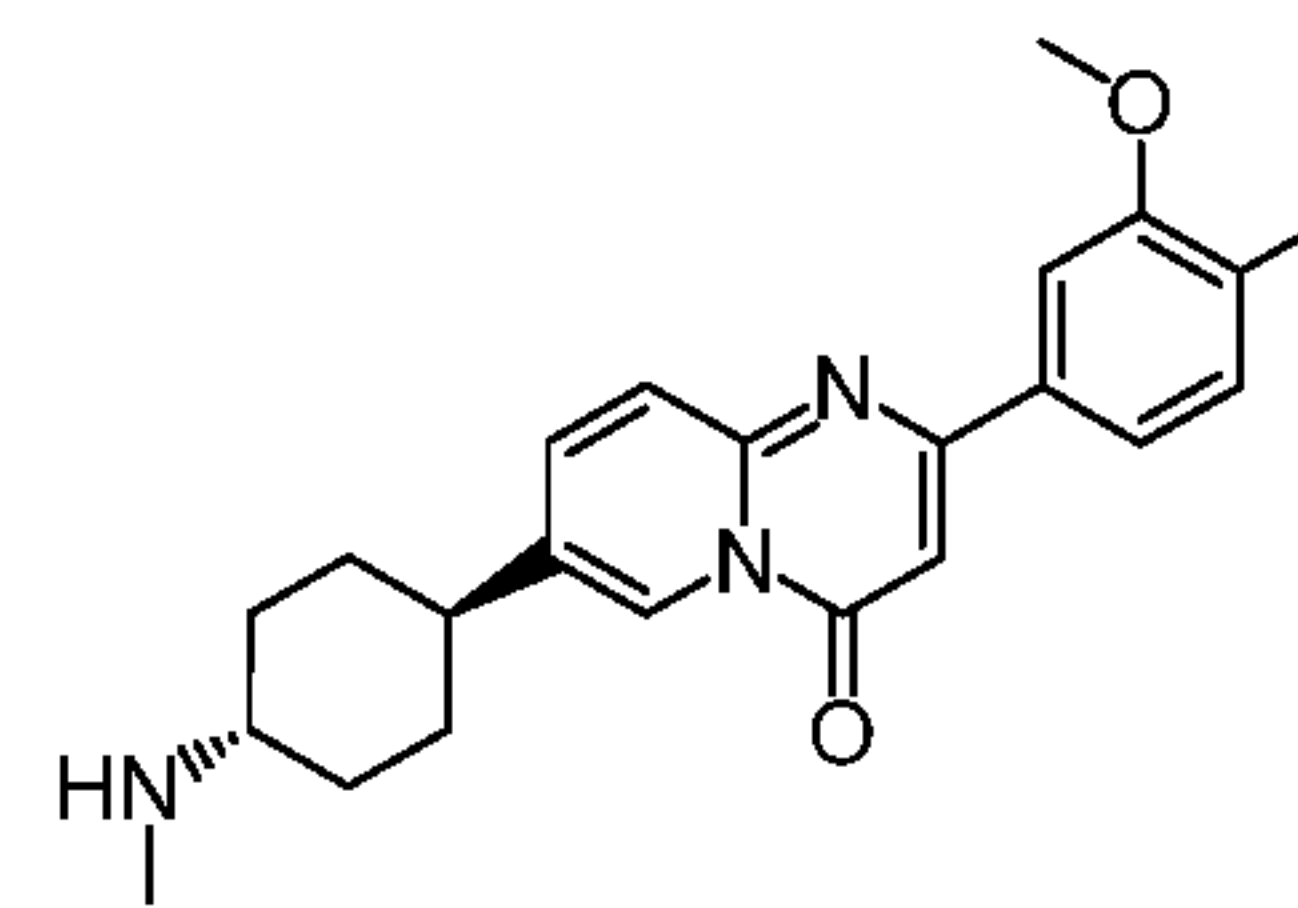
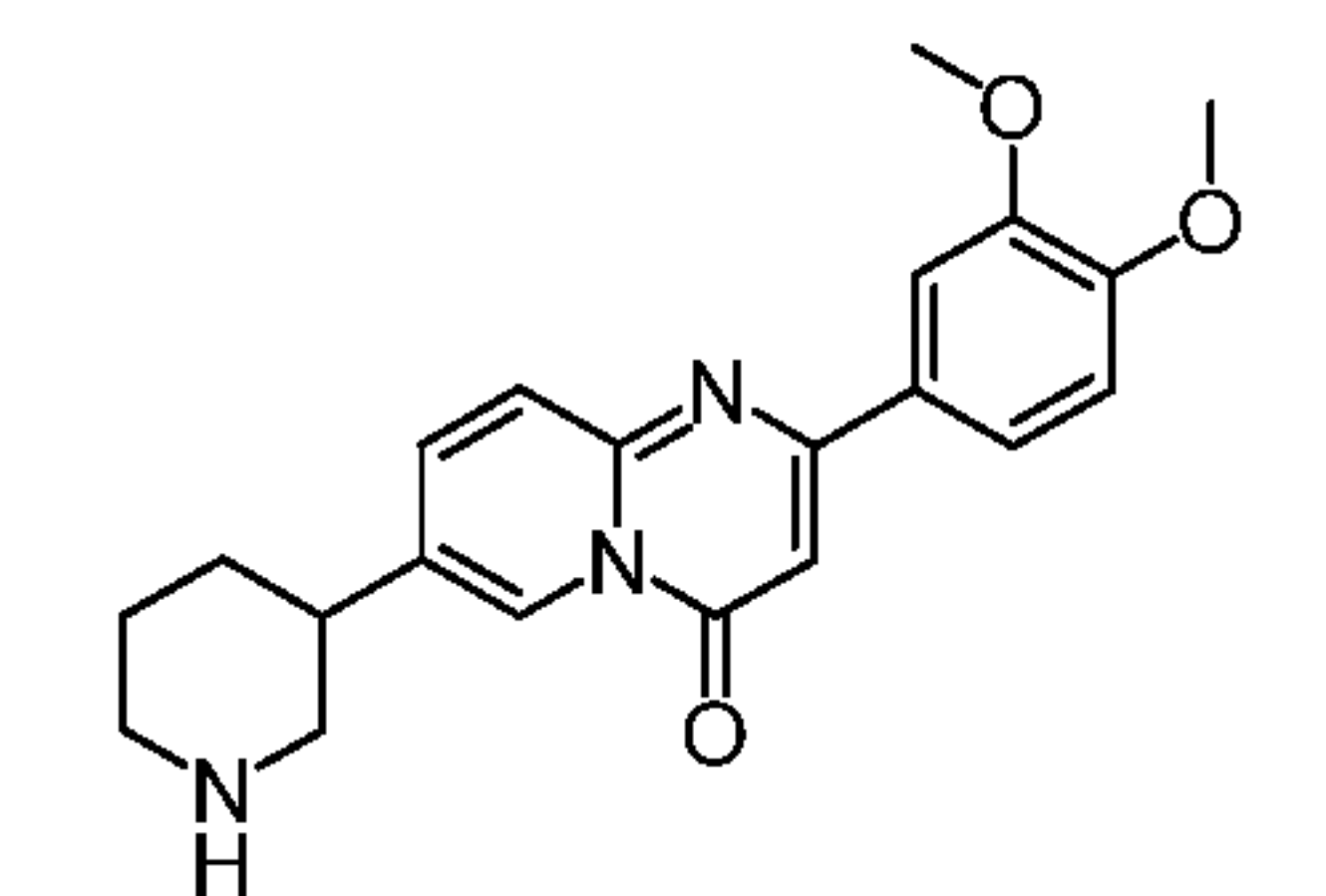
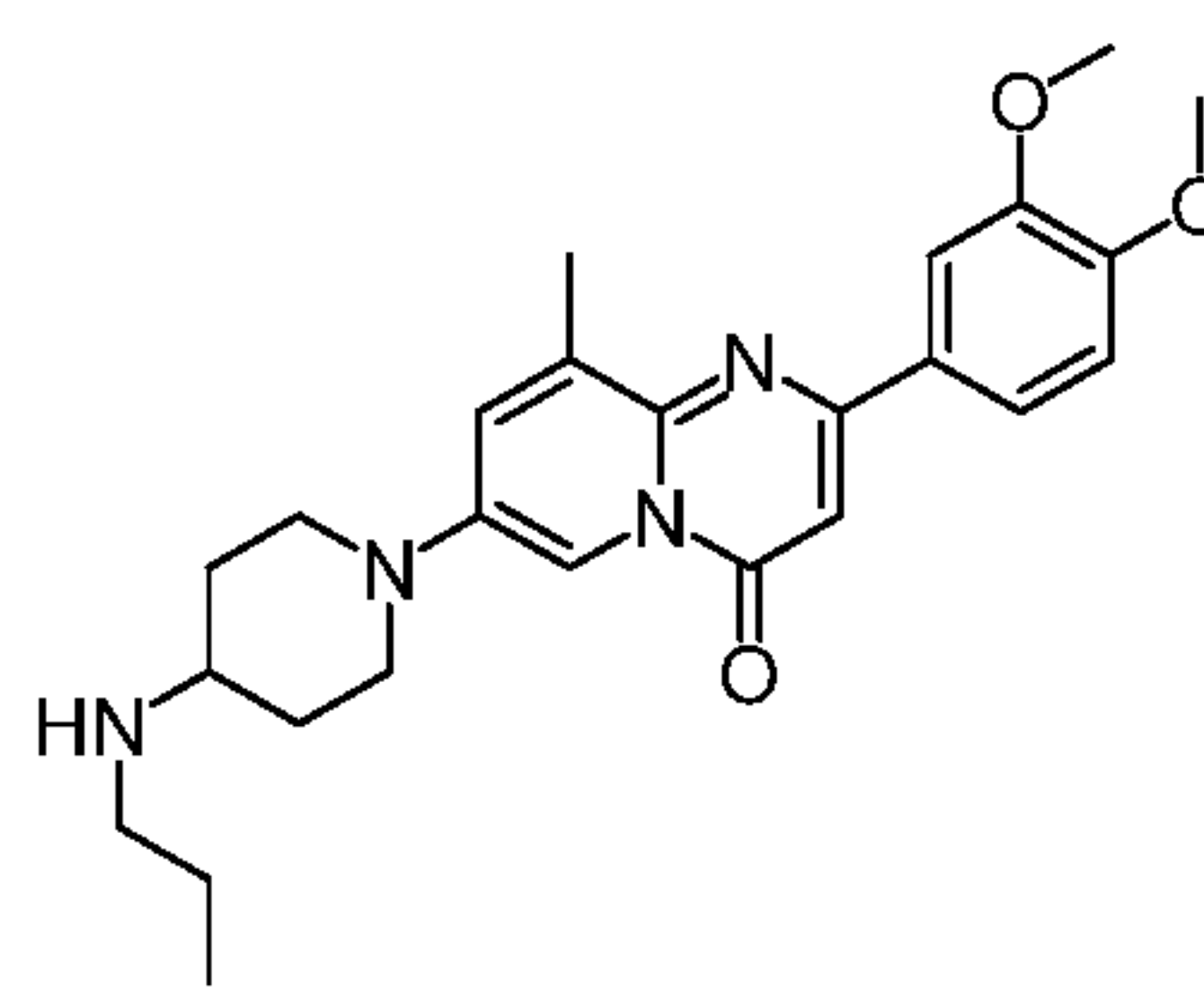
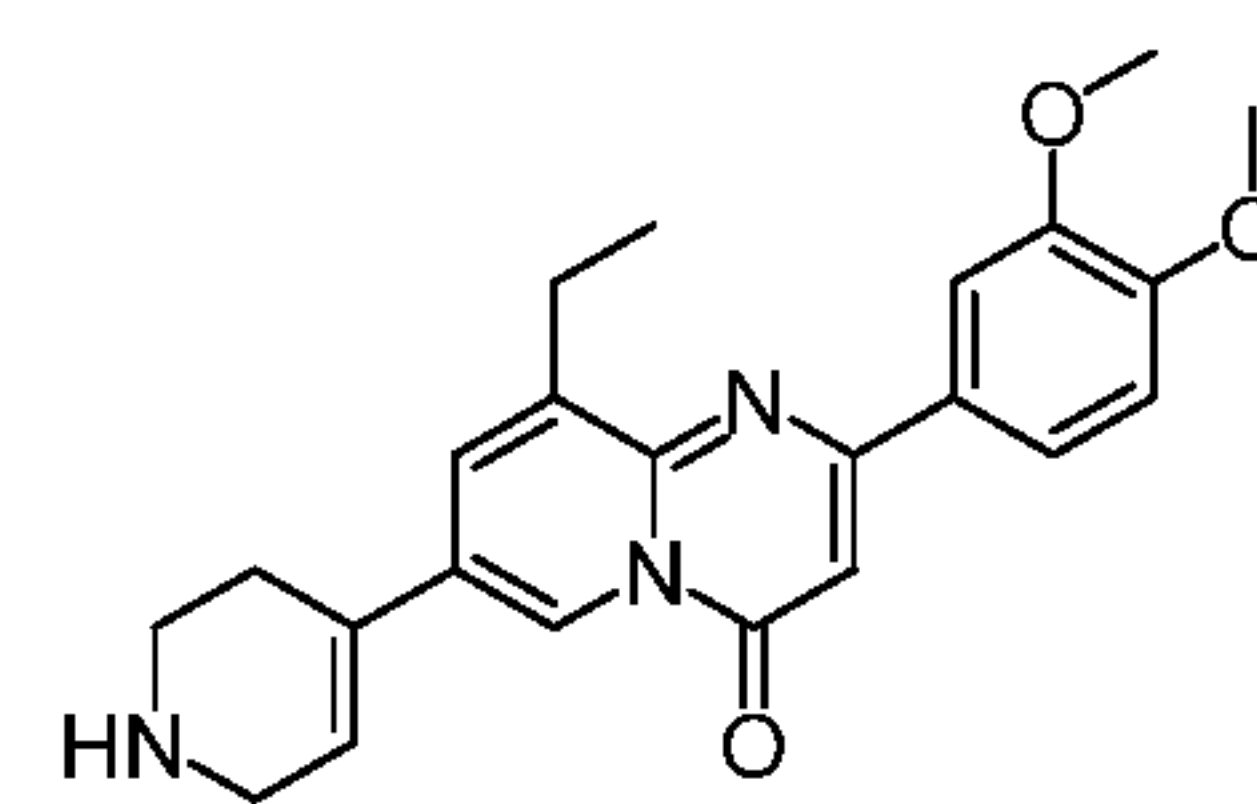


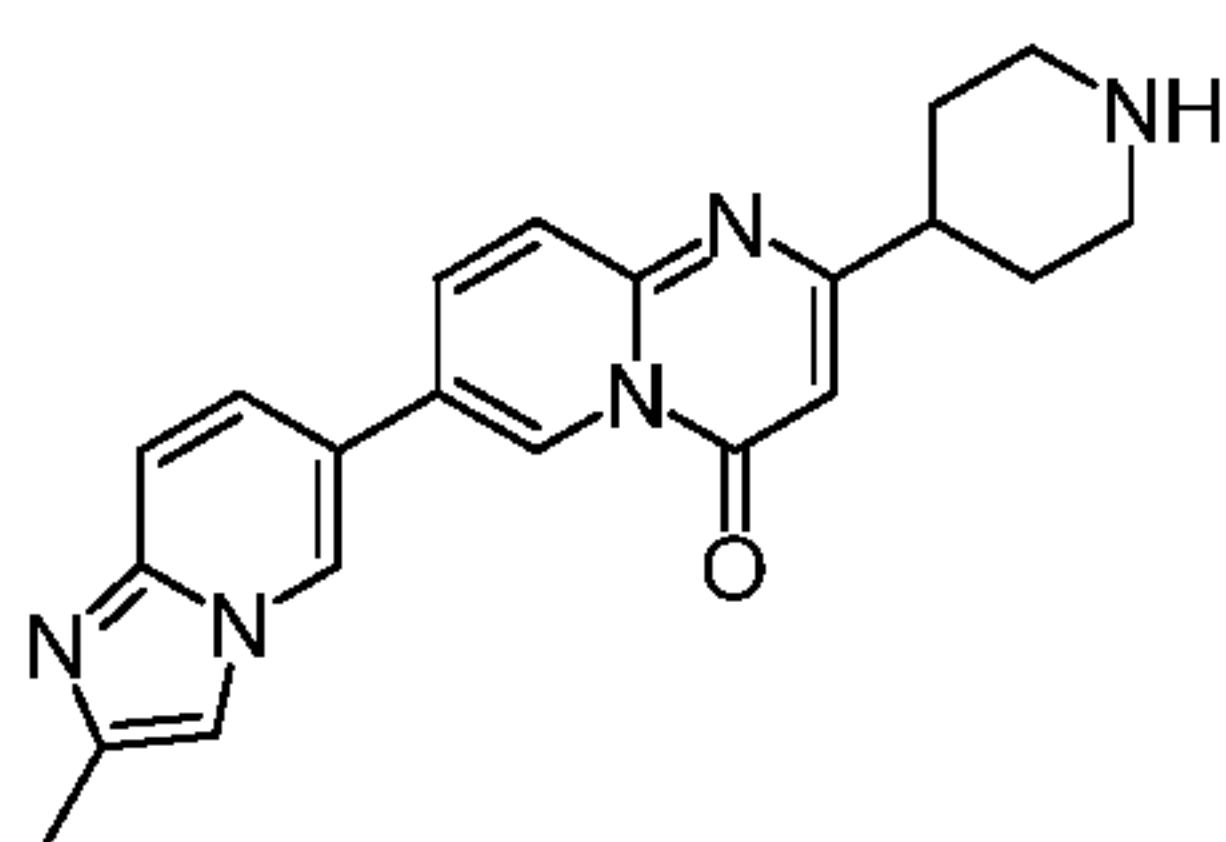
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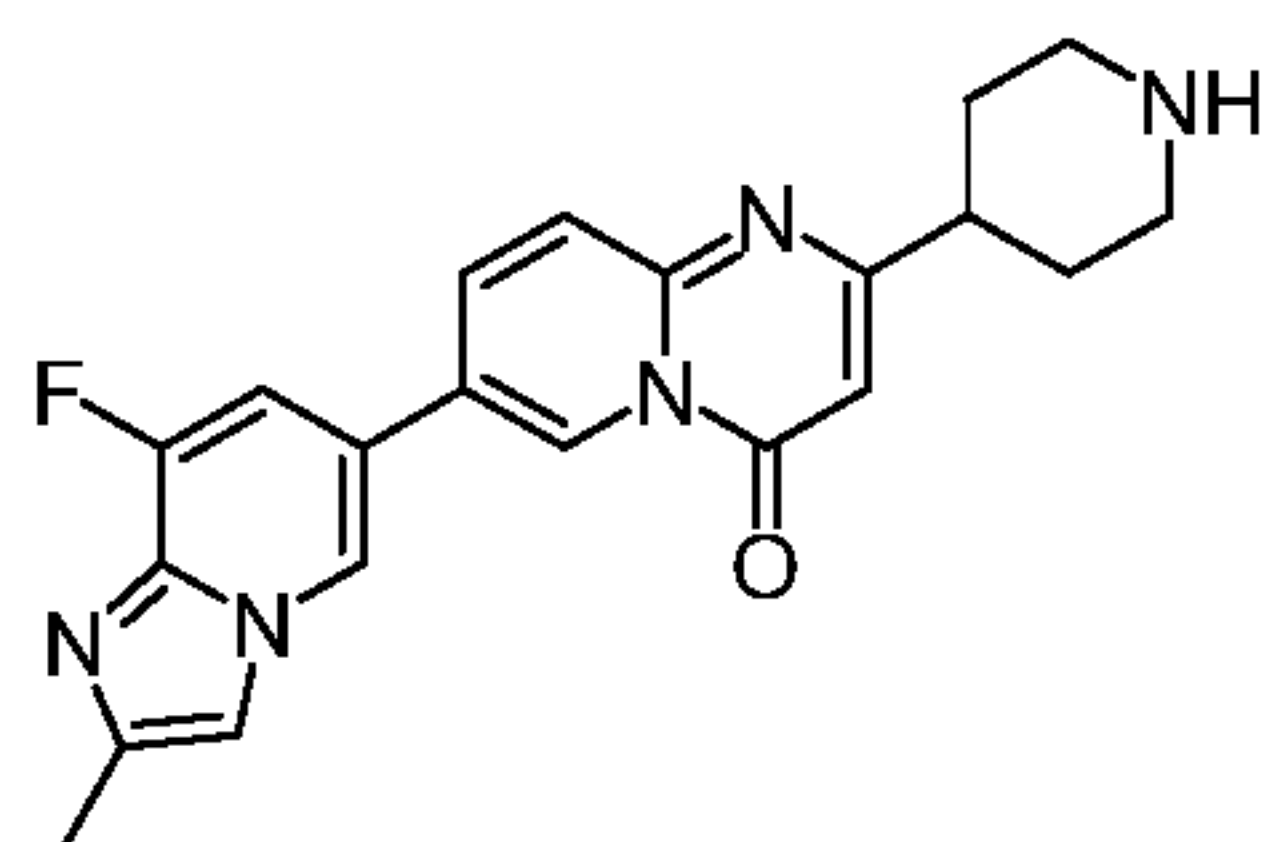
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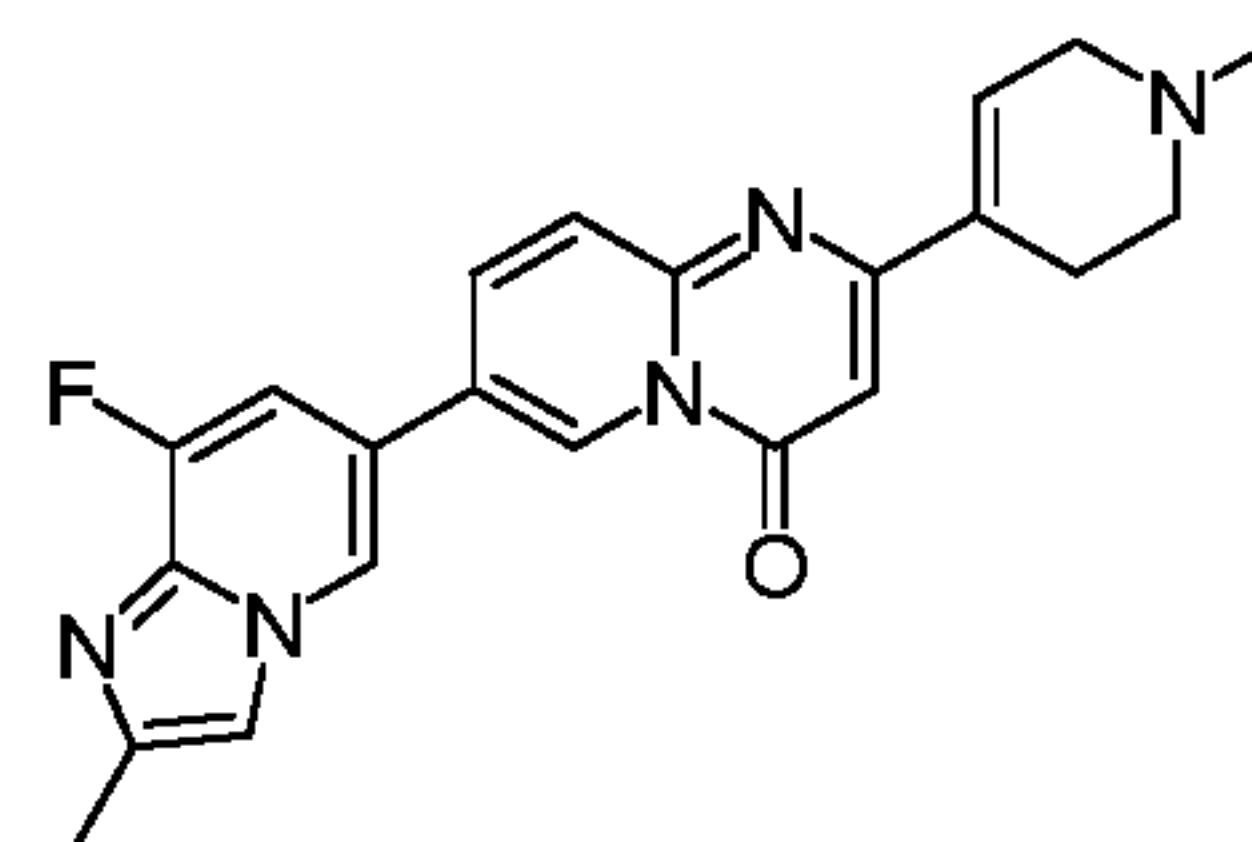
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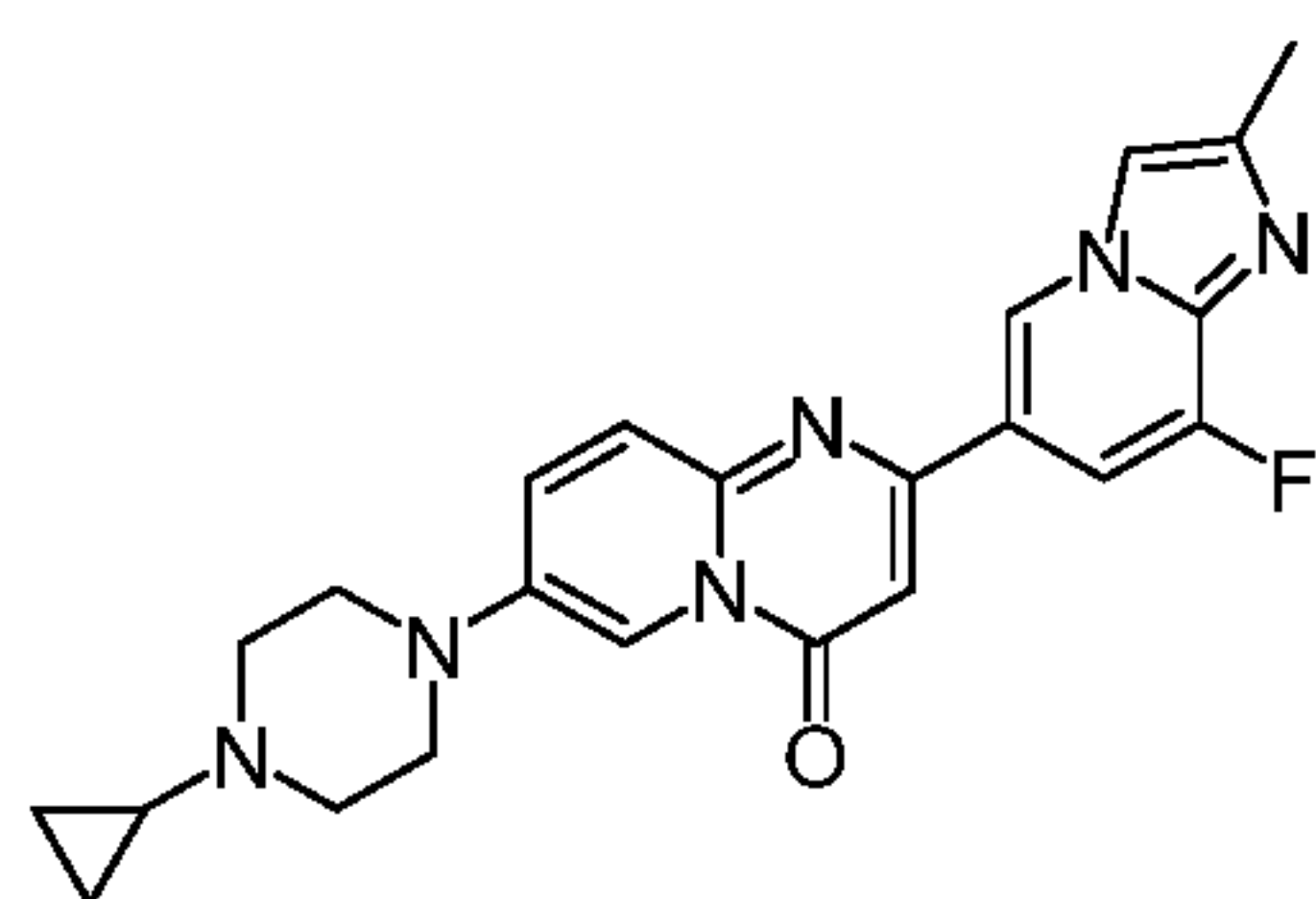
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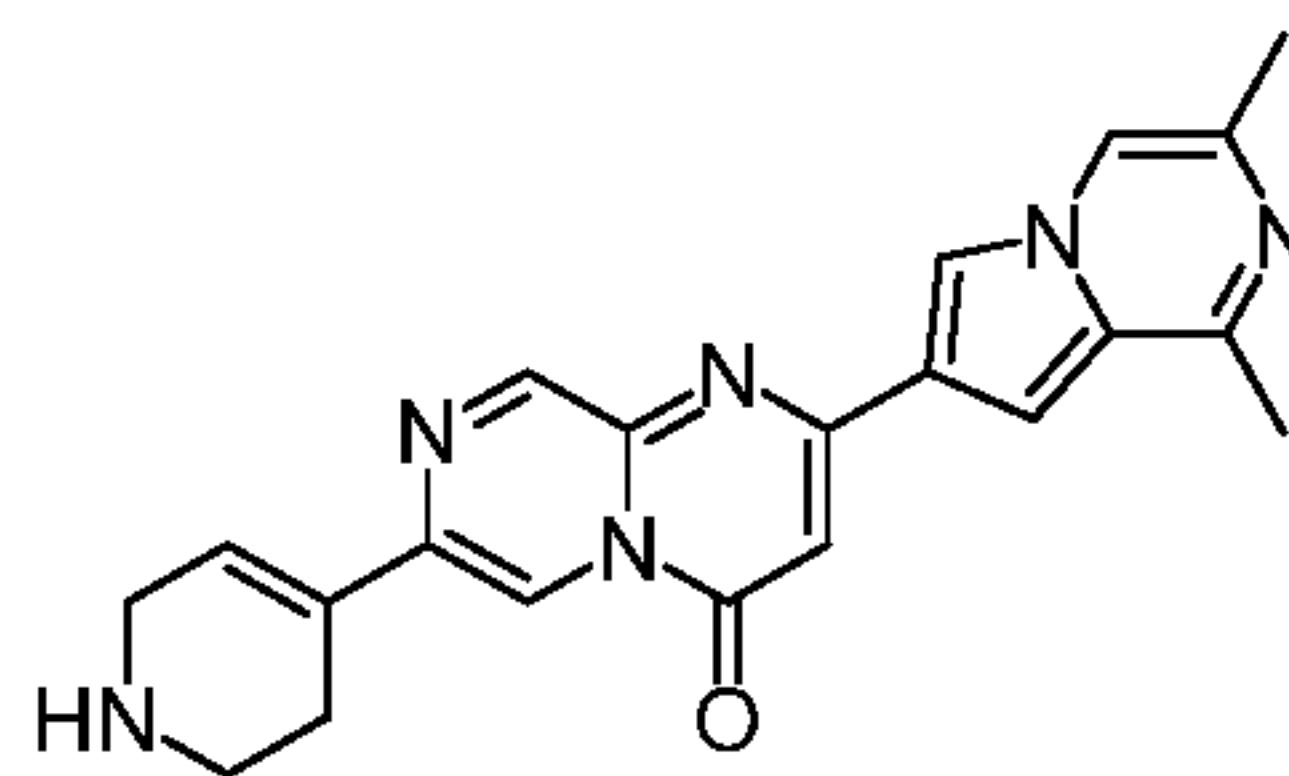
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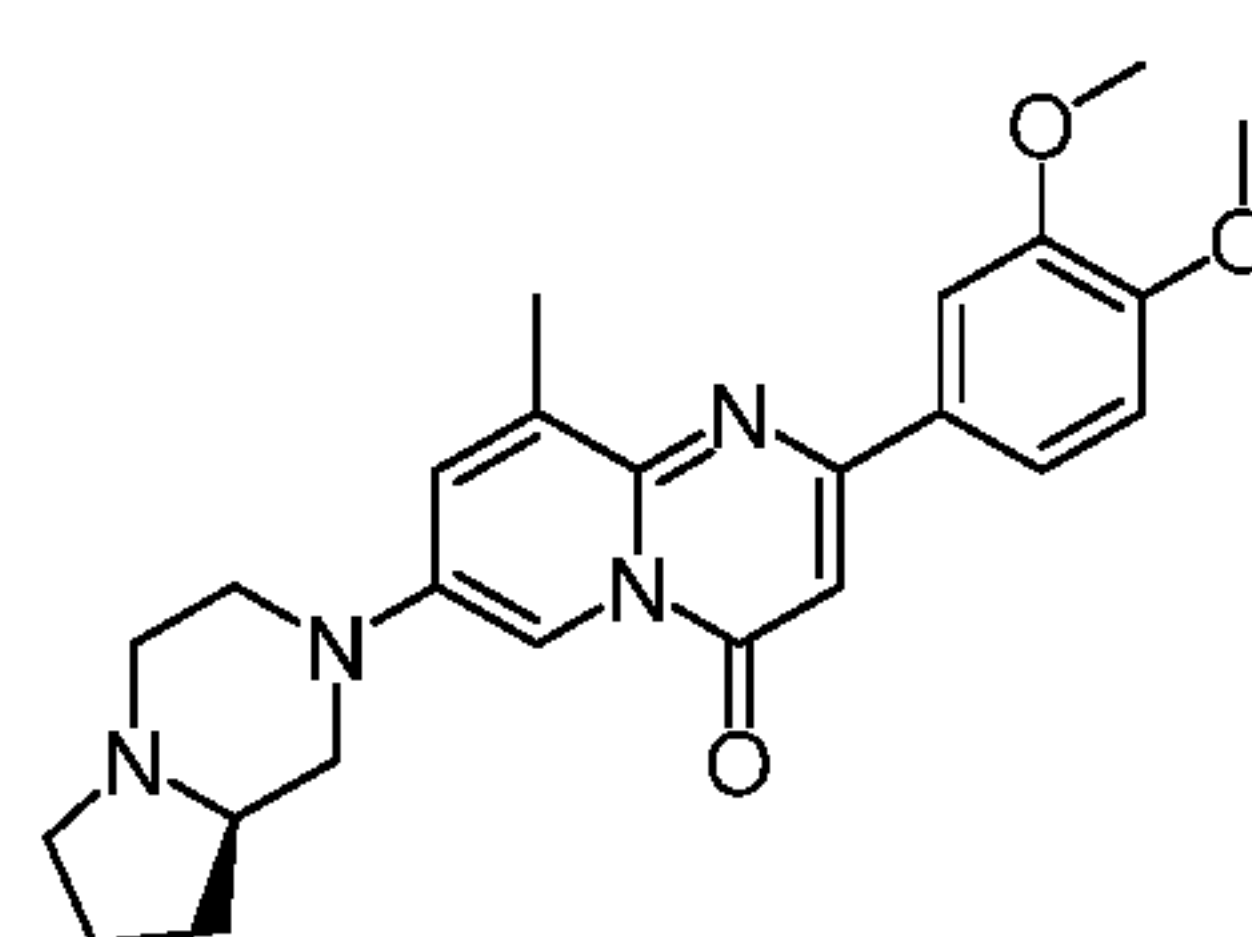
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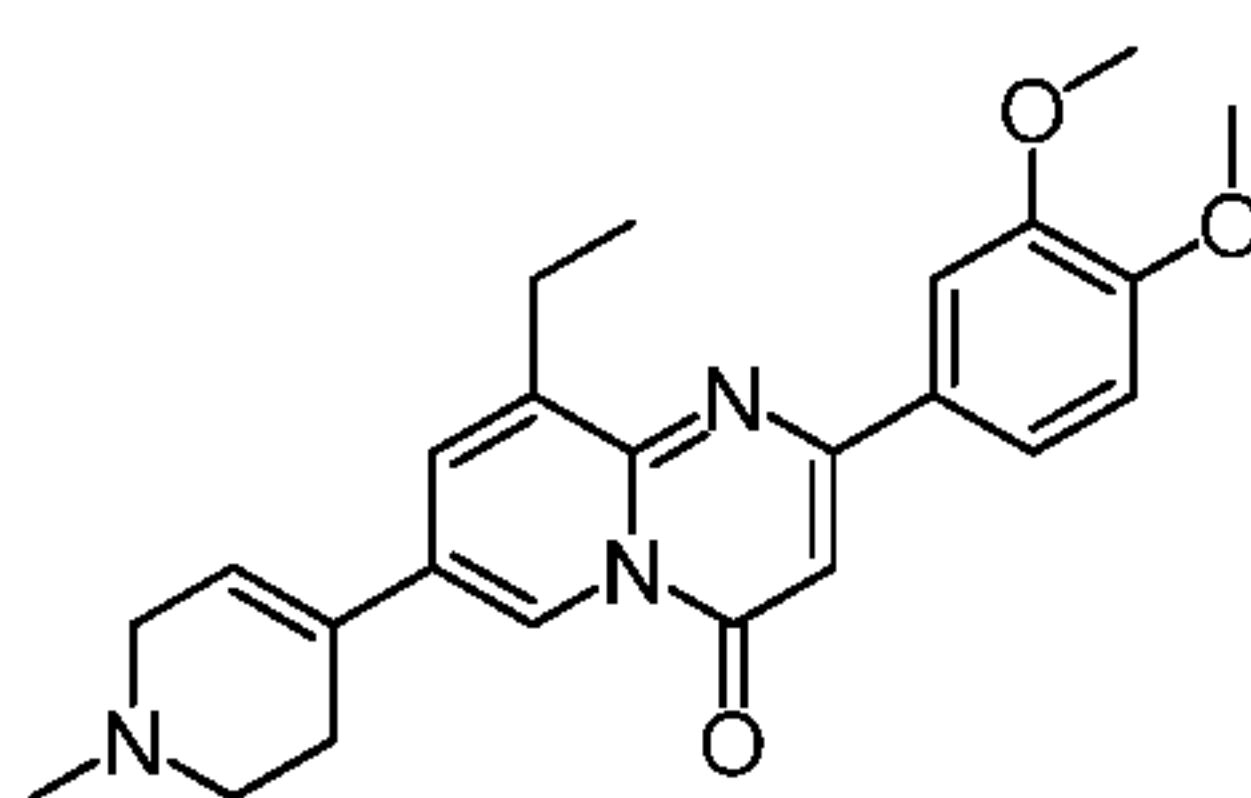
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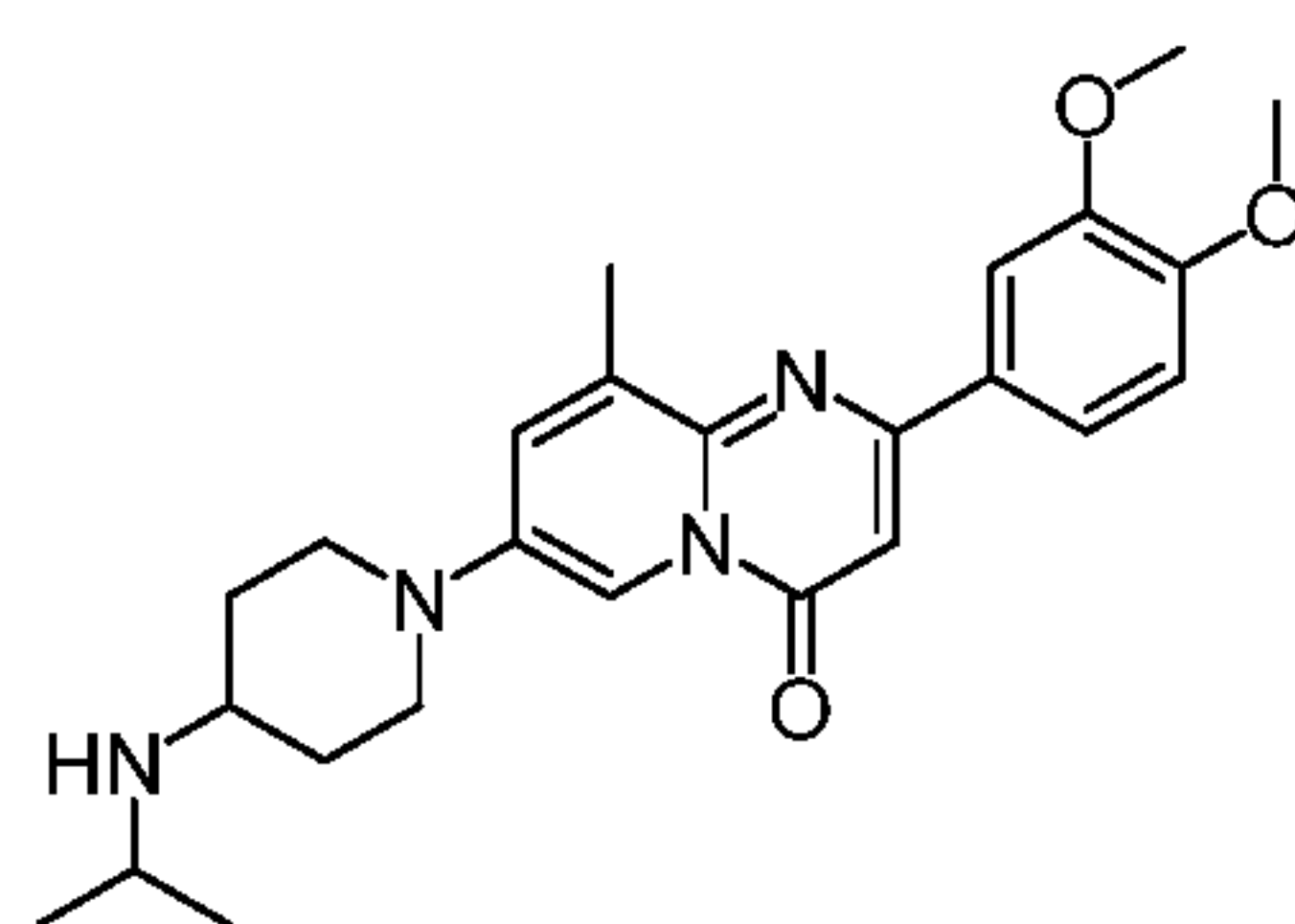
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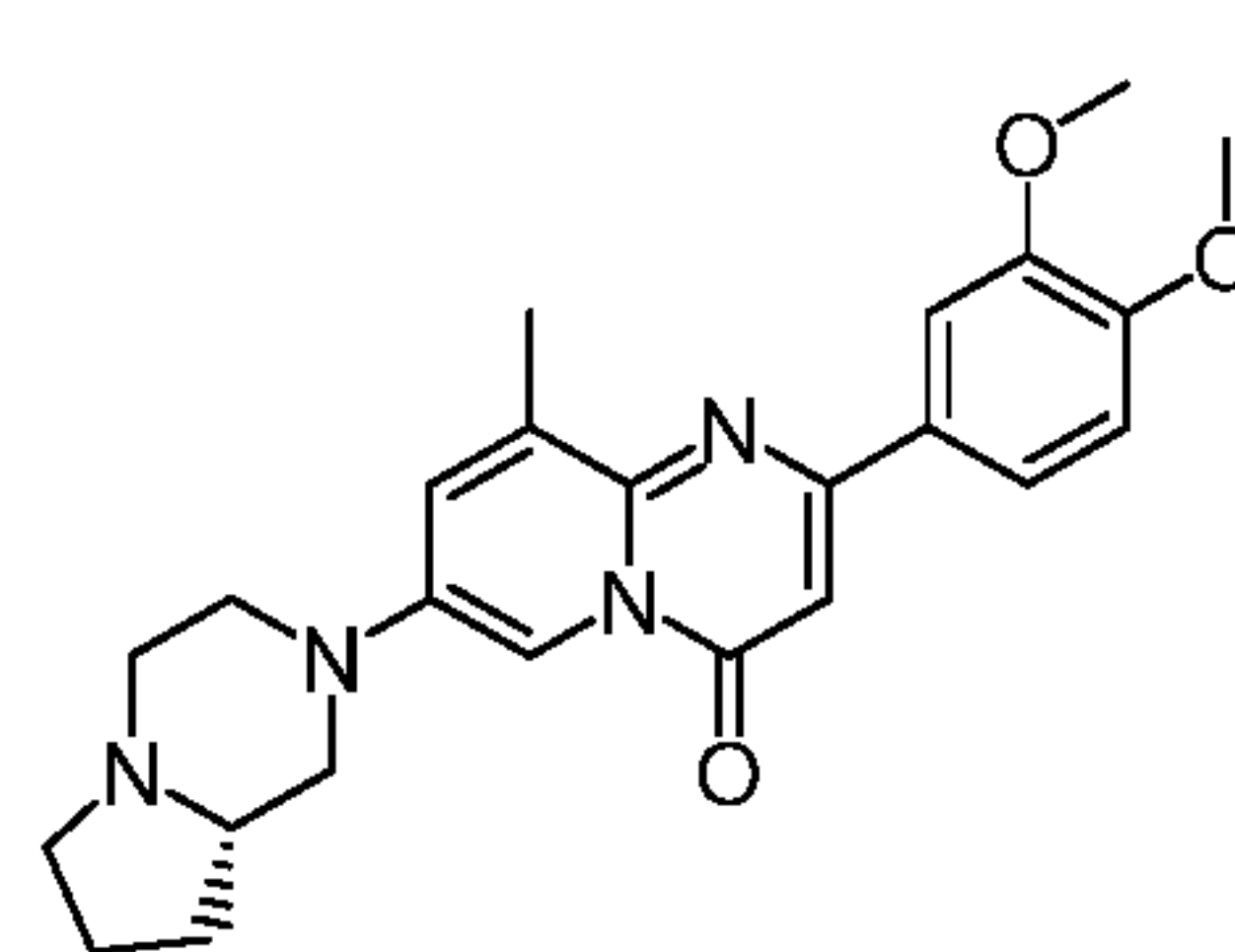
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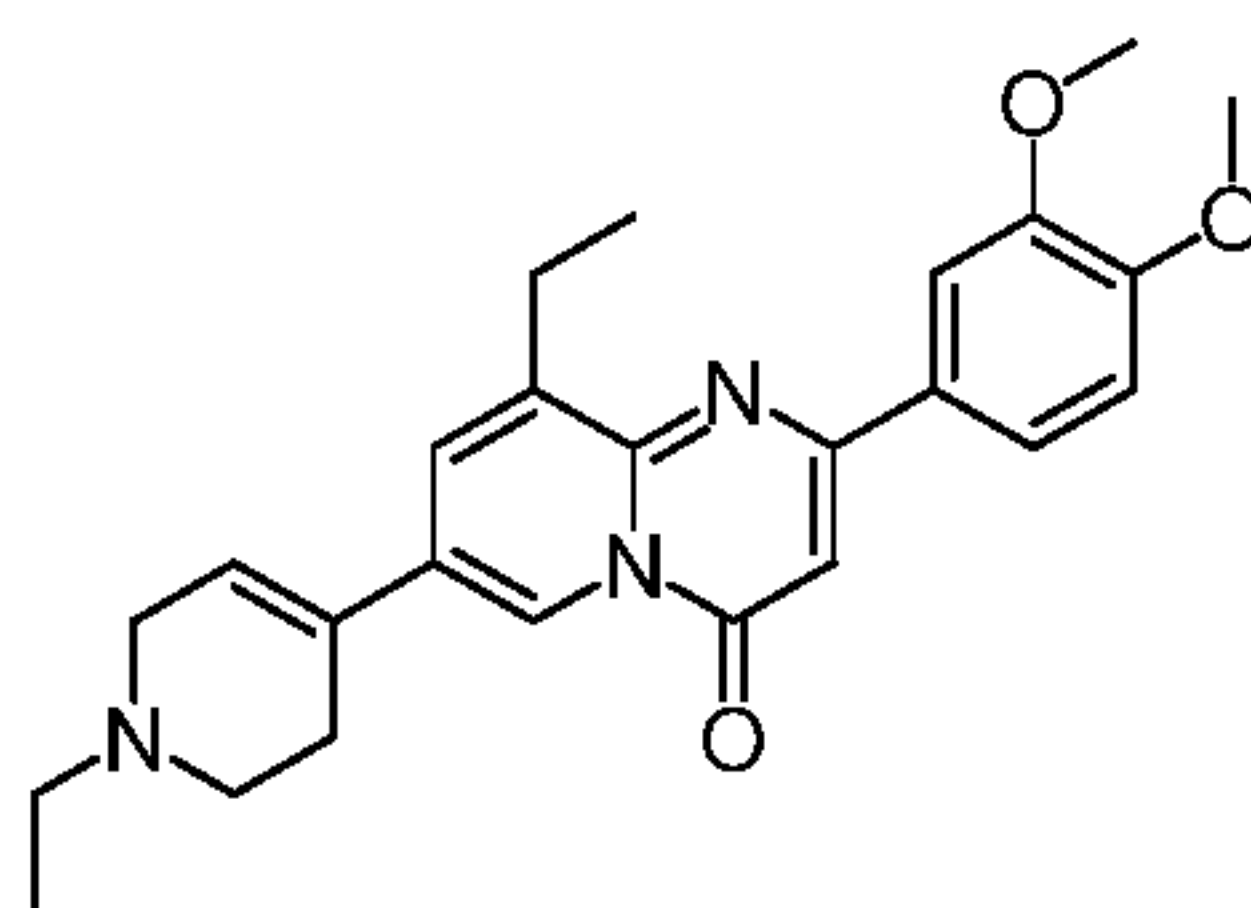
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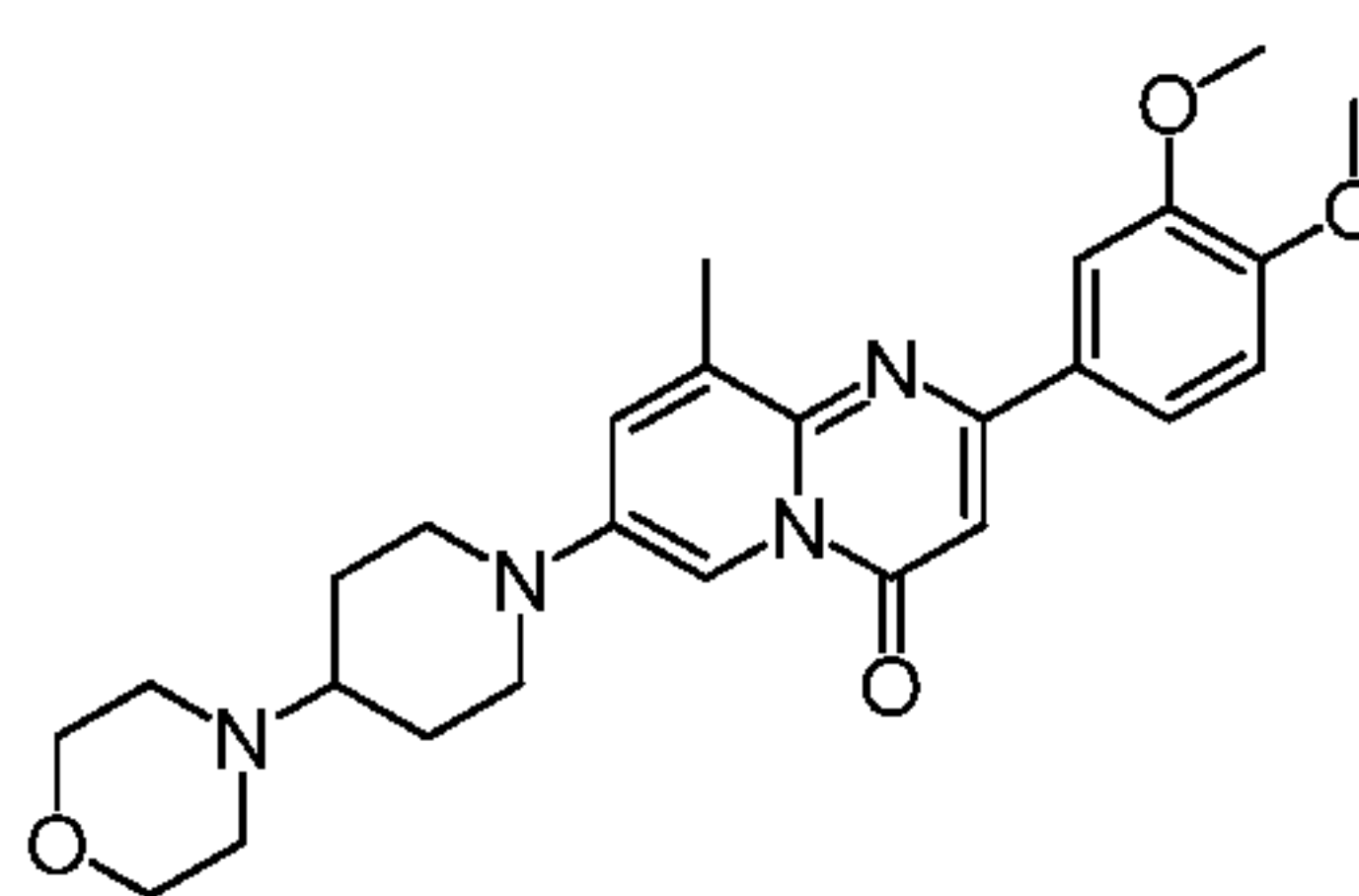
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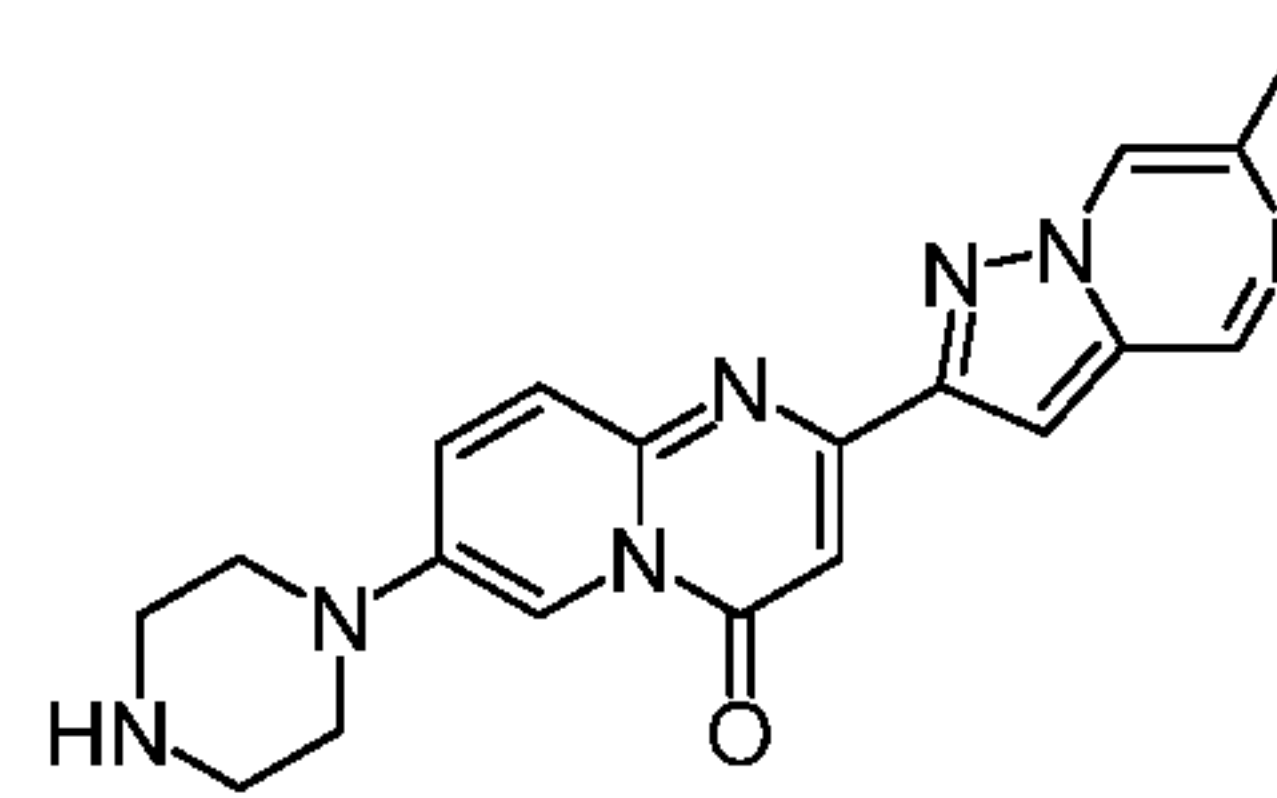
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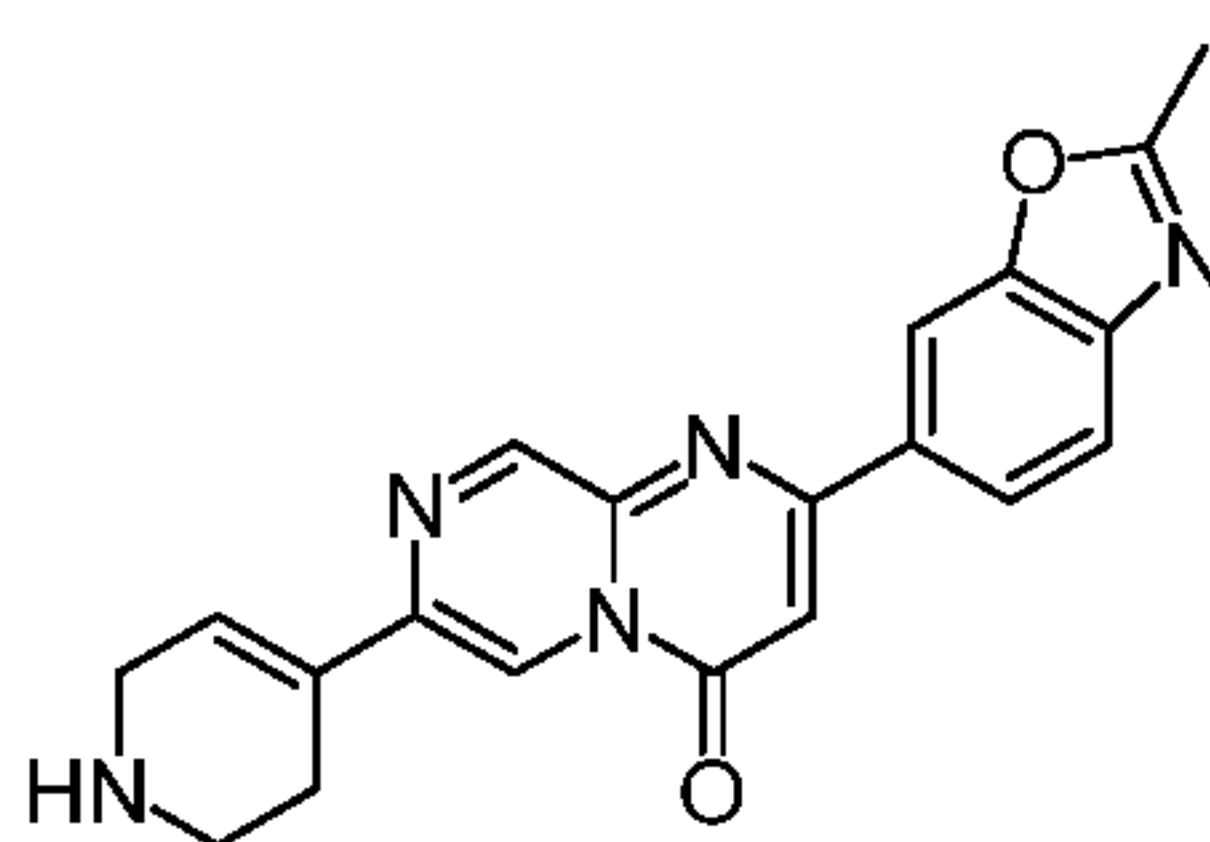
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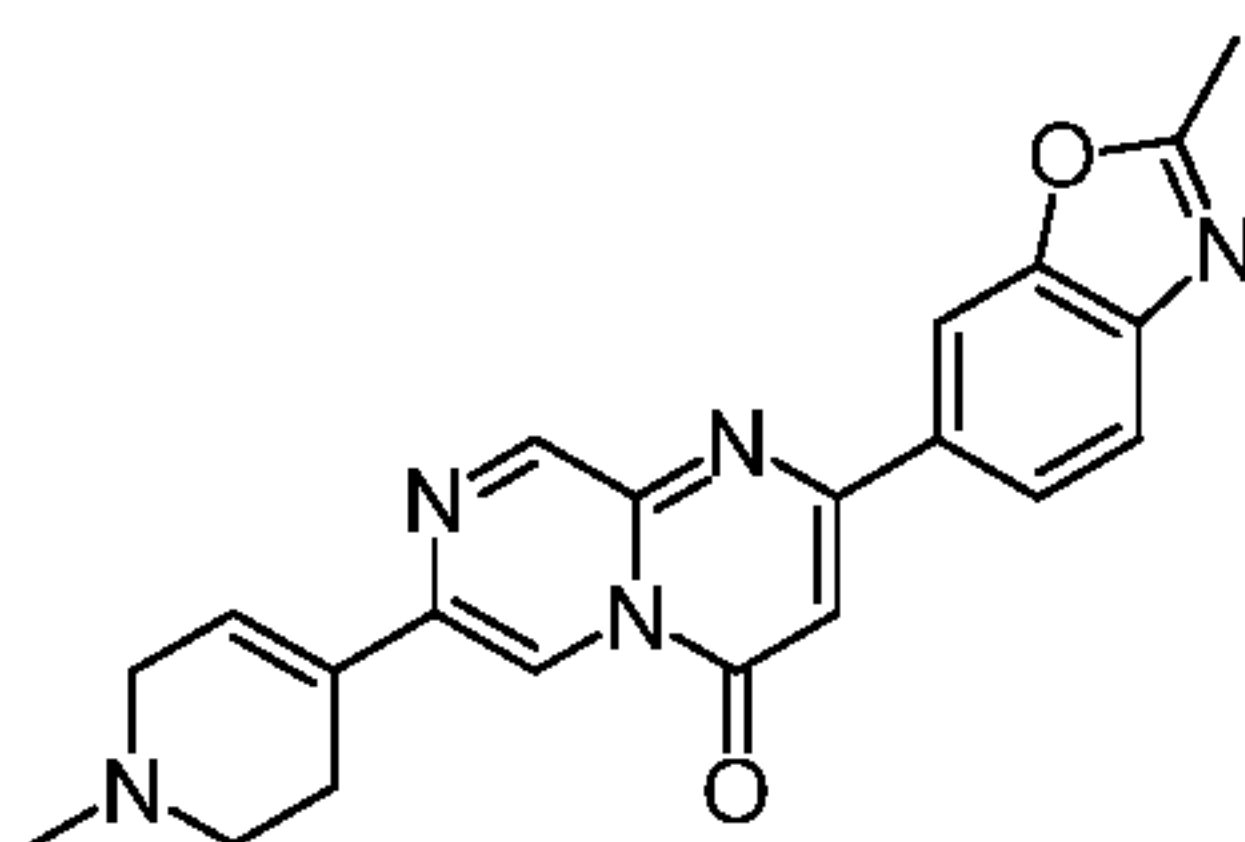
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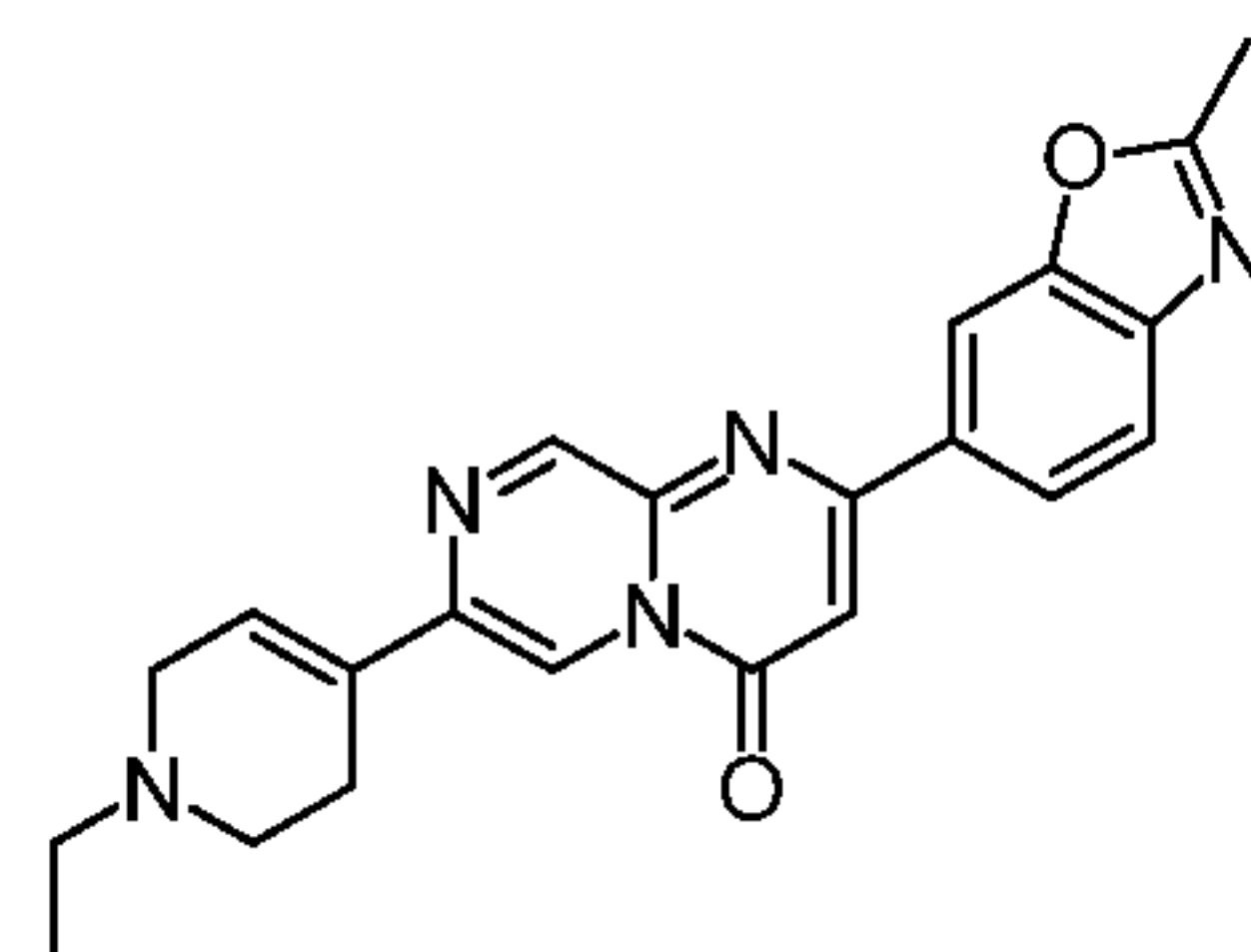
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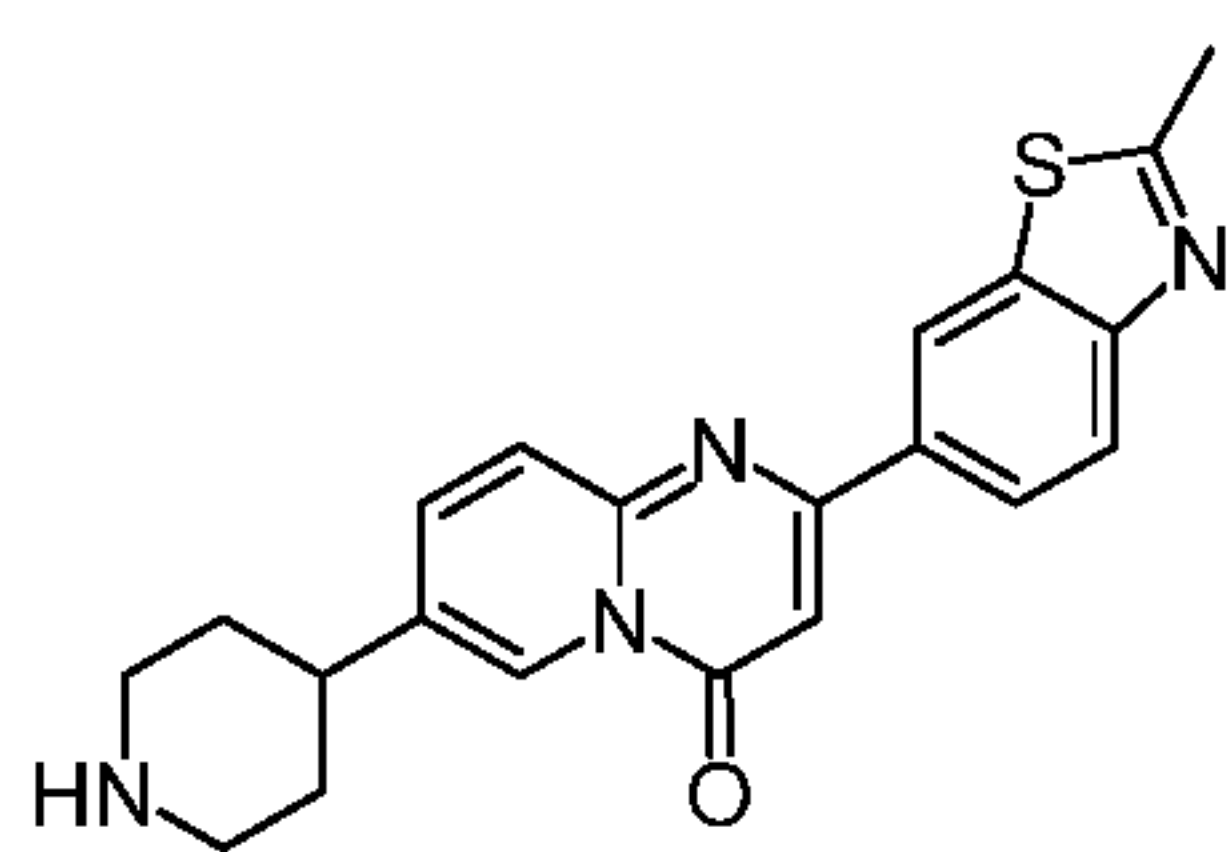
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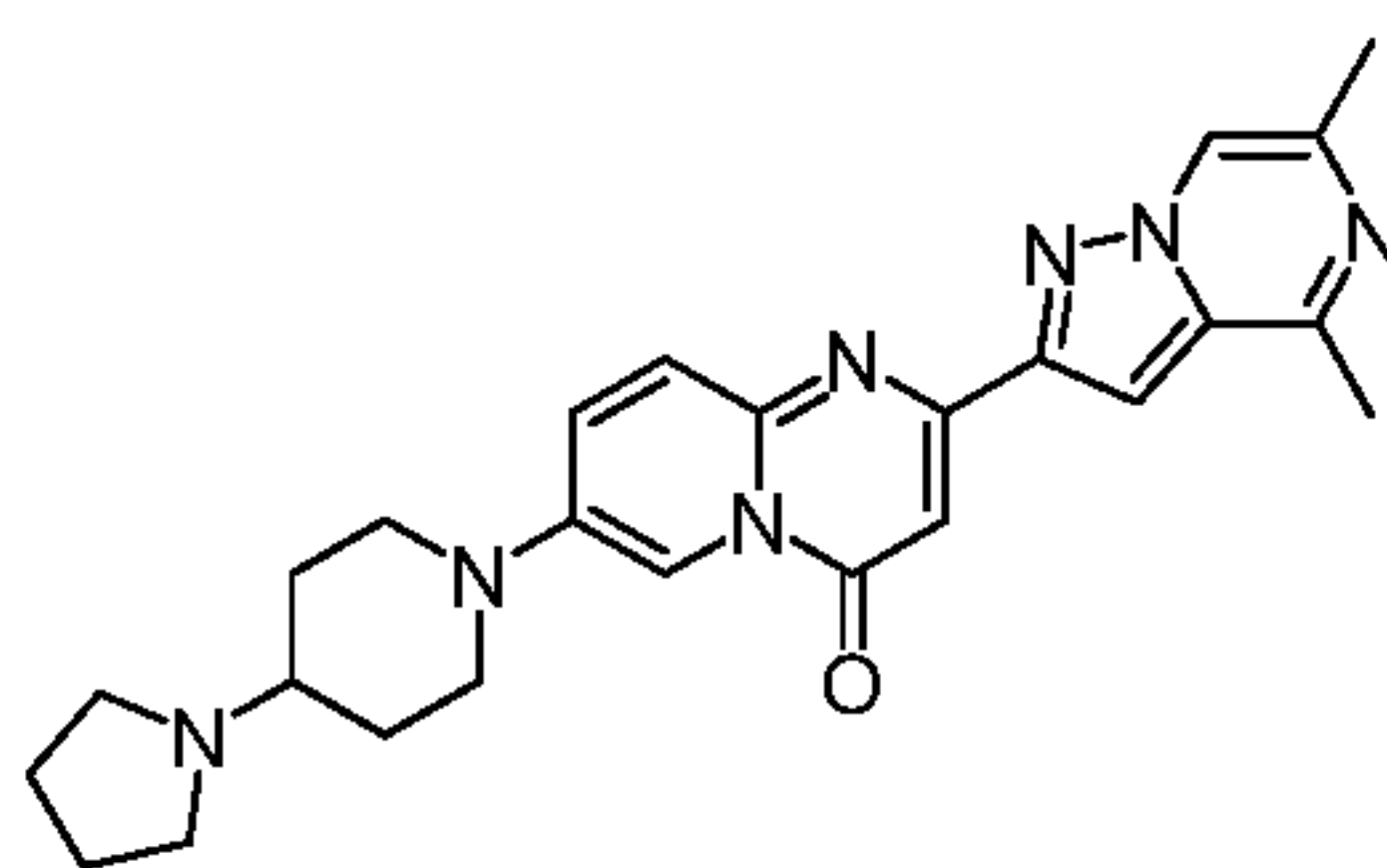
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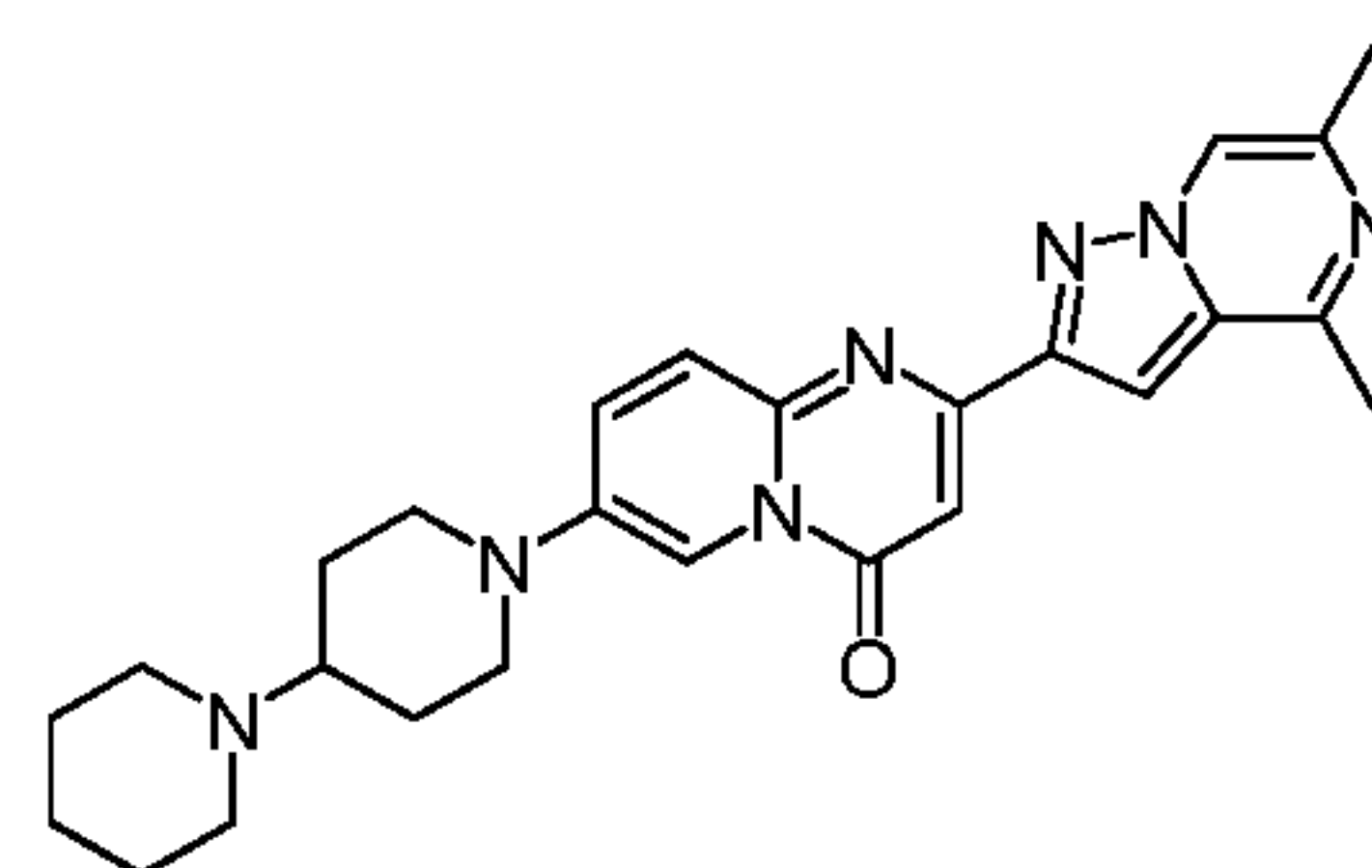
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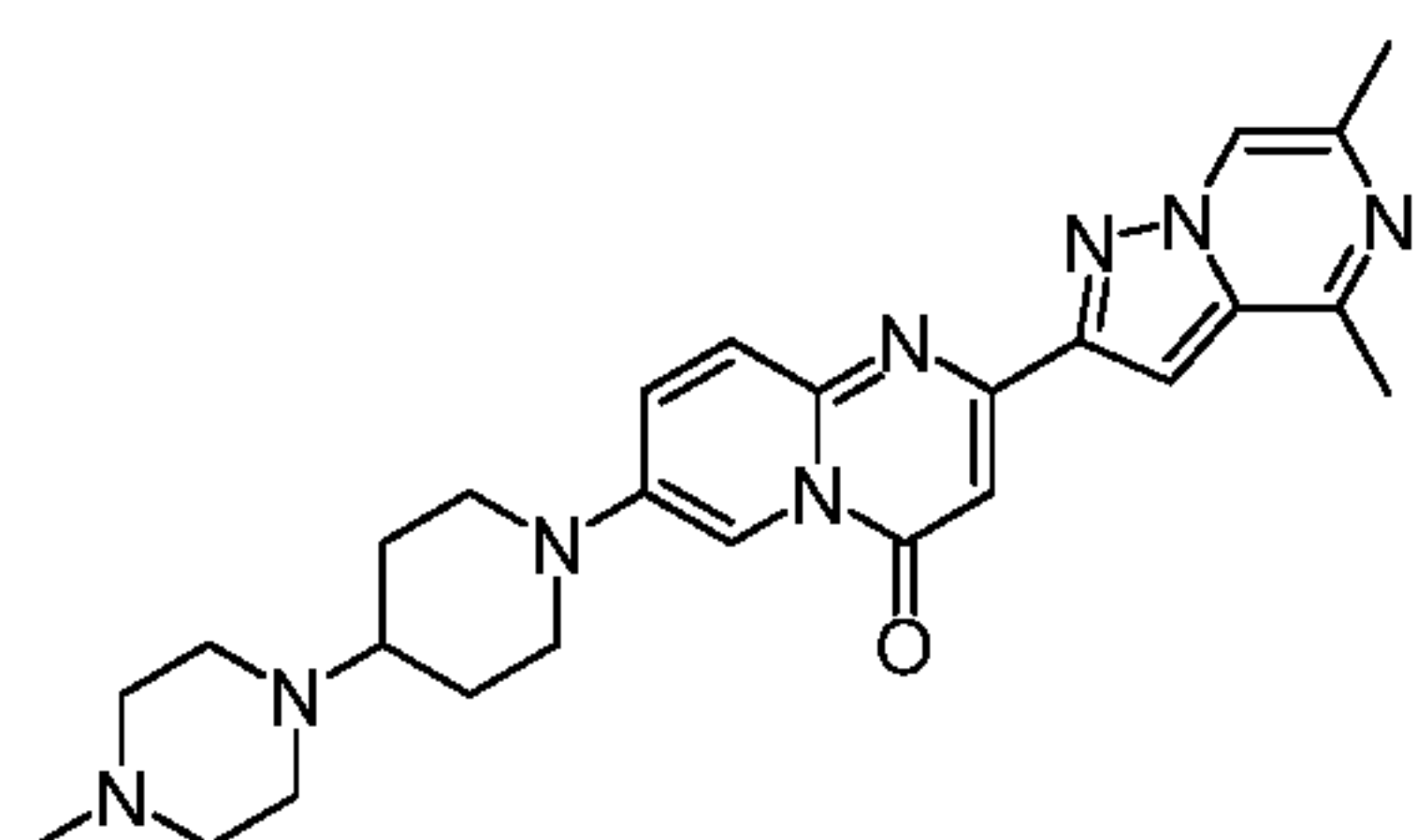
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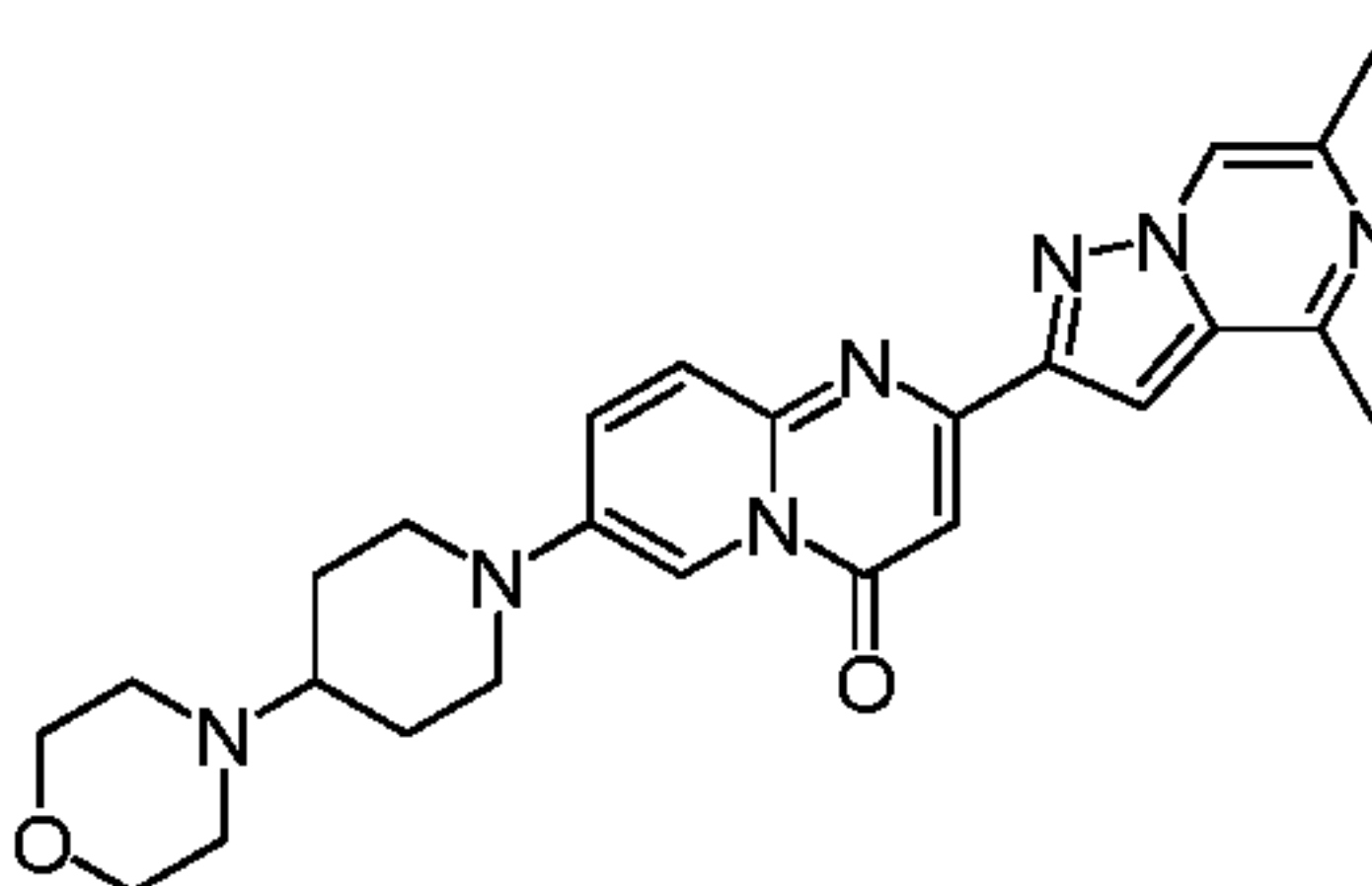
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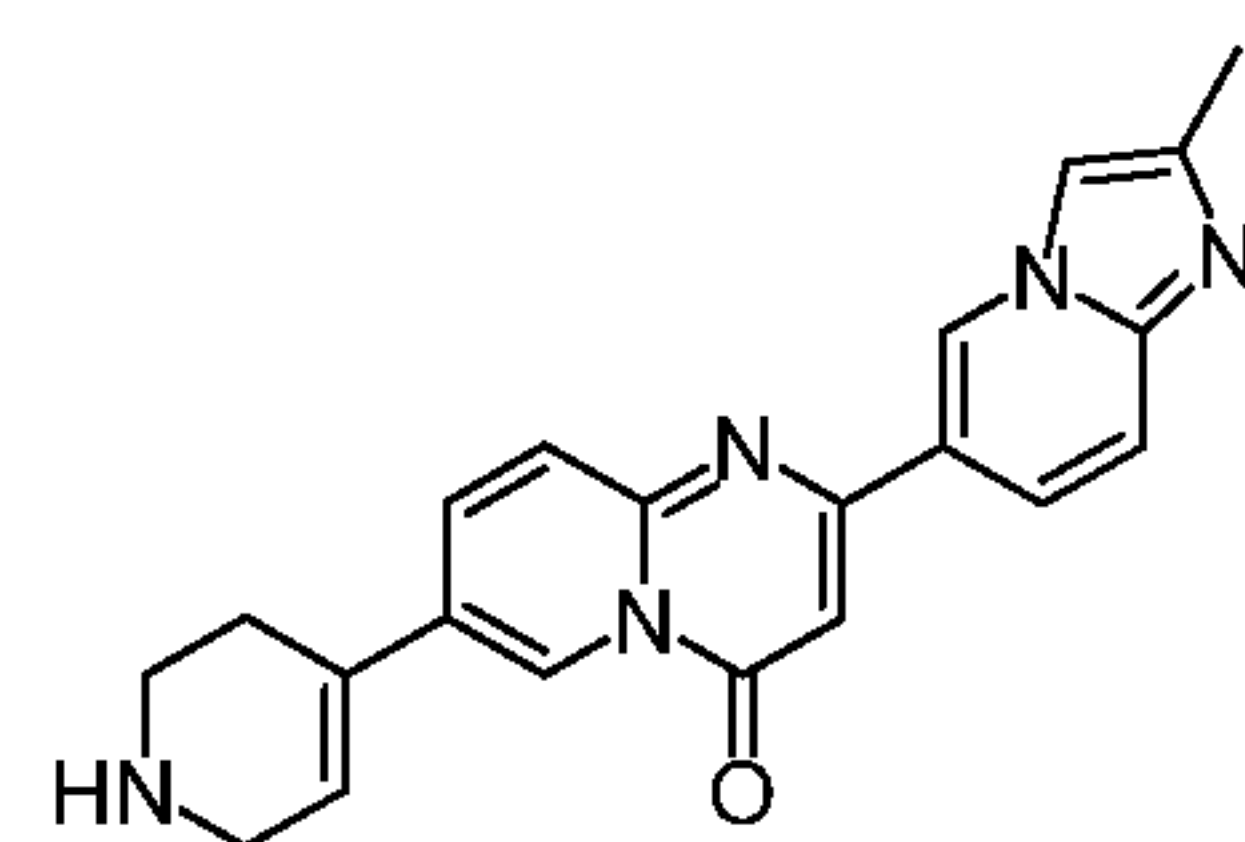
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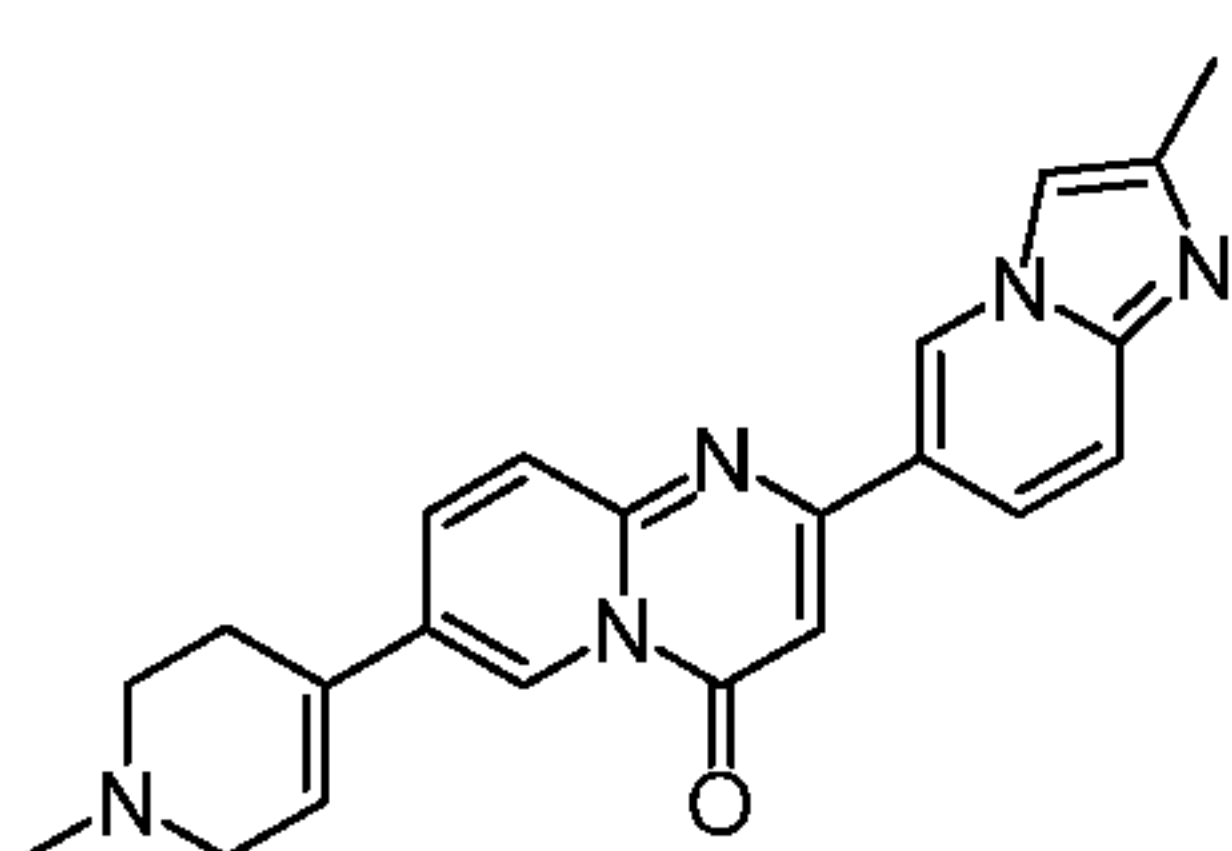
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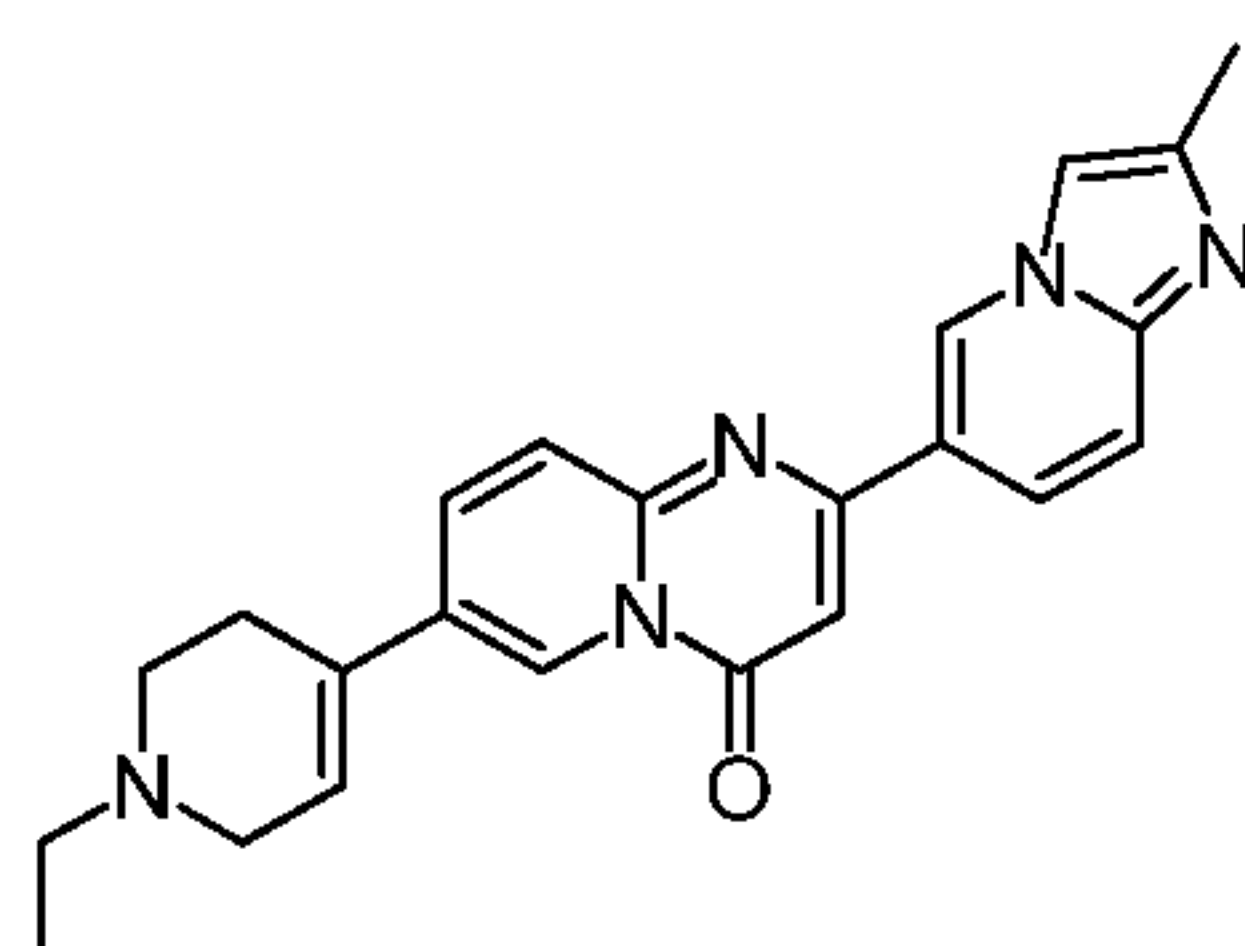
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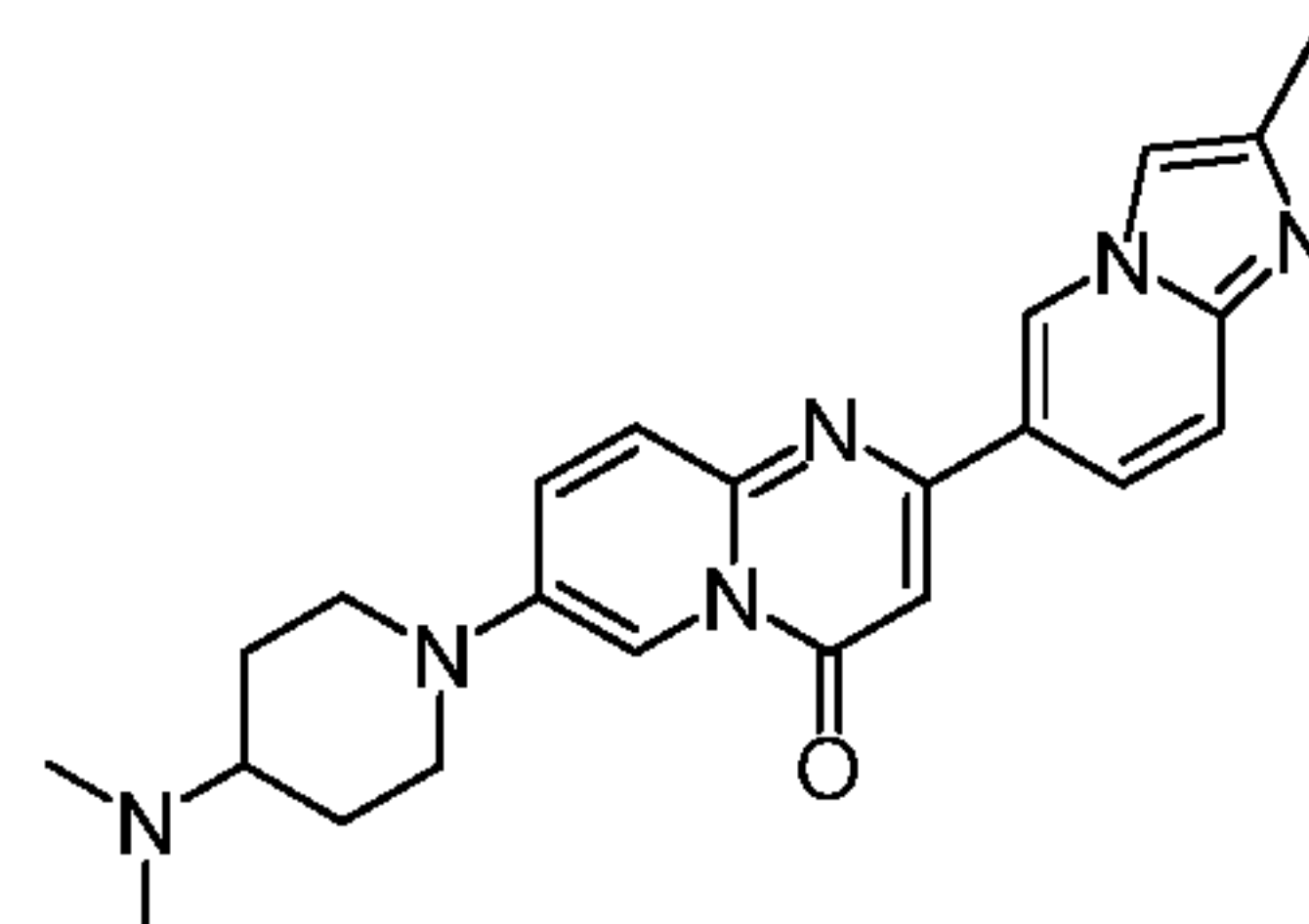
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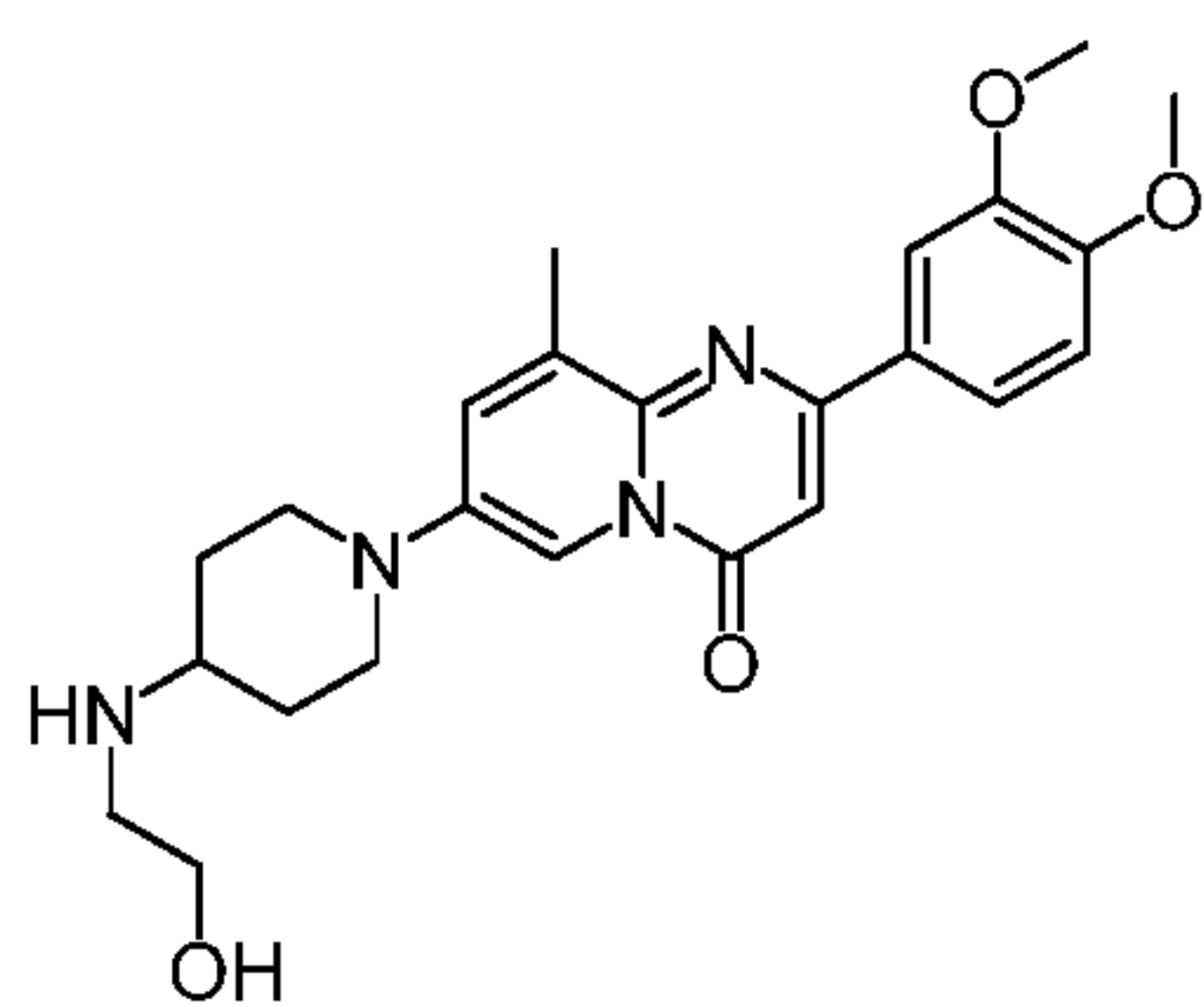
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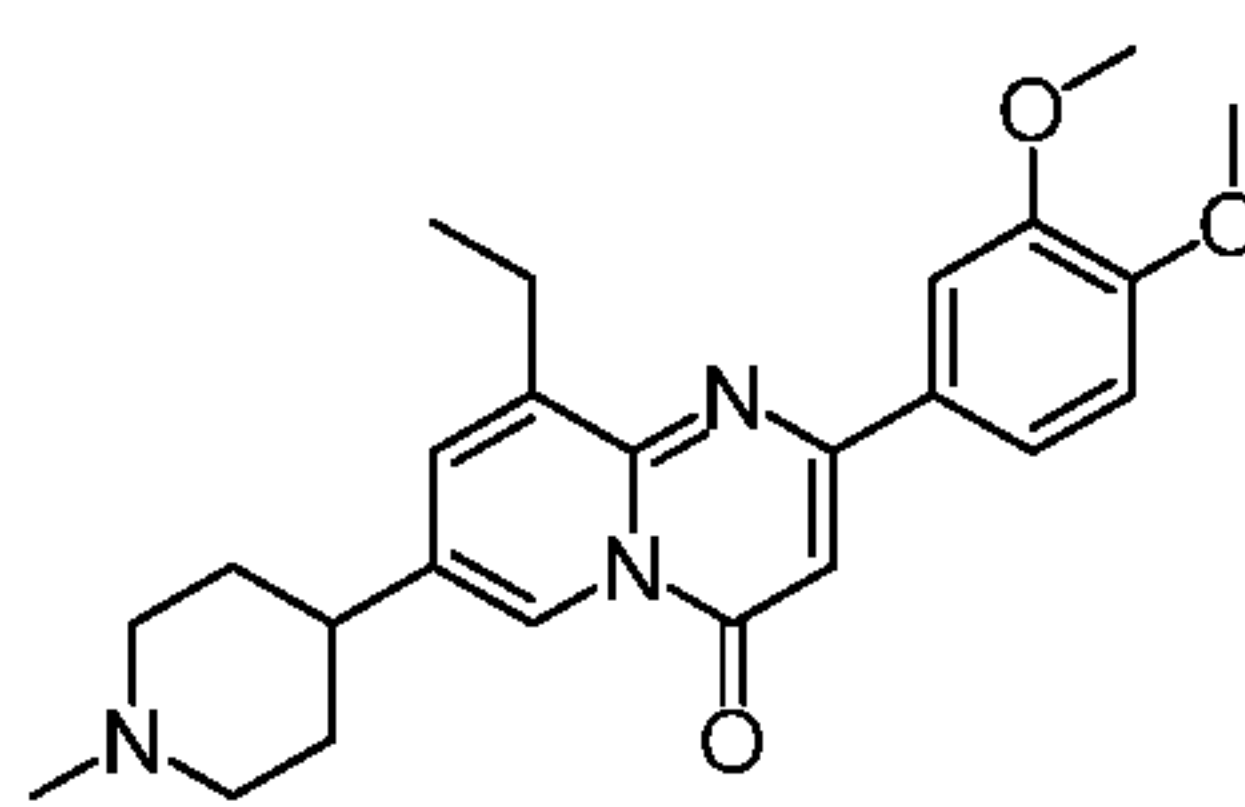
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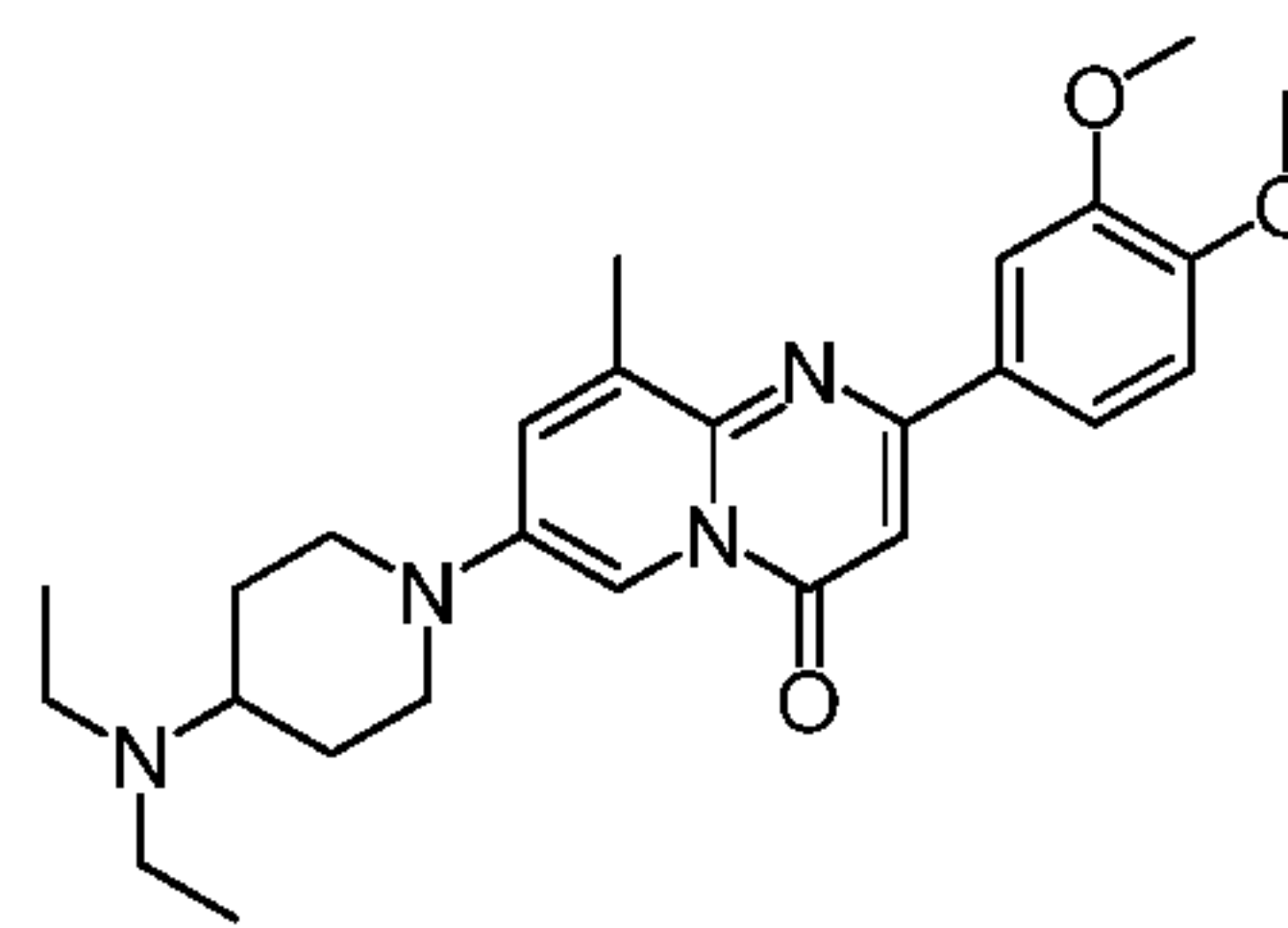
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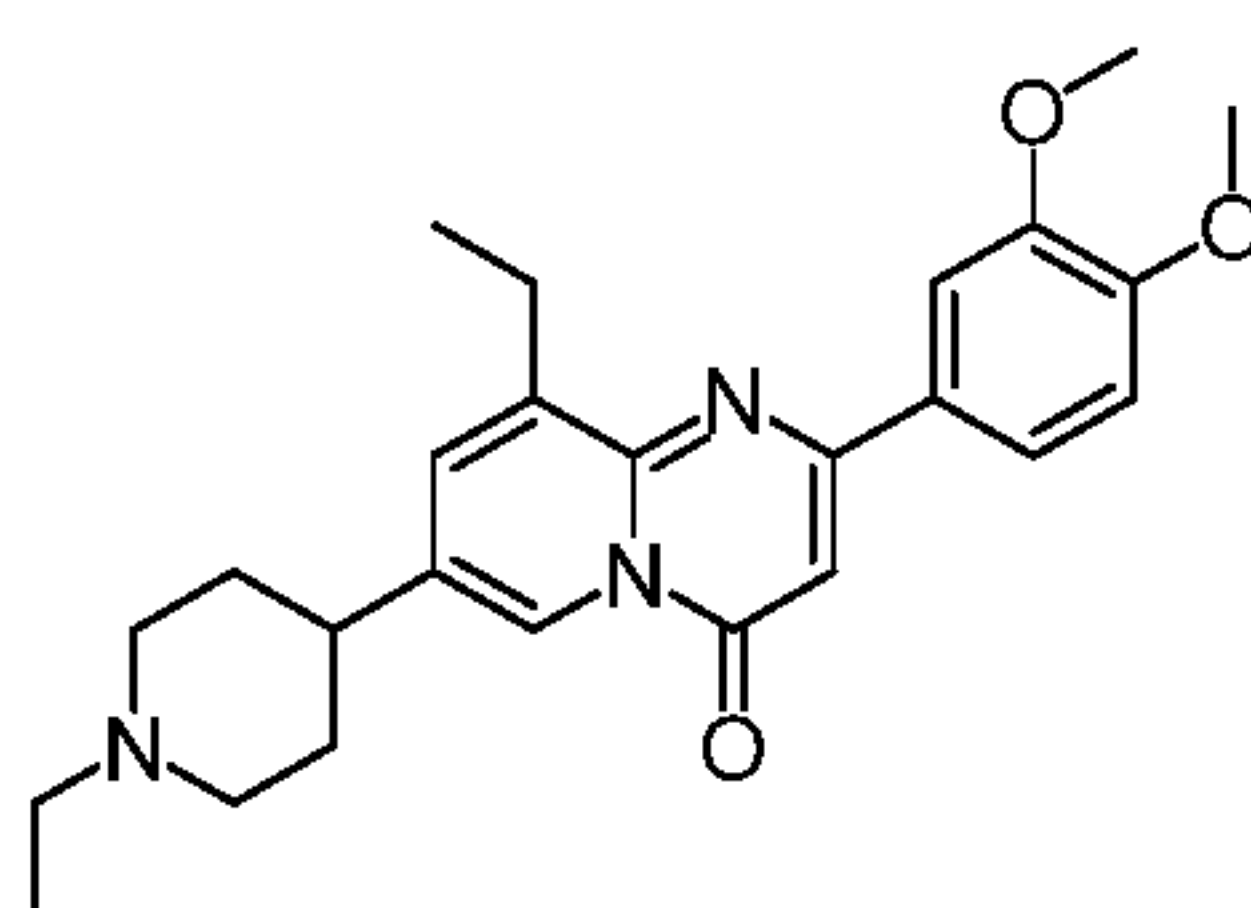
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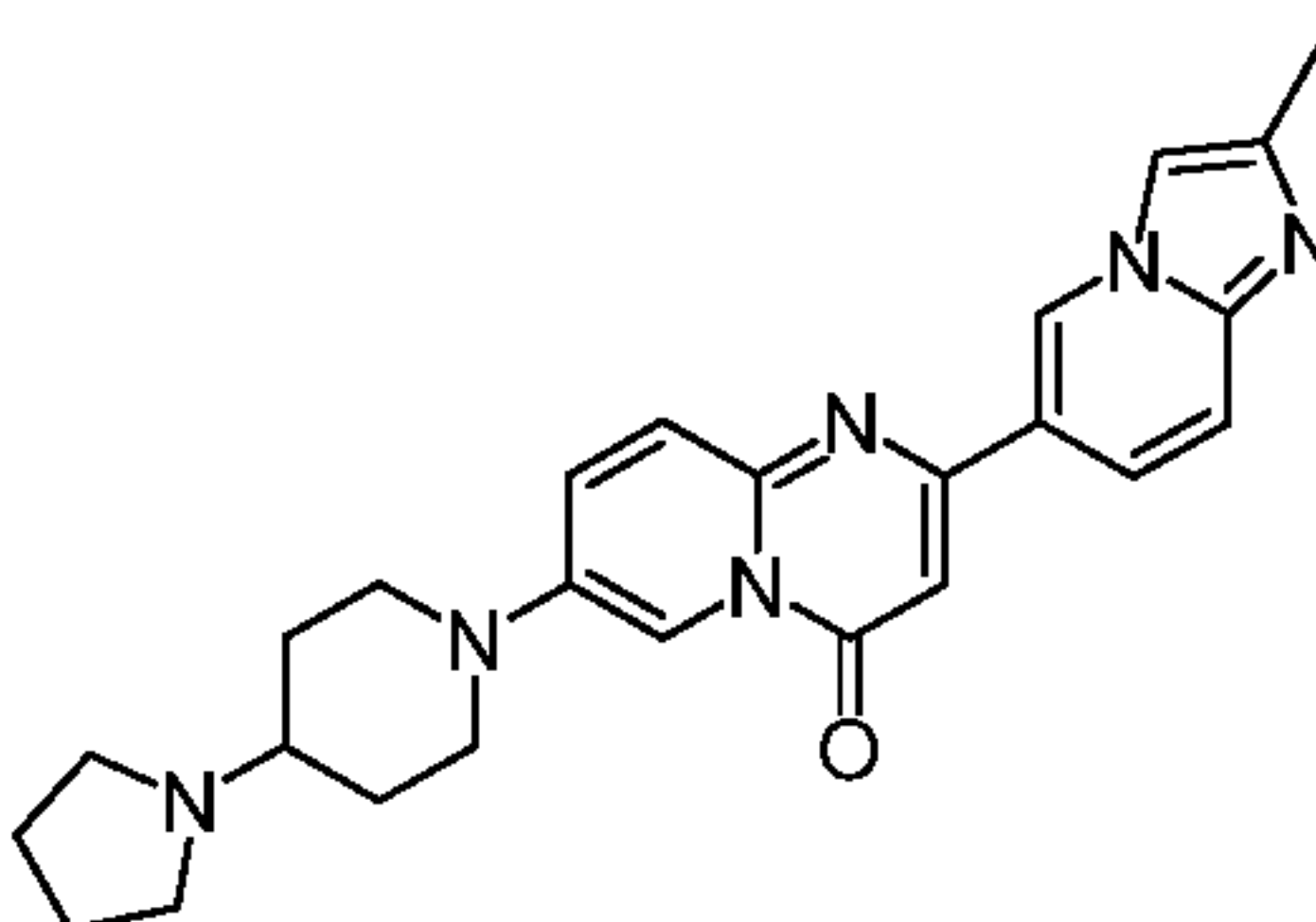
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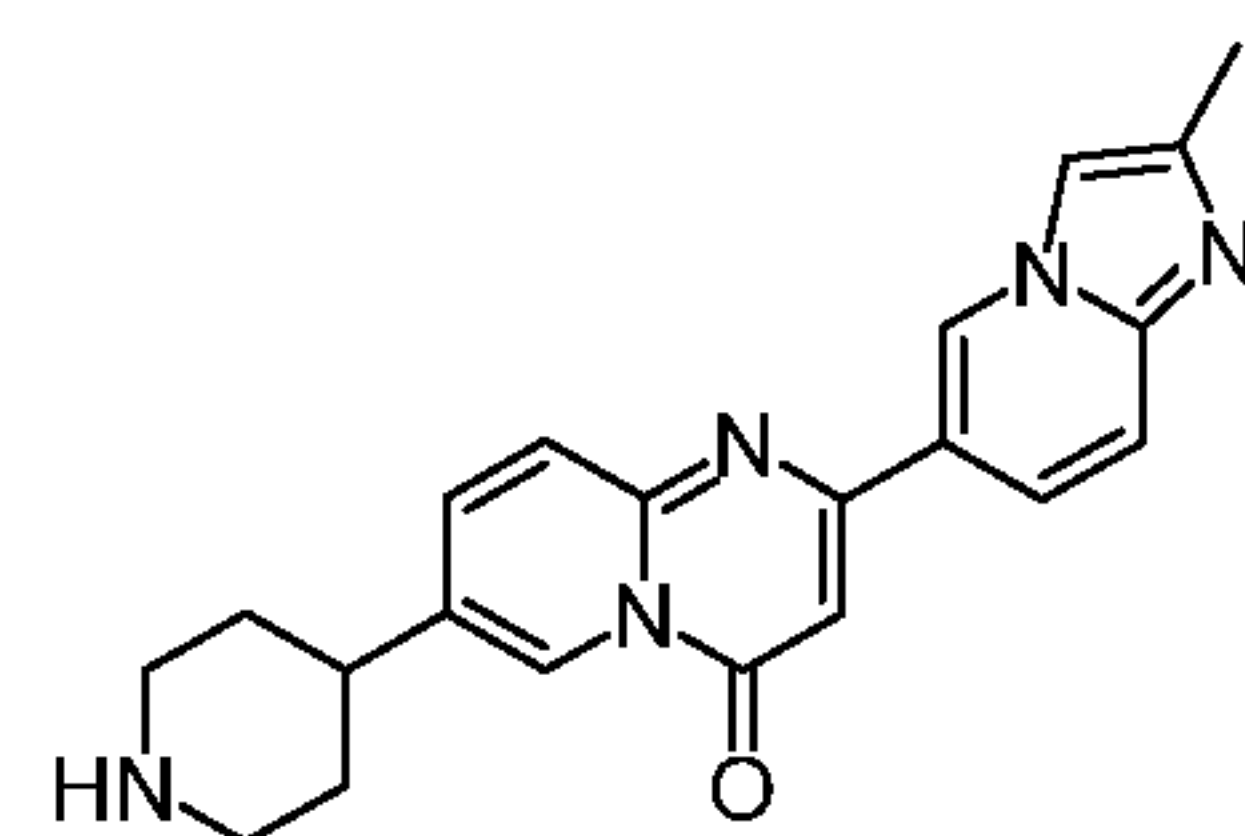
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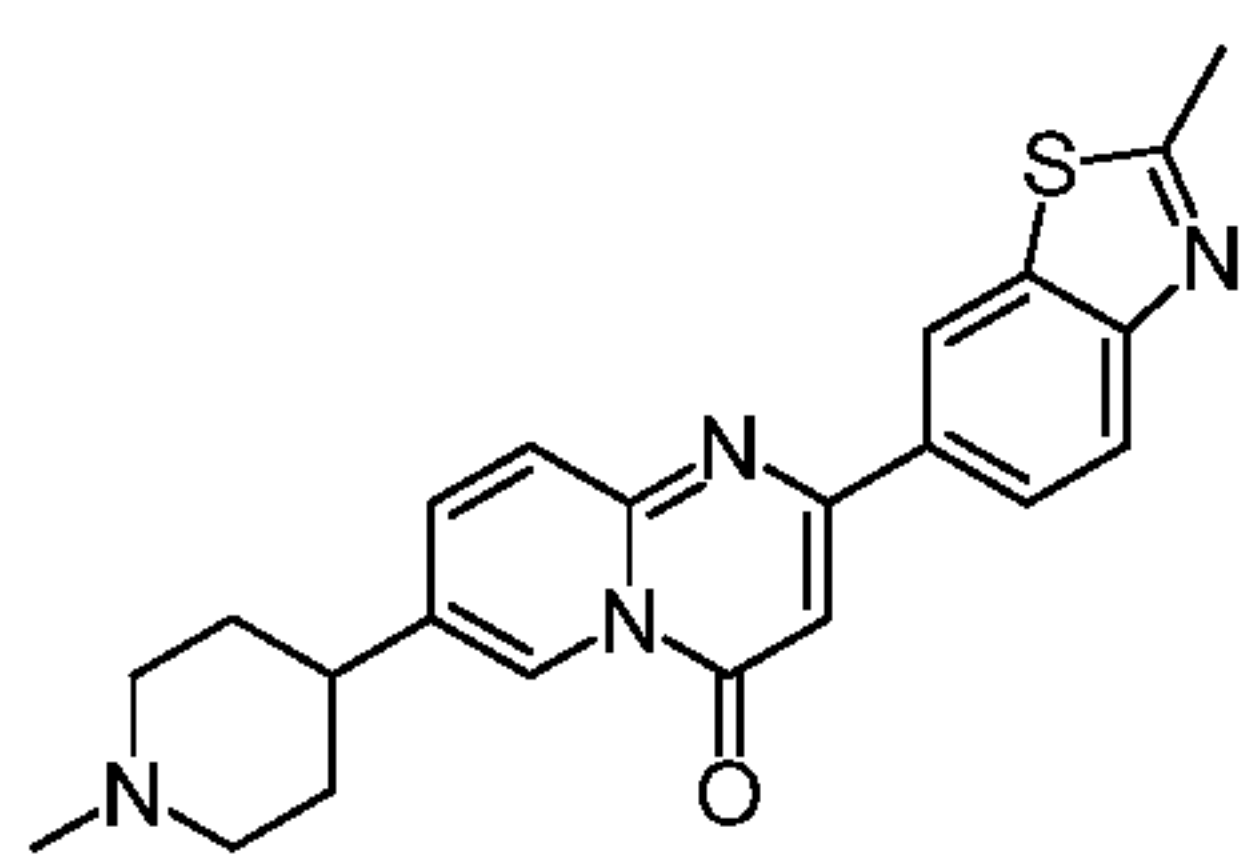
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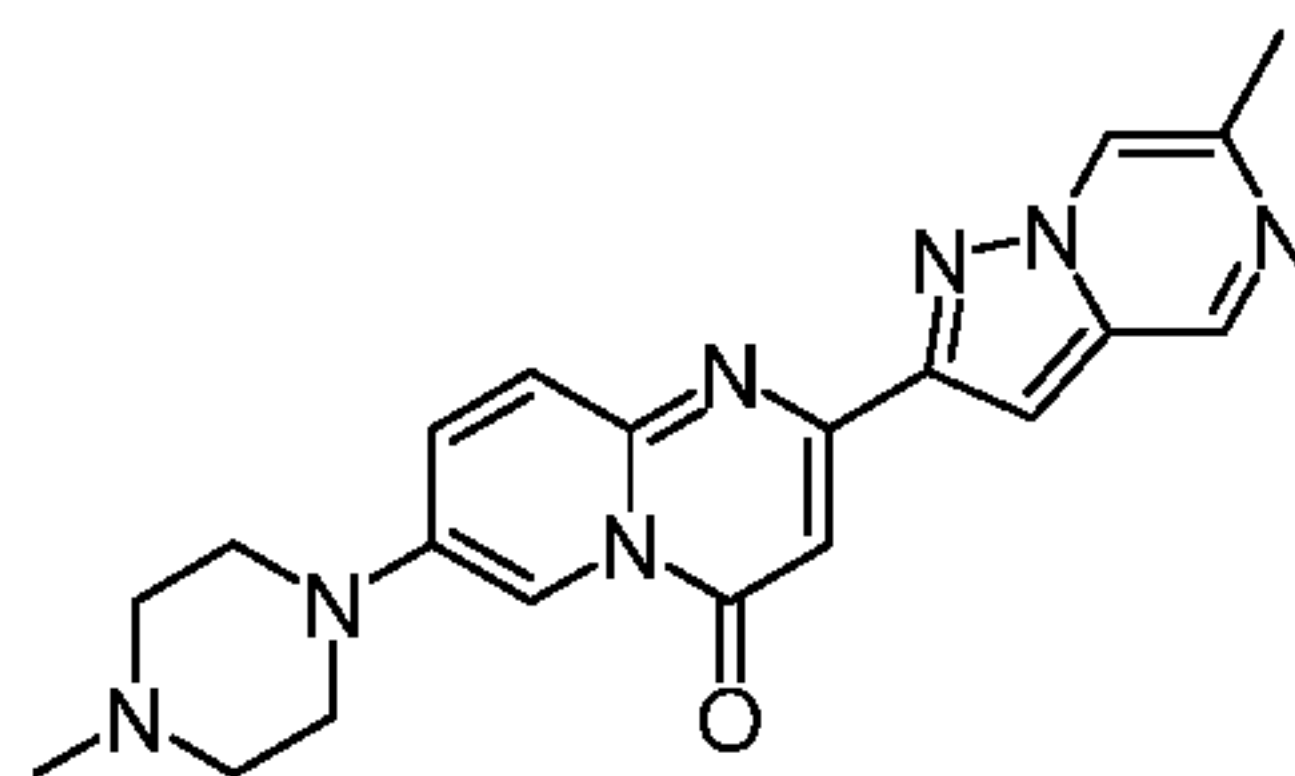
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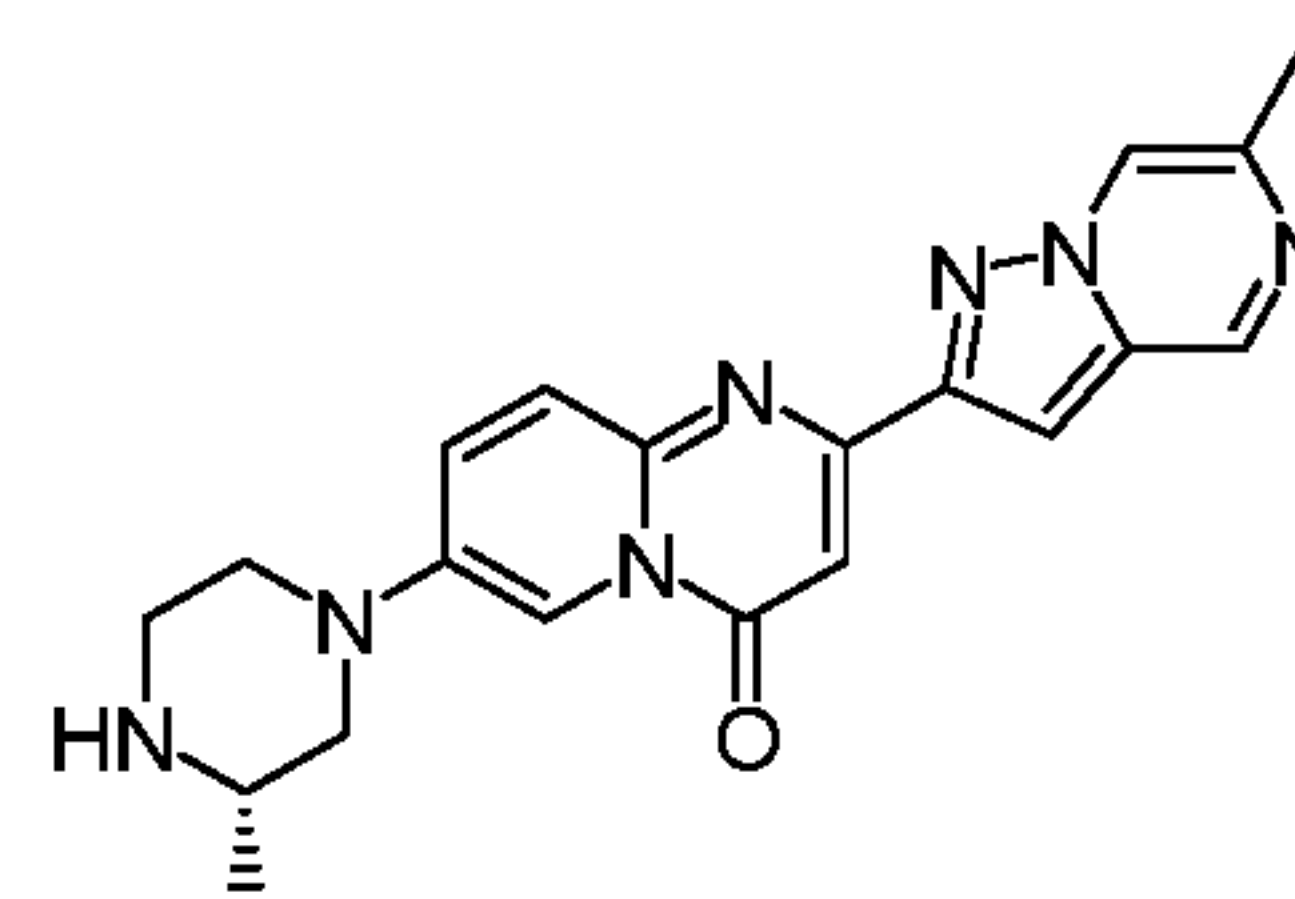
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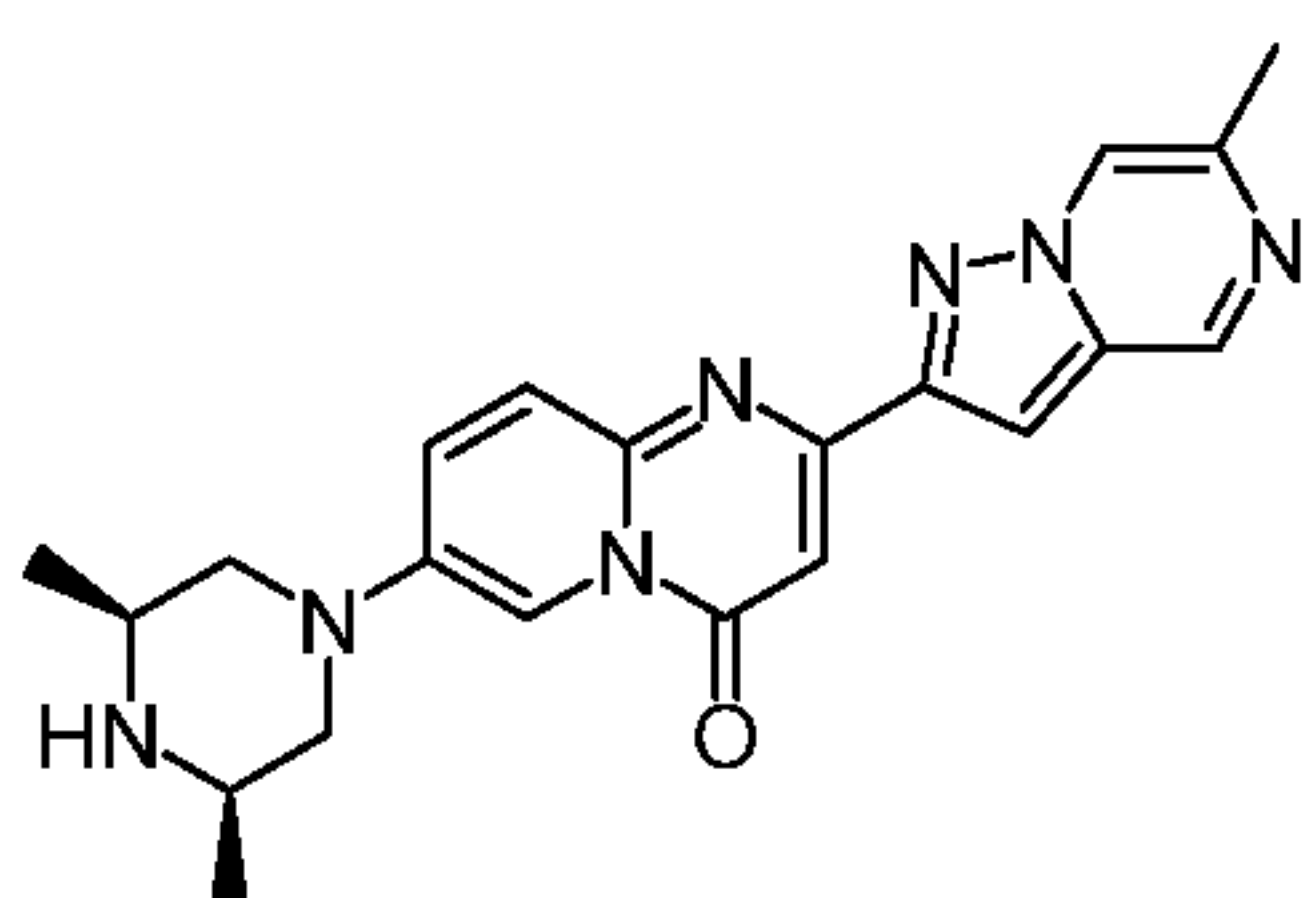
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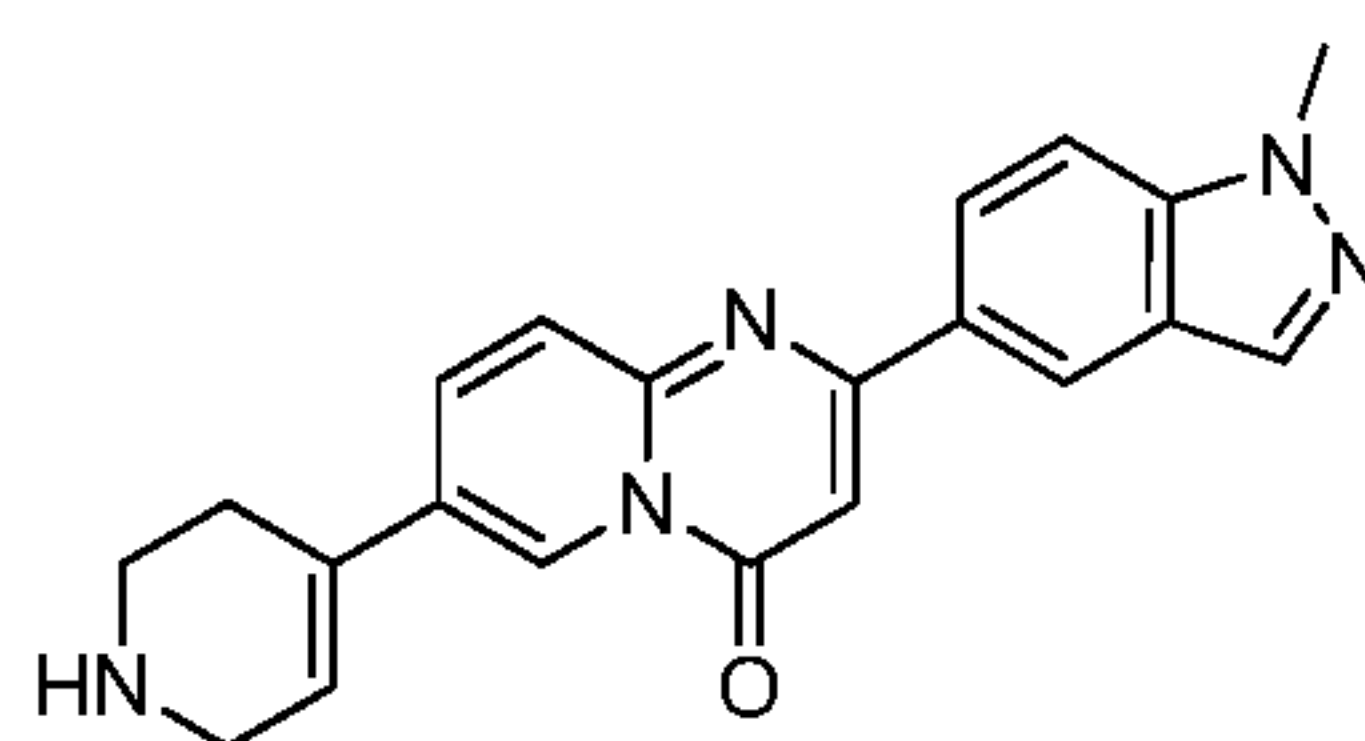
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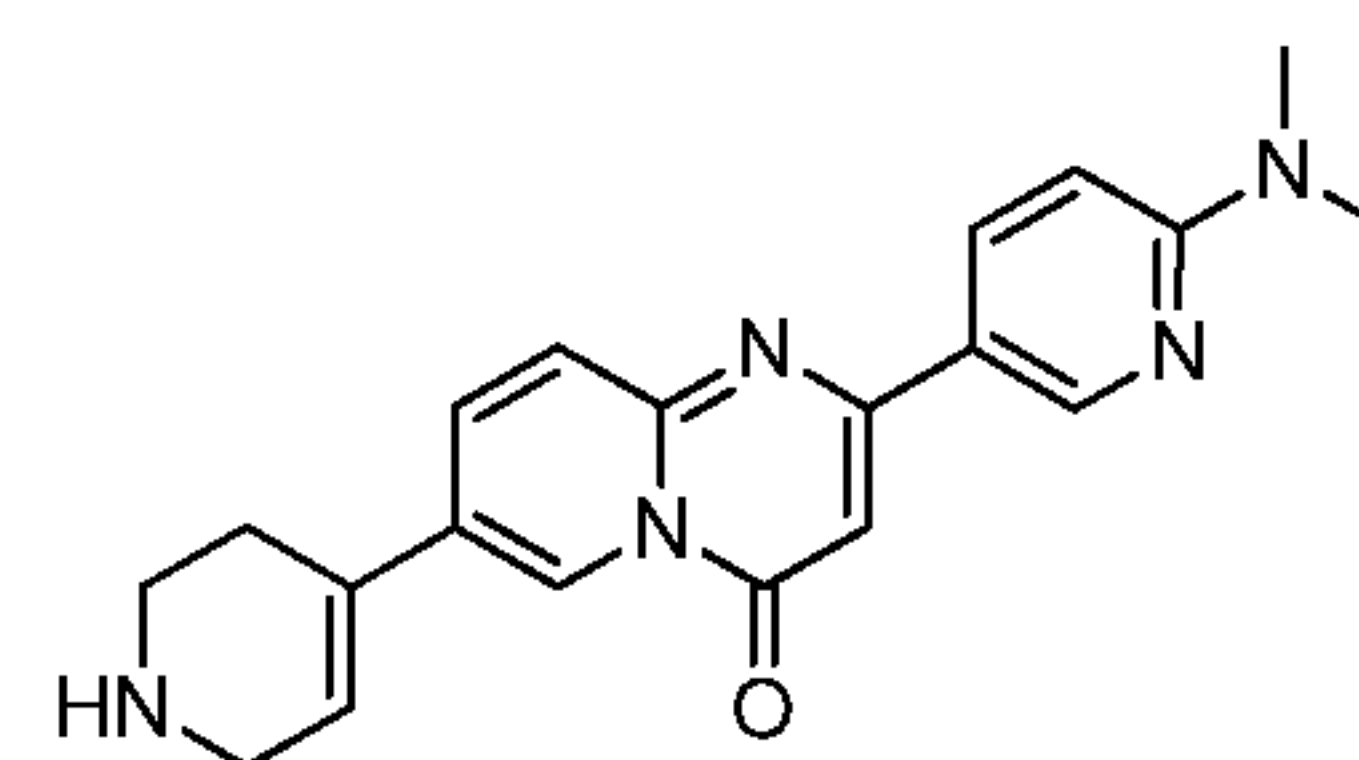
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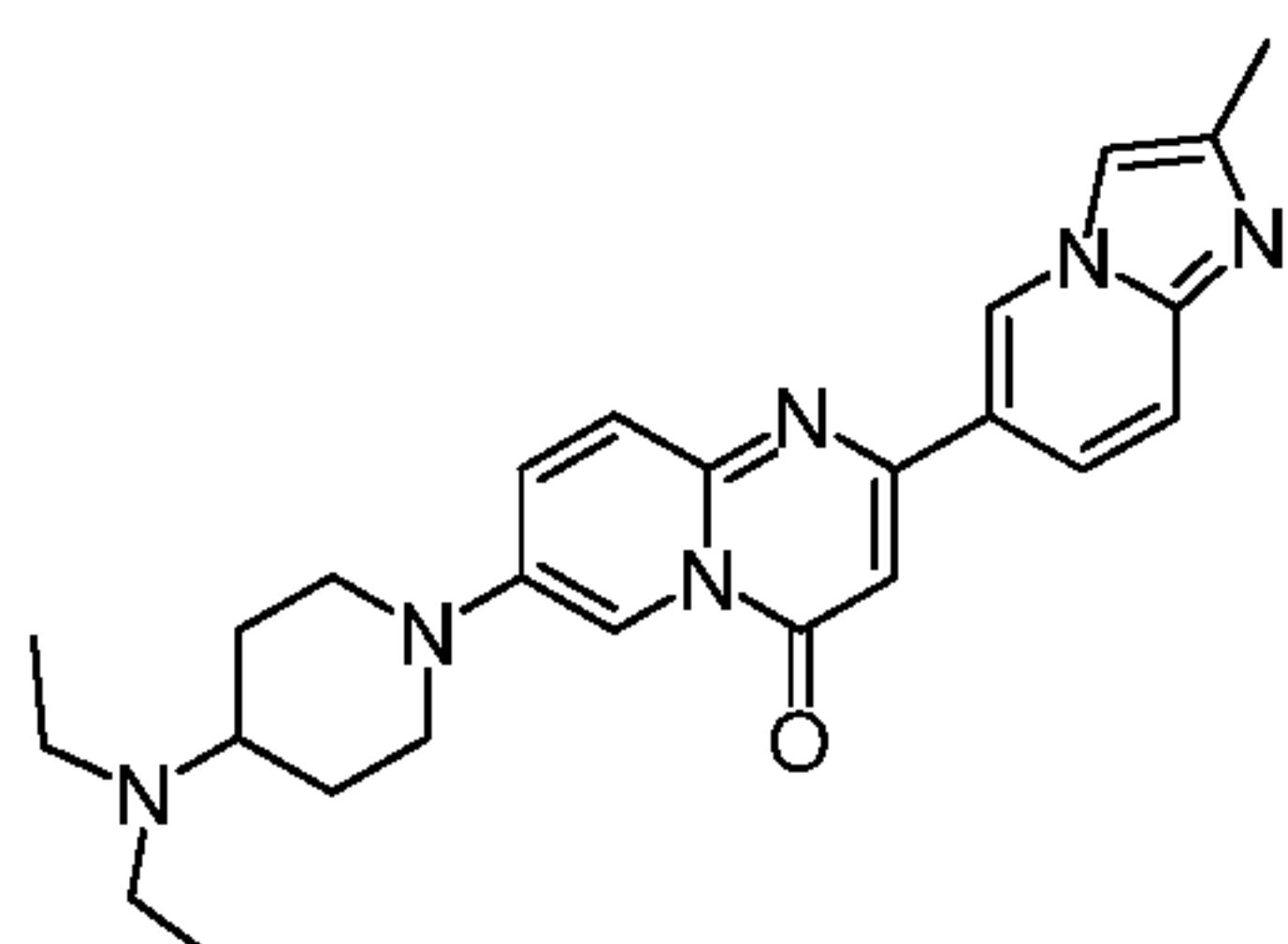
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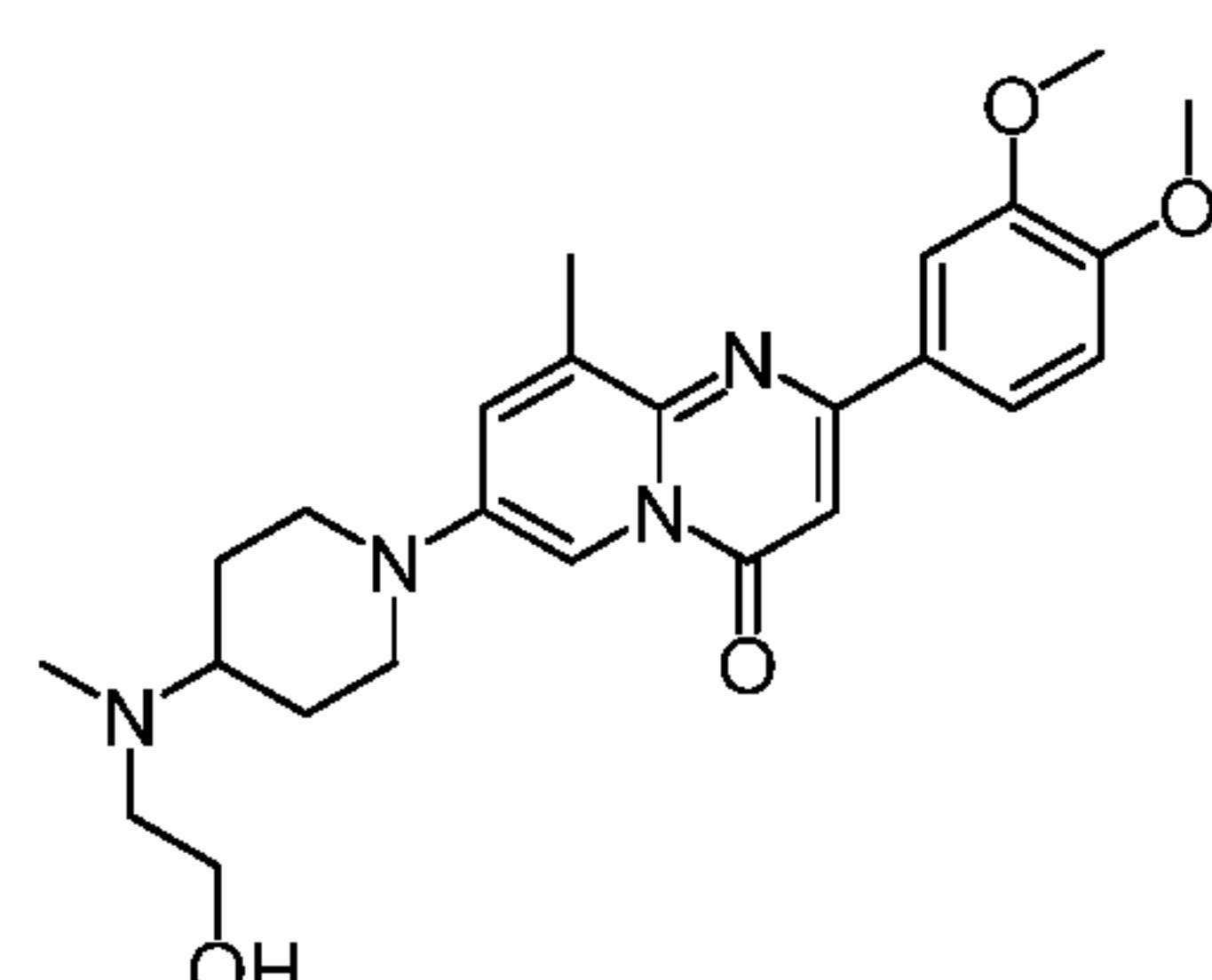
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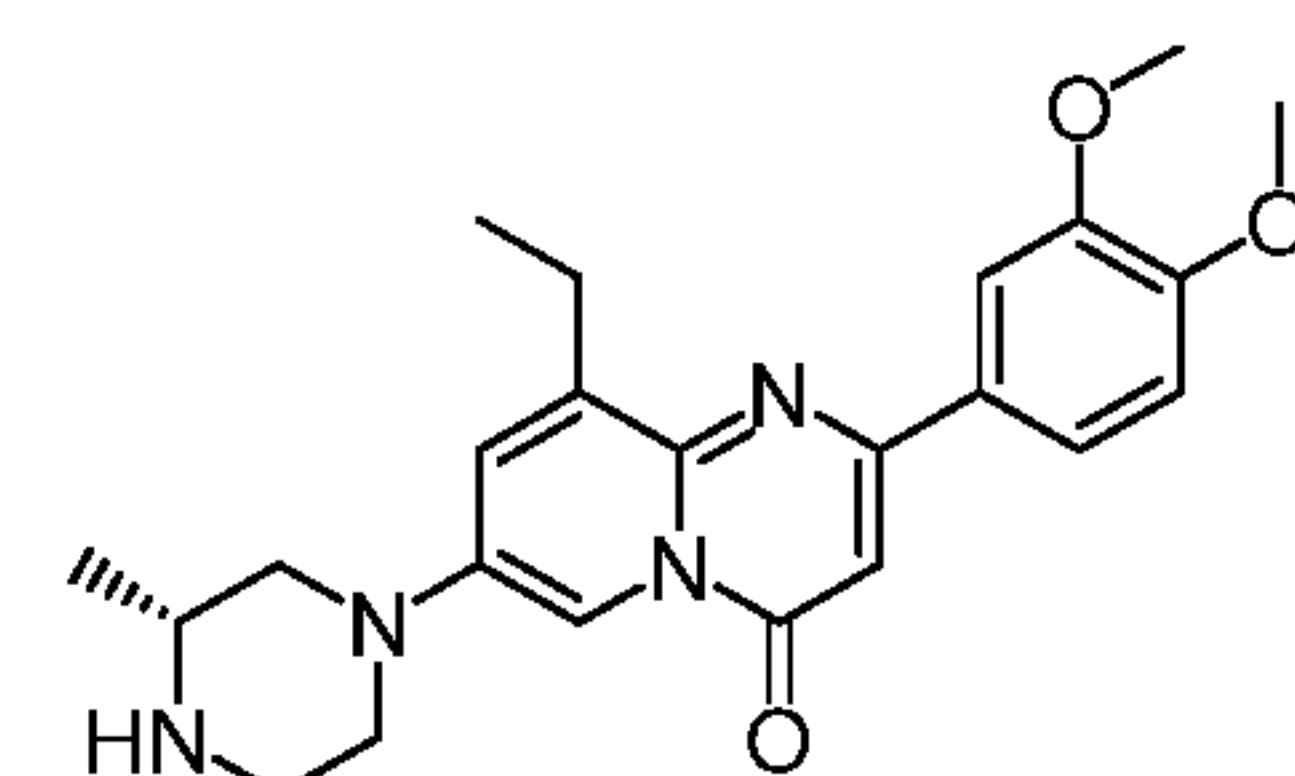
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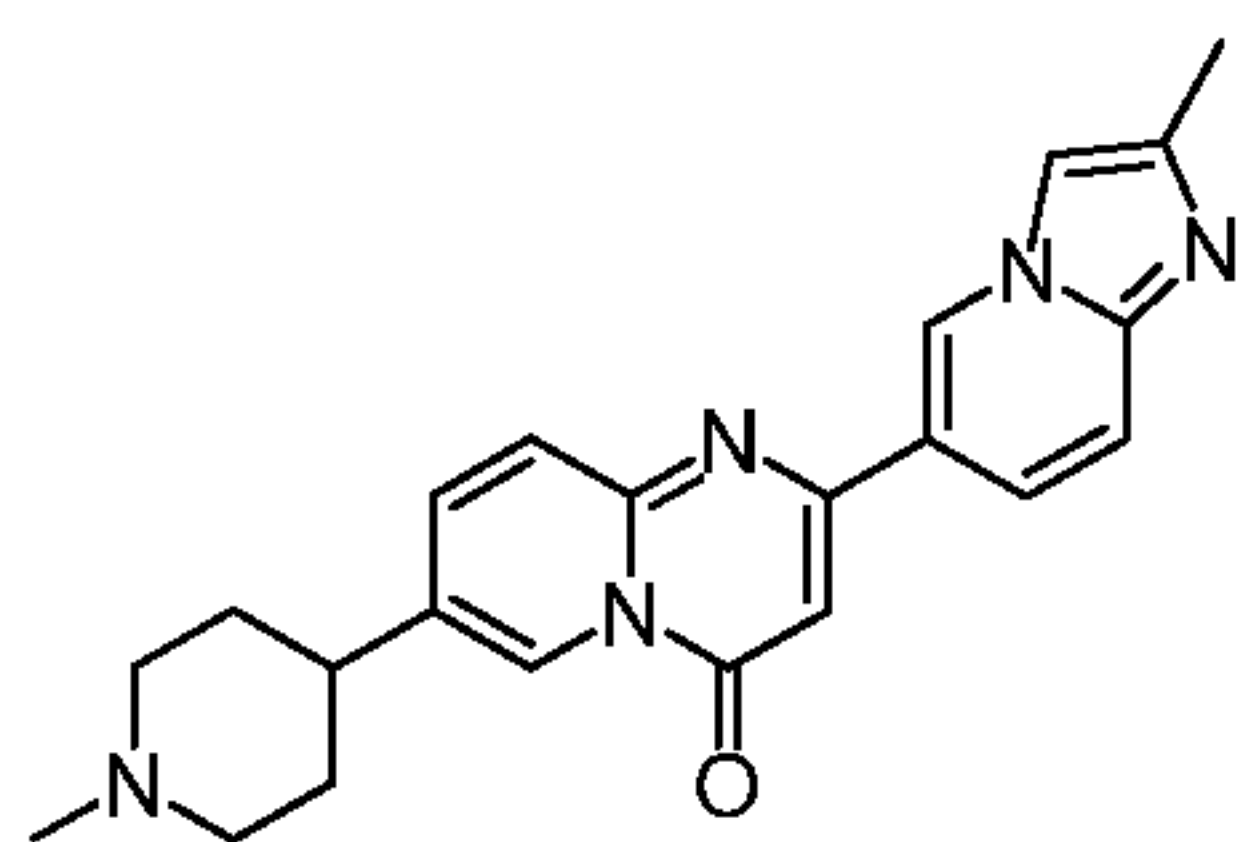
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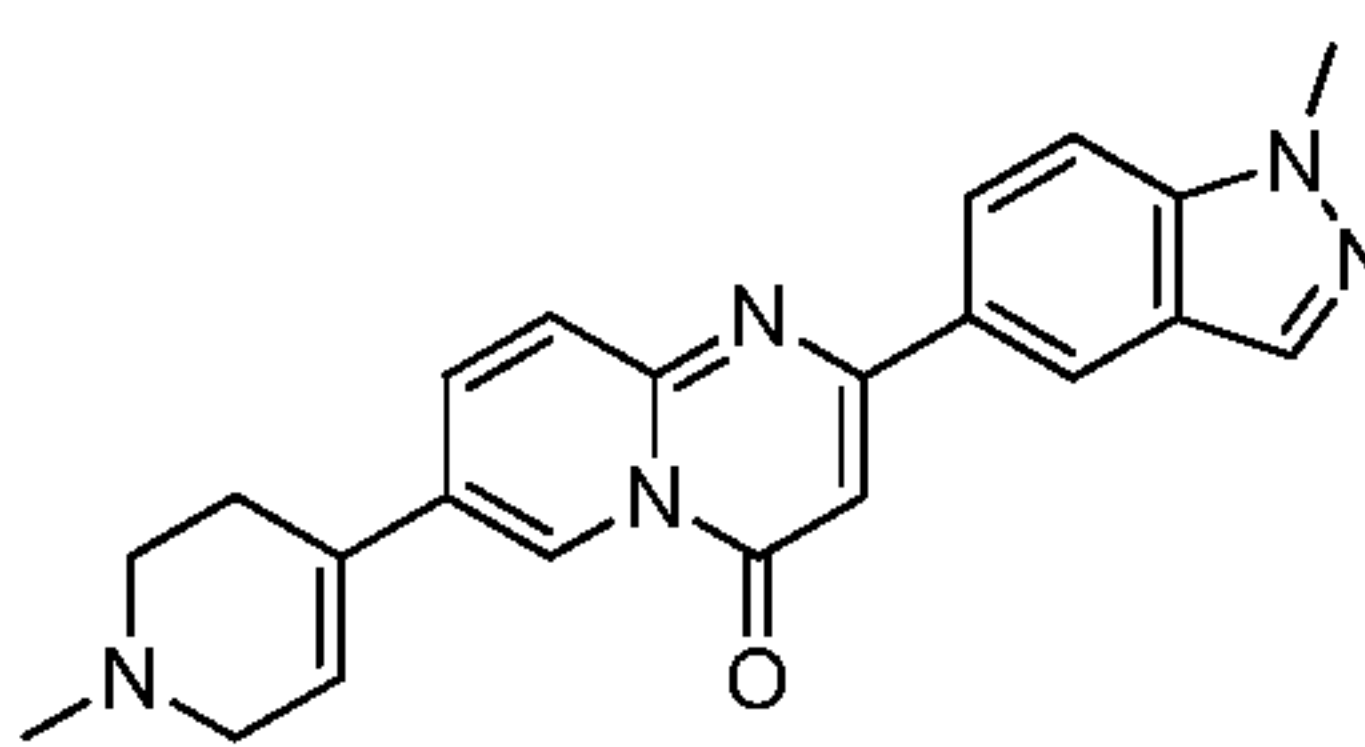
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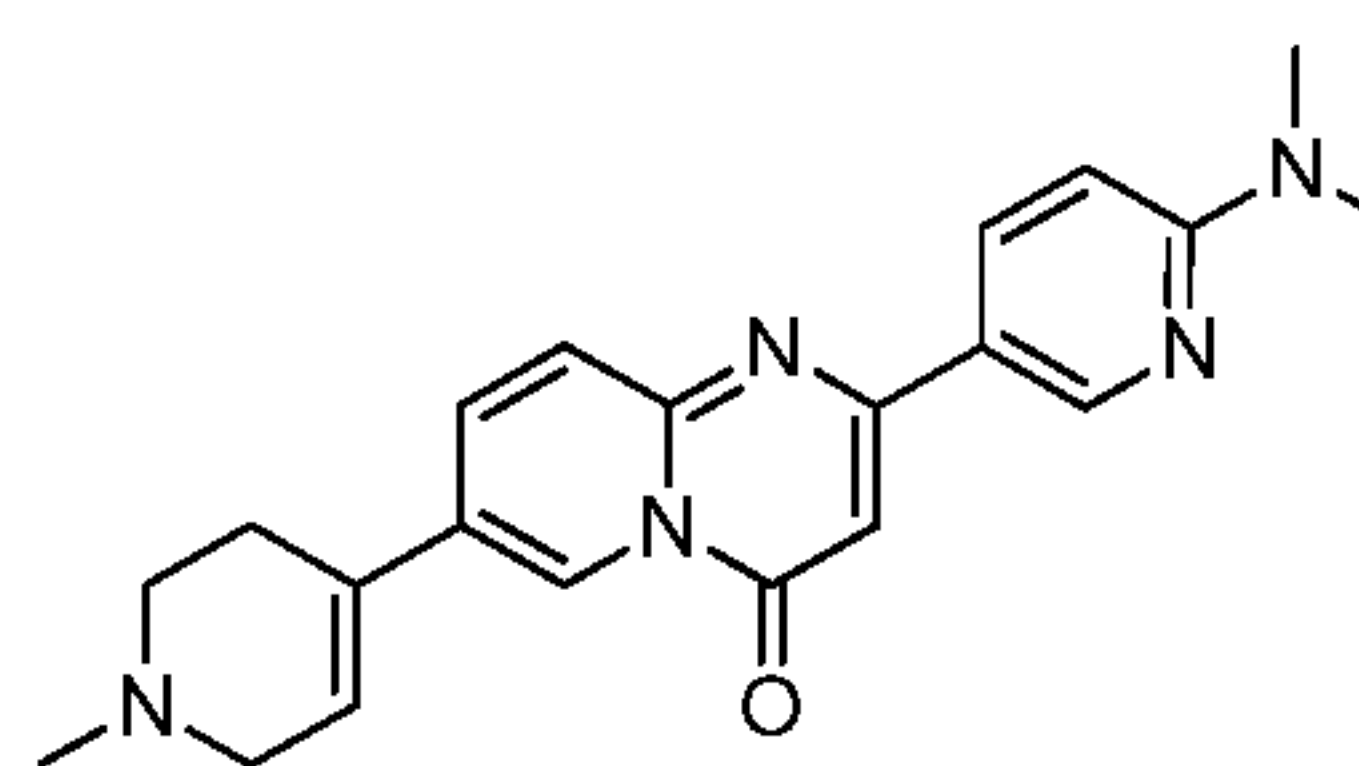
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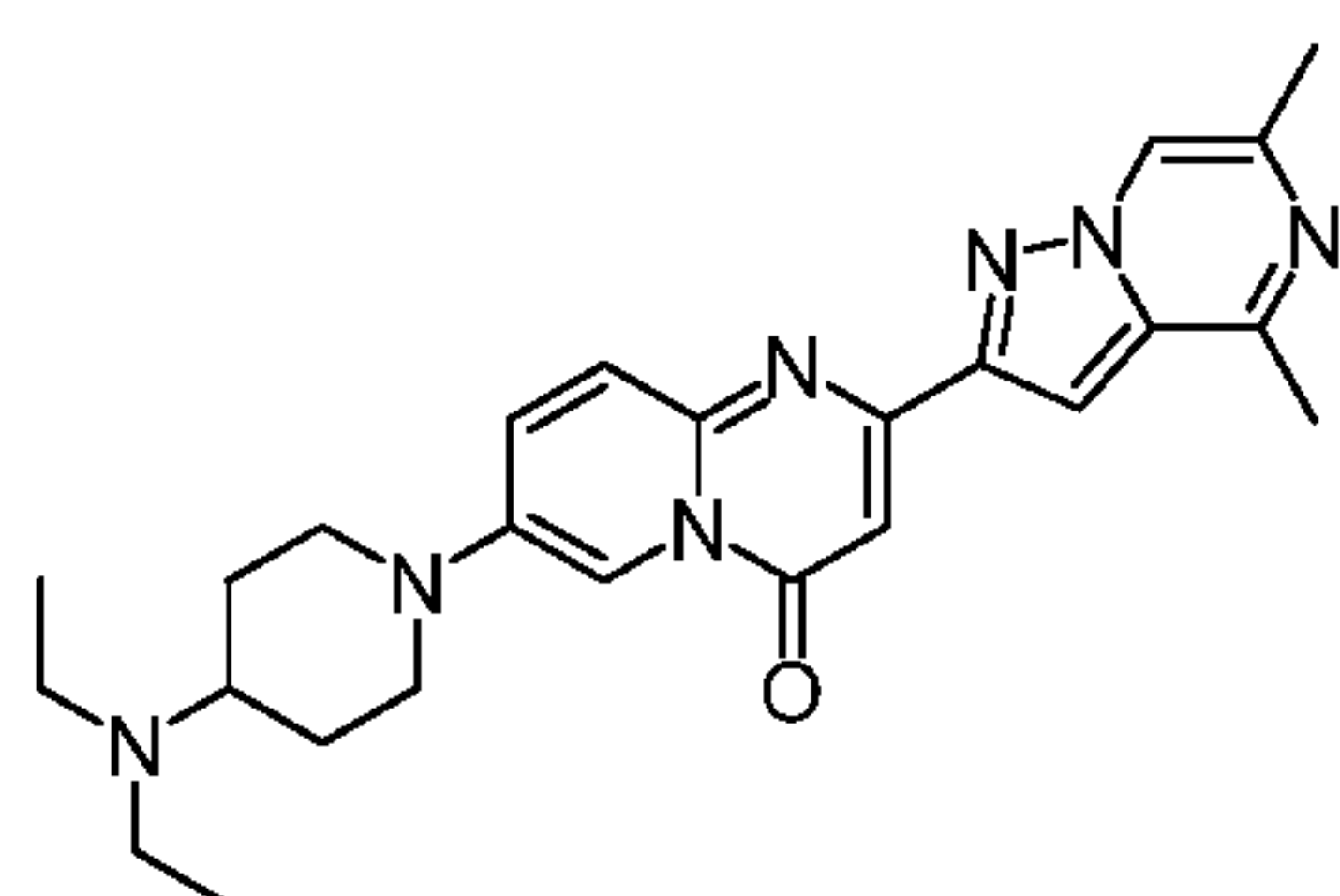
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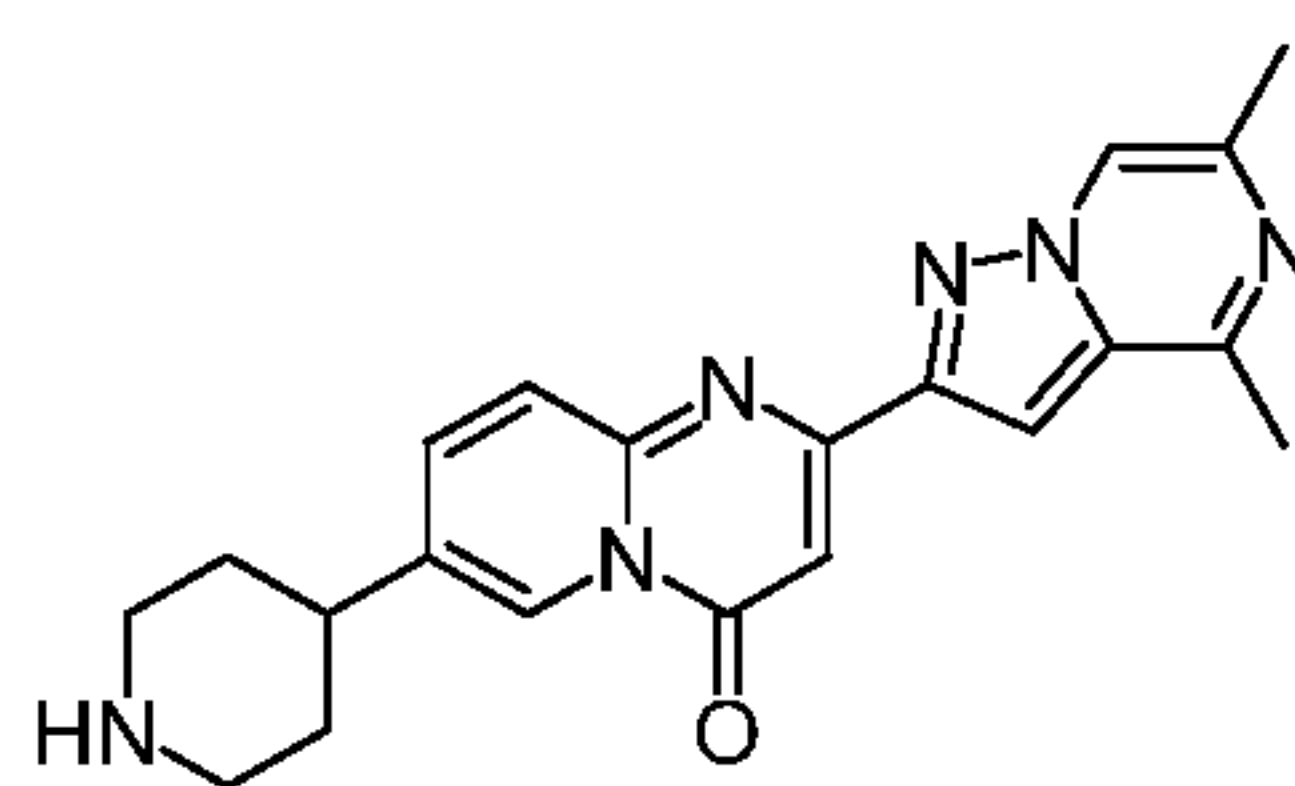
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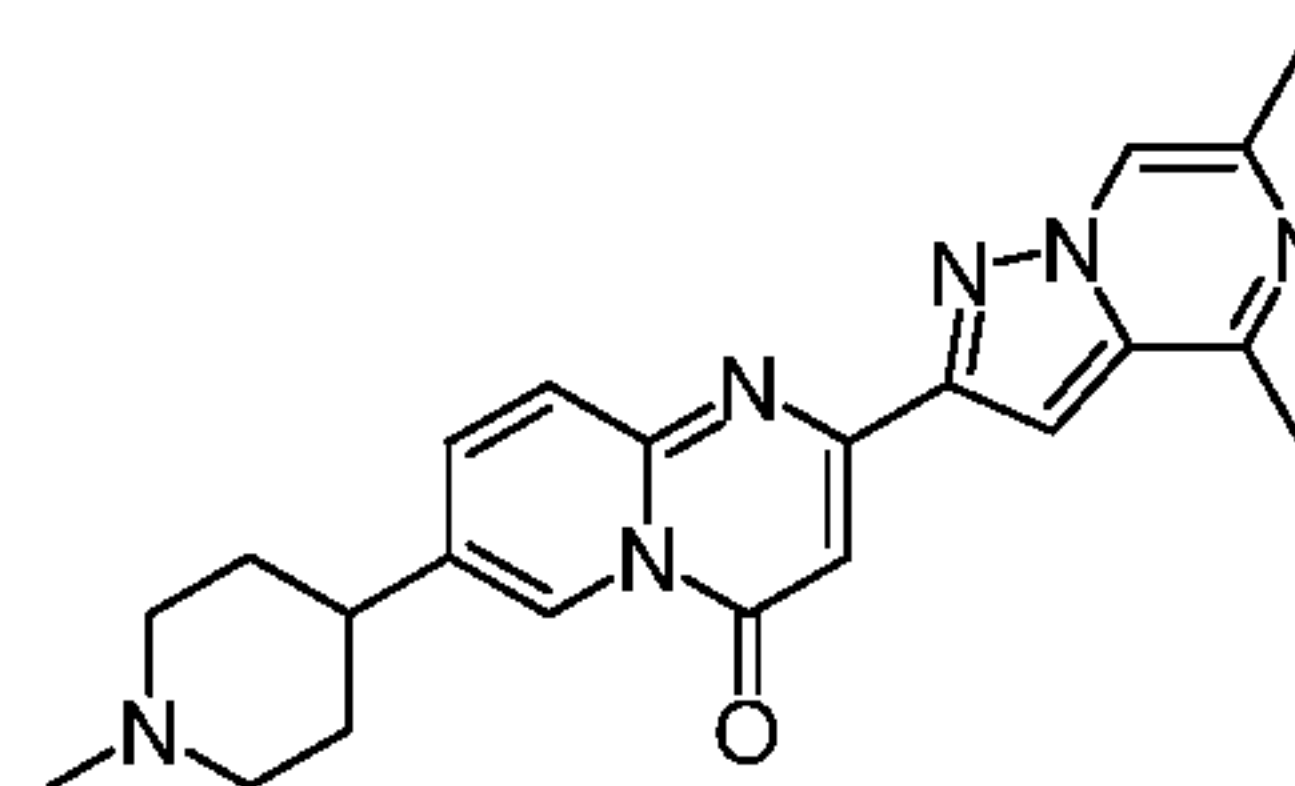
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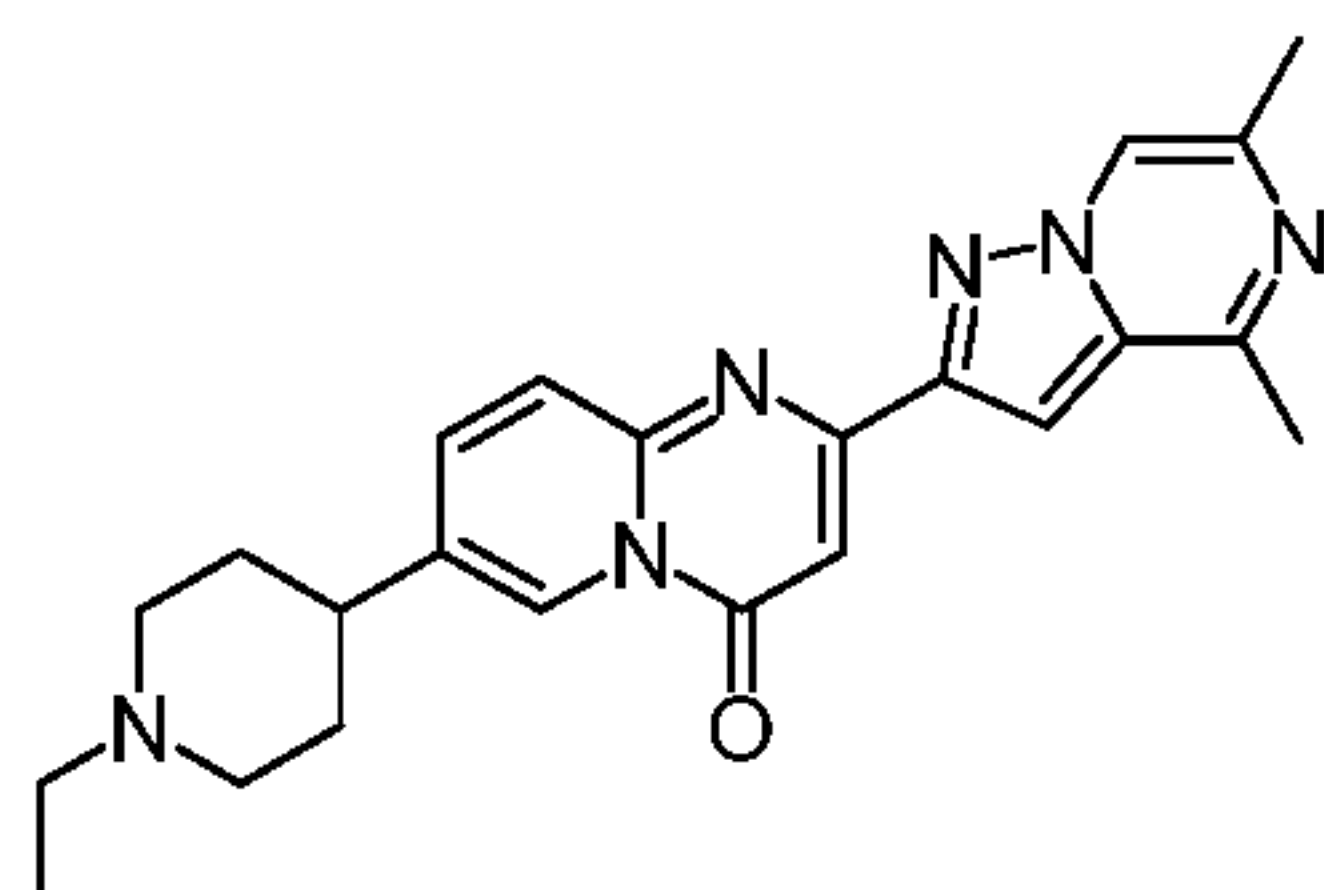
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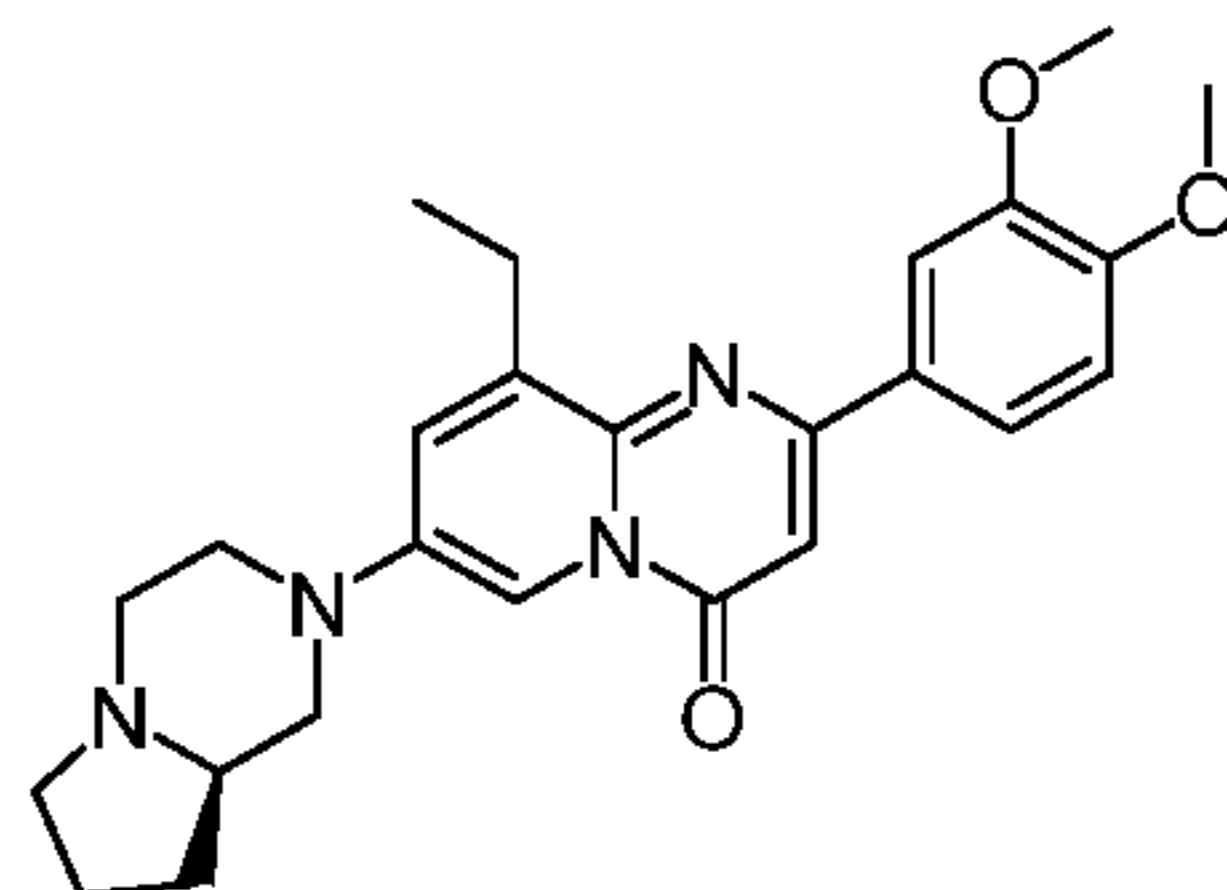
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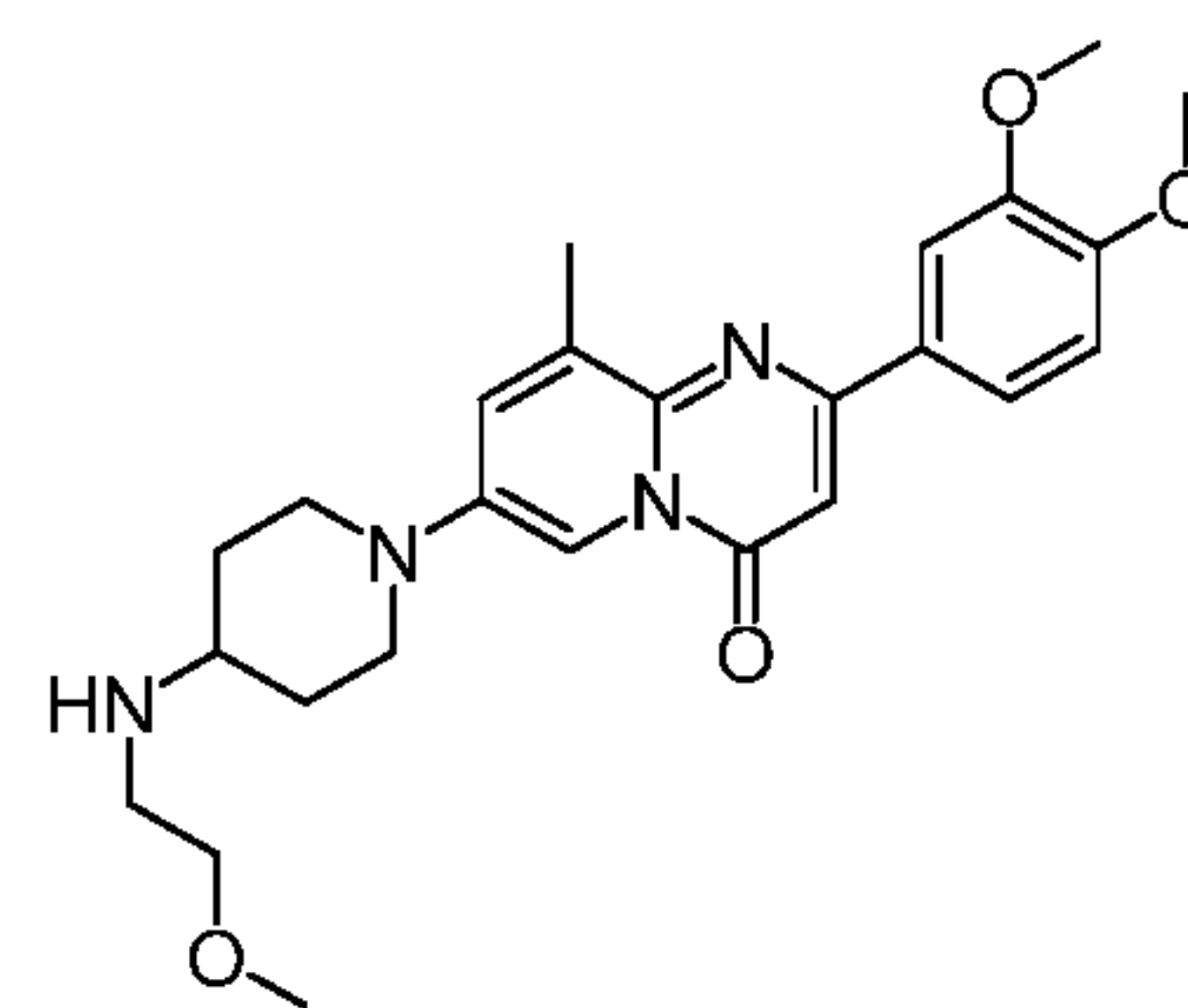
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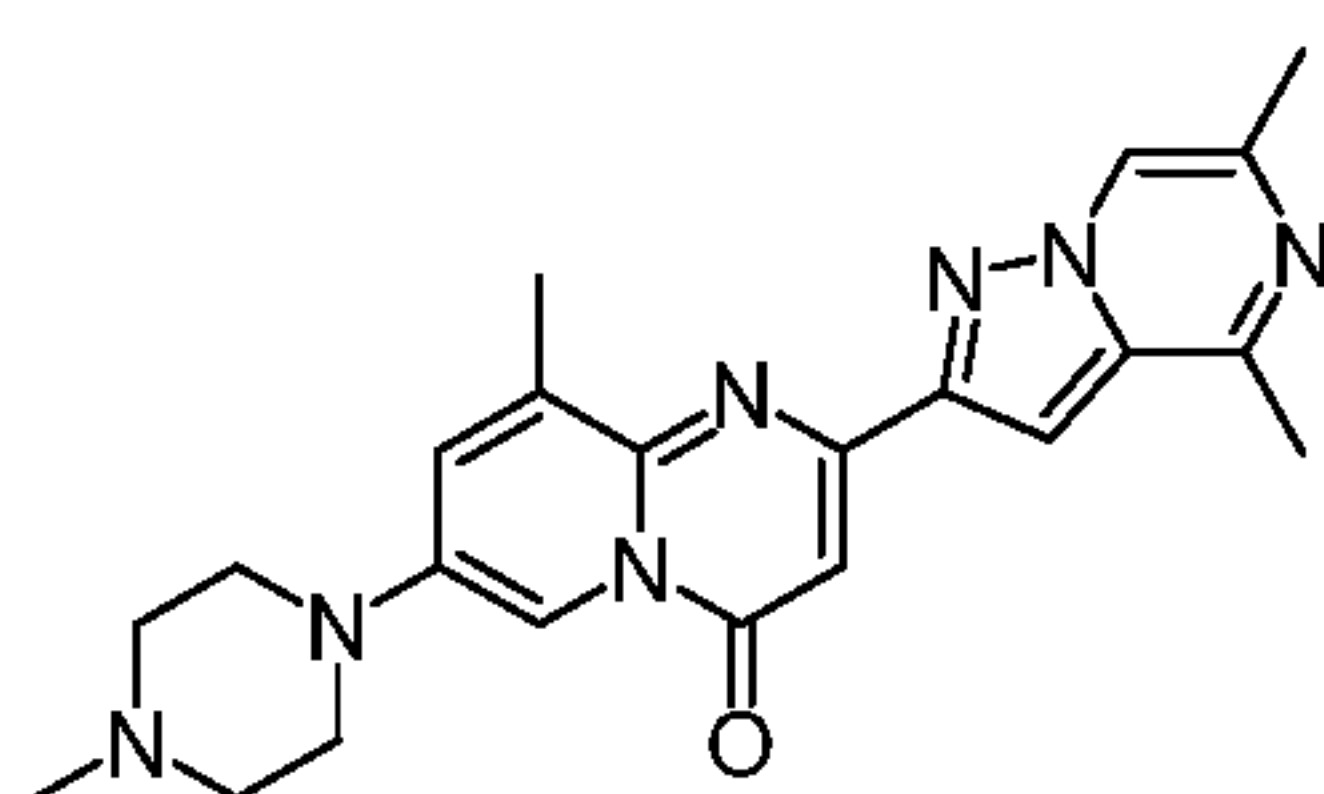
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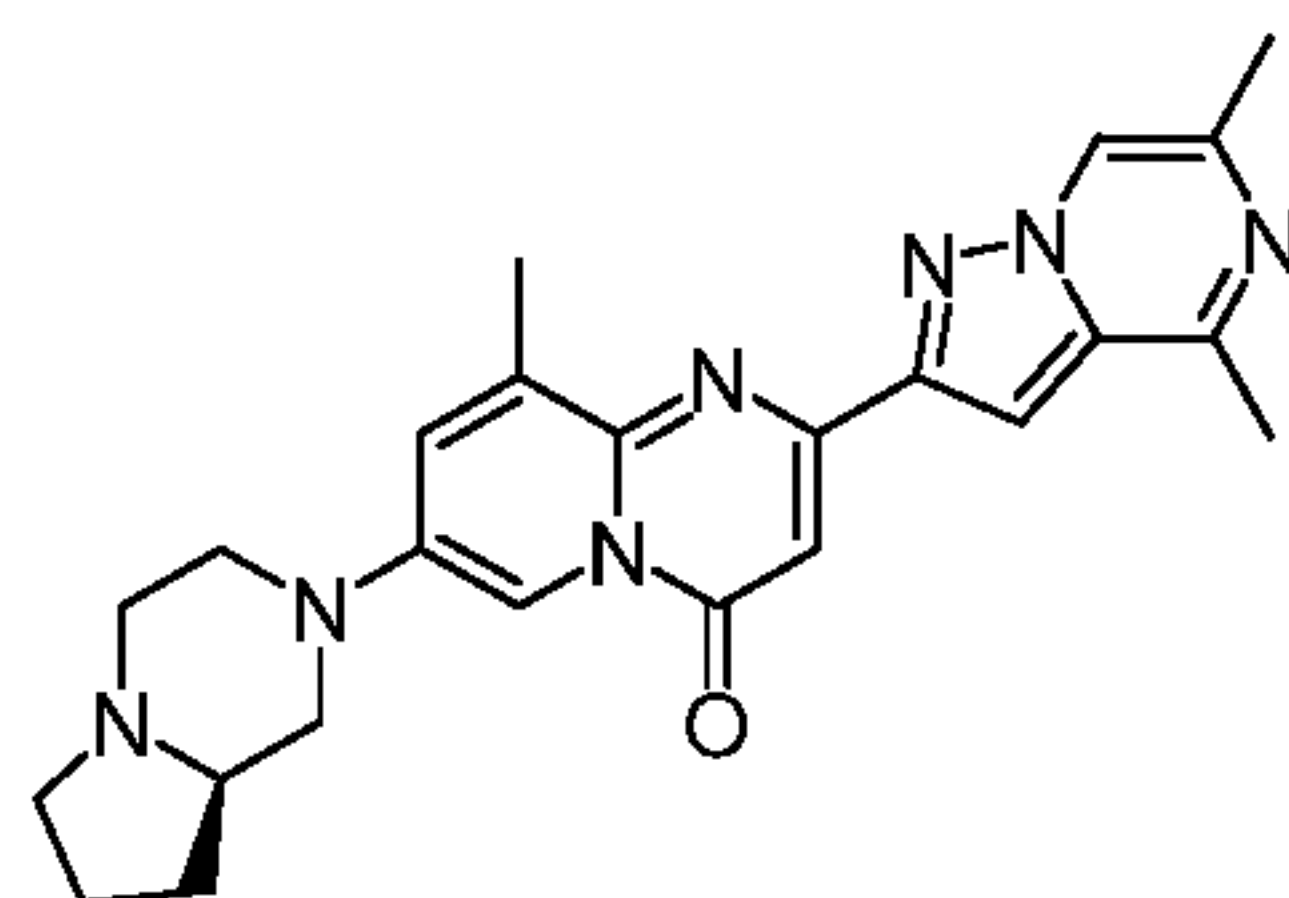
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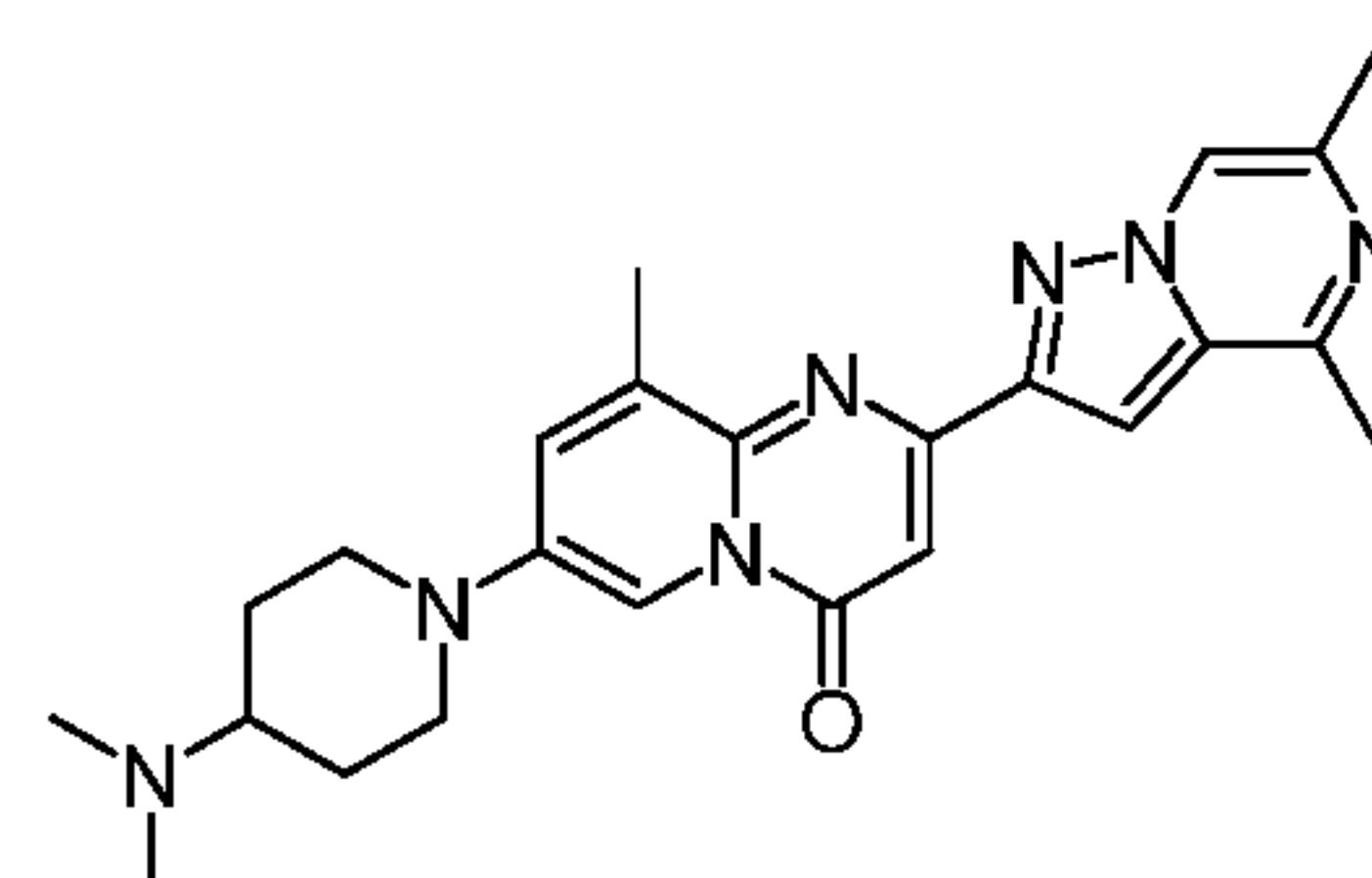
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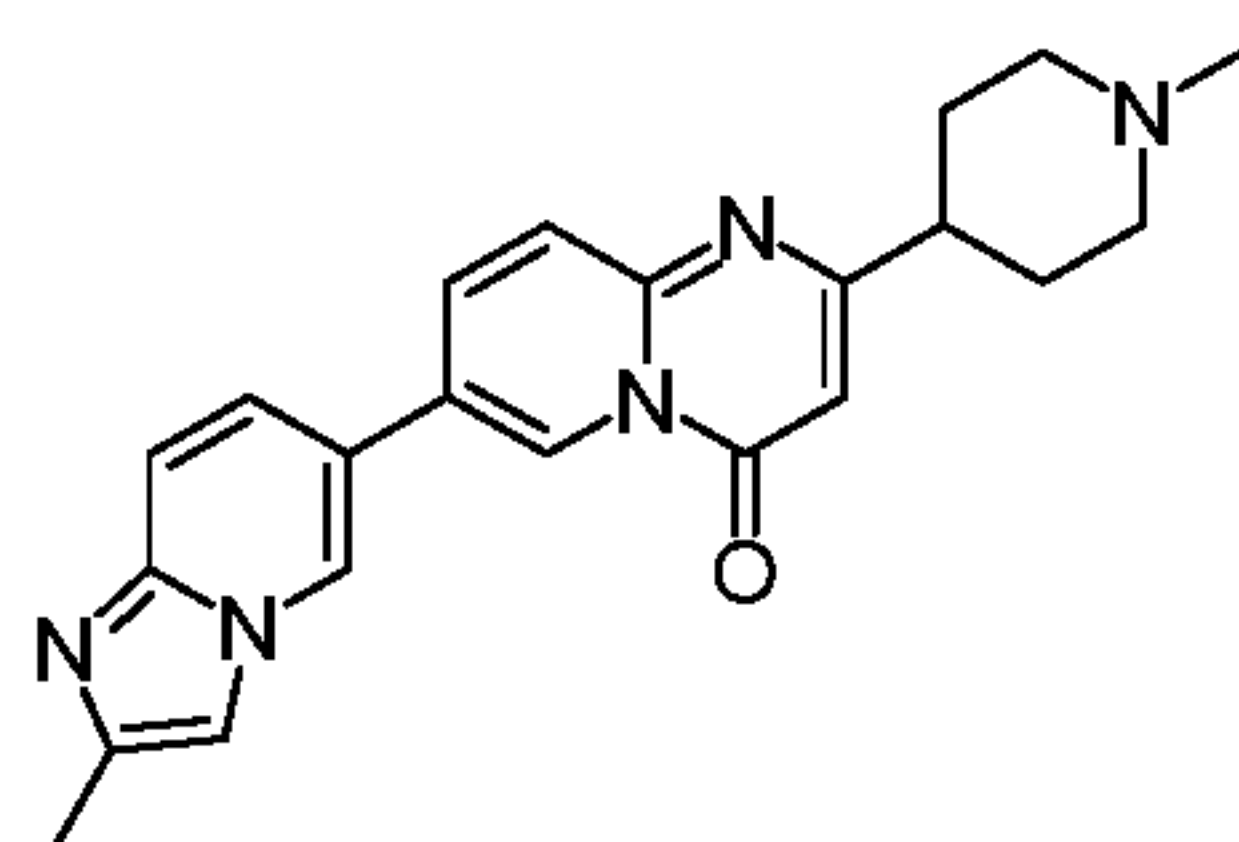
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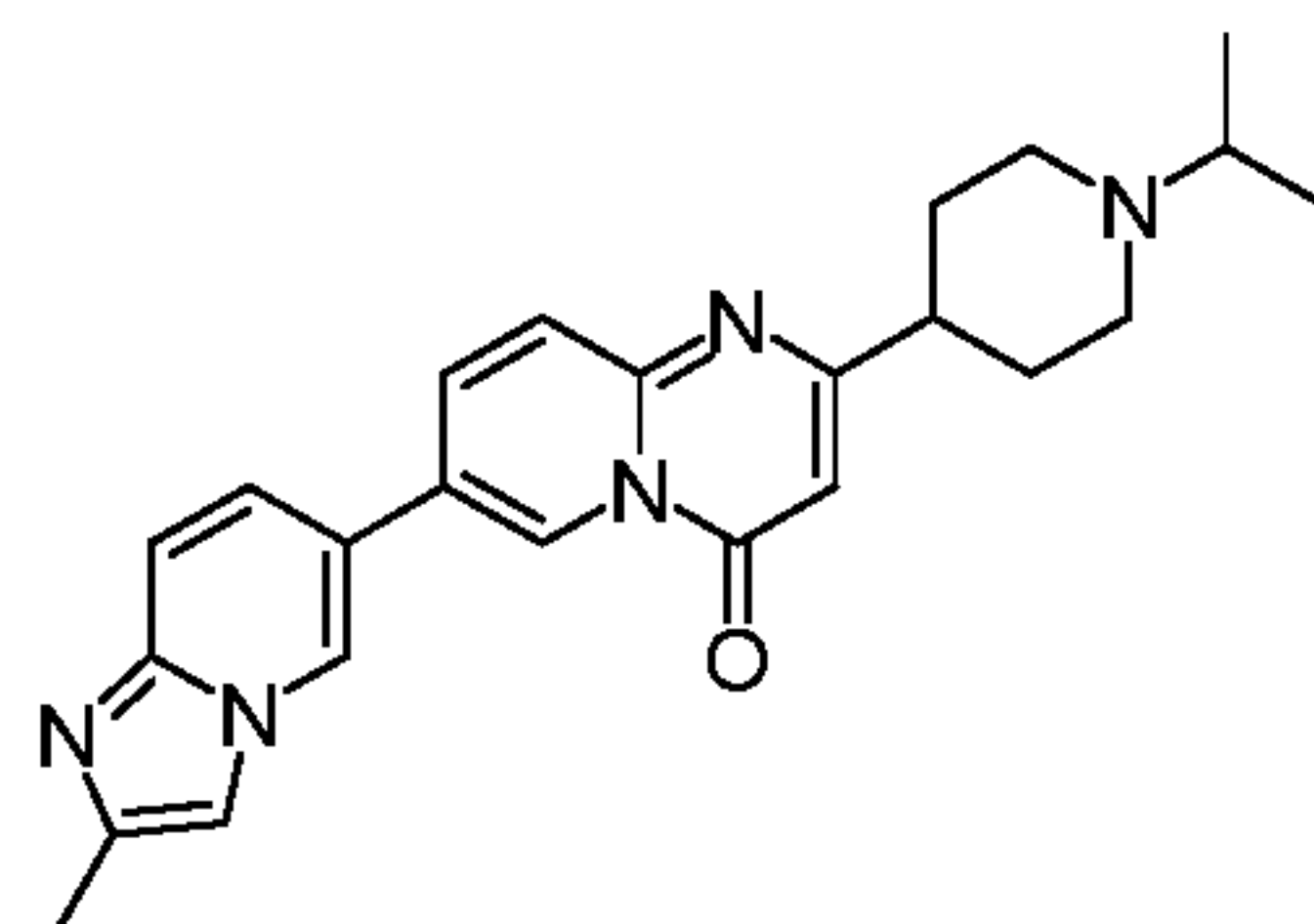
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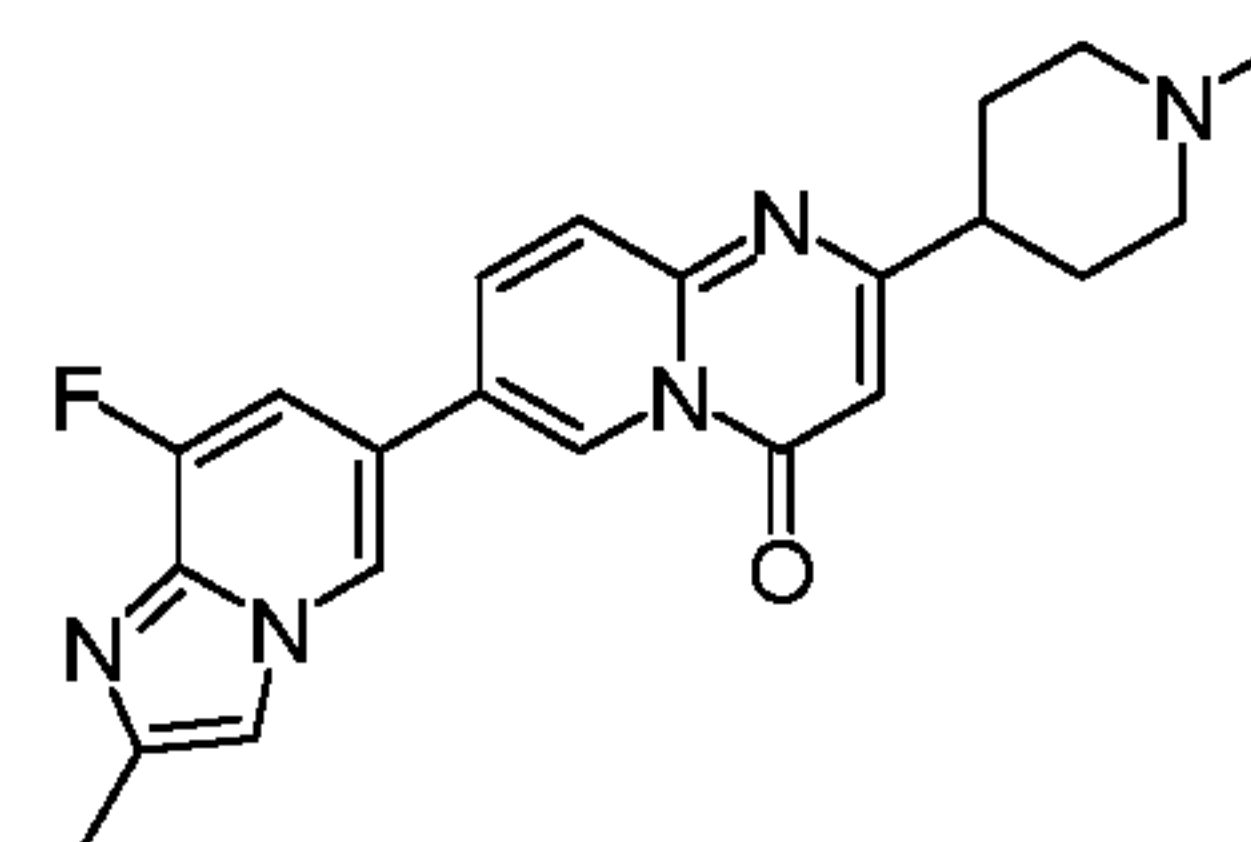
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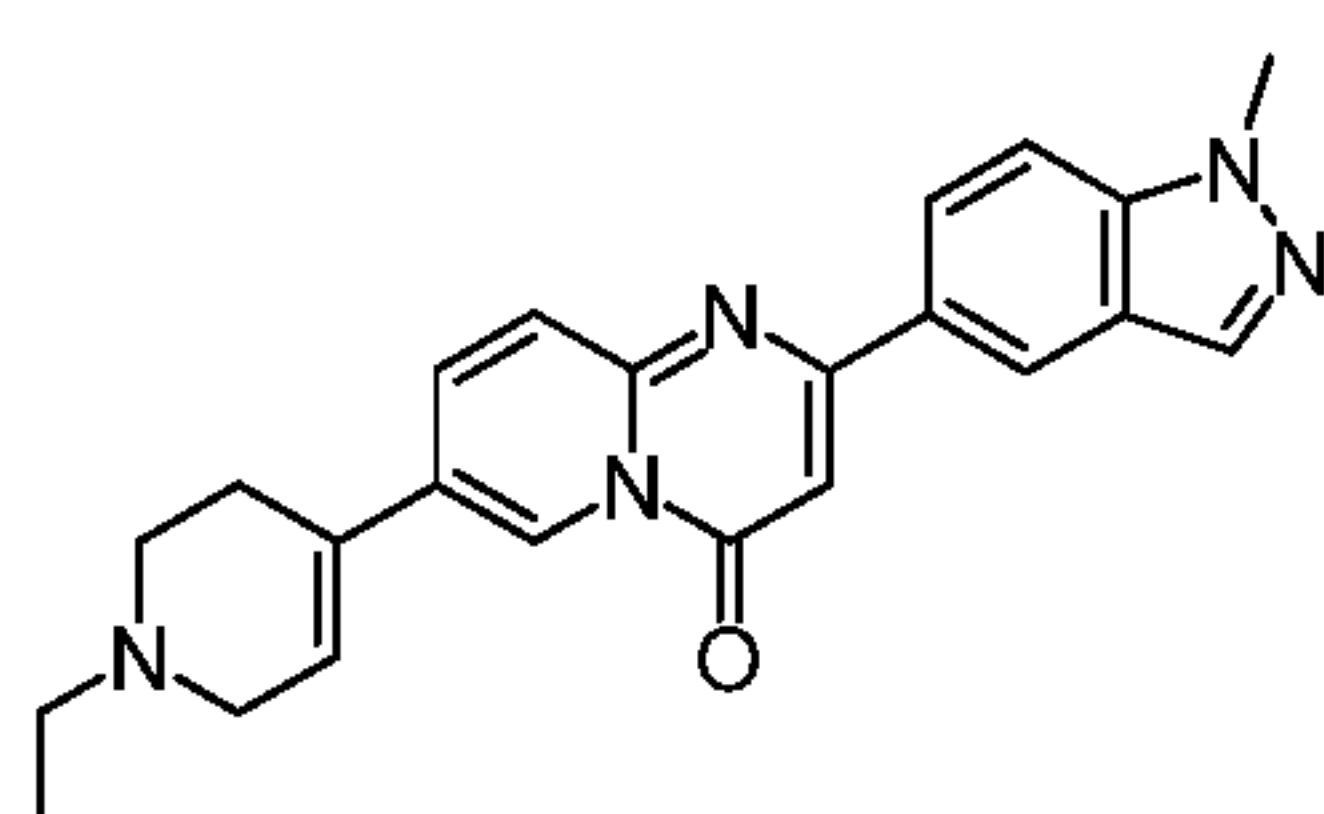
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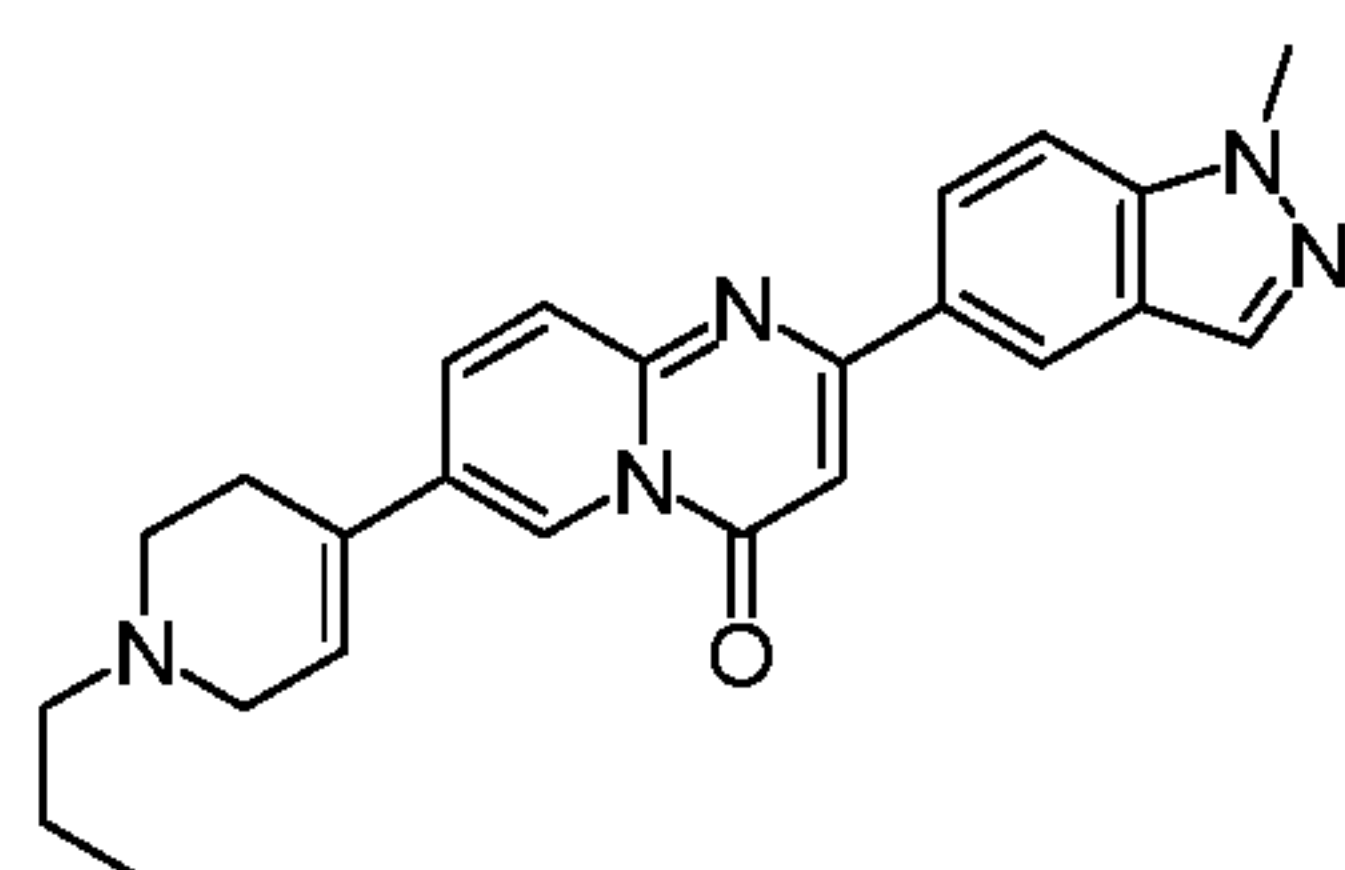
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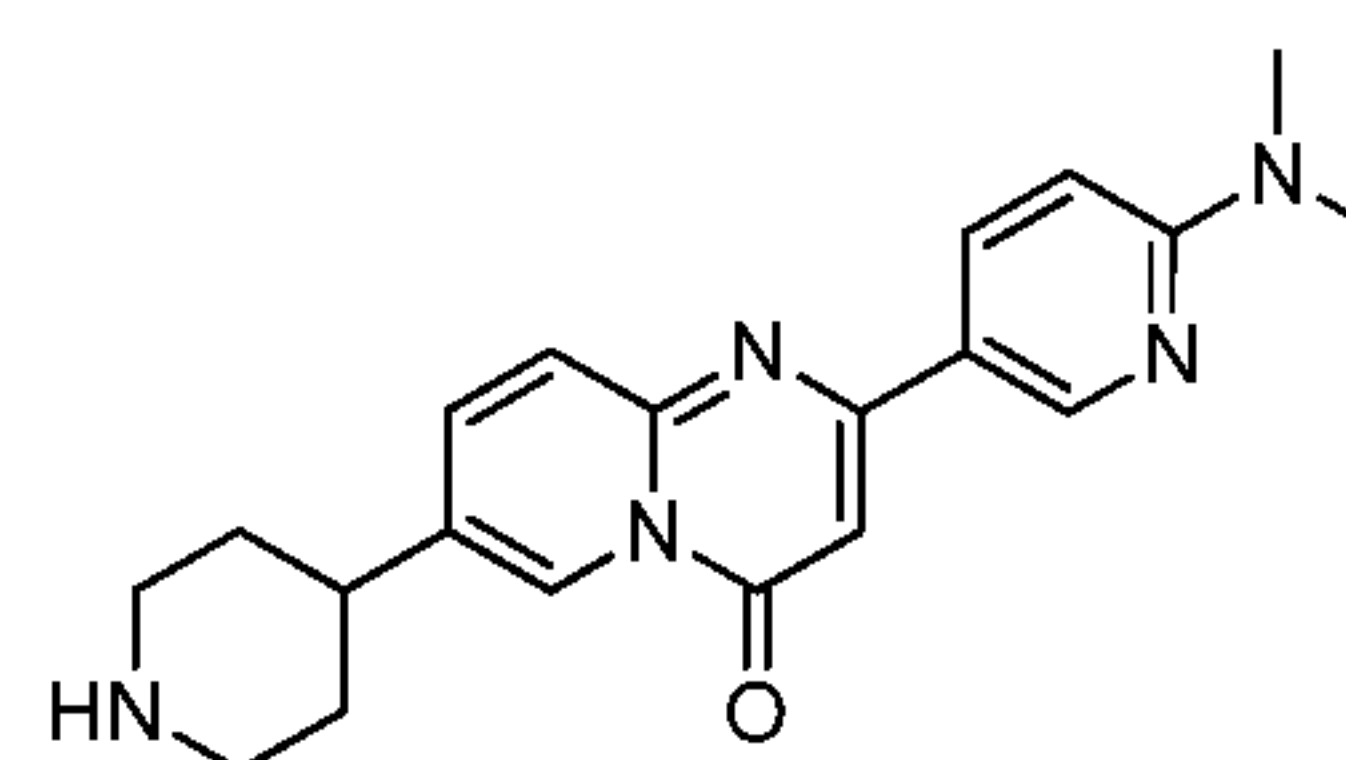
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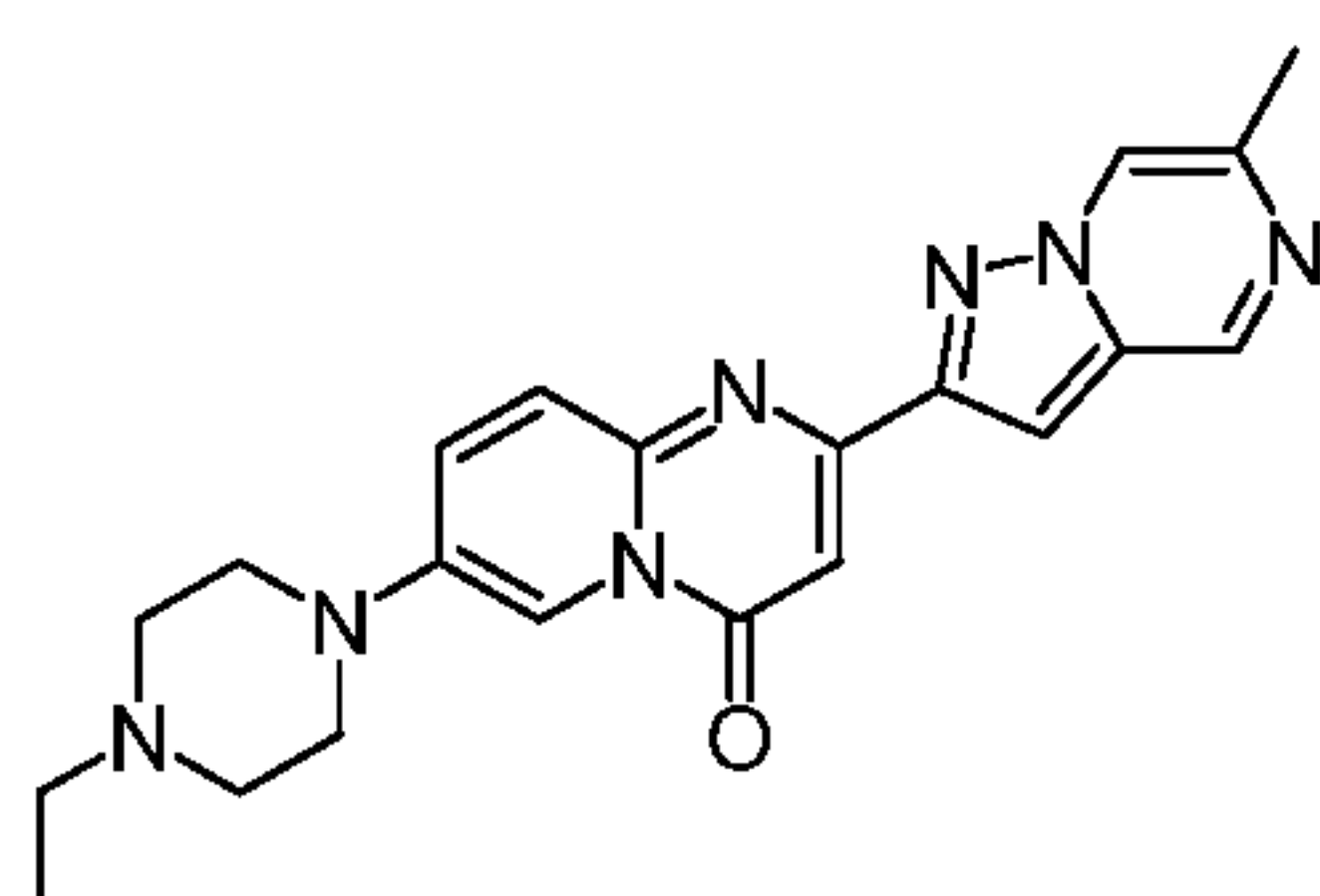
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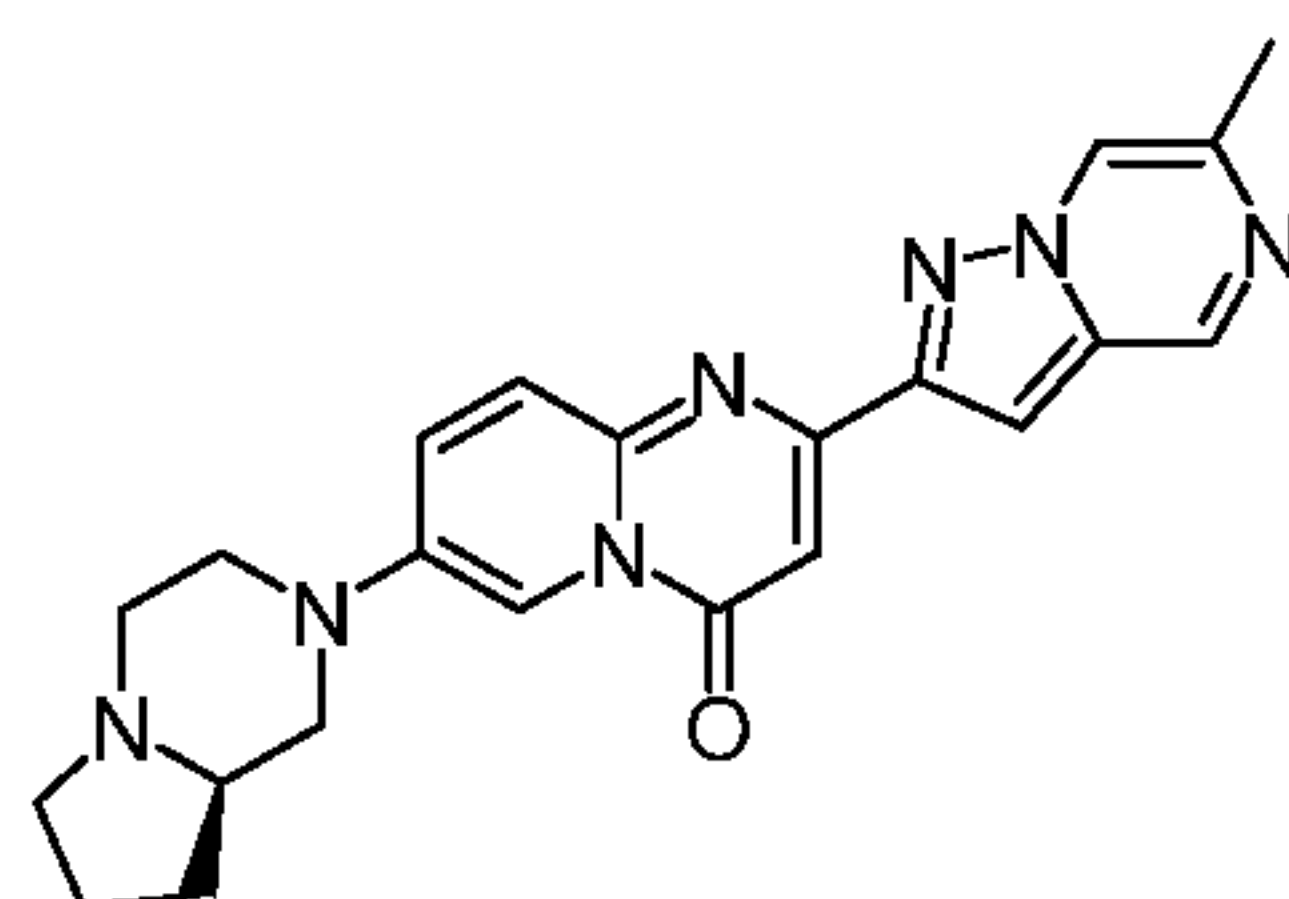
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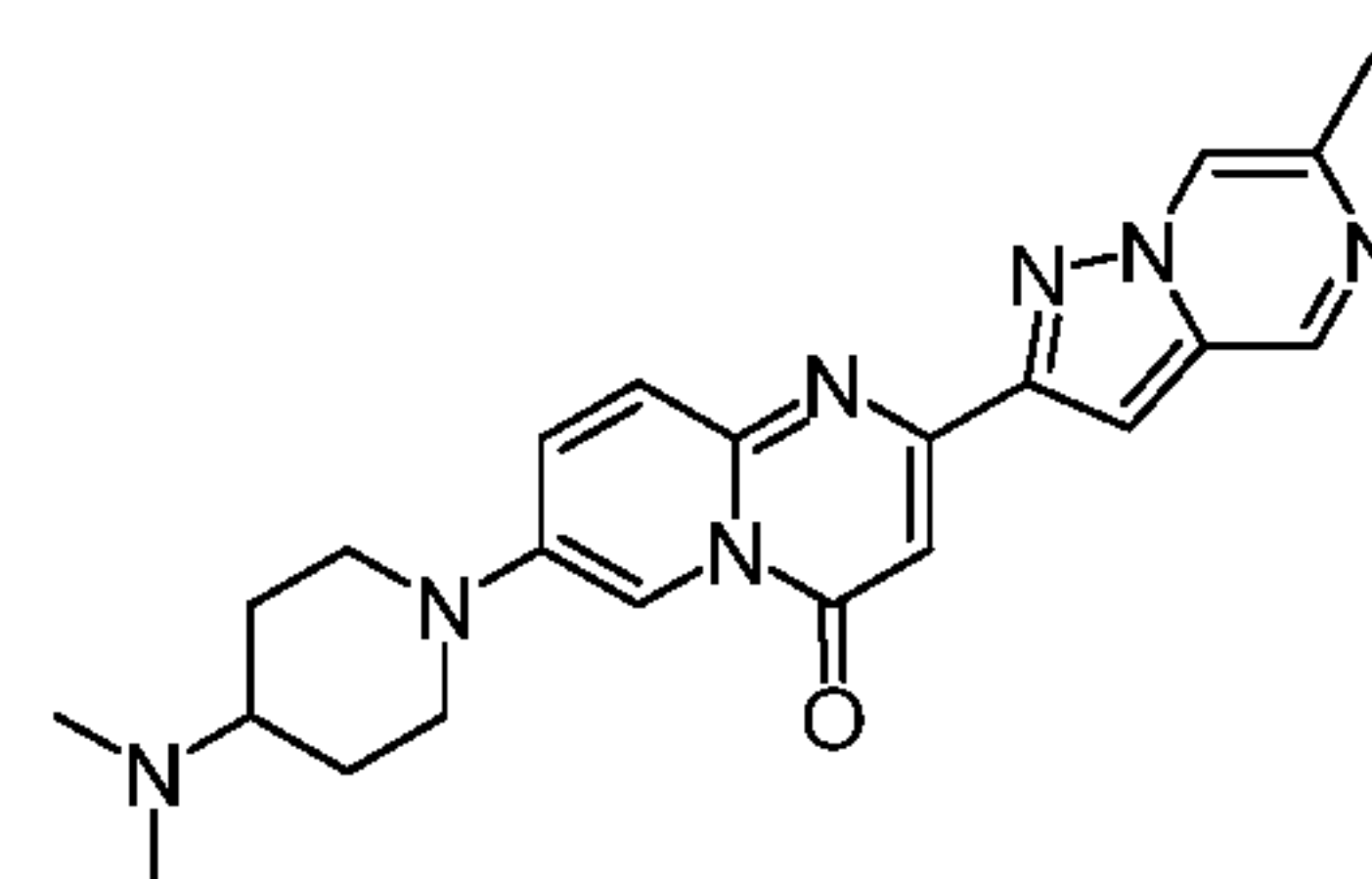
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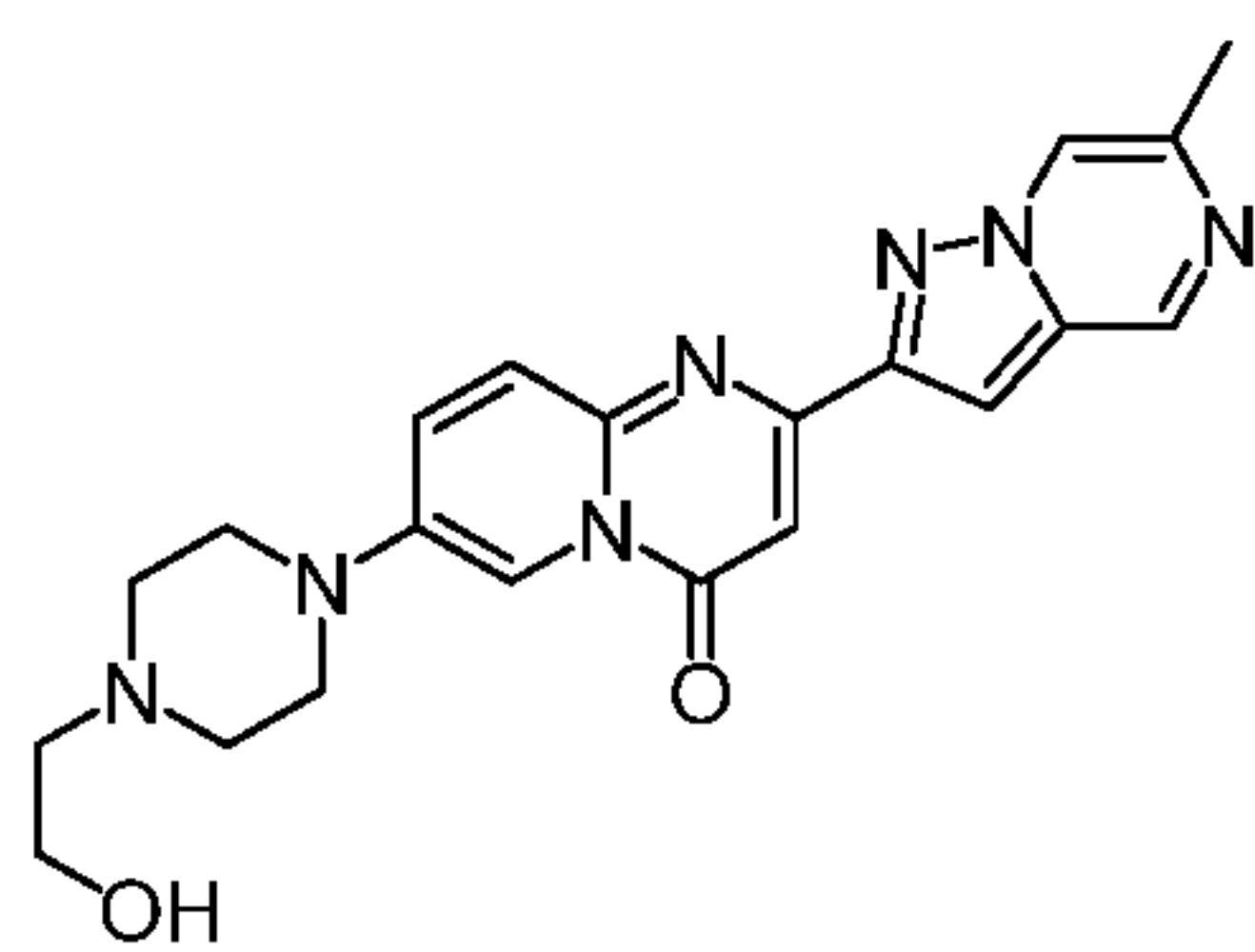
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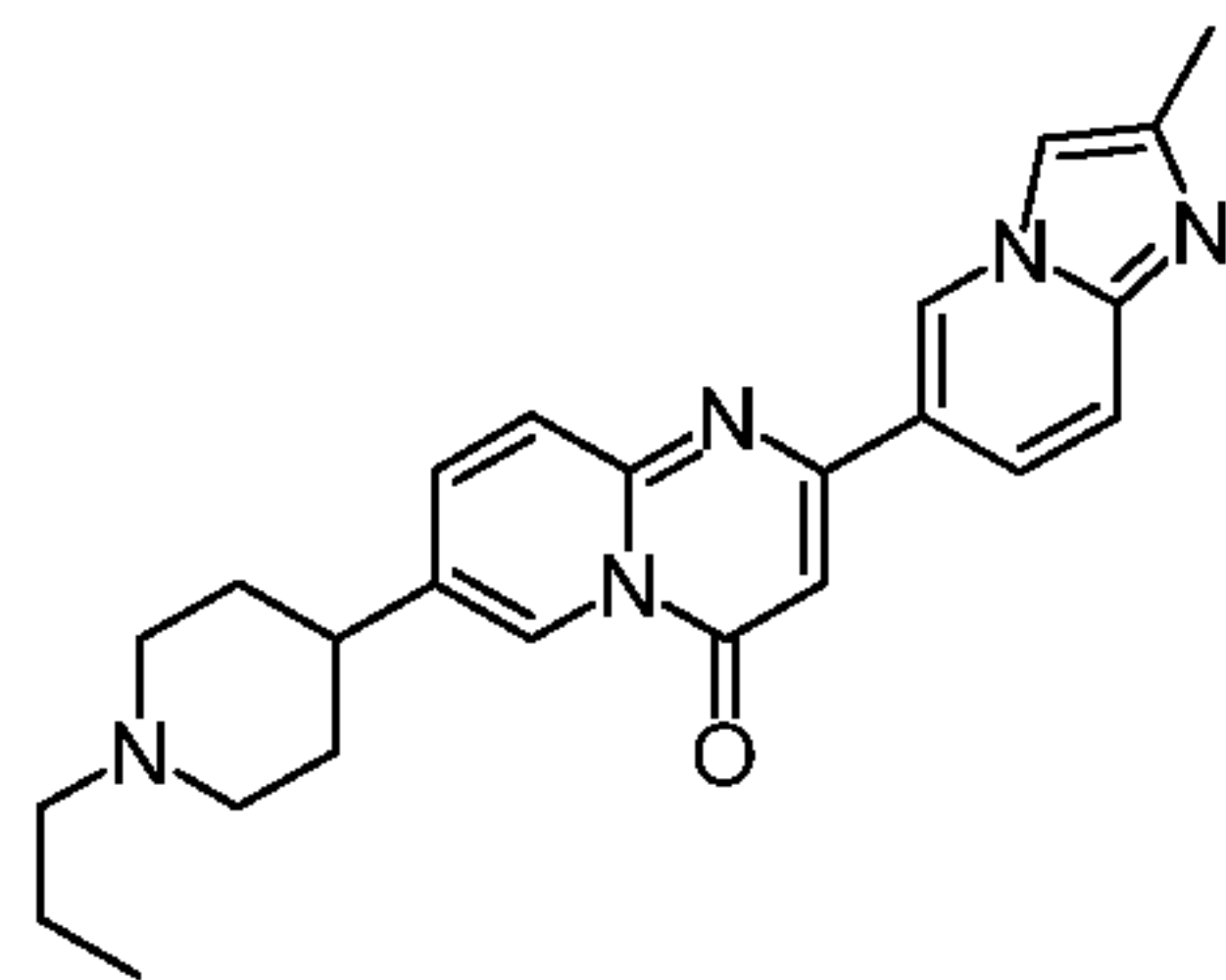
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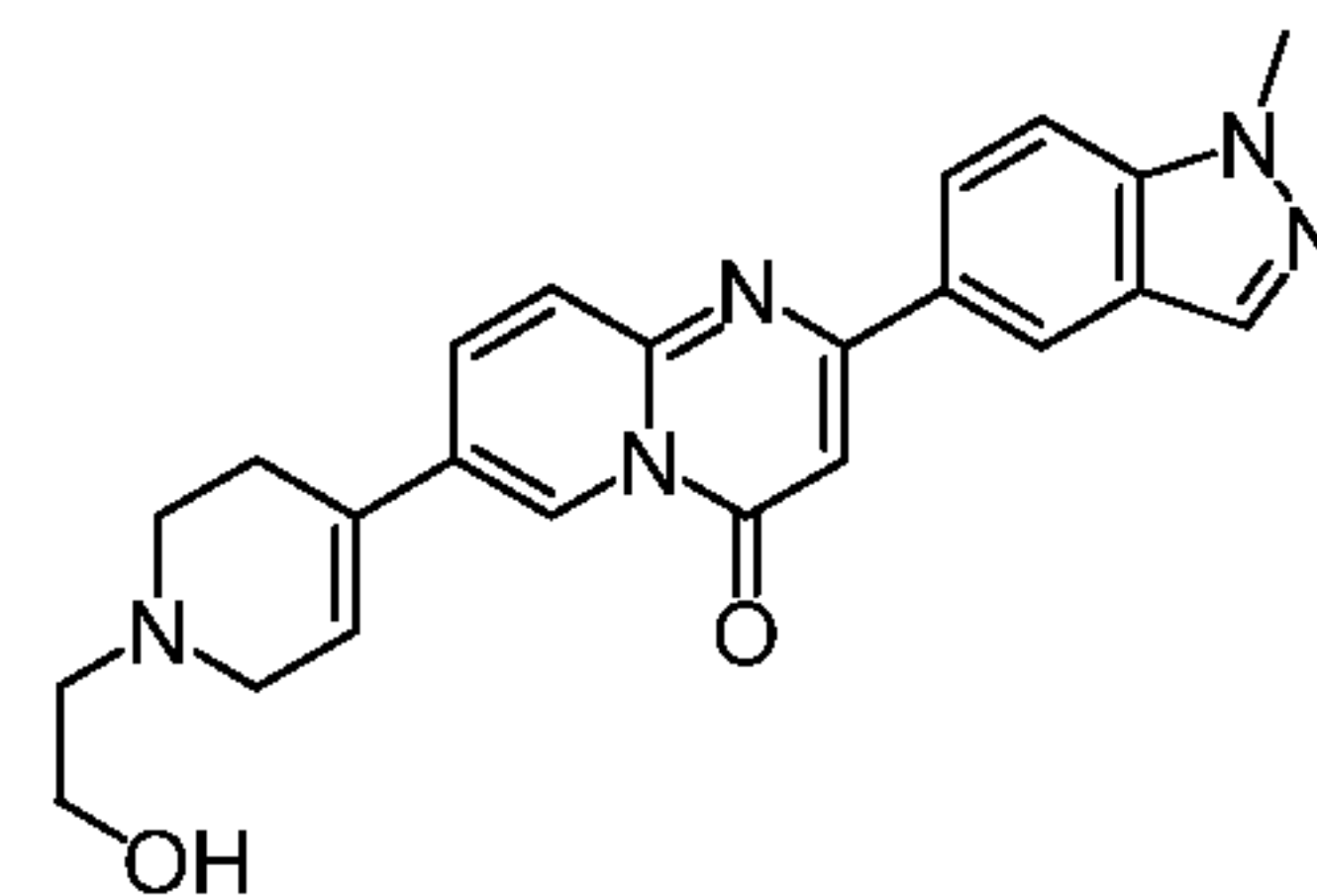
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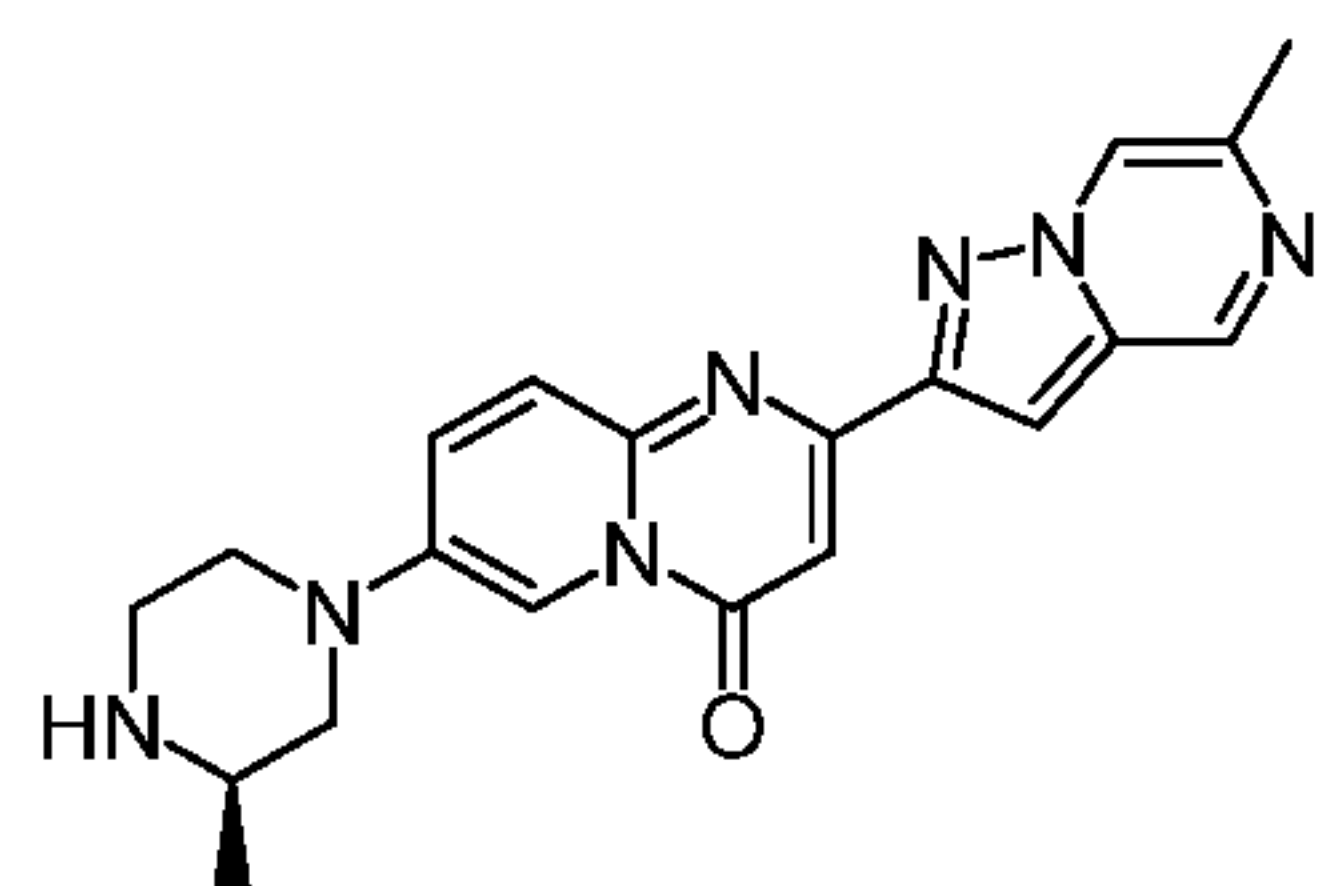
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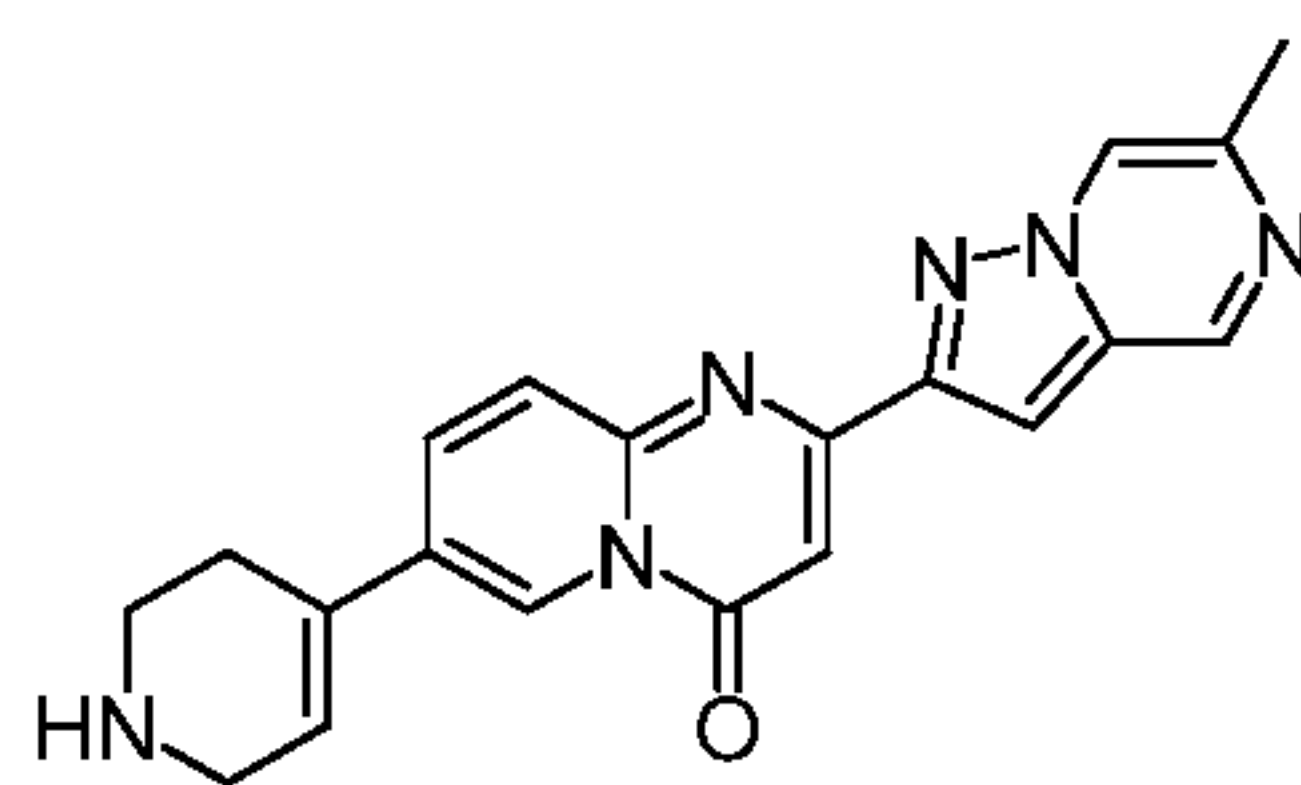
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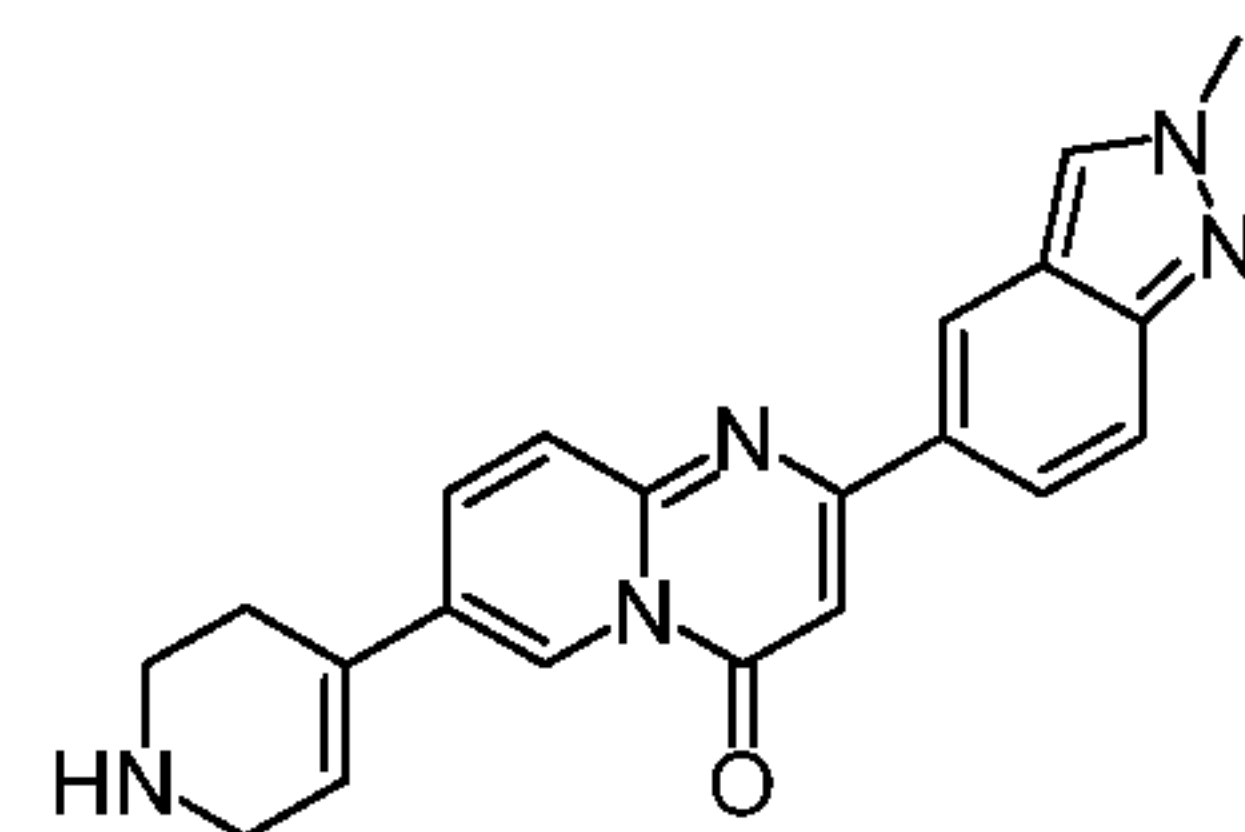
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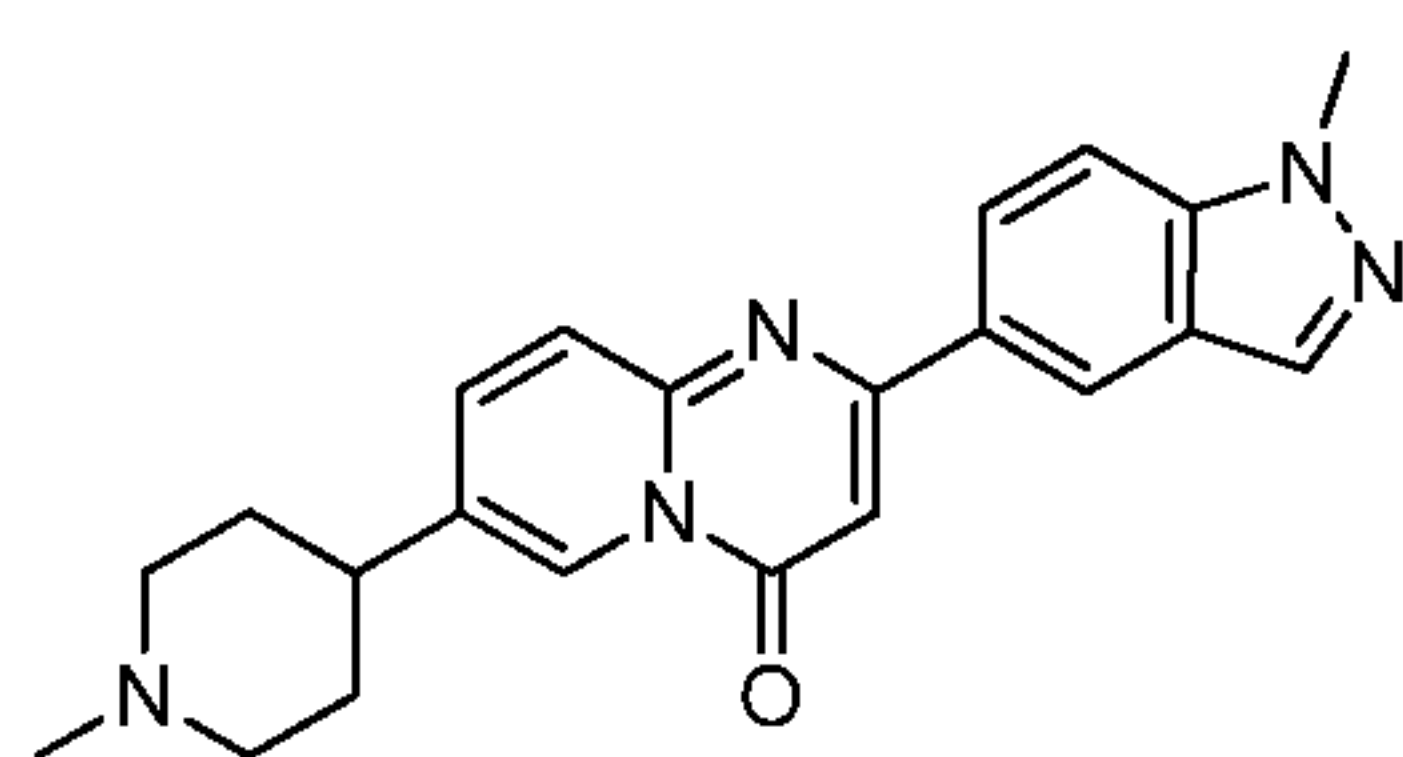
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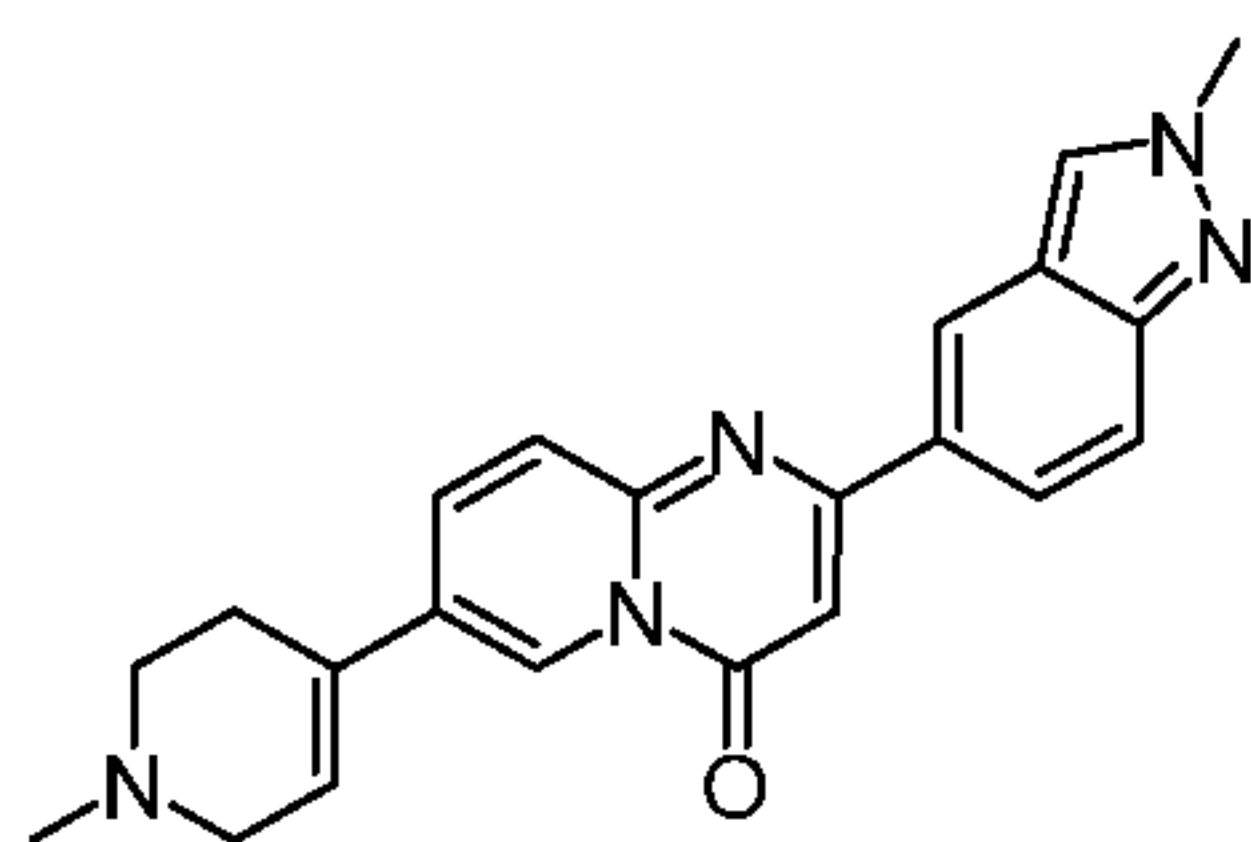
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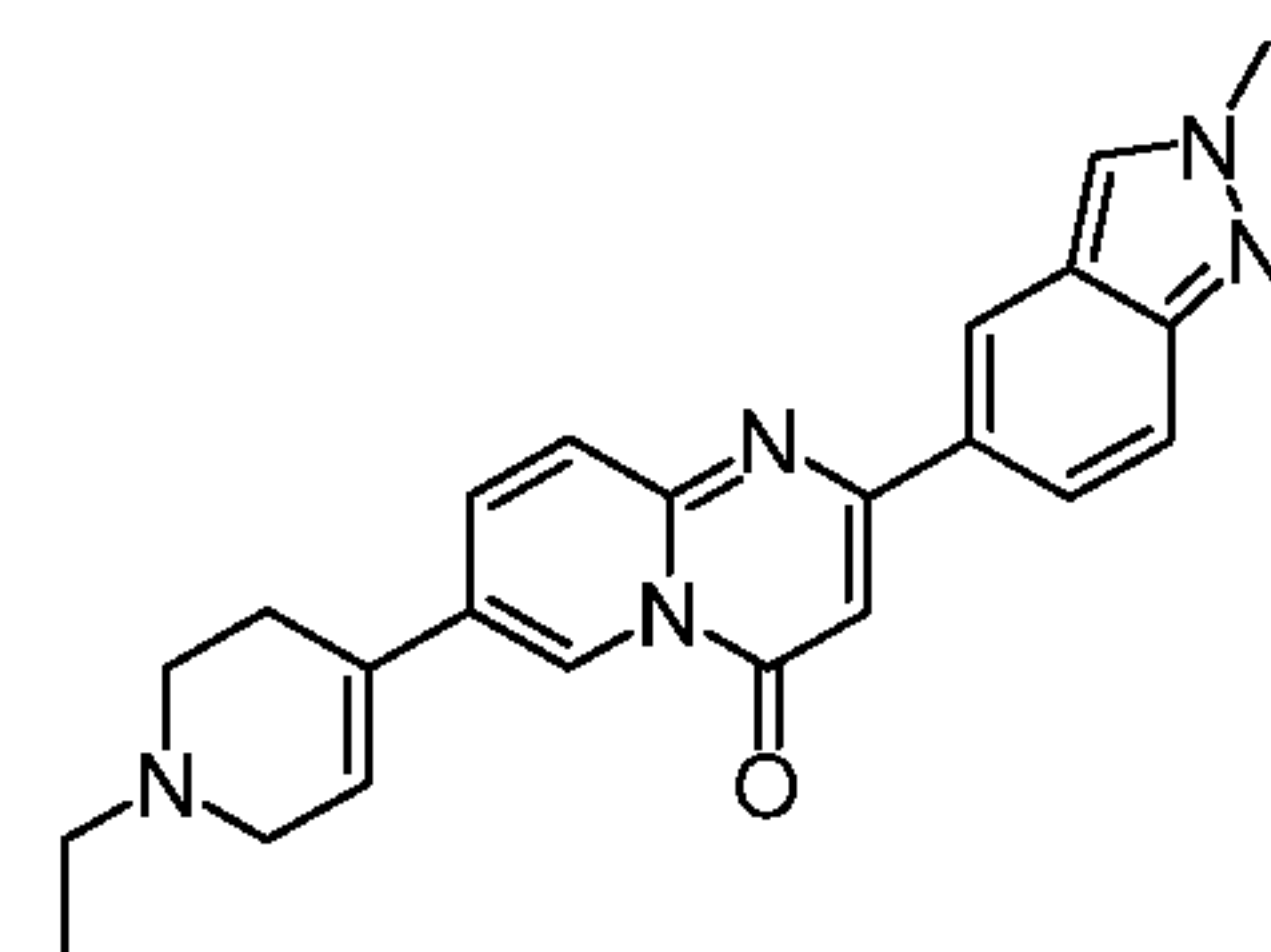
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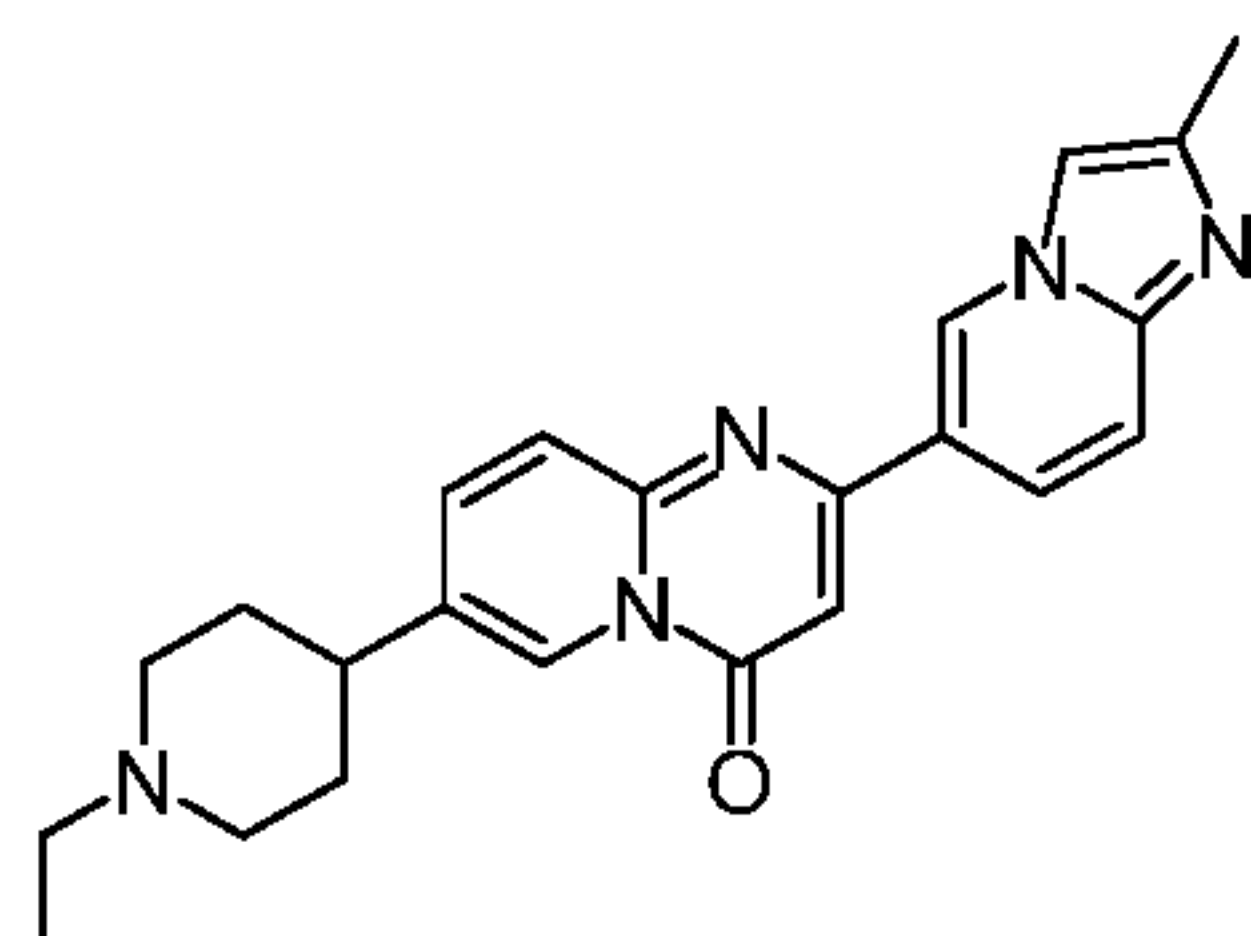
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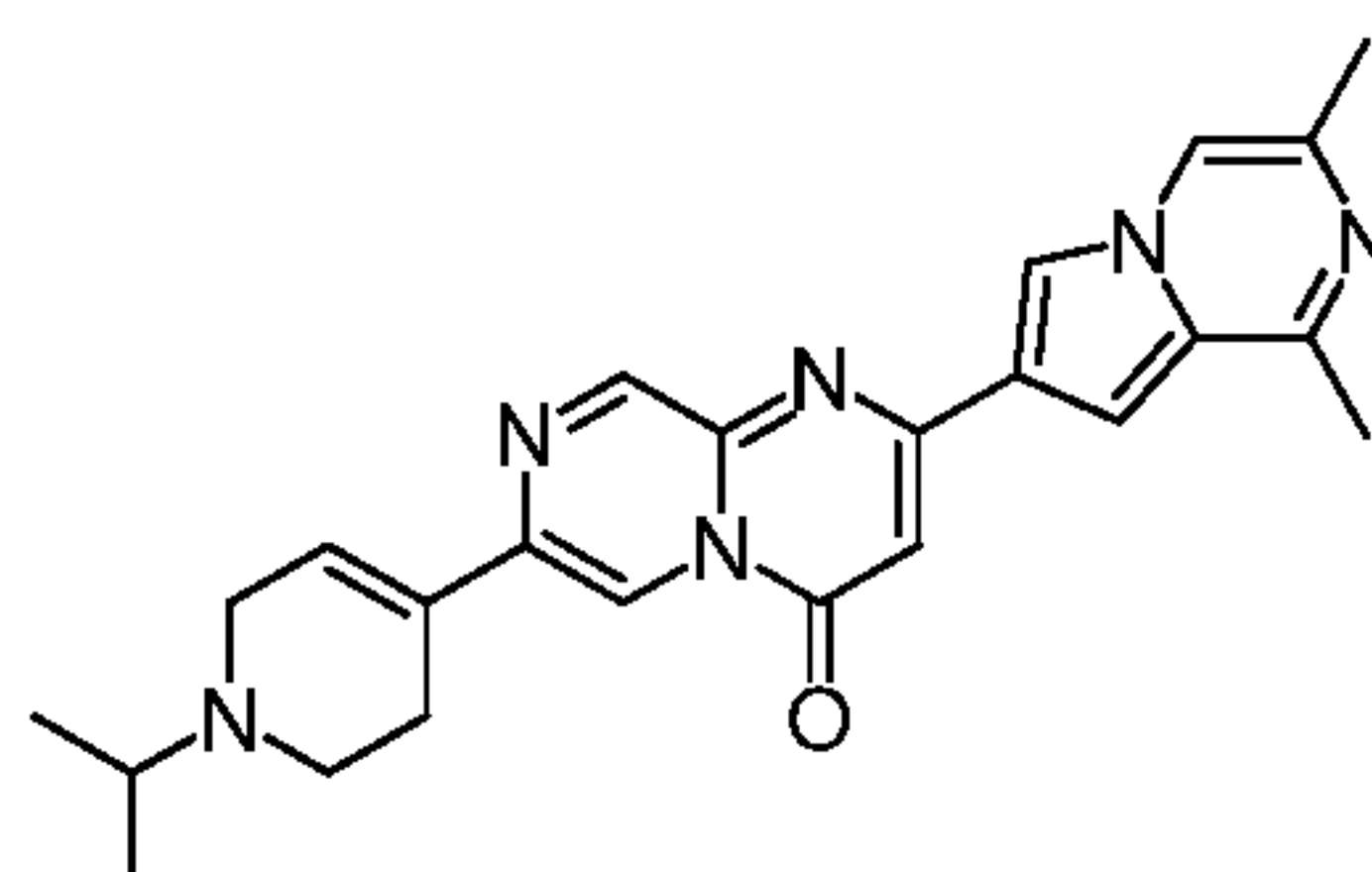
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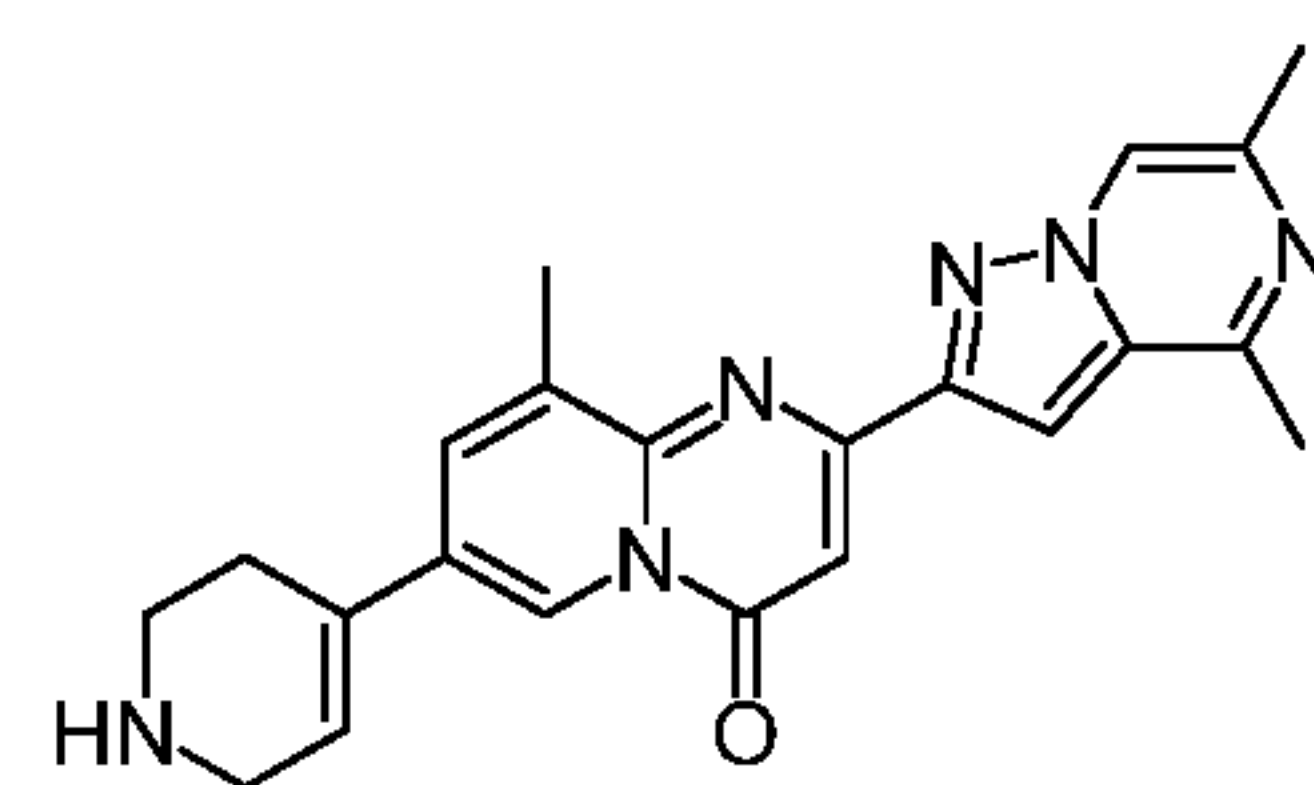
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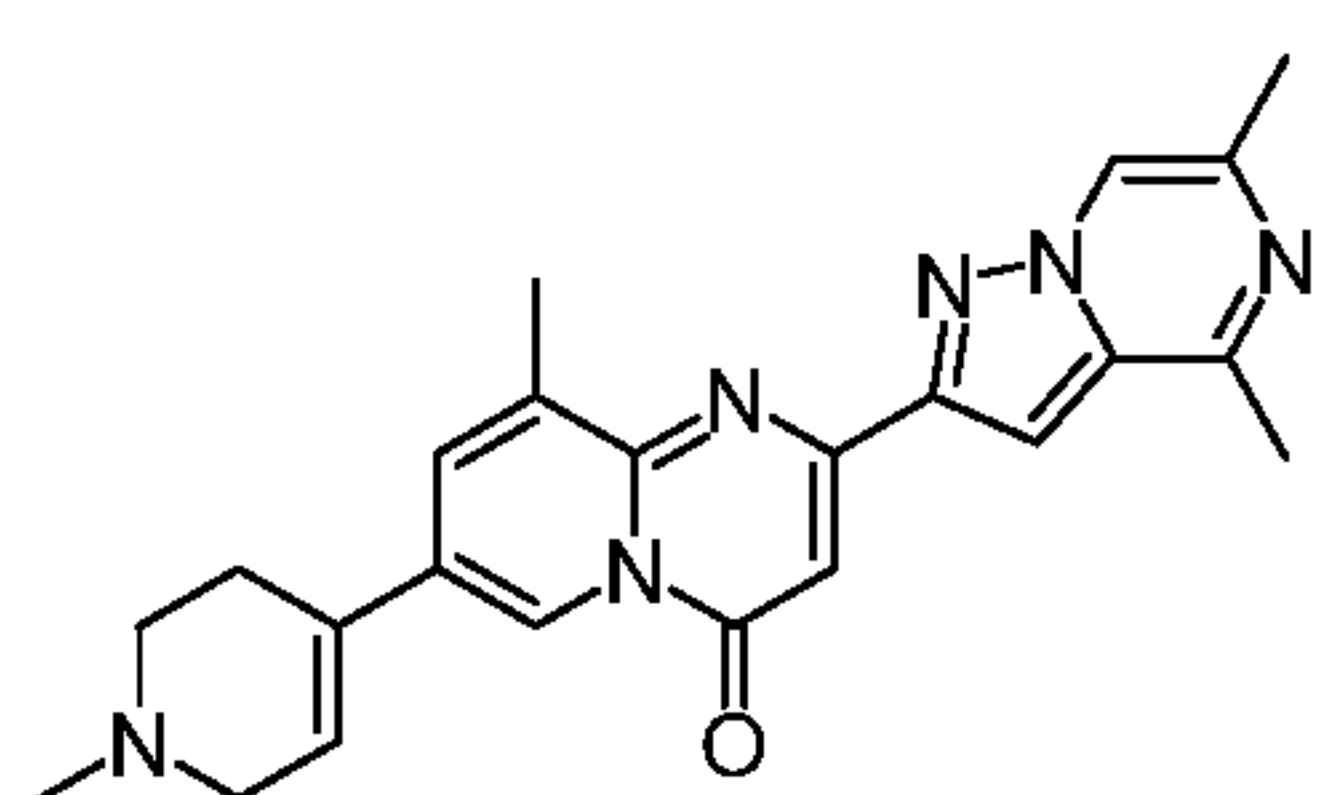
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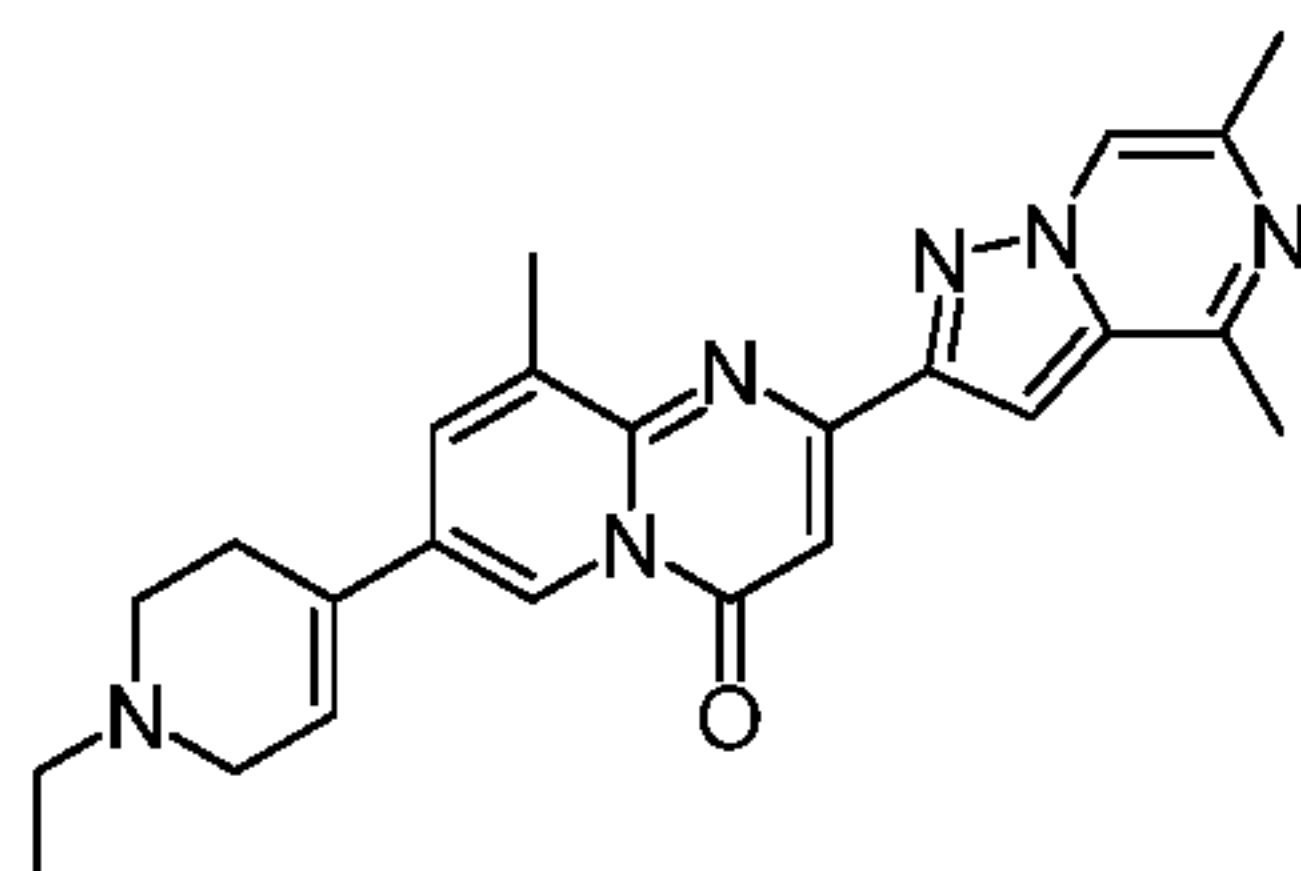
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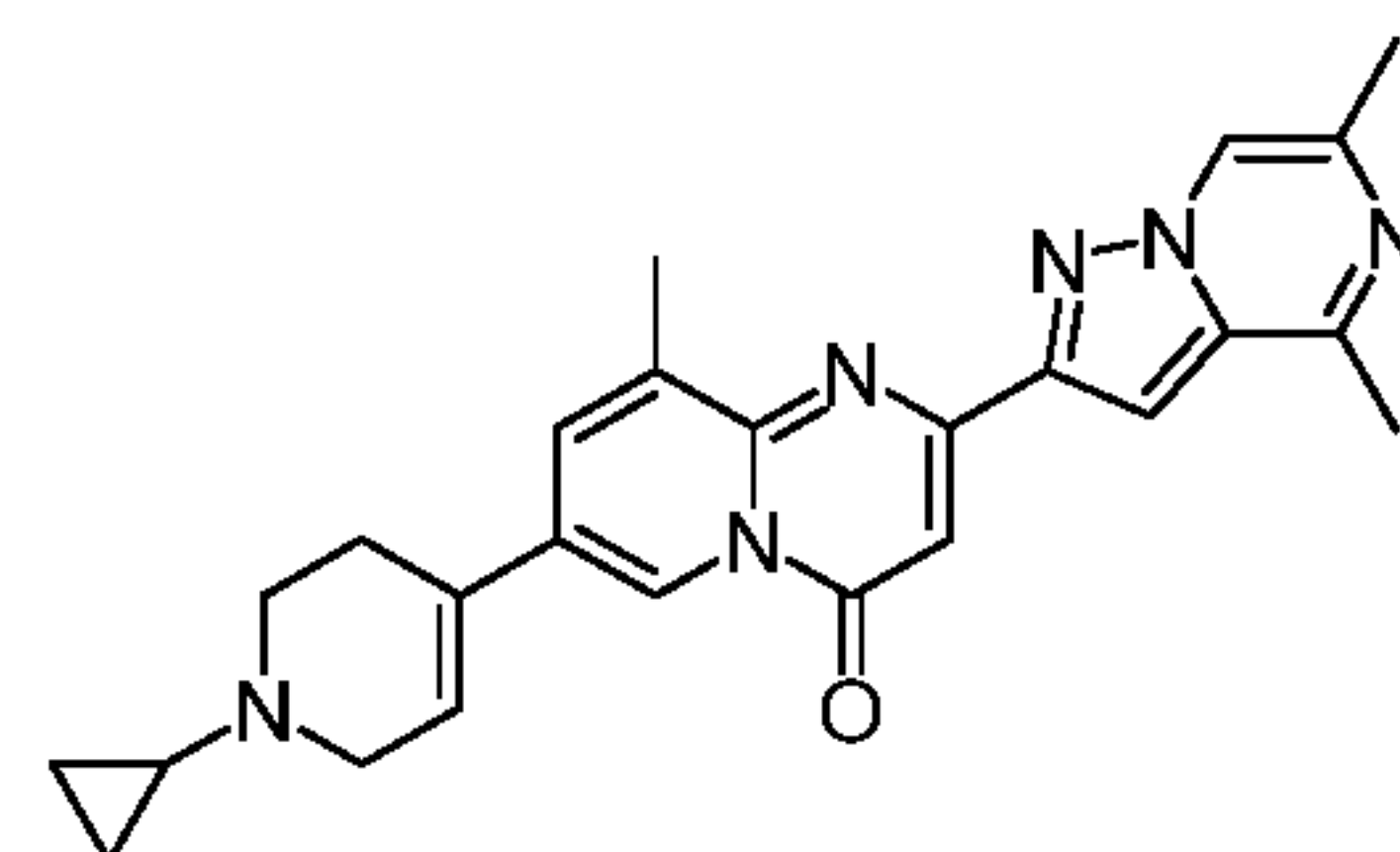
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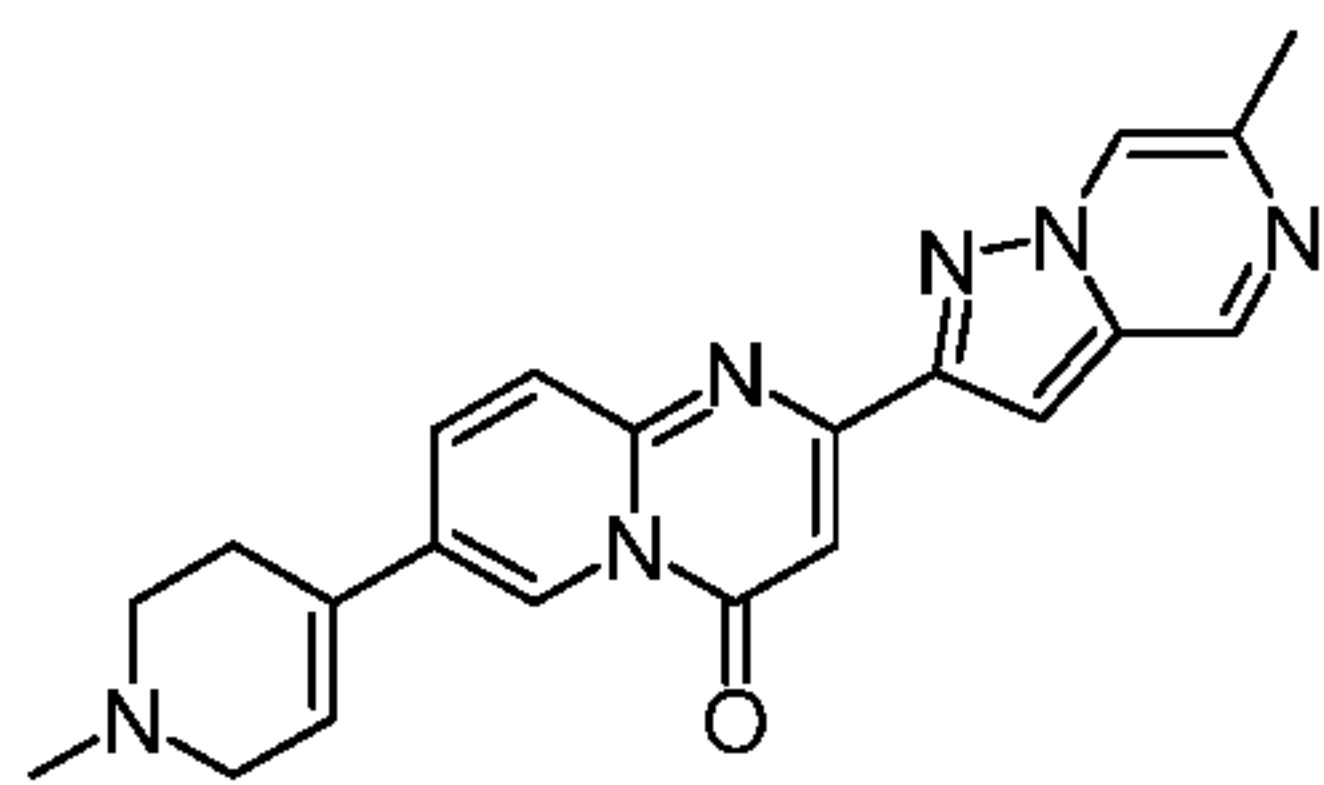
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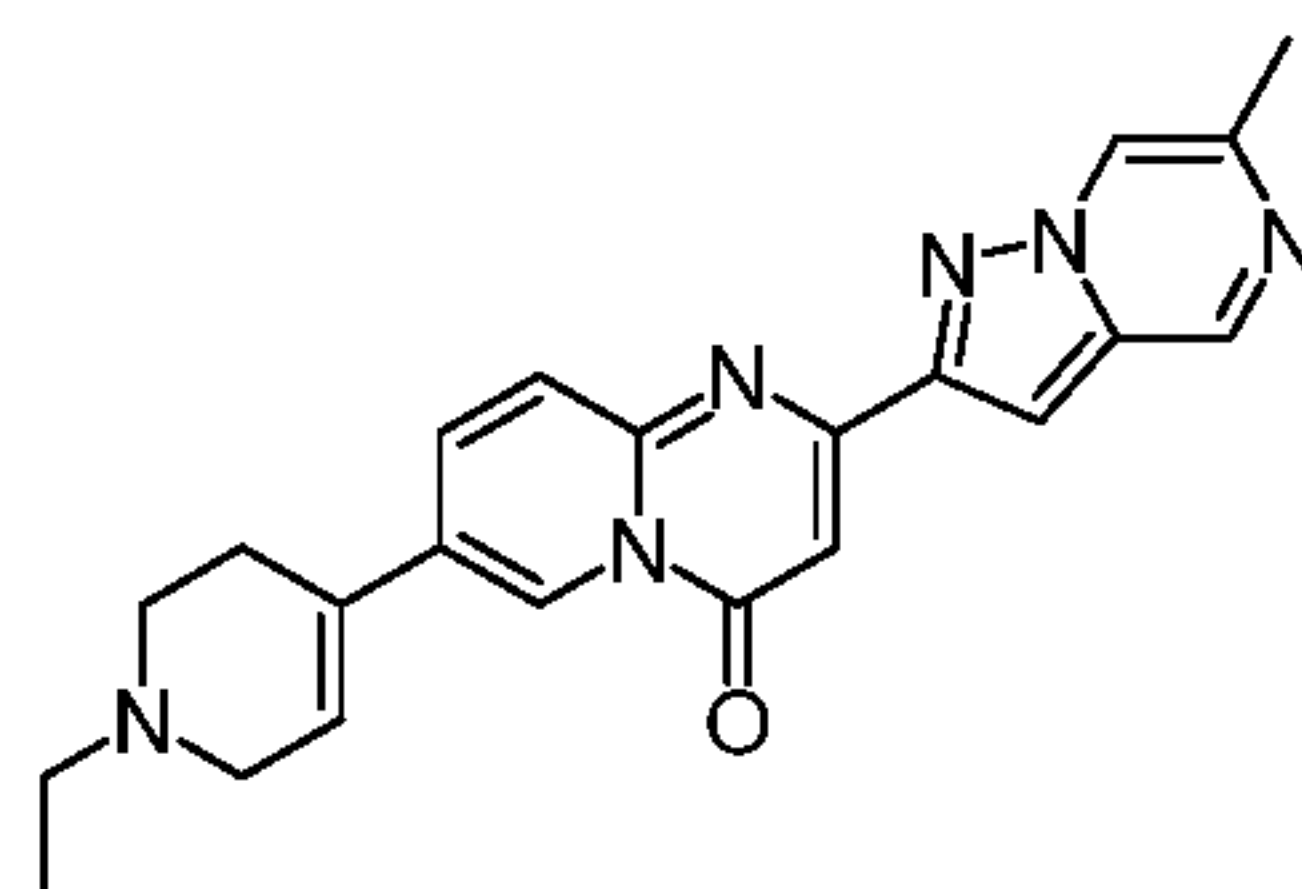
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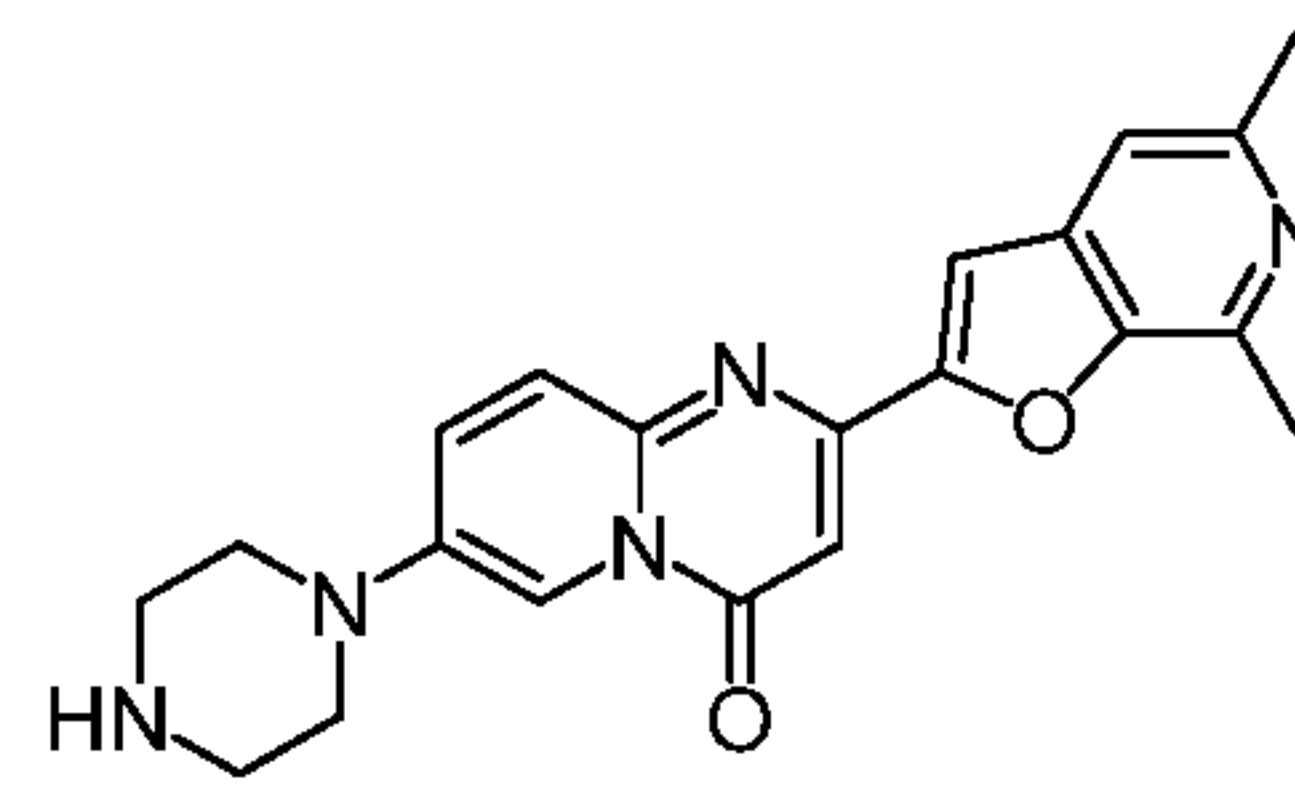
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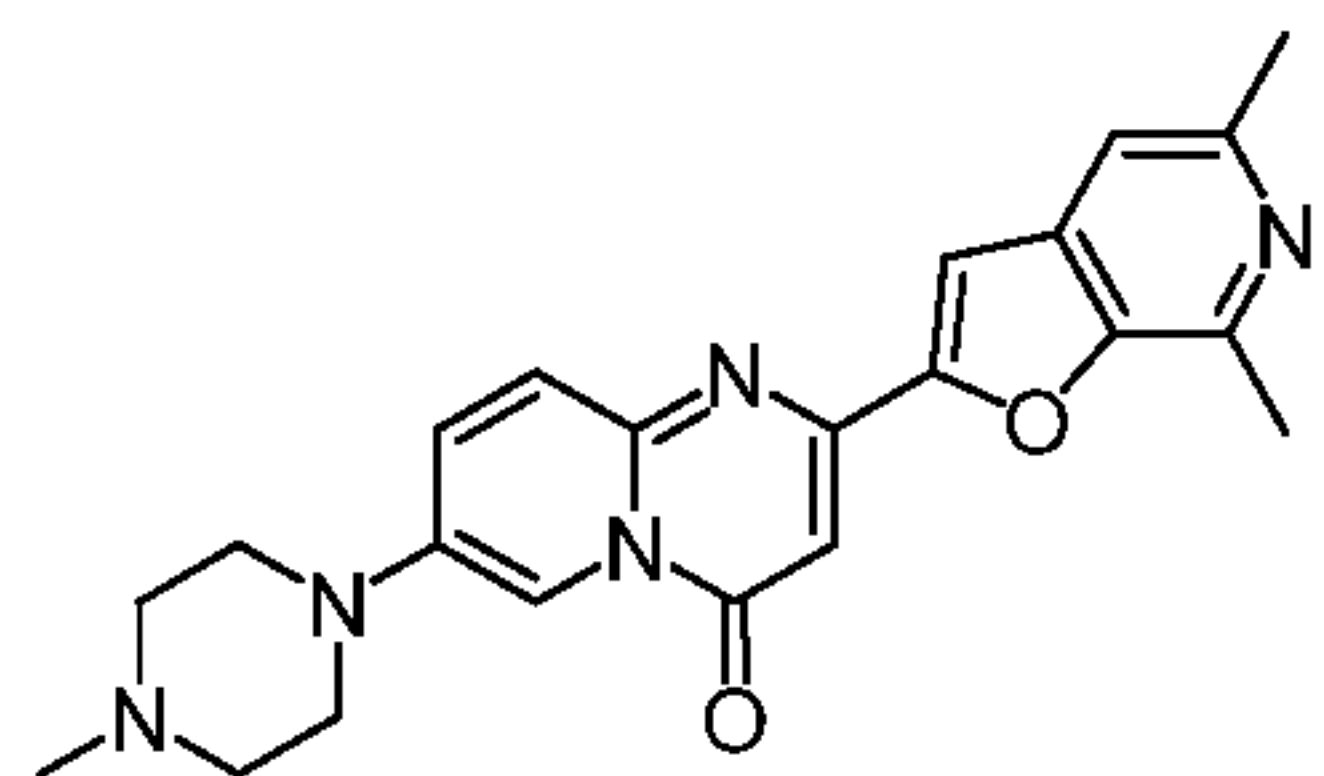
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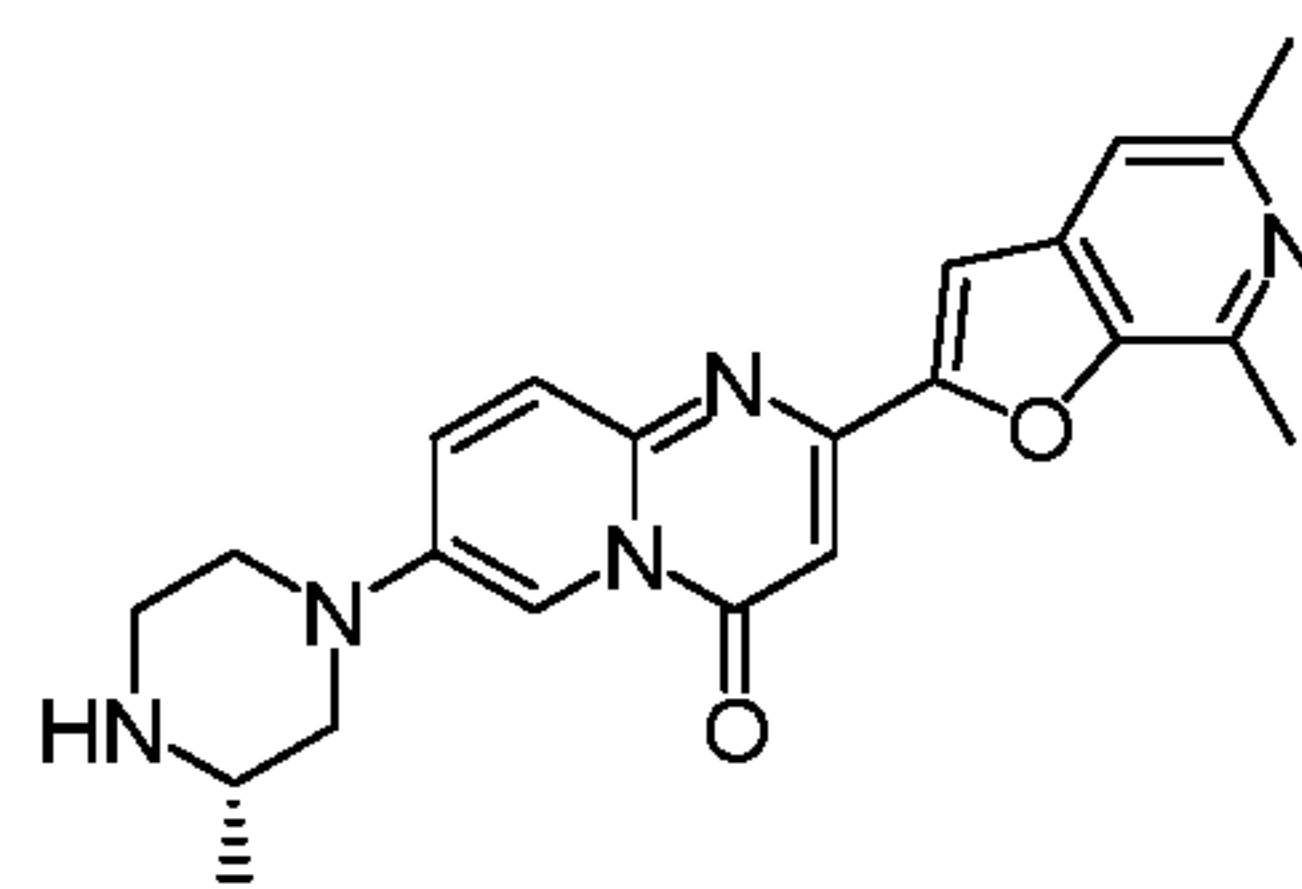
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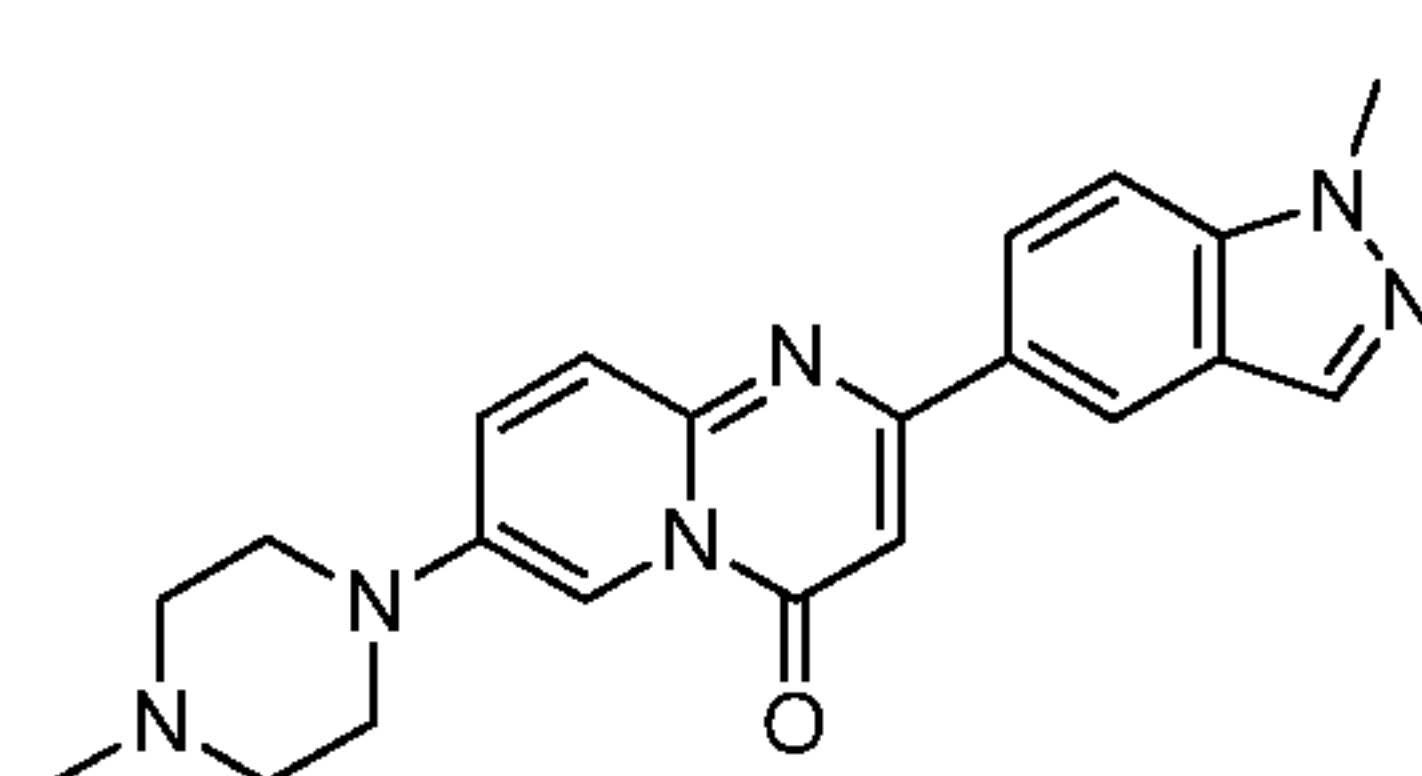
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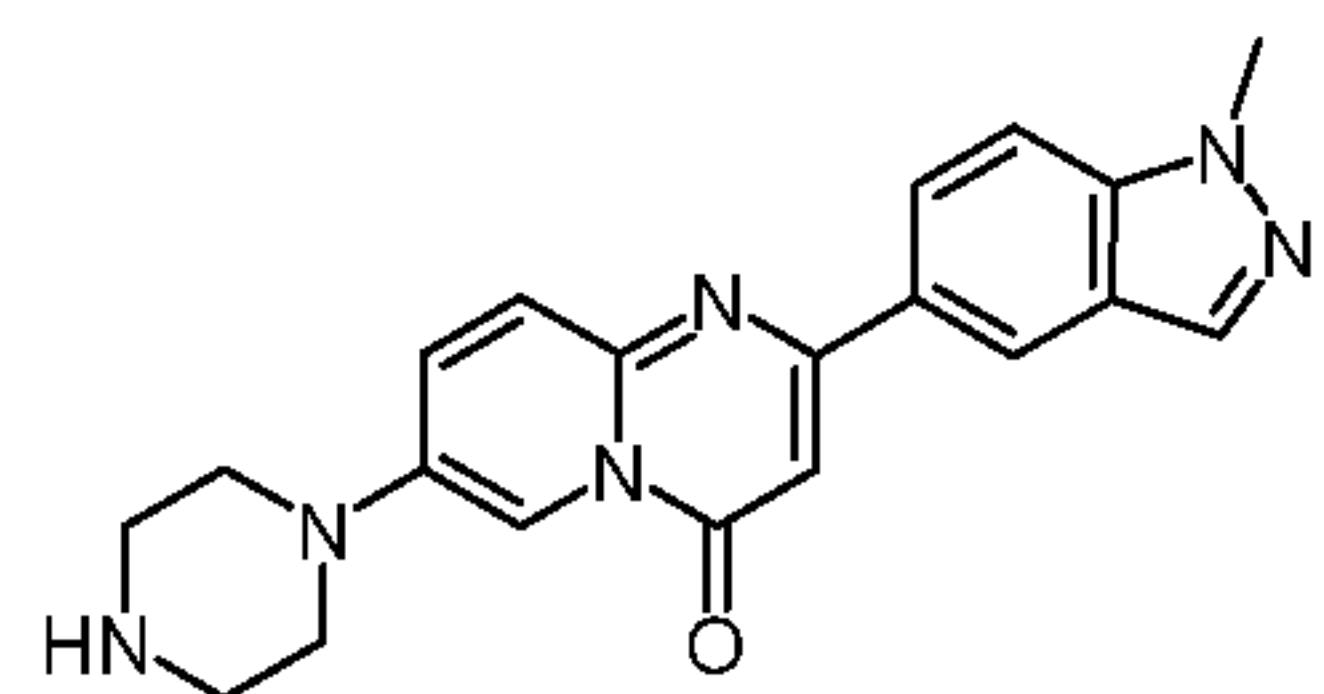
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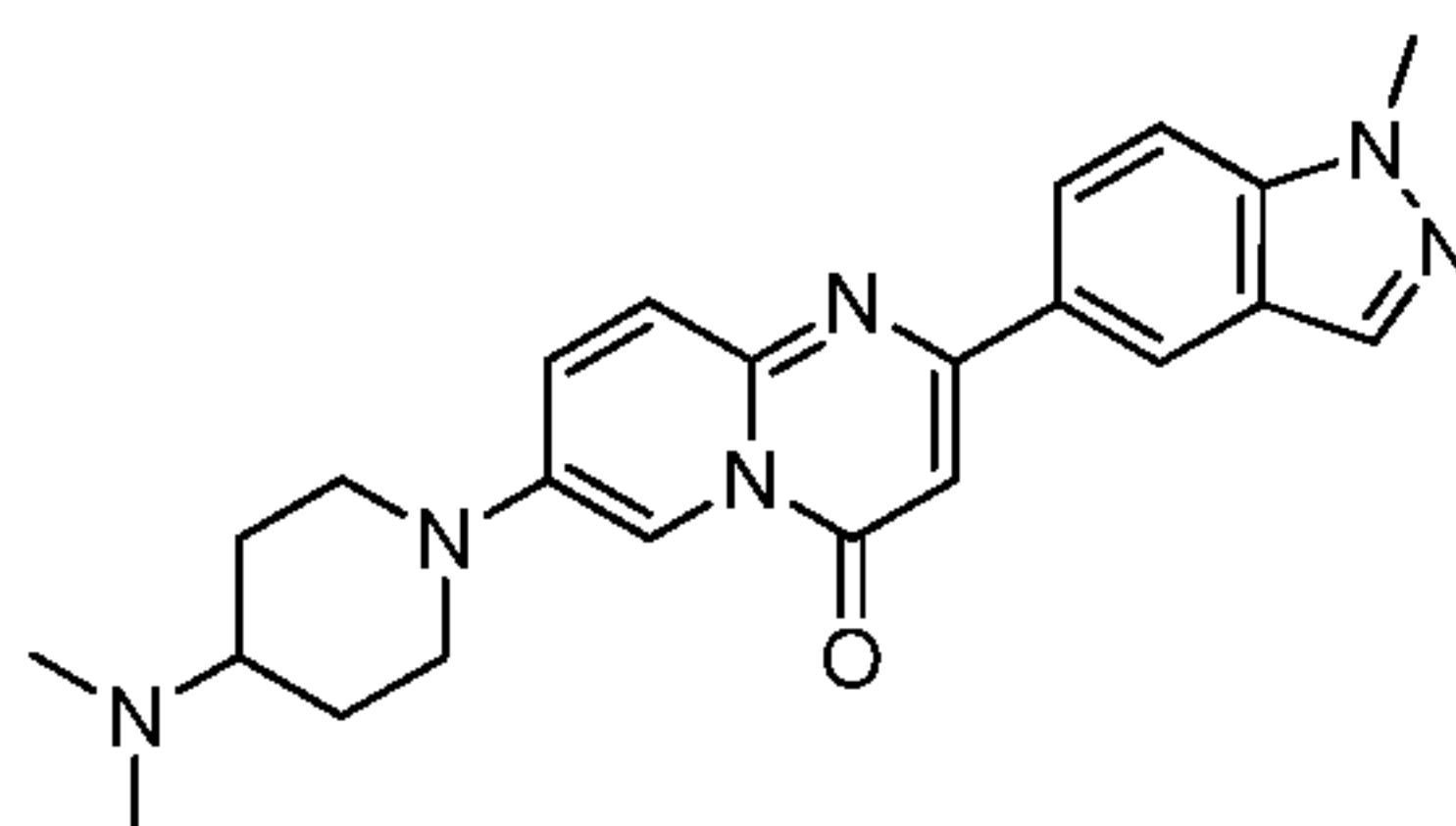
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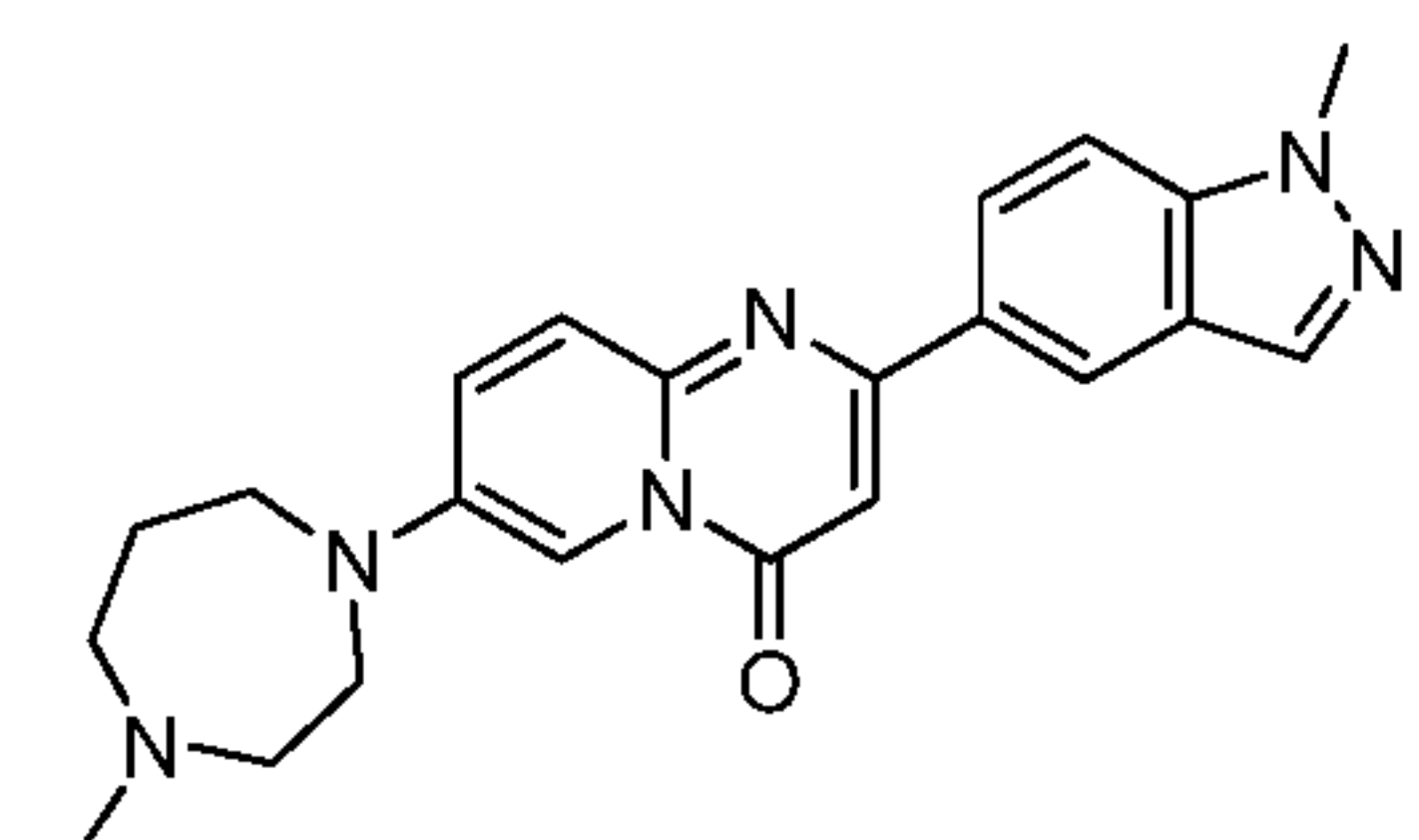
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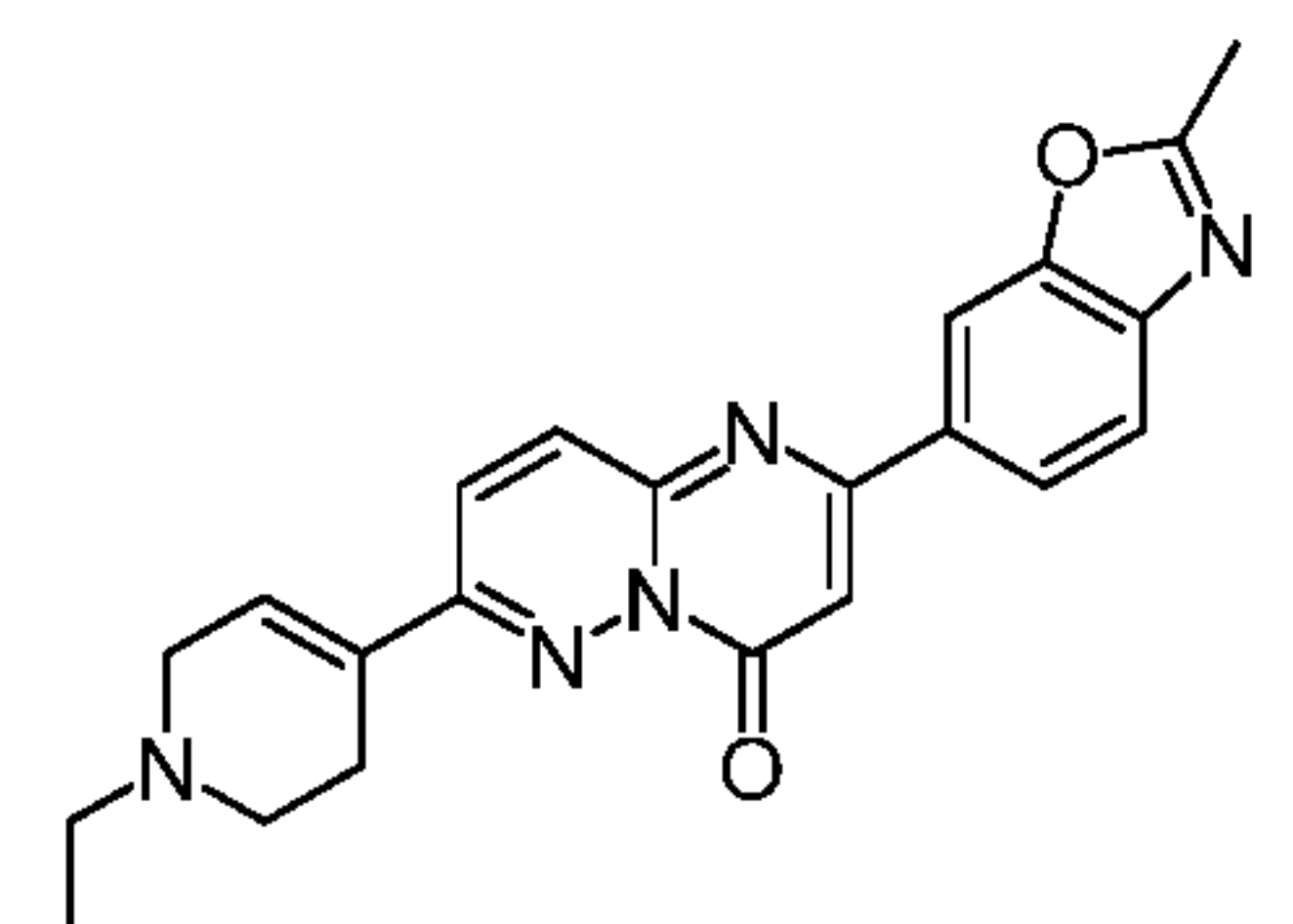
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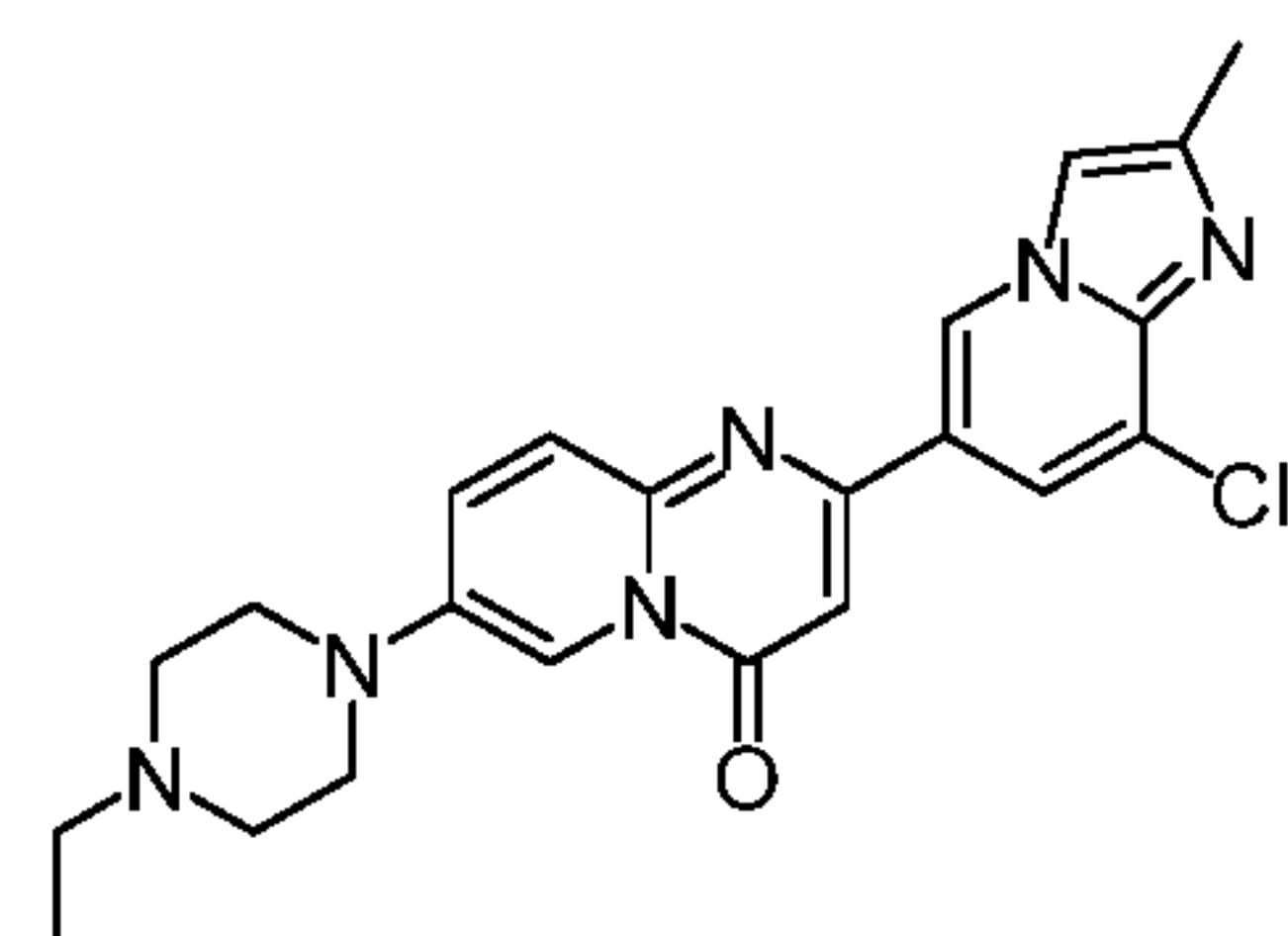
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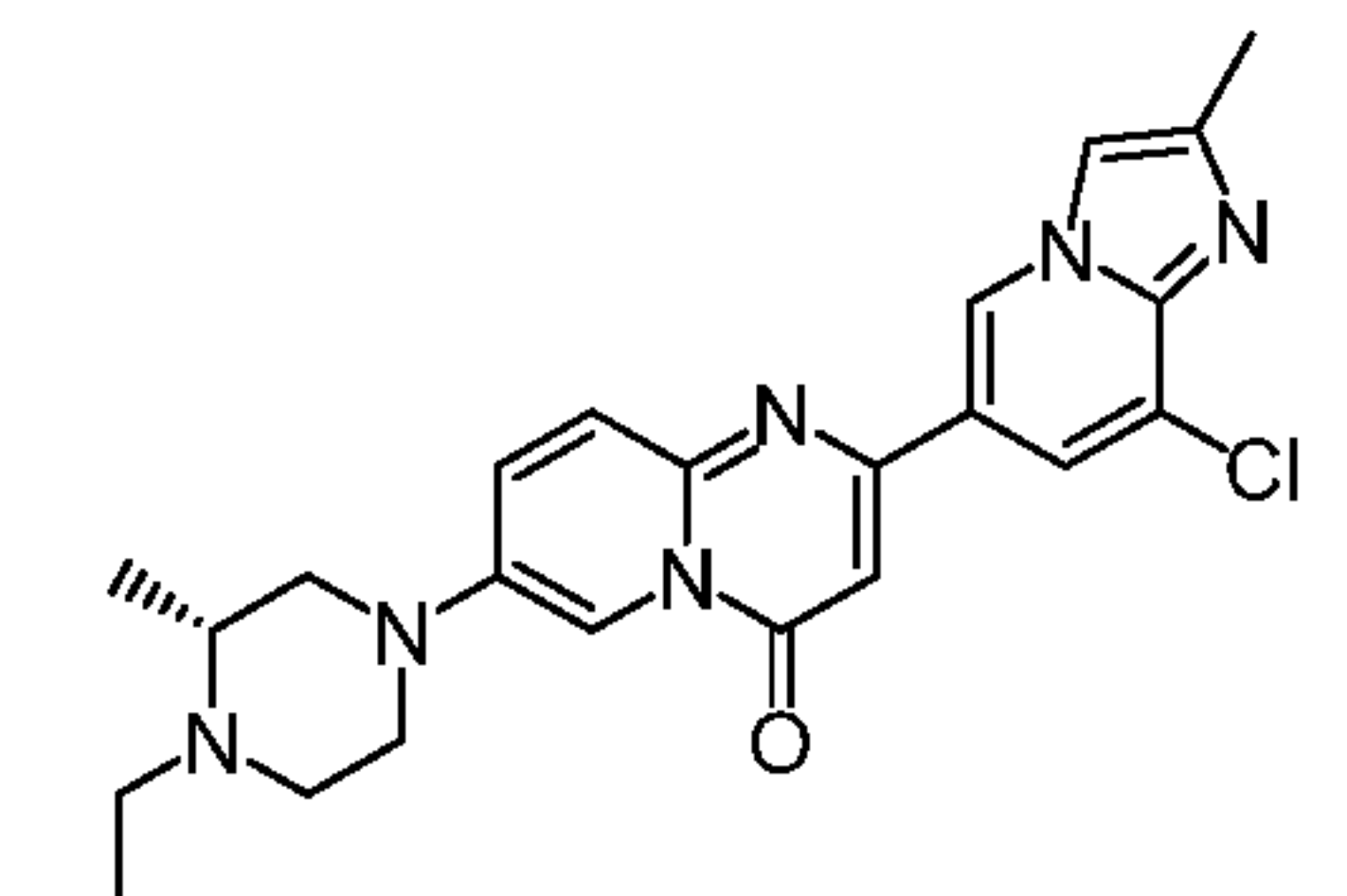
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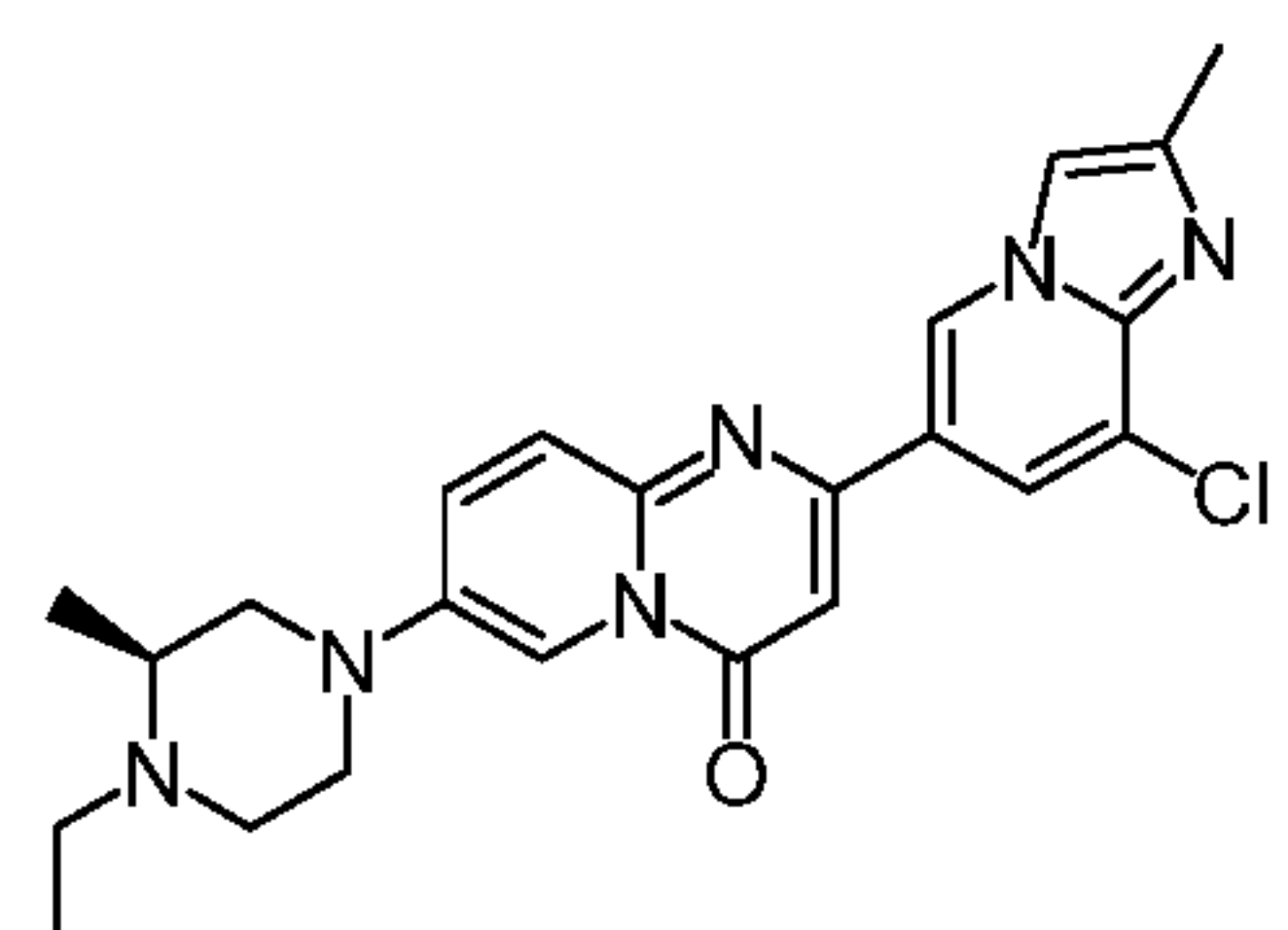
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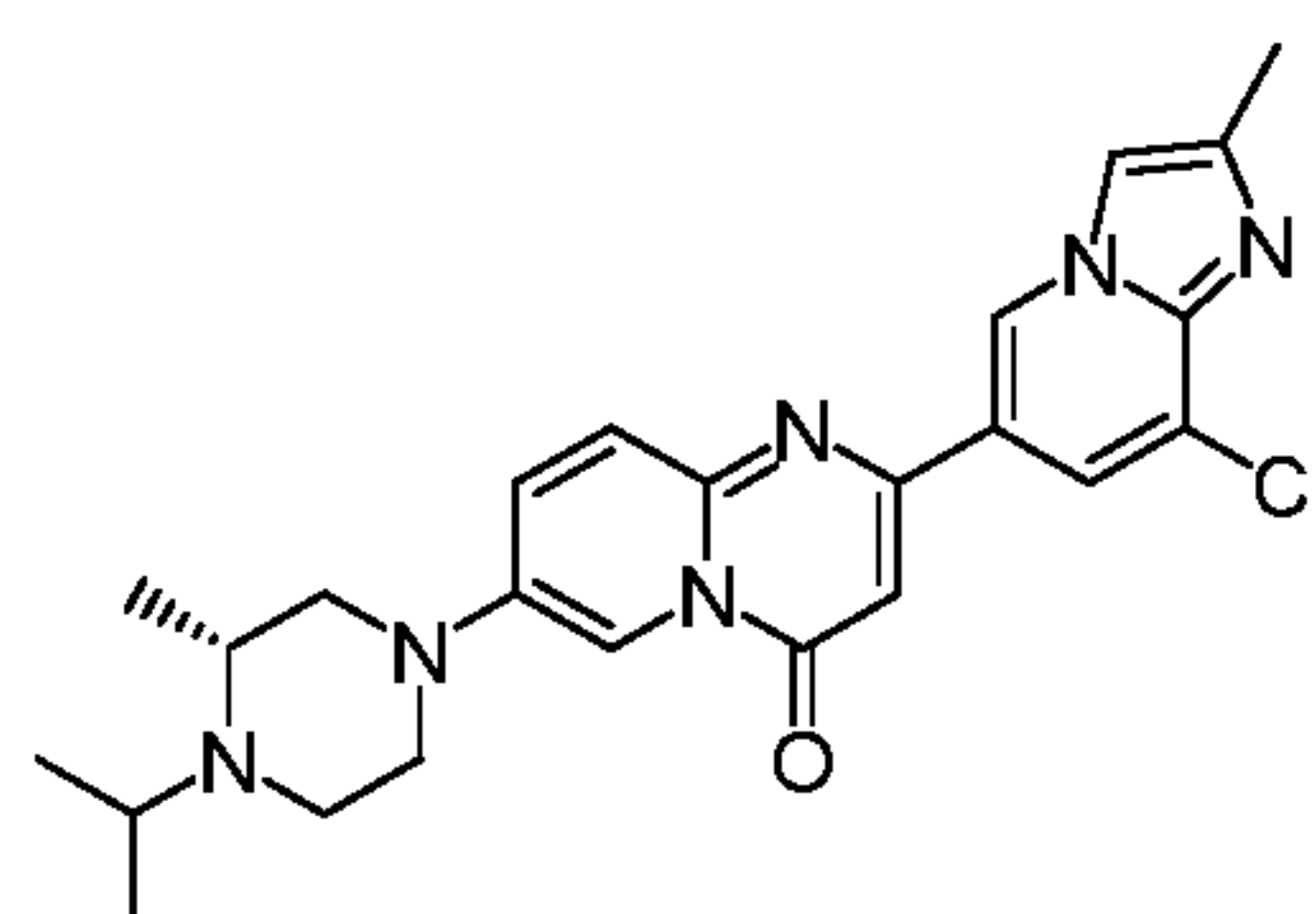
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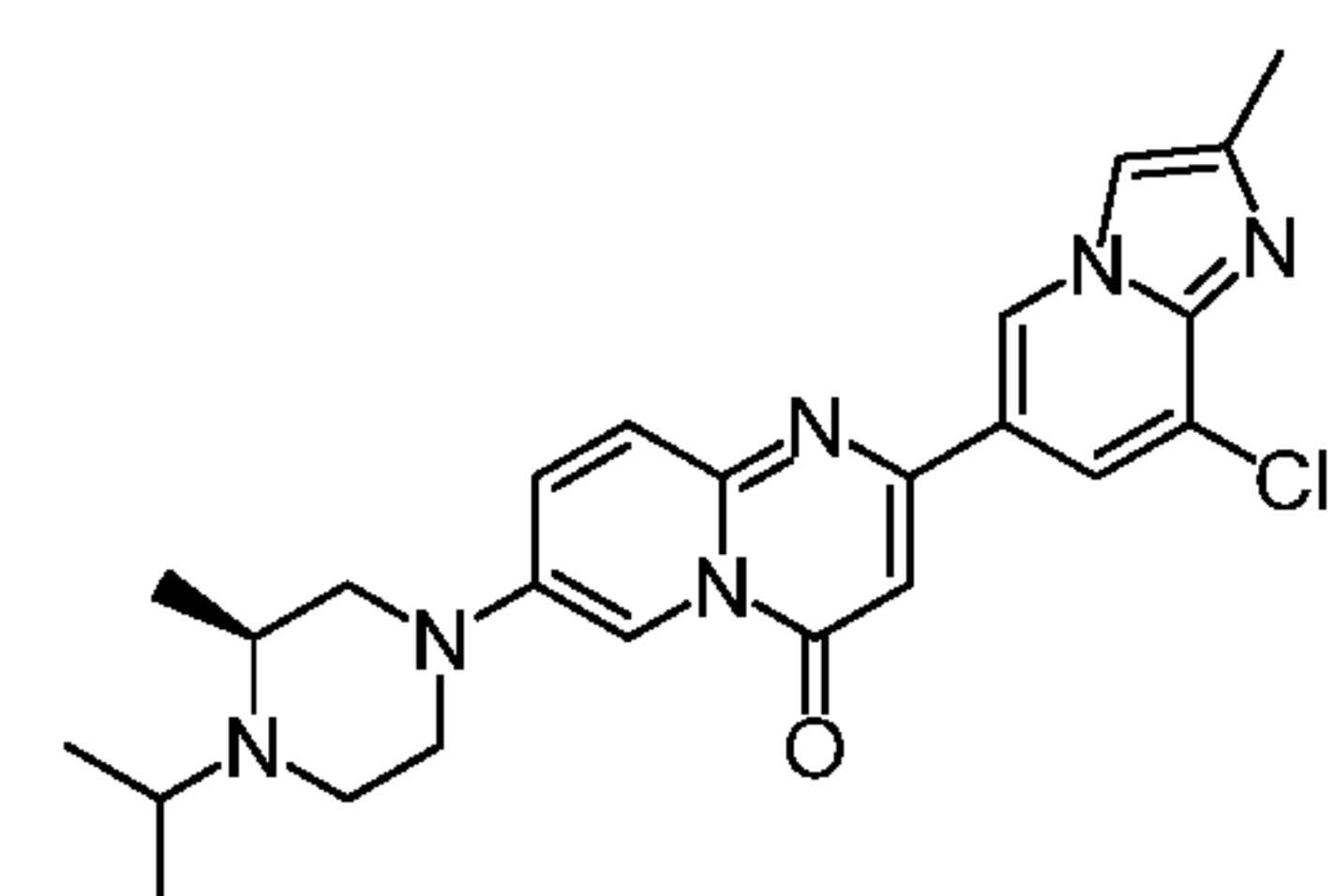
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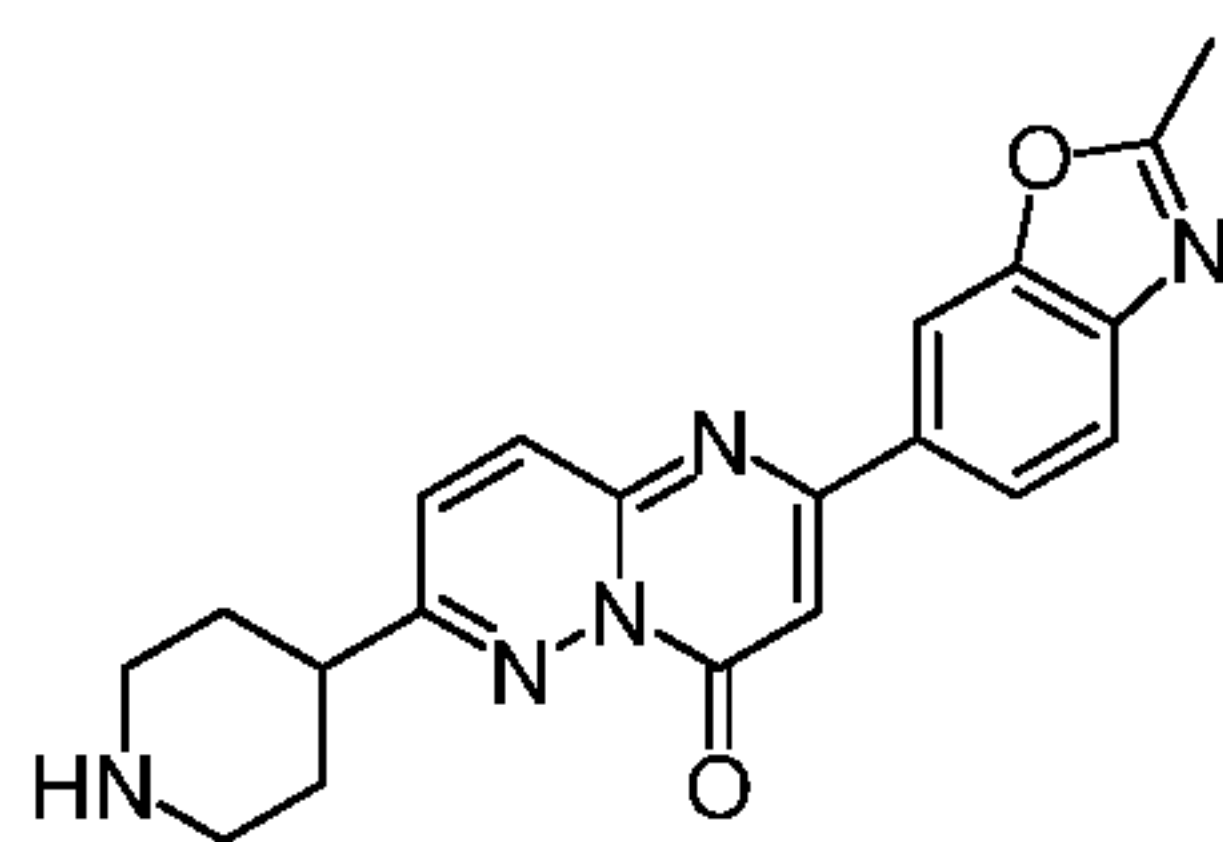
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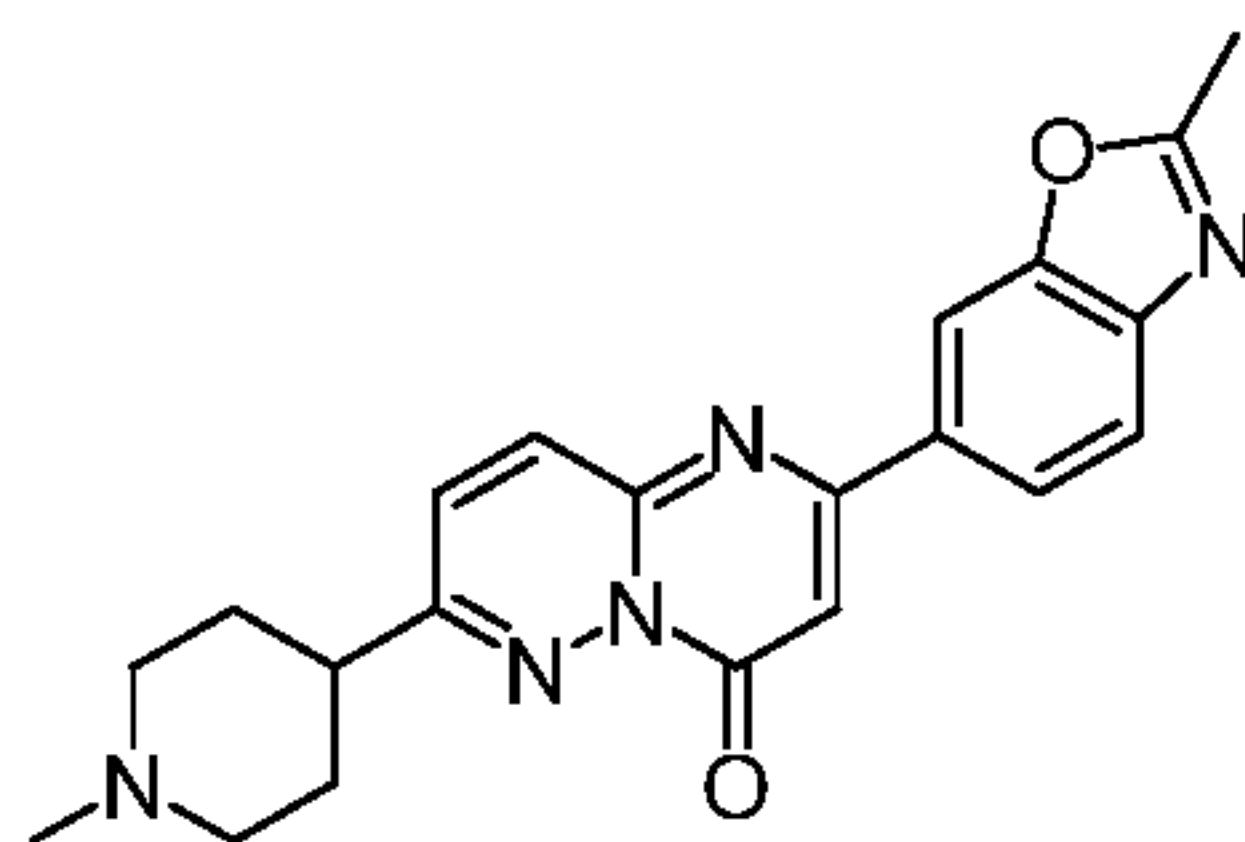
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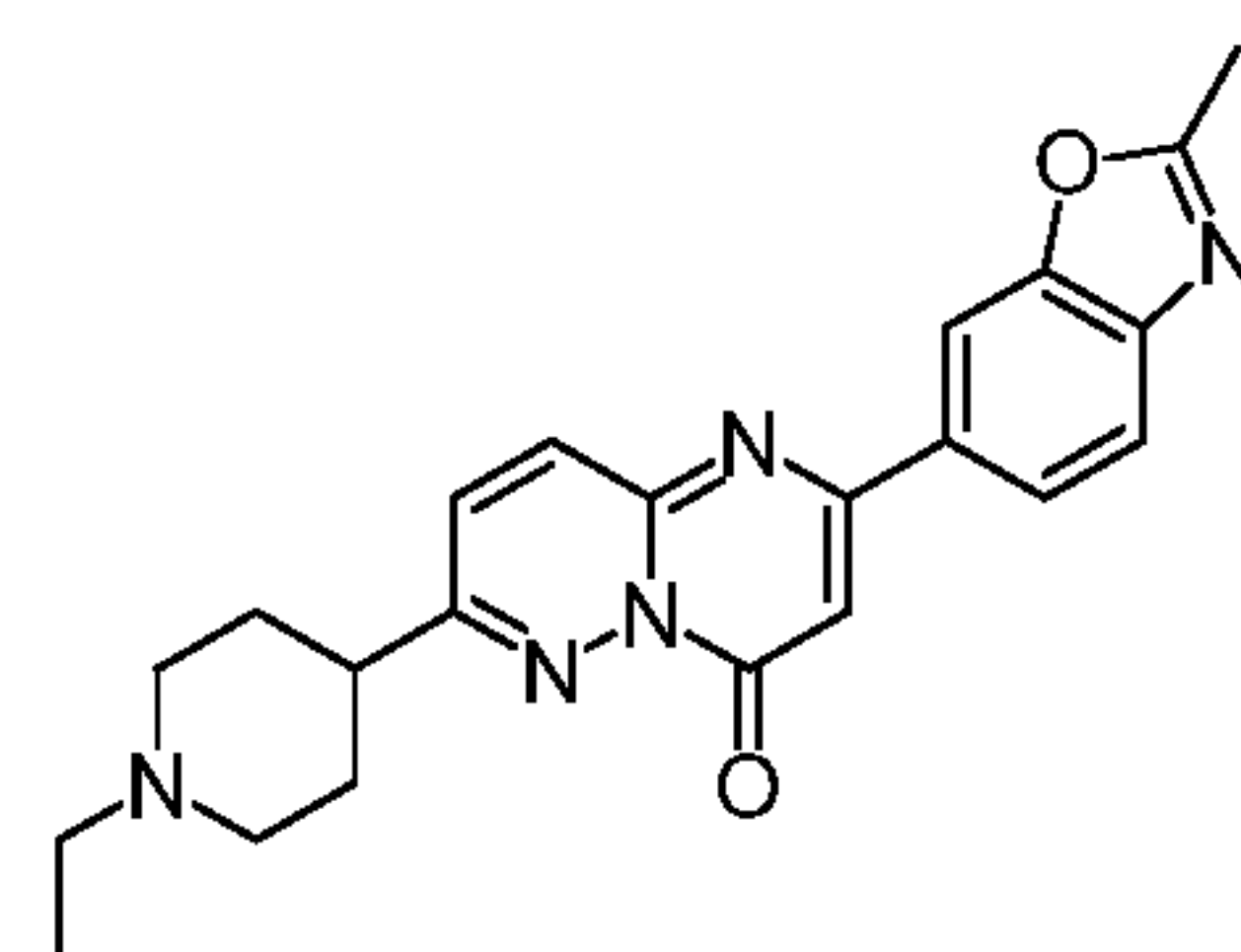
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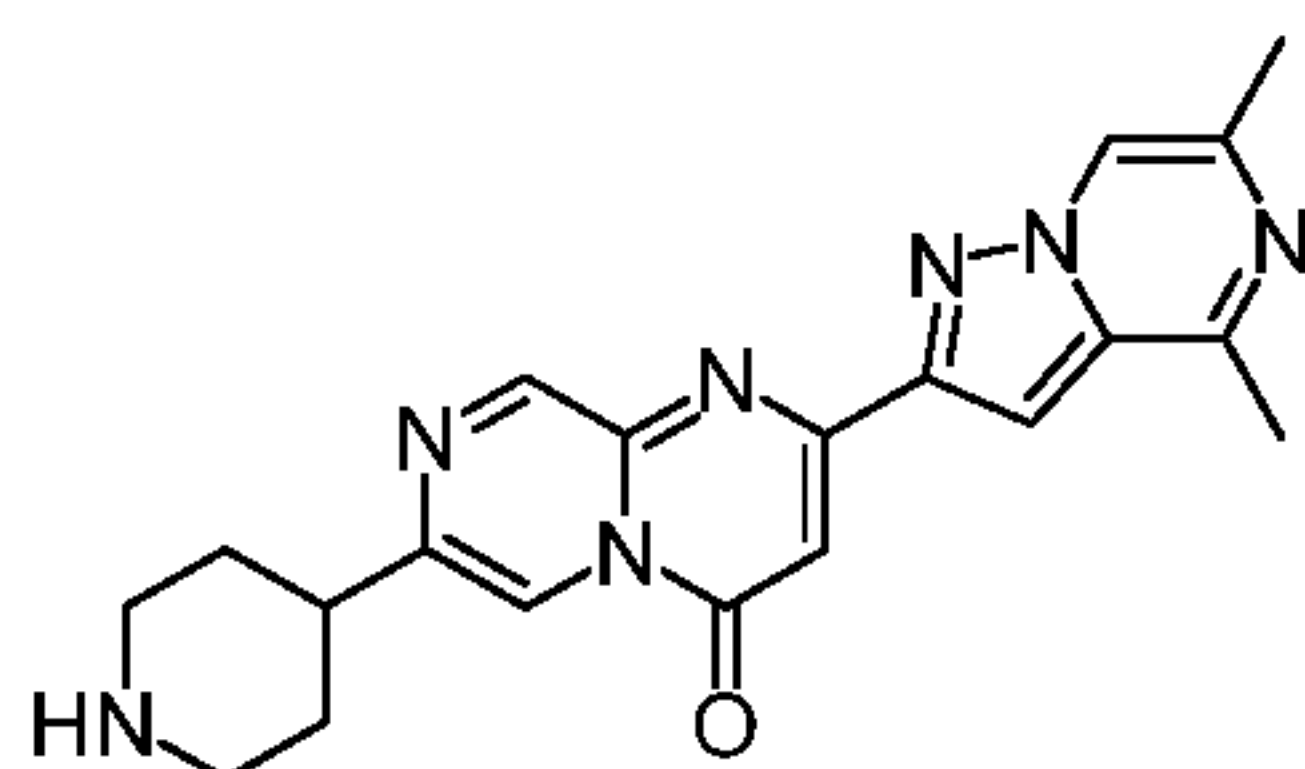
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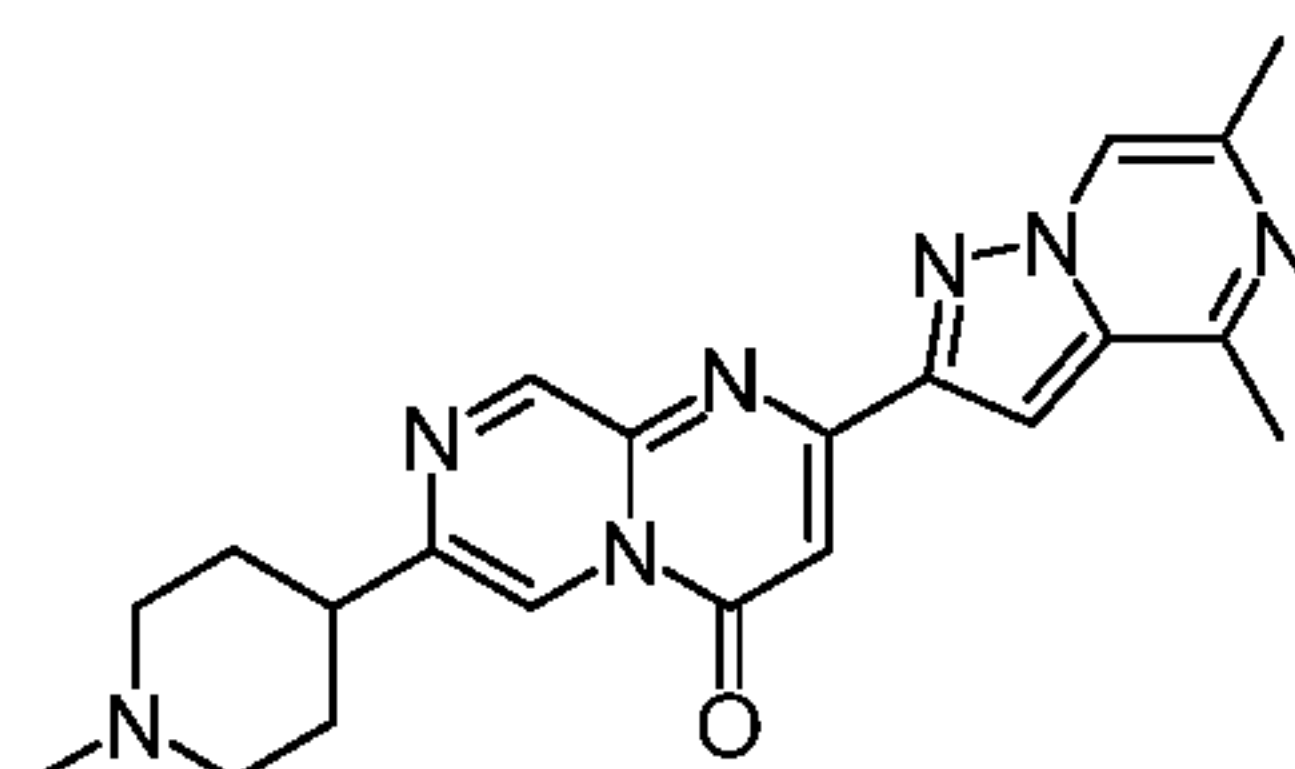
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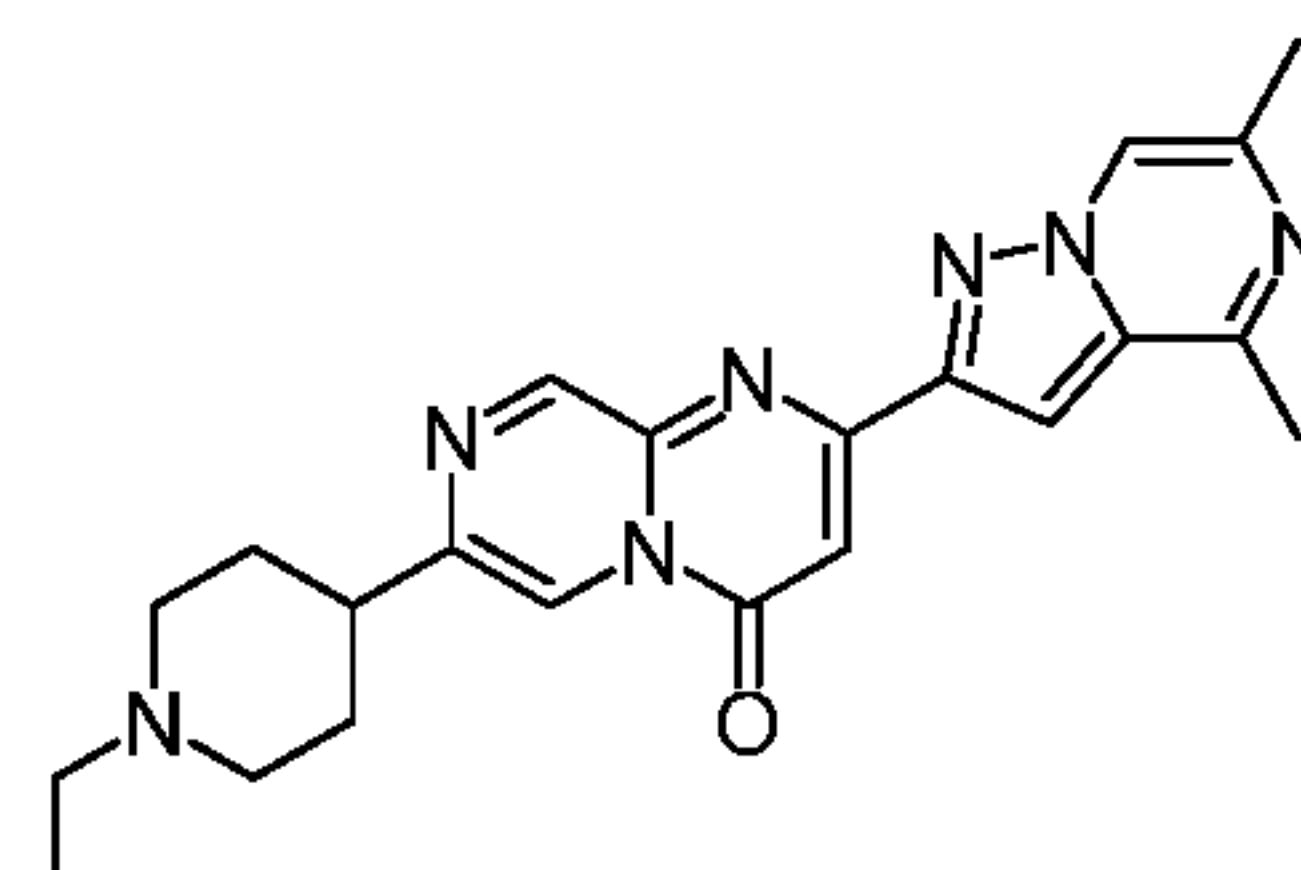
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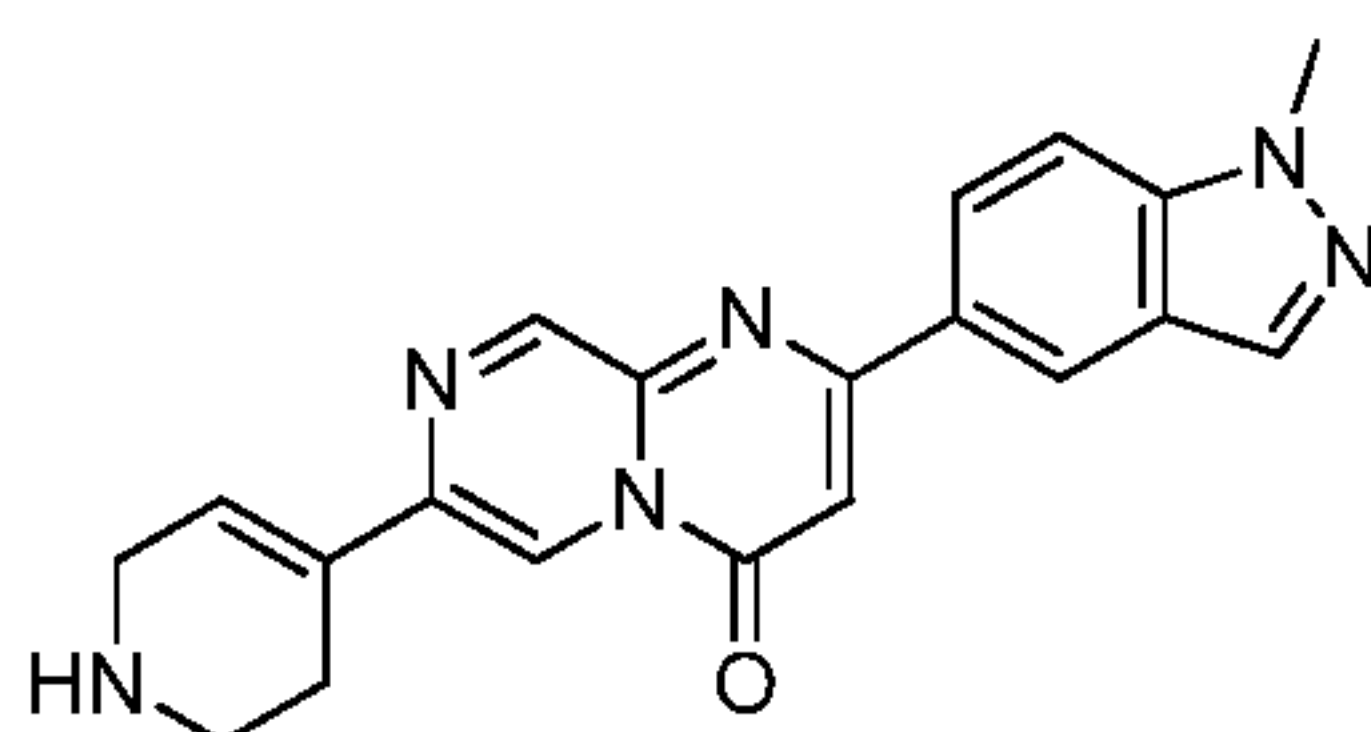
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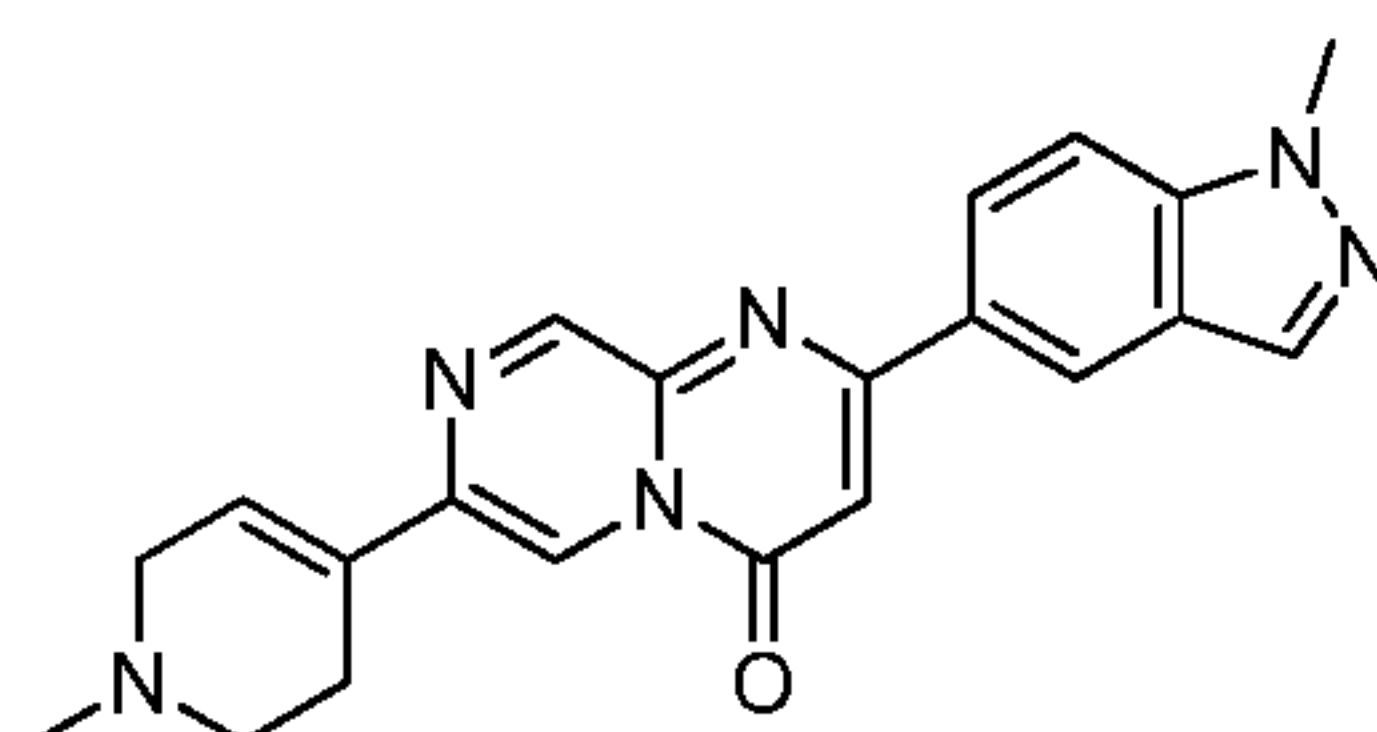
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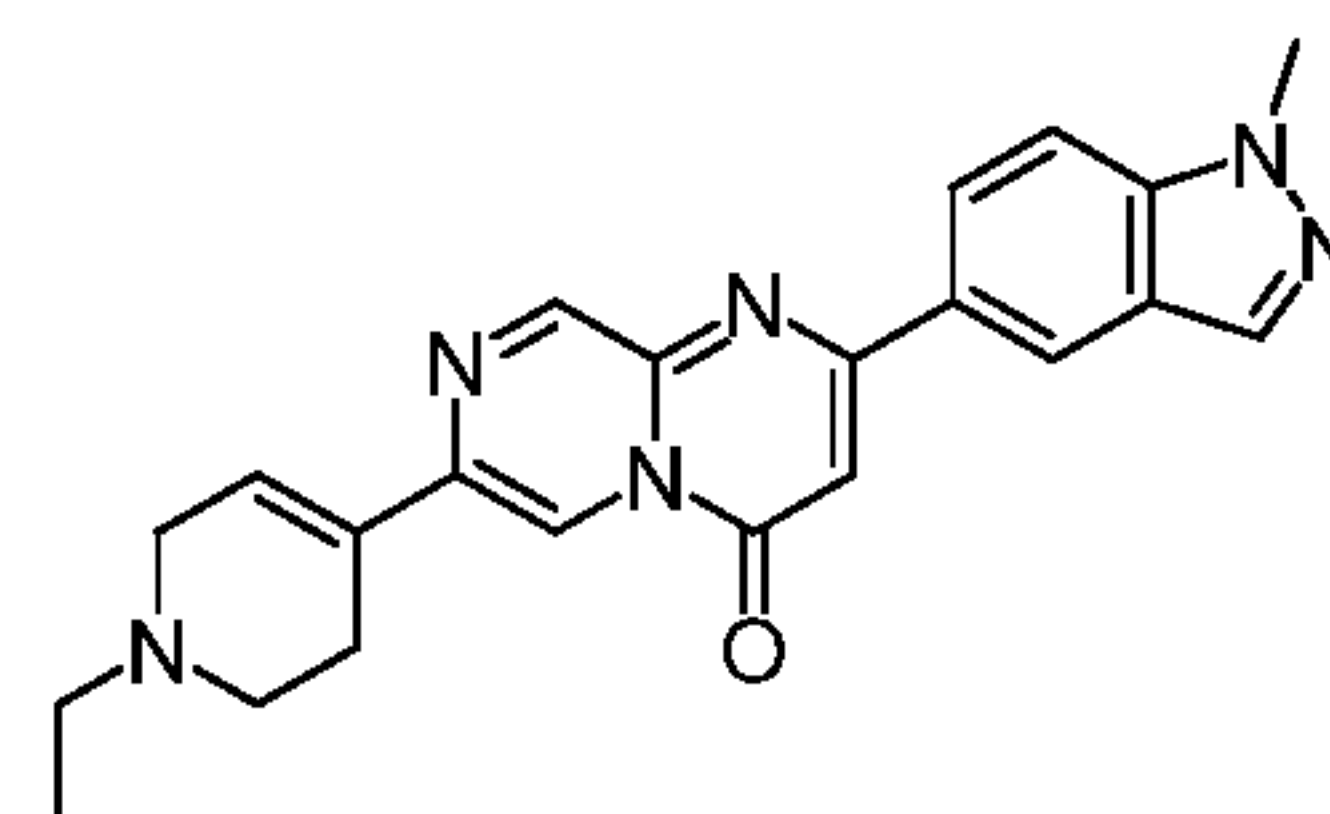
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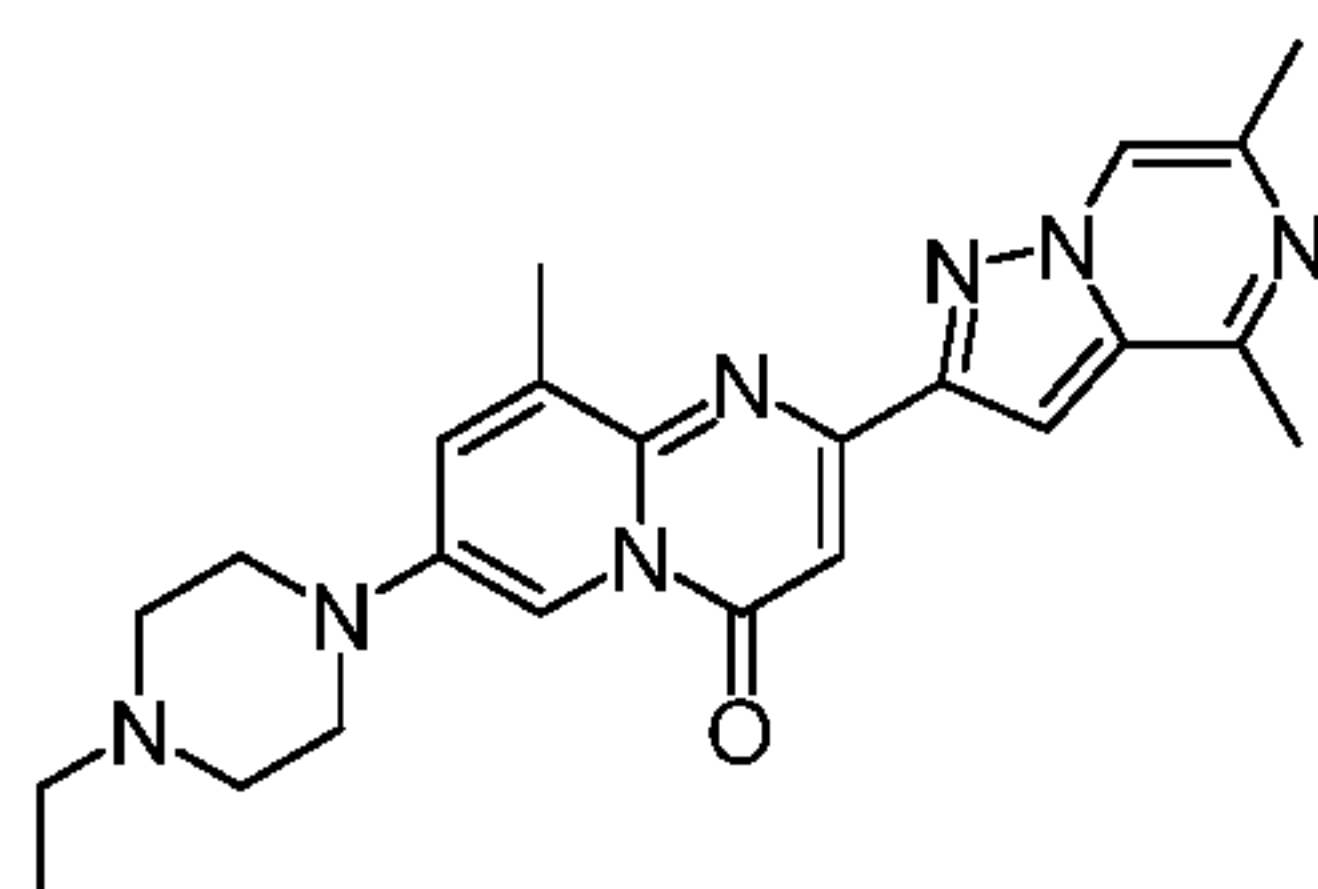
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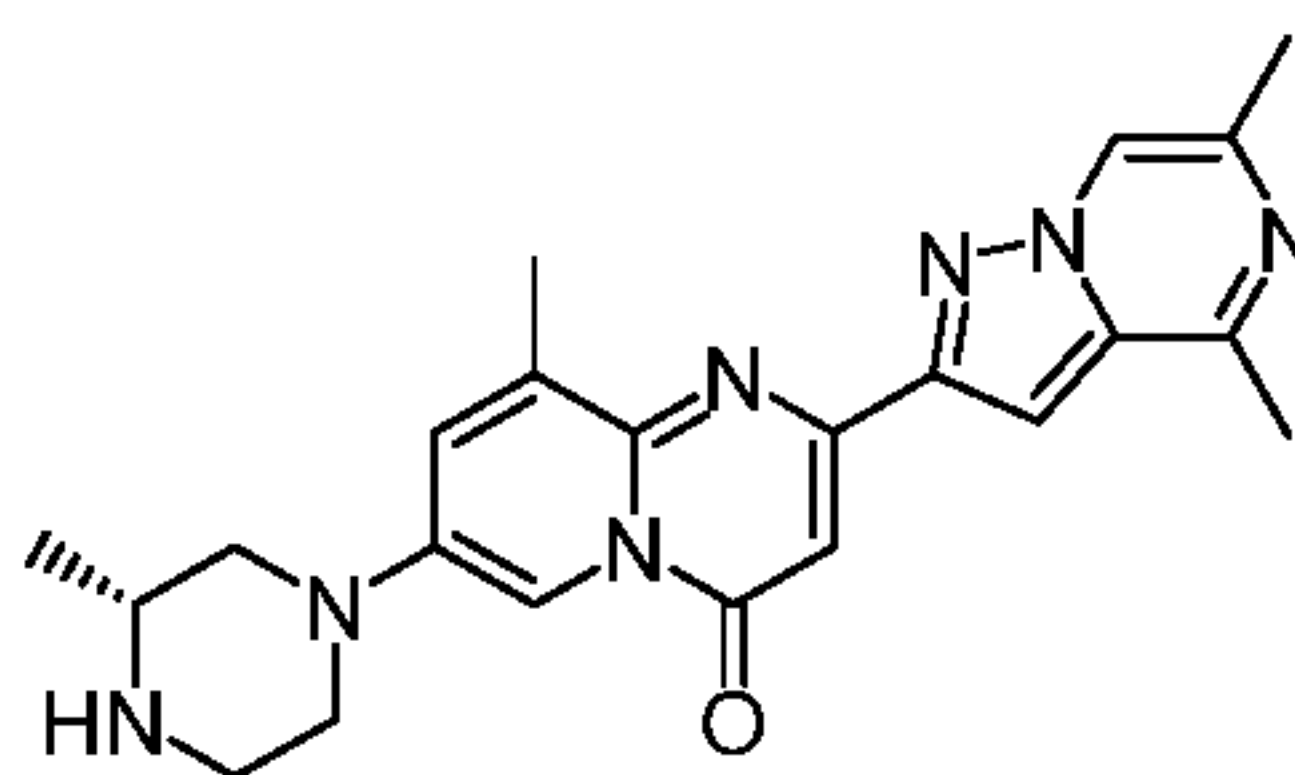
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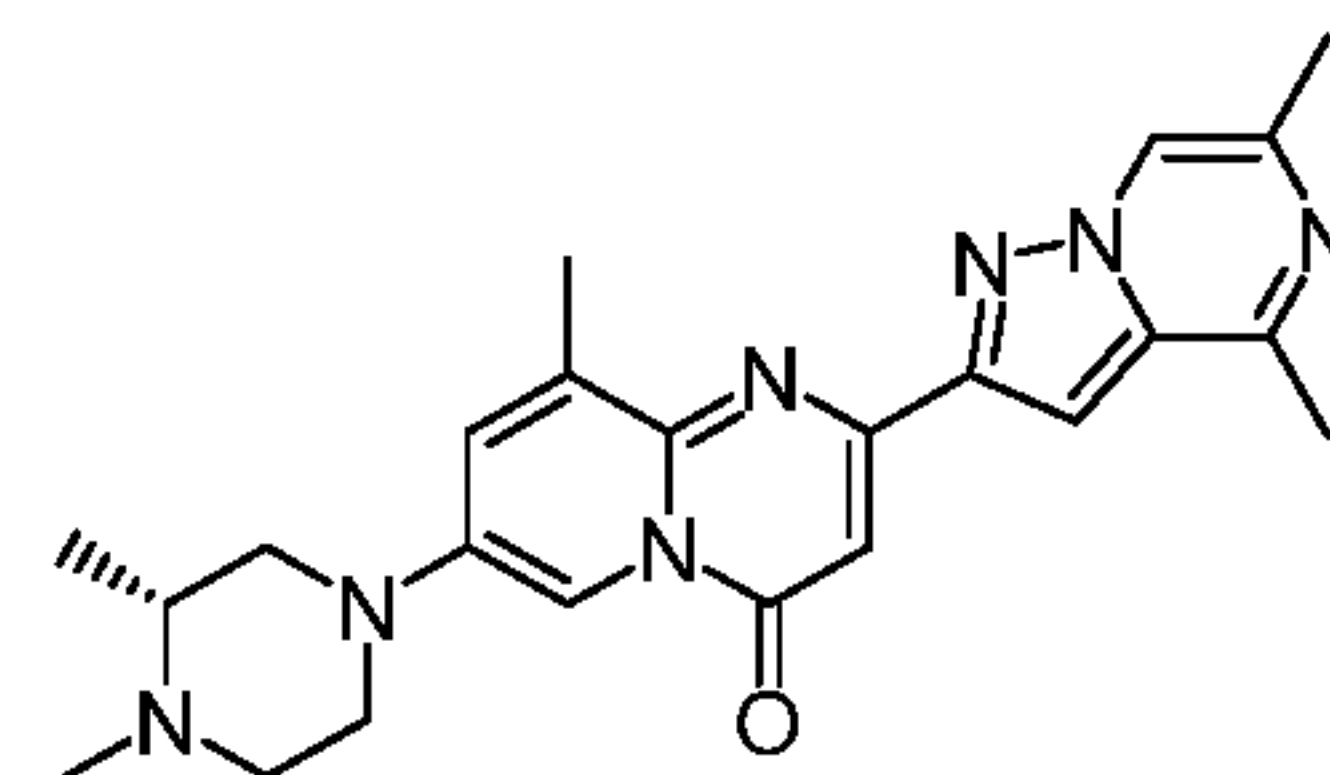
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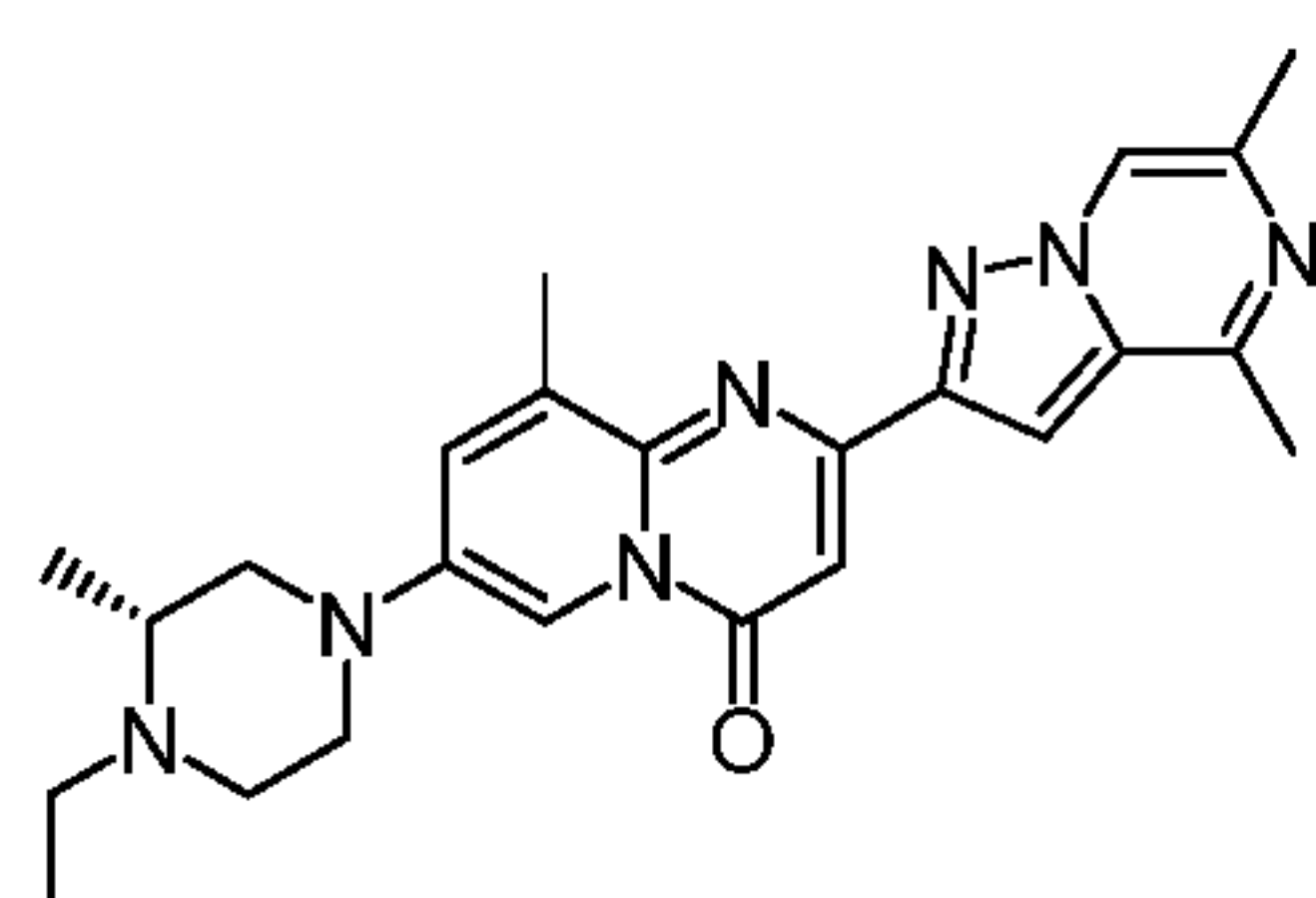
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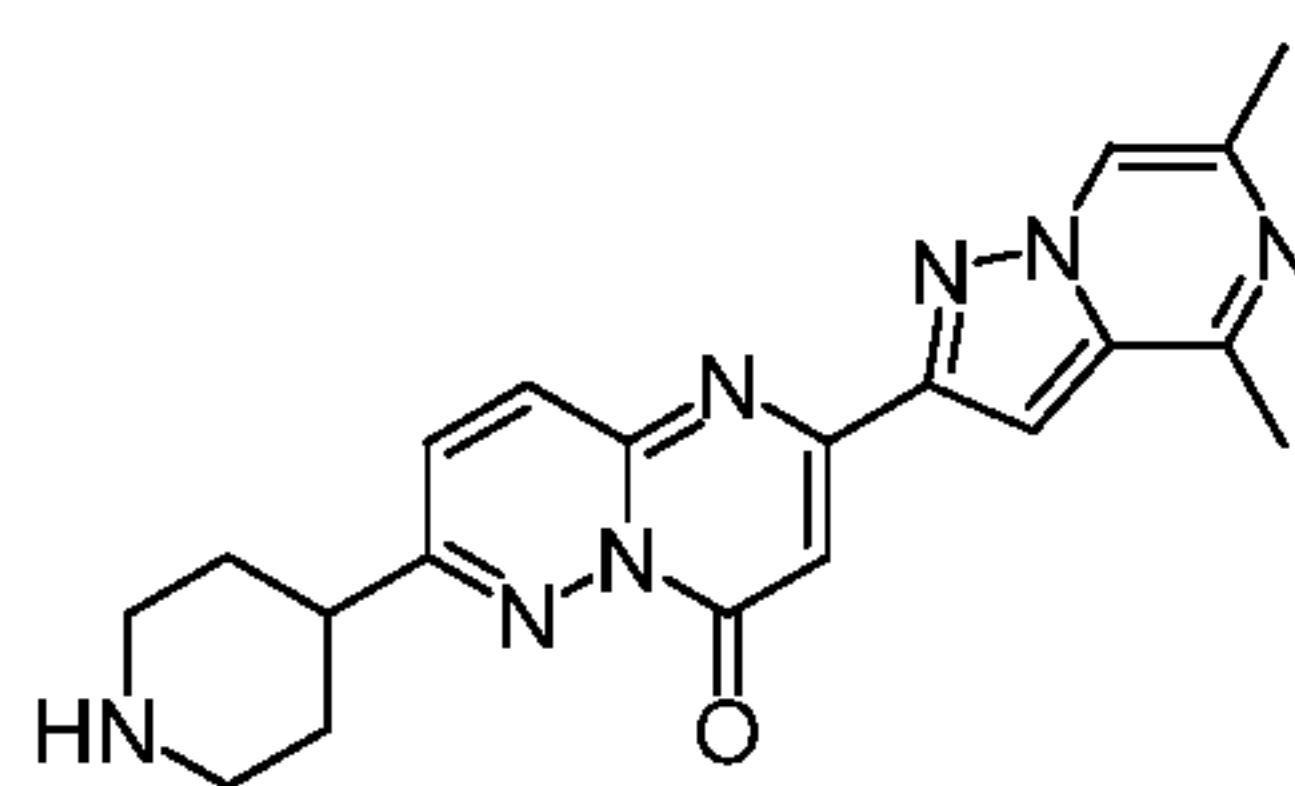
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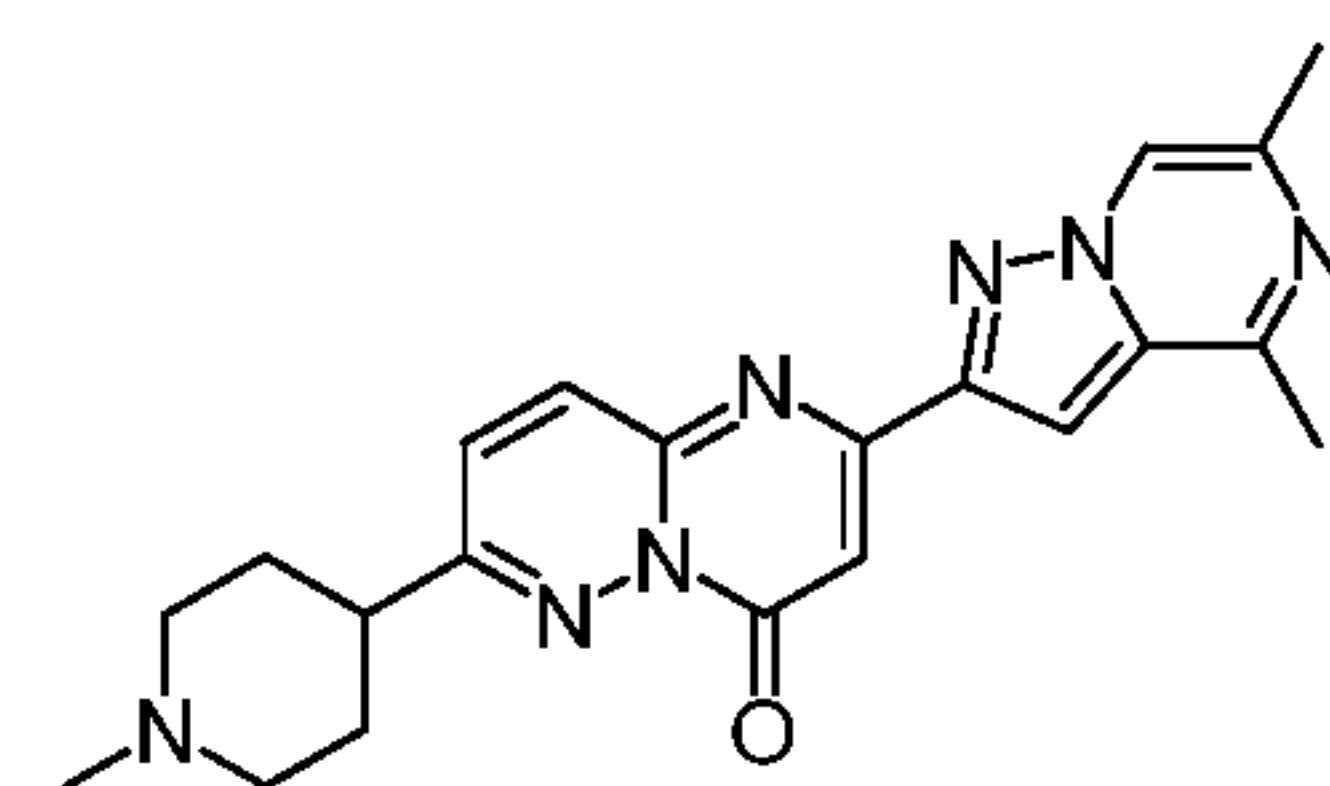
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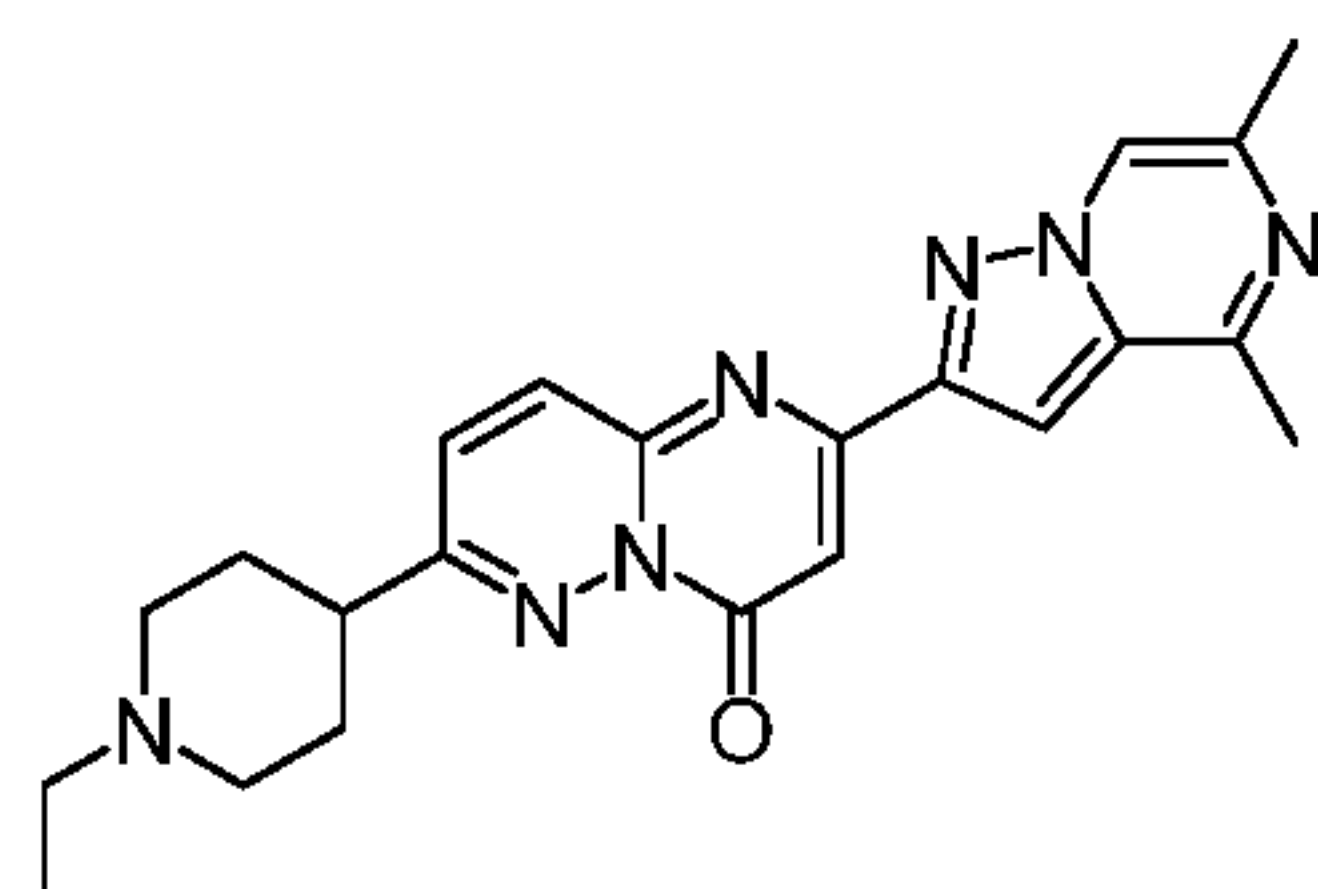
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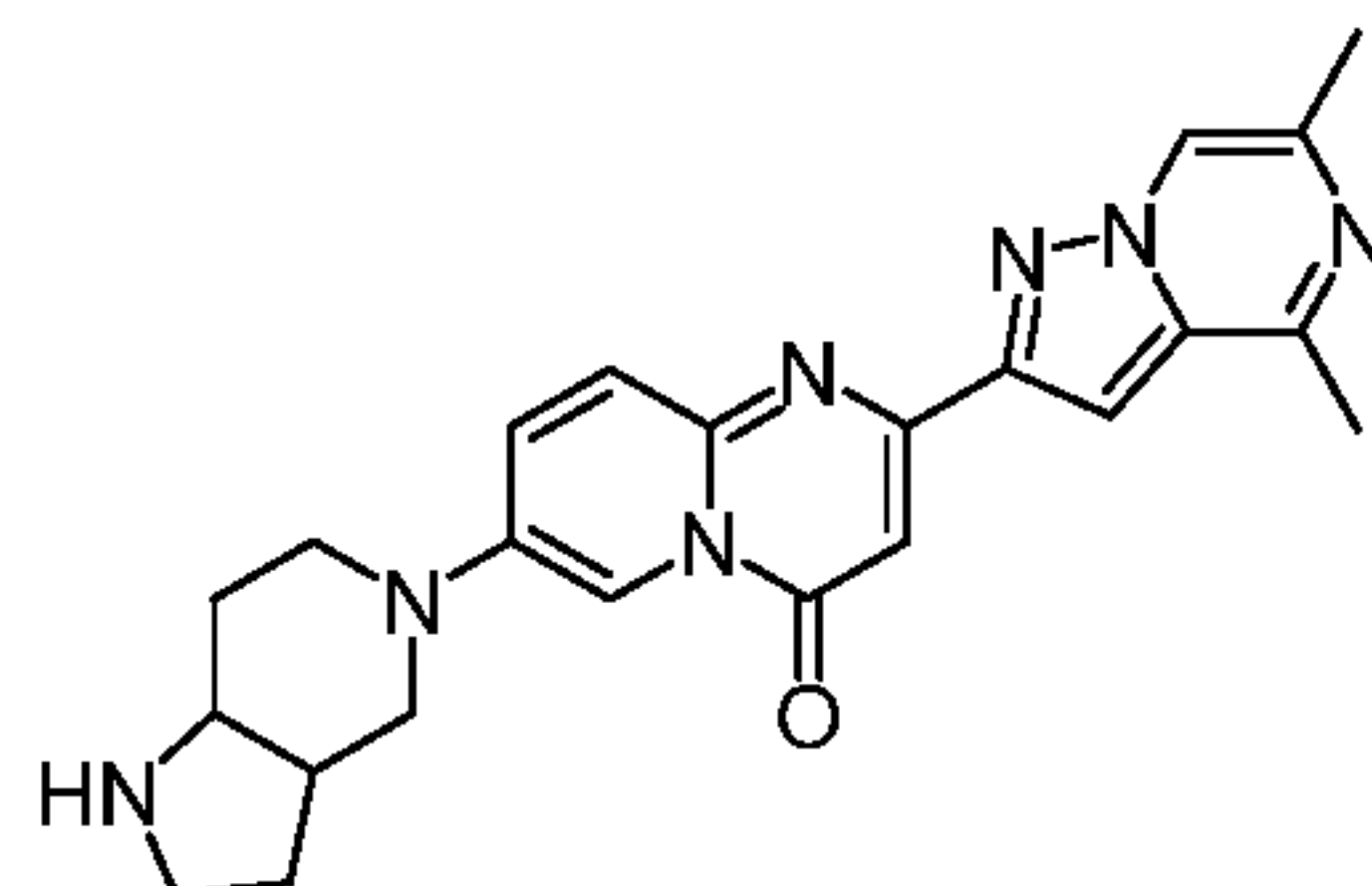
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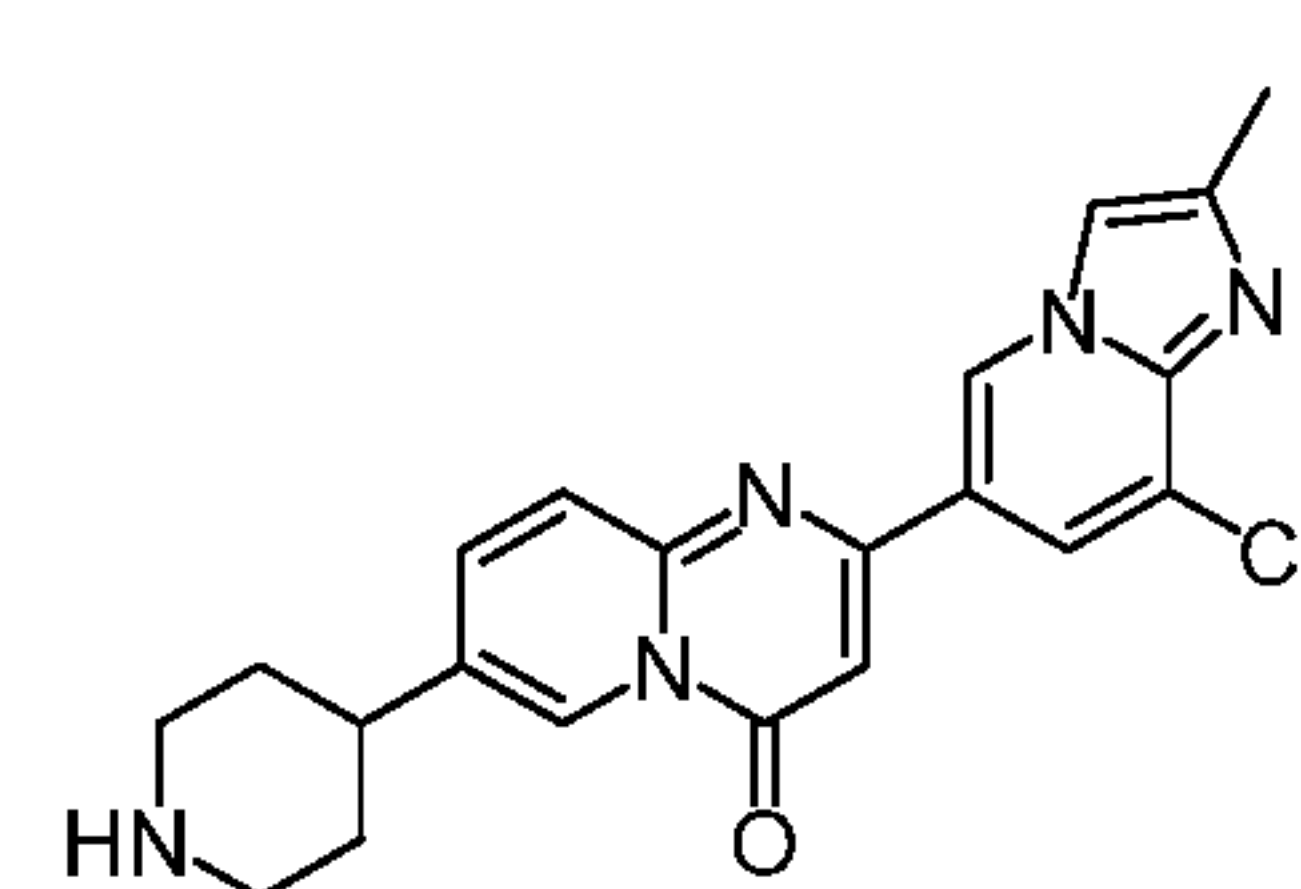
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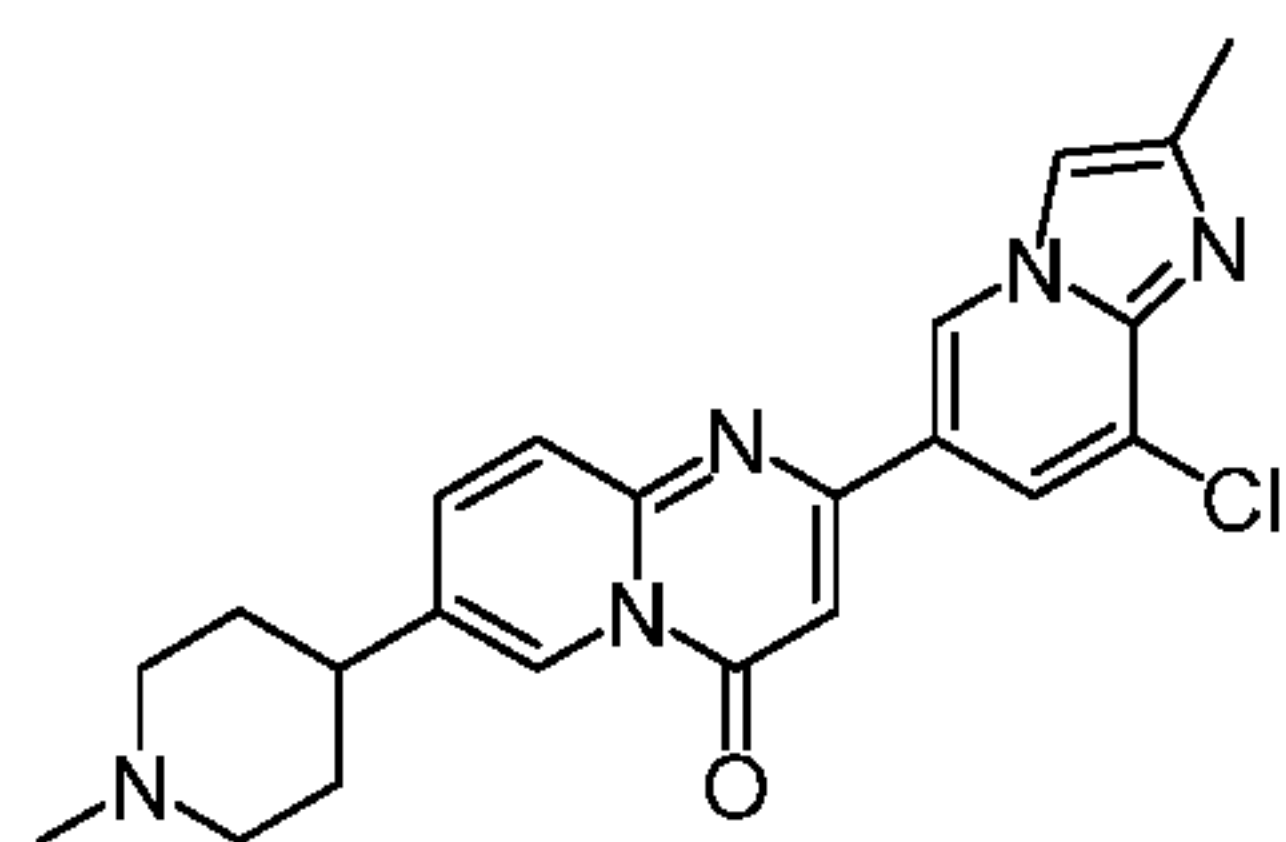
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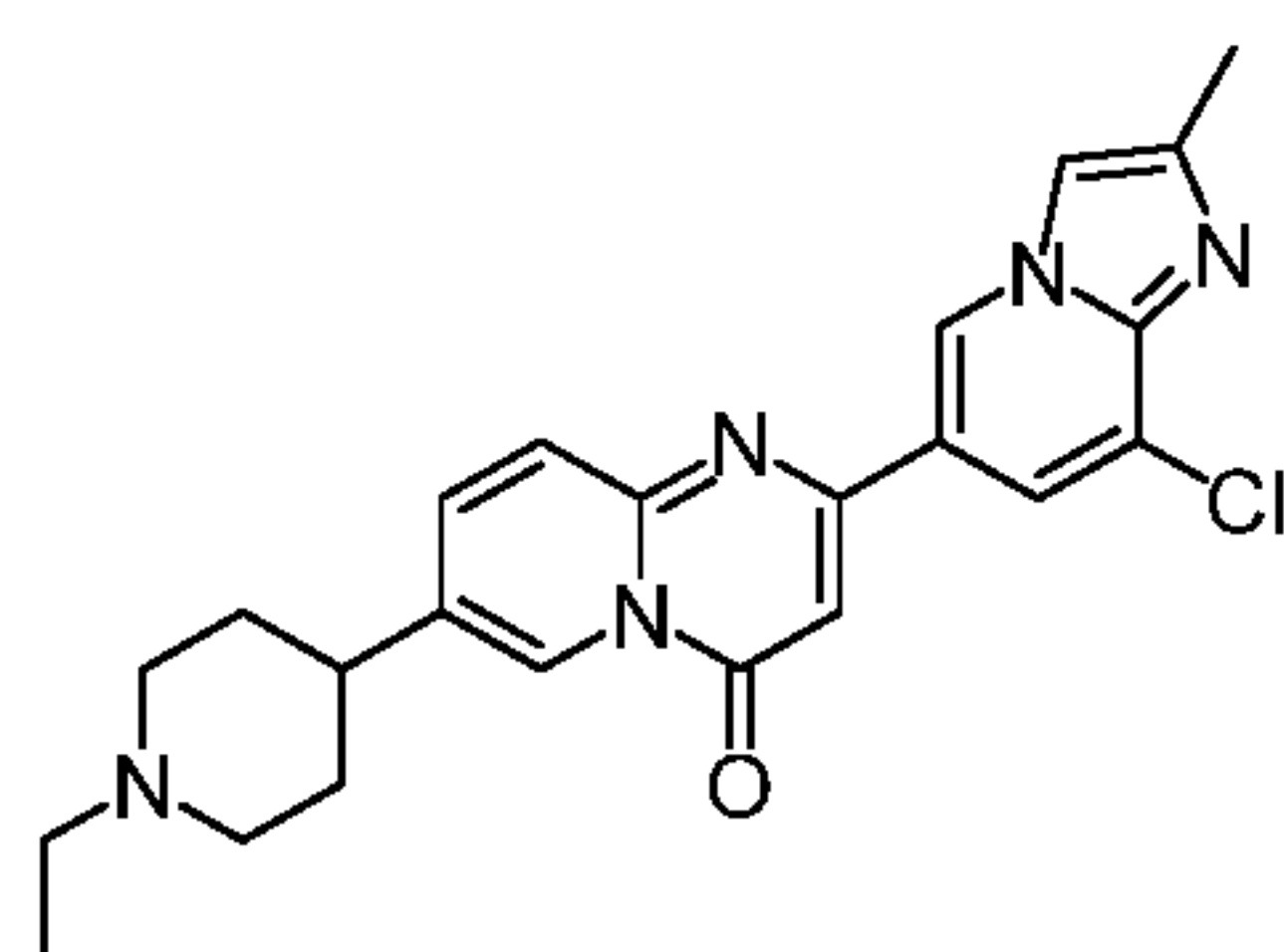
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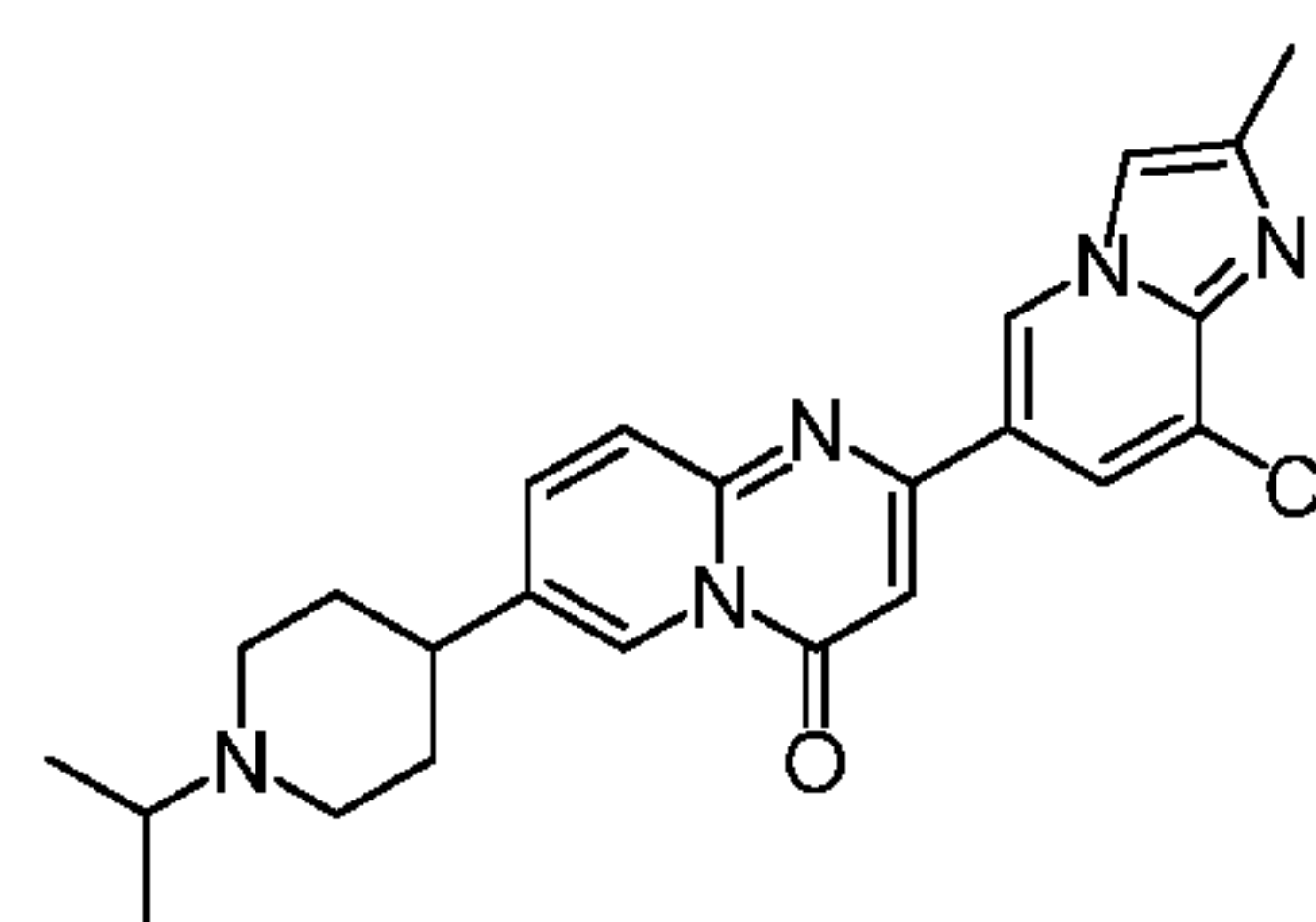
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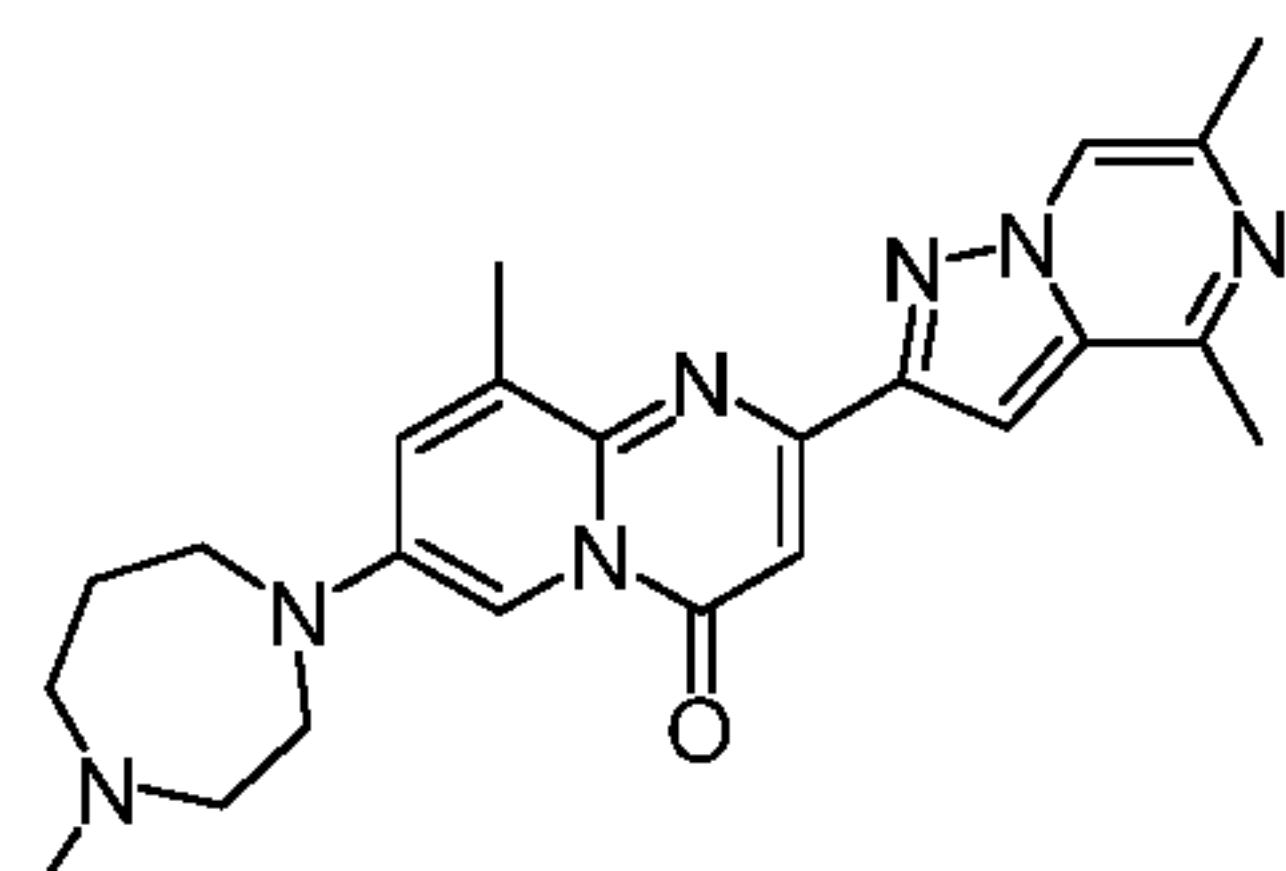
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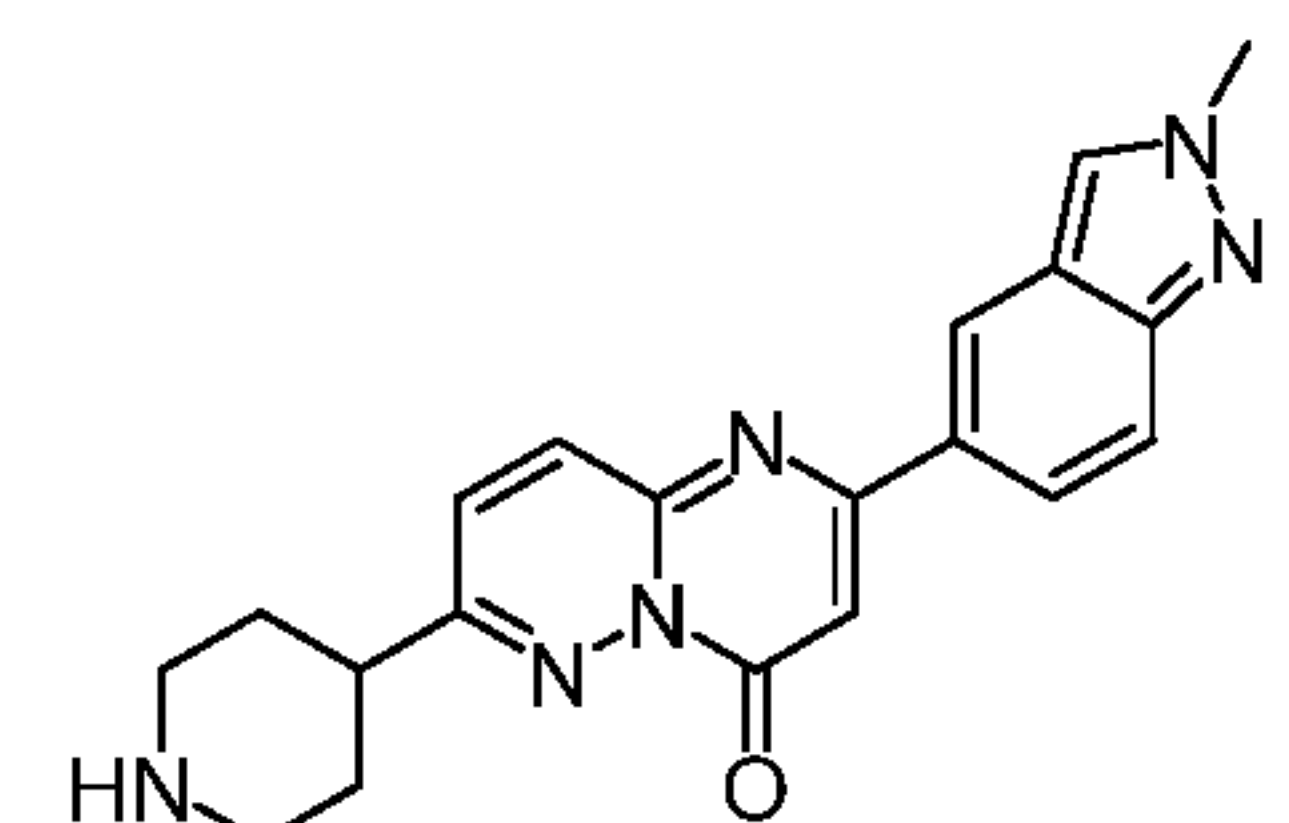
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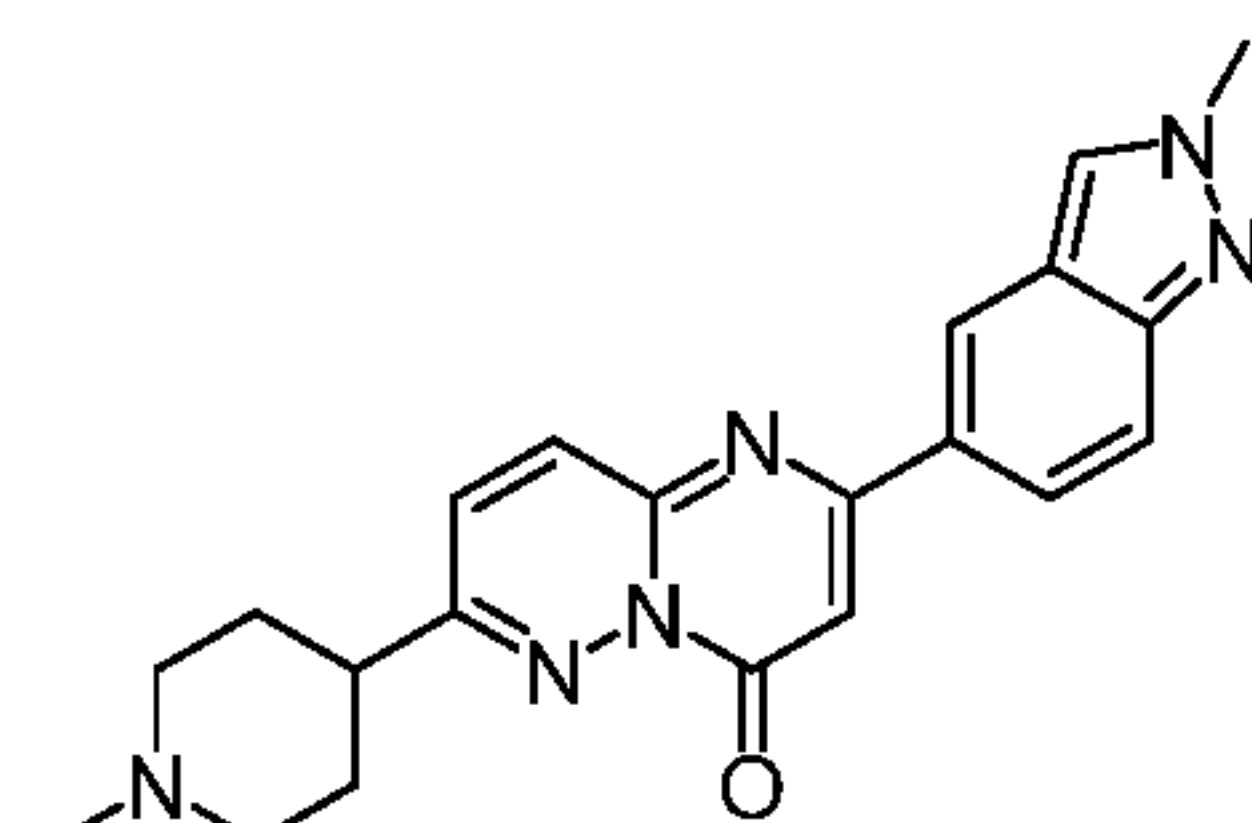
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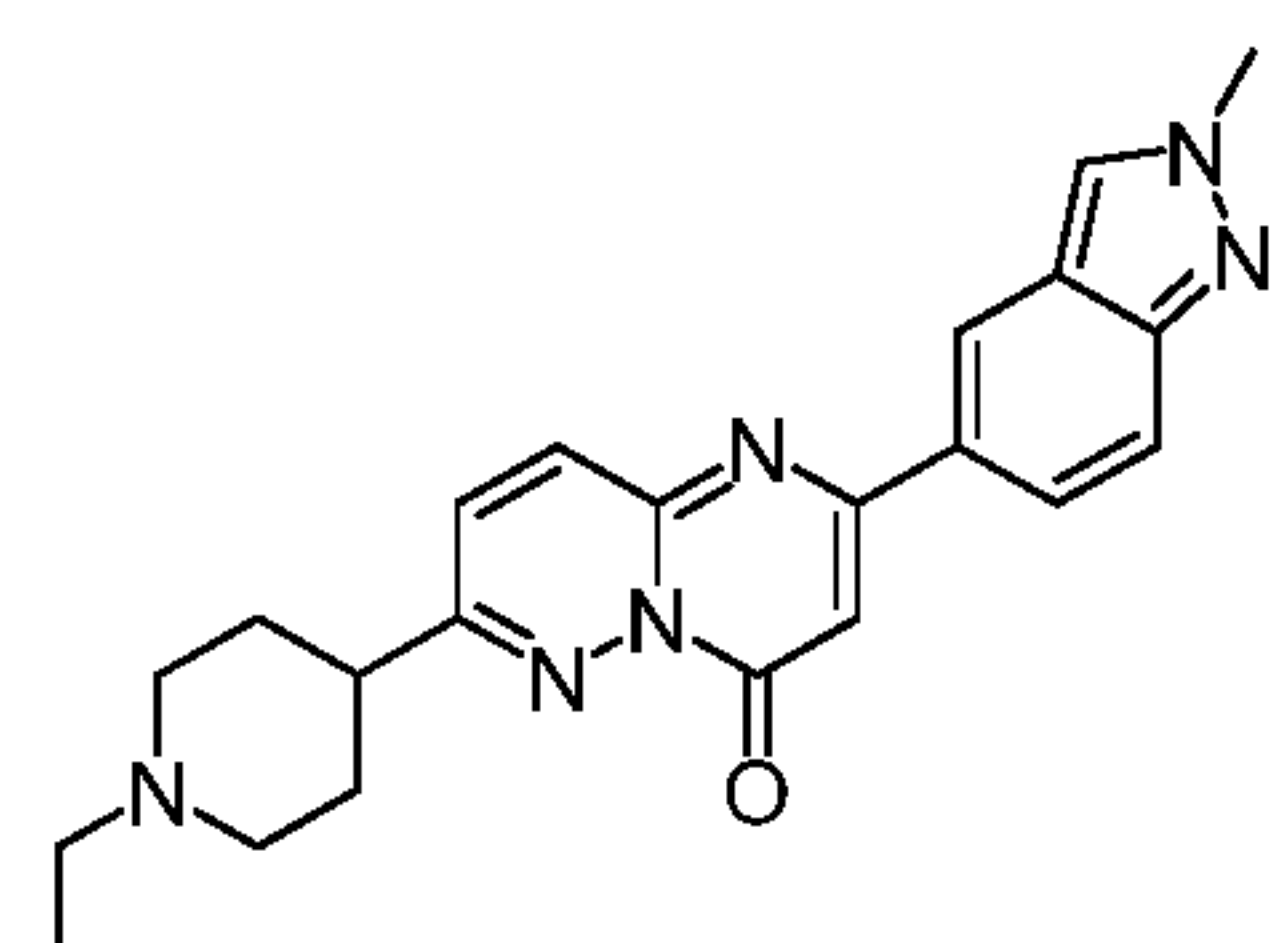
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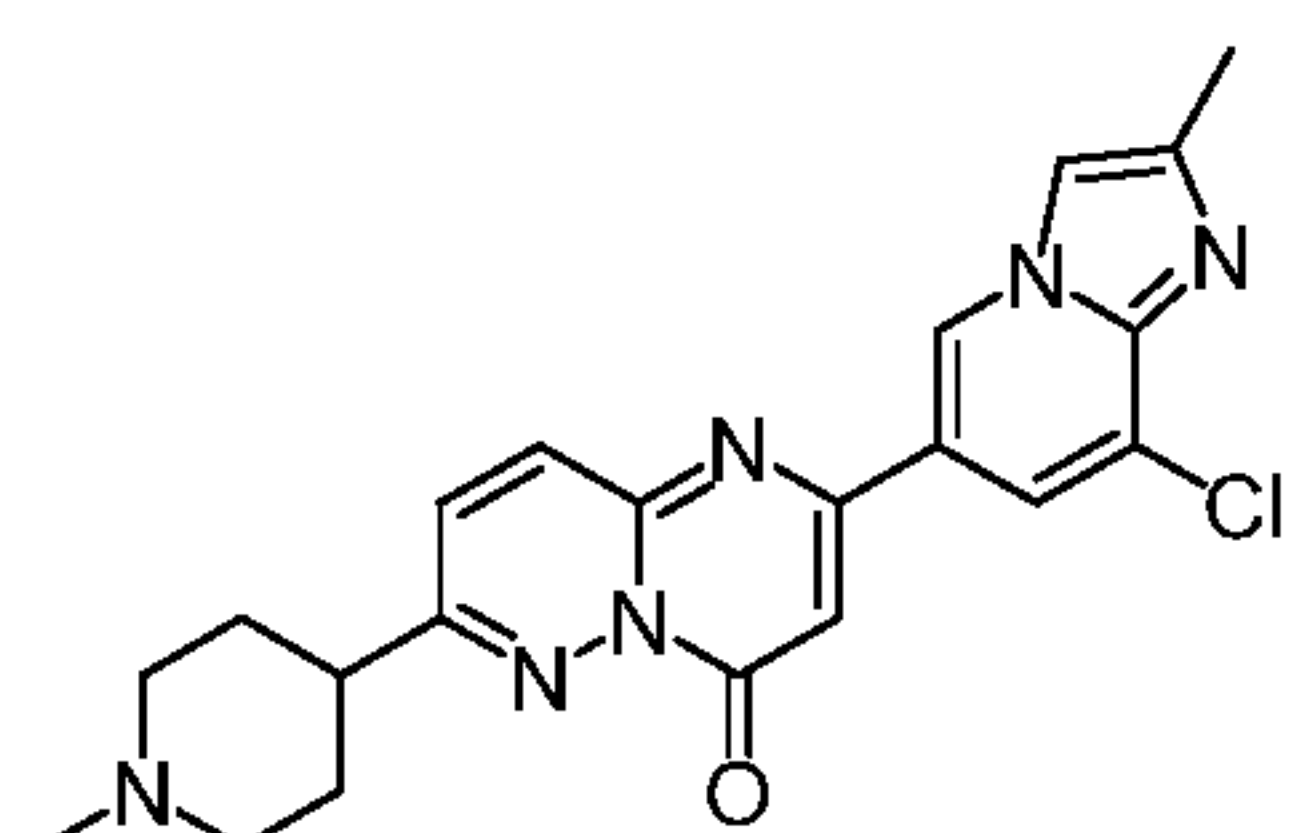
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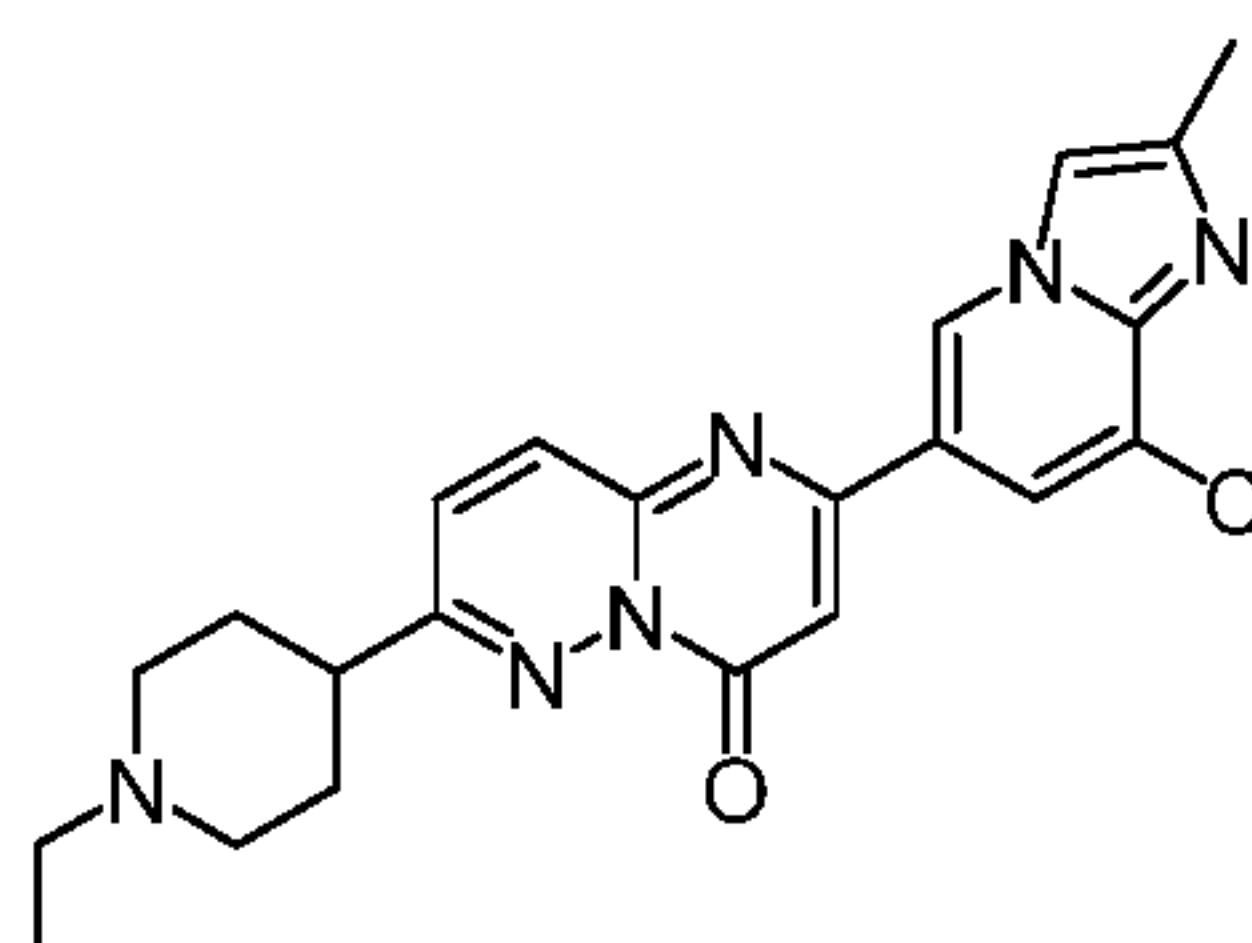
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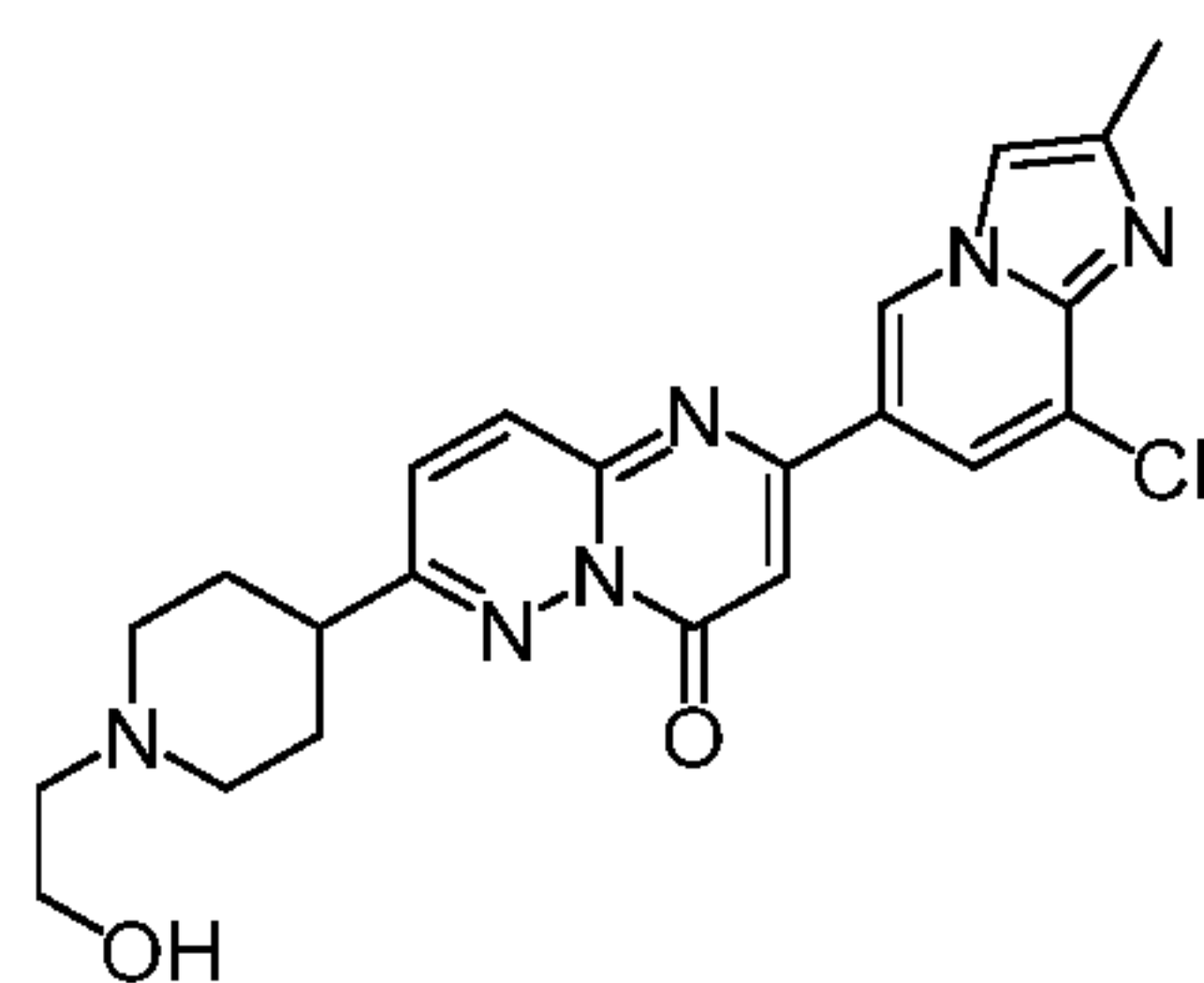
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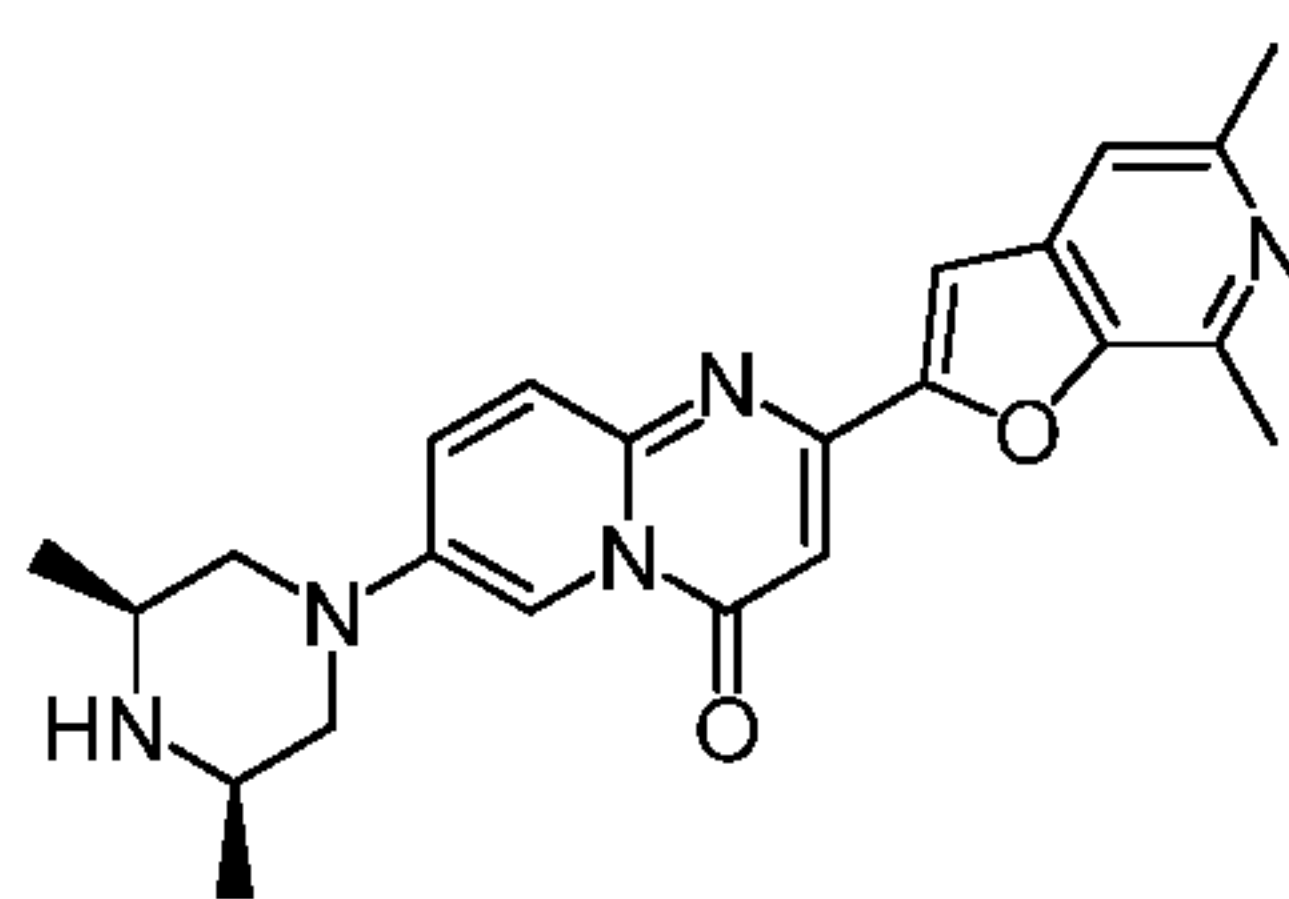
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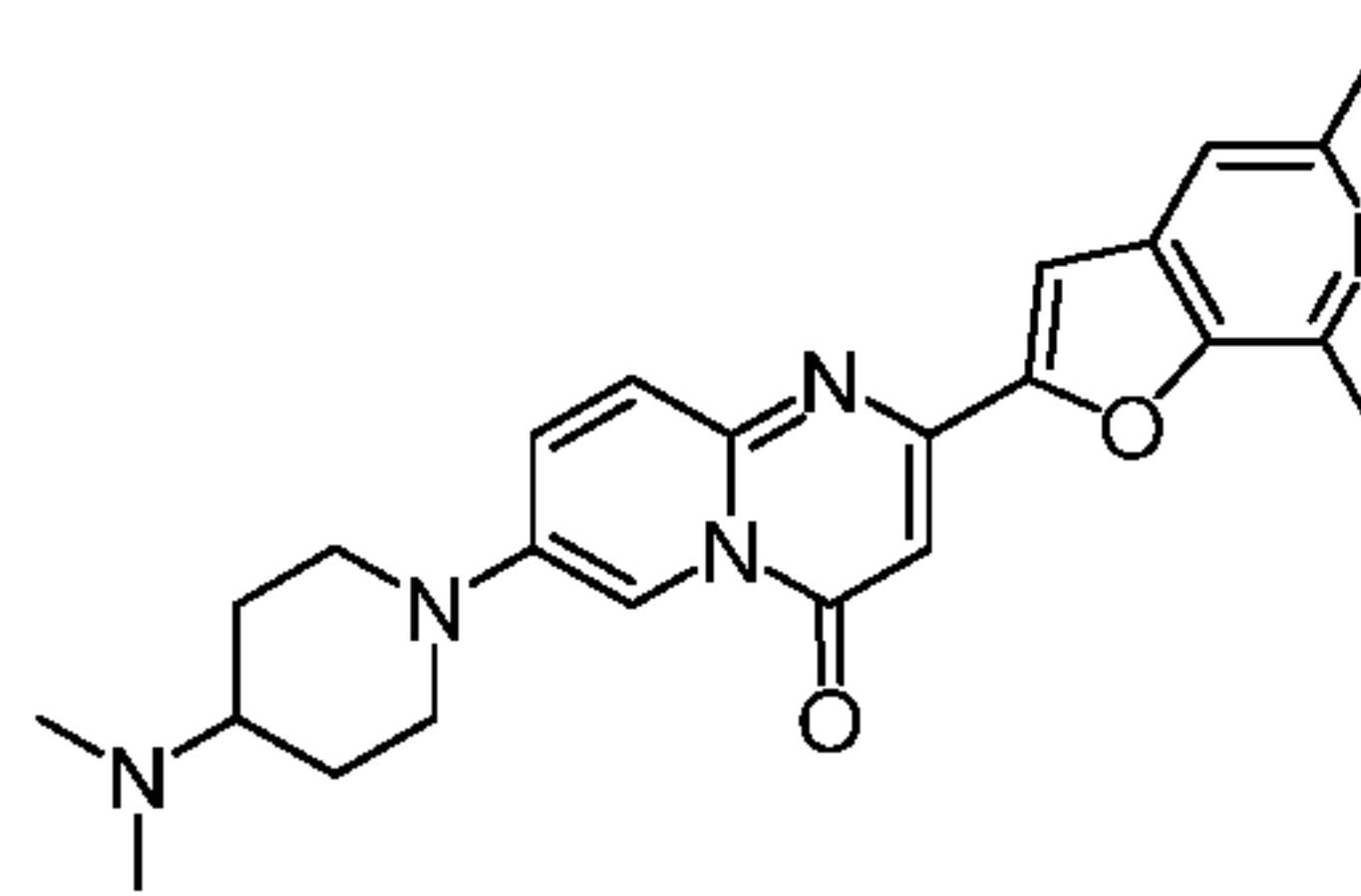
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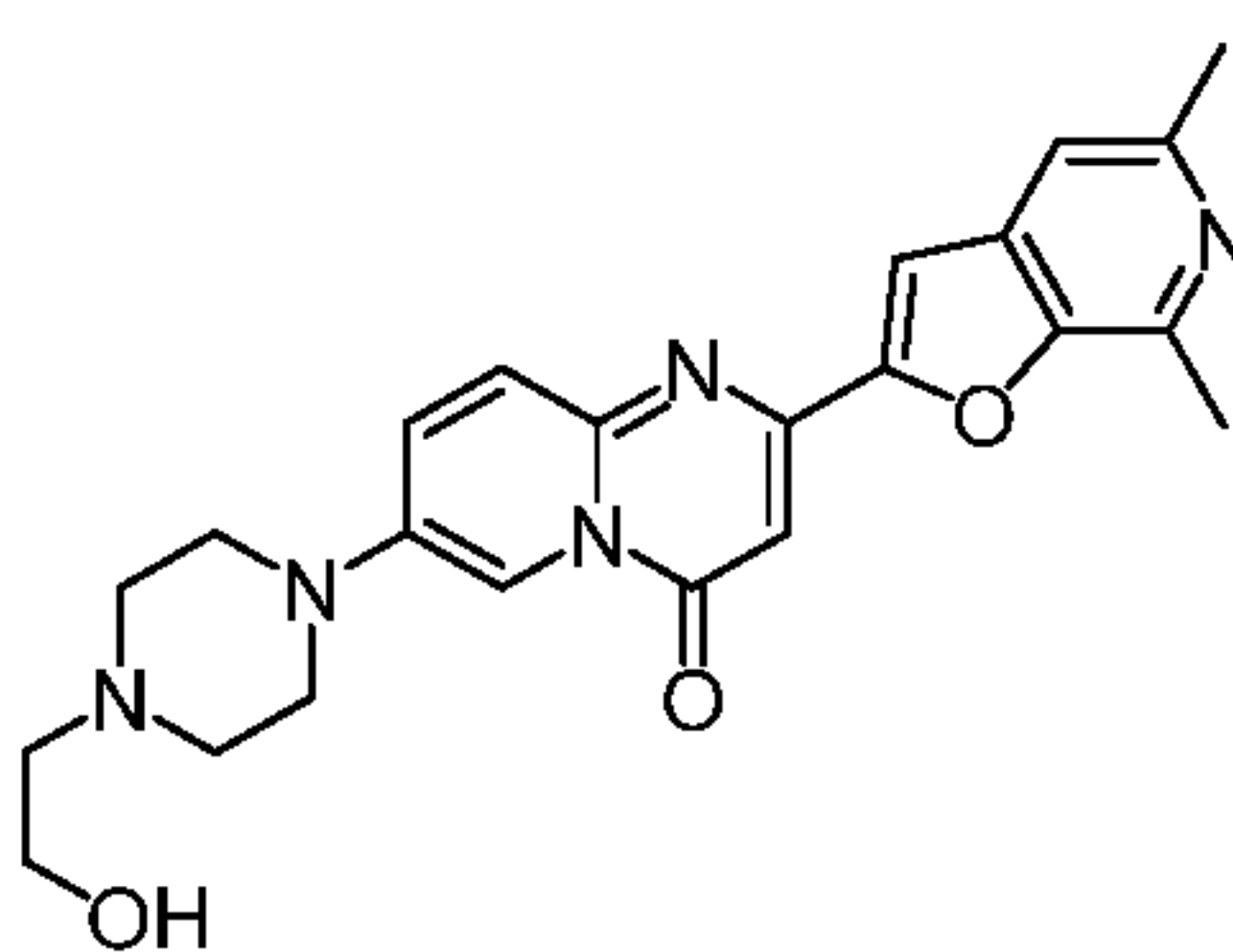
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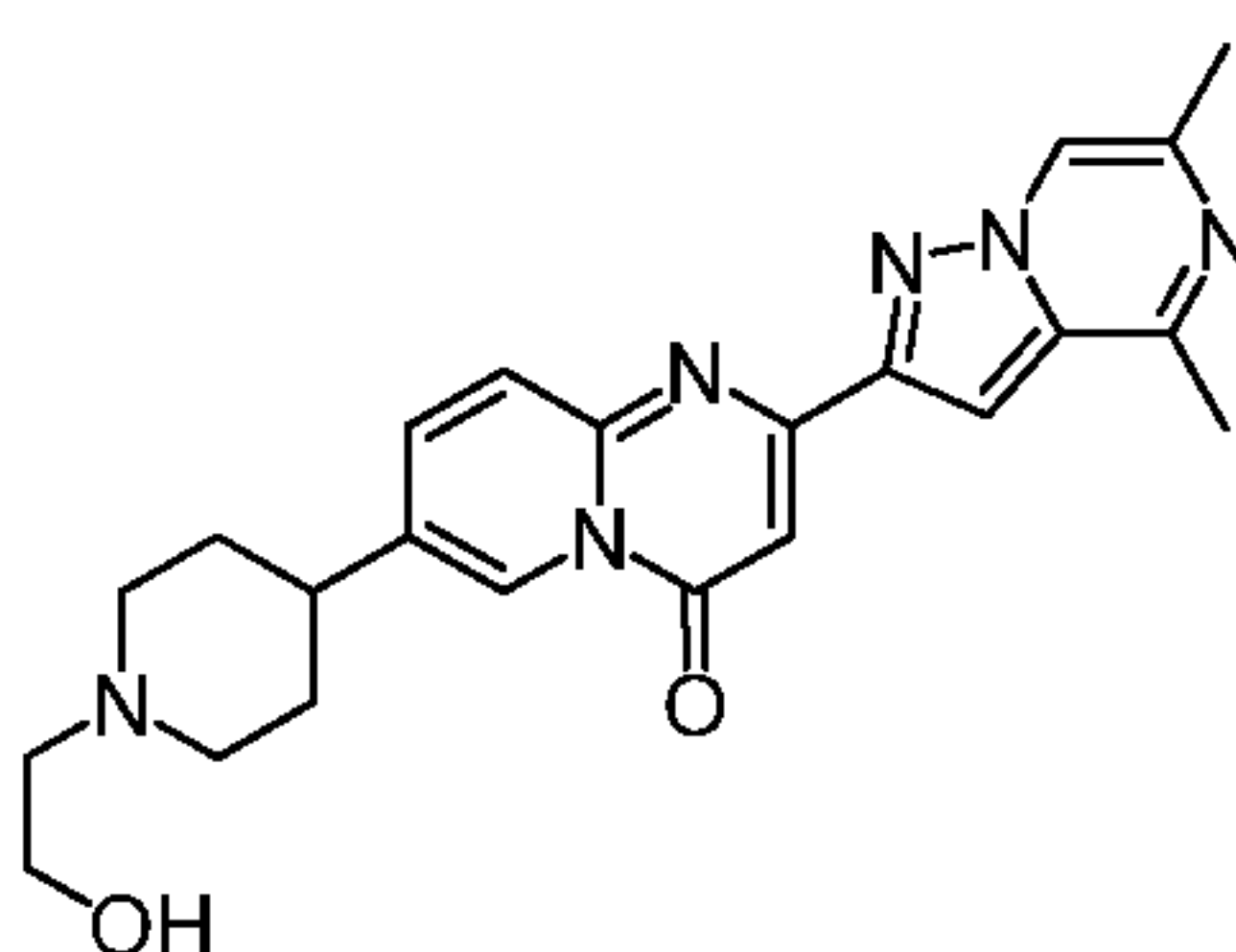
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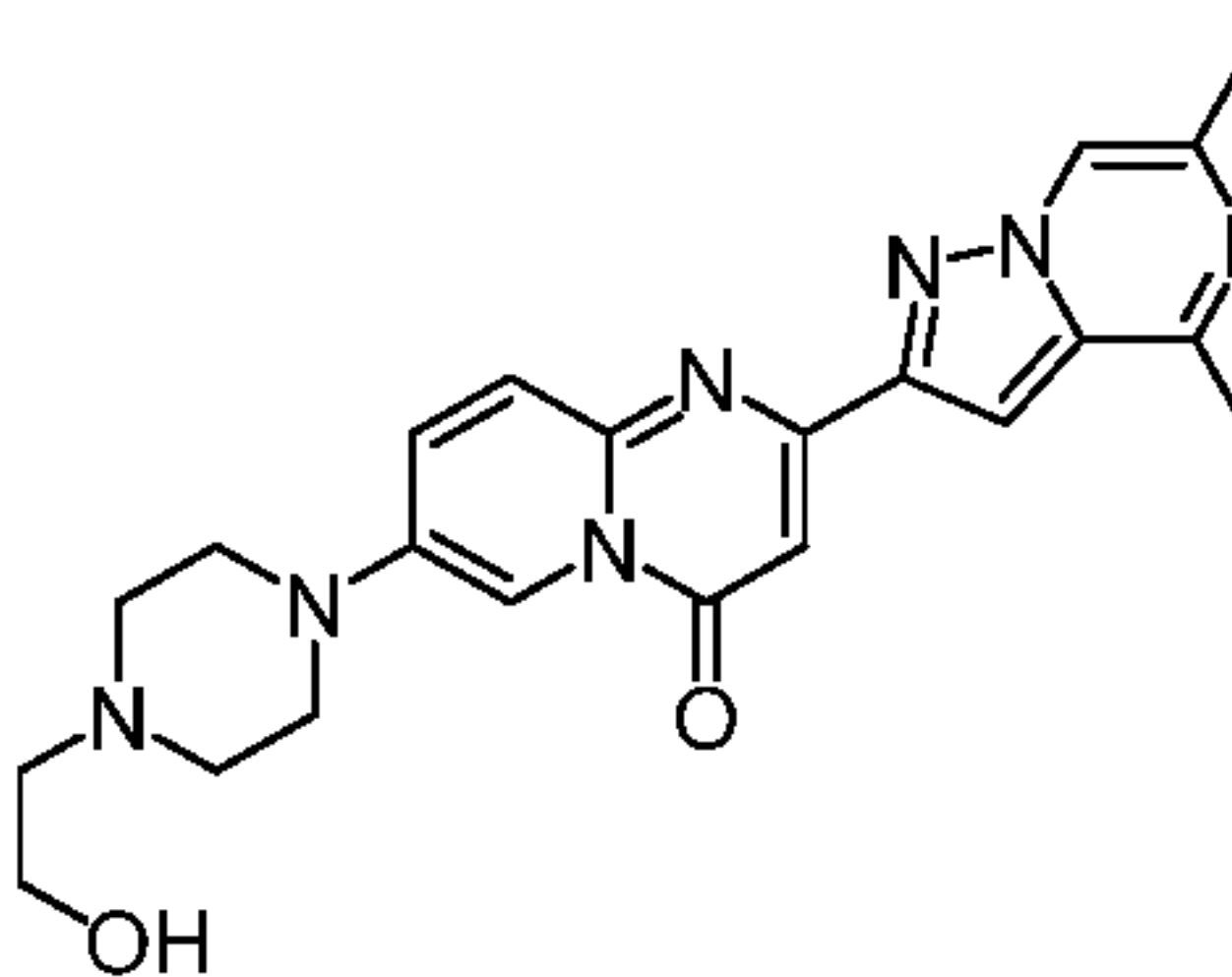
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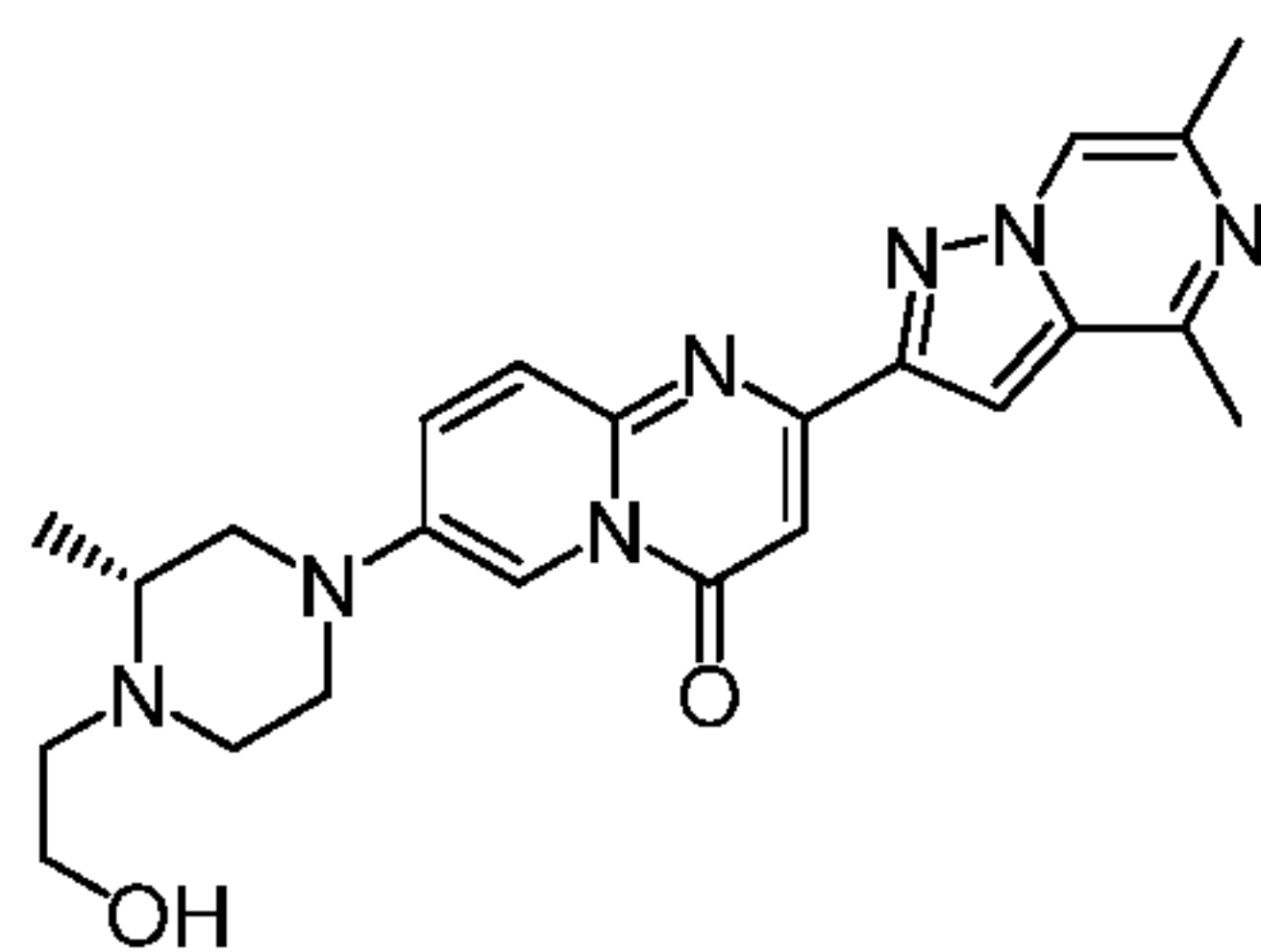
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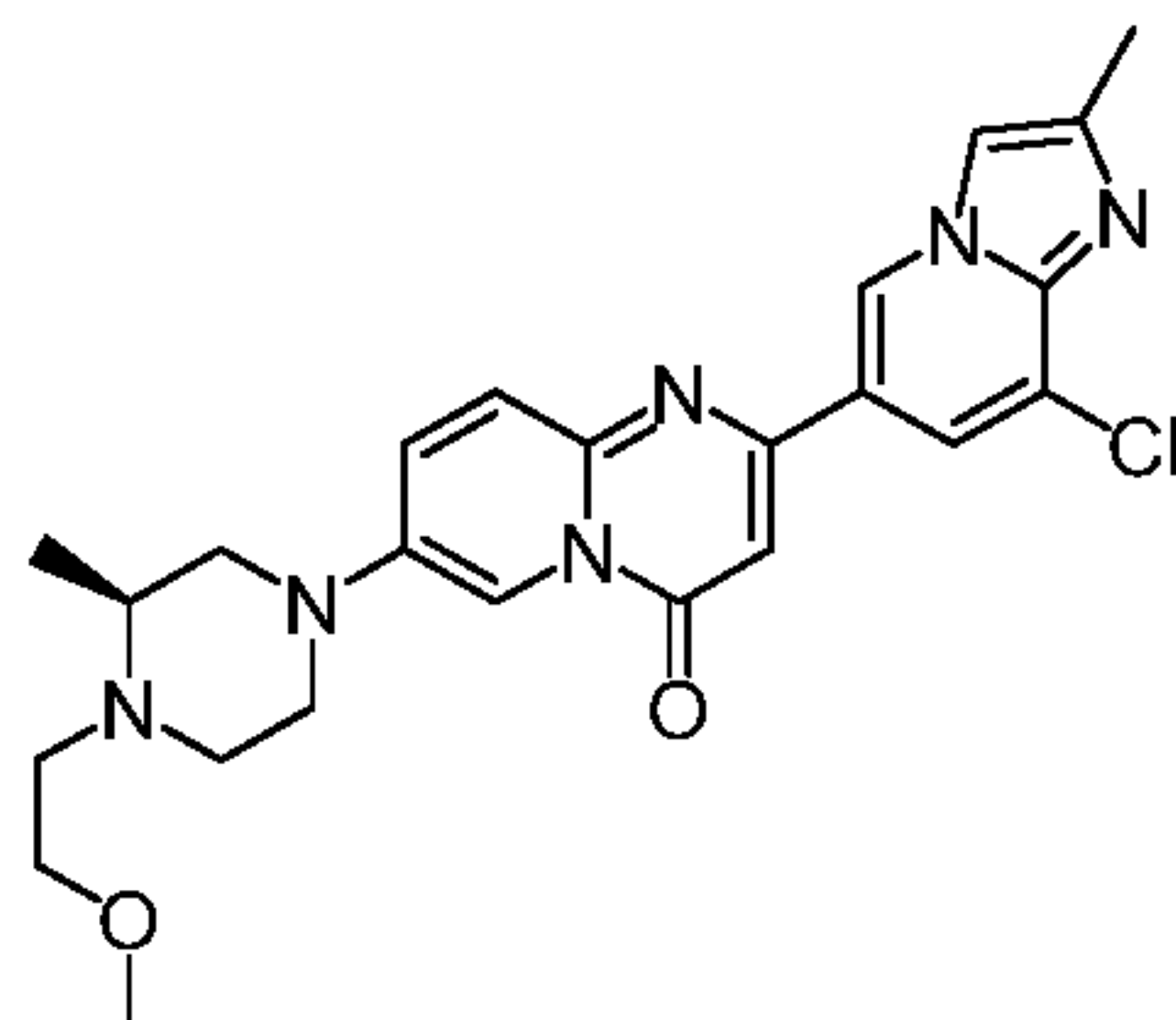
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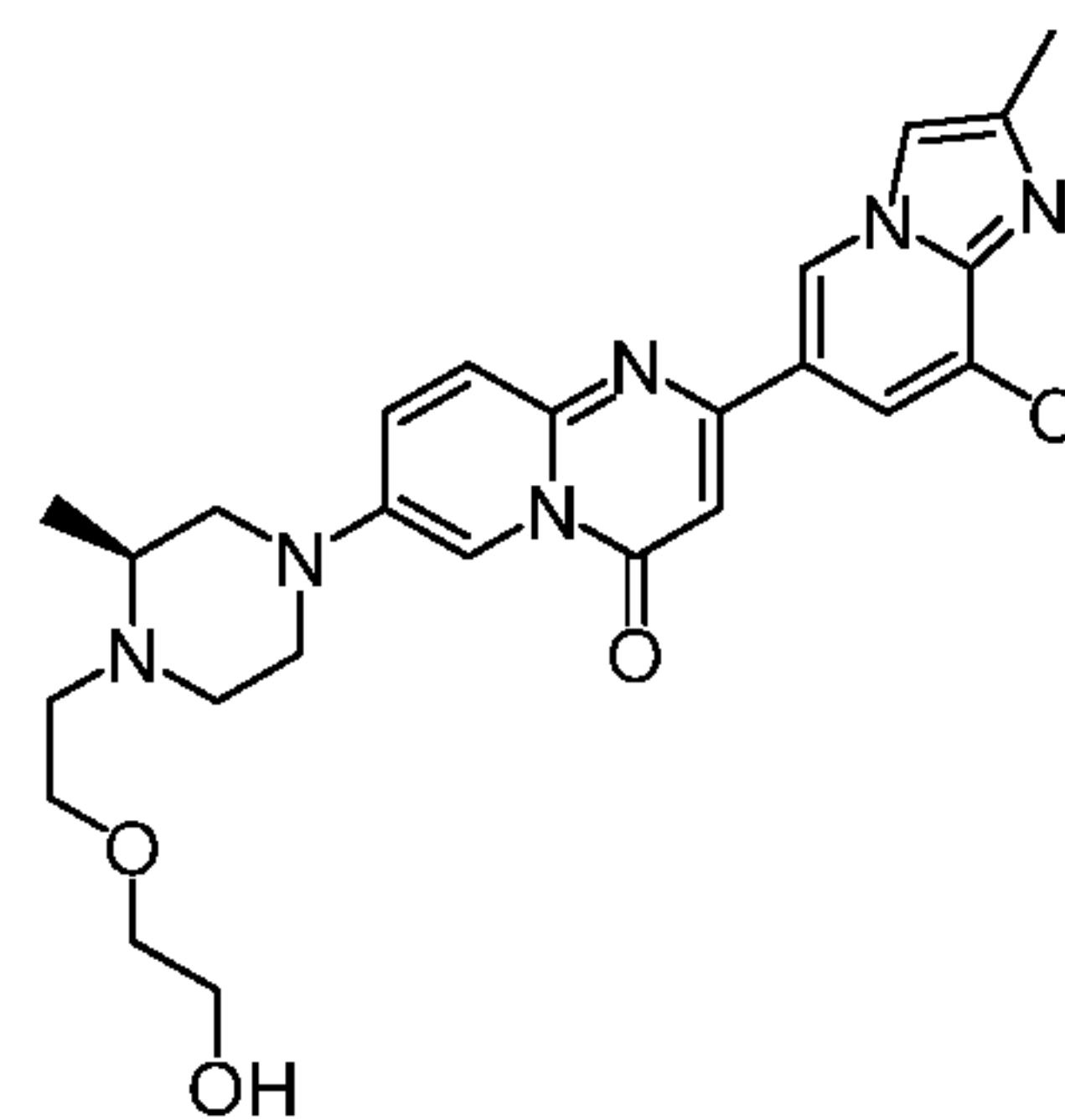
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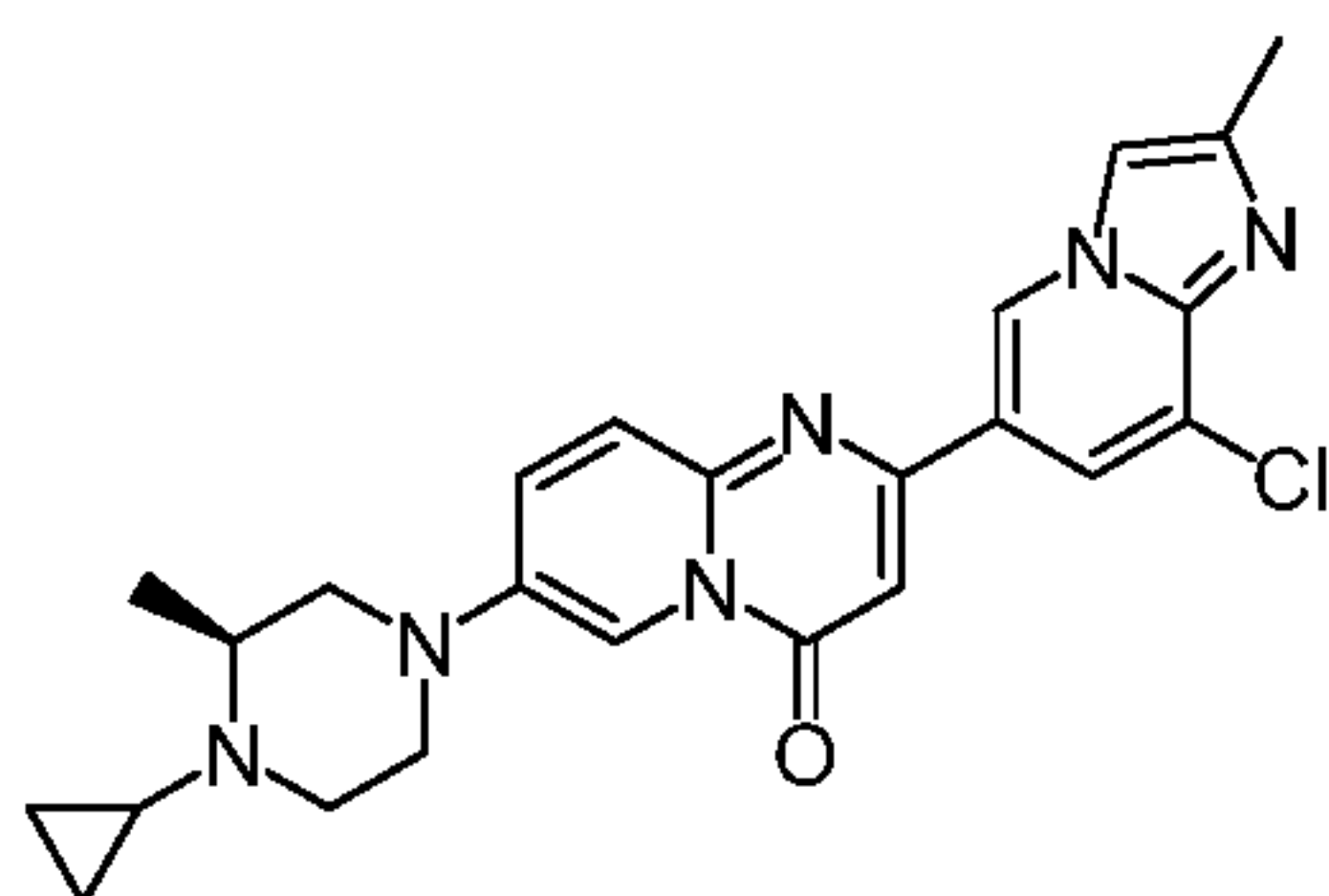
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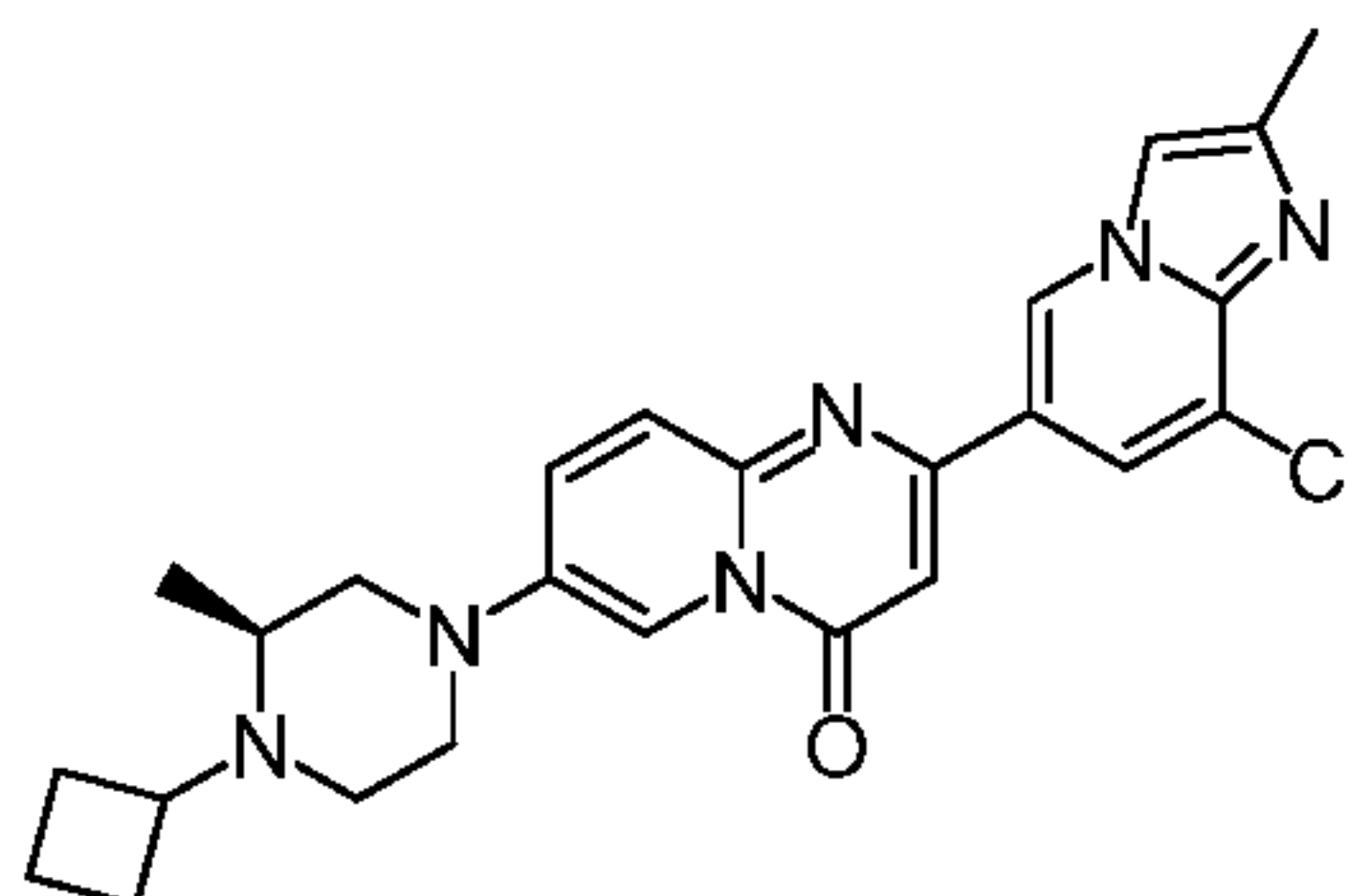
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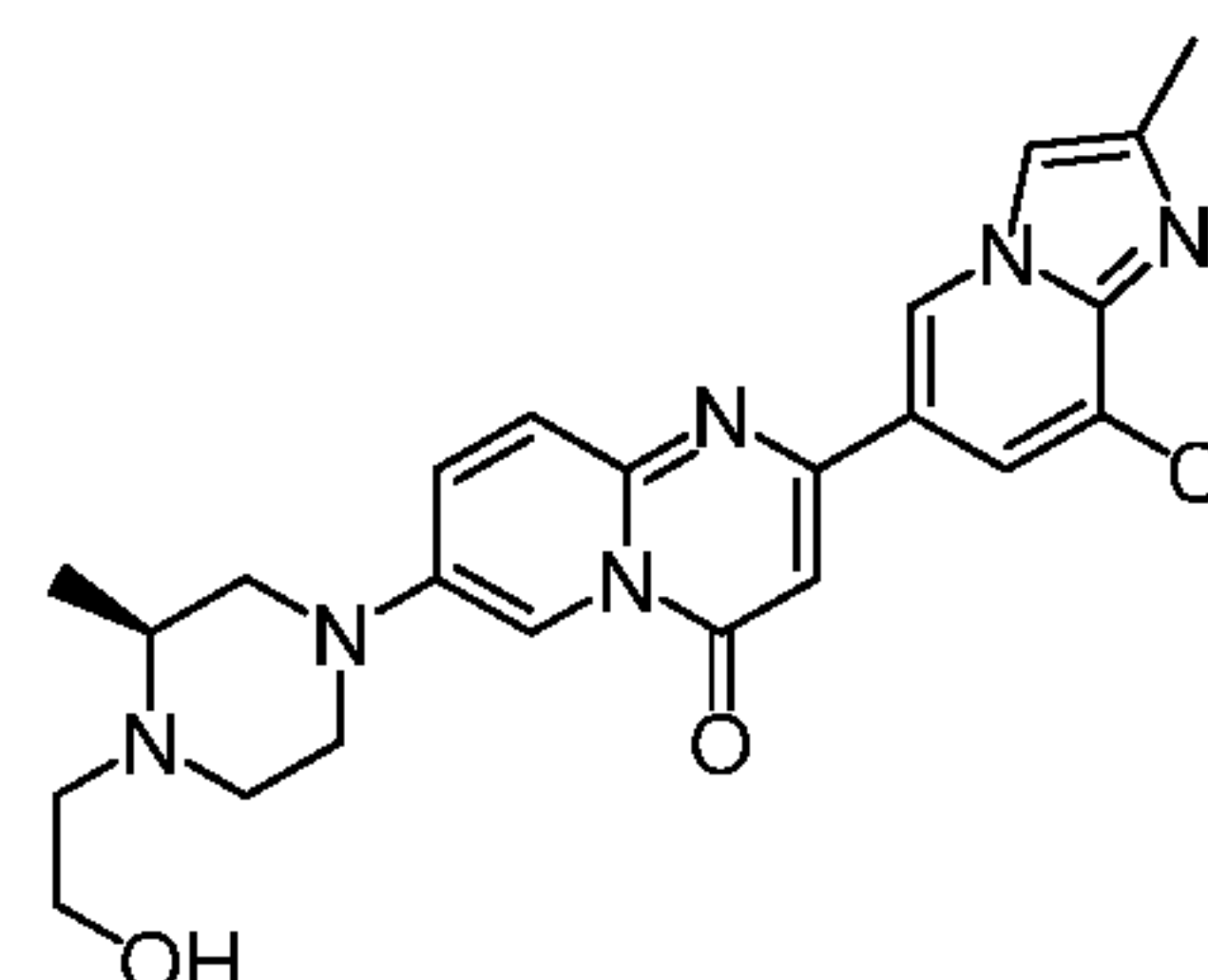
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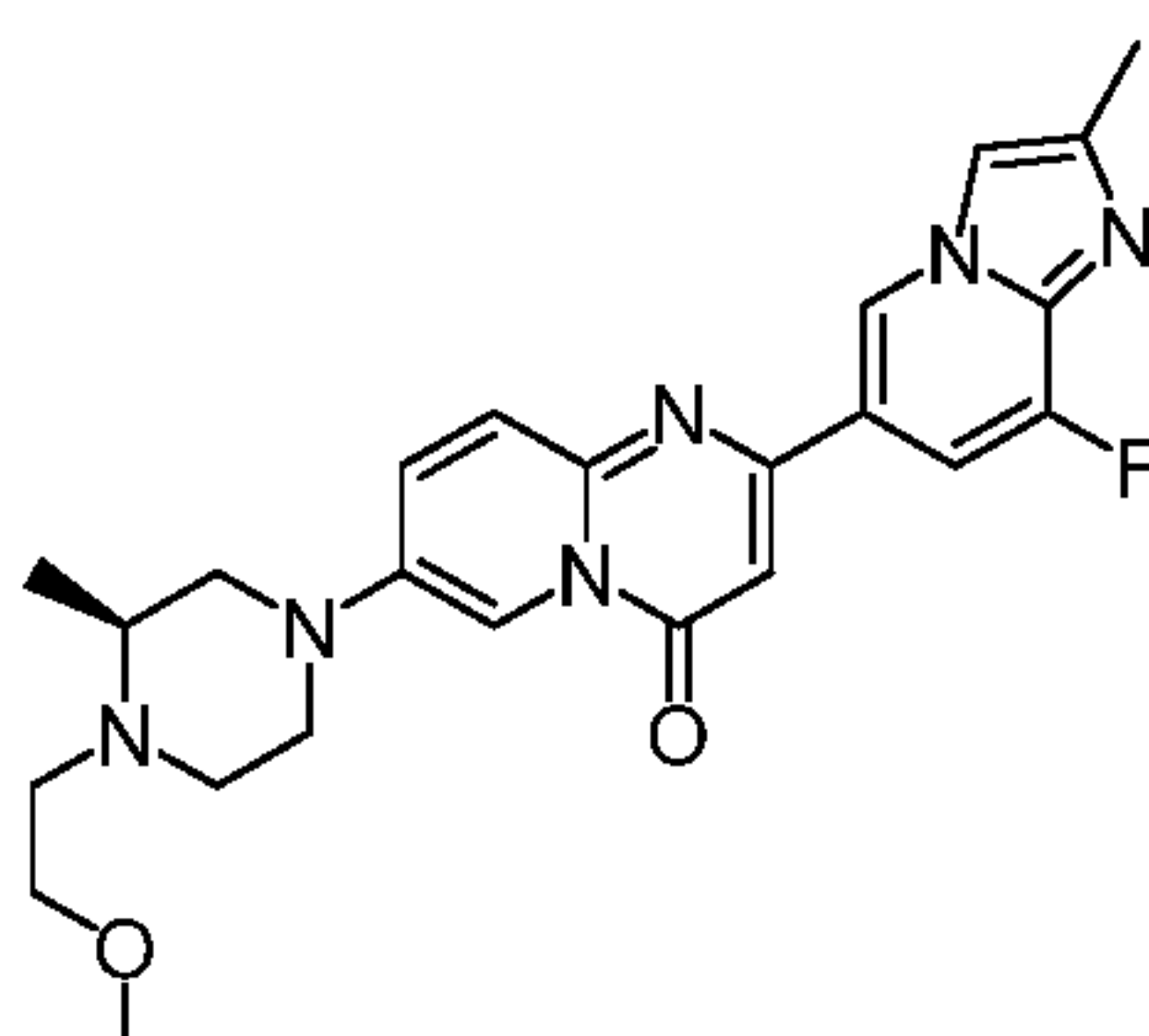
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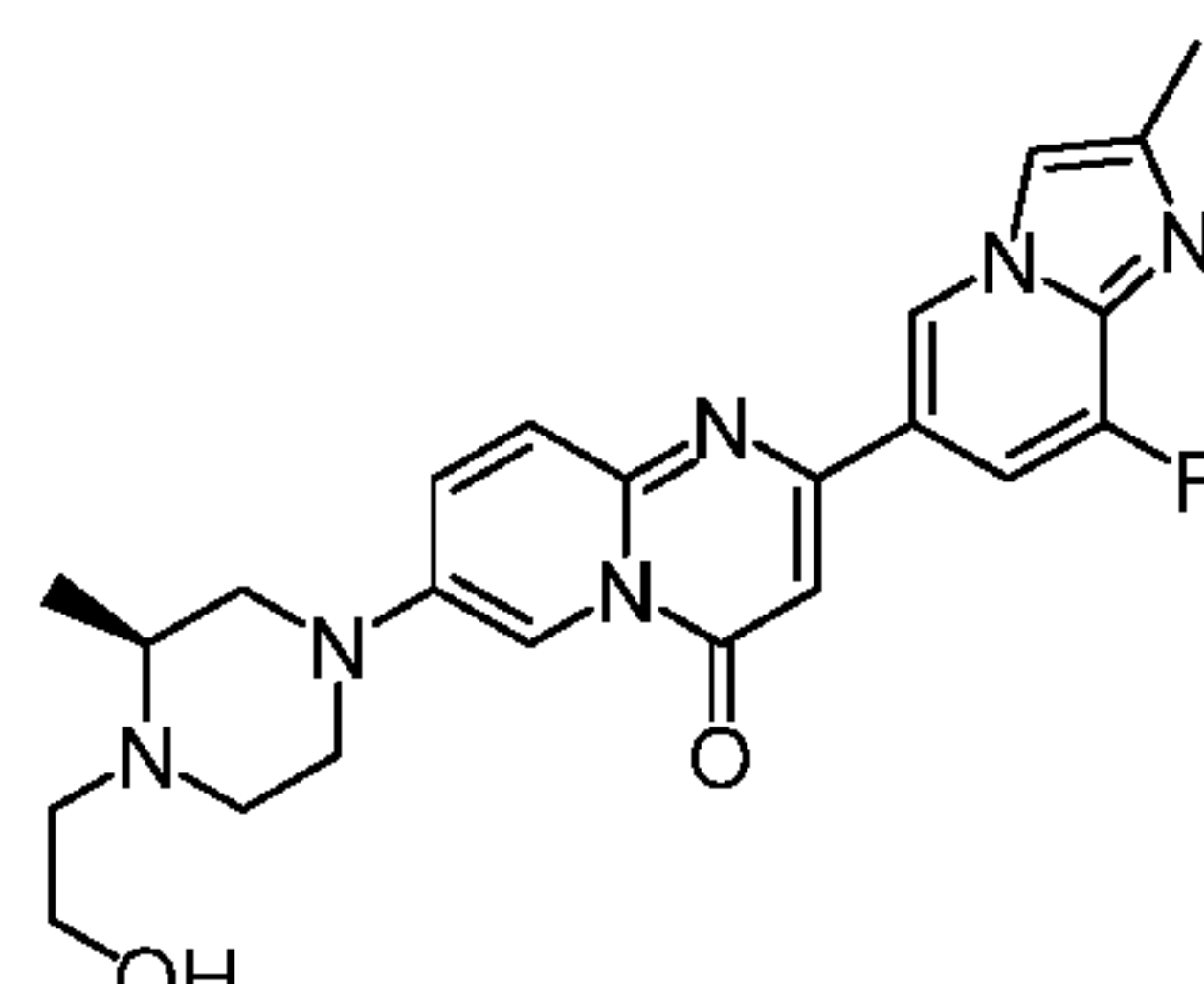
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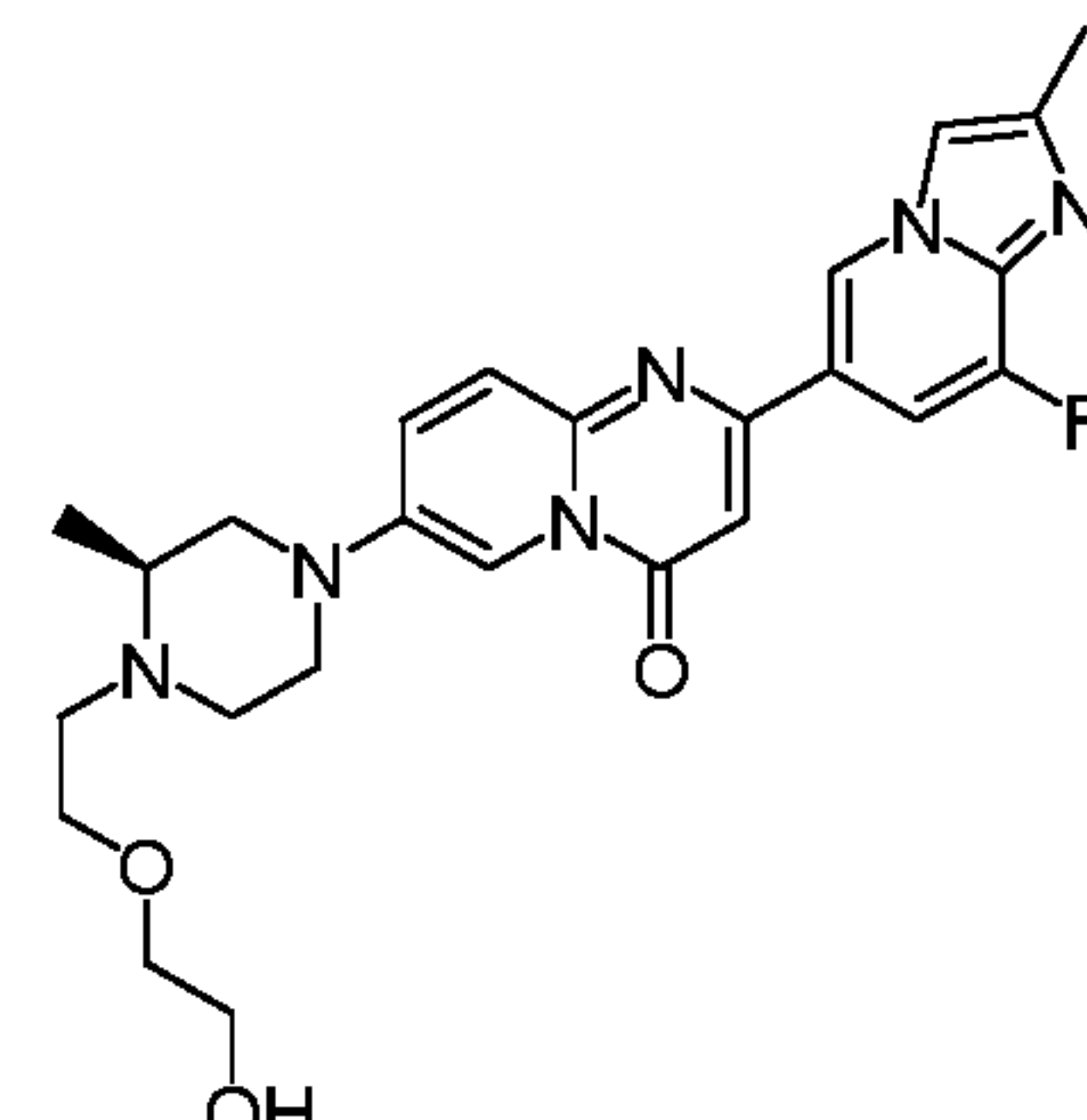
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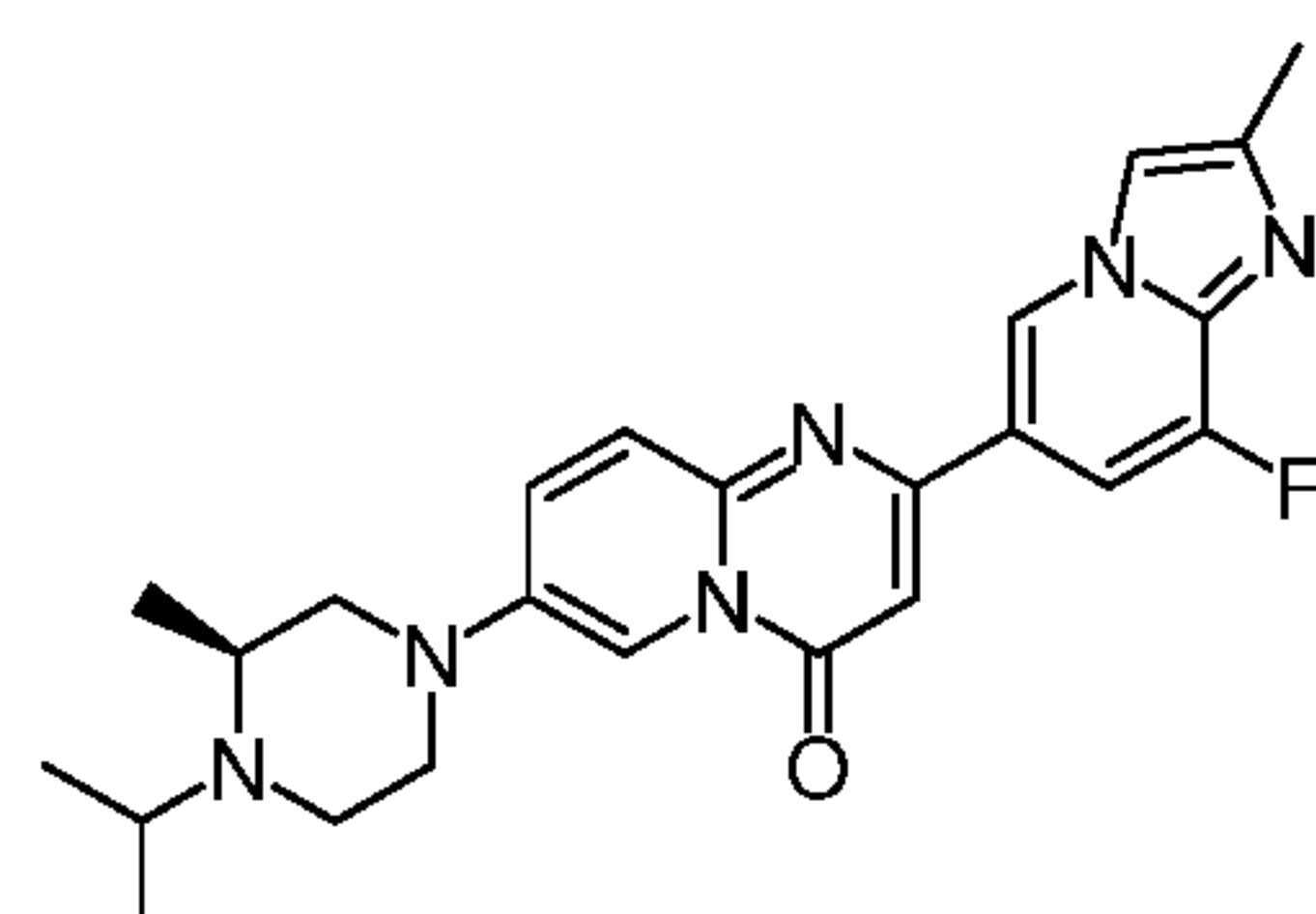
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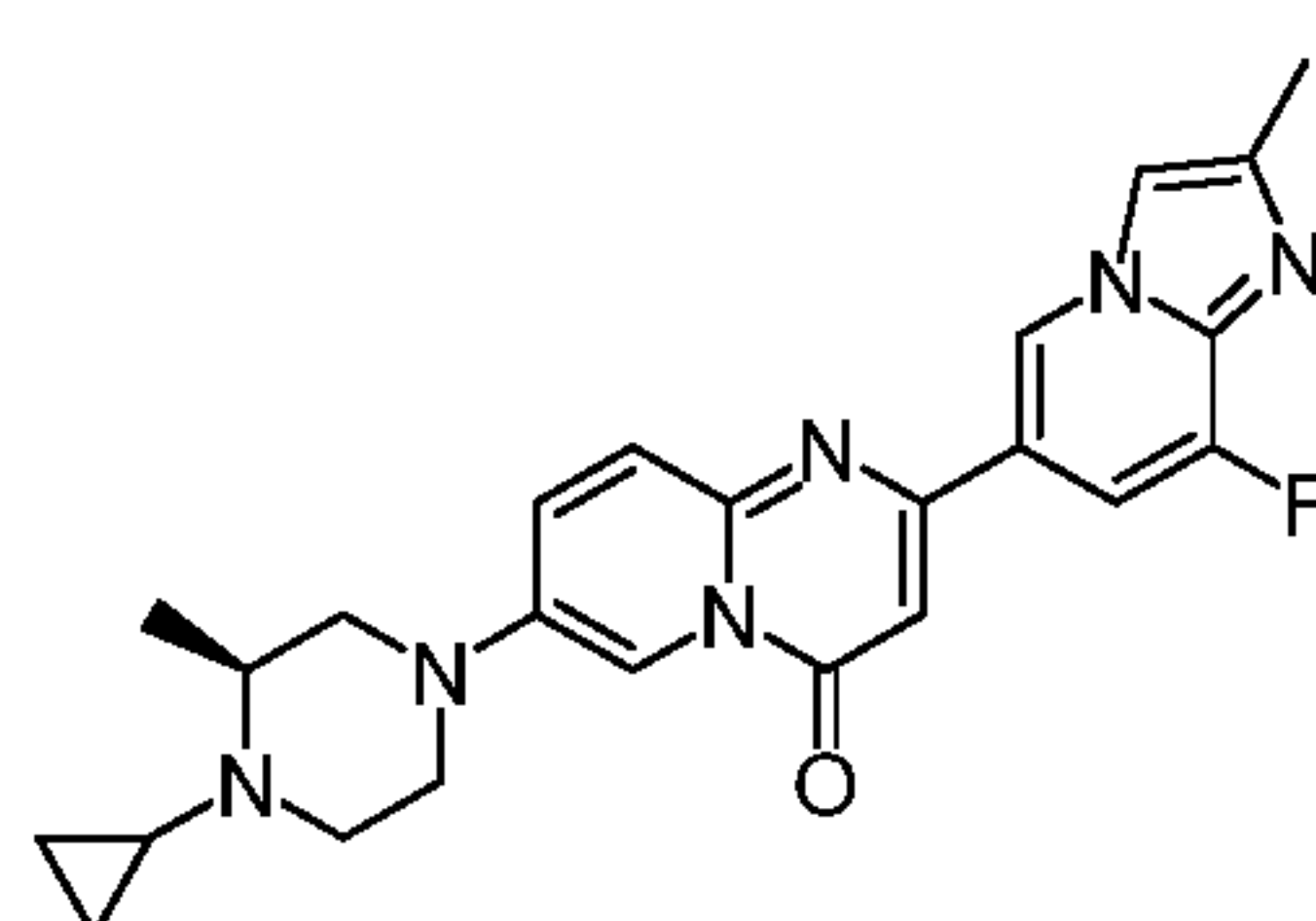
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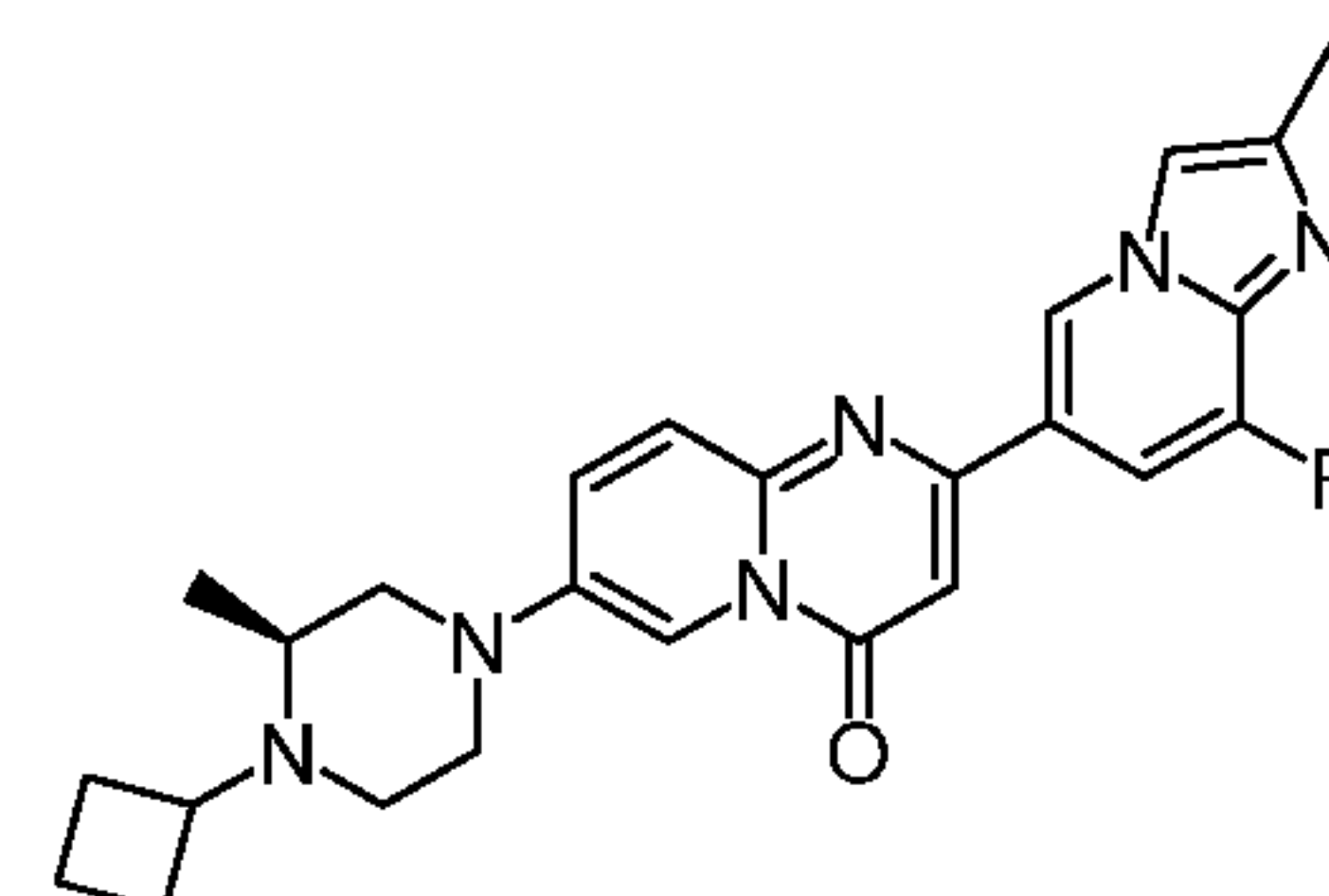
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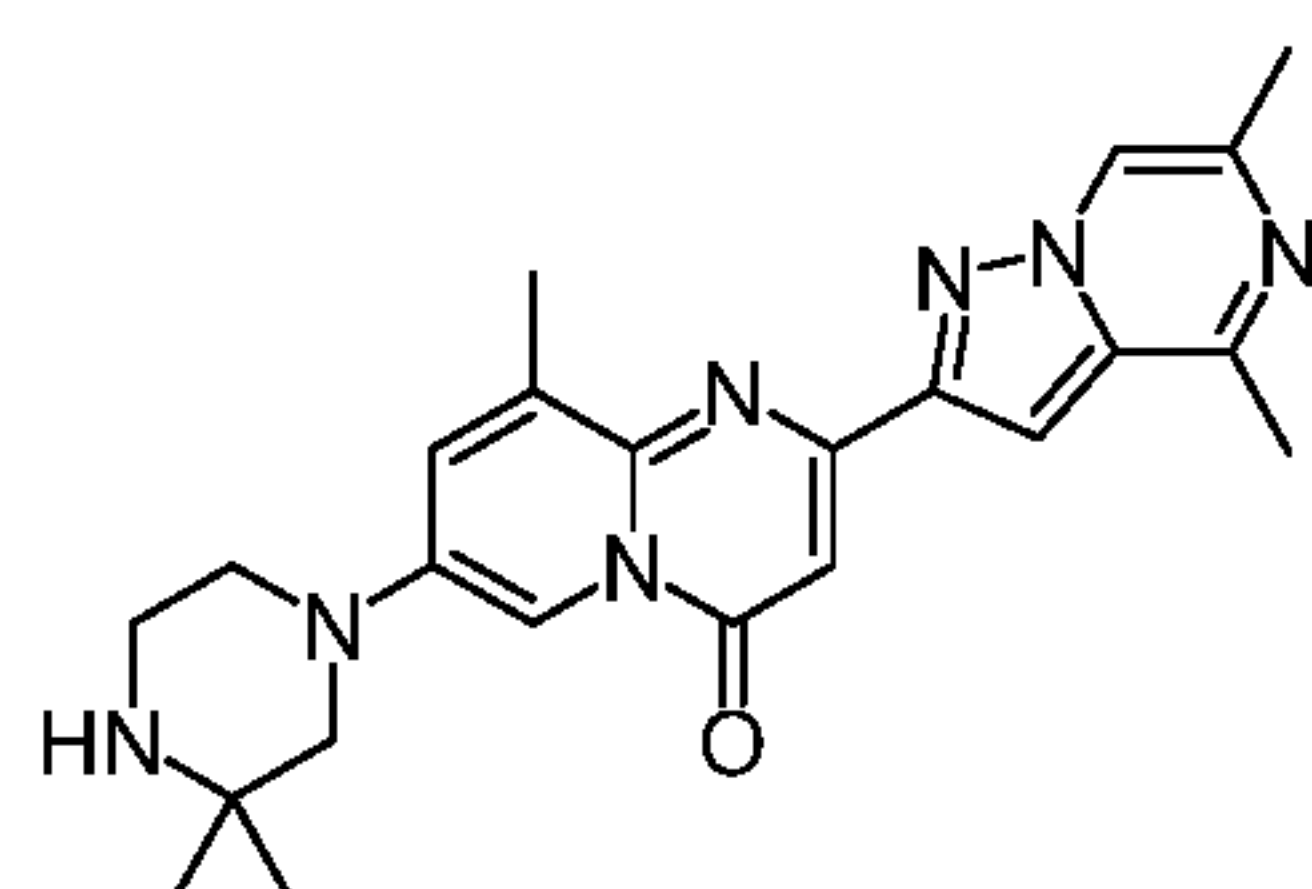
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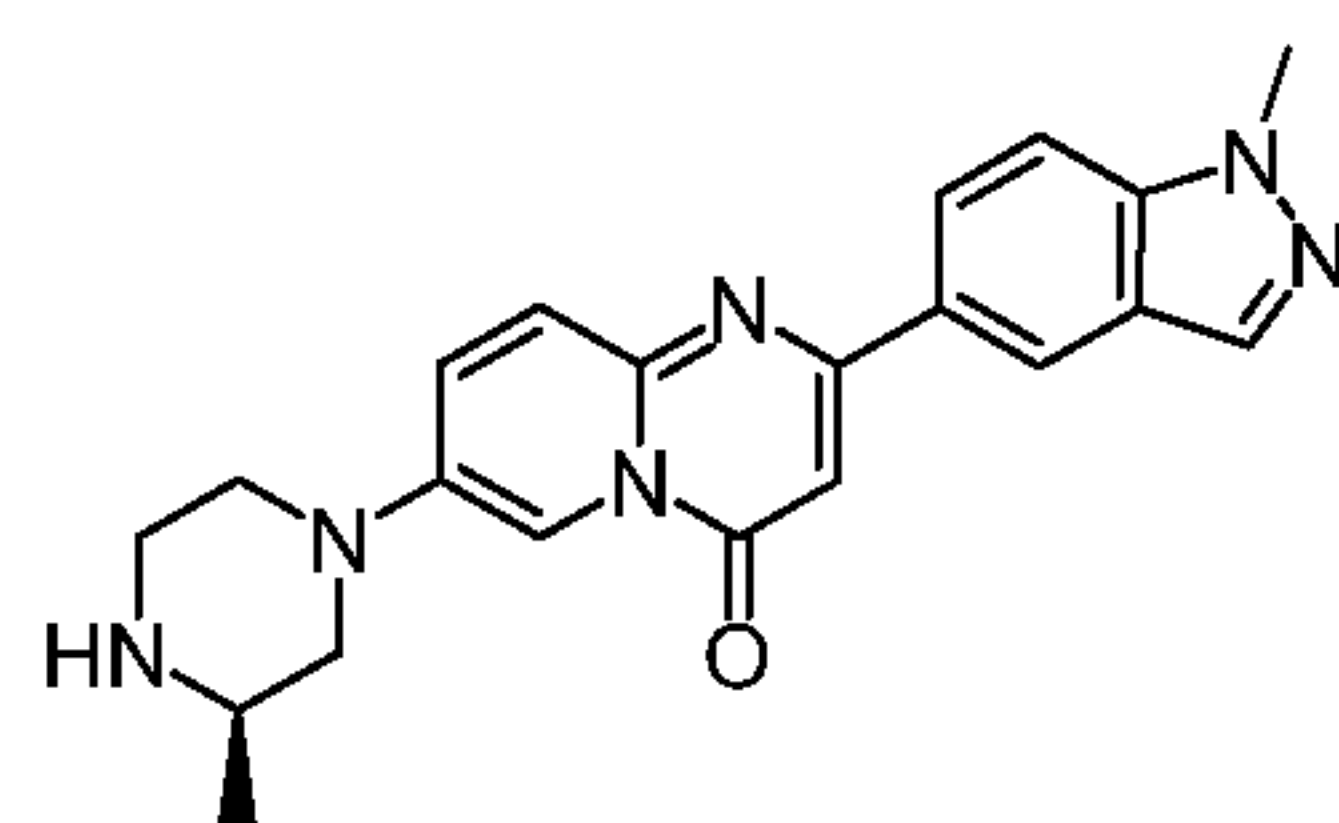
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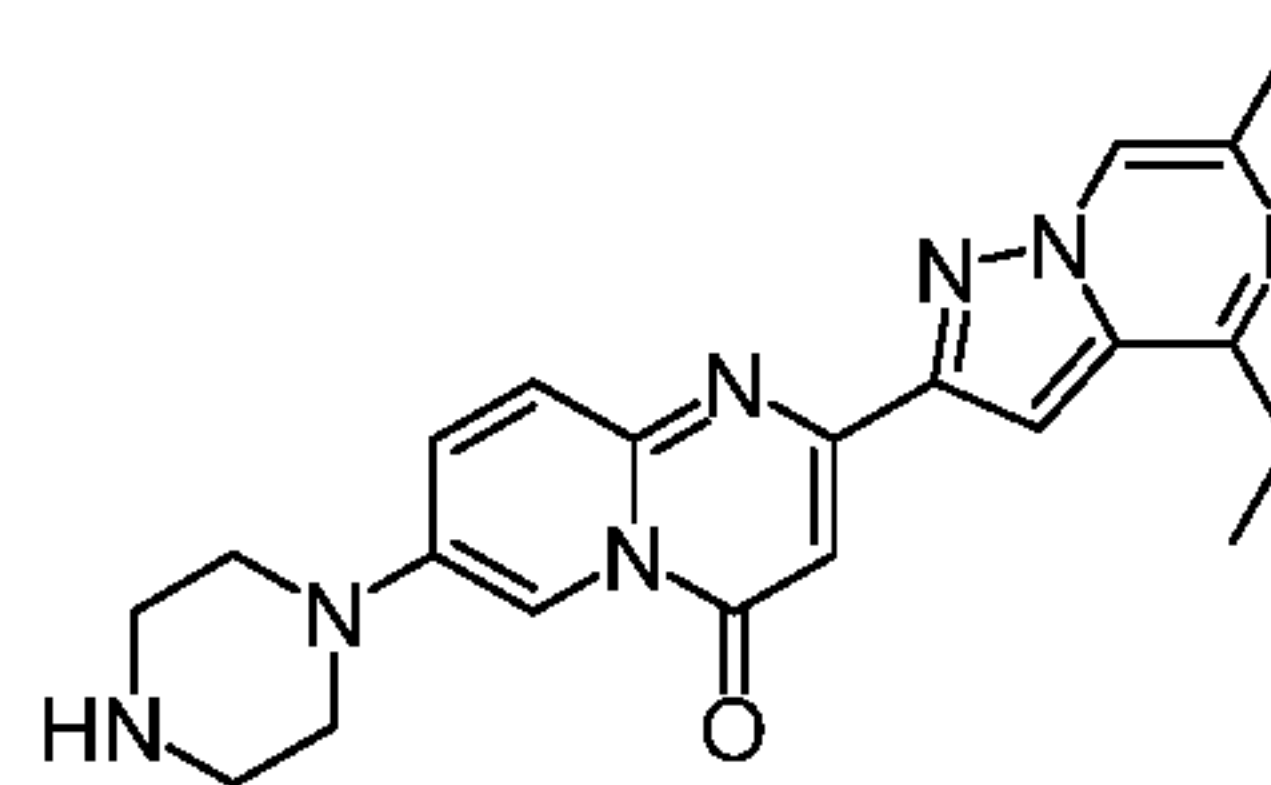
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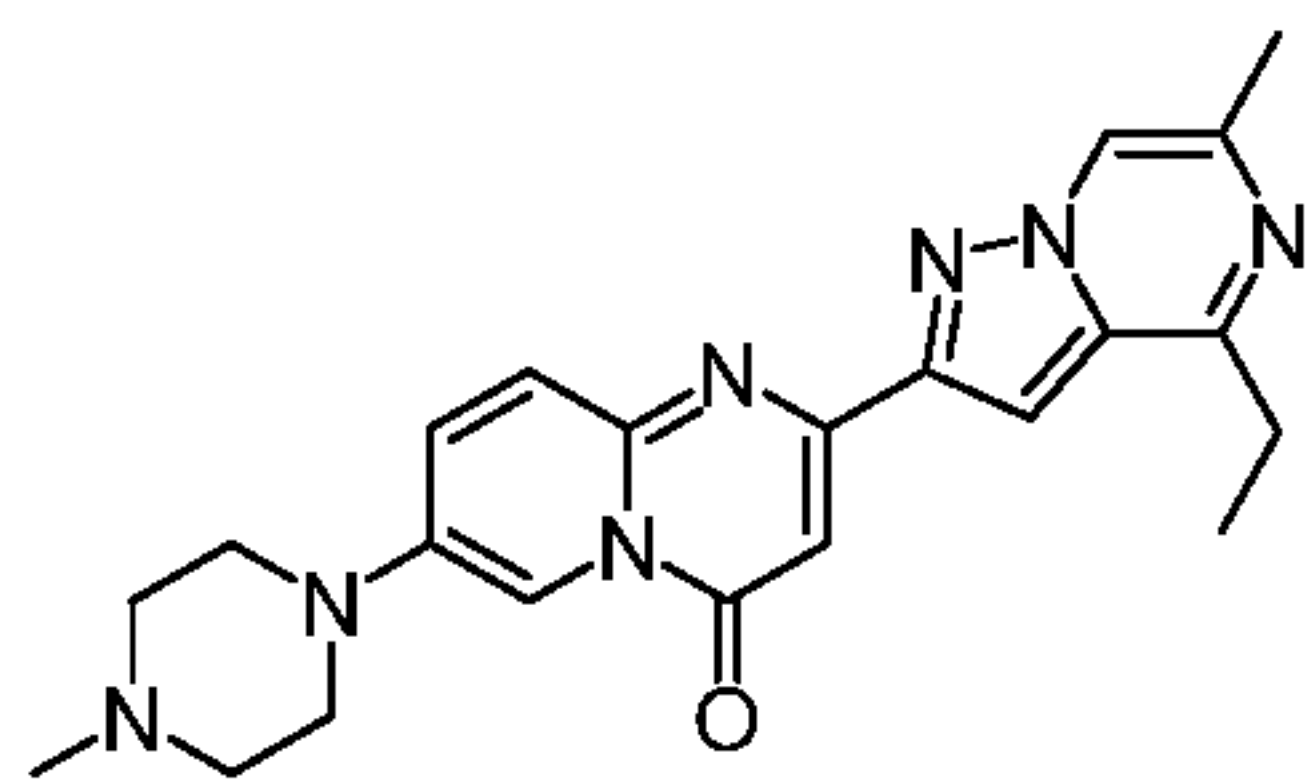
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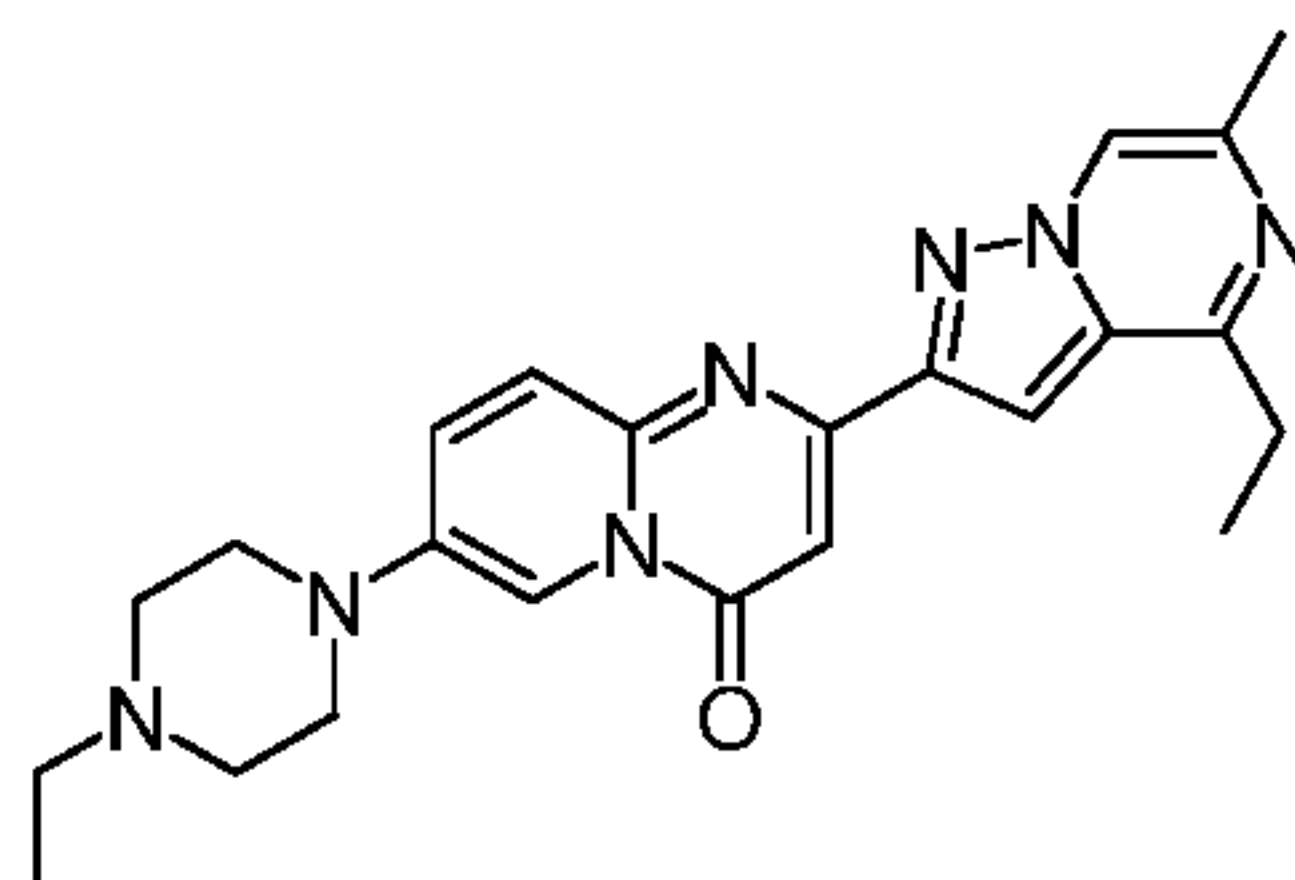
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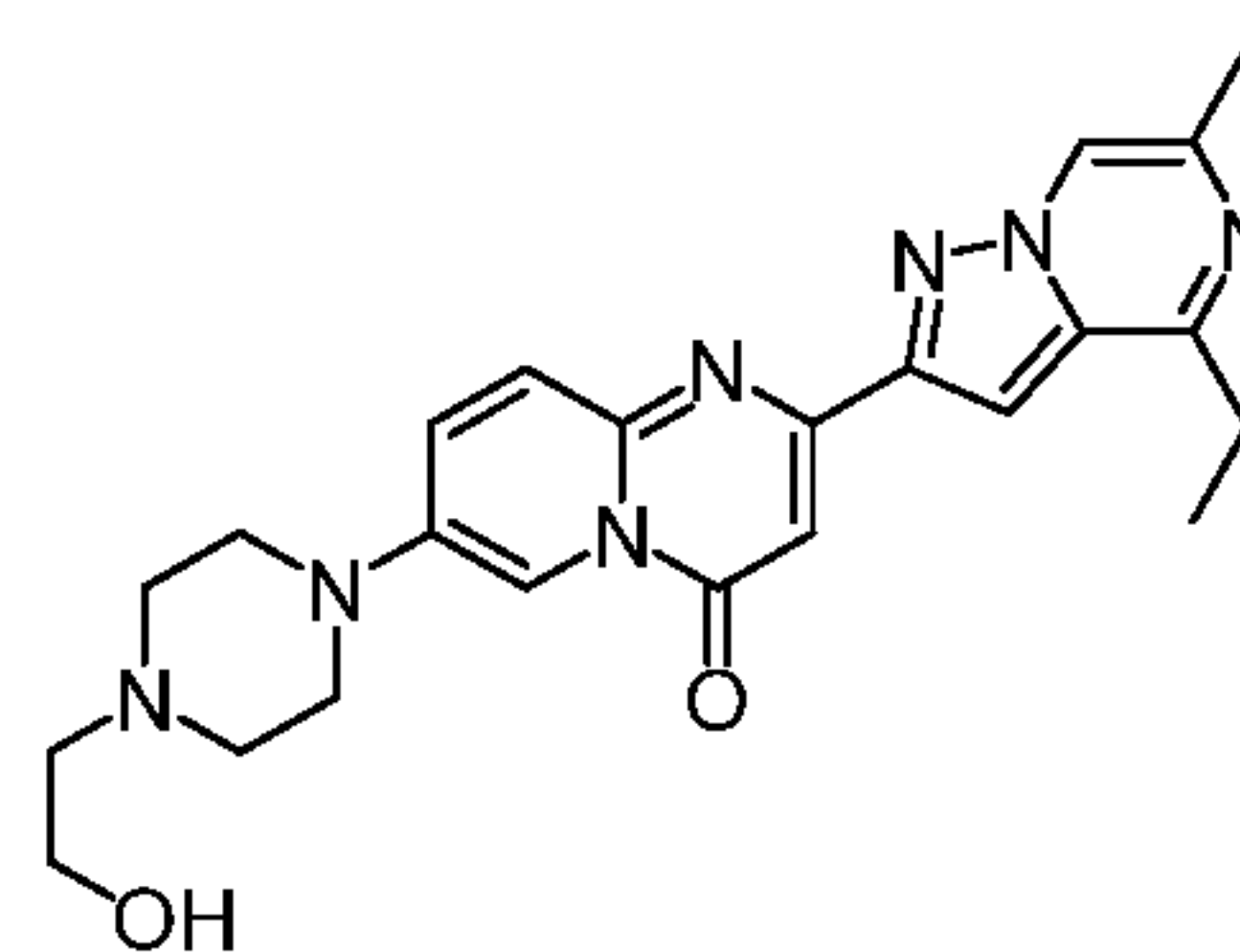
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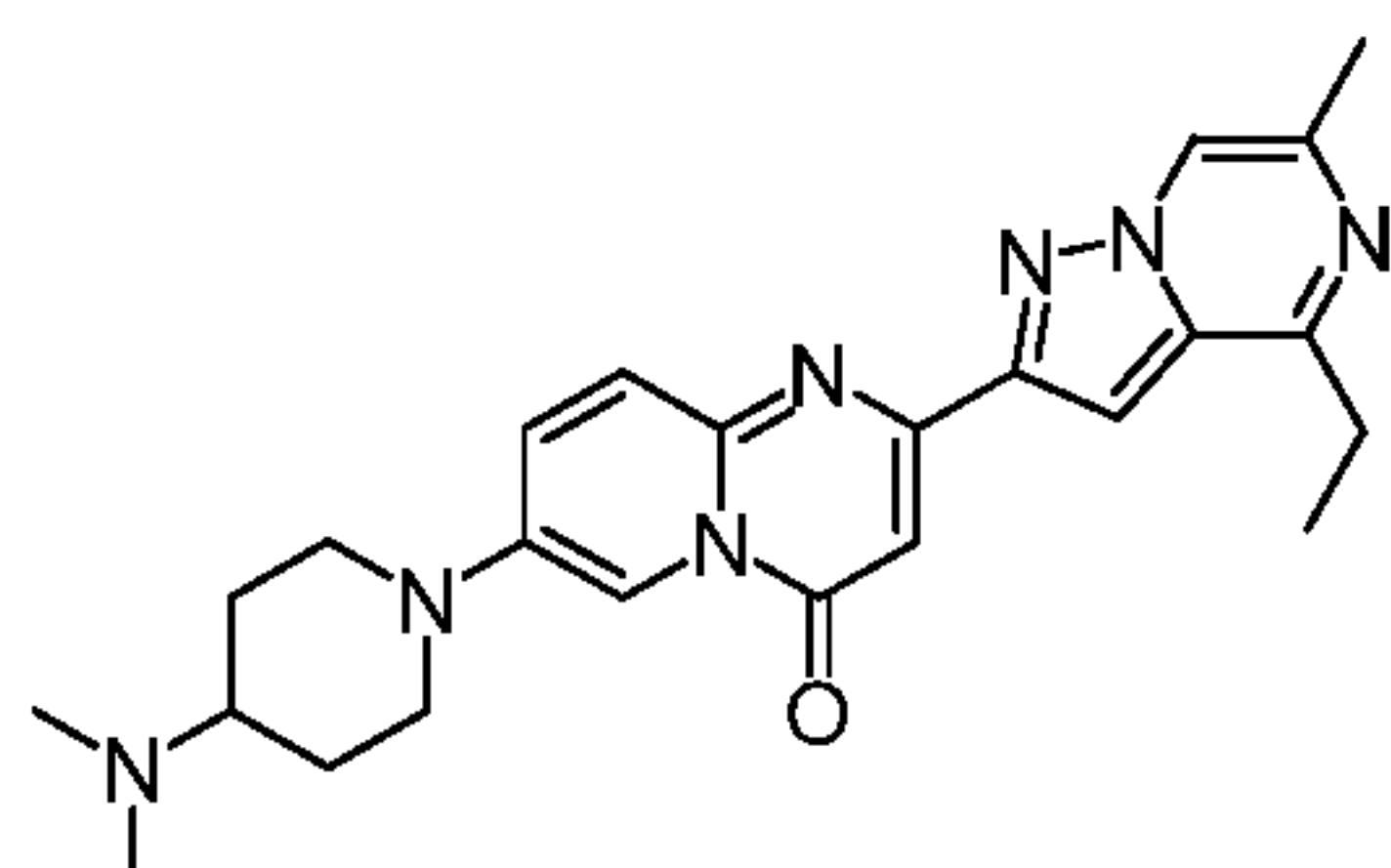
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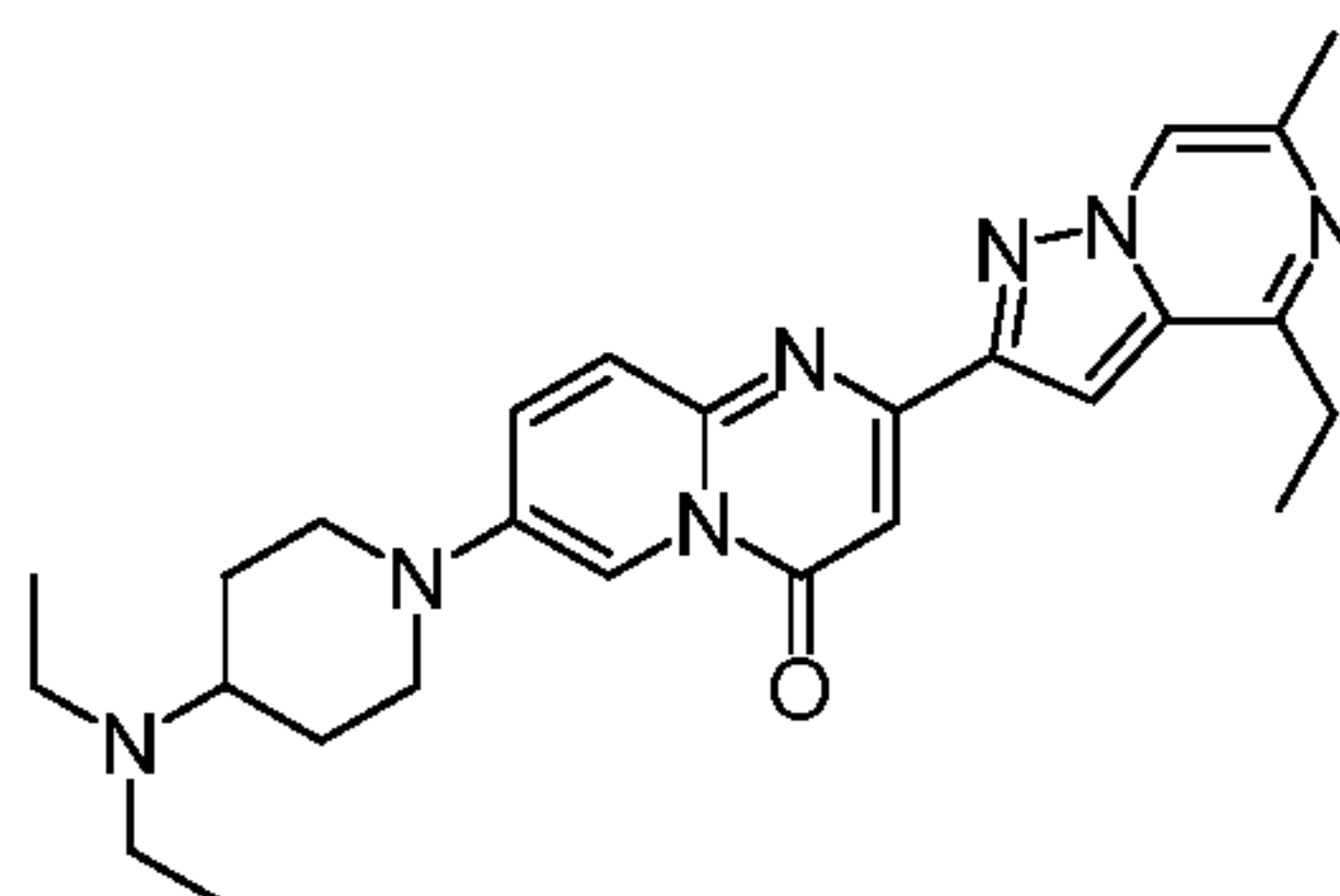
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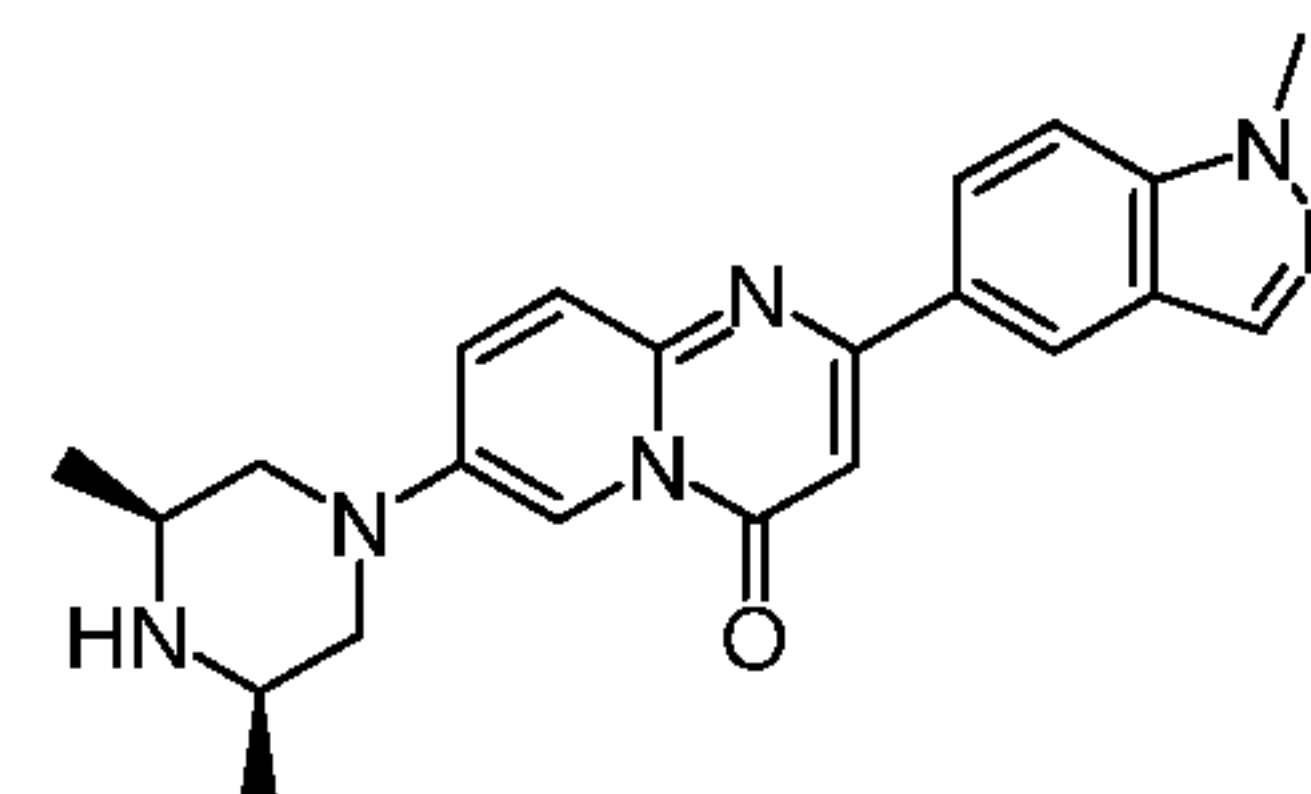
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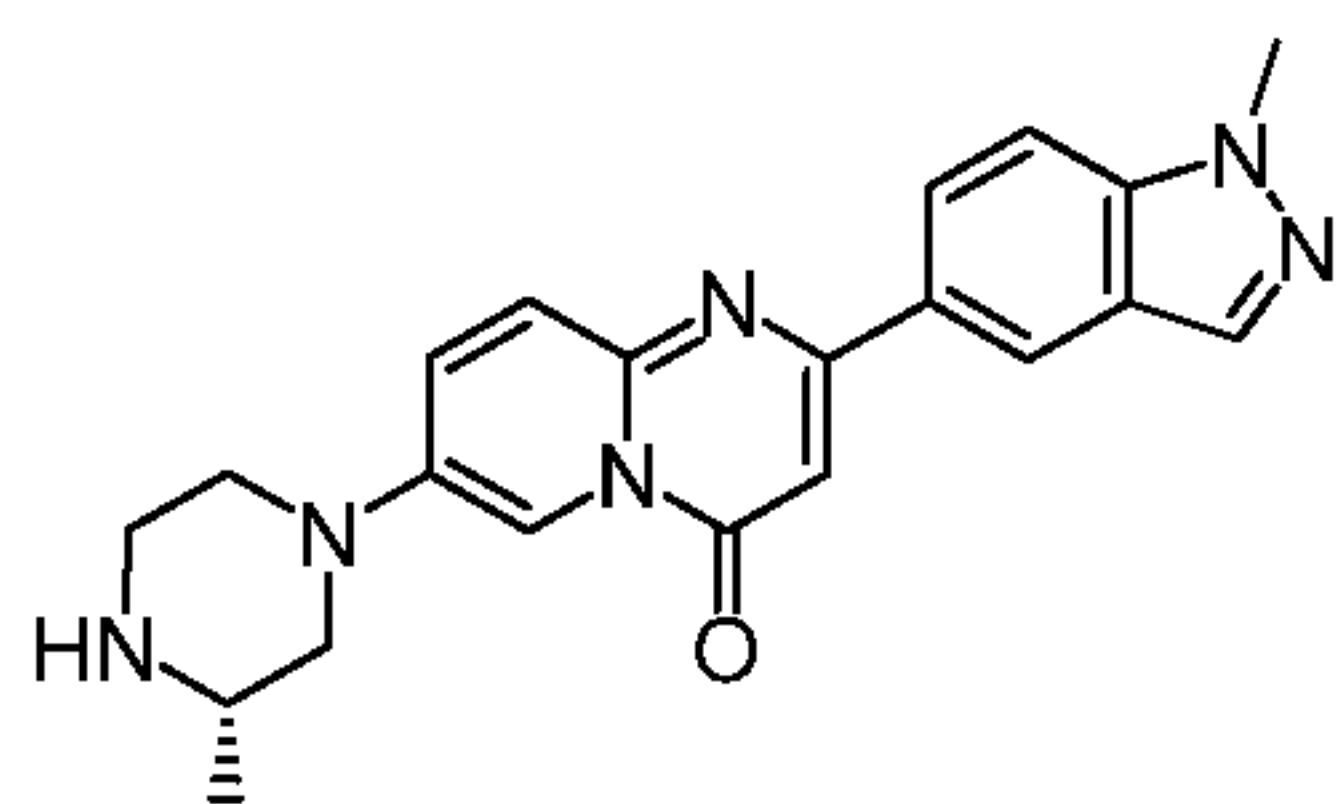
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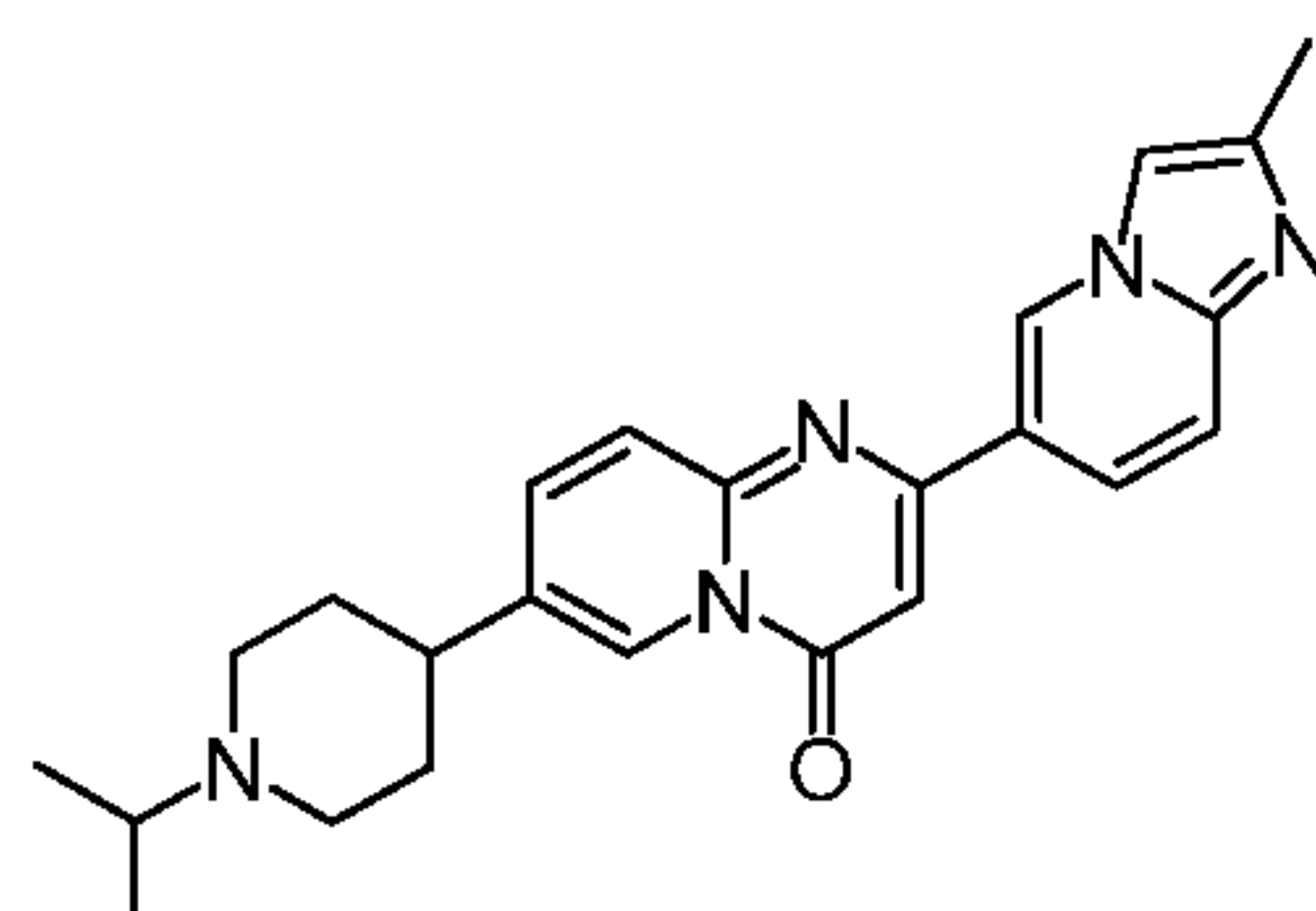
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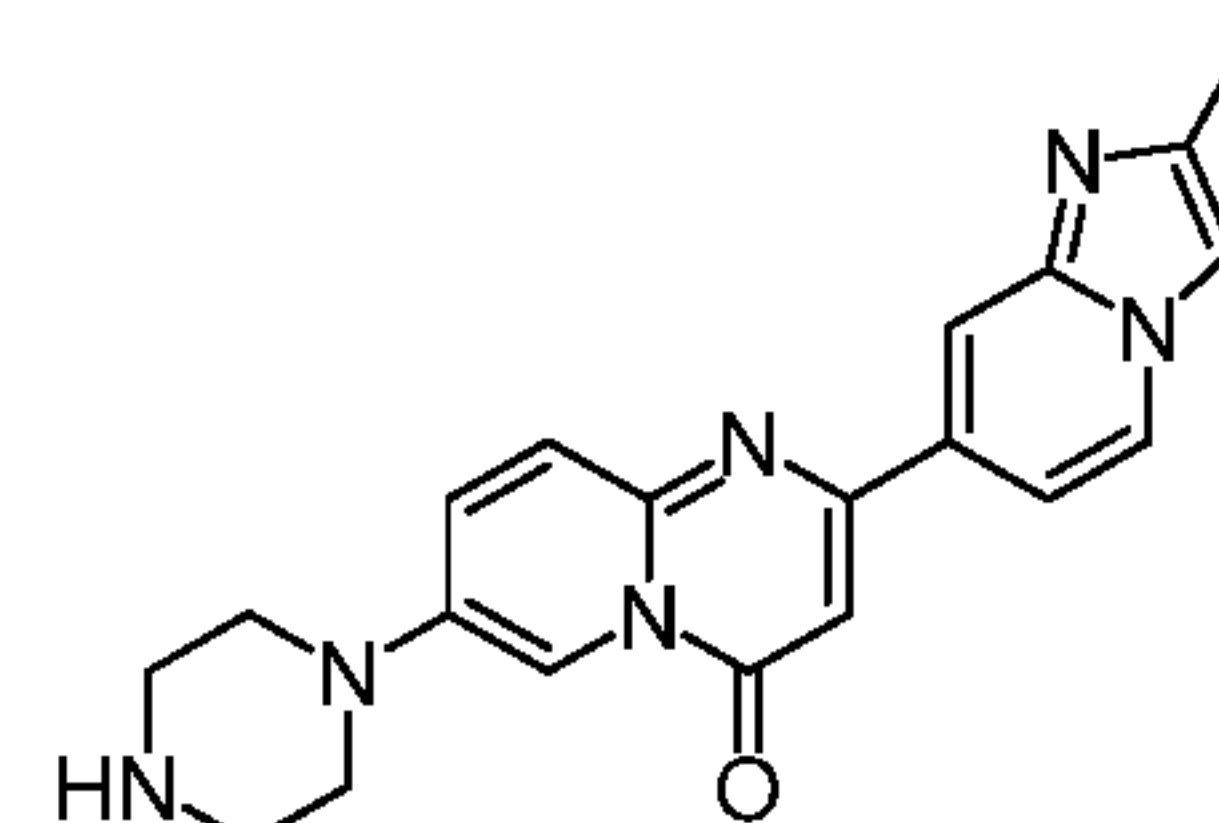
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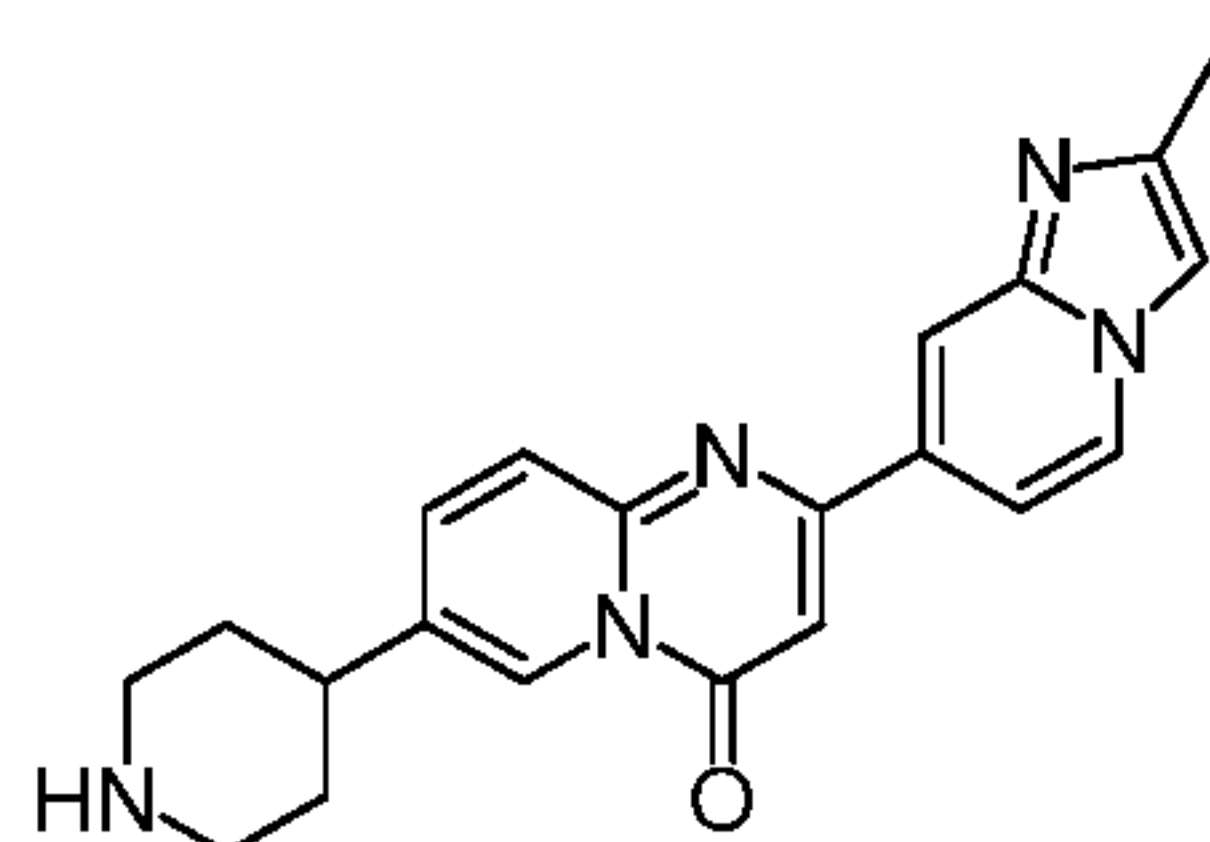
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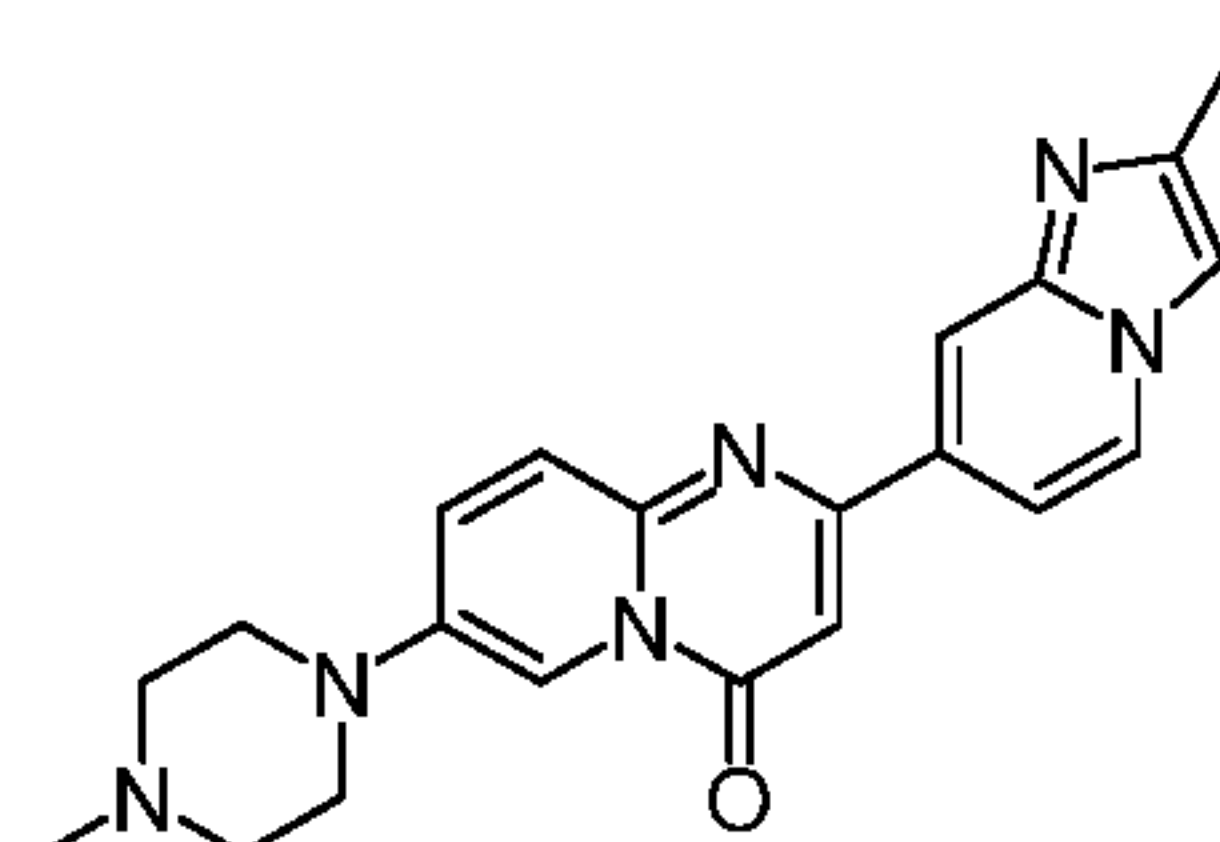
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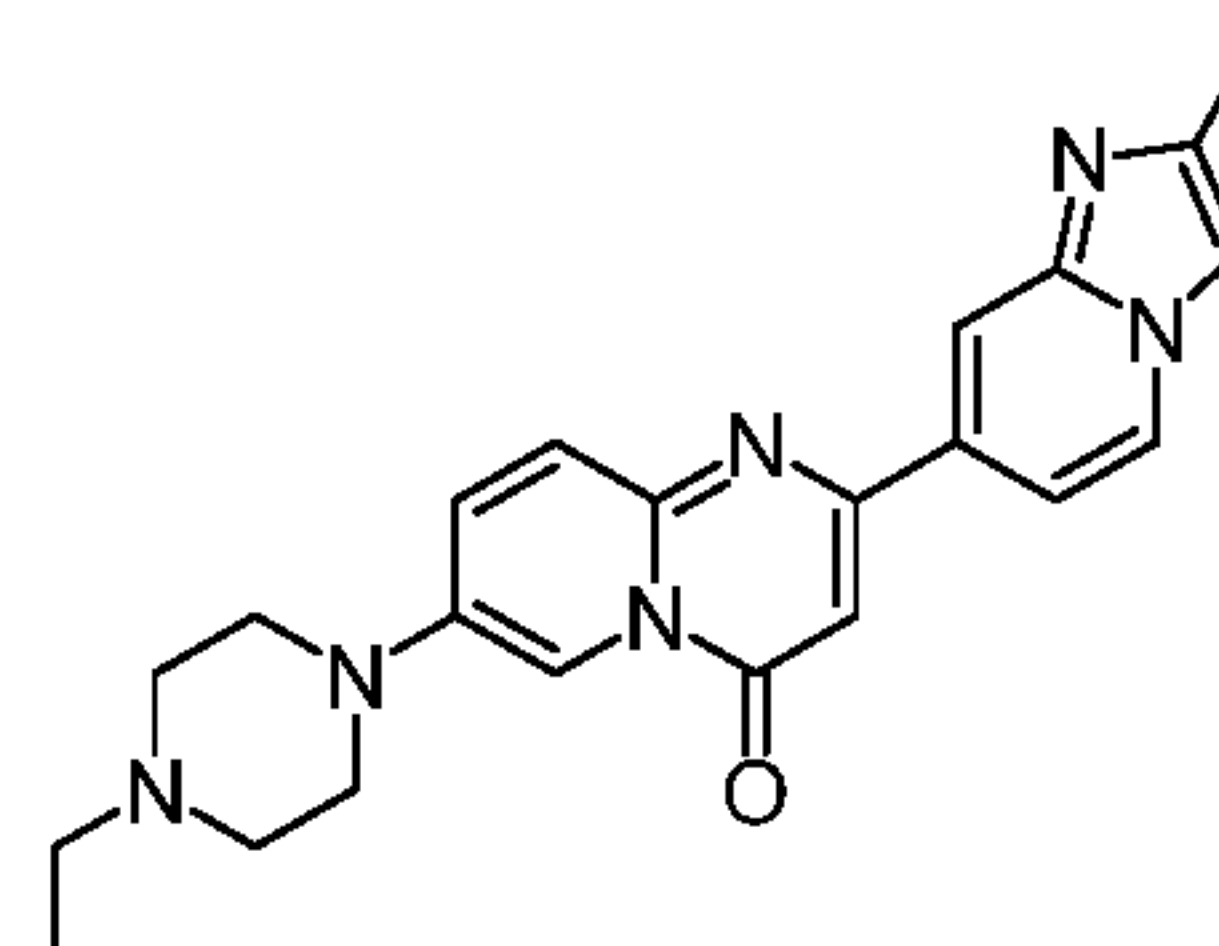
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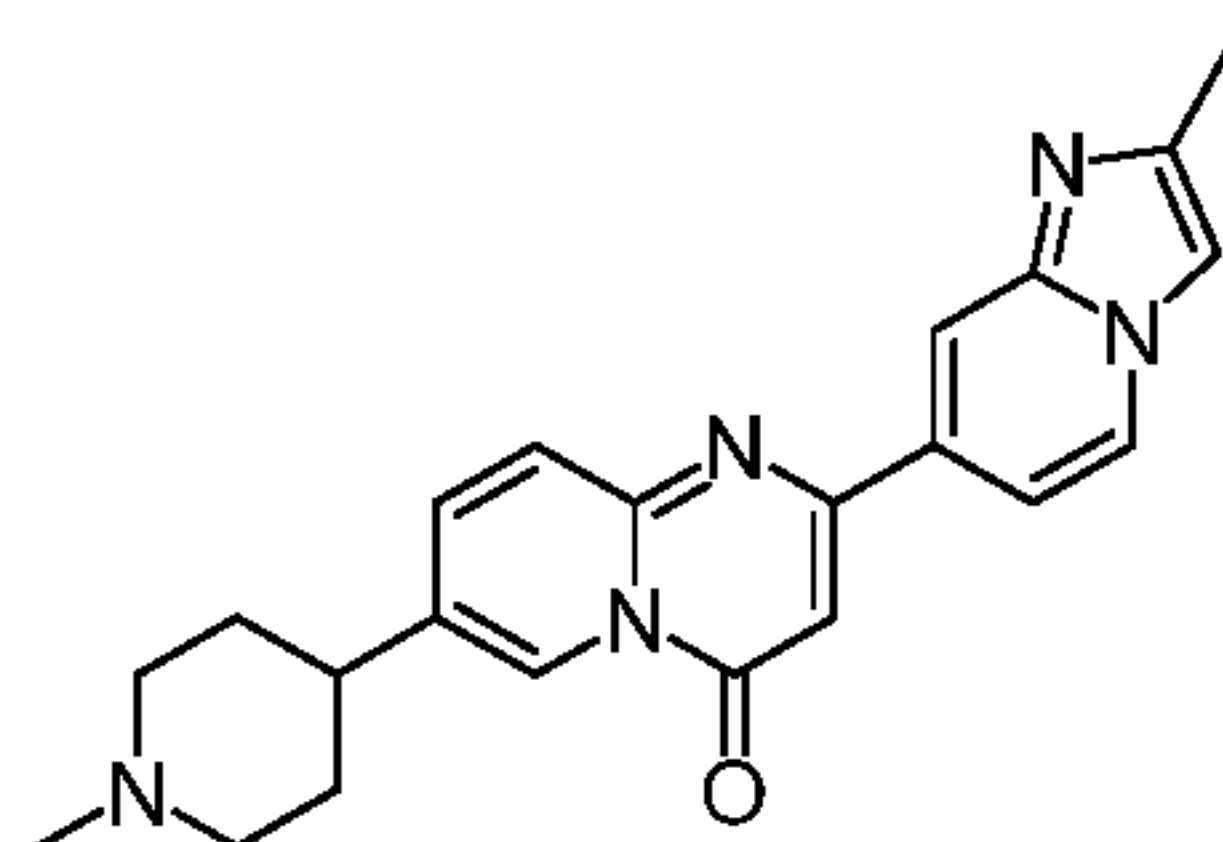
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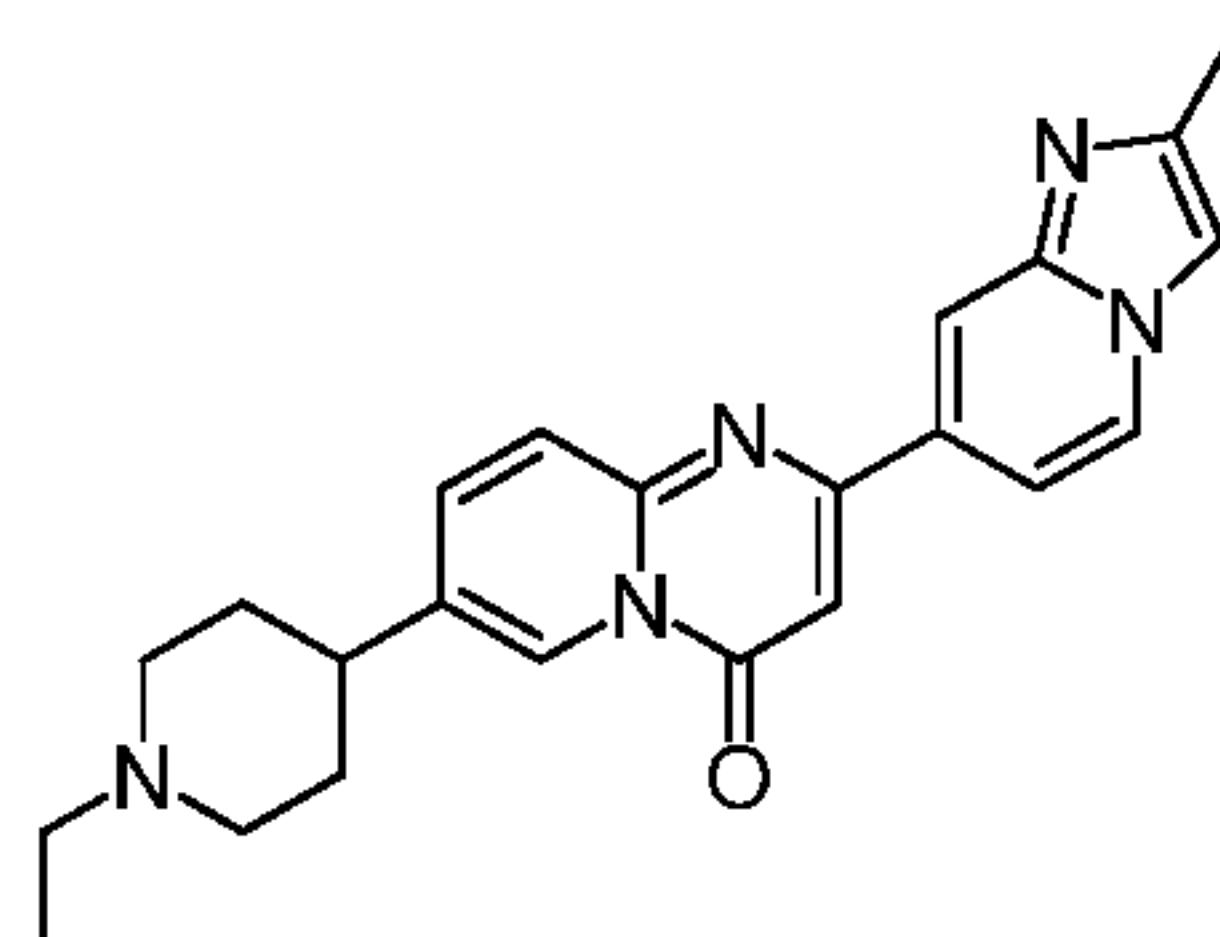
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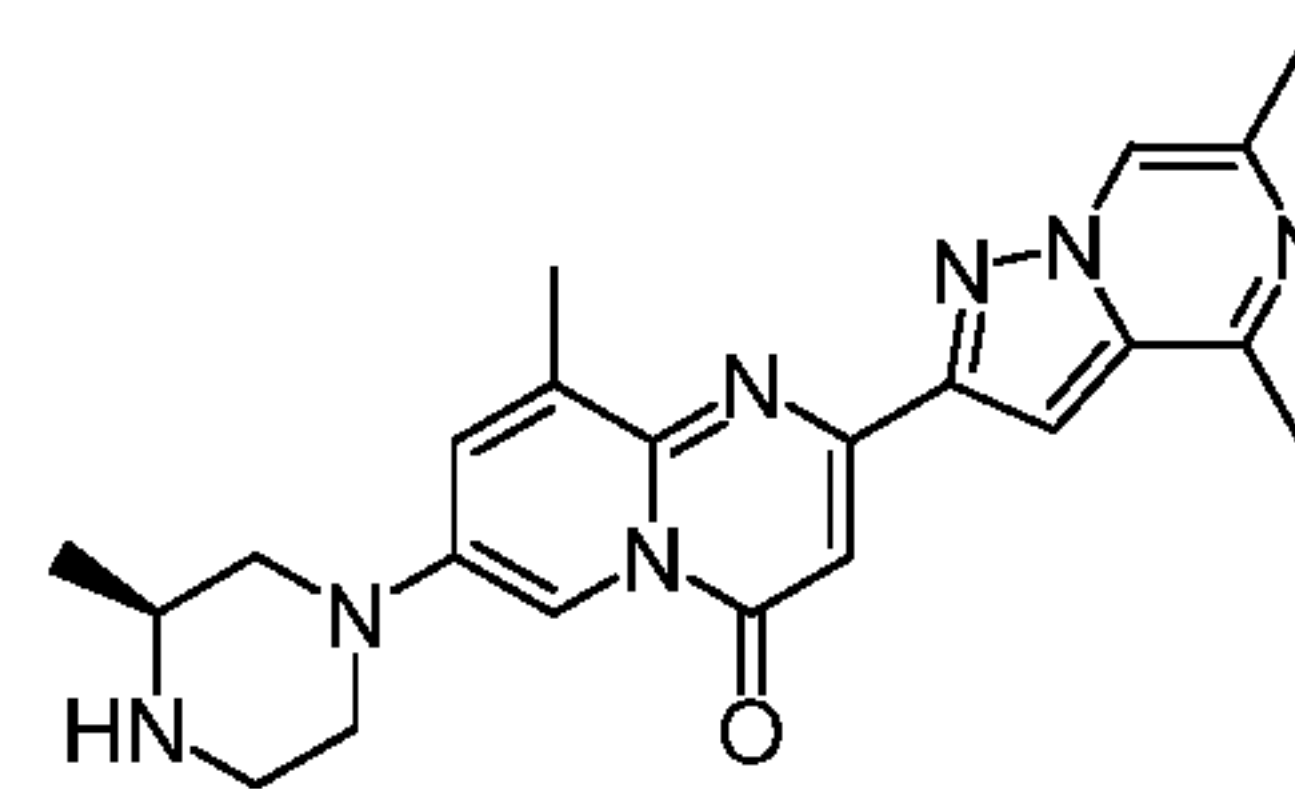
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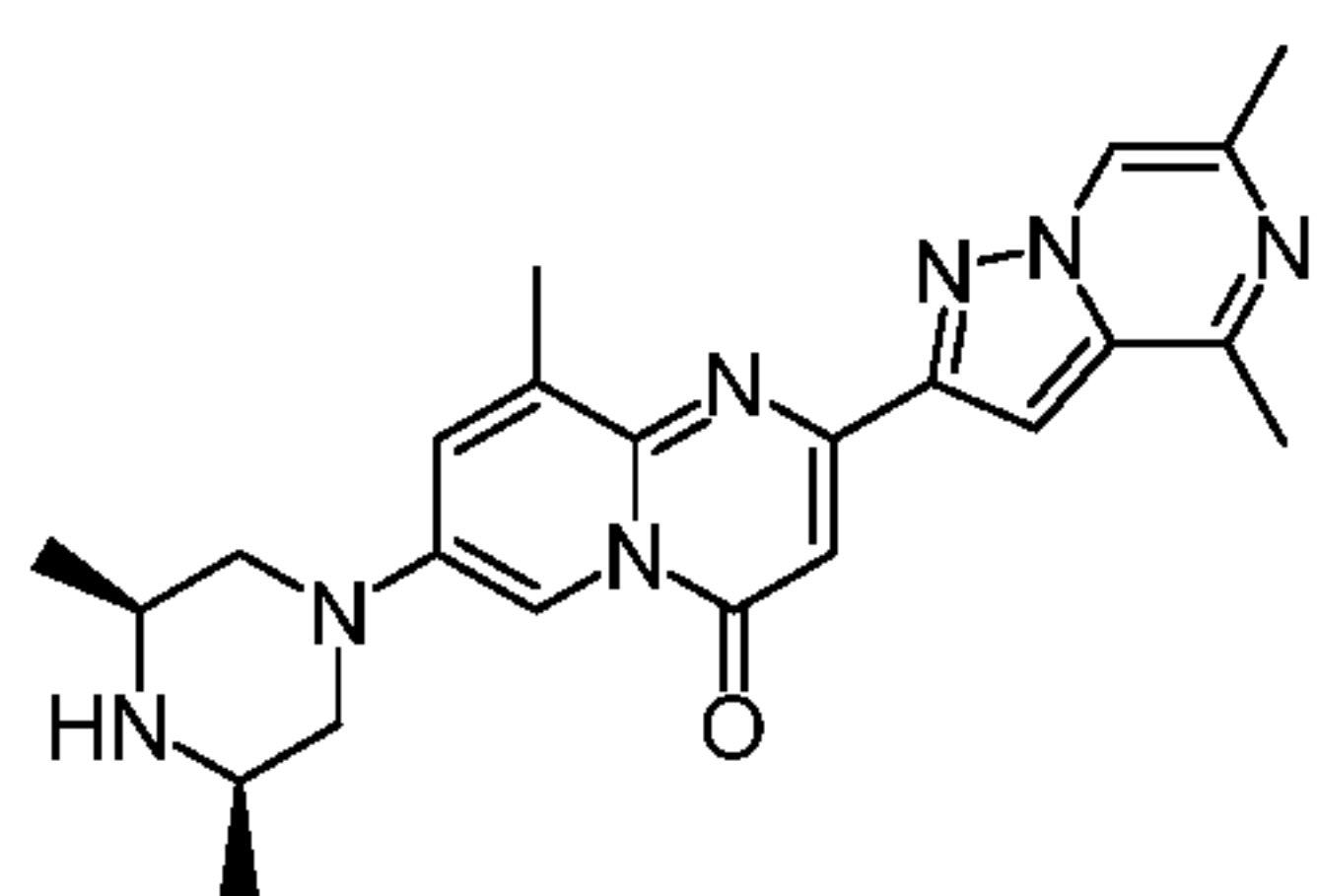
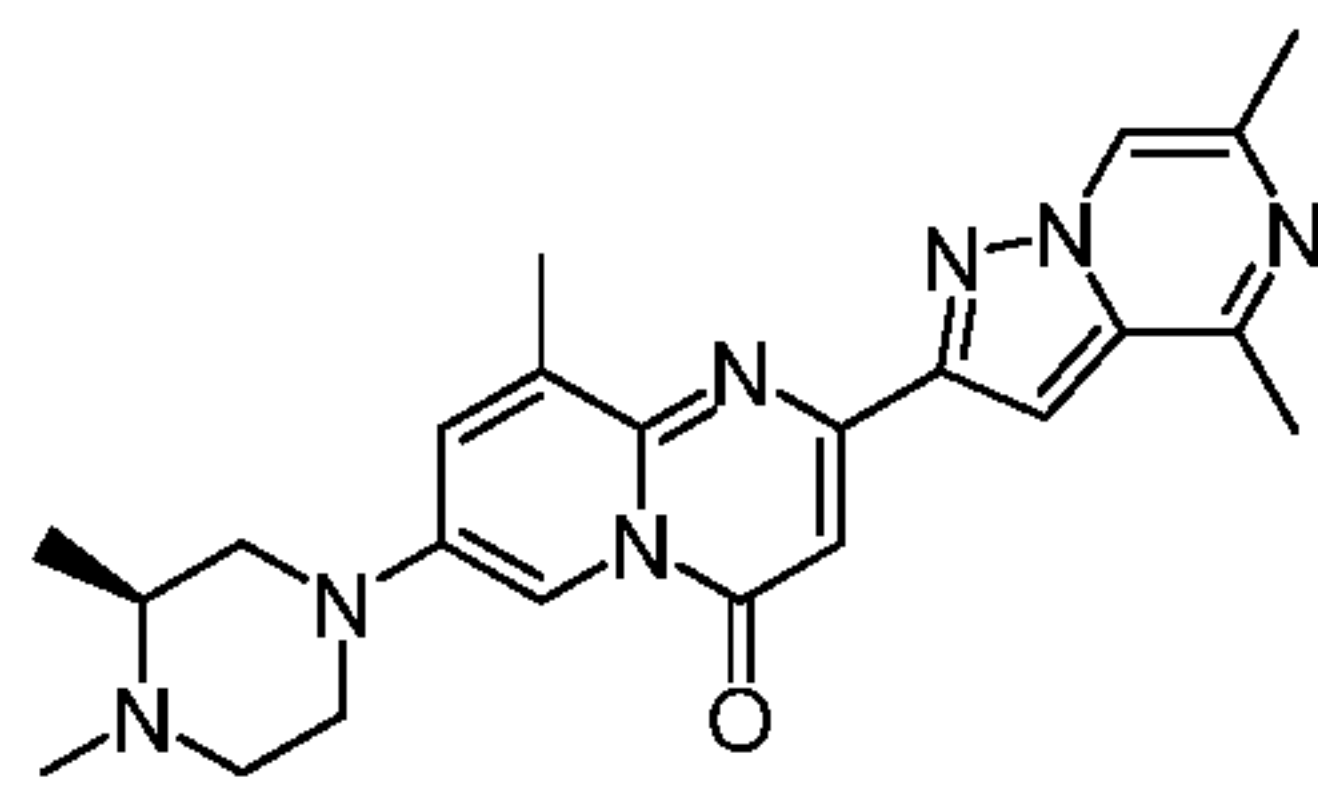
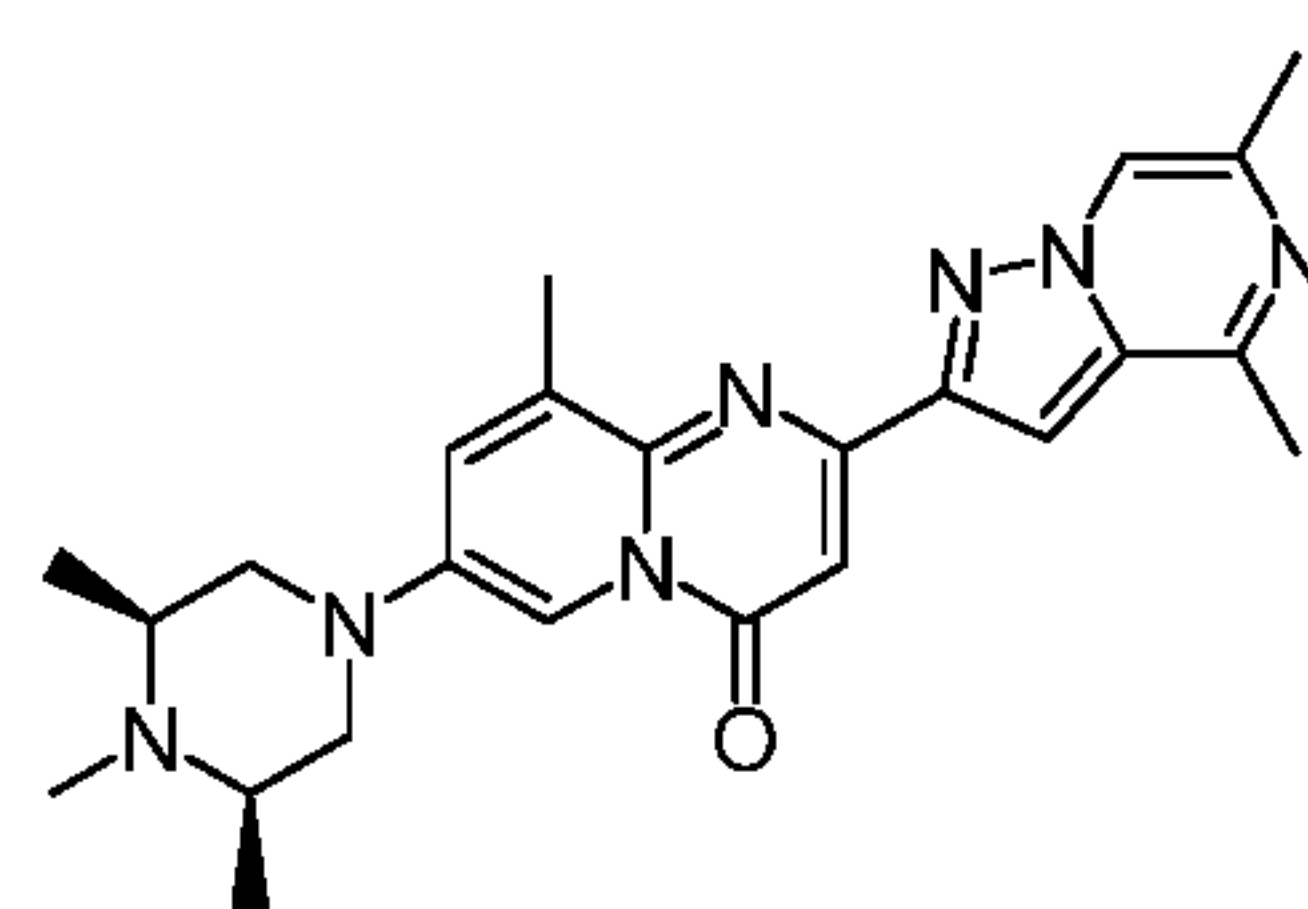
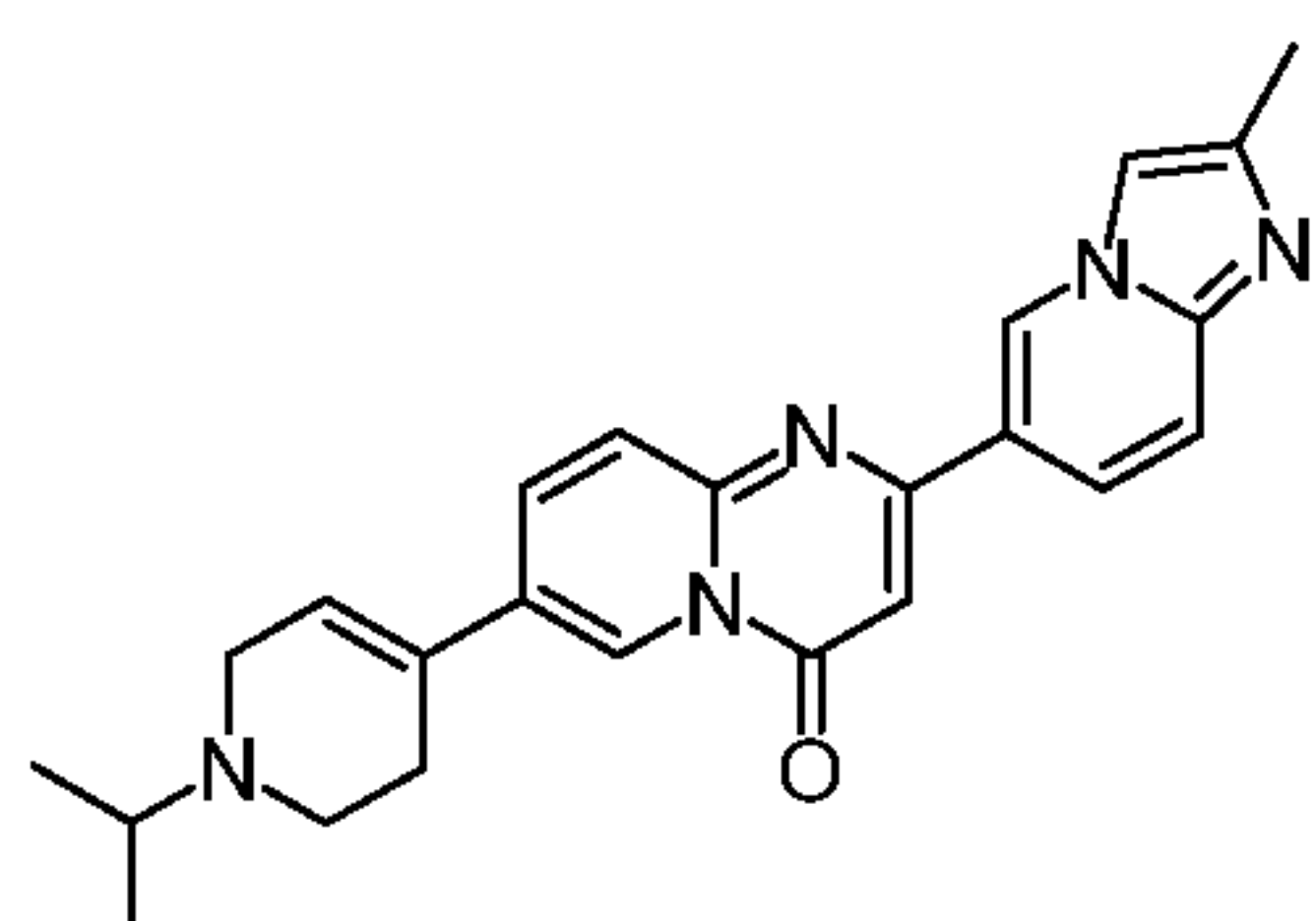
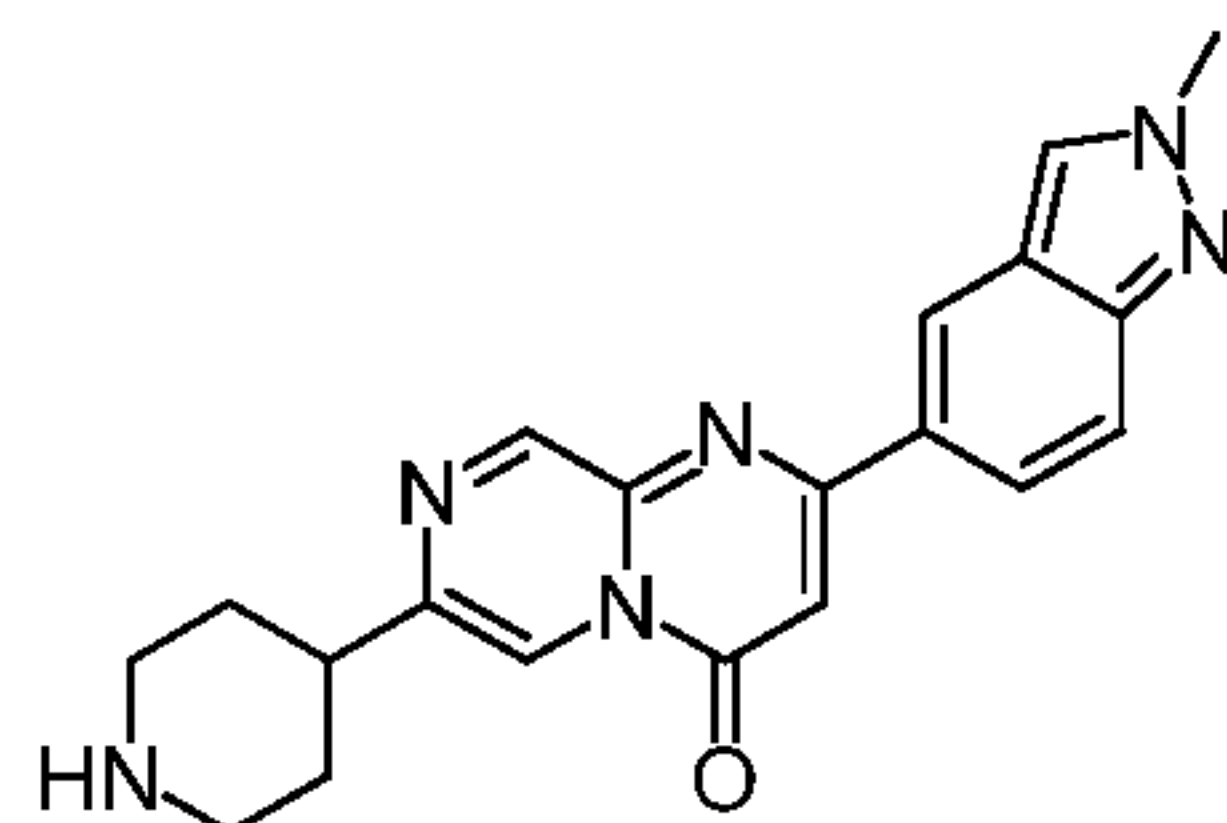
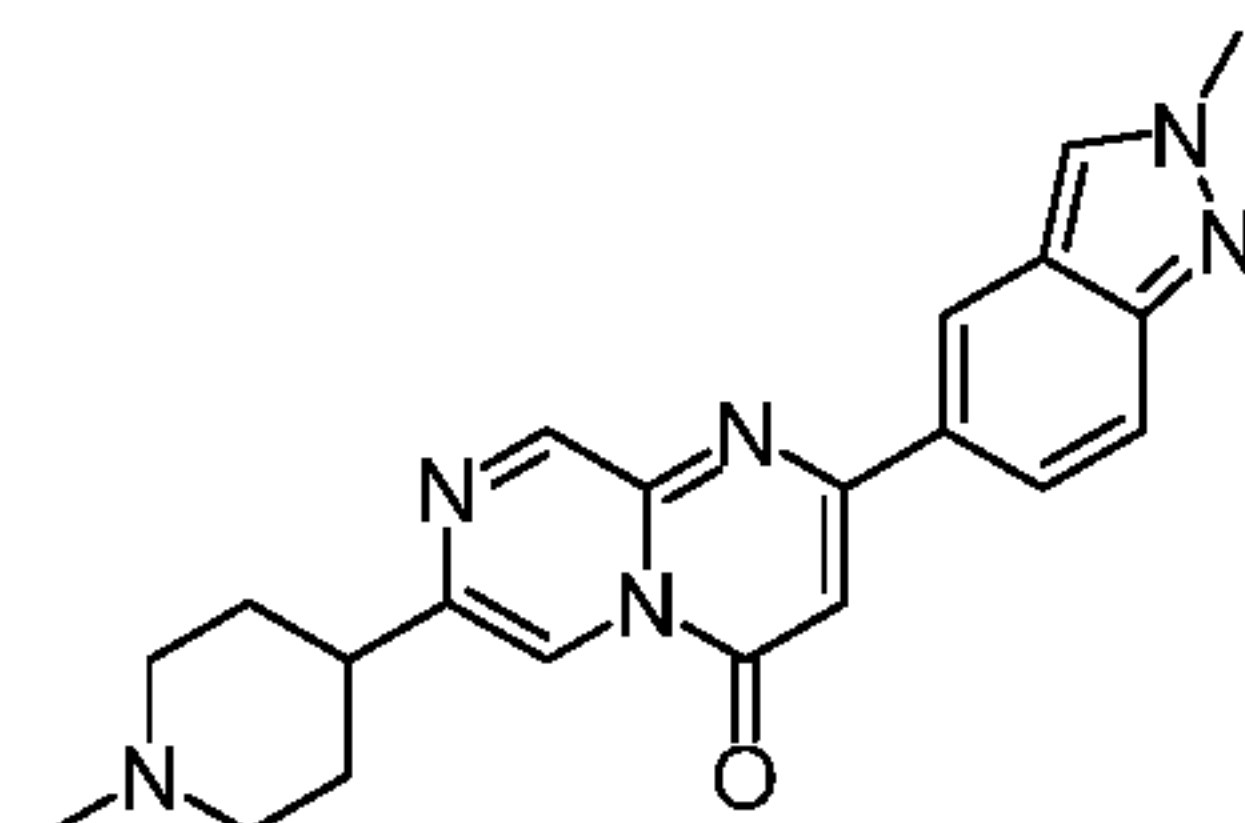
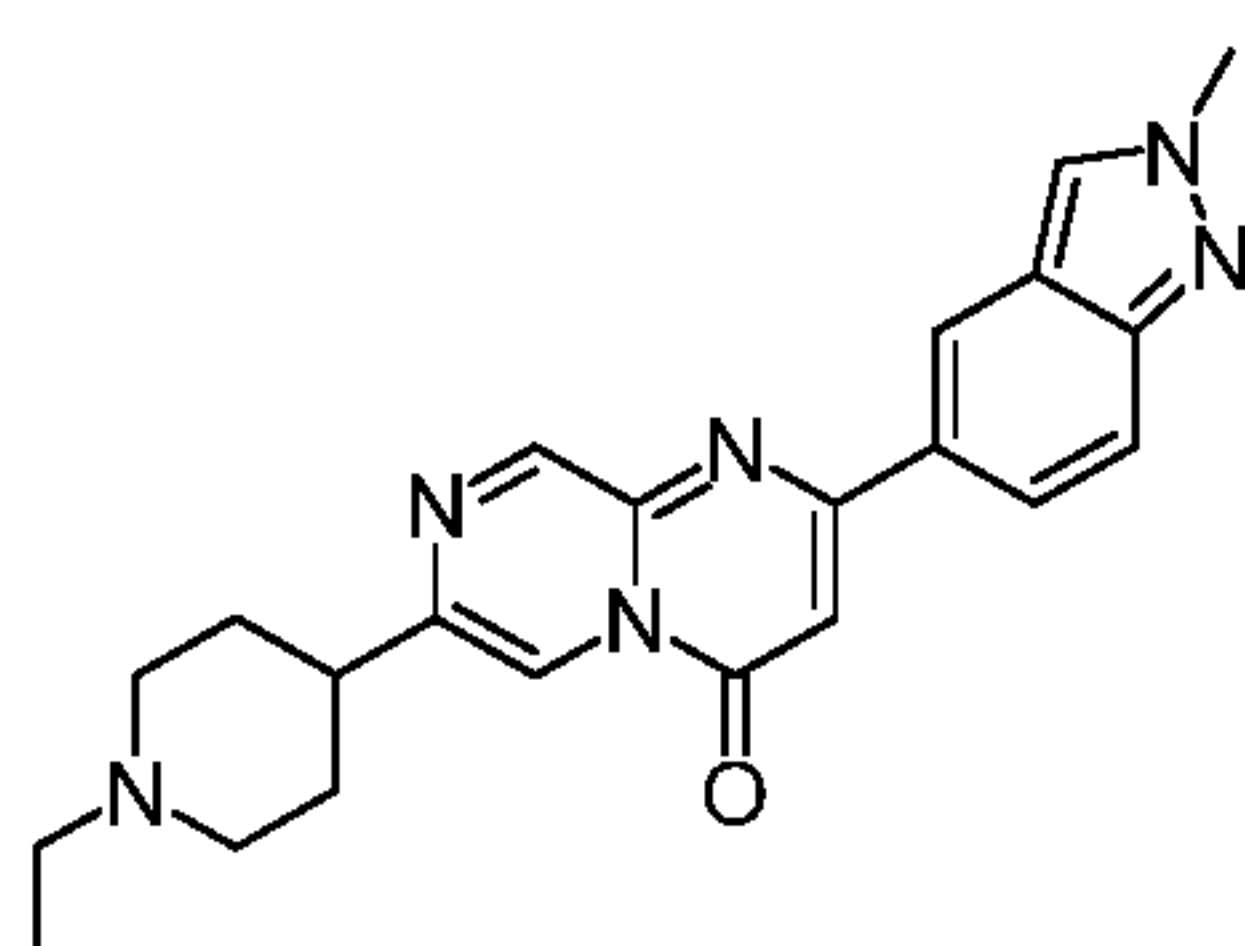
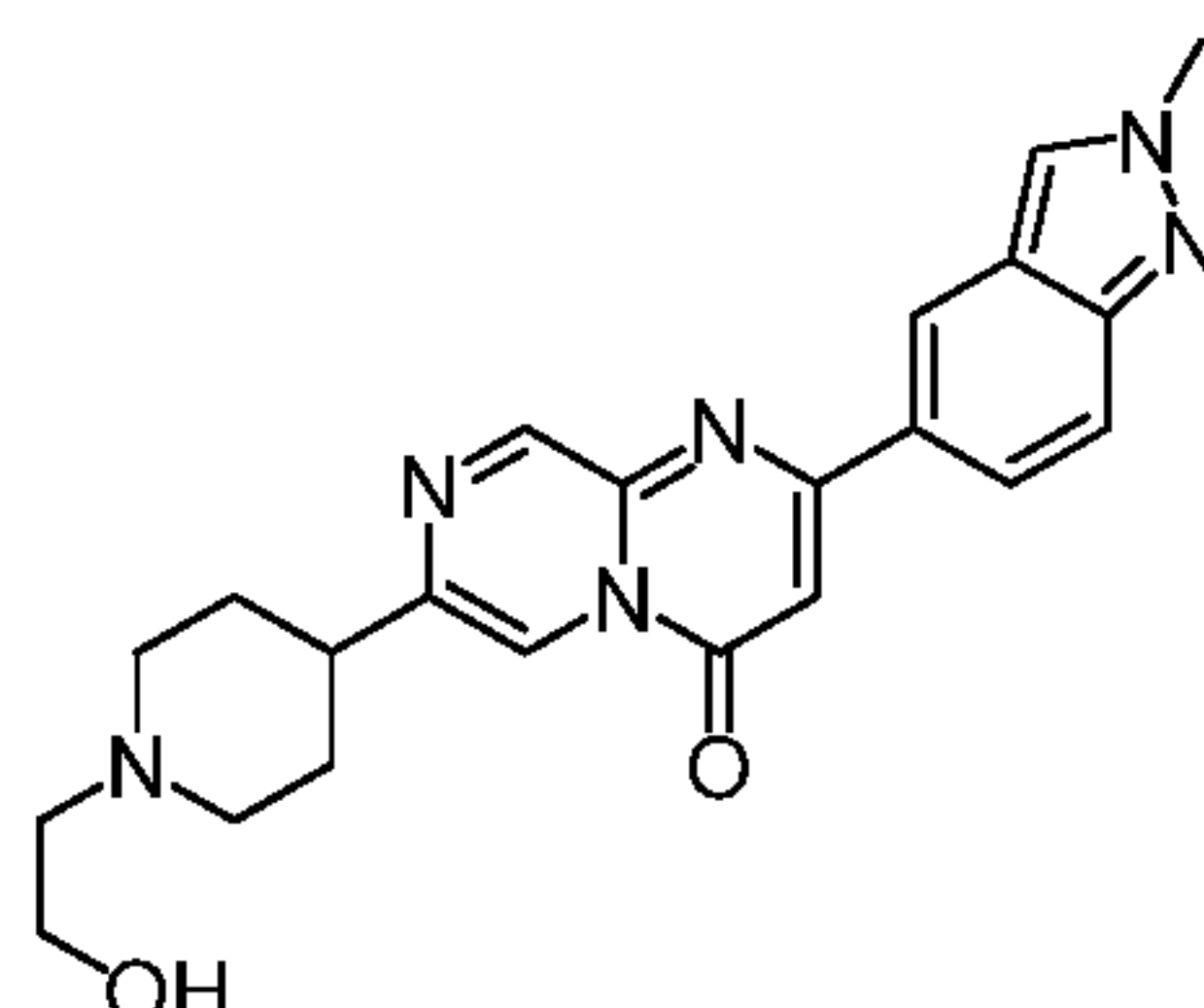
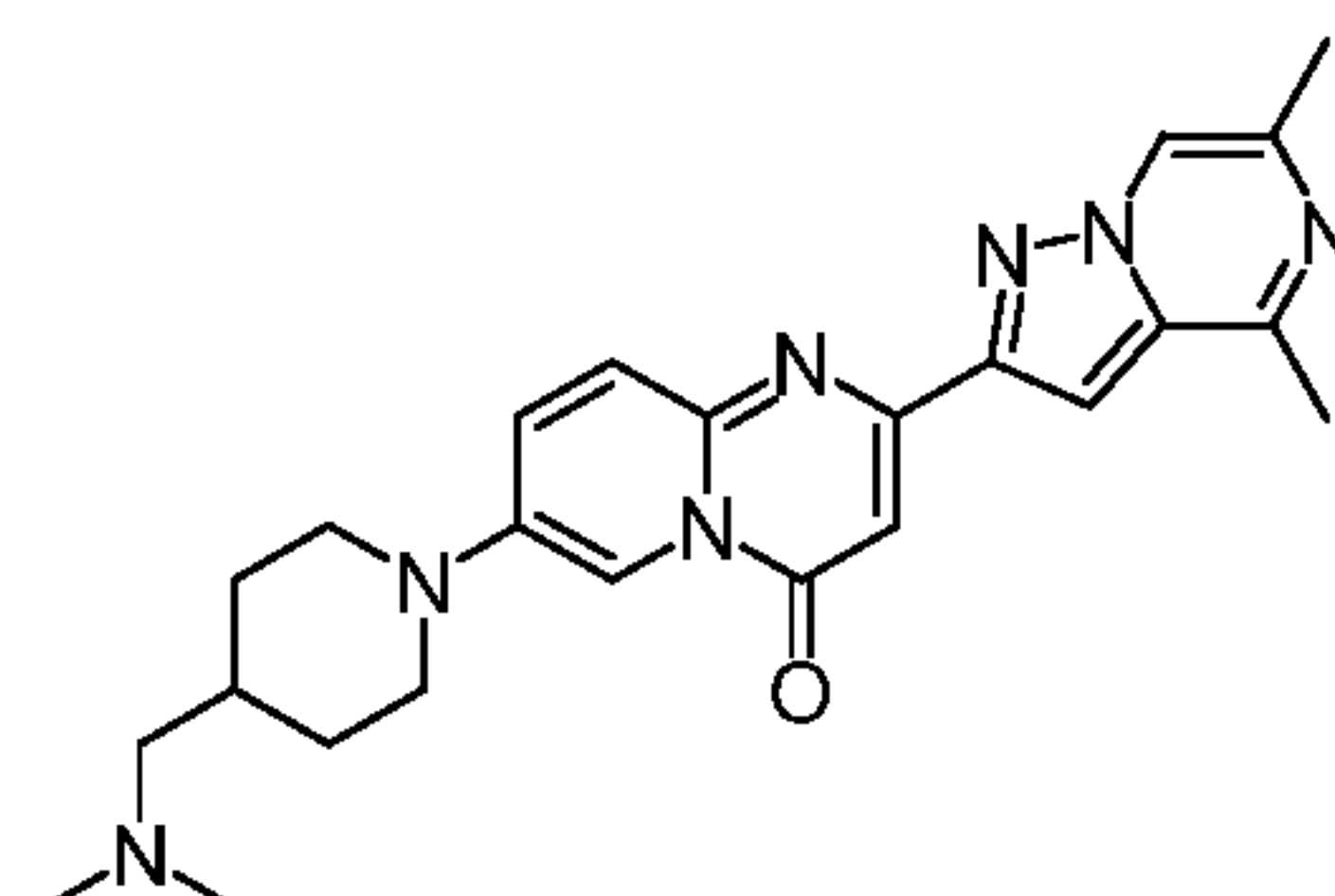
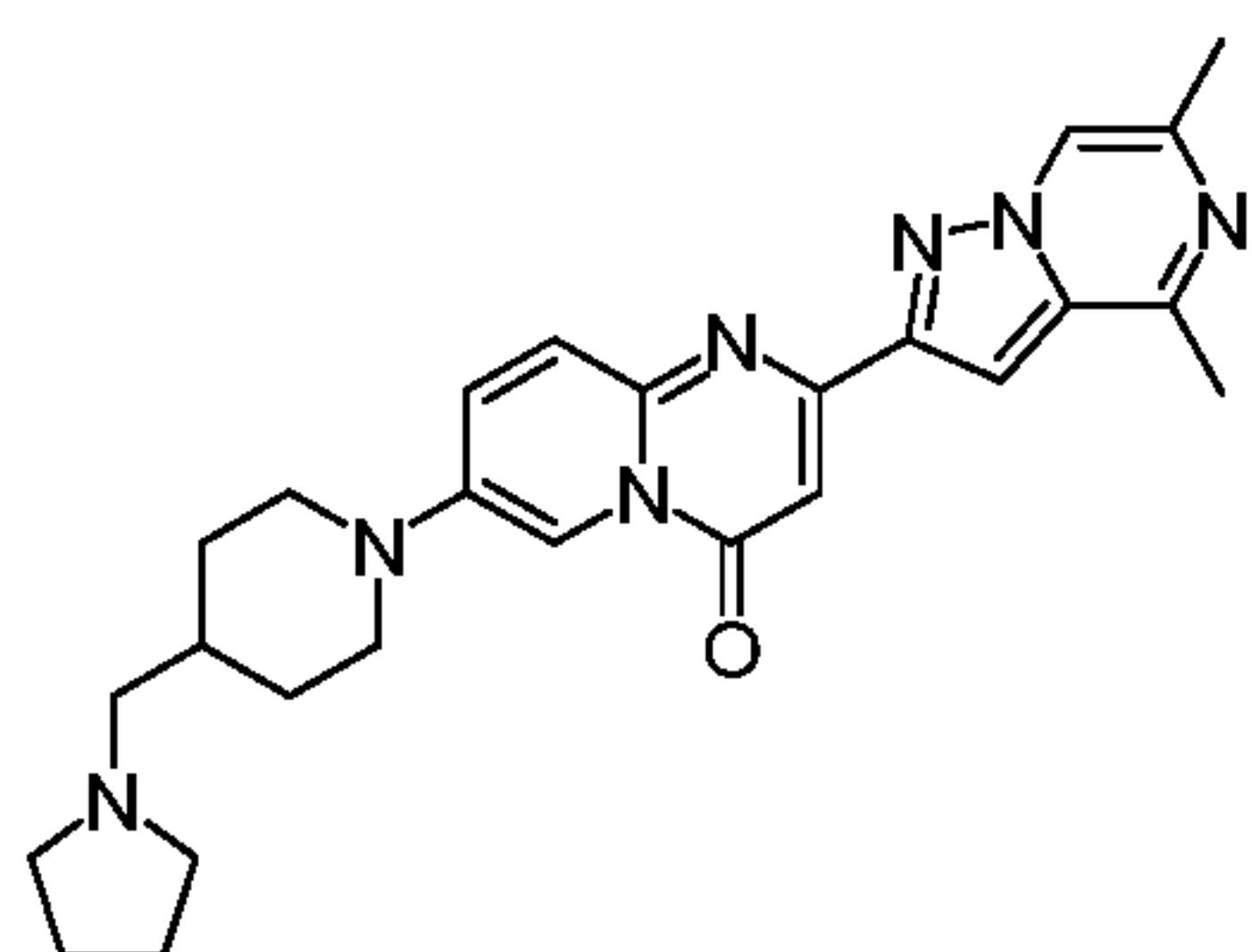
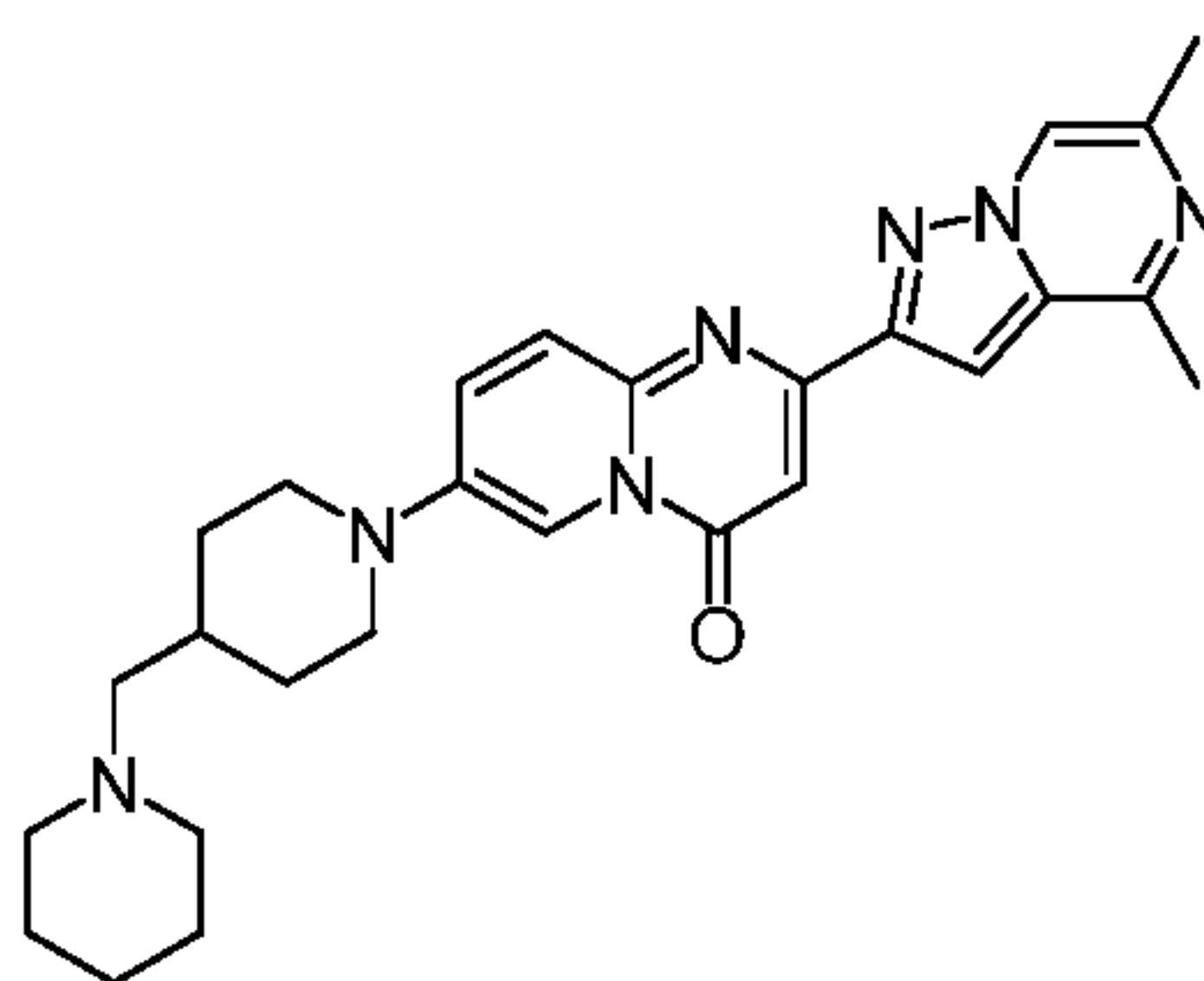
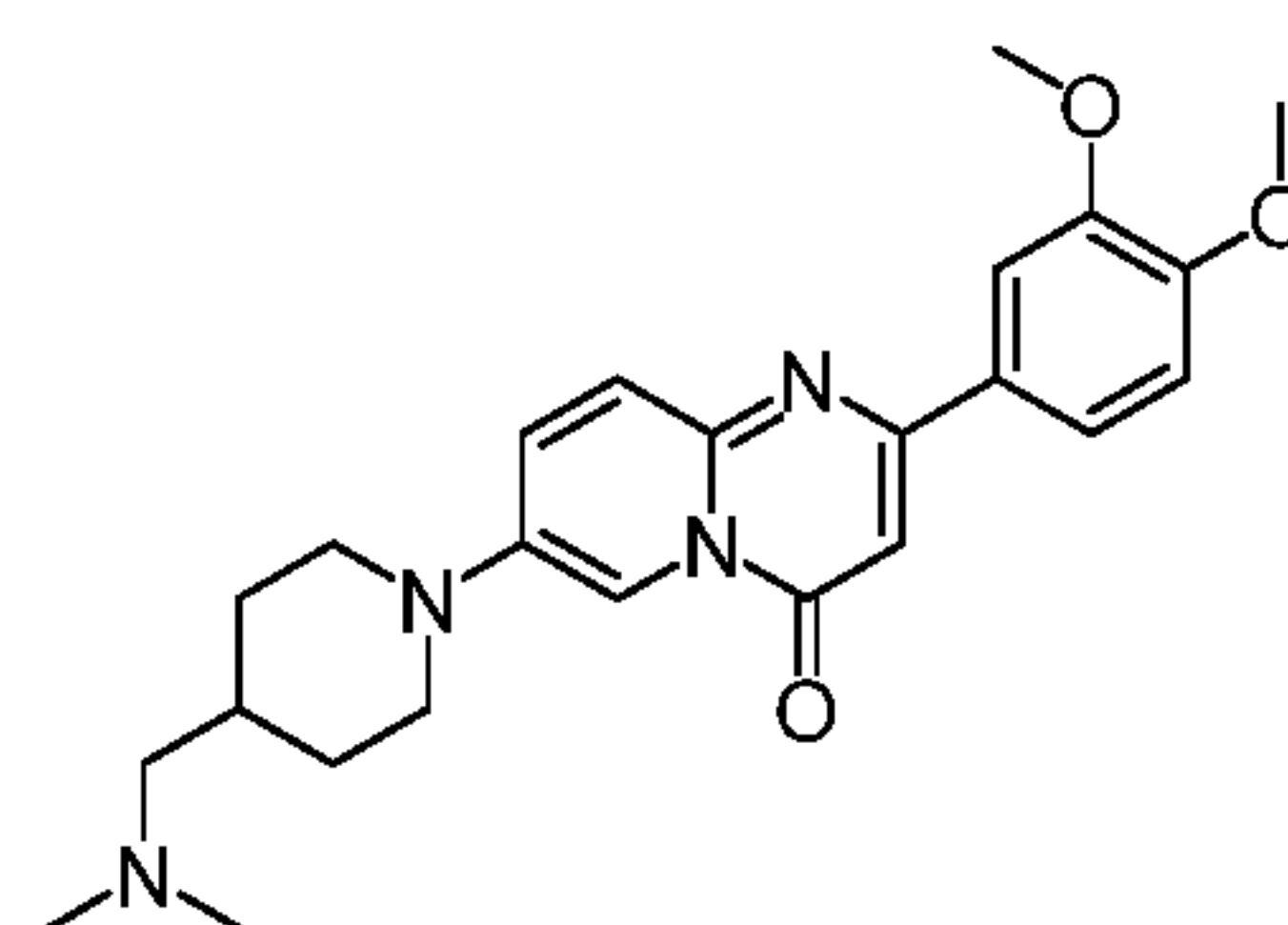
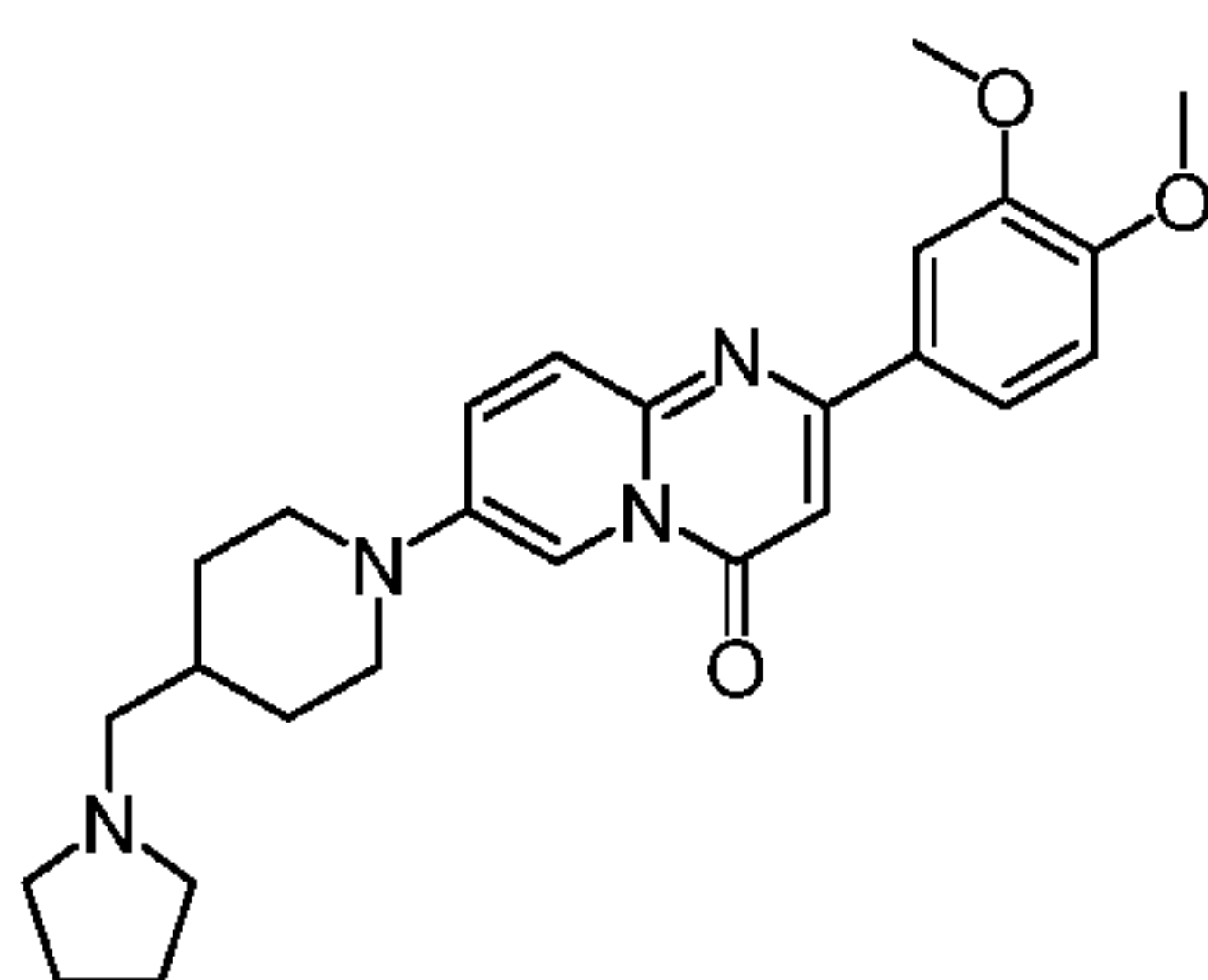
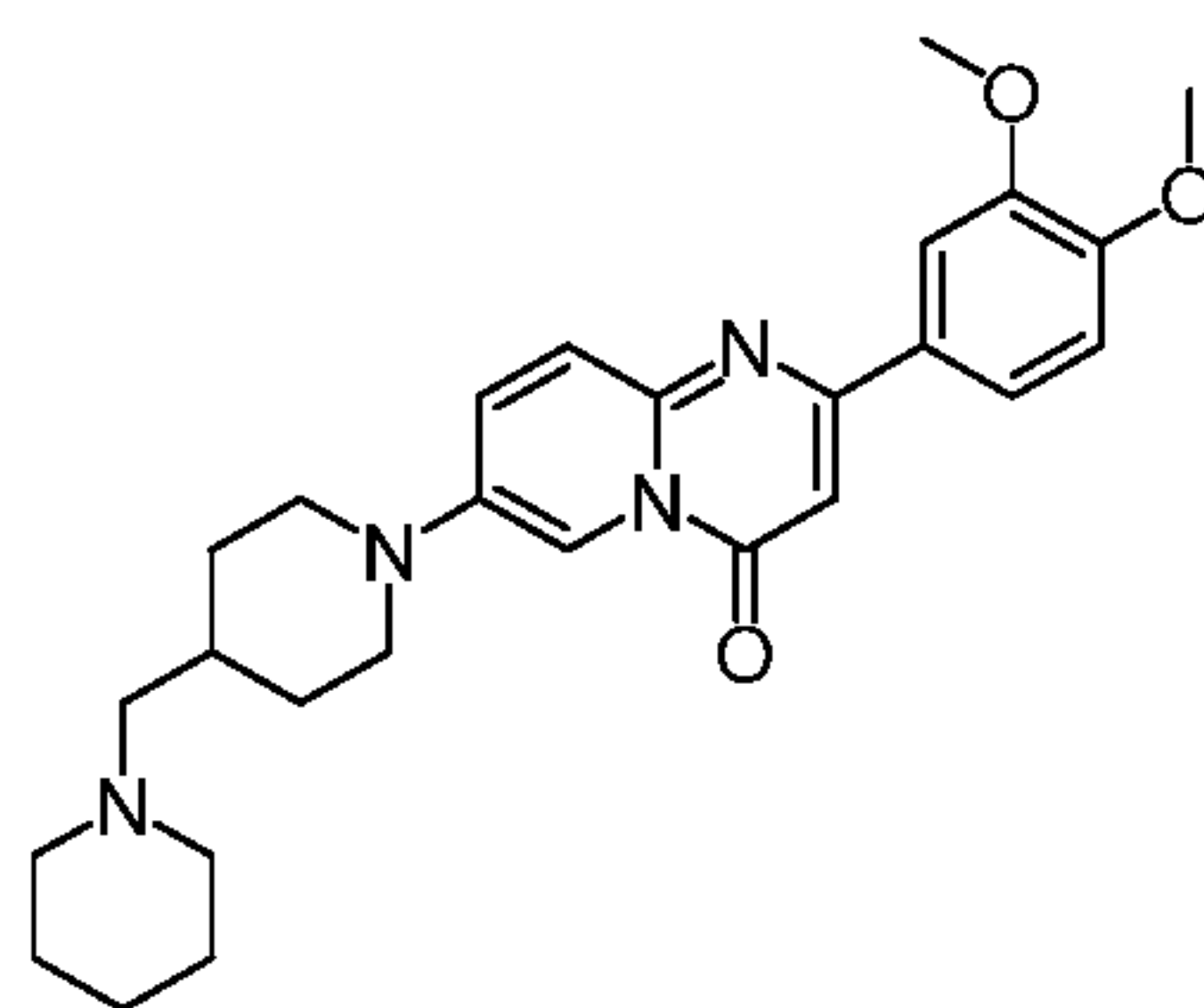
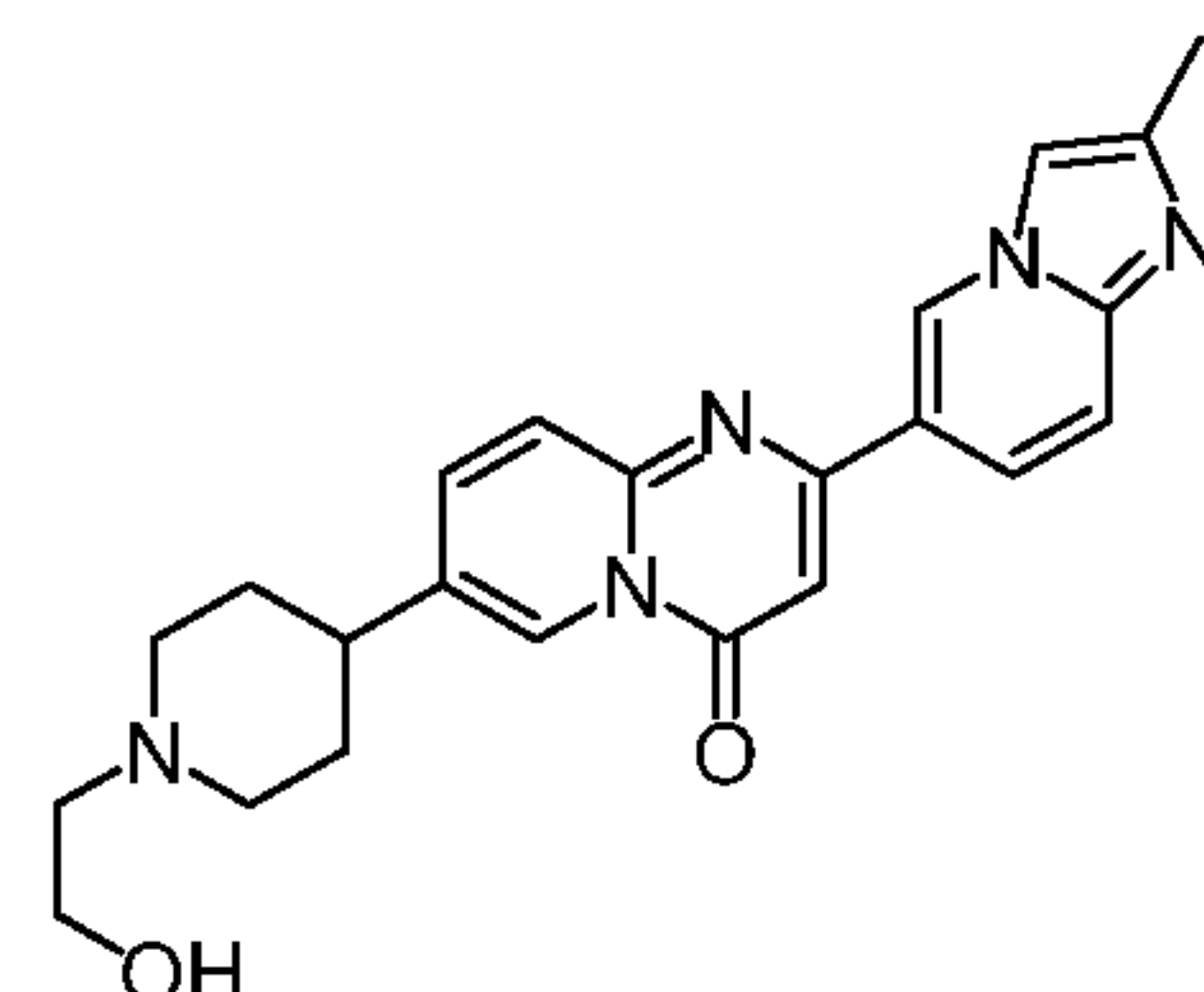
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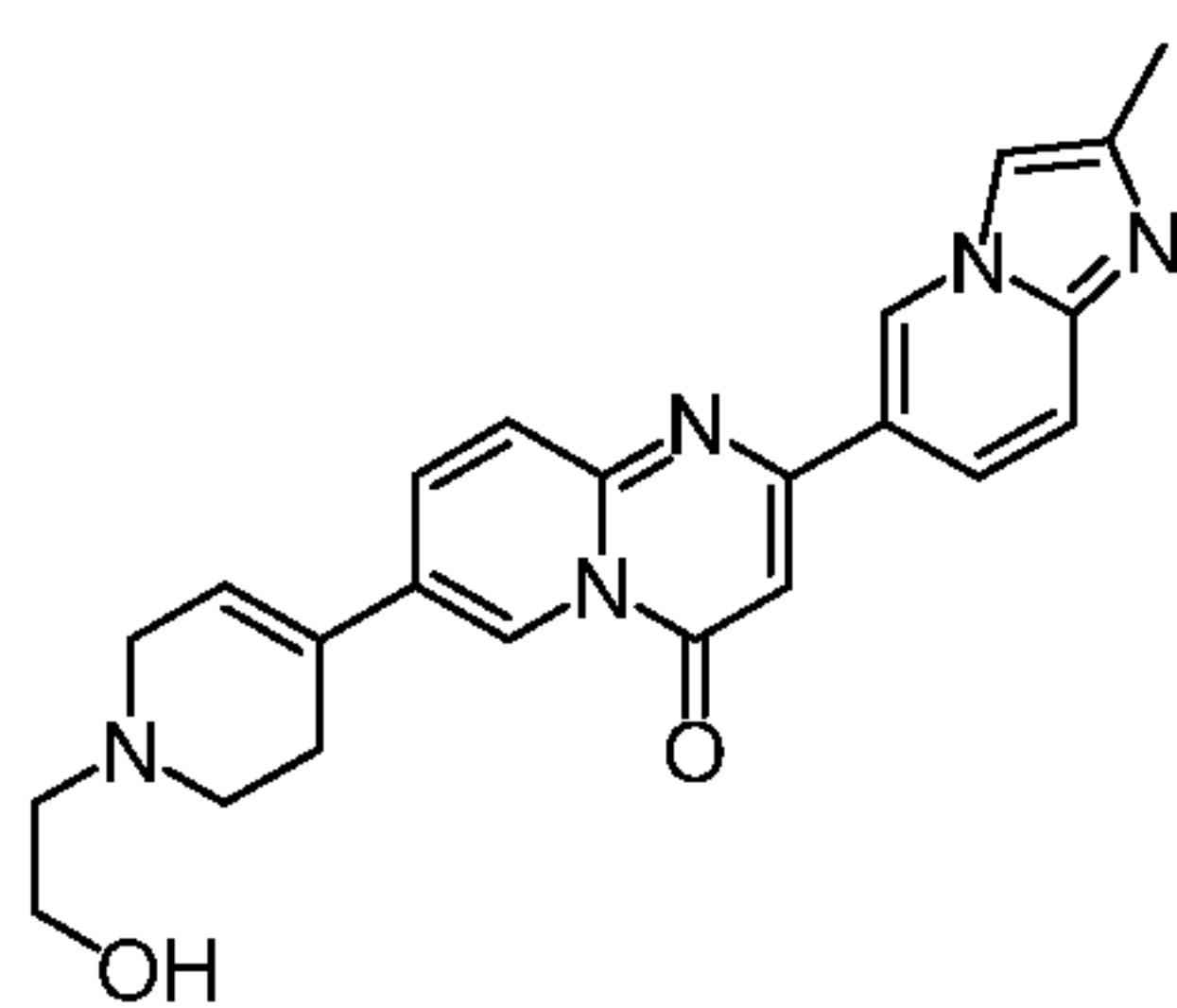
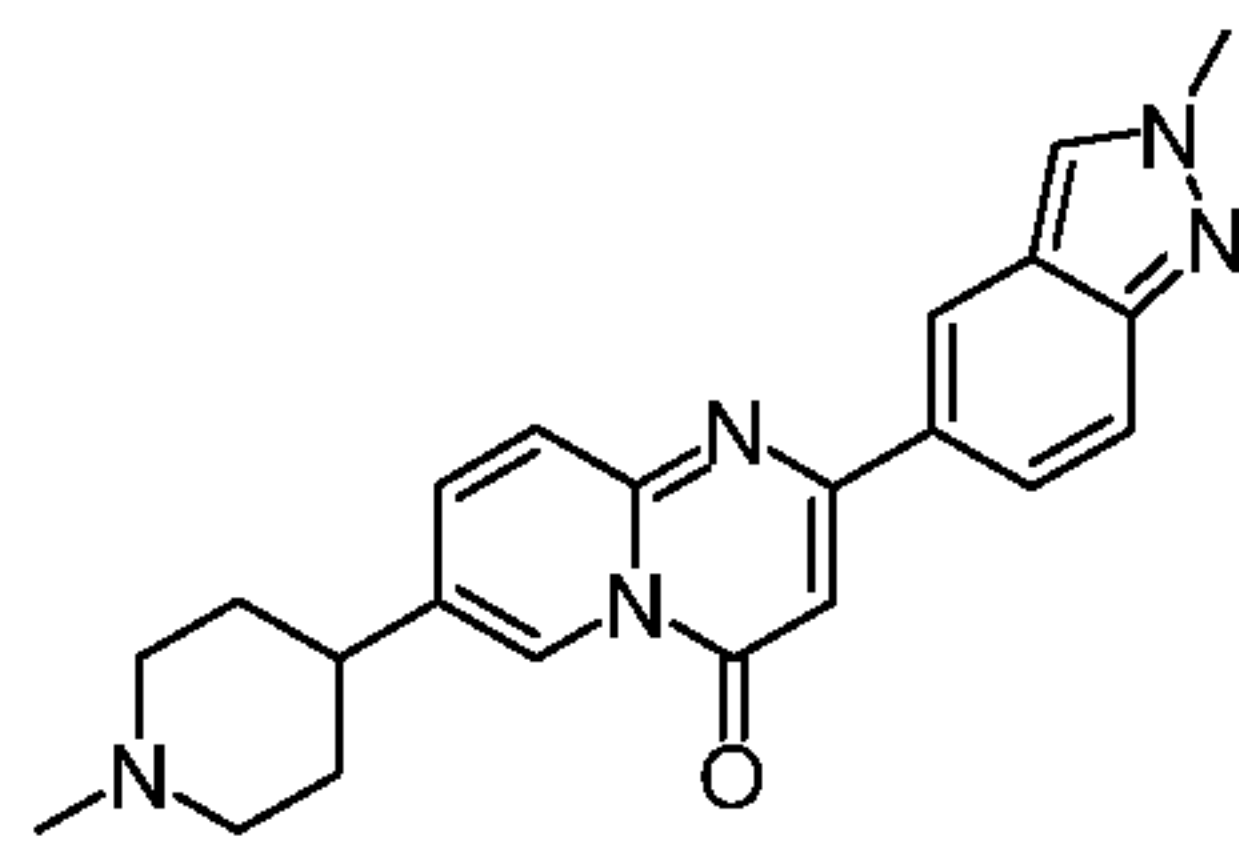
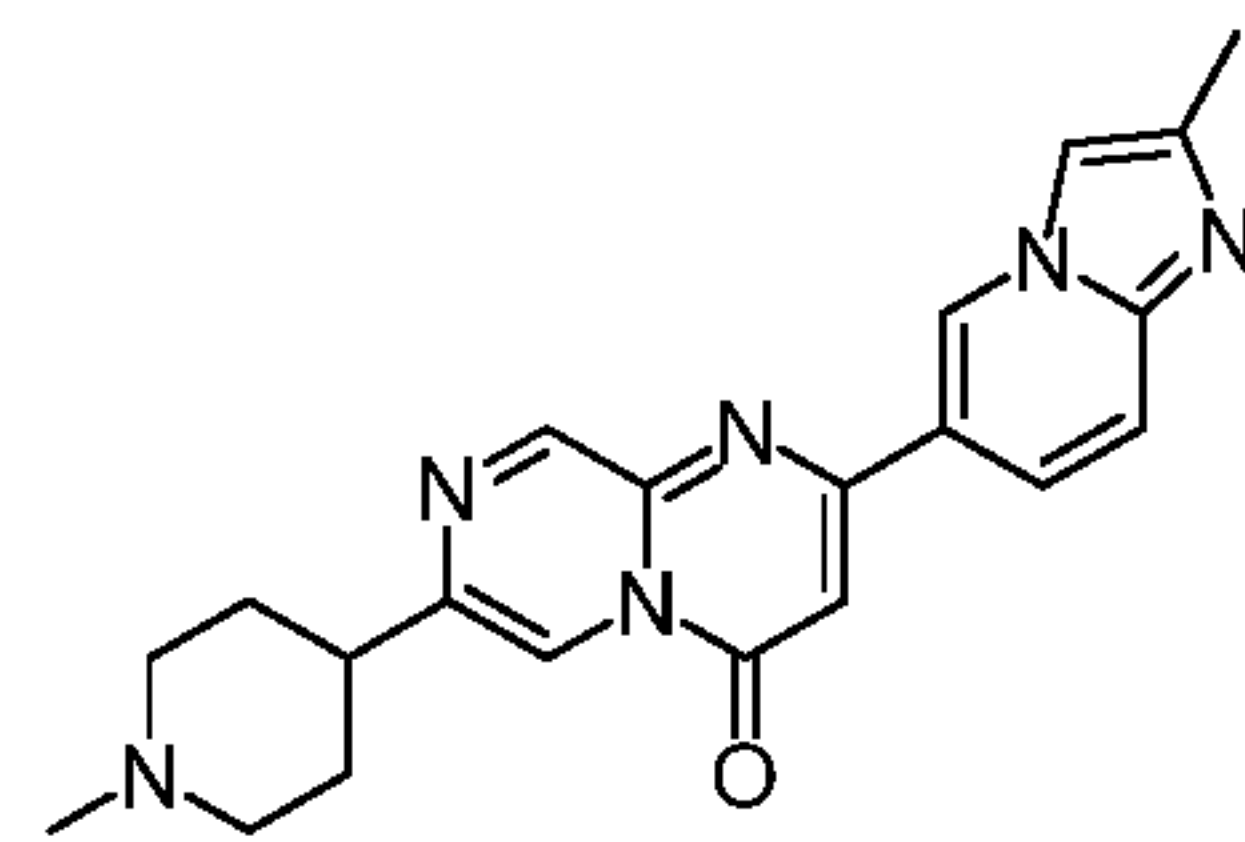
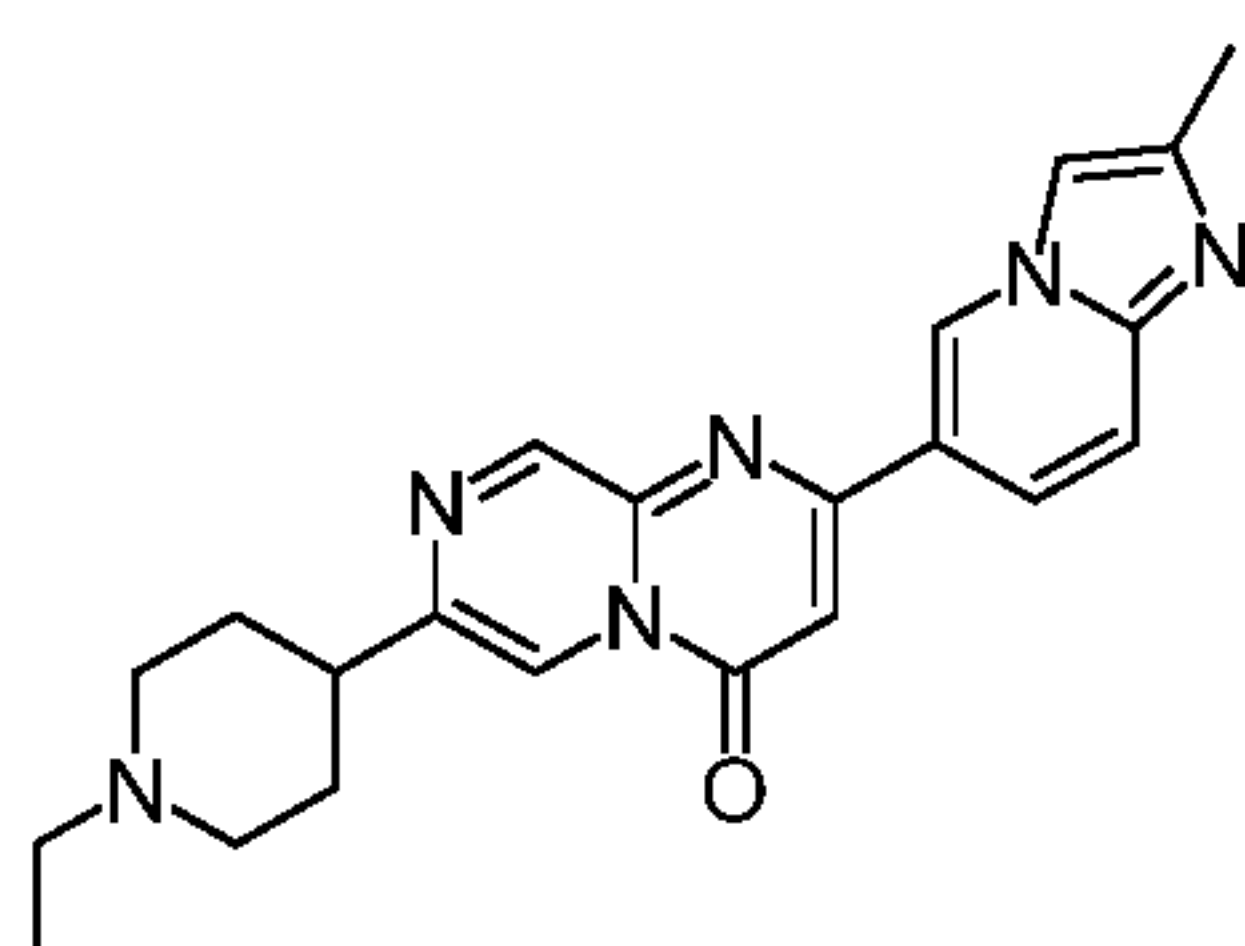
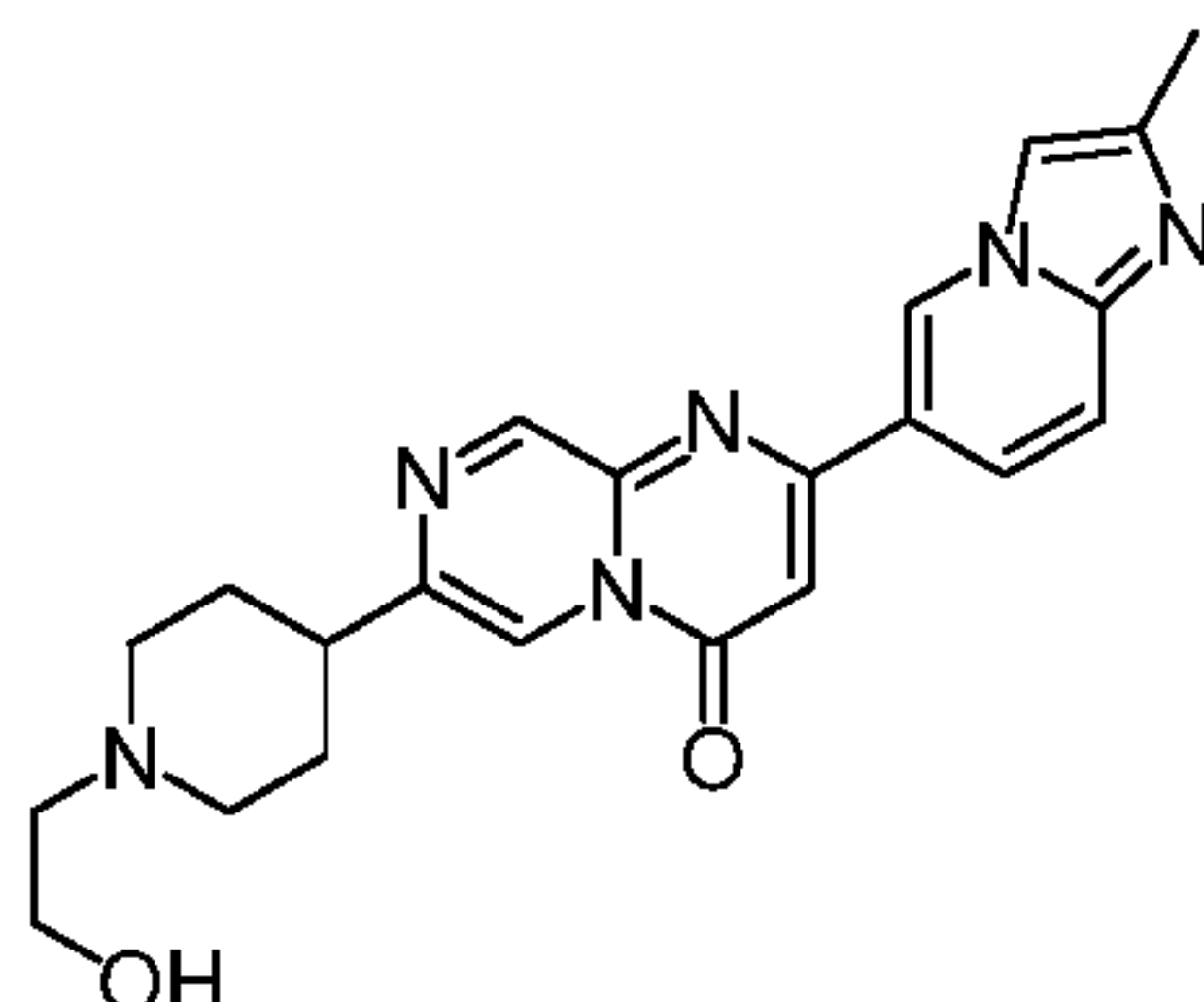
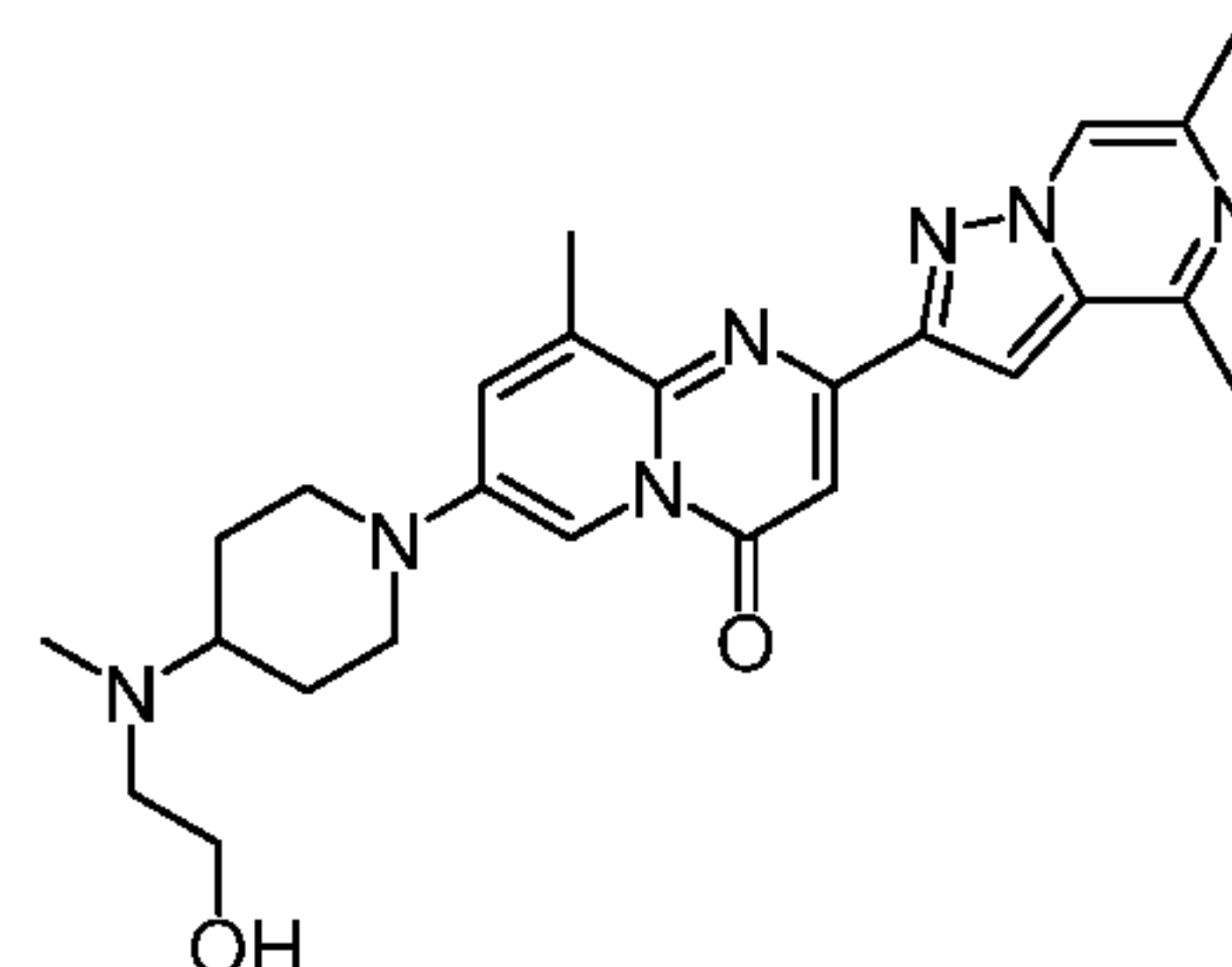
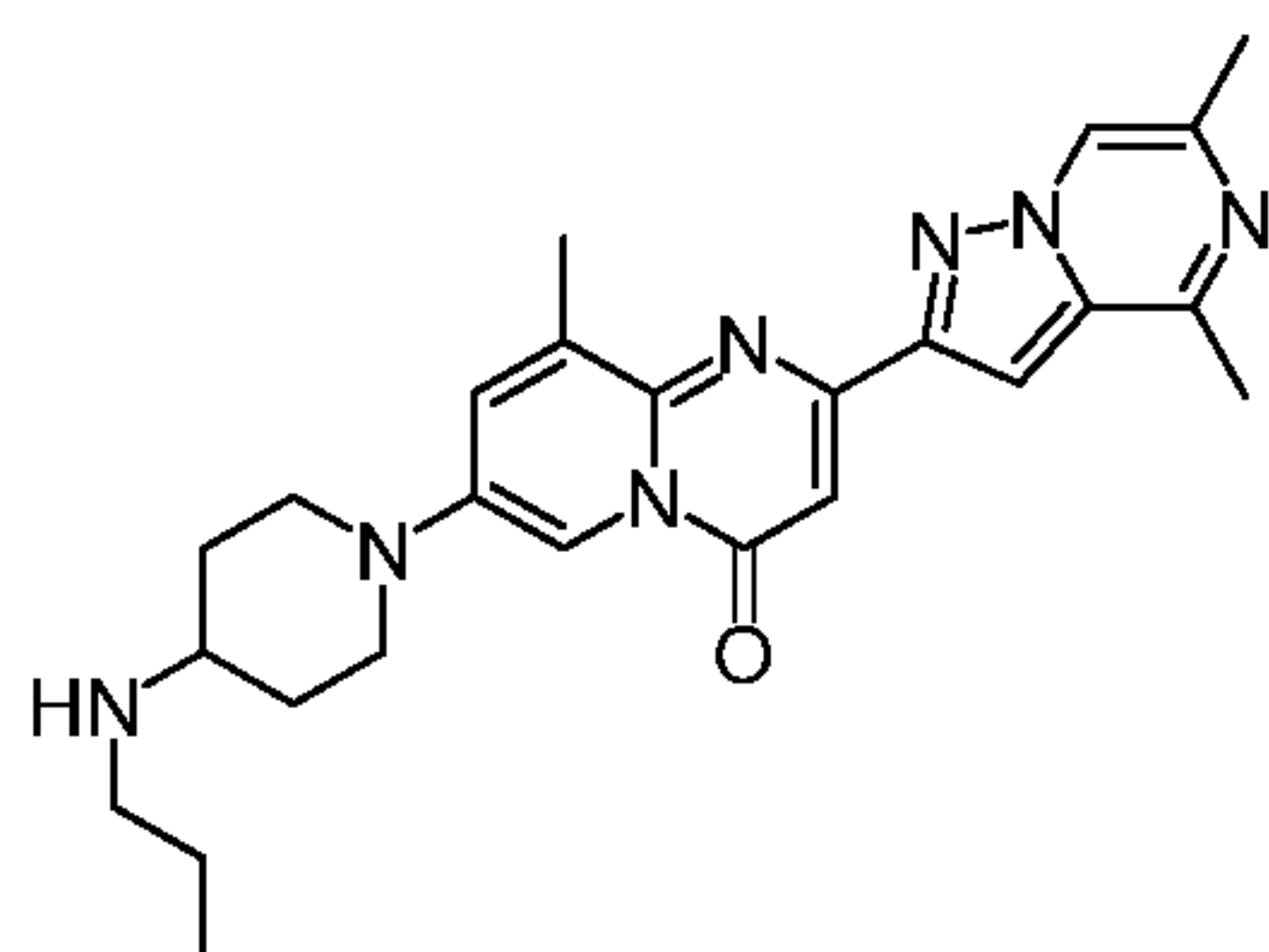
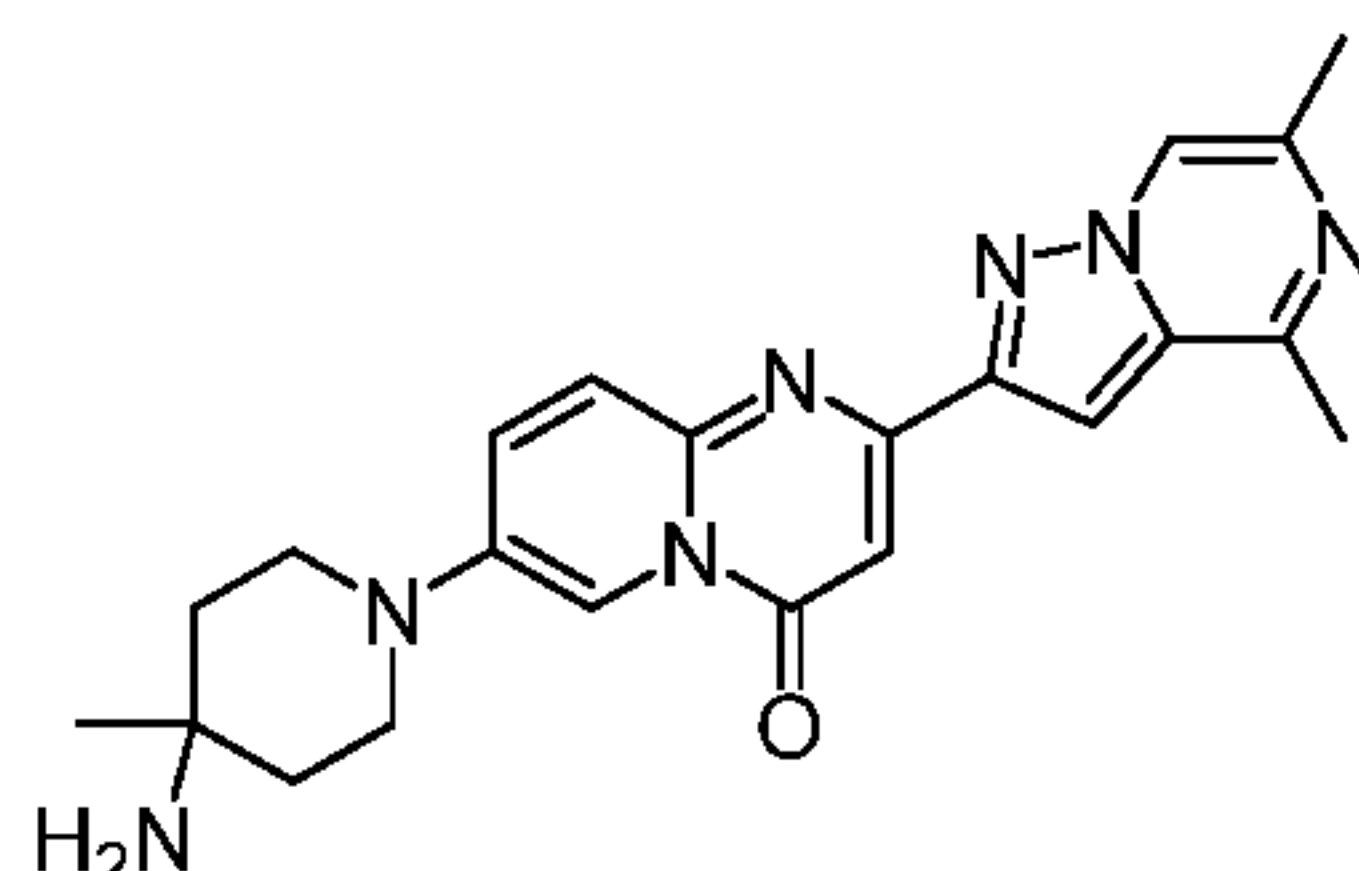
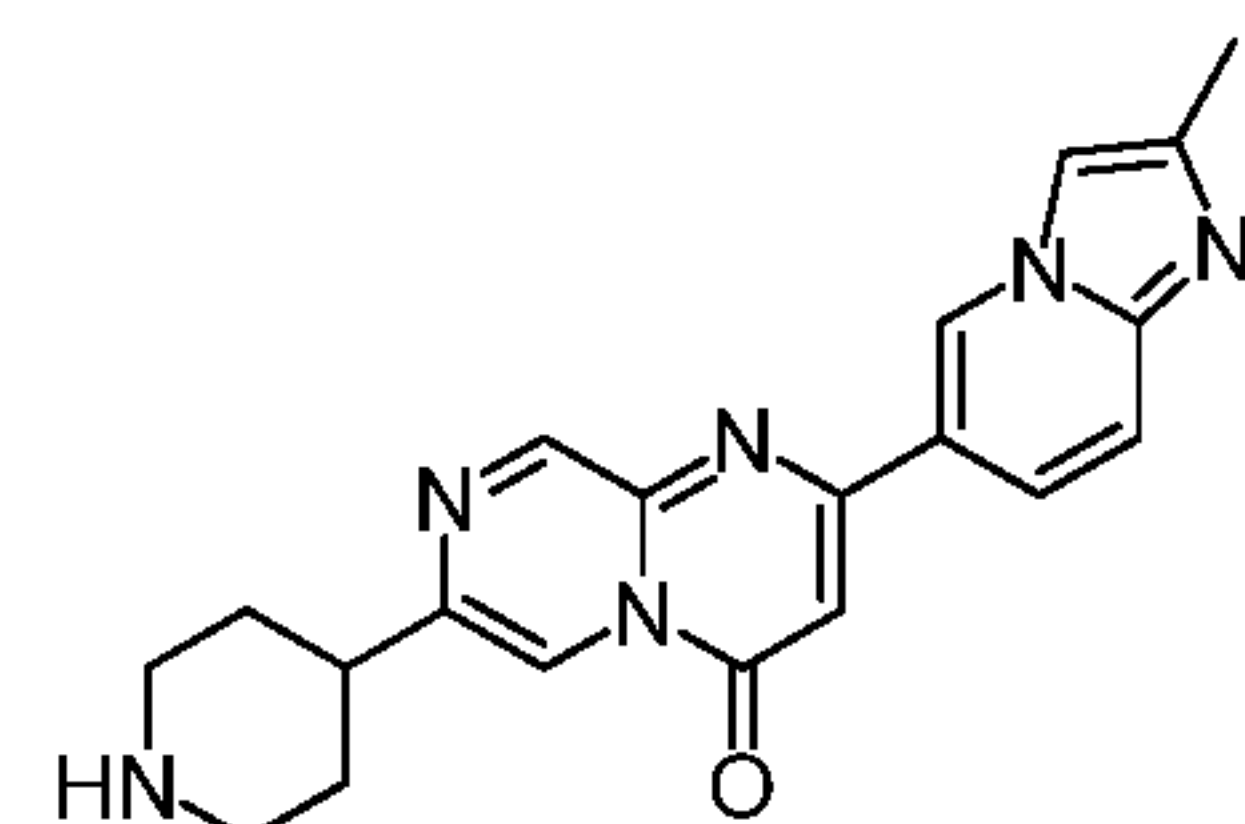
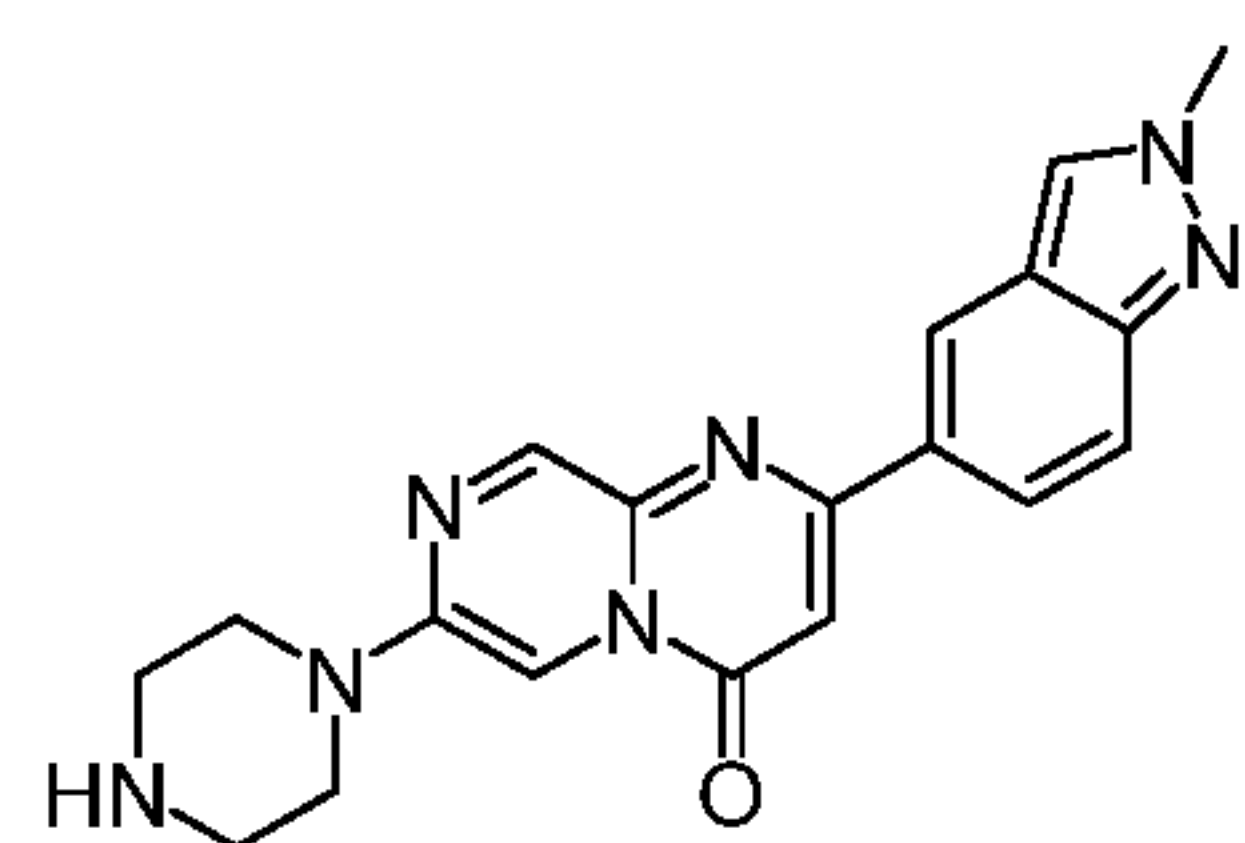
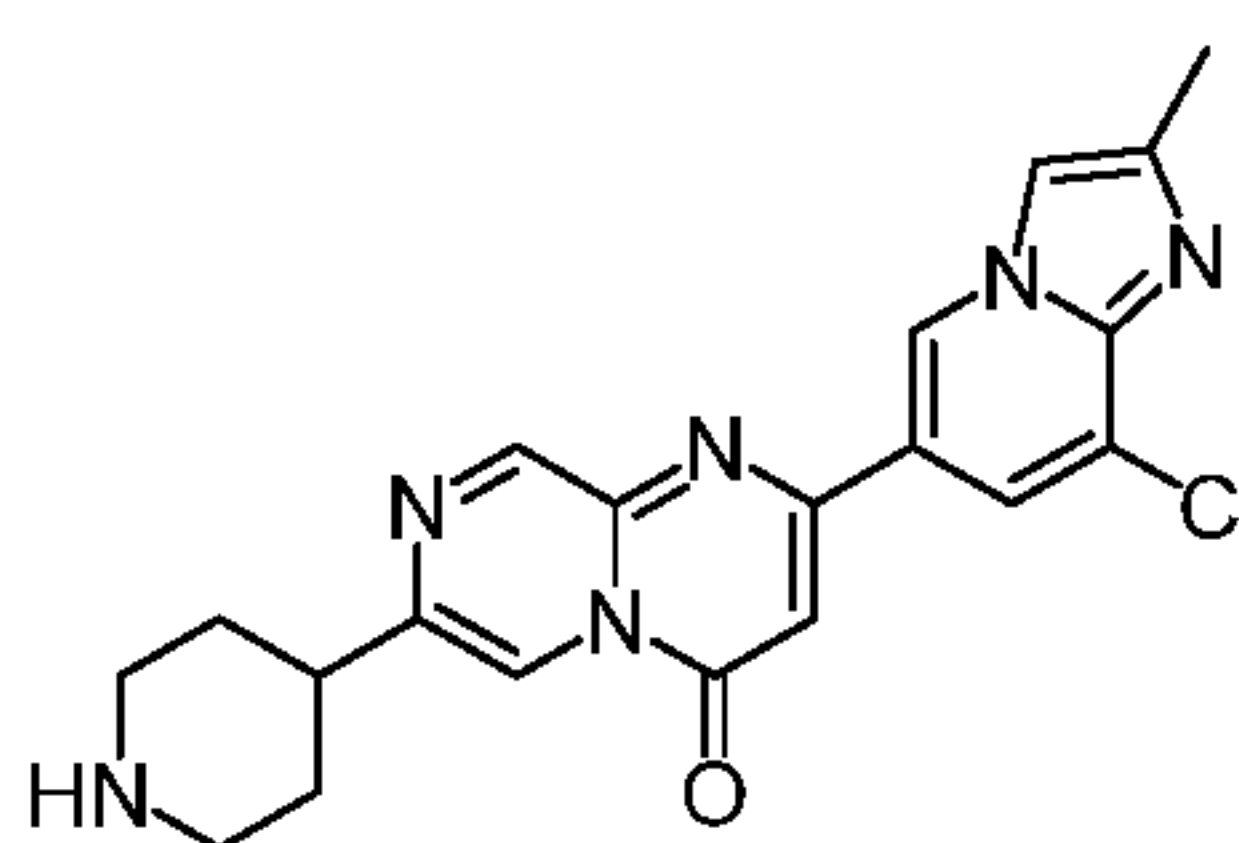
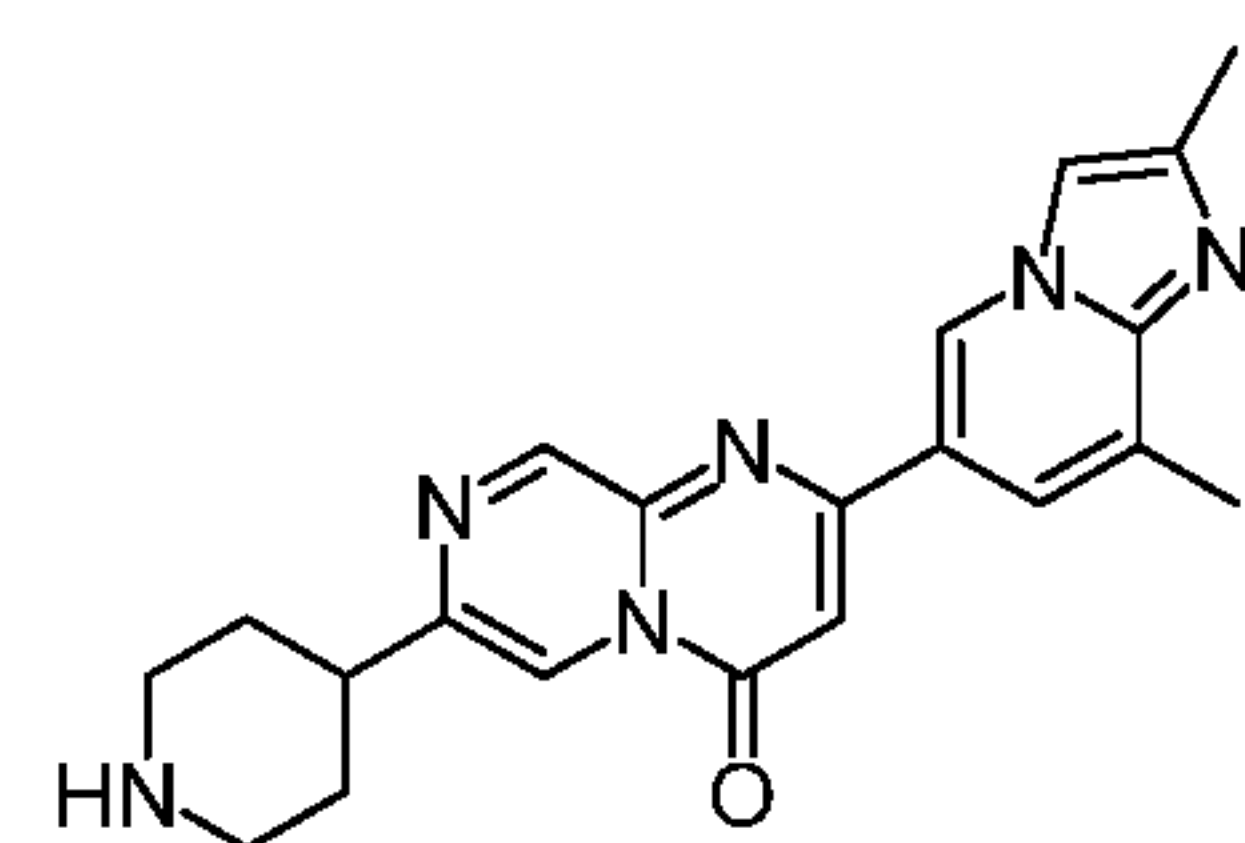
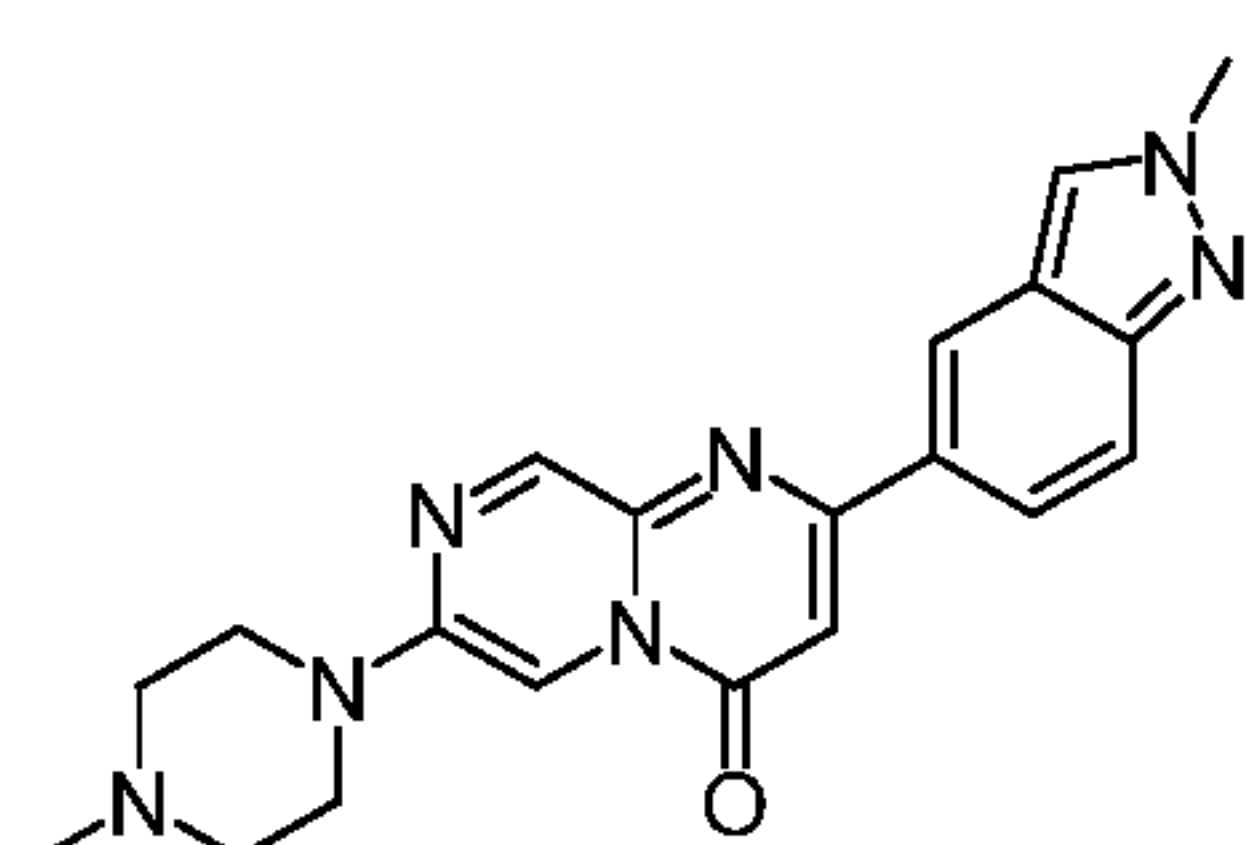
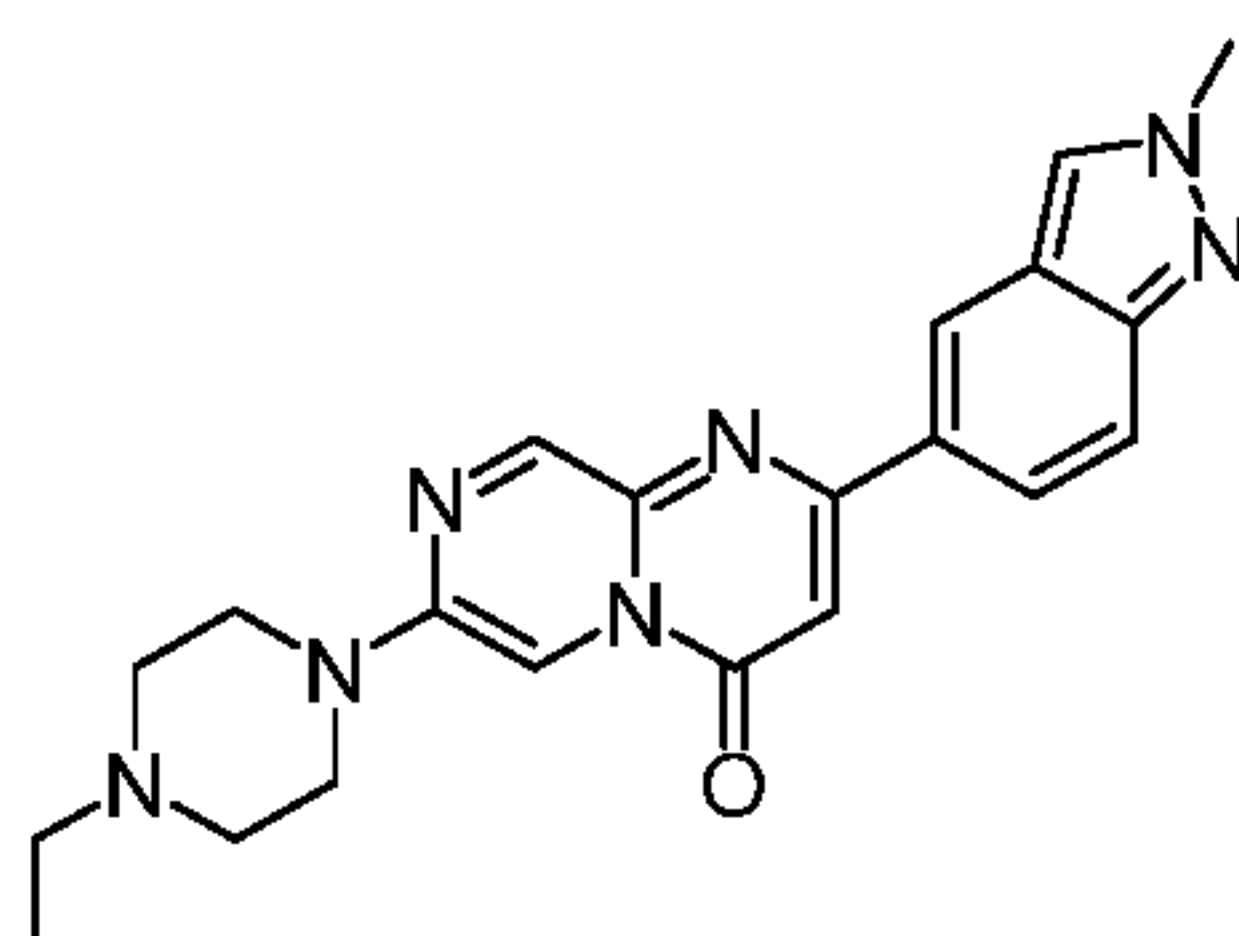
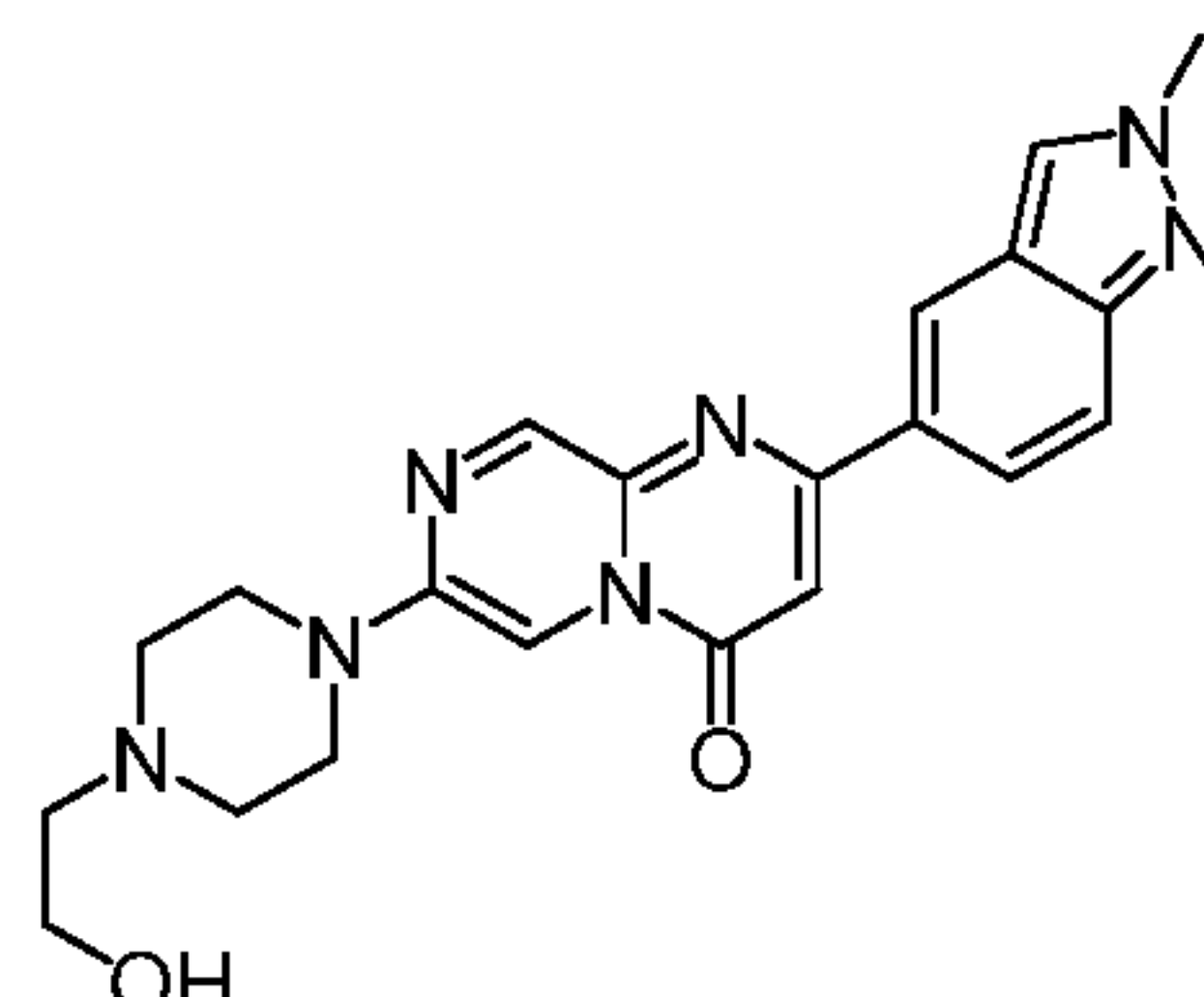


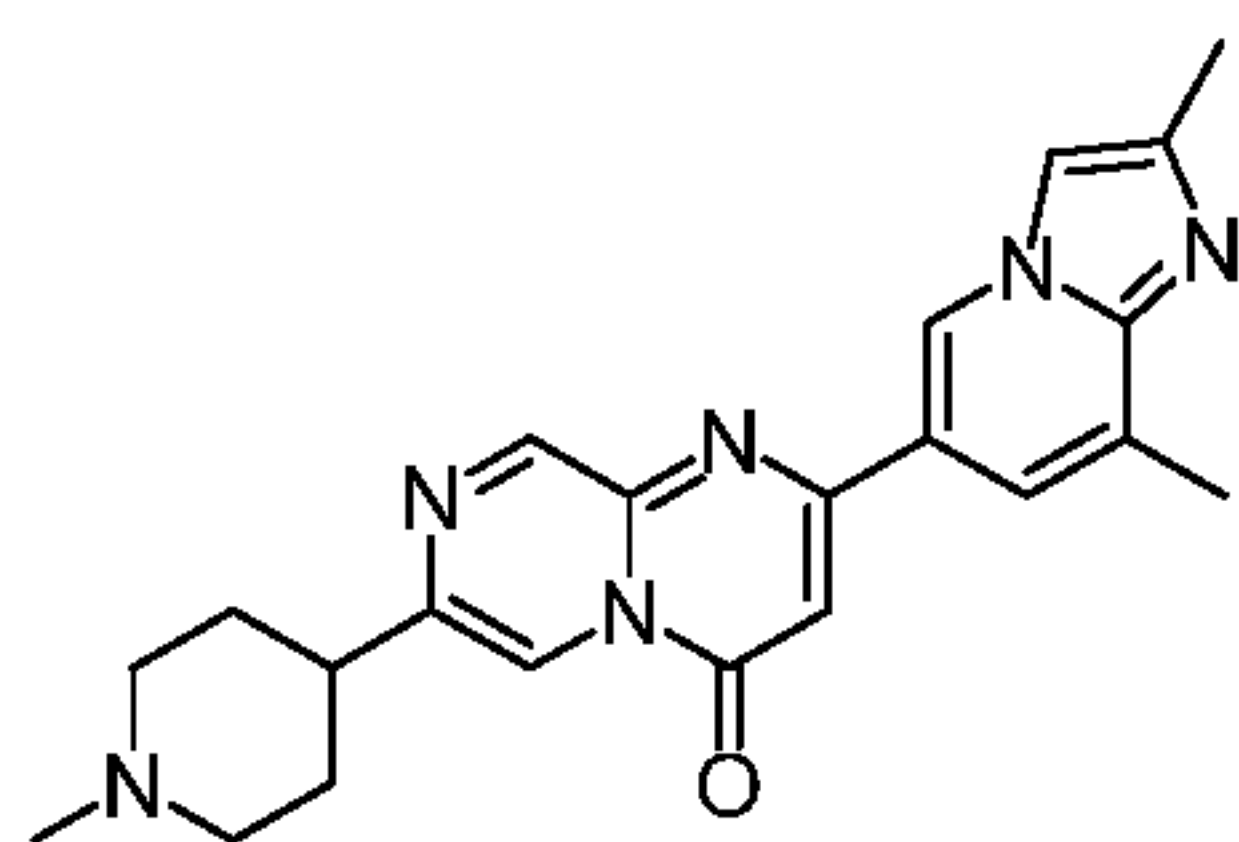
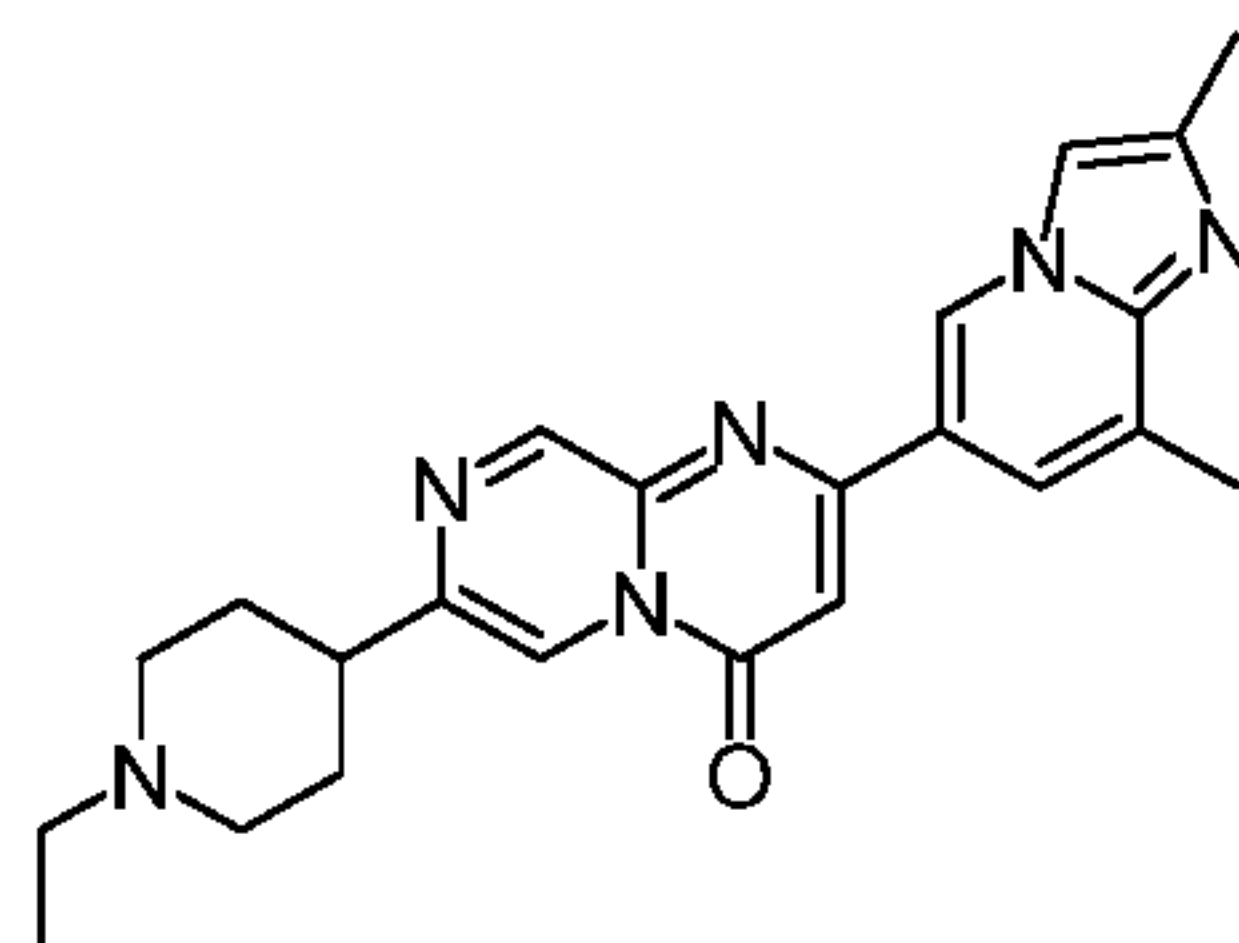
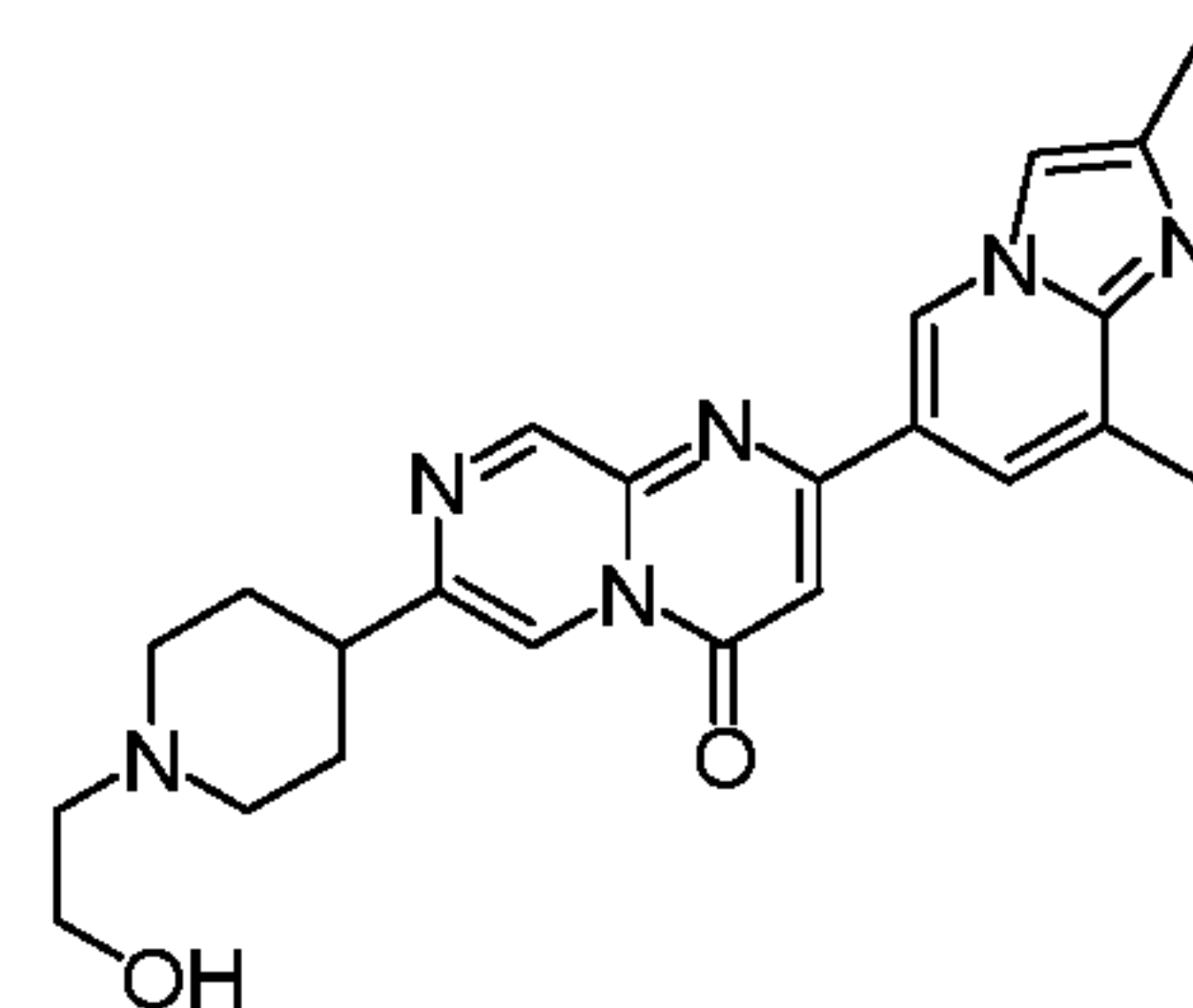
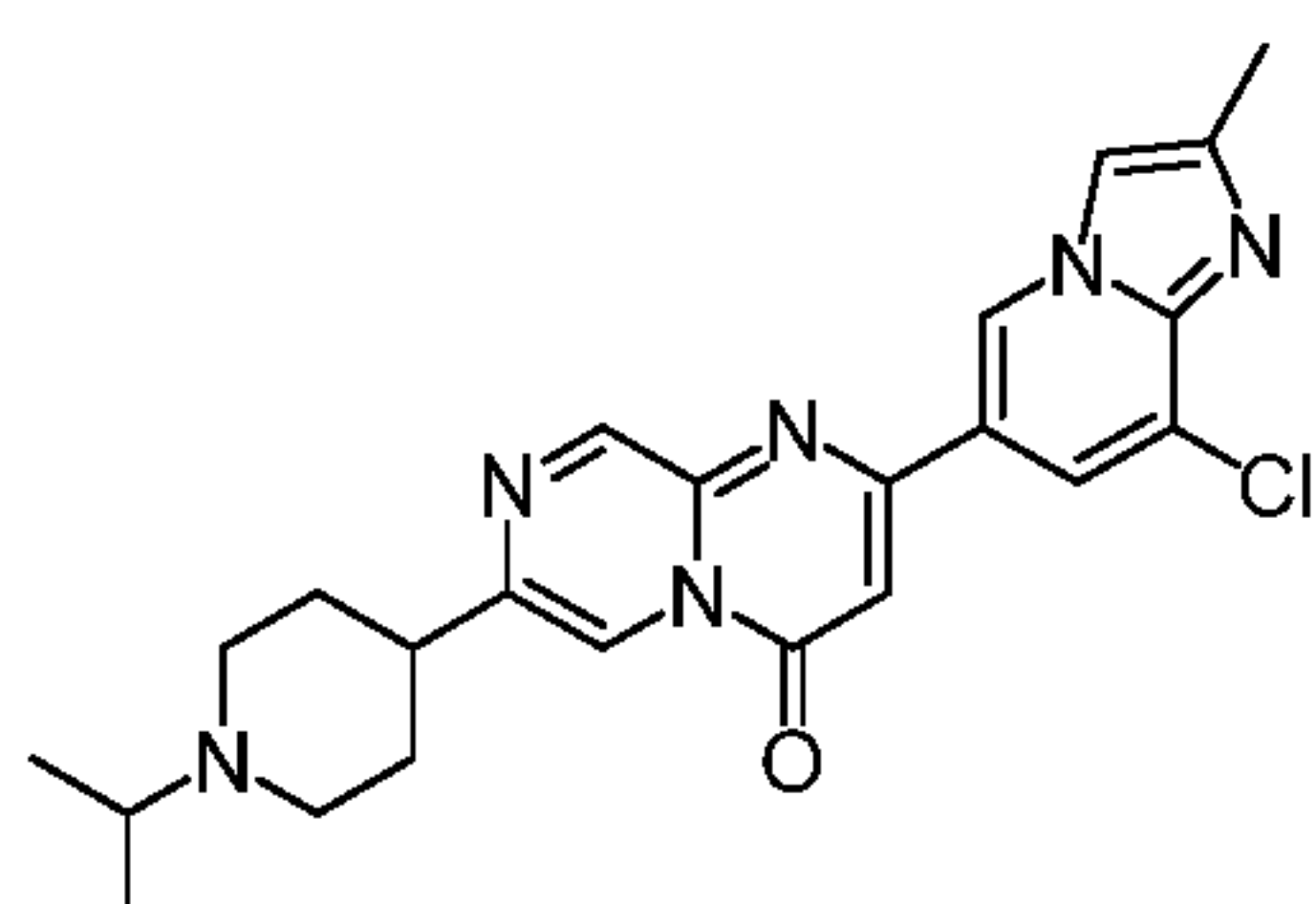
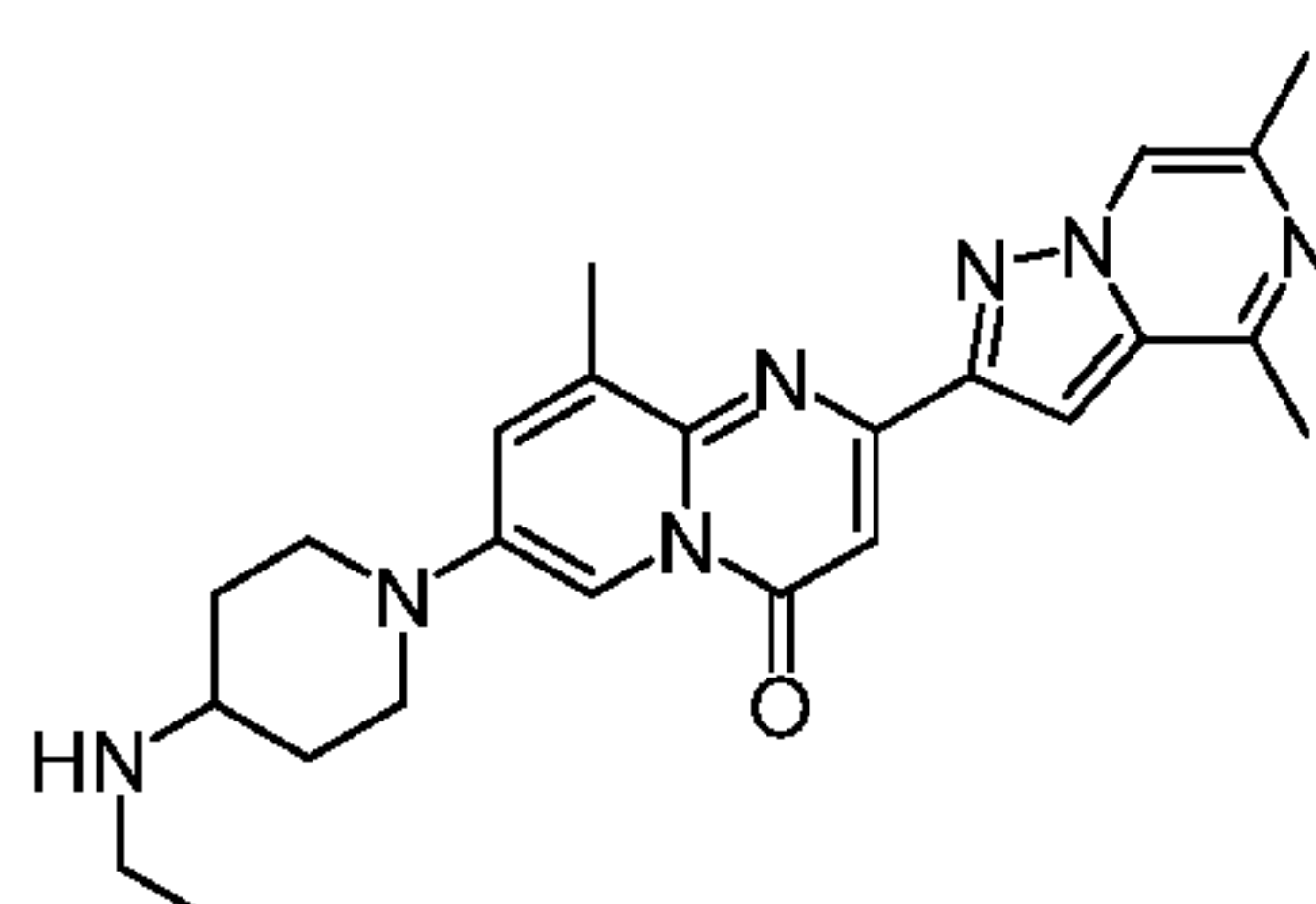
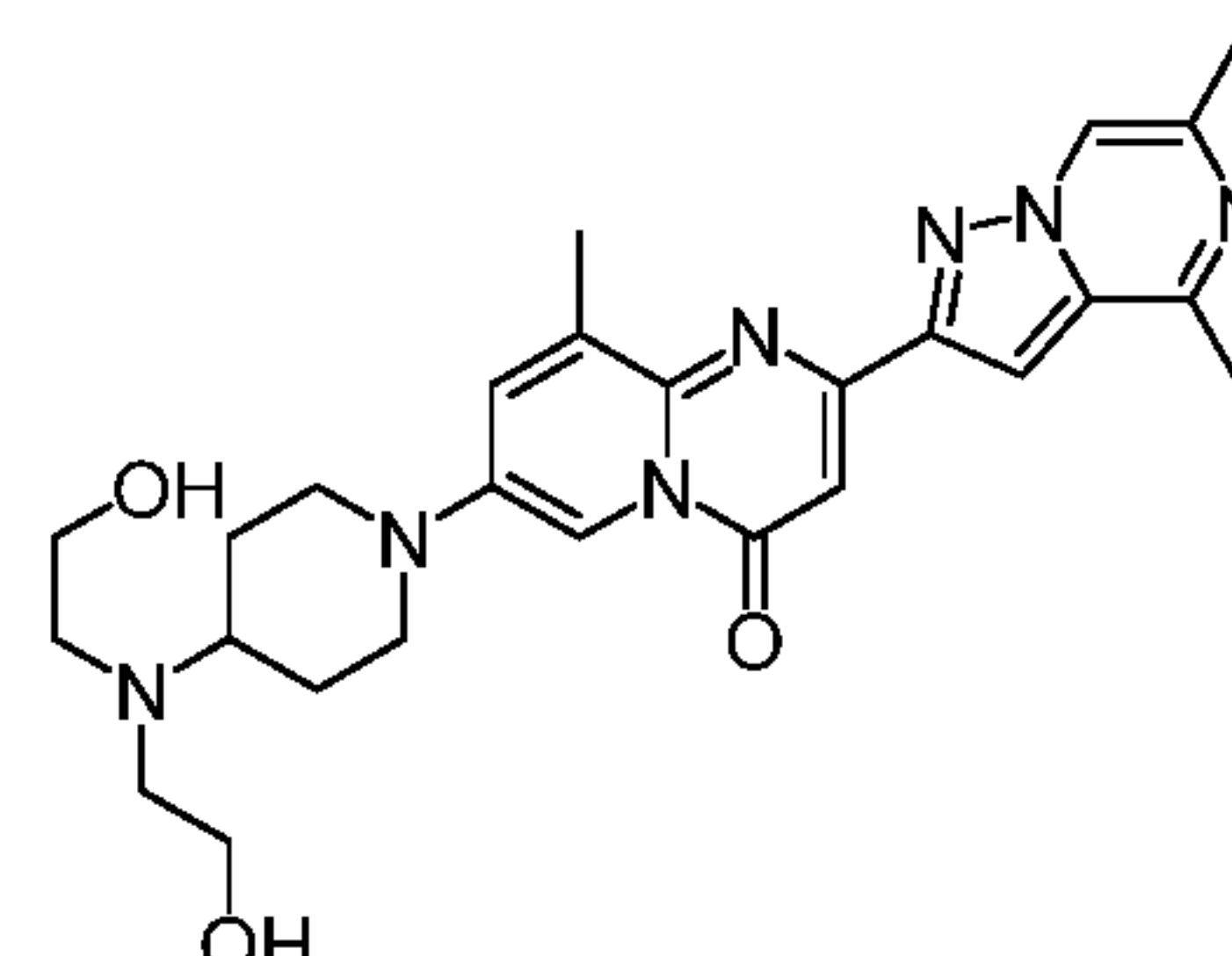
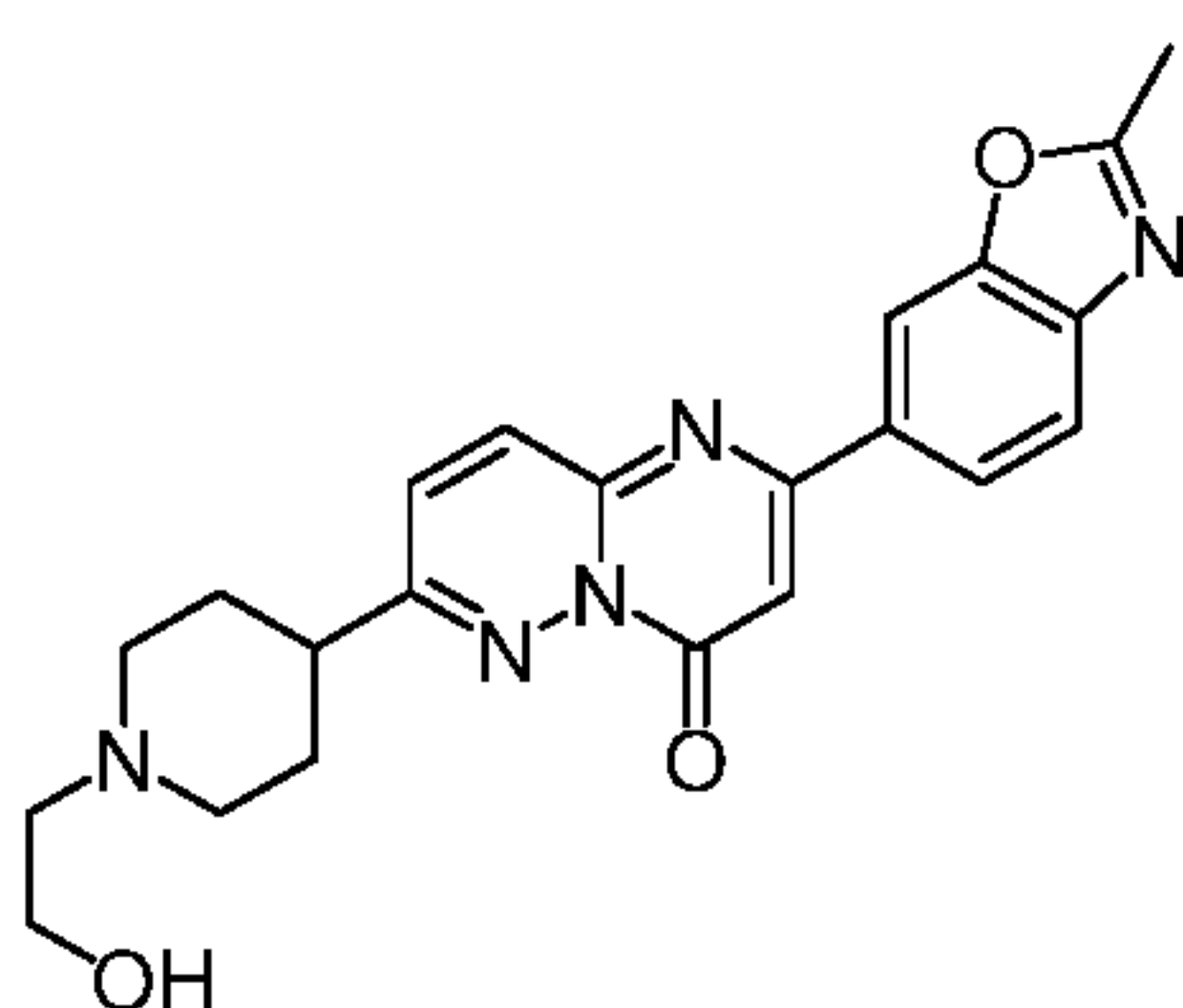
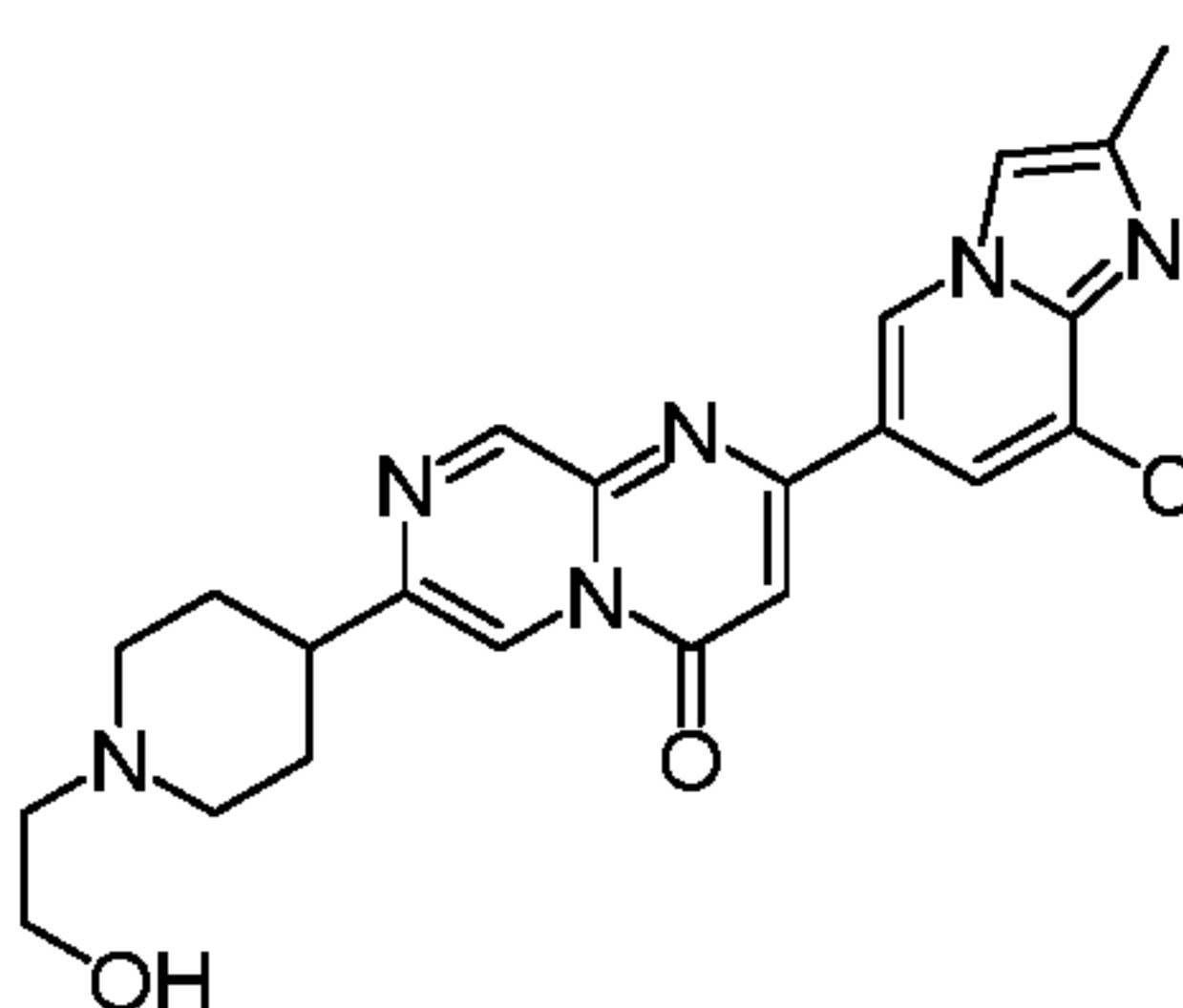
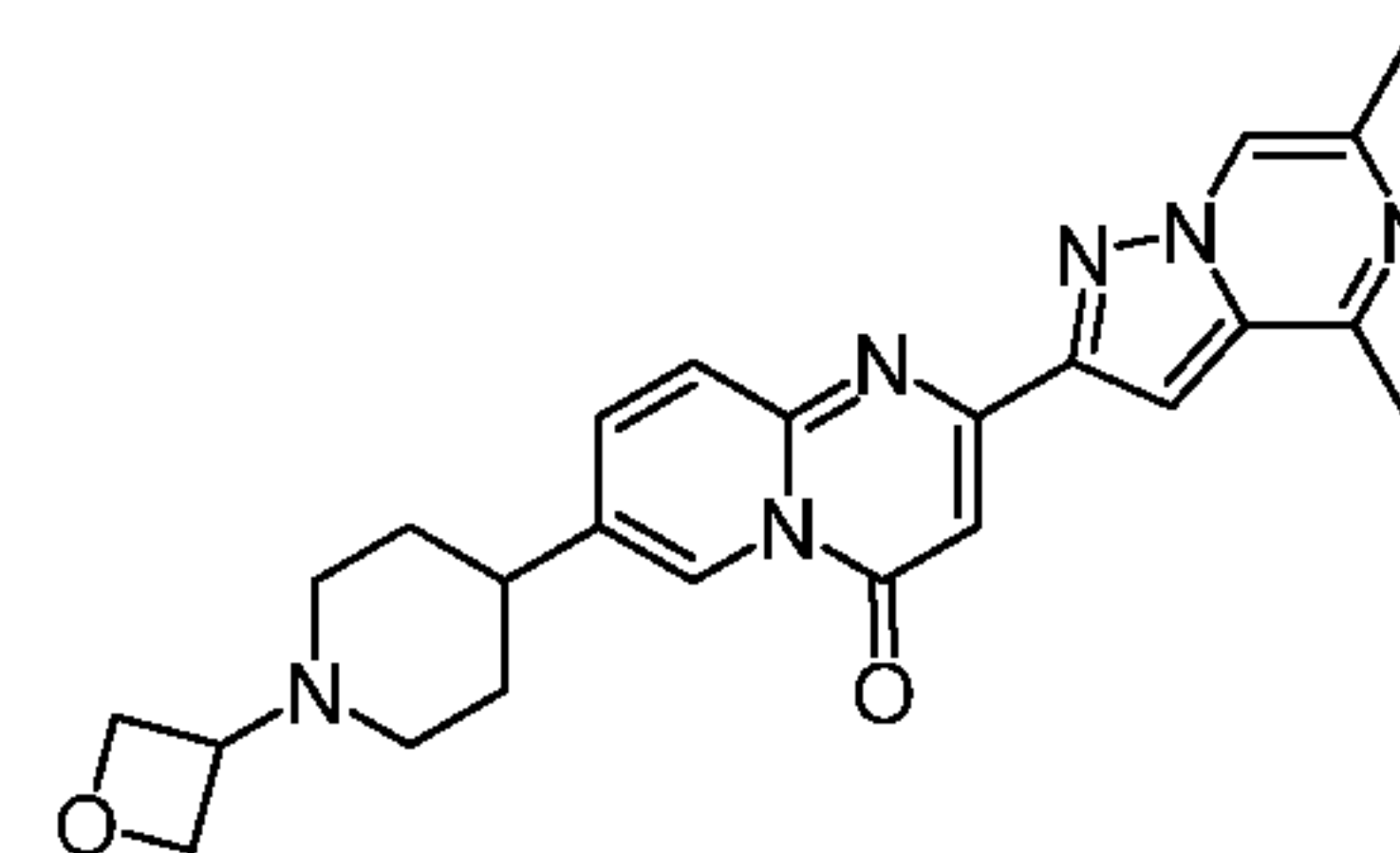
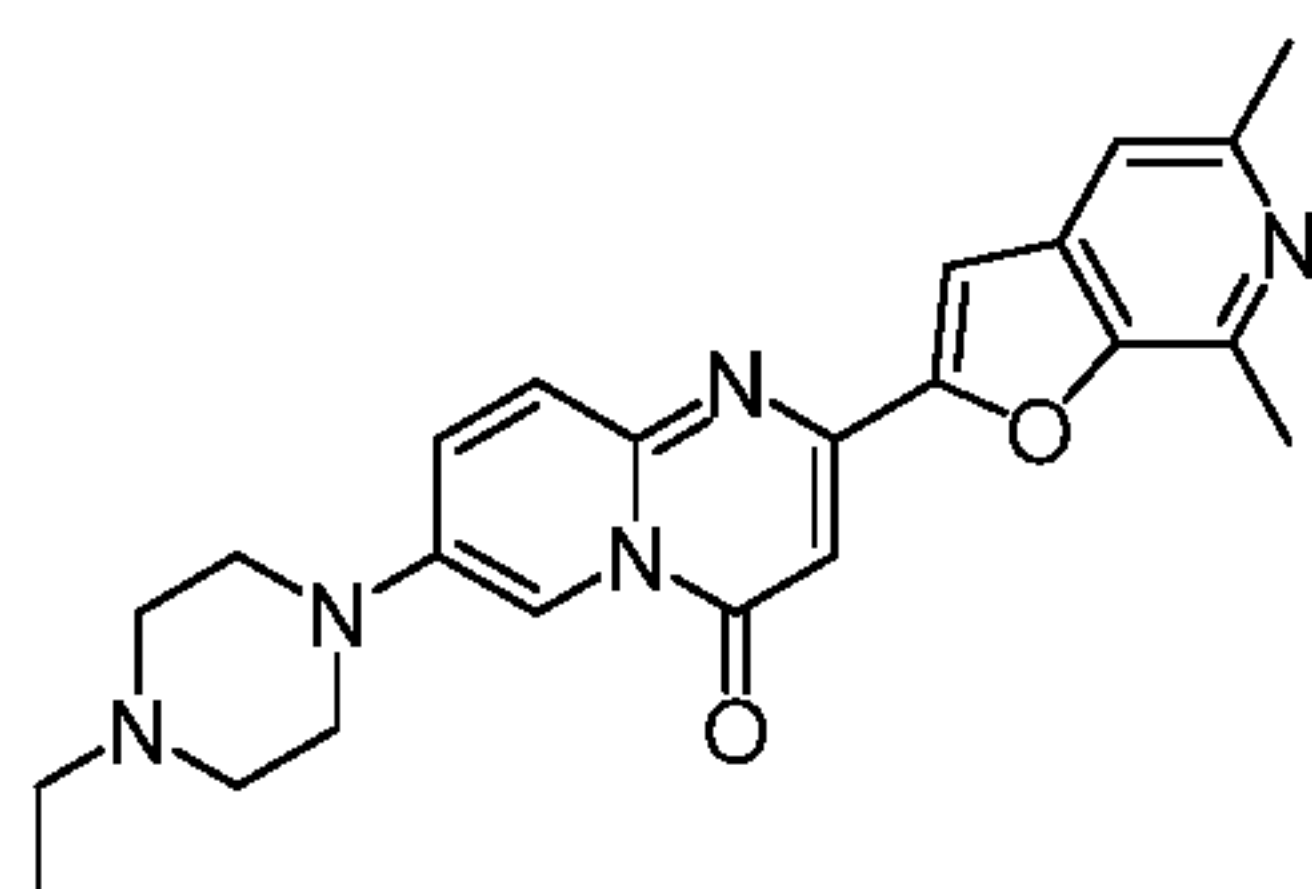
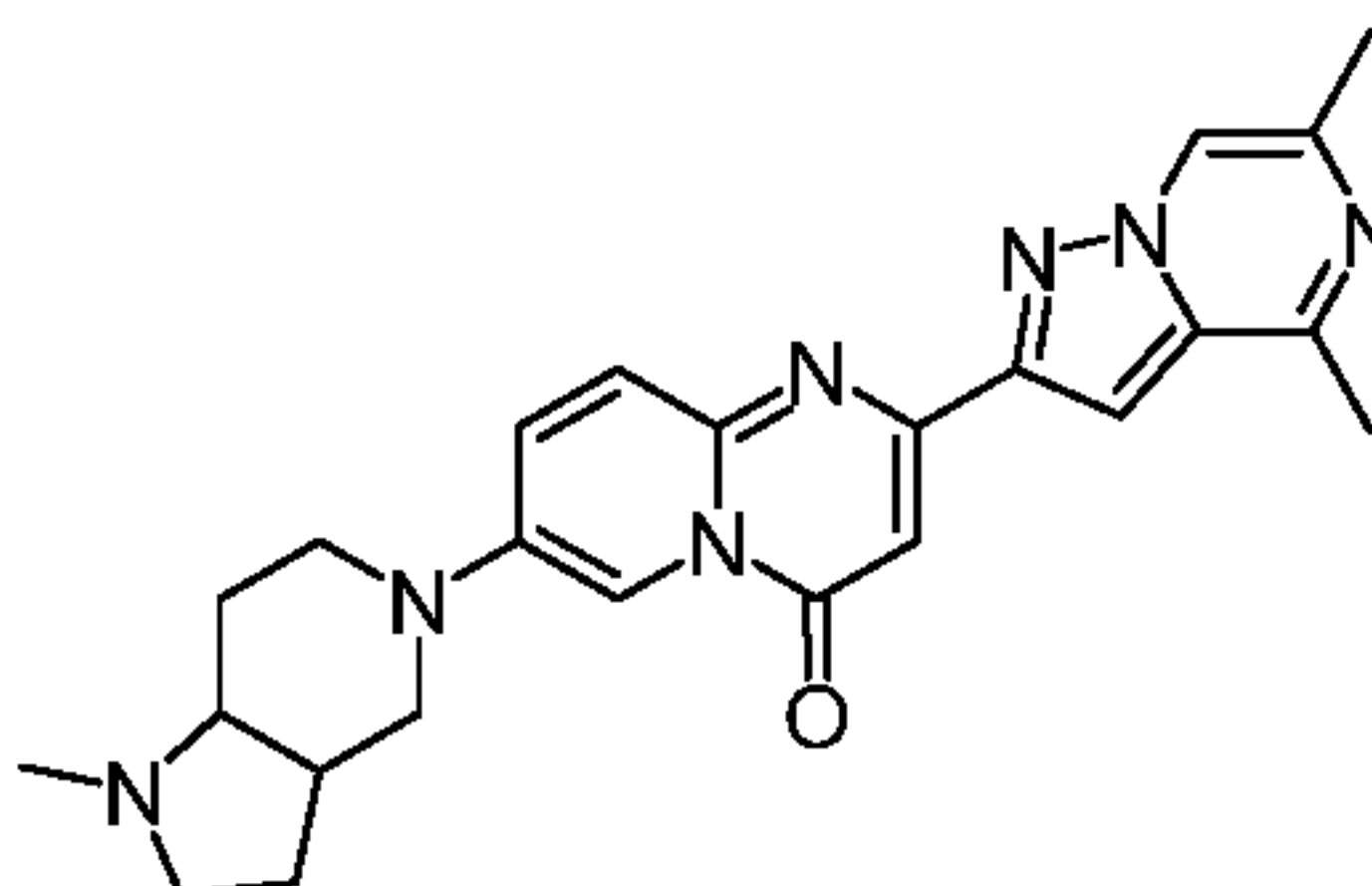
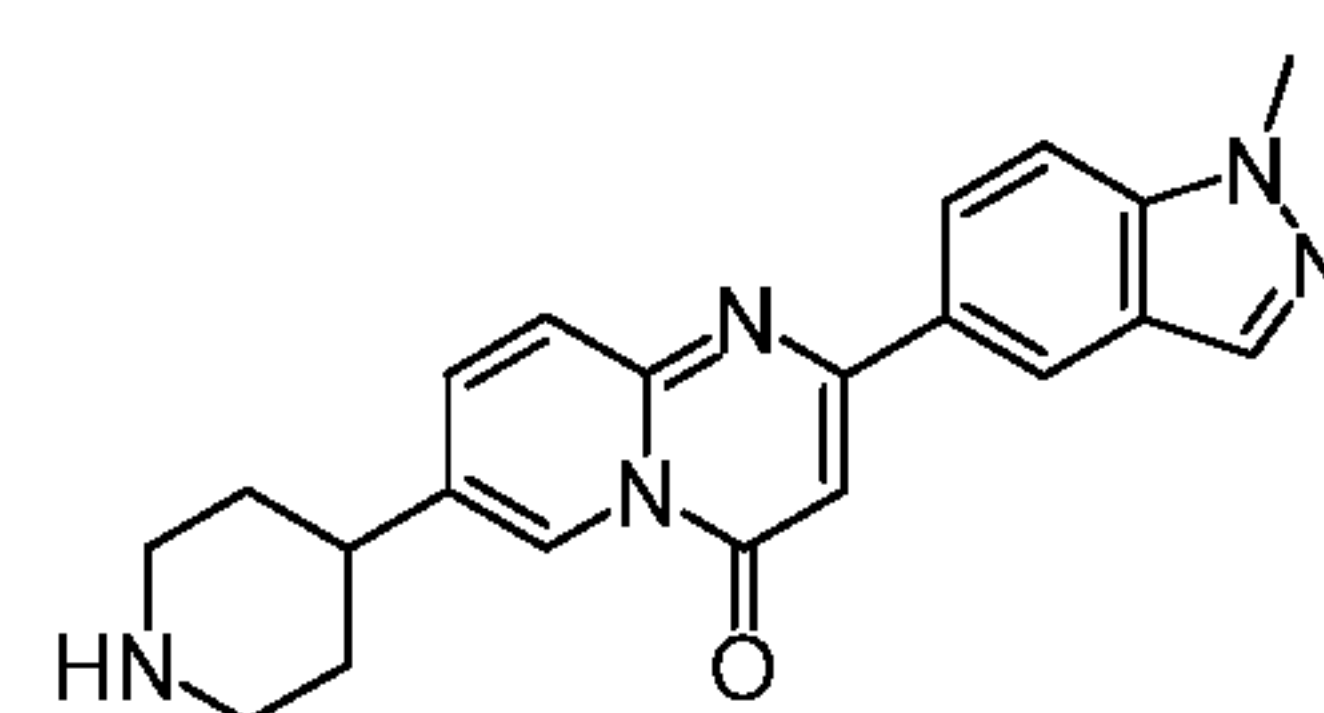
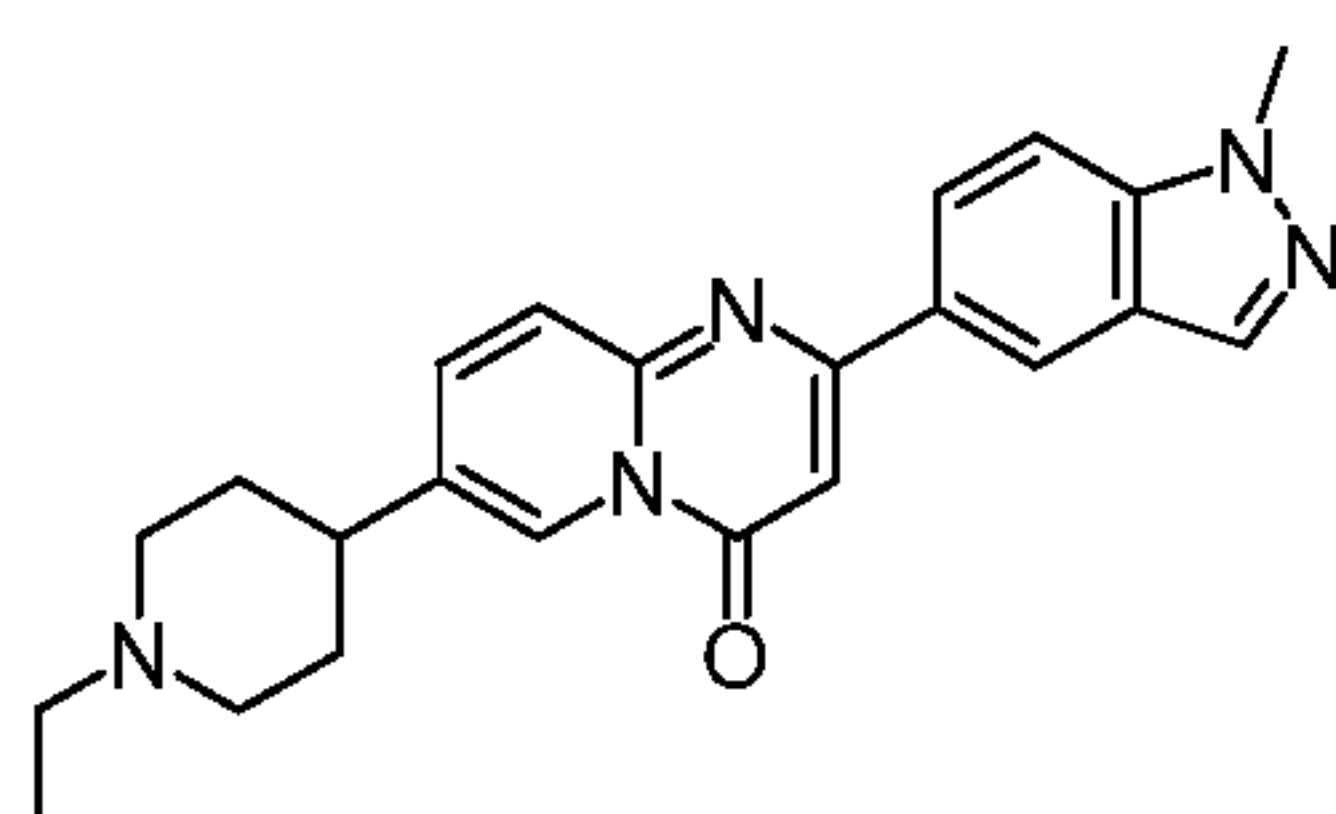
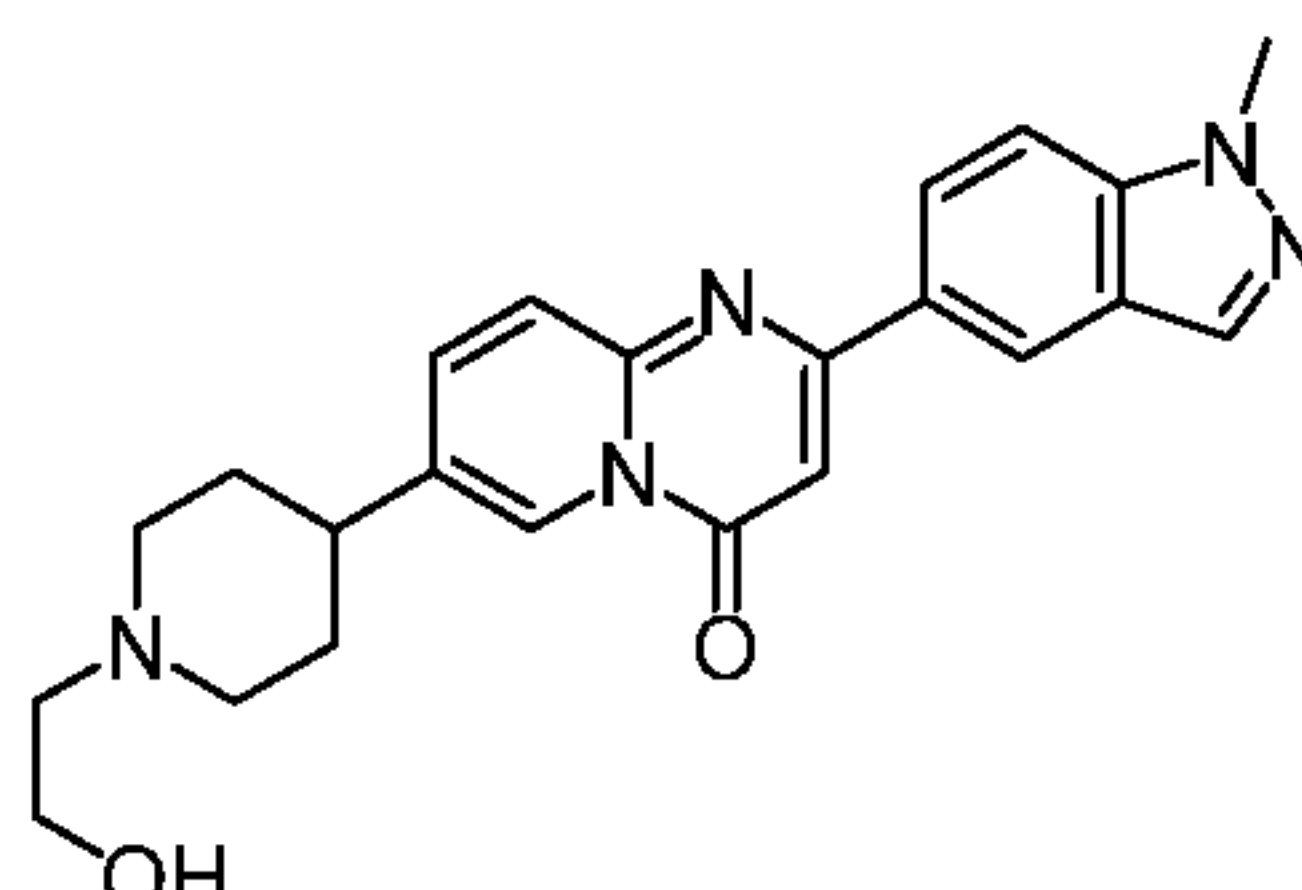
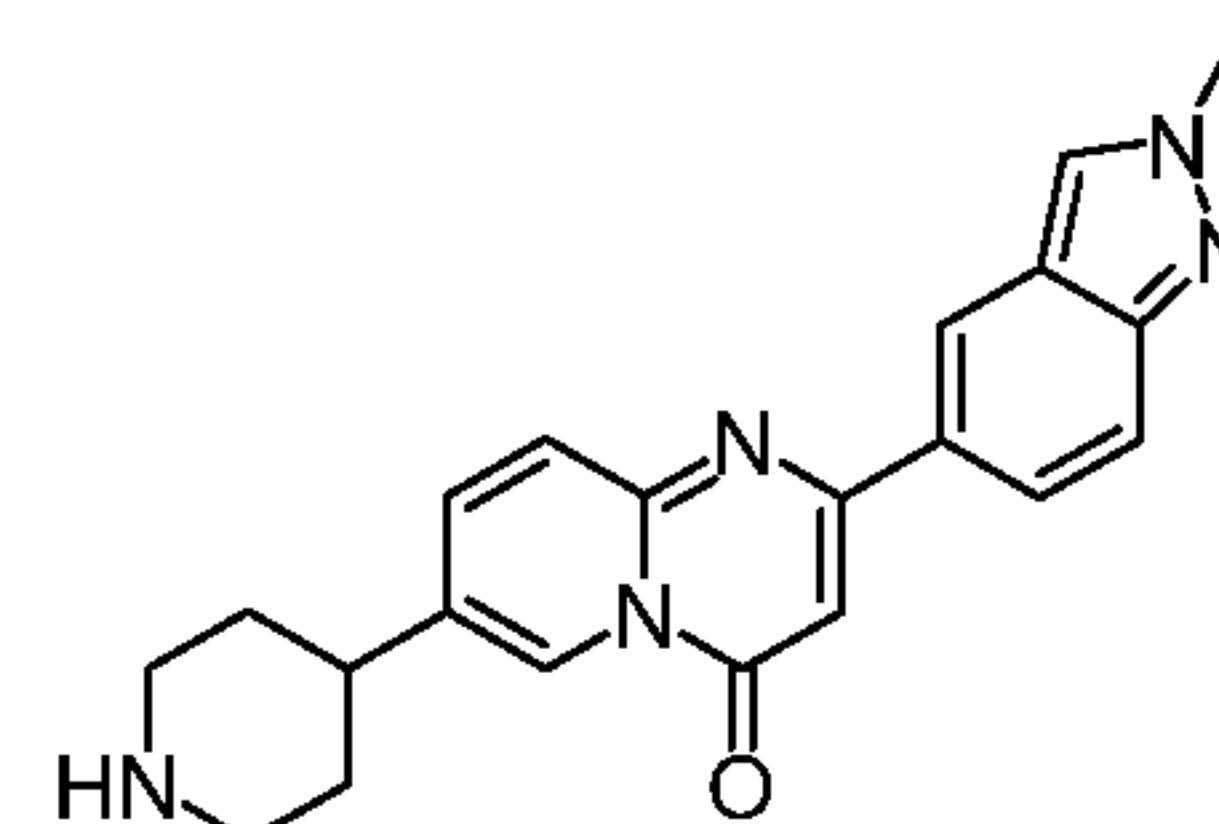
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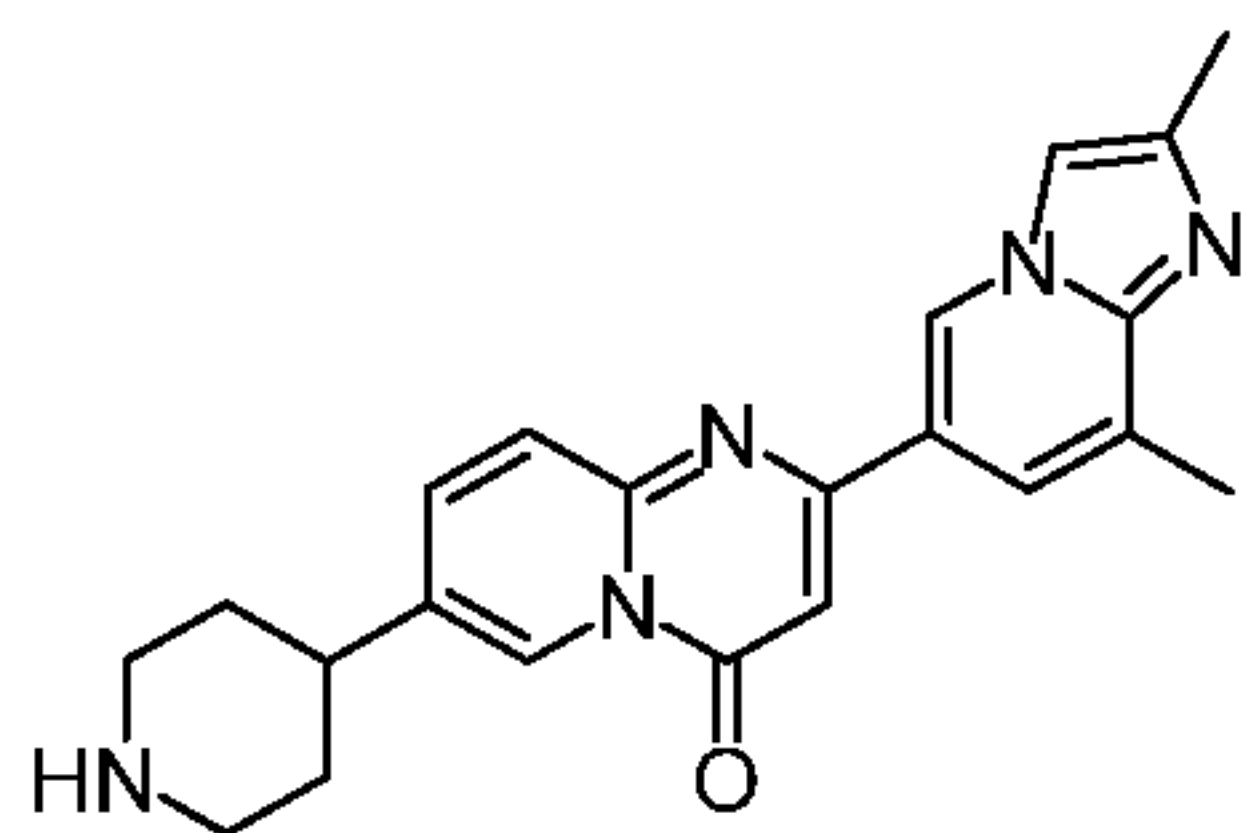


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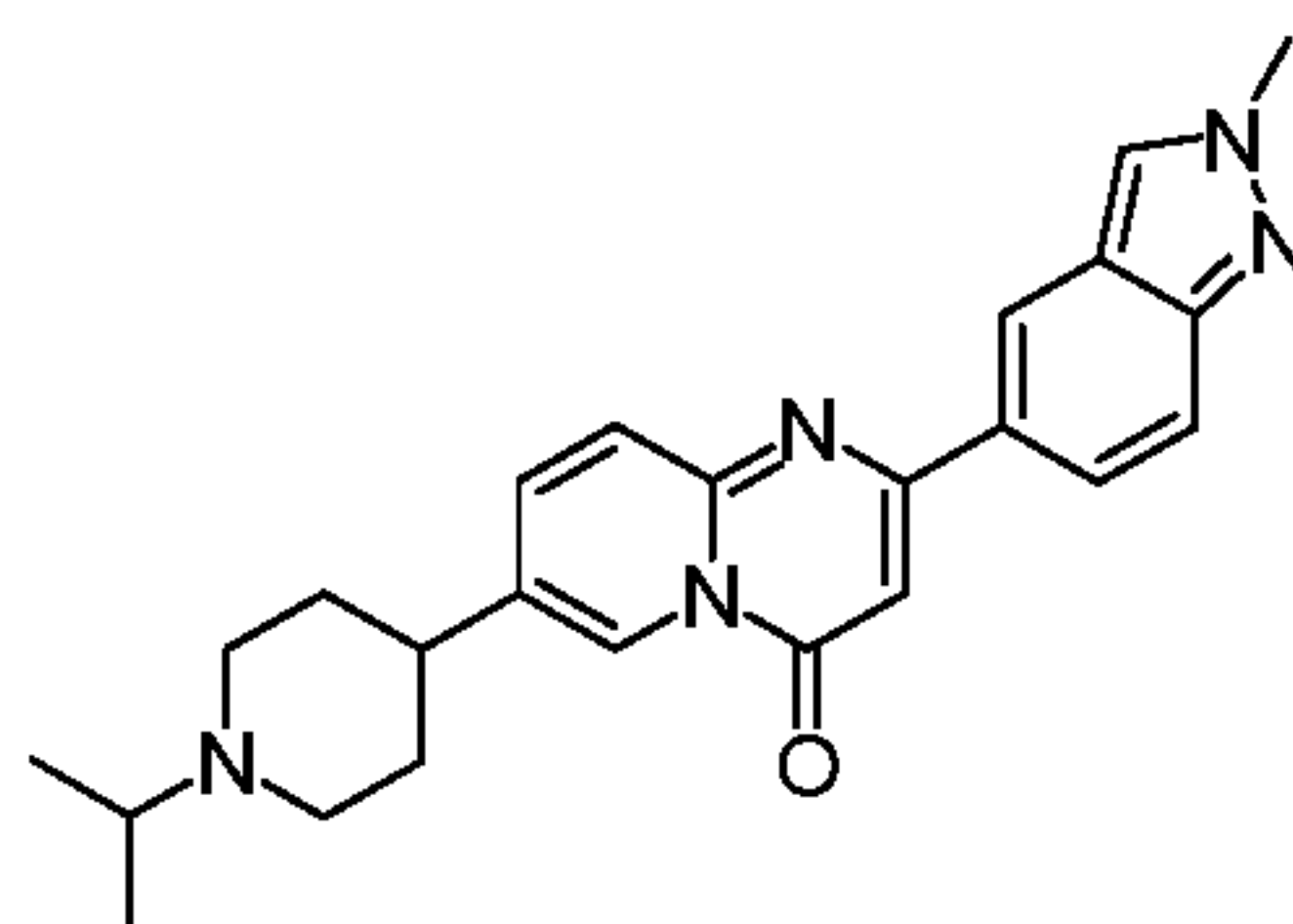
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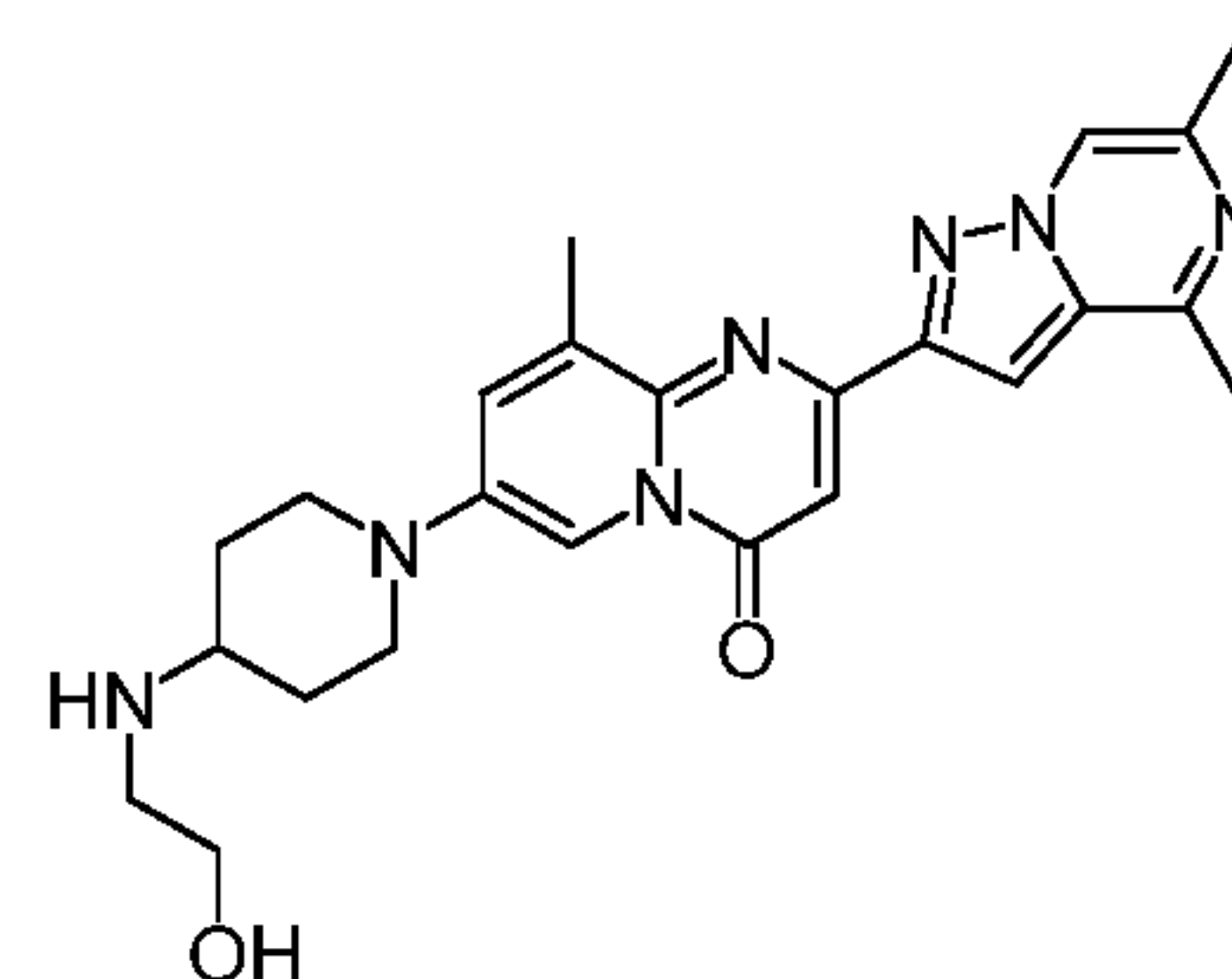
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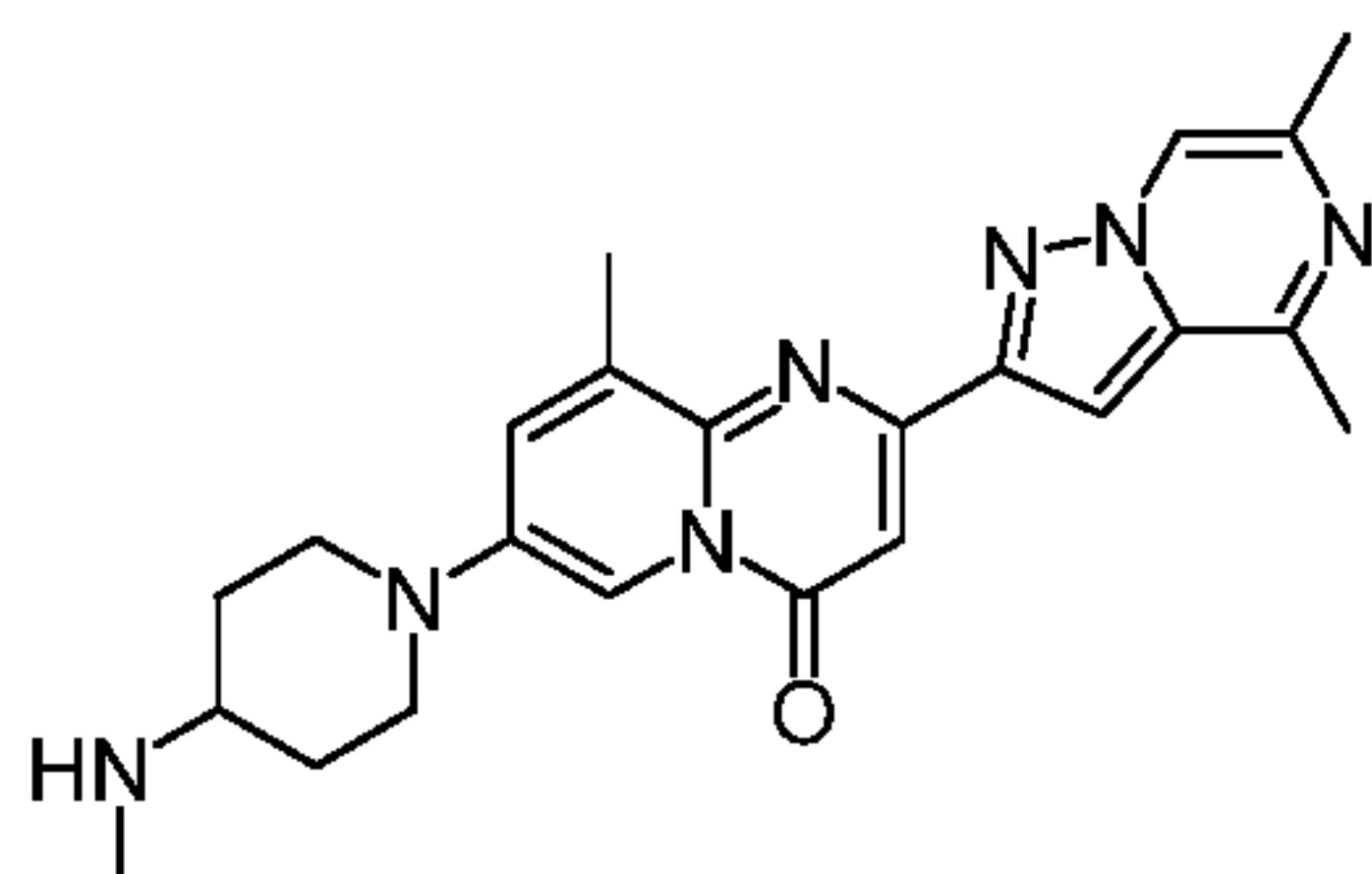
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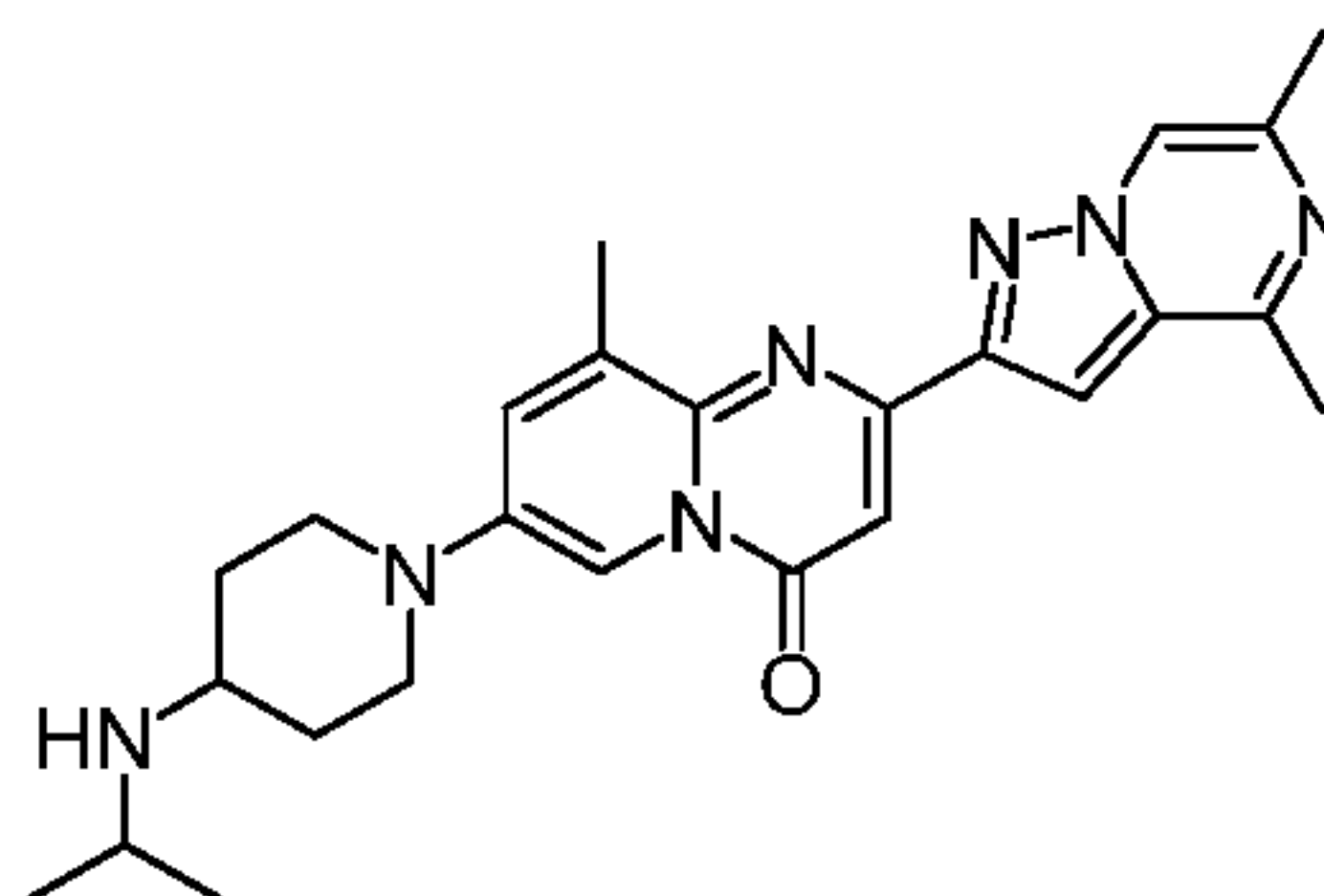
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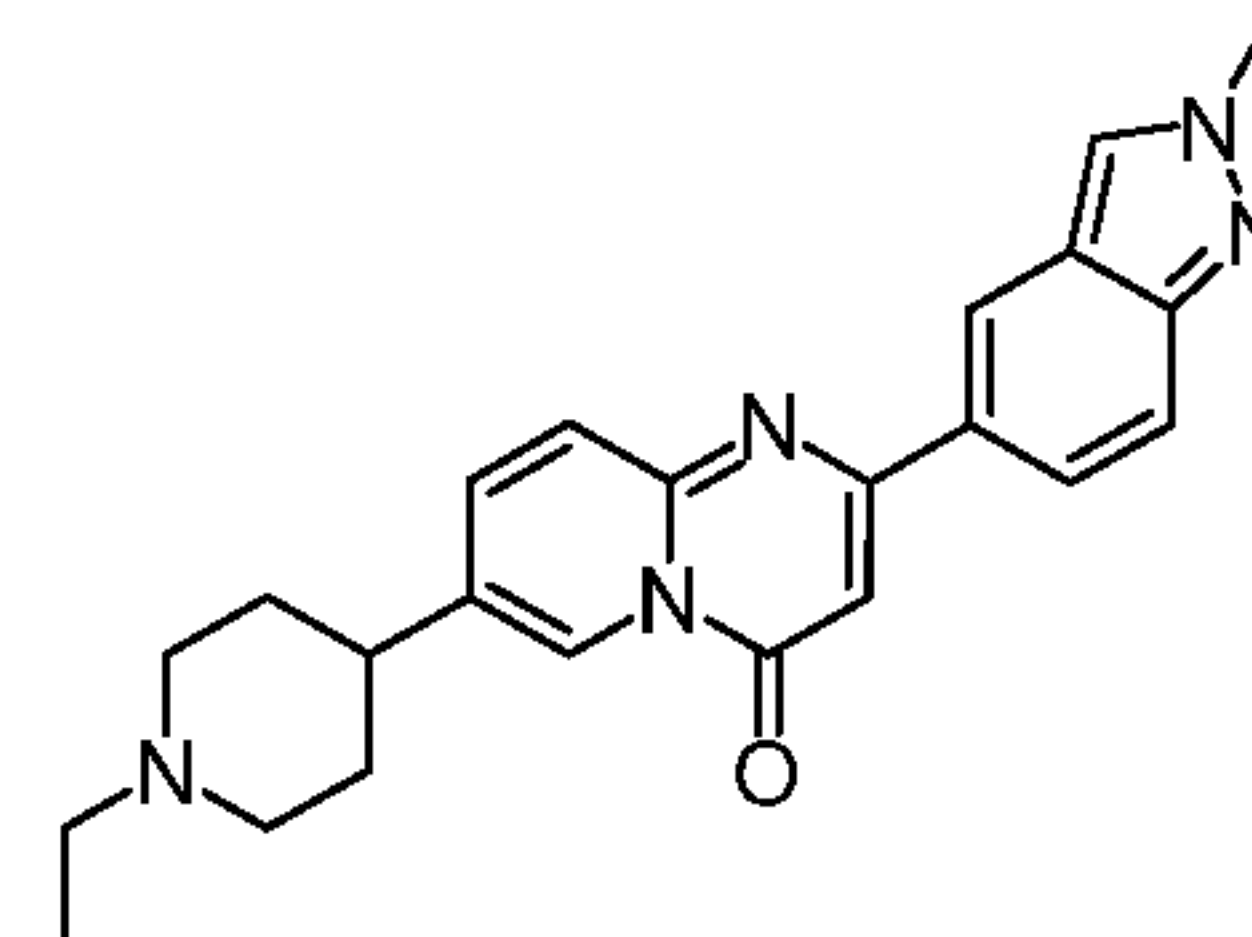
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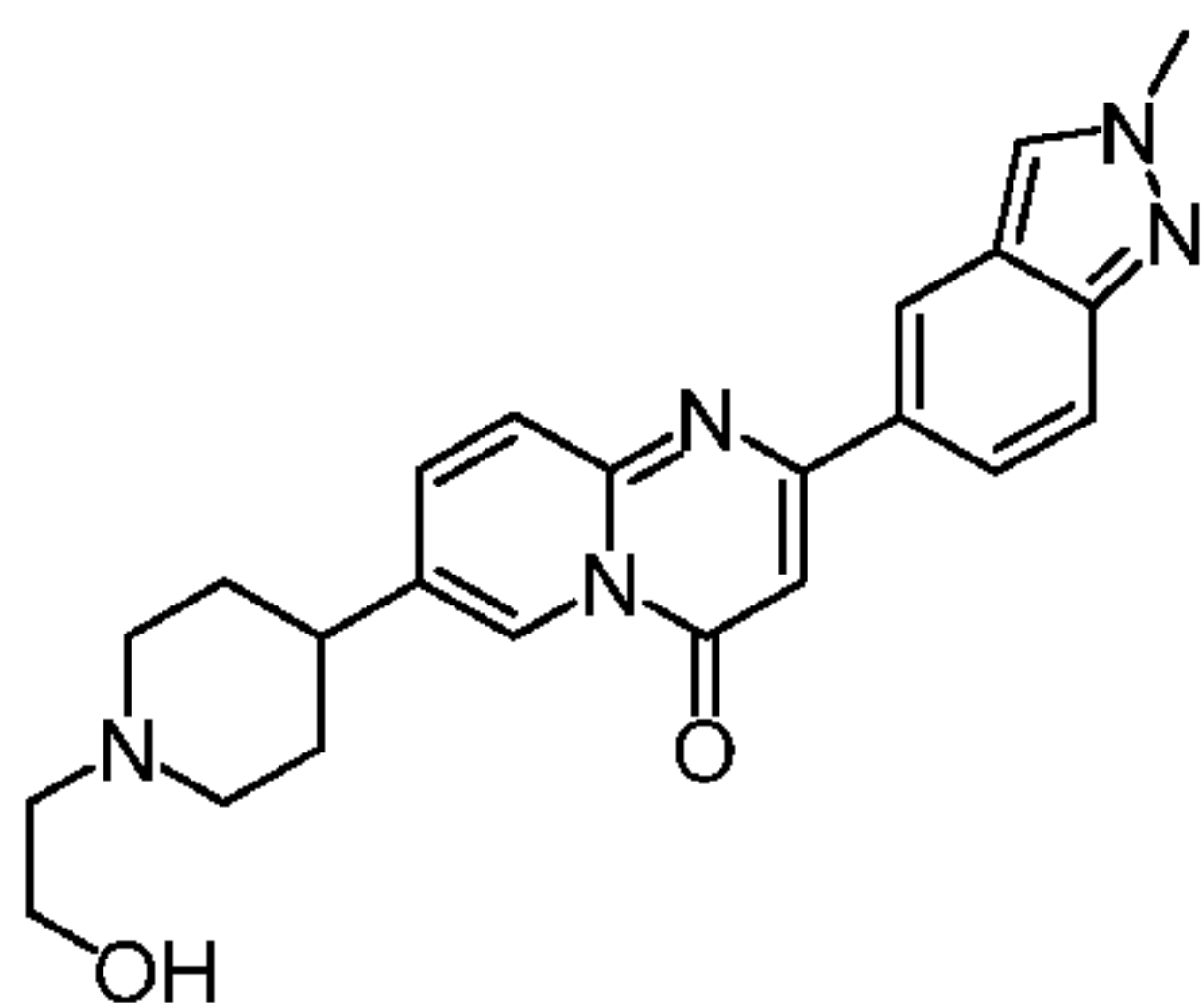
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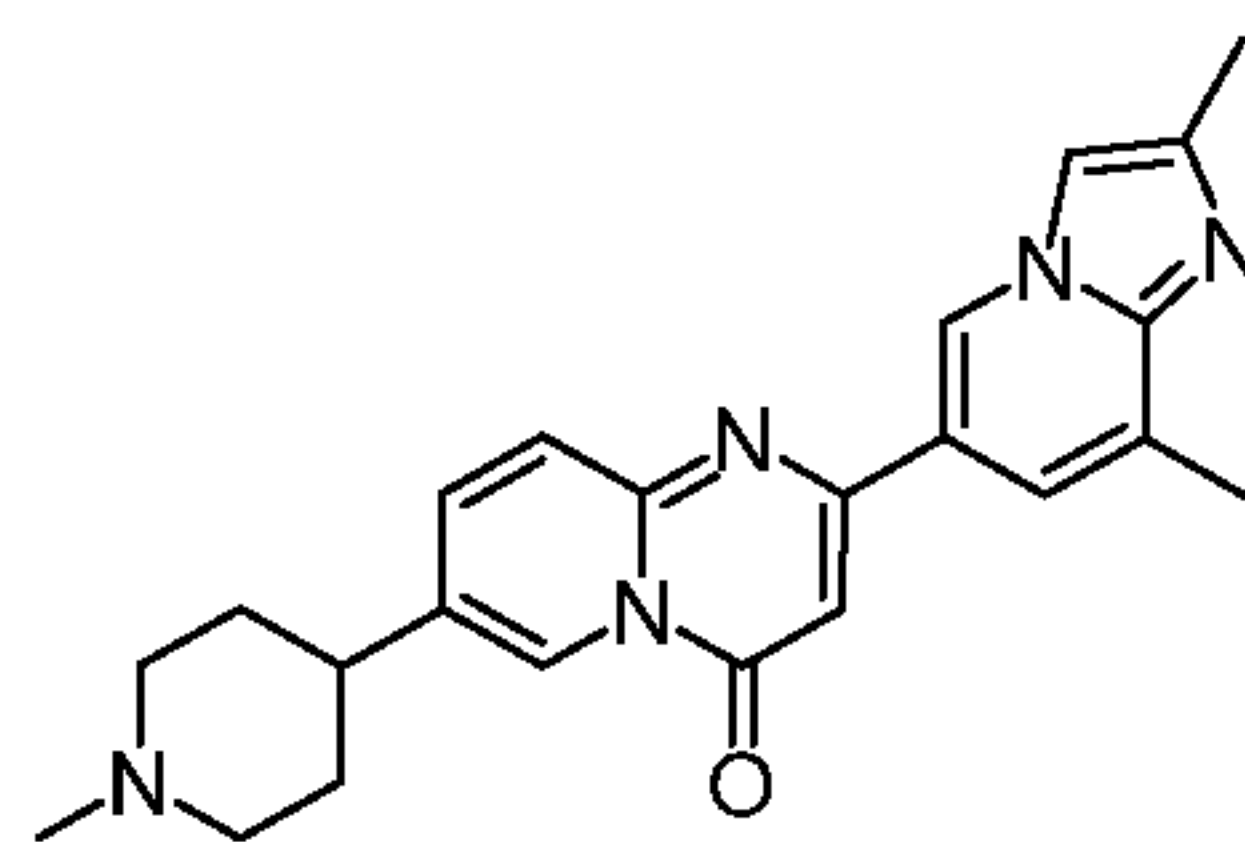
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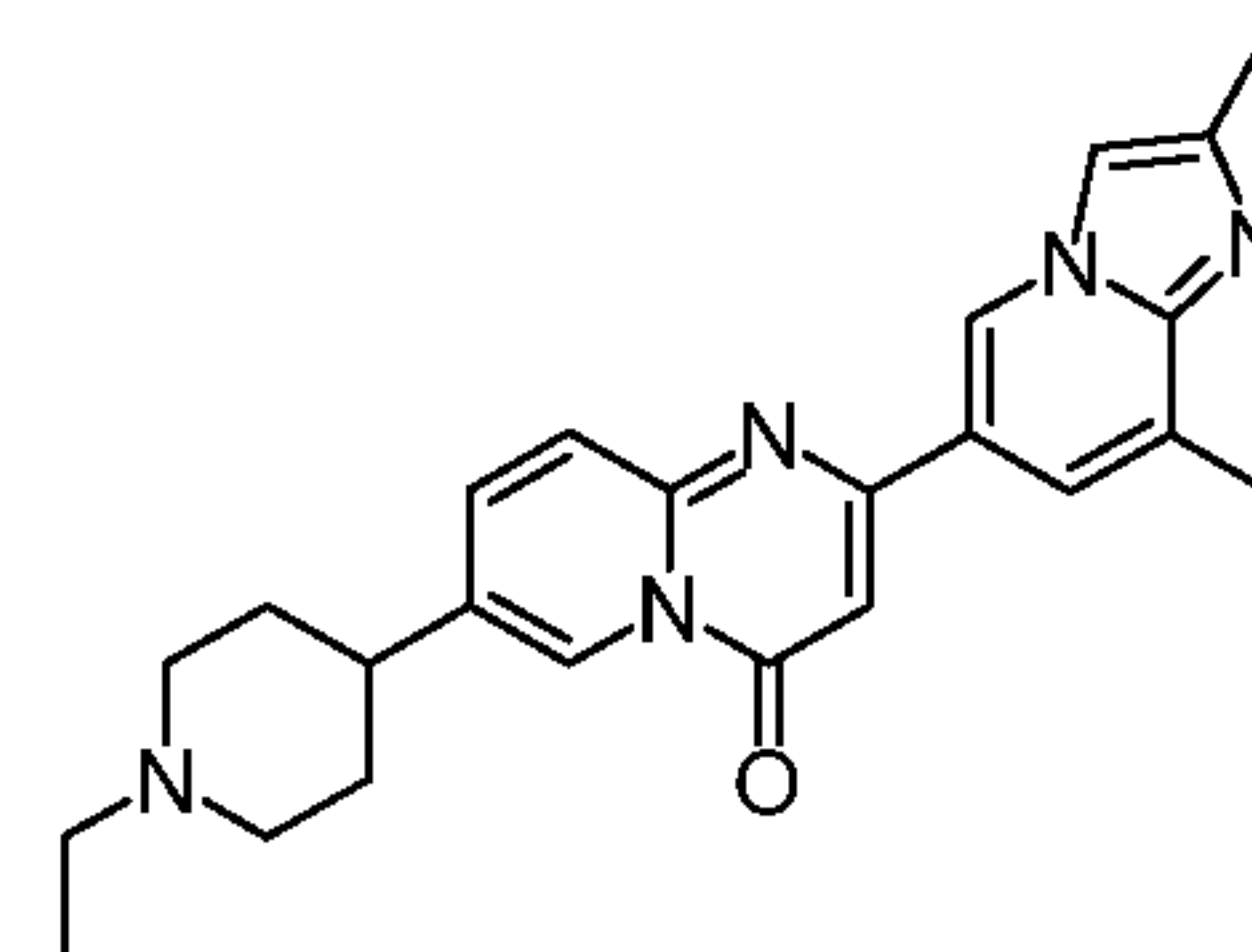
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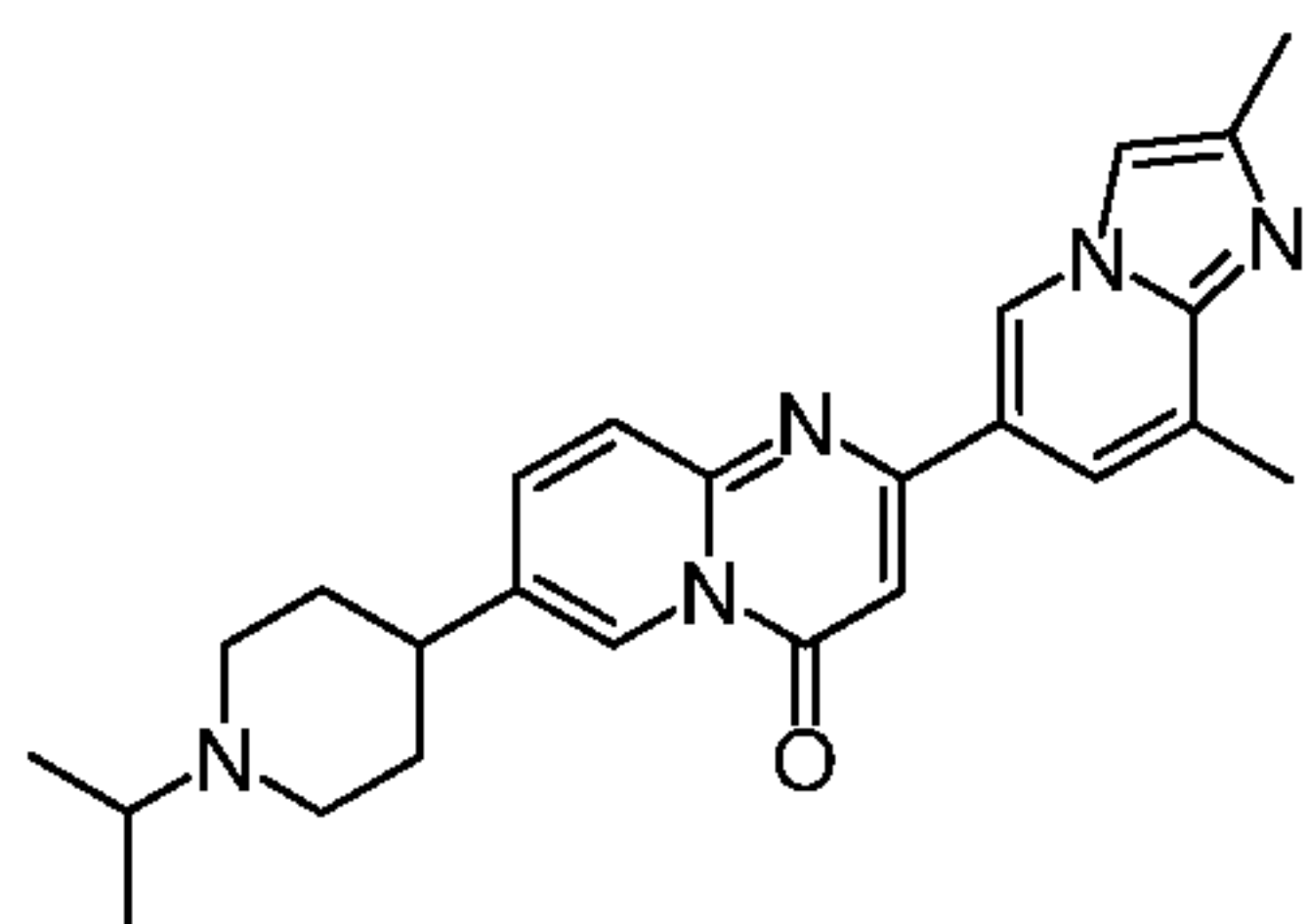
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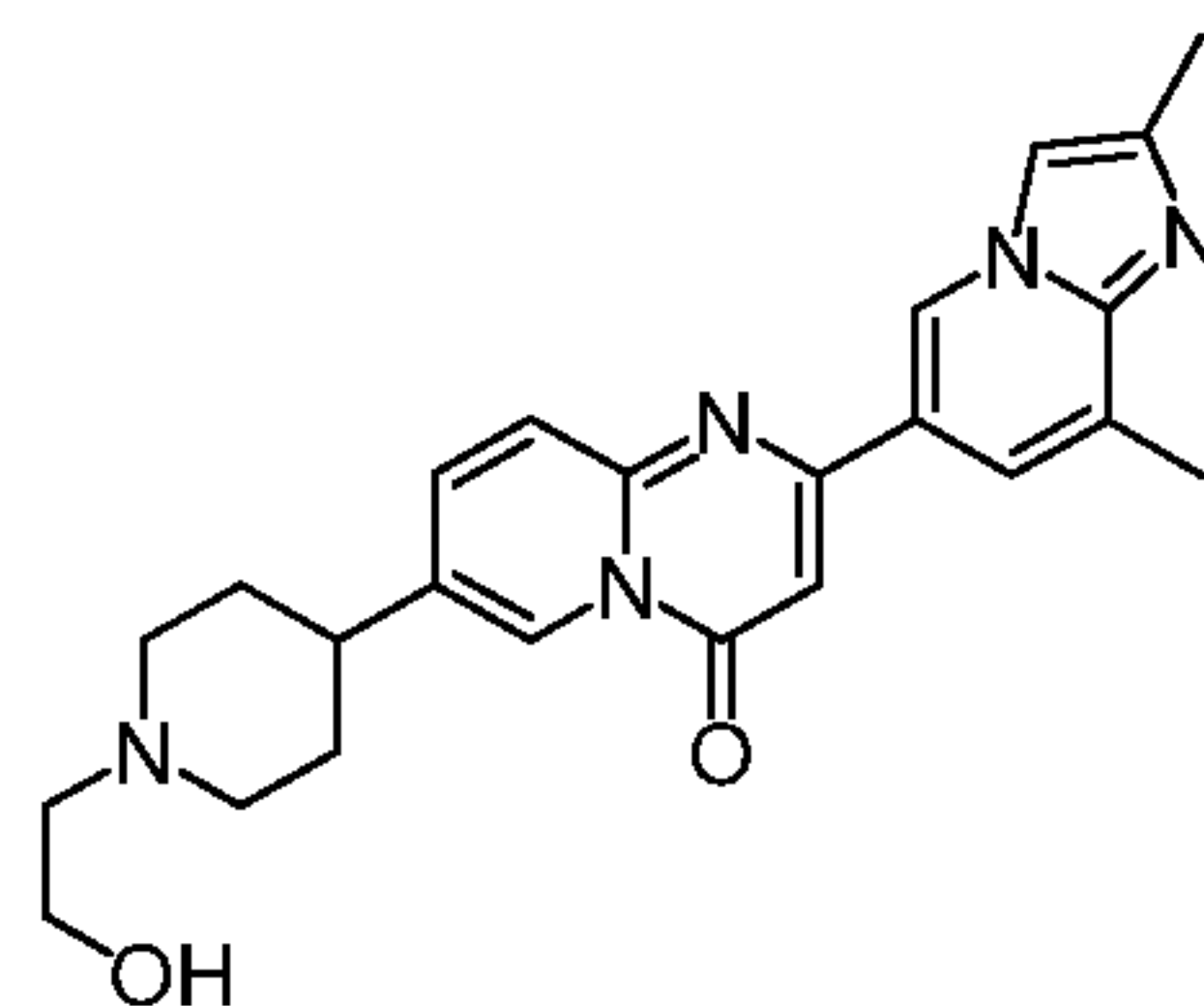
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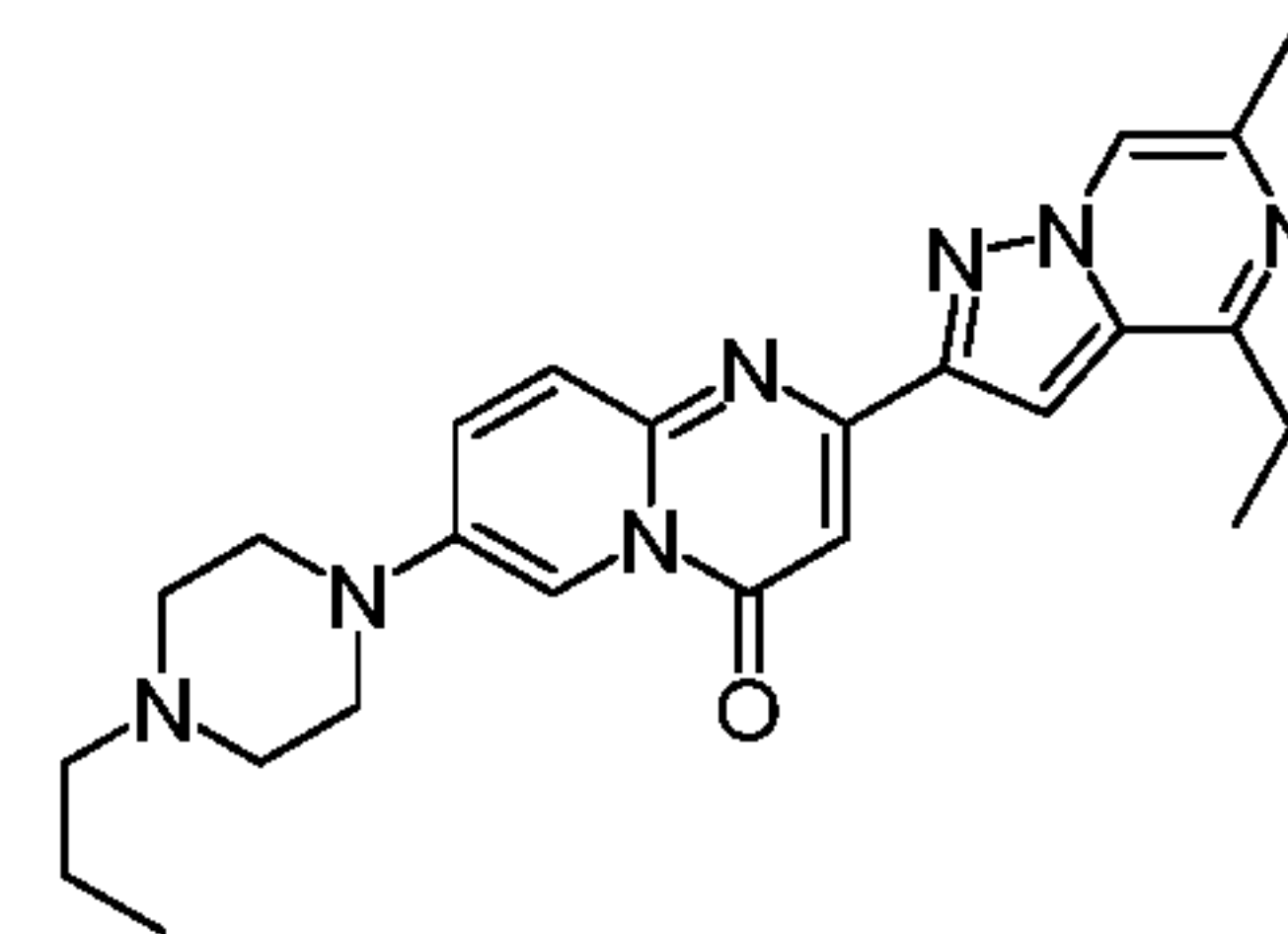
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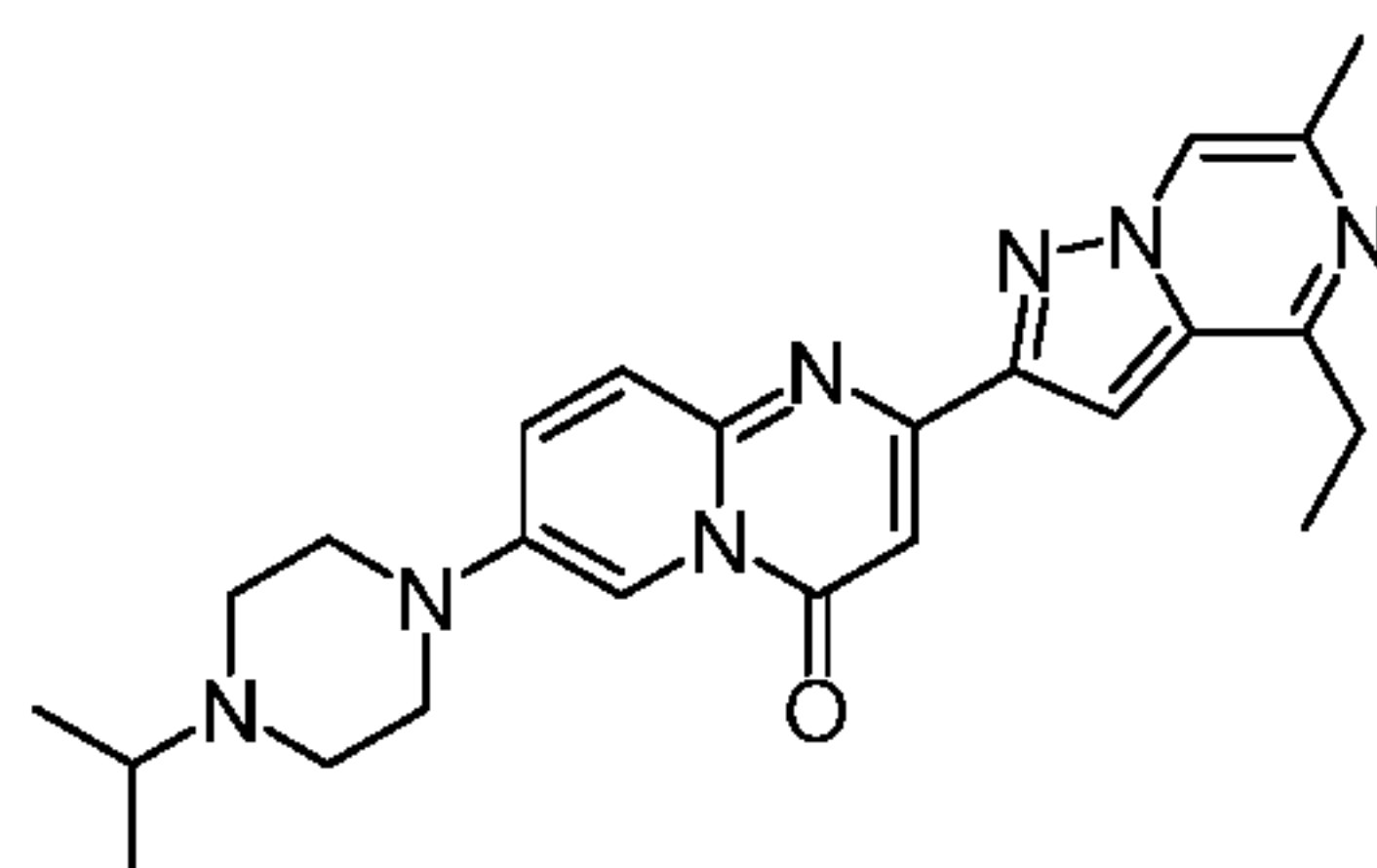
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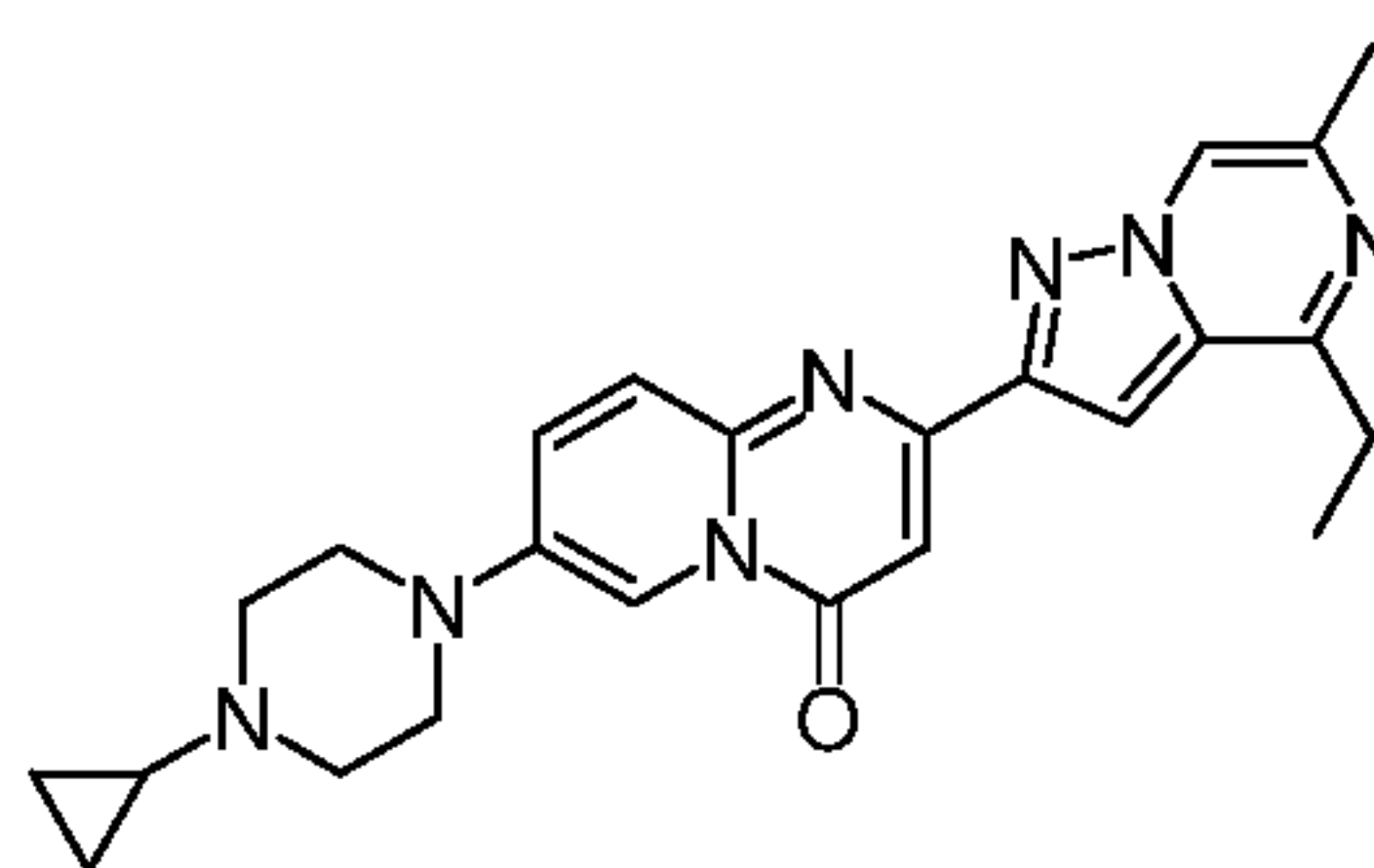
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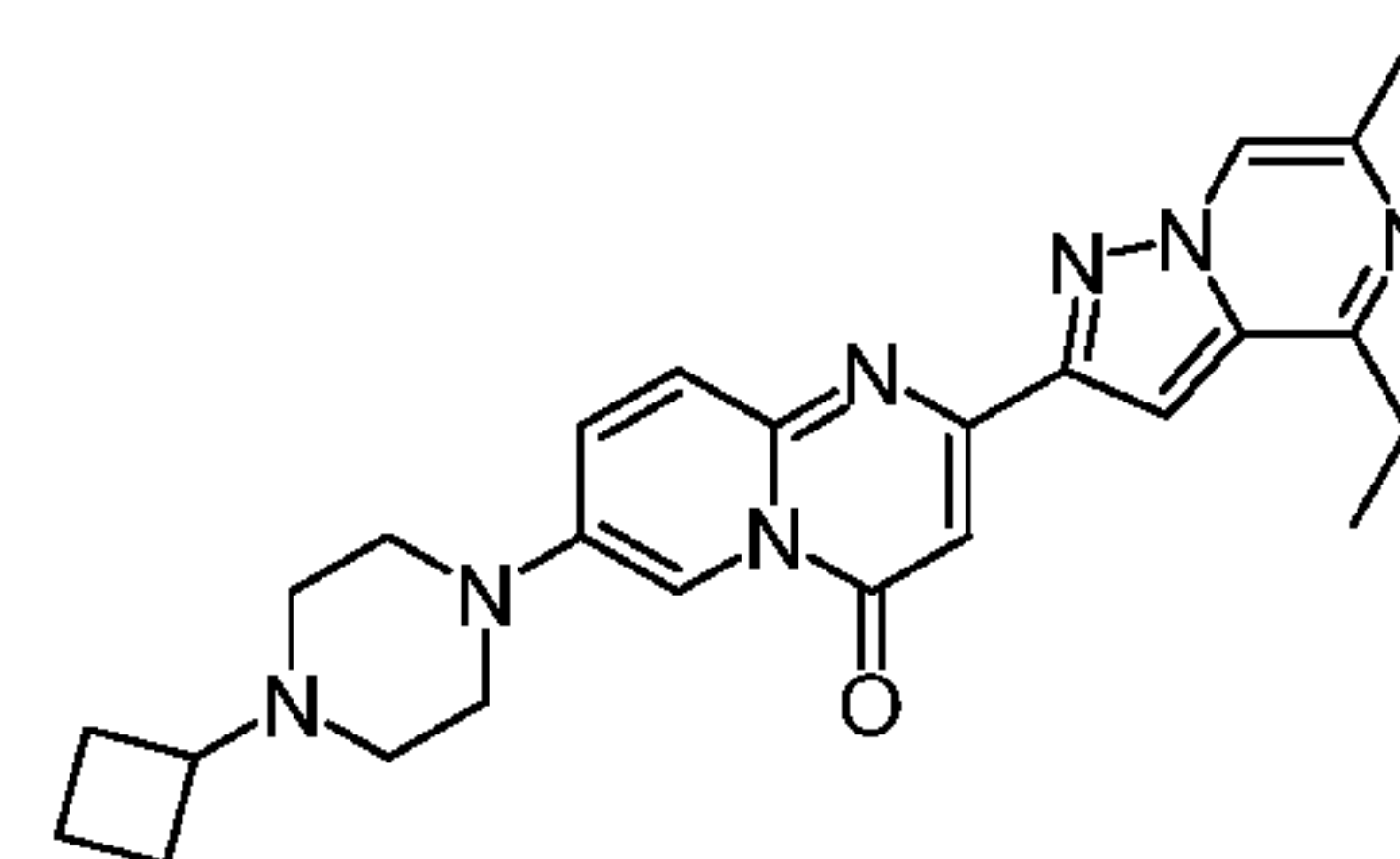
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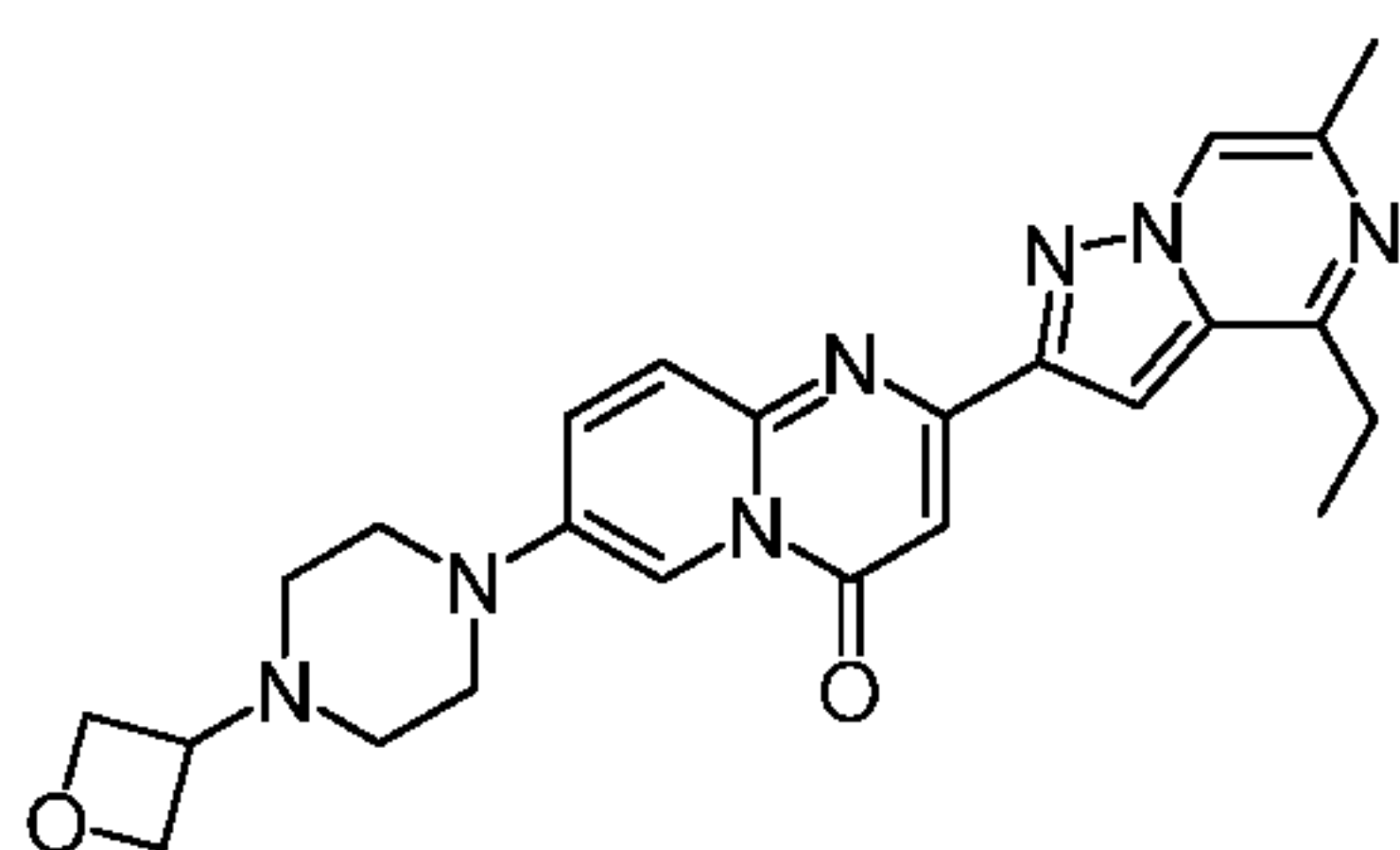
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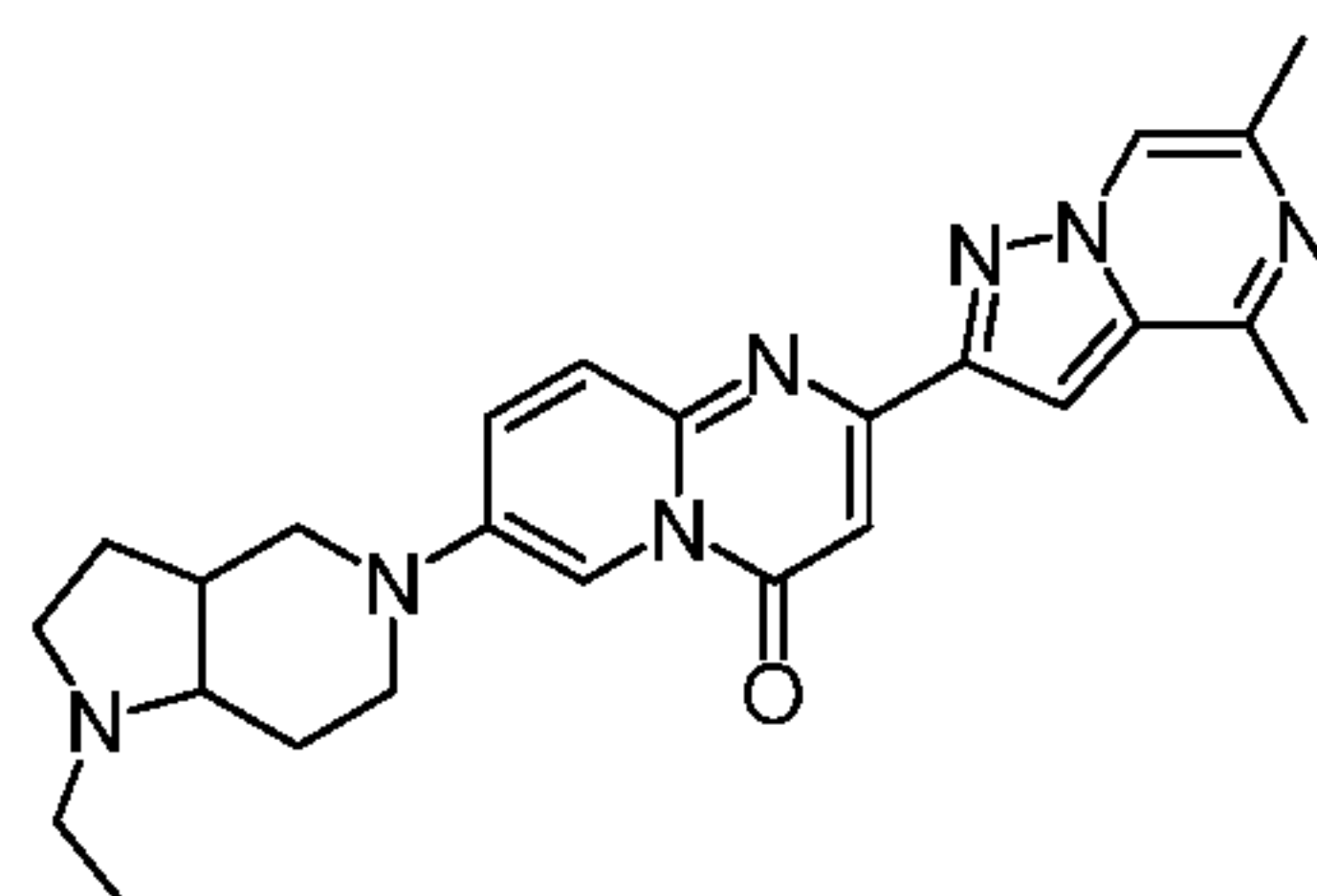
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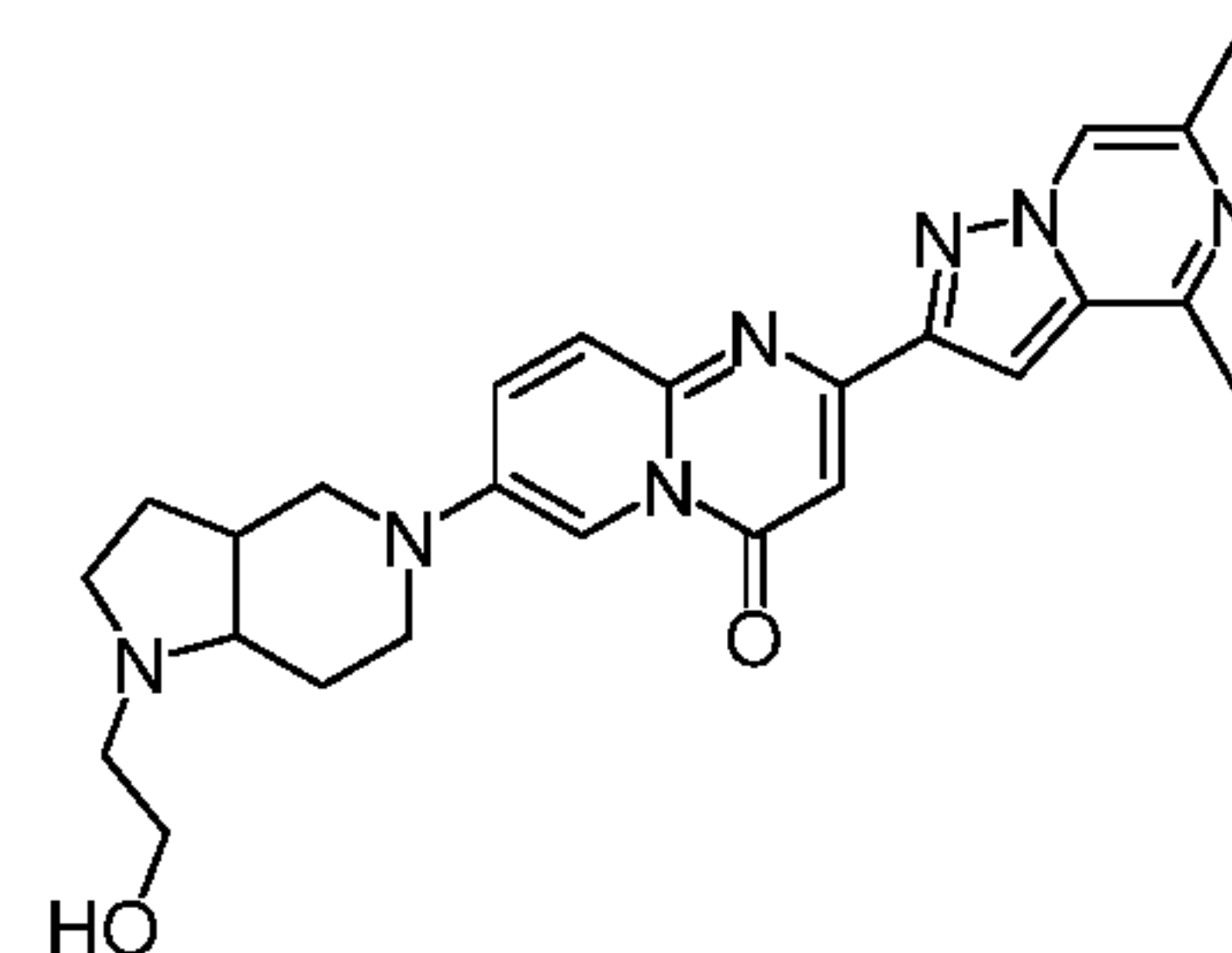
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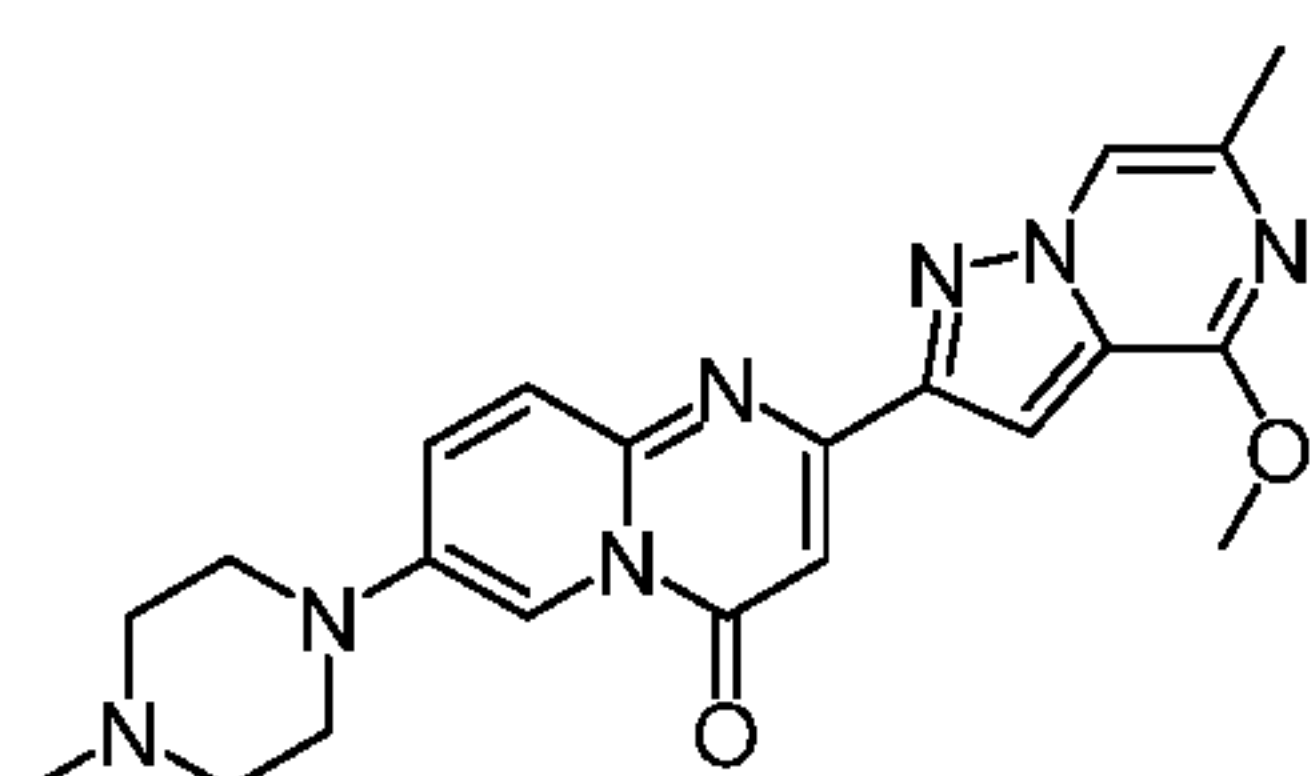
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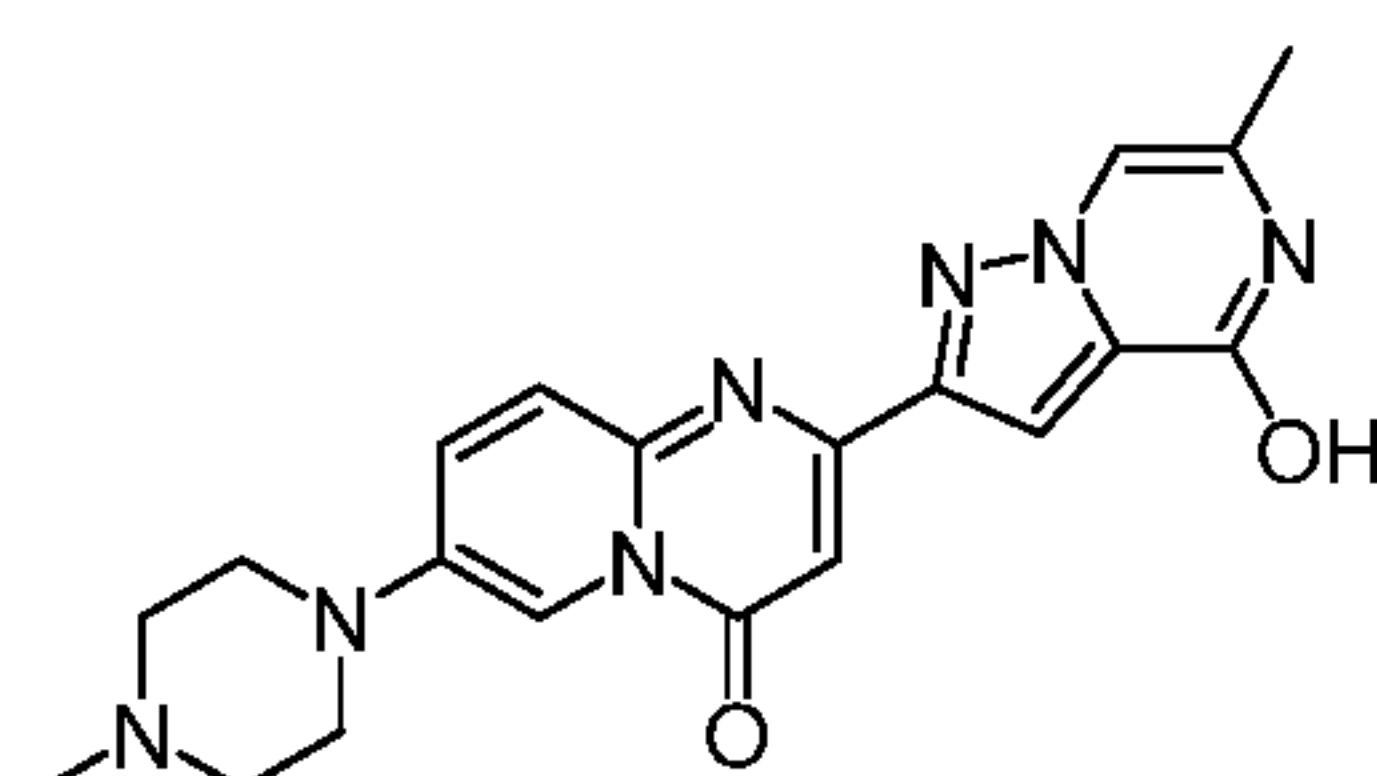
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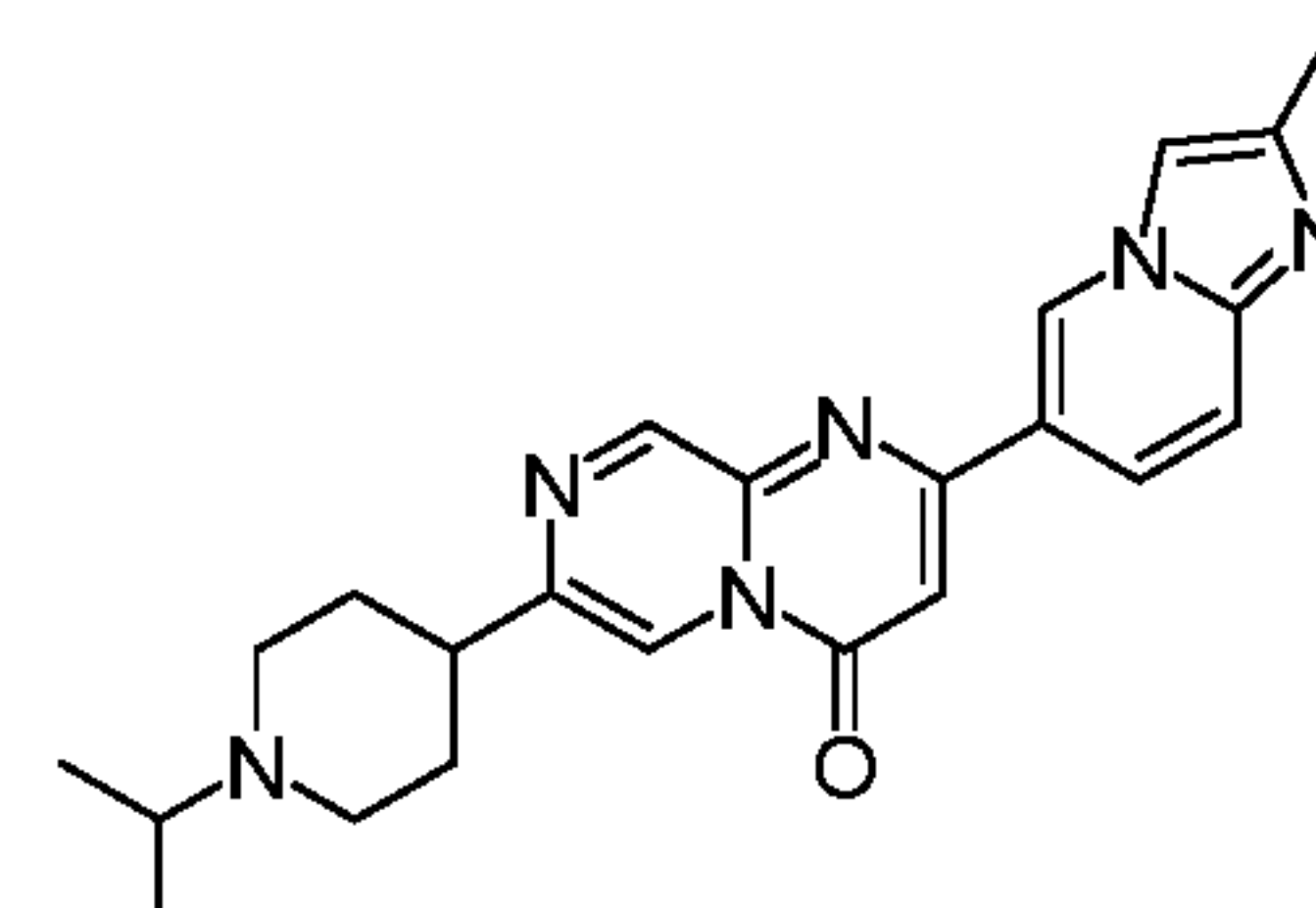
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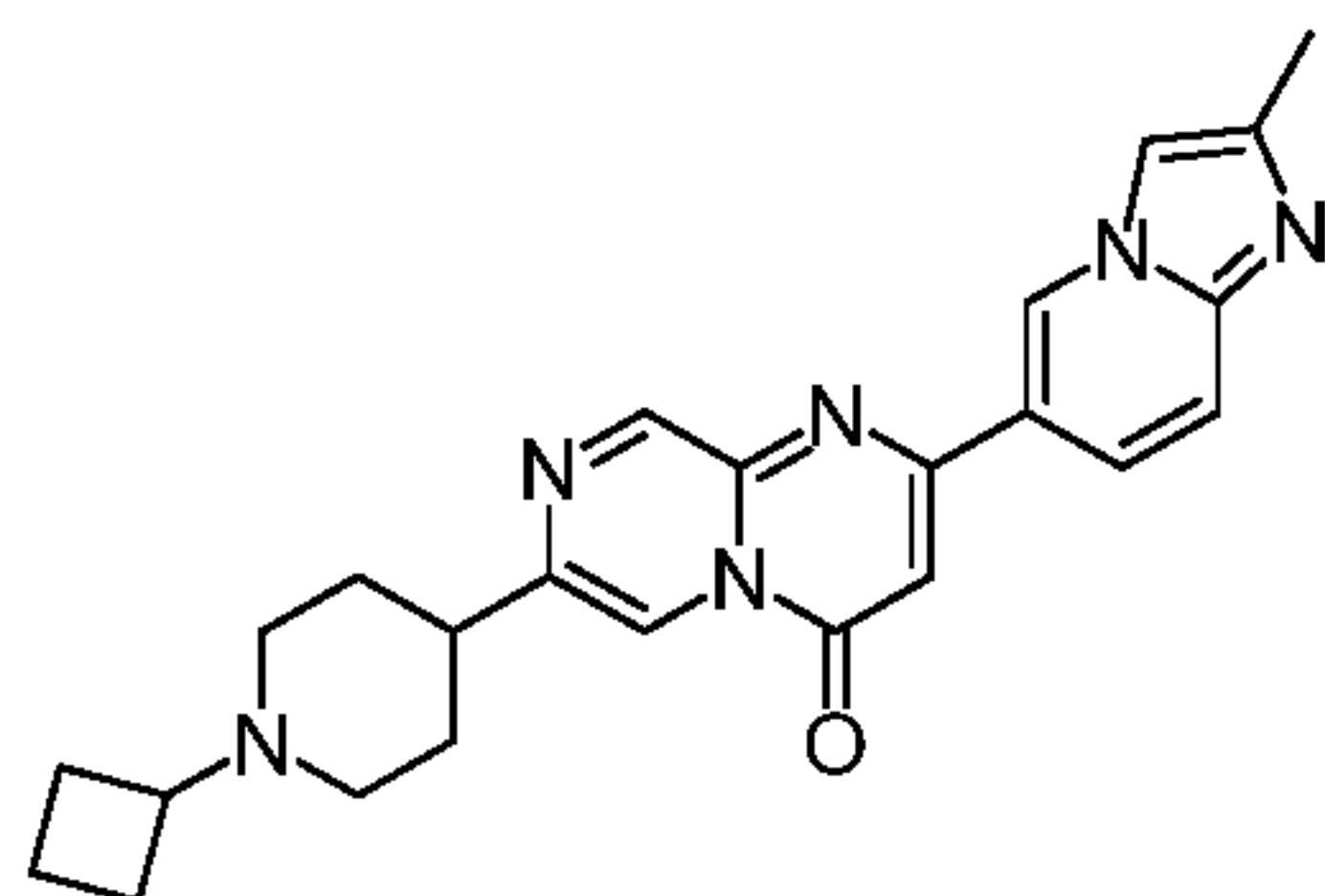
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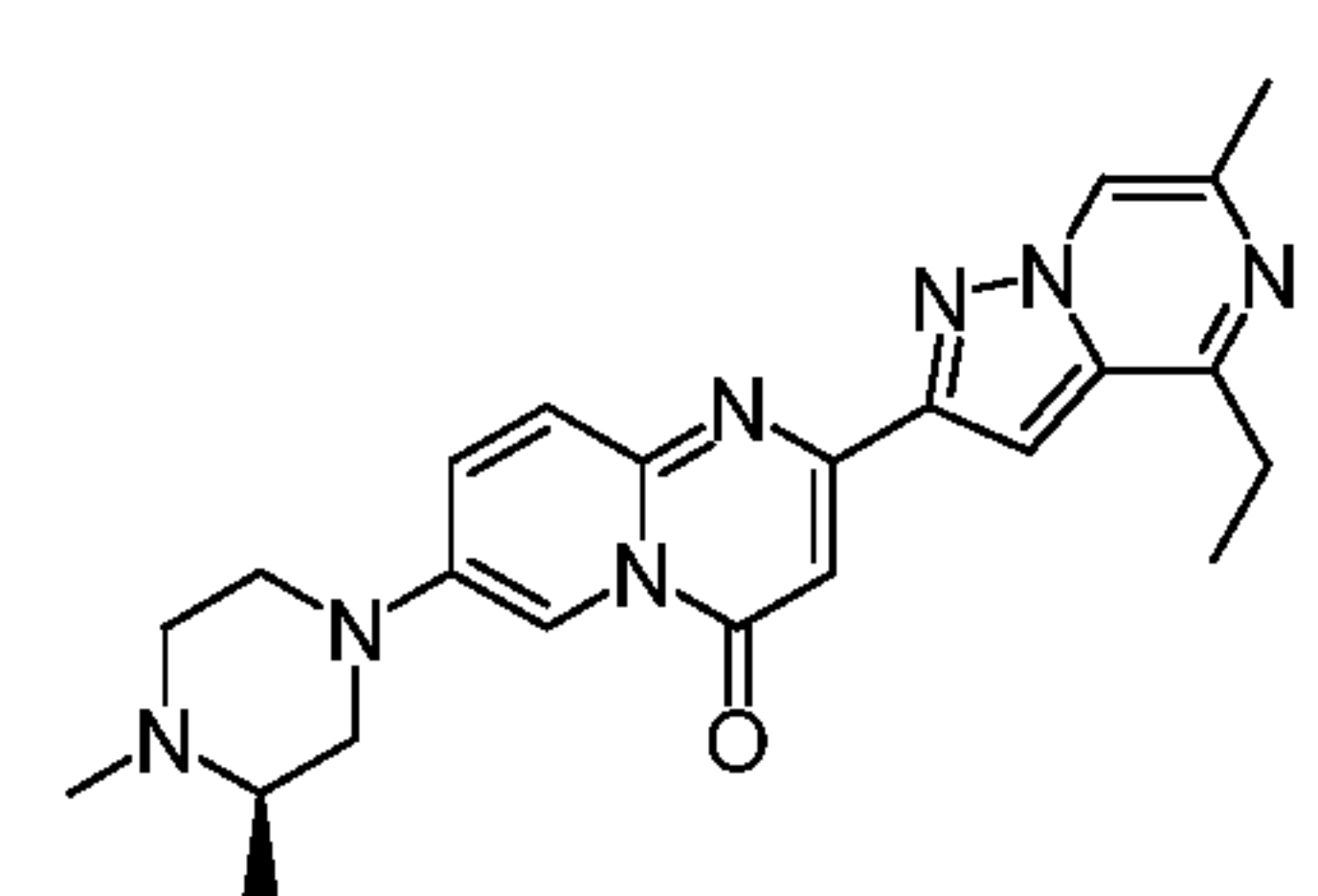
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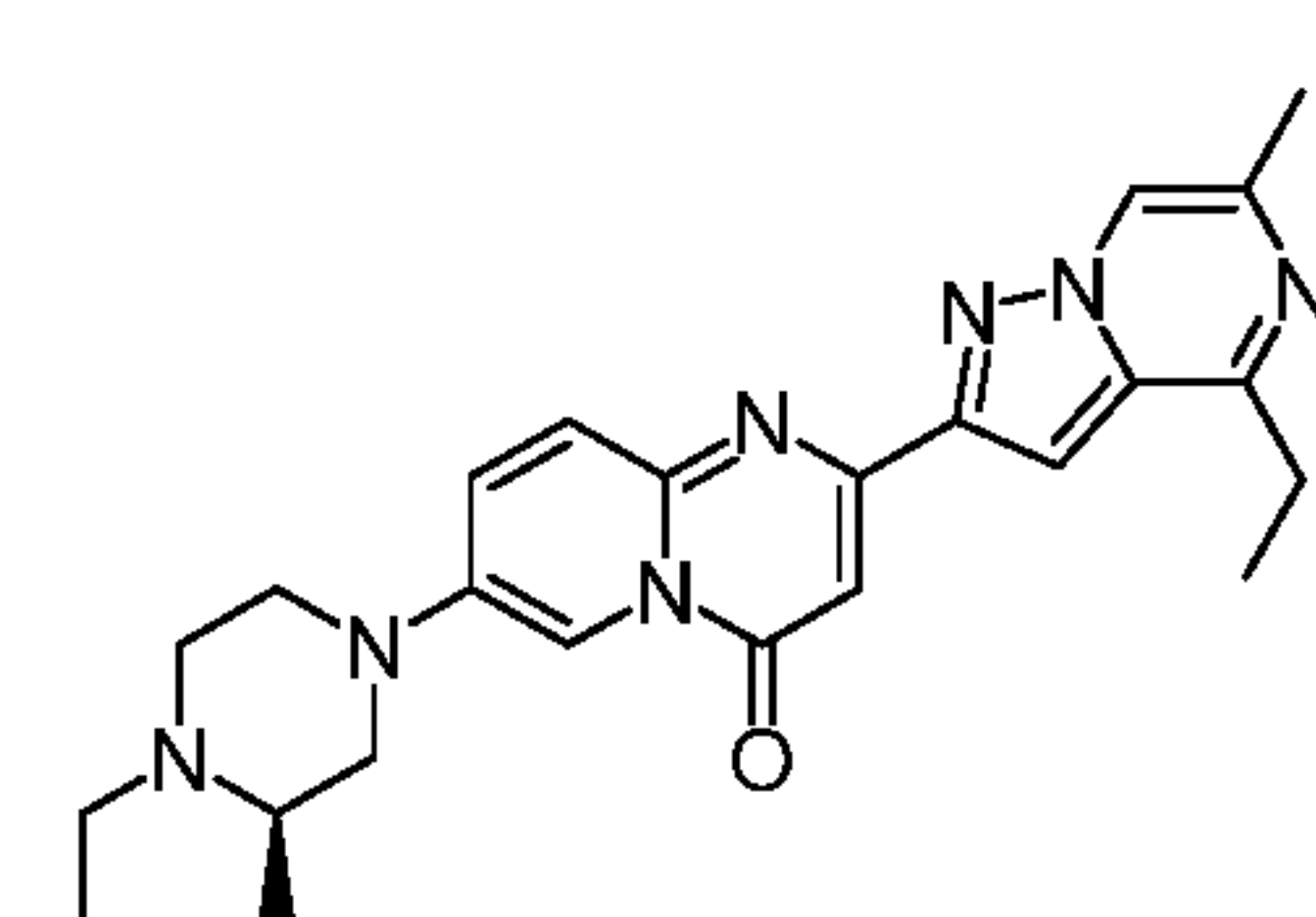
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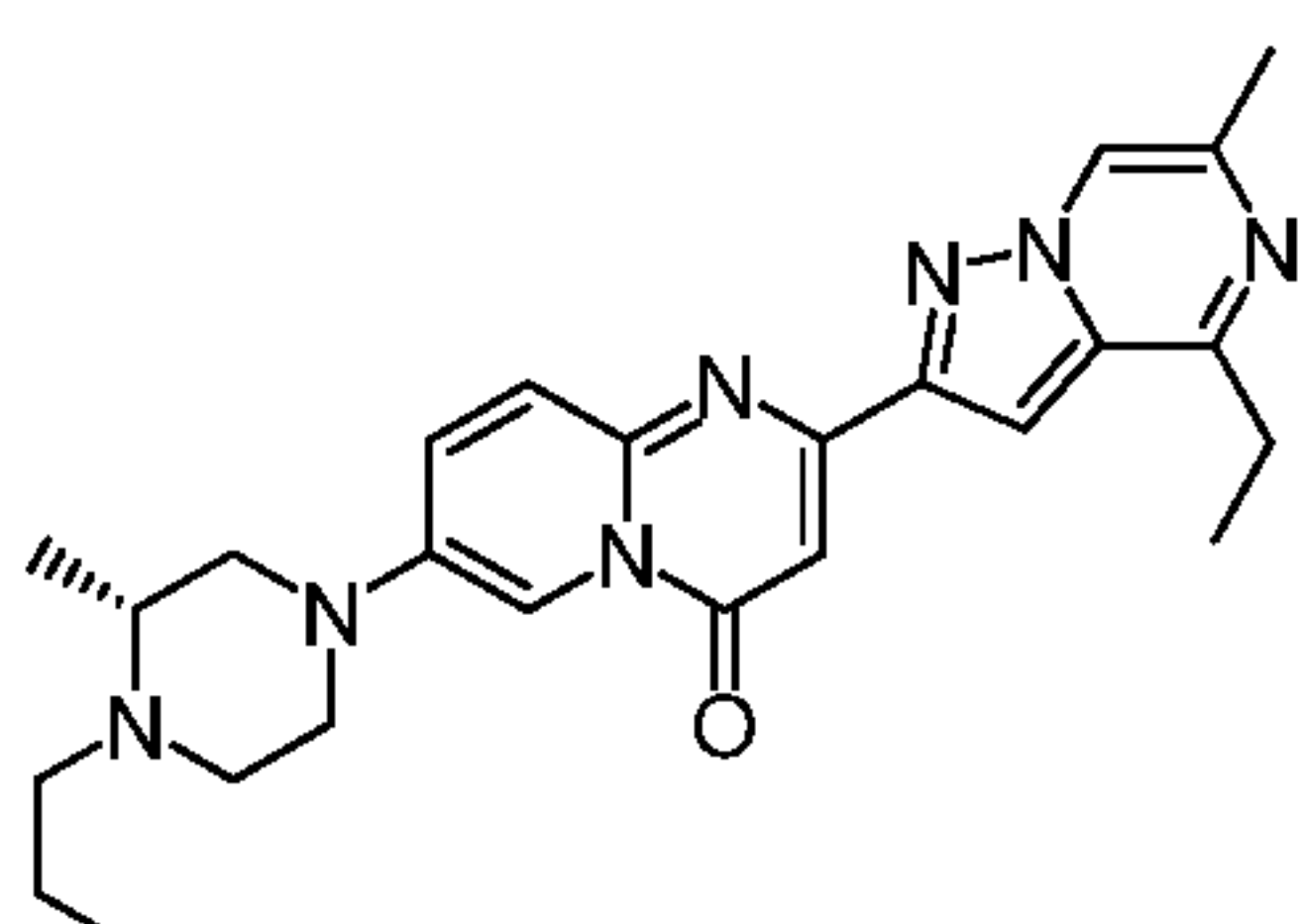
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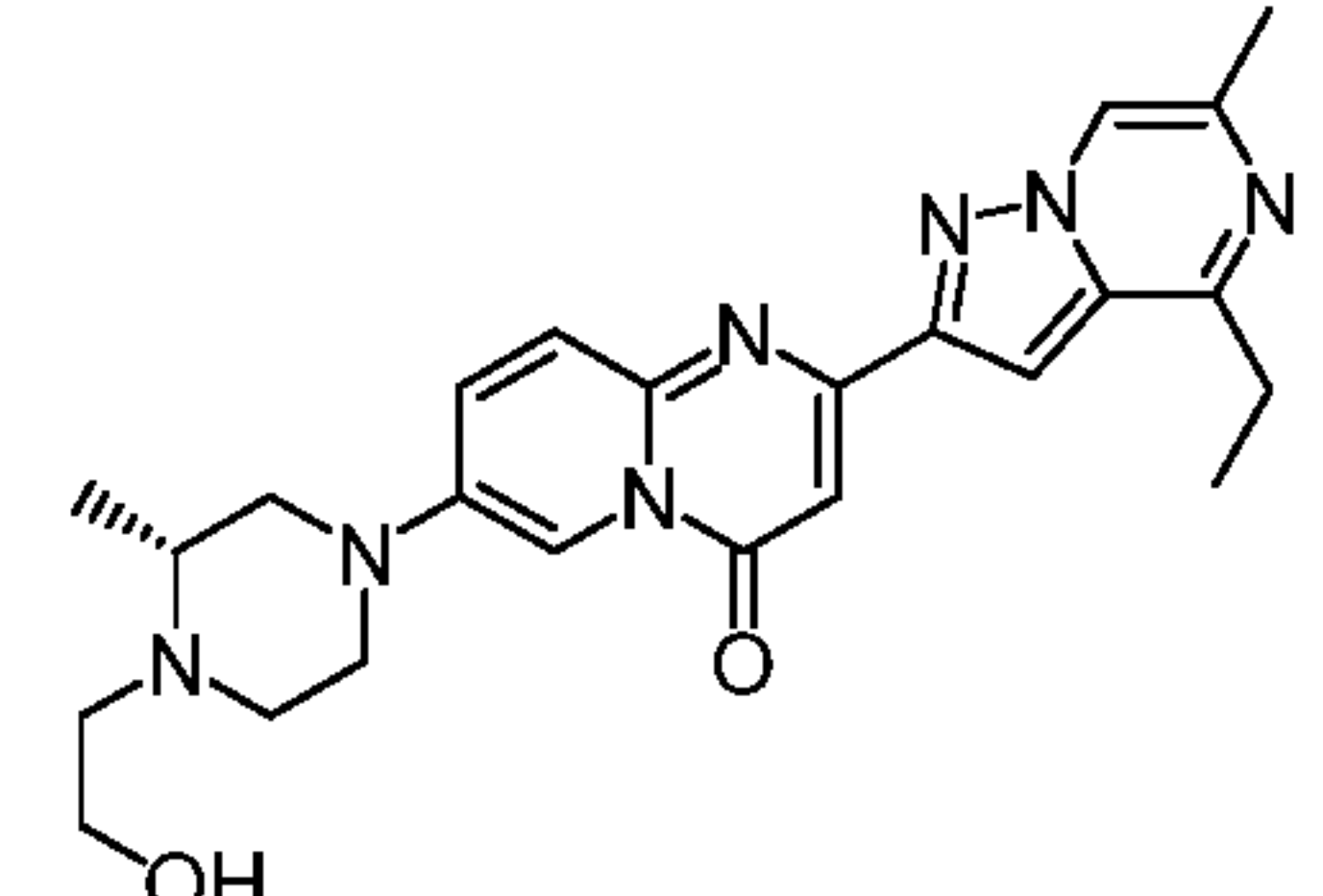
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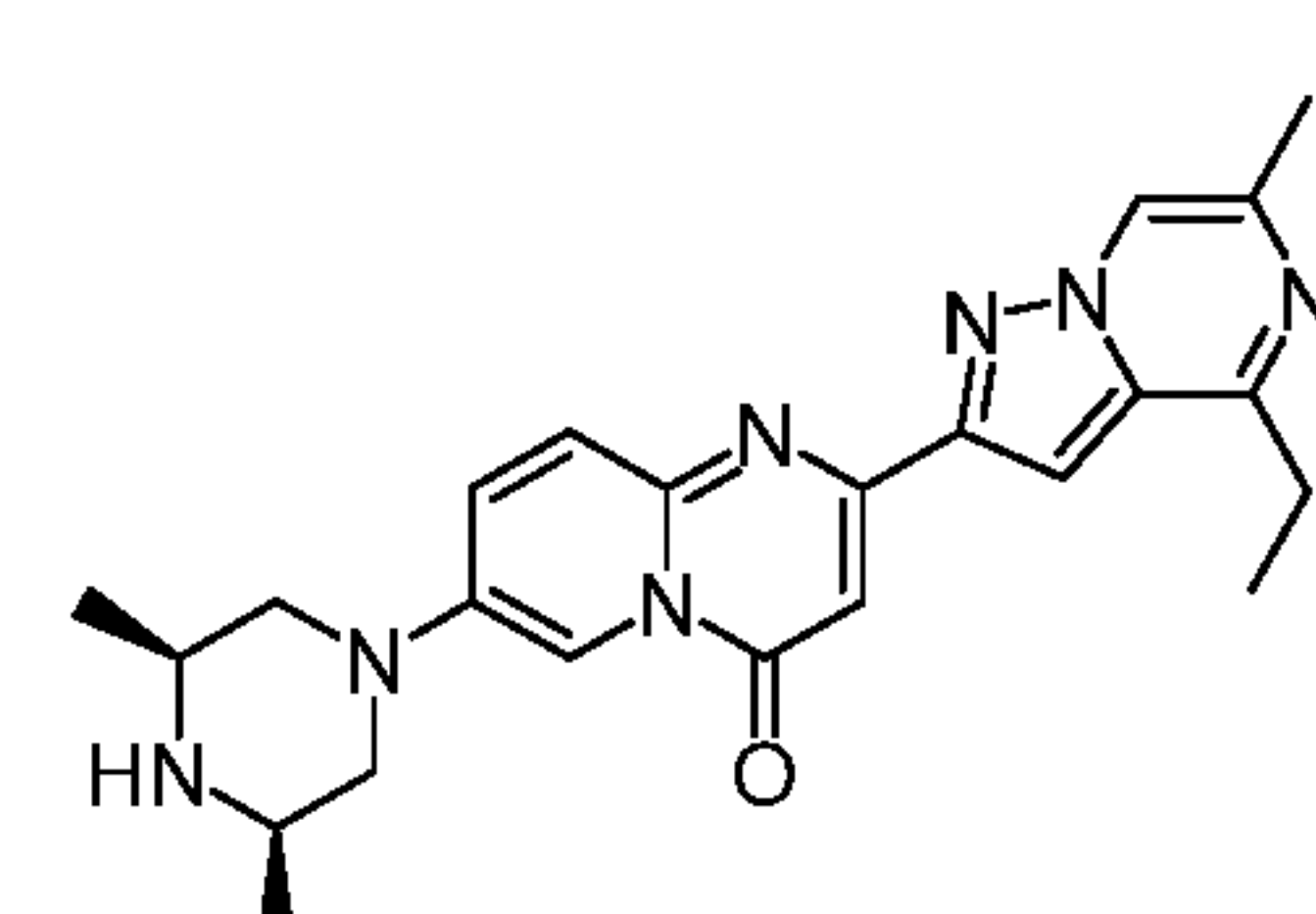
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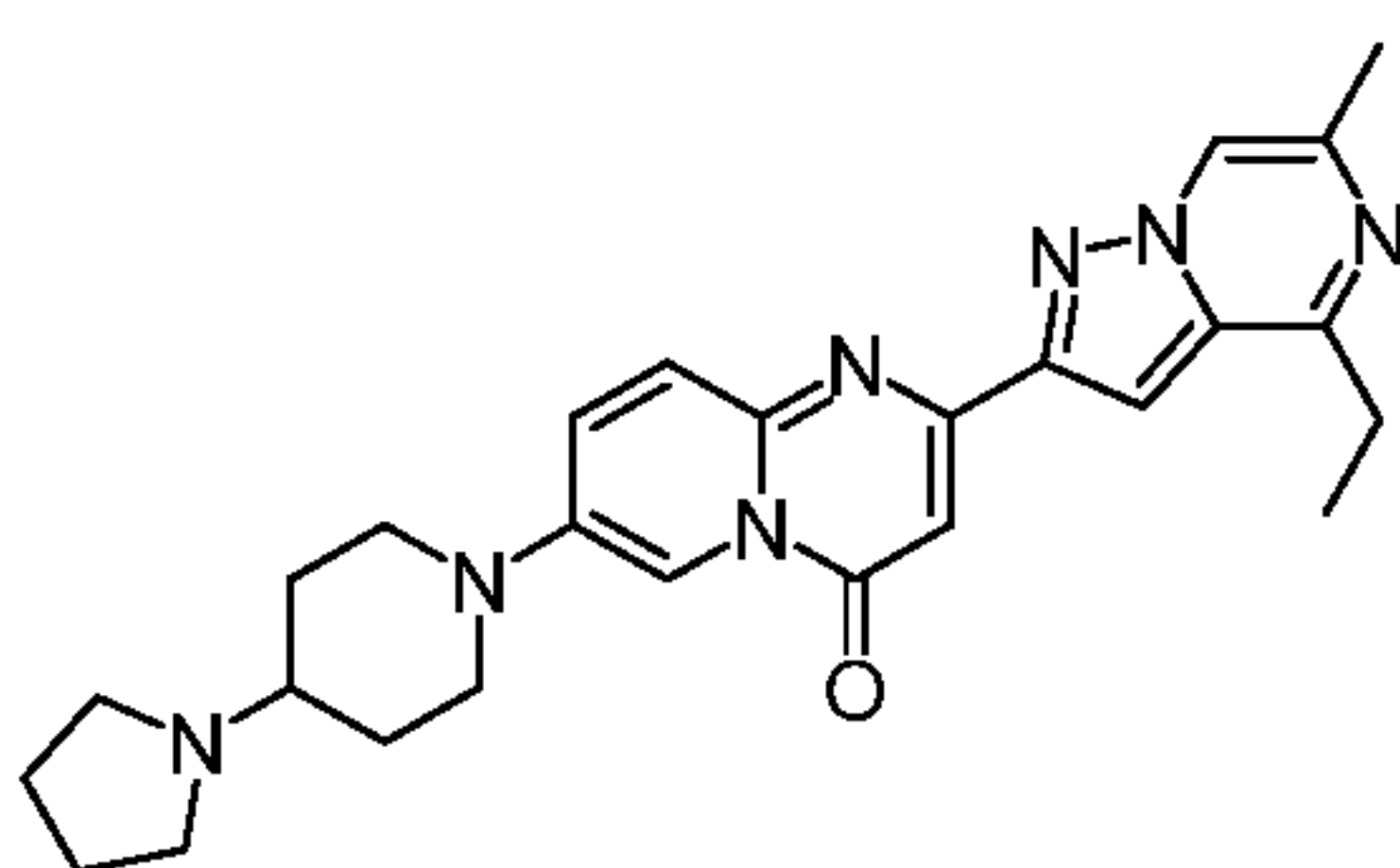
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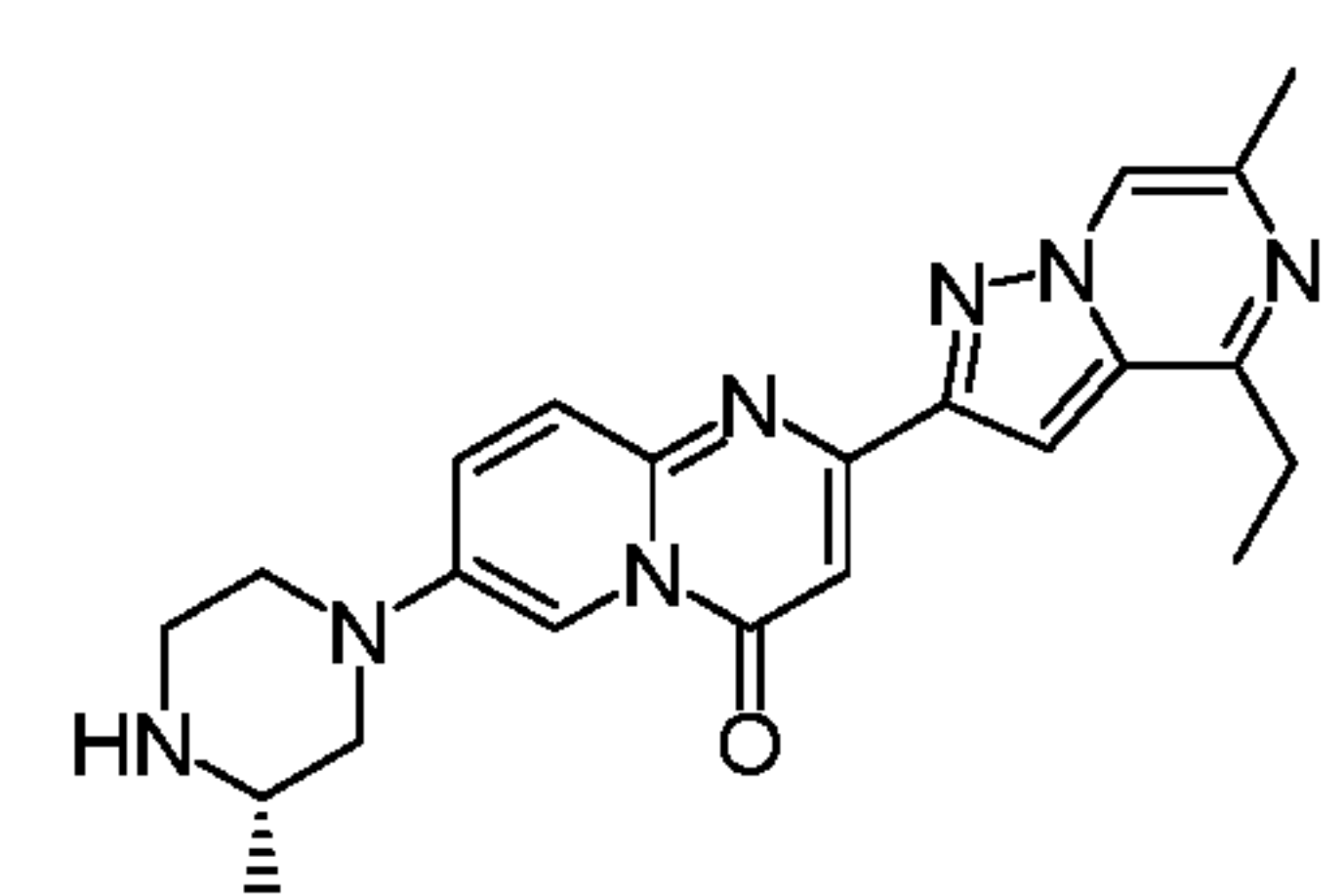
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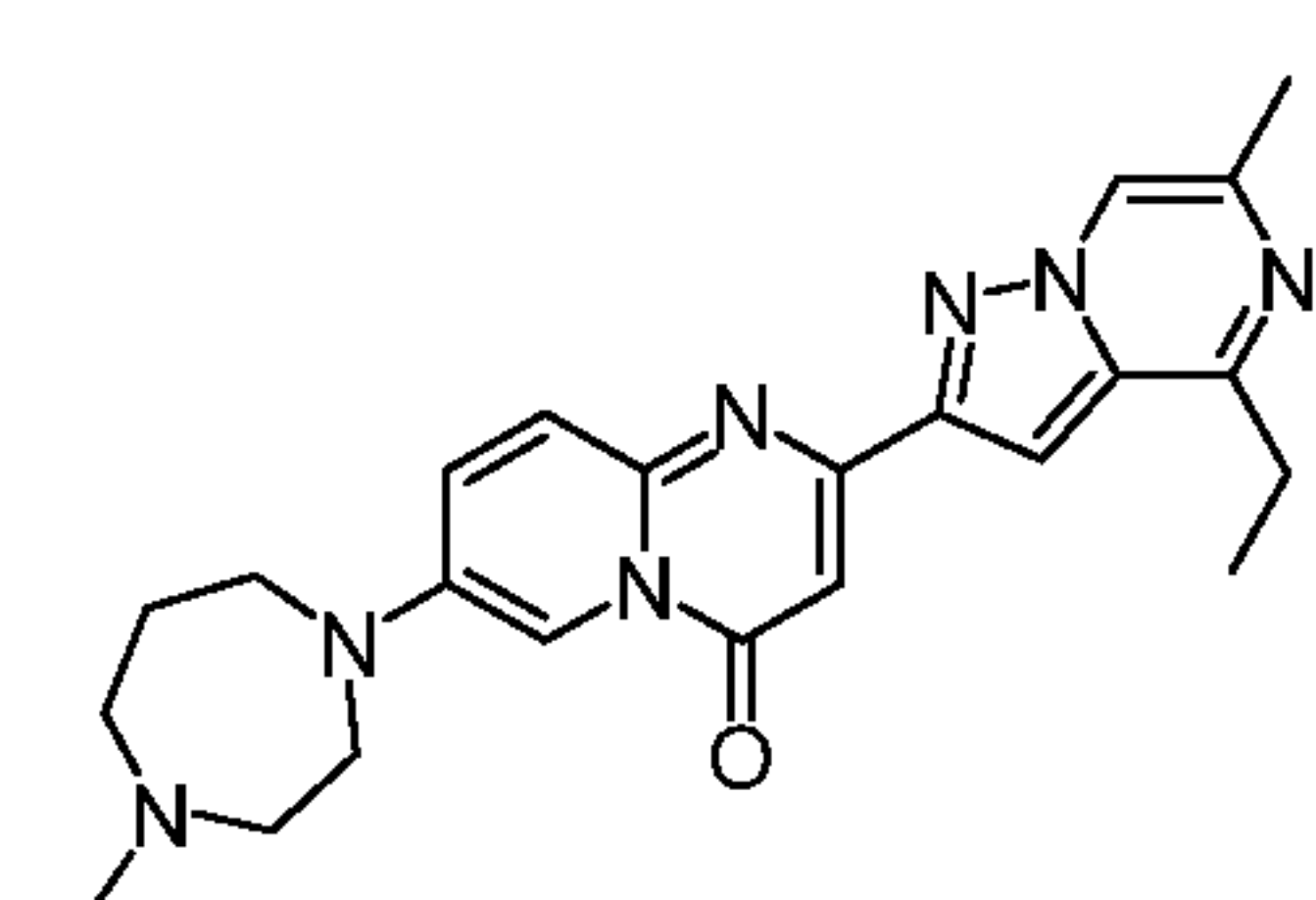
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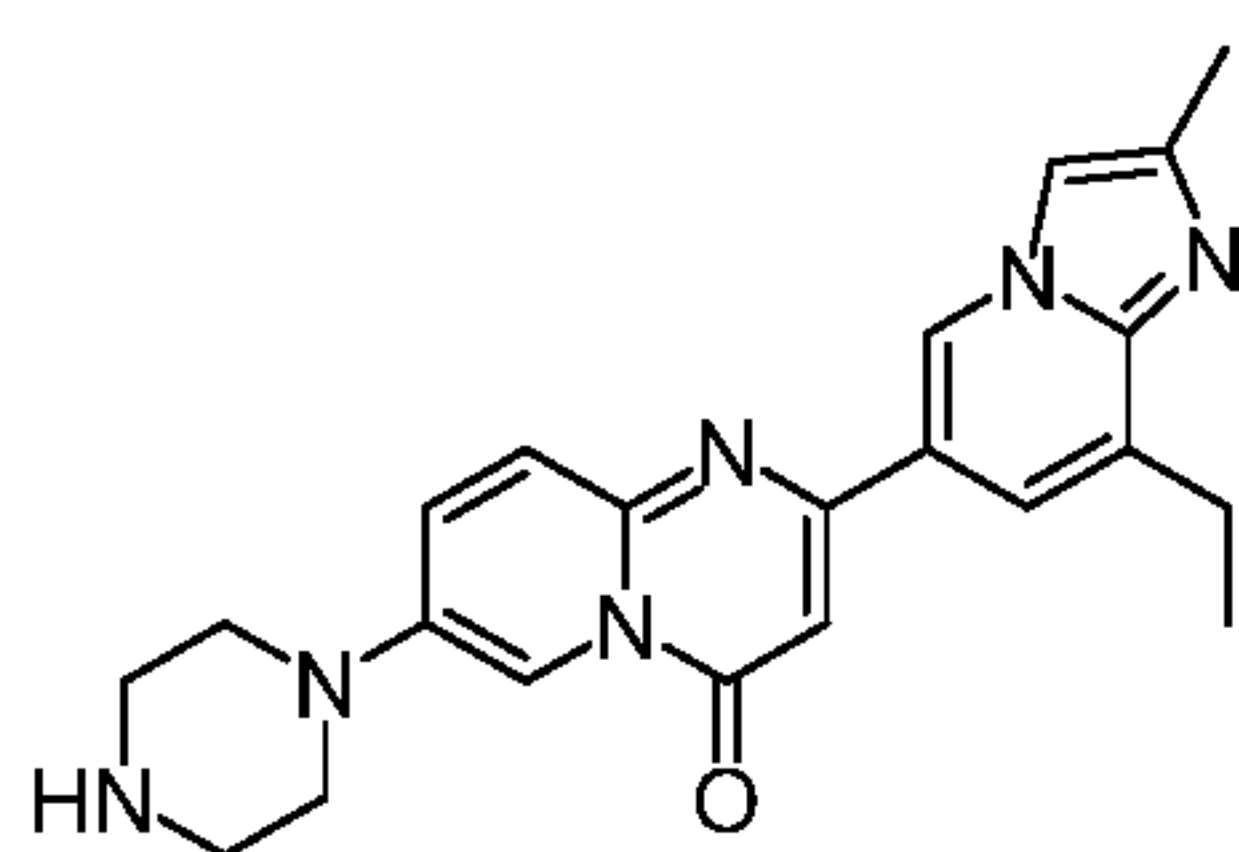
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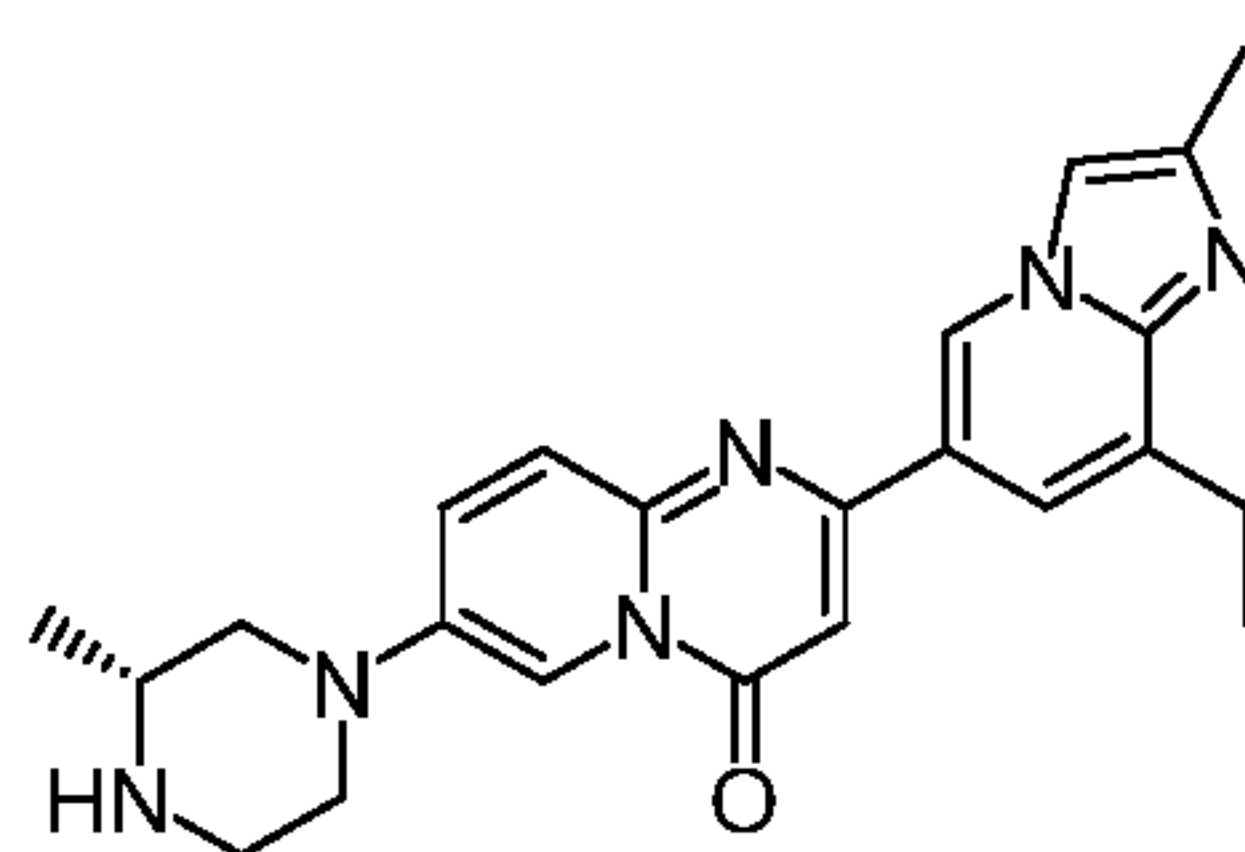
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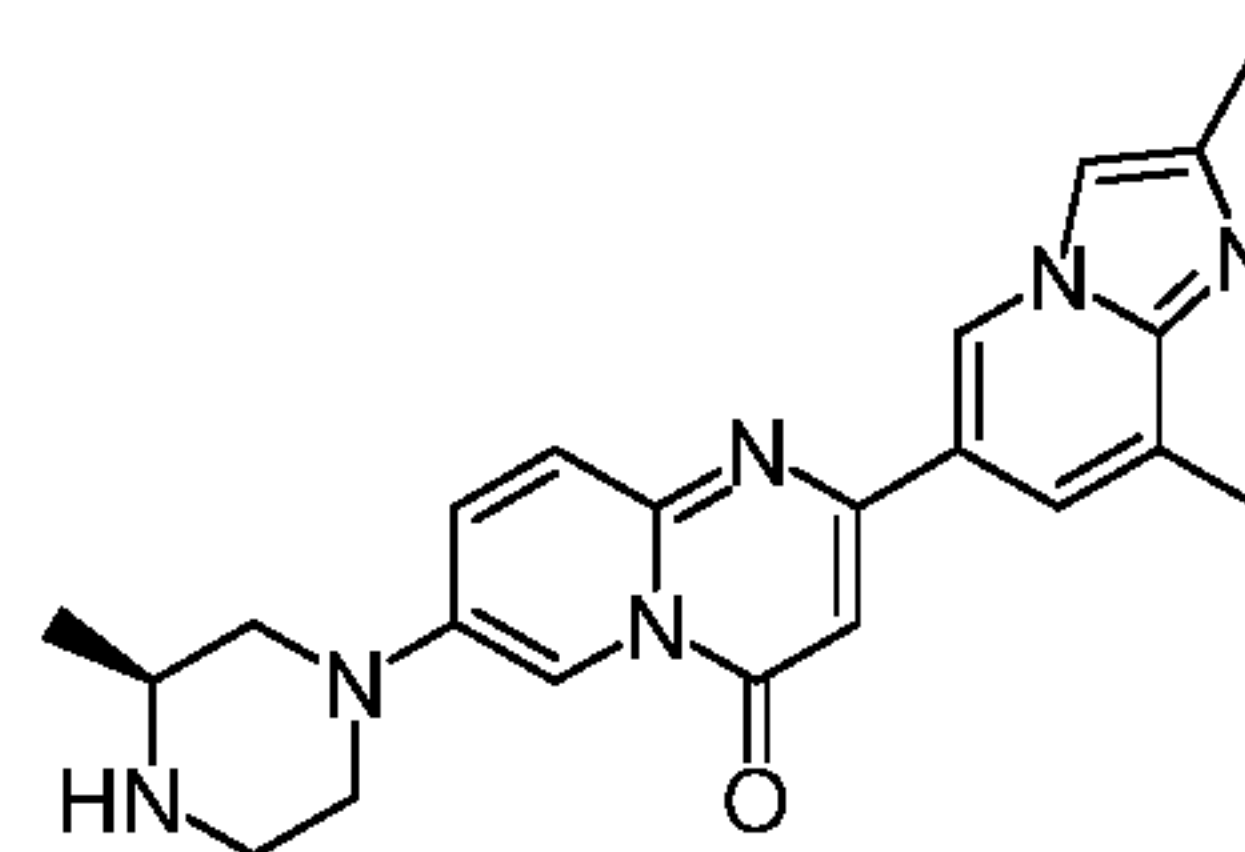
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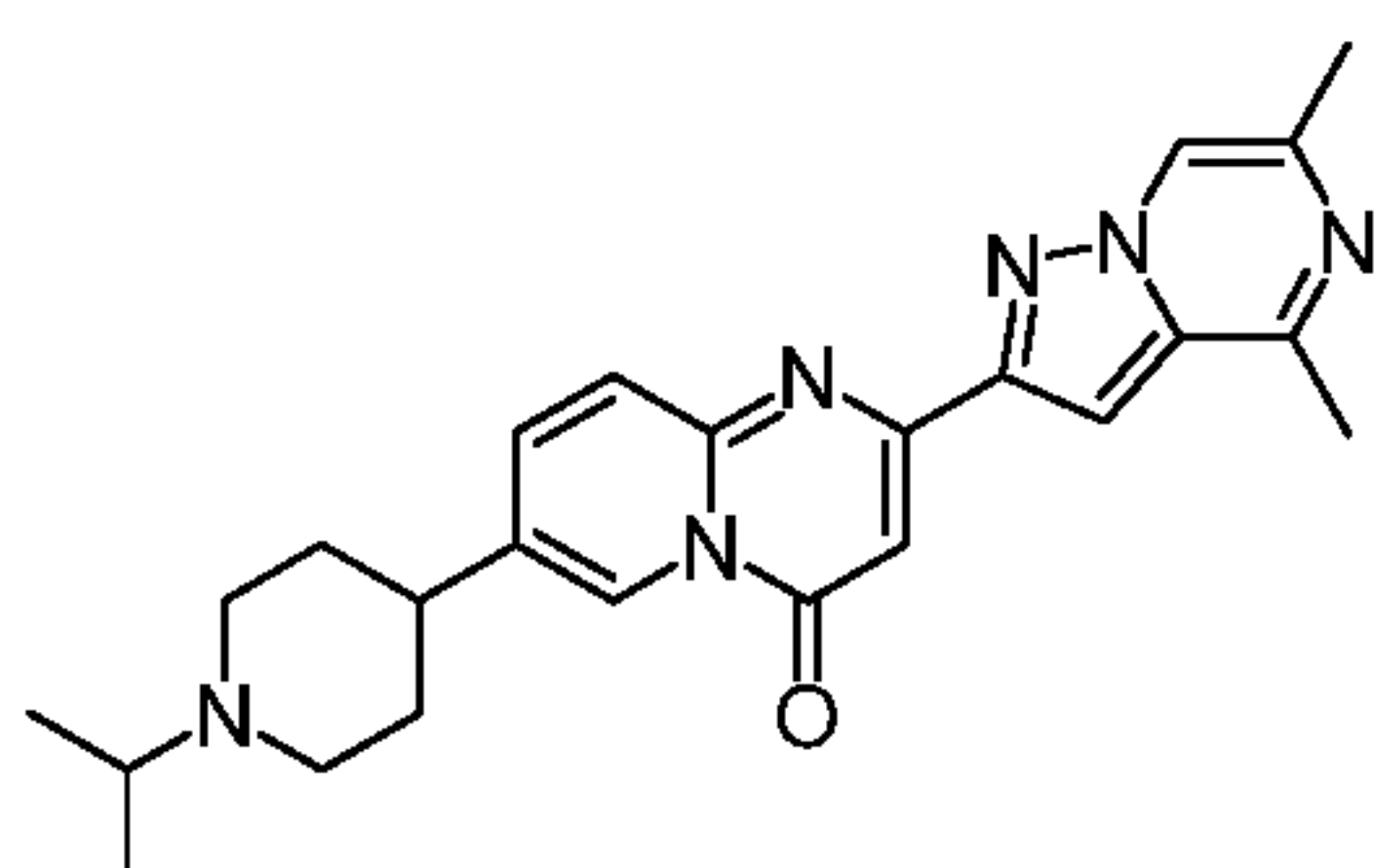
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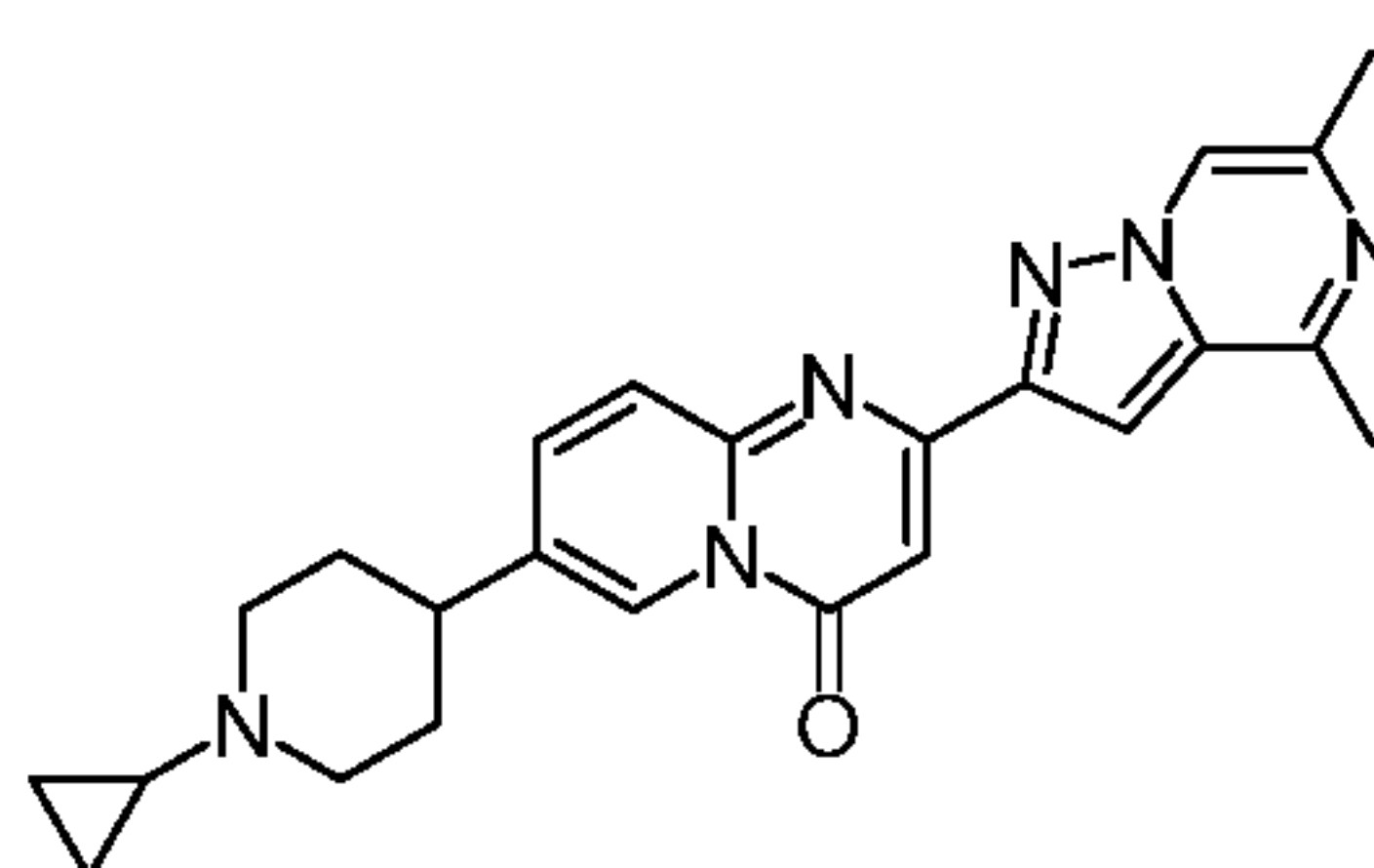
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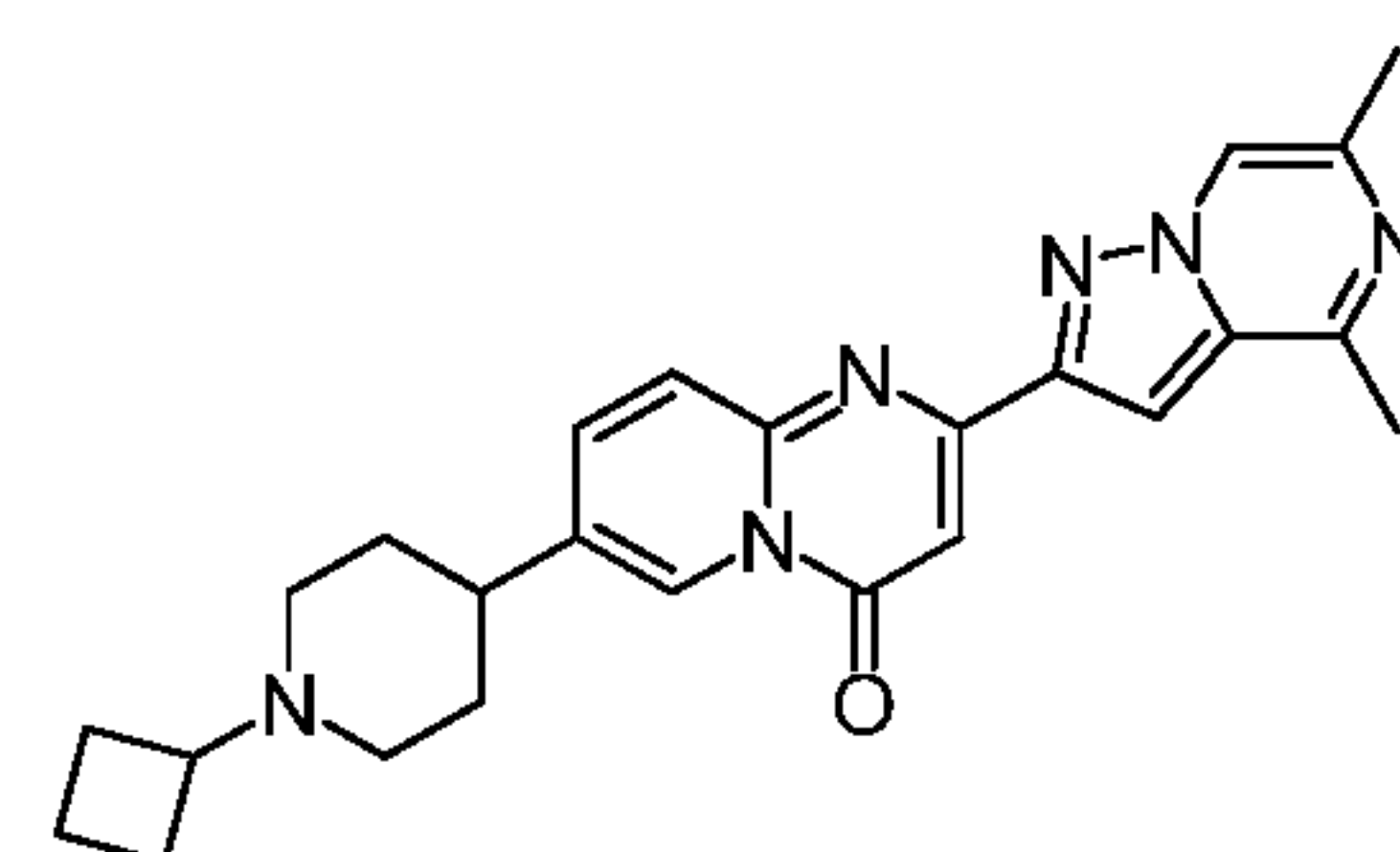
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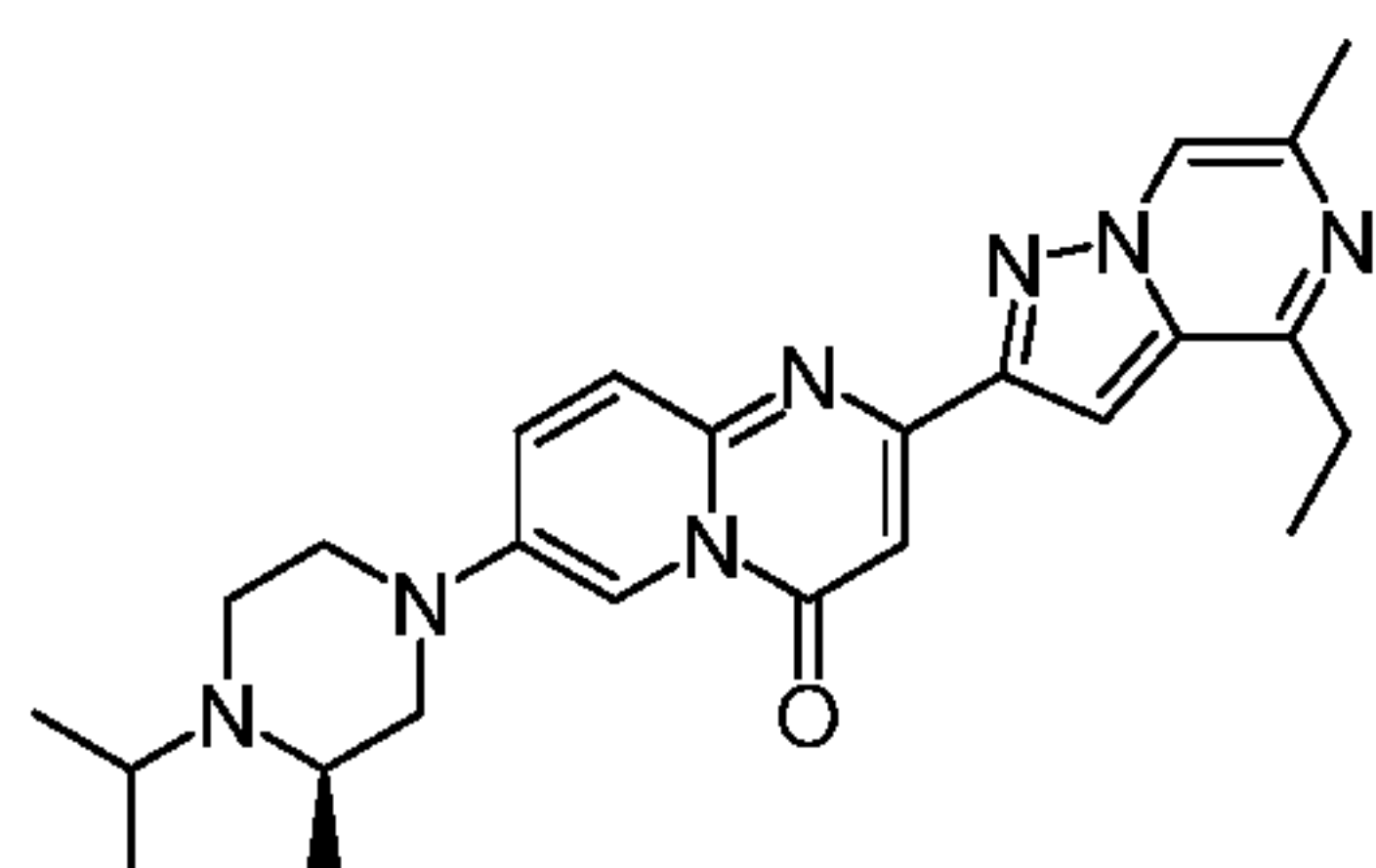
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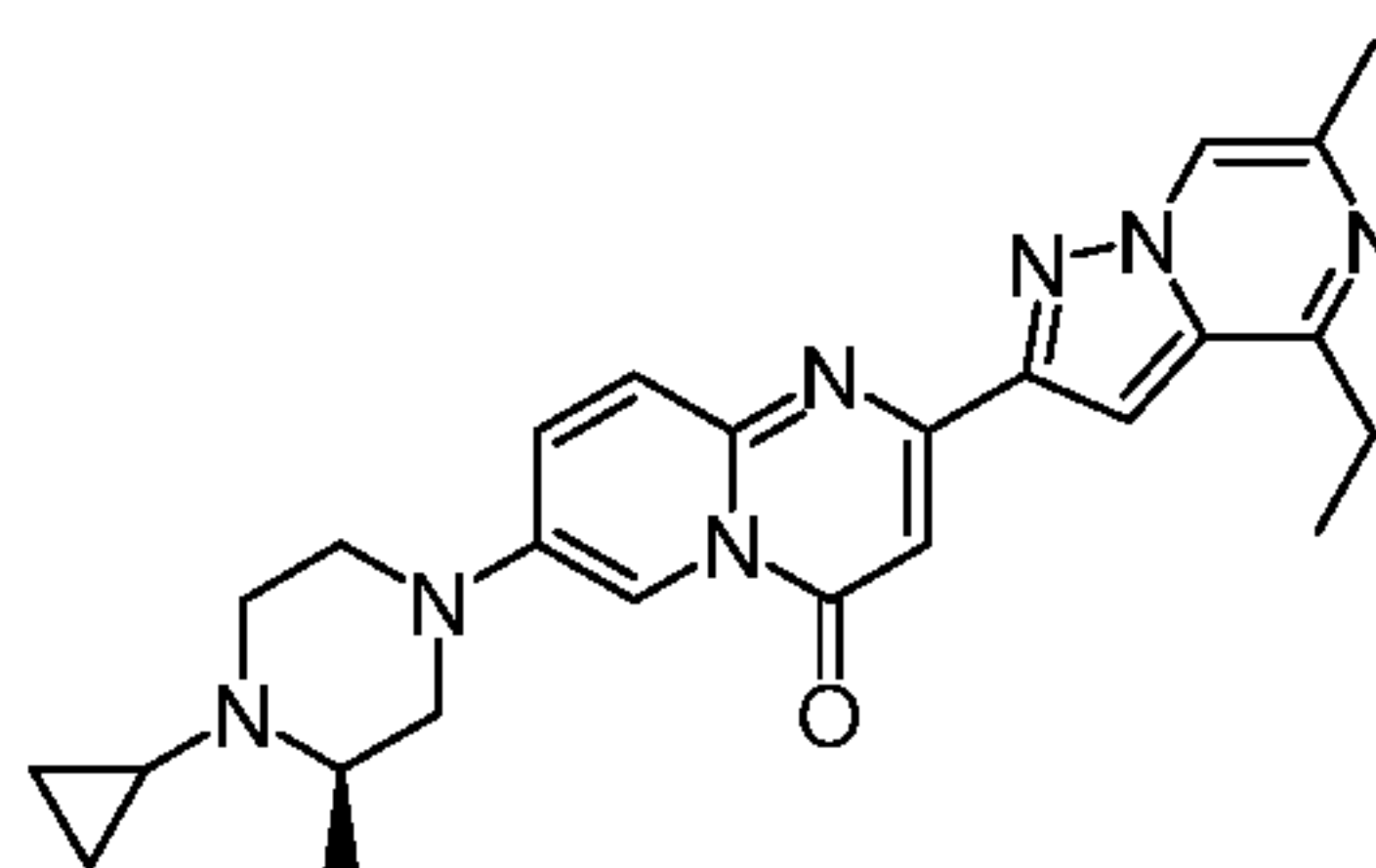
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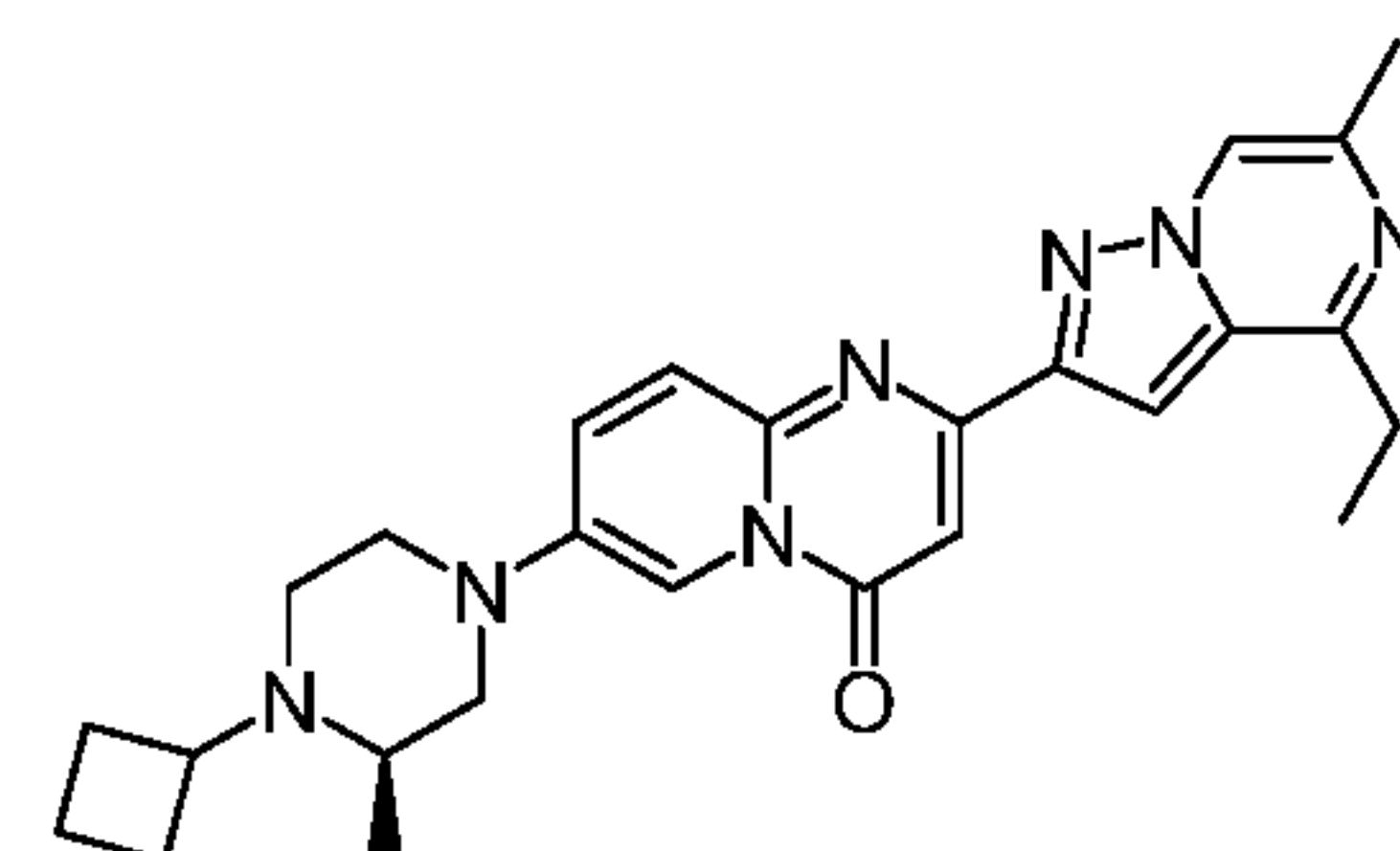
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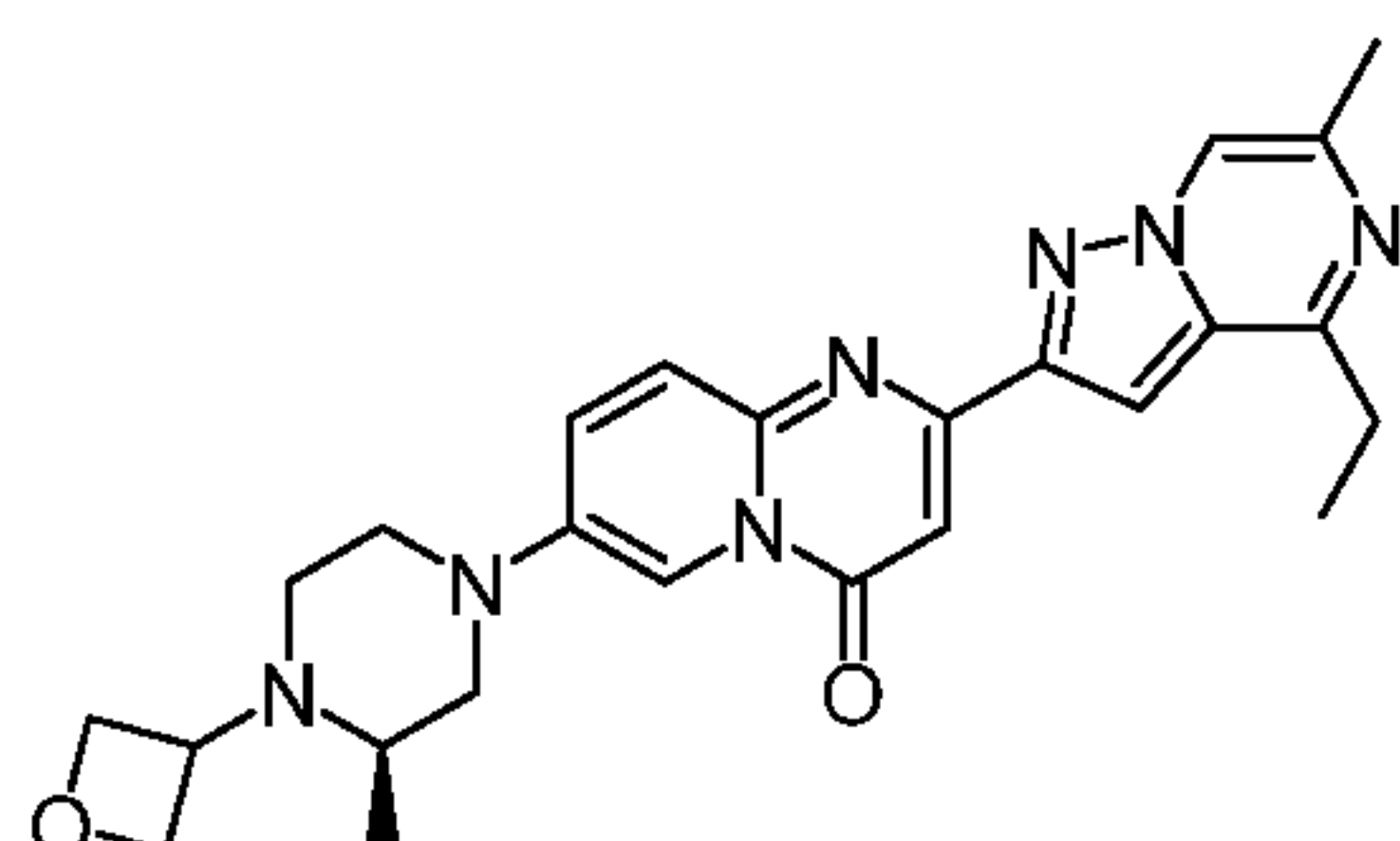
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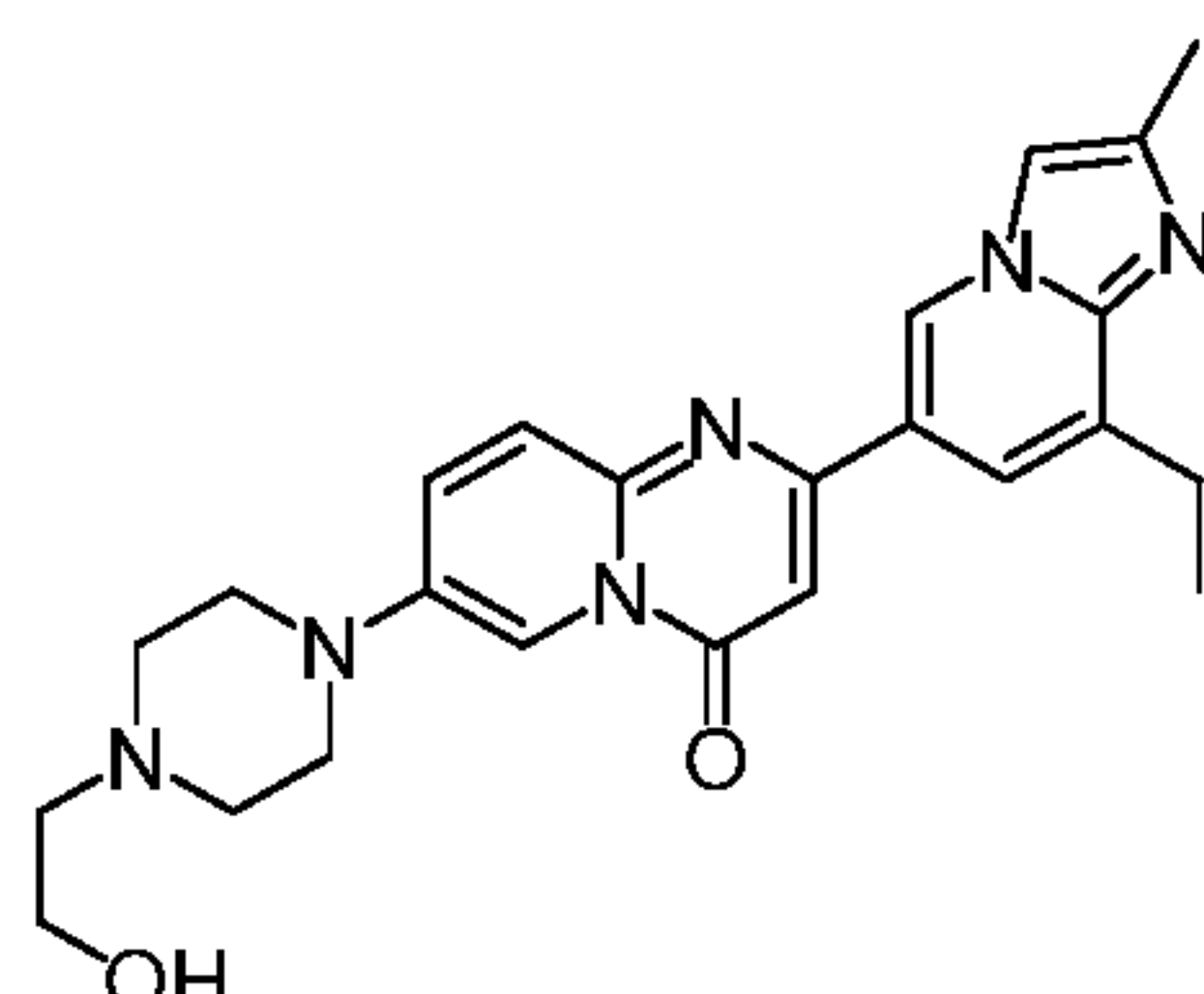
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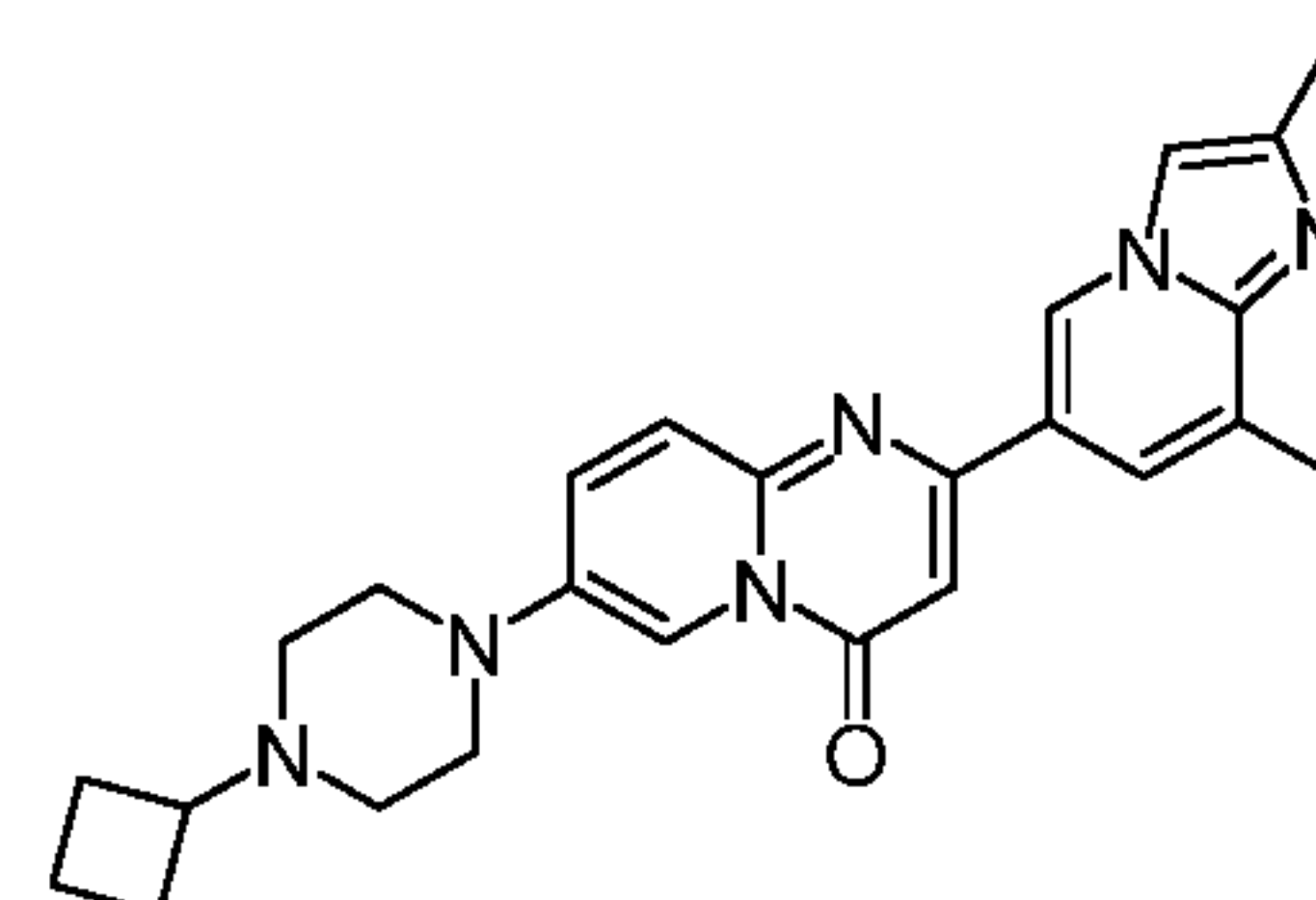
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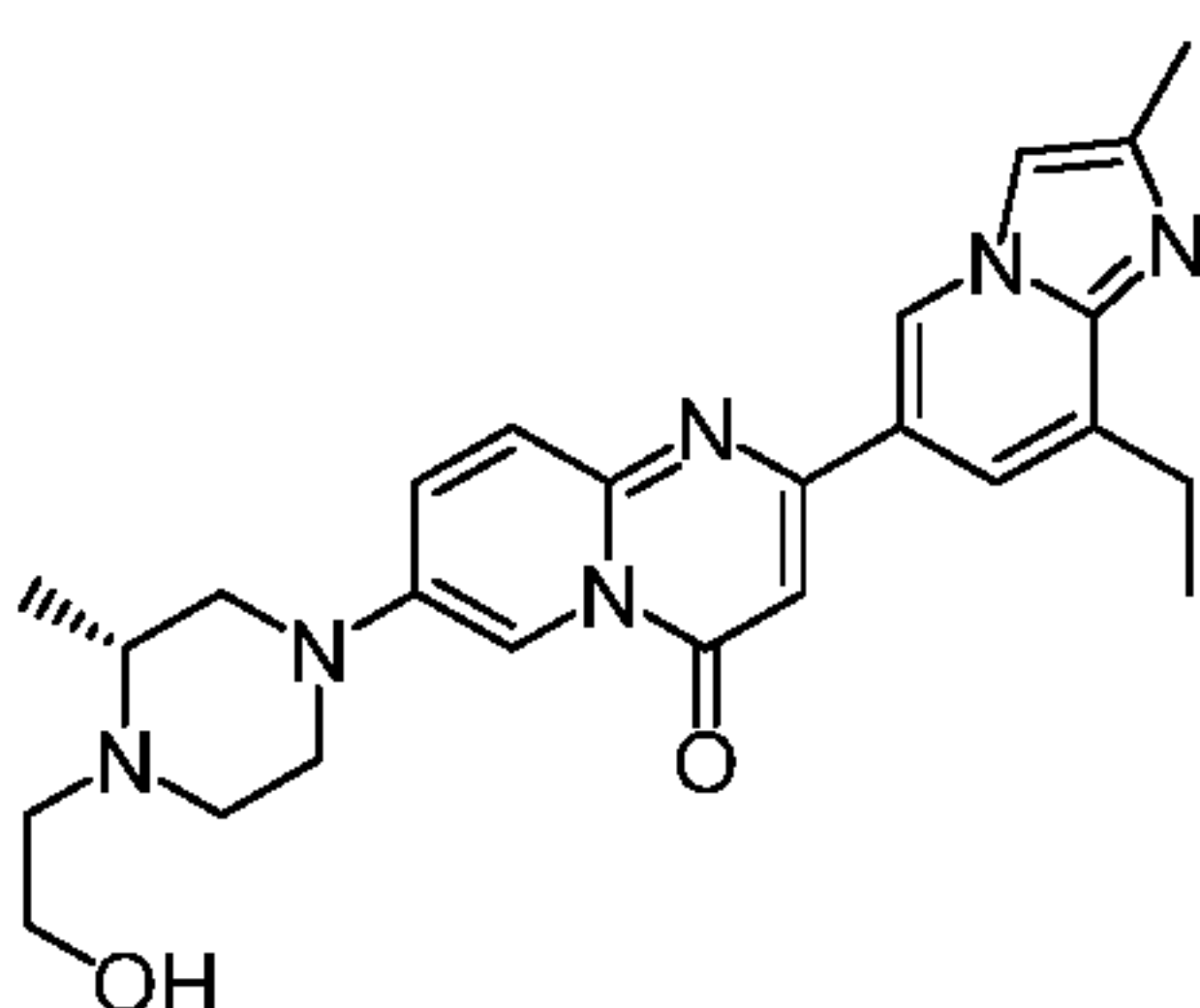
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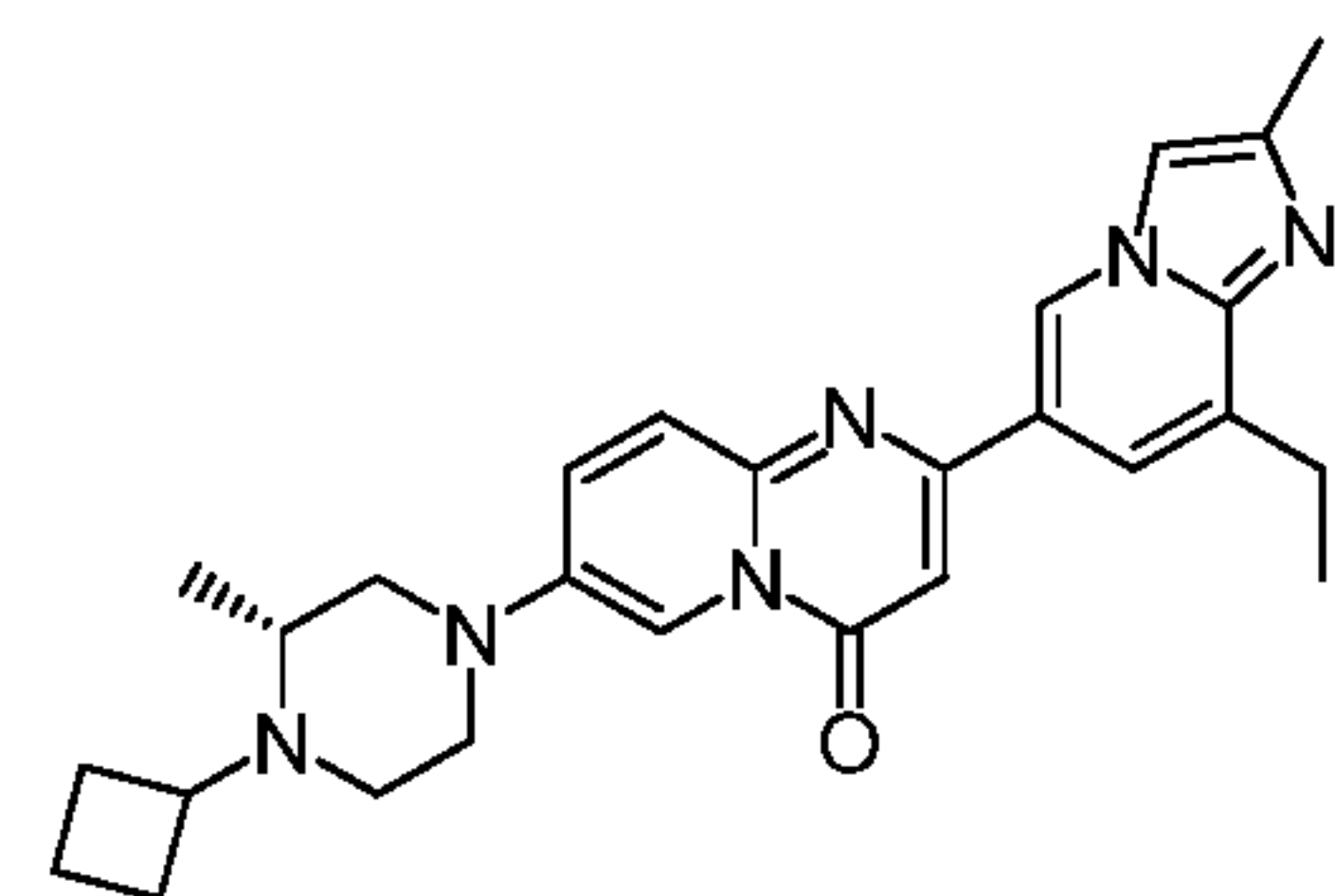
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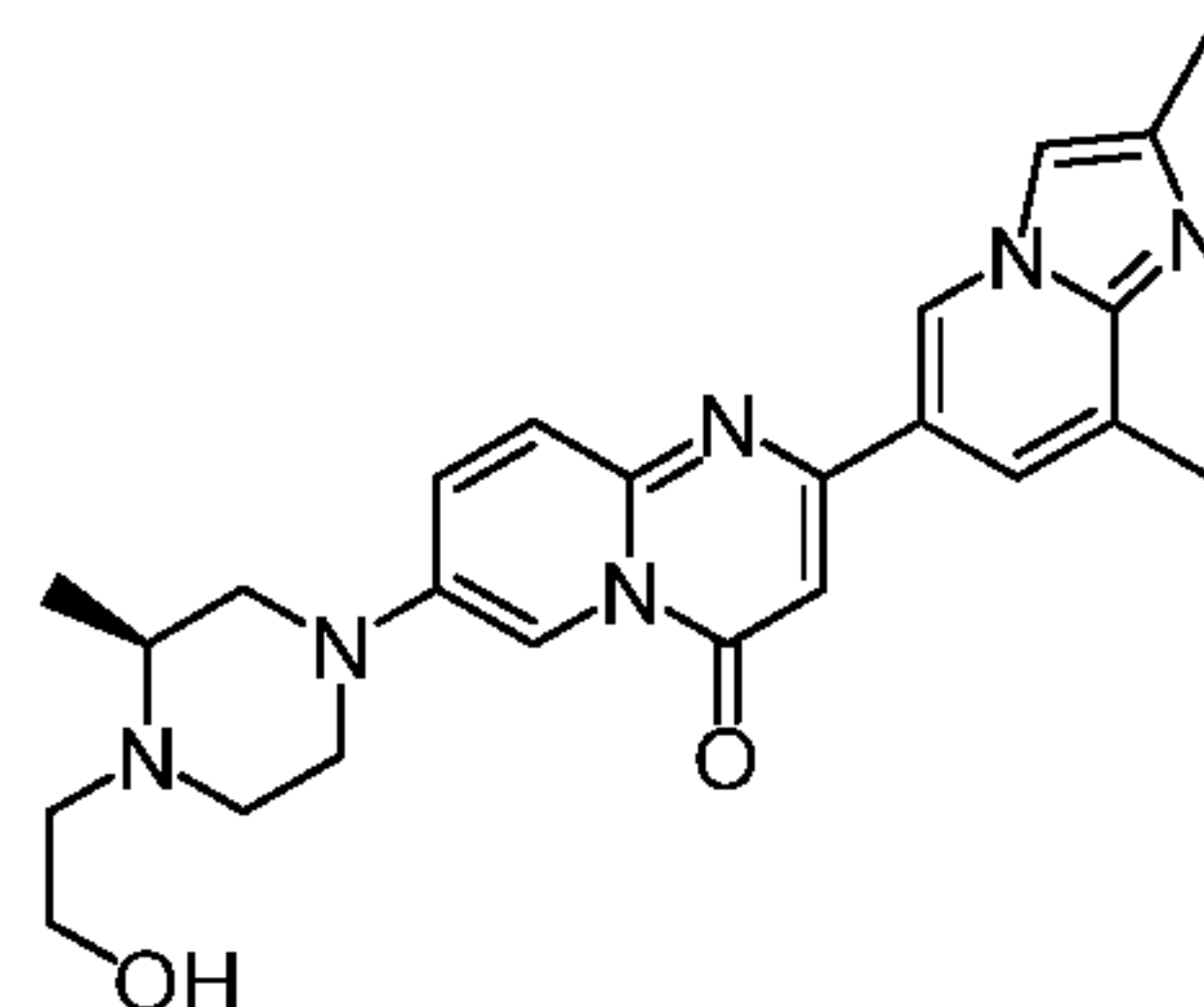
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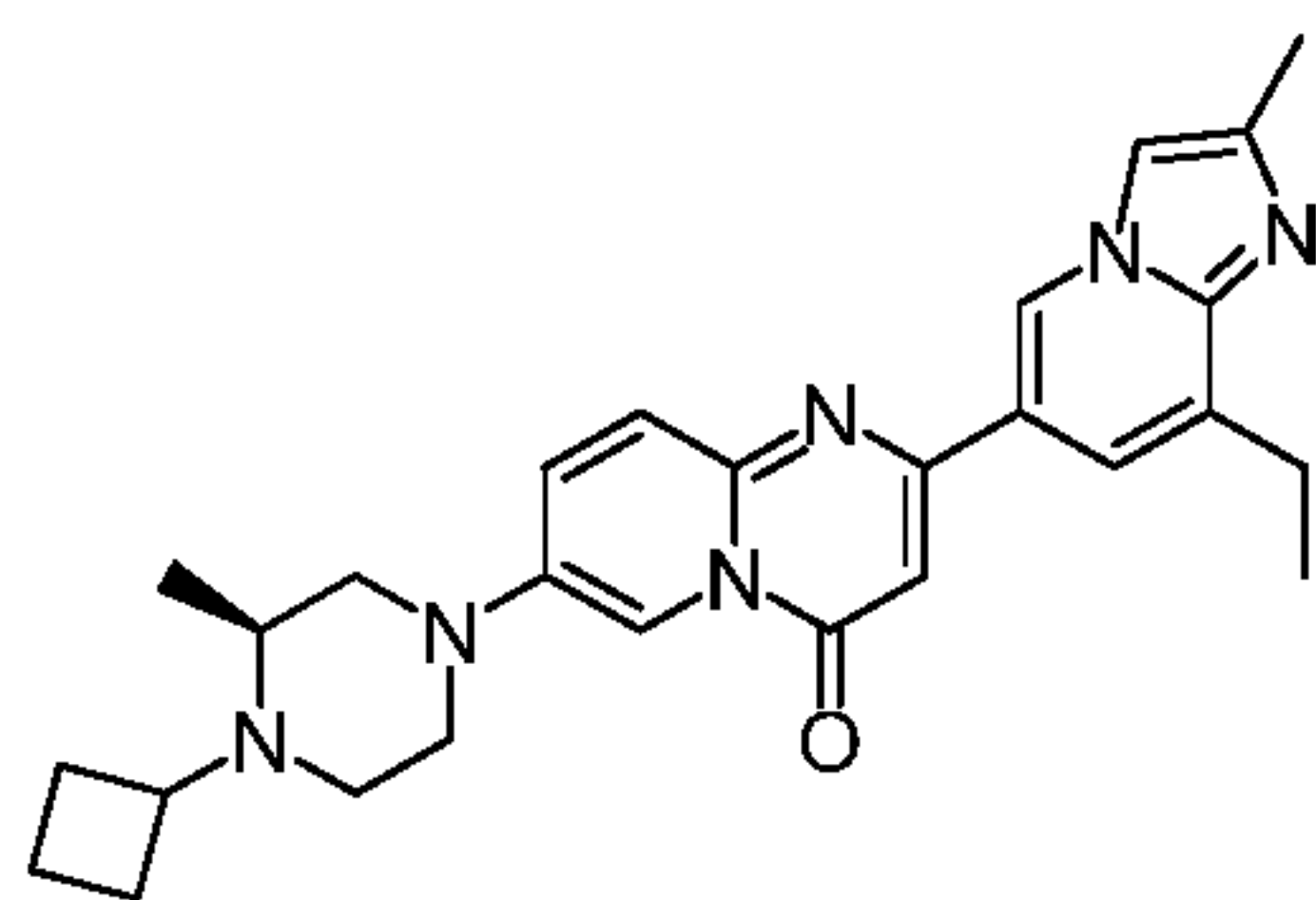
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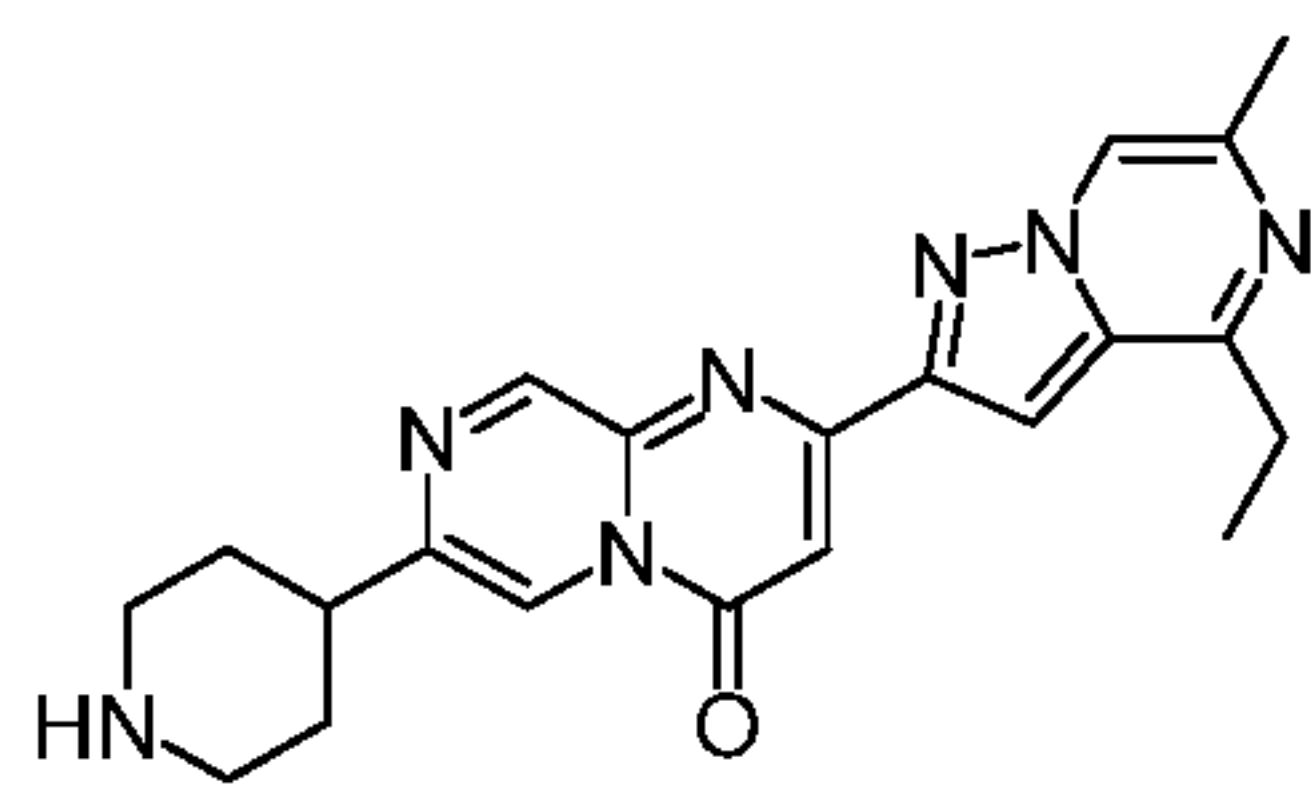
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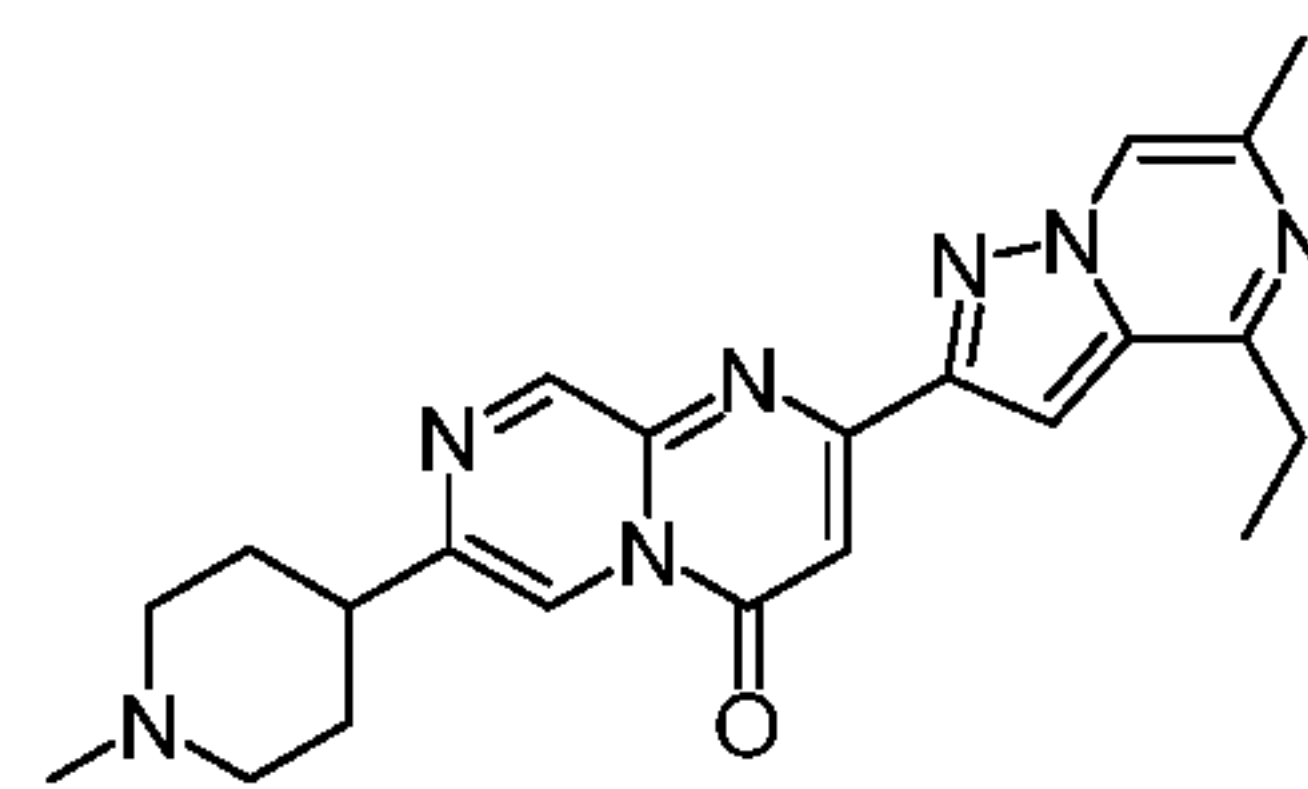
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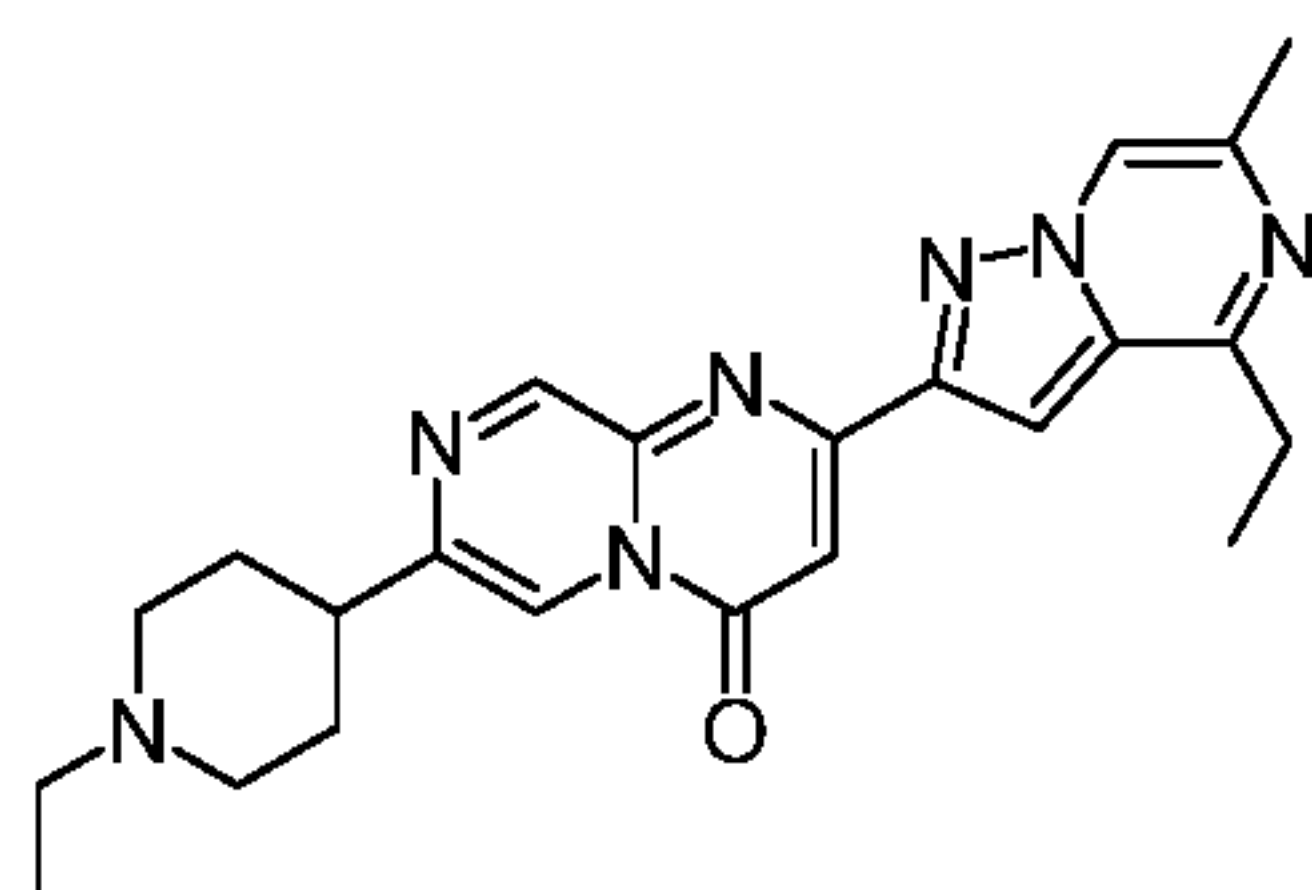
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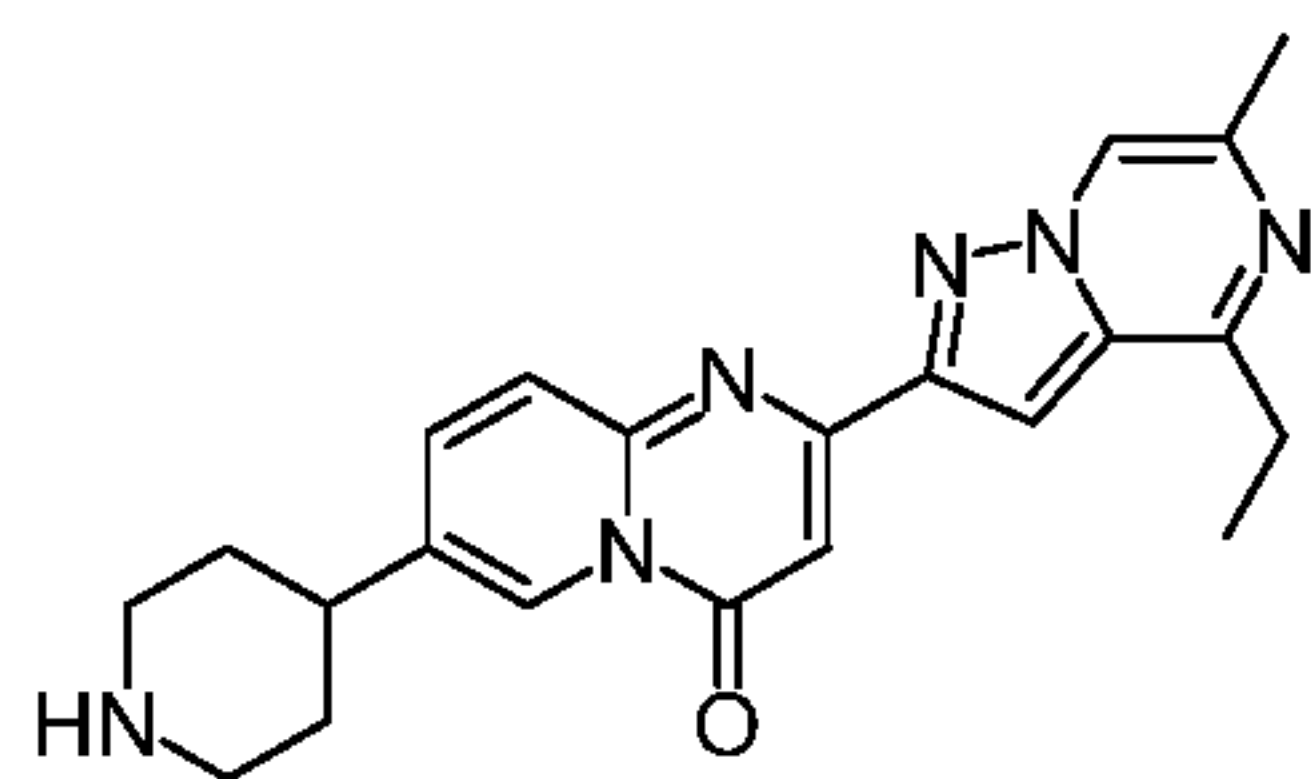
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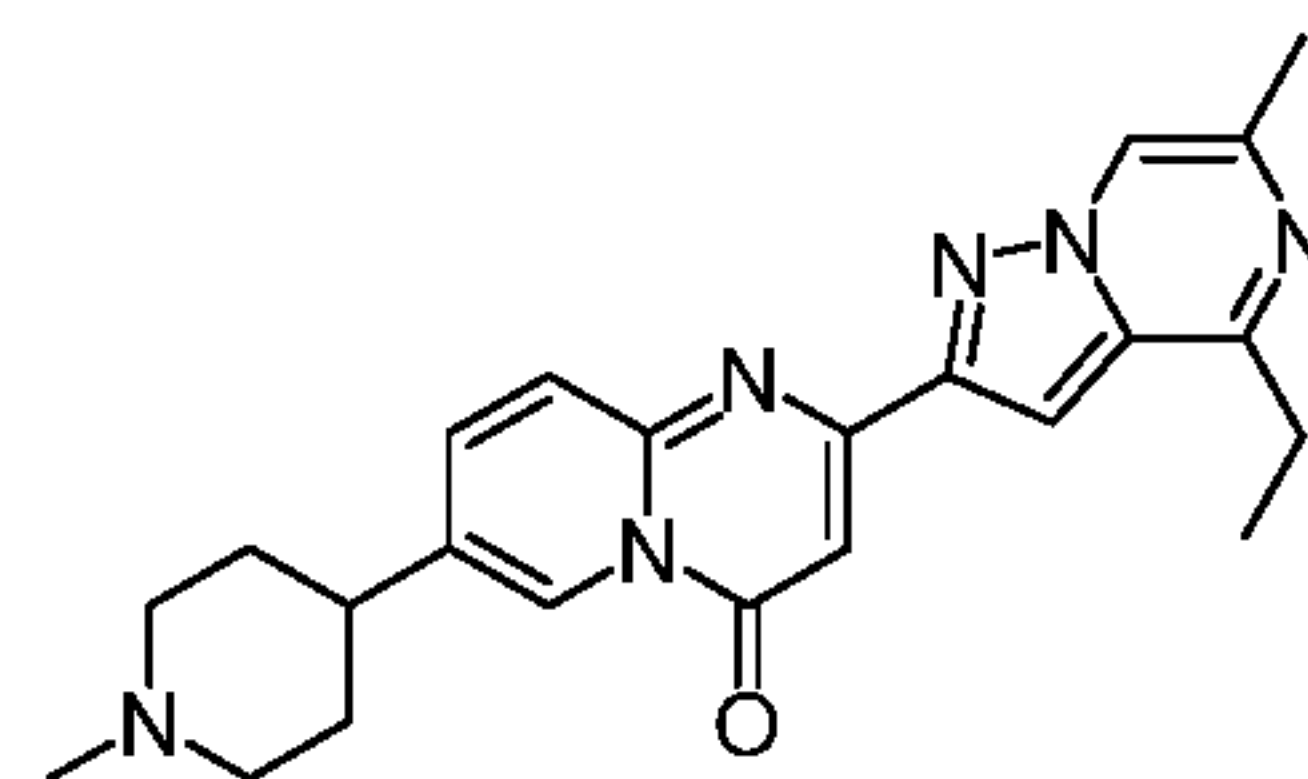
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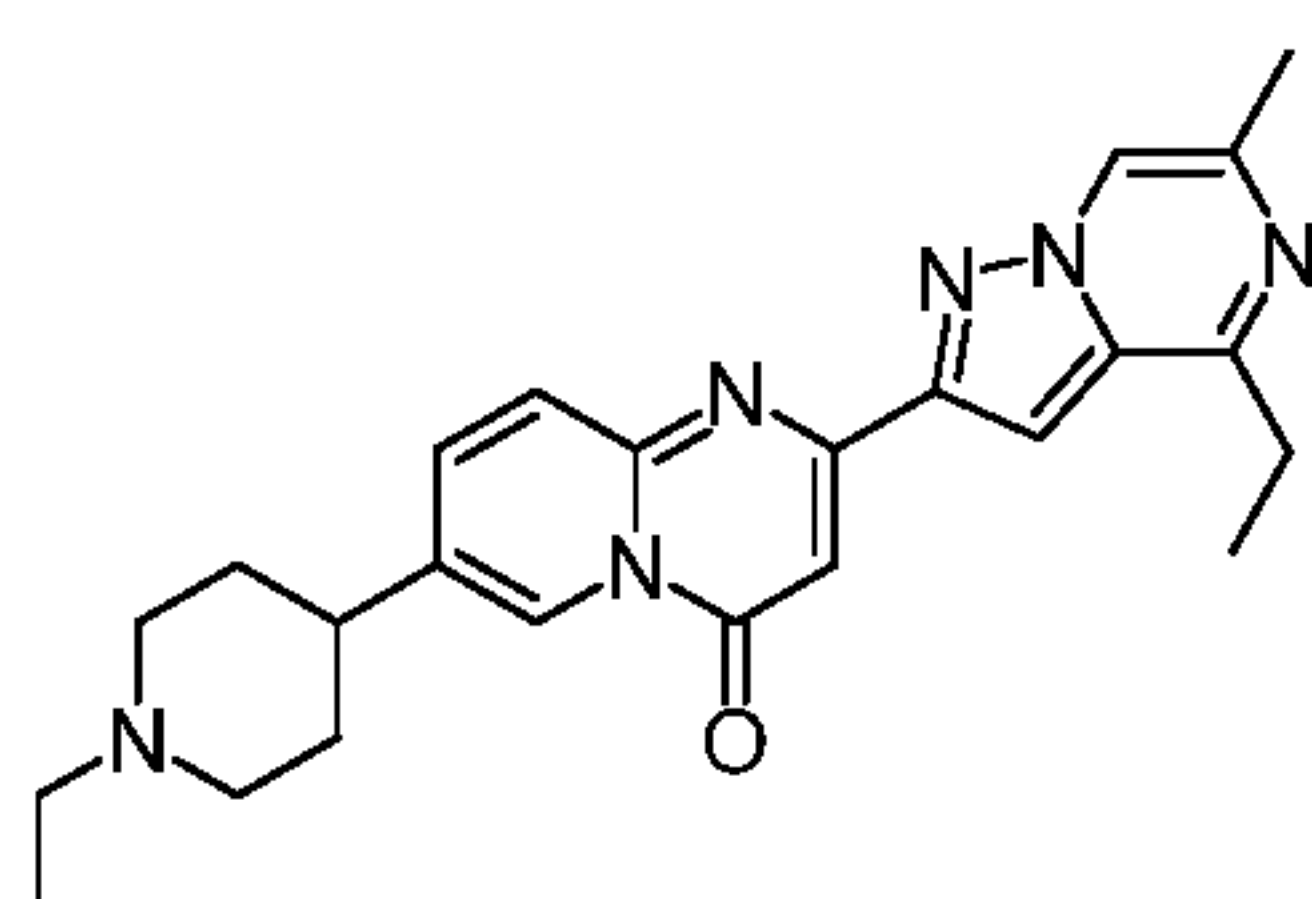
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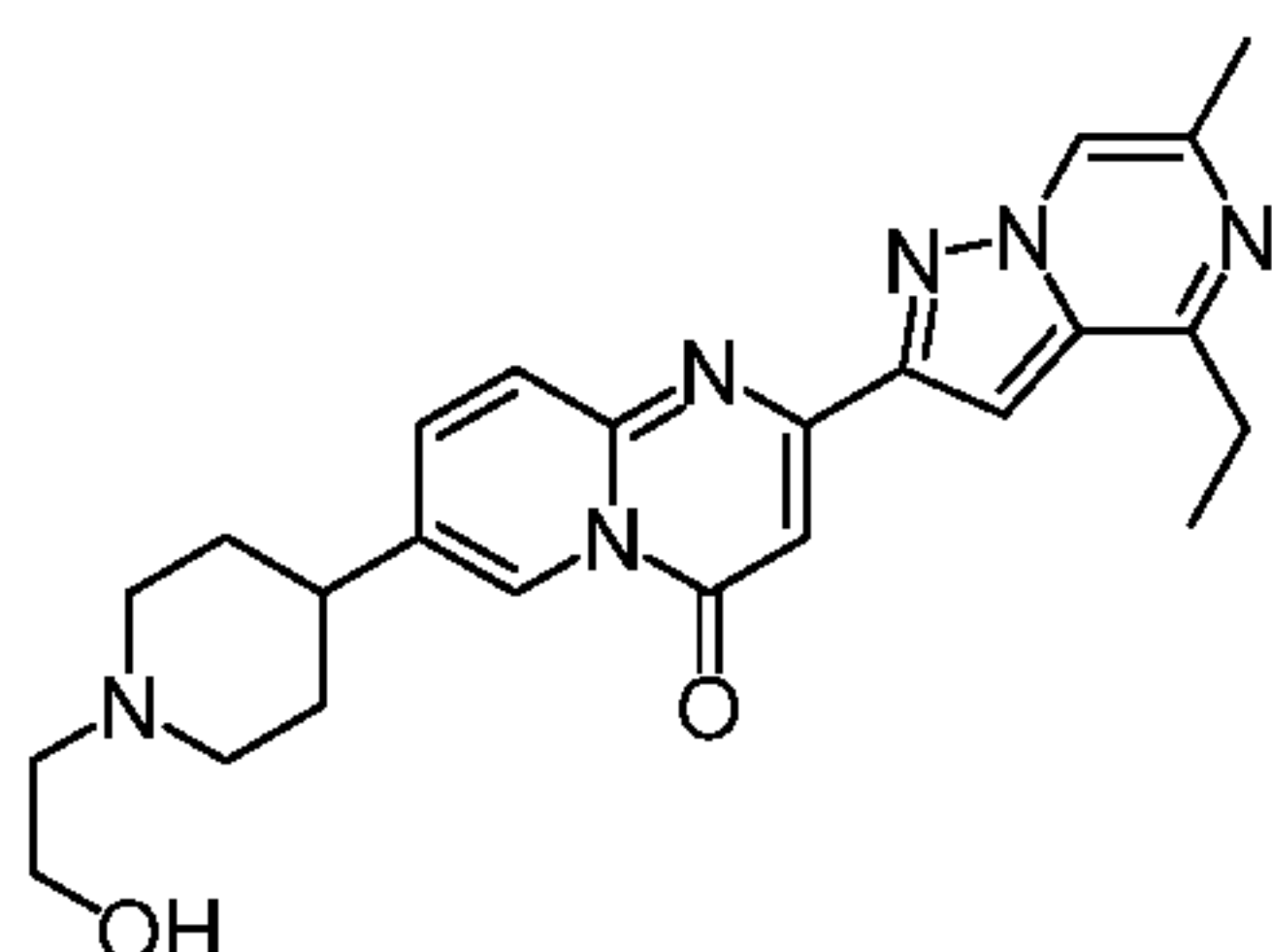
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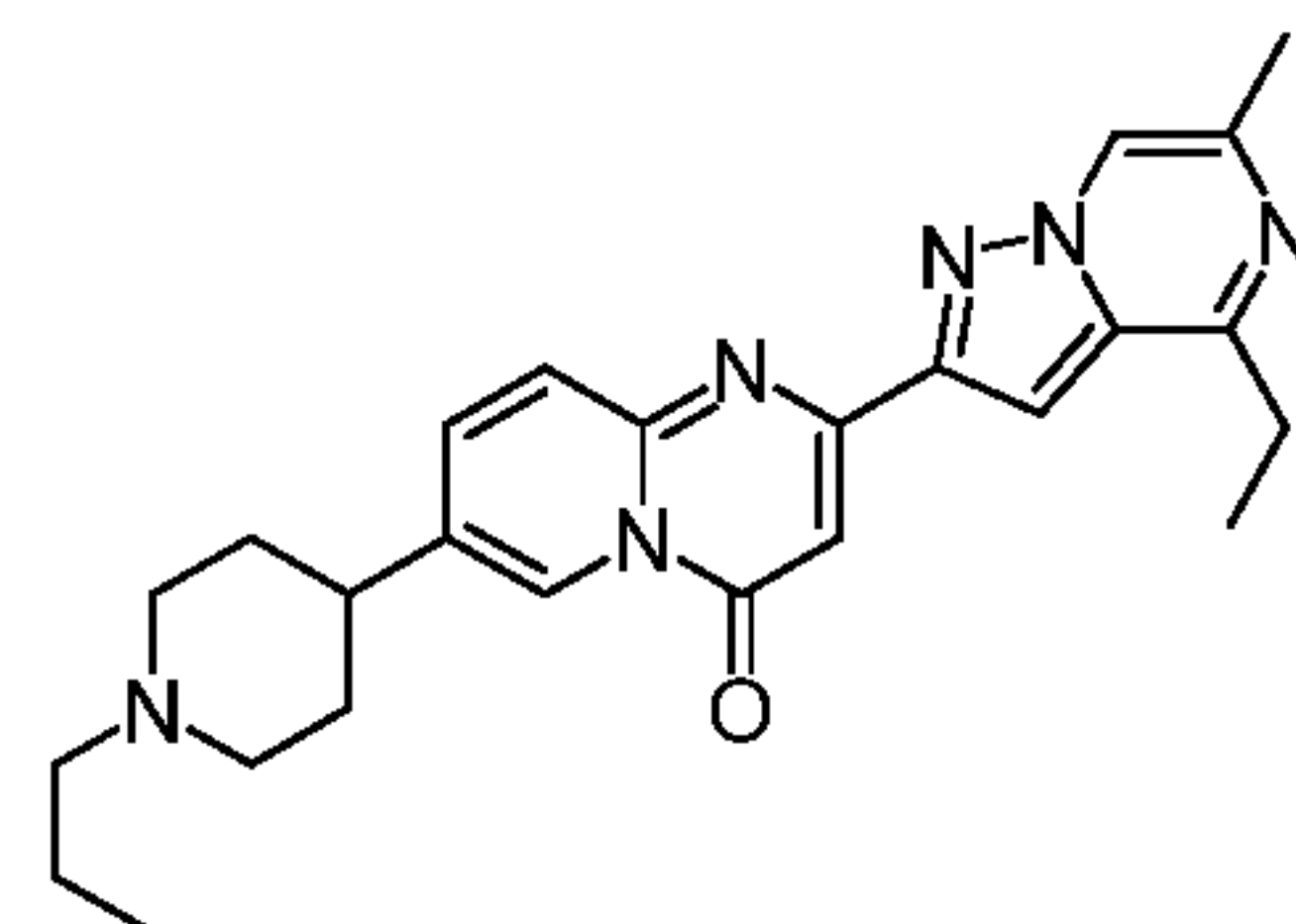
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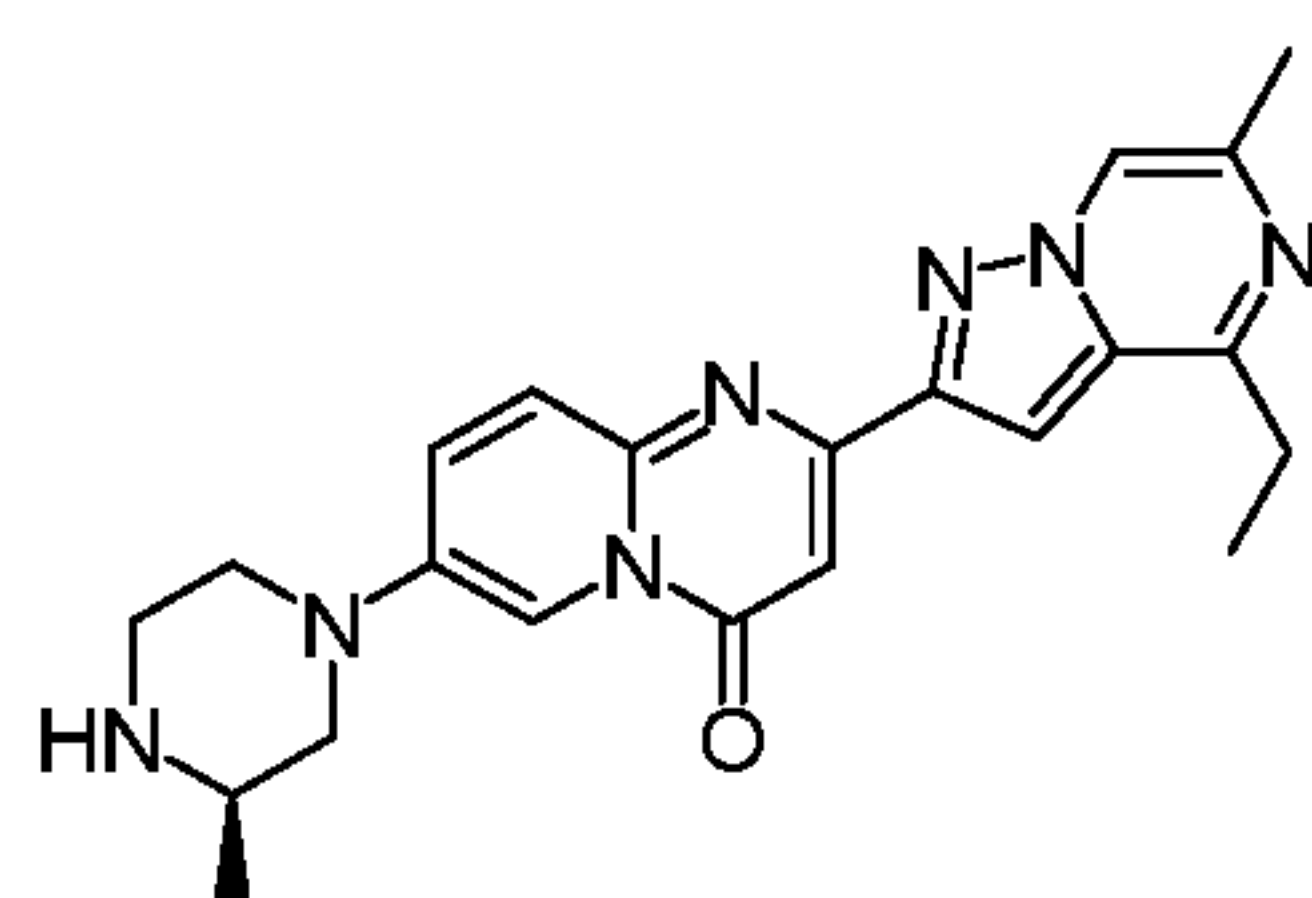
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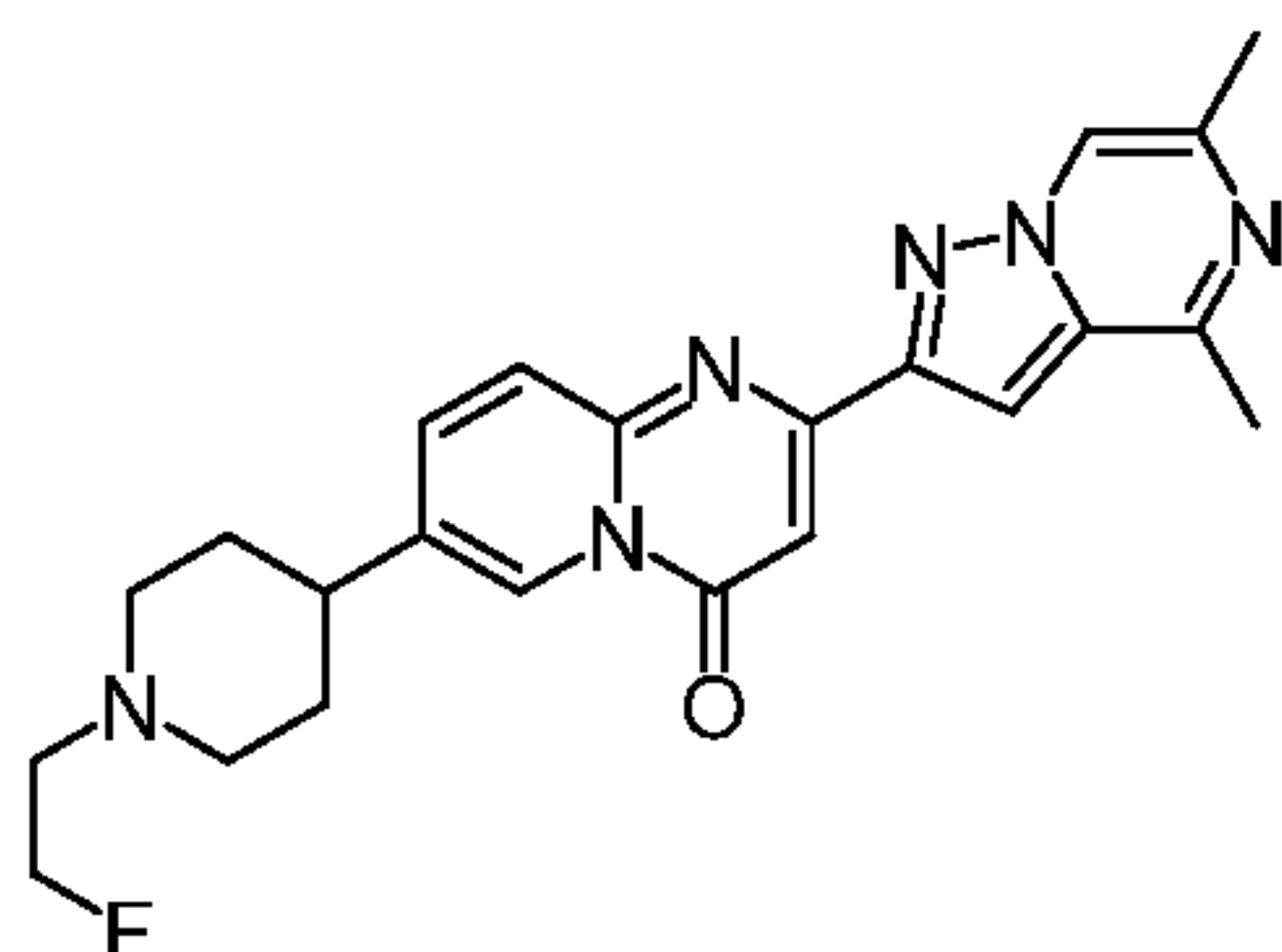
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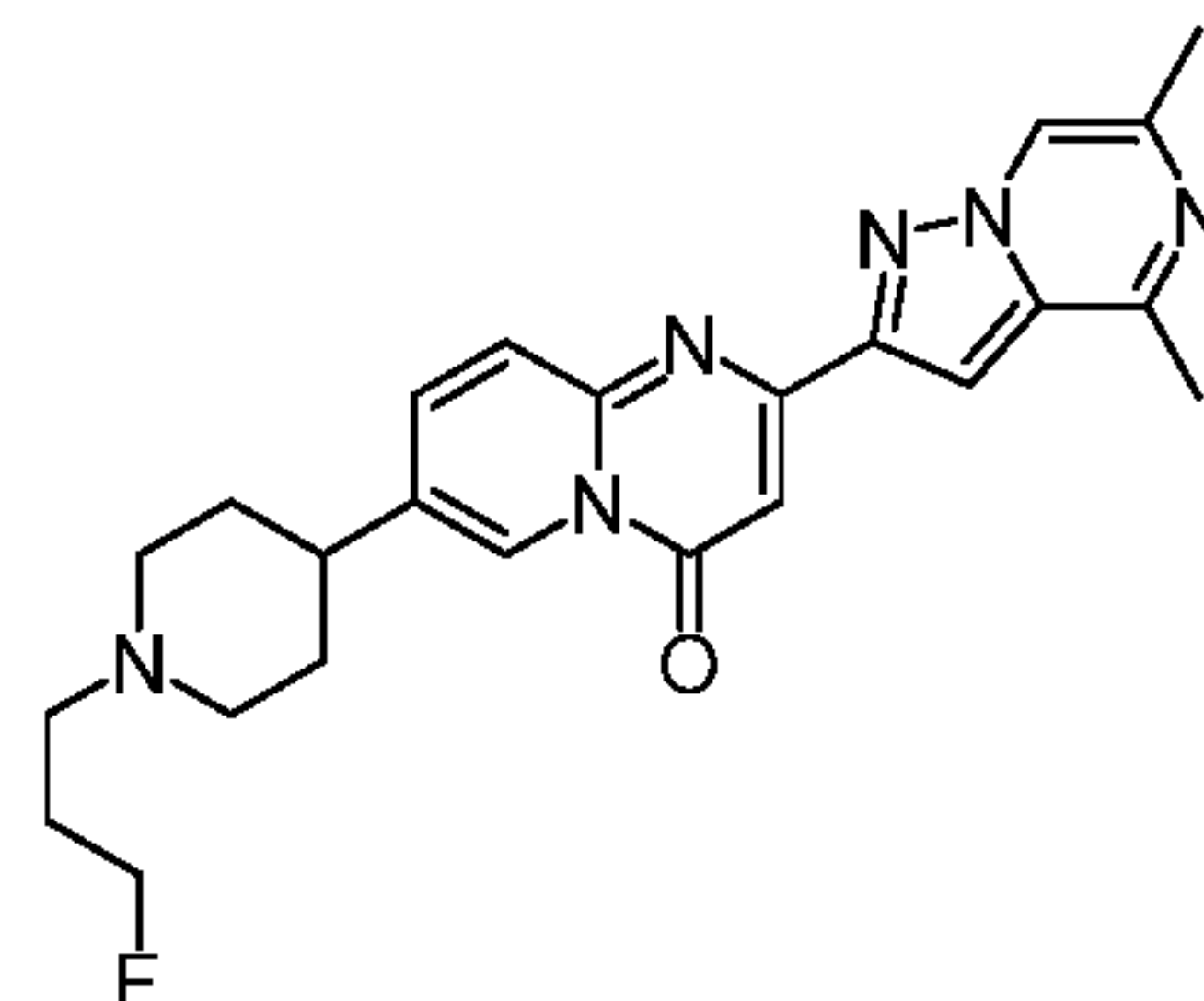
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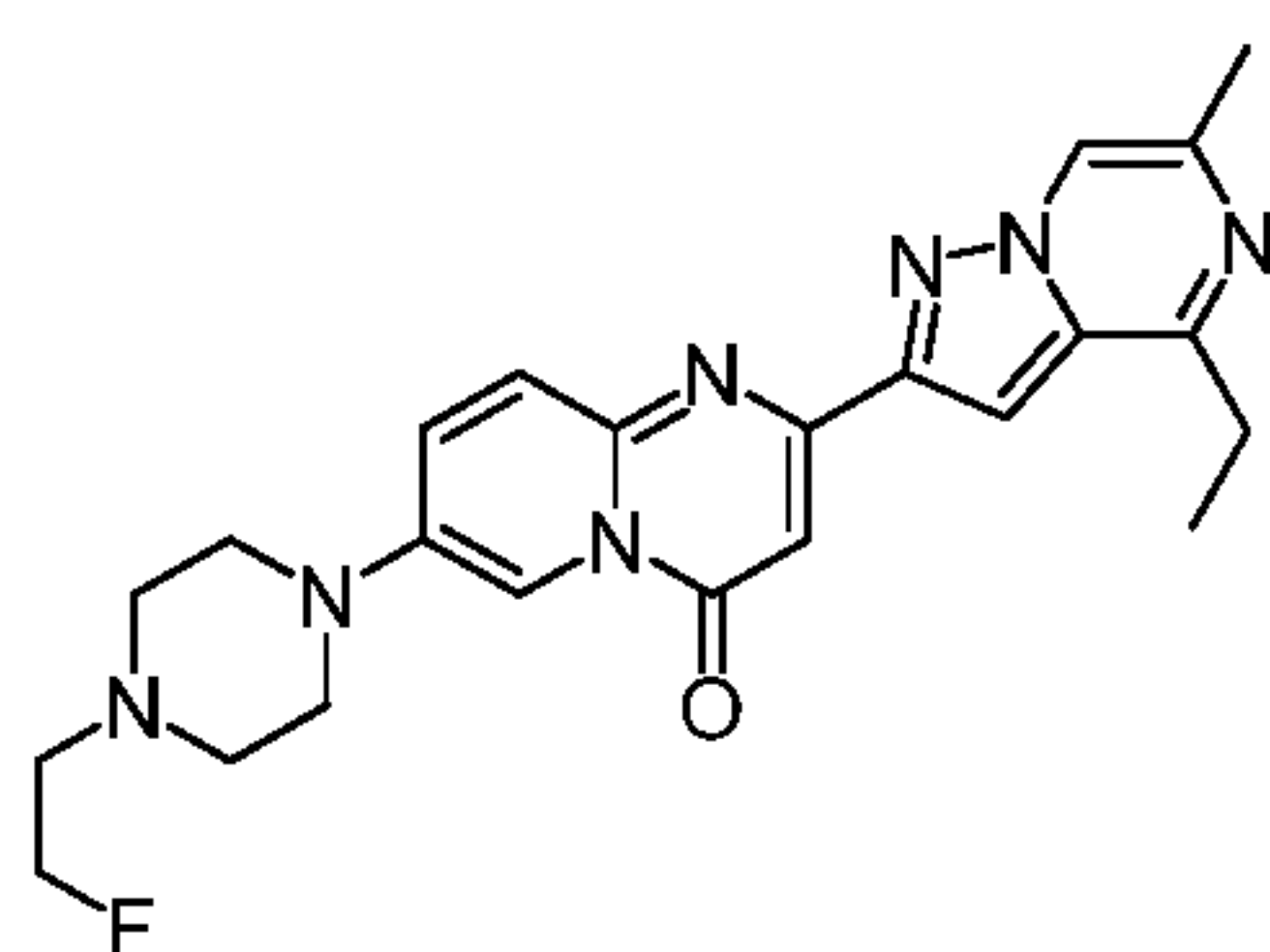
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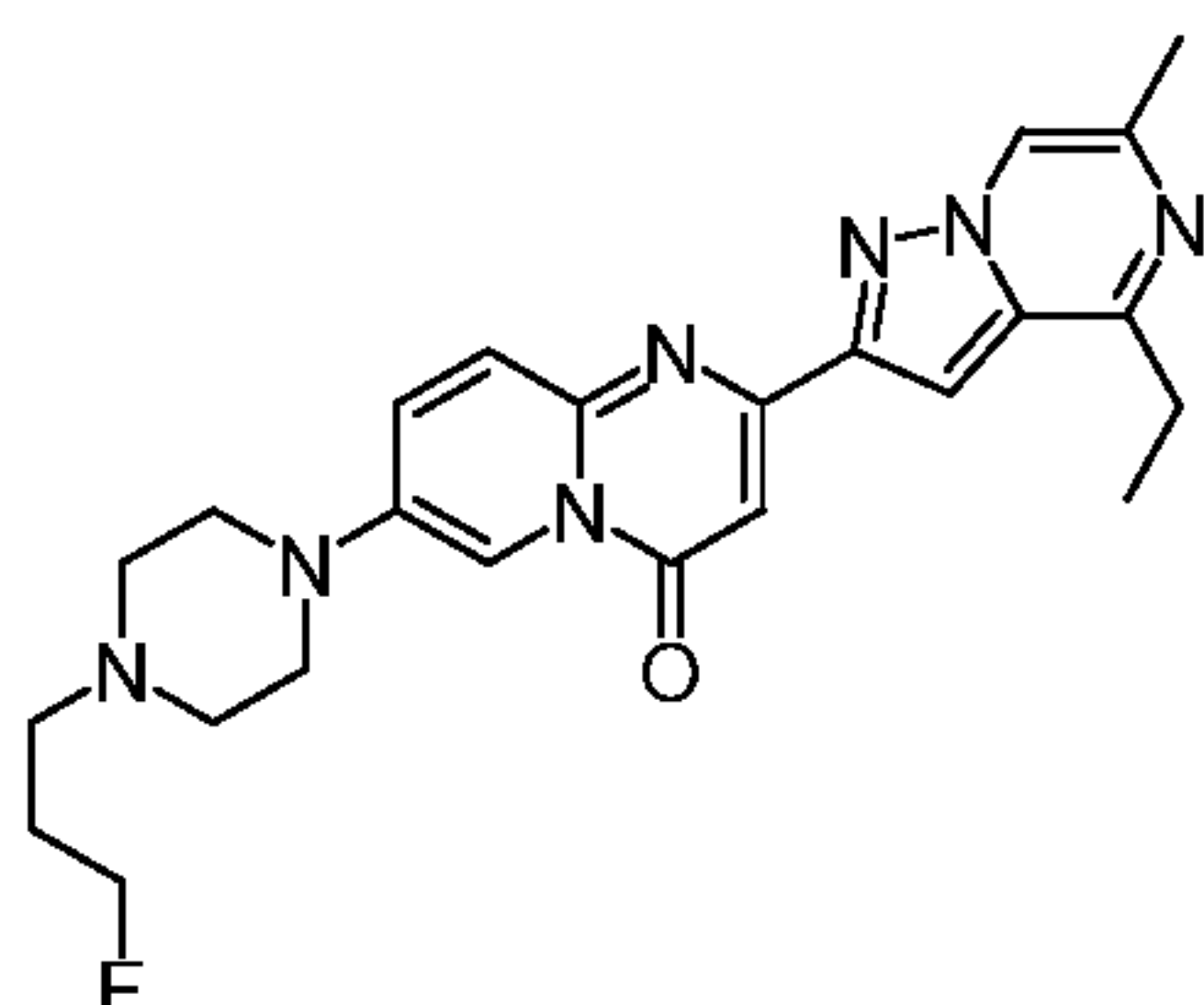
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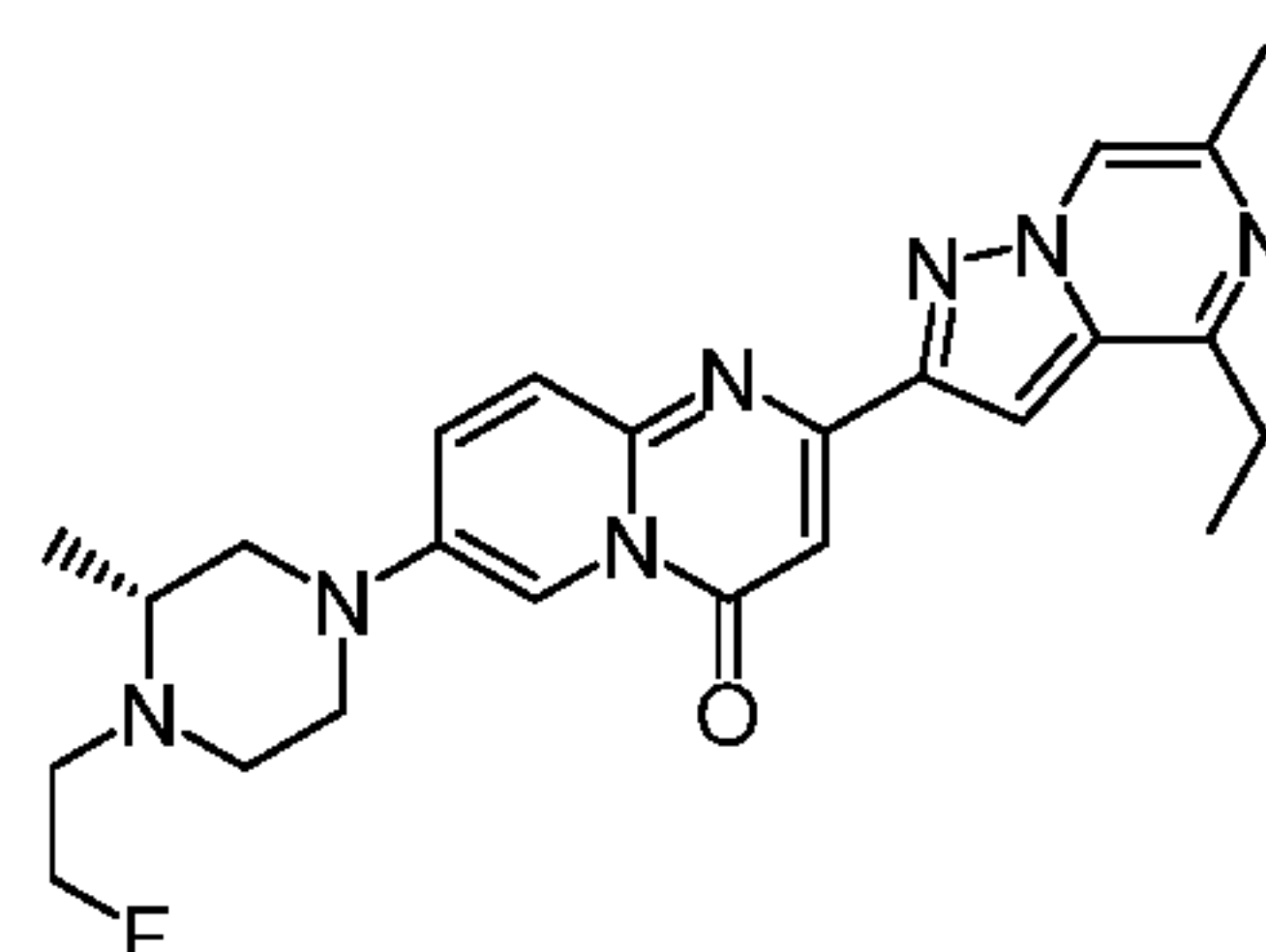
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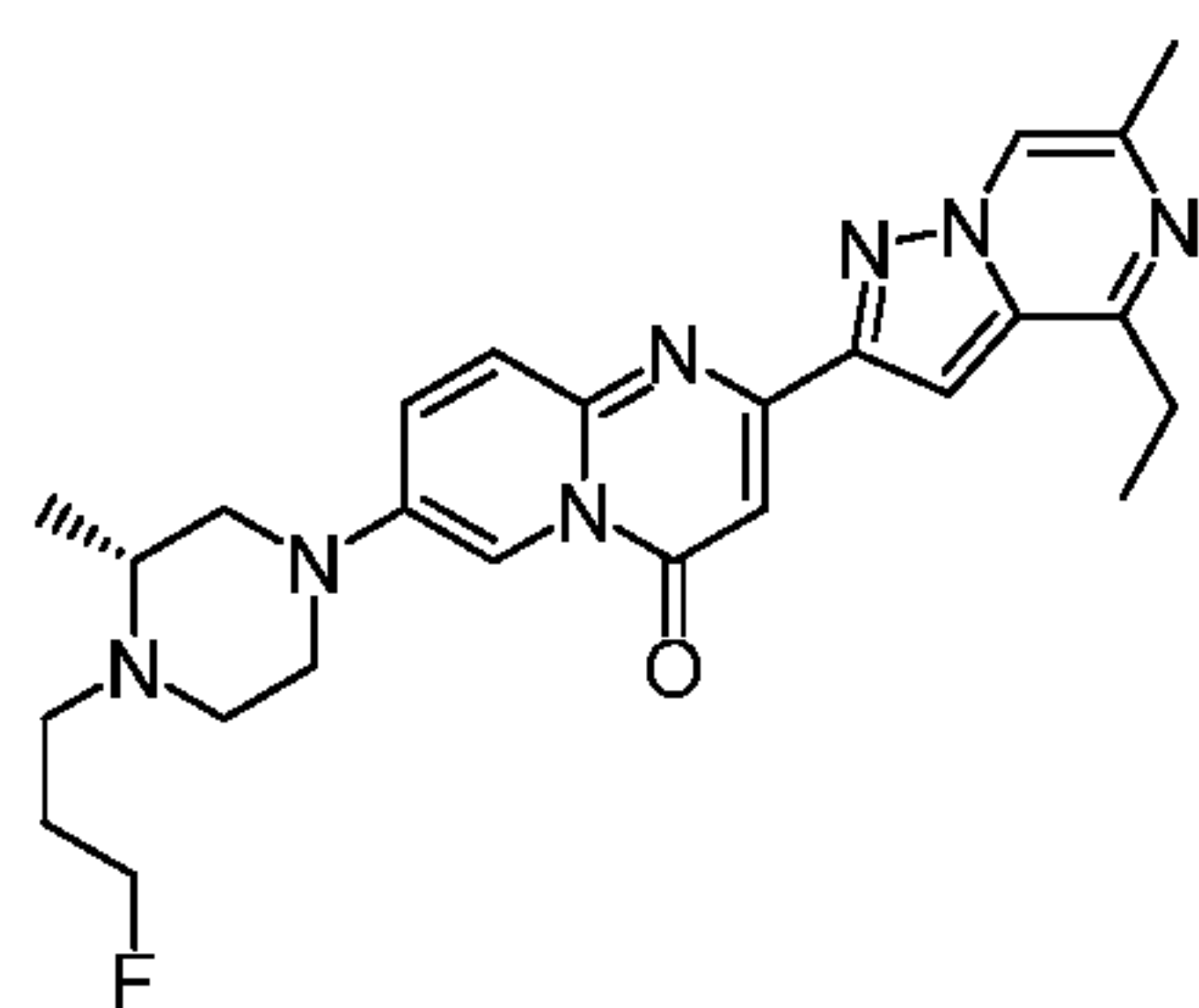
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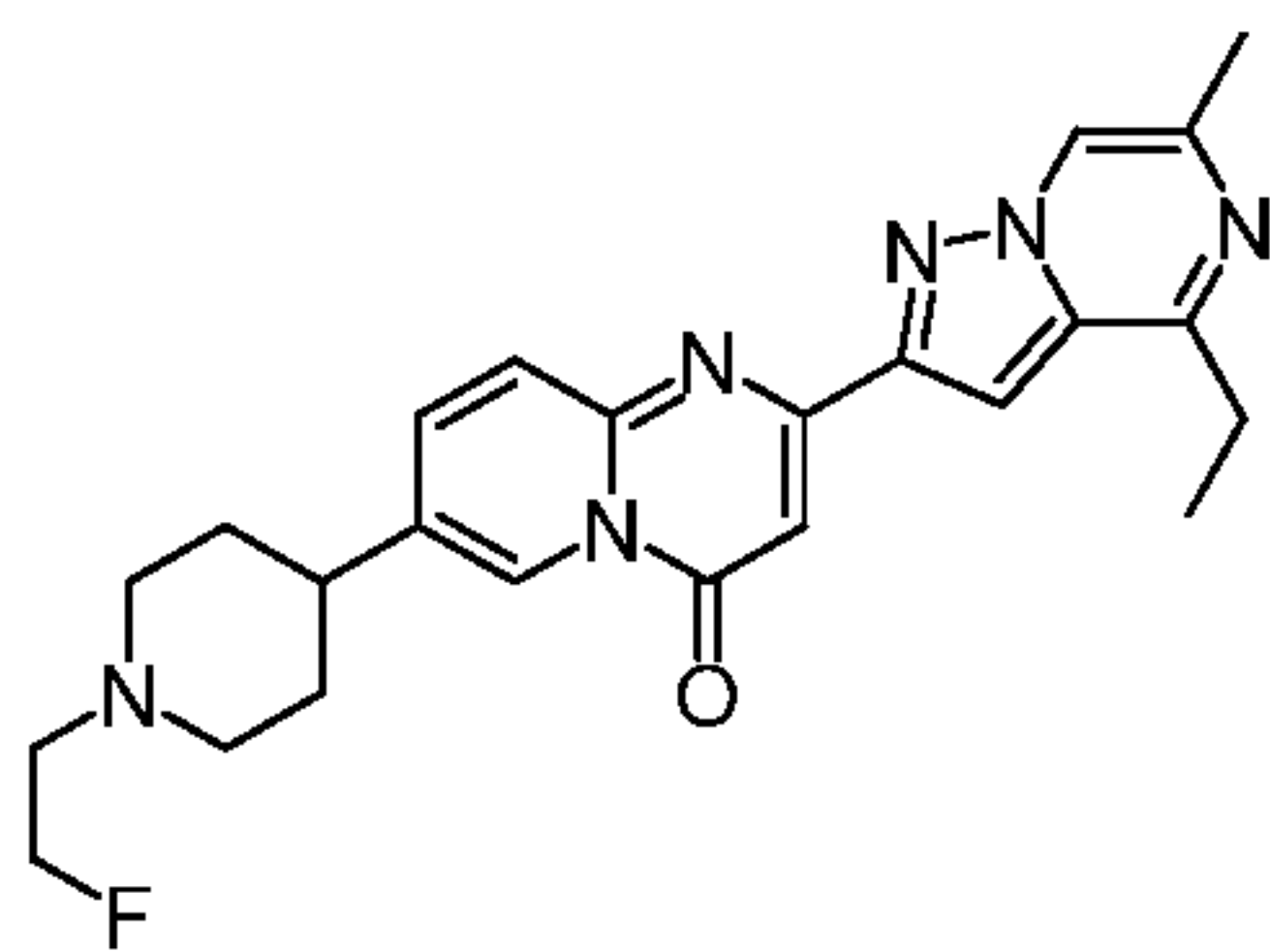
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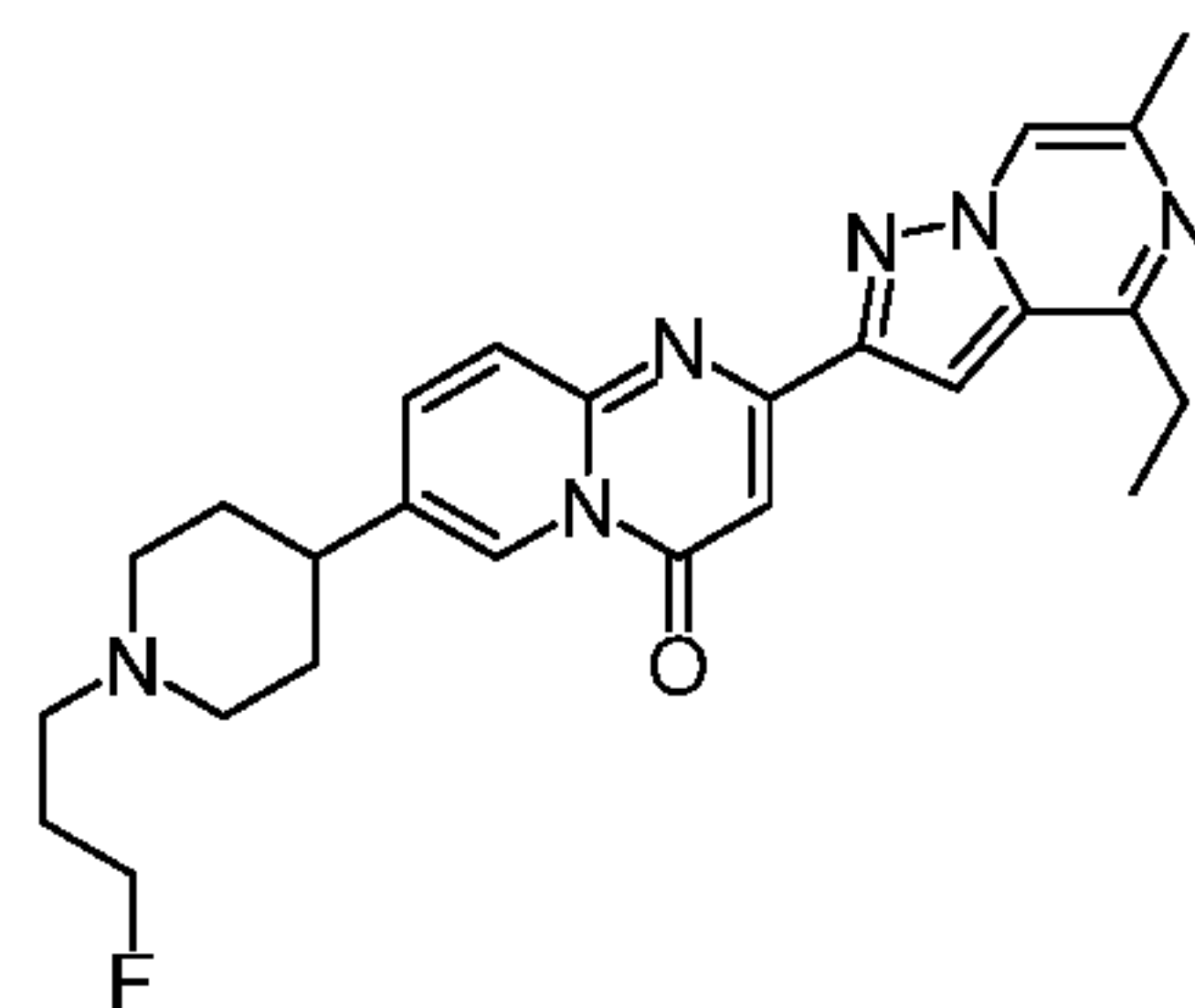
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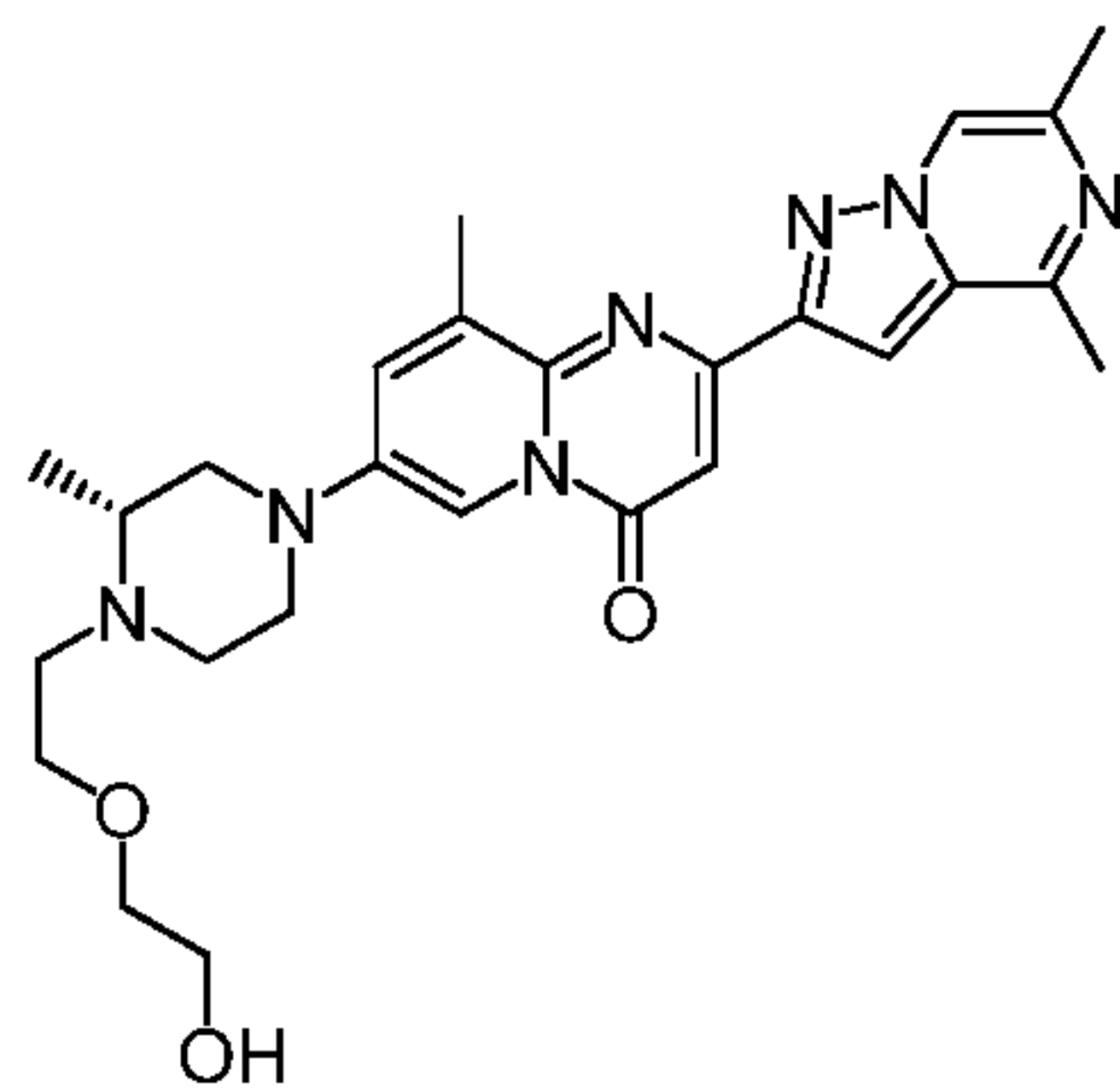
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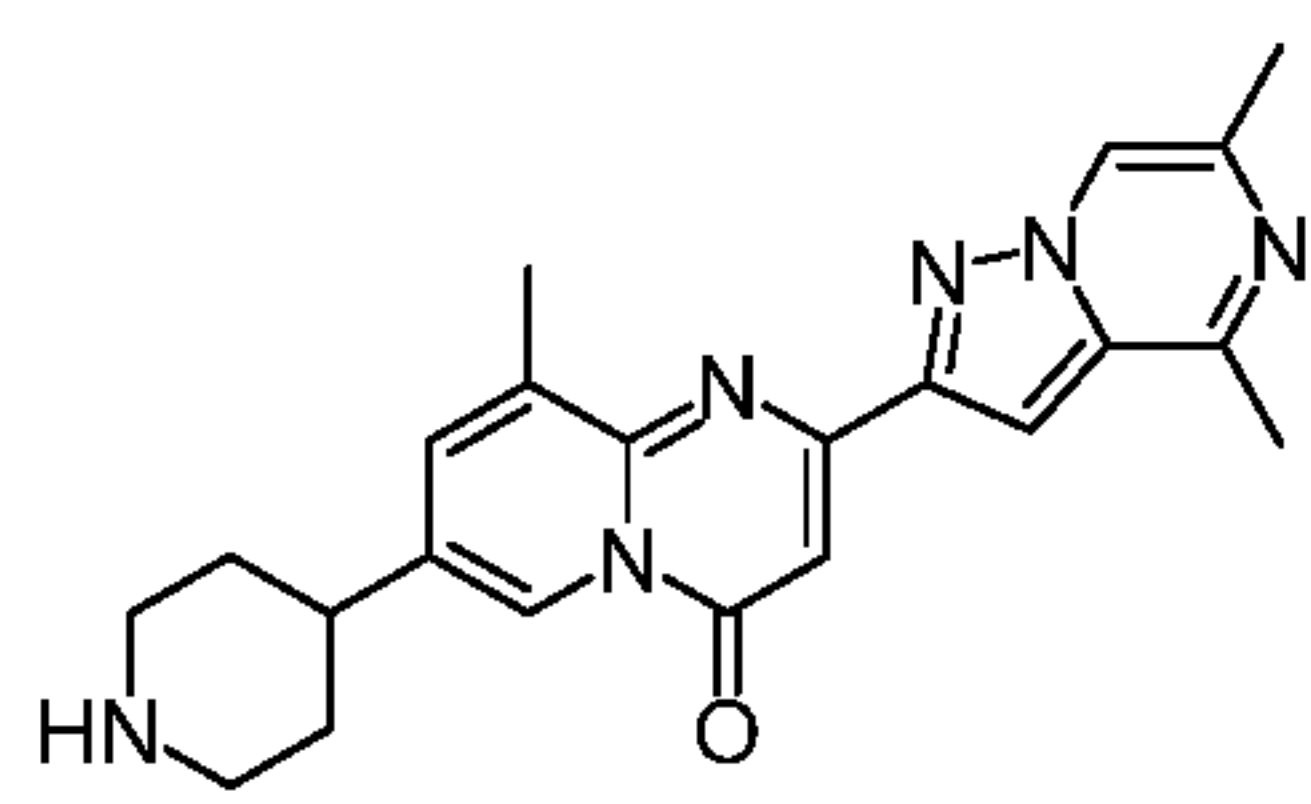
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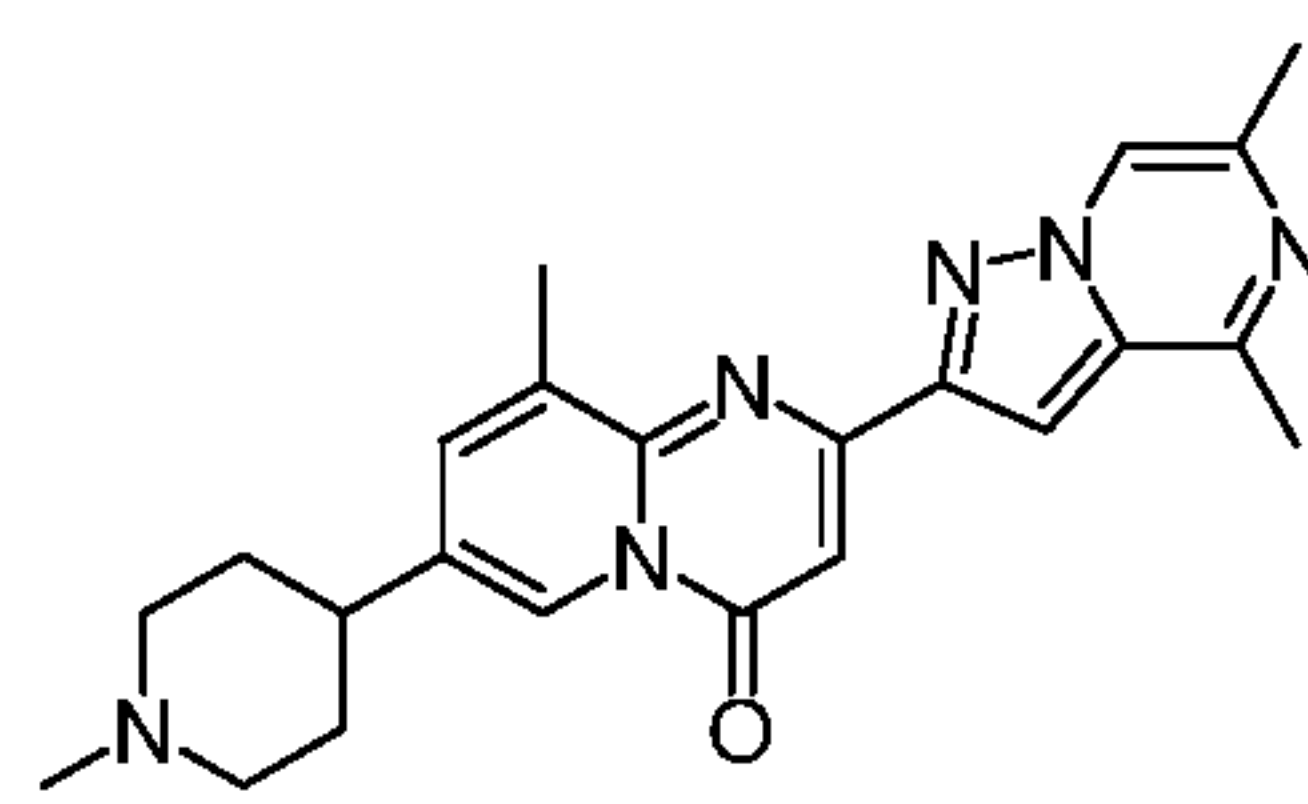
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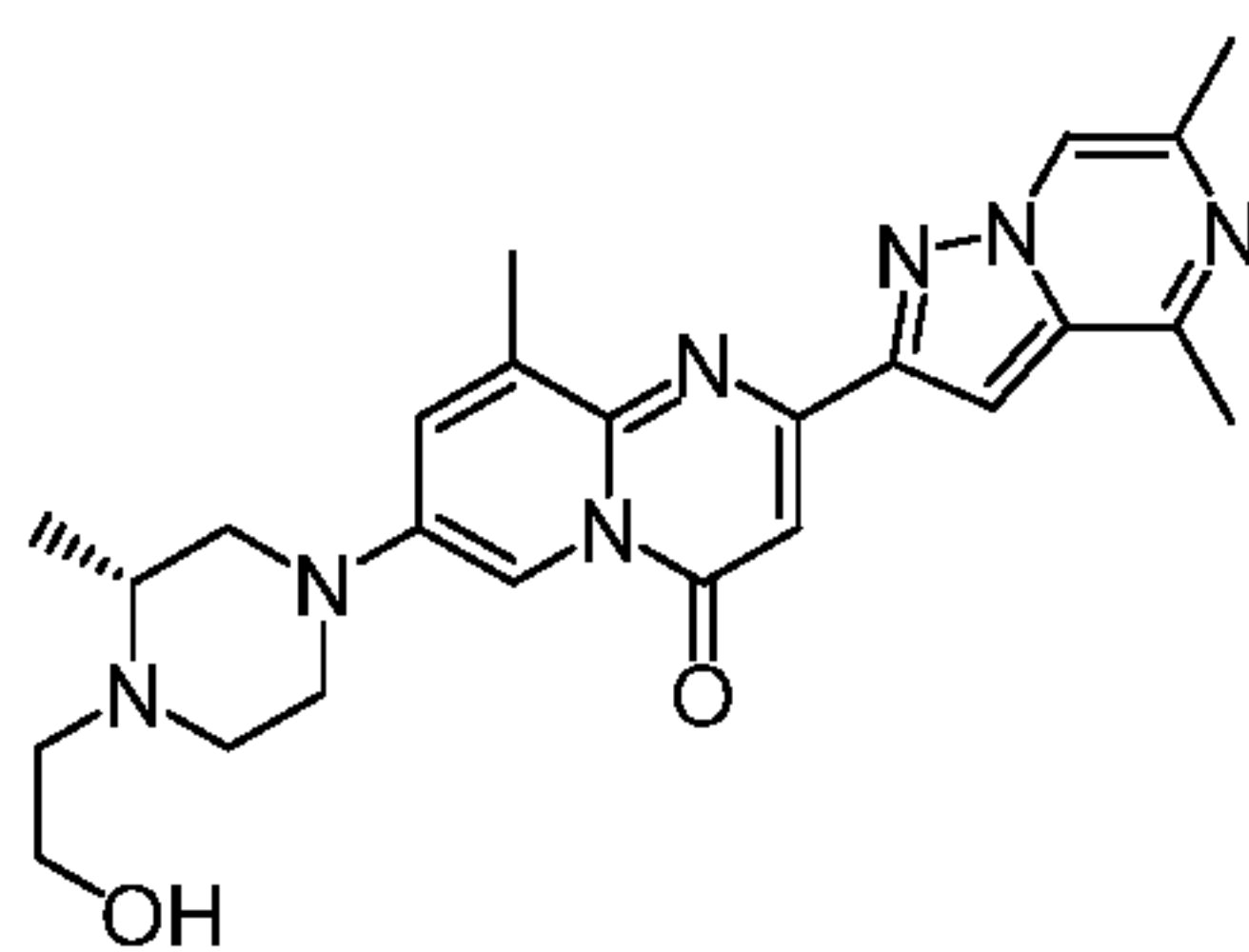
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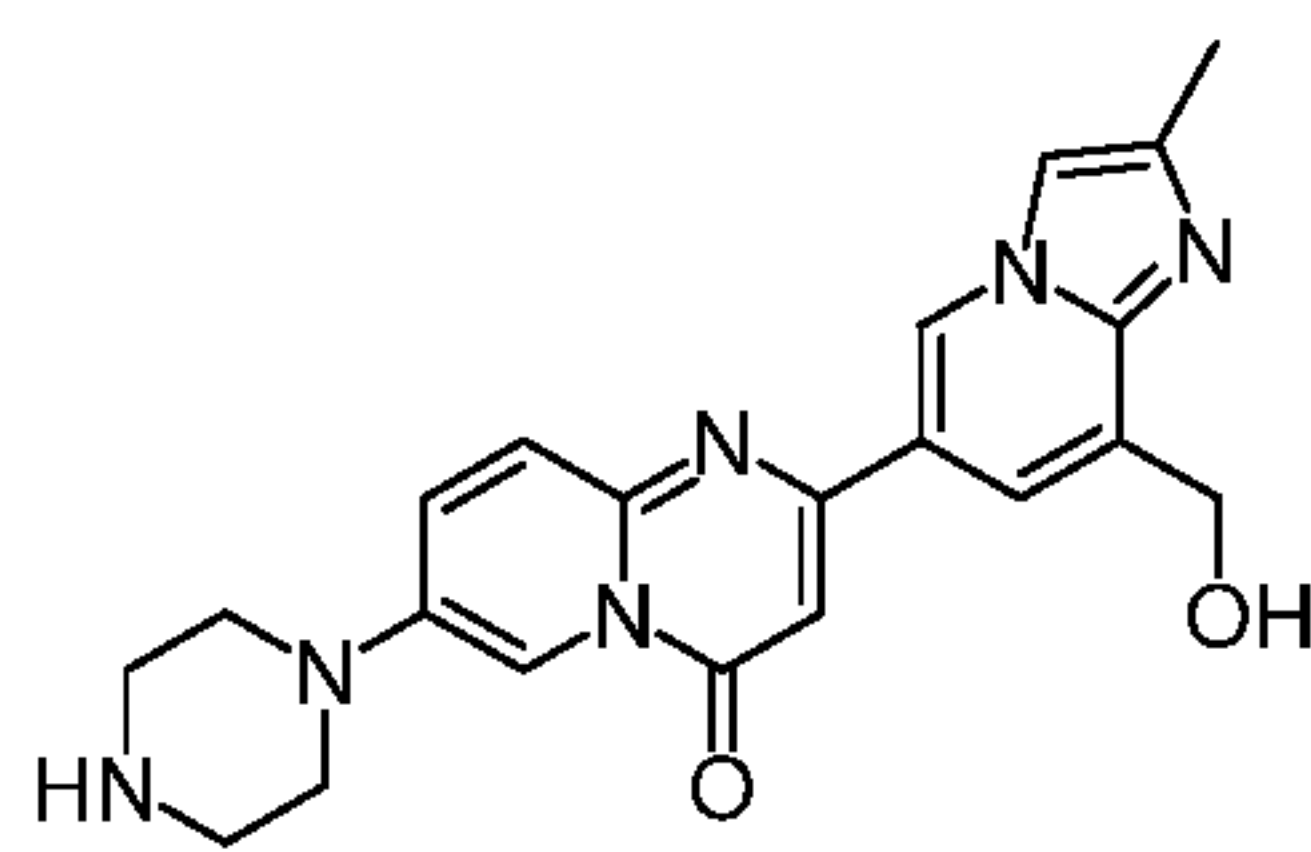
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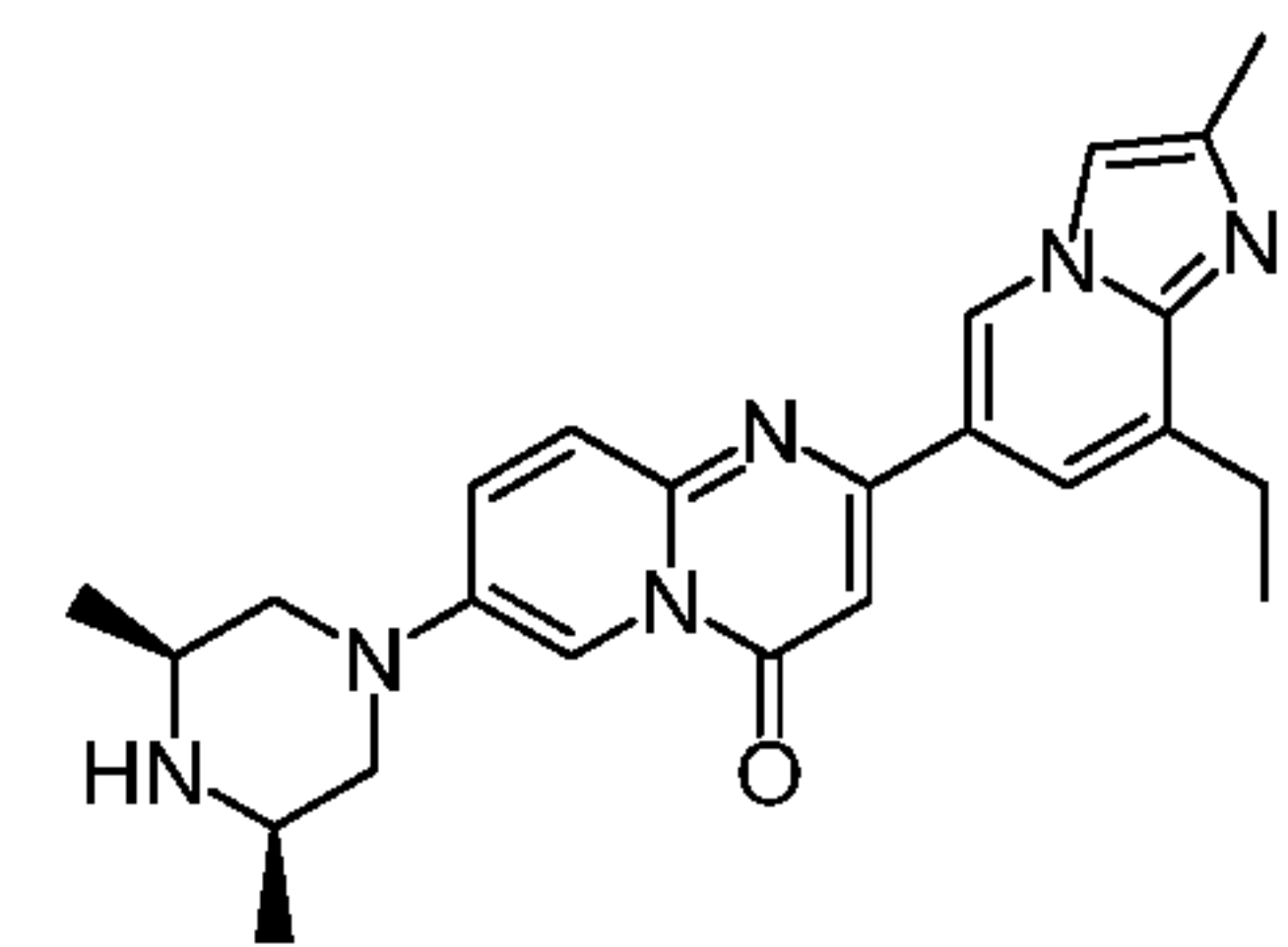
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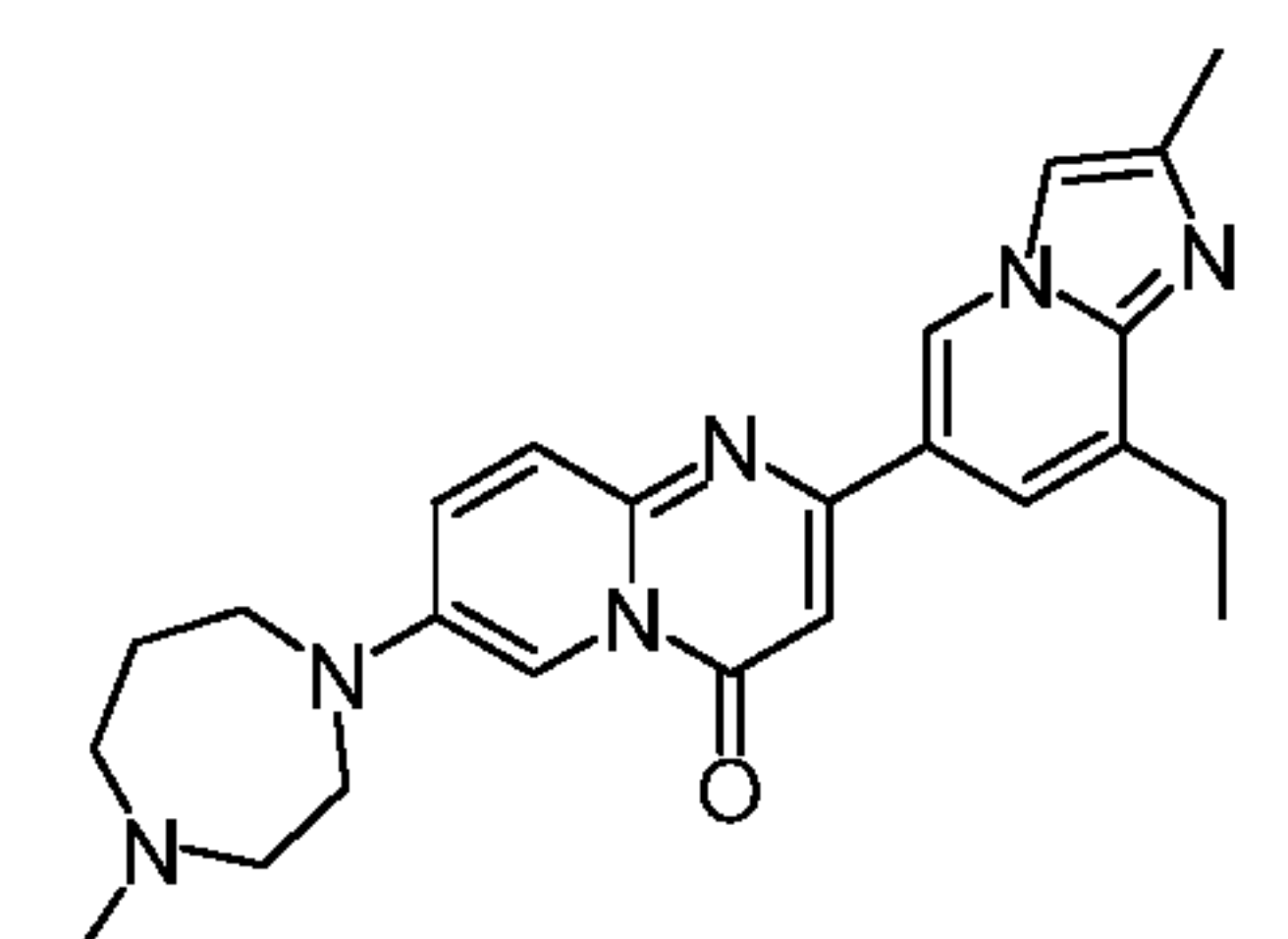
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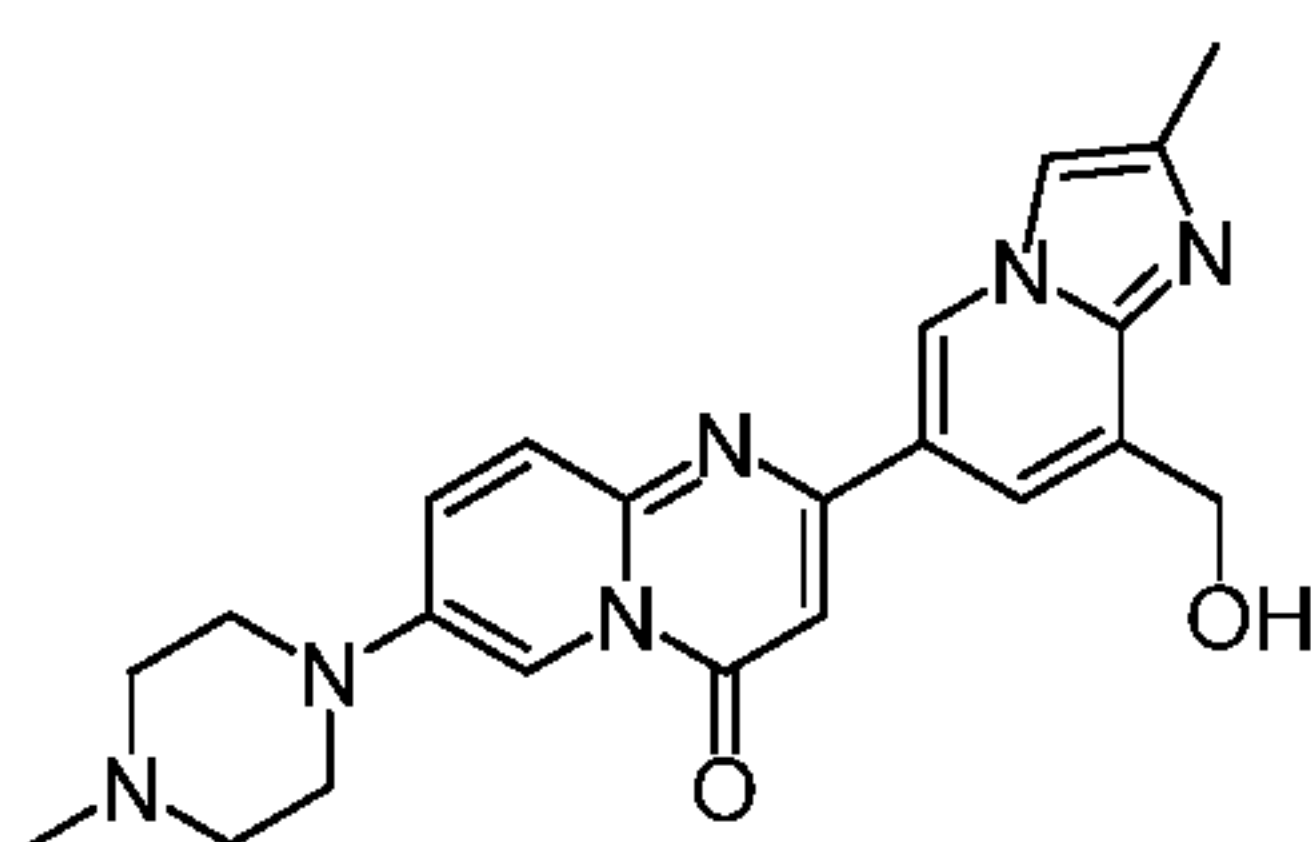
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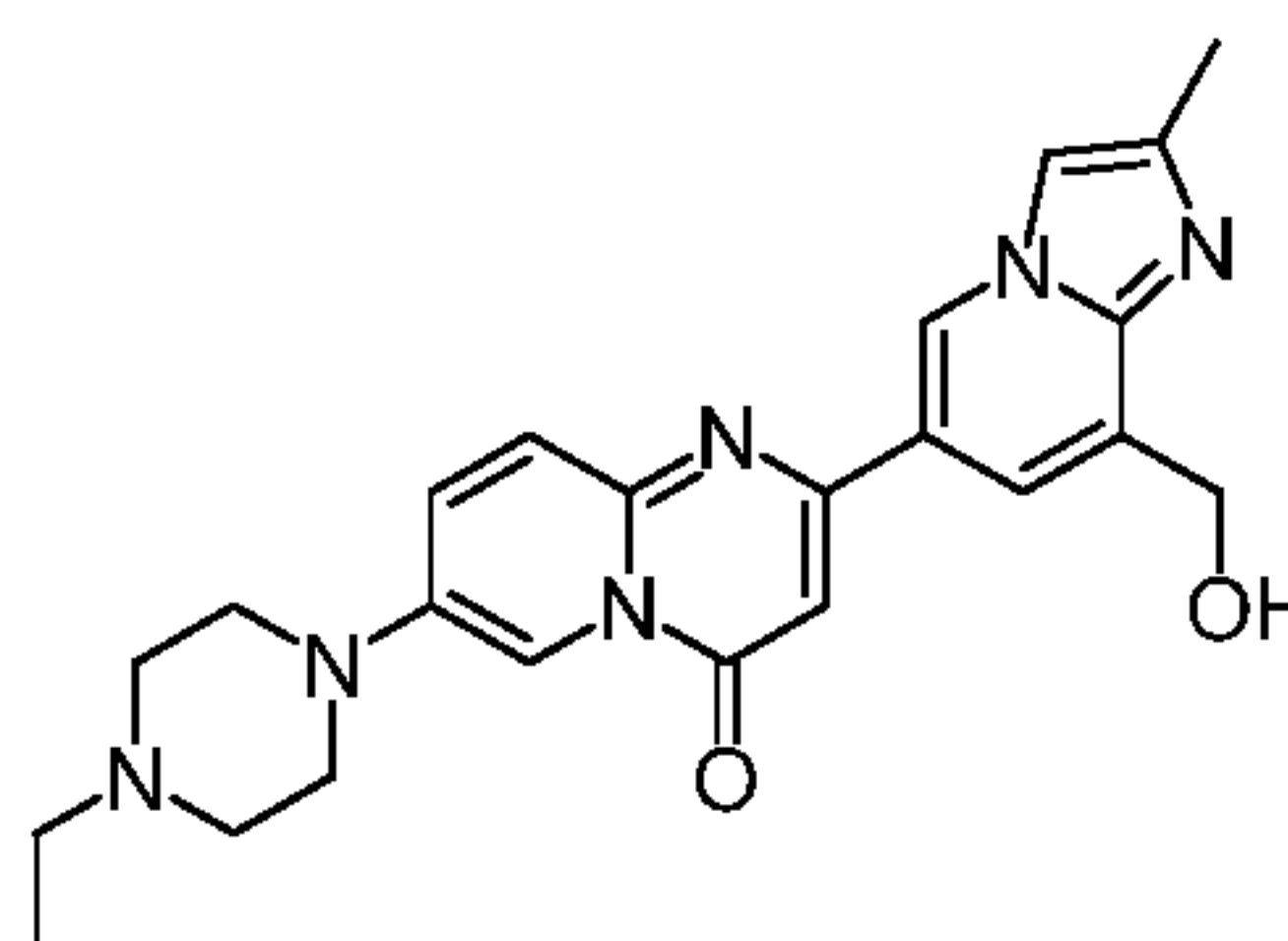
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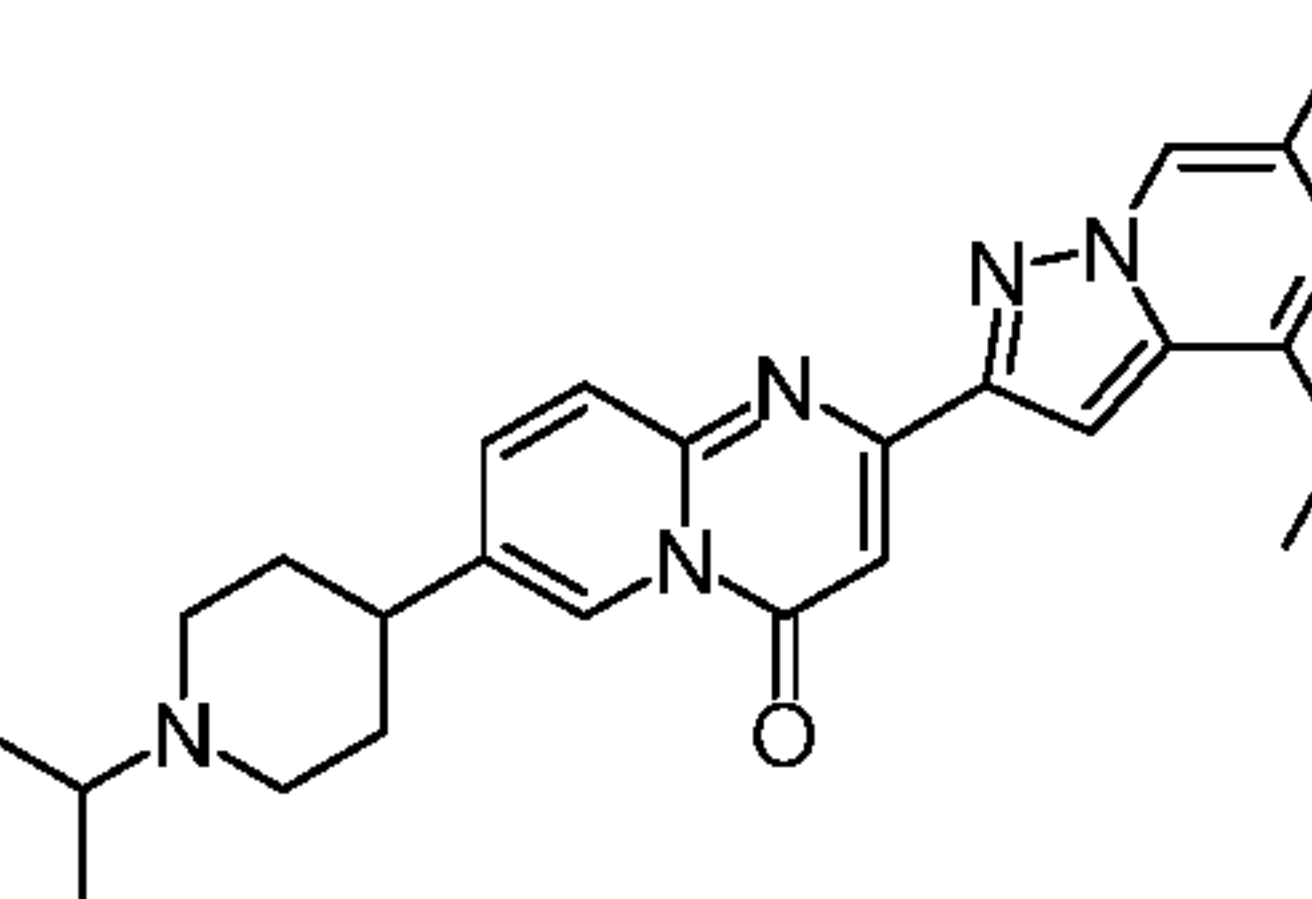
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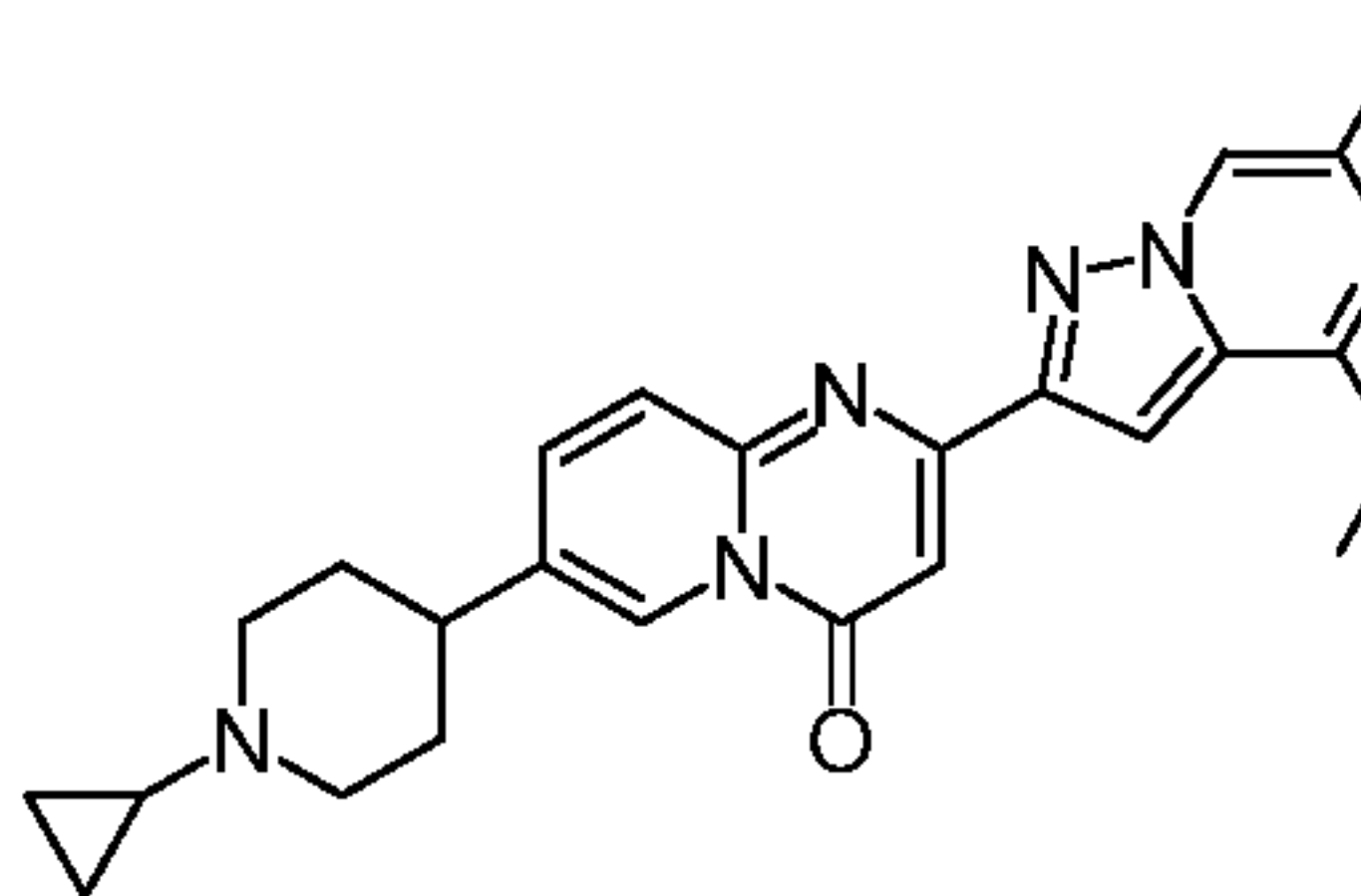
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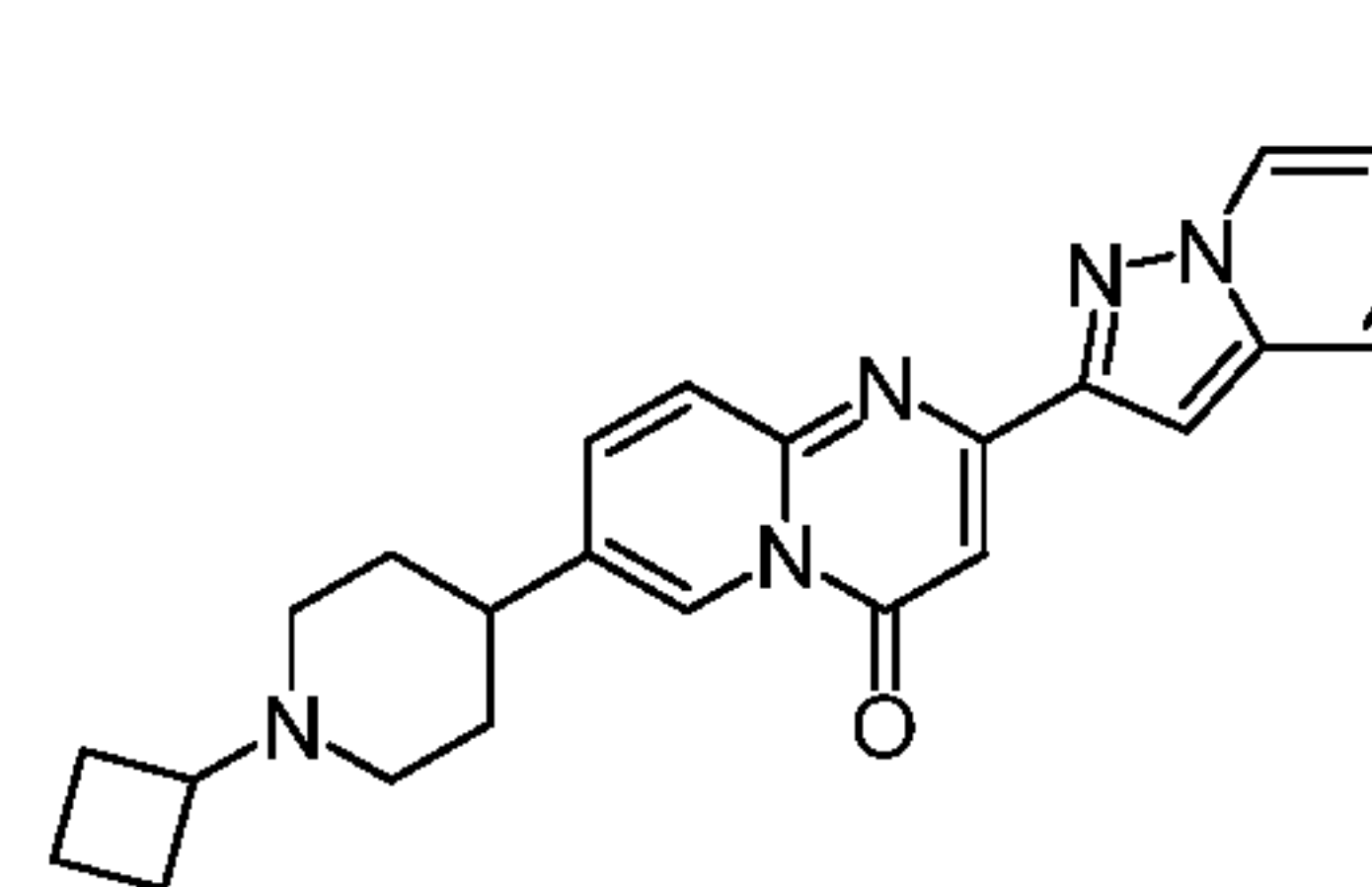
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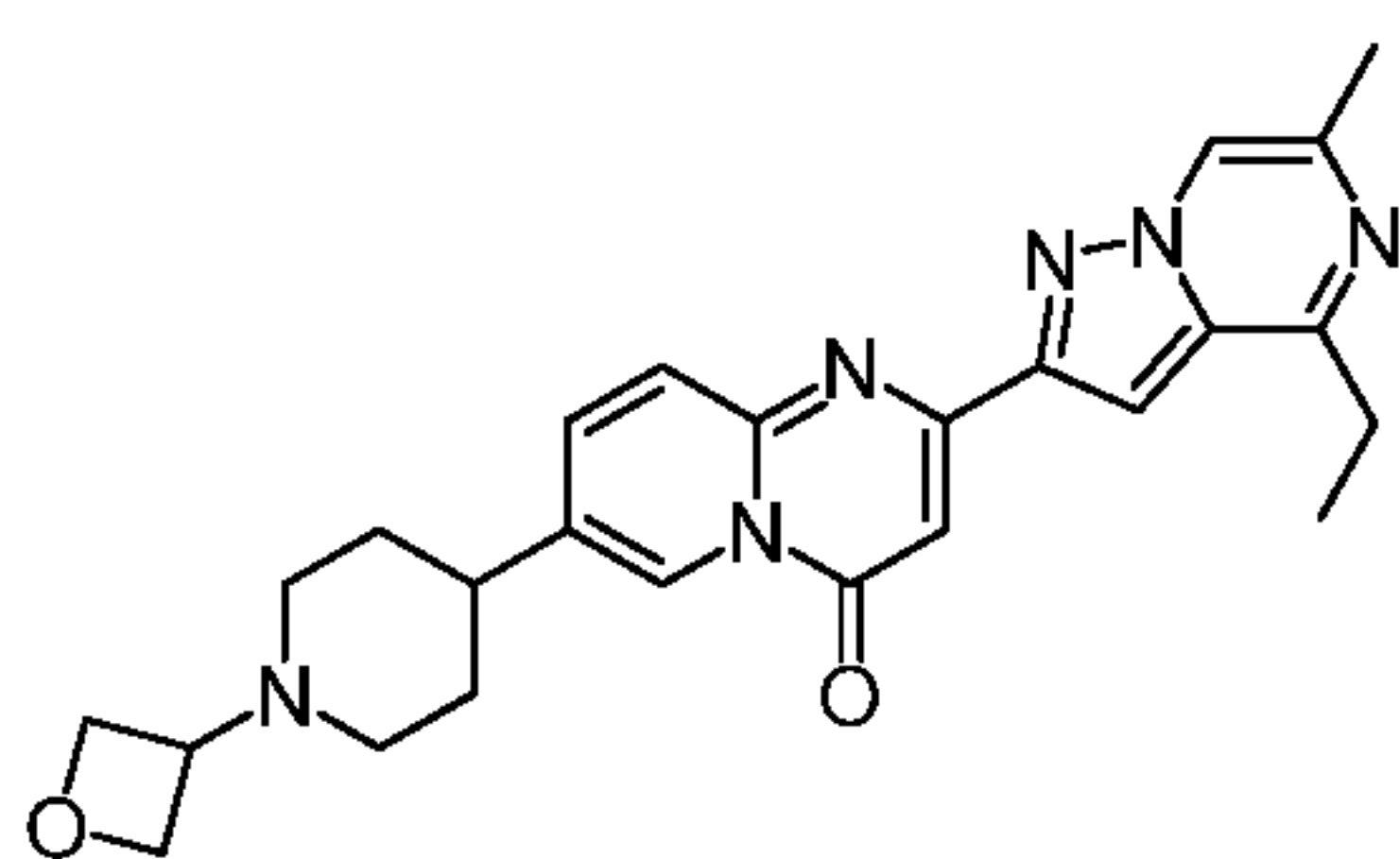
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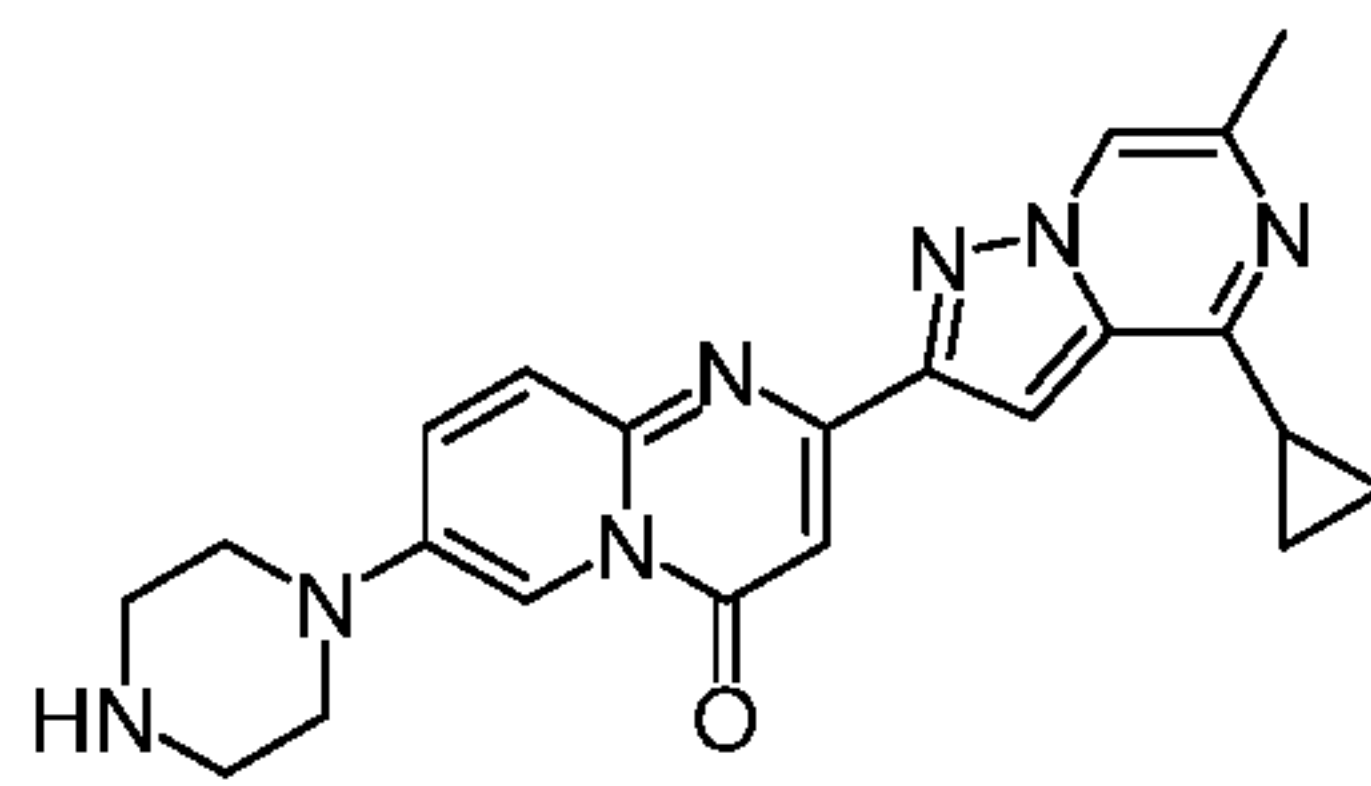
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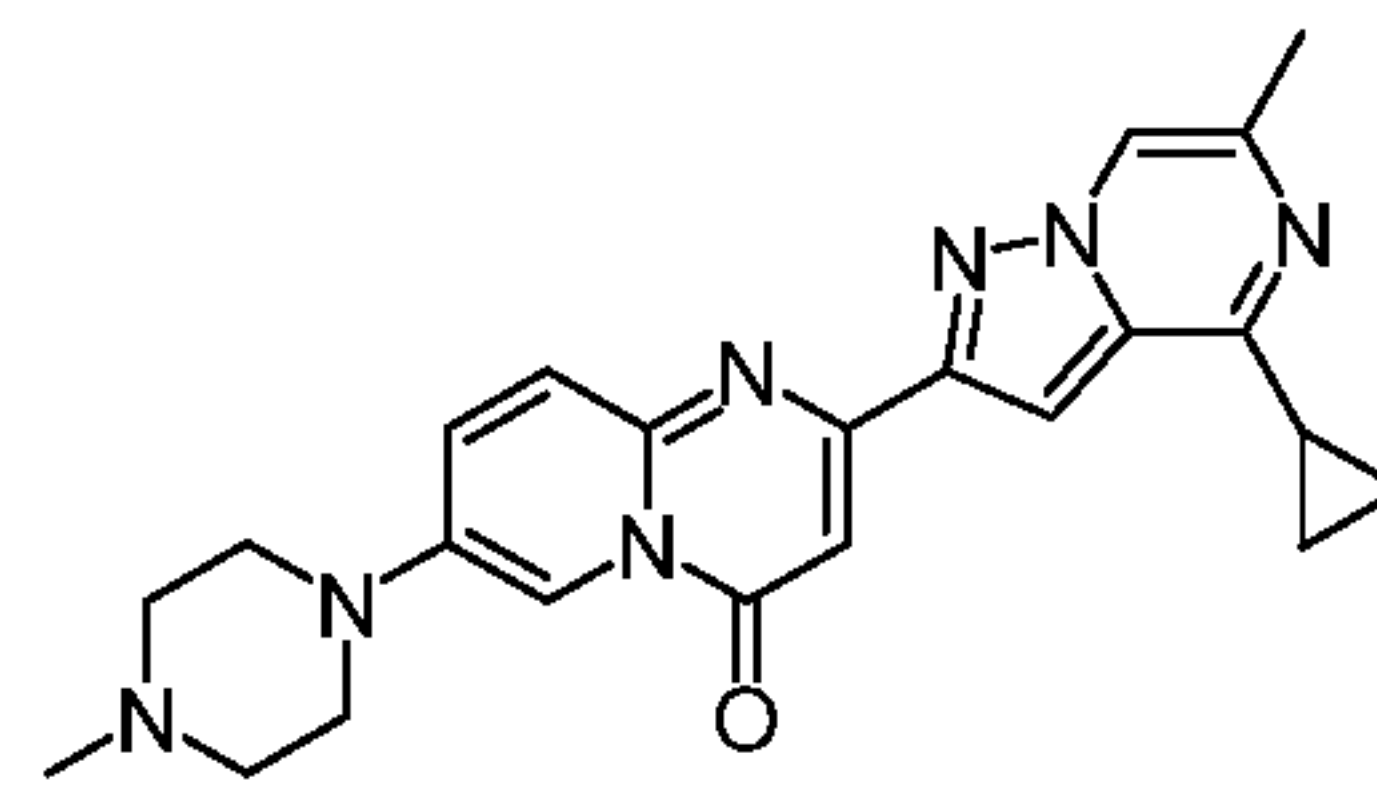
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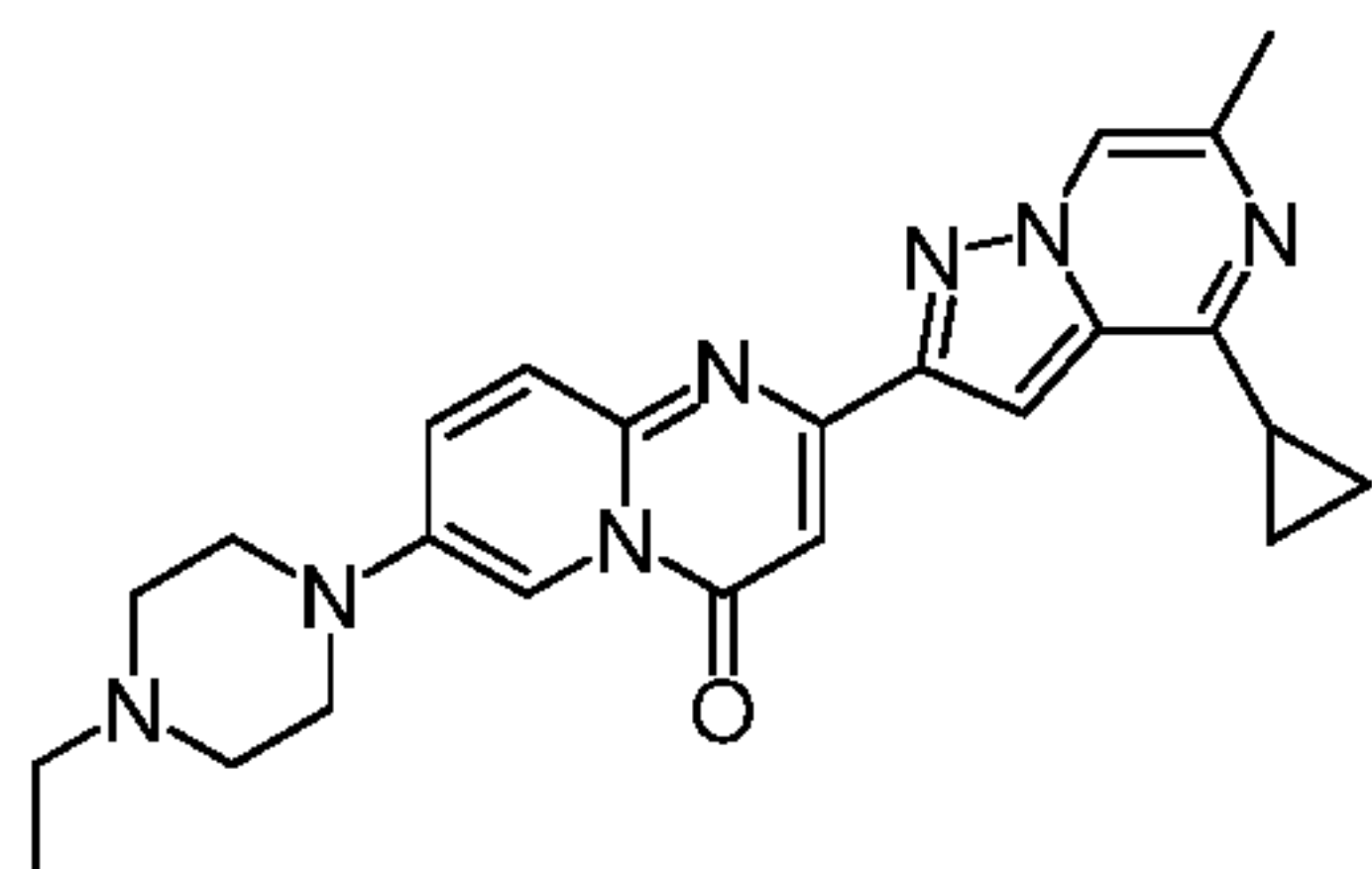
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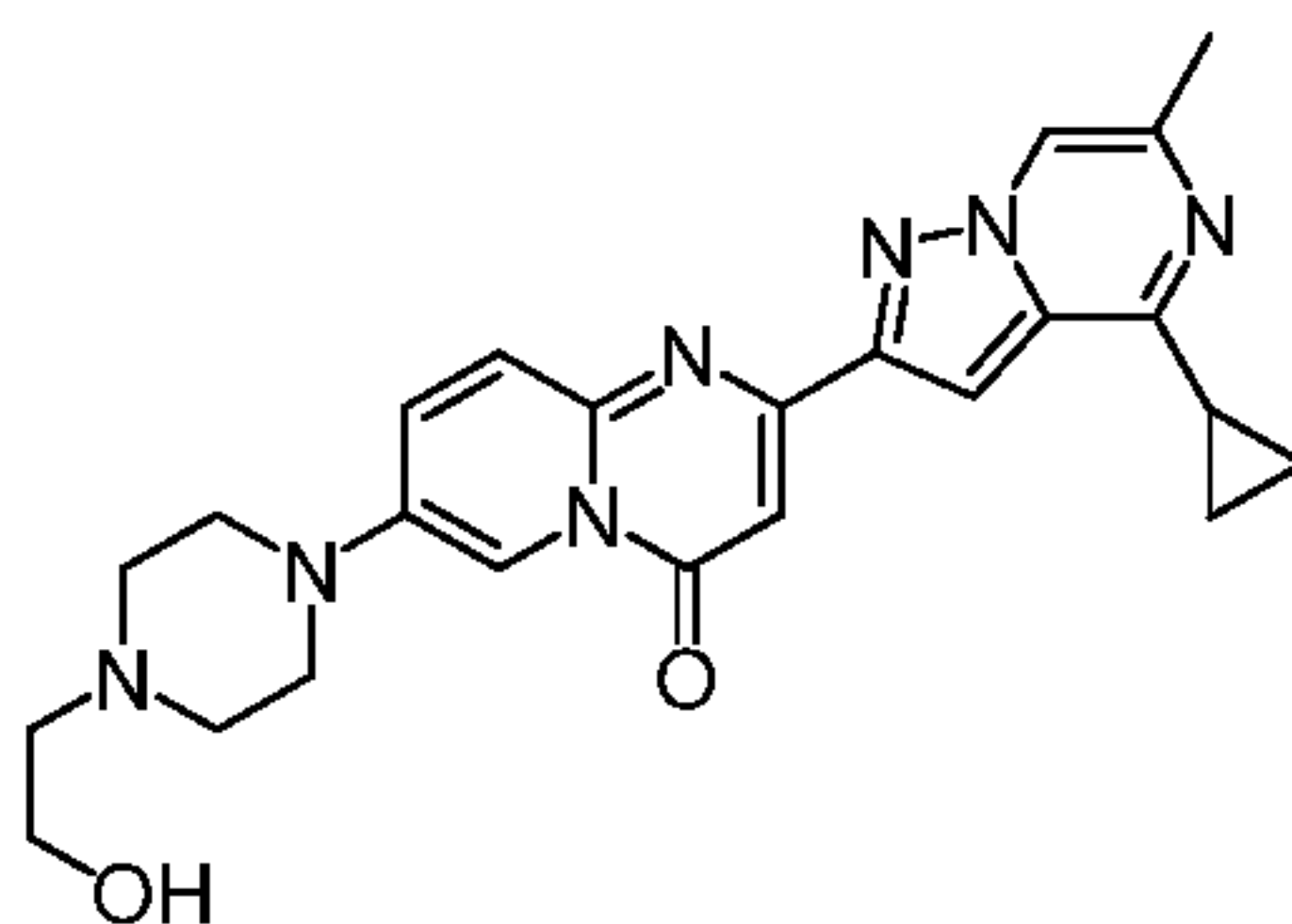
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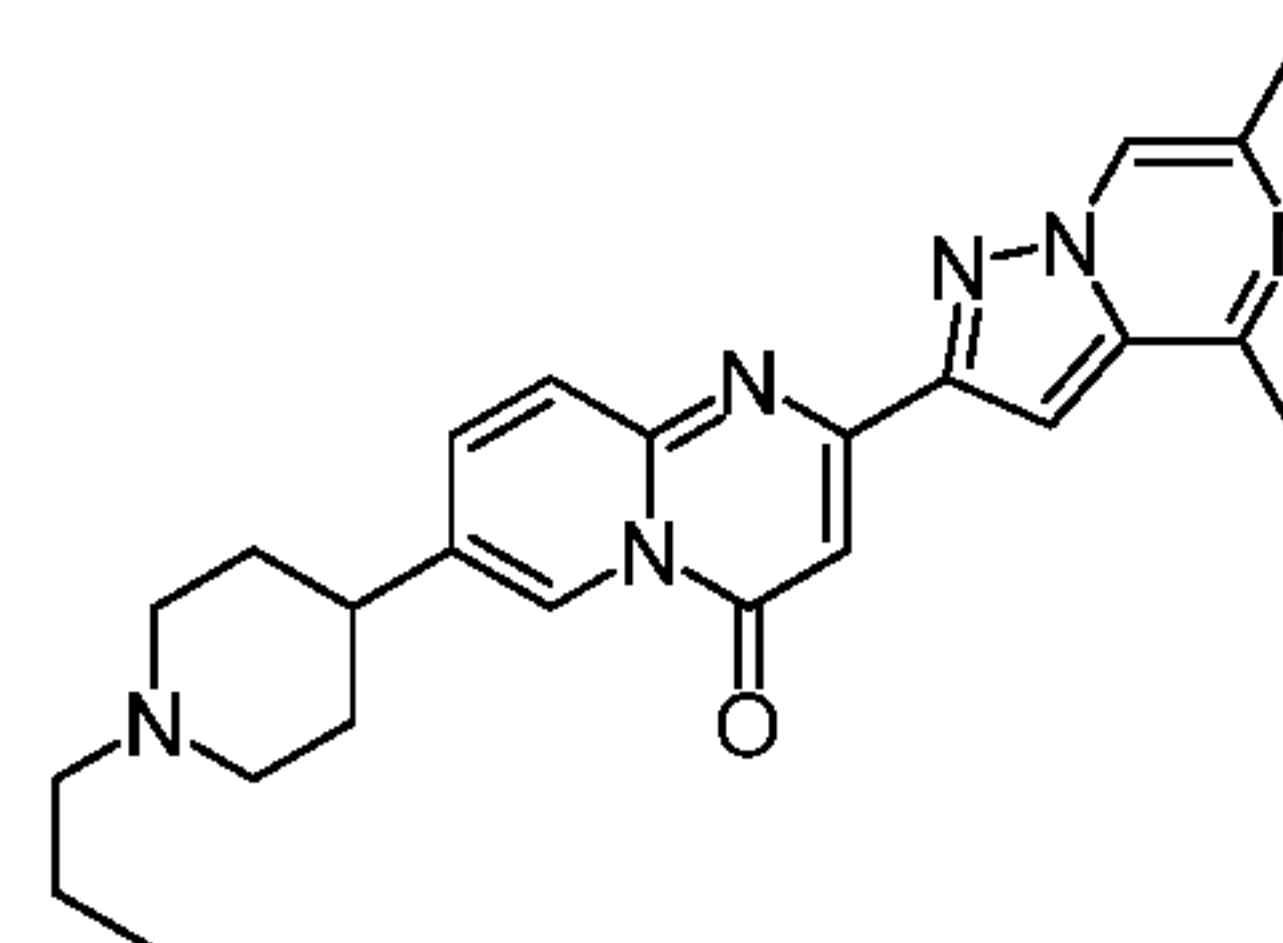
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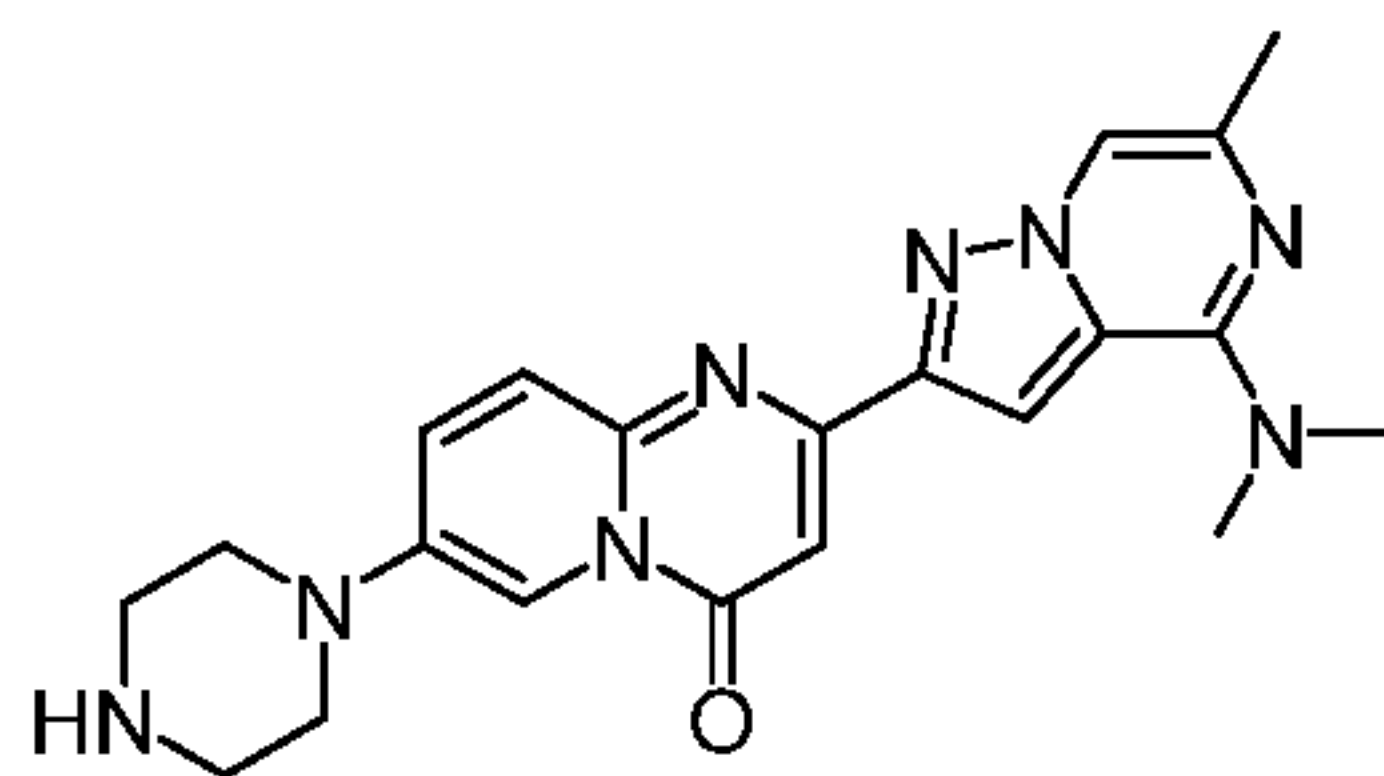
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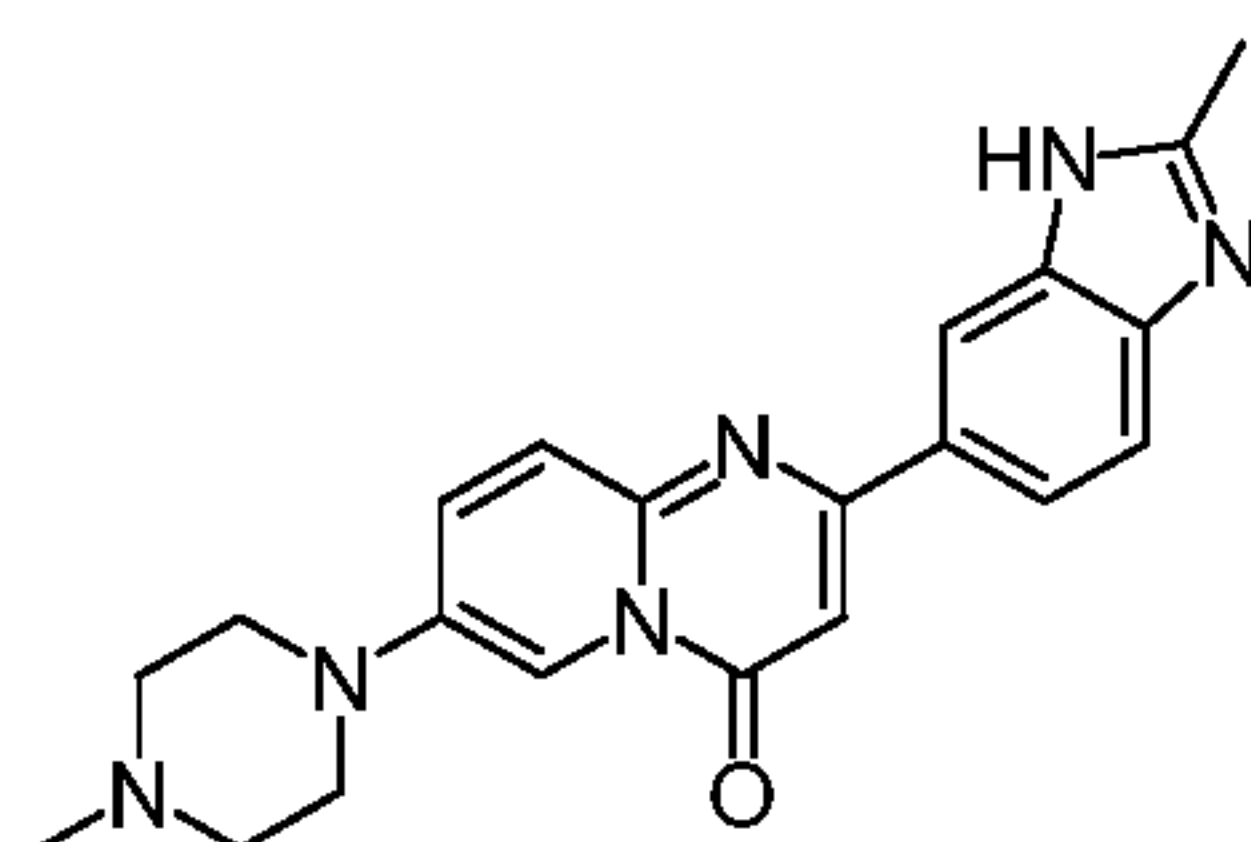
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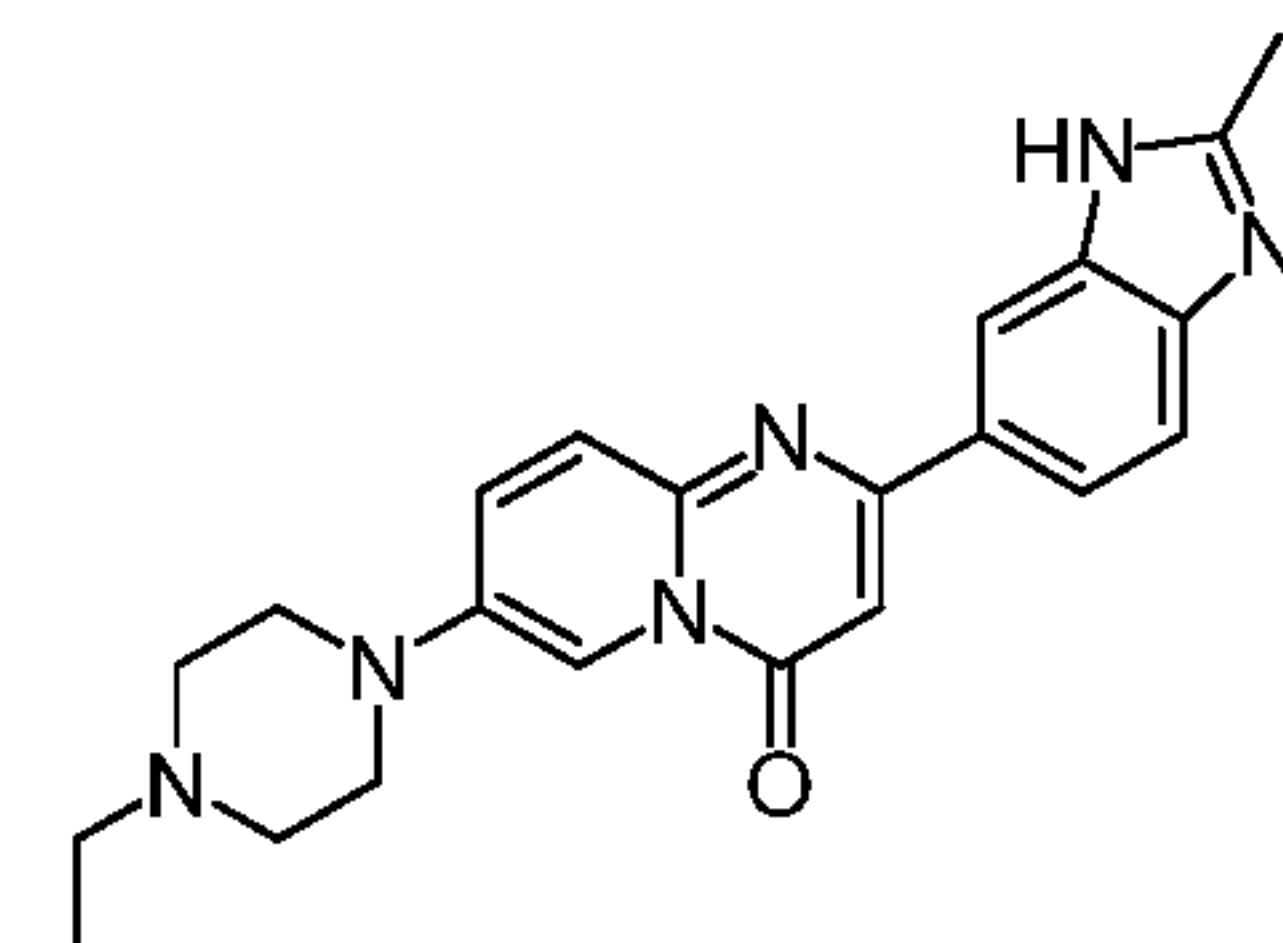
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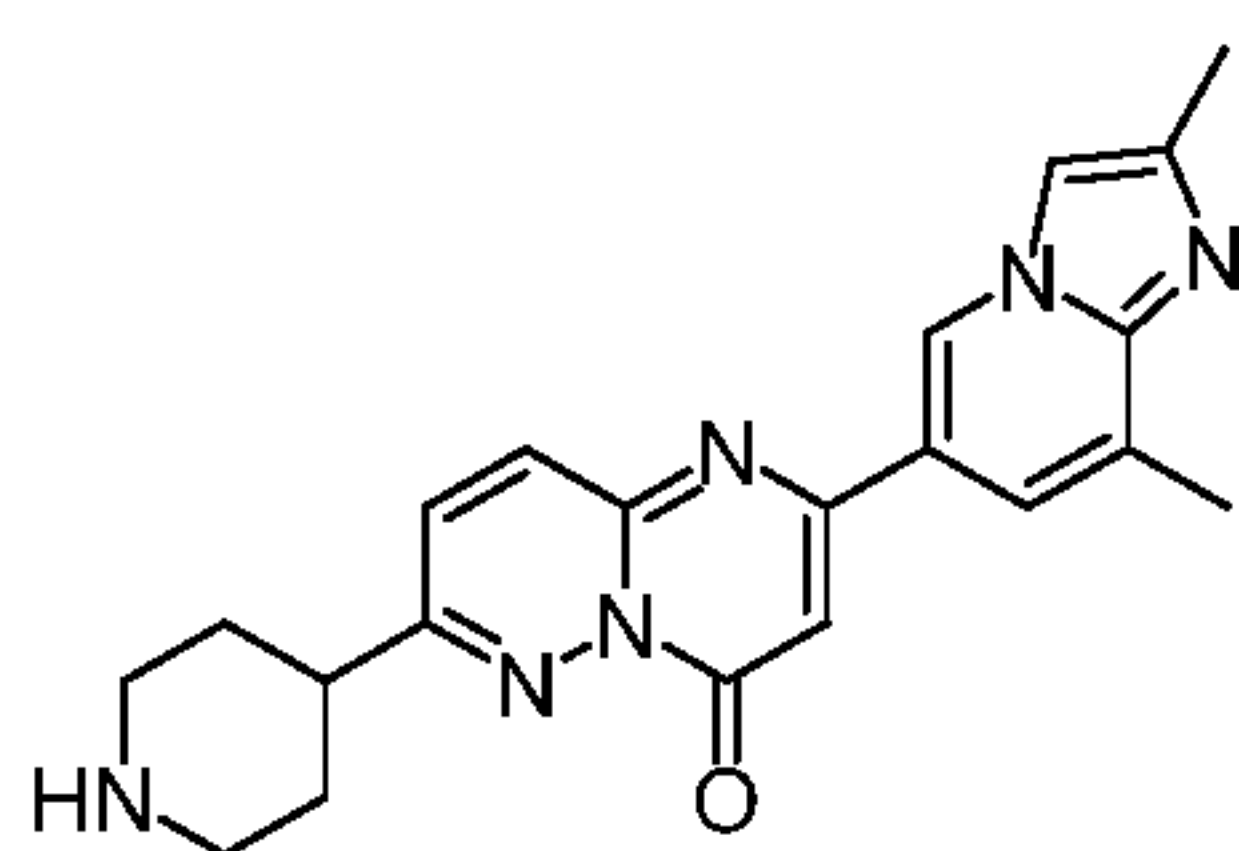
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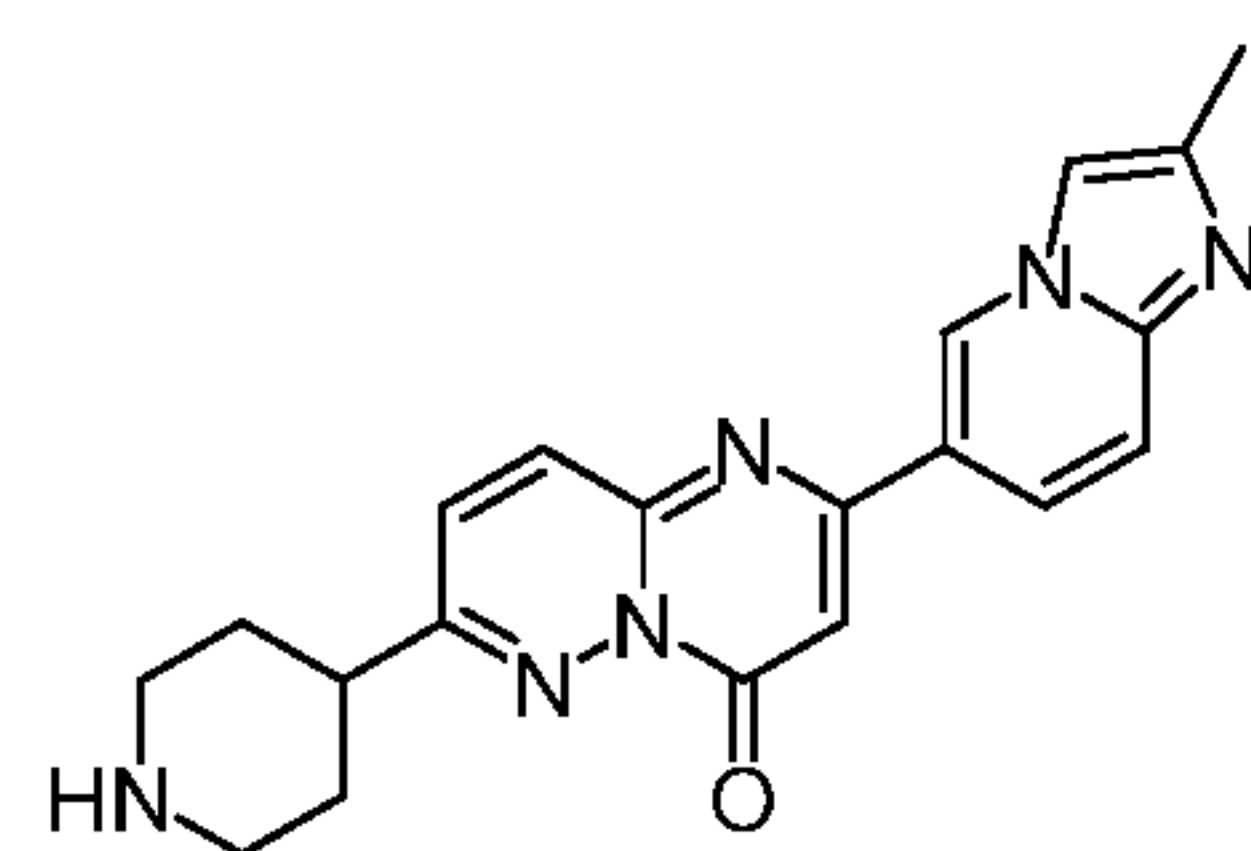
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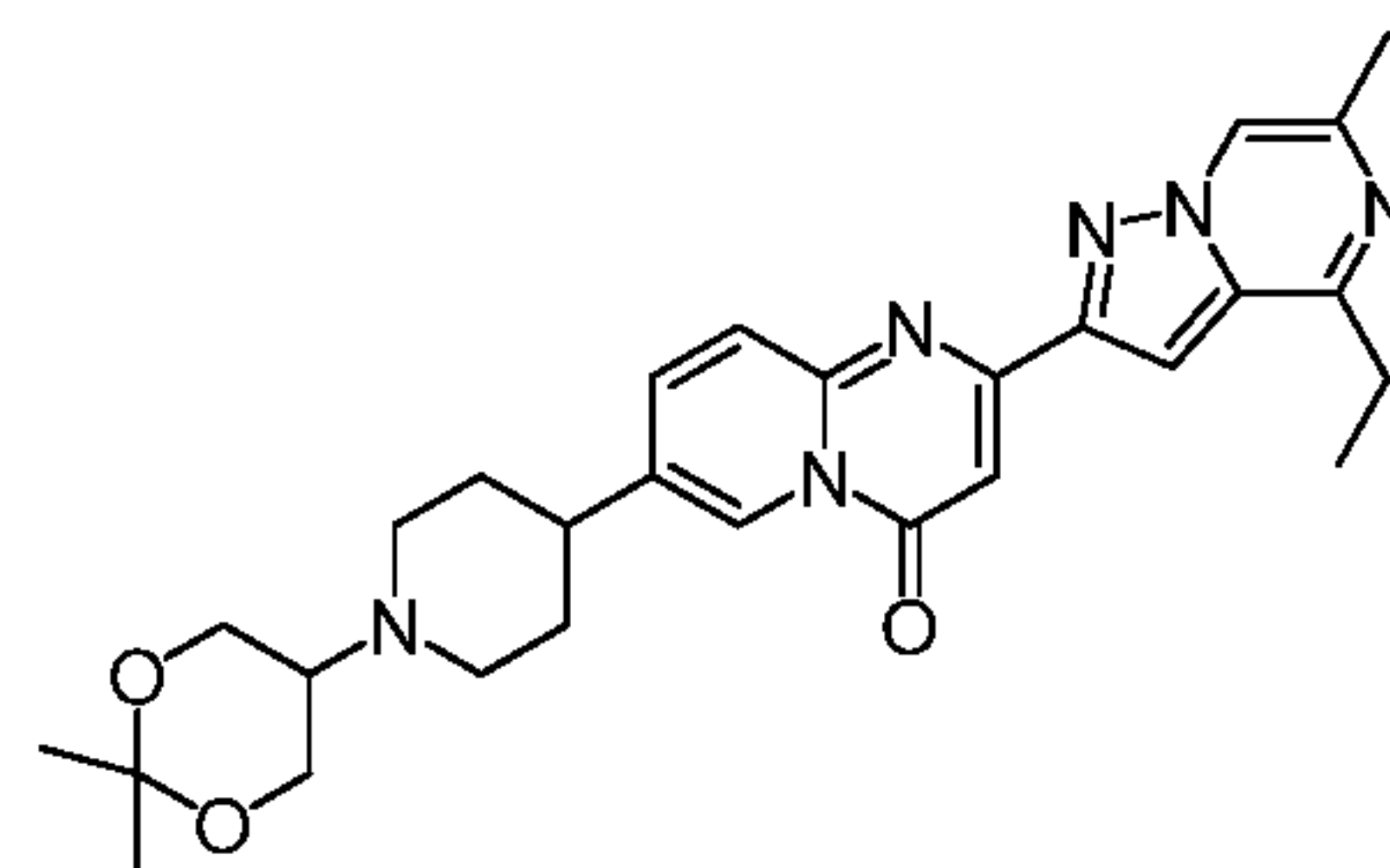
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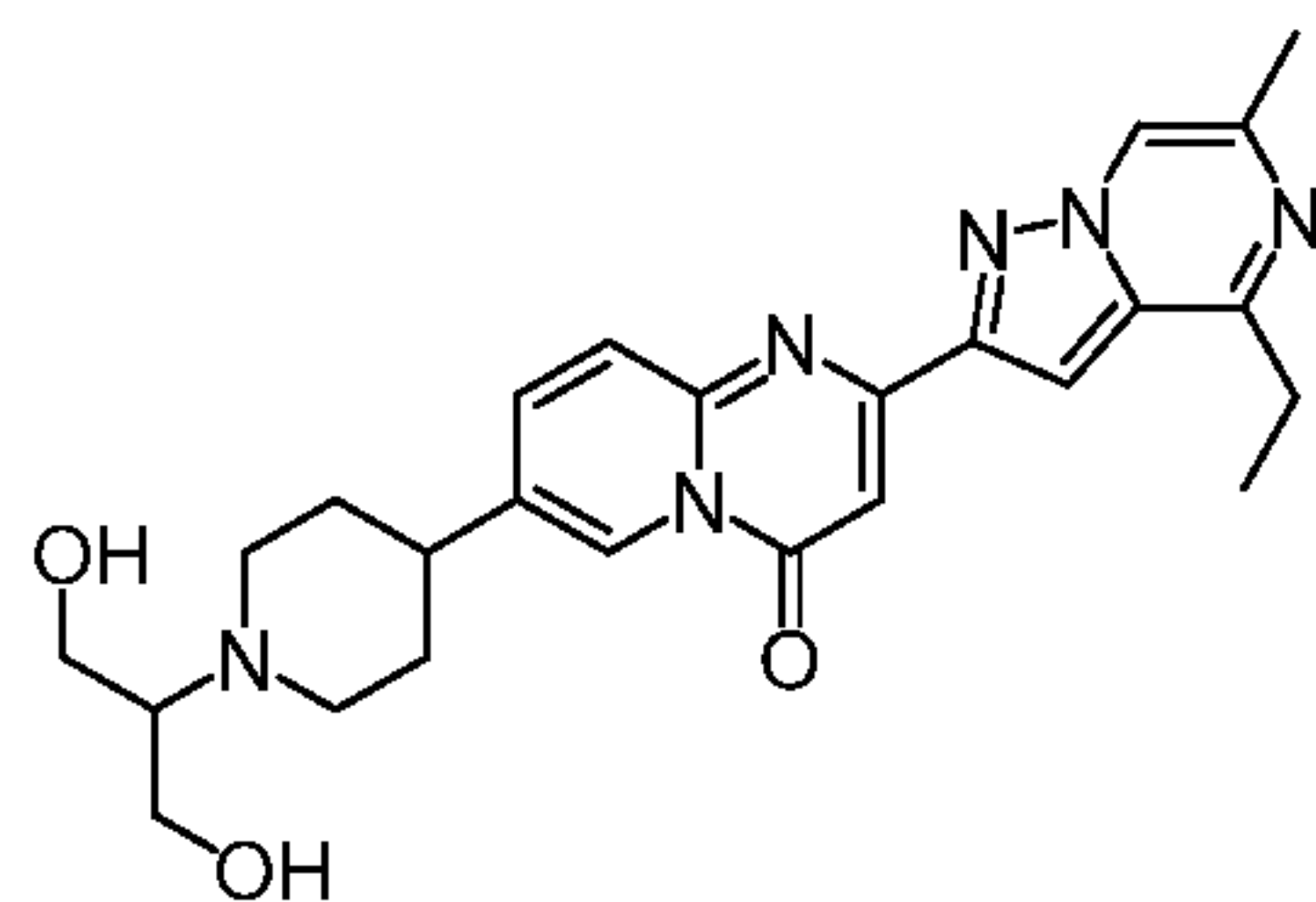
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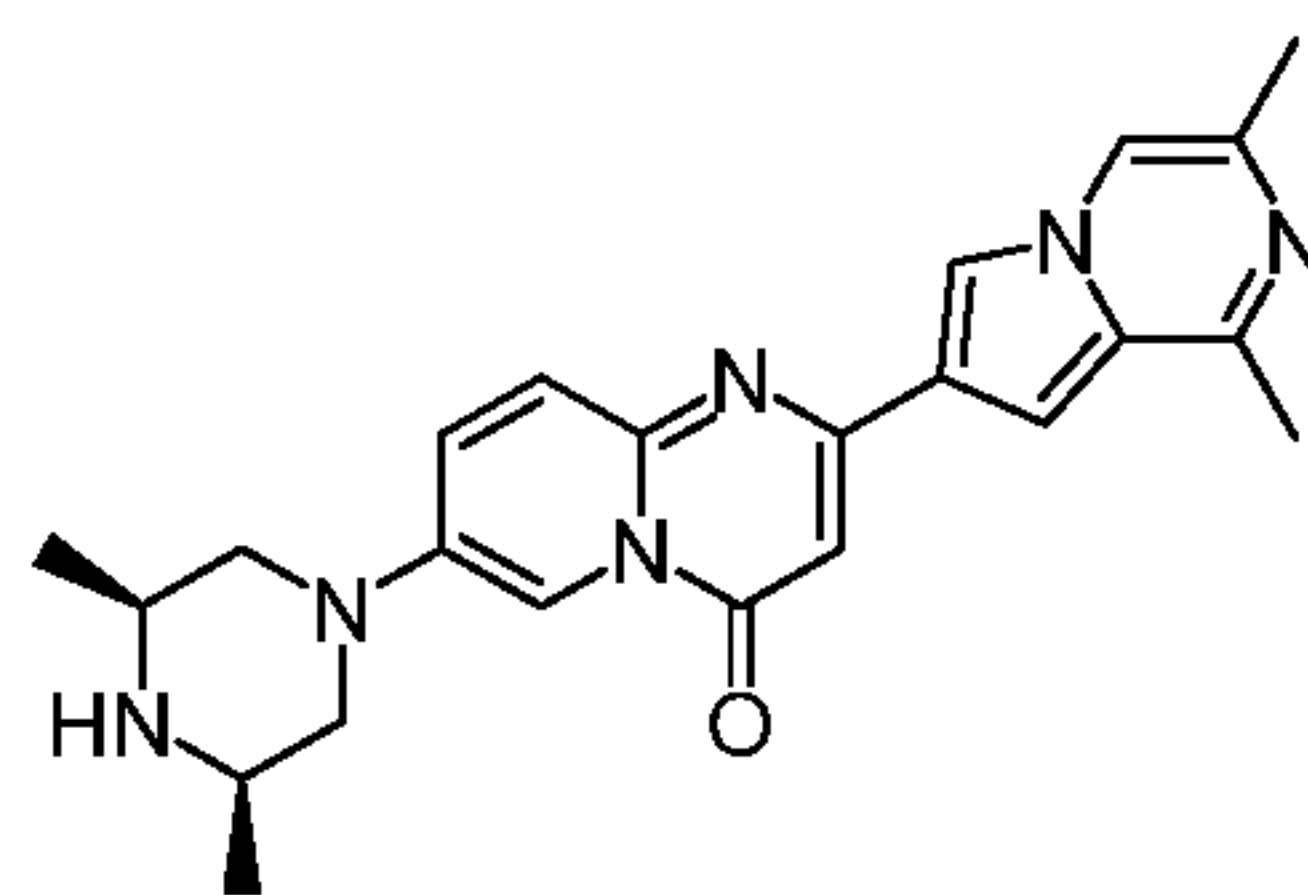
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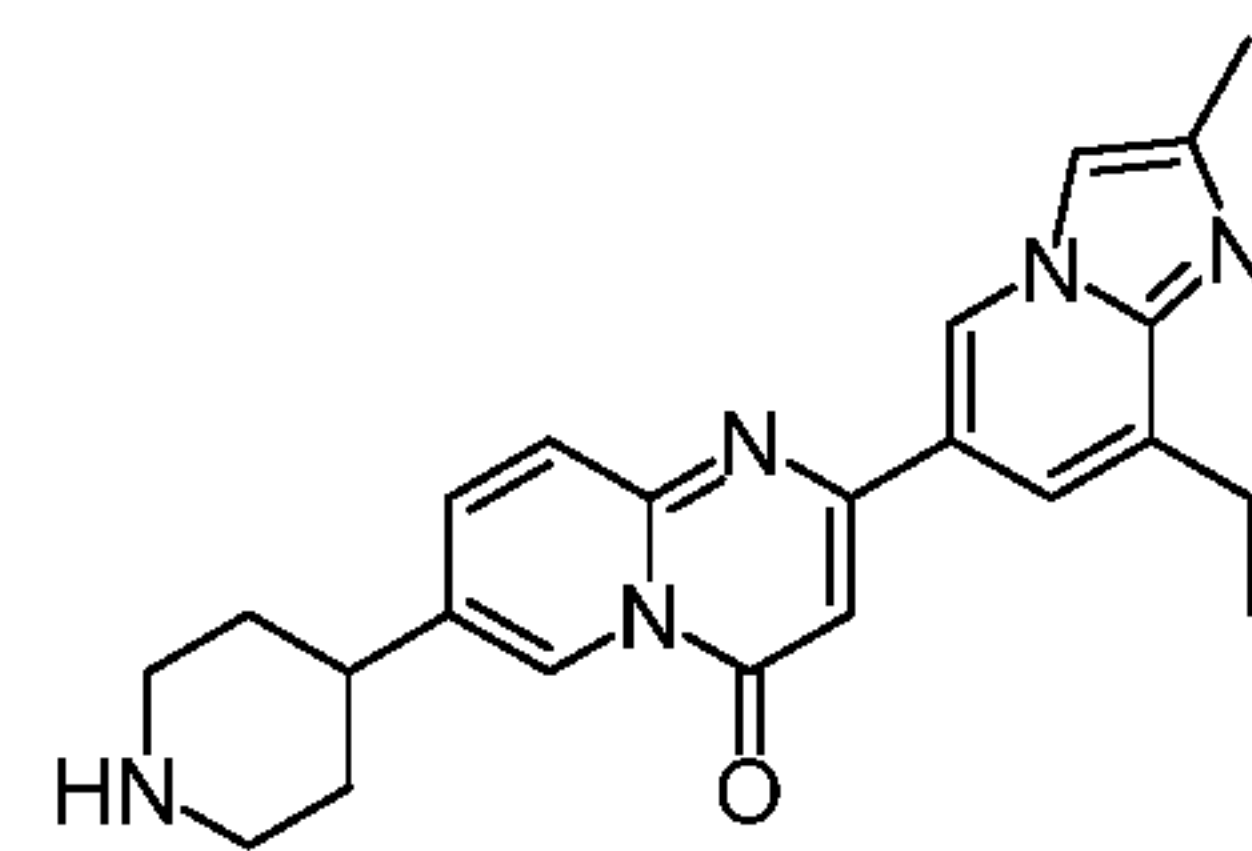
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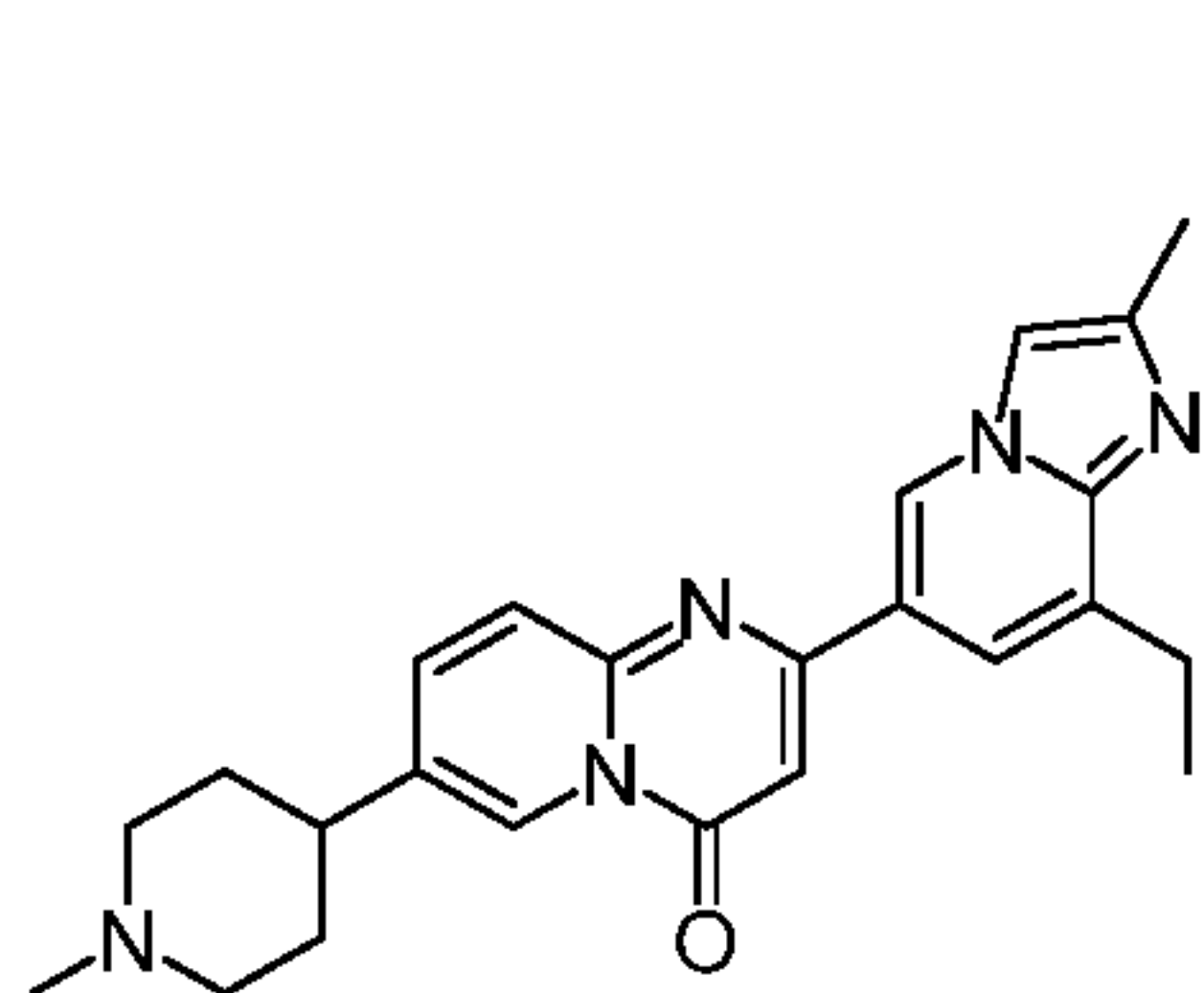
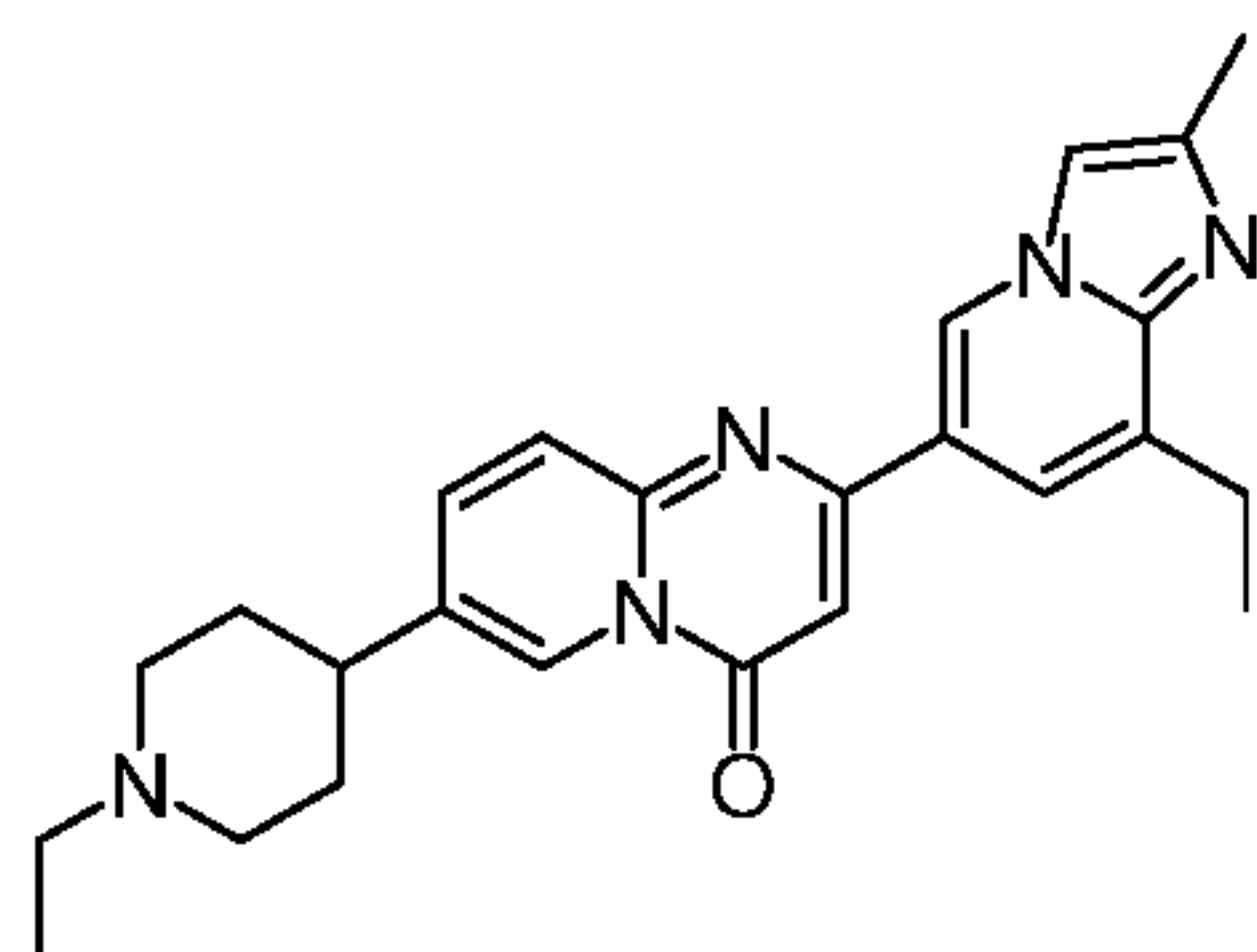
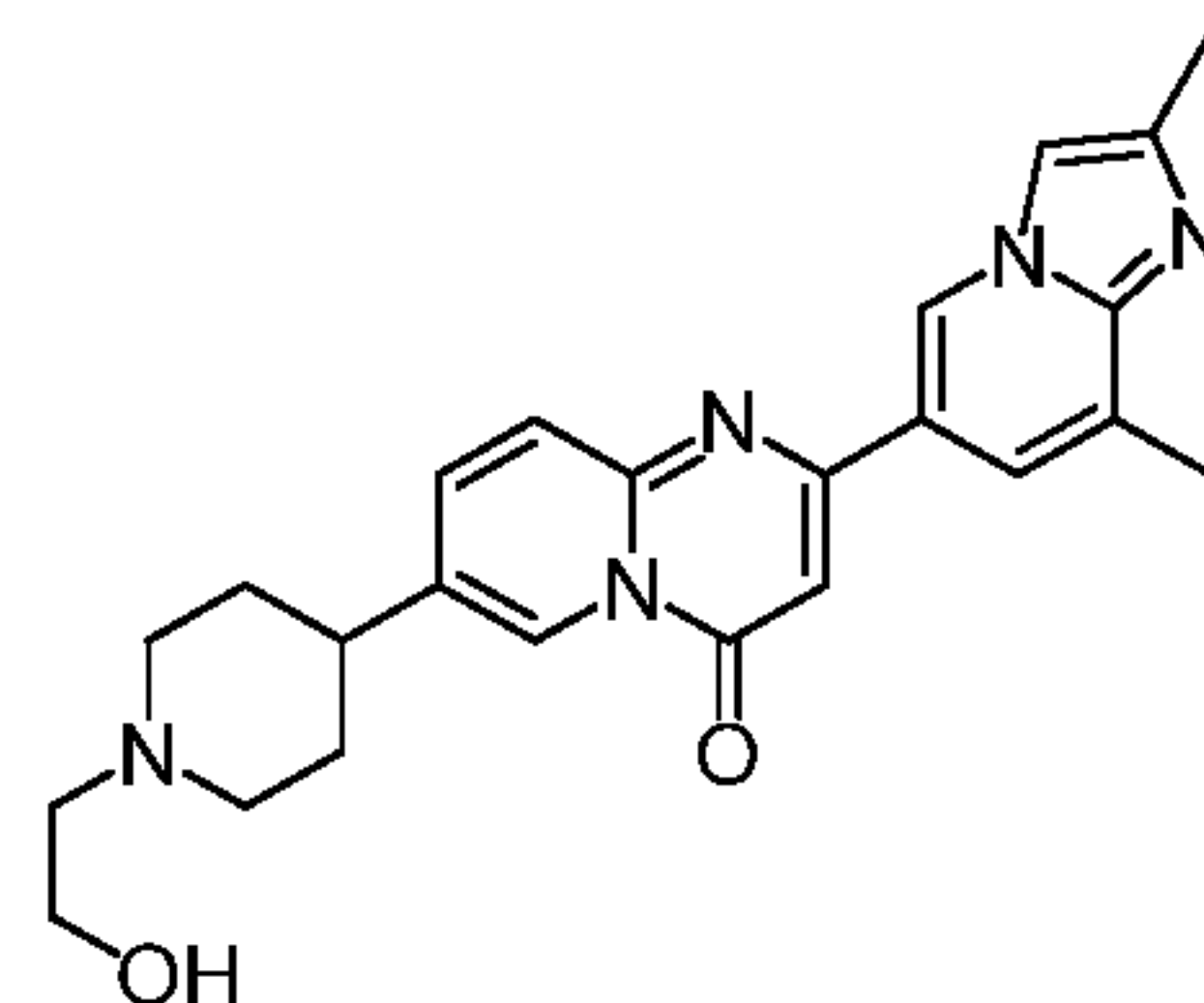
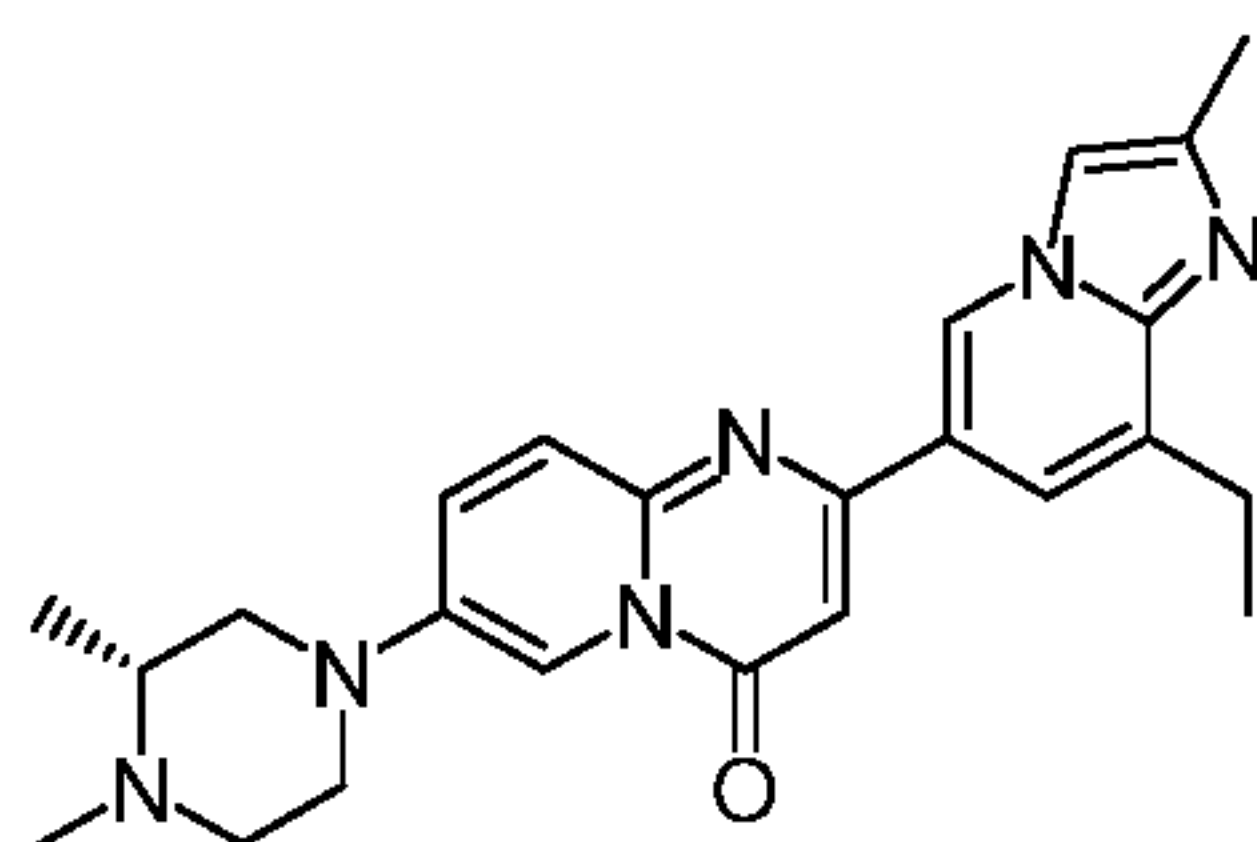
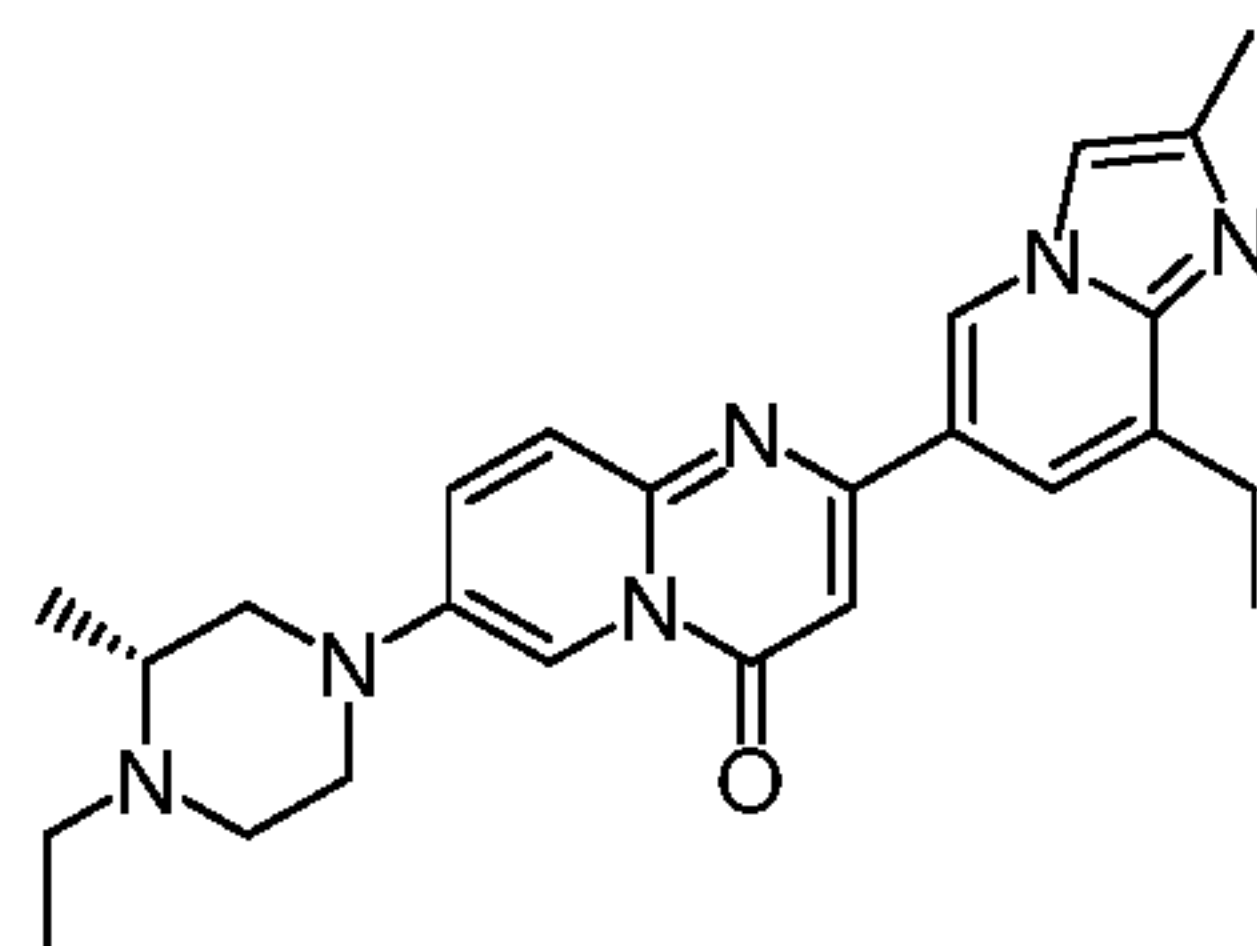
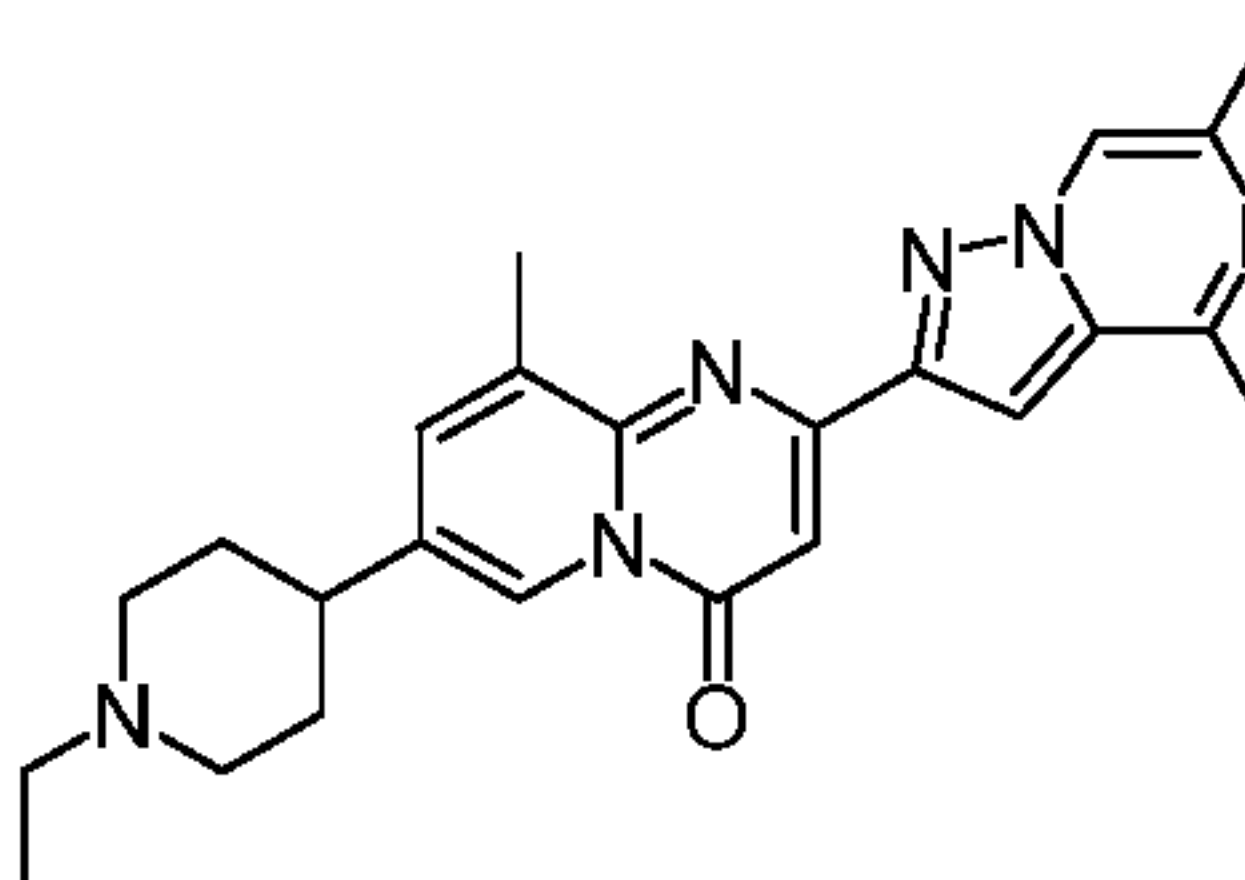
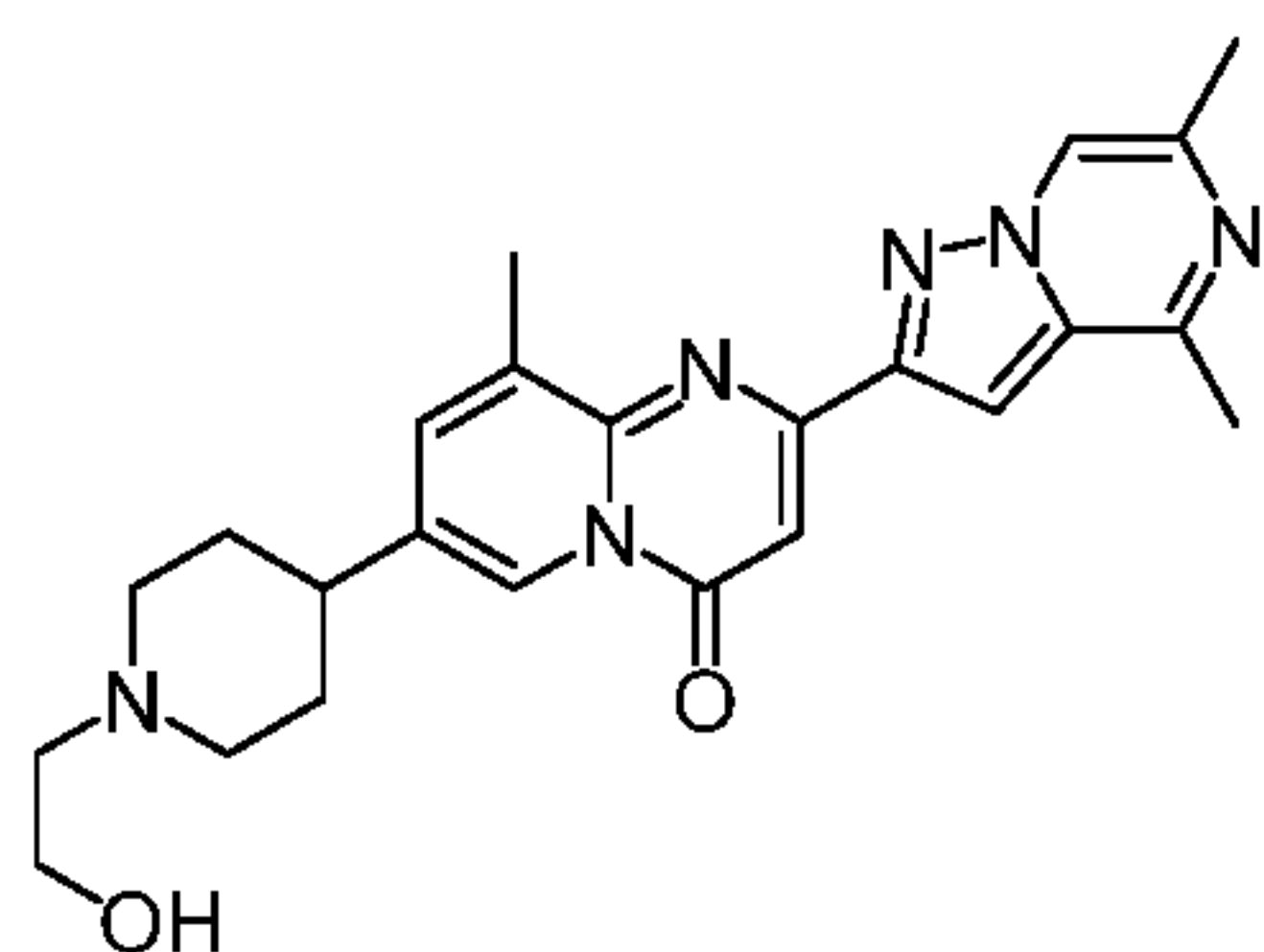
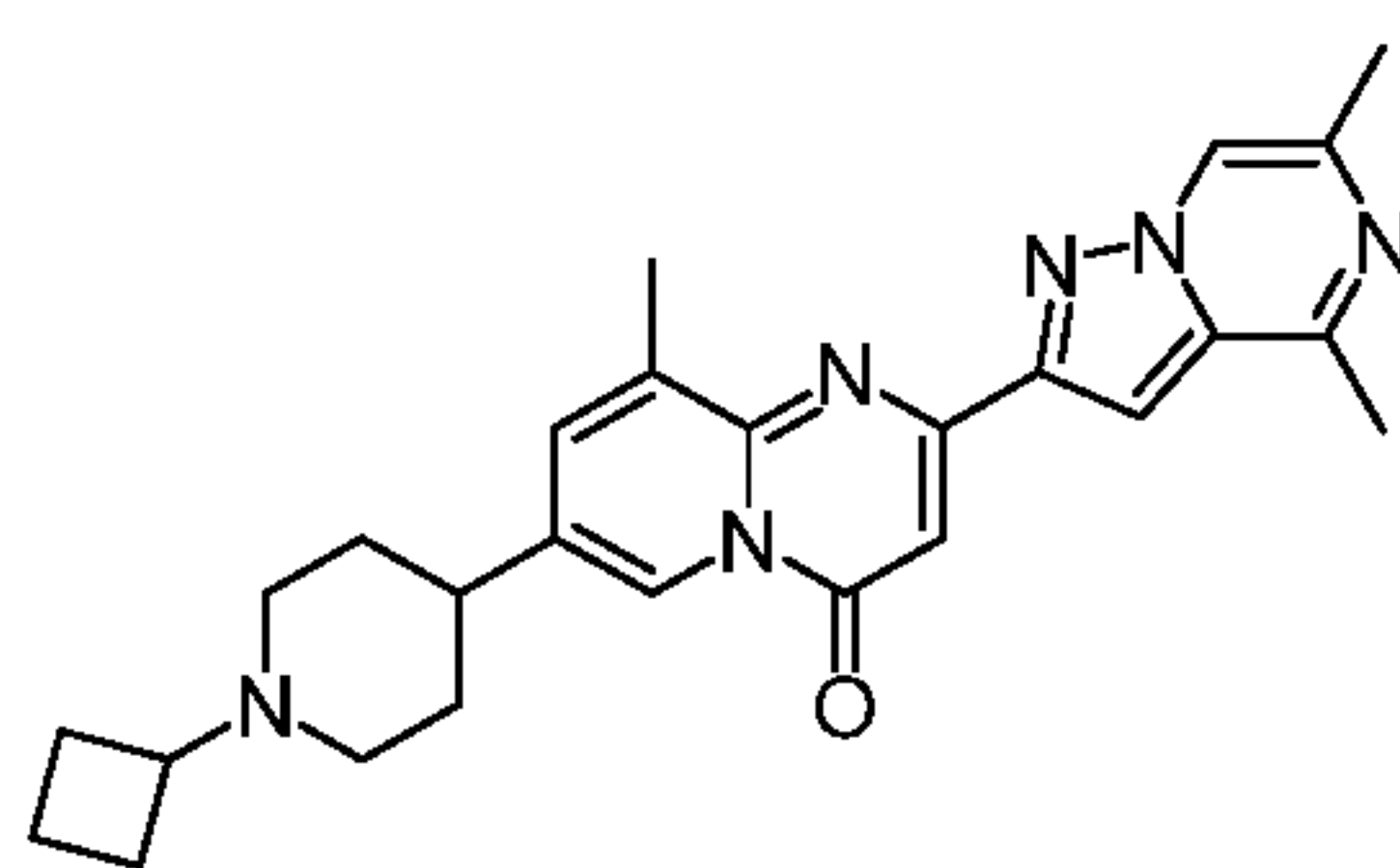
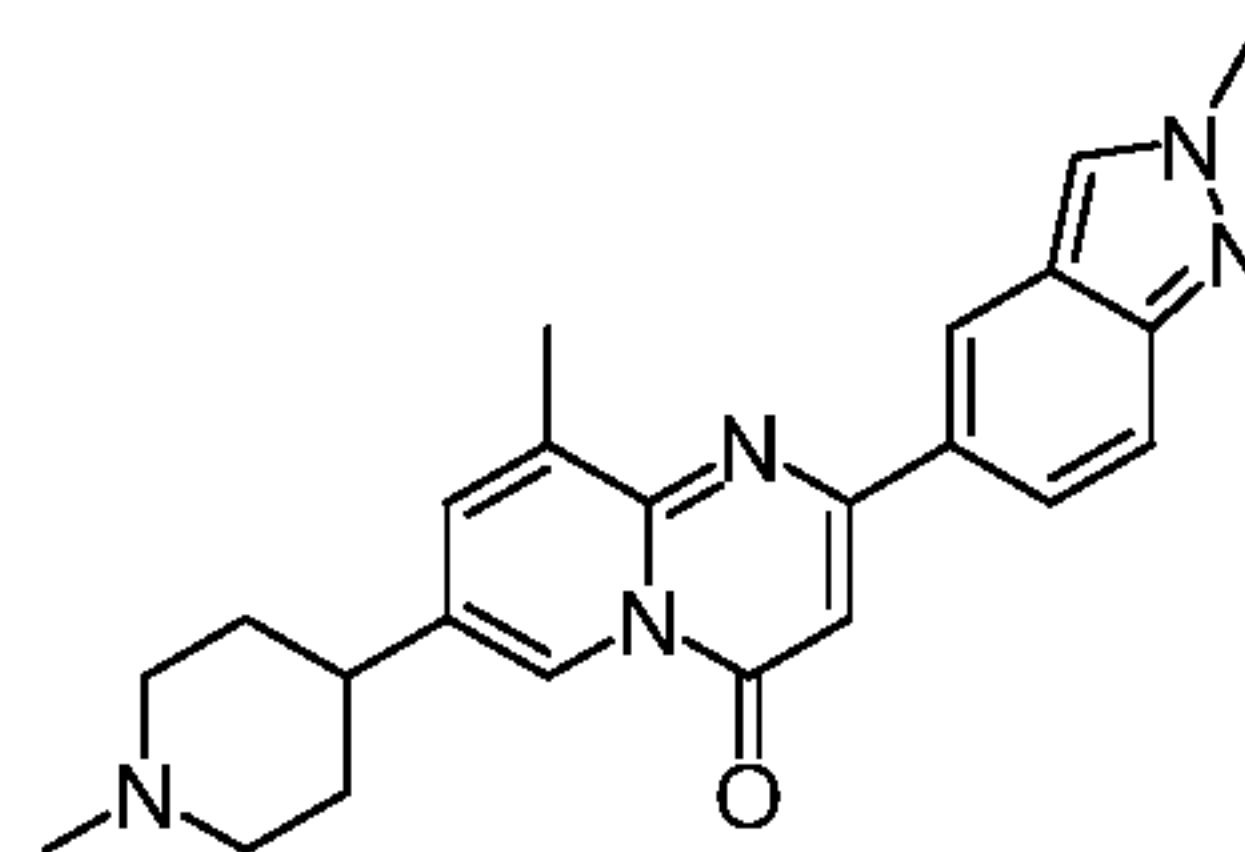
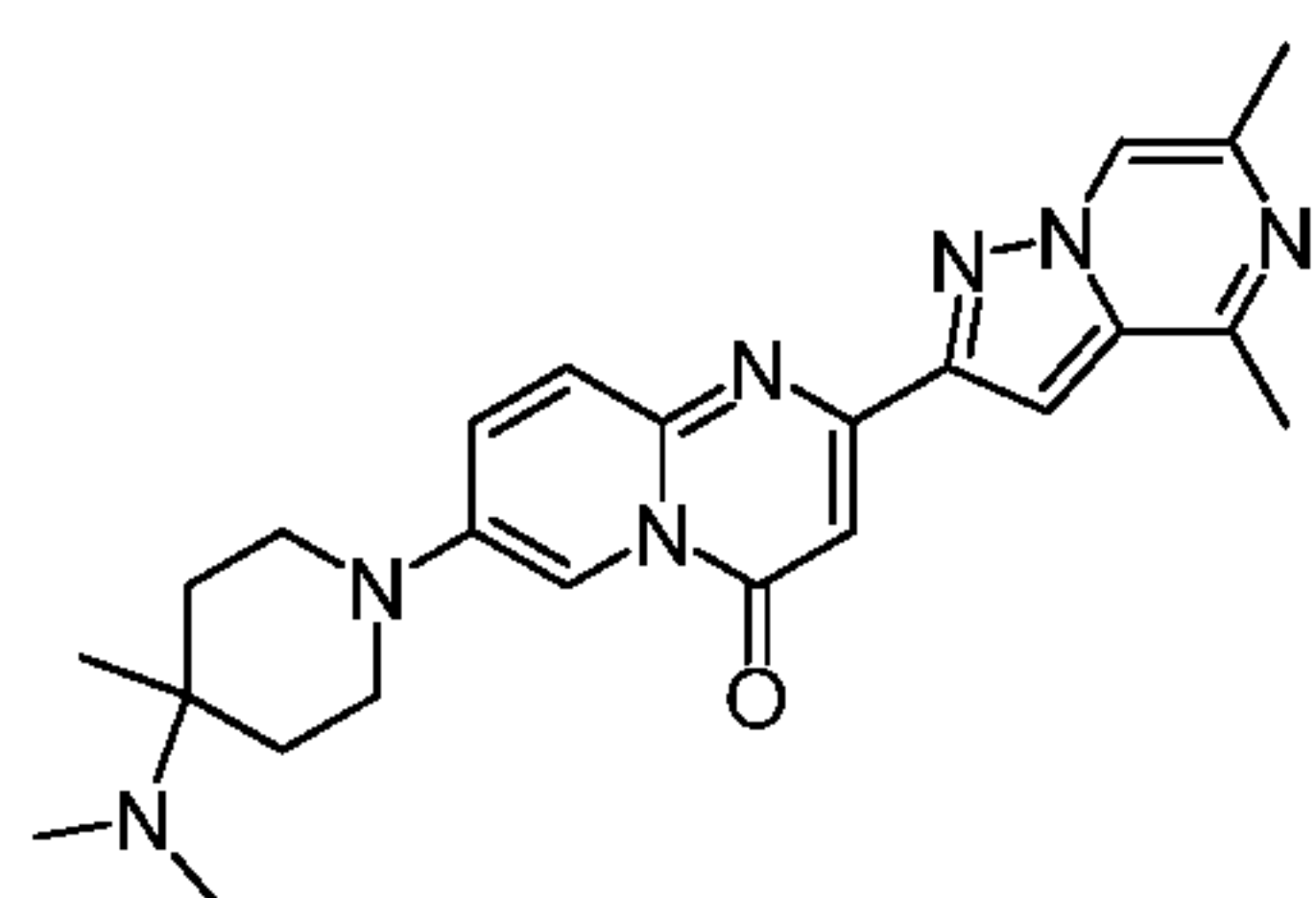
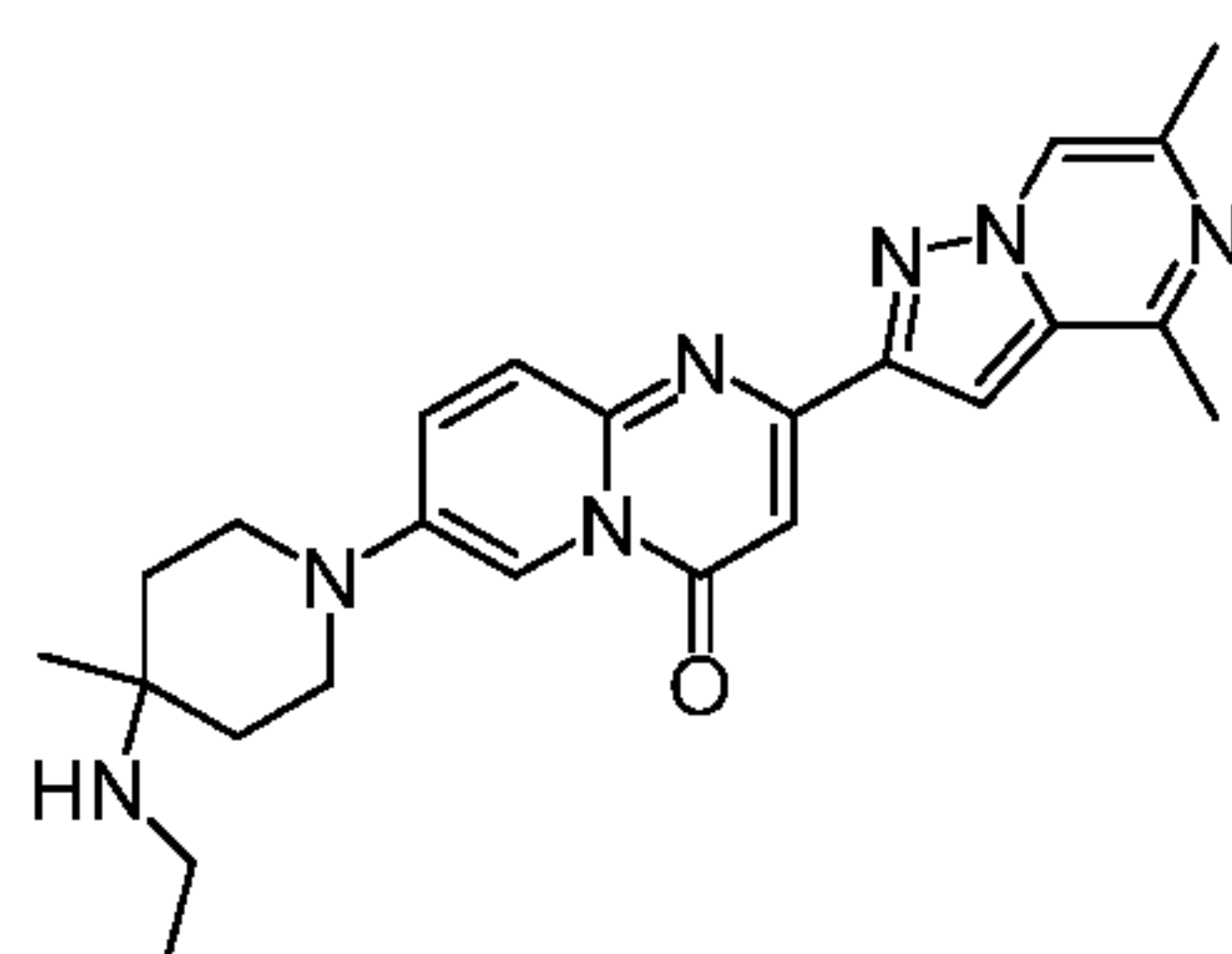
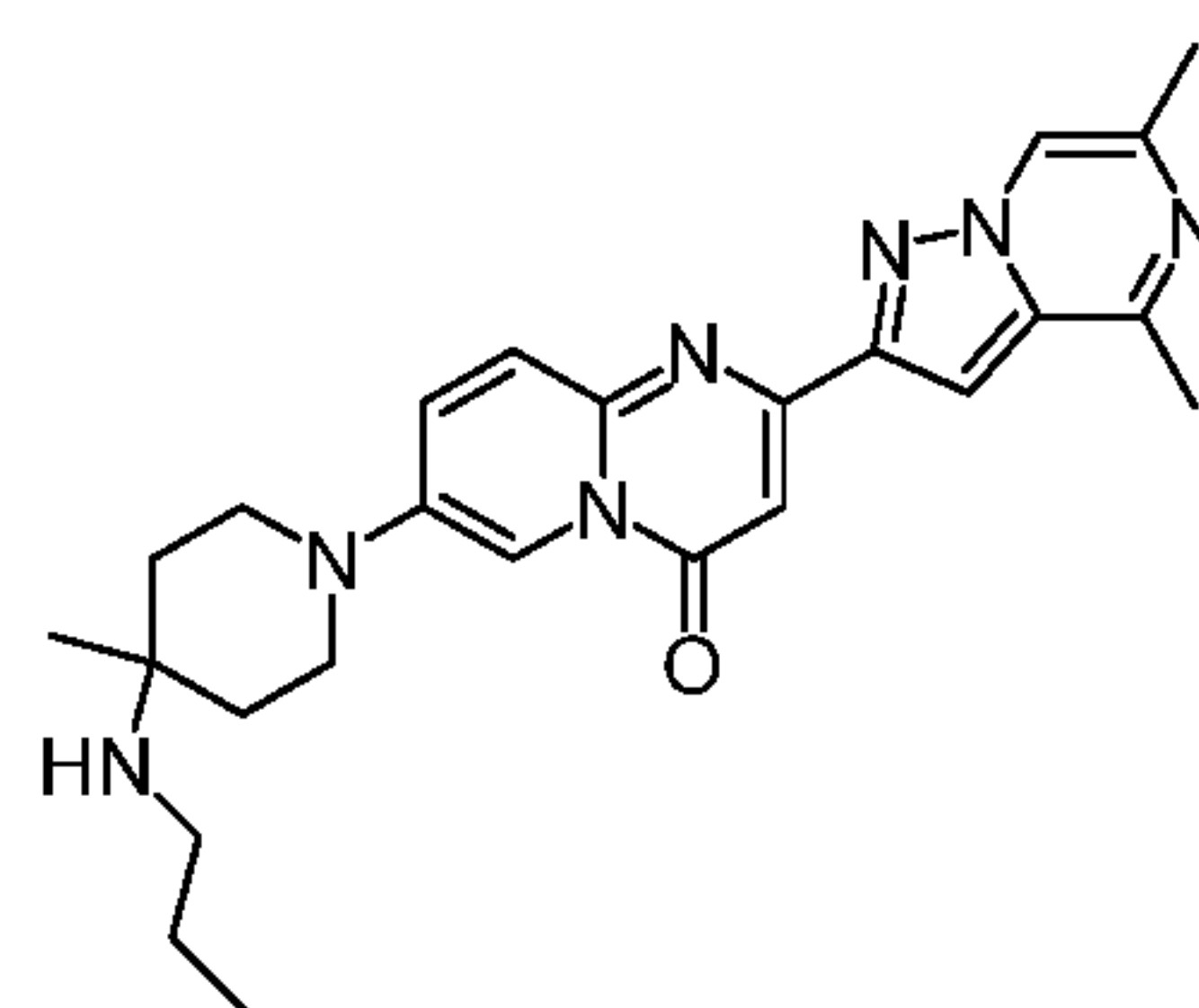
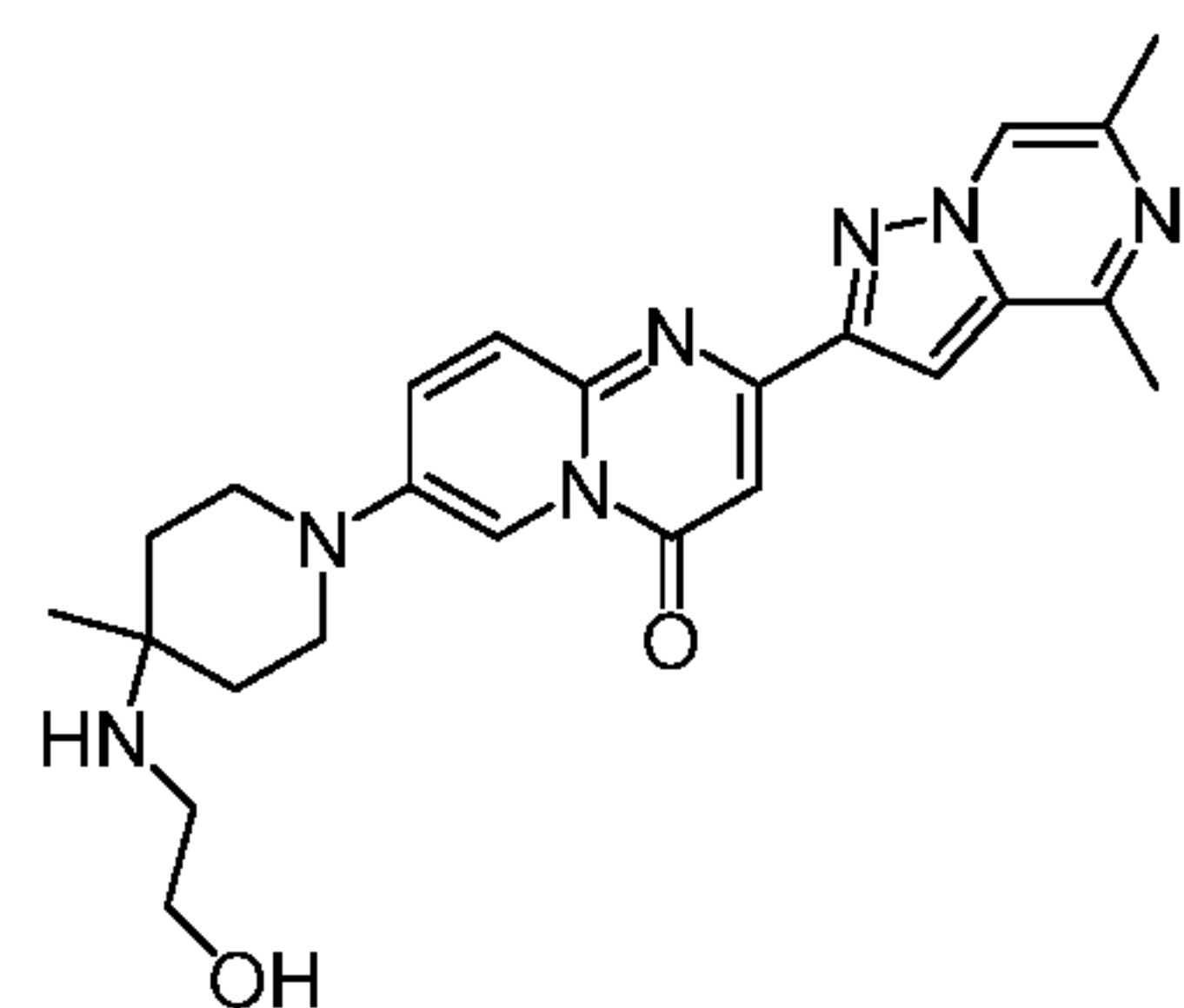
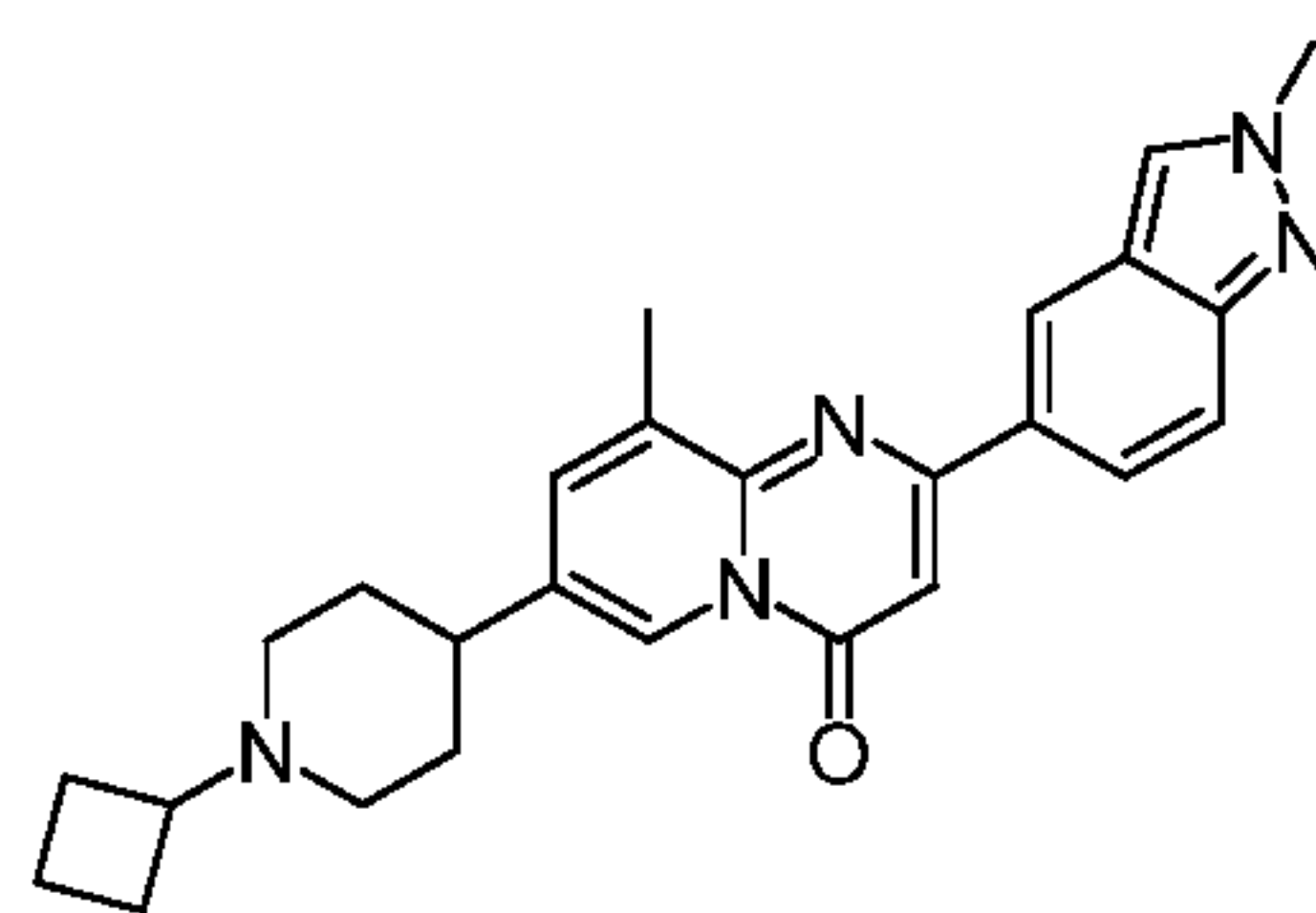
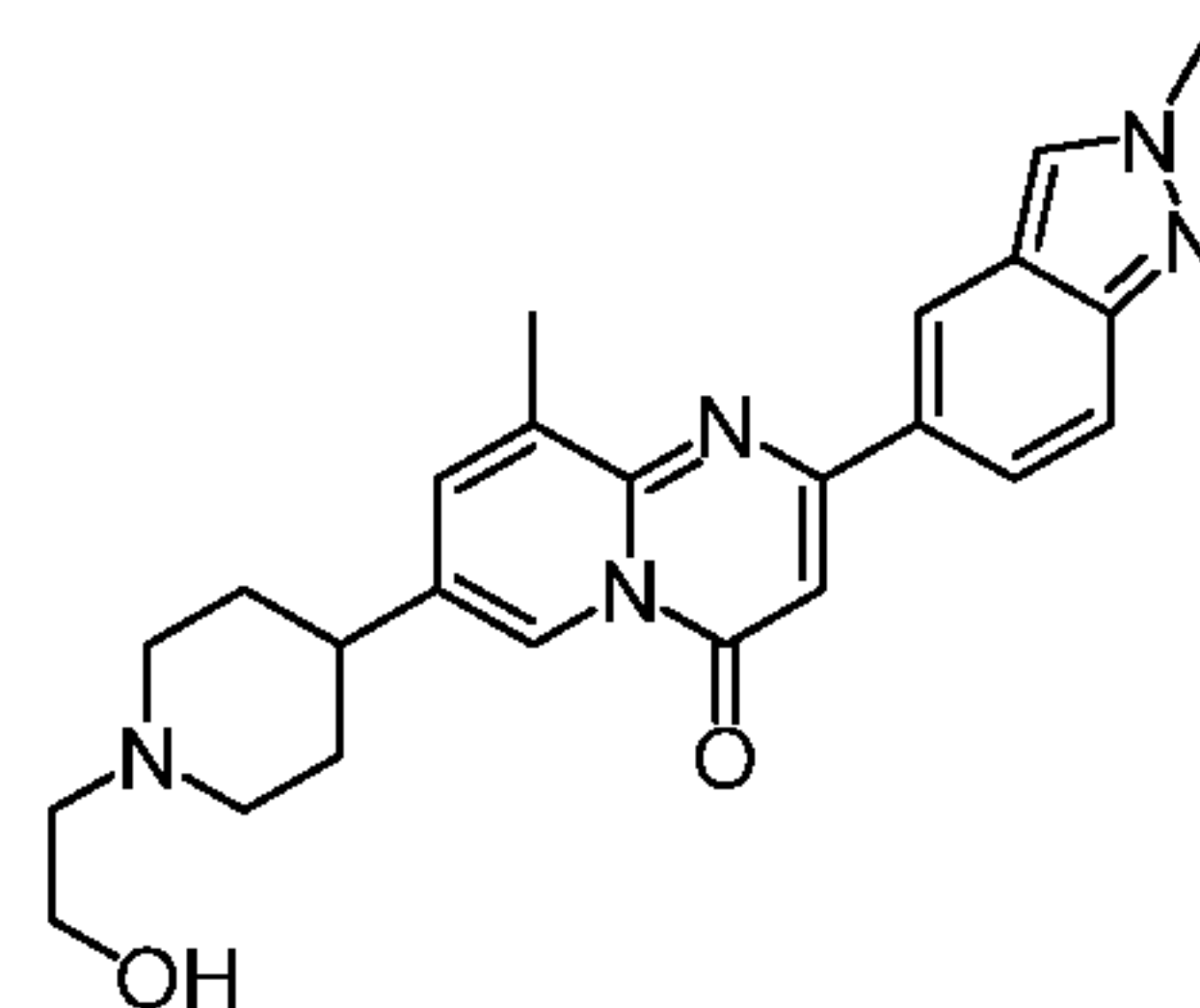
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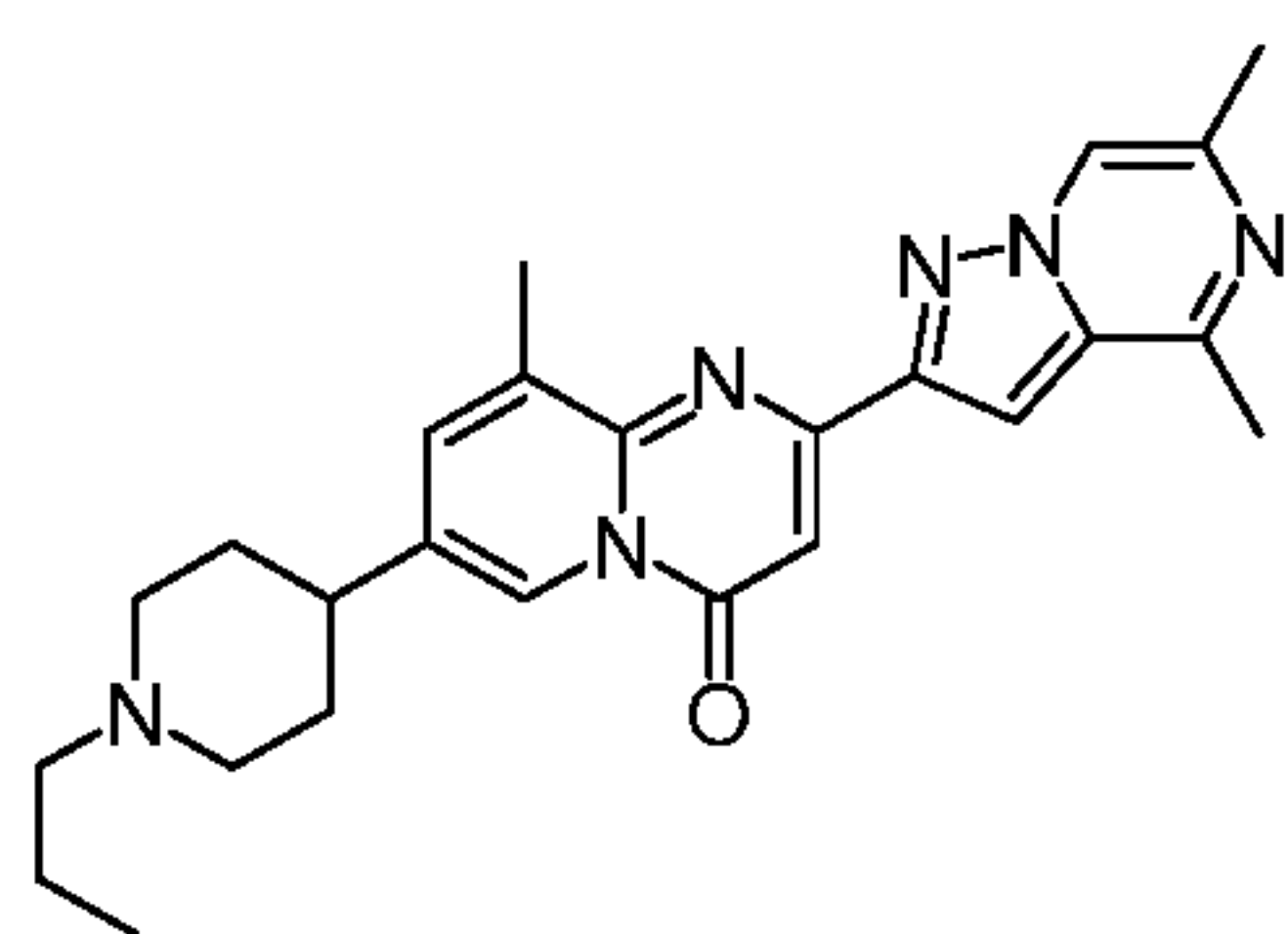


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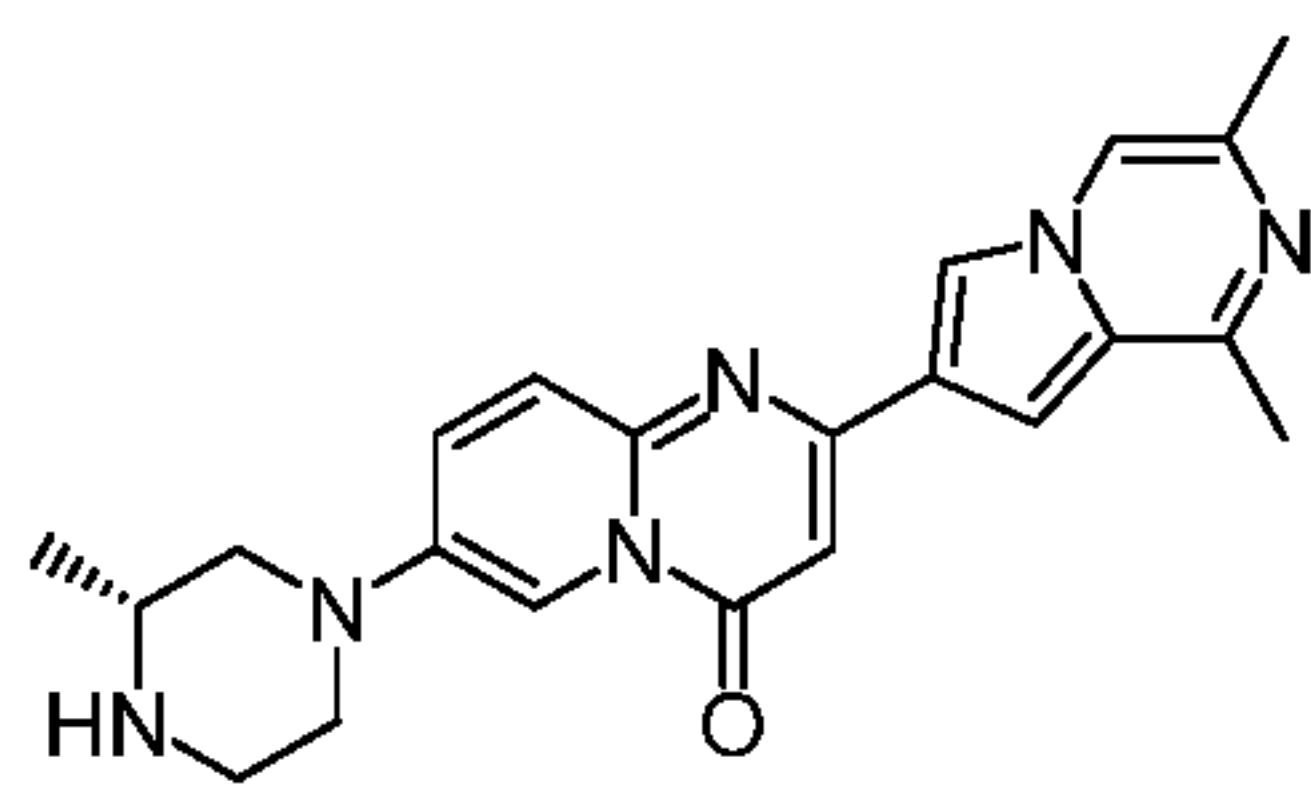


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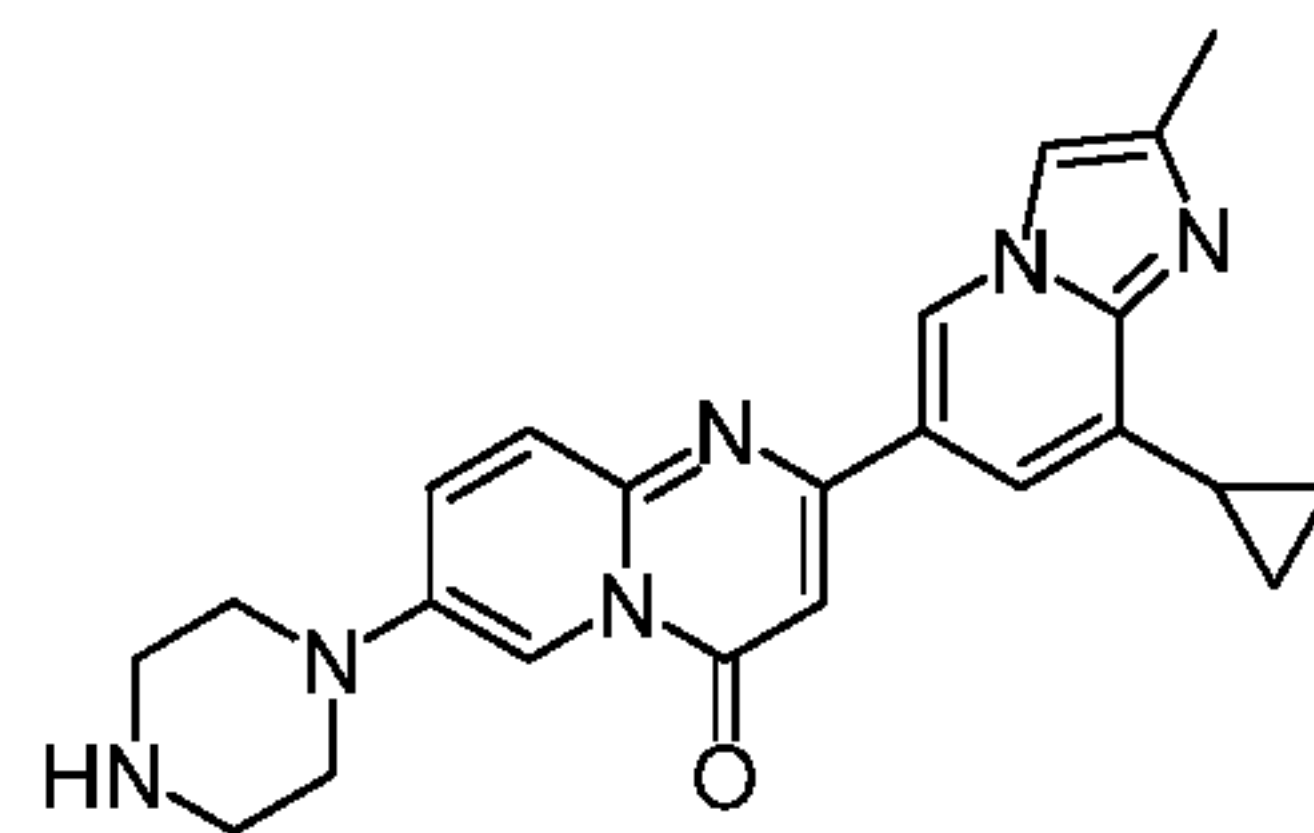
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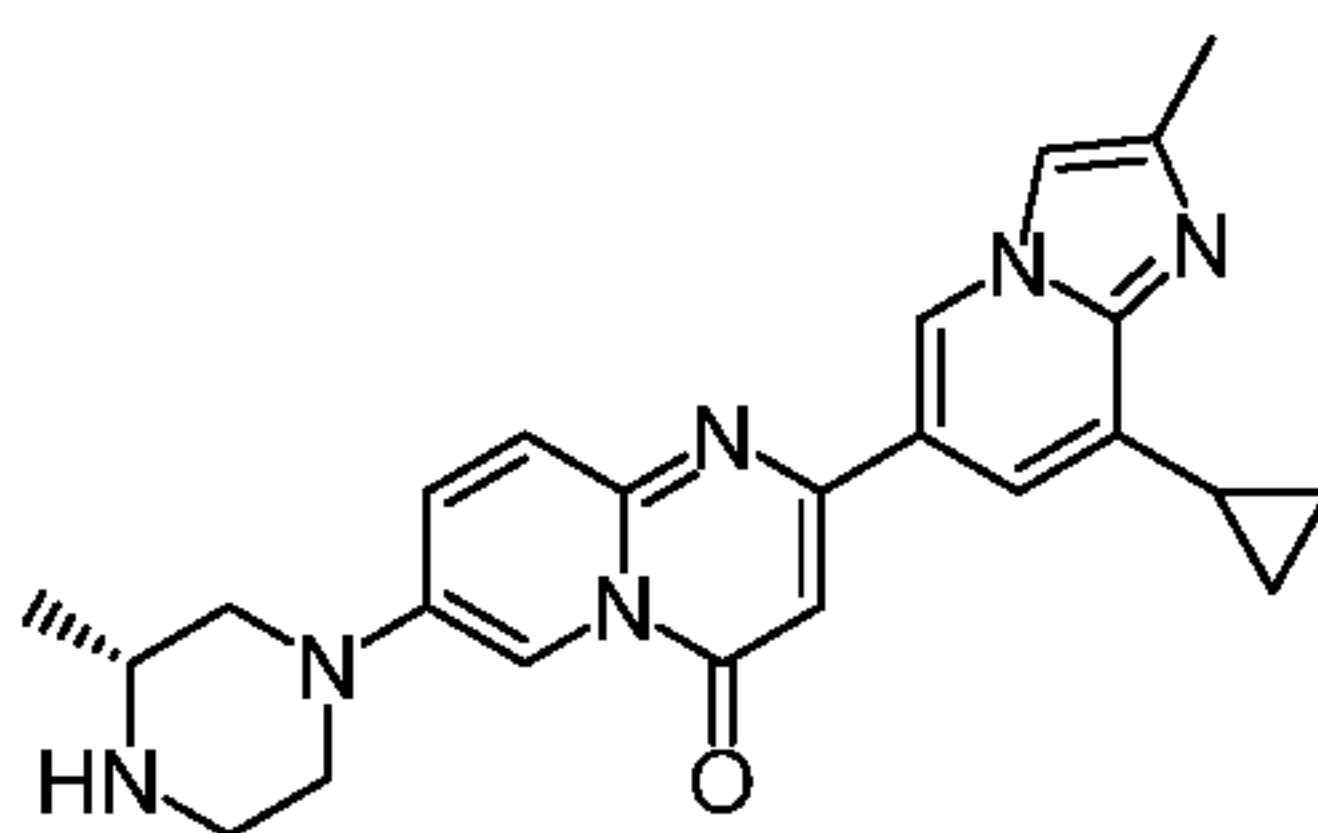
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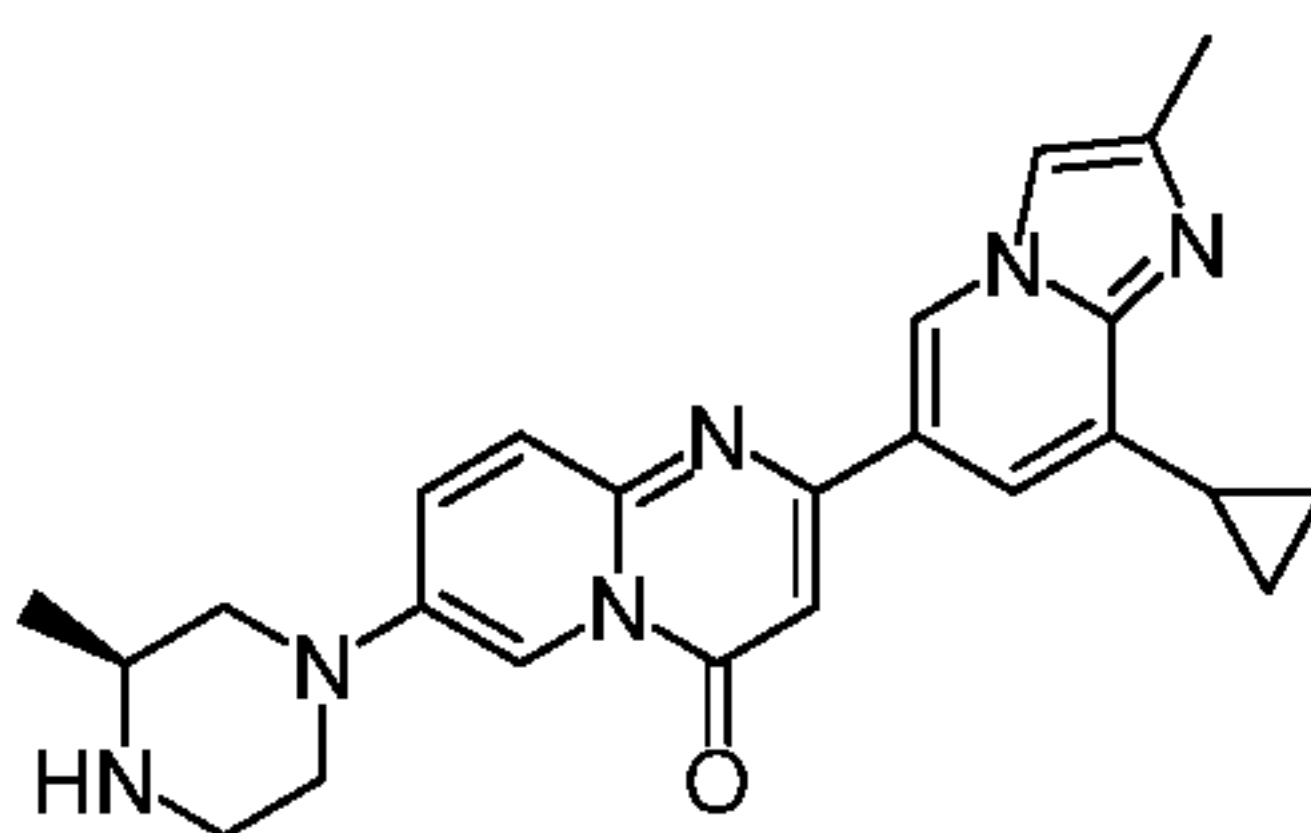
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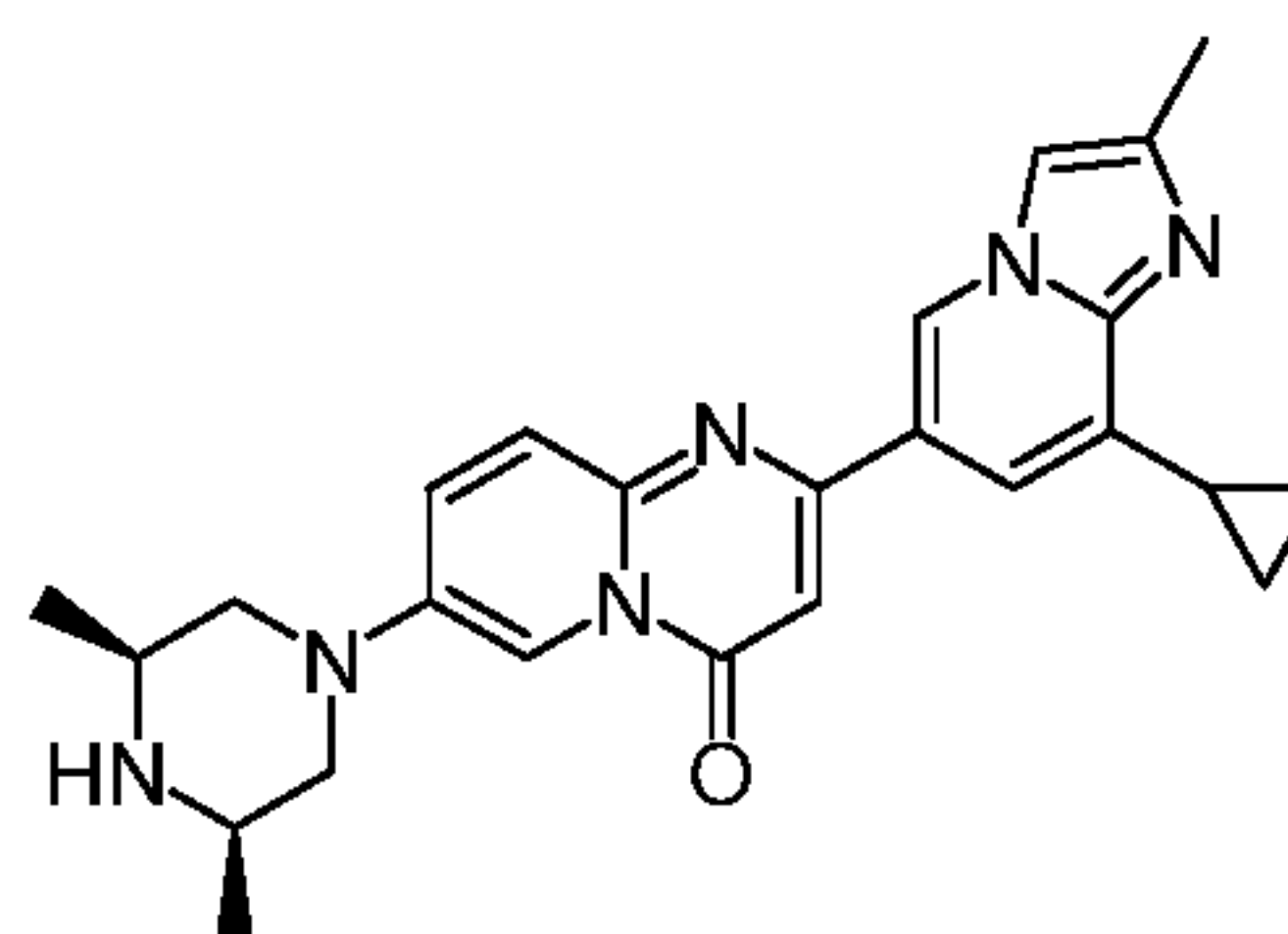
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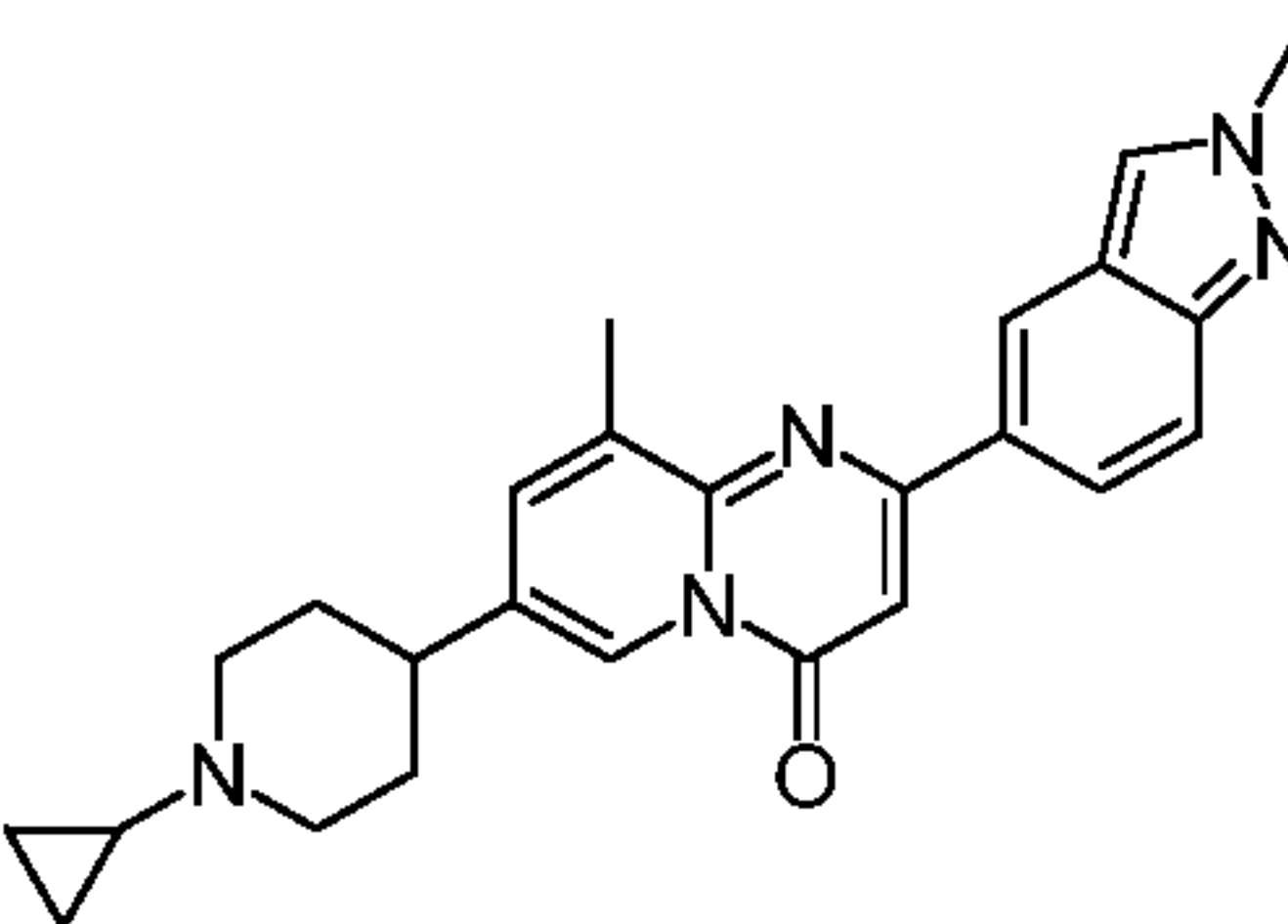
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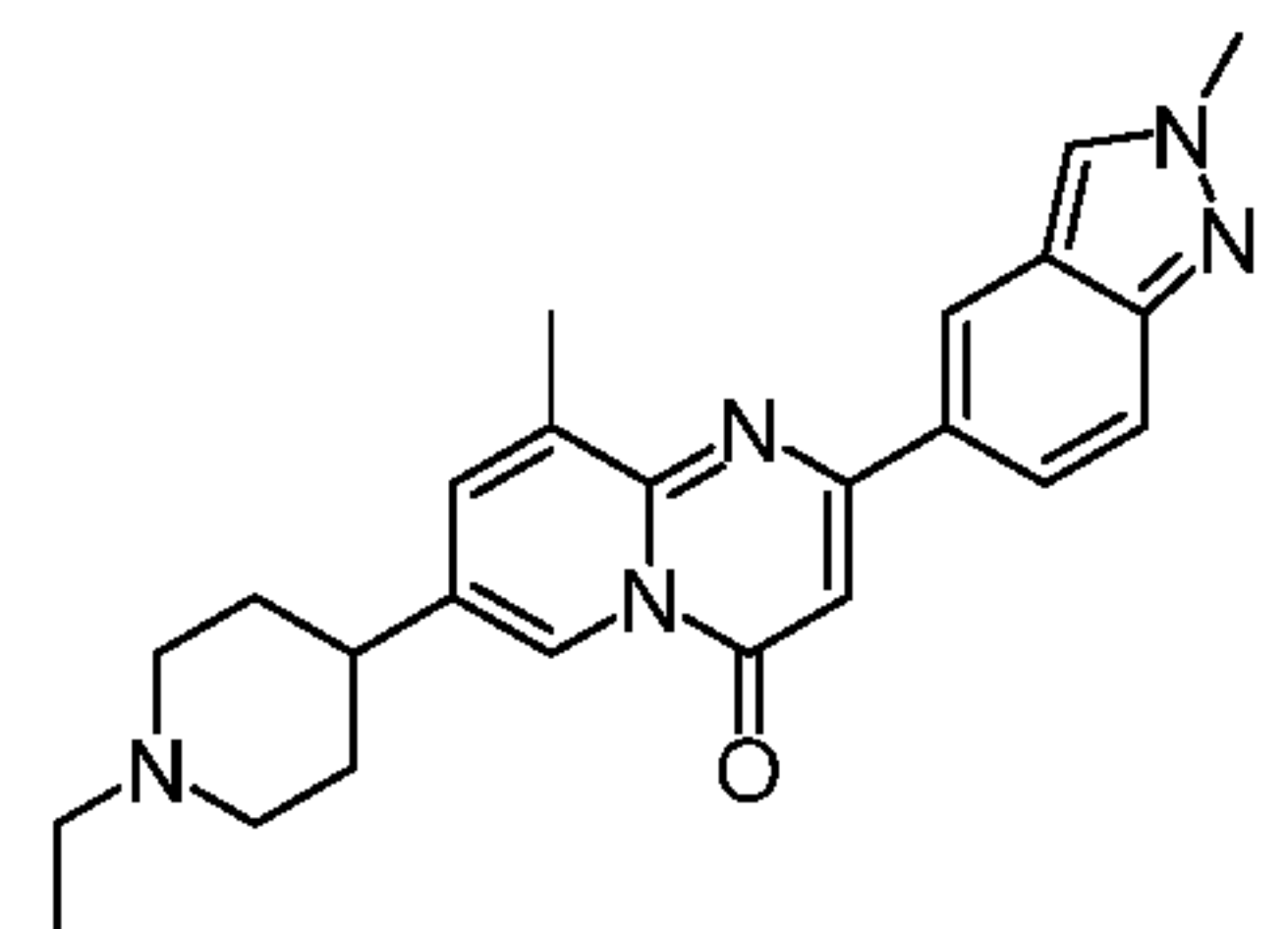
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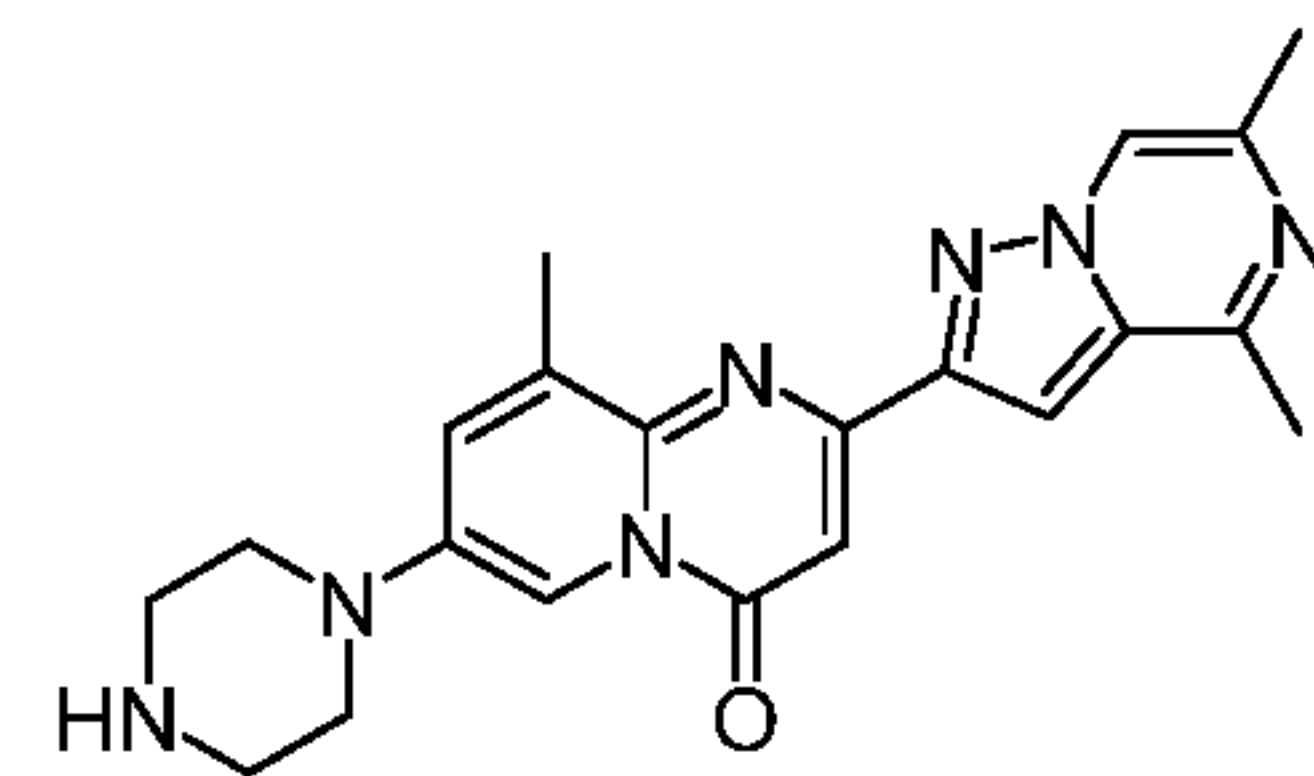
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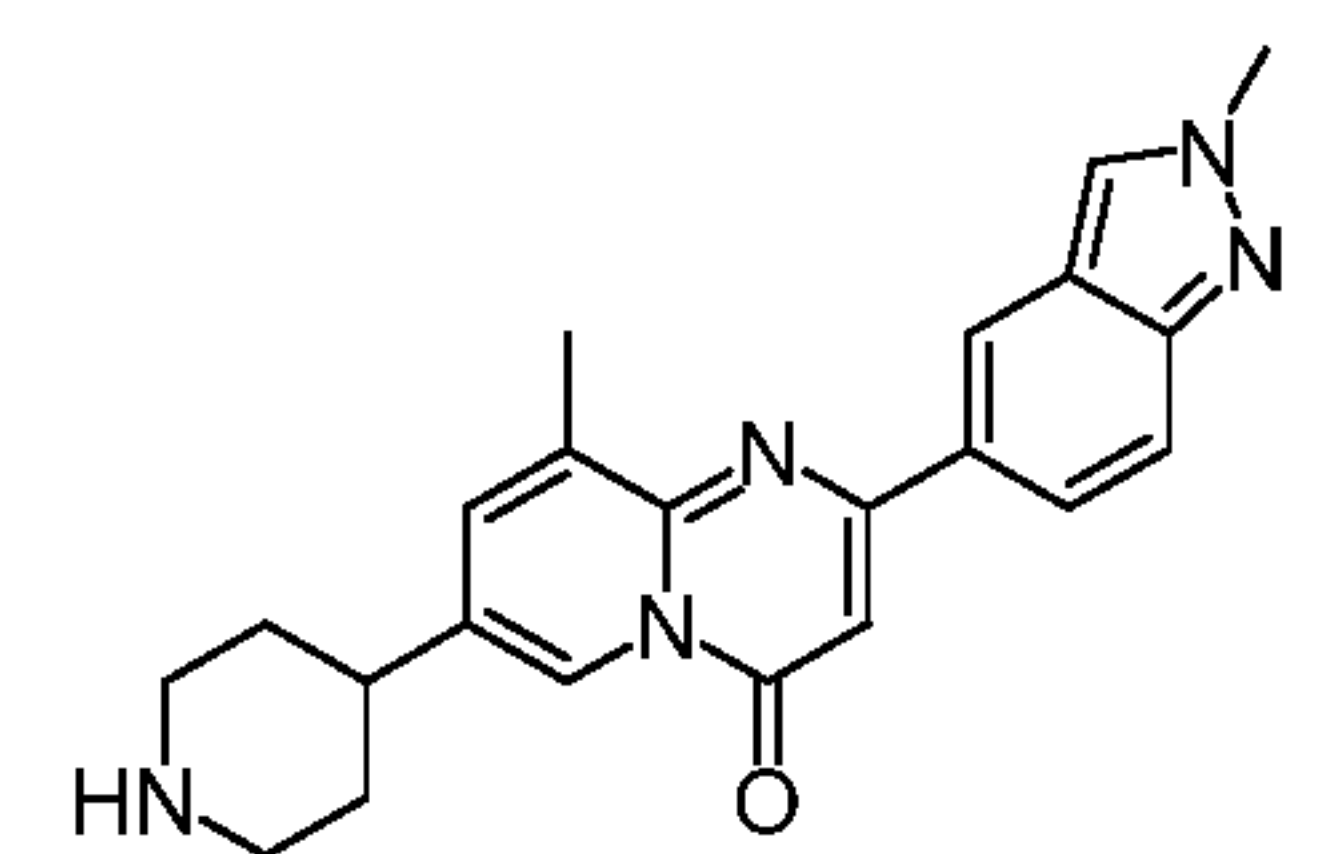
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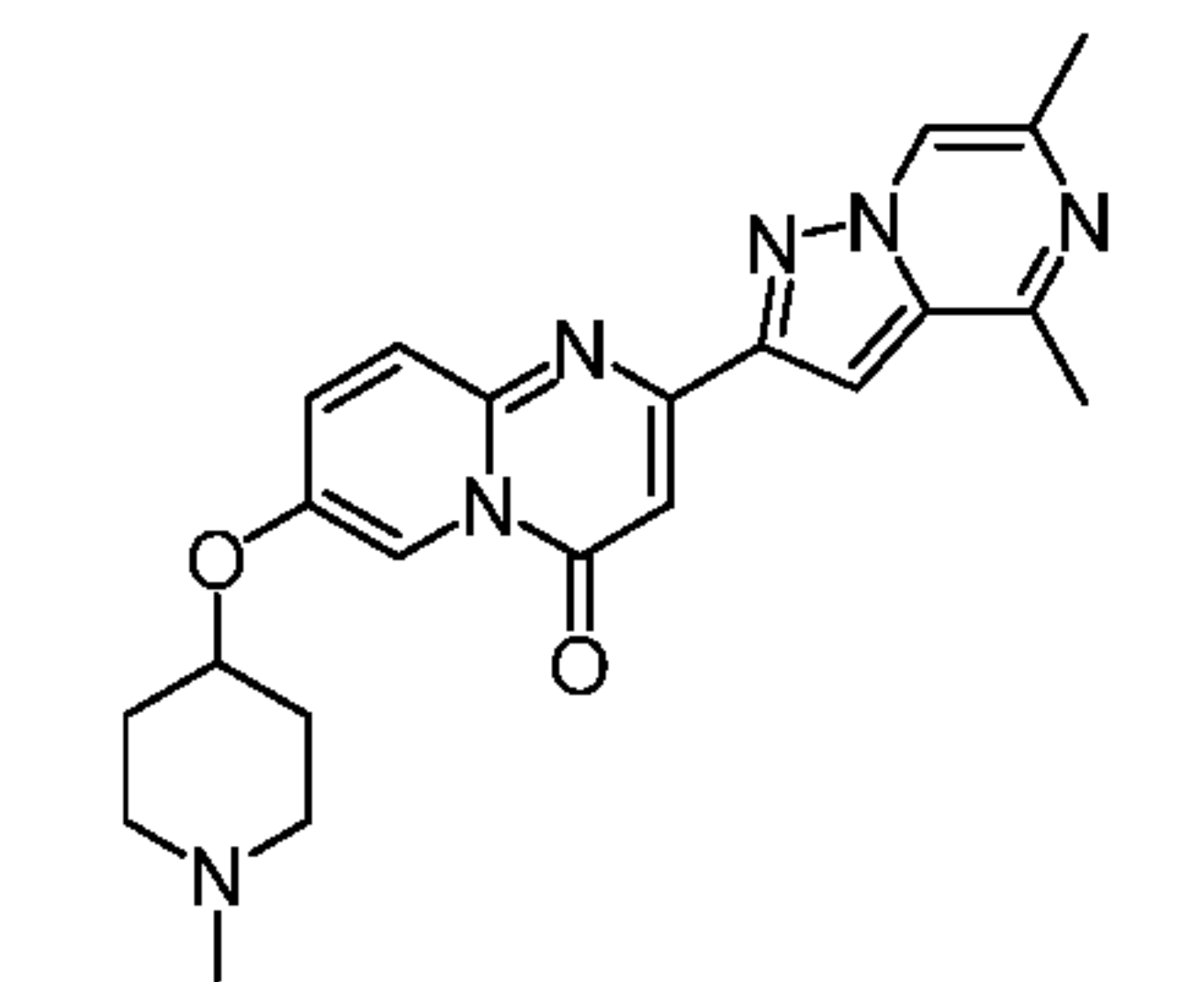
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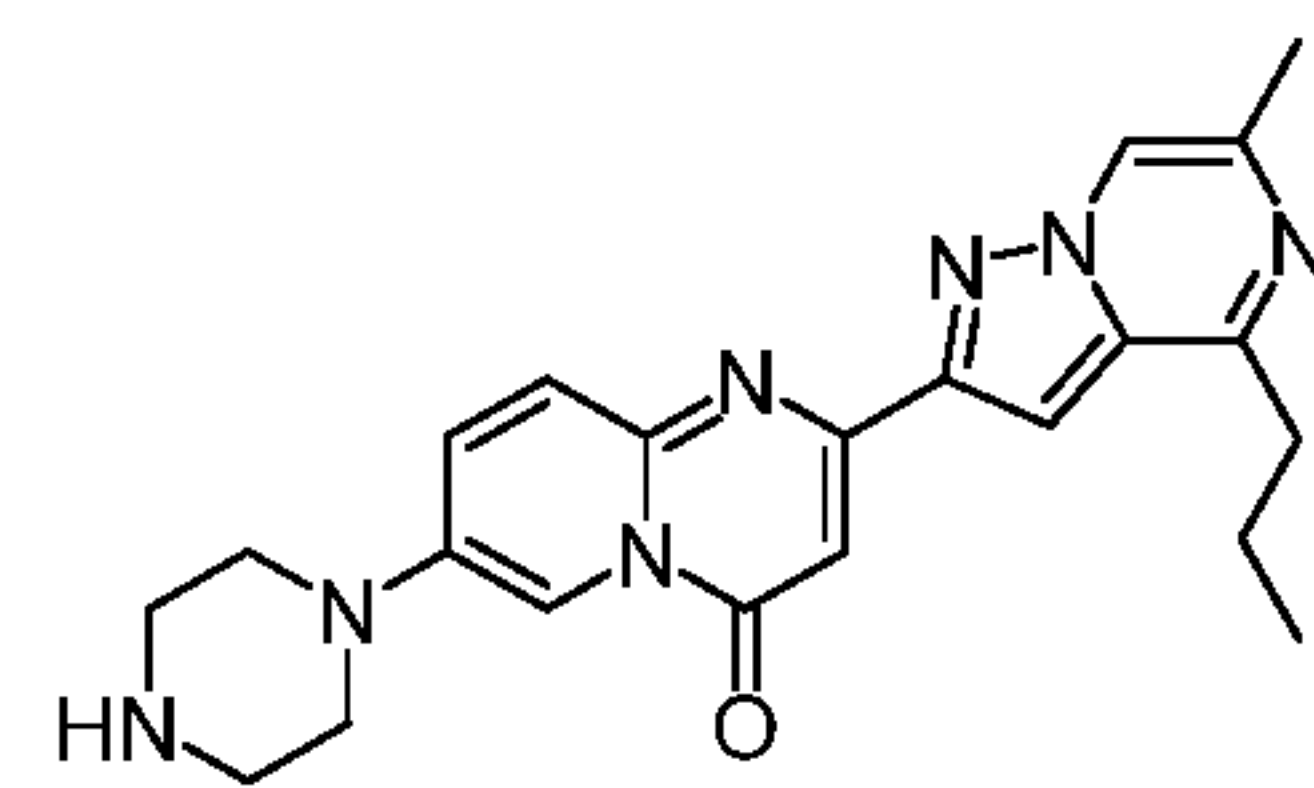
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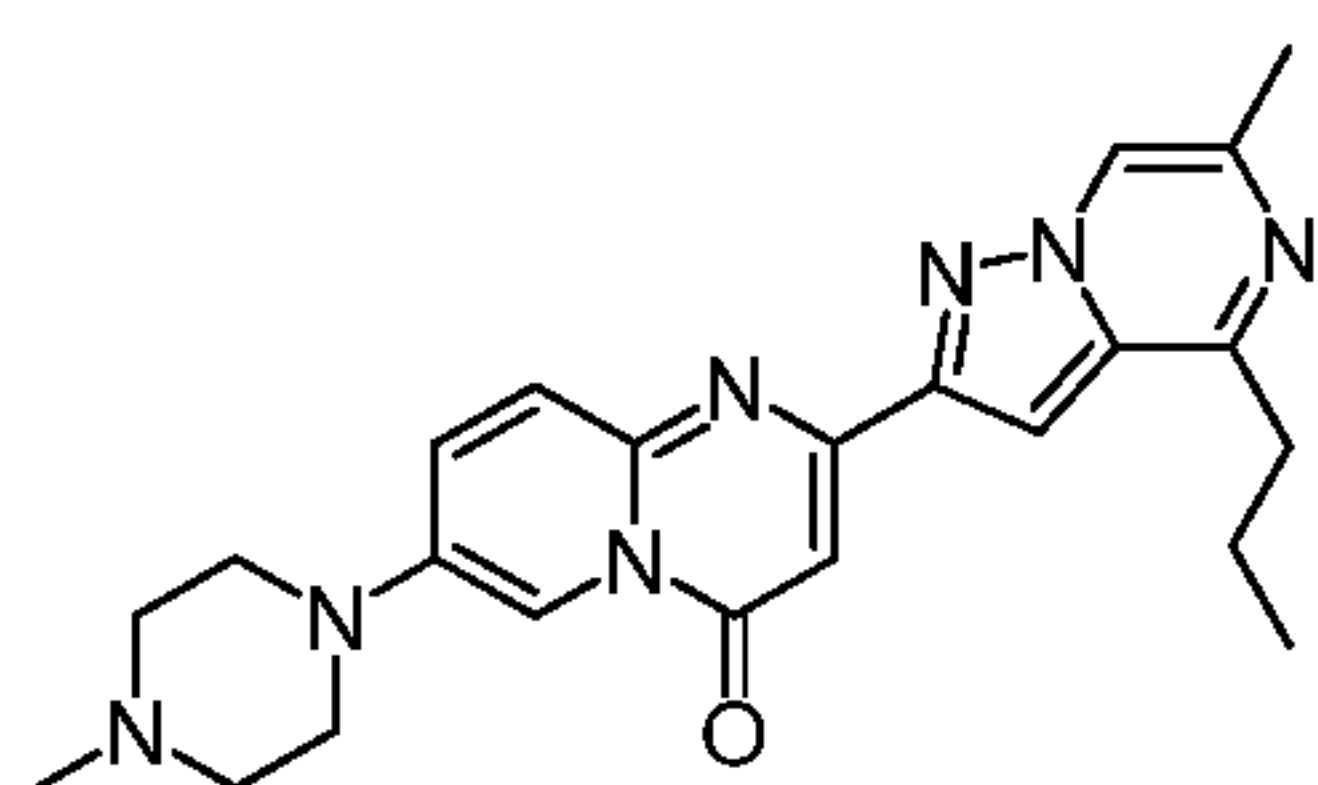
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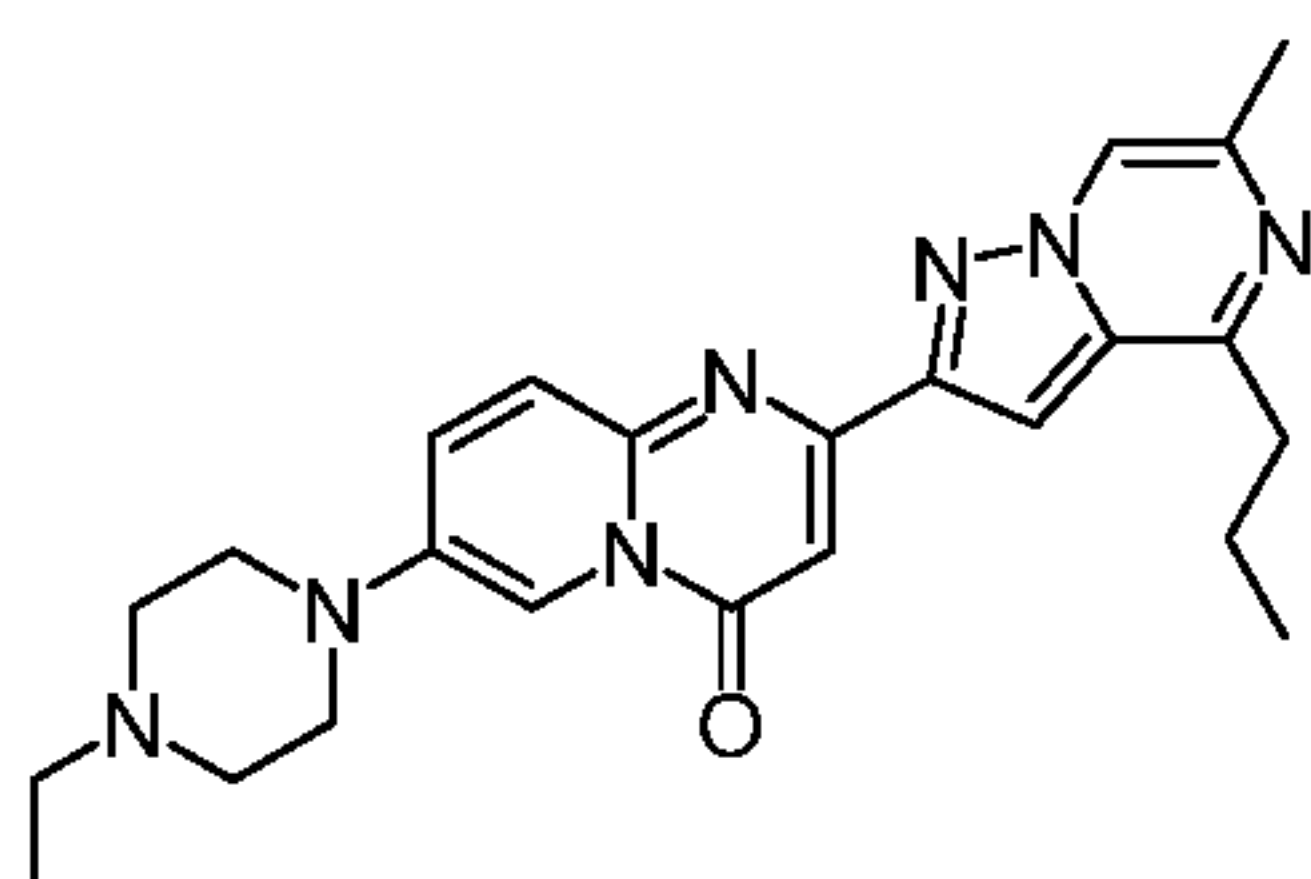
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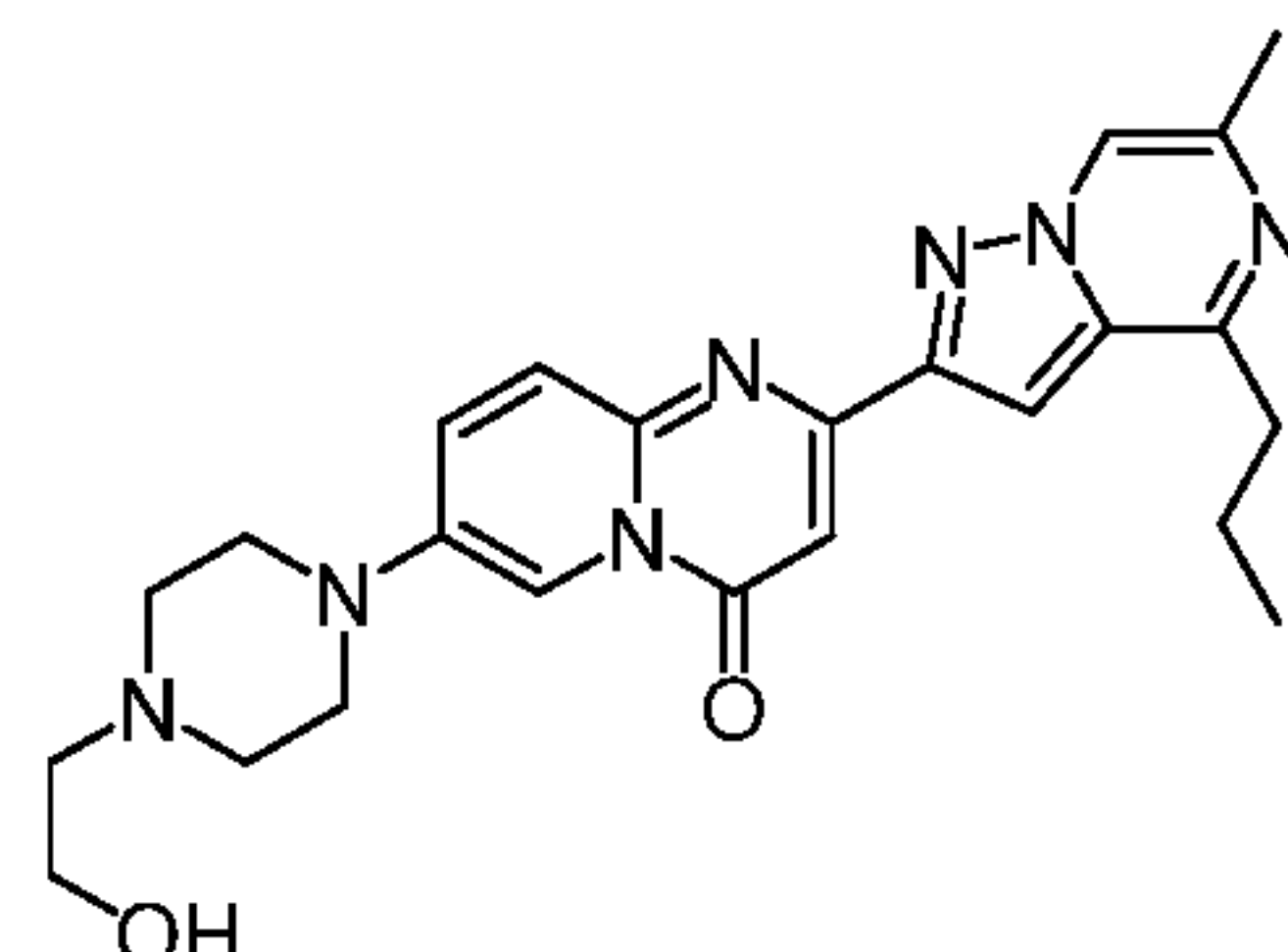
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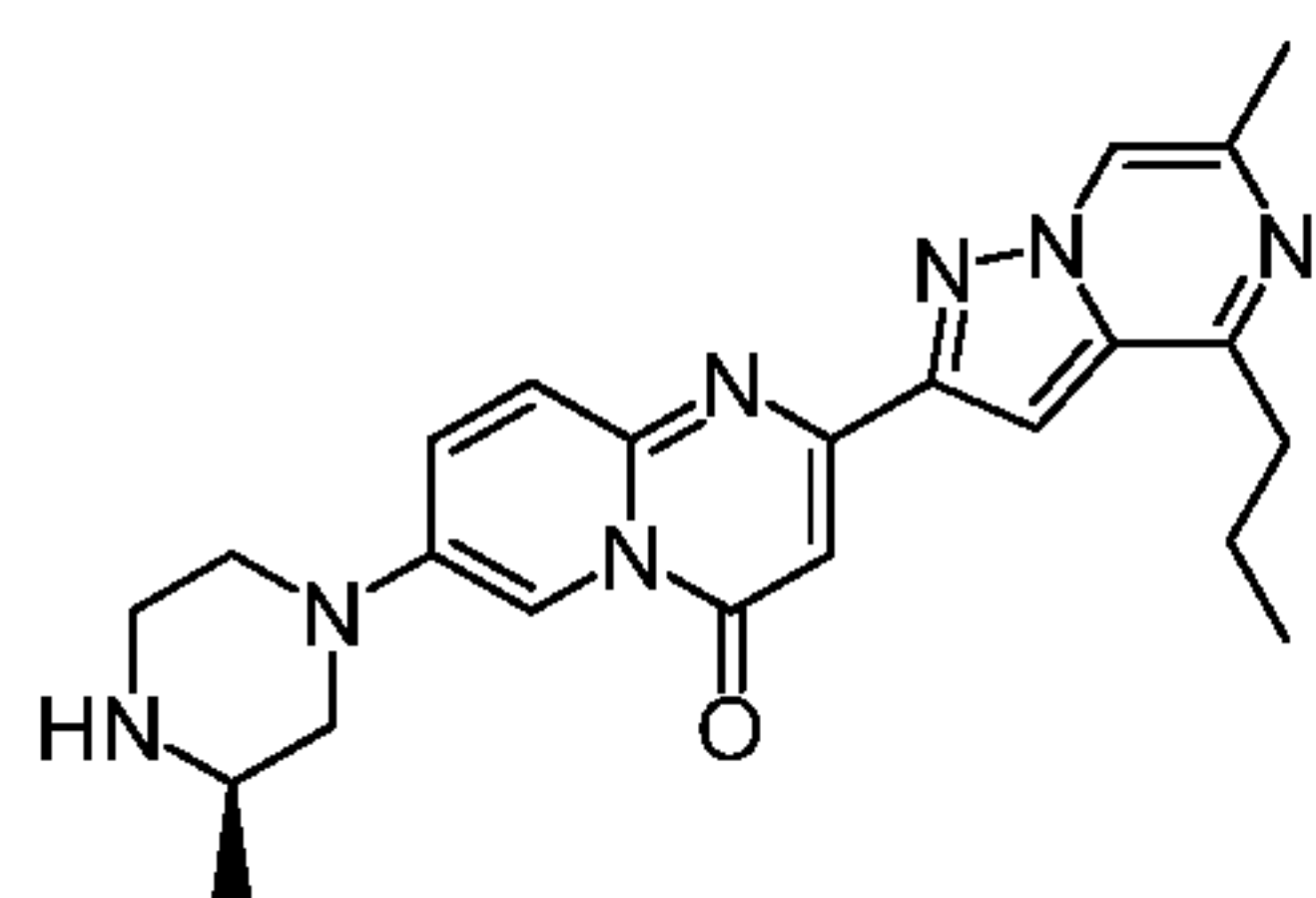
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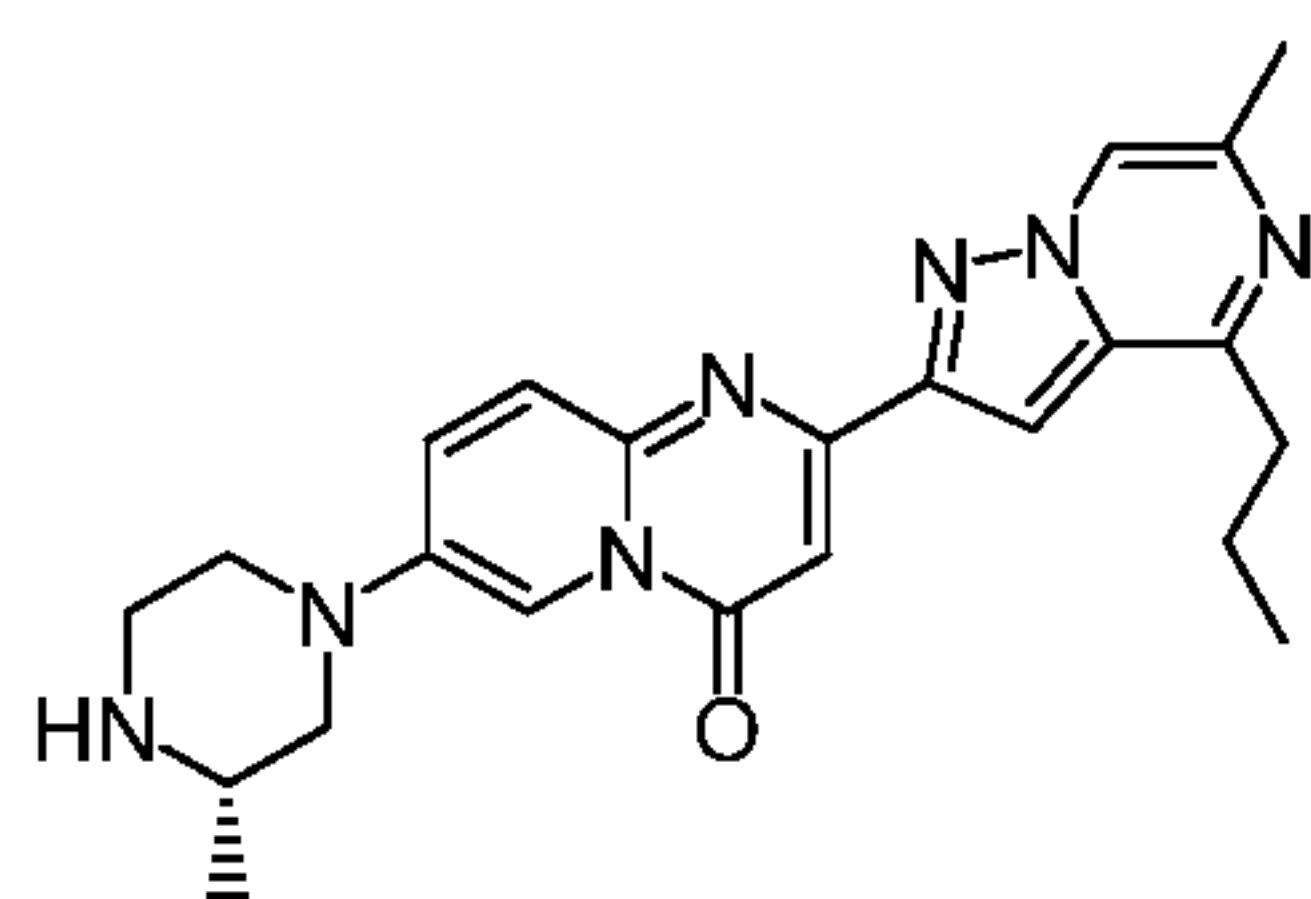
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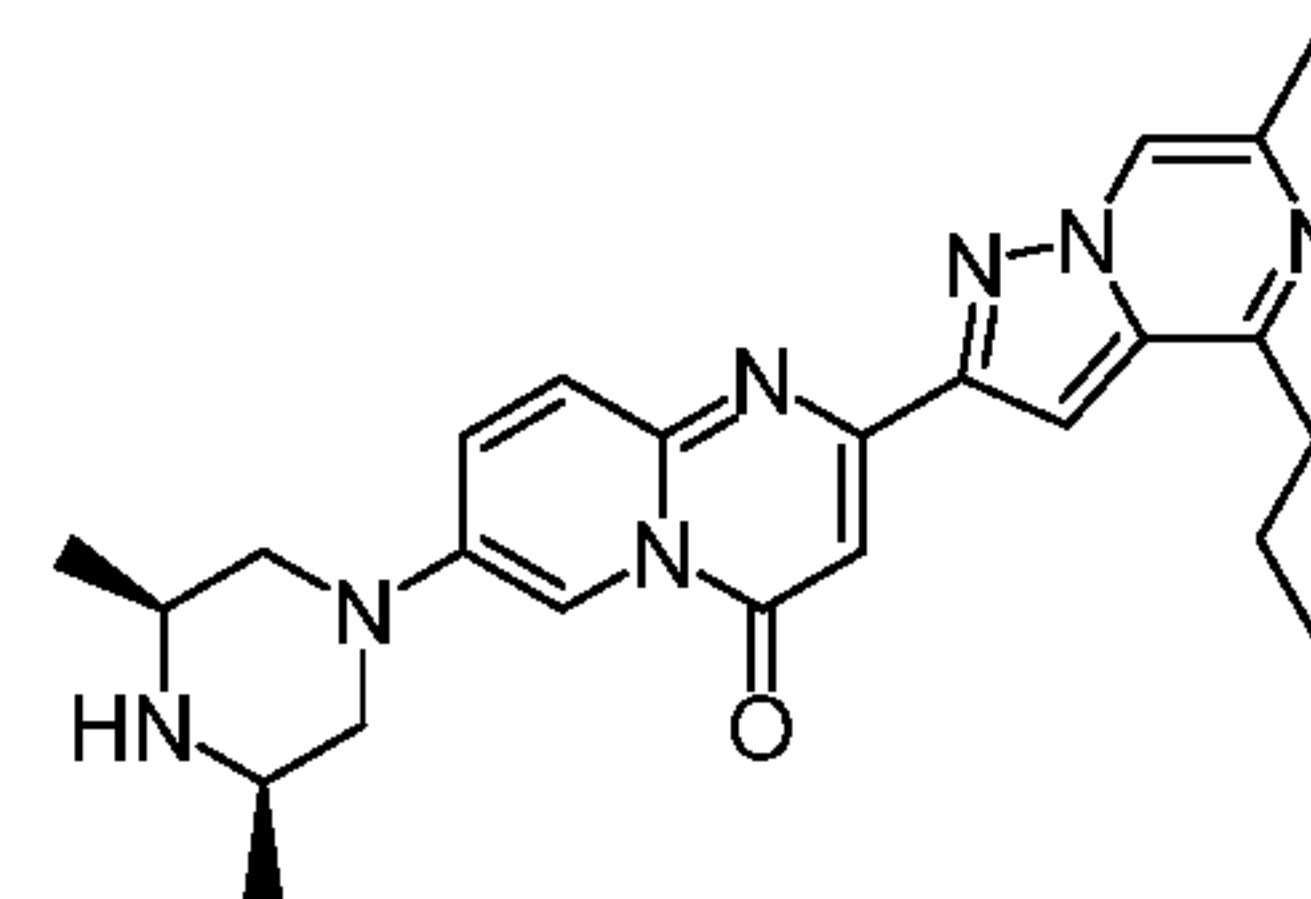
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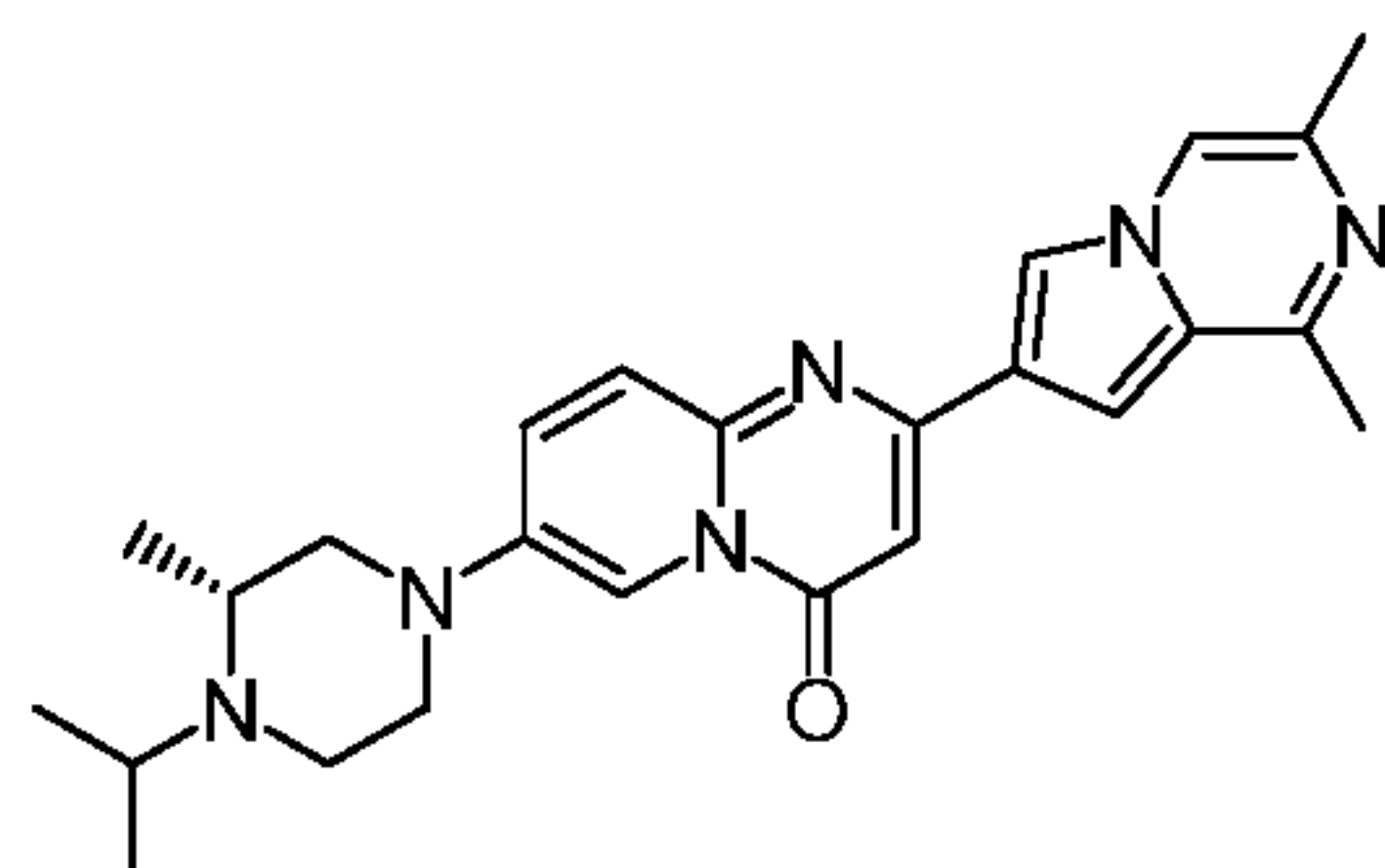
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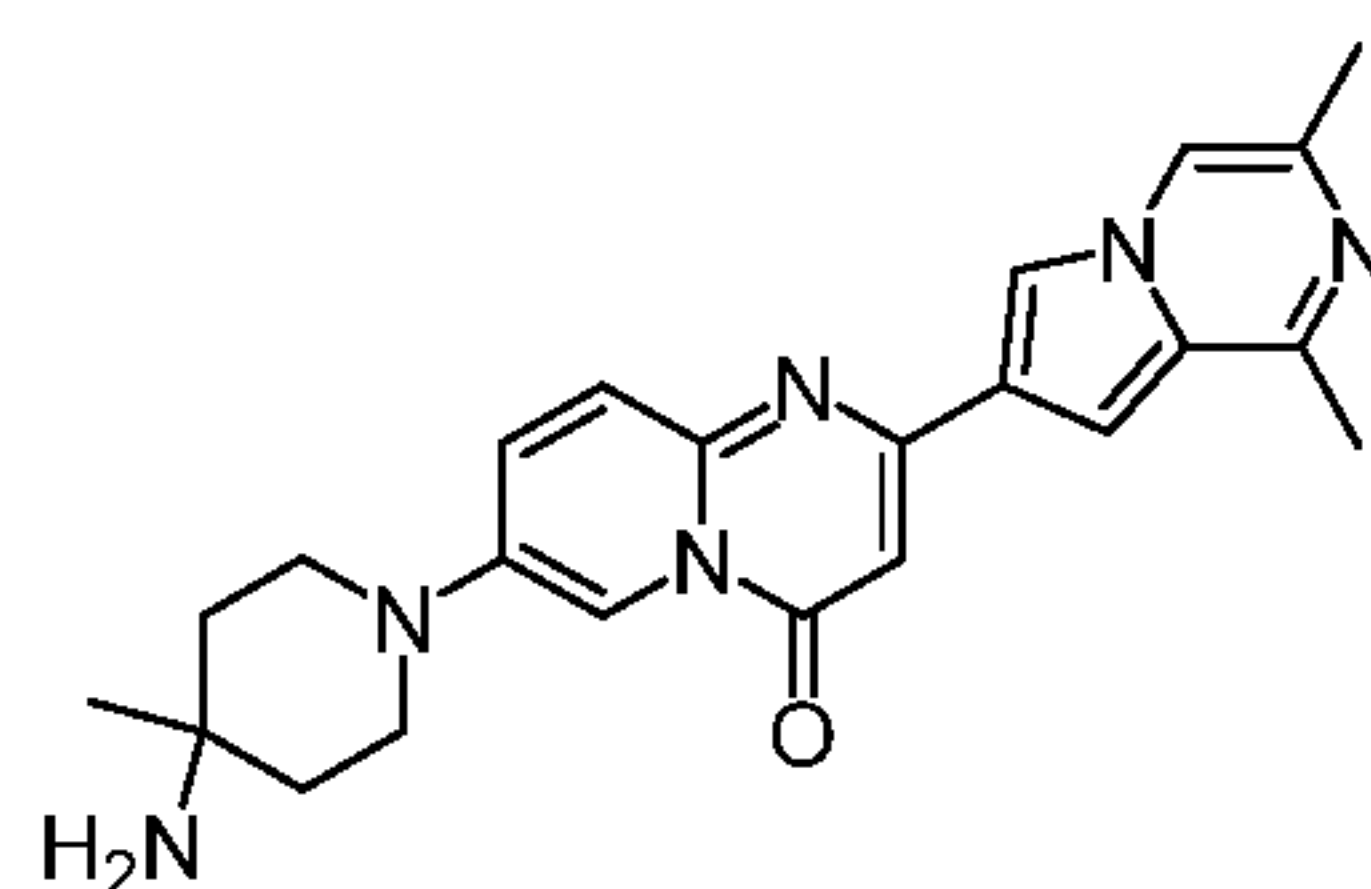
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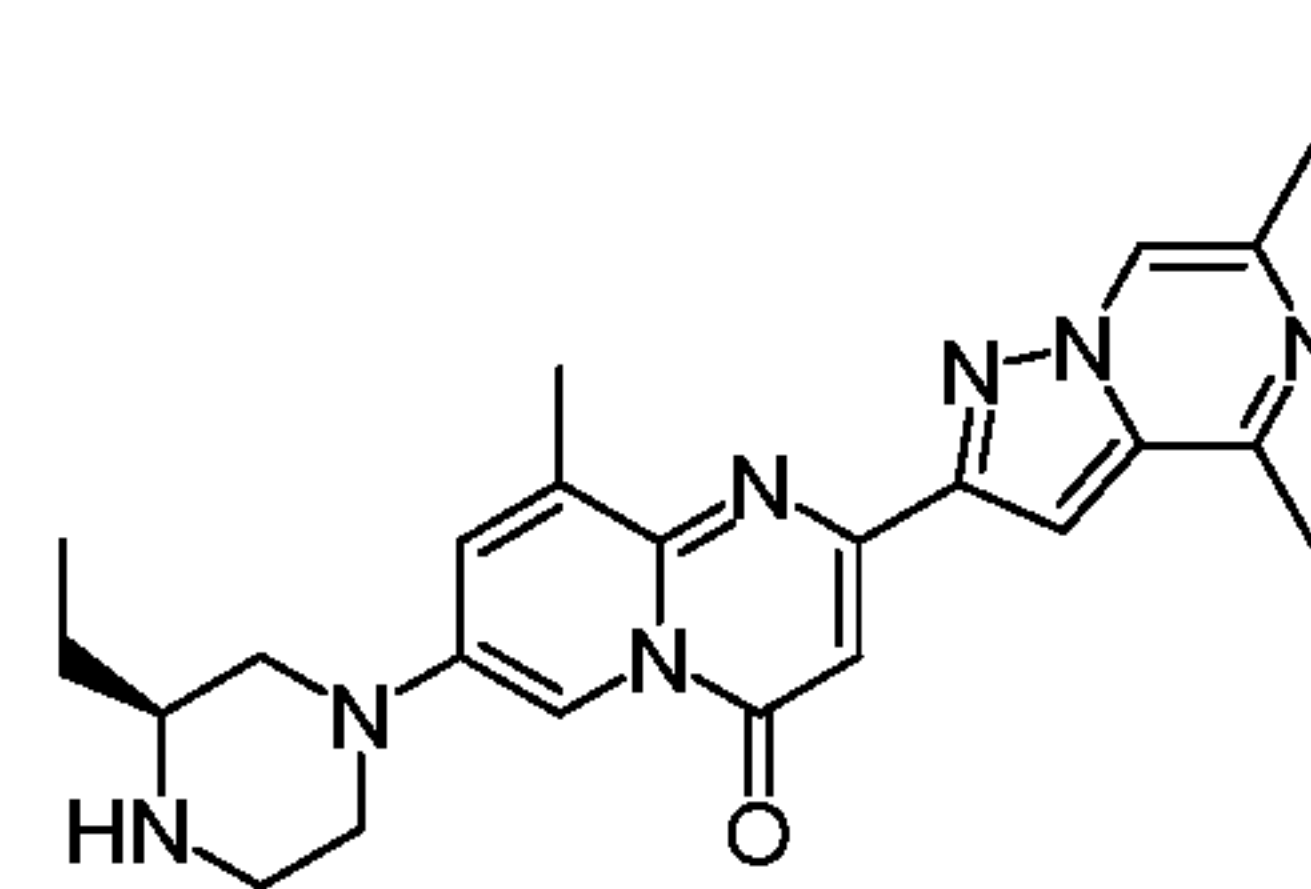
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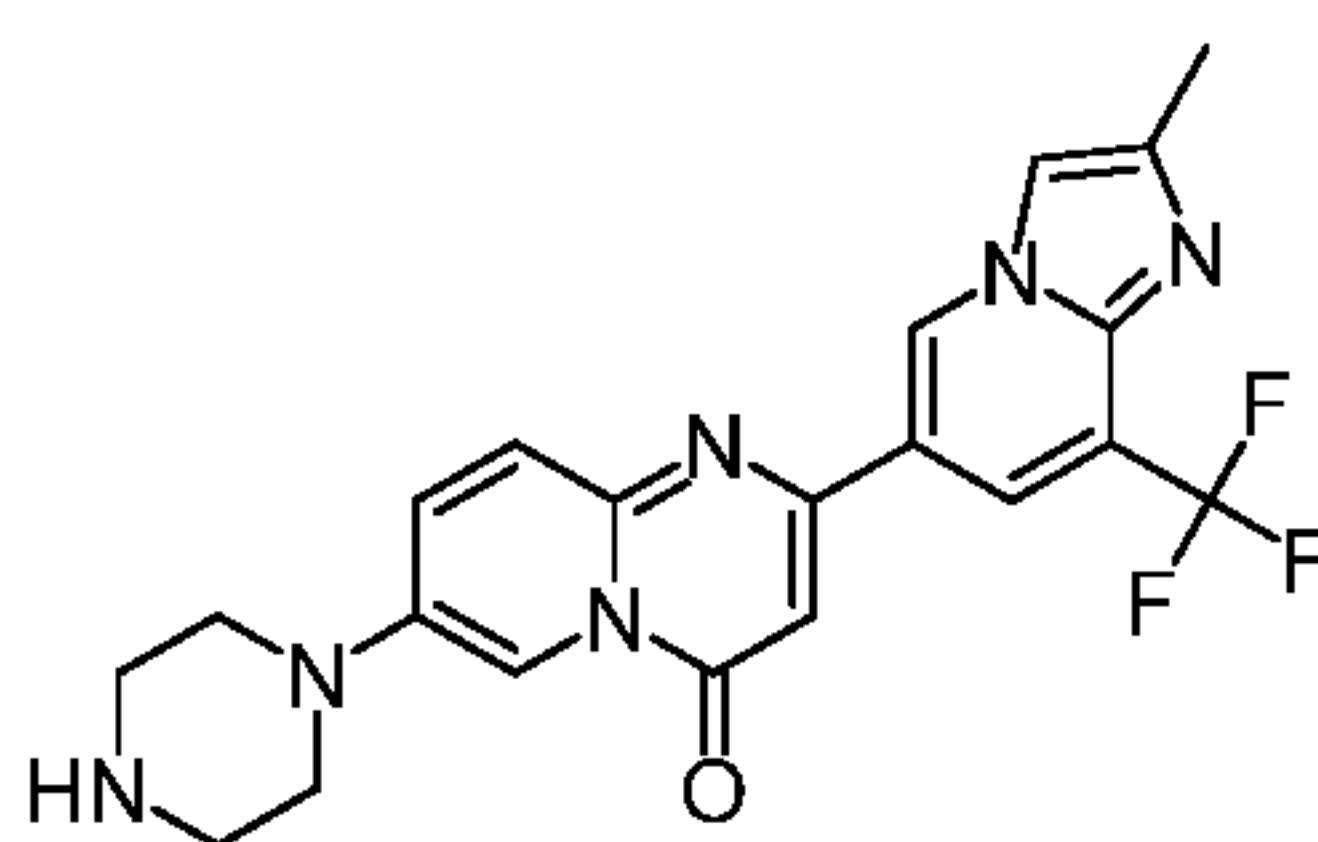
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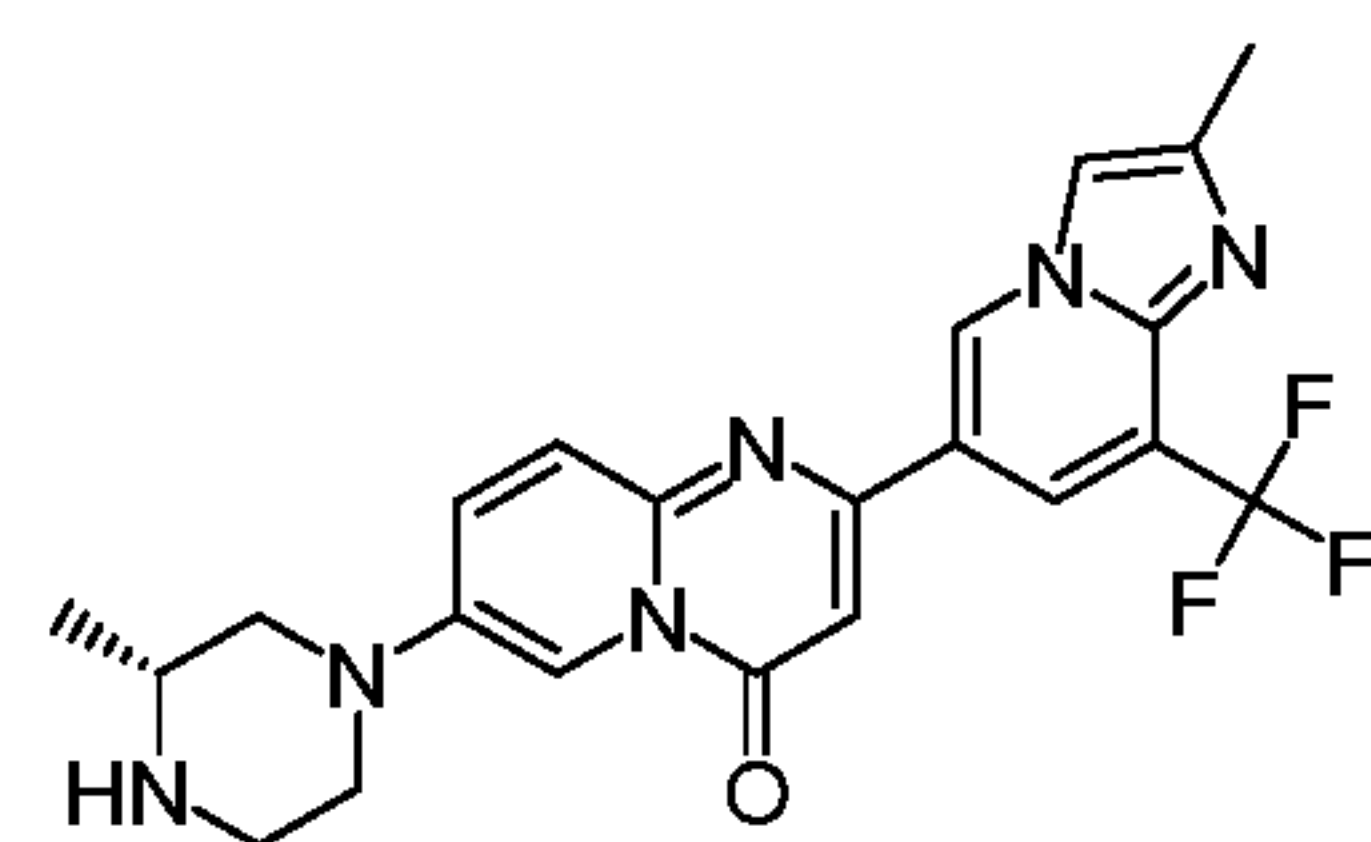
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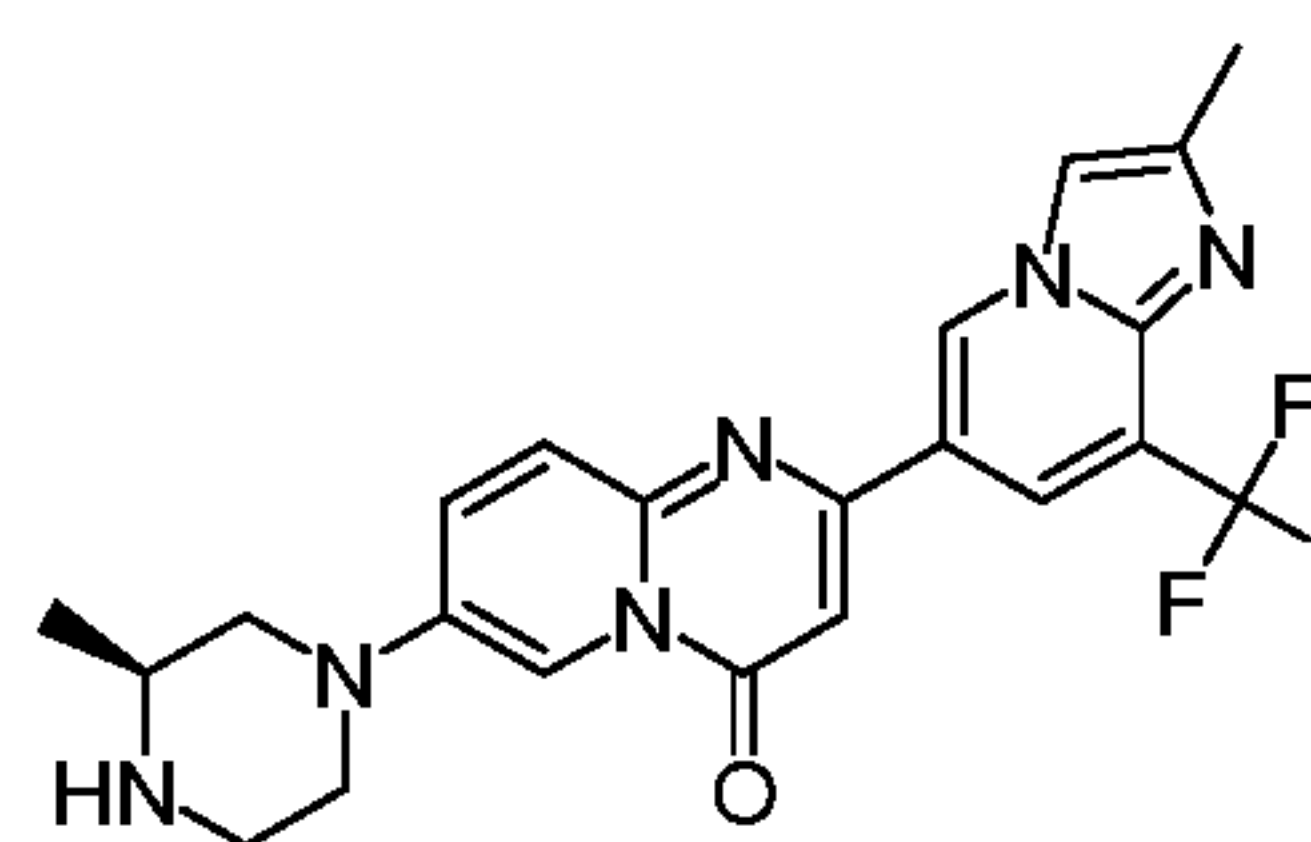
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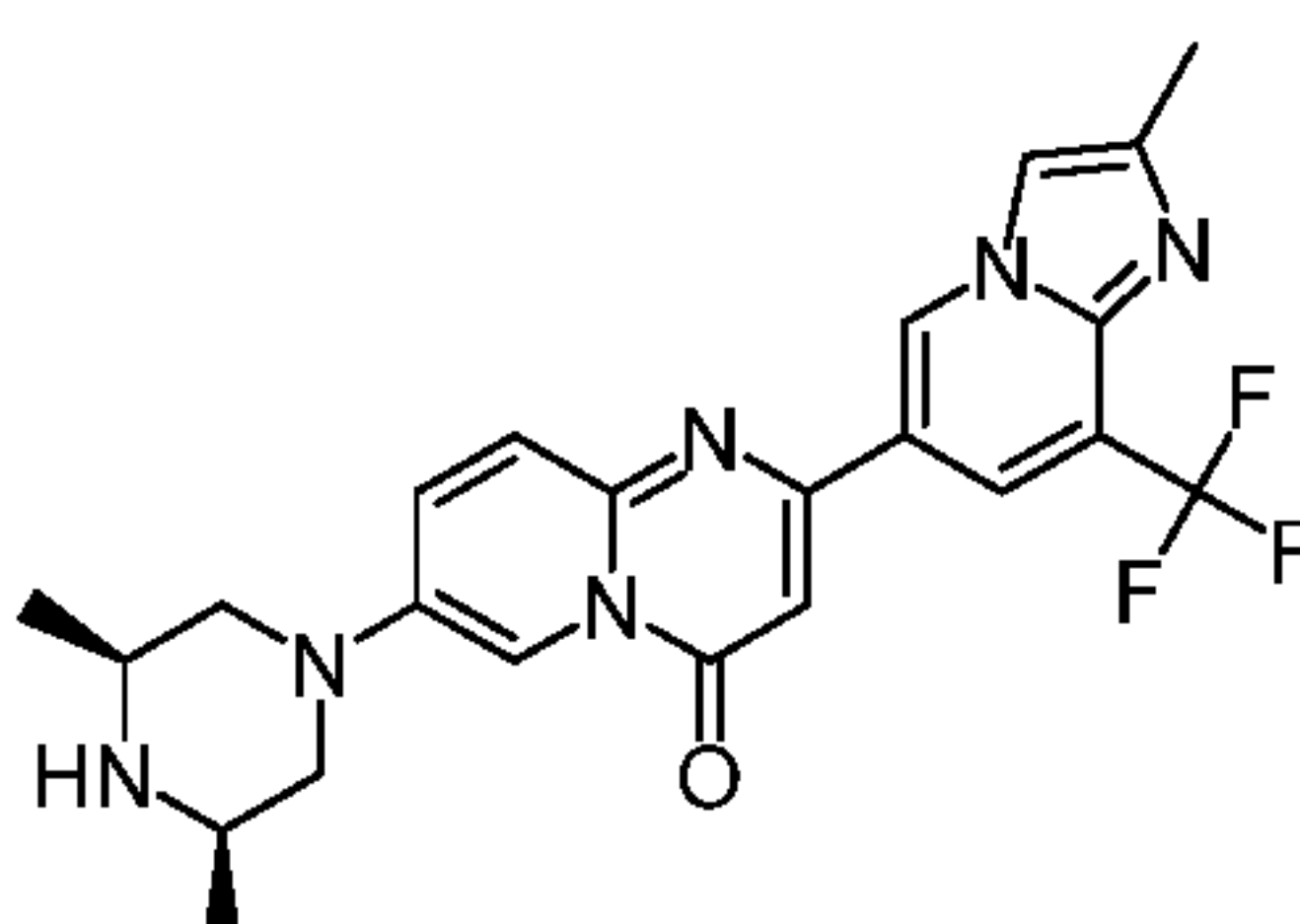
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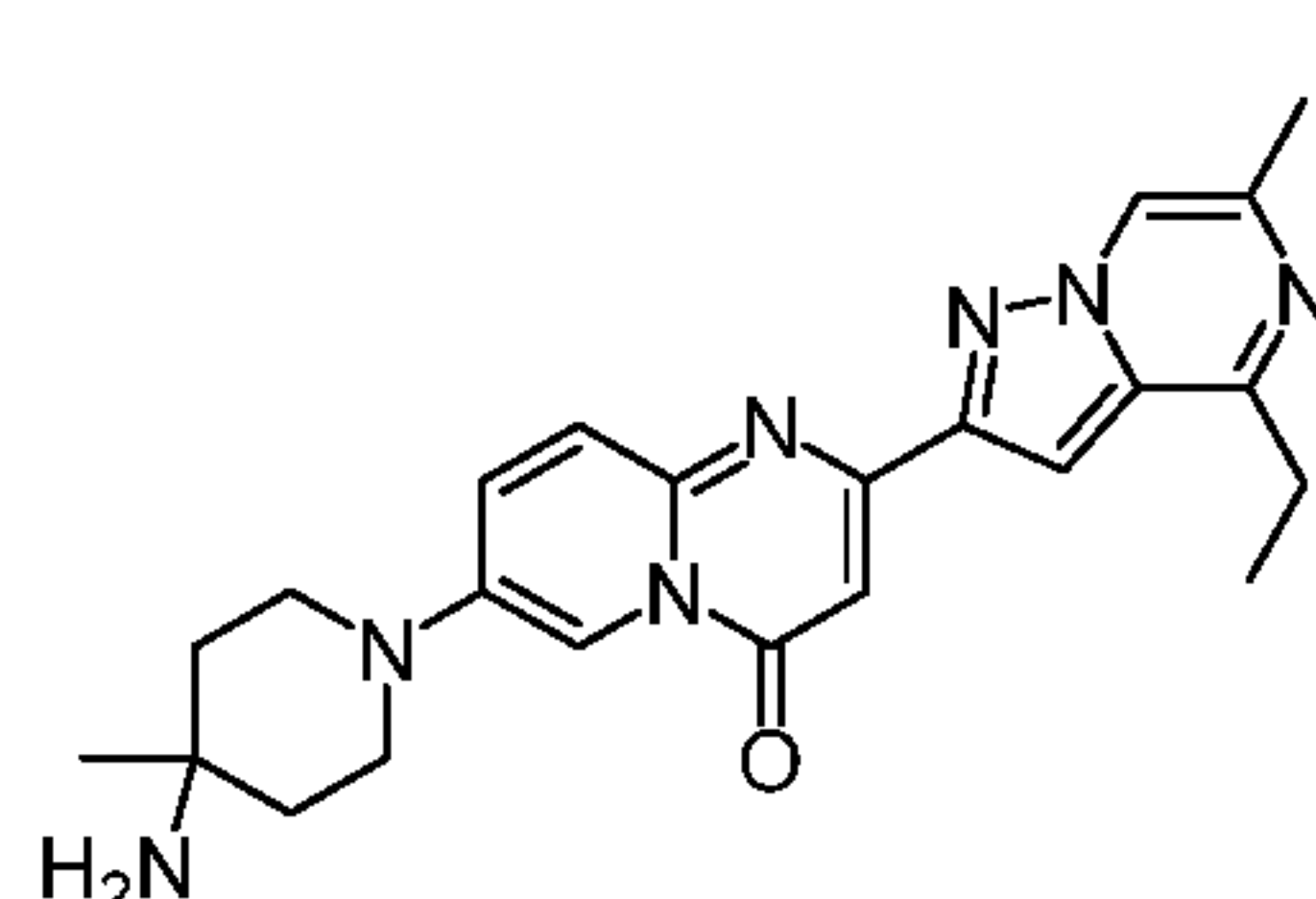
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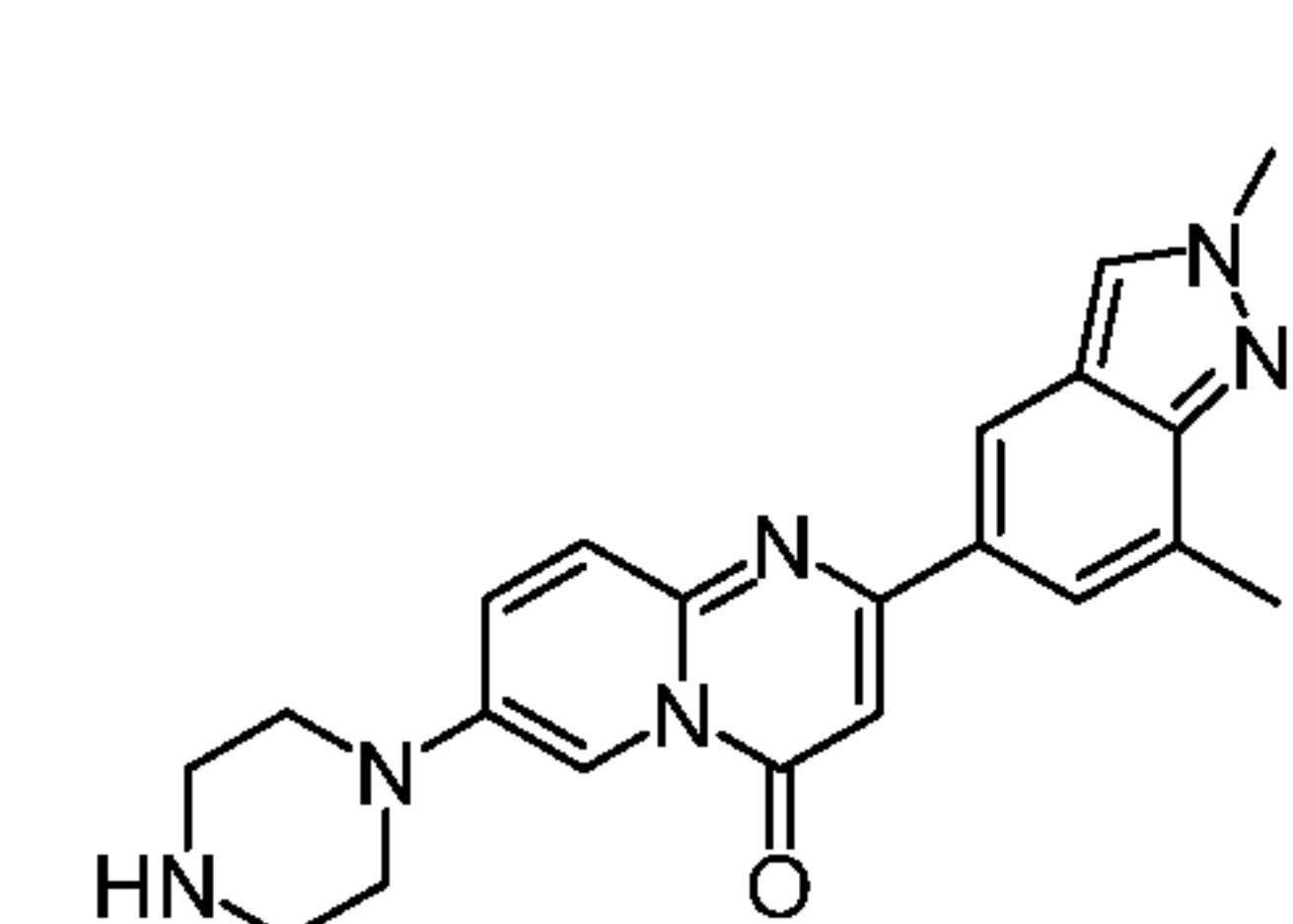
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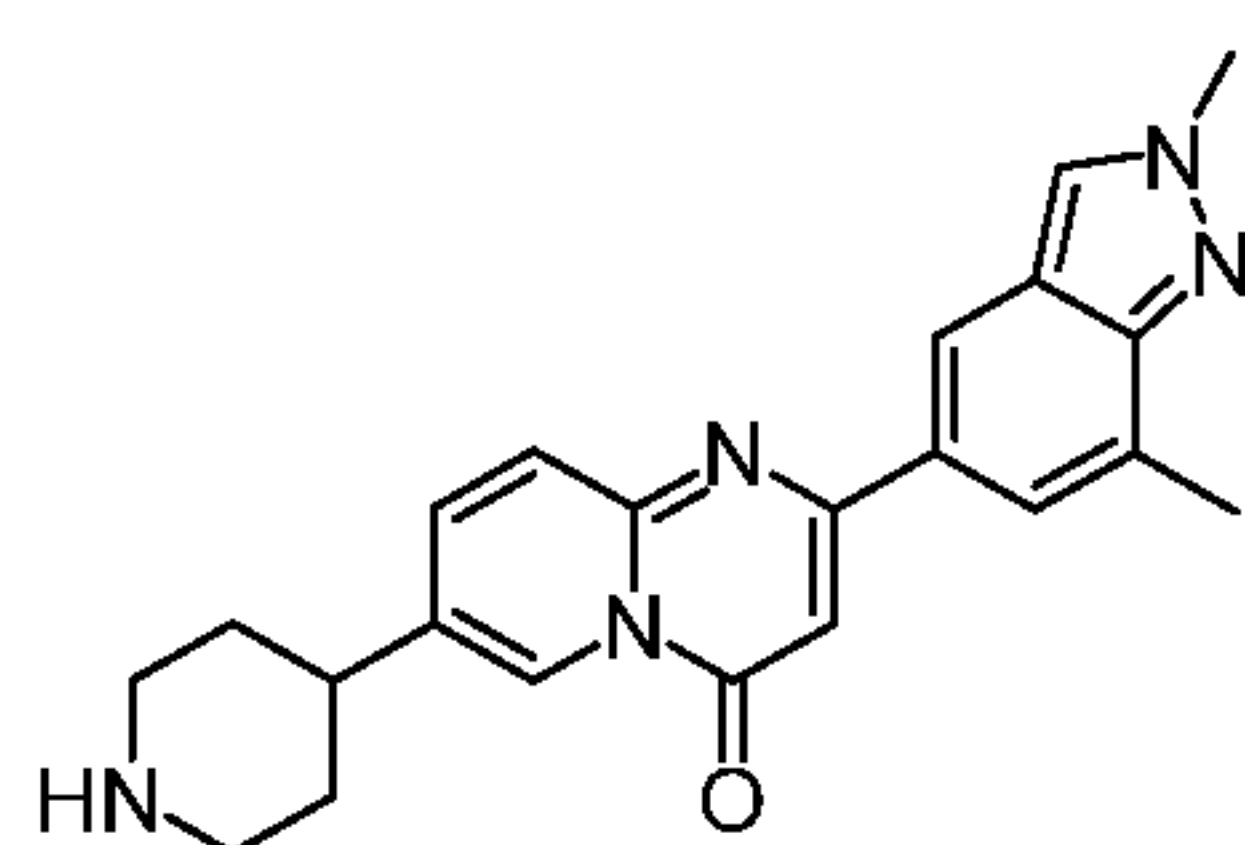
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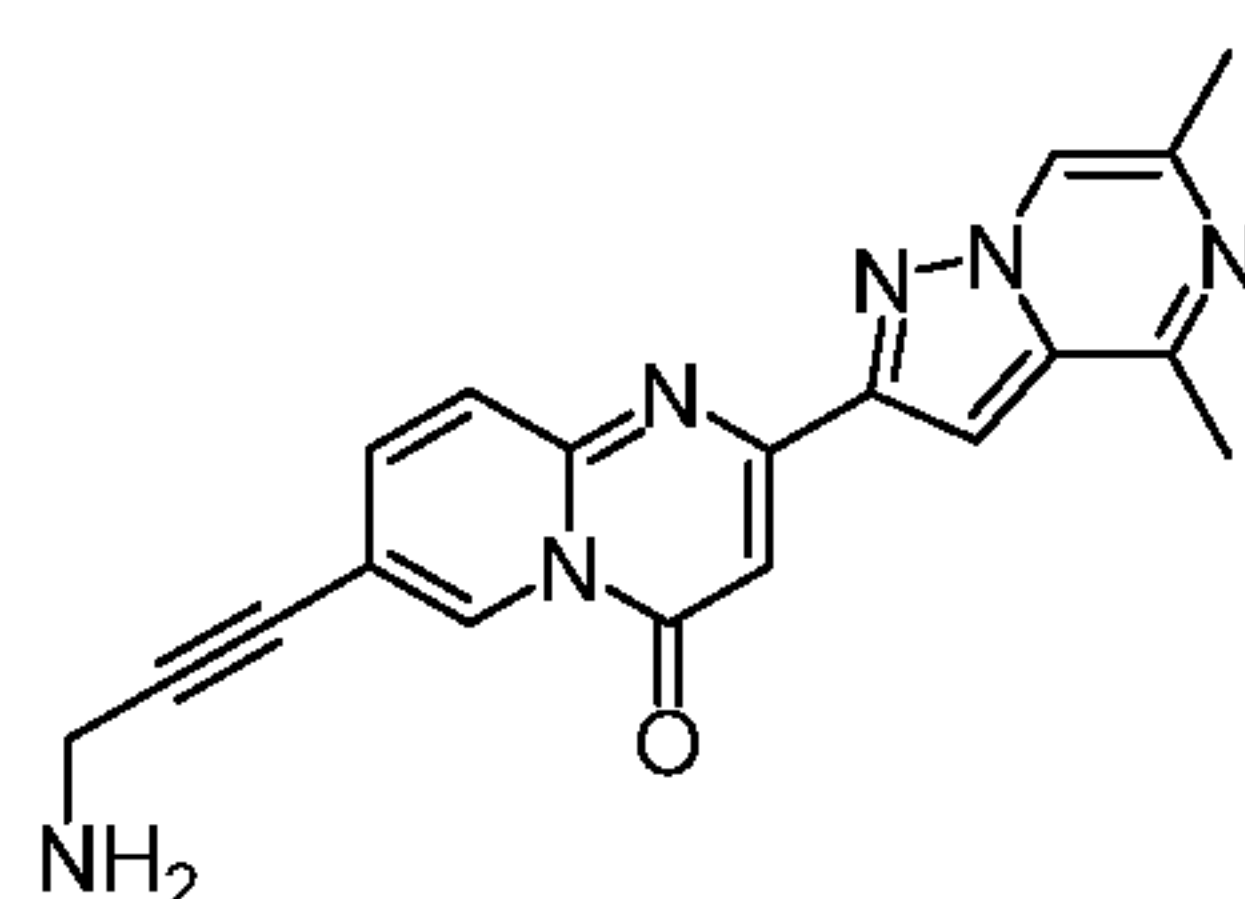
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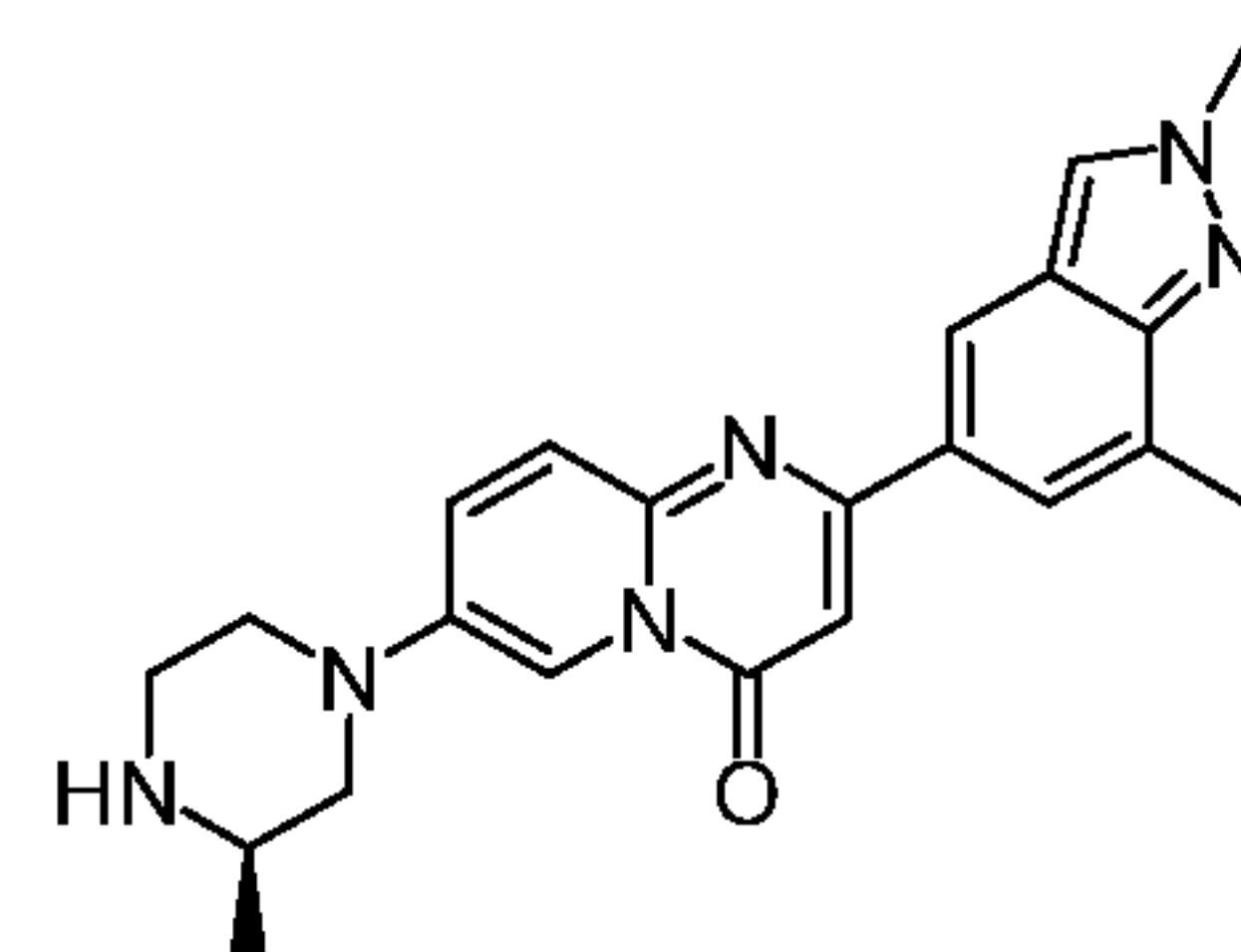
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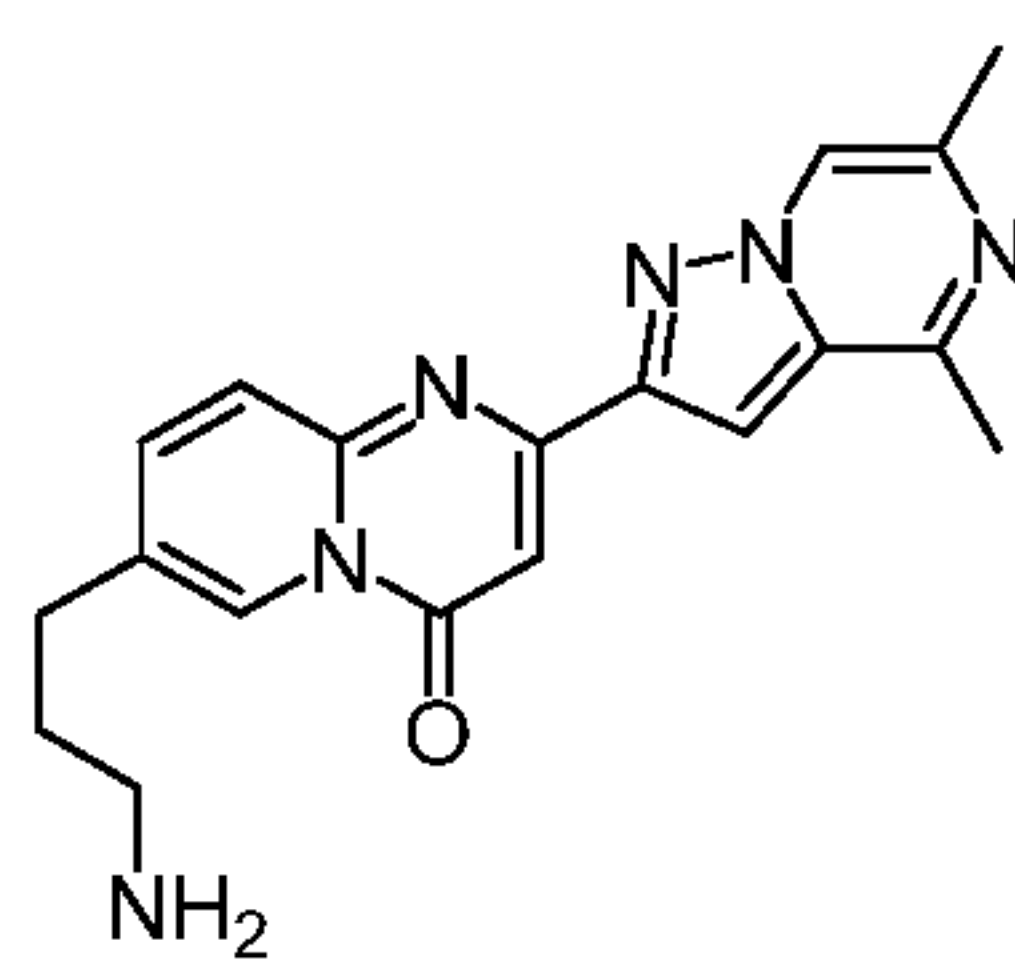
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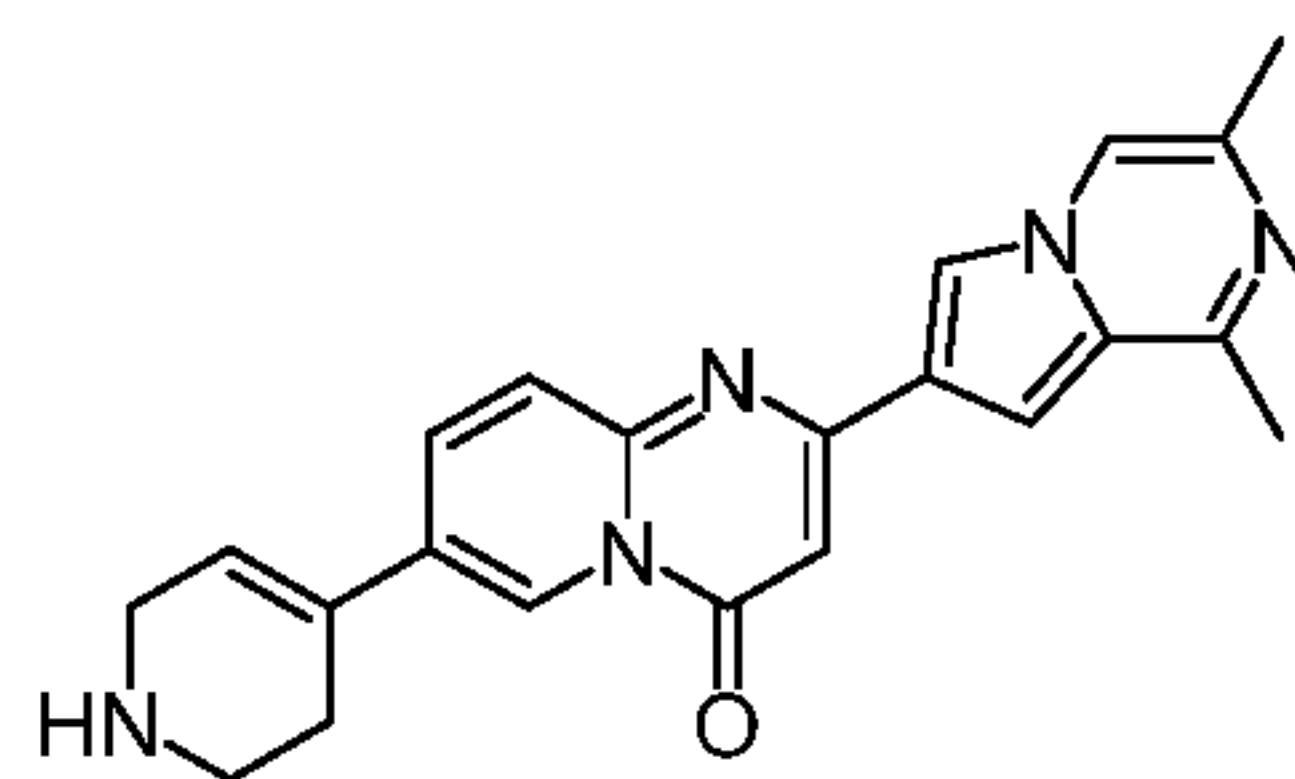
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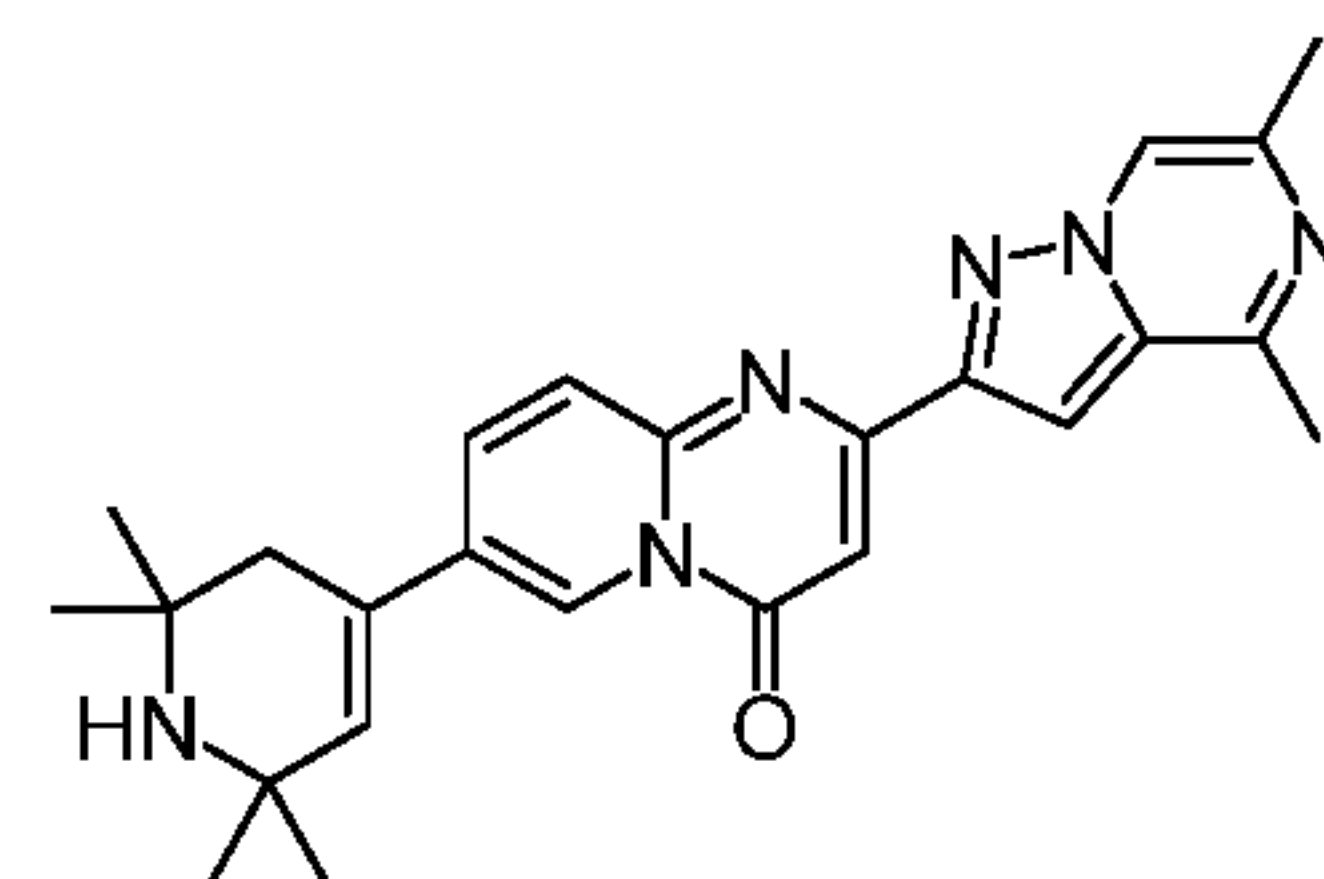
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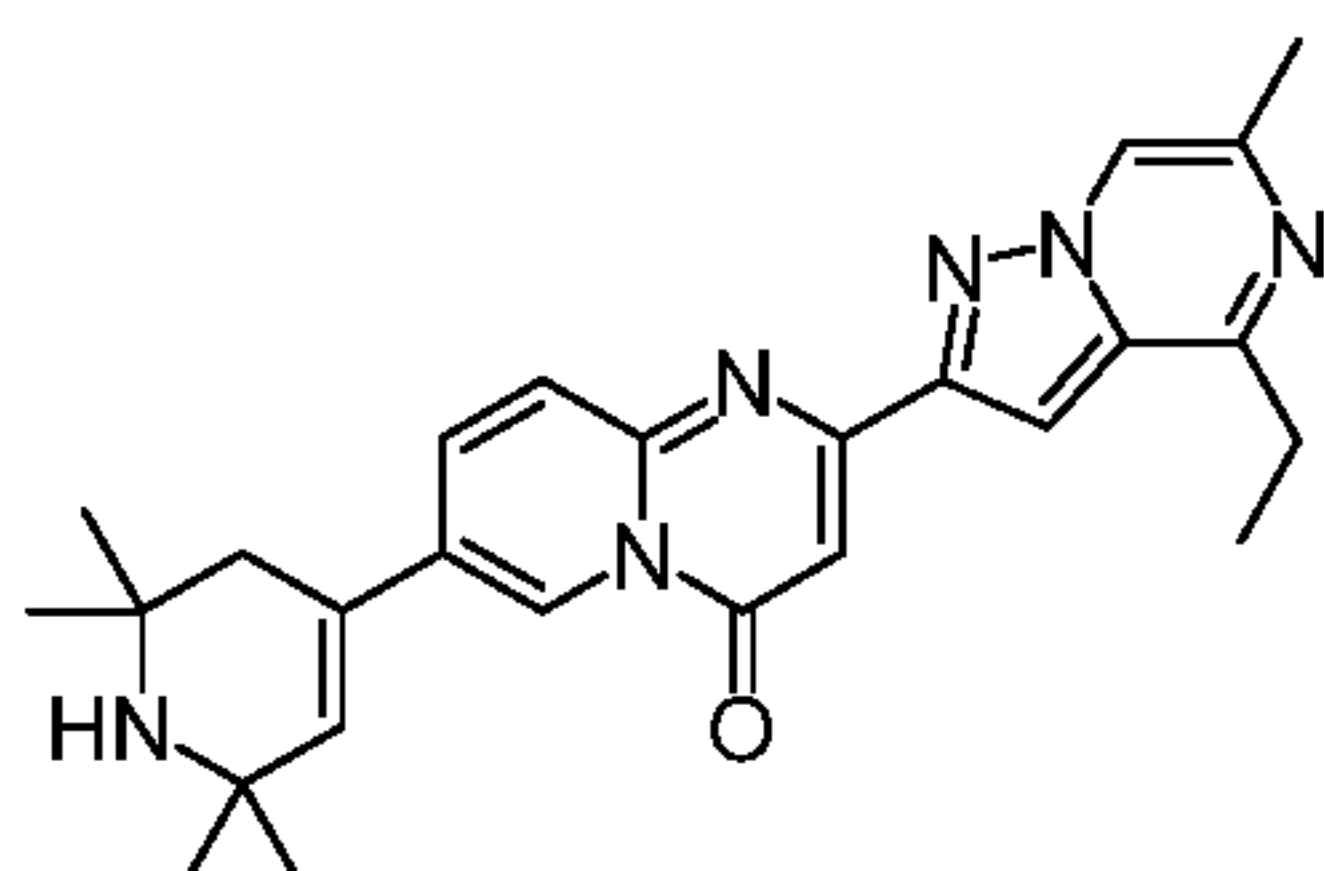
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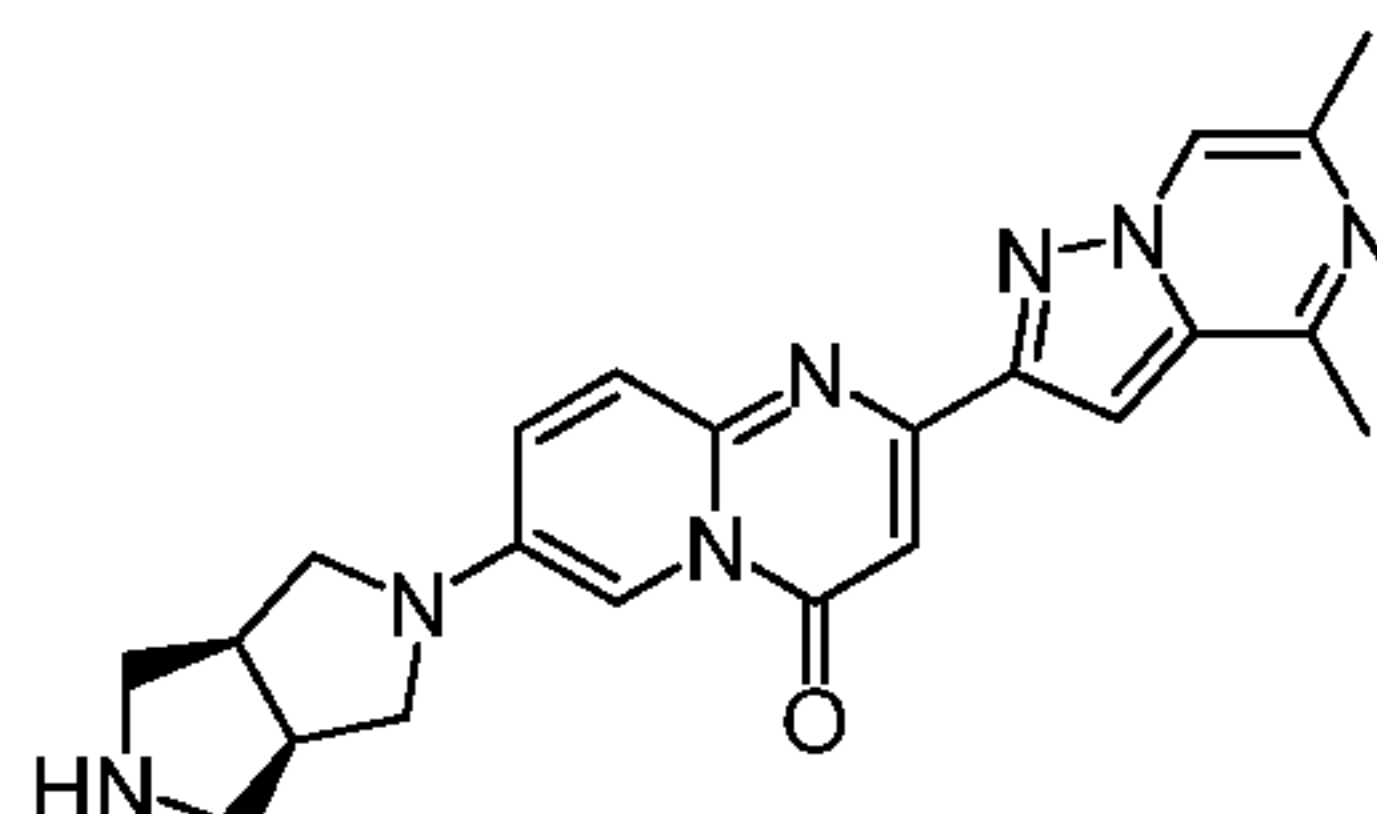
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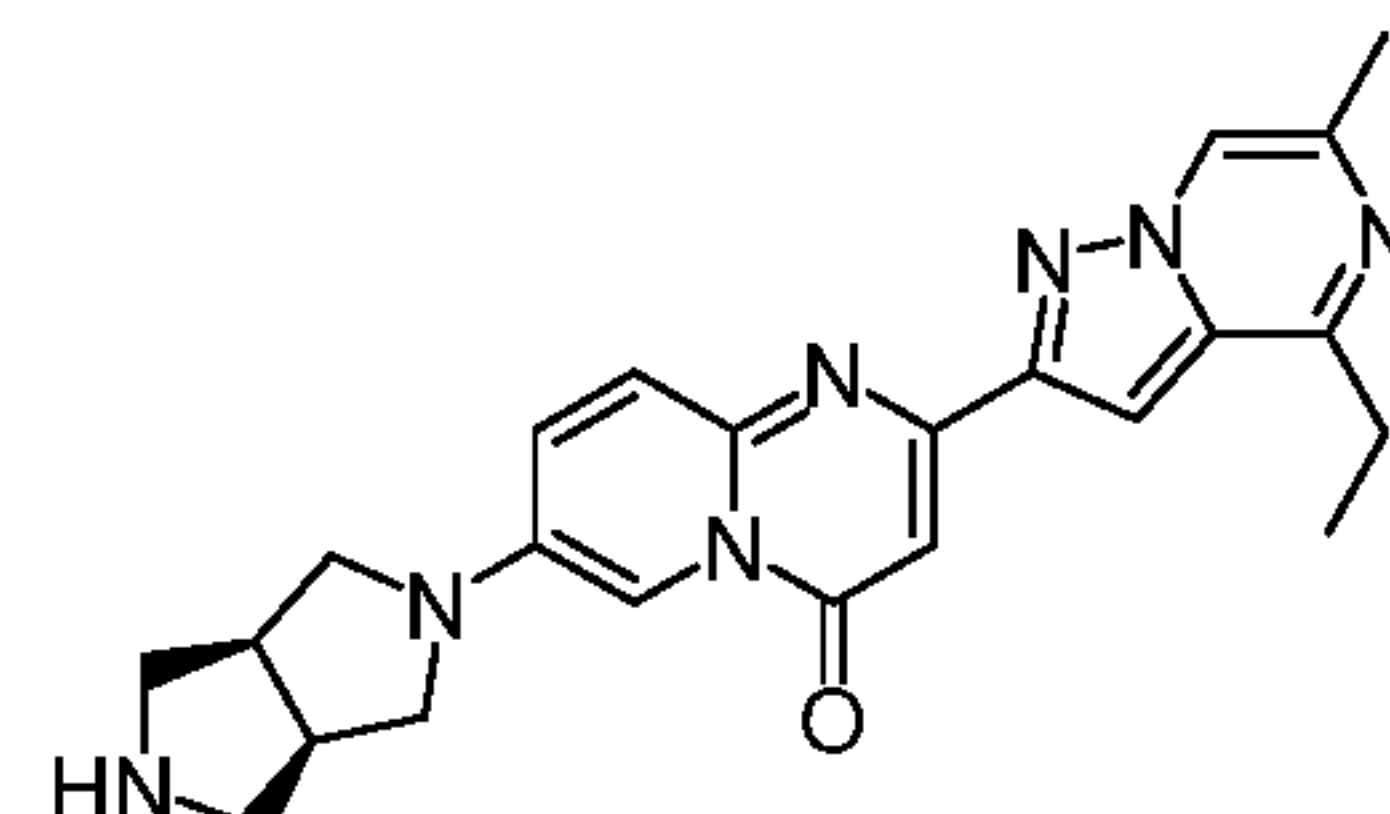
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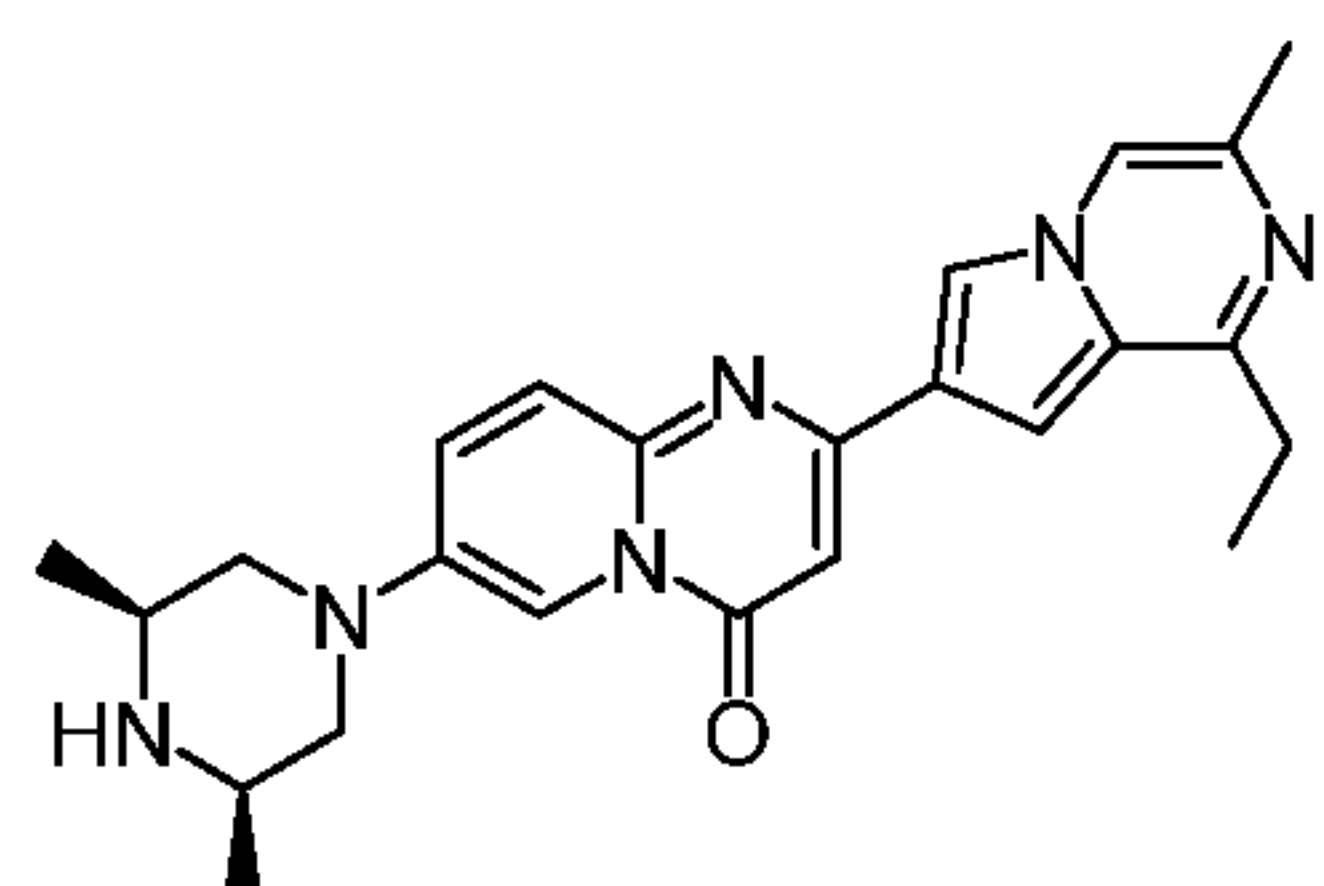
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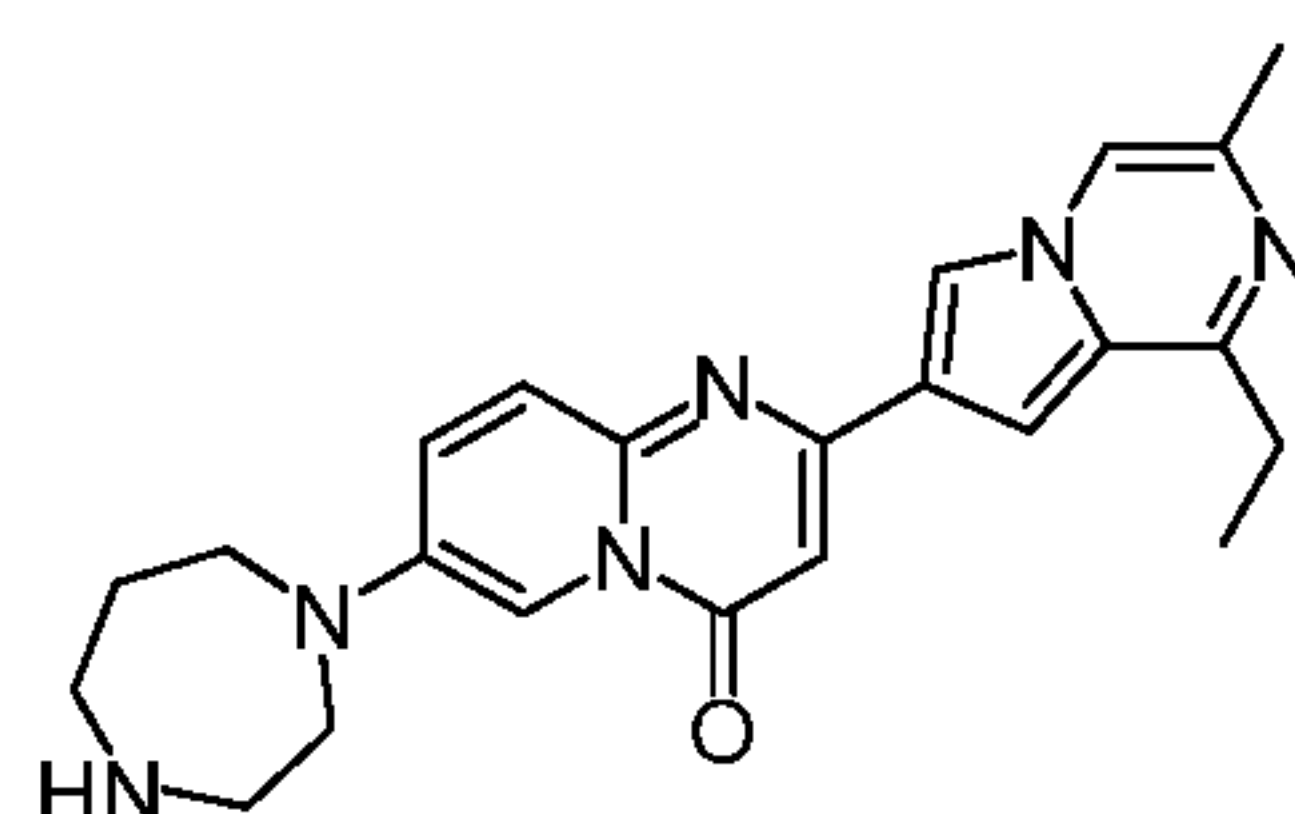
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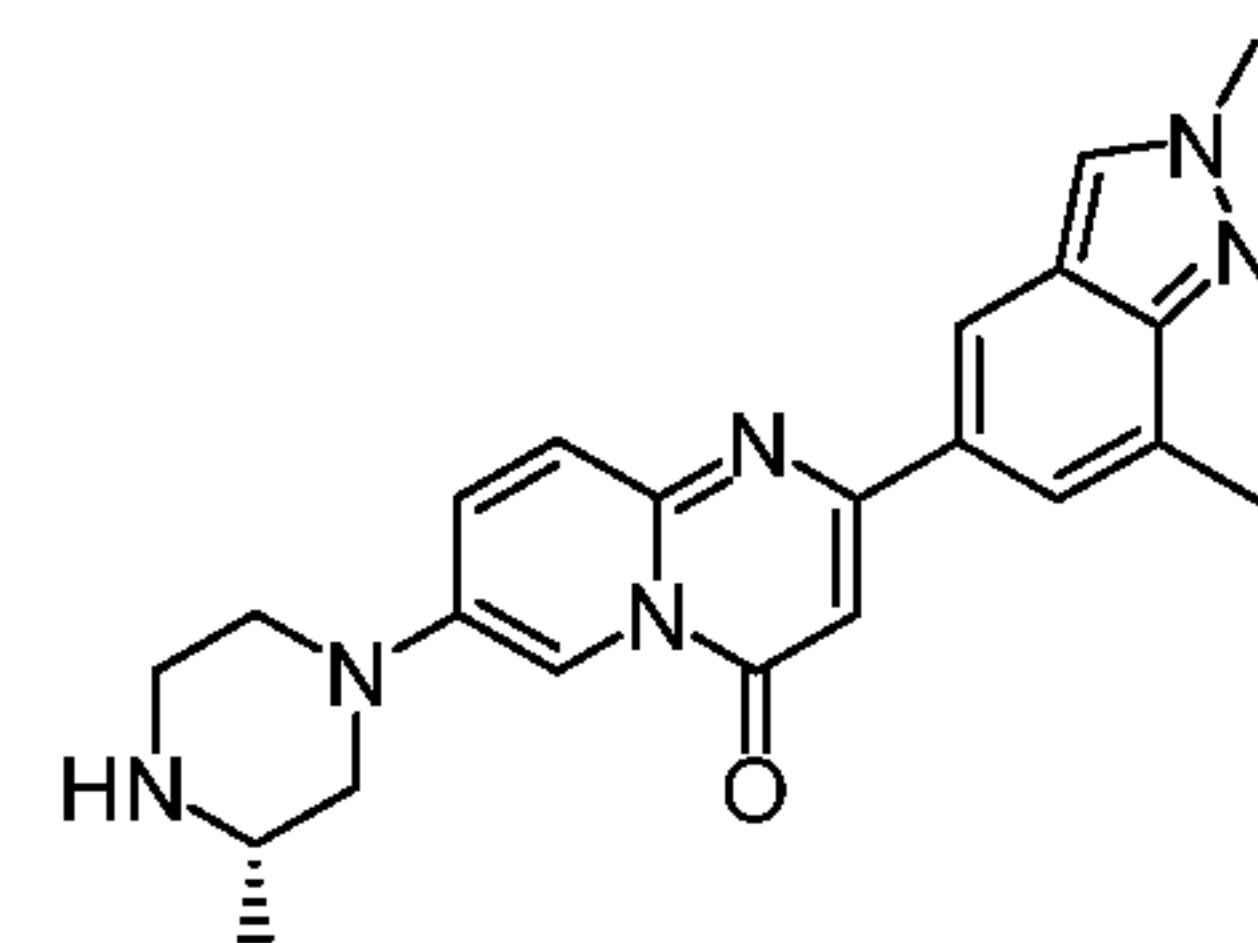
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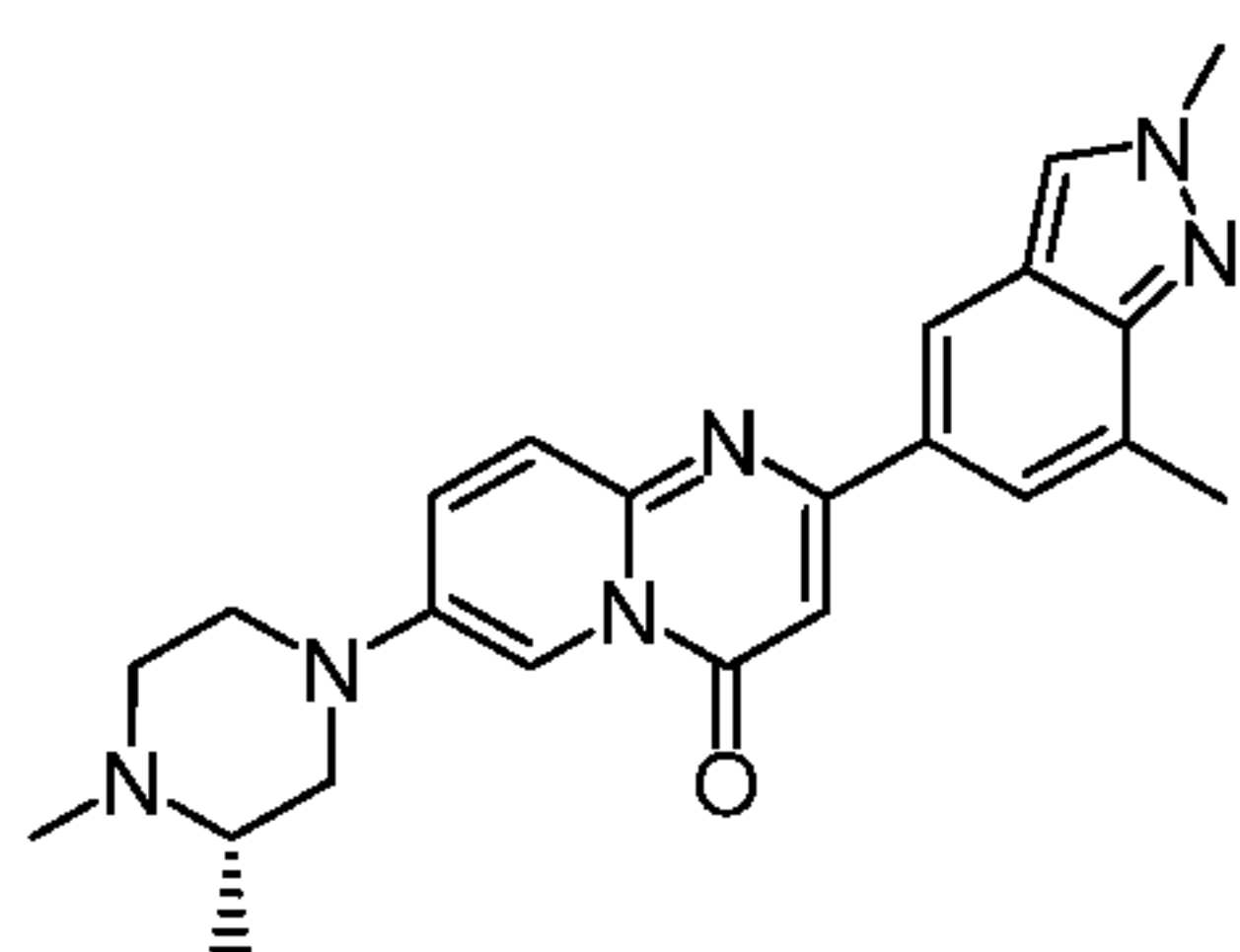
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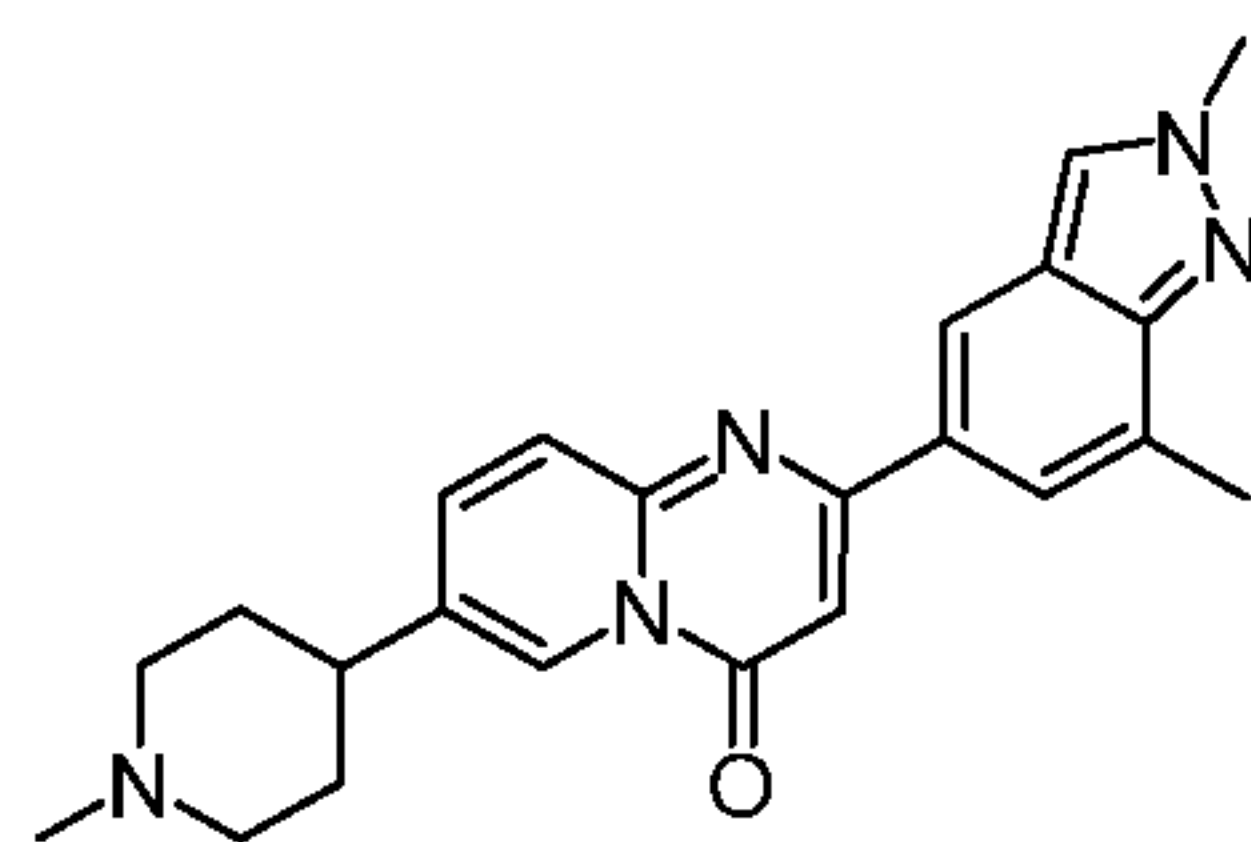
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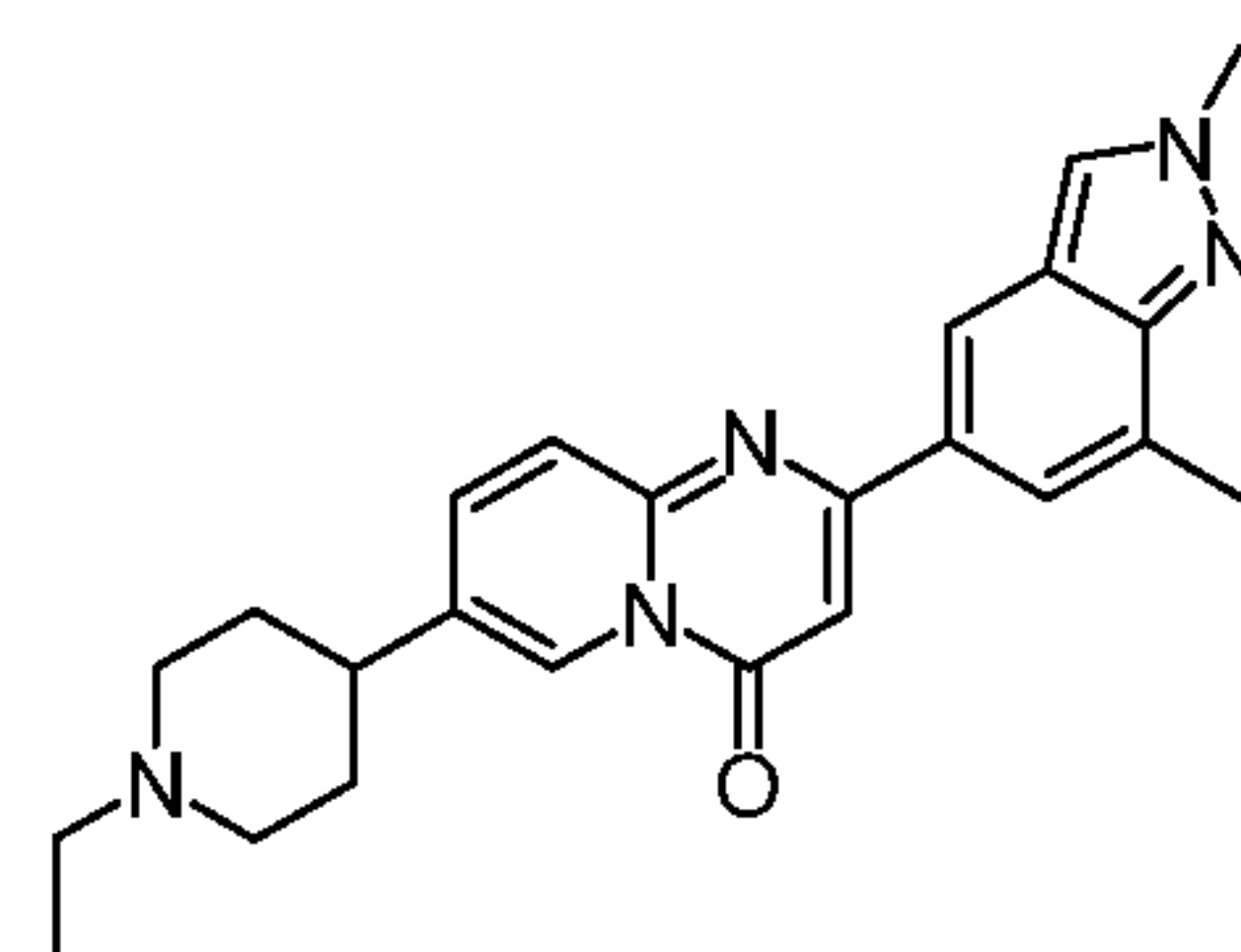
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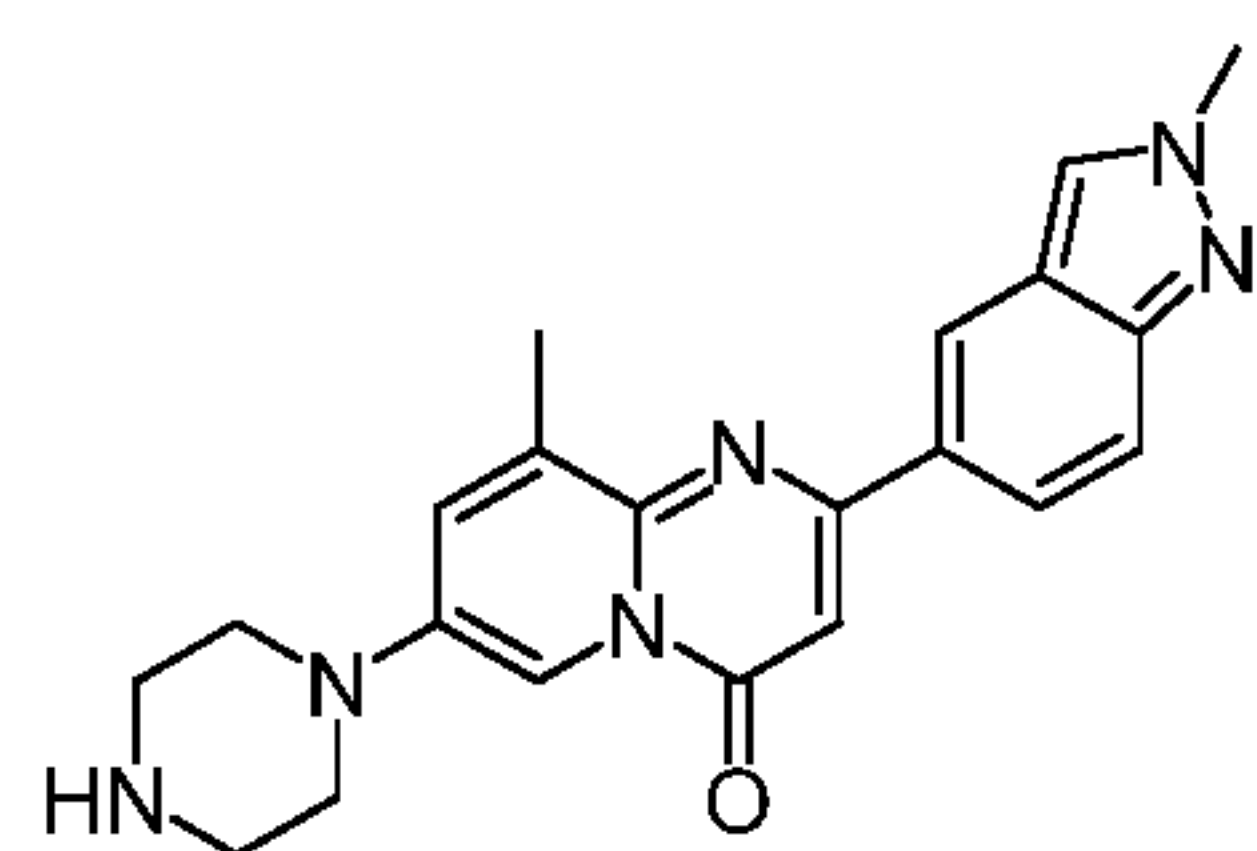
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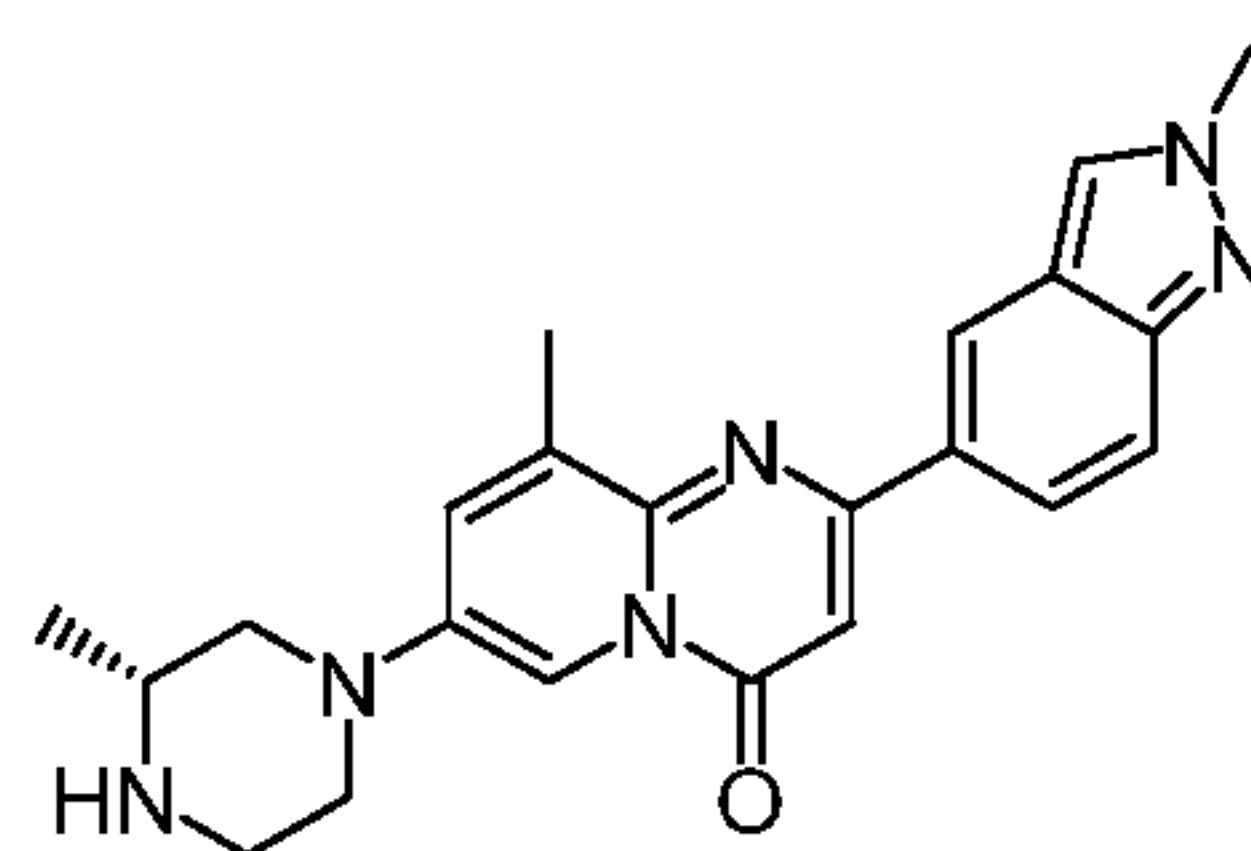
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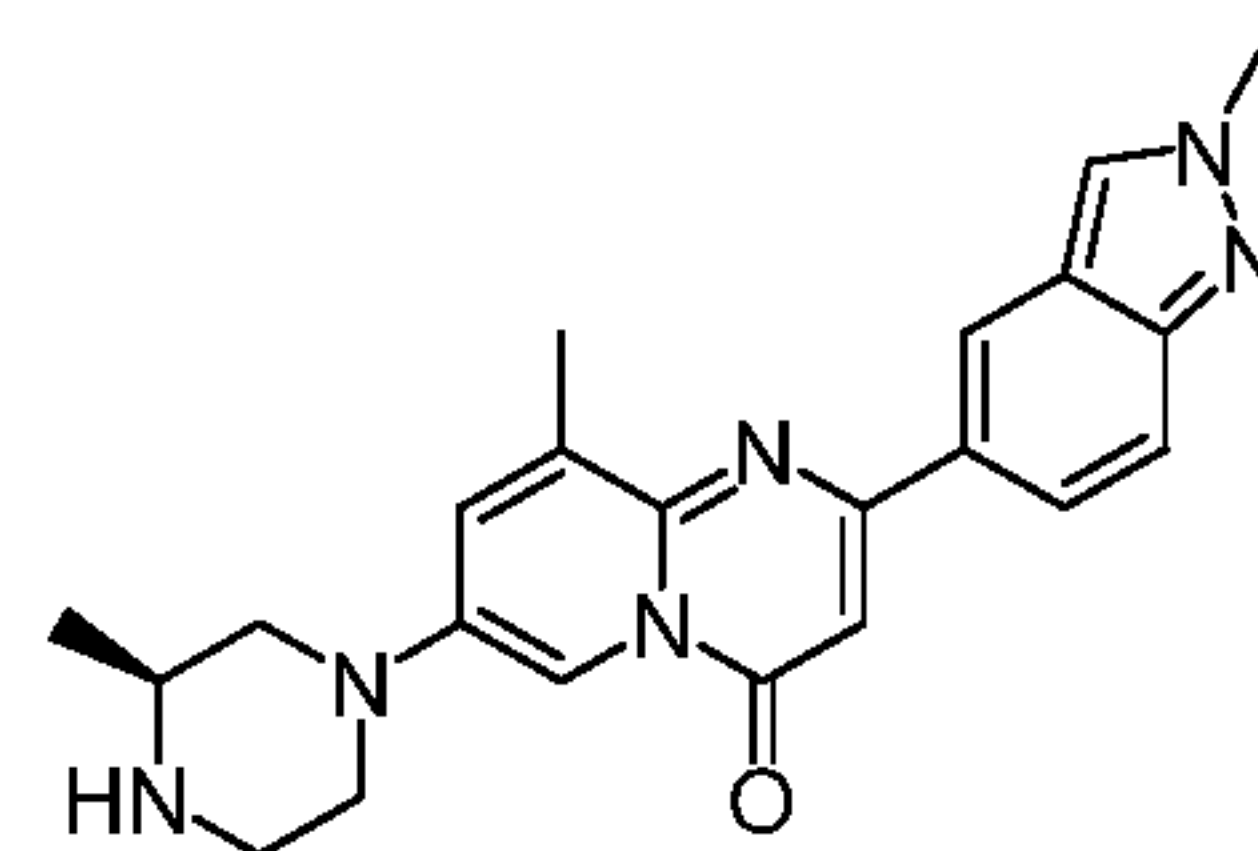
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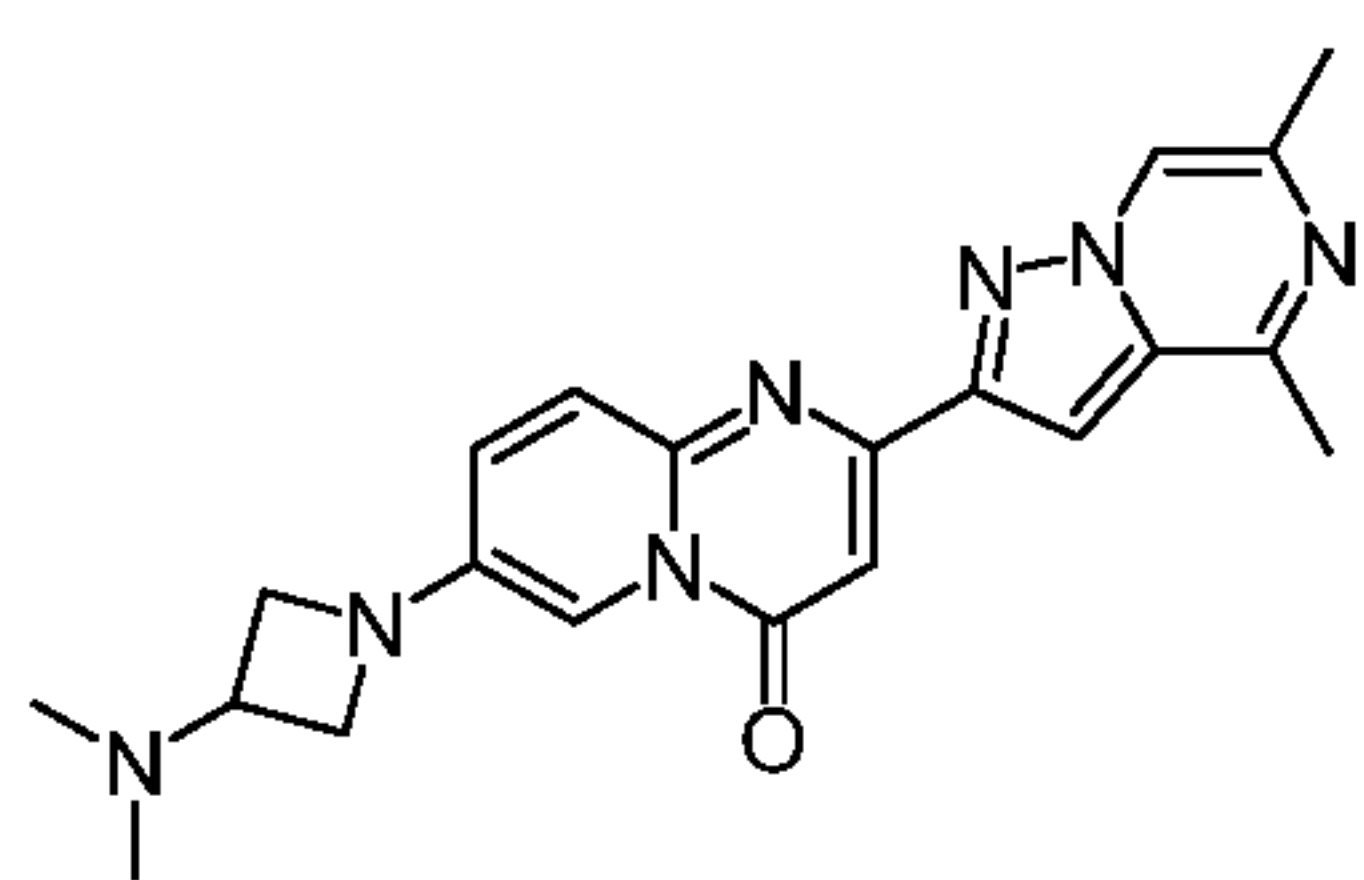
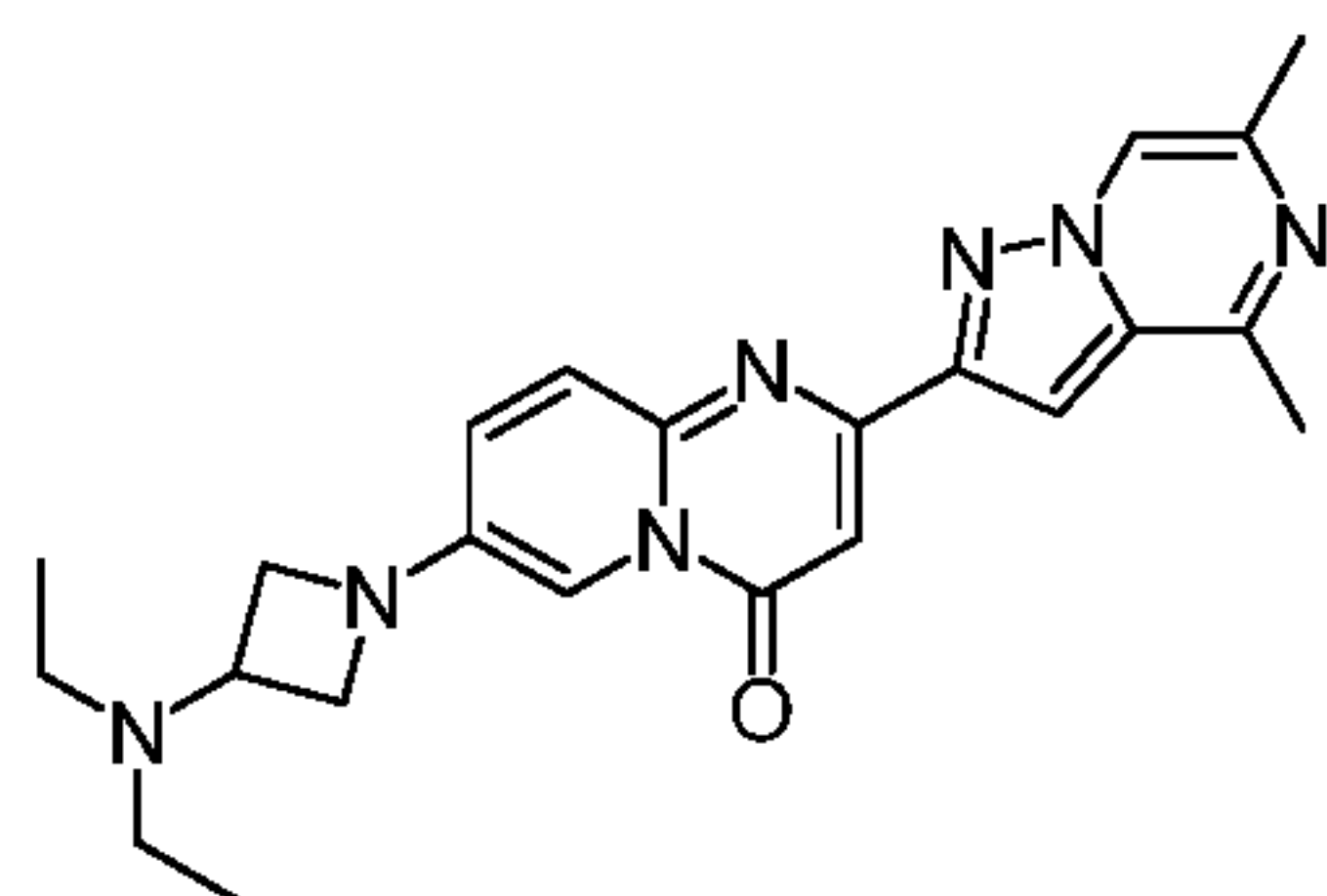
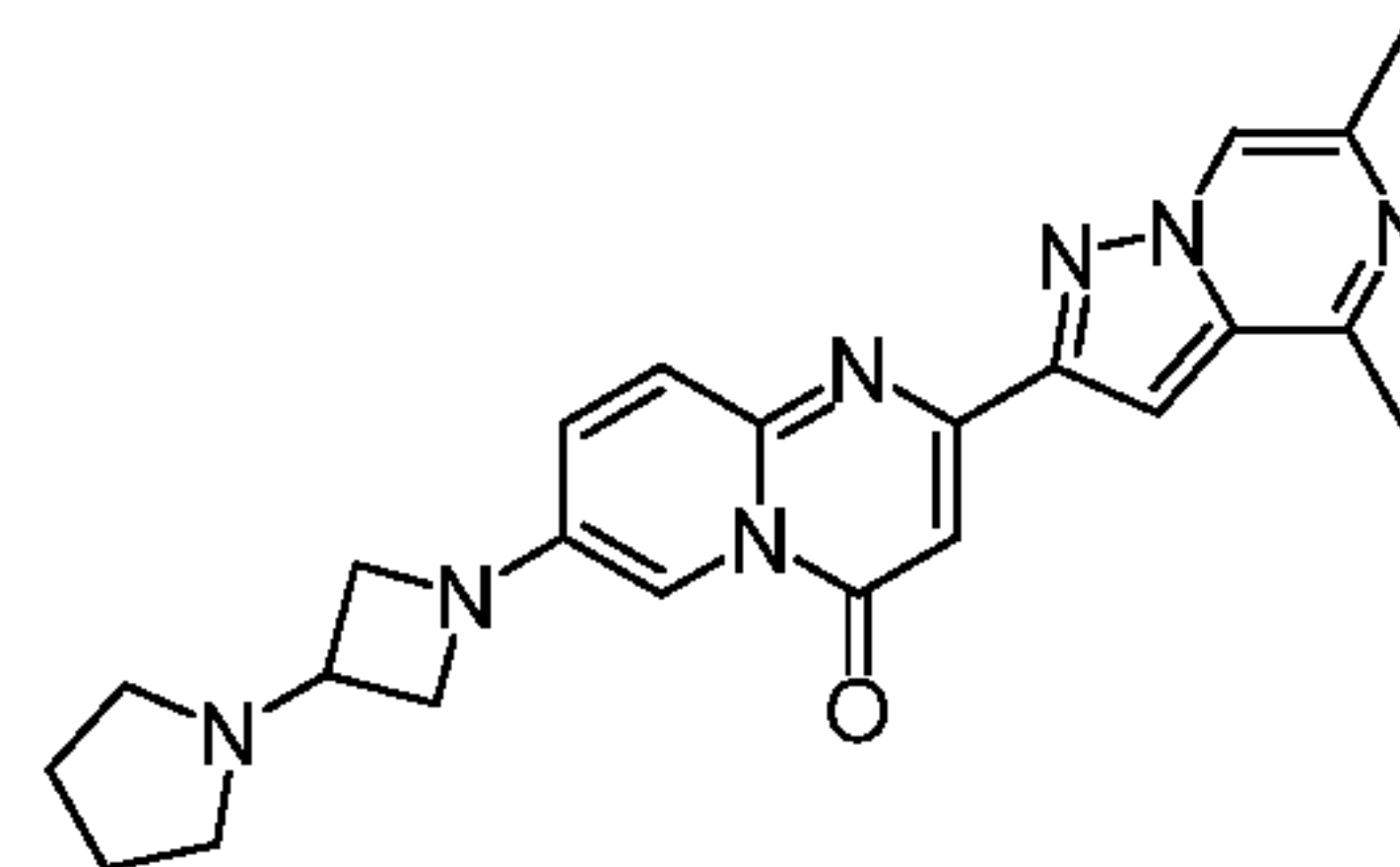
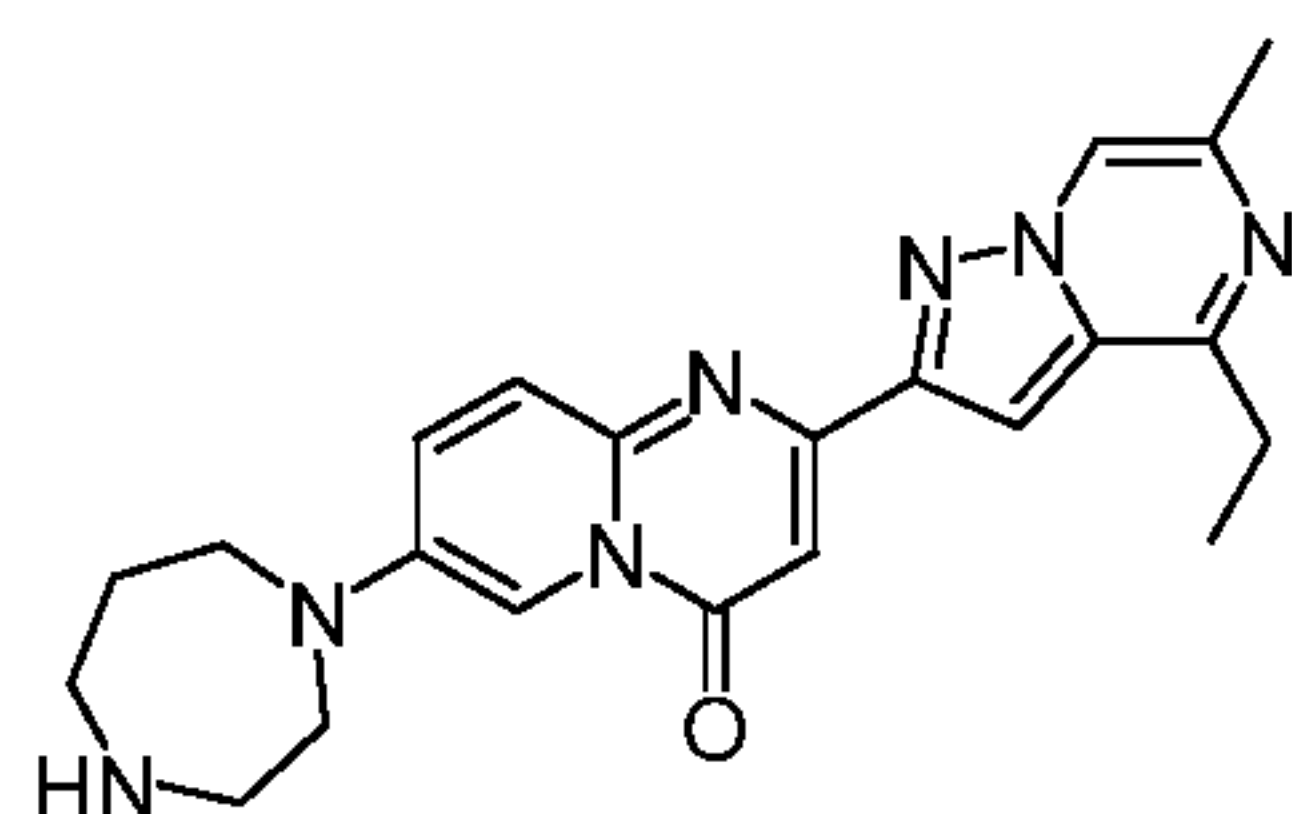
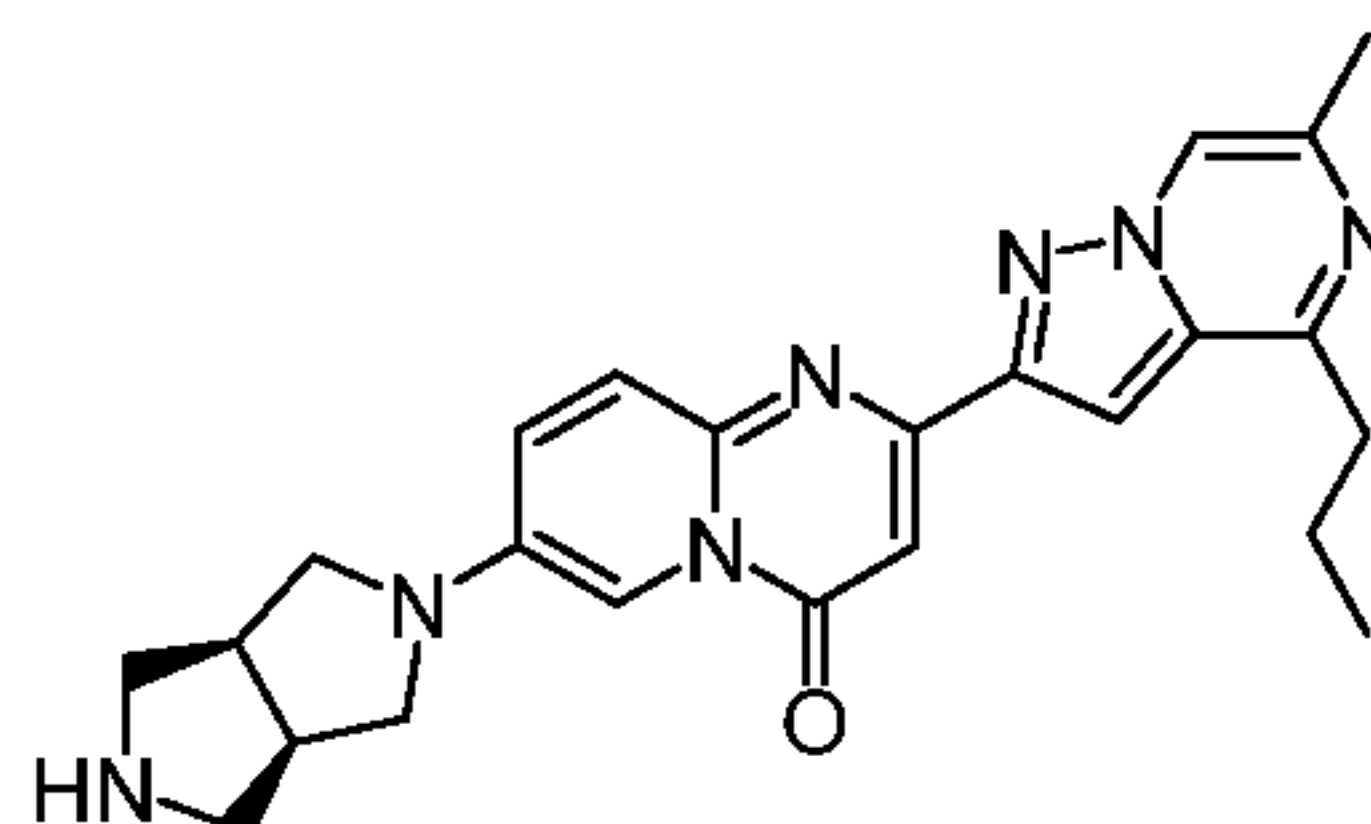
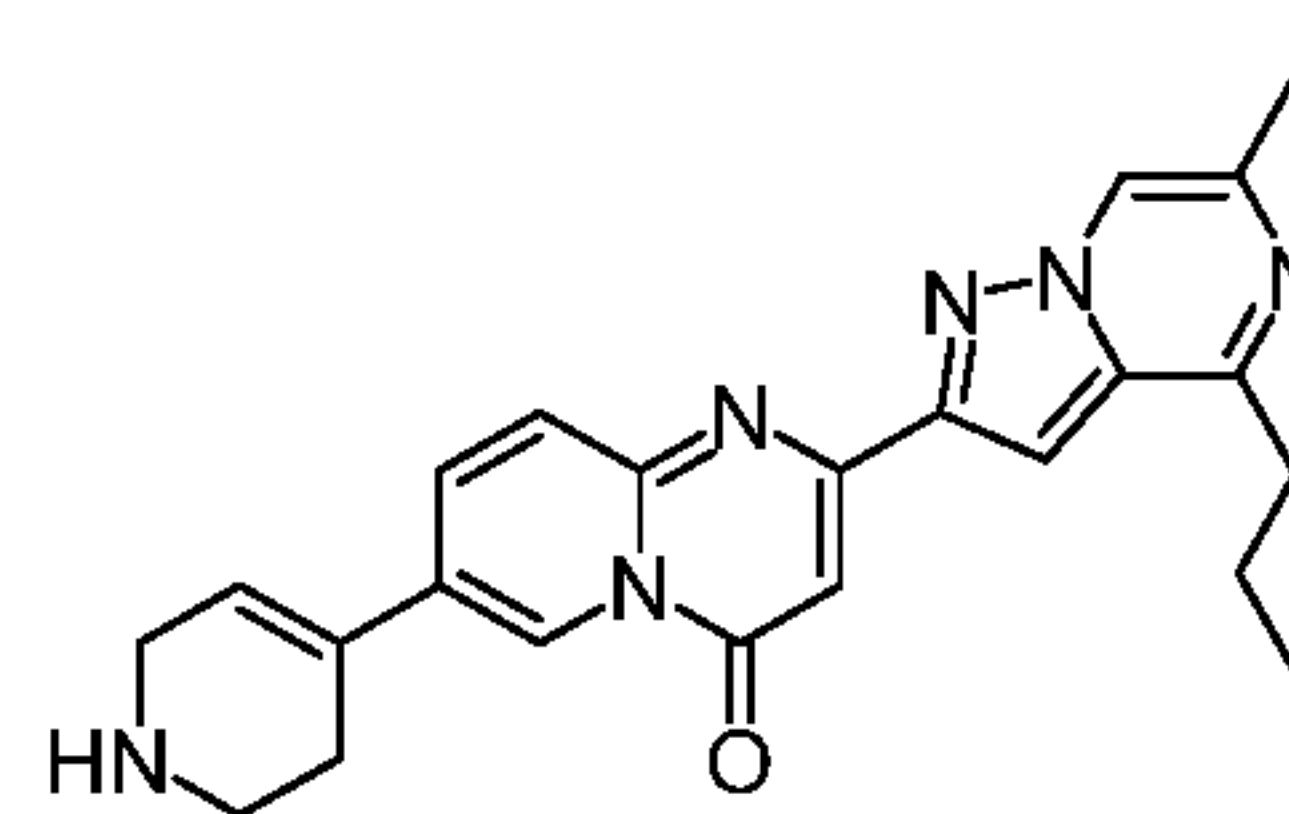
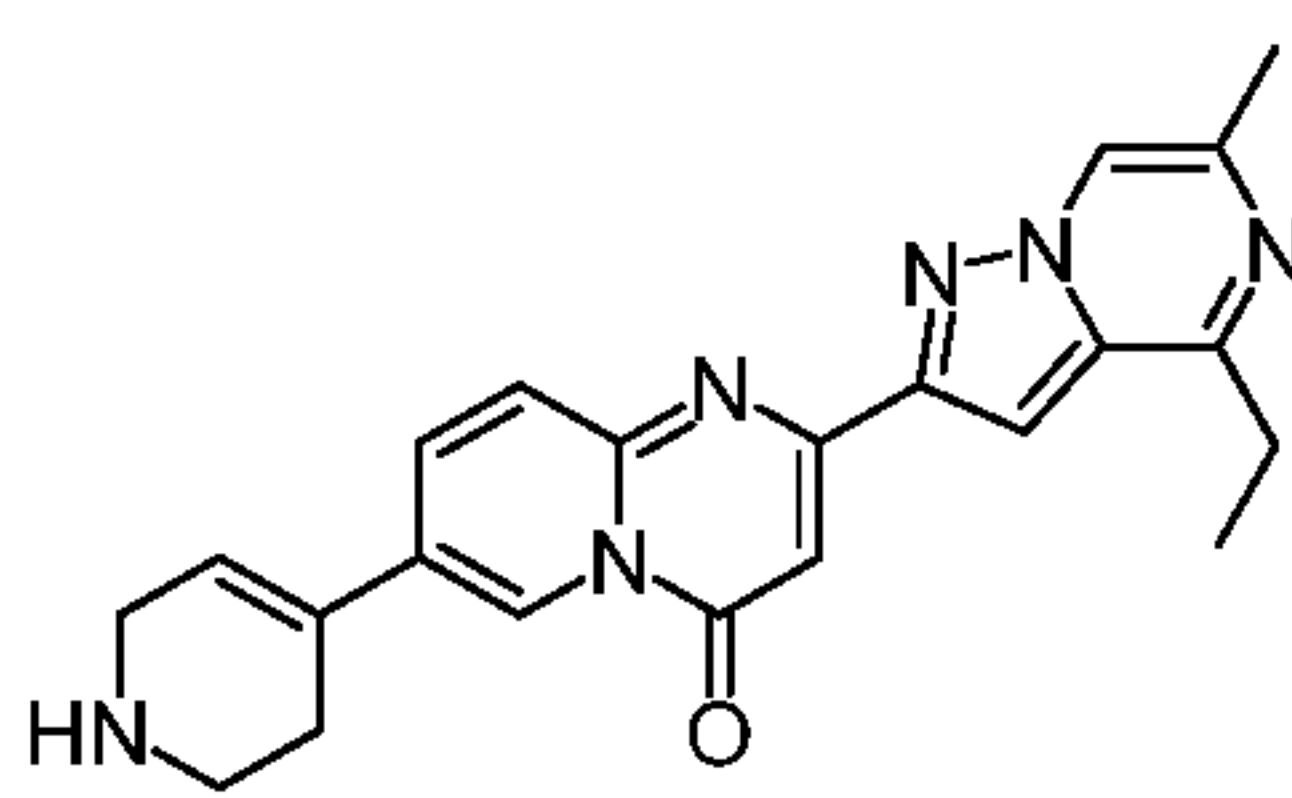
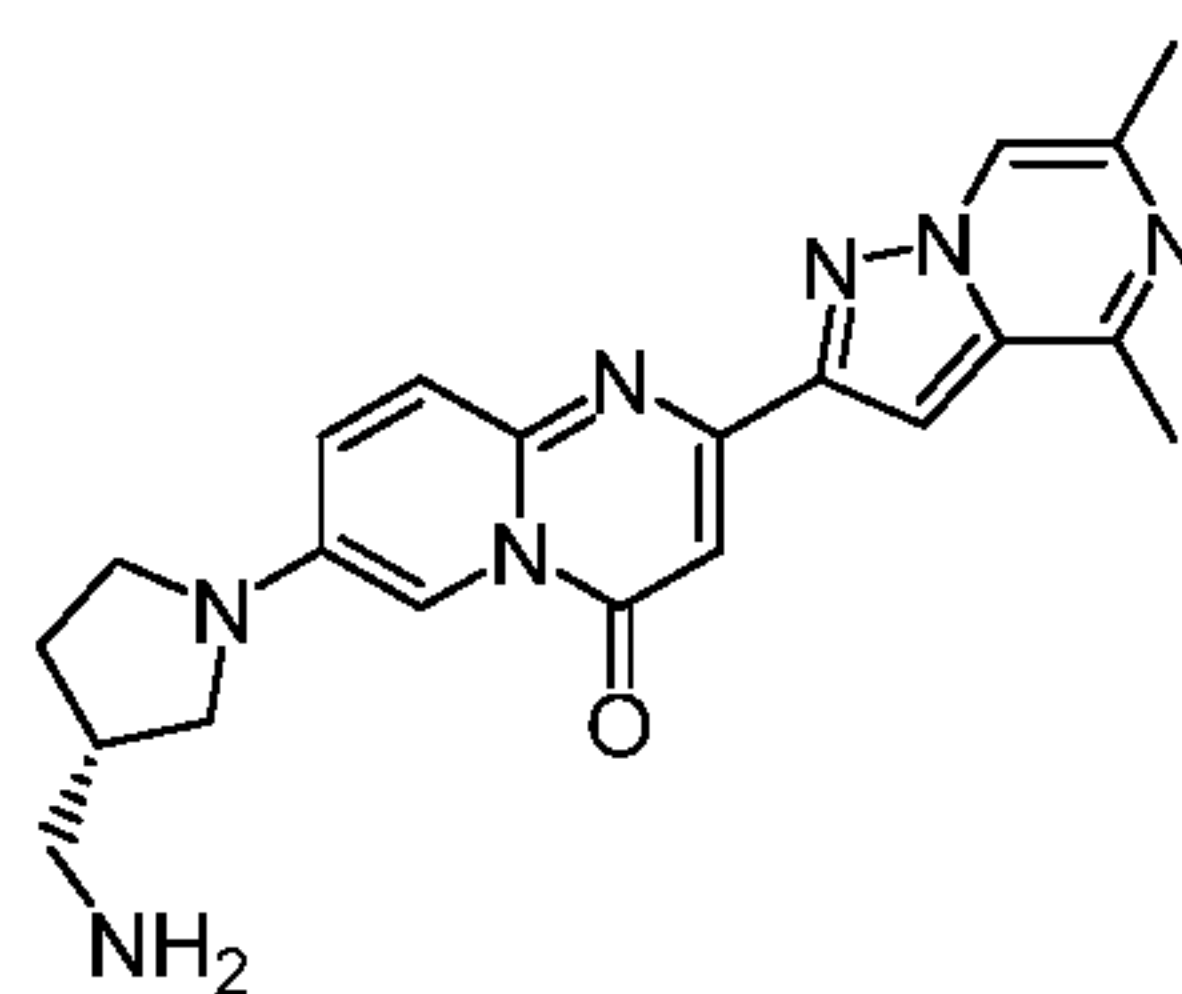
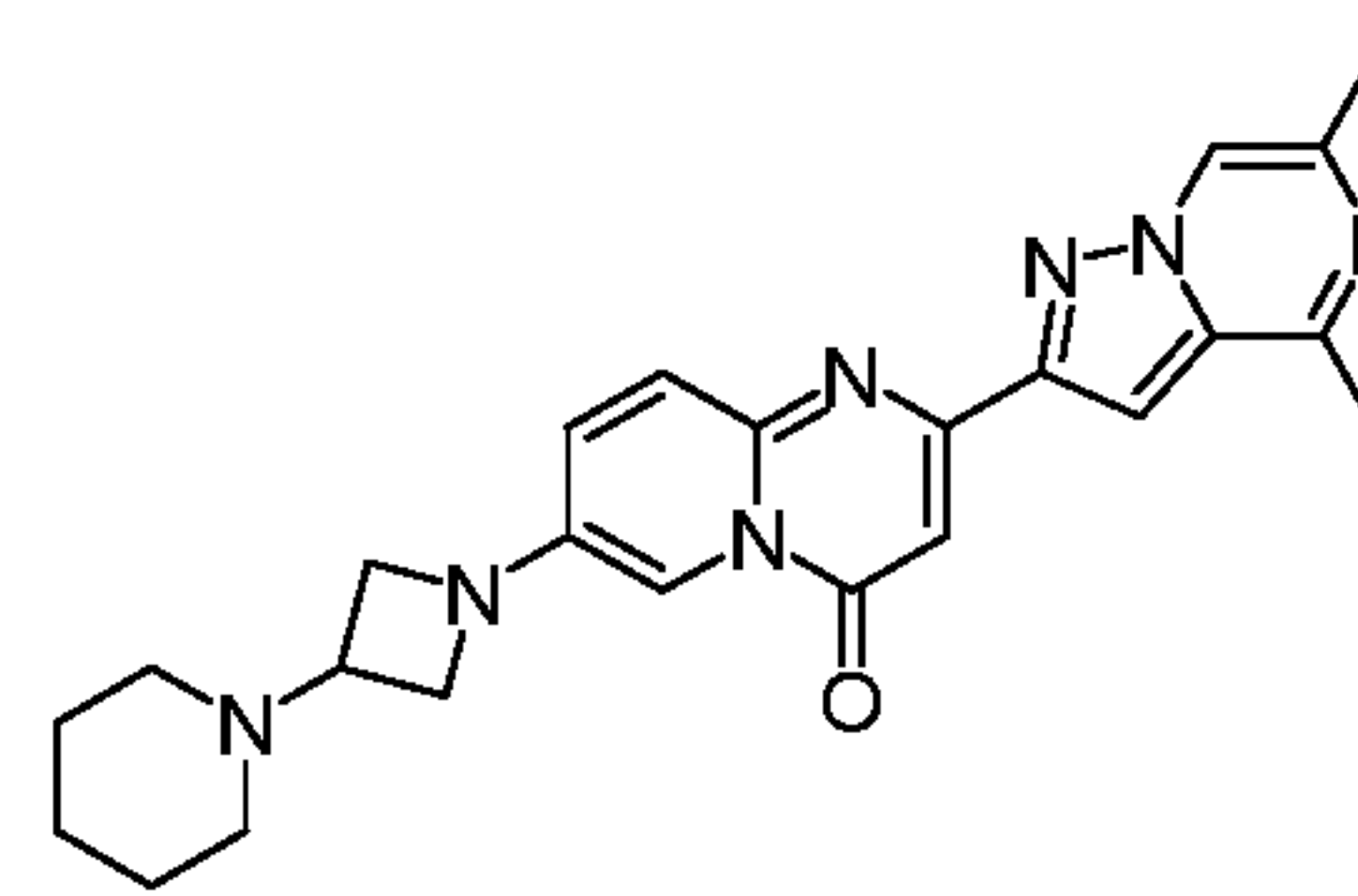
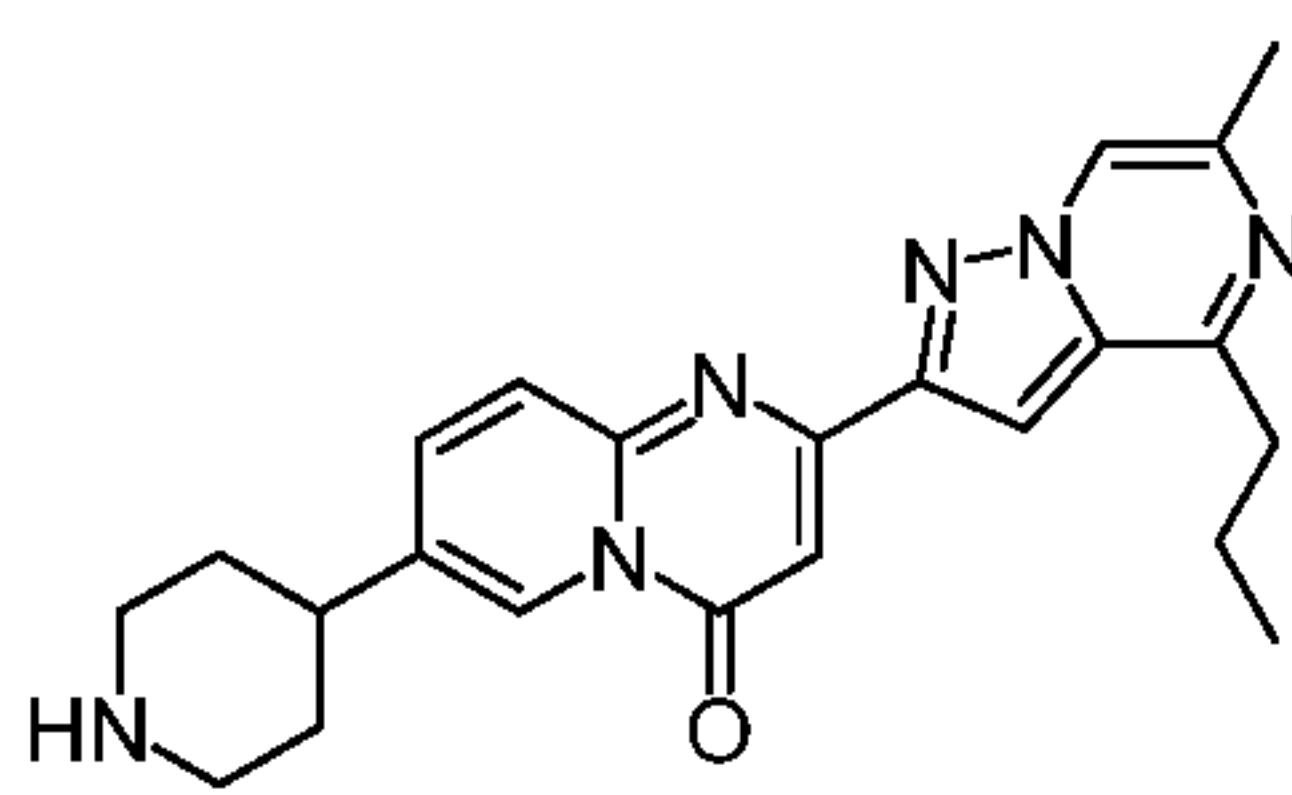
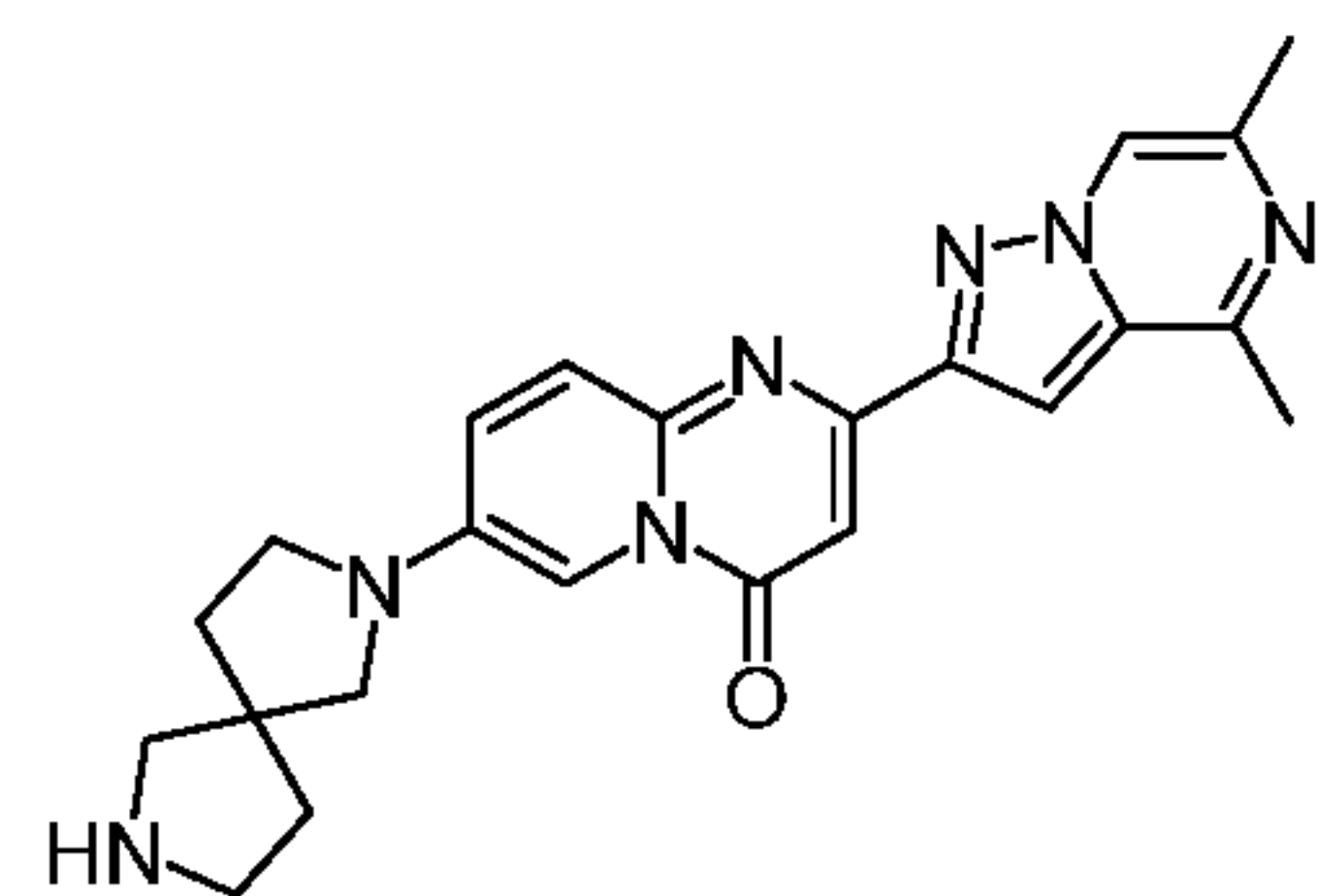
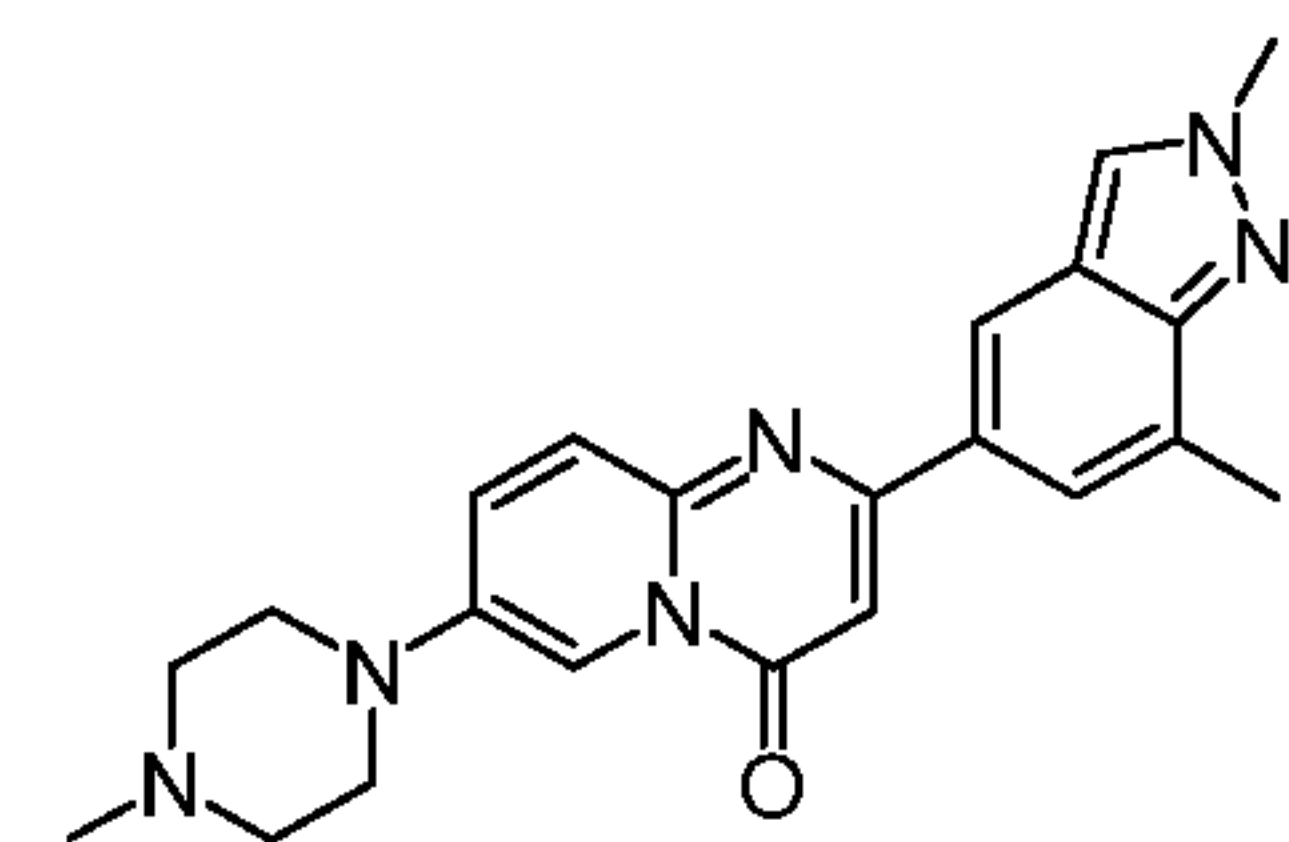
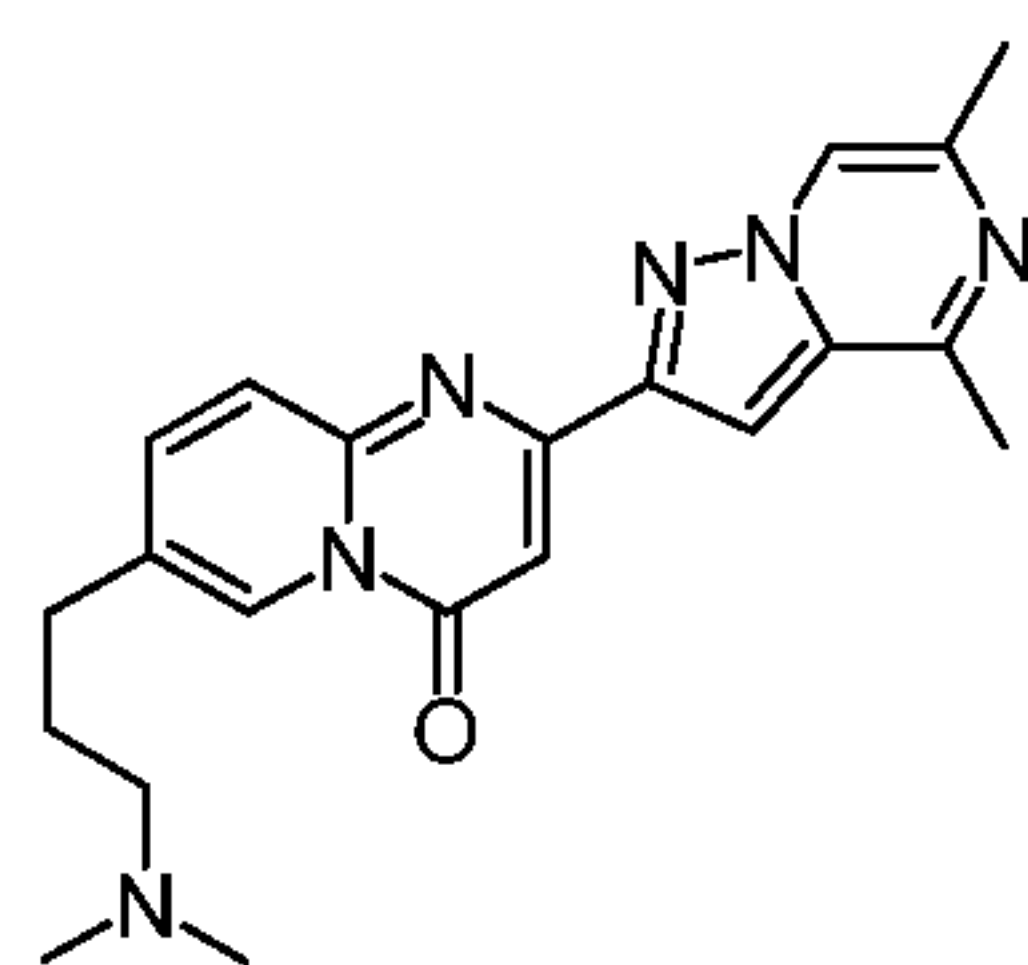
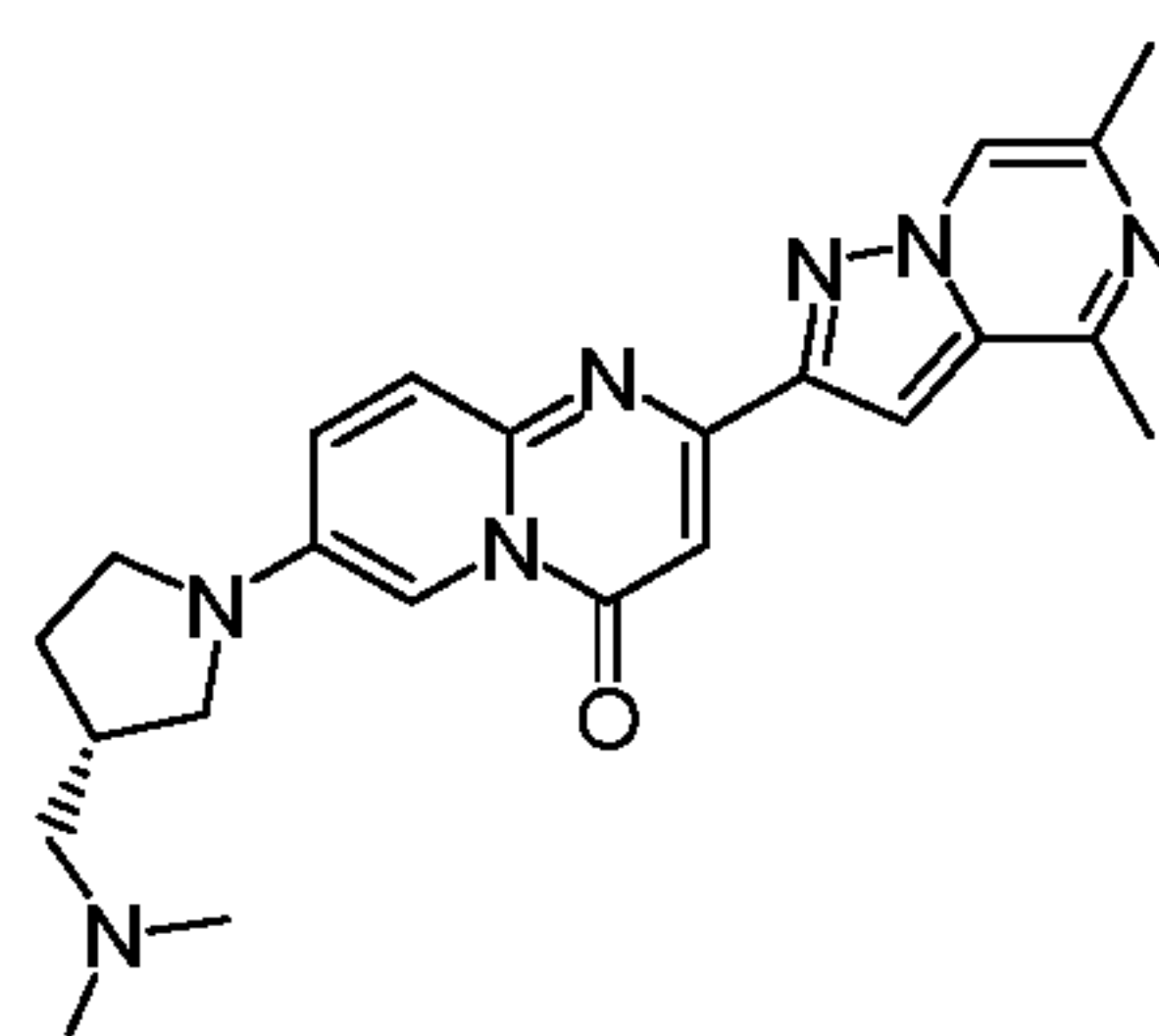
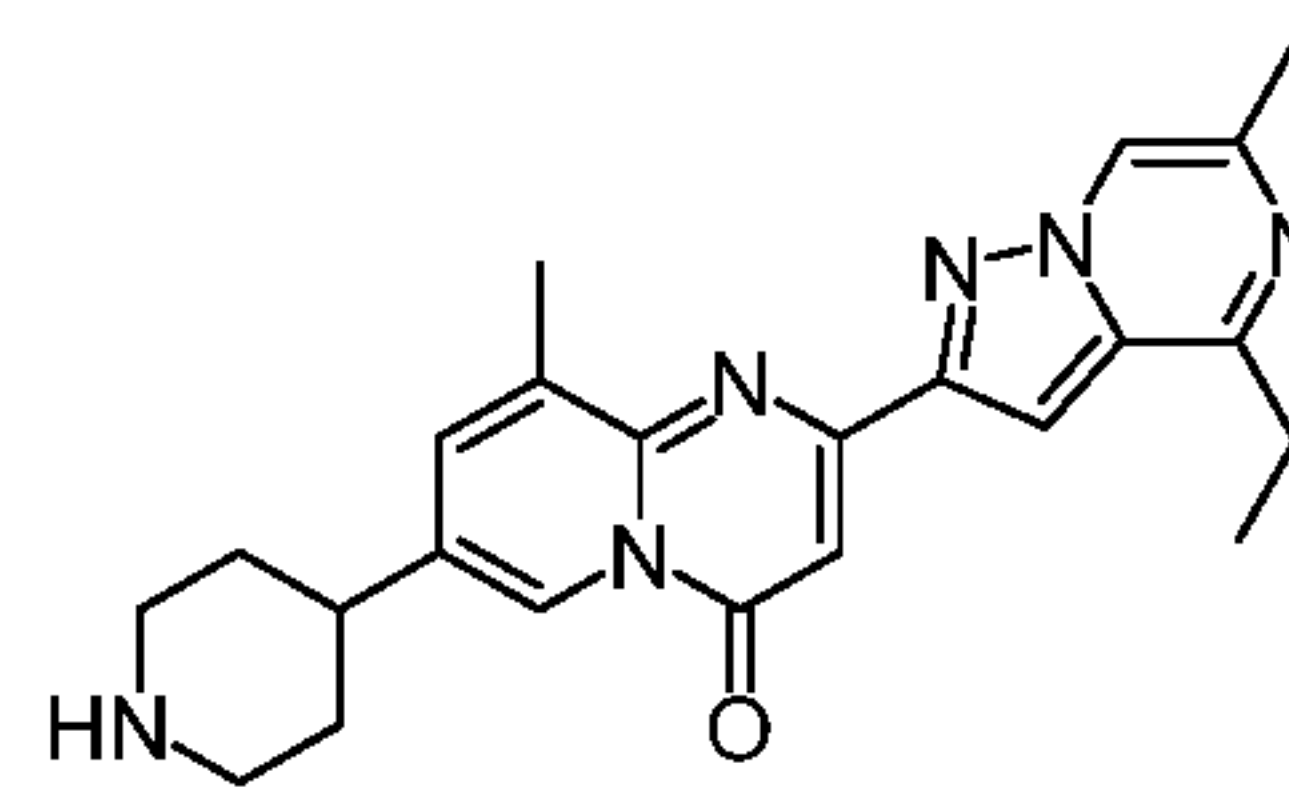
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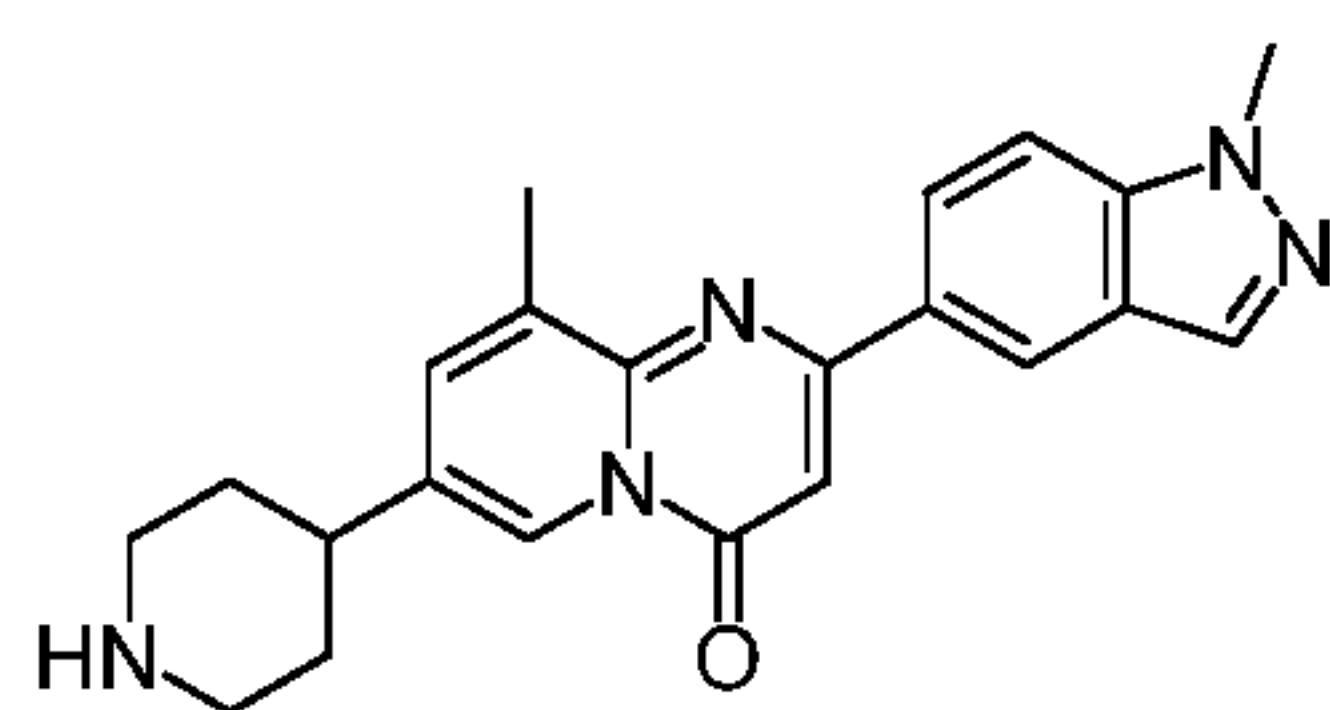


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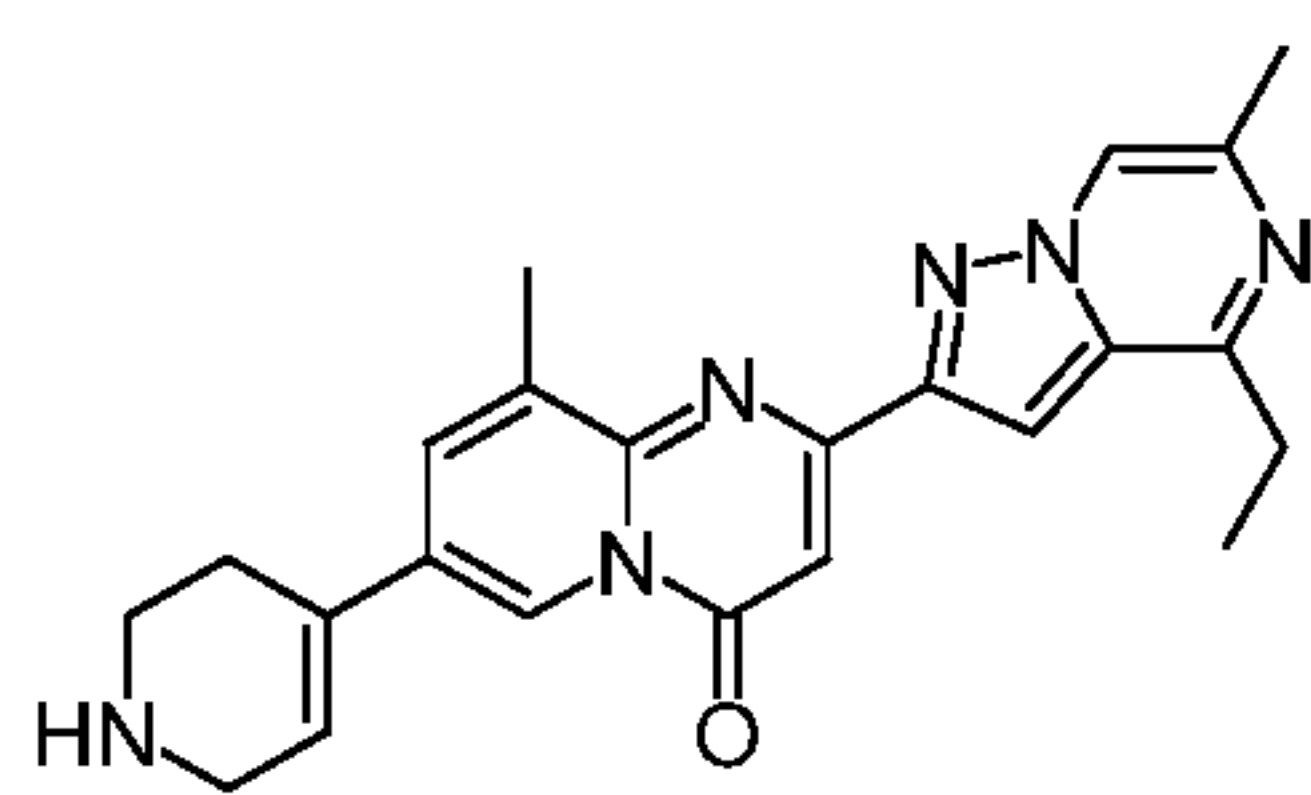


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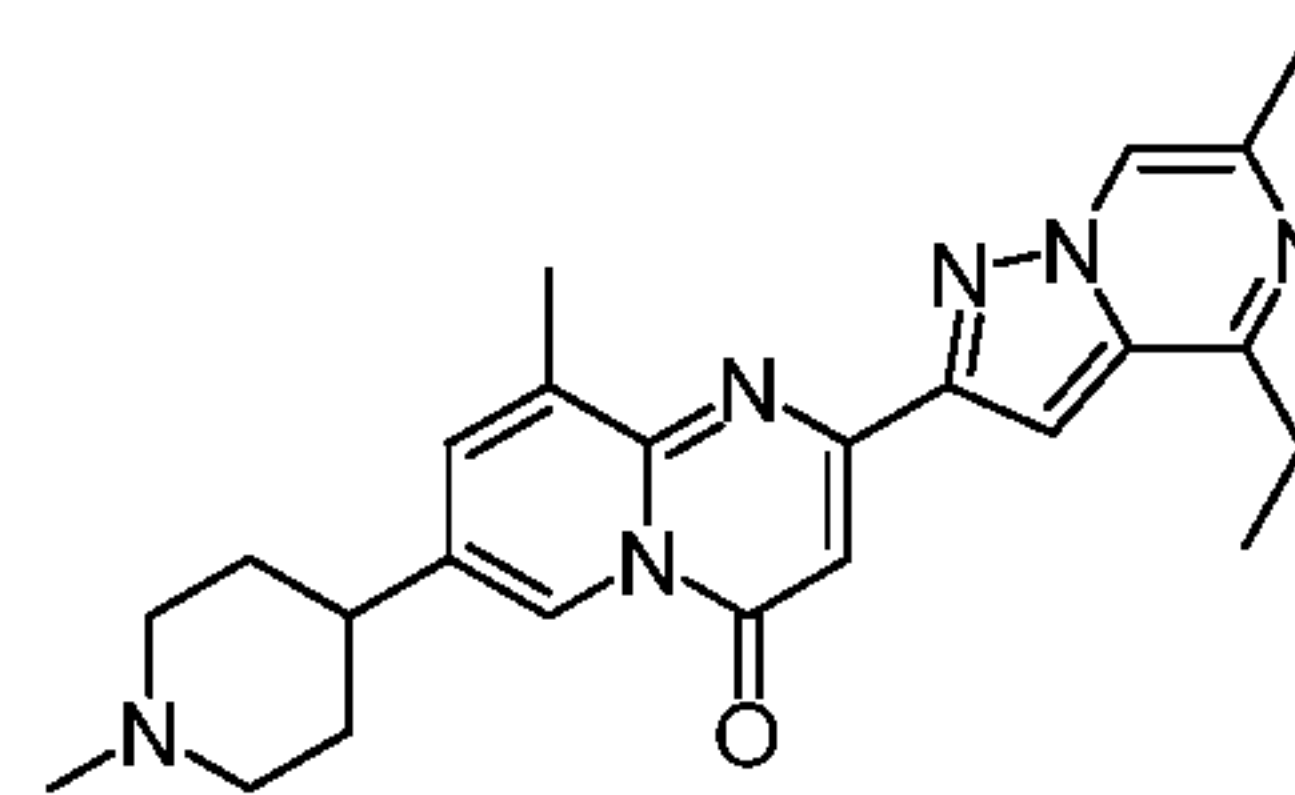
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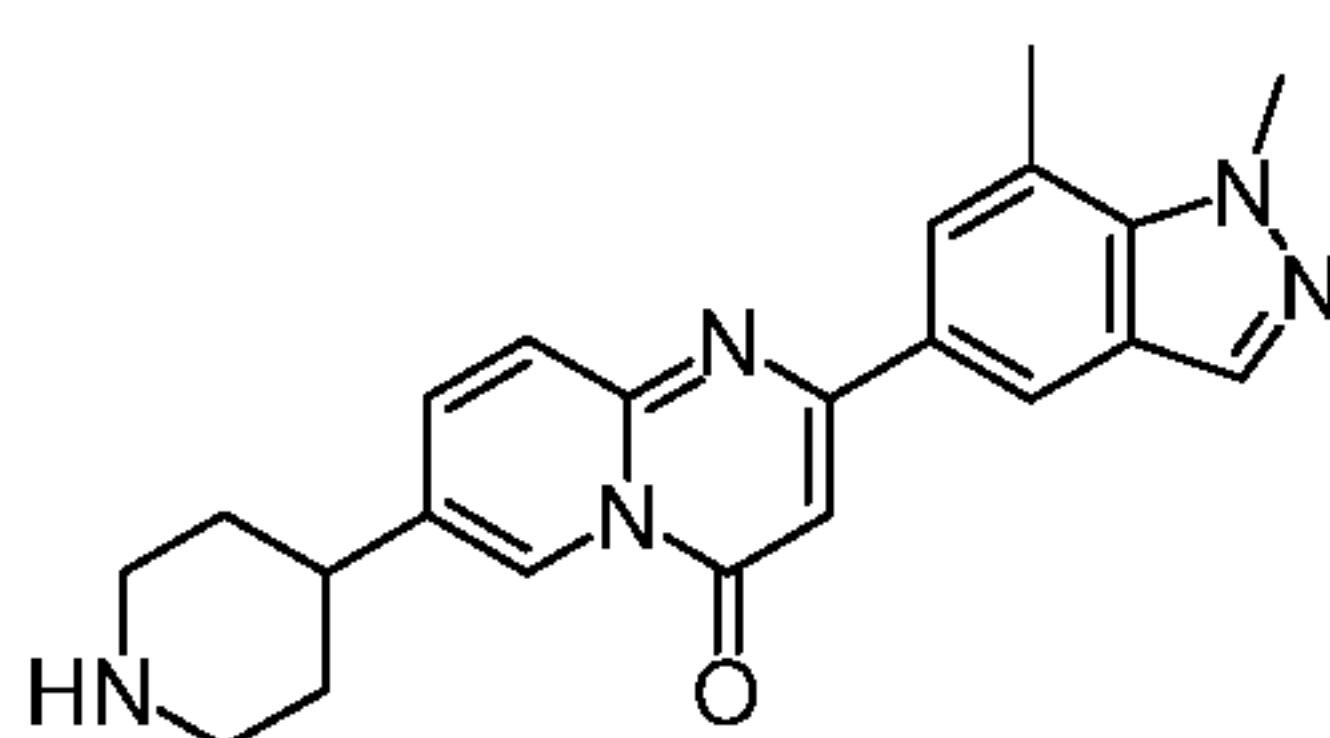
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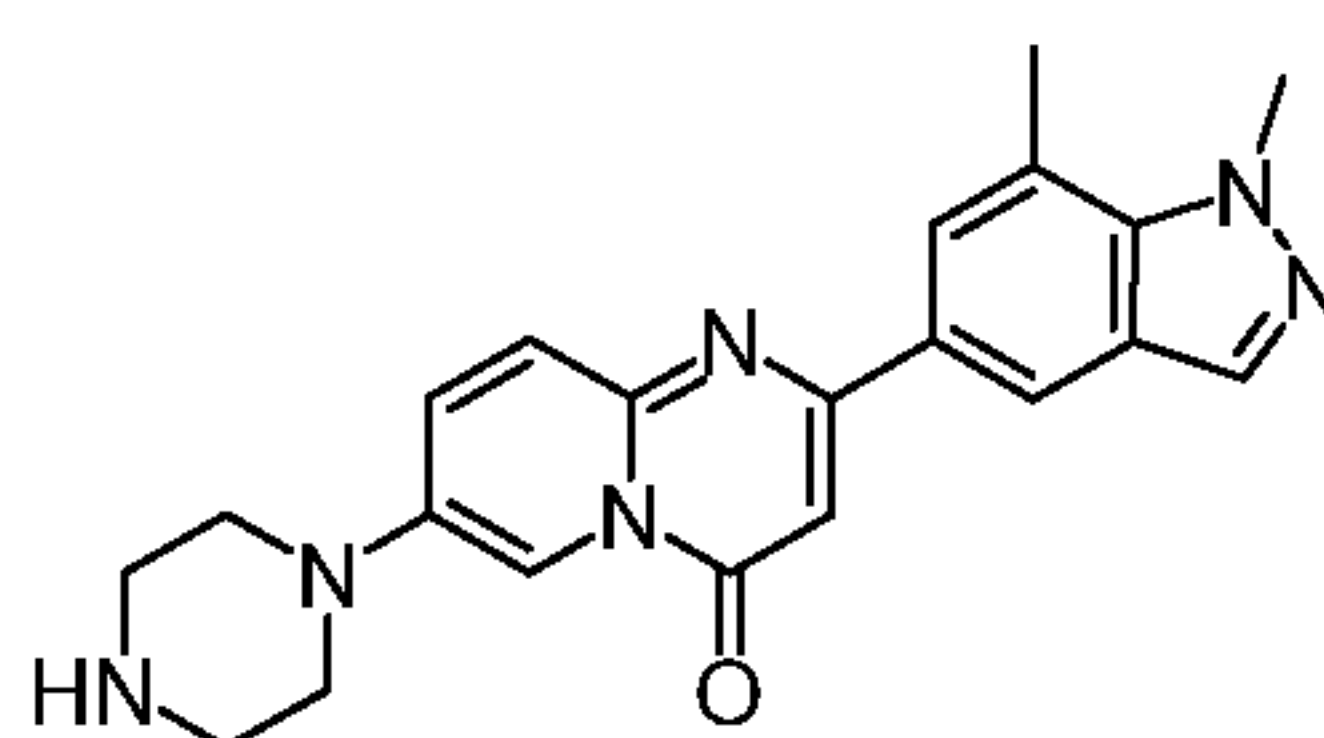
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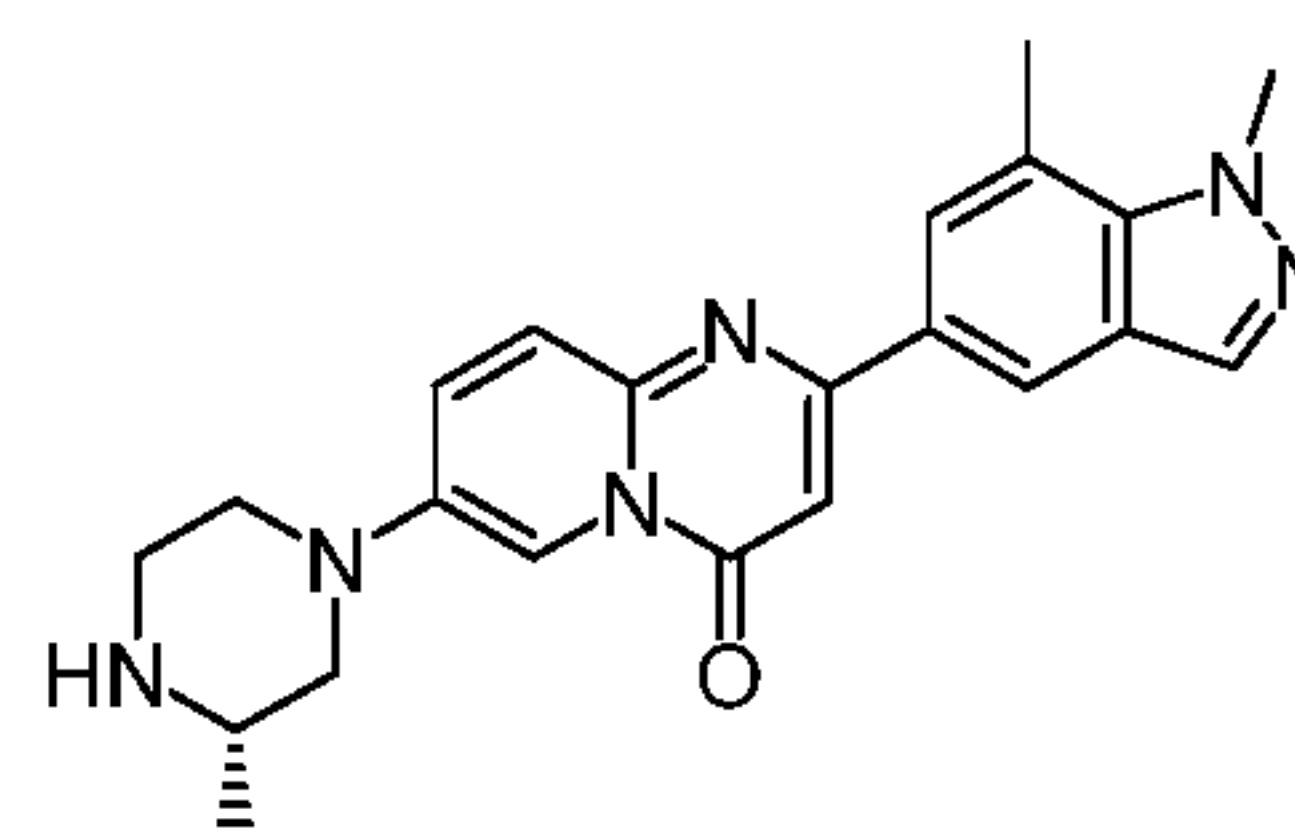
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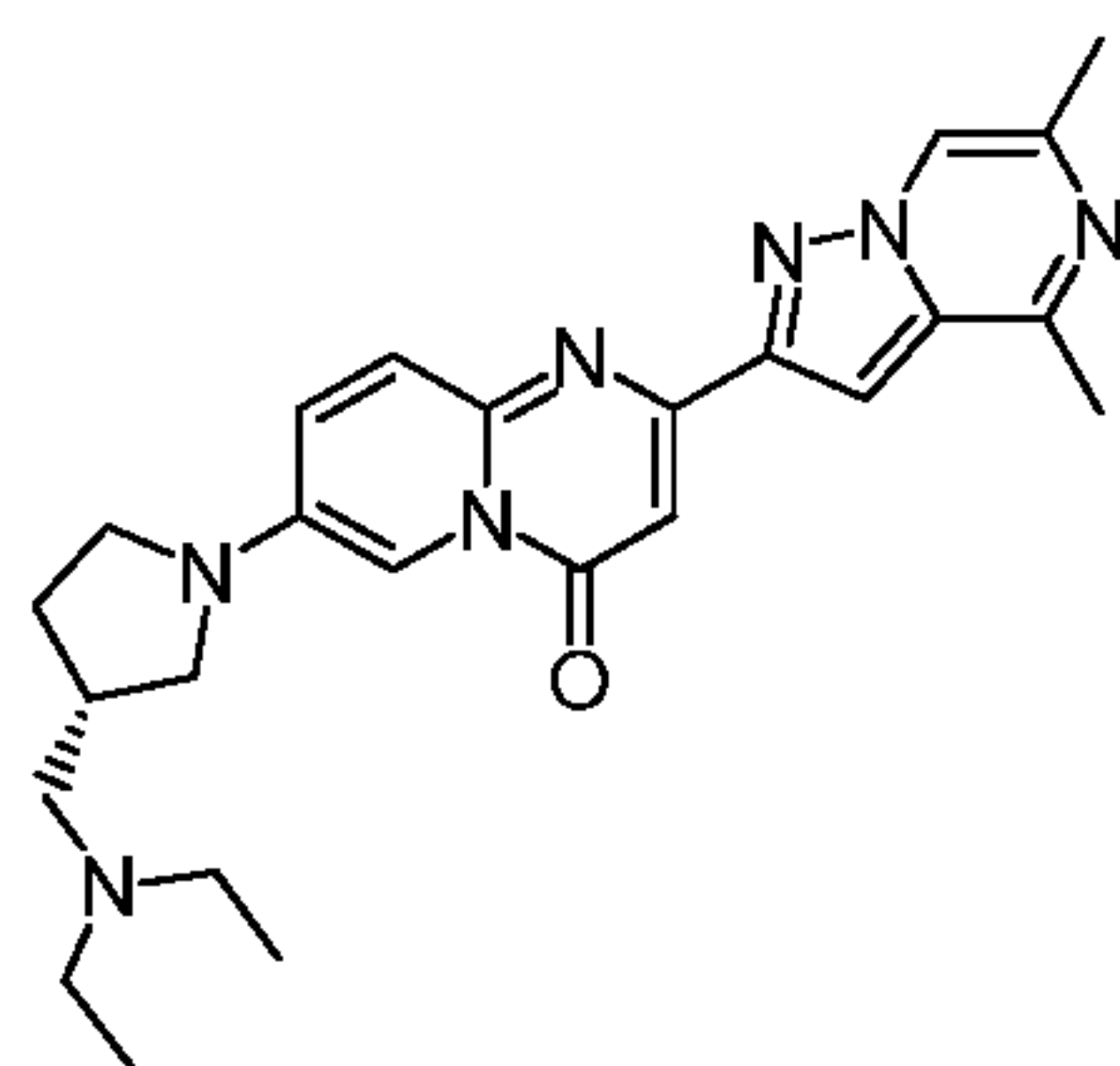
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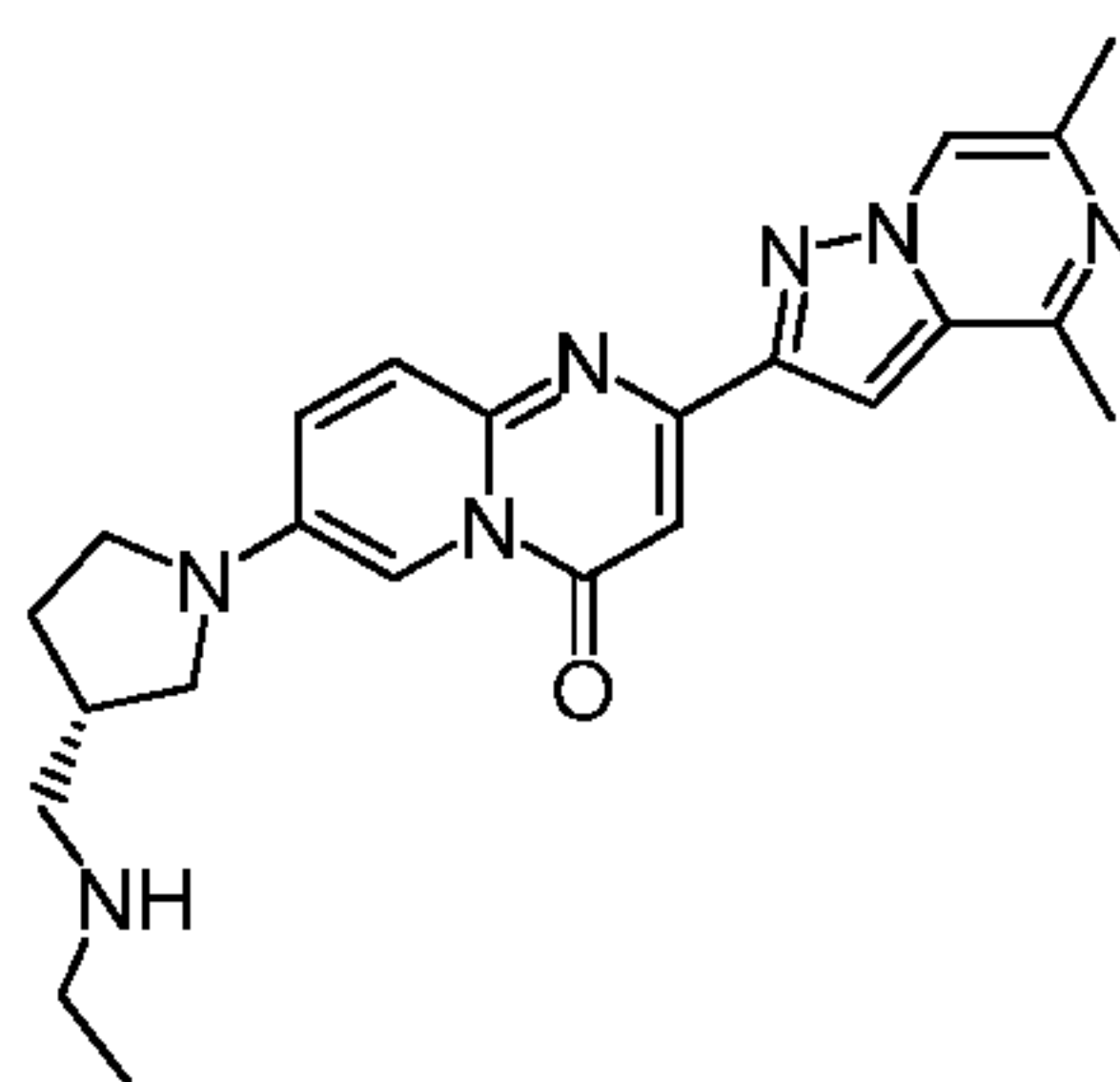
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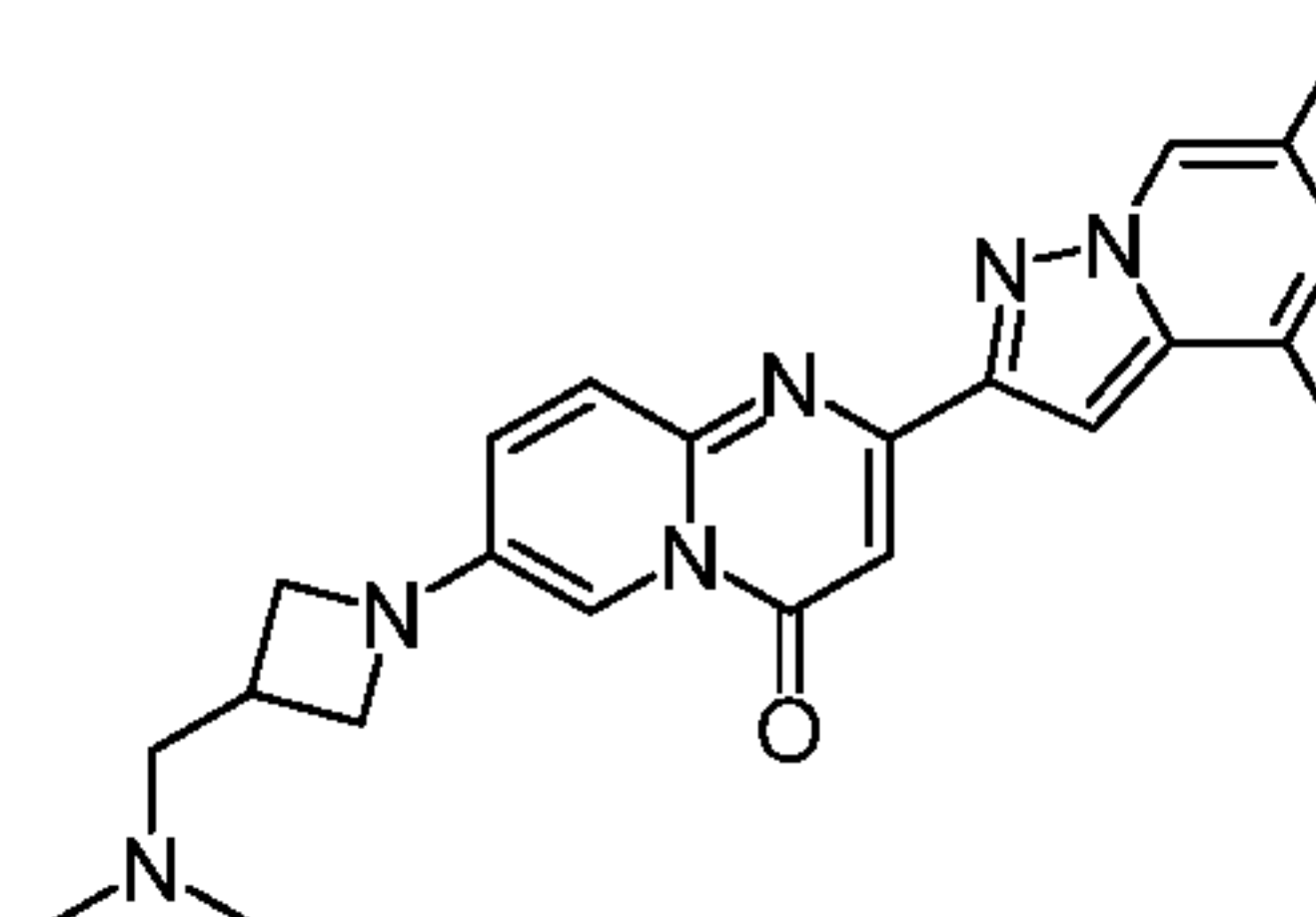
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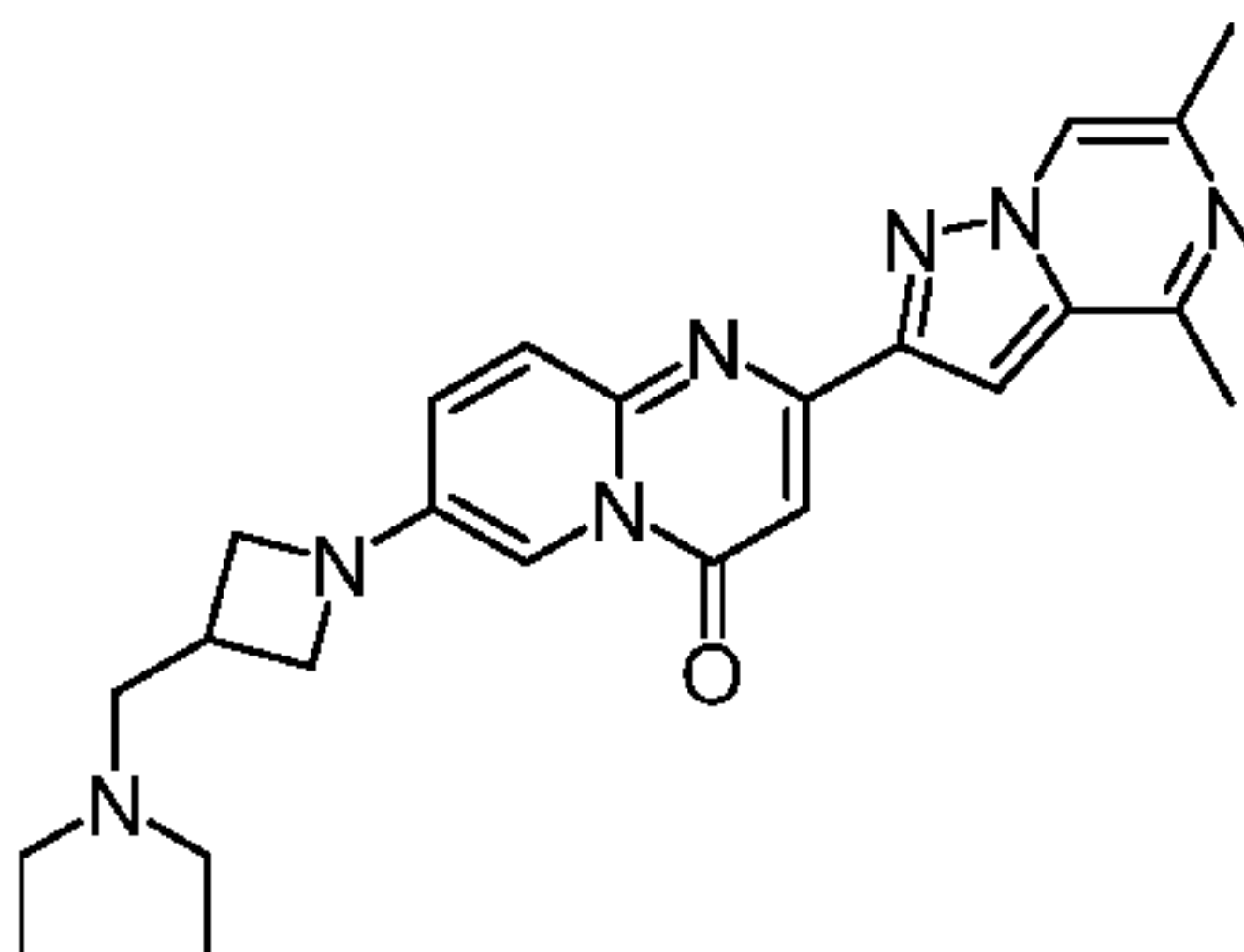
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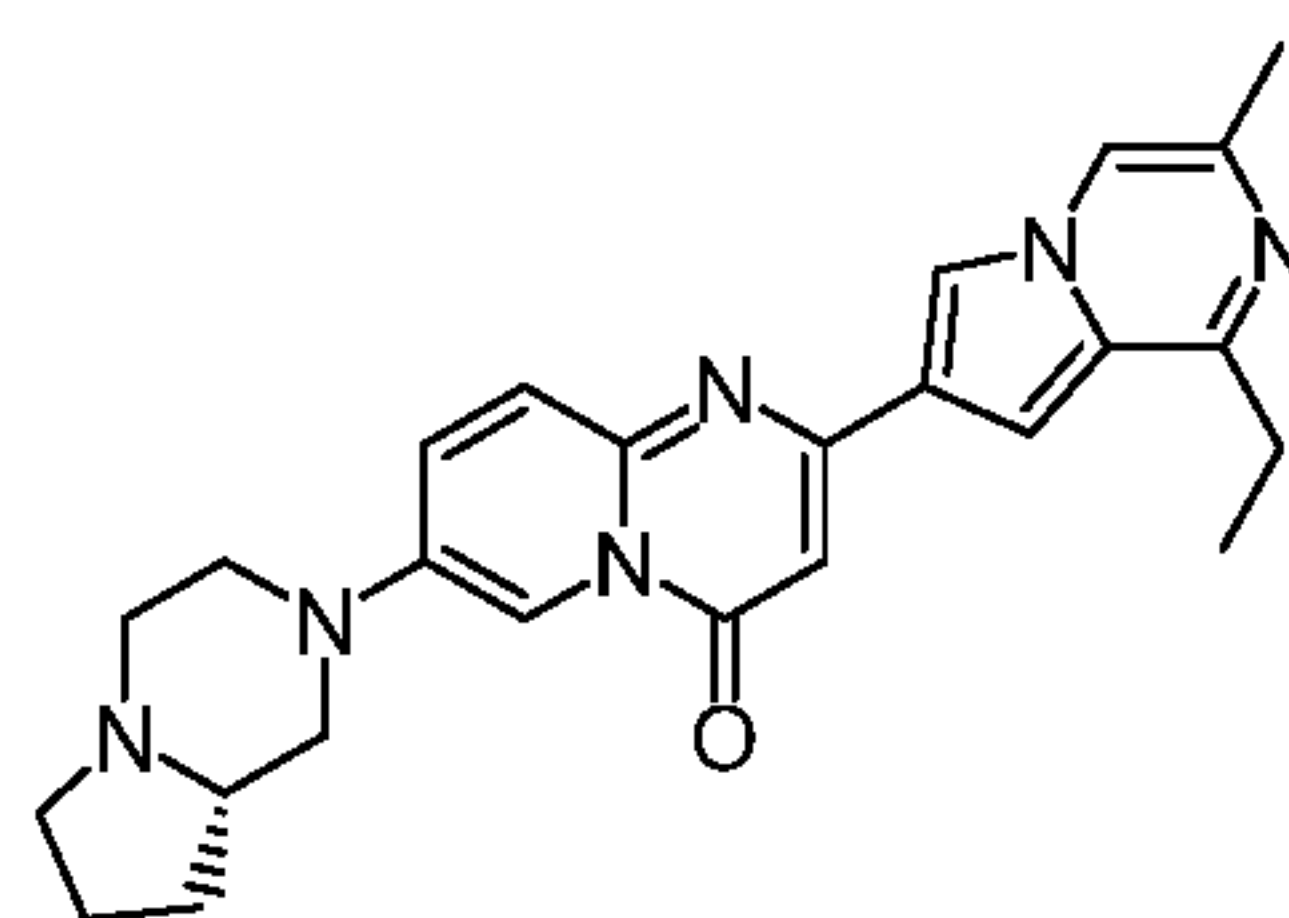
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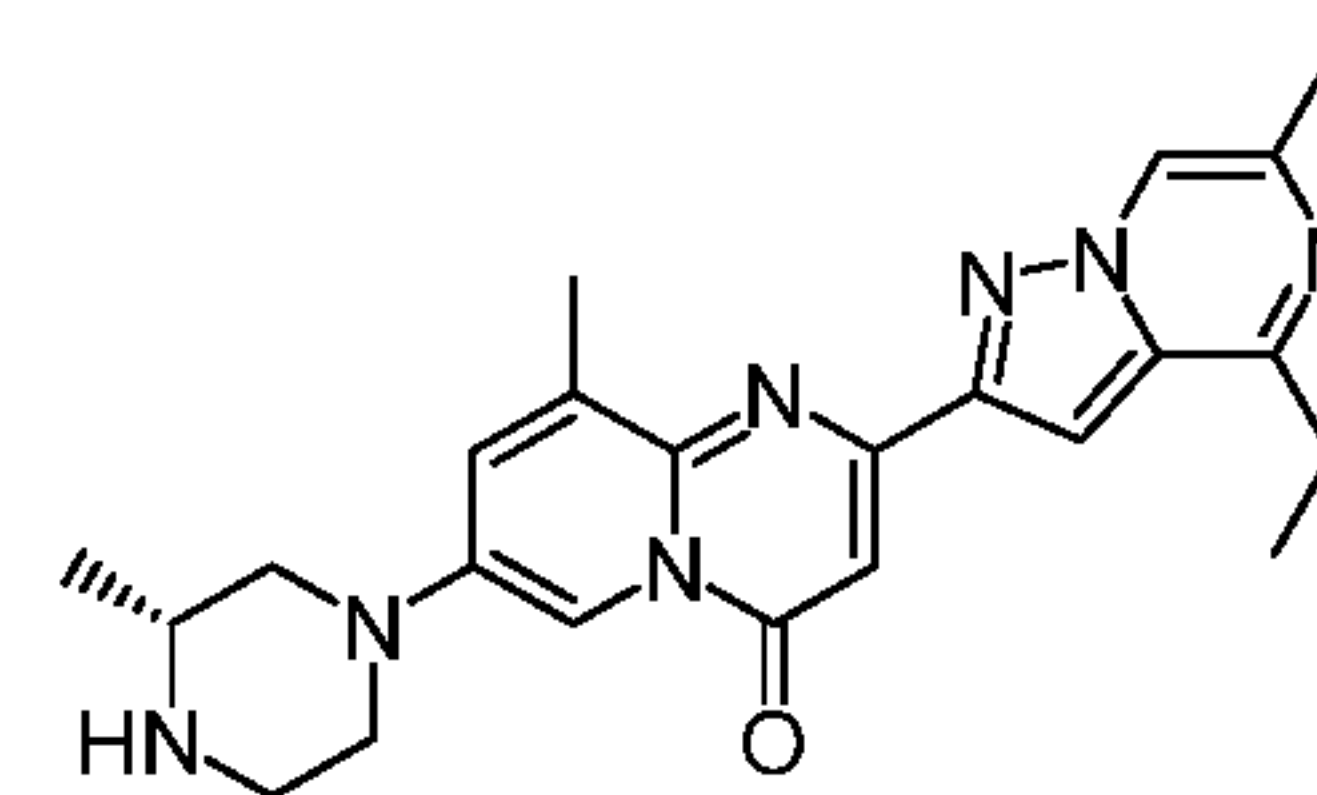
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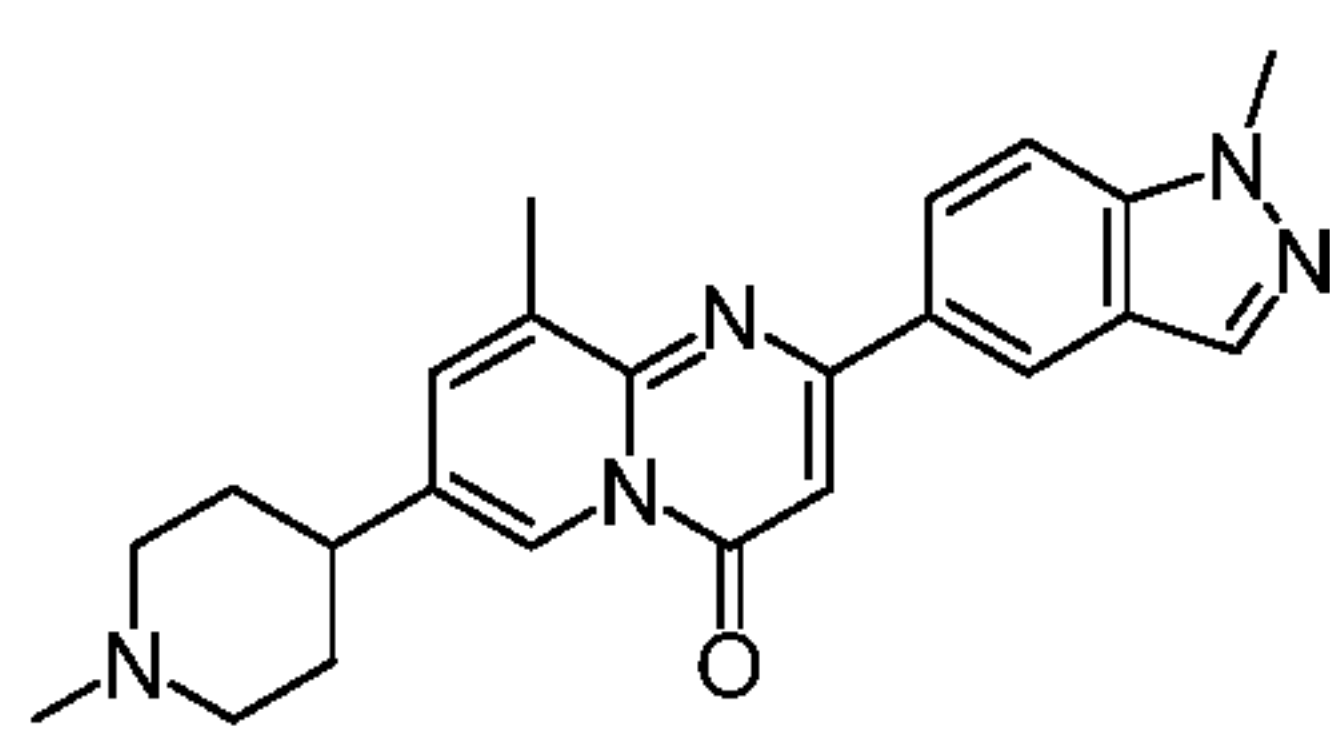
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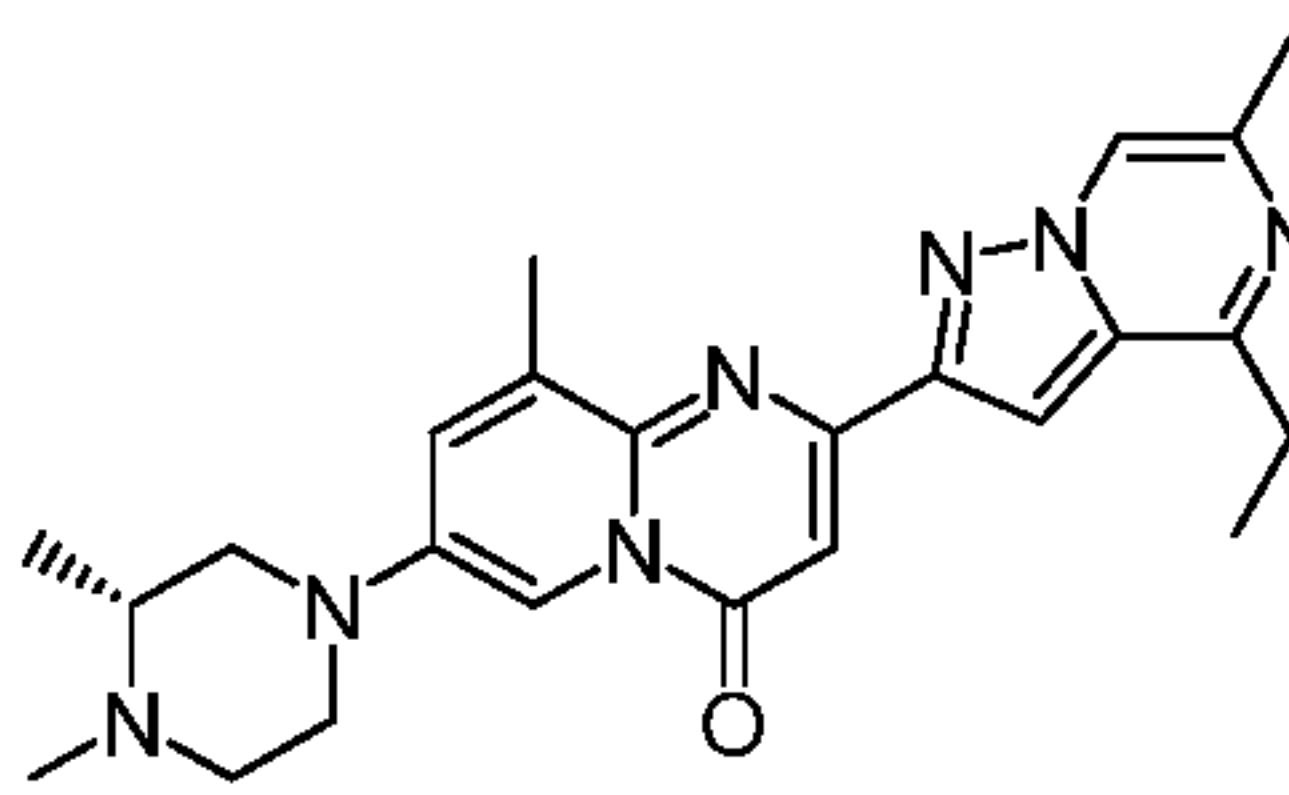
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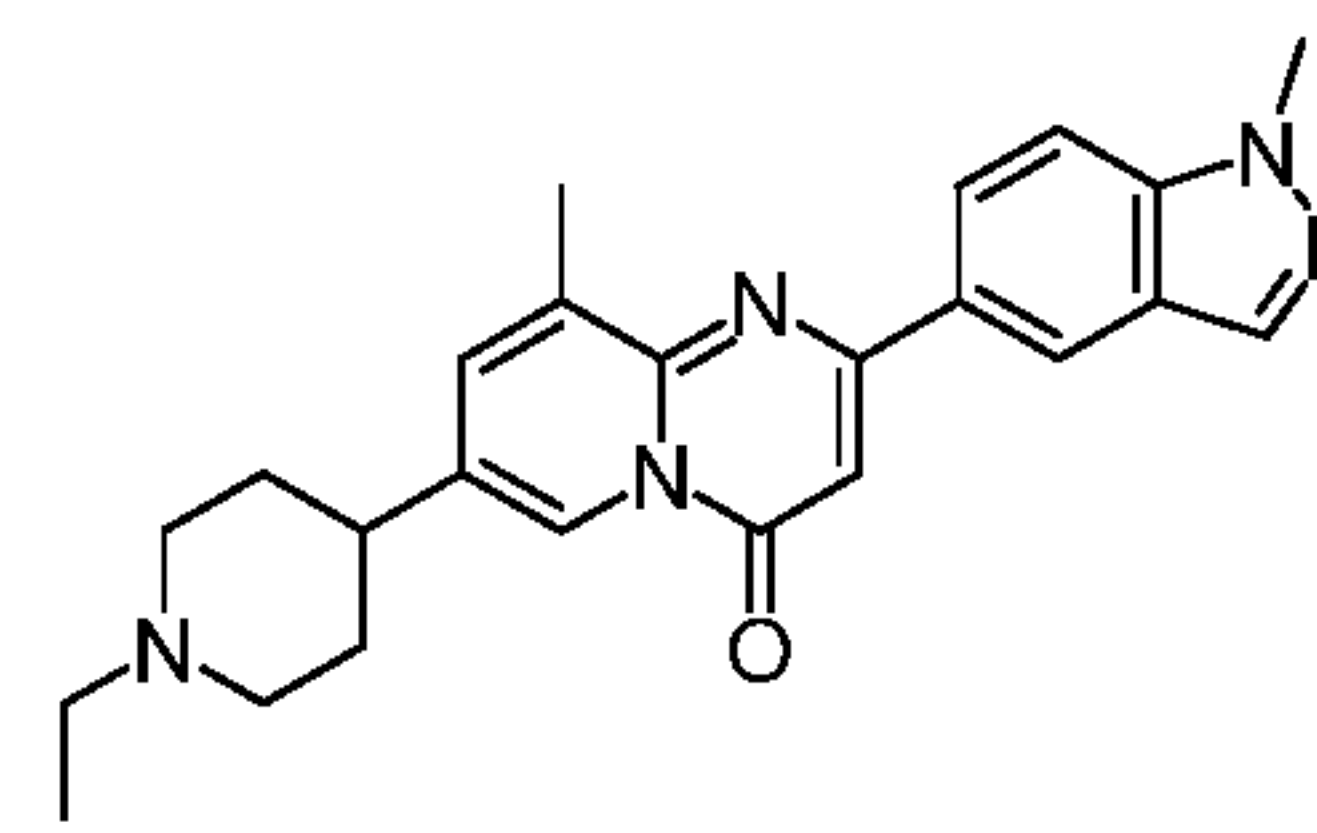
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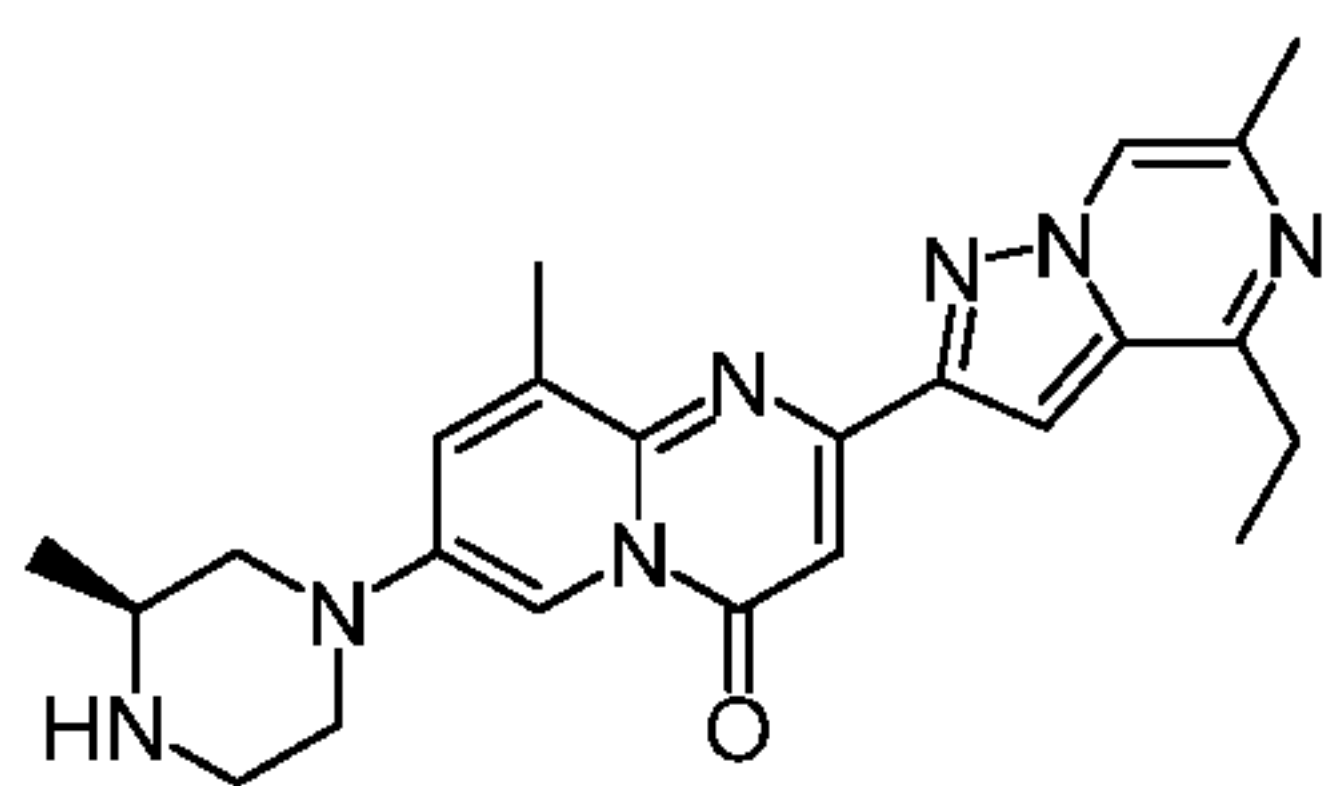
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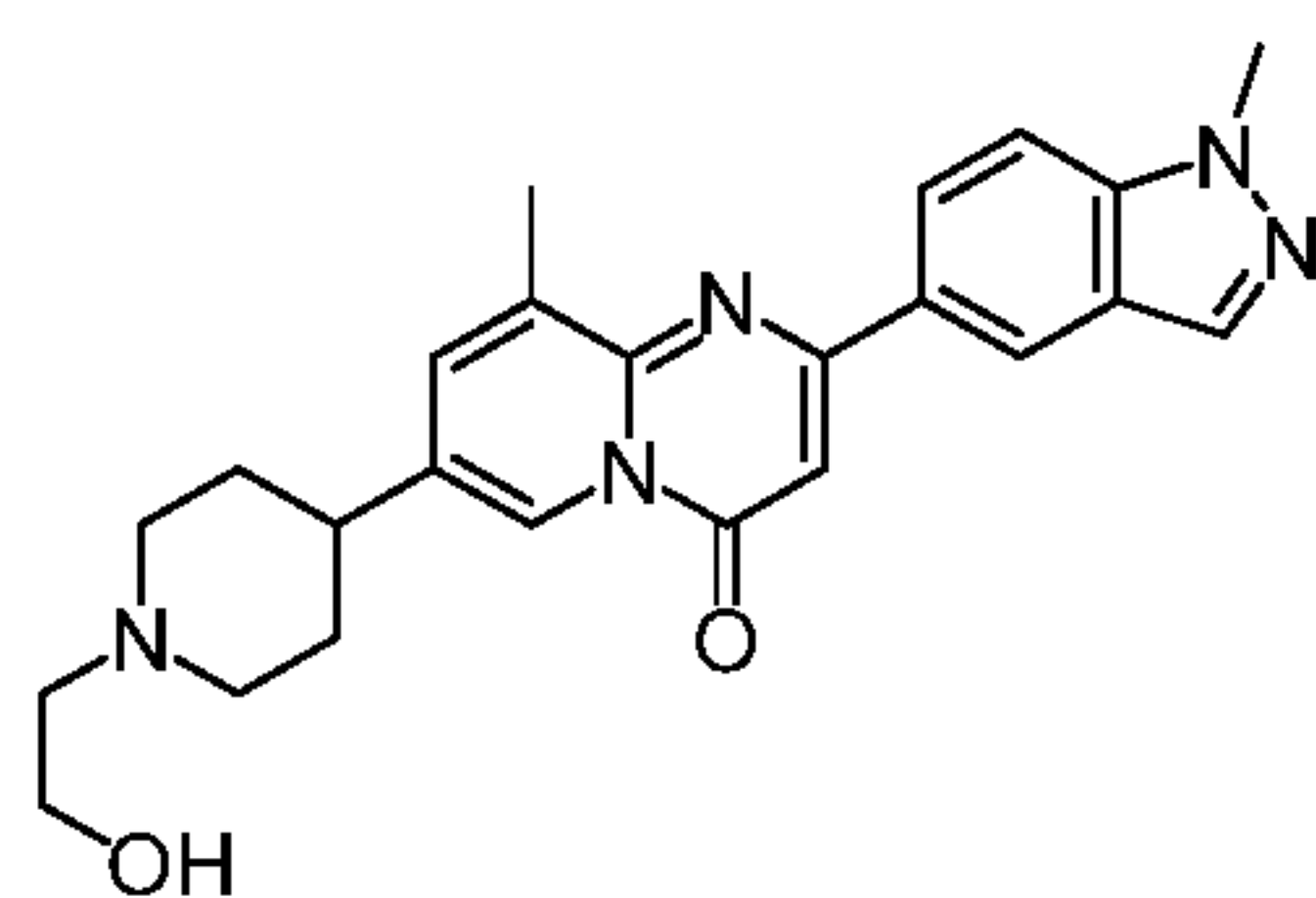
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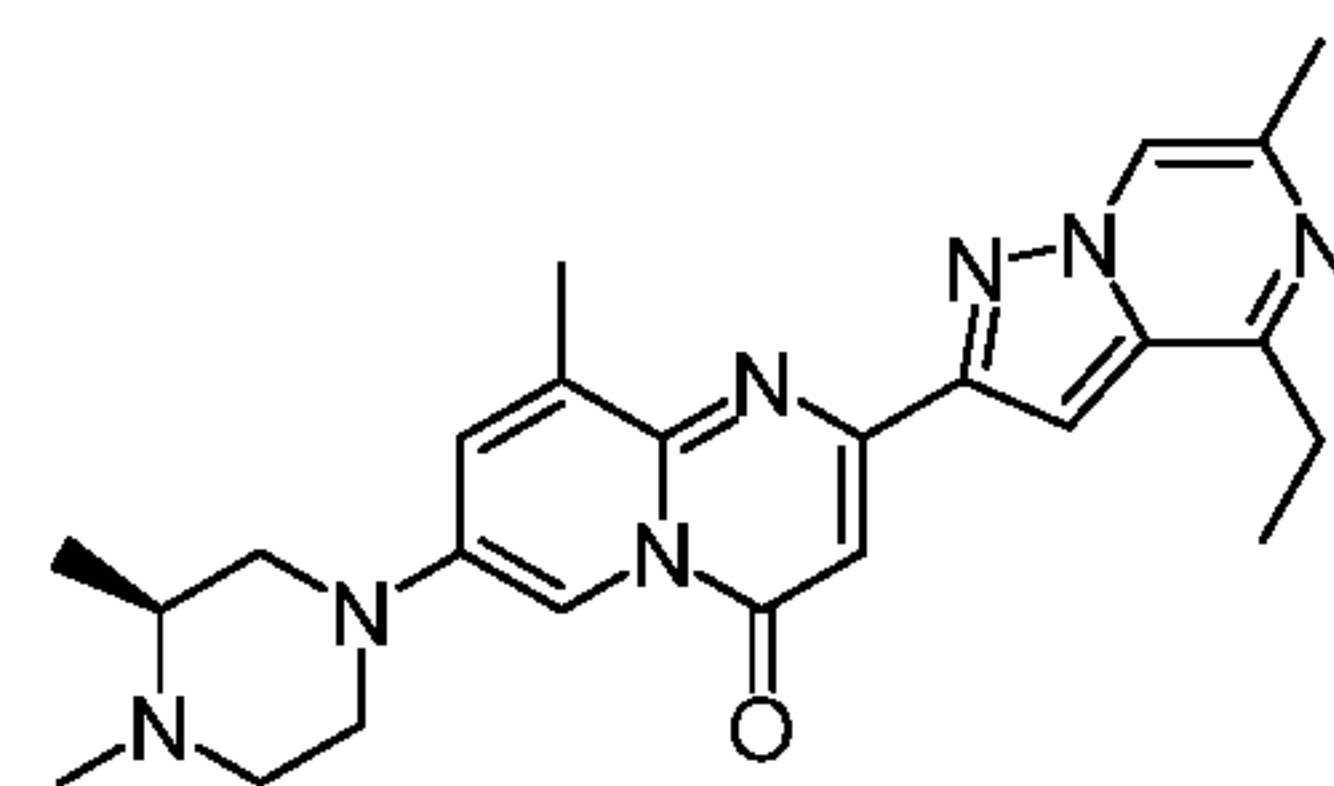
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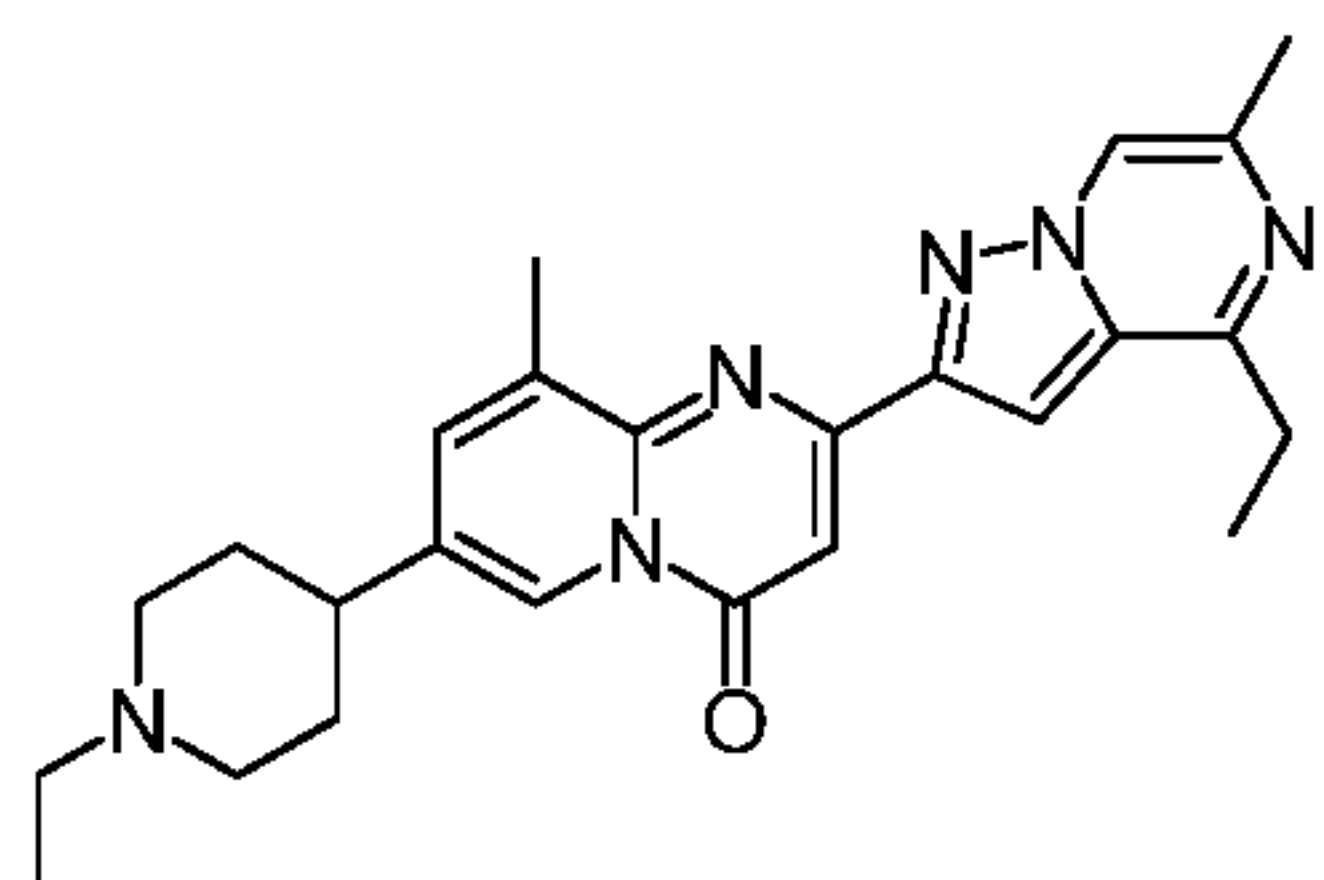
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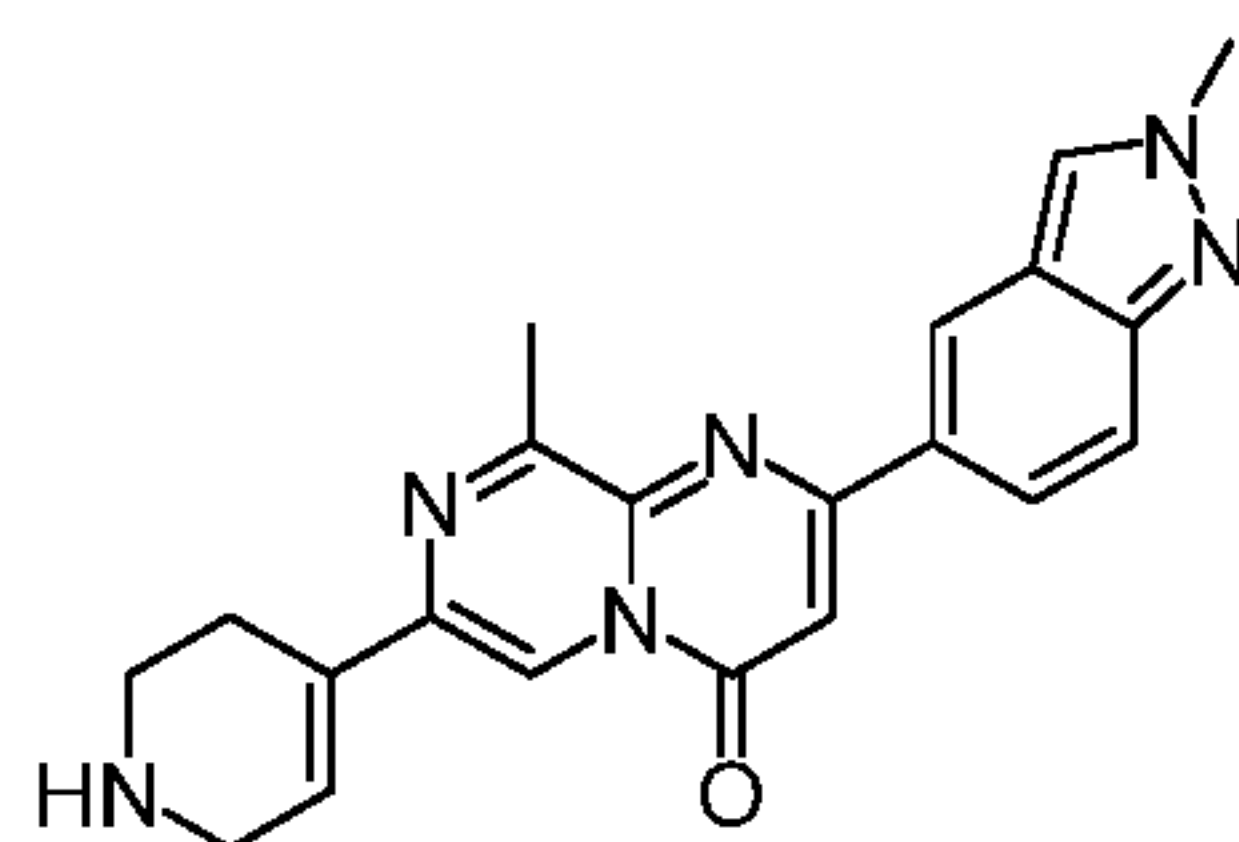
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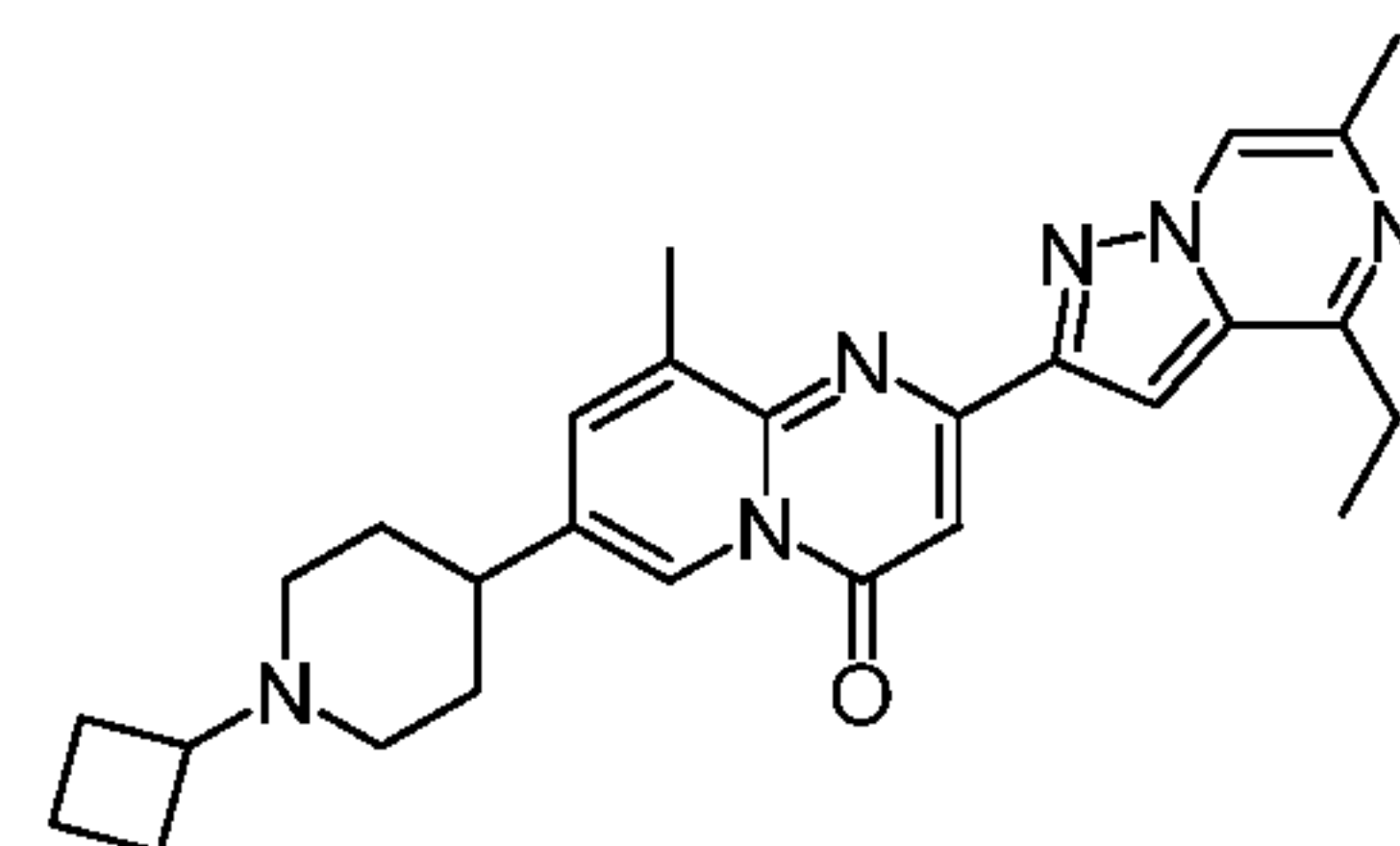
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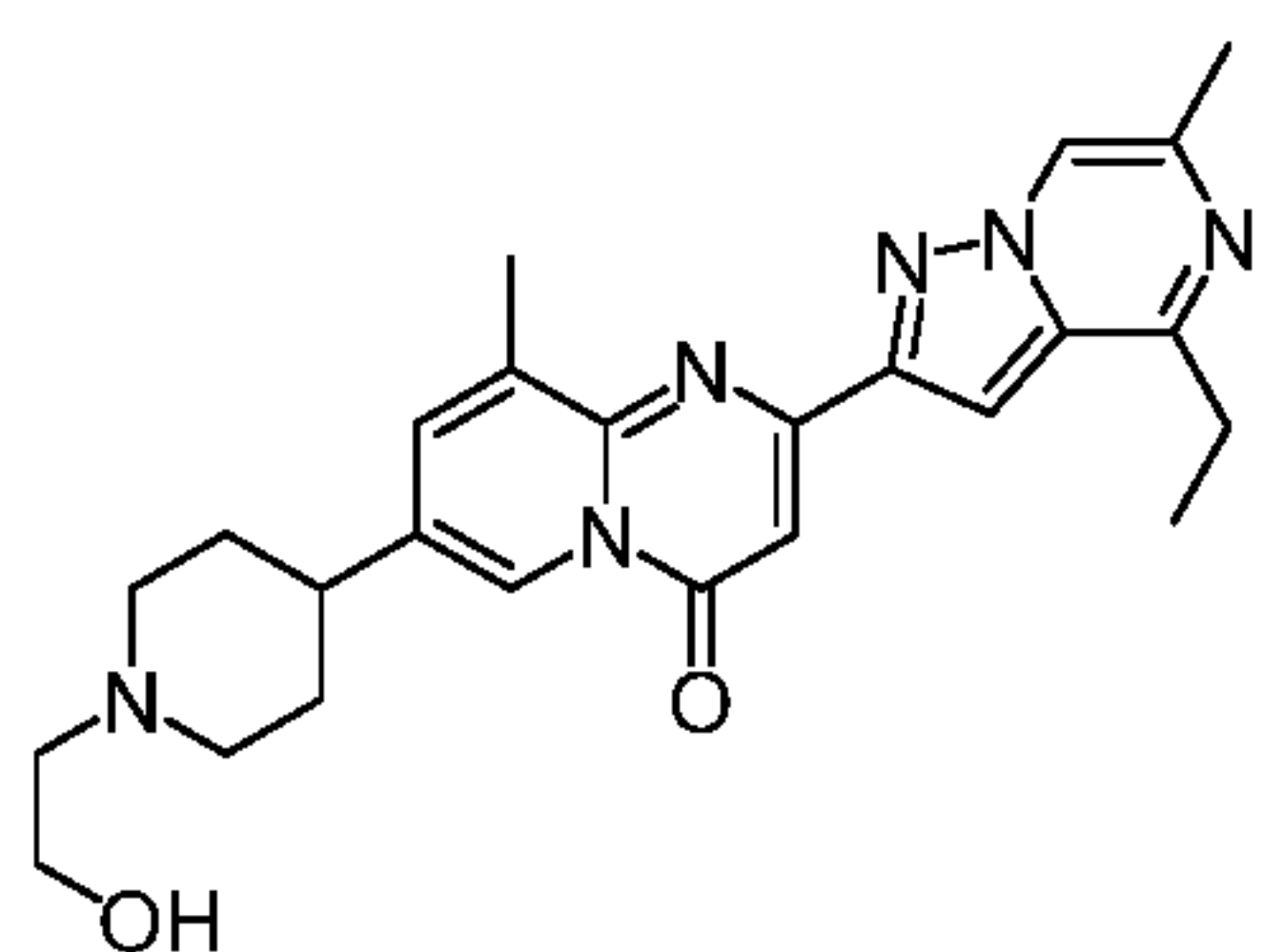
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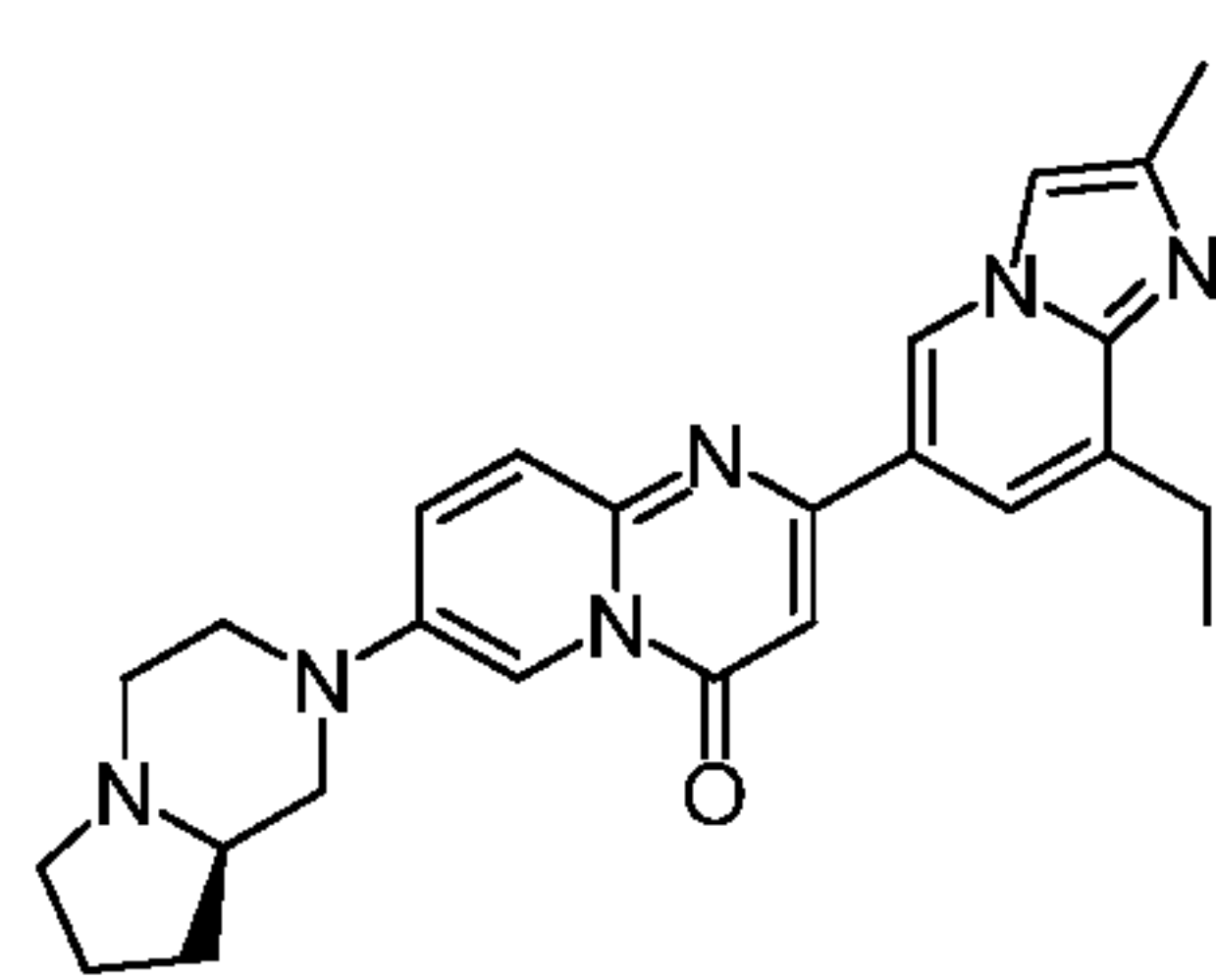
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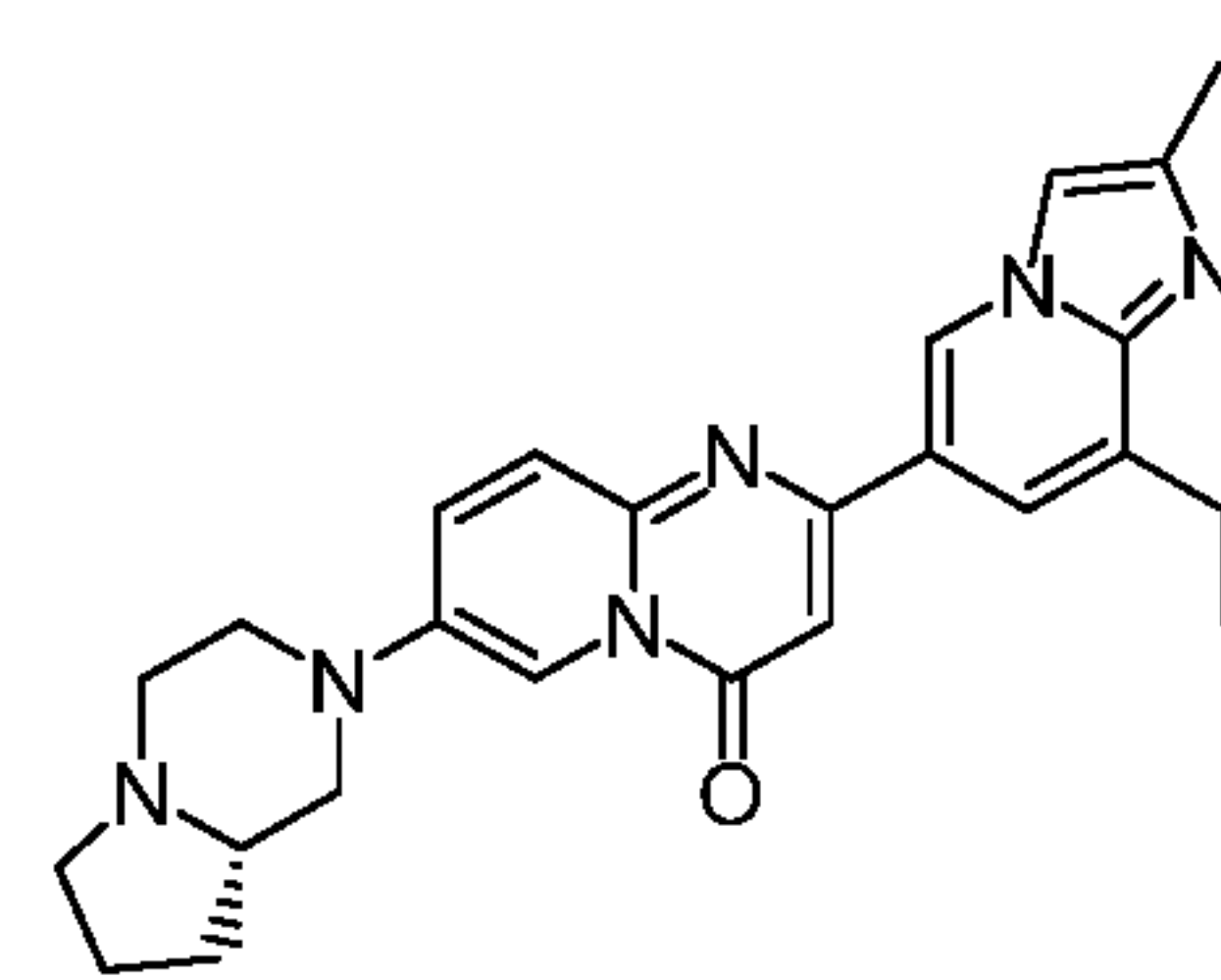
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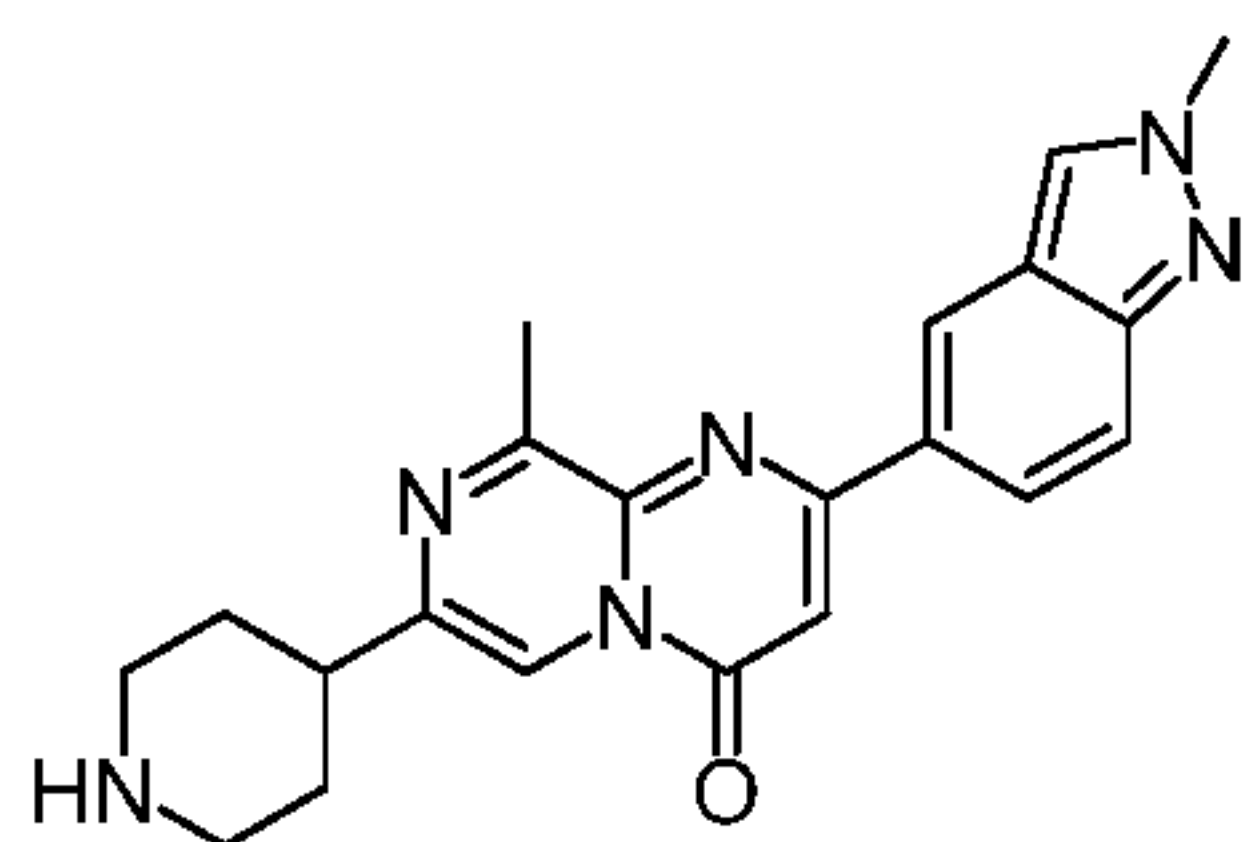
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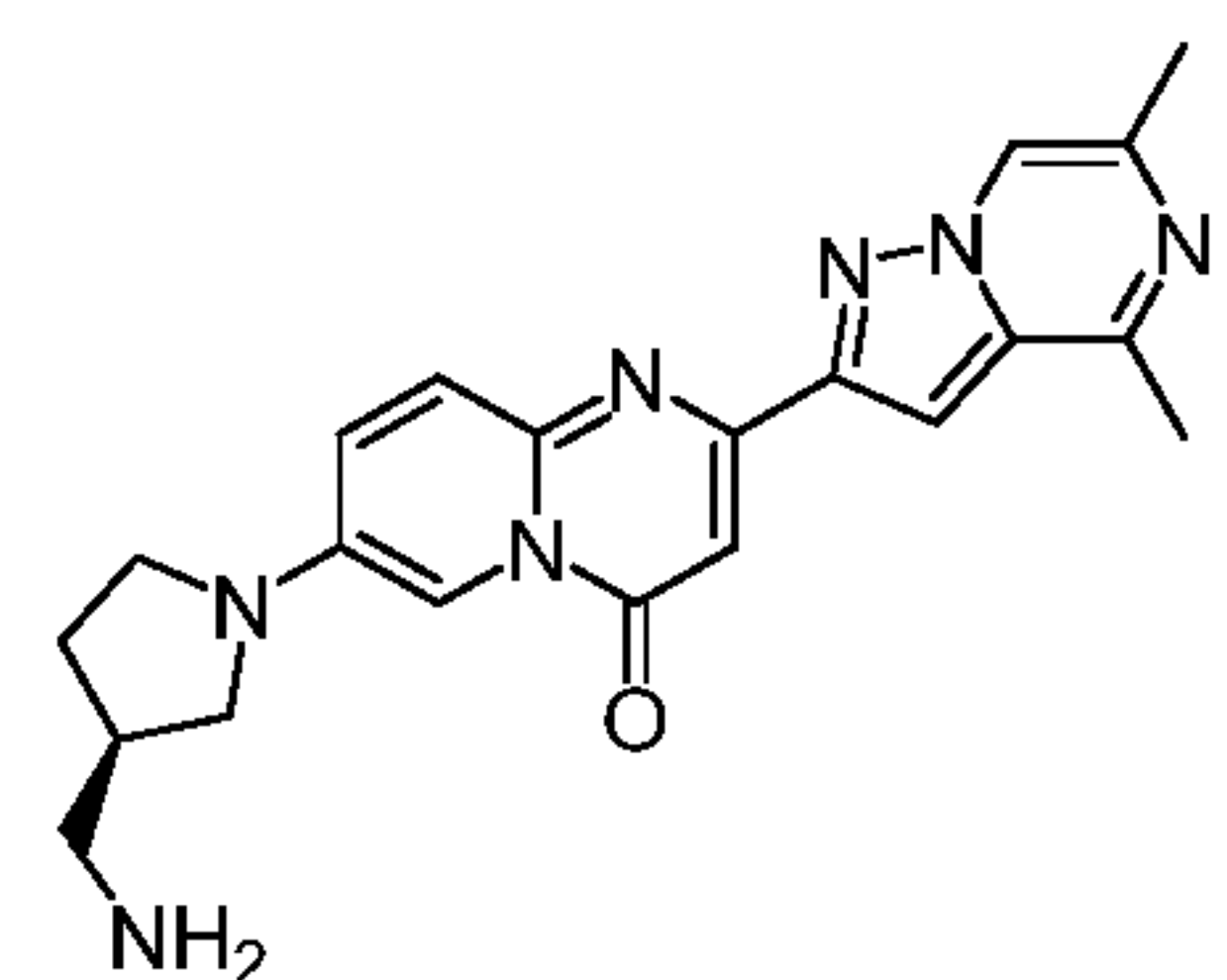
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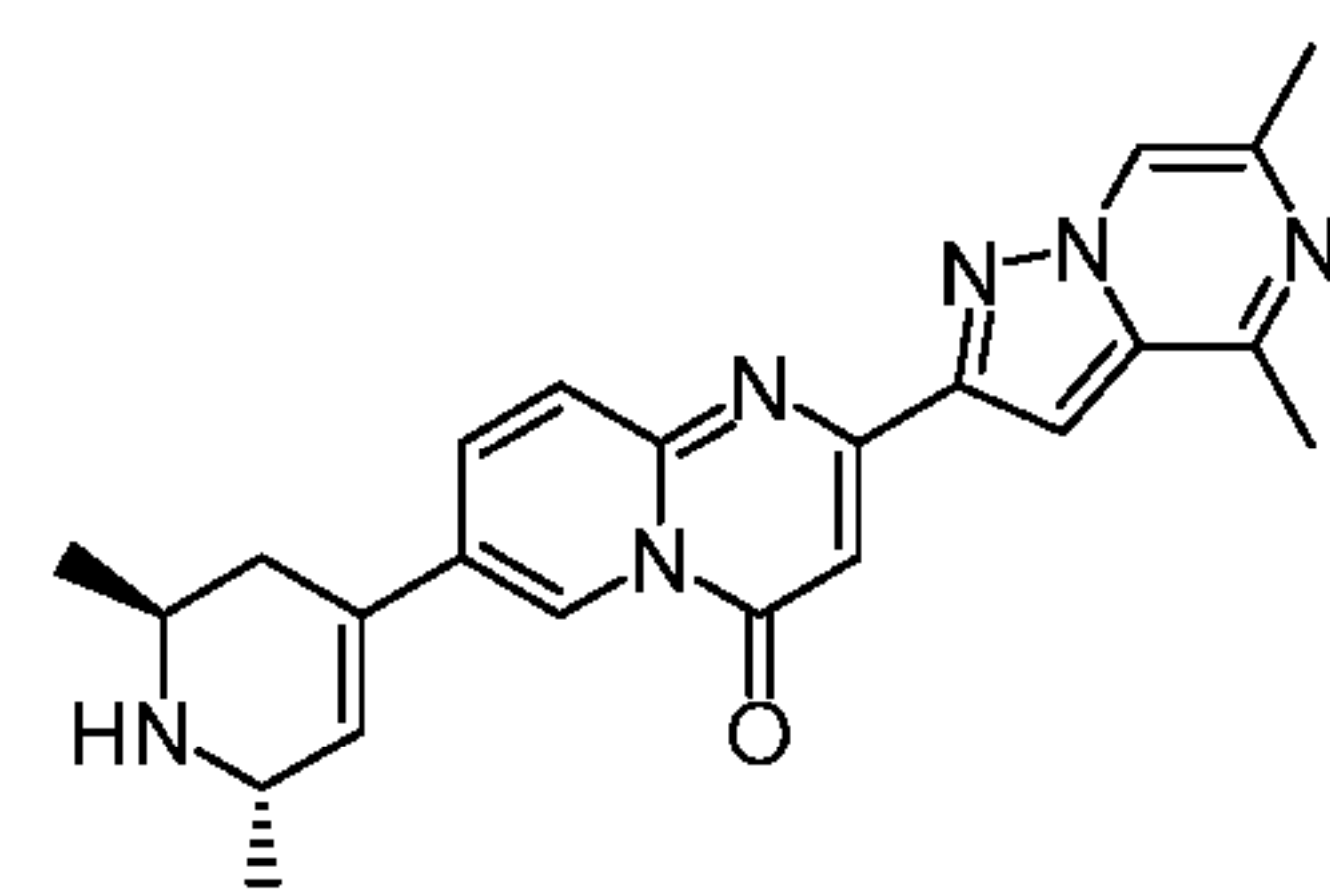
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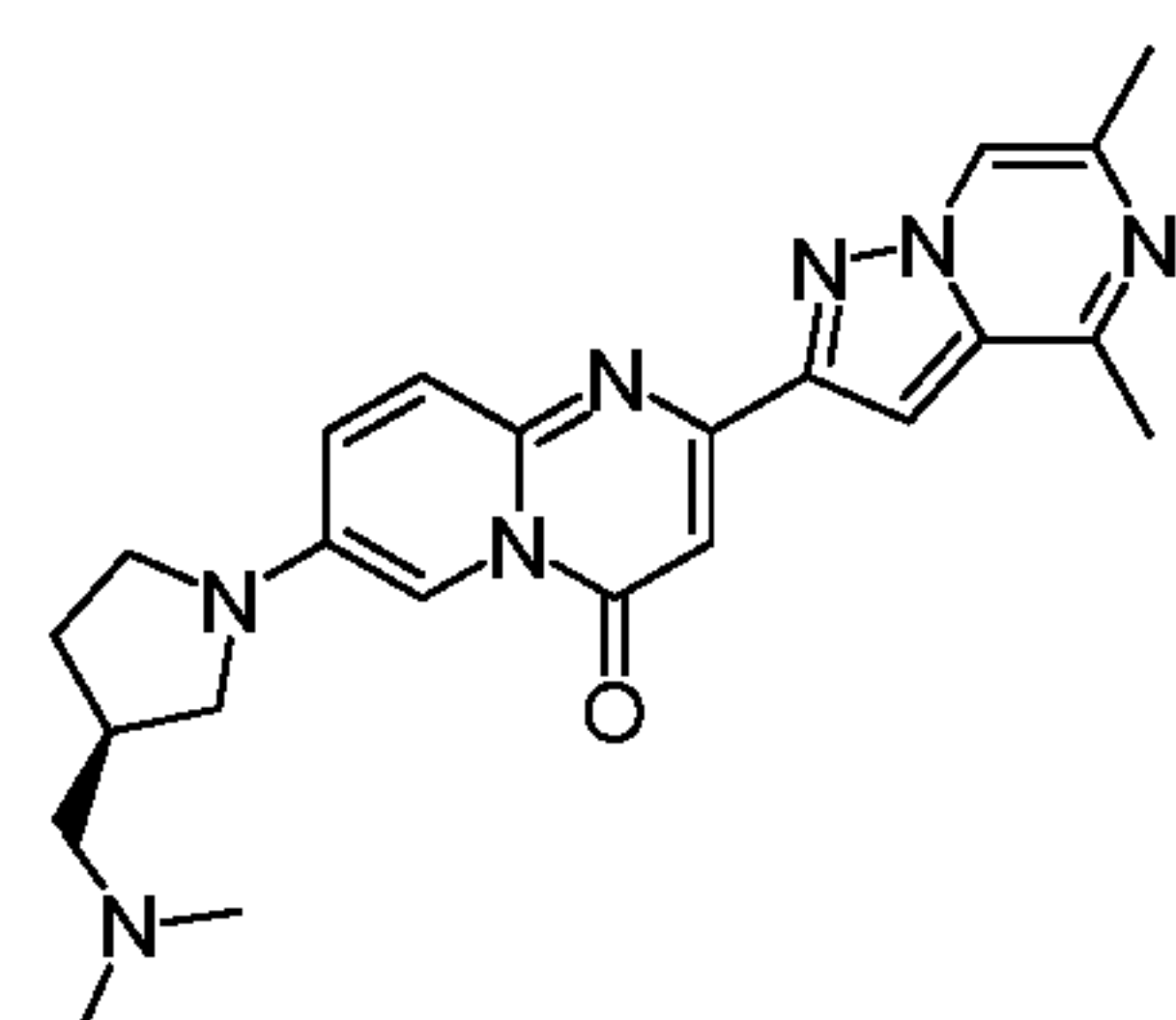
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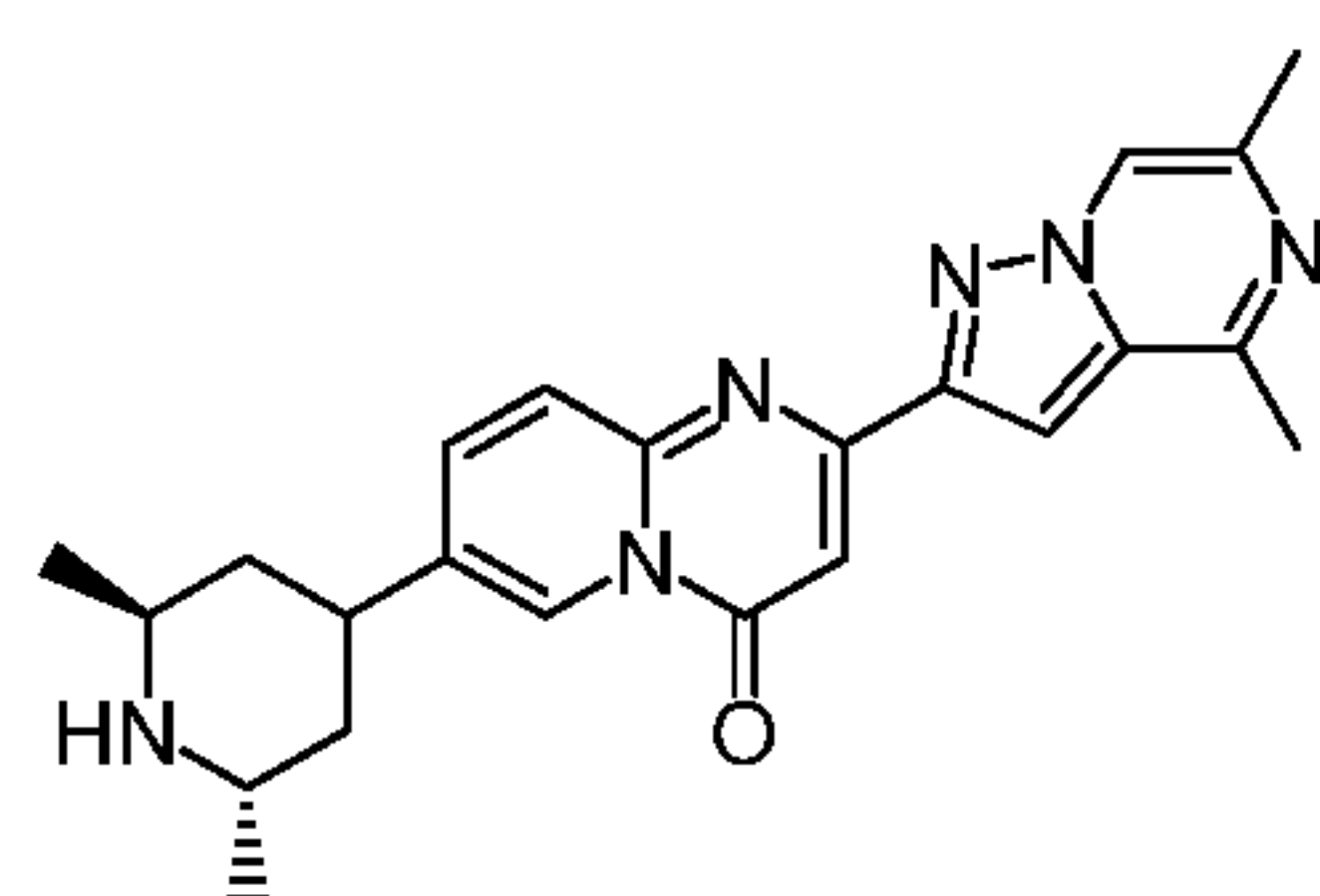
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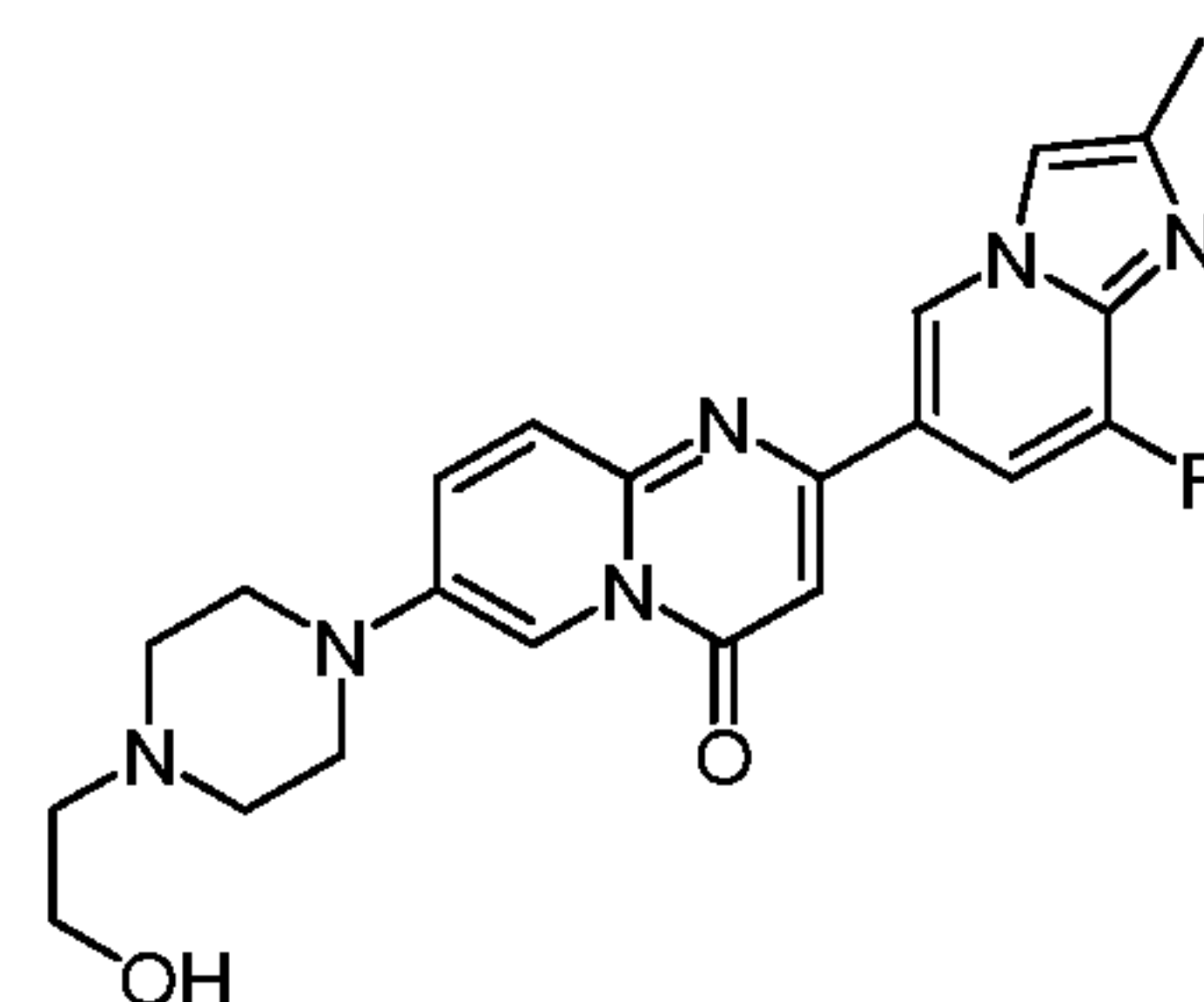
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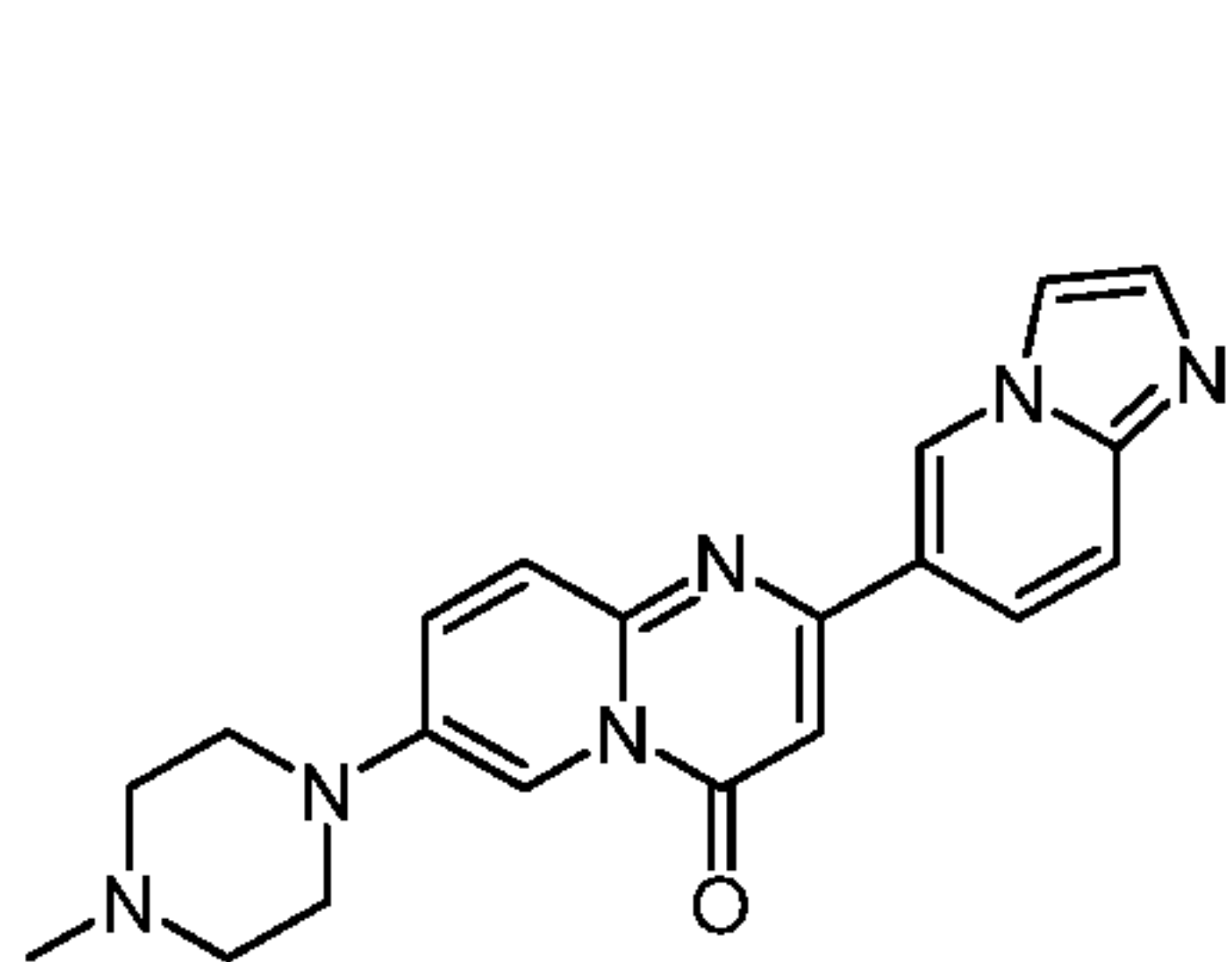
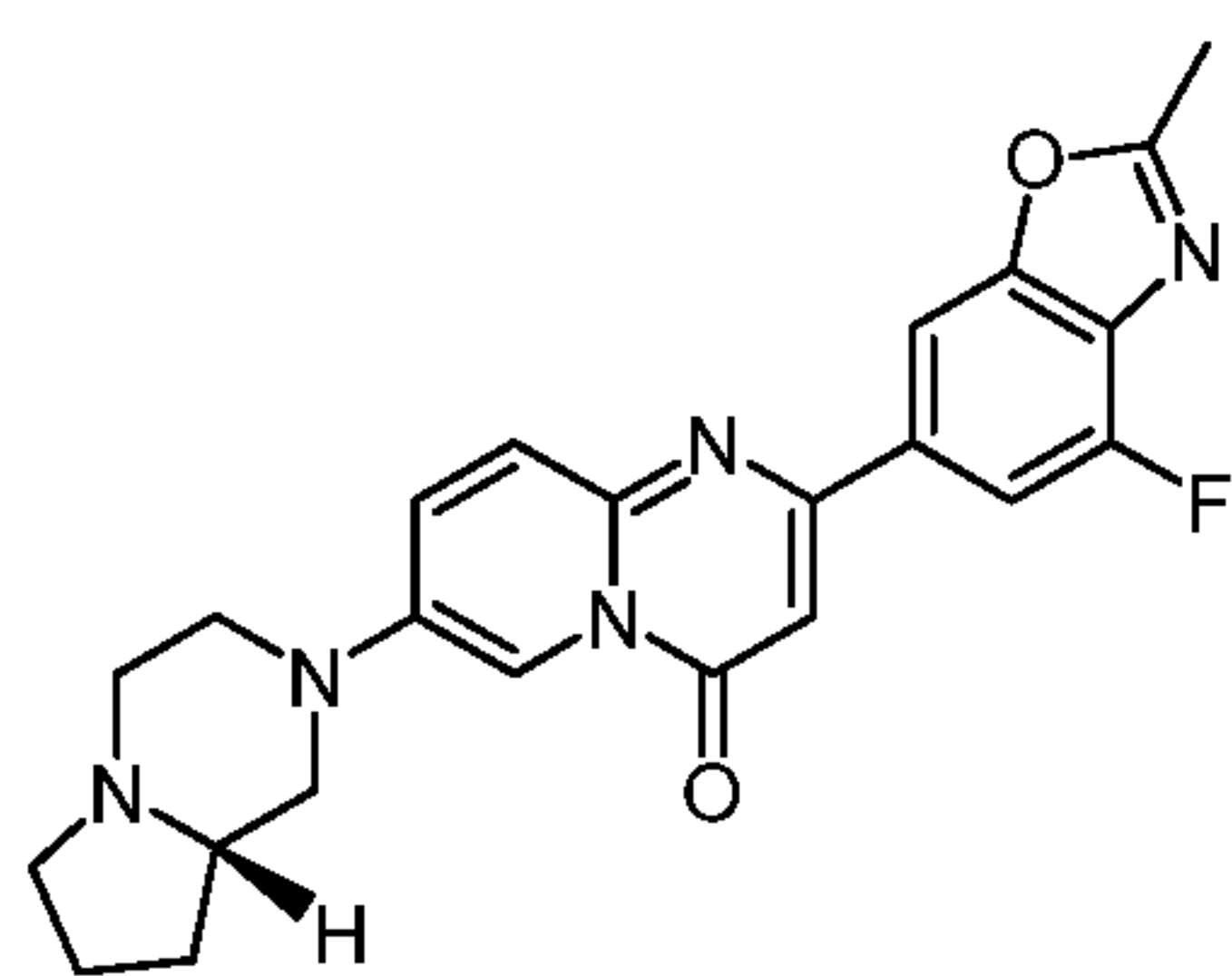
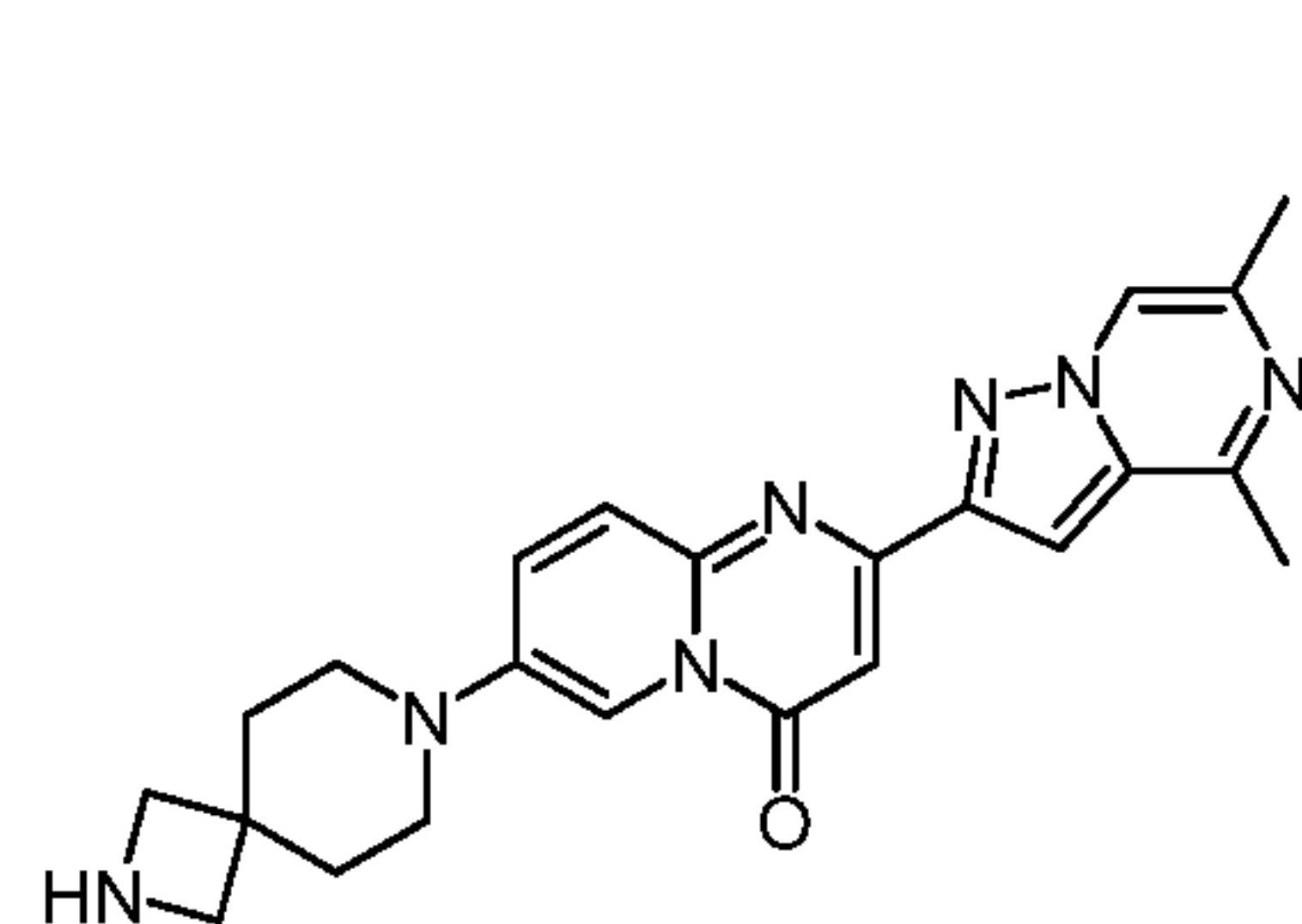
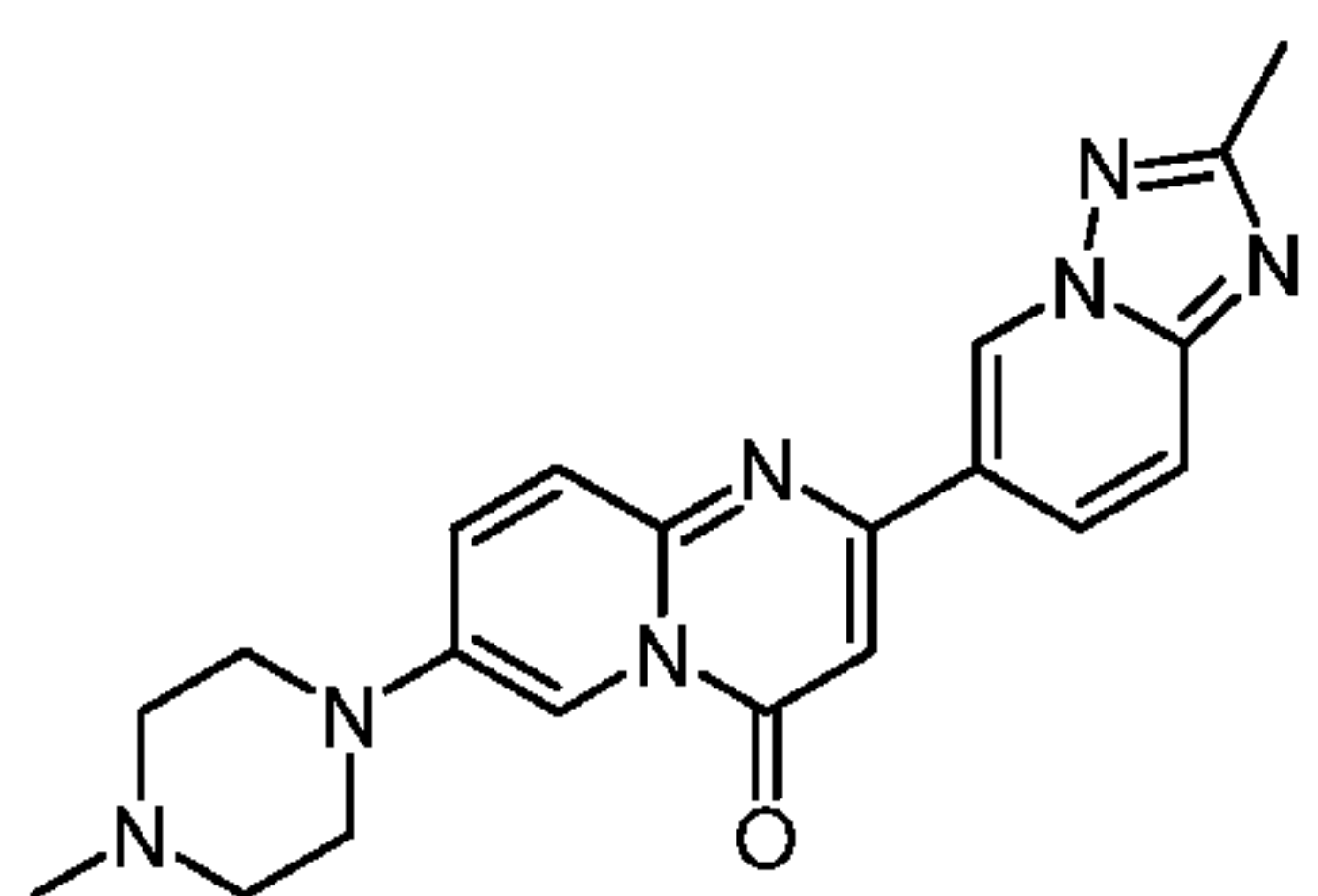
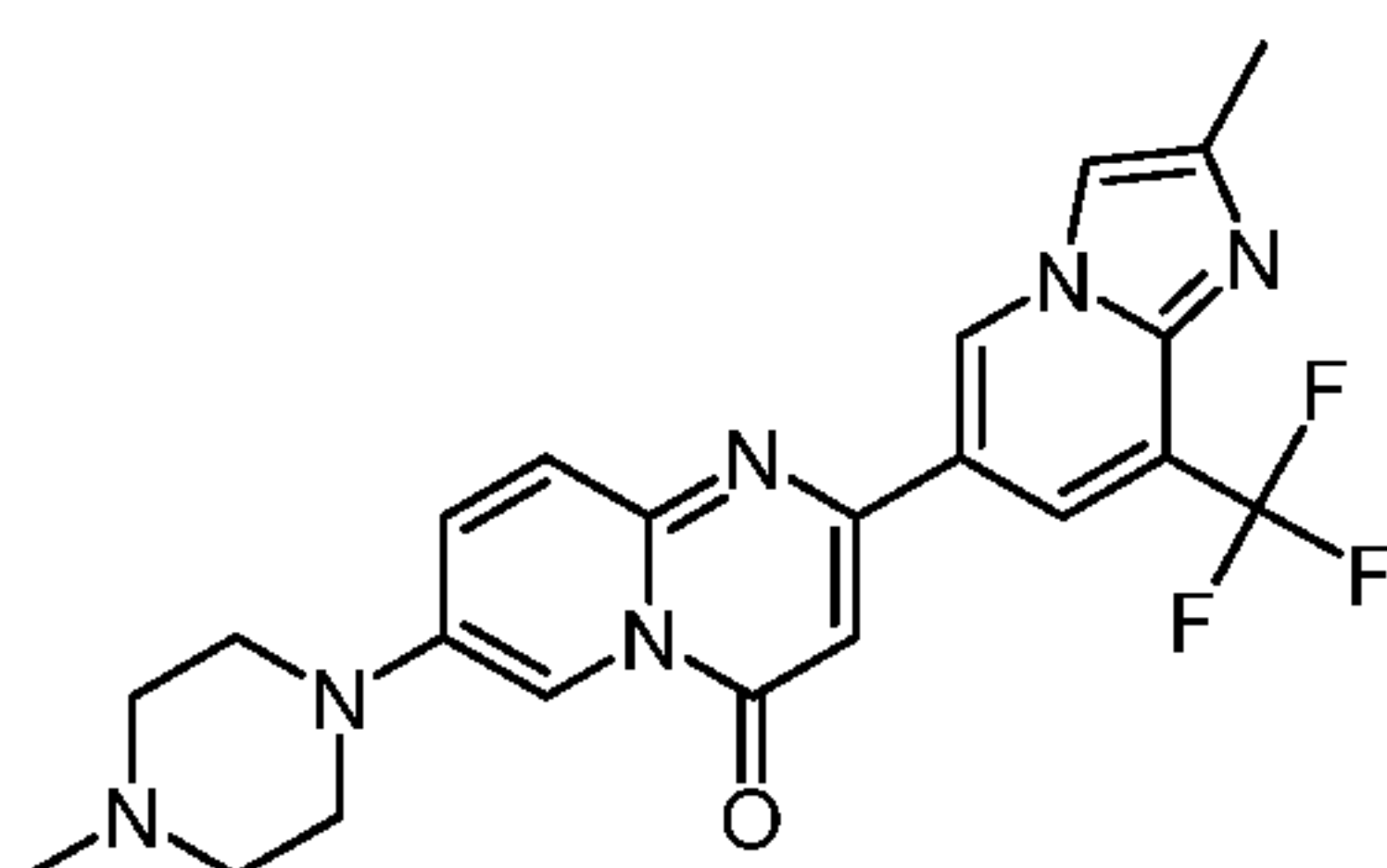
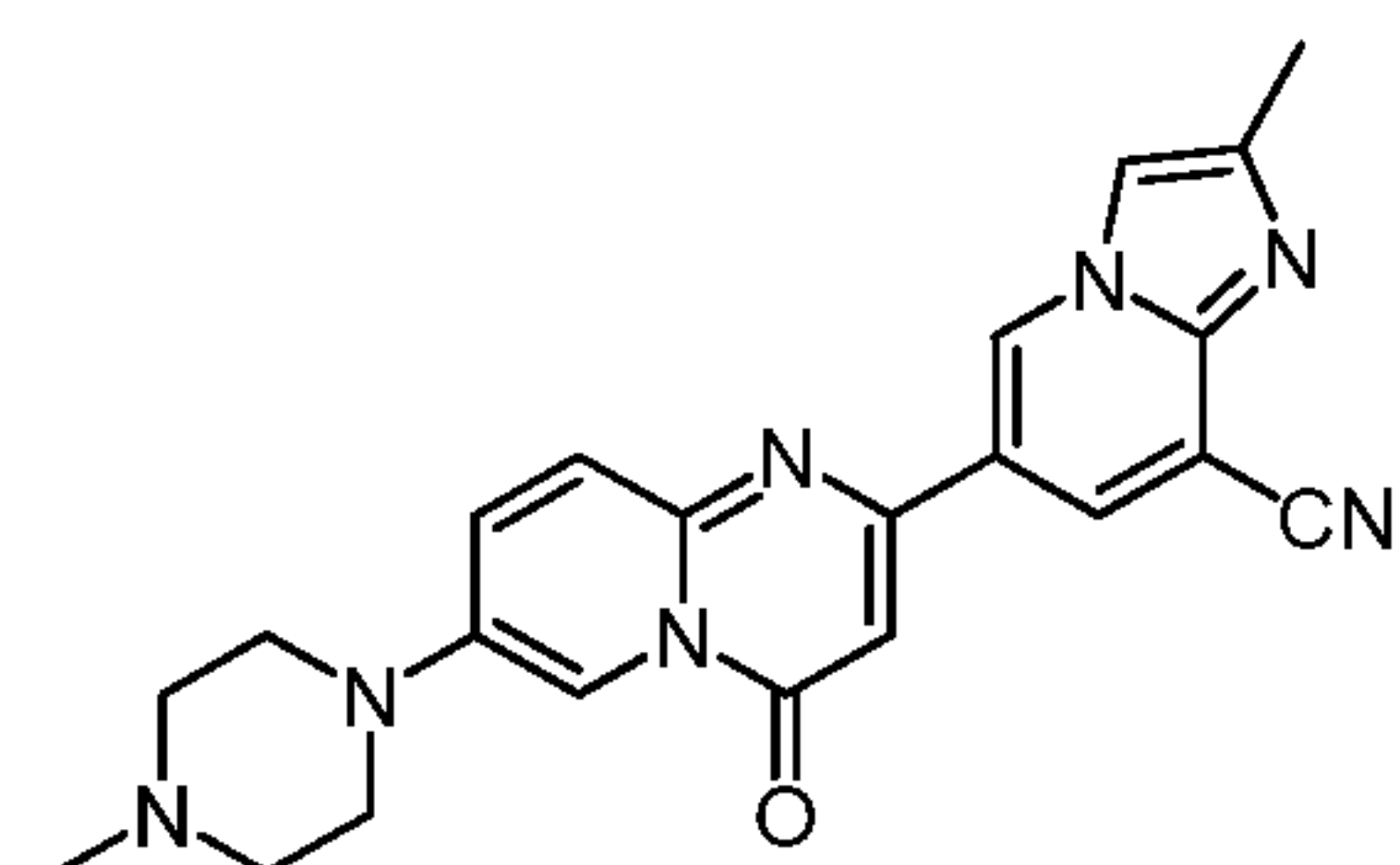
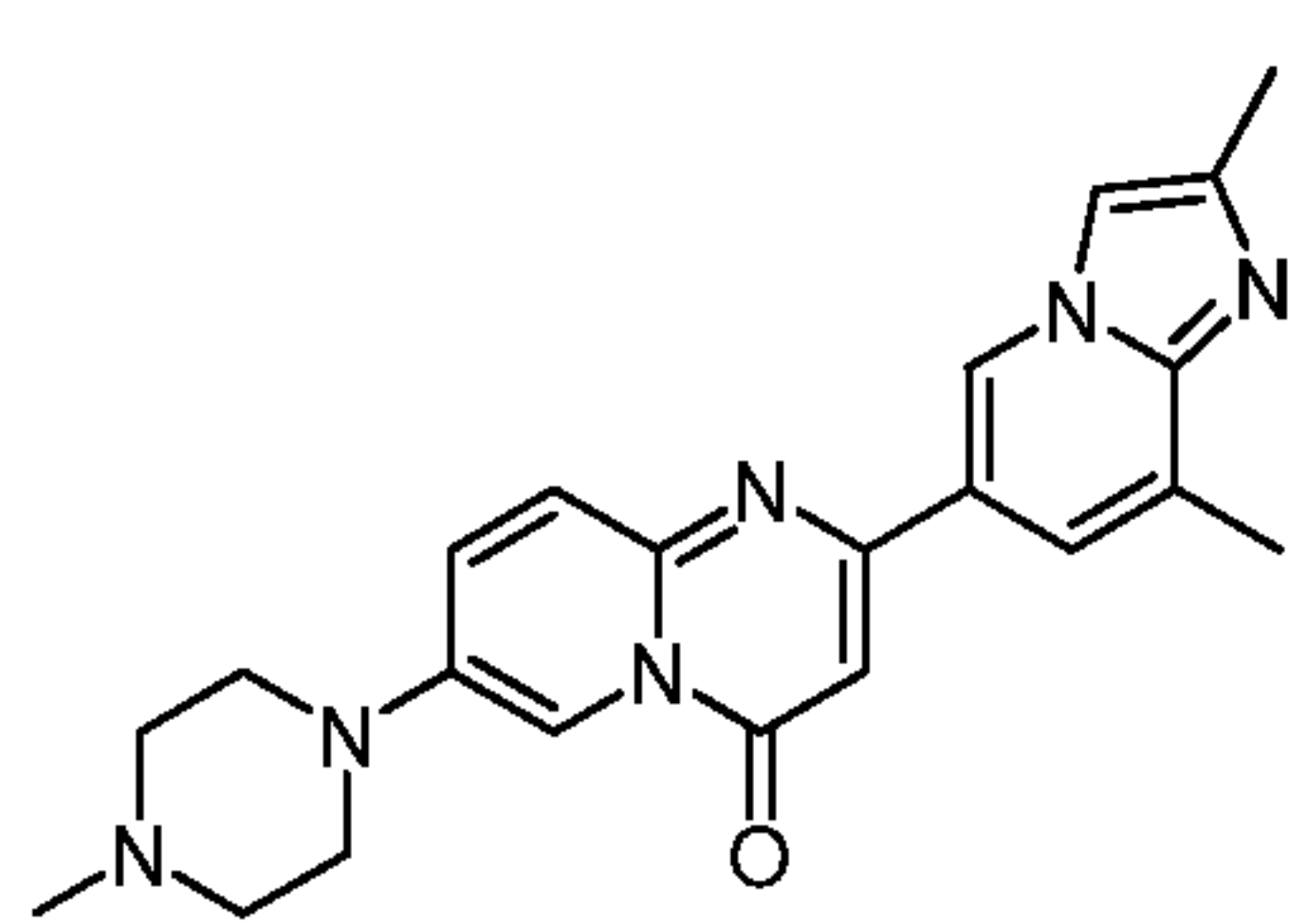
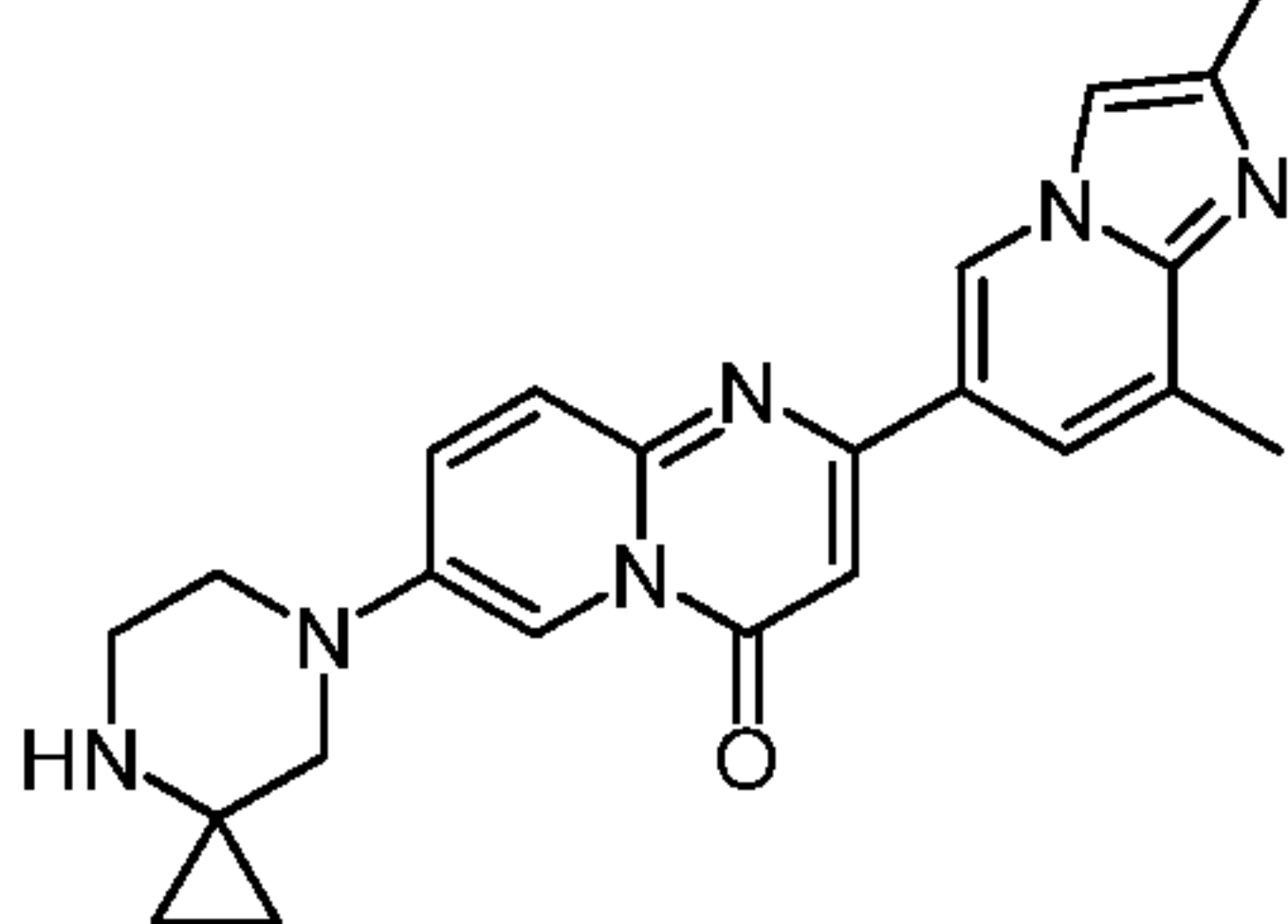
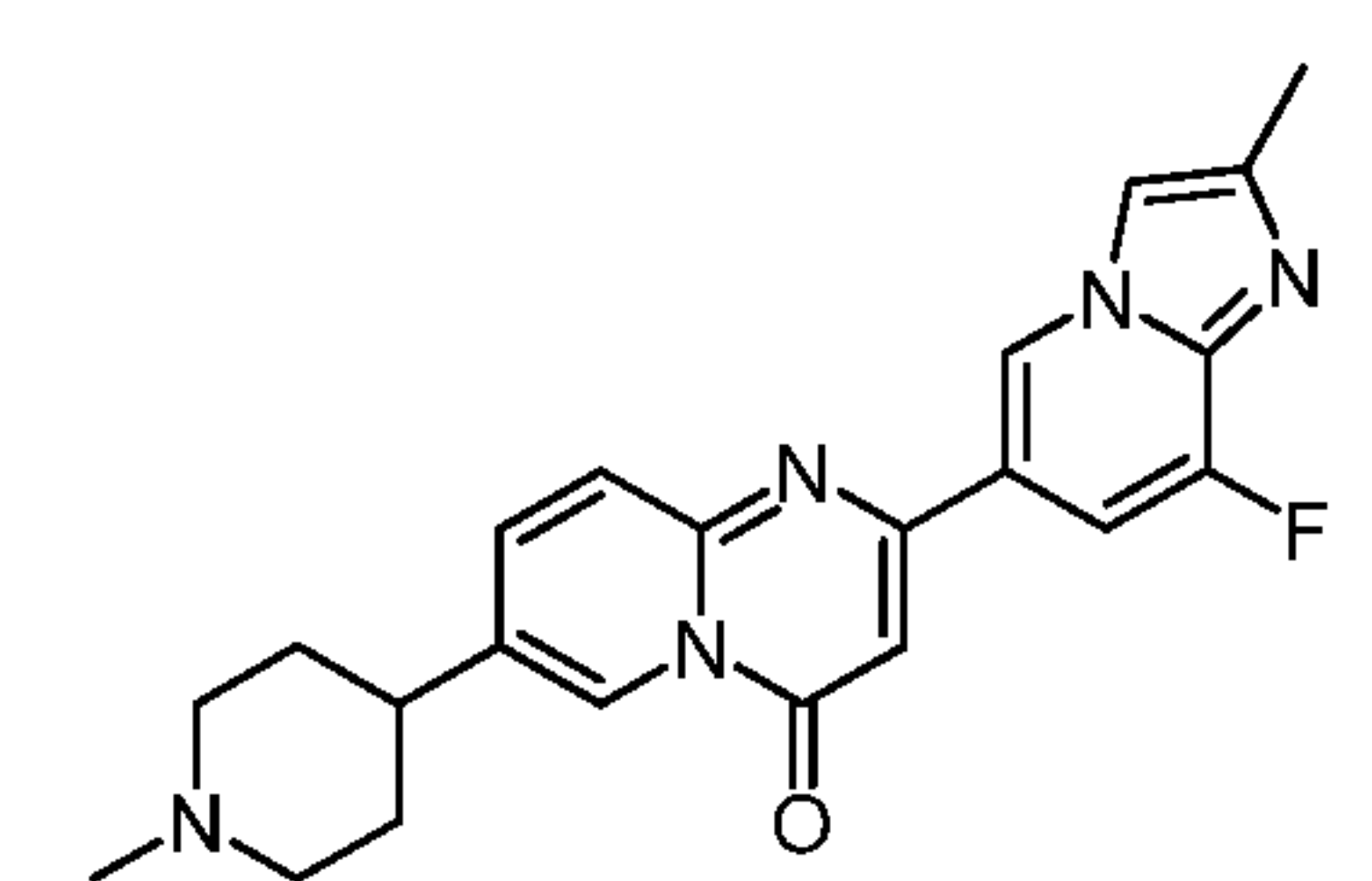
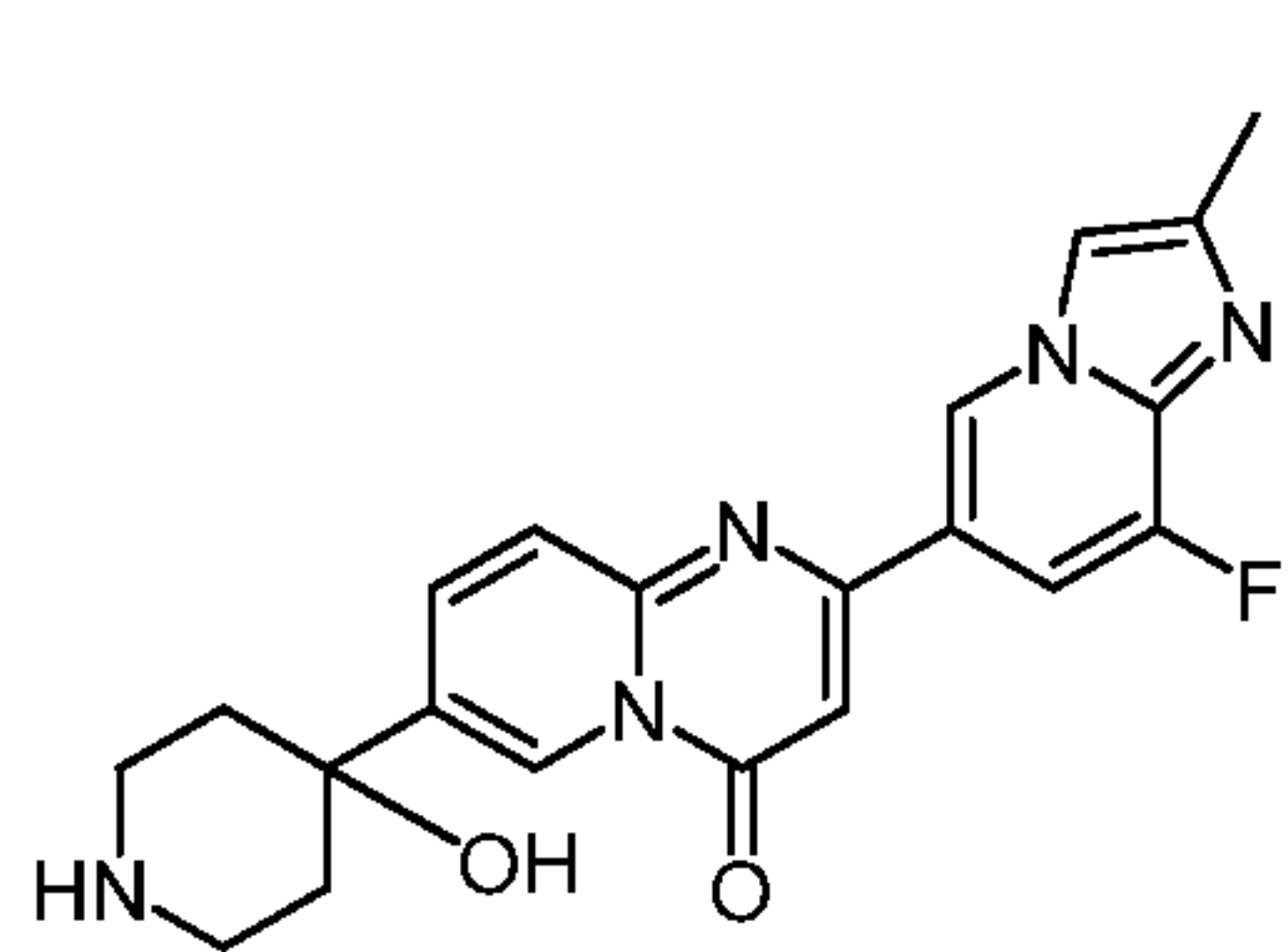
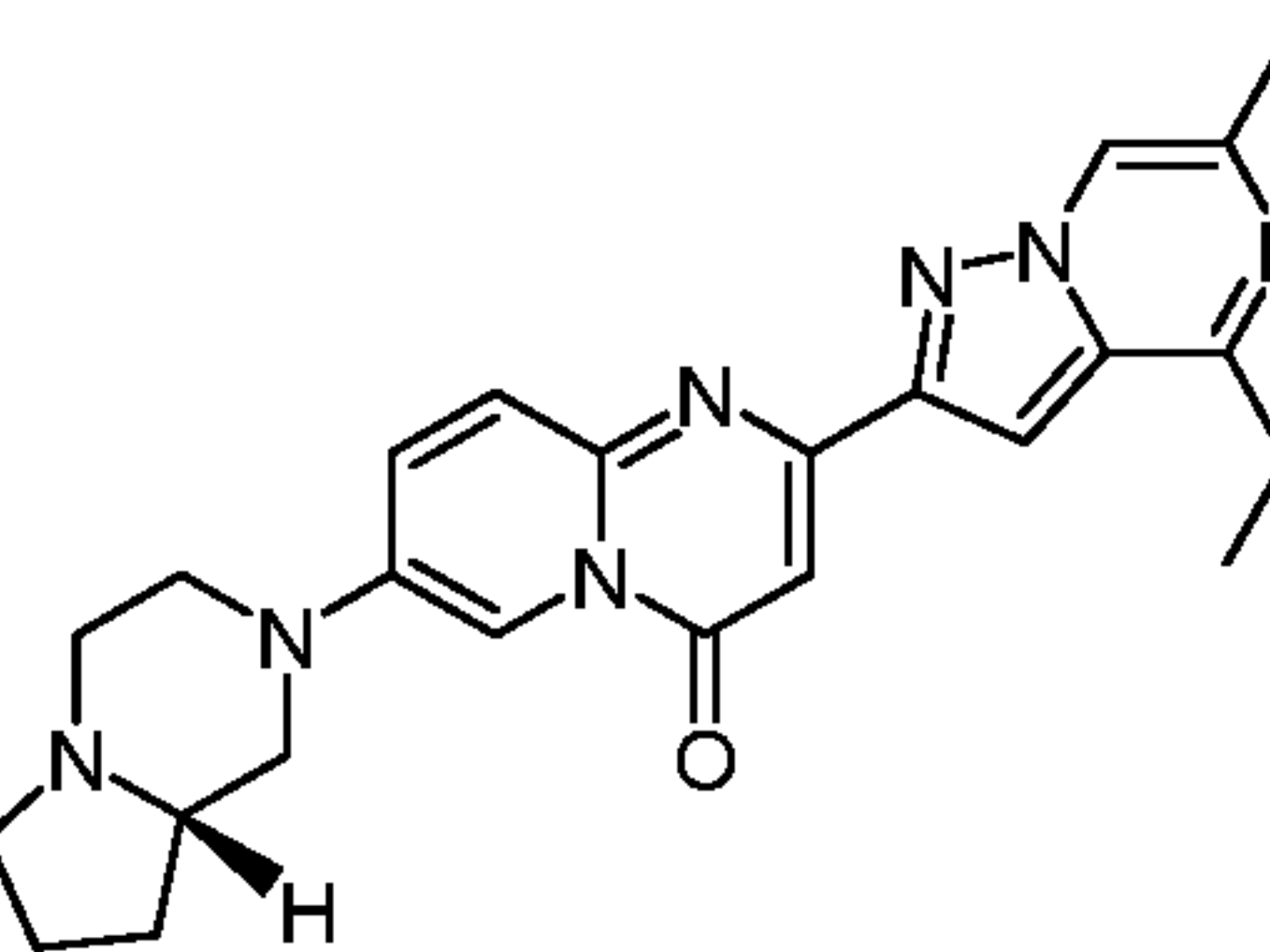
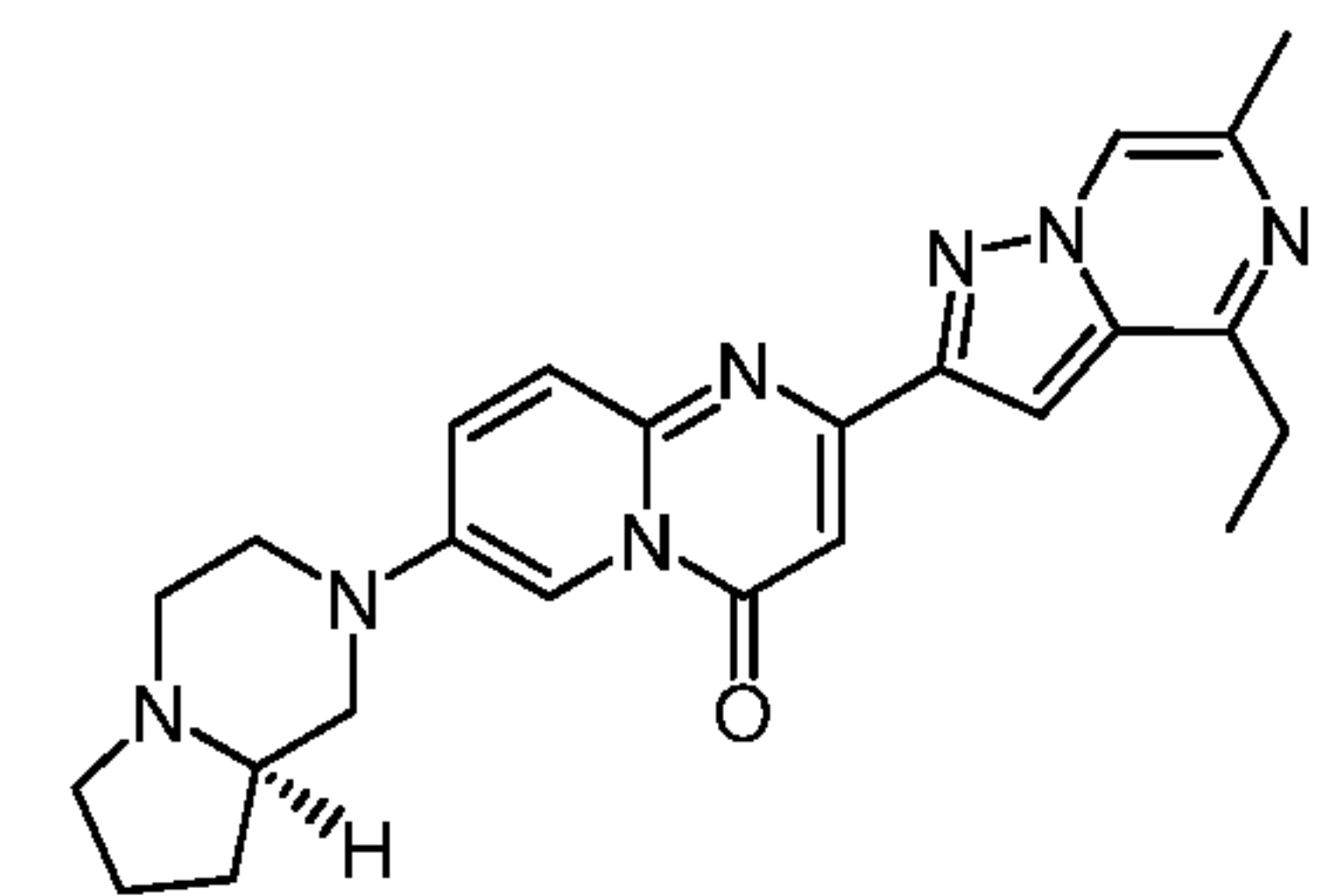
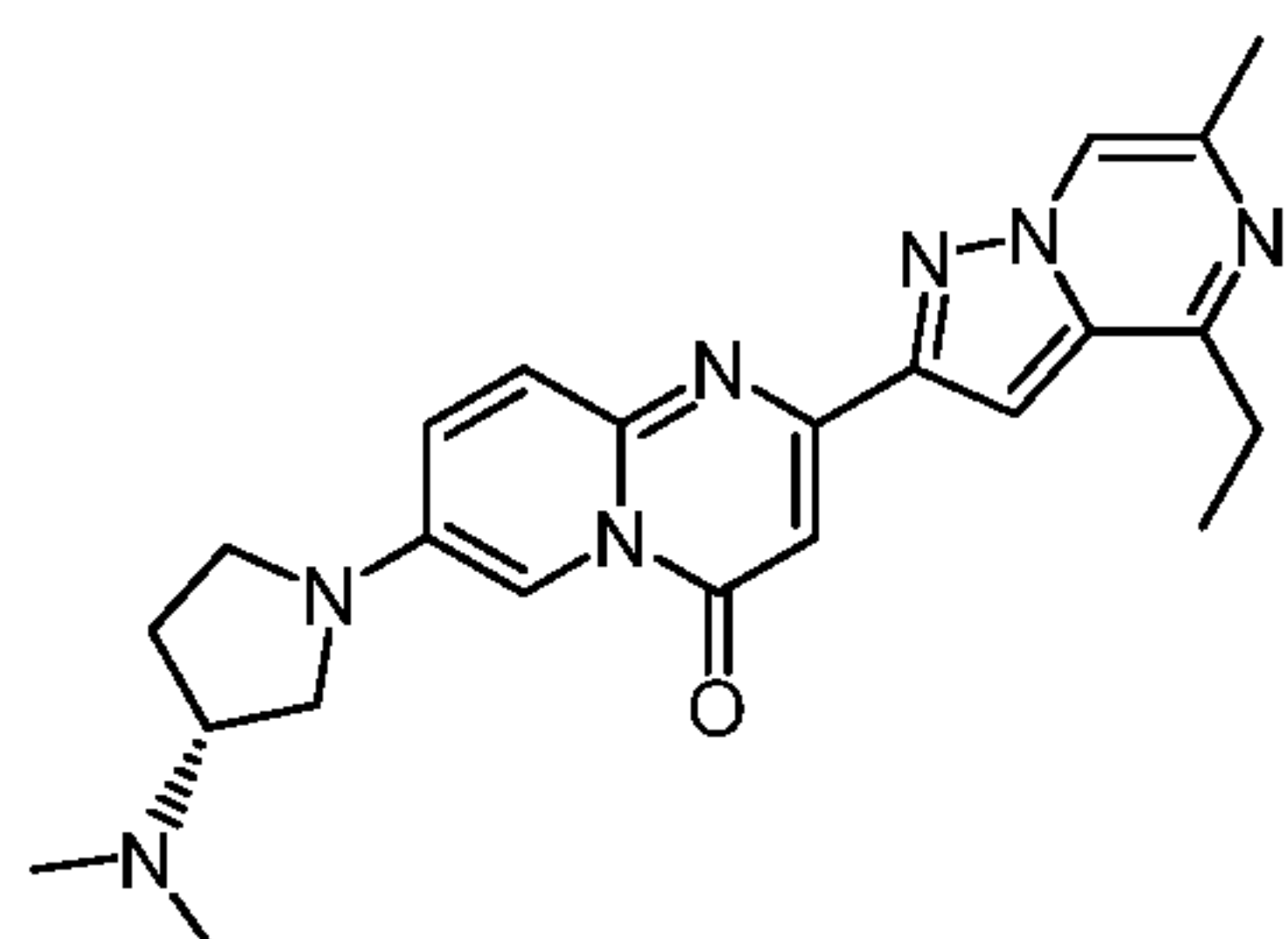
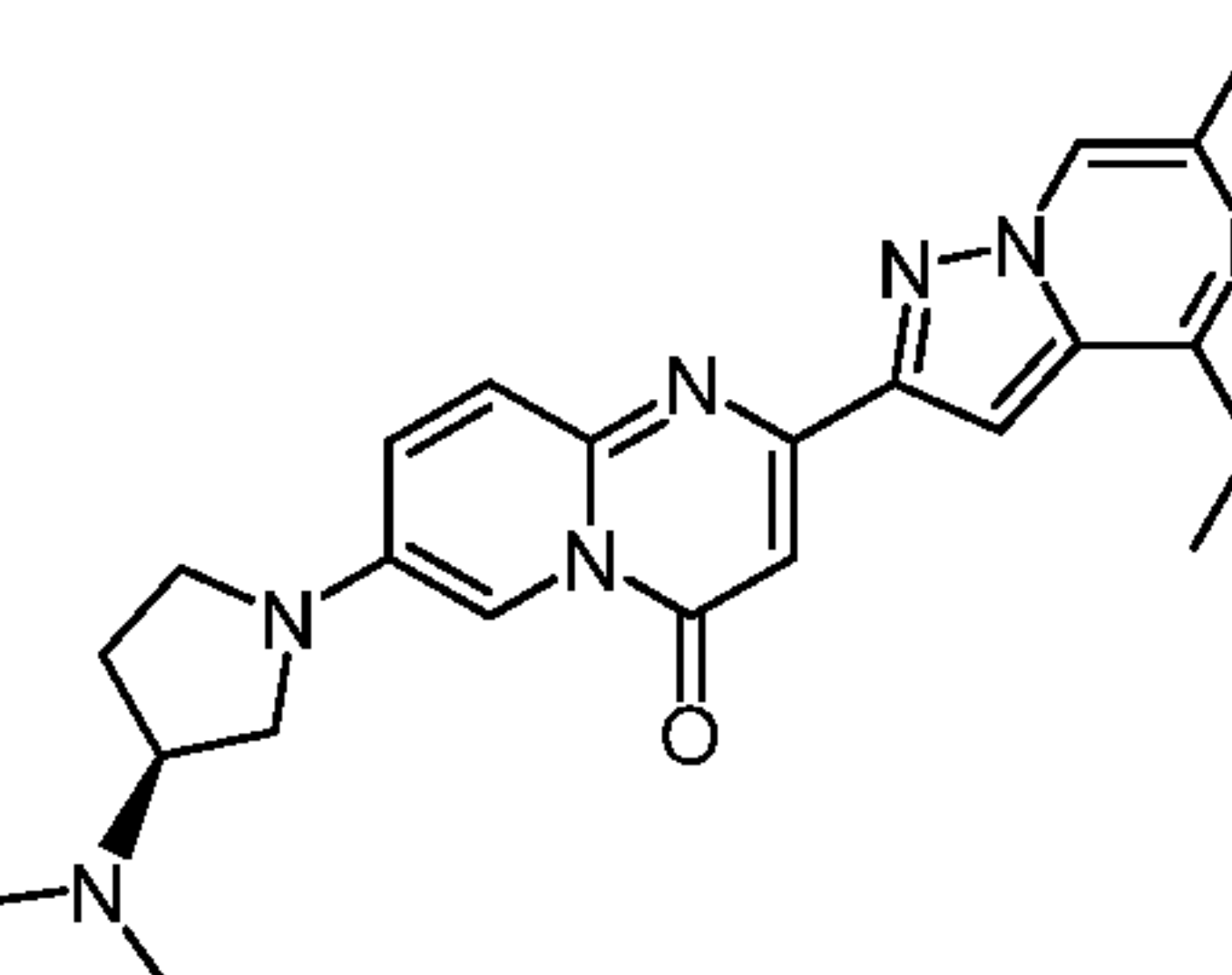
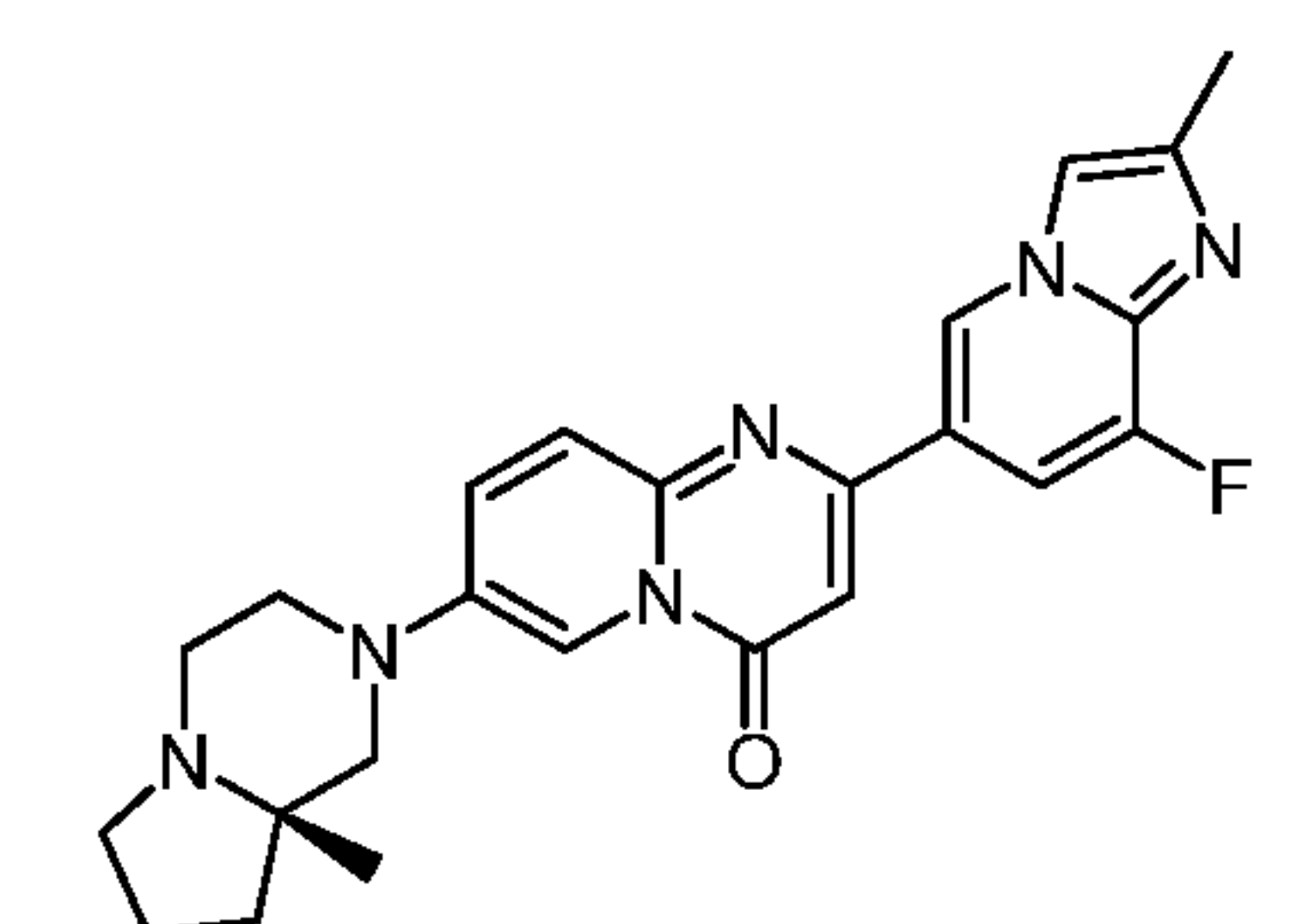
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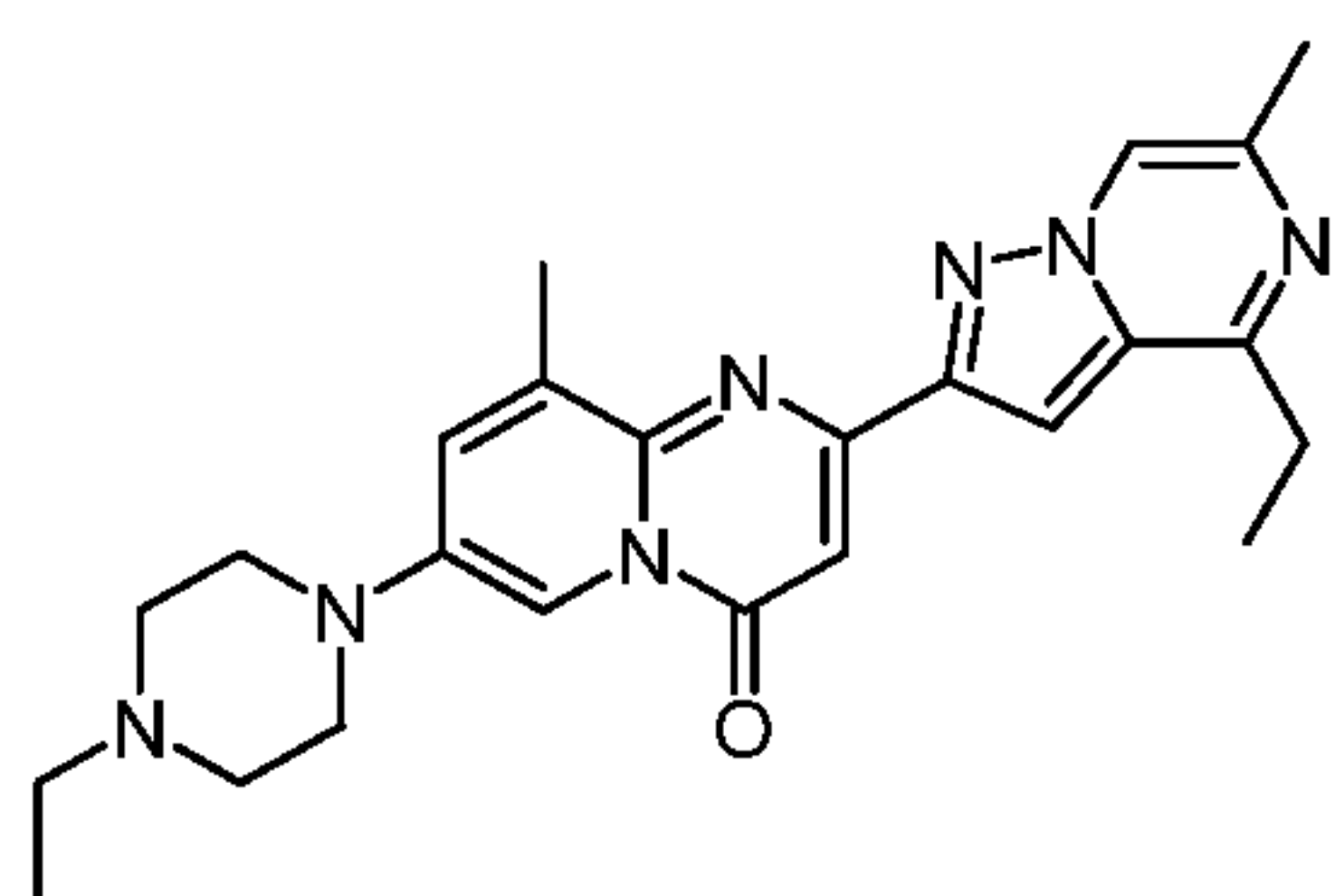


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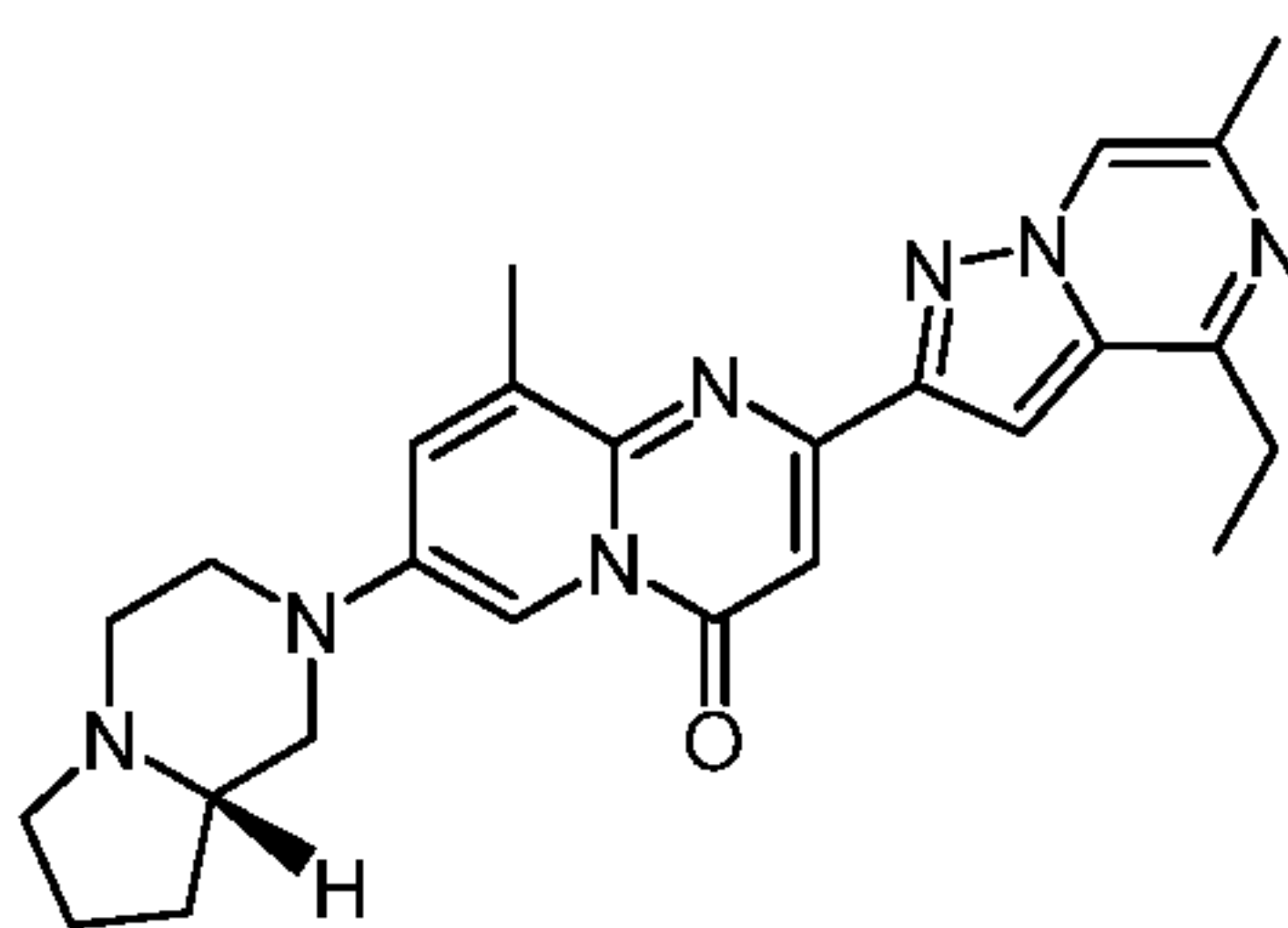


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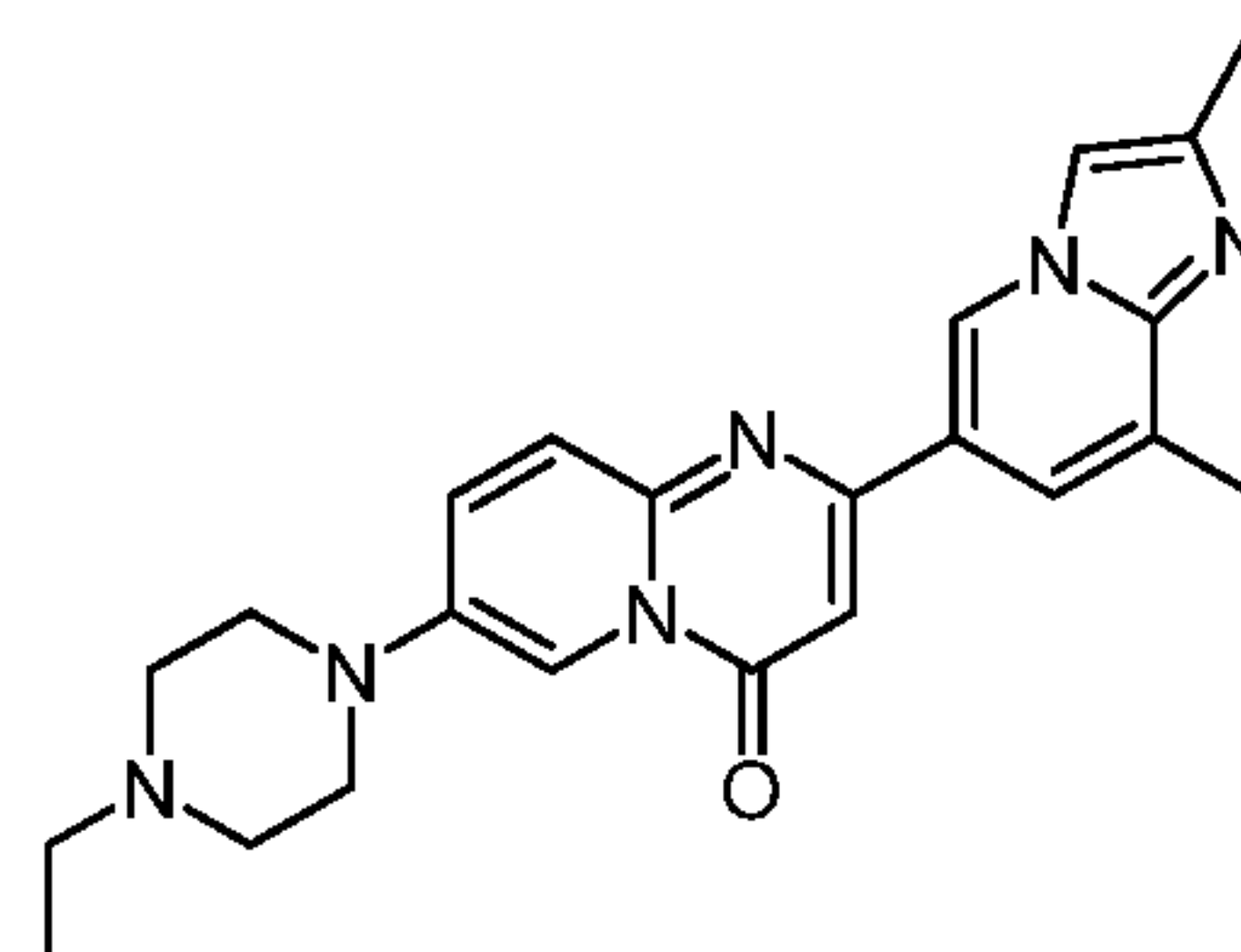
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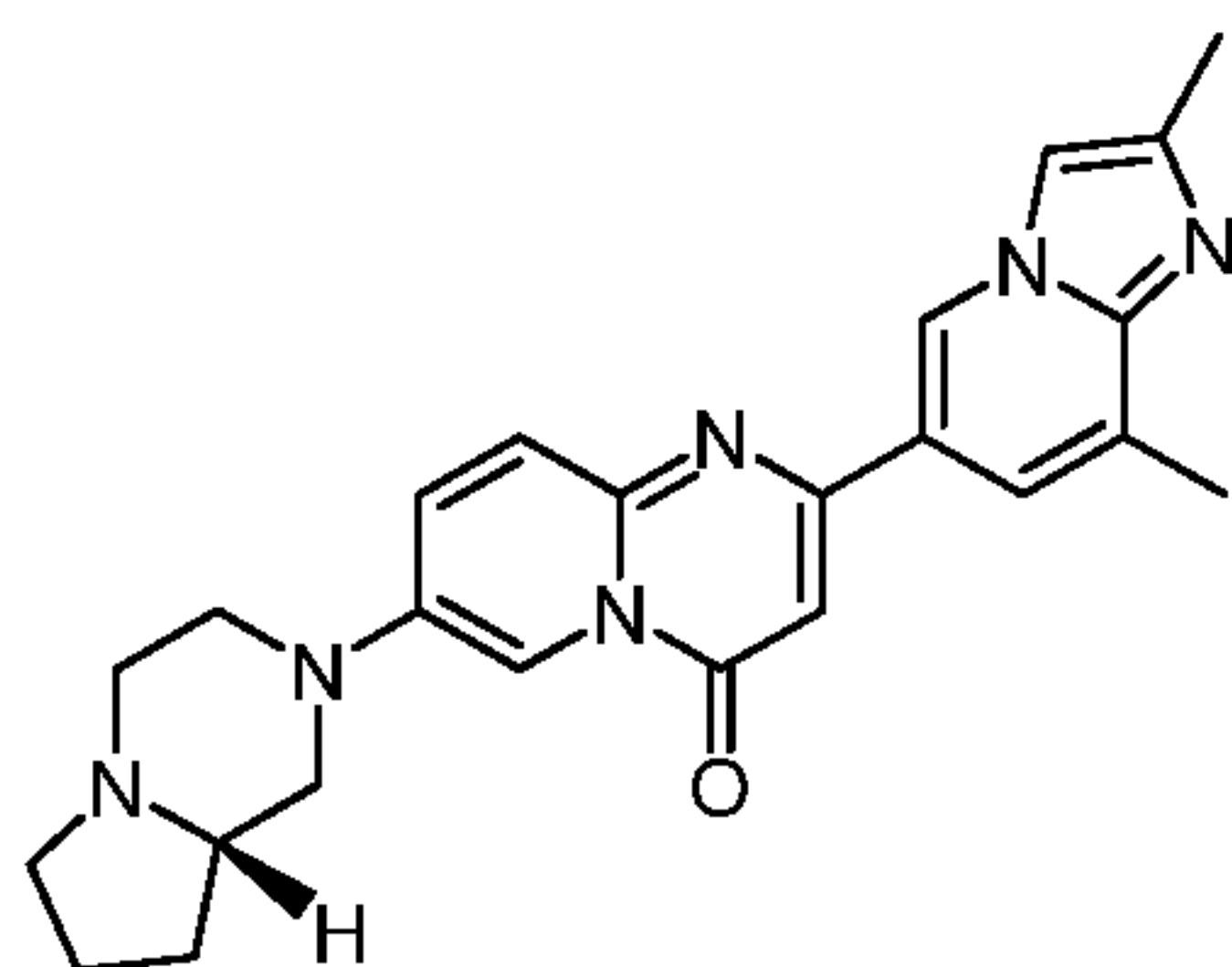
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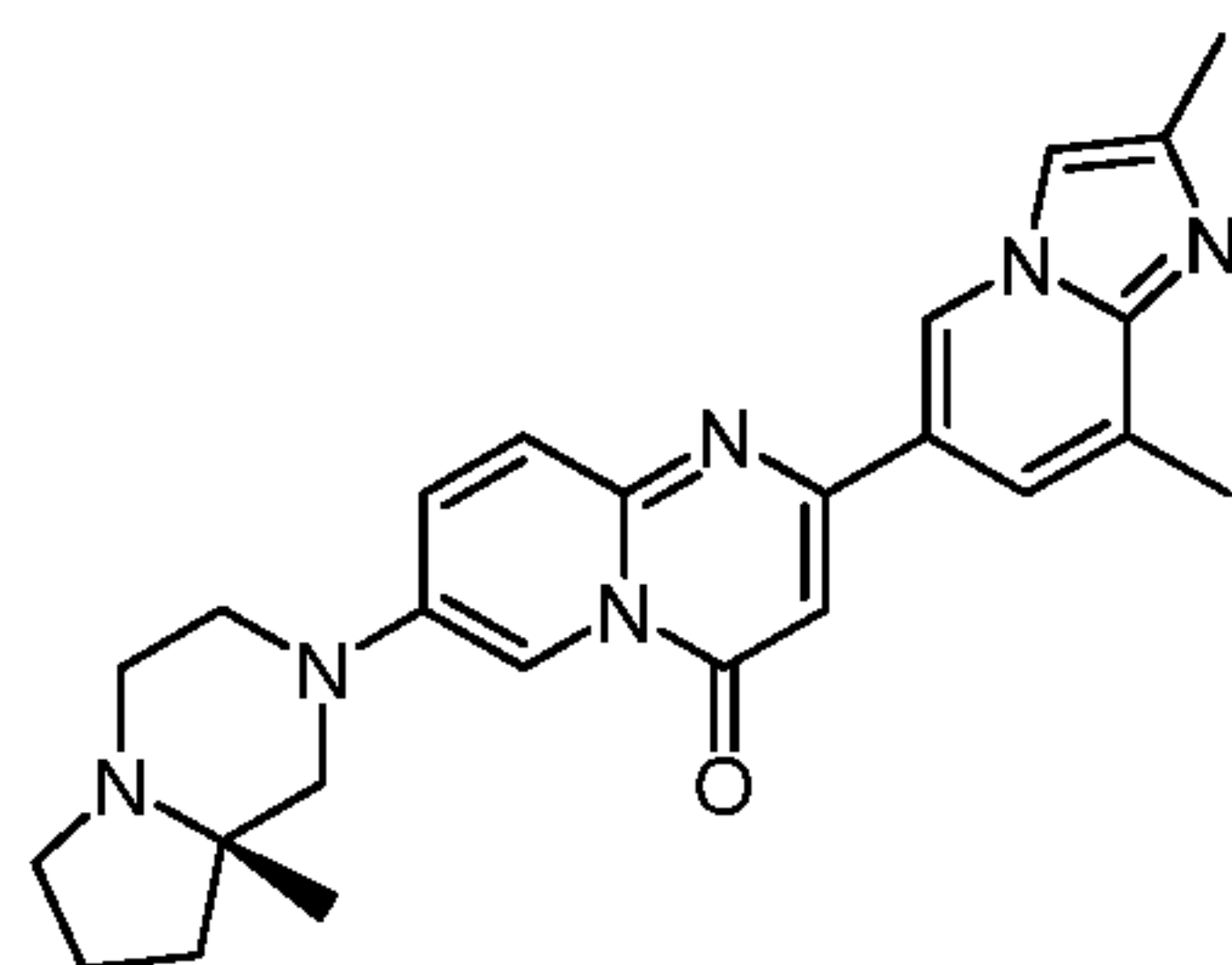
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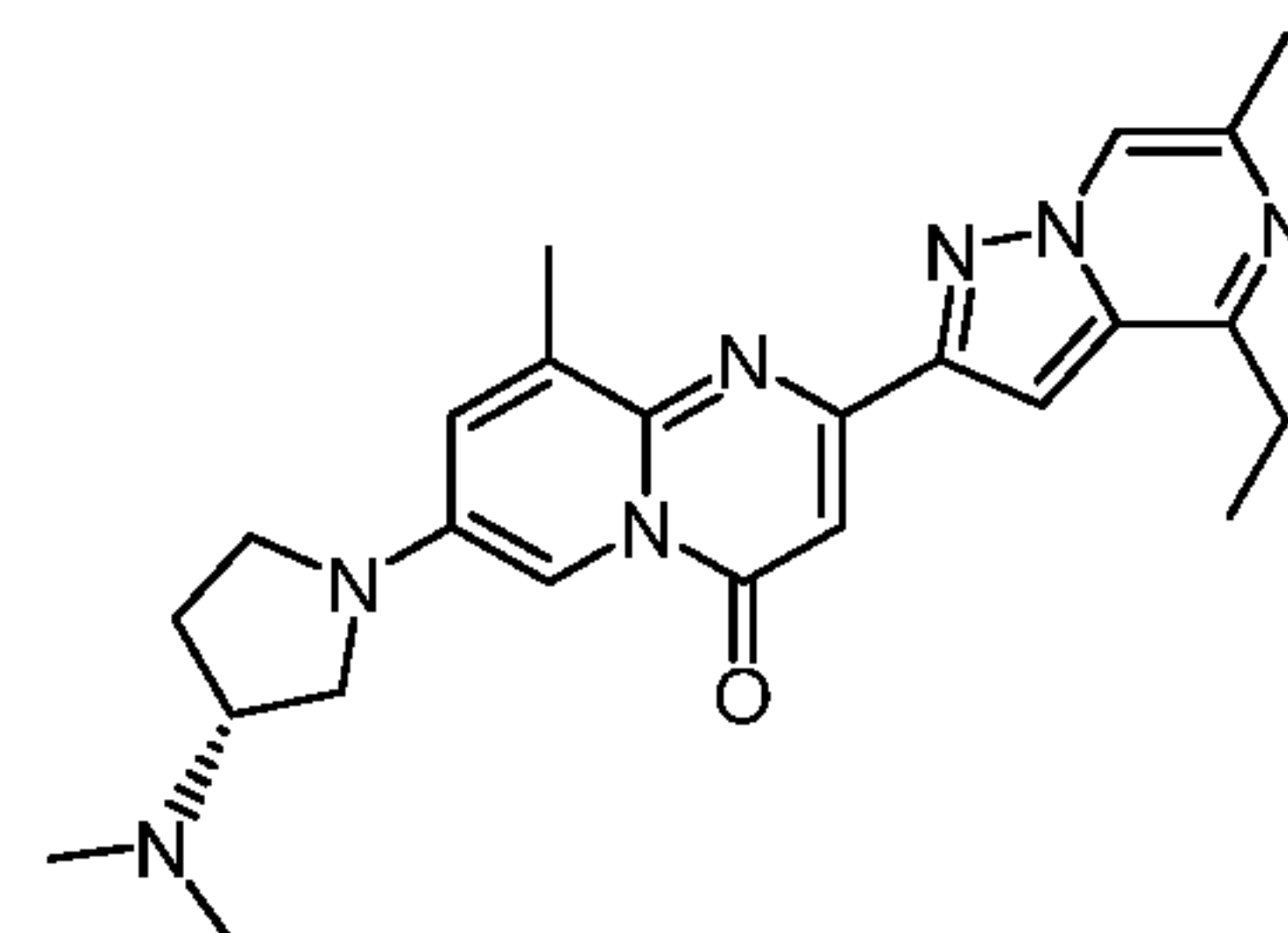
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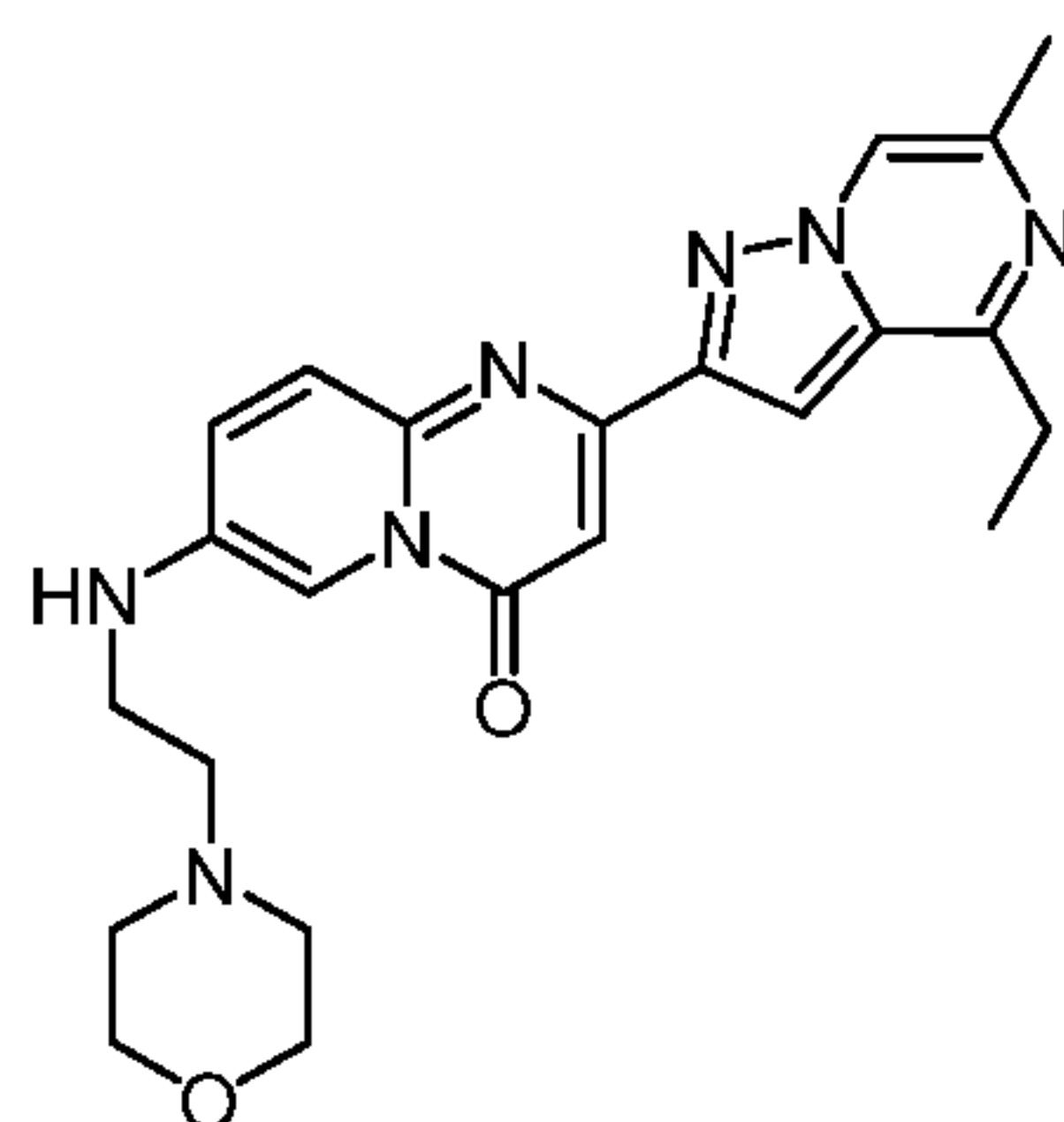
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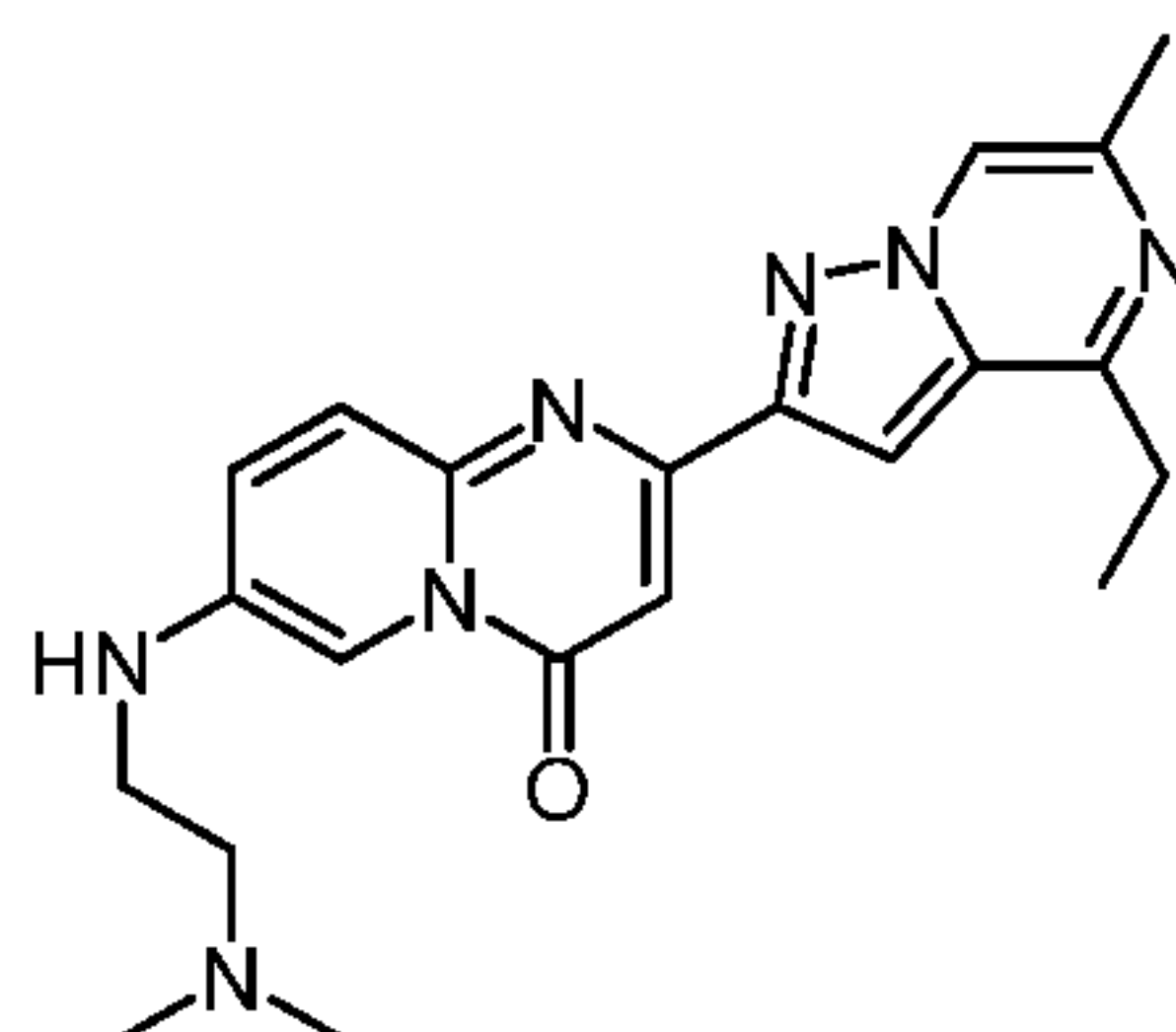
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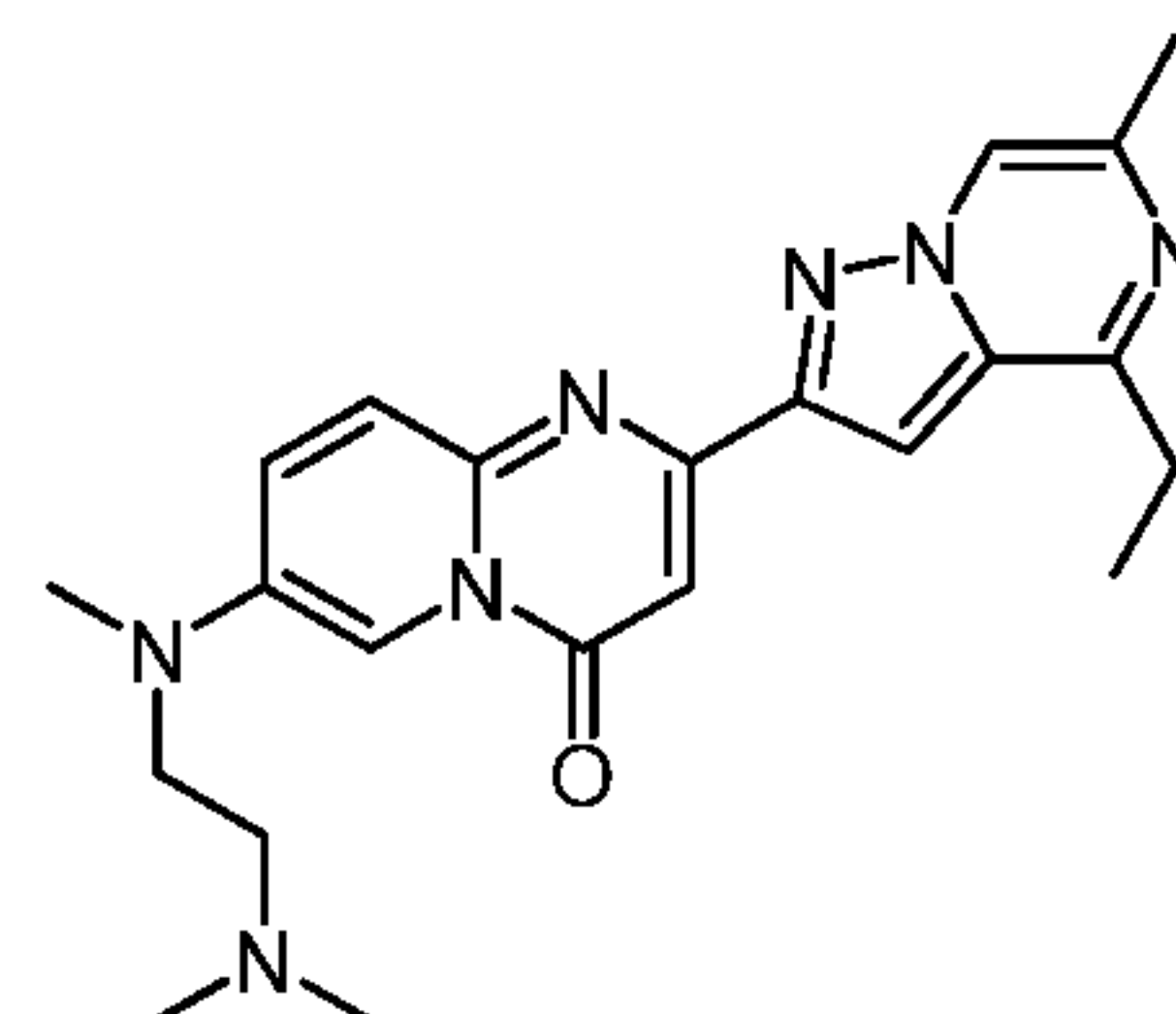
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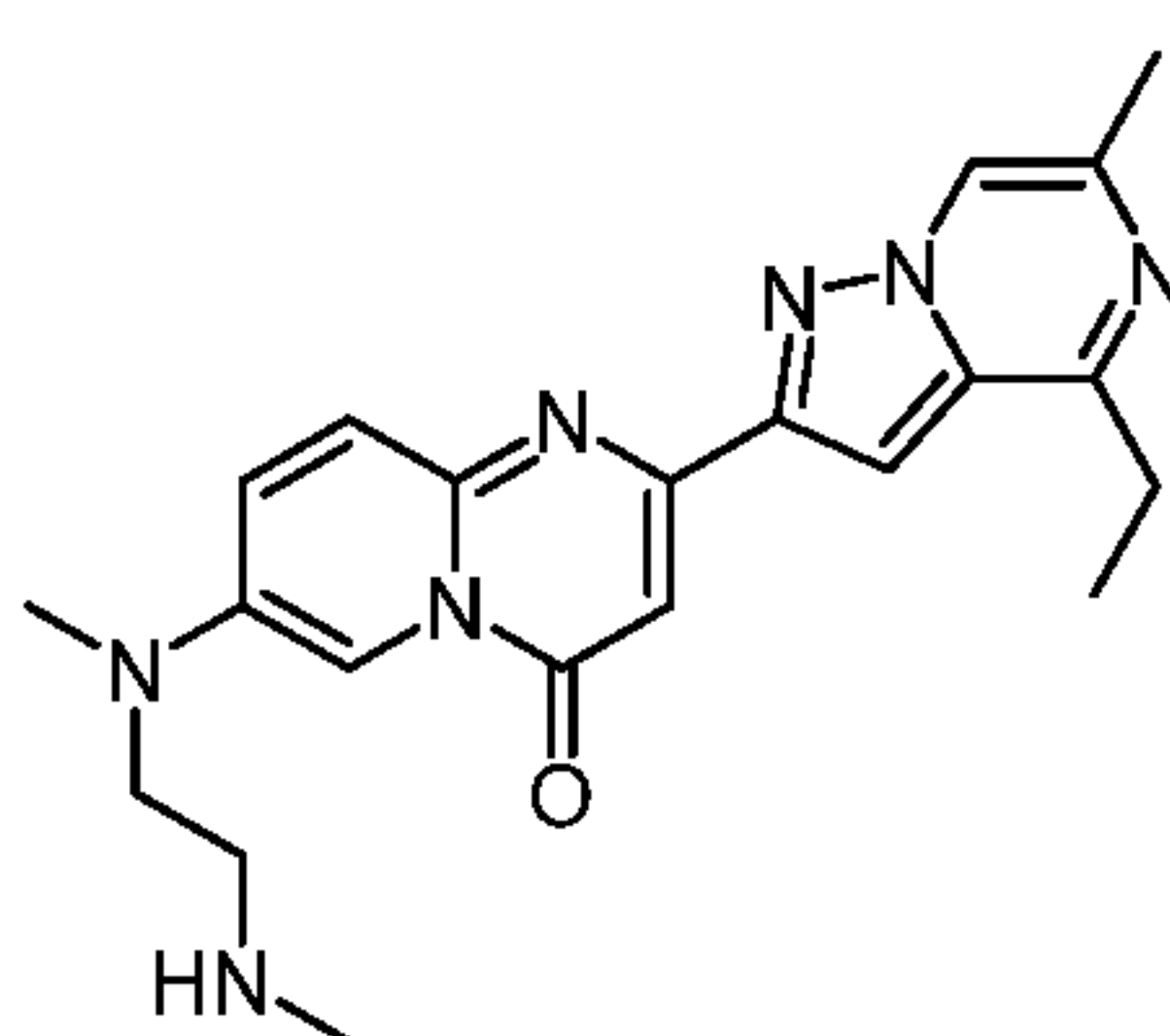
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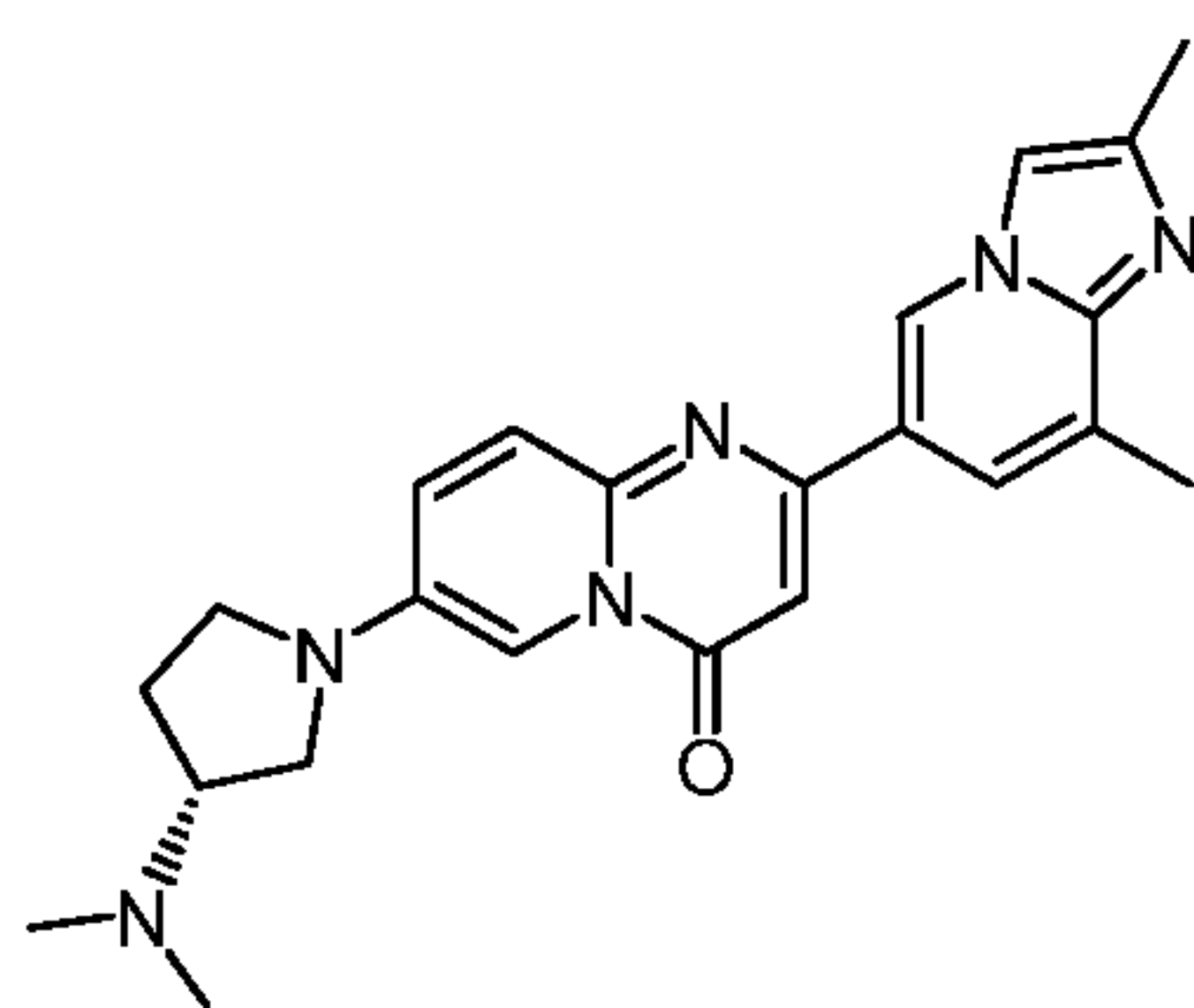
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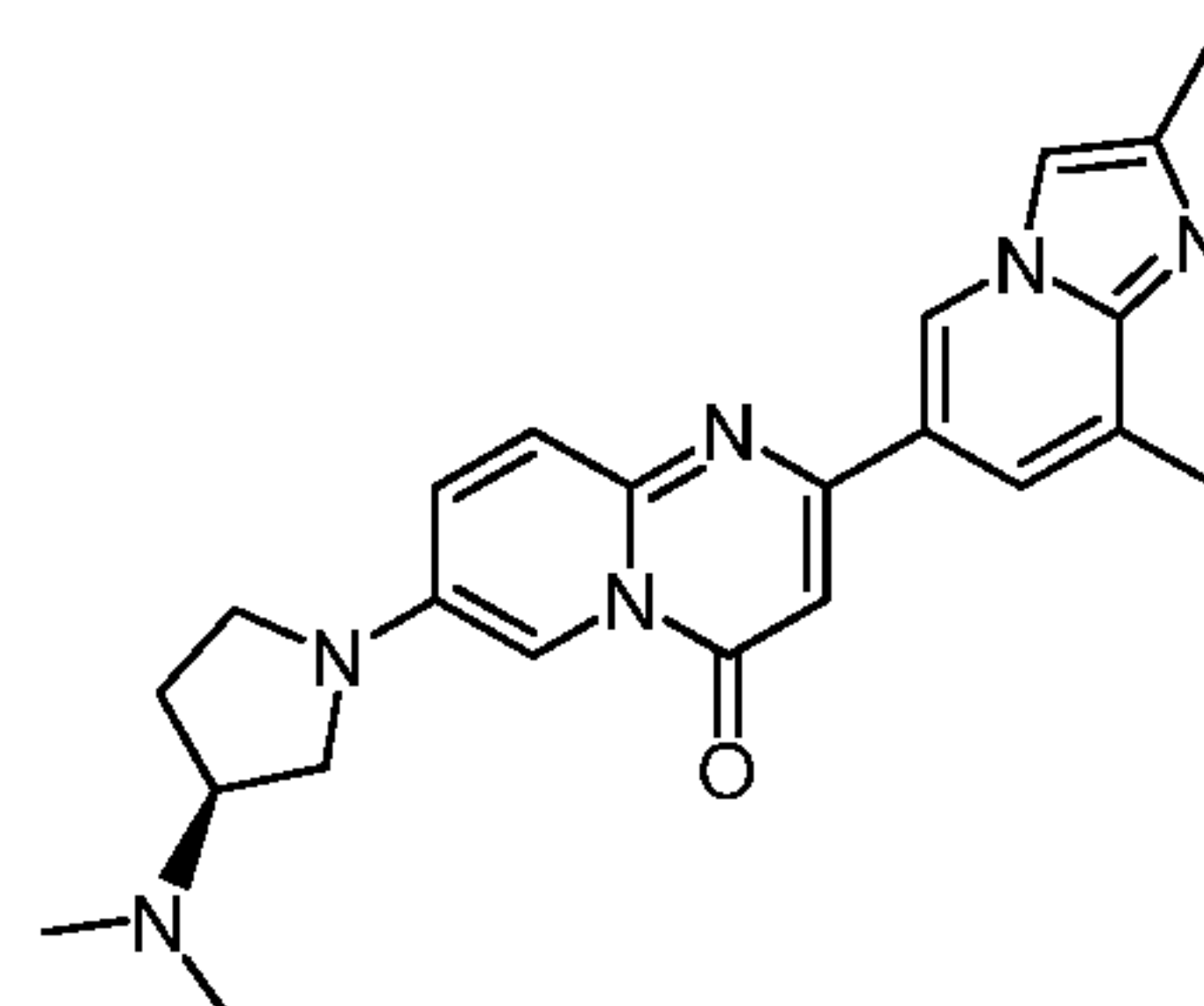
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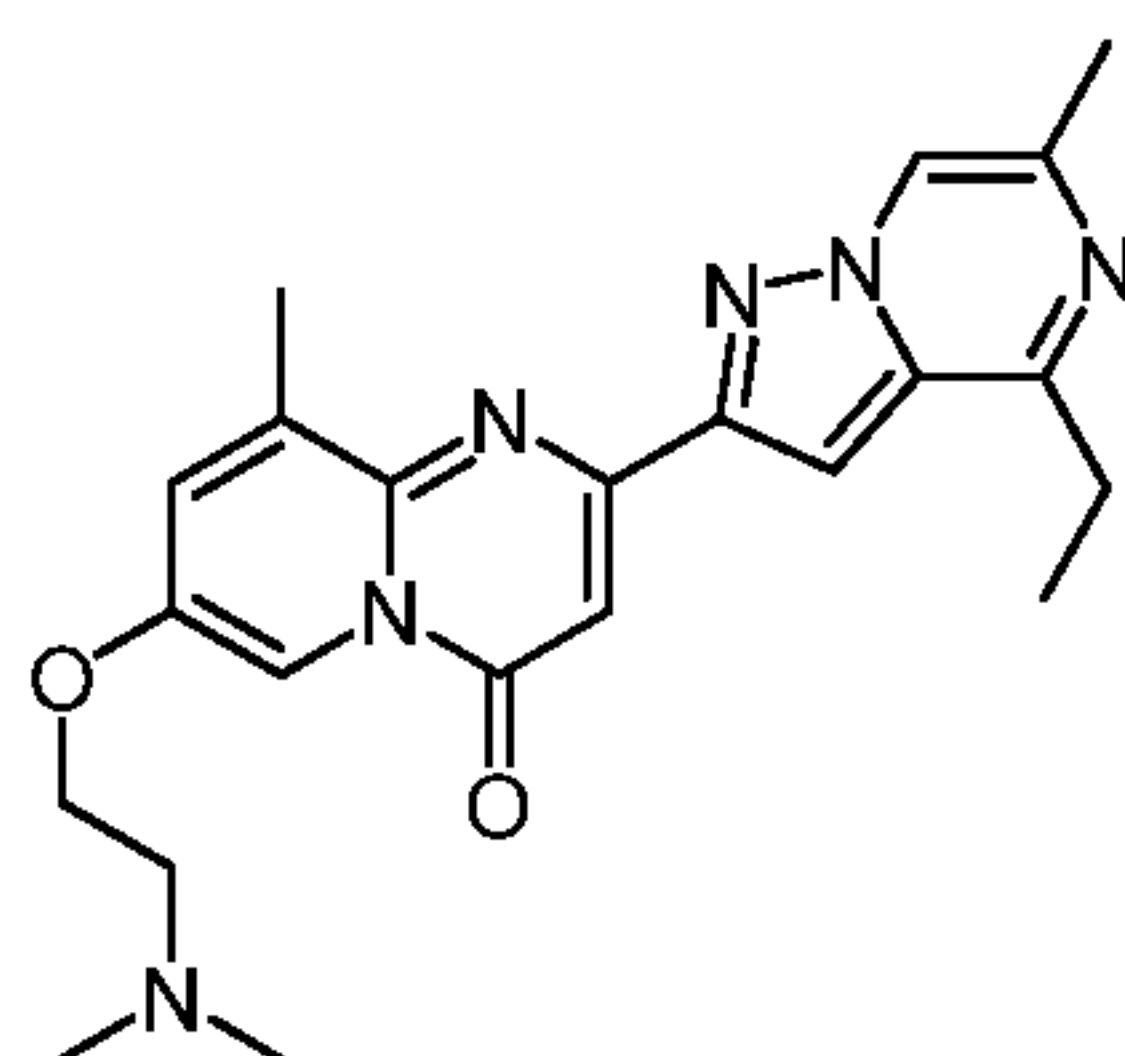
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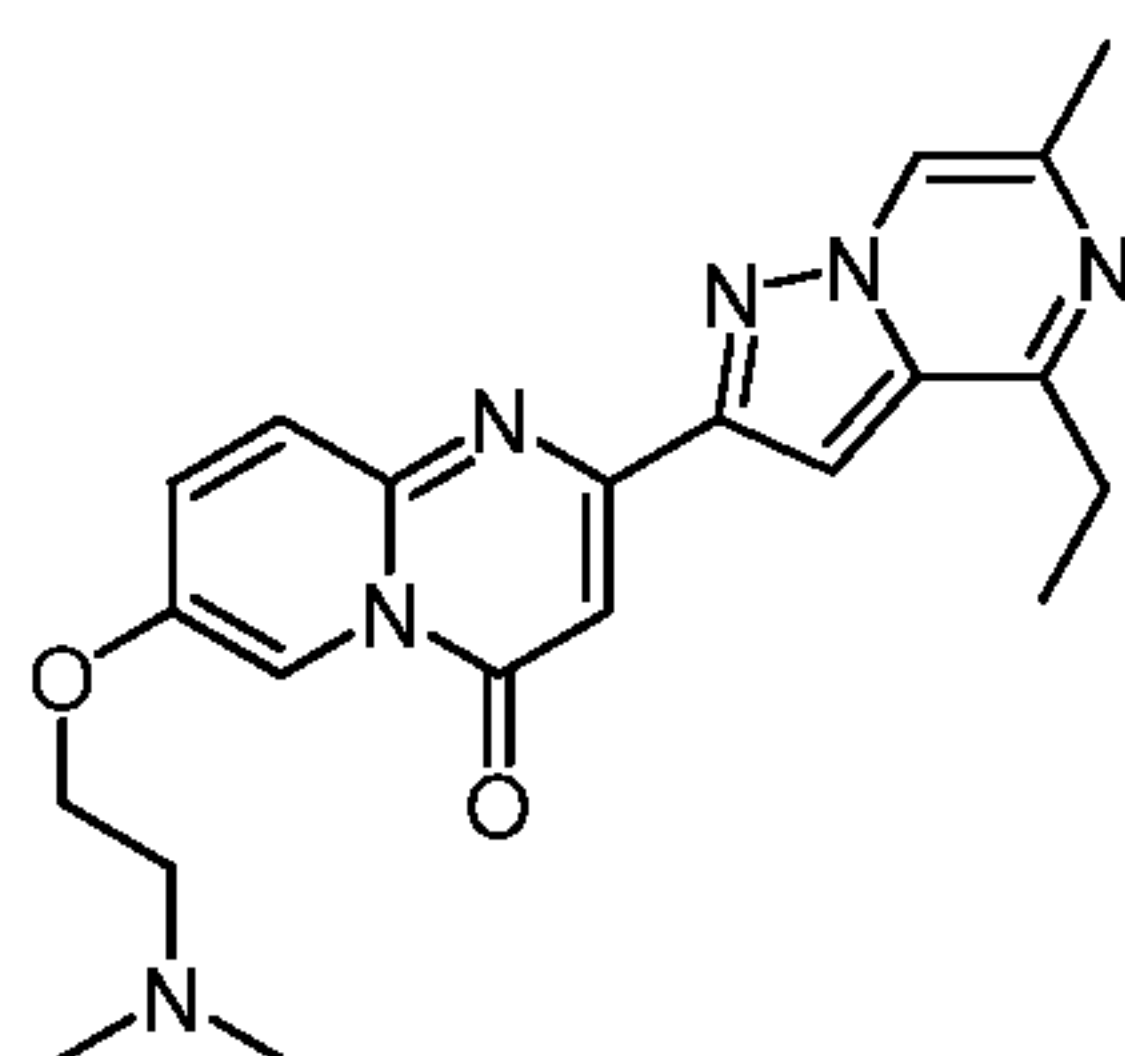
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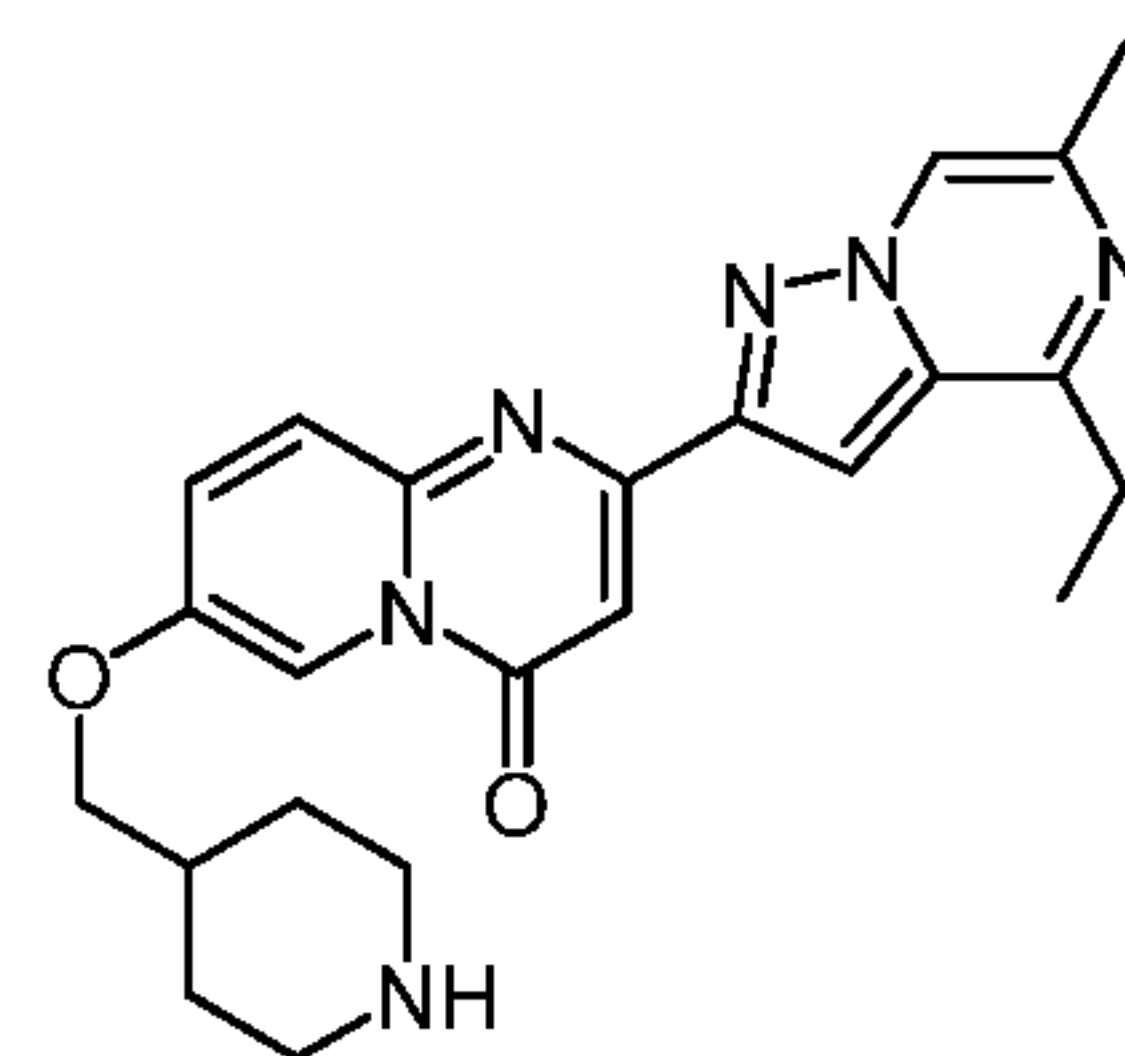
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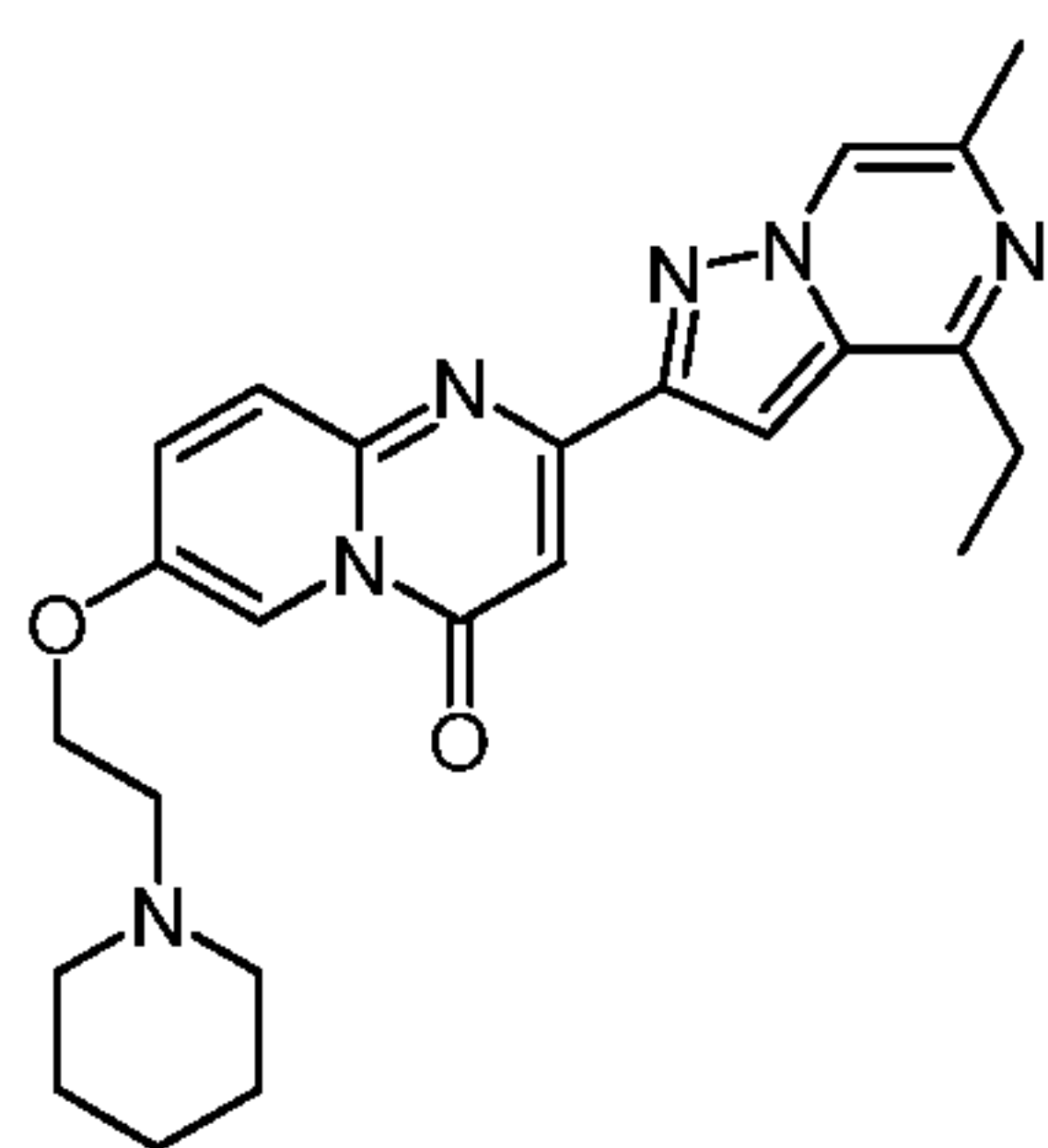
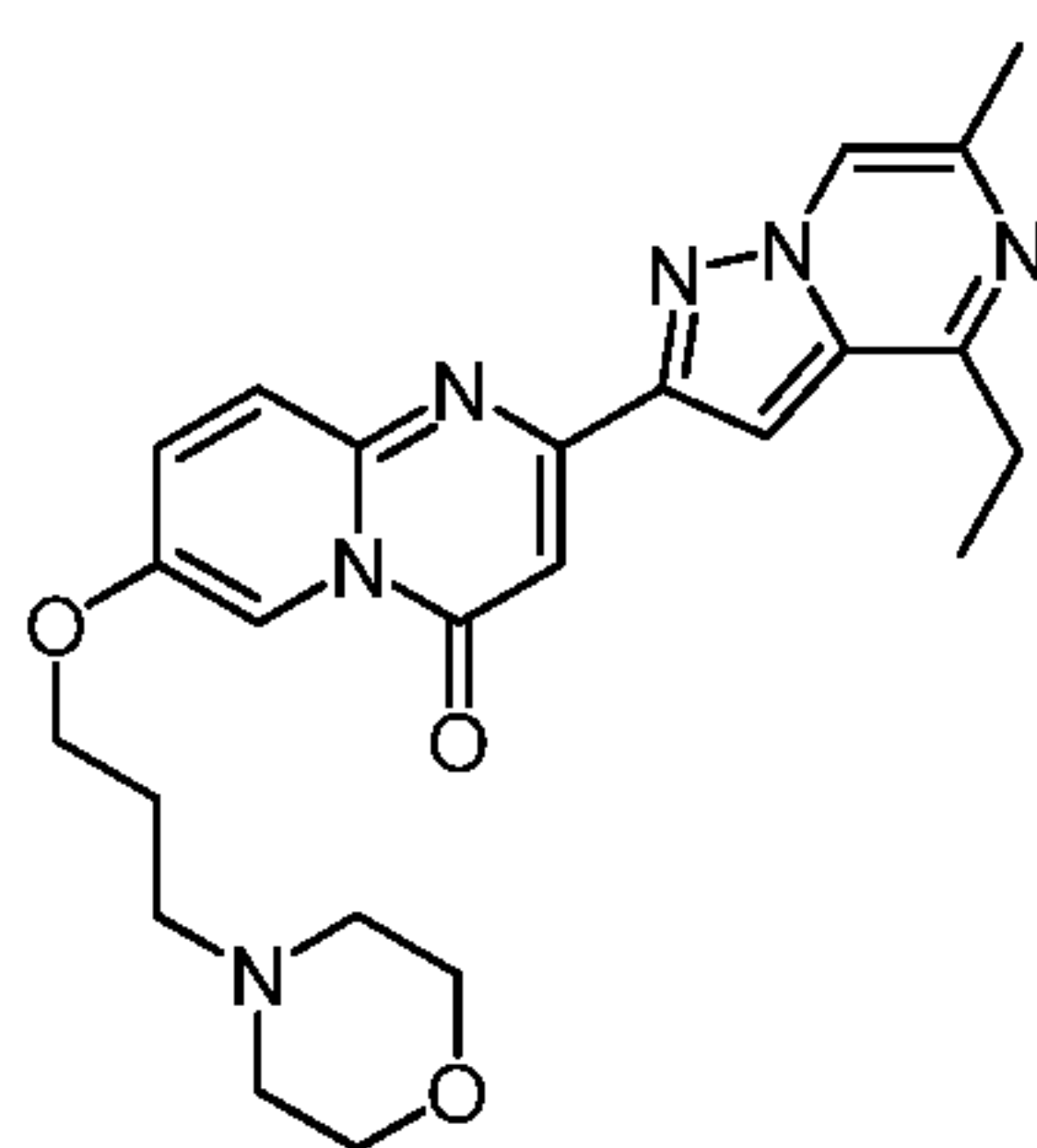
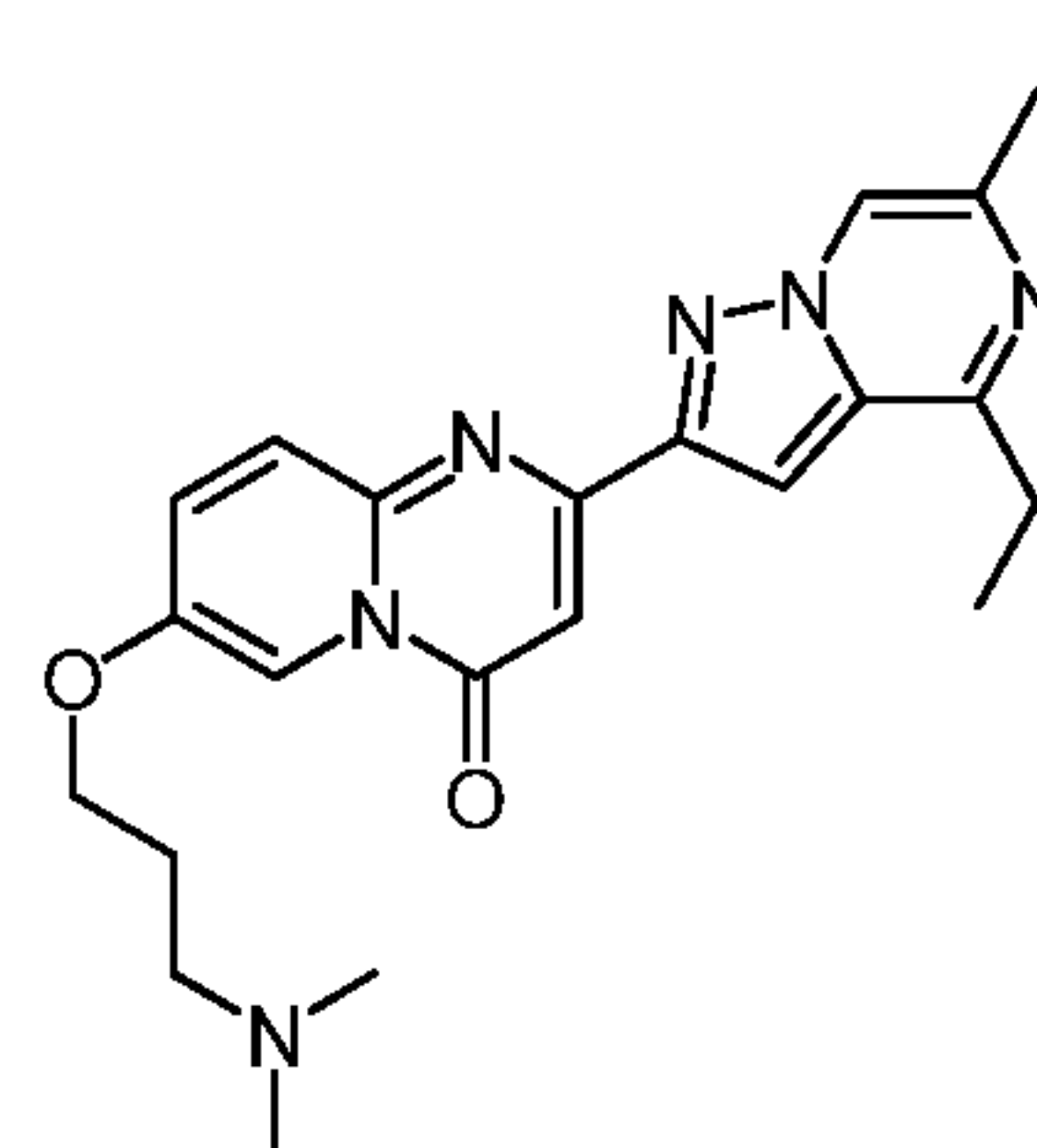
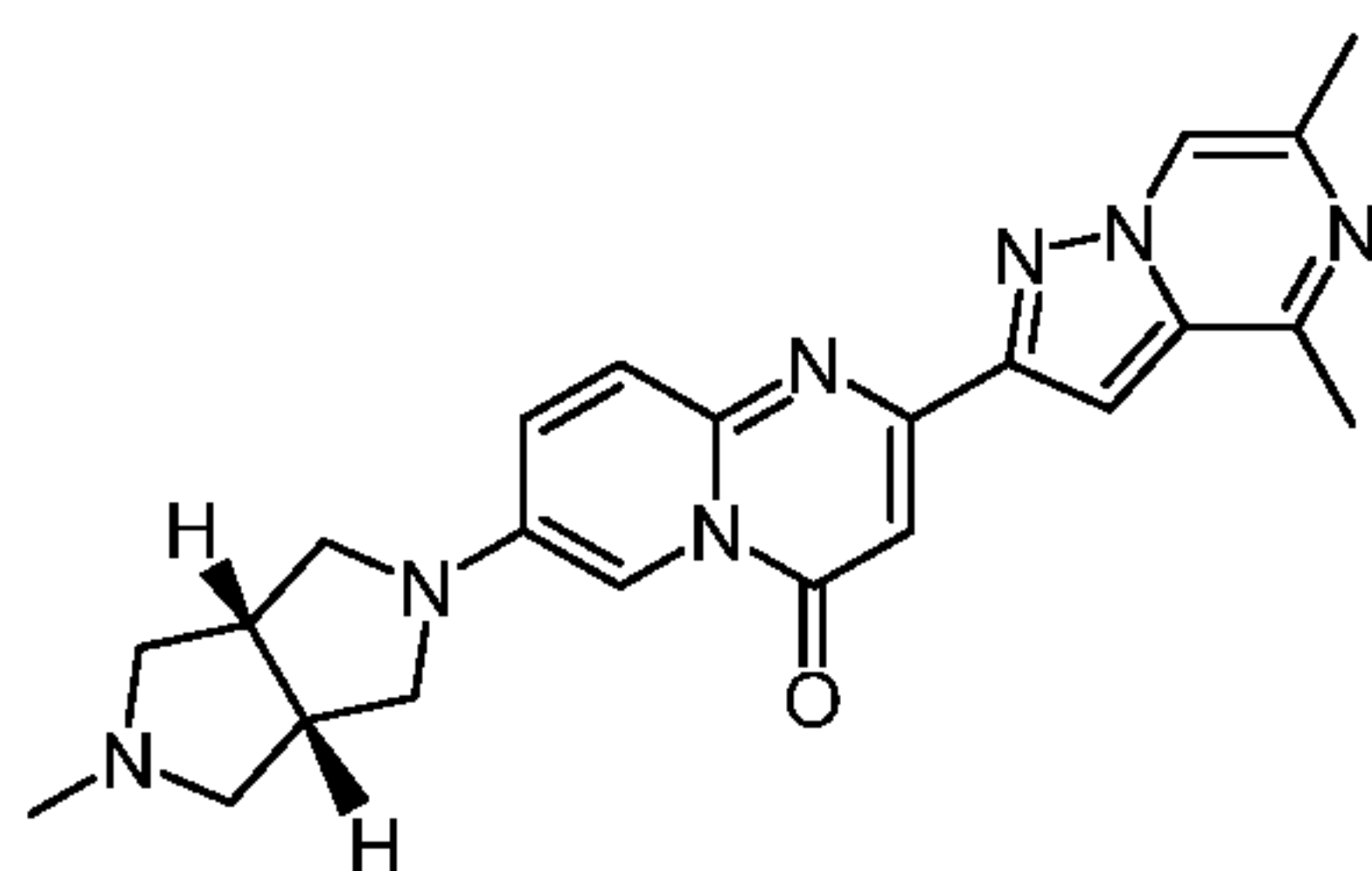
829



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831

**832****833****834****835**

[00642] or a form thereof.

[00643] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound selected from the group consisting of:

2-(4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

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

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

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

2-(4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

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

2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

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

2-(4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3,3-dimethylpiperazin-1-yl)-2-(4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-benzodioxol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-benzodioxol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-benzodioxol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-benzodioxol-5-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-methoxyphenyl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(3-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methylimidazo[1,2-a]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-phenyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-methylpiperazin-1-yl]-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(2,3-dihydro-1,4-benzodioxin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dihydro-1,4-benzodioxin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-fluoro-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-chlorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(piperazin-1-yl)-2-[3-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(piperazin-1-yl)-2-[4-(trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-fluoro-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(dimethylamino)phenyl]-9-fluoro-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(dimethylamino)phenyl]-9-fluoro-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 3-(3,4-dimethoxyphenyl)-8-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-(dimethylamino)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-(dimethylamino)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(difluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(difluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-fluoro-4,5-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3,8-diazabicyclo[3.2.1]oct-3-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-methoxy-3-(trifluoromethyl)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methoxy-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 4-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile
 2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-fluoro-5-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-fluoro-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[2-methoxy-3-(trifluoromethyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,5-difluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(piperazin-1-yl)-2-[3-(trifluoromethoxy)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-methoxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-hydroxy-3-(trifluoromethoxy)phenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-4-oxo-7-(piperazin-1-yl)-4H-quinolizine-1-carbonitrile
 2-(3-fluoro-4-methoxyphenyl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one
 2-(5-fluoropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-fluoropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-chloropyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-chloropyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-chloro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1H-indol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1H-indol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-(difluoromethoxy)-4-methoxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-(difluoromethoxy)-4-hydroxyphenyl]-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one
 2-(3,5-difluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-quinolizin-4-one
 2-(imidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(imidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-chloro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-chloro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-ethoxy-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-ethoxy-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6,8-dimethylimidazo[1,2-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(2-methylpyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(piperazin-1-yl)-2-[2-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-ethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,3-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-aminopiperidin-1-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4,5-dimethoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(4-hydroxypiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-methoxy-3-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

3-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile
 2-methoxy-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile
 2-(3-fluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethoxy-3-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-fluoro-4-(2,2,2-trifluoroethoxy)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methylphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methylphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-methylpiperazin-1-yl]-2-(4-methyl-1,3-thiazol-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-methyl-1,3-thiazol-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3S)-3-(propan-2-ylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-methoxy-3-nitrophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[3-fluoro-4-(methylsulfanyl)phenyl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-fluoro-6-methoxypyridin-3-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(5-fluoro-6-methoxypyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-5-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methyl-1H-imidazol-1-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methyl-1H-imidazol-1-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5-fluoro-6-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluoro-4-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,5-difluoro-4-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-4-ylamino)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-5-fluorophenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-chloro-5-fluorophenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-methylpiperazin-1-yl]-2-(1-methyl-1H-pyrazol-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-pyrazol-4-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

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

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

7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,5-dimethoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one
 7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,4R)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-aminopiperidin-1-yl)-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-3-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-3-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-difluoro-5-methoxyphenyl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-difluoro-5-methoxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3-fluoro-4-methoxyphenyl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3S)-3-(methylamino)pyrrolidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-{4-[(methylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-aminopyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-{[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one
 7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methoxypyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(piperazin-1-yl)-2-(pyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5-methoxypyridin-3-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 3-fluoro-5-{7-[(3S)-3-methylpiperazin-1-yl]-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl}benzonitrile
 3-fluoro-5-[4-oxo-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-2-yl]benzonitrile
 2-(3-fluoro-4-methoxyphenyl)-7-[(3'S,4'S)-4'-hydroxy-1,3'-bipyrrolidin-1'-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-pyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3S)-pyrrolidin-3-yloxy]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-{methyl[(3R)-1-methylpyrrolidin-3-yl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-quinolizin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1,4-diazepan-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(1R,5S)-8-azabicyclo[3.2.1]oct-2-en-3-yl]-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-(1,2,5,6-tetrahydropyridin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-ethyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-ethyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-aminopiperidin-1-yl)-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(2-hydroxyethyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-[(3aR,6aS)-5-(propan-2-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yloxy)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3-fluoro-4-methoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[4-(dimethylamino)piperidin-1-yl]-7-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3aR,6aS)-5-ethylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-7-[(4aR,7aR)-1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3-fluoro-4-methoxyphenyl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3-fluoro-4-methoxyphenyl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(1R,5S)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(2R)-2-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-quinolizin-4-one
 2-(2-methyl-1,3-benzoxazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-quinolizin-4-one
 7-[(3S)-4-ethyl-3-methylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-quinolizin-4-one
 2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3-fluoro-4-methoxyphenyl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(cyclopropylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-[(3R)-3,4-dimethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-cyclopropylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)piperidin-1-yl]-9-ethyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(2-methyl-1,3-benzothiazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(methylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(dimethylamino)cyclohex-1-en-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[ethyl(methyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[methyl(propyl)amino]cyclohex-1-en-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,4-dimethoxyphenyl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,4-dimethoxyphenyl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(4-aminopiperidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminopyrrolidin-1-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-methoxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(oxetan-3-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-8-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzothiazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1S,4S)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(3-fluoro-4-methoxyphenyl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[cis-4-(methylamino)cyclohexyl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-(piperidin-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclopropylpiperazin-1-yl)-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-methyl-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:1)

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4'-bipiperidin-1'-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(morpholin-4-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(diethylamino)piperidin-1-yl]-2-(3,4-dimethoxyphenyl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(3,4-dimethoxyphenyl)-9-ethyl-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-1,3-benzothiazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-methylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[6-(dimethylamino)pyridin-3-yl]-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(diethylamino)piperidin-1-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[6-(dimethylamino)pyridin-3-yl]-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(diethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-9-ethyl-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(2-methoxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2-methylimidazo[1,2-a]pyridin-6-yl)-2-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-2-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-propyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[6-(dimethylamino)pyridin-3-yl]-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-cyclopropyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methyl-1,4-diazepan-1-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

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

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

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methyl-1,3-benzoxazol-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(1-methyl-1H-indazol-5-yl)-7-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrimido[1,2-b]pyridazin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)piperidin-1-yl]-2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

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

2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

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

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

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

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-methoxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-{(3S)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(dimethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(diethylamino)piperidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-7-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R,5S)-3,4,5-trimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-{4-[(dimethylamino)methyl]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-{4-[(dimethylamino)methyl]piperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(pyrrolidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(3,4-dimethoxyphenyl)-7-[4-(piperidin-1-ylmethyl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)(methyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-amino-4-methylpiperidin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)piperidin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-{4-[bis(2-hydroxyethyl)amino]piperidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-1,3-benzoxazol-6-yl)-4H-pyrimido[1,2-b]pyridazin-4-one
 2-(8-chloro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(5,7-dimethylfuro[2,3-c]pyridin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethylpiperidin-4-yl)-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2-methyl-2H-indazol-5-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]piperidin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(methylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[4-(propan-2-ylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(1-ethylpiperidin-4-yl)-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[1-(2-hydroxyethyl)piperidin-4-yl]-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-propylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-cyclopropylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-cyclobutylpiperazin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-methoxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-hydroxy-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-propylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(pyrrolidin-1-yl)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclopropyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methyl-4-(oxetan-3-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-cyclobutylpiperazin-1-yl)-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-4-cyclobutyl-3-methylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-fluoroethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(3-fluoropropyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-fluoroethyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(3-fluoropropyl)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-fluoroethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(3-fluoropropyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3R)-4-[2-(2-hydroxyethoxy)ethyl]-3-methylpiperazin-1-yl}-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3R)-4-(2-hydroxyethyl)-3-methylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-methyl-1,4-diazepan-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-[8-(hydroxymethyl)-2-methylimidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(propan-2-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(oxetan-3-yl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-cyclopropyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-[4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-1H-benzimidazol-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methyl-1H-benzimidazol-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

2-(2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one

7-[1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(1,3-dihydroxypropan-2-yl)piperidin-4-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-4-ethyl-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[4-(dimethylamino)-4-methylpiperidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-(ethylamino)-4-methylpiperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[4-methyl-4-(propylamino)piperidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{4-[(2-hydroxyethyl)amino]-4-methylpiperidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-propylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-cyclopropyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-cyclopropylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-9-methyl-2-(2-methyl-2H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(1-methylpiperidin-4-yl)oxy]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-methylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-ethylpiperazin-1-yl)-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[4-(2-hydroxyethyl)piperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-methylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(3R)-3-methyl-4-(propan-2-yl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-amino-4-methylpiperidin-1-yl)-2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3S)-3-ethylpiperazin-1-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
 2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-methylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(4-amino-4-methylpiperidin-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,7-dimethyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminoprop-1-yn-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3-aminopropyl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-[(3S)-3,4-dimethylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,7-dimethyl-2H-indazol-5-yl)-7-(1-ethylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(diethylamino)azetidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(pyrrolidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[(3S)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(piperidin-1-yl)azetidin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(6-methyl-4-propylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-(2,7-diazaspiro[4.4]non-2-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(2,7-dimethyl-2H-indazol-5-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-[3-(dimethylamino)propyl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 7-{(3S)-3-[(dimethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,7-dimethyl-1H-indazol-5-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(1,7-dimethyl-1H-indazol-5-yl)-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
 7-{(3S)-3-[(diethylamino)methyl]pyrrolidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-{(3S)-3-[(ethylamino)methyl]pyrrolidin-1-yl}-4H-pyrido[1,2-a]pyrimidin-4-one

7-{3-[(dimethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-{3-[(diethylamino)methyl]azetidin-1-yl}-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(1-ethyl-3-methylpyrrolo[1,2-a]pyrazin-7-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3R)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(1-methyl-1H-indazol-5-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1-ethylpiperidin-4-yl)-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-7-[(3S)-3-methylpiperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-2-(1-methyl-1H-indazol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3,4-dimethylpiperazin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(1-ethylpiperidin-4-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-(1-cyclobutylpiperidin-4-yl)-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[1-(2-hydroxyethyl)piperidin-4-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-ethyl-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-2H-indazol-5-yl)-7-(piperidin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one

7-[(3R)-3-(aminomethyl)pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydropyridin-4-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-[(dimethylamino)methyl]pyrrolidin-1-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(2S,6S)-2,6-dimethylpiperidin-4-yl]-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(imidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-(2,7-diazaspiro[3.5]non-7-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methylpiperazin-1-yl)-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-methyl-6-[7-(4-methylpiperazin-1-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]imidazo[1,2-a]pyridine-8-carbonitrile

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

7-(4,7-diazaspiro[2.5]oct-7-yl)-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-hydroxypiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{[2-(morpholin-4-yl)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-{[2-(dimethylamino)ethyl]amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-{[2-(dimethylamino)ethyl](methyl)amino}-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-{methyl[2-(methylamino)ethyl]amino}-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

7-[2-(dimethylamino)ethoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(piperidin-4-ylmethoxy)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[2-(piperidin-1-yl)ethoxy]-4H-pyrido[1,2-a]pyrimidin-4-one

2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[3-(morpholin-4-yl)propoxy]-4H-pyrido[1,2-a]pyrimidin-4-one

7-[3-(dimethylamino)propoxy]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one, or

2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

or a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00644] In another embodiment, the compound of Formula (I) used in a method disclosed herein is a compound selected from the group consisting of:

2-(3,5-difluoro-4-hydroxyphenyl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one hydrochloride

7-[4-(dimethylamino)piperidin-1-yl]-2-(3-fluoro-4-methoxyphenyl)-4H-quinolizin-4-one acetate

2-(2-methyl-1,3-benzothiazol-6-yl)-7-(piperidin-4-yl)-4H-pyrimido[1,2-b]pyridazin-4-one trifluoroacetate (1:1), or

2-(1,3-dimethylpyrrolo[1,2-a]pyrazin-7-yl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-4H-pyrazino[1,2-a]pyrimidin-4-one hydrochloride (1:2)

or a free base, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00645] Compounds of Formula (I) can be prepared using reagents and methods known in the art, including the methods provided in International Application No. PCT/US2013/025292, filed on February 8, 2013, and published as International Publication No. WO 2013/119916 on August 15, 2013, the entire contents which are incorporated herein by reference (see in particular, General Synthetic Methods, Schemes A-J, at paragraphs [001126] to [001159]; and Specific Synthetic Examples, at paragraphs [001160] to [001573] and Table 1, therein).

TERMINOLOGY

[00646] 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.

[00647] As used herein, the term “C₁₋₈alkyl” 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, C₁₋₈alkyl includes, but is not limited to, C₁₋₆alkyl, C₁₋₄alkyl and the like. A C₁₋₈alkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00648] As used herein, the term “C₂₋₈alkenyl” 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, C₂₋₈alkenyl includes, but is not limited to, C₂₋₆alkenyl, C₂₋₄alkenyl and the like. A C₂₋₈alkenyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00649] As used herein, the term “C₂₋₈alkynyl” generally refers to partially unsaturated hydrocarbon radicals having from two to eight carbon atoms in a straight or branched chain configuration and one or more carbon-carbon triple bonds therein, including, but not limited to, ethynyl, propynyl, butynyl and the like. In some embodiments, C₂₋₈alkynyl includes, but is not limited to, C₂₋₆alkynyl, C₂₋₄alkynyl and the like. A C₂₋₈alkynyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00650] As used herein, the term “C₁₋₈alkoxy” generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration of the formula: -O-C₁₋₈alkyl, 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, C₁₋₈alkoxy includes, but is not limited to, C₁₋₆alkoxy, C₁₋₄alkoxy and the like. A C₁₋₈alkoxy radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00651] As used herein, the term “C₃₋₁₄cycloalkyl” generally refers to a saturated or partially unsaturated monocyclic, bicyclic or polycyclic hydrocarbon radical, including, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctyl, 1H-indanyl, indenyl, tetrahydro-naphthalenyl and the like. In some embodiments, C₃₋₁₄cycloalkyl includes, but is not limited to, C₃₋₈cycloalkyl, C₅₋₈cycloalkyl, C₃₋₁₀cycloalkyl and the like. A C₃₋₁₄cycloalkyl radical is optionally substituted with substituent species as described herein where allowed by available valences.

[00652] 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.

[00653] 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, 2H-pyrrolyl, 3H-pyrrolyl, pyrazolyl, 1H-pyrazolyl, imidazolyl, 1H-imidazolyl, isoxazolyl, isothiazolyl, oxazolyl, 1,3-thiazolyl, triazolyl (such as 1H-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 1H-tetrazolyl, 2H-tetrazolyl and the like), pyridinyl (also referred to as pyridyl), pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, 1H-indolyl, indazolyl, 1H-indazolyl, 2H-indazolyl, indoliziny, isoindolyl, benzofuranyl, benzothienyl (also referred to as benzothiophenyl), benzoimidazolyl, 1H-benzoimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl (also referred to as 1,3-benzooxazolyl), purinyl, 9H-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, 1H-pyrrolo[2,3-b]pyridinyl, 1H-pyrrolo[2,3-c]pyridinyl, 1H-pyrrolo[3,2-b]pyridinyl, pyrrolo[1,2-a]pyrazinyl, pyrrolo[1,2-b]pyridazinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrazinyl, imidazo[1,2-a]pyridinyl, 3H-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyrimidinyl, imidazo[1,2-c]pyrimidinyl, imidazo[1,2-b]pyridazinyl, imidazo[1,2-a]pyrazinyl, imidazo[2,1-b][1,3]thiazolyl, imidazo[2,1-b][1,3,4]thiadiazolyl, [1,2,4]triazolo[1,5-a]pyridinyl, [1,2,4]triazolo[4,3-a]pyridinyl and the like. A heteroaryl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

[00654] 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, azetidiny, 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-(1H)-yl, (3aS,6aS)-hexahydropyrrolo[3,4-b]pyrrol-(1H)-yl, (3aR,6aR)-hexahydropyrrolo[3,4-b]pyrrol-(1H)-yl, hexahydropyrrolo[3,4-b]pyrrol-(2H)-yl, (3aS,6aS)-hexahydropyrrolo[3,4-b]pyrrol-(2H)-yl, (3aR,6aR)-hexahydropyrrolo[3,4-b]pyrrol-(2H)-yl, hexahydropyrrolo[3,4-c]pyrrol-(1H)-yl, (3aR,6aS)-hexahydropyrrolo[3,4-c]pyrrol-(1H)-yl, (3aR,6aR)-hexahydropyrrolo[3,4-c]pyrrol-(1H)-yl, octahydro-5H-pyrrolo[3,2-c]pyridinyl, octahydro-6H-pyrrolo[3,4-b]pyridinyl, (4aR,7aR)-octahydro-6H-pyrrolo[3,4-b]pyridinyl, (4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridinyl, hexahydropyrrolo[1,2-a]pyrazin-(1H)-yl, (7R,8aS)-hexahydropyrrolo[1,2-a]pyrazin-(1H)-yl, (8aS)-hexahydropyrrolo[1,2-a]pyrazin-(1H)-yl, (8aR)-hexahydropyrrolo[1,2-a]pyrazin-(1H)-yl, (8aS)-octahydropyrrolo[1,2-a]pyrazin-(1H)-yl, (8aR)-octahydropyrrolo[1,2-a]pyrazin-(1H)-yl, hexahydropyrrolo[1,2-a]pyrazin-(2H)-one, octahydro-2H-pyrido[1,2-a]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, (1R,5S)-3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, (1R,5S)-8-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]oct-2-enyl, (1R,5S)-8-azabicyclo[3.2.1]oct-2-enyl, 9-azabicyclo[3.3.1]nonyl, (1R,5S)-9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, (1S,4S)-2,5-diazabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.2]octyl, 3,8-diazabicyclo[3.2.1]octyl, (1R,5S)-3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, azaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl, 6,9-diazaspiro[4.5]decyl and the like. A heterocyclyl radical is optionally substituted on a carbon or nitrogen atom ring member with substituent species as described herein where allowed by available valences.

[00655] As used herein, the term “C₁₋₈alkoxy-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-O-C₁₋₈alkyl.

[00656] As used herein, the term “C₁₋₈alkoxy-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-O-C₁₋₈alkyl.

[00657] As used herein, the term “(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-O-C₁₋₈alkyl)₂.

[00658] As used herein, the term “C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-NH-C₁₋₈alkyl-O-C₁₋₈alkyl.

[00659] As used herein, the term “(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-N(C₁₋₈alkyl-O-C₁₋₈alkyl)₂.

[00660] As used herein, the term “(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-O-C₁₋₈alkyl).

[00661] As used herein, the term “C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl-O-C₁₋₈alkyl.

[00662] As used herein, the term “(C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl-O-C₁₋₈alkyl)₂.

[00663] As used herein, the term “(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-O-C₁₋₈alkyl).

[00664] As used herein, the term “C₁₋₈alkoxy-carbonyl” refers to a radical of the formula: -C(O)-O-C₁₋₈alkyl.

[00665] As used herein, the term “C₁₋₈alkoxy-carbonyl-C₂₋₈alkenyl” refers to a radical of the formula: -C₂₋₈alkenyl-C(O)-O-C₁₋₈alkyl.

[00666] As used herein, the term “C₁₋₈alkoxy-carbonyl-amino” refers to a radical of the formula: -NH-C(O)-O-C₁₋₈alkyl.

[00667] As used herein, the term “C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl.

[00668] As used herein, the term “(C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl)₂.

[00669] As used herein, the term “C₁₋₈alkyl-amino-C₂₋₈alkenyl” refers to a radical of the formula: -C₂₋₈alkenyl-NH-C₁₋₈alkyl.

[00670] As used herein, the term “(C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl” refers to a radical of the formula: -C₂₋₈alkenyl-N(C₁₋₈alkyl)₂.

[00671] As used herein, the term “C₁₋₈alkyl-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-NH-C₁₋₈alkyl.

[00672] As used herein, the term “(C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-N(C₁₋₈alkyl)₂.

[00673] As used herein, the term “C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl.

[00674] As used herein, the term “(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)₂.

[00675] As used herein, the term “C₁₋₈alkyl-amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-NH-C₁₋₈alkyl.

[00676] As used herein, the term “(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-N(C₁₋₈alkyl)₂.

[00677] As used herein, the term “(C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-NH-C₁₋₈alkyl)₂.

[00678] As used herein, the term “[C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino” refers to a radical of the formula: -N[C₁₋₈alkyl-N(C₁₋₈alkyl)₂]₂.

[00679] As used herein, the term “(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-NH-C₁₋₈alkyl).

[00680] As used herein, the term “[C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)[C₁₋₈alkyl-N(C₁₋₈alkyl)₂].

[00681] As used herein, the term “C₁₋₈alkyl-amino-C₂₋₈alkynyl” refers to a radical of the formula: -C₂₋₈alkynyl-NH-C₁₋₈alkyl.

[00682] As used herein, the term “(C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl” refers to a radical of the formula: -C₂₋₈alkynyl-N(C₁₋₈alkyl)₂.

[00683] As used herein, the term “C₁₋₈alkyl-carbonyl” refers to a radical of the formula: -C(O)-C₁₋₈alkyl.

[00684] As used herein, the term “C₁₋₈alkyl-carbonyl-amino” refers to a radical of the formula: -NH-C(O)-C₁₋₈alkyl.

[00685] As used herein, the term “C₁₋₈alkyl-thio” refers to a radical of the formula: -S-C₁₋₈alkyl.

[00686] As used herein, the term “amino-C₂₋₈alkenyl” refers to a radical of the formula: -C₂₋₈alkenyl-NH₂.

[00687] As used herein, the term “amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-NH₂.

[00688] As used herein, the term “amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH₂.

[00689] As used herein, the term “amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-NH₂.

[00690] As used herein, the term “(amino-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-NH₂)₂.

[00691] As used herein, the term “(amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-NH₂).

[00692] As used herein, the term “amino-C₂₋₈alkynyl” refers to a radical of the formula: -C₂₋₈alkynyl-NH₂.

[00693] As used herein, the term “aryl-C₁₋₈alkoxy-carbonyl” refers to a radical of the formula: -C(O)-O-C₁₋₈alkyl-aryl.

[00694] As used herein, the term “aryl-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-aryl.

[00695] As used herein, the term “aryl-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-aryl.

[00696] As used herein, the term “(aryl-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-aryl)₂.

[00697] As used herein, the term “(aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-aryl).

[00698] As used herein, the term “aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl-aryl.

[00699] As used herein, the term “(aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl-aryl)₂.

[00700] As used herein, the term “(aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-aryl).

[00701] As used herein, the term “aryl-amino” refers to a radical of the formula: -NH-aryl.

[00702] As used herein, the term “aryl-amino-carbonyl” refers to a radical of the formula: -C(O)-NH-aryl .

[00703] As used herein, the term “aryl-sulfonyloxy- C_{1-8} alkyl” refers to a radical of the formula: $\text{-C}_{1-8}\text{alkyl-O-SO}_2\text{-aryl}$.

[00704] As used herein, the term “benzoxy-carbonyl” refers to a radical of the formula: $\text{-C(O)O-CH}_2\text{-phenyl}$.

[00705] As used herein, the term “ C_{3-14} cycloalkyl- C_{1-8} alkyl” refers to a radical of the formula: $\text{-C}_{1-8}\text{alkyl-C}_{3-14}\text{cycloalkyl}$.

[00706] As used herein, the term “ C_{3-14} cycloalkyl-amino” refers to a radical of the formula: $\text{-NH-C}_{3-14}\text{cycloalkyl}$.

[00707] As used herein, the term “ C_{3-14} cycloalkyl-oxy” refers to a radical of the formula: $\text{-O-C}_{3-14}\text{cycloalkyl}$.

[00708] As used herein, the term “halo” or “halogen” generally refers to a halogen atom radical, including fluoro, chloro, bromo and iodo.

[00709] As used herein, the term “halo- C_{1-8} alkoxy” refers to a radical of the formula: $\text{-O-C}_{1-8}\text{alkyl-halo}$, wherein C_{1-8} alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

[00710] As used herein, the term “halo- C_{1-8} alkyl” refers to a radical of the formula: $\text{-C}_{1-8}\text{alkyl-halo}$, wherein C_{1-8} alkyl is partially or completely substituted with one or more halogen atoms where allowed by available valences.

[00711] As used herein, the term “halo- C_{1-8} alkyl-amino” refers to a radical of the formula: $\text{-NH-C}_{1-8}\text{alkyl-halo}$.

[00712] As used herein, the term “(halo- C_{1-8} alkyl)(C_{1-8} alkyl)amino” refers to a radical of the formula: $\text{-N(C}_{1-8}\text{alkyl)(C}_{1-8}\text{alkyl-halo)}$.

[00713] As used herein, the term “(halo- C_{1-8} alkyl) $_2$ -amino” refers to a radical of the formula: $\text{-N(C}_{1-8}\text{alkyl-halo)}_2$.

[00714] As used herein, the term “heteroaryl- C_{1-8} alkoxy” refers to a radical of the formula: $\text{-O-C}_{1-8}\text{alkyl-heteroaryl}$.

[00715] As used herein, the term “heteroaryl- C_{1-8} alkyl” refers to a radical of the formula: $\text{-C}_{1-8}\text{alkyl-heteroaryl}$.

[00716] As used herein, the term “heteroaryl-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-heteroaryl.

[00717] As used herein, the term “(heteroaryl-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-heteroaryl)₂.

[00718] As used herein, the term “(heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-heteroaryl).

[00719] As used herein, the term “heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl-heteroaryl.

[00720] As used herein, the term “(heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl-heteroaryl)₂.

[00721] As used herein, the term “(heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-heteroaryl).

[00722] As used herein, the term “heteroaryl-amino” refers to a radical of the formula: -NH-heteroaryl.

[00723] As used herein, the term “heterocyclyl-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-heterocyclyl.

[00724] As used herein, the term “heterocyclyl-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-heterocyclyl.

[00725] As used herein, the term “heterocyclyl-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-heterocyclyl.

[00726] As used herein, the term “(heterocyclyl-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-heterocyclyl)₂.

[00727] As used herein, the term “(heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-heterocyclyl).

[00728] As used herein, the term “heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl-heterocyclyl.

[00729] As used herein, the term “(heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl-heterocyclyl)₂.

[00730] As used herein, the term “(heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-heterocyclyl).

[00731] As used herein, the term “heterocyclyl-amino” refers to a radical of the formula: -NH-heterocyclyl.

[00732] As used herein, the term “(heterocyclyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(heterocyclyl).

[00733] As used herein, the term “heterocyclyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-heterocyclyl.

[00734] As used herein, the term “heterocyclyl-carbonyl” refers to a radical of the formula: -C(O)-heterocyclyl.

[00735] As used herein, the term “heterocyclyl-carbonyl-oxy” refers to a radical of the formula: -O-C(O)-heterocyclyl.

[00736] As used herein, the term “heterocyclyl-oxy” refers to a radical of the formula: -O-heterocyclyl.

[00737] As used herein, the term “hydroxy” refers to a radical of the formula: -OH.

[00738] As used herein, the term “hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-O-C₁₋₈alkyl-OH.

[00739] As used herein, the term “hydroxy-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-OH, wherein C₁₋₈alkyl is partially or completely substituted with one or more hydroxy radicals where allowed by available valences.

[00740] As used herein, the term “hydroxy-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-OH.

[00741] As used herein, the term “(hydroxy-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-OH)₂.

[00742] As used herein, the term “(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-OH).

[00743] As used herein, the term “hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-NH-C₁₋₈alkyl-OH.

[00744] As used herein, the term “(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl-OH)₂.

[00745] As used herein, the term “(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl” refers to a radical of the formula: -C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-OH).

[00746] As used herein, the term “hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-NH-C₁₋₈alkyl-OH.

[00747] As used herein, the term “(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-N(C₁₋₈alkyl-OH)₂.

[00748] As used herein, the term “(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy” refers to a radical of the formula: -O-C₁₋₈alkyl-N(C₁₋₈alkyl)(C₁₋₈alkyl-OH).

[00749] As used herein, the term “hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-NH-C₁₋₈alkyl-OH.

[00750] As used herein, the term “(hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino” refers to a radical of the formula: -N(C₁₋₈alkyl-NH-C₁₋₈alkyl-OH)₂.

[00751] As used herein, the term “(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-N(C₁₋₈alkyl-OH)₂.

[00752] As used herein, the term “(hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)(C₁₋₈alkyl-NH-C₁₋₈alkyl-OH).

[00753] As used herein, the term “[hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)[C₁₋₈alkyl-N(C₁₋₈alkyl-OH)₂].

[00754] As used herein, the term “(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino” refers to a radical of the formula: -NH-C₁₋₈alkyl-N(C₁₋₈alkyl, C₁₋₈alkyl-OH).

[00755] As used herein, the term “[(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino” refers to a radical of the formula: -N(C₁₋₈alkyl)[C₁₋₈alkyl -N(C₁₋₈alkyl)(C₁₋₈alkyl -OH)].

[00756] 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.

[00757] 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.

[00758] As used herein, the terms “independently selected,” or “each selected” refer to functional variables in a substituent list that may be attached more than once on the structure of a core molecule, where the pattern of substitution at each occurrence is independent of the pattern at any other occurrence. Further, the use of a generic substituent on a core structure for a compound provided herein is understood to include the replacement of the generic substituent with specie substituents that are included within the particular genus, e.g., aryl may be independently replaced with phenyl or naphthalenyl (also referred to as naphthyl) and the like, such that the resulting compound is intended to be included within the scope of the compounds described herein.

[00759] As used herein, the term “each instance of” when used in a phrase such as “...aryl, aryl-C₁₋₈alkyl, heterocyclyl and heterocyclyl-C₁₋₈alkyl, 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-C₁₋₈alkyl and heterocyclyl-C₁₋₈alkyl.

[00760] 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.

[00761] 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.

[00762] 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.

[00763] As used herein the term “aberrant” refers to a deviation from the norm of, *e.g.*, the average healthy subject or a cell(s) or tissue sample from a healthy subject. The term “aberrant expression,” as used herein, refers to abnormal expression (up-regulated or down-regulated resulting in an excessive or deficient amount thereof) of a gene product (*e.g.*, RNA transcript or protein) by a cell, tissue sample, or subject relative to a corresponding normal, healthy cell, tissue sample or subject. In a specific embodiment, the “aberrant expression” refers to an altered level of a gene product (*e.g.*, RNA transcript or protein) in a cell, tissue sample, or subject relative to a corresponding normal, healthy cell, tissue sample or subject. The term “aberrant amount” as used herein refers to an altered level of a gene product (*e.g.*, RNA, protein, polypeptide, or peptide) in a cell, tissue sample, or subject relative to a corresponding normal, healthy cell, tissue sample or subject. In specific embodiments, the amount of a gene product (*e.g.*, RNA, protein, polypeptide, or peptide) in a cell, tissue sample, or subject relative to a corresponding cell or tissue sample from a healthy subject or a healthy subject, is considered aberrant if it is 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6-fold or more above or below the amount of the gene product in the corresponding cell or tissue sample from a healthy subject or healthy subject.

[00764] The term “intronic REMS” refers to a REMS sequence present in an intron that functions as a 5’ splice site in the presence of a compound described herein. The intronic REMS, when downstream of a first branch point (BP) sequence and a first 3’ splice site (3’ ss) sequence and upstream of a second branch point (BP) sequence and a second 3’ splice site (3’ ss) sequence) (as shown in Figure 1A) and in the presence of a compound described herein, can function as a 5’ splice site. The intronic REMS may also function as a 5’ splice site when upstream of a first branch point and a first 3’ splice site in the presence of a compound described herein (see Figure 1B or 1C). Any one, two, three, or more or all of the following may be present endogenously or non-endogenously in the affected intron: the intronic REMS, the first BP, the second BP, the first 3’ ss, and the second 3’ ss.

[00765] As used herein, a “non-endogenous” nucleotide sequence (such as a non-endogenous 5’ splice site, a non-endogenous branch point or a non-endogenous 3’ splice site) is a nucleotide sequence not naturally found to be part of a pre-RNA or a DNA sequence encoding a pre-RNA

sequence. In other words, the hand of man is required to synthesize or manipulate the RNA or DNA sequence to introduce the nucleotide sequence.

[00766] As used herein, the term “non-endogenous intronic REMS” refers to a REMS sequence not naturally found to be part of an RNA sequence or naturally encoded by a DNA sequence. In other words, the hand of man is required to manipulate the RNA or DNA sequence to introduce the intronic REMS or the nucleotide sequence encoding the REMS into an intron.

[00767] As used herein, the terms “intron-derived exon,” “intronic exon,” “iExon” and “intronic exon” (collectively iExon) refers to the formation of an exon from an RNA sequence present in an intron following splicing of an RNA transcript in the presence of a compound described herein or another agent which results in an iREMS functioning as an intronic 5' splice site. In particular, an iExon comprises the following RNA sequence as an exon when RNA splicing of an RNA transcript comprising two exons and an intron occurs in the presence of a compound described herein, wherein a first exon is upstream of the intron and a second exon is downstream of the intron, and wherein the intron comprises a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point, and a second 3' splice site: the RNA sequence between the first 3' splice site and the iREMS, as shown in Figure 1A. One or more of the iREMS sequence, branch point and 3' splice site may be naturally present in an intron or may be introduced into the intron. When all such elements are present or introduced, in the presence of a compound described herein the elements define an exonic boundary that enables the splicing machinery to generate an iExon in RNA, a result that would not naturally occur without the addition of a splicing modulator compound.

[00768] As used herein, the term “pseudoexon” refers to a potential exon in intronic regions of pre-mRNA that is not normally spliced into mature mRNA. A subset of pseudoexons are spliced in the presence of a compound described herein or another agent resulting from an iREMS functioning as a 5' splice site within the pseudoexon, to form an iExon. An intronic REMS-containing pseudoexon is not known to be endogenously recognized by the splicing machinery for producing an iExon, but in the presence of a splicing modulator compound as described herein, the splicing machinery produces an iExon. Accordingly, production of an iExon from a pseudoexon is intended to be included within the scope of various aspects of the collective term “iExon.”

[00769] As used herein, the term “unannotated exon” refers to endogenous sequences that are naturally present as exons in mature mRNA product according to experimental evidence but are not annotated in NCBI’s RefSeq database (<https://www.ncbi.nlm.nih.gov/refseq/>). Some unannotated exons contain an intronic REMS at the 5’ splice site. A REMS-containing unannotated exon is not known to be endogenously recognized by the splicing machinery for producing an iExon, but in the presence of a splicing modulator compound as described herein, the splicing machinery produces an iExon. Accordingly, production of an iExon from an unannotated exon is intended to be included within the scope of various aspects of the collective term “iExon.”

[00770] As used herein, the term “substantial change” in the context of the amount of one or more RNA transcripts (*e.g.*, rRNA, tRNA, miRNA, siRNA, piRNA, lncRNA, pre-mRNA or mRNA transcripts), an alternative splice variant thereof or an isoform thereof, or one or more proteins thereof, each expressed as the product of one or more of genes, means that the amount of such products changes by a statistically significant amount such as, in a nonlimiting example, a p value less than a value selected from 0.1, 0.01, 0.001, or 0.0001.

[00771] 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. Non-limiting 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.

[00772] As used herein, the term “functional protein” refers to a form of a protein that retains a certain biological function or the functions of a full length protein or protein isoform encoded by a gene. Accordingly, inclusion of an iExon that is located in the protein coding region of an mRNA that expresses a functional protein is intended to be included within the scope of the description herein.

[00773] As used herein, the term “non-functional protein” refers to a form of a protein that does not retain any biological function compared to full length protein or a protein isoform encoded by a gene in the absence of a splicing modifier compound as described herein. Accordingly, inclusion of an iExon that is located in the protein coding region of an mRNA that

expresses a non-functional protein is intended to be included within the scope of the description herein.

[00774] As used herein, in the context of a functional protein produced from an artificial construct, the term “produce substantially less” means that the amount of functional protein produced in the presence of a compound described herein is at least substantially 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, or 100% less than the amount of functional protein produced in the absence of the compound.

COMPOUND FORMS

[00775] As used herein, the terms “a compound of Formula (Ia),” “a compound of Formula (Ia1),” “a compound of Formula (Ia2),” “a compound of Formula (Ia3),” “a compound of Formula (Ia4),” “a compound of Formula (II),” “a compound of Formula (IIa),” “a compound of Formula (IIa1),” “a compound of Formula (IIa2),” “a compound of Formula (IIa3),” “a compound of Formula (IIa4),” “a compound of Formula (III),” “a compound of Formula (IIIa),” “a compound of Formula (IIIa1),” “a compound of Formula (IIIa2),” “a compound of Formula (IIIa3),” “a compound of Formula (IIIa4),” “a compound of Formula (IV),” “a compound of Formula (IVa),” “a compound of Formula (IVa1),” “a compound of Formula (IVa2),” “a compound of Formula (V),” “a compound of Formula (Va),” “a compound of Formula (Va1),” “a compound of Formula (Va2),” “a compound of Formula (VI),” “a compound of Formula (VIa),” “a compound of Formula (VIa1),” “a compound of Formula (VIa2),” “a compound of Formula (VIa3),” “a compound of Formula (VIa4),” “a compound of Formula (VII),” “a compound of Formula (VIIa),” “a compound of Formula (VIIa1),” “a compound of Formula (VIIa2),” “a compound of Formula (VIII),” “a compound of Formula (VIIIa),” “a compound of Formula (VIIIa1),” “a compound of Formula (VIIIa2),” “a compound of Formula (IX),” “a compound of Formula (IXa),” “a compound of Formula (IXa1),” “a compound of Formula (IXa2),” “a compound of Formula (IXa3),” “a compound of Formula (IXa4),” “a compound of Formula (X),” “a compound of Formula (Xa),” “a compound of Formula (Xa1),” “a compound of Formula (Xa2),” “a compound of Formula (XI),” “a compound of Formula (XIa),” “a compound of Formula (XIa1),” “a compound of Formula (XIa2),” “a compound of Formula (XII),” “a compound of Formula (XIIa),” “a compound of Formula (XIIa1),” “a compound of Formula (XIIa2),” “a compound of Formula (XIIa3),” “a compound of Formula (XIIa4),” “a

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

[00776] Rather than repeat embodiments for the various subgenera of the compound of Formula (I), in certain embodiments, the term “a compound of Formula (I) or a form thereof” is used to inclusively refer to a compound of Formula (Ia) or a form thereof, a compound of Formula (Ia1) or a form thereof, a compound of Formula (Ia2) or a form thereof, a compound of Formula (Ia3) or a form thereof, a compound of Formula (Ia4) or a form thereof, a compound of Formula (II) or a form thereof, a compound of Formula (IIa) or a form thereof, a compound of Formula (IIa1) or a form thereof, a compound of Formula (IIa2) or a form thereof, a compound of Formula (IIa3) or a form thereof, a compound of Formula (IIa4) or a form thereof, a compound of Formula (III) or a form thereof, a compound of Formula (IIIa) or a form thereof, a compound of Formula (IIIa1) or a form thereof, a compound of Formula (IIIa2) or a form thereof, a compound of Formula (IIIa3) or a form thereof, a compound of Formula (IIIa4) or a form thereof, a compound of Formula (IV) or a form thereof, a compound of Formula (IVa) or a form thereof, a compound of Formula (IVa1) or a form thereof, a compound of Formula (IVa2) or a form thereof, a compound of Formula (V) or a form thereof, a compound of Formula (Va) or a form thereof, a compound of Formula (Va1) or a form thereof, a compound of Formula (Va2) or a form thereof, a compound of Formula (VI) or a form thereof, a compound of Formula (VIa) or a form thereof, a compound of Formula (VIa1) or a form thereof, a compound of Formula (VIa2) or a form thereof, a compound of Formula (VIa3) or a form thereof, a compound of Formula (VIa4) or a form thereof, a compound of Formula (VII) or a form thereof, a compound of Formula (VIIa) or a form thereof, a compound of Formula (VIIa1) or a form thereof, a compound of Formula (VIIa2) or a form thereof, a compound of Formula (VIII) or a form thereof, a compound of Formula (VIIIa) or a form thereof, a compound of Formula (VIIIa1) or a form thereof, a compound of Formula (VIIIa2) or a form thereof, a compound of Formula (IX) or a form thereof, a compound of Formula (IXa) or a form thereof, a compound of Formula (IXa1) or a form thereof, a compound of Formula (IXa2) or a form thereof, a compound of Formula (IXa3) or a form thereof, a compound of Formula (IXa4) or a form thereof, a compound of Formula (X) or a form thereof, a compound of Formula (Xa) or a form thereof, a compound of

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

[00777] Thus, embodiments and references to “a compound of Formula (I)” are intended to be inclusive of compounds of Formula (Ia), Formula (Ia1), Formula (Ia2), Formula (Ia3), Formula (Ia4), Formula (II), Formula (IIa), Formula (IIa1), Formula (IIa2), Formula (IIa3), Formula (IIa4), Formula (III), Formula (IIIa), Formula (IIIa1), Formula (IIIa2), Formula (IIIa3), Formula (IIIa4), Formula (IV), Formula (IVa), Formula (IVa1), Formula (IVa2), Formula (V), Formula (Va), Formula (Va1), Formula (Va2), Formula (VI), Formula (VIa), Formula (VIa1), Formula (VIa2), Formula (VIa3), Formula (VIa4), Formula (VII), Formula (VIIa), Formula (VIIa1), Formula (VIIa2), Formula (VIII), Formula (VIIIa), Formula (VIIIa1), Formula (VIIIa2), Formula (IX), Formula (IXa), Formula (IXa1), Formula (IXa2), Formula (IXa3), Formula (IXa4), Formula (X), Formula (Xa), Formula (Xa1), Formula (Xa2), Formula (XI), Formula (XIa), Formula (XIa1), Formula (XIa2), Formula (XII), Formula (XIIa), Formula (XIIa1), Formula (XIIa2), Formula (XIIa3), Formula (XIIa4), Formula (XIII), Formula (XIIIa), Formula (XIIIa1), Formula (XIIIa2), Formula (XIV), Formula (XIVa), Formula (XIVa1) and Formula (XIVa2).

[00778] 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.

[00779] In certain embodiments described herein, the form of the compound of Formula (I) is selected from a salt, isotopologue, stereoisomer, racemate, enantiomer, diastereomer or tautomer thereof.

[00780] 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.

[00781] 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.

[00782] In certain embodiments described herein, the form of the compound of Formula (I) is a free acid, free base or salt thereof.

[00783] In certain embodiments described herein, the form of the compound of Formula (I) is an isotopologue thereof.

[00784] In certain embodiments described herein, the form of the compound of Formula (I) is a stereoisomer, racemate, enantiomer or diastereomer thereof.

[00785] In certain embodiments described herein, the form of the compound of Formula (I) is a tautomer thereof.

[00786] In certain embodiments described herein, the form of the compound of Formula (I) is a pharmaceutically acceptable form.

[00787] In certain embodiments described herein, the compound of Formula (I) or a form thereof is isolated for use.

[00788] 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.

[00789] 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.

[00790] Prodrugs of a compound of Formula (I) or a form thereof are also contemplated herein.

[00791] 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.

[00792] 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.

[00793] 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.

[00794] 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.

[00795] 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.

[00796] 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. One or more embodiments of 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.

[00797] Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl et al, Camille G. (eds.) Handbook of Pharmaceutical Salts. Properties, Selection and Use. (2002) Zurich: Wiley-VCH; S. Berge et al, Journal of Pharmaceutical Sciences (1977) 66(1) 1-19; P. Gould, International J. of Pharmaceutics (1986) 33, 201-217; Anderson et al, The Practice of Medicinal Chemistry (1996), Academic Press, New York; and in The Orange Book (see, website for Food & Drug Administration, Washington, D.C.). These disclosures are incorporated herein by reference thereto.

[00798] 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.

[00799] All such acid salts and base salts are intended to be pharmaceutically acceptable salts within the scope of the description herein and all such acid and base salts are considered equivalent to the free forms of the corresponding compounds for the purposes described herein.

[00800] Compounds of Formula I and forms thereof may further exist in a tautomeric form. All such tautomeric forms are contemplated herein as part of the present description.

[00801] 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.

[00802] 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.

[00803] 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.

[00804] 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%.

[00805] 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%.

[00806] 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.

[00807] 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.

[00808] 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.

[00809] 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.

[00810] 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.

[00811] 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.

[00812] 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.

[00813] Certain isotopically-enriched compounds described herein (*e.g.*, those labeled with H^3 and C^{14}) are useful in compound and/or substrate tissue distribution assays. Tritiated (*i.e.*, H^3) and carbon-14 (*i.e.*, C^{14}) isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium (*i.e.*, “deuterium enriched”) may afford certain therapeutic advantages resulting from greater metabolic stability (*e.g.*, increased in vivo half-life or reduced dosage requirements) and hence may be preferred in some circumstances. Isotopically-enriched compounds of Formula (I) can generally be prepared using procedures known to persons of ordinary skill in the art by substituting an appropriate isotopically-enriched reagent for a non-isotopically-enriched reagent.

[00814] When the compounds are enriched with deuterium, the deuterium-to-hydrogen ratio on the deuterated atoms of the molecule substantially exceeds the naturally occurring deuterium-to-hydrogen ratio.

[00815] An embodiment described herein may include an isotopologue form of the compound of Formula (I), wherein the isotopologue is substituted on one or more atom members of the compound of Formula (I) with one or more deuterium atoms in place of one or more hydrogen atoms.

[00816] 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.

[00817] 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.

[00818] 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 ethanlates, methanlates, and the like.

[00819] 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).

[00820] As used herein, the term “hydrate” means a solvate wherein the solvent molecule is water.

[00821] 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

METHODS FOR DETERMINING WHICH GENES MAY BE MODULATED BY THE COMPOUNDS

[00822] In another aspect, provided herein are methods for determining whether the splicing of the precursor RNA of a gene is likely to be modulated by a compound of Formula (I) or a form thereof, comprising searching for the presence of an intronic REMS (i.e., a sequence functioning as a 5' splice site) in a gene intronic sequence, wherein the presence of the intronic REMS 3' splice site and an intronic branch point in the gene sequence indicates that the splicing of the precursor RNA of the gene is likely to be modulated by the compound of Formula (I) or a form thereof, and the absence of the intronic REMS and an intronic 3' splice site and an intronic branch point in the gene sequence indicates that the splicing of the precursor RNA of the gene is unlikely to be modulated by the compound of Formula (I) or a form thereof. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described herein. In specific embodiments, the methods further comprise searching for the presence of the combination of an intronic REMS, an intronic 3' splice site and an intronic branch point in the gene sequence.

[00823] In another aspect, provided herein are methods for determining whether the amount of a product (e.g., an mRNA transcript or protein) of a gene is likely to be modulated by a compound of Formula (I) or a form thereof, comprising searching for the presence of an intronic REMS in the gene sequence, wherein the presence of the combination of an intronic REMS, an intronic 3' splice site and an intronic branch point in the gene sequence indicates that the amount of a product (e.g., an mRNA transcript or protein) of the gene is likely to be modulated by the compound of Formula (I) or a form thereof, and the absence of the combination of an intronic REMS, an intronic 3' splice site and an intronic branch point in the gene sequence indicates that the amount of a product (e.g., an mRNA transcript or protein) of the gene is unlikely to be modulated by the compound of Formula (I) or a form thereof. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described herein. In specific embodiments, the methods further comprise searching for the presence of any of an intronic REMS, an intronic 3' splice site, and an intronic branch point in the gene sequence.

[00824] The step of searching for the presence of an intronic REMS, an intronic 3' splice site, and an intronic branch point in the gene sequence described herein can be performed by a computer system comprising a memory storing instructions for searching for the presence of the intronic REMS, the intronic 3' splice site, and the intronic branch point in the gene sequence, or such a search can be performed manually.

[00825] In another aspect, provided herein are methods for determining whether the splicing of the precursor RNA of a gene is likely to be modulated via iExon inclusion by a compound of Formula (I) or a form thereof. In one particular aspect, the method comprises searching for the presence of an intronic REMS (i.e., a sequence functioning as a 5' splice site) in combination with, in order, an upstream branch point and an upstream 3' splice site in a gene intronic sequence. The presence of these elements with the intronic REMS and the endogenous presence of a downstream 3' splice site and a downstream branch point in the gene sequence indicates that the splicing of the precursor RNA of the gene is likely to be modulated by the compound of Formula (I) or a form thereof. In this aspect, the presence of an upstream branch point and upstream 3' splice site and the REMS in the intron enable the presence of the compound of Formula (I) or a form thereof to modulate iExon inclusion, i.e., splicing the iExon with the downstream endogenous exon (as shown in Figure 1A). Otherwise, in the absence of these elements, the iREMS will be either ignored by the spliceosome or, in a limited set of circumstances, will become an extended/cryptic 5' splice site for the upstream endogenous exon (as shown in Figure 1B and 1C). The absence of the intronic REMS in the gene sequence indicates that the splicing of the precursor RNA of the gene is unlikely to be modulated via iExon inclusion by the compound of Formula (I) or a form thereof. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described herein. In other specific embodiments, the methods further comprise searching for the presence of the combination of, in 5' to 3' order: an upstream branch point, an upstream 3' splice site, an intronic REMS, a downstream branch point and a downstream 3' splice site in the gene sequence.

[00826] In another aspect, provided herein are methods for determining whether the amount of a product (e.g., an mRNA transcript or protein) of a gene is likely to be modulated via iExon inclusion by a compound of Formula (I) or a form thereof, comprising searching for the presence

of an intronic REMS in the gene sequence, wherein the presence of the combination of at least an upstream branch point, an upstream 3' splice site and an intronic REMS in the gene sequence indicates that the amount of a product (*e.g.*, an mRNA transcript or protein) of the gene is likely to be modulated via iExon inclusion by the compound of Formula (I) or a form thereof, and the absence of the combination of an upstream branch point, an upstream 3' splice site and an intronic REMS in the gene sequence indicates that the amount of a product (*e.g.*, an mRNA transcript or protein) of the gene is unlikely to be modulated via iExon inclusion by the compound of Formula (I) or a form thereof. In certain embodiments, a compound of Formula (I) is a compound of Formula (II), Formula (III), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), Formula (IX), Formula (X), Formula (XI), Formula (XII), Formula (XIII), or Formula (XIV) described herein. In specific embodiments, the methods further comprise searching for the presence of any of, in 5' to 3' order: an upstream branch point, an upstream 3' splice site, an intronic REMS, a downstream 3' splice site, and a downstream branch point in the gene sequence.

[00827] The step of searching for the presence of an upstream branch point, an upstream 3' splice site and an intronic REMS in any of the gene sequences in any of the genes described herein can be performed by a computer system comprising a memory storing instructions for searching for the presence of the intronic REMS, the upstream 3' splice site, and the upstream branch point in the gene sequence, or such a search can be performed manually.

[00828] In certain embodiments, the splicing of a precursor RNA containing an intronic REMS is assessed by contacting a compound described herein with the precursor RNA in cell culture. In some embodiments, the splicing of a precursor RNA containing an intronic REMS is assessed by contacting a compound described herein with the precursor RNA in a cell-free extract. In a specific embodiment, the compound is one known to modulate the splicing of a precursor RNA containing an exonic REMS. *See, e.g.*, the section below relating to methods for determining whether a compound modulates the expression of certain genes, and the example below for techniques that could be used in these assessments.

METHODS FOR DETERMINING WHICH COMPOUNDS OF FORMULA (I) MODULATE THE EXPRESSION OF CERTAIN GENES

[00829] Provided herein are methods for determining whether a compound of Formula (I) or a form thereof modulates the amount of one, two, three or more RNA transcripts (e.g., pre-mRNA or mRNA transcripts or isoforms thereof) of one, two, three or more genes. In some embodiments, the gene is any one of the genes disclosed in Tables 2-7 or any one of the genes disclosed in Table 1. In certain embodiments, the gene is a gene disclosed in Tables 2-6. In some embodiments, the gene is a gene disclosed in Table 7. In other embodiments, the gene is a gene disclosed in Table 1. In certain embodiments, the gene is a gene not disclosed in either International Publication No. WO 2015/105657, International Publication No. WO 2016/196386, or both.

[00830] In one embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript, comprising: (a) contacting a cell(s) with a compound of Formula (I) or a form thereof, and (b) determining the amount of the RNA transcript produced by the cell(s), wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (e.g., a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (e.g., an mRNA transcript), comprising: (a) contacting a first cell(s) with a compound of Formula (I) or a form thereof, (b) contacting a second cell(s) with a negative control (e.g., a vehicle control, such as PBS or DMSO); and (c) determining the amount of the RNA transcript produced by the first cell(s) and the second cell(s); and (d) comparing the amount of the RNA transcript produced by the first cell(s) to the amount of the RNA transcript expressed by the second cell(s), wherein an alteration in the amount of the RNA transcript produced by the first cell(s) relative to the amount of the RNA transcript produced by the second cell(s) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In certain embodiments, the contacting of the cell(s) with the compound occurs in cell culture. In other embodiments, the contacting of the cell(s) with the compound occurs in a subject, such as a non-human animal subject.

[00831] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (*e.g.*, an mRNA transcript), comprising: (a) culturing a cell(s) in the presence of a compound of Formula (I) or a form thereof; and (b) determining the amount of the two or more RNA transcript splice variants produced by the cell(s), wherein an alteration in the amount of the two or more RNA transcript in the presence of the compound relative to the amount of the two or more RNA transcript splice variants in the absence of the compound or the presence of a negative control (*e.g.*, a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the splicing of the RNA transcript.

[00832] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (*e.g.*, an mRNA transcript), comprising: (a) culturing a cell(s) in the presence of a compound of Formula (I) or a form thereof; (b) isolating two or more RNA transcript splice variants from the cell(s) after a certain period of time; and (c) determining the amount of the two or more RNA transcript splice variants produced by the cell(s), wherein an alteration in the amount of the two or more RNA transcript in the presence of the compound relative to the amount of the two or more RNA transcript splice variants in the absence of the compound or the presence of a negative control (*e.g.*, a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the splicing of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (*e.g.*, an mRNA transcript), comprising (a) culturing a first cell(s) in the presence of a compound of Formula (I) or a form thereof; (b) culturing a second cell(s) in the presence of a negative control (*e.g.*, a vehicle control, such as PBS or DMSO); (c) isolating two or more RNA transcript splice variants produced by the first cell(s) and isolating two or more RNA transcript splice variants produced by the second cell(s); (d) determining the amount of the two or more RNA transcript splice variants produced by the first cell(s) and the second cell(s); and (e) comparing the amount of the two or more RNA transcript splice variants produced by the first cell(s) to the amount of the two or more RNA transcript splice variants produced by the second cell(s), wherein an alteration in the amount of the two or more RNA transcript splice variants produced by the first cell(s) relative to the amount of the

two or more RNA transcript splice variants produced by the second cell(s) indicates that the compound of Formula (I) or a form thereof modulates the splicing of the RNA transcript.

[00833] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (e.g., an mRNA transcript), comprising: (a) contacting a cell-free system with a compound of Formula (I) or a form thereof, and (b) determining the amount of the RNA transcript produced by the cell-free system, wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (e.g., a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (e.g., an mRNA transcript), comprising: (a) contacting a first cell-free system with a compound of Formula (I) or a form thereof, (b) contacting a second cell-free system with a negative control (e.g., a vehicle control, such as PBS or DMSO); and (c) determining the amount of the RNA transcript produced by the first cell-free system and the second cell-free system; and (d) comparing the amount of the RNA transcript produced by the first cell-free system to the amount of the RNA transcript expressed by the second cell-free system, wherein an alteration in the amount of the RNA transcript produced by the first cell-free system relative to the amount of the RNA transcript produced by the second cell-free system indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In certain embodiments, the cell-free system comprises purely synthetic RNA, synthetic or recombinant (purified) enzymes, and protein factors. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template, synthetic or recombinant (purified) enzymes, and protein factors. In other embodiments, the cell-free system comprises purely synthetic RNA and nuclear extract. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template and nuclear extract. In other embodiments, the cell-free system comprises purely synthetic RNA and whole cell extract. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template and whole cell extract. In certain embodiments, the cell-free system additionally comprises regulatory RNAs (e.g., microRNAs).

[00834] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (e.g., an mRNA transcript), comprising: (a) contacting a cell-free system with a compound of Formula (I) or a form thereof; and (b) determining the amount of two or more RNA transcript splice variants produced by the cell-free system, wherein an alteration in the amount of the two or more RNA transcript splice variants in the presence of the compound relative to the amount of the two or more RNA transcript splice variants in the absence of the compound or the presence of a negative control (e.g., a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the splicing of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (e.g., an mRNA transcript), comprising: (a) contacting a first cell-free system with a compound of Formula (I) or a form thereof; (b) contacting a second cell-free system with a negative control (e.g., a vehicle control, such as PBS or DMSO); and (c) determining the amount of two or more RNA transcript splice variants produced by the first cell-free system and the second cell-free system; and (d) comparing the amount of the two or more RNA transcript splice variants produced by the first cell-free system to the amount of the RNA transcript expressed by the second cell-free system, wherein an alteration in the amount of the two or more RNA transcript splice variants produced by the first cell-free system relative to the amount of the two or more RNA transcript splice variants produced by the second cell-free system indicates that the compound of Formula (I) or a form thereof modulates the splicing of the RNA transcript. In certain embodiments, the cell-free system comprises purely synthetic RNA, synthetic or recombinant (purified) enzymes, and protein factors. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template, synthetic or recombinant (purified) enzymes, and protein factors. In other embodiments, the cell-free system comprises purely synthetic RNA and nuclear extract. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template and nuclear extract. In other embodiments, the cell-free system comprises purely synthetic RNA and whole cell extract. In other embodiments, the cell-free system comprises RNA transcribed from a synthetic DNA template and whole cell extract. In certain embodiments, the cell-free system additionally comprises regulatory RNAs (e.g., microRNAs).

[00835] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (*e.g.*, an mRNA transcript), comprising: (a) culturing a cell(s) in the presence of a compound of Formula (I) or a form thereof, (b) isolating the RNA transcript from the cell(s) after a certain period of time; and (c) determining the amount of the RNA transcript produced by the cell(s), wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (*e.g.*, a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (*e.g.*, an mRNA transcript), comprising (a) culturing a first cell(s) in the presence of a compound of Formula (I) or a form thereof, (b) culturing a second cell(s) in the presence of a negative control (*e.g.*, a vehicle control, such as PBS or DMSO); (c) isolating the RNA transcript produced by the first cell(s) and isolating the RNA transcript produced by the second cell(s); (d) determining the amount of the RNA transcript produced by the first cell(s) and the second cell(s); and (e) comparing the amount of the RNA transcript produced by the first cell(s) to the amount of the RNA transcript produced by the second cell(s), wherein an alteration in the amount of the RNA transcript produced by the first cell(s) relative to the amount of the RNA transcript produced by the second cell(s) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript.

[00836] In certain embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a primary cell(s) from a subject. In some embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a primary cell(s) from a subject with a disease. In specific embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a primary cell(s) from a subject with a disease associated with an aberrant amount of an RNA transcript(s) for a particular gene(s). In some specific embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a primary cell(s) from a subject with a disease associated with an aberrant amount of an isoform(s) of a particular gene(s). In some embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a fibroblast (*e.g.*, GM03813 or PNN 1-46 fibroblasts), an immune cell (*e.g.*, a T cell, B cell, natural killer cell, macrophage), or

a muscle cell. In certain embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a cancer cell.

[00837] In certain embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is from a cell line. In some embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a cell line derived from a subject with a disease. In certain embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is from a cell line known to have aberrant RNA transcript levels for a particular gene(s). In specific embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is from a cell line derived from a subject with a disease known to have aberrant RNA transcript levels for a particular gene(s). In certain embodiments, the cell(s) contacted or cultured with a compound of Formula (I) or a form thereof is a cancer cell line. In some specific embodiments, the cell(s) contacted or cultured with the compound of Formula (I) or a form thereof is from a cell line derived from a subject with a disease known to have an aberrant amount of an RNA isoform(s) and/or protein isoform(s) of a particular gene(s). Non-limiting examples of cell lines include 3T3, 4T1, 721, 9L, A2780, A172, A20, A253, A431, A-549, ALC, B16, B35, BCP-1, BEAS-2B, bEnd.3, BHK, BR 293, BT2O, BT483, BxPC3, C2C12, C3H-10T1/2, C6/36, C6, Cal-27, CHO, COR-L23, COS, COV-434, CML T1, CMT, CRL7030, CT26, D17, DH82, DU145, DuCaP, EL4, EM2, EM3, EMT6, FM3, H1299, H69, HB54, HB55, HCA2, HDF (human dermal fibroblasts), HEK-293, HeLa, Hepa1c1c7, HL-60, HMEC, Hs578T, HsS78Bst, HT-29, HTB2, HUVEC, Jurkat, J558L, JY, K562, Ku812, KCL22, KG1, KYO1, LNCap, Ma-Mel, MC-38, MCF-7, MCF-10A, MDA-MB-231, MDA-MB-468, MDA-MB-435, MDCK, MG63, MOR/0.2R, MONO-MAC 6, MRC5, MTD-1A, NCI-H69, NIH-3T3, NALM-1, NS0, NW-145, OPCN, OPCT, PNT-1A, PNT-2, Raji, RBL, RenCa, RIN-5F, RMA, Saos-2, Sf21, Sf9, SH-SY5Y, SiHa, SKBR3, SKOV-3, T2, T-47D, T84, THP1, U373, U87, U937, VCaP, Vero, VERY, W138, WM39, WT-49, X63, YAC-1, and YAR cells. In one embodiment, the cells are from a patient. In another embodiment, the patient cells are GM03813 cells.

[00838] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (*e.g.*, an mRNA transcript), comprising: (a) contacting a tissue sample with a compound of Formula (I) or a form thereof; and (b) determining the amount of the RNA transcript produced by the tissue

sample, wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (*e.g.*, a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (*e.g.*, an mRNA transcript), comprising: (a) contacting a first tissue sample with a compound of Formula (I) or a form thereof, (b) contacting a second tissue sample with a negative control (*e.g.*, a vehicle control, such as PBS or DMSO); and (c) determining the amount of the RNA transcript produced by the first tissue sample and the second tissue sample; and (d) comparing the amount of the RNA transcript produced by the first tissue sample to the amount of the RNA transcript produced by the second tissue sample, wherein an alteration in the amount of the RNA transcript produced by the first tissue sample relative to the amount of the RNA transcript produced by the second tissue sample indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. Any tissue sample containing cells may be used in the accordance with these methods. In certain embodiments, the tissue sample is a blood sample, a skin sample, a muscle sample, or a tumor sample. Techniques known to one skilled in the art may be used to obtain a tissue sample from a subject.

[00839] In some embodiments, a dose-response assay is performed. In one embodiment, the dose response assay comprises: (a) contacting a cell(s) with a concentration of a compound of Formula (I) or a form thereof; (b) determining the amount of the RNA transcript produced by the cell(s), wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (*e.g.*, a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript; (c) repeating steps (a) and (b), wherein the only experimental variable changed is the concentration of the compound or a form thereof; and (d) comparing the amount of the RNA transcript produced at the different concentrations of the compound or a form thereof. In another embodiment, the dose response assay comprises: (a) culturing a cell(s) in the presence of a compound of Formula (I) or a form thereof, (b) isolating the RNA transcript from the cell(s) after a certain period of time; (c) determining the amount of the RNA transcript produced by the

cell(s), wherein an alteration in the amount of the RNA transcript in the presence of the compound relative to the amount of the RNA transcript in the absence of the compound or the presence of a negative control (e.g., a vehicle control such as PBS or DMSO) indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript; (d) repeating steps (a), (b), and (c), wherein the only experimental variable changed is the concentration of the compound or a form thereof; and (e) comparing the amount of the RNA transcript produced at the different concentrations of the compound or a form thereof. In another embodiment, the dose-response assay comprises: (a) contacting each well of a microtiter plate containing cells with a different concentration of a compound of Formula (I) or a form thereof; (b) determining the amount of an RNA transcript produced by cells in each well; and (c) assessing the change of the amount of the RNA transcript at the different concentrations of the compound or form thereof.

[00840] In one embodiment, the dose response assay comprises: (a) contacting a cell(s) with a concentration of a compound of Formula (I) or a form thereof, wherein the cells are within the wells of a tissue culture container (e.g., a 96-well plate) at about the same density within each well, and wherein the cells are contacted with different concentrations of compound in different wells; (b) isolating the RNA from said cells in each well; (c) determining the amount of the RNA transcript produced by the cell(s) in each well; and (d) assessing change in the amount of the RNA transcript in the presence of one or more concentrations of compound relative to the amount of the RNA transcript in the presence of a different concentration of the compound or the absence of the compound or the presence of a negative control (e.g., a vehicle control such as PBS or DMSO).

[00841] In certain embodiments, the contacting of the cell(s) with the compound occurs in cell culture. In other embodiments, the contacting of the cell(s) with the compound occurs in a subject, such as a non-human animal subject.

[00842] In certain embodiments described herein, the cell(s) is contacted or cultured with a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a compound of Formula (I) or a form thereof, or a negative control for a period of 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 8 hours, 12 hours, 18 hours, 24 hours, 48 hours, 72 hours or more. In other embodiments described herein, the cell(s) is contacted or cultured with a compound of Formula (I) or a form thereof, or a tissue sample is

contacted with a compound of Formula (I) or a form thereof, or a negative control for a period of 15 minutes to 1 hour, 1 to 2 hours, 2 to 4 hours, 6 to 12 hours, 12 to 18 hours, 12 to 24 hours, 28 to 24 hours, 24 to 48 hours, 48 to 72 hours.

[00843] In certain embodiments described herein, the cell(s) is contacted or cultured with a certain concentration of a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a certain concentration of a compound of Formula (I) or a form thereof, wherein the certain concentration is 0.0001 μ M, 0.0003 μ M, 0.001 μ M, 0.003 μ M, 0.01 μ M, 0.05 μ M, 1 μ M, 2 μ M, 5 μ M, 10 μ M, 15 μ M, 20 μ M, 25 μ M, 50 μ M, 75 μ M, 100 μ M, or 150 μ M. In other embodiments described herein, the cell(s) is contacted or cultured with a certain concentration of a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a certain concentration of a compound of Formula (I) or a form thereof, wherein the certain concentration is 0.0001 μ M, 0.0003 μ M, 0.0005 μ M, 0.001 μ M, 0.003 μ M, 0.005 μ M, 0.01 μ M, 0.03 μ M, 0.05 μ M, 0.1 μ M, 0.3 μ M, 0.5 μ M or 1 μ M. In other embodiments described herein, the cell(s) is contacted or cultured with a certain concentration of a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a certain concentration of a compound of Formula (I) or a form thereof, wherein the certain concentration is 175 μ M, 200 μ M, 250 μ M, 275 μ M, 300 μ M, 350 μ M, 400 μ M, 450 μ M, 500 μ M, 550 μ M, 600 μ M, 650 μ M, 700 μ M, 750 μ M, 800 μ M, 850 μ M, 900 μ M, 950 μ M or 1 mM. In some embodiments described herein, the cell(s) is contacted or cultured with a certain concentration of a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a certain concentration of a compound of Formula (I) or a form thereof, wherein the certain concentration is 5 nM, 10 nM, 20 nM, 30 nM, 40 nM, 50 nM, 60 nM, 70 nM, 80 nM, 90 nM, 100 nM, 150 nM, 200 nM, 250 nM, 300 nM, 350 nM, 400 nM, 450 nM, 500 nM, 550 nM, 600 nM, 650 nM, 700 nM, 750 nM, 800 nM, 850 nM, 900 nM, or 950 nM. In certain embodiments described herein, the cell(s) is contacted or cultured with a certain concentration of a compound of Formula (I) or a form thereof, or a tissue sample is contacted with a certain concentration of a compound of Formula (I) or a form thereof, wherein the certain concentration is between 0.0001 μ M to 0.001 μ M, 0.0001 μ M to 0.01 μ M, 0.0003 μ M to 0.001 μ M, 0.0003 μ M to 0.01 μ M, 0.001 μ M to 0.01 μ M, 0.003 μ M to 0.01 μ M, 0.01 μ M to 0.1 μ M, 0.1 μ M to 1 μ M, 1 μ M to 50 μ M, 50 μ M to 100 μ M, 100 μ M to 500 μ M, 500 μ M to 1 nM, 1 nM to 10 nM, 10 nM to 50 nM, 50 nM to 100 nM, 100 nM to 500 nM, 500 nM to 1000 nM.

[00844] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (e.g., an mRNA transcript), comprising: (a) administering a compound of Formula (I) or a form thereof to a subject (in certain embodiments, a non-human animal); and (b) determining the amount of the RNA transcript in a sample obtained from the subject, wherein an alteration in the amount of the RNA transcript measured in the sample from the subject administered the compound or form thereof relative to the amount of the RNA transcript in a sample from the subject prior to administration of the compound or form thereof or a sample from a different subject from the same species not administered the compound or form thereof indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the amount of an RNA transcript (e.g., an mRNA transcript), comprising: (a) administering a compound of Formula (I) or a form thereof to a first subject (in certain embodiments, a non-human animal); (b) administering a negative control (e.g., a pharmaceutical carrier) to a second subject (in certain embodiments, a non-human animal) of the same species as the first subject; and (c) determining the amount of the RNA transcript in a first tissue sample from the first subject and the amount of the RNA transcript in the second tissue sample from the second subject; and (d) comparing the amount of the RNA transcript in the first tissue sample to the amount of the RNA transcript in the second tissue sample, wherein an alteration in the amount of the RNA transcript in the first tissue sample relative to the amount of the RNA transcript in the second tissue sample indicates that the compound of Formula (I) or a form thereof modulates the amount of the RNA transcript. In certain embodiments, a compound of Formula (I) or form thereof is administered to a subject at a dose of about 0.001 mg/kg/day to about 500 mg/kg/day. In some embodiments, a single dose of a compound of Formula (I) or a form thereof is administered to a subject in accordance with the methods described herein. In other embodiments, 2, 3, 4, 5 or more doses of a compound of Formula (I) is administered to a subject in accordance with the methods described herein. In specific embodiments, the compound of Formula (I) or a form thereof is administered in a subject in a pharmaceutically acceptable carrier, excipient or diluent.

[00845] In another embodiment, provided herein is a method for determining whether a compound of Formula (I) or a form thereof modulates the splicing of an RNA transcript (e.g., an

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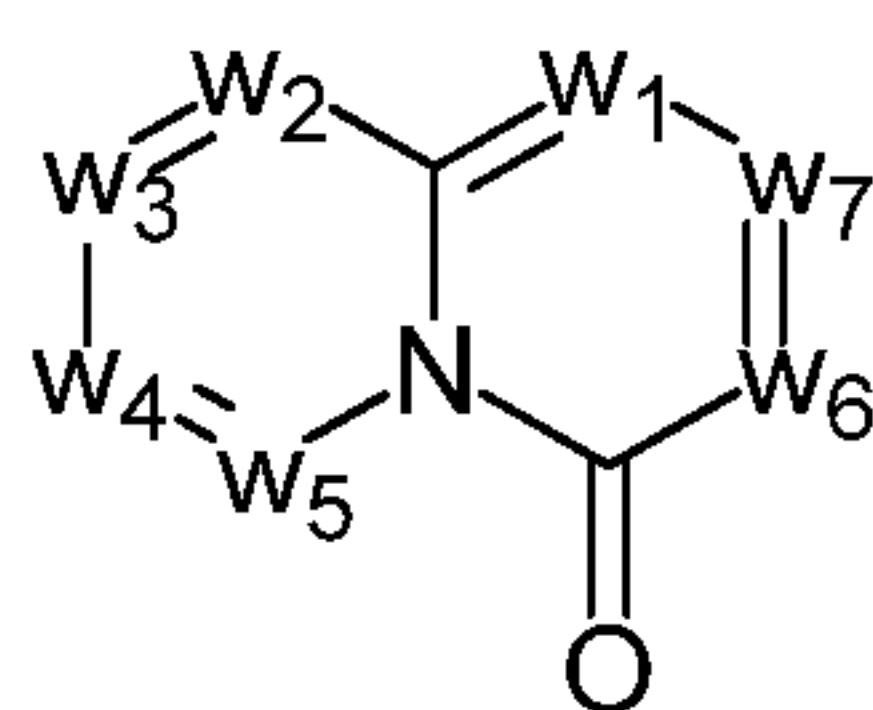
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What is claimed is:

1. A method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a pre-mRNA transcript with a compound of Formula (I) or a form thereof, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCB8, ABCC3, ADAM17, ADCY3, AGPAT4, ANKRA2, ANXA11, APIP, APPL2, ARHGAP1, ARL15, ASAP1, ASPH, ATAD2B, ATXN1, BECN1, BHMT2, BICD1, BTN3A1, C11orf30, C11orf73, C12orf4, C14orf132, C8orf44, C8orf44-SGK3, C8orf88, CASC3, CASP7, CCDC122, CDH13, CECR7, CENPI, CEP112, CEP192, CHEK1, CMAHP, CNRIP1, COPS7B, CPSF4, CRISPLD2, CRYBG3, CSNK1E, CSNK1G1, DCAF17, DCUN1D4, DDX42, DENND1A, DENND5A, DGKA, DHFR, DIAPH3, DNAJC13, DNMBP, DOCK1, DYRK1A, EIF2B3, ENAH, ENOX1, EP300, ERC1, ERLIN2, ERFFI1, EVC, FAF1, FAIM, FAM126A, FAM13A, FAM162A, FAM174A, FBN2, FER, FHOD3, FOCAD, GALC, GCFC2, GGACT, GLCE, GOLGA4, GOLGB1, GPSM2, GULP1, GXYLT1, HDX, HLTF, HMGA2, HNMT, HSD17B12, HSD17B4, HTT, IFT57, IVD, KDM6A, KIAA1524, KIAA1715, LETM2, LOC400927, LRRC42, LUC7L3, LYRM1, MB21D2, MCM10, MED13L, MEDAG, MEMO1, MFN2, MMS19, MRPL45, MRPS28, MTERF3, MYCBP2, MYLK, MYOF, NGF, NREP, NSUN4, NT5C2, OSMR, OXCT1, PAPD4, PCM1, PDE7A, PDS5B, PDXDC1, PIGN, PIK3CD, PIK3R1, PIKFYVE, PITPNB, PLEKHA1, PLSCR1, PMS1, POMT2, PPARG, PPIP5K2, PPP1R26, PRPF31, PRSS23, PSMA4, PXX, RAF1, RAPGEF1, RARS2, RBKS, RERE, RFWD2, RPA1, RPS10, SAMD4A, SAR1A, SCO1, SEC24A, SENP6, SERGEF, SGK3, SLC12A2, SLC25A17, SLC44A2, SMYD3, SNAP23, SNHG16, SNX7, SOS2, SPATA5, SPIDR, SPRYD7, SRGAP1, SRRM1, STAT1, STXBP6, SUPT20H, TAF2, TASP1, TBC1D15, TCF12, TCF4, TIAM1, TJP2, TMC3, TMEM214, TNRC6A, TNS3, TOE1, TRAF3, TSPAN2, TTC7B, TYW5, UBAP2L, URGCP, VAV2, WDR27, WDR37, WDR91, WNK1, XRN2, ZCCHC8, ZFP82, ZNF138, ZNF232 or ZNF37BP, and wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino; wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

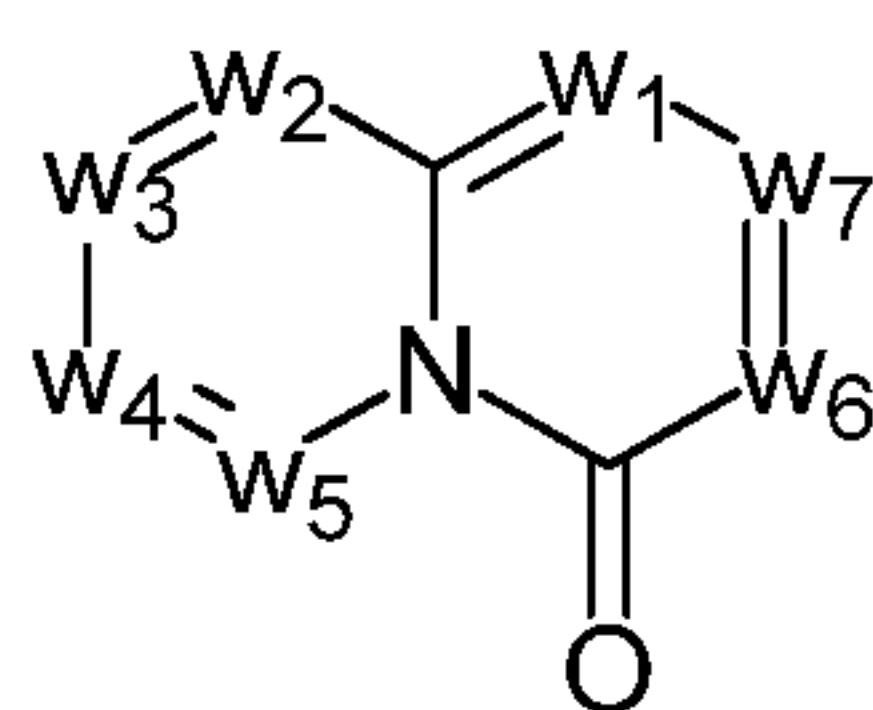
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

2. A method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting the pre-mRNA transcript with a compound of Formula (I) or a form thereof, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: an endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein the pre-mRNA transcript is a pre-mRNA transcript of a gene that is selected from ABCA10, ABCB8, ABCC3, ACTA2, ADAL, ADAMTS1, ADCY3, ADD1, ADGRG6, ADH6, ADHFE1, AFF3, AGPAT4, AKAP3, ANK1, ANK3, ANKRA2, ANKRD33B, ANKRD36, AP4B1-AS1, APIP, ARHGAP1, ARHGAP12, ARHGEF16, ARID5B, ARL15, ARL9, ARM CX6, ASIC1, ATG5, ATP2A3, ATXN1, B3GALT2, B3GNT6, BCL2L15, BCYRN1, BECN1, BHMT2, BIN3-IT1, BIRC3, BIRC6, BTG2, BTN3A1, C10orf54, C11orf70, C11orf94, C12orf4, C12orf56, C14orf132, C19orf47, C1orf86, C3, C7orf31, C8orf34, C8orf44, C8orf44-SGK3, C8orf88, CA13, CA3, CACNA2D2, CACNB1, CADM1, CAND2, CASP7, CCDC122, CCDC79, CCER2, CCNF, CECR7, CELSR1, CEMIP, CENPI, CEP112, CEP170, CEP192, CFH, CHEK1, CIITA, CLDN23, CLTA, CMAHP, CNGA4, CNRIP1, CNTD1, COL11A1, COL14A1, COL15A1, COL5A1, COL5A3, COL6A6, COL8A1, COLEC12, COMP, CPA4, CPQ, CPSF4, CRISPLD2, CRLF1, CRYBG3, CRYL1, CSNK1E, CSNK1G1, CYB5R2, CYGB, CYP1B1, DAGLB, DCAF17, DCLK1, DCN, DDIT4L, DDX50, DEGS1, DEPTOR, DFNB59, DIRAS3, DLG5, DLGAP4, DNAH8, DNAJC13, DNAJC27, DNMBP, DOCK11, DYNC1I1, DYRK1A, DZIP1L, EFEMP1, EGR3, ELN, ELP4, EMX2OS, ENAH, ENPP1, EP300, ERCC1, ERCC8, ERGIC3, ERLIN2, ERFFI1, ESM1, EVC, EVC2, F2R, FAIM, FAM126A, FAM13A, FAM160A1, FAM162A, FAM174A, FAM20A, FAM46B, FAM65B, FAP, FARP1, FBLN2, FBN2, FBXL6, FCHO1, FGFR2, FGL2, FLT1, FRAS1, FSCN2, GAL3ST4, GALNT15, GATA6, GBGT1, GCNT1, GDF6, GGACT, GLCE, GNAQ, GPR183, GPR50, GPRC5A, GPRC5B, GRTP1, GUCA1B, GULP1, GXYLT1, HAPLN1, HAPLN2, HAS3, HAVCR2, HDAC5, HDX, HECTD2-AS1, HEPH, HEY1, HMGA2, HMGN3-AS1, HNMT, HOOK3, HPS1, HSPA1L, HTATIP2, IFT57, IGDCC4, IGF2R, IGFBP3, IL16, INA, INPP5K, INTU, IQCG, ITGA11, ITGA8, ITGB8, ITIH1, ITPKA, IVD,

KAT6B, KCNS1, KCNS2, KDM6A, KDSR, KIAA1456, KIAA1462, KIAA1755, KIT, KLF17, KLRG1, KMT2D, KRT7, KRTAP1-1, KRTAP1-5, L3MBTL2, LAMB2P1, LETM2, LGI2, LGR4, LHX9, LINC00472, LINC00570, LINC00578, LINC00607, LINC00678, LINC00702, LINC00886, LINC00961, LINC01011, LINC01118, LINC01204, LMOD1, LOC400927, LRBA, LRP4, LRRC32, LRRC39, LRRC42, LSAMP, LUM, LYPD1, LYRM1, MAFB, MAMDC2, MAN2A1, MAN2C1, MAPK13, MASP1, MB, MB21D2, MC4R, MCM10, MED13L, MEGF6, MFN2, MIAT, MIR612, MLLT10, MMP10, MMP24, MN1, MOXD1, MRPL45, MRPL55, MRPS28, MRVI1, MSH4, MTERF3, MXRA5, MYCBP2, NA, NAALADL2, NAE1, NAGS, NDNF, NGF, NGFR, NHLH1, NLN, NOTCH3, NOTUM, NOVA2, NOX4, NRROS, OCLN, OLR1, OSBPL10, OXCT1, OXCT2, PAIP2B, PBLD, PDE1C, PDE5A, PDGFD, PDGFRB, PDS5B, PEAR1, PHACTR3, PIGN, PIK3CD, PIK3R1, PIKFYVE, PIM2, PITPNM3, PLEK2, PLEKHA1, PLEKHA6, PLEKHH2, PLSCR1, PNISR, PODN, POLN, POLR1A, POMT2, PPARG, PPIP5K2, PPM1E, PPP1R26, PPP3CA, PRKCA, PRKG1, PRPF31, PRPH2, PRRG4, PRUNE2, PSMD6-AS2, PTGIS, PTX3, P XK, RAB30, RAB38, RAB44, RAD9B, RAF1, RAPGEF1, RARS, RARS2, RBBP8, RBKS, RDX, RERE, RFX3-AS1, RGCC, ROR1, ROR2, RPA1, RPS10, RPS6KB2, SAMD4A, SCARNA9, SEC24A, SENP6, SERGEF, SGK3, SH3YL1, SHROOM3, SIGLEC10, SKA2, SLC12A2, SLC24A3, SLC35F3, SLC39A10, SLC44A2, SLC46A2, SLC4A11, SLC6A15, SLC7A11, SLC9A3, SLIT3, SMG1P3, SMTN, SNED1, SNX7, SORBS2, SORCS2, SOX7, SPATA18, SPATA5, SPDYA, SPEF2, SPIDR, SPRYD7, SRGAP1, SRRM1, STAC2, STAT4, STK32B, STRN4, STS, STXBP6, SULF1, SVEP1, SYNGR2, SYNPO, SYNPO2, SYNPO2L, TAGLN3, TANGO6, TASP1, TCF12, TCF4, TGFA, TGFB2, TGFB3, TGM2, THBS2, TIAM1, TMC3, TMEM102, TMEM119, TMEM134, TMEM189-UBE2V1, TMEM214, TMEM256-PLSCR3, TMEM50B, TNFAIP8L3, TNFRSF14, TNRC18P1, TNRC6A, TNXB, TP53AIP1, TPRG1, TRIM66, TRPC4, TSHZ2, TSPAN11, TSPAN18, TSPAN7, TSSK3, TTC7B, TUBE1, TXNIP, TYW5, URGCP, USP27X, UVRAG, VAV2, VIM-AS1, VPS41, VSTM2L, VWF, WDR27, WDR91, WISP1, WNK1, WNT10B, YDJC, ZBTB26, ZCCHC5, ZCCHC8, ZFP82, ZMIZ1-AS1, ZNF138, ZNF212, ZNF232, ZNF350, ZNF431, ZNF660, ZNF680, ZNF79, or ZNF837, and, wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino; wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

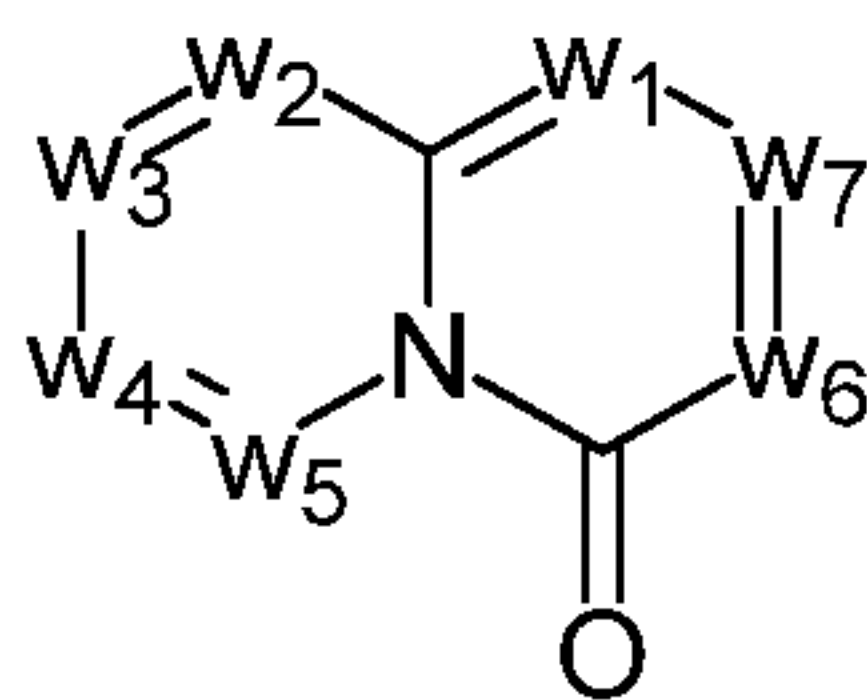
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

3. The method of claim 2, wherein the intron further comprises a first 5' splice site, a second branch point, and a second 3' splice site upstream of the iREMS.

4. A method for producing a mature mRNA transcript comprising an iExon, the method comprising contacting a pre-mRNA transcript with a compound of Formula (I) or a form thereof, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, a non-endogenous intronic recognition element for splicing modifier (iREMS), a second branch point, and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,
 (amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,
 C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,
 (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,
 C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,
 C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,
 (halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,
 hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,
 (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,
 (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,
 (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,
 [(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl, heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino, heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino, (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl, (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino; wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

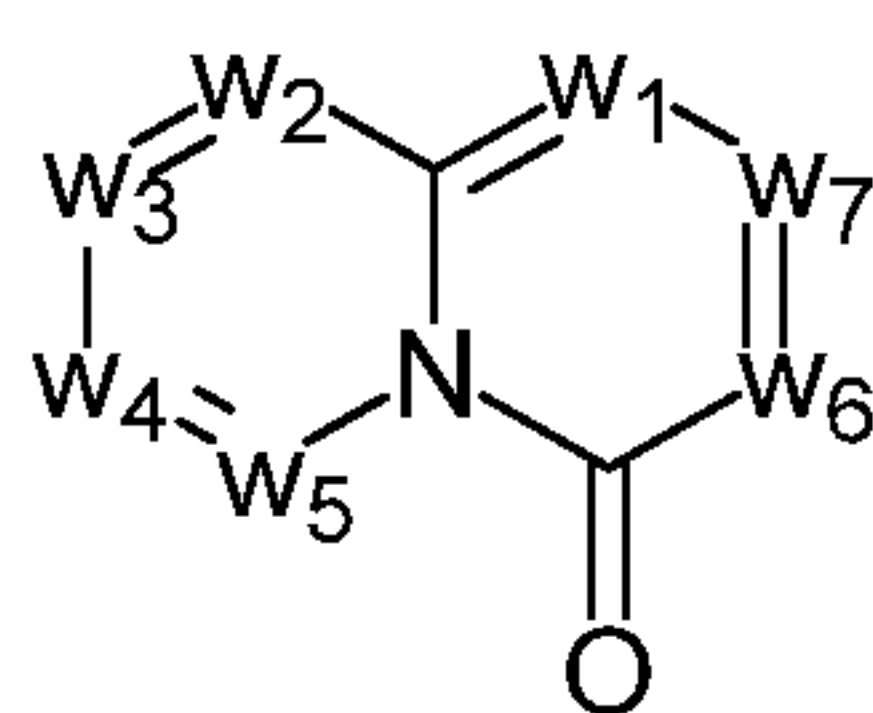
R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and,

R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

5. A method for modulating the amount of a mature mRNA transcript produced by a pre-mRNA transcript, the method comprising contacting the pre-mRNA transcript with the a compound of Formula (I) or a form thereof, wherein the pre-mRNA transcript comprises two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the intron comprises a RNA nucleotide sequence comprising in 5' to 3' order: a non-endogenous intronic recognition element for splicing modifier (iREMS), a first branch point, and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide, and wherein wherein Formula (I) is:



(I),

wherein:

w₁ and w₅ are independently C-R_a or N;

w₂ is C-R_b or N;

w₃, w₄ and w₇ are independently C-R₁, C-R₂, C-R_a or N;

w₆ is C-R₁, C-R₂, C-R_c or N;

wherein one of w₃, w₄, w₆ and w₇ is C-R₁ and one other of w₃, w₄, w₆ and w₇ is C-R₂, provided that,

when w₃ is C-R₁, then w₆ is C-R₂ and w₄ and w₇ are independently C-R_a or N; or,

when w₃ is C-R₂, then w₆ is C-R₁ and w₄ and w₇ are independently C-R_a or N; or,

when w₄ is C-R₁, then w₇ is C-R₂ and w₃ is C-R_a or N and w₆ is C-R_c or N; or,

when w₄ is C-R₂, then w₇ is C-R₁ and w₃ is C-R_a or N and w₆ is C-R_c or N; and,

wherein any one, two or three of w₁, w₂, w₃, w₄, w₅, w₆ and w₇ may optionally be N;

R₁ is C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino,

(amino-C₁₋₈alkyl)₂-amino, (amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

[(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, amino-C₁₋₈alkoxy,

C₁₋₈alkyl-amino-C₁₋₈alkoxy, (C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy,

(C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy, amino-C₂₋₈alkenyl,

C₁₋₈alkyl-amino-C₂₋₈alkenyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkenyl, amino-C₂₋₈alkynyl,

C₁₋₈alkyl-amino-C₂₋₈alkynyl, (C₁₋₈alkyl)₂-amino-C₂₋₈alkynyl, halo-C₁₋₈alkyl-amino,

(halo-C₁₋₈alkyl)₂-amino, (halo-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl,

hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkoxy, (hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkoxy,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkoxy,

hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino,

(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino,

(hydroxy-C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino,

(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl-amino,

[(hydroxy-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino,
 [(hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, heterocyclyl,
 heterocyclyl-C₁₋₈alkyl, heterocyclyl-C₁₋₈alkoxy, heterocyclyl-amino,
 (heterocyclyl)(C₁₋₈alkyl)amino, heterocyclyl-amino-C₁₋₈alkyl,
 heterocyclyl-C₁₋₈alkyl-amino, (heterocyclyl-C₁₋₈alkyl)₂-amino,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heterocyclyl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl,
 (heterocyclyl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heterocyclyl-oxy,
 heterocyclyl-carbonyl, heterocyclyl-carbonyl-oxy, C₃₋₁₄cycloalkyl, aryl-C₁₋₈alkyl-amino,
 (aryl-C₁₋₈alkyl)₂-amino, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, aryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (aryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, (aryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl, heteroaryl,
 heteroaryl-C₁₋₈alkyl, heteroaryl-C₁₋₈alkoxy, heteroaryl-amino,
 heteroaryl-C₁₋₈alkyl-amino, (heteroaryl-C₁₋₈alkyl)₂-amino,
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino, heteroaryl-C₁₋₈alkyl-amino-C₁₋₈alkyl,
 (heteroaryl-C₁₋₈alkyl)₂-amino-C₁₋₈alkyl or
 (heteroaryl-C₁₋₈alkyl)(C₁₋₈alkyl)amino-C₁₋₈alkyl;

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two or three R₃ substituents and optionally, with one additional R₄ substituent; or,

wherein, each instance of heterocyclyl, C₃₋₁₄cycloalkyl, aryl and heteroaryl is optionally substituted with one, two, three or four R₃ substituents;

R₂ is aryl, aryl-amino, aryl-amino-carbonyl, heterocyclyl, heteroaryl or heteroaryl-amino;

wherein, each instance of aryl, heterocyclyl and heteroaryl is optionally substituted with one, two or three R₆ substituents and optionally, with one additional R₇ substituent;

R_a is, in each instance, independently selected from hydrogen, halogen, C₁₋₈alkyl or deuterium;

R_b is hydrogen, halogen, C₁₋₈alkyl, C₁₋₈alkoxy or deuterium;

R_c is hydrogen, halogen, C₁₋₈alkyl or deuterium;

R₃ is, in each instance, independently selected from cyano, halogen, hydroxy, oxo, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkyl-carbonyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy,

C₁₋₈alkoxy-C₁₋₈alkyl, C₁₋₈alkoxy-carbonyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino,

amino-C₁₋₈alkyl, C₁₋₈alkyl-amino-C₁₋₈alkyl, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl, amino-C₁₋₈alkyl-amino, C₁₋₈alkyl-amino-C₁₋₈alkyl-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)₂-amino, (C₁₋₈alkyl)₂-amino-C₁₋₈alkyl-amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl]₂-amino, (C₁₋₈alkyl-amino-C₁₋₈alkyl)(C₁₋₈alkyl)amino, [(C₁₋₈alkyl)₂-amino-C₁₋₈alkyl](C₁₋₈alkyl)amino, C₁₋₈alkoxy-C₁₋₈alkyl-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)₂-amino, (C₁₋₈alkoxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino, C₁₋₈alkyl-carbonyl-amino, C₁₋₈alkoxy-carbonyl-amino, hydroxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkoxy-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl-amino, (hydroxy-C₁₋₈alkyl)₂-amino or (hydroxy-C₁₋₈alkyl)(C₁₋₈alkyl)amino;

R₄ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-C₁₋₈alkyl, C₃₋₁₄cycloalkyl-amino, aryl-C₁₋₈alkyl, aryl-C₁₋₈alkoxy-carbonyl, aryl-sulfonyloxy-C₁₋₈alkyl, heterocyclyl or heterocyclyl-C₁₋₈alkyl; wherein, each instance of C₃₋₁₄cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R₅ substituents;

R₅ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, halo-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio;

R₆ is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C₁₋₈alkyl, C₂₋₈alkenyl, halo-C₁₋₈alkyl, hydroxy-C₁₋₈alkyl, C₁₋₈alkoxy, halo-C₁₋₈alkoxy, C₁₋₈alkoxy-C₁₋₈alkyl, amino, C₁₋₈alkyl-amino, (C₁₋₈alkyl)₂-amino or C₁₋₈alkyl-thio; and, R₇ is C₃₋₁₄cycloalkyl, C₃₋₁₄cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl.

6. The method of any one of claims 1-5, wherein the iREMS comprises an RNA sequence GAguragu, and wherein r is adenine or guanine.

7. The method of any one of claims 1-5, wherein the iREMS comprises an RNA sequence NNGAgurngn (SEQ ID NO: 1), and wherein r is adenine or guanine and n or N is any nucleotide.

8. The method of claim 7, wherein the RNA sequence NNGAgurngn (SEQ ID NO: 1) is selected from the group consisting of ANGAgurngn (SEQ ID NO: 29), CNGAgurngn (SEQ ID NO: 35), GNGAgurngn (SEQ ID NO: 41), UNGAgurngn (SEQ ID NO: 47), NAGAgurngn (SEQ ID NO: 30), NCGAgurngn (SEQ ID NO: 36),

NGGAgurngn (SEQ ID NO: 42), NUGAgurngn (SEQ ID NO: 48), AAGAgurngn (SEQ ID NO: 31), ACGAgurngn (SEQ ID NO: 37), AGGAgurngn (SEQ ID NO: 43), AUGAgurngn (SEQ ID NO: 49), CAGAgurngn (SEQ ID NO: 32), CCGAgurngn (SEQ ID NO: 38), CGGAgurngn (SEQ ID NO: 44), CUGAgurngn (SEQ ID NO: 50), GAGAgurngn (SEQ ID NO: 33), GCGAgurngn (SEQ ID NO: 39), GGGAgurngn (SEQ ID NO: 45), GUGAgurngn (SEQ ID NO: 51), UAGAgurngn (SEQ ID NO: 34), UCGAgurngn (SEQ ID NO: 40), UGGAgurngn (SEQ ID NO: 46) and UUGAgurngn (SEQ ID NO: 52), wherein r is adenine or guanine and n or N is any nucleotide.

9. The method of any one of claims 1-5, wherein the iREMS comprises an RNA sequence NNGAguragu (SEQ ID NO: 3862), wherein r is adenine or guanine and N is any nucleotide.

10. The method of claim 9, wherein the RNA sequence NNGAguragu (SEQ ID NO: 3862) is selected from the group consisting of ANGAguragu (SEQ ID NO: 437), CNGAguragu (SEQ ID NO: 443), GNGAguragu (SEQ ID NO: 449), UNGAguragu (SEQ ID NO: 455), NAGAguragu (SEQ ID NO: 438), NCGAguragu (SEQ ID NO: 444), NGGAguragu (SEQ ID NO: 450), NUGAguragu (SEQ ID NO: 456), AAGAguragu (SEQ ID NO: 439), ACGAguragu (SEQ ID NO: 445), AGGAguragu (SEQ ID NO: 451), AUGAguragu (SEQ ID NO: 457), CAGAguragu (SEQ ID NO: 440), CCGAguragu (SEQ ID NO: 446), CGGAguragu (SEQ ID NO: 452), CUGAguragu (SEQ ID NO: 458), GAGAguragu (SEQ ID NO: 441), GCGAguragu (SEQ ID NO: 447), GGGAguragu (SEQ ID NO: 453), GUGAguragu (SEQ ID NO: 459), UAGAguragu (SEQ ID NO: 442), UCGAguragu (SEQ ID NO: 448), UGGAguragu (SEQ ID NO: 454) and UUGAguragu (SEQ ID NO: 460), wherein r is adenine or guanine, and N is any nucleotide.

11. An artificial gene construct comprising an RNA sequence comprising exons and one or more introns, wherein at least one intron comprises an iREMS that is downstream of a

branch point and a 3' splice site, and wherein the iREMS comprises the sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

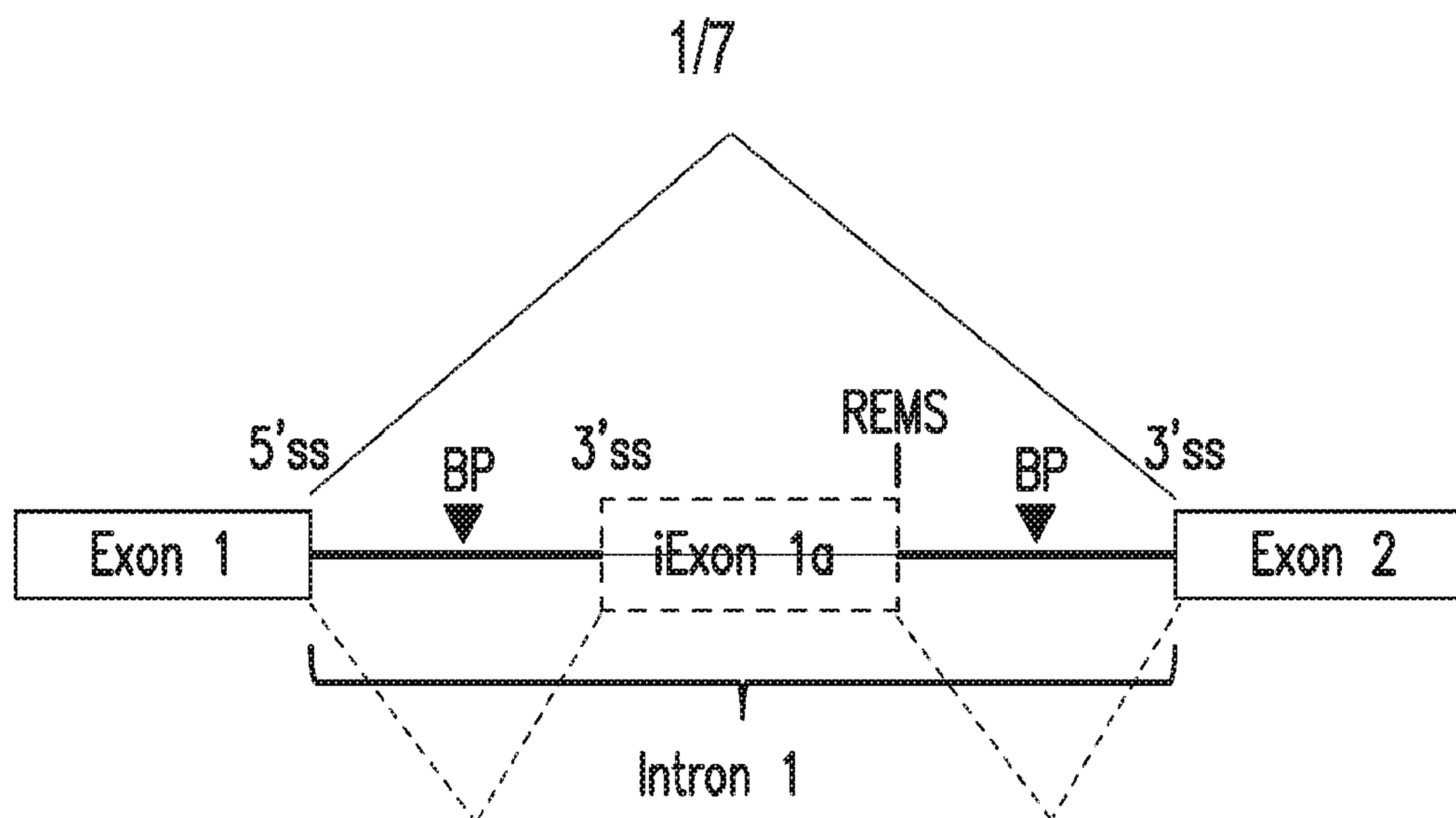
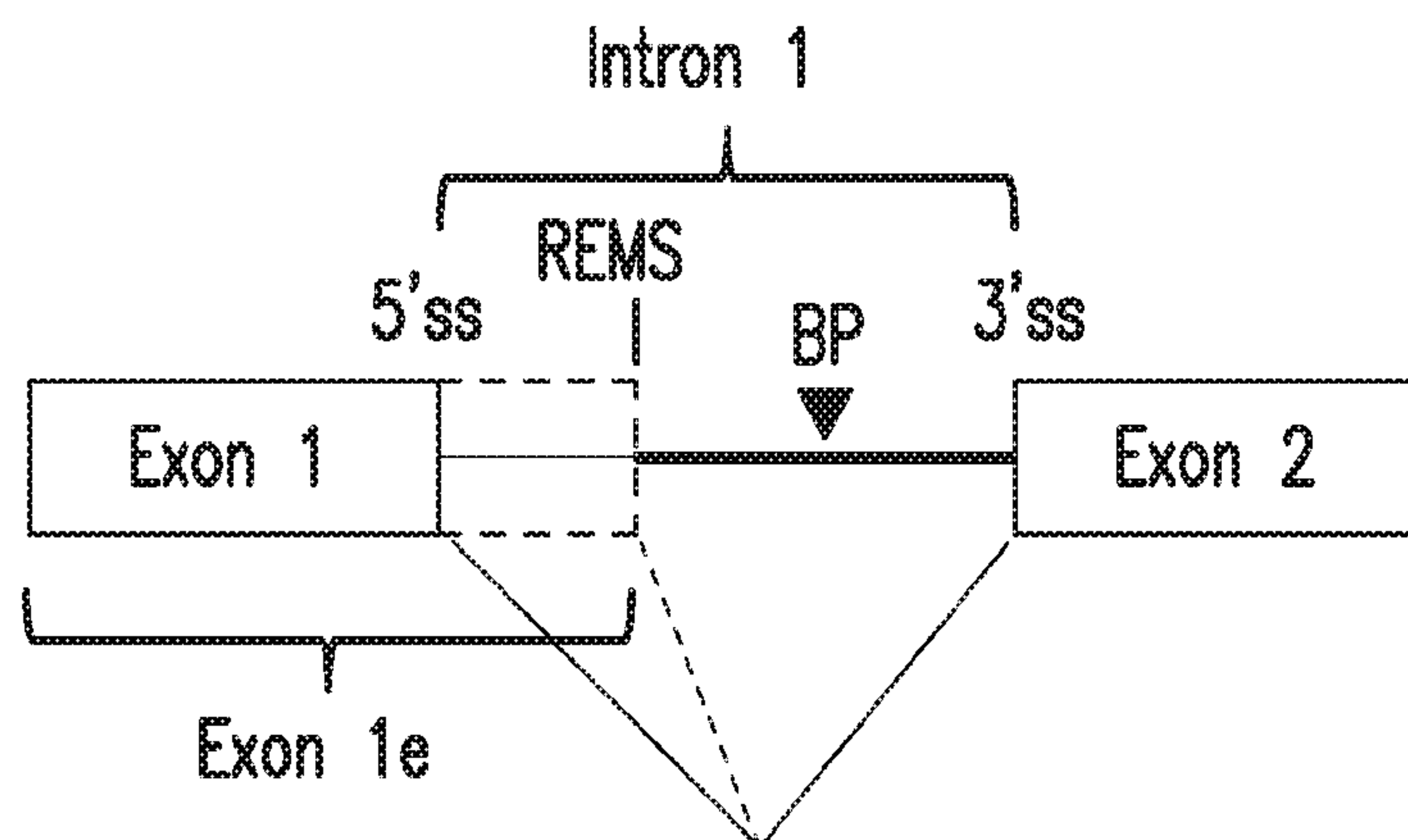
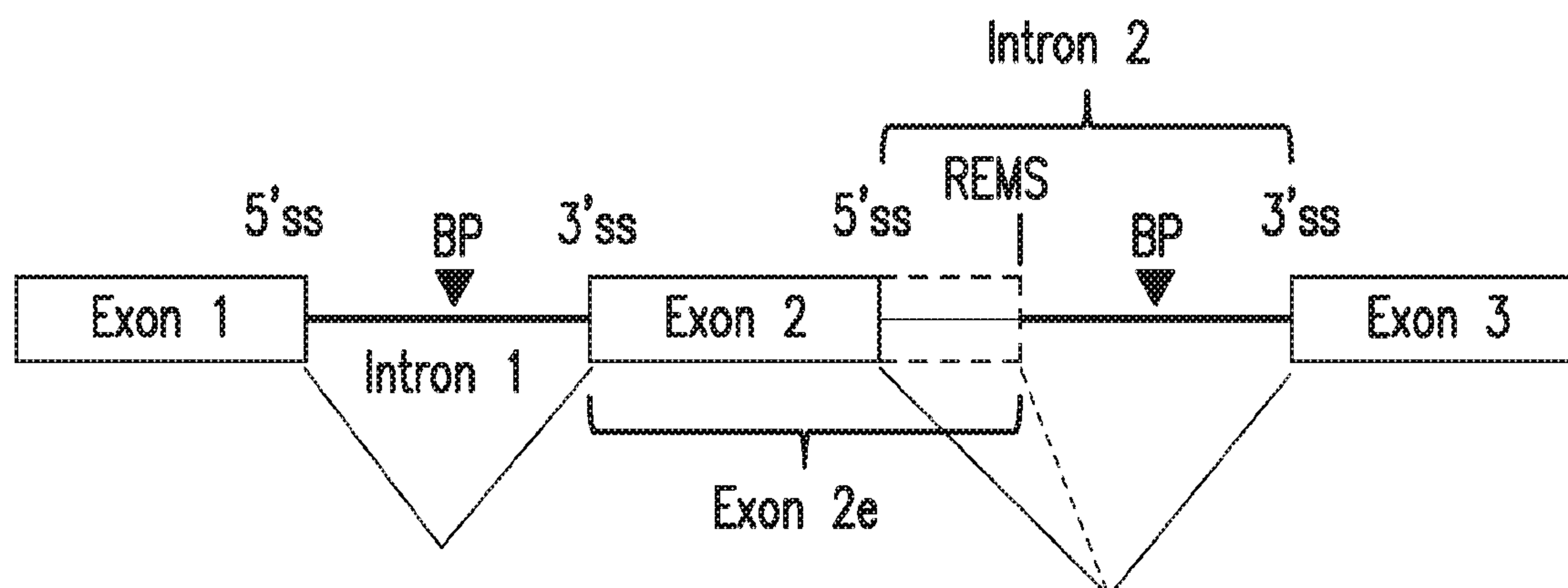
12. An artificial gene construct comprising an RNA sequence comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: a first 5' splice site, a first branch point, a first 3' splice site, an iREMS, a second branch point and a second 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

13. An artificial gene construct comprising an RNA sequence comprising two exons and an intron, wherein one exon is upstream of the intron and the other exon is downstream of the intron, wherein the RNA nucleotide sequence of the intron comprises in 5' to 3' order: an iREMS, a first branch point and a first 3' splice site, wherein the iREMS comprises an RNA sequence GAgurngn (SEQ ID NO: 2), wherein r is adenine or guanine and n is any nucleotide.

14. The method of any one of claims 1-10, wherein the pre-mRNA transcript is in a cell or a lysate of the cell and the method comprises contacting the cell or cell lysate with the compound.

15. The method of claim 14, wherein the modulation of the production of the mature mRNA transcript modulates the amount and/or type of a protein translated from the mature mRNA transcript and produced in the cell or lysate of the cell.

16. The method of any one of claims 1-10, 14 and 15, wherein the pre-mRNA transcript encodes a detectable reporter protein.

**FIG. 1A****FIG. 1B****FIG. 1C**

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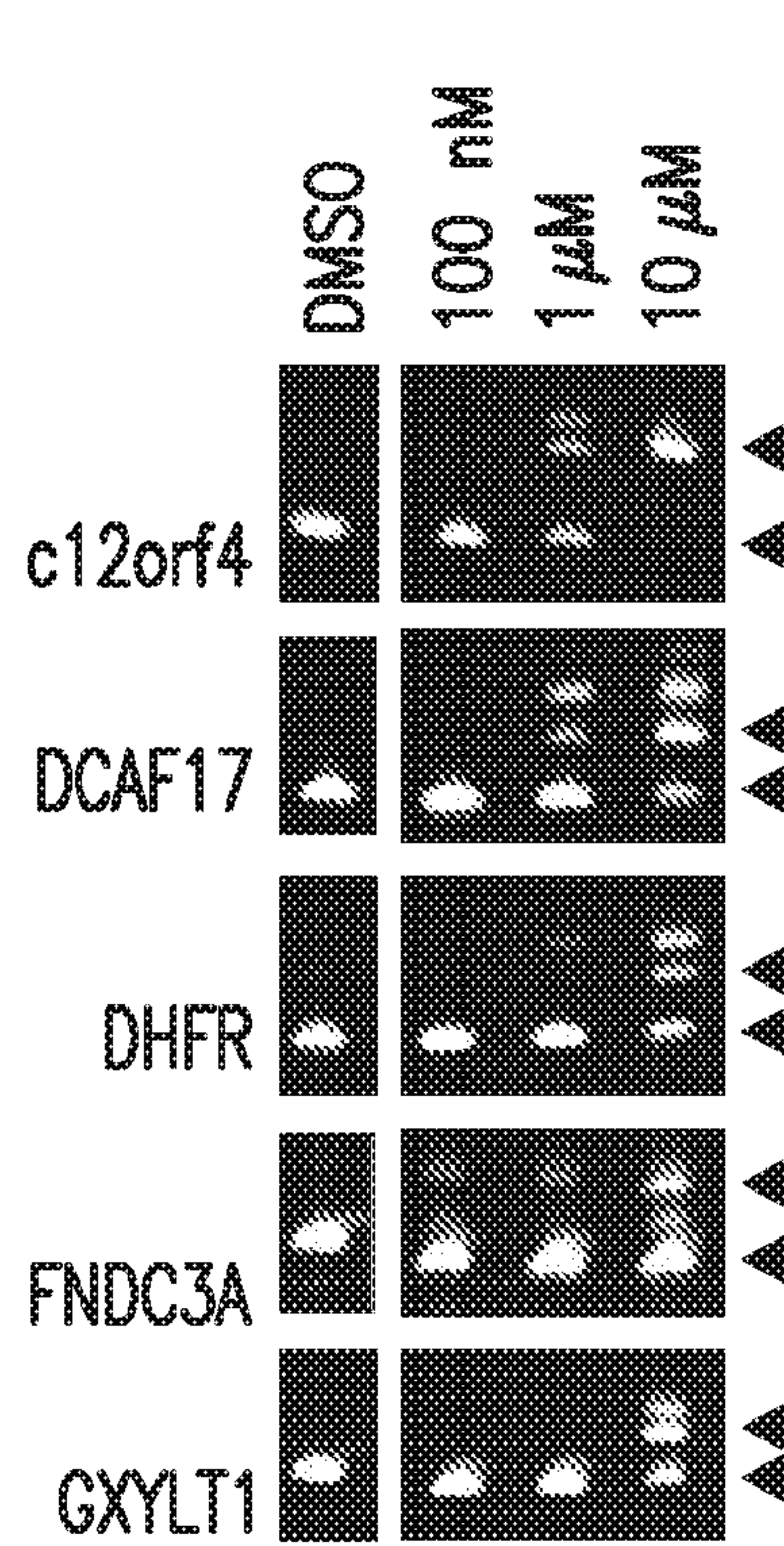


FIG. 2A

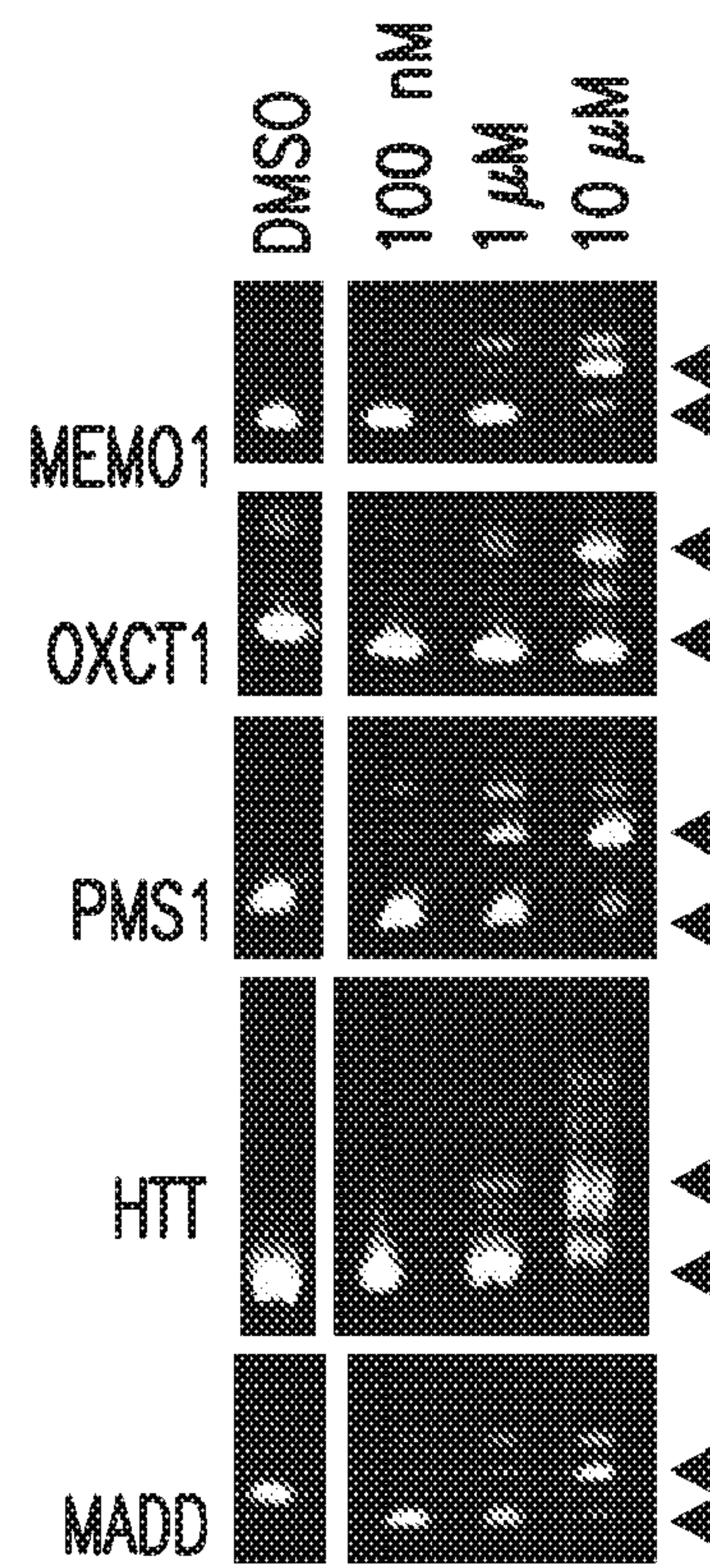


FIG. 2B

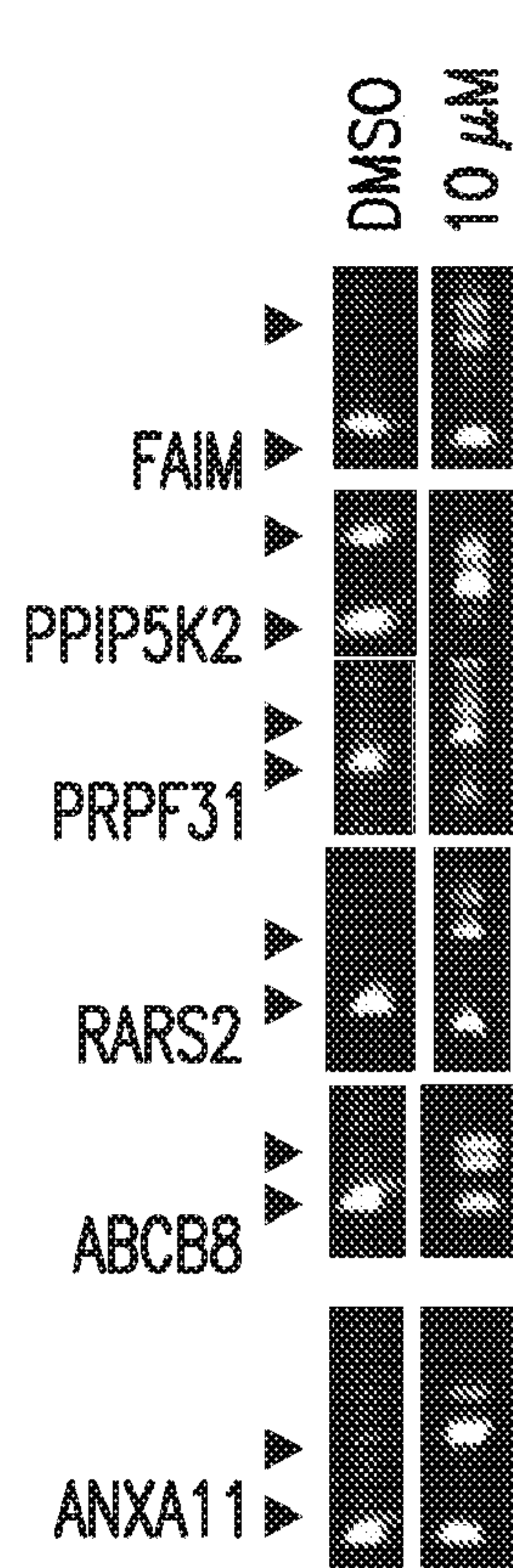


FIG. 2C

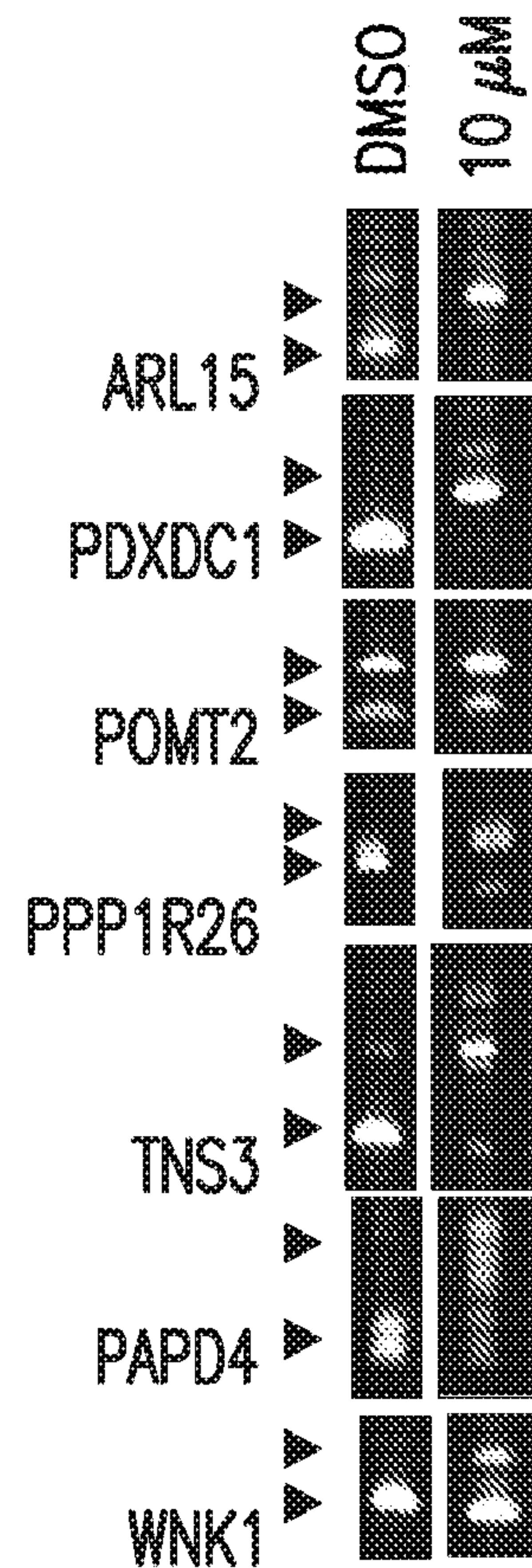


FIG. 2D

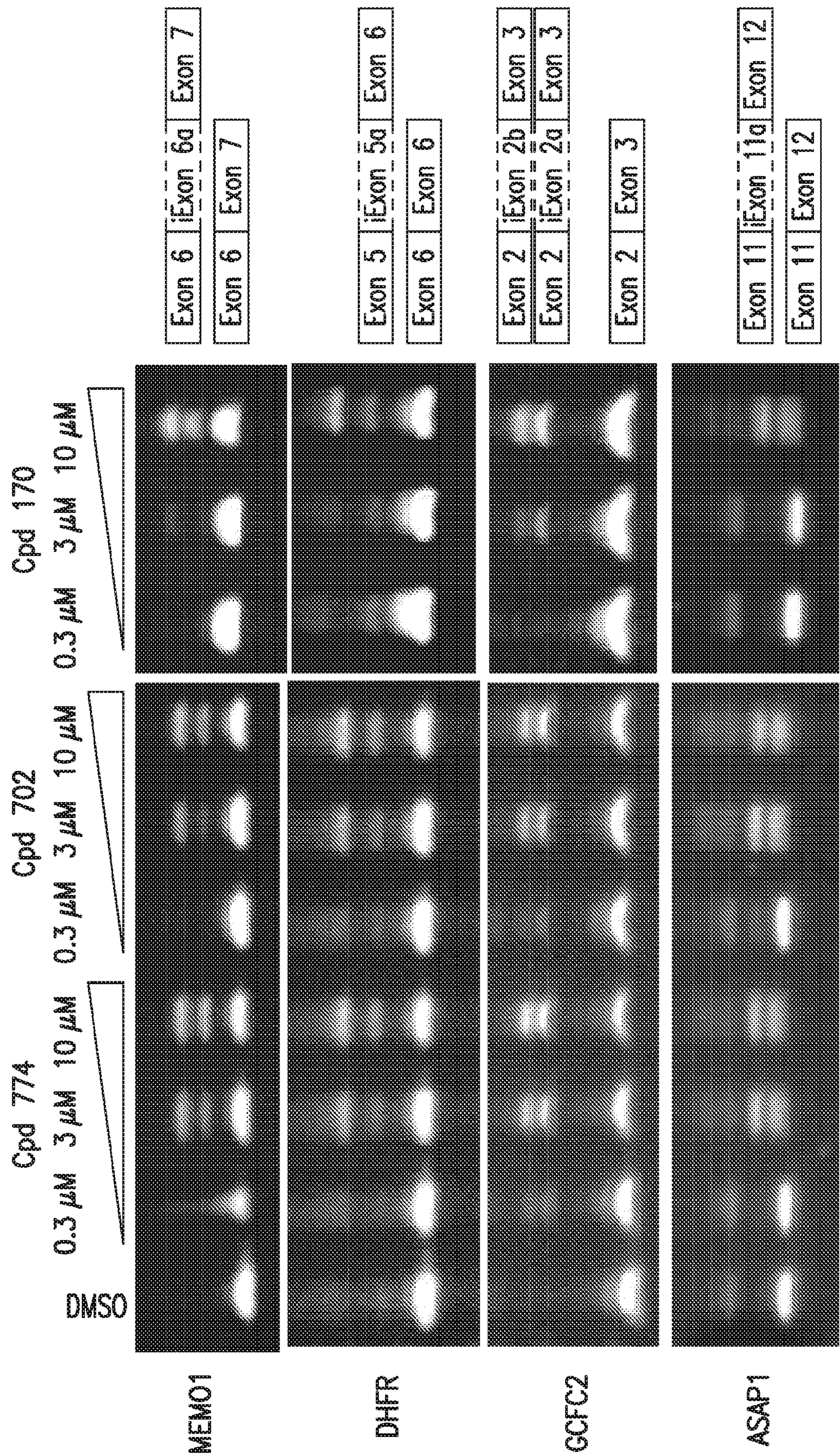


FIG. 3

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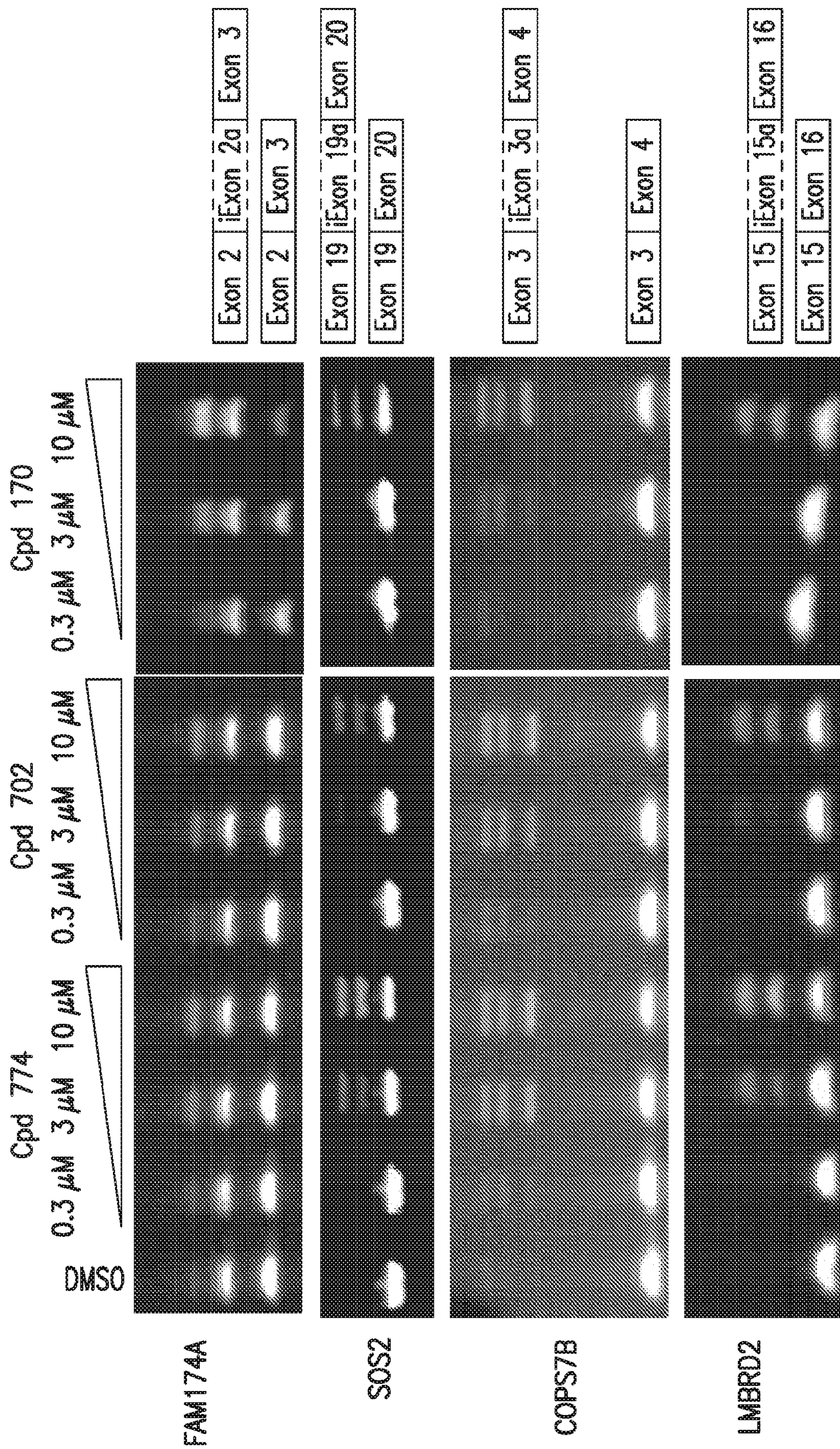


FIG. 4

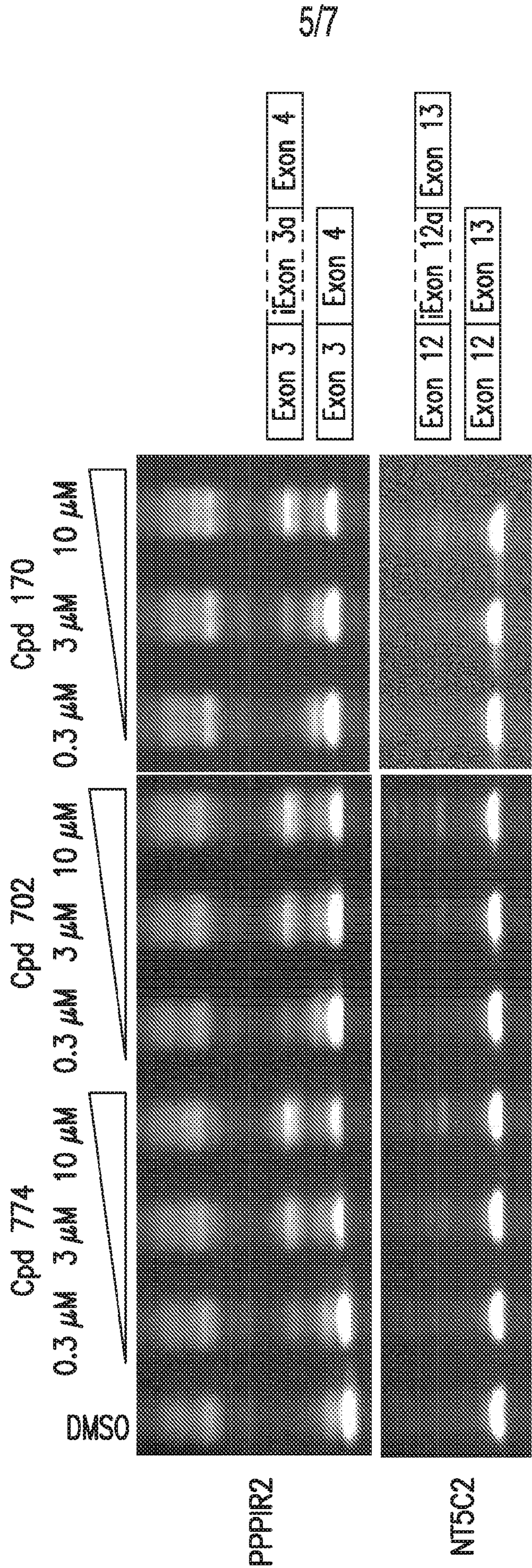


FIG. 5

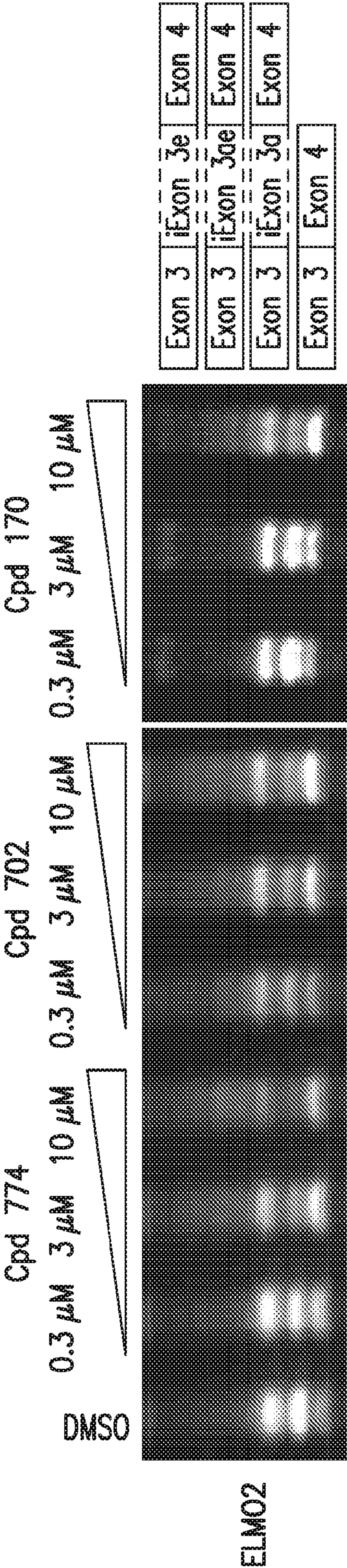


FIG. 6A

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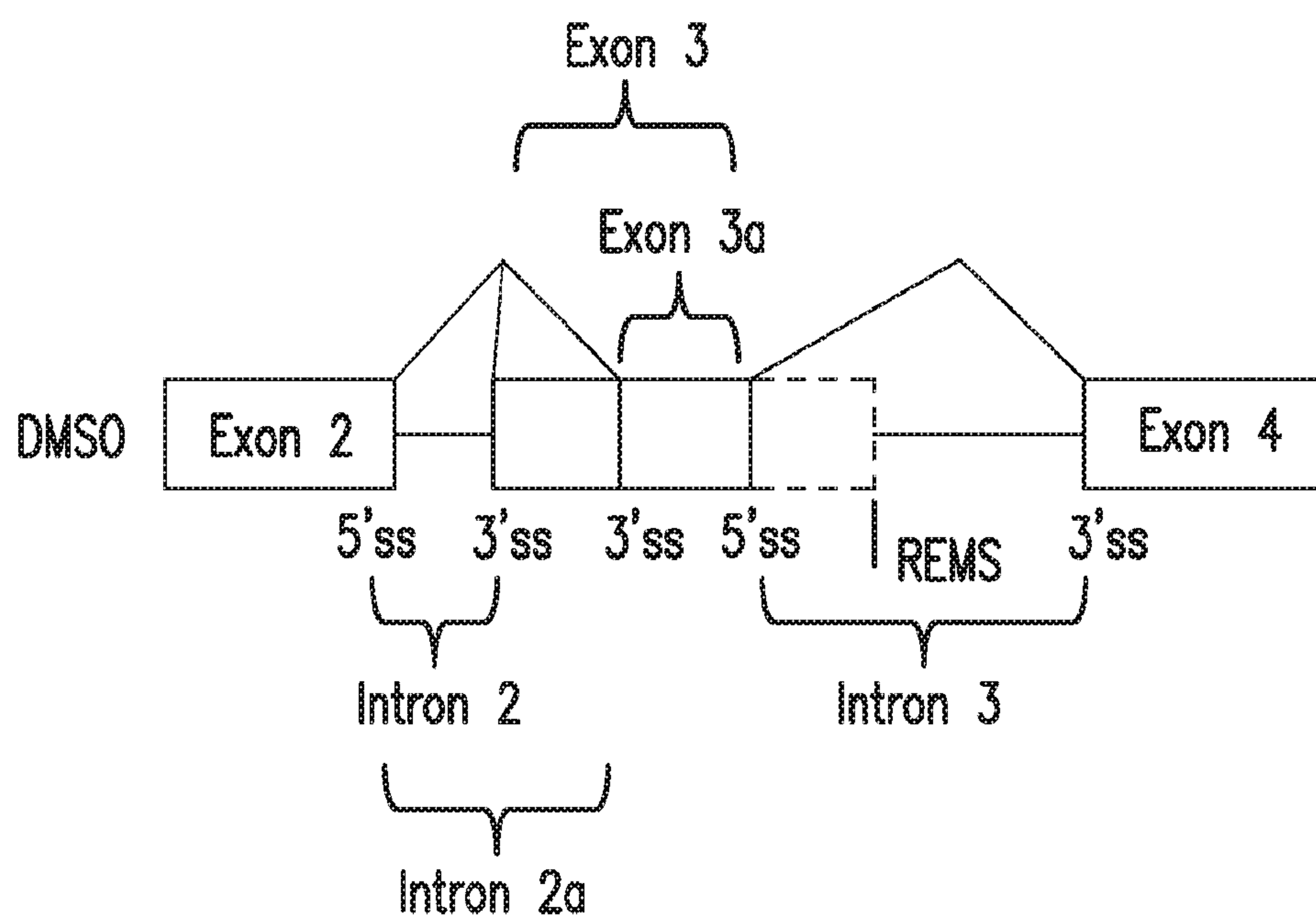


FIG. 6B

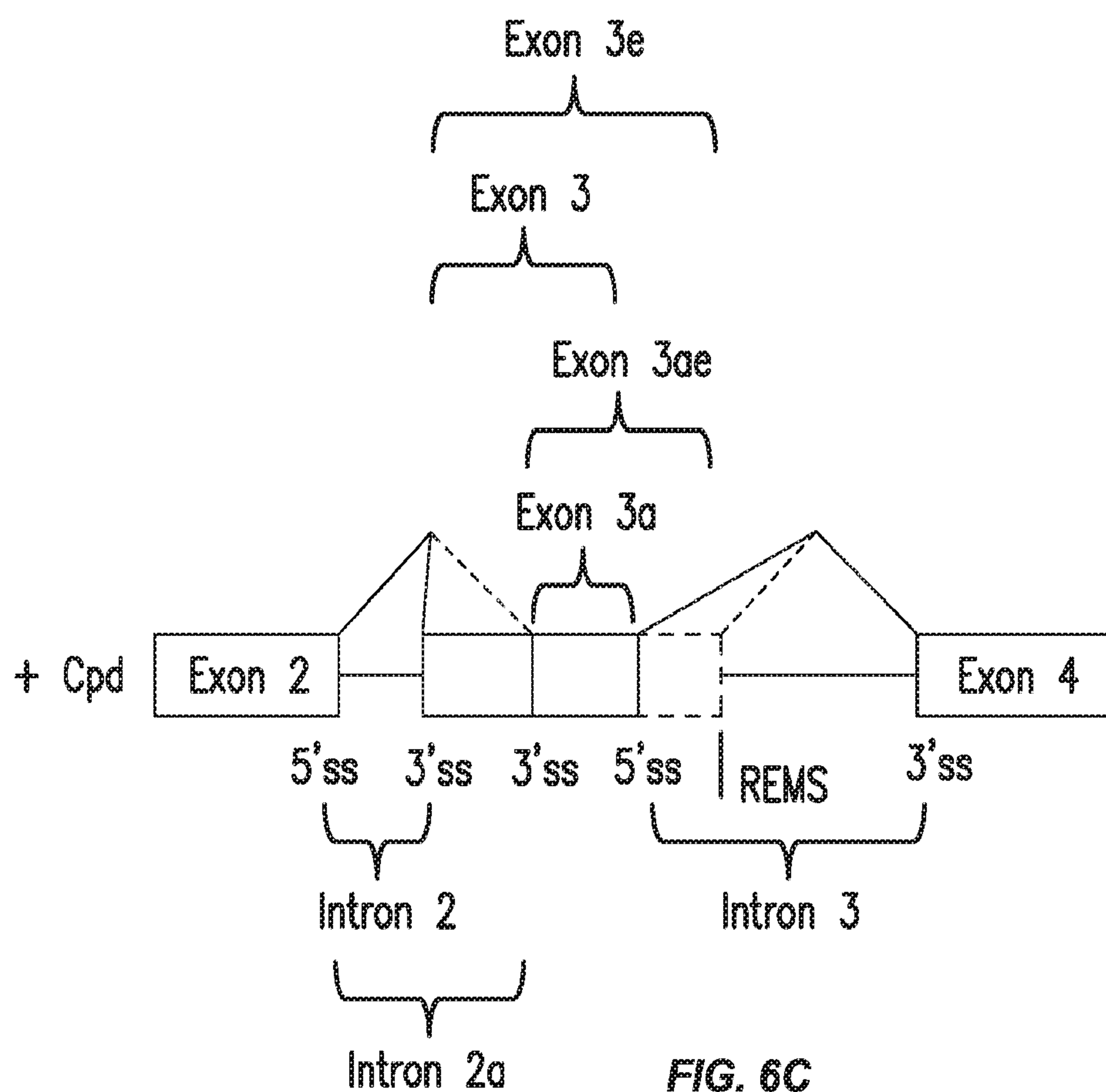


FIG. 6C

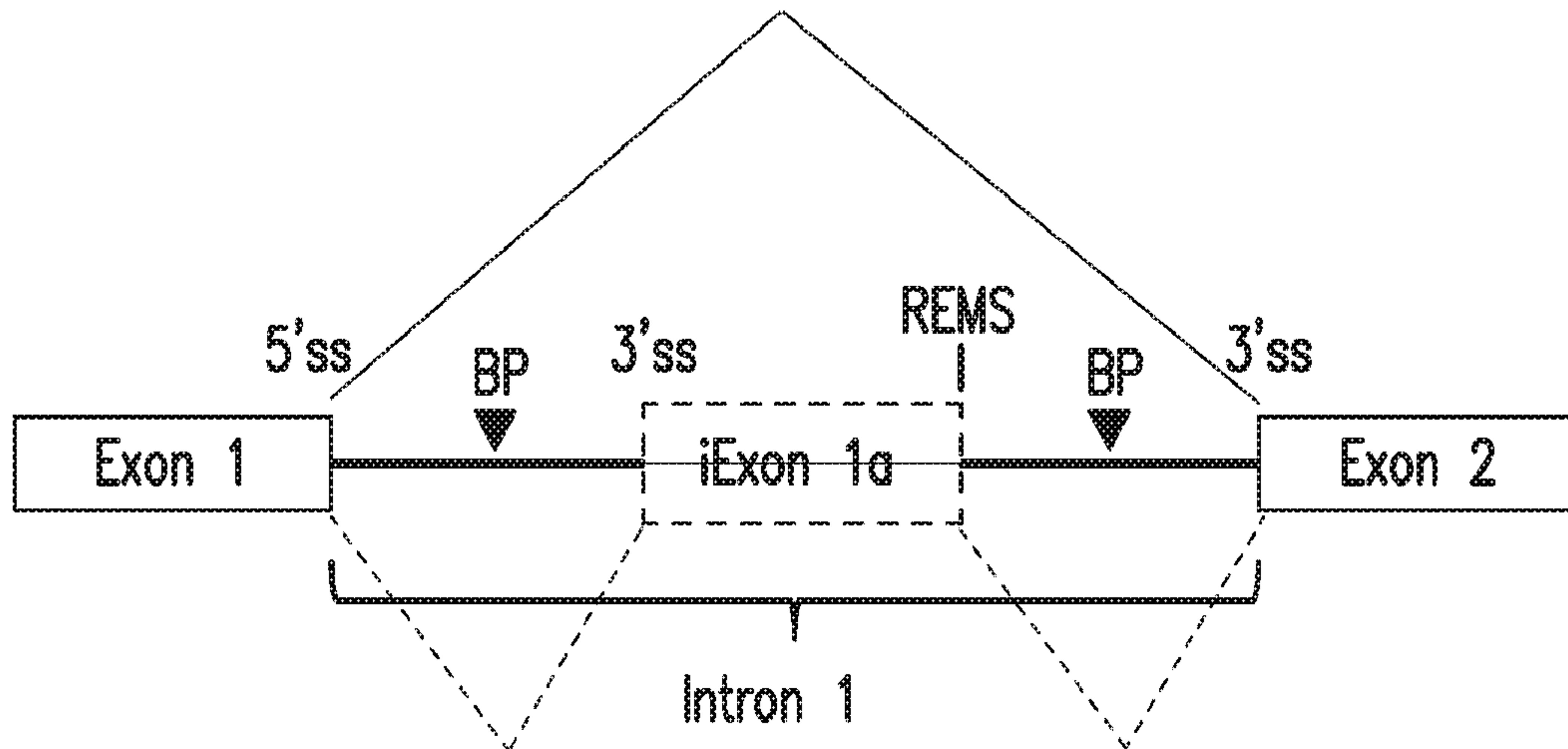


FIG. 1A