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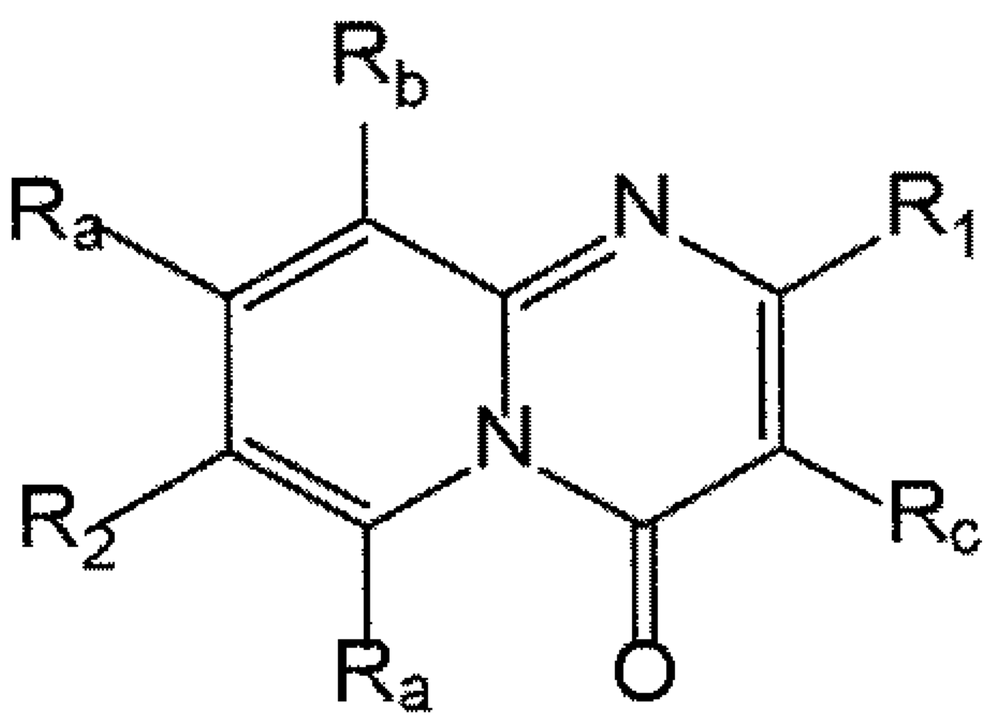
(54) Titre : METHODES DE TRAITEMENT DE LA MALADIE DE HUNTINGTON
(54) Title: METHODS FOR TREATING HUNTINGTON'S DISEASE



(I)

(57) Abrégé/Abstract:
The present description relates to a method or use of a compound for treating or ameliorating HD (Huntington's Disease) in a subject in need thereof comprising administering to the subject an effective amount of a compound of Formula (I): or a form thereof, wherein R_1, R_2, R_a, R_b and R_c are as defined herein. In particular, the present description relates to a method of use of a compound of Formula (I) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound or a form or composition thereof to the subject.

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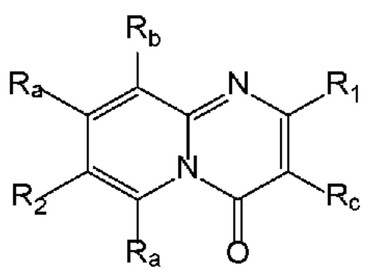
(54) Title: METHODS FOR TREATING HUNTINGTON'S DISEASE



(I)

(57) Abstract: The present description relates to a method or use of a compound for treating or ameliorating HD (Huntington's Disease) in a subject in need thereof comprising administering to the subject an effective amount of a compound of Formula (I): or a form thereof, wherein R_1, R_2, R_a, R_b and R_c are as defined herein. In particular, the present description relates to a method of use of a compound of Formula (I) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound or a form or composition thereof to the subject.

METHODS FOR TREATING HUNTINGTON'S DISEASE

The present description relates to compounds, forms, and pharmaceutical compositions thereof and methods of using such compounds, forms, or compositions thereof for treating or ameliorating Huntington's disease. In particular, the present description relates to substituted monocyclic heteroaryl compounds, forms and pharmaceutical compositions thereof and methods of using such compounds, forms, or compositions thereof for treating or ameliorating Huntington's disease.

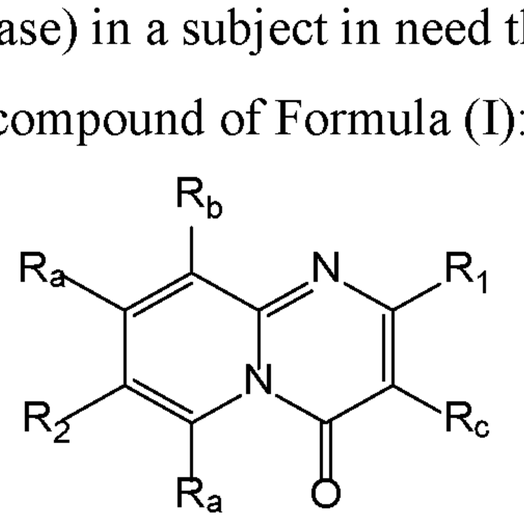
BACKGROUND

Huntington's Disease (HD) is a progressive, autosomal dominant neurodegenerative disorder of the brain, having symptoms characterized by involuntary movements, cognitive impairment, and mental deterioration. Death, typically caused by pneumonia or coronary artery disease, usually occurs 13 to 15 years after the onset of symptoms. The prevalence of HD is between three and seven individuals per 100,000 in populations of western European descent. In North America, an estimated 30,000 people have HD, while an additional 200,000 people are at risk of inheriting the disease from an affected parent. The disease is caused by an expansion of uninterrupted trinucleotide CAG repeats in the "mutant" huntingtin (Htt) gene, leading to production of HTT (Htt protein) with an expanded poly-glutamine (polyQ) stretch, also known as a "CAG repeat" sequence. There are no current small molecule therapies targeting the underlying cause of the disease, leaving a high unmet need for medications that can be used for treating or ameliorating HD. Consequently, there remains a need to identify and provide a small molecule compound for use in treating or ameliorating HD.

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

SUMMARY

The present description relates to a method or use of a compound for treating or ameliorating HD (Huntington's Disease) in a subject in need thereof comprising administering to the subject an effective amount of a compound of Formula (I):

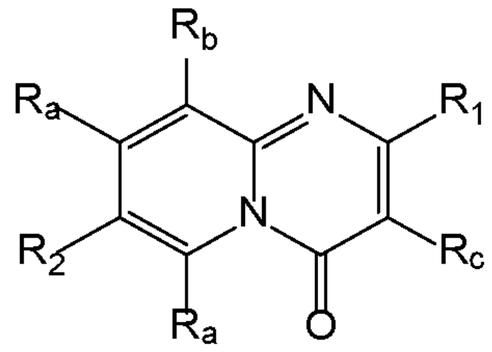


(I)

or a form thereof, wherein R_1, R_2, R_a, R_b and R_c are as defined herein. In particular, the present description relates to a method of use of a compound of Formula (I) or a form or composition thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound or a form or composition thereof to the subject.

DETAILED DESCRIPTION

The present description relates to a method or use of a compound for treating or ameliorating HD (Huntington's Disease) in a subject in need thereof comprising administering to the subject an effective amount of a compound of Formula (I):



(I)

or a form thereof, wherein:

R_1 is heterocyclyl optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or, optionally substituted with one, two, three or four R_3 substituents;

R_2 is heteroaryl optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent;

R_a is, in each instance, independently selected from hydrogen, halogen or $C_{1\text{-}8}$alkyl;

R_b and R_c are, in each instance, independently selected from hydrogen, halogen or $C_{1\text{-}8}$alkyl;

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

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

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

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

R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl; and,

wherein the form of the compound is selected from the group consisting of a salt, prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

In one aspect of the use of a compound of Formula (I),

R_1 is heterocyclyl selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, 3,6-dihydropyridinyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl,

(3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, 1,3,3a,4,6,6a-hexahydropyrrolo[3,4-*c*]pyrrolyl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazinyl, (8a*R*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazinyl, (8a*S*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (8a*R*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, octahydro-2H-pyrido[1,2-*a*]pyrazinyl, (3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-(3H)-yl, 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, 3,6-diazabicyclo[3.2.0]heptyl, 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, 4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.4]octyl, 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 one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or, optionally, with one, two, three or four R_3 substituents.

In another aspect of the use of a compound of Formula (I),

R_1 is heterocyclyl selected from pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, 1,3,3a,4,6,6a-hexahydropyrrolo[3,4-*c*]pyrrolyl, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazinyl, (8a*R*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazinyl, (8a*S*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (8a*R*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-(3H)-yl, 3,6-diazabicyclo[3.2.0]heptyl, 2,6-diazaspiro[3.3]heptyl, 4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.4]octyl or 2,7-diazaspiro[3.5]nonyl; wherein, each instance of heterocyclyl is optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or, optionally, with one, two, three or four R_3 substituents.

In another aspect of the use of a compound of Formula (I),

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

(7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*S*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl,
(8a*R*)-3,4,6,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl,
(8a*S*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazin-2-yl,
(8a*R*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazin-2-yl,
(8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl, octahydro-2H-pyrido[1,2-*a*]pyrazin-2-yl,
(3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-2(3H)-yl,
3-azabicyclo[3.1.0]hex-3-yl, 8-azabicyclo[3.2.1]oct-3-yl,
(1R,5S)-8-azabicyclo[3.2.1]oct-3-yl, 8-azabicyclo[3.2.1]oct-2-en-3-yl,
(1*R*,5*S*)-8-azabicyclo[3.2.1]oct-2-en-3-yl, 9-azabicyclo[3.3.1]non-3-yl,
(1*R*,5*S*)-9-azabicyclo[3.3.1]non-3-yl, 2,5-diazabicyclo[2.2.1]hept-2-yl,
(1*S*,4*S*)-2,5-diazabicyclo[2.2.1]hept-2-yl, 2,5-diazabicyclo[2.2.2]oct-2-yl,
3,6-diazabicyclo[3.2.0]hept-3-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, 4,7-diazaspiro[2.5]oct-7-yl,
2,6-diazaspiro[3.4]oct-2-yl, 2,7-diazaspiro[3.5]non-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 one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or, optionally, with one, two, three or four R_3 substituents.

In another aspect of the use of a compound of Formula (I),

R_1 is substituted heterocyclyl selected from (3*R*)-3-pyrrolidin-1-ylpyrrolidin-1-yl,
1-methylpiperidin-4-yl, 1-ethylpiperidin-4-yl, 2,2,6,6-tetramethylpiperidin-4-yl,
(3S)-3-methylpiperazin-1-yl, 4-methylpiperazin-1-yl, 4-ethylpiperazin-1-yl,
3-(trifluoromethyl)piperazin-1-yl, 1-tert-butoxy-carbonyl-3,6-dihydropyridin-4-yl,
1-ethyl-1,2,3,6-tetrahydropyridin-4-yl, 2,2,6,6-tetramethyl-1,2,3,6-tetrahydropyridin-4-yl,
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-methyl-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazin-2-yl,
(8a*R*)-8a-methyl-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazin-2-yl,
(8a*S*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(8a*R*)-8a-methyloctahydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl,
(1*R*,5*S*,6s)-6-(dimethylamino)-3-azabicyclo[3.1.0]hex-3-yl,
(1*R*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl, 9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(3-exo)-9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(1*R*,5*S*)-9-methyl-9-azabicyclo[3.3.1]non-3-yl,
(1*S*,4*S*)-5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl,
(1*S*,4*S*)-5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl or 6-methyl-2,6-diazaspiro[3.3]hept-2-yl.

In one aspect of the use of a compound of Formula (I), R_3 is selected from cyano, halogen, hydroxy, oxo, $C_{1\text{-}8}$alkyl, halo-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkyl-carbonyl, $C_{1\text{-}8}$alkoxy, halo-$C_{1\text{-}8}$alkoxy, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkoxy-carbonyl, amino, $C_{1\text{-}8}$alkyl-amino, $(C_{1\text{-}8}alkyl)_2$-amino, amino-$C_{1\text{-}8}$alkyl, $C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl, $(C_{1\text{-}8}alkyl)_2$-amino-$C_{1\text{-}8}$alkyl, amino-$C_{1\text{-}8}$alkyl-amino, $C_{1\text{-}8}$alkyl-amino-$C_{1\text{-}8}$alkyl-amino, $(C_{1\text{-}8}alkyl)_2$-amino-$C_{1\text{-}8}$alkyl-amino, $C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl-amino, $C_{1\text{-}8}$alkyl-carbonyl-amino, $C_{1\text{-}8}$alkoxy-carbonyl-amino, hydroxy-$C_{1\text{-}8}$alkyl, hydroxy-$C_{1\text{-}8}$alkoxy-$C_{1\text{-}8}$alkyl, hydroxy-$C_{1\text{-}8}$alkyl-amino, $(hydroxy\text{-}C_{1\text{-}8}alkyl)_2$-amino or (hydroxy-$C_{1\text{-}8}$alkyl)($C_{1\text{-}8}$alkyl)amino.

In another aspect of the use of a compound of Formula (I), R_3 is selected from cyano, halogen, hydroxy, oxo, C_{1-8}alkyl, halo-C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, C_{1-8}alkoxy-carbonyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino, amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl, $(C_{1-8}alkyl)_2$-amino-C_{1-8}alkyl, C_{1-8}alkyl-amino-C_{1-8}alkyl-amino, C_{1-8}alkoxy-C_{1-8}alkyl-amino, C_{1-8}alkoxy-carbonyl-amino, hydroxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkoxy-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl-amino, $(hydroxy\text{-}C_{1-8}alkyl)_2$-amino or (hydroxy-$C_{1-8}$alkyl)($C_{1-8}$alkyl)amino.

In another aspect of the use of a compound of Formula (I), R_3 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

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

In another aspect of the use of a compound of Formula (I), R_3 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

In another aspect of the use of a compound of Formula (I), R_3 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

In another aspect of the use of a compound of Formula (I), R_3 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

In another aspect of the use of a compound of Formula (I), R_3 is C_{1-8}alkoxy-carbonyl-amino selected from methoxy-carbonyl-amino, ethoxy-carbonyl-amino, propoxy-carbonyl-amino, isopropoxy-carbonyl-amino, tert-butoxy-carbonyl-amino.

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

In another aspect of the use of a compound of Formula (I), R_4 is C_{3-14}cycloalkyl-C_{1-8}alkyl, wherein C_{3-14}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl

or cycloheptyl; and, wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is C_{3-14}cycloalkyl-amino, wherein C_{3-14}cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl; and, wherein, each instance of C_{3-14}cycloalkyl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is aryl-C_{1-8}alkyl, aryl-C_{1-8}alkoxy-carbonyl or aryl-sulfonyloxy-C_{1-8}alkyl, wherein aryl is selected from phenyl; and, wherein, each instance of aryl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is heterocyclyl selected from oxetanyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,3-dioxanyl or morpholinyl, wherein each instance of heterocyclyl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, 1,3-dioxan-5-yl or morpholin-4-yl, wherein each instance of heterocyclyl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is heterocyclyl-C_{1-8}alkyl, wherein each instance of heterocyclyl is selected from pyrrolidinyl or piperidinyl; and, wherein, each instance of heterocyclyl is optionally substituted with one, two or three R_5 substituents.

In another aspect of the use of a compound of Formula (I), R_4 is heterocyclyl-C_{1-8}alkyl selected from pyrrolidin-1-yl-C_{1-8}alkyl or piperidin-1-yl-C_{1-8}alkyl, wherein each instance of heterocyclyl is optionally substituted with one, two or three R_5 substituents.

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

In another aspect of the use of a compound of Formula (I), R_5 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl, n-butyl or tert-butyl.

In another aspect of the use of a compound of Formula (I), R_5 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, halo-ethyl, trihalo-propyl, dihalo-propyl or halo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

In another aspect of the use of a compound of Formula (I), R_5 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

In another aspect of the use of a compound of Formula (I), R_5 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

In one aspect of the use of a compound of Formula (I),

R_2 is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 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, quinazolinyl, quinoxalinyl, 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, pyrazolo[4,3-b]pyridinyl, pyrazolo[3,4-*c*]pyridinyl, imidazo[1,2-*a*]pyridinyl, 3*H*-imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, [1,2,4]triazolo[1,5-a]pyrimidinyl, [1,2,4]triazolo[1,5-b]pyridazinyl, pyrido[1,2-a]pyrimidinyl or pyrido[1,2-a]pyrimidinone; wherein, each instance of heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent.

In another aspect of the use of a compound of Formula (I),

R_2 is heteroaryl selected from 1,3-benzoxazolyl, pyrazolo[1,5-*a*]pyrazinyl, imidazo[1,2-*a*]pyridinyl, imidazo[1,2-*b*]pyridazinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[1,5-a]pyrimidinyl or [1,2,4]triazolo[1,5-b]pyridazinyl; wherein, each

instance of heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent.

In another aspect of the use of a compound of Formula (I),

R_2 is heteroaryl selected from thien-2-yl, thien-3-yl, 1*H*-pyrazol-3-yl, 1*H*-pyrazol-4-yl, 1*H*-pyrazol-5-yl, 1*H*-imidazol-1-yl, 1*H*-imidazol-4-yl, 1,3-thiazol-2-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-4-yl, 1*H*-indol-3-yl, 1*H*-indol-4-yl, 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, quinazolin-6-yl, quinoxalin-2-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*]pyridin-5-yl, pyrazolo[1,5-*a*]pyrazin-2-yl, pyrazolo[4,3-b]pyridin-5-yl, pyrazolo[3,4-*c*]pyridin-5-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-*b*]pyridazin-6-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, [1,2,4]triazolo[1,5-a]pyridin-6-yl, [1,2,4]triazolo[1,5-a]pyrimidin-6-yl, [1,2,4]triazolo[1,5-b]pyridazin-6-yl, pyrido[1,2-a]pyrimidin-4-yl or pyrido[1,2-a]pyrimidin-4-one; wherein, each instance of heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent.

In another aspect of the use of a compound of Formula (I),

R_2 is substituted heteroaryl selected from 4-methylthien-2-yl, 1-methyl-1*H*-pyrazol-3-yl, 4-methyl-1*H*-pyrazol-3-yl, 1-phenyl-1*H*-pyrazol-3-yl, 1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazol-4-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, (5-fluoro-6-hydroxy)pyridin-3-yl, 2-methylpyrimidin-4-yl,
2-(propan-2-yl)pyrimidin-4-yl, 2-cyclopropylpyrimidin-4-yl, 1-methyl-1H-indol-3-yl,
1,7-dimethyl-1H-indazol-5-yl, 2-methyl-2*H*-indazol-5-yl, 2,7-dimethyl-2H-indazol-5-yl,
7-fluoro-2-methyl-2H-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,
(4-hydroxy-2-methyl)quinazolin-6-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,
2-methylpyrazolo[1,5-a]pyridin-5-yl, 5-methylpyrazolo[1,5-*a*]pyridin-2-yl,
4-(dimethylamino)-6-methylpyrazolo[1,5-a]pyrazin-2-yl,
4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl, 4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl,
1,7-dimethyl-1H-pyrazolo[4,3-b]pyridin-5-yl,
1,7-dimethyl-1H-pyrazolo[3,4-c]pyridin-5-yl,
2,7-dimethyl-2H-pyrazolo[3,4-c]pyridin-5-yl,
2,7-dimethyl-2H-pyrazolo[4,3-b]pyridin-5-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-methylimidazo[1,2-*b*]pyridazin-6-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, 2-methylimidazo[2,1-*b*][1,3,4]thiadiazol-6-yl,

2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl, 2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl, 2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl or 4H,4'H-2,7'-bipyrido[1,2-a]pyrimidine-4,4'-dione.

In one aspect of the use of a compound of Formula (I), R_6 is, in each instance, independently selected from halogen, hydroxy, cyano, nitro, C_{1-8}alkyl, C_{2-8}alkenyl, halo-C_{1-8}alkyl, hydroxy-C_{1-8}alkyl, C_{1-8}alkoxy, halo-C_{1-8}alkoxy, C_{1-8}alkoxy-C_{1-8}alkyl, amino, C_{1-8}alkyl-amino, $(C_{1-8}alkyl)_2$-amino or C_{1-8}alkyl-thio; wherein, halogen and halo is selected from fluoro, chloro, bromo or iodo.

In another aspect of the use of a compound of Formula (I), R_6 is C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

In another aspect of the use of a compound of Formula (I), R_6 is C_{2-8}alkenyl selected from ethenyl, allyl or buta-1,3-dienyl.

In another aspect of the use of a compound of Formula (I), R_6 is halo-C_{1-8}alkyl selected from trihalo-methyl, dihalo-methyl, halo-methyl, trihalo-ethyl, dihalo-ethyl, halo-ethyl, trihalo-propyl, dihalo-propyl or halo-propyl; wherein, halo is selected from fluoro, chloro, bromo or iodo.

In another aspect of the use of a compound of Formula (I), R_6 is hydroxy-C_{1-8}alkyl selected from hydroxy-methyl, hydroxy-ethyl, hydroxy-propyl, dihydroxy-propyl, hydroxy-butyl or dihydroxy-butyl.

In another aspect of the use of a compound of Formula (I), R_6 is C_{1-8}alkoxy selected from methoxy, ethoxy, propoxy or isopropoxy.

In another aspect of the use of a compound of Formula (I), R_6 is halo-C_{1-8}alkoxy selected from trihalo-methoxy, dihalo-methoxy, halo-methoxy, trihalo-ethoxy, dihalo-ethoxy, halo-ethoxy, trihalo-propoxy, dihalo-propoxy or halo-propoxy; wherein, halo is selected from fluoro, chloro, bromo or iodo.

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

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

In another aspect of the use of a compound of Formula (I), R_7 is aryl selected from phenyl.

In another aspect of the use of a compound of Formula (I), R_7 is heterocyclyl selected from oxetanyl, pyrrolidinyl or 1,2,3,6-tetrahydropyridinyl.

In another aspect of the use of a compound of Formula (I), R_7 is heterocyclyl selected from oxetan-3-yl, pyrrolidin-1-yl or 1,2,3,6-tetrahydropyridin-4-yl.

In another aspect of the use of a compound of Formula (I), R_7 is heteroaryl selected from thienyl or pyridinyl.

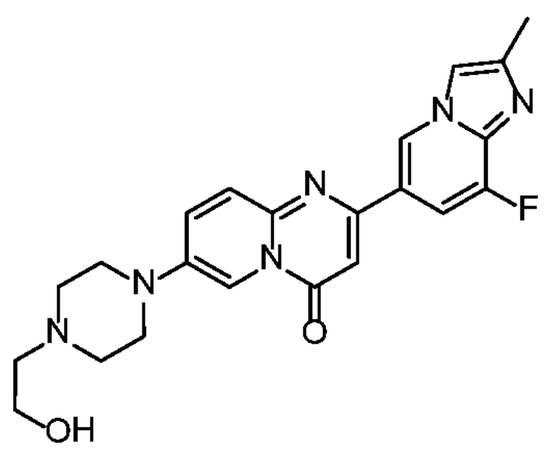
In another aspect of the use of a compound of Formula (I), R_7 is heteroaryl selected from thien-2-yl or pyridin-2-yl.

In one aspect of the use of a compound of Formula (I), R_a, R_b and R_c are each independently selected from hydrogen or C_{1-8}alkyl.

In another aspect of the use of a compound of Formula (I), R_a, R_b and R_c are each independently selected from hydrogen or C_{1-8}alkyl.

In another aspect of the use of a compound of Formula (I), R_a, R_b and R_c are each independently C_{1-8}alkyl selected from methyl, ethyl, propyl, isopropyl or tert-butyl.

In one aspect of the use of a compound of Formula (I) or a form thereof, the compound is selected from the group consisting of:



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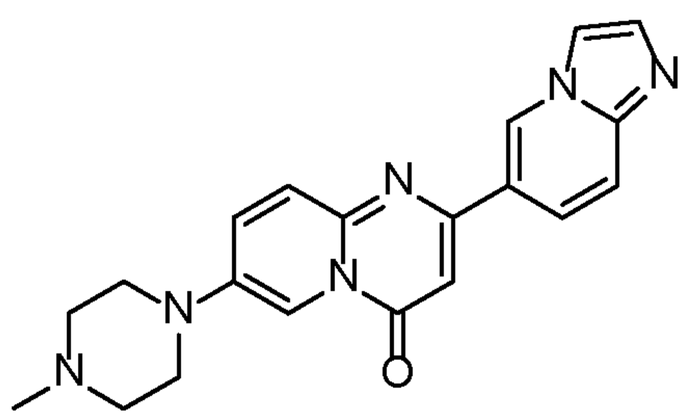

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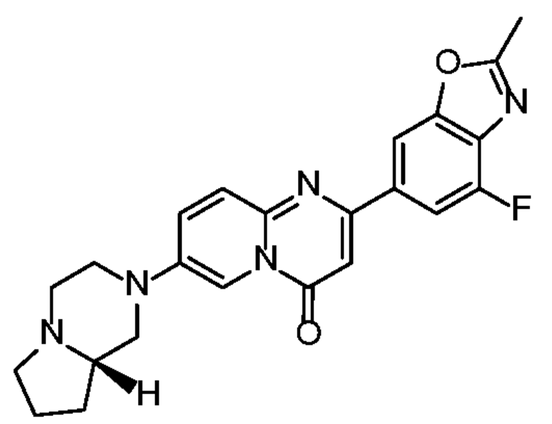

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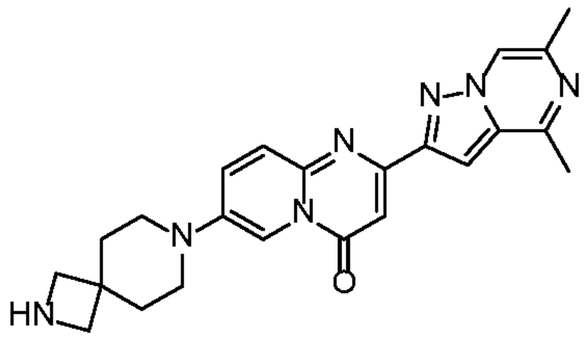

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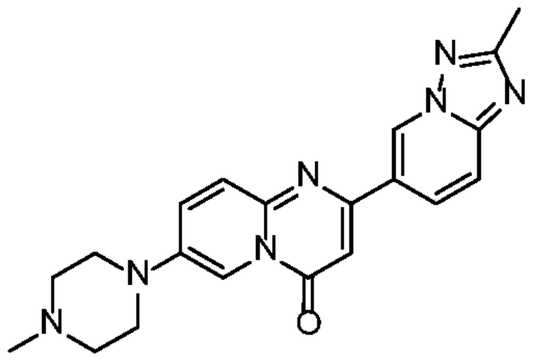

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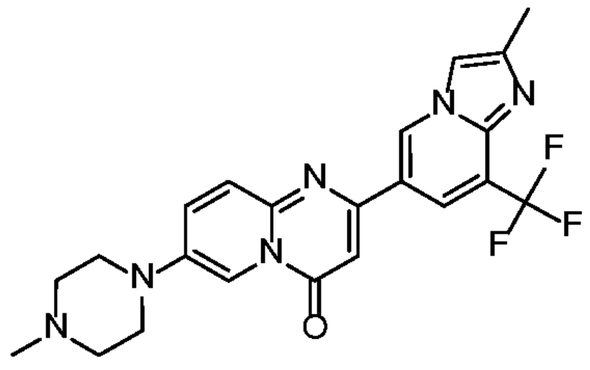

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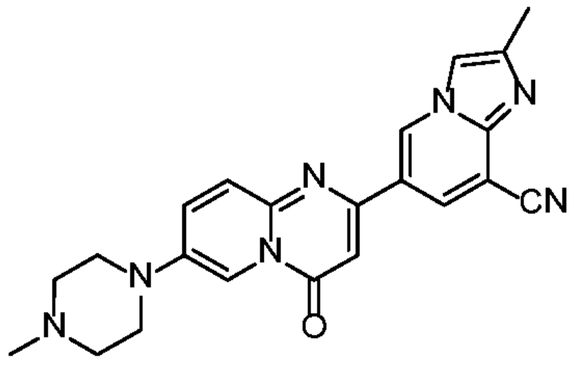

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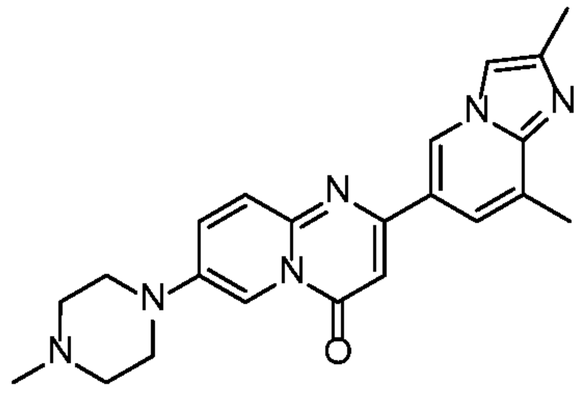

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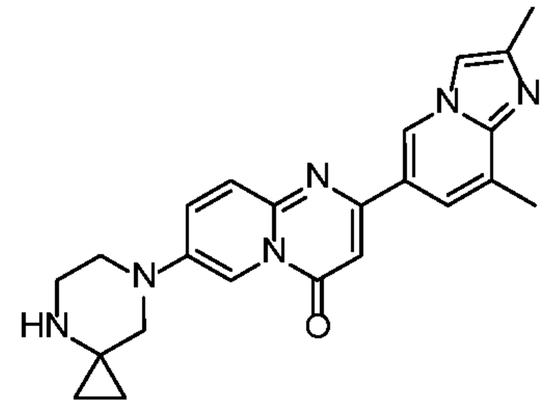

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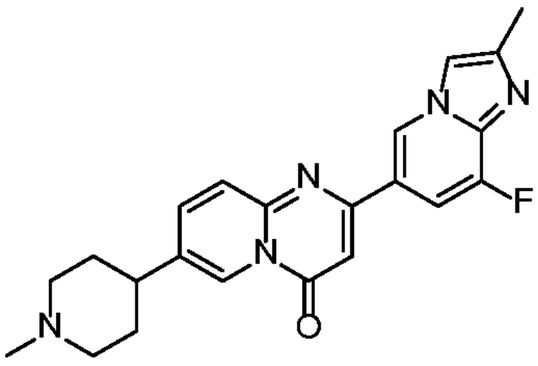

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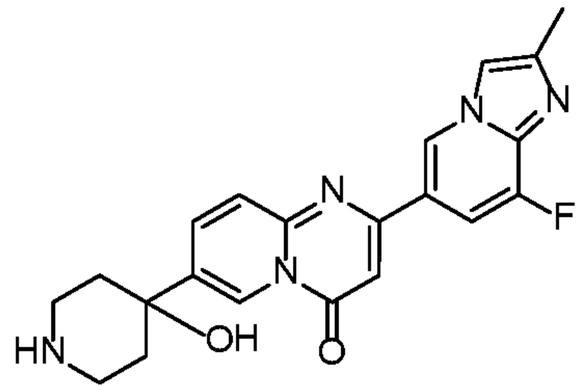

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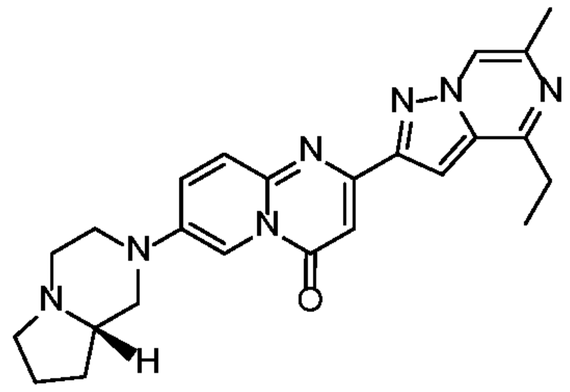

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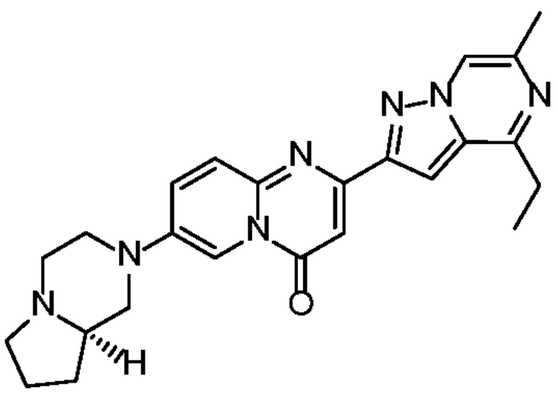

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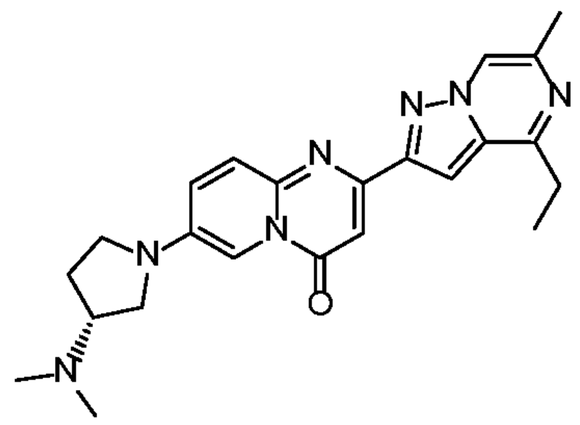

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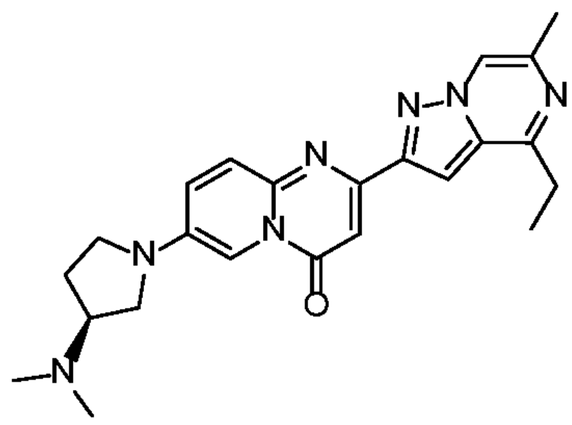

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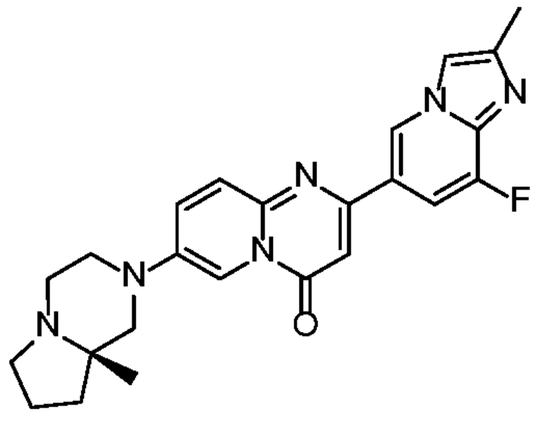

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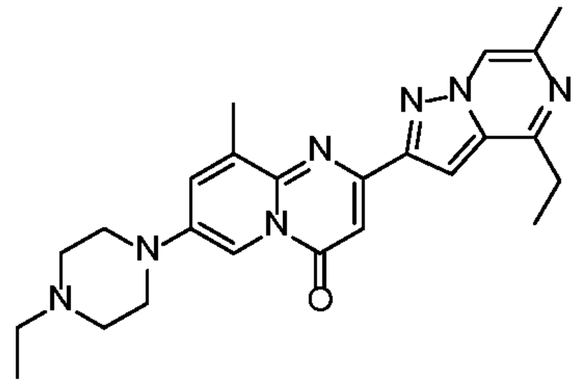

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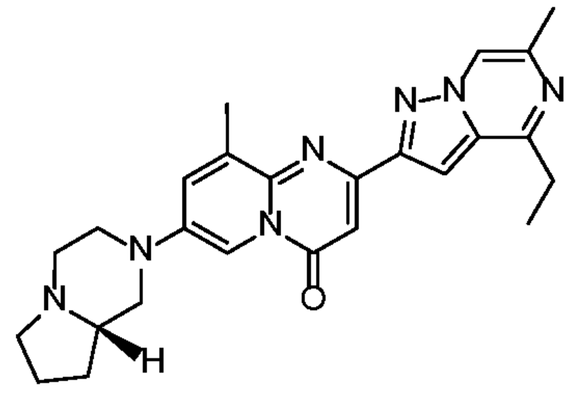

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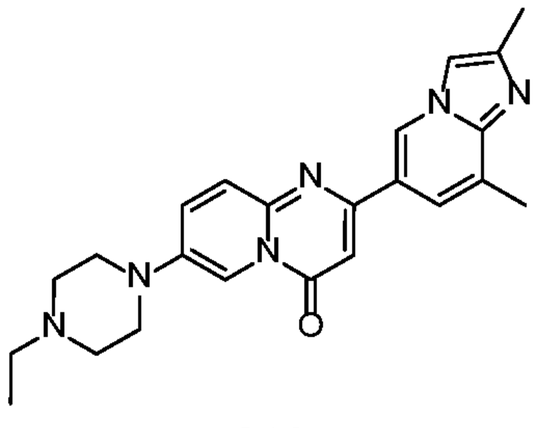

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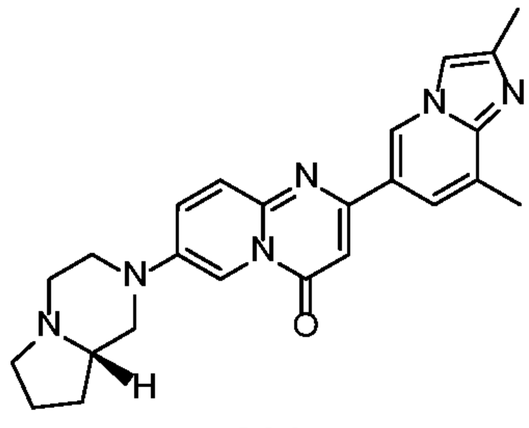

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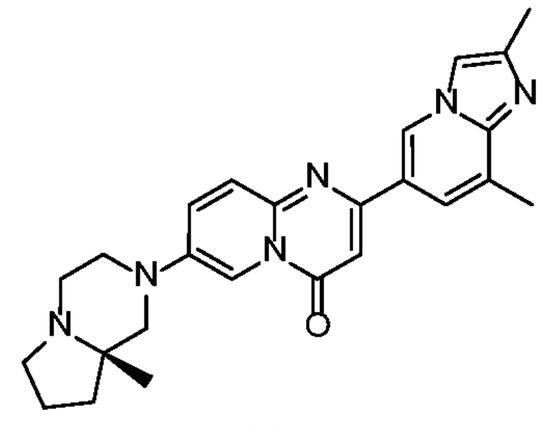

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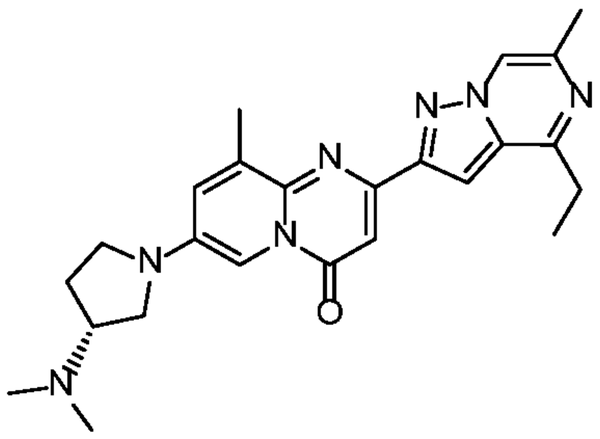

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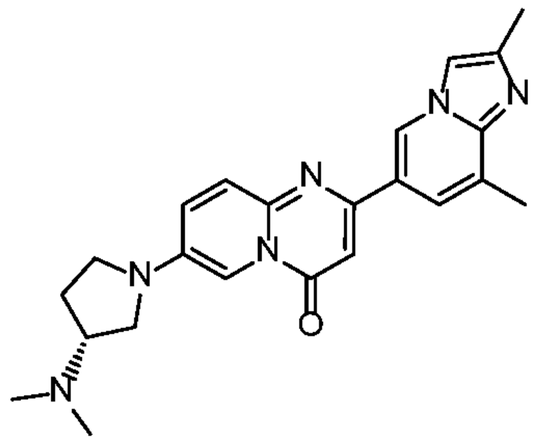

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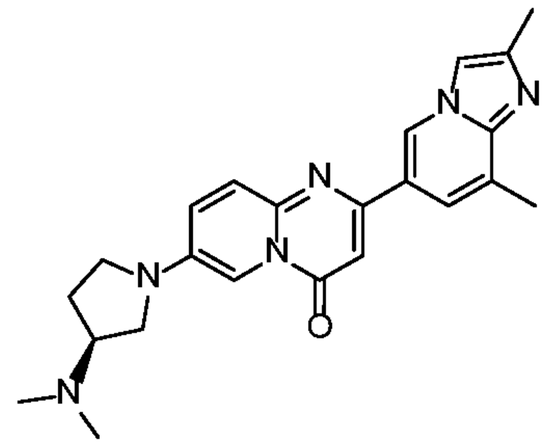

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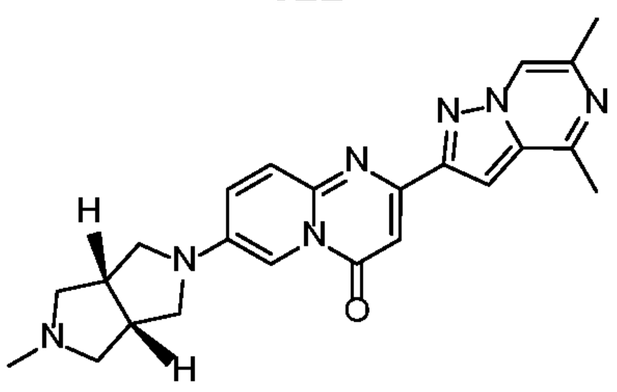

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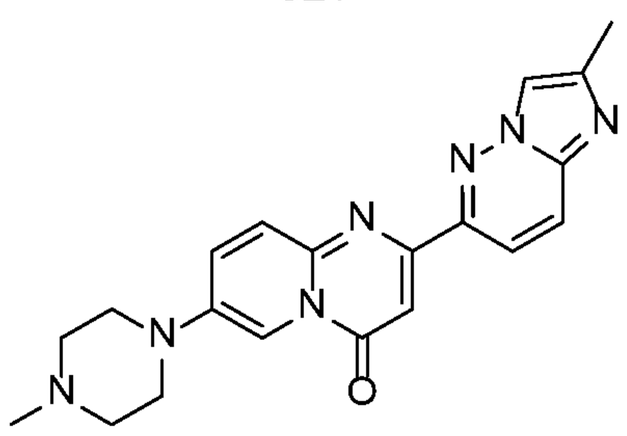

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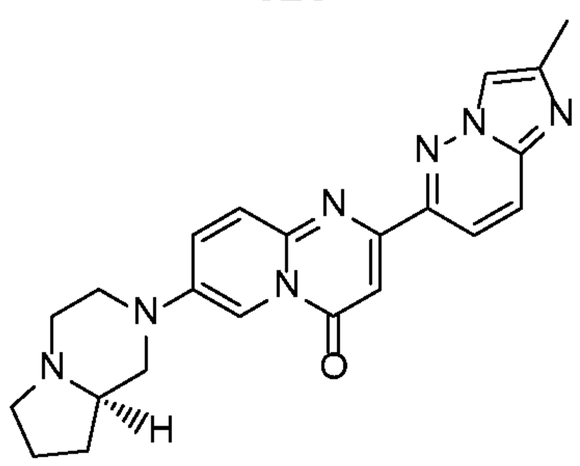

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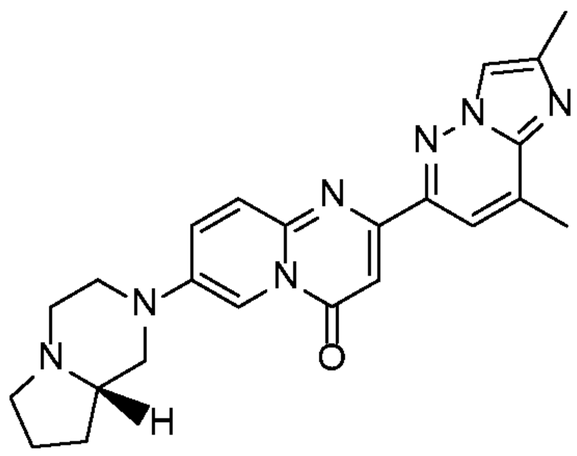

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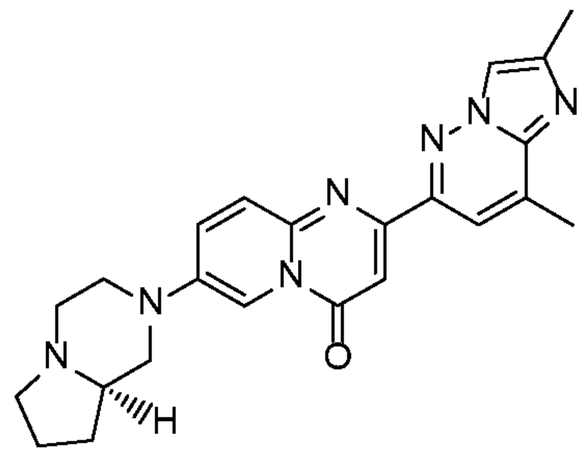

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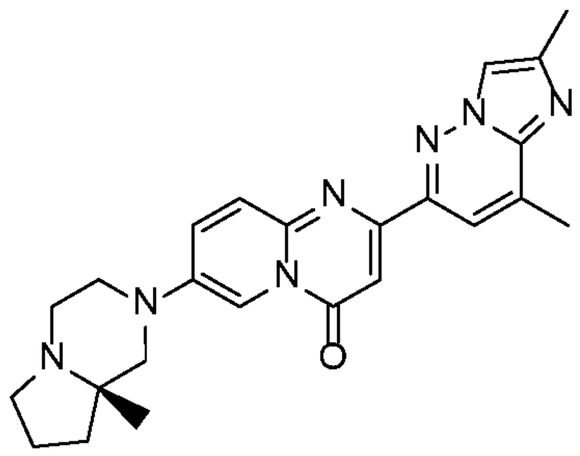

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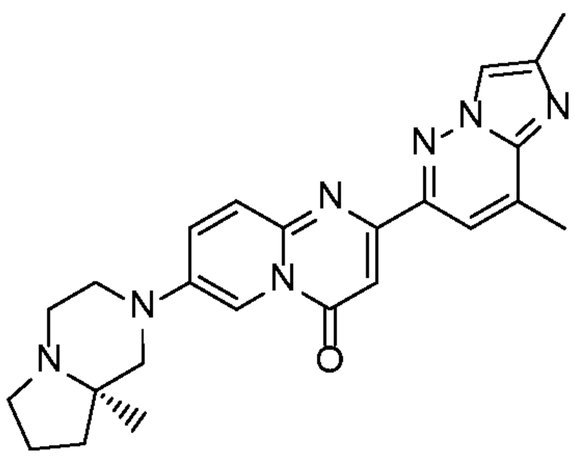

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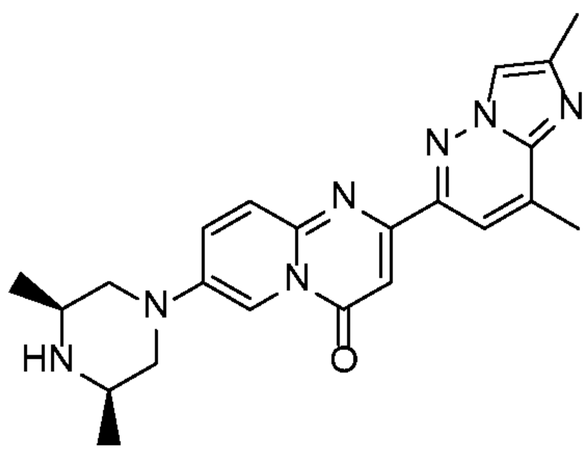

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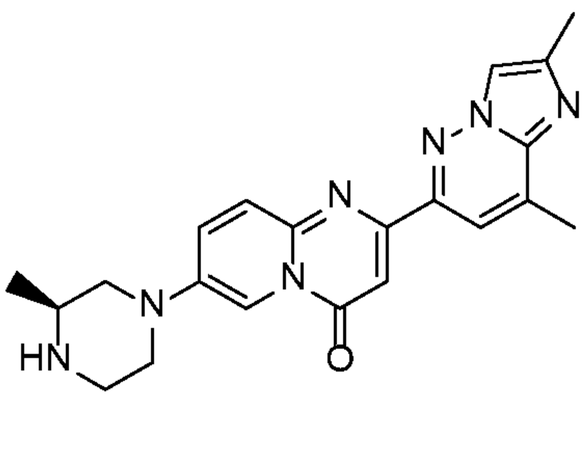

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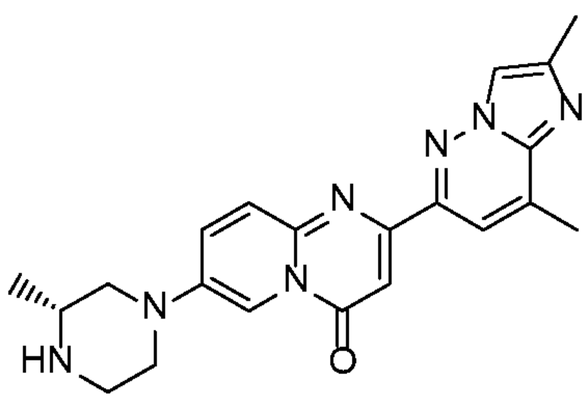

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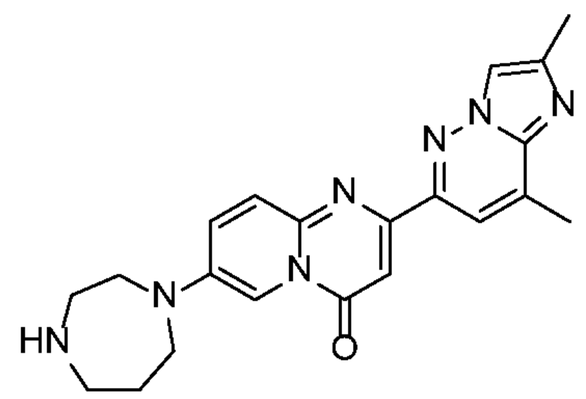

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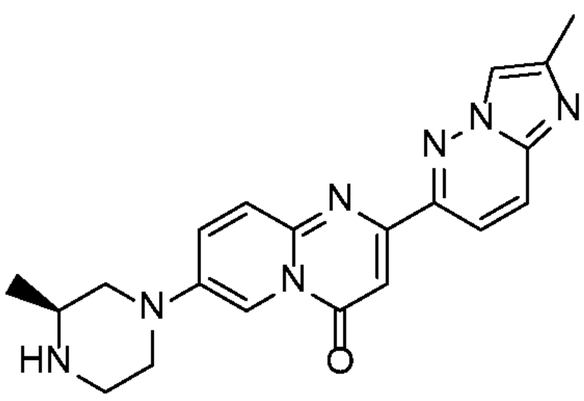

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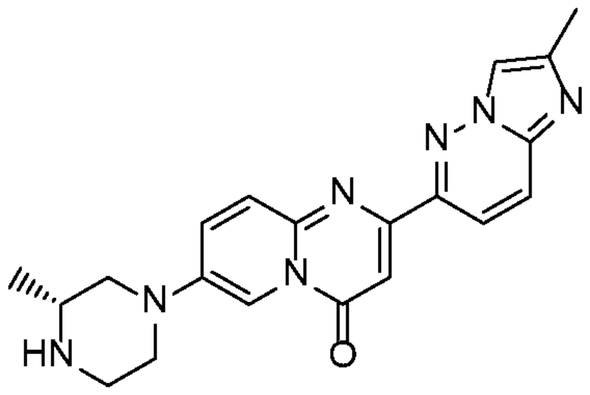

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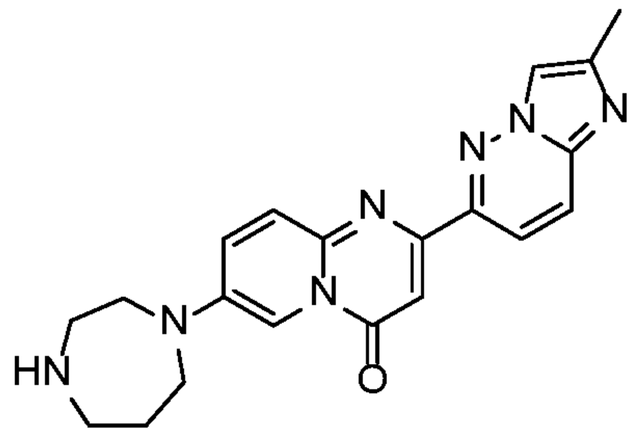

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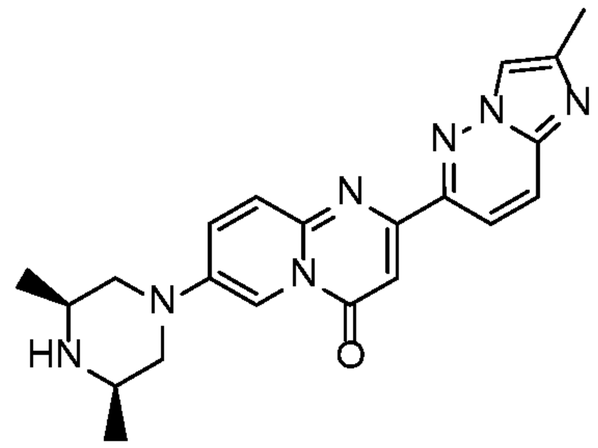

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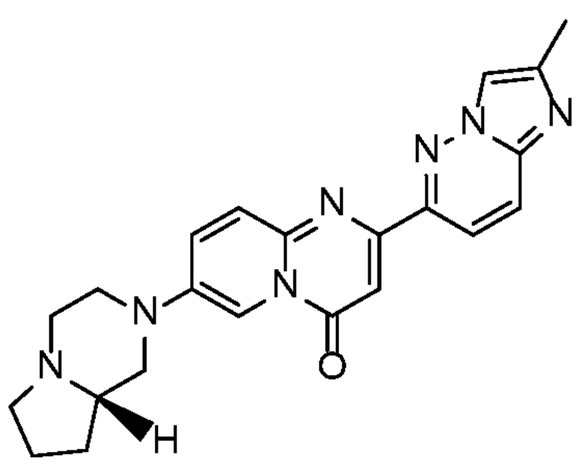

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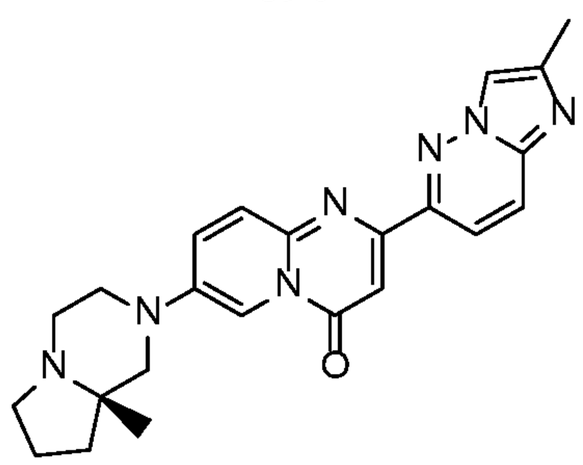

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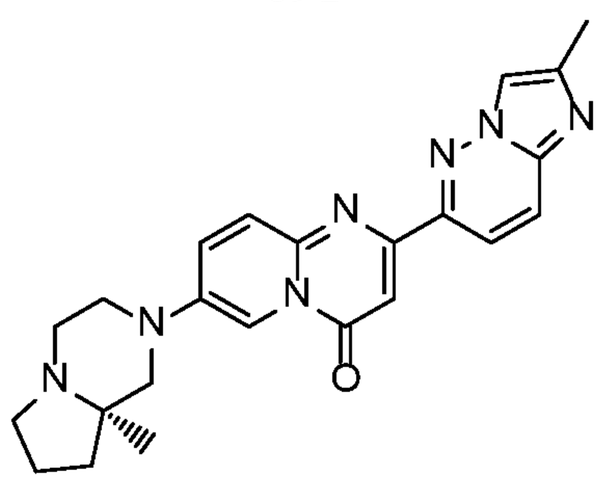

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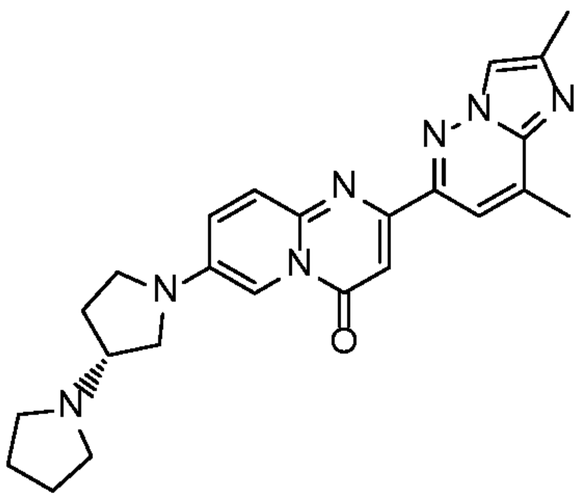

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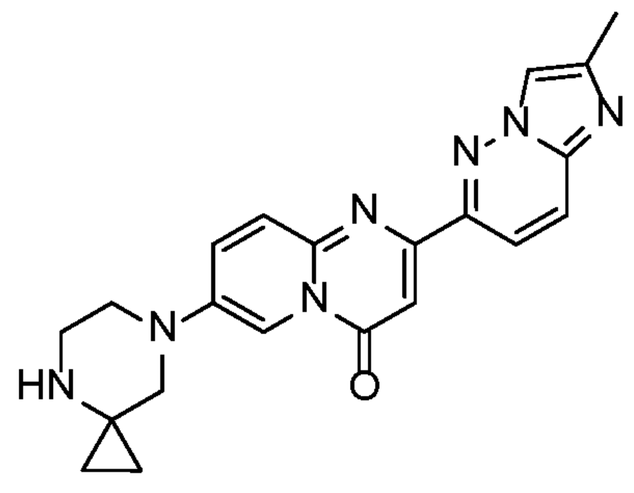

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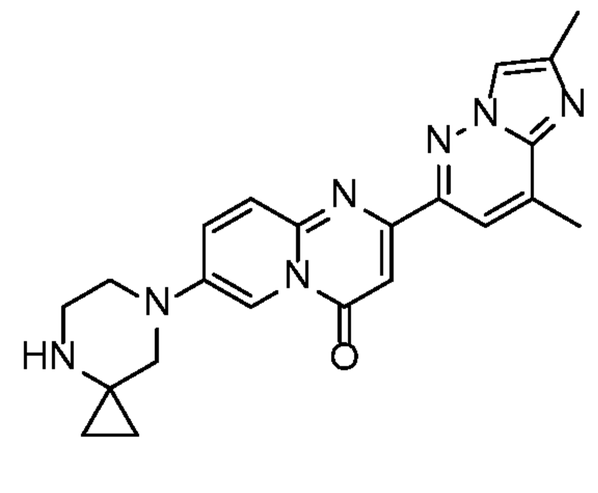

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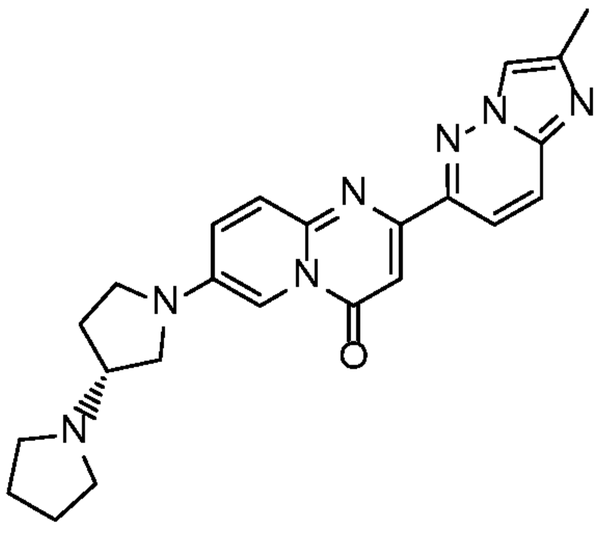

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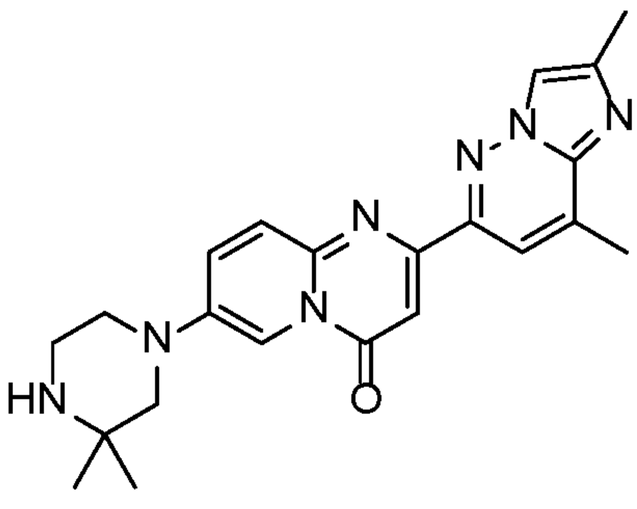

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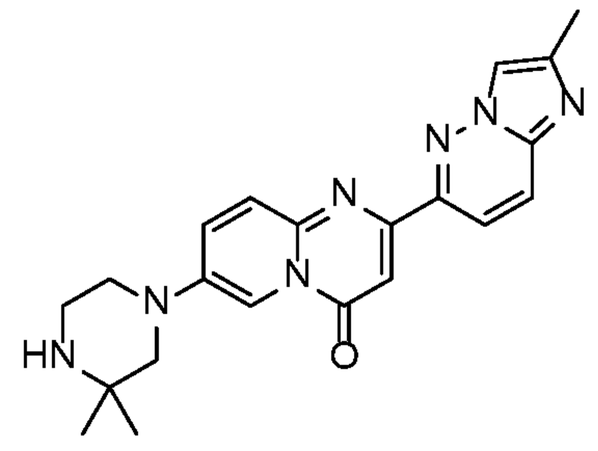

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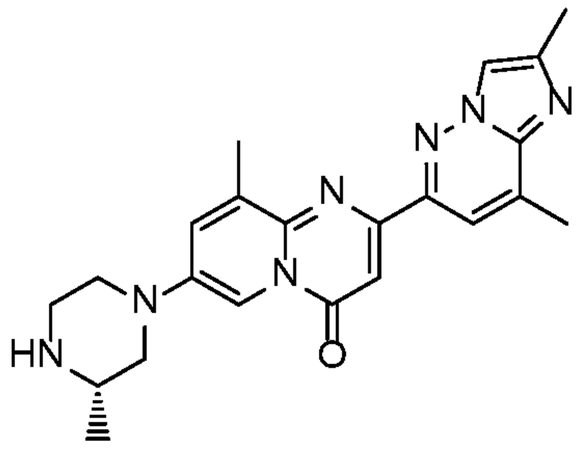

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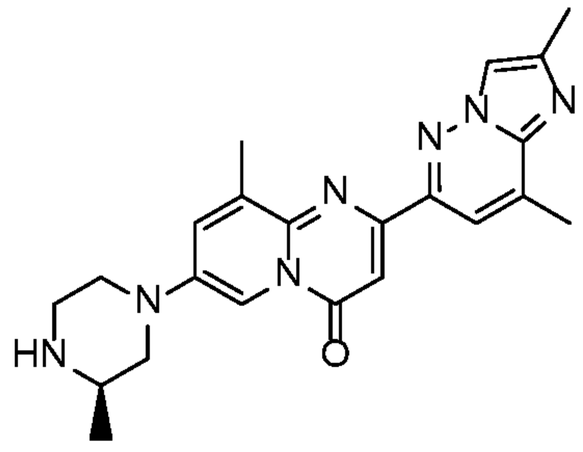

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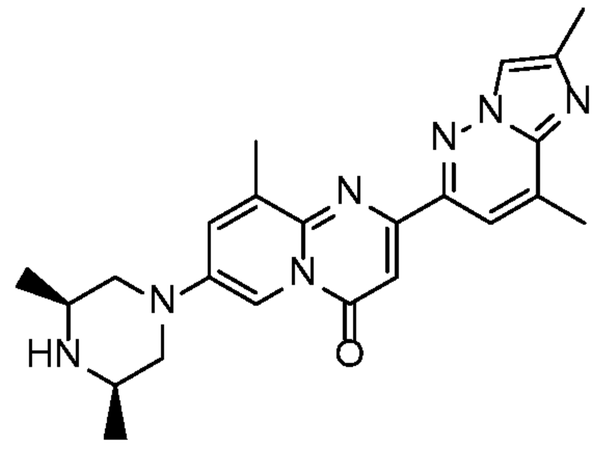

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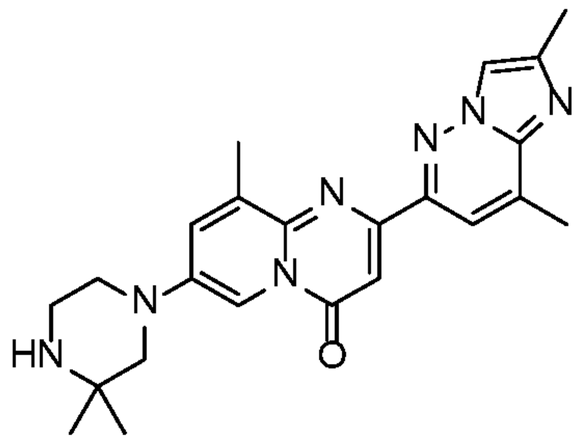

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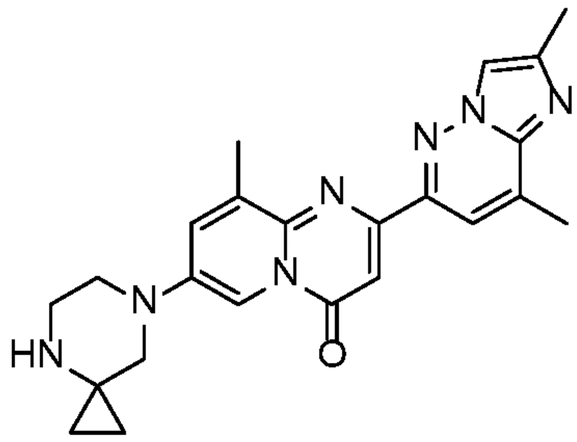

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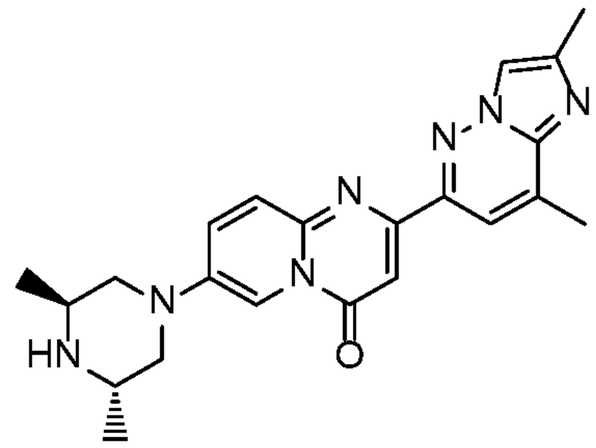

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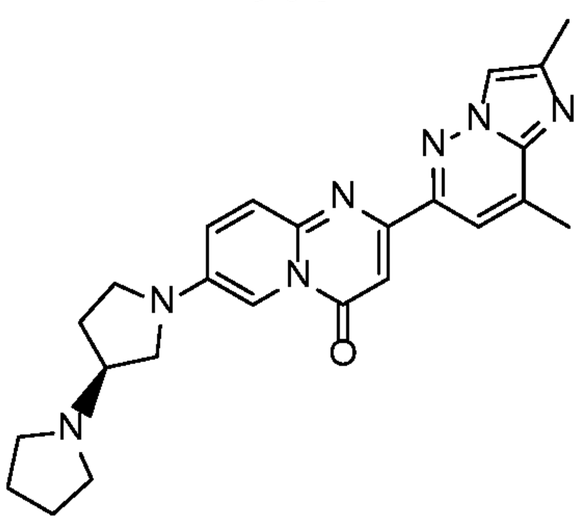

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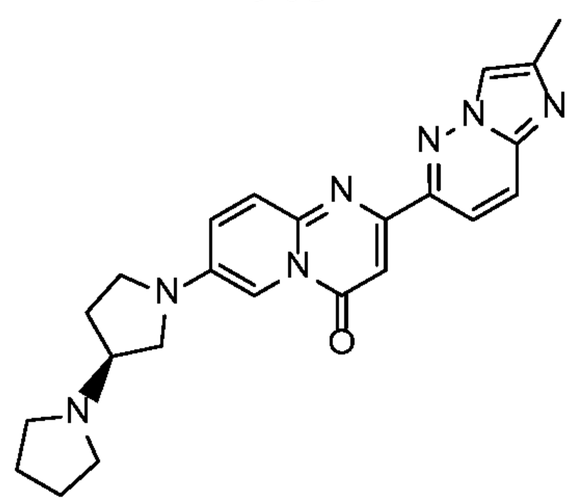

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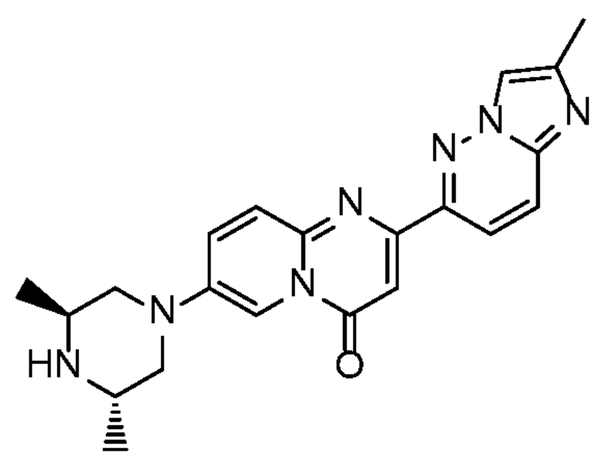

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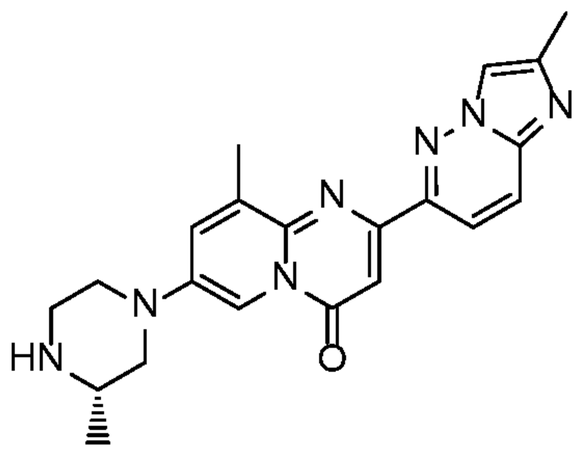

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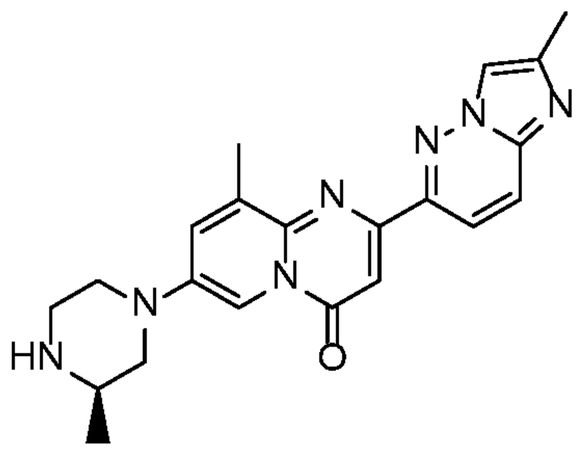

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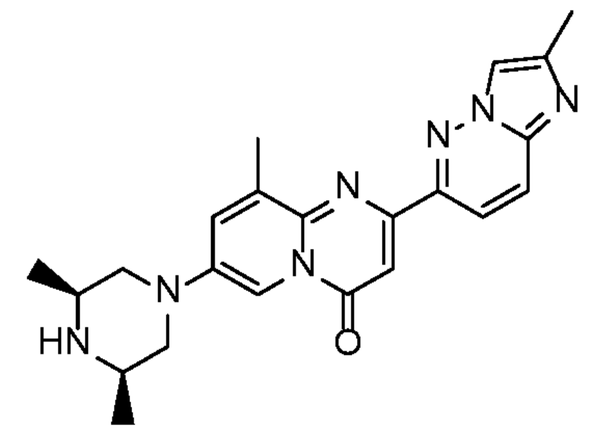

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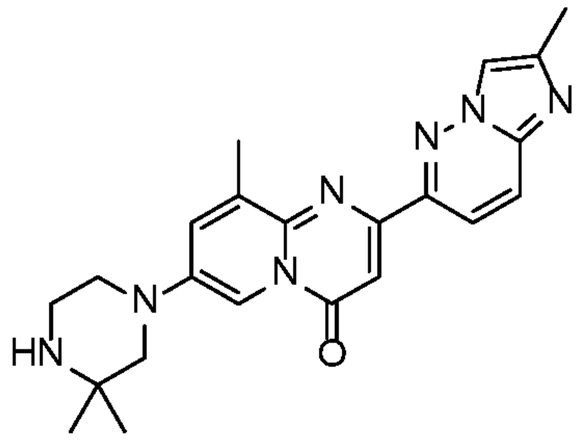

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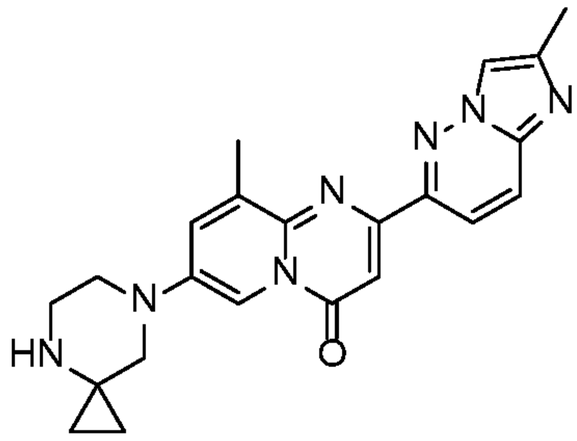

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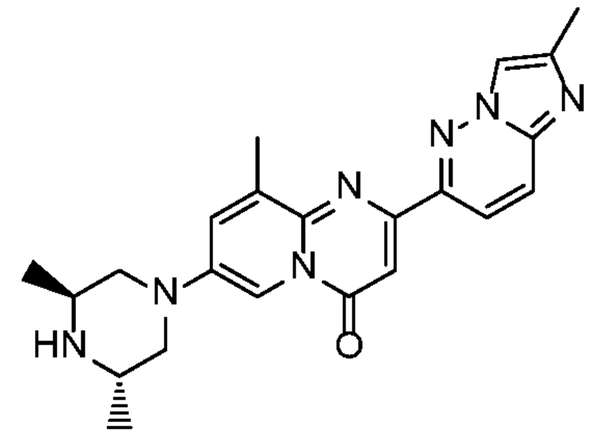

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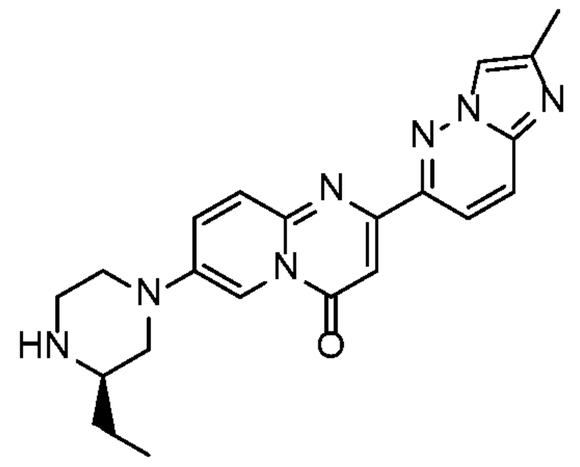

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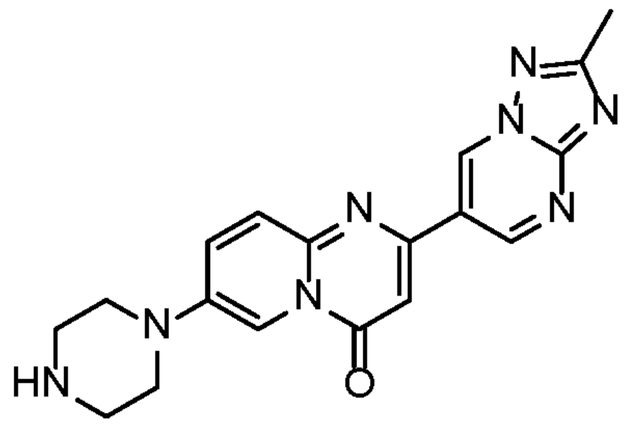

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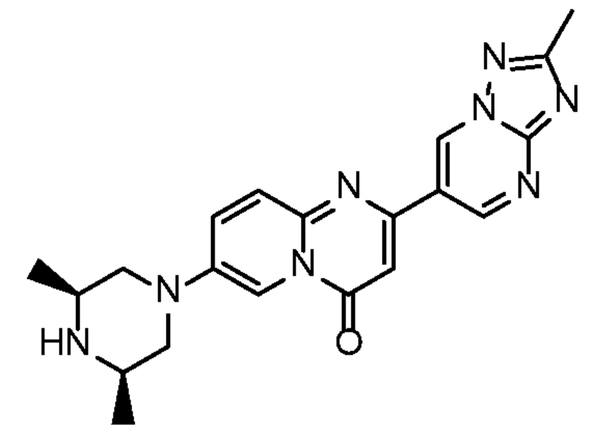

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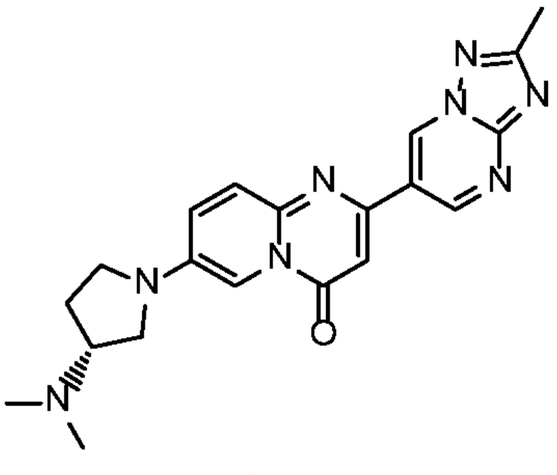

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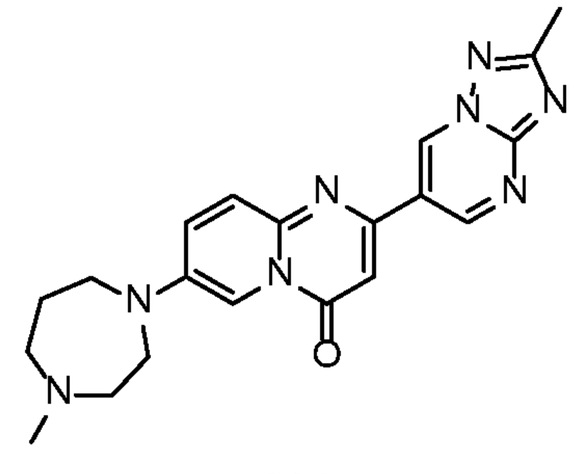

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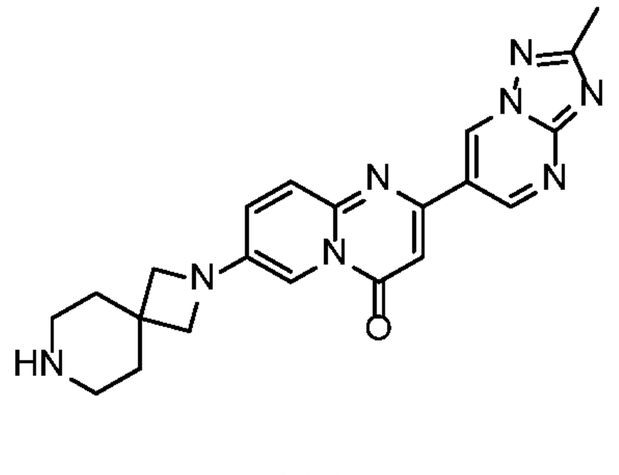

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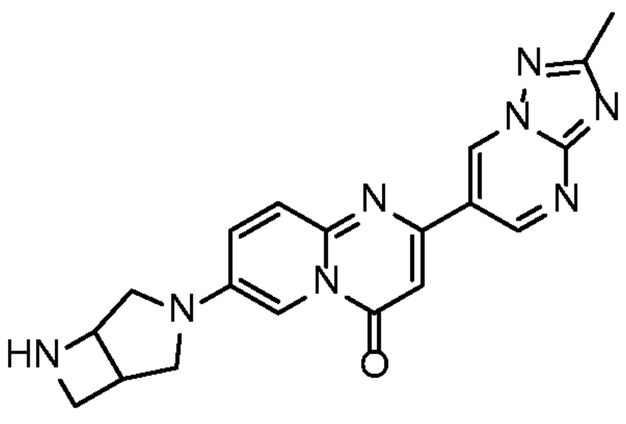

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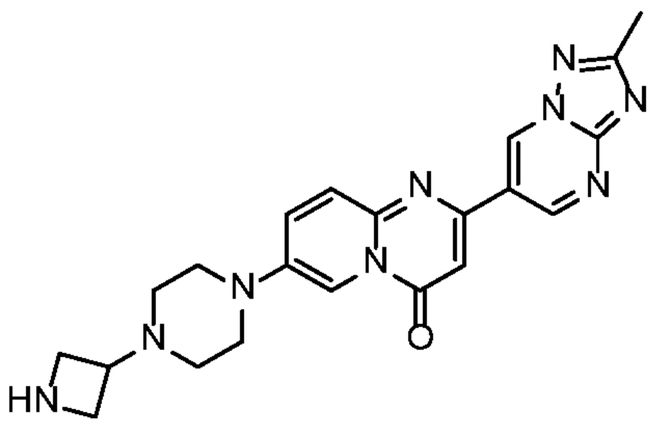

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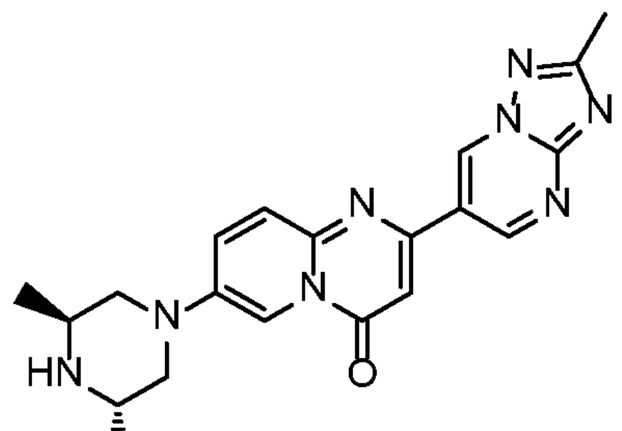

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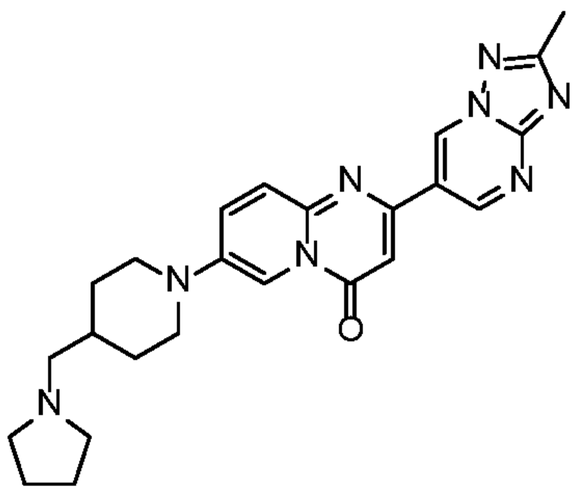

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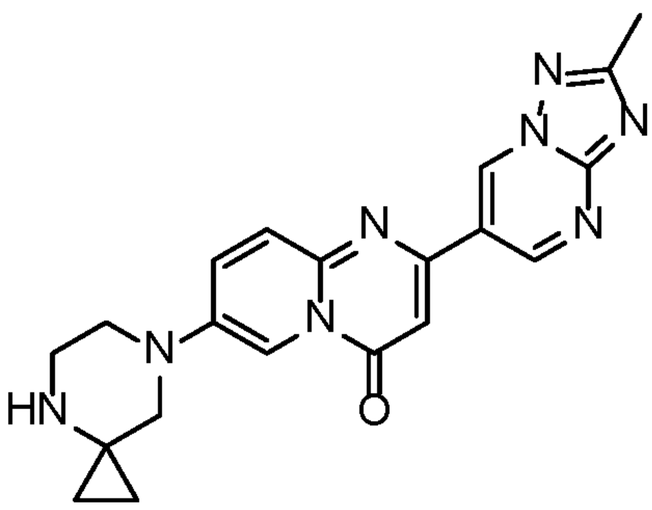

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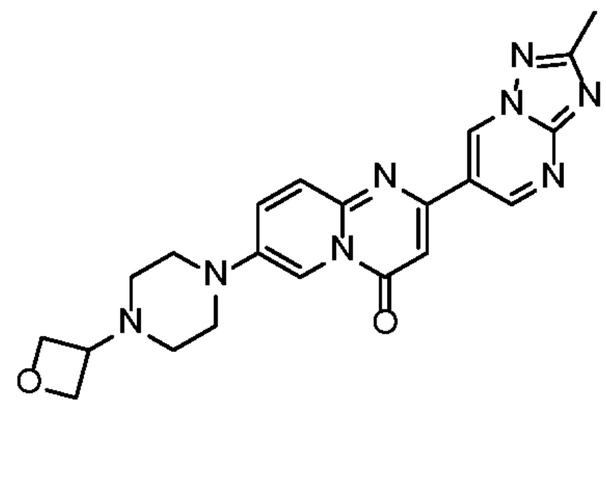

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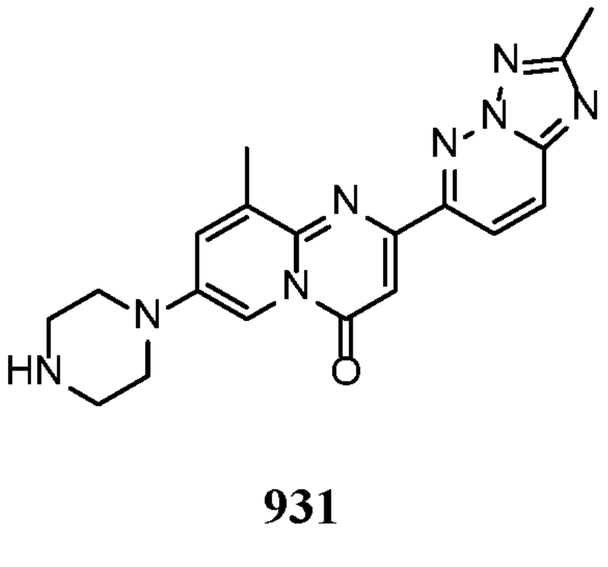

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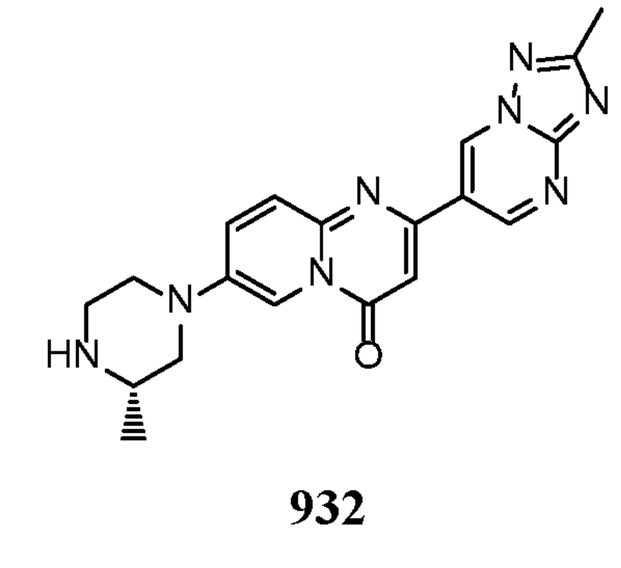

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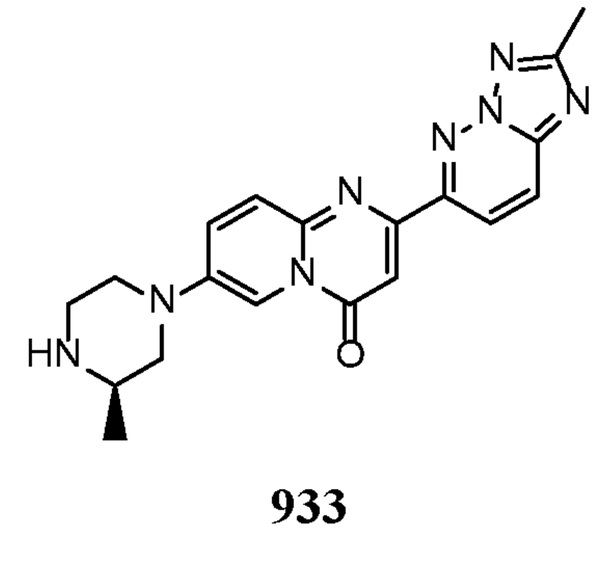

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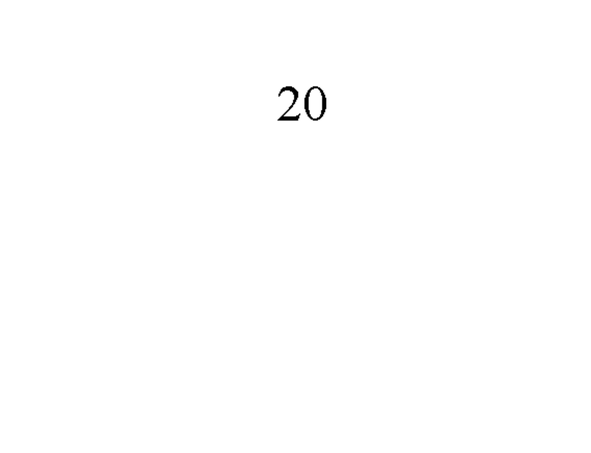

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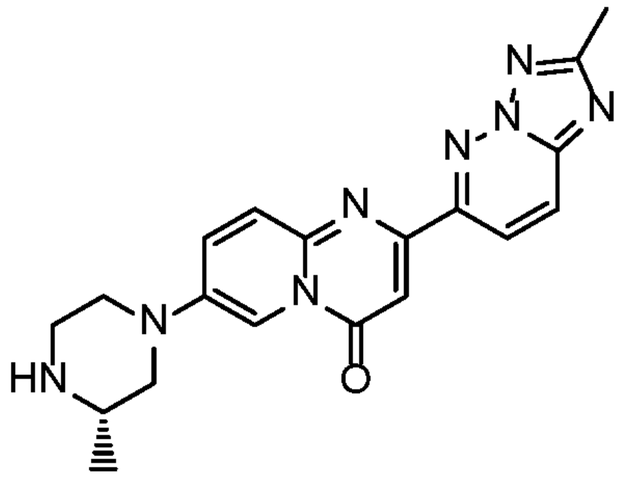

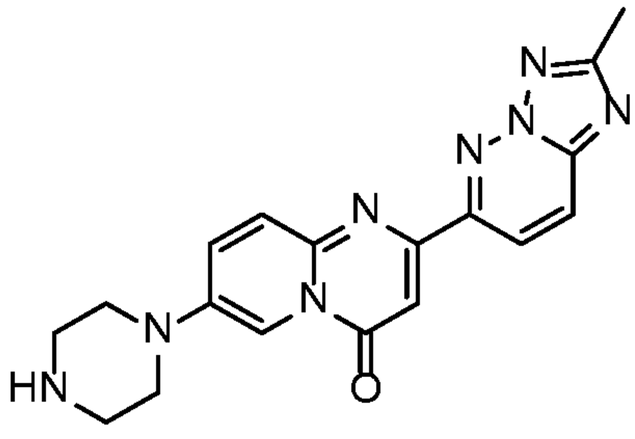

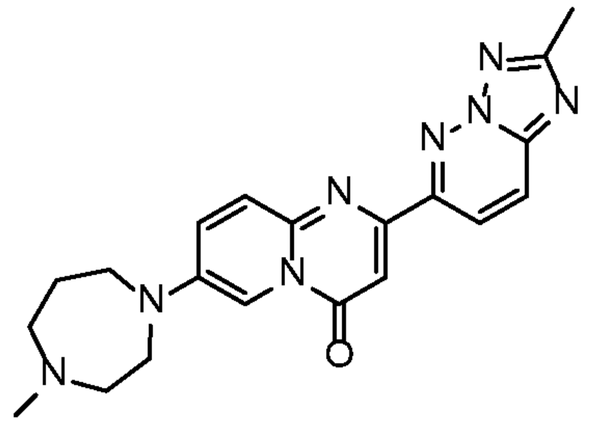

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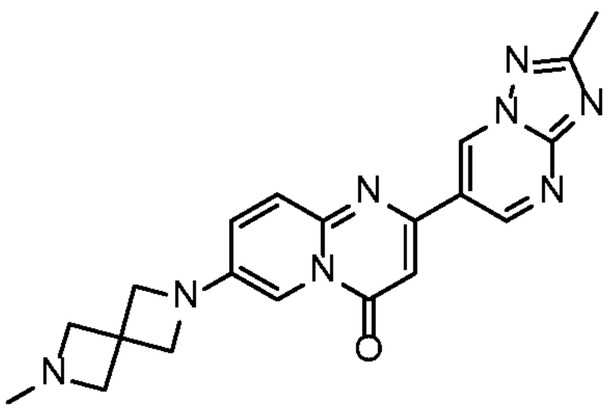

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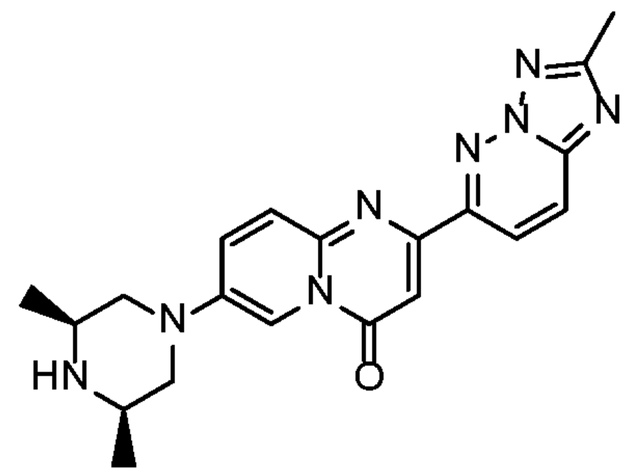

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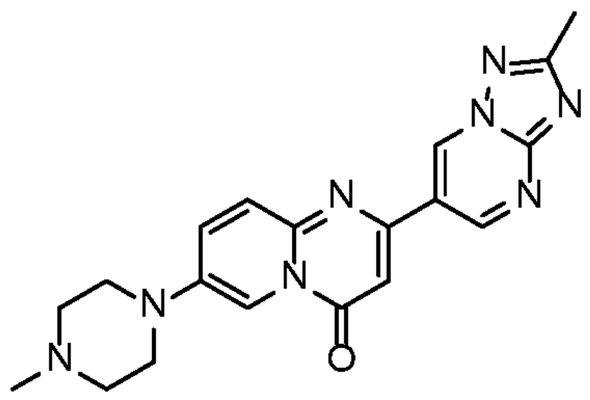

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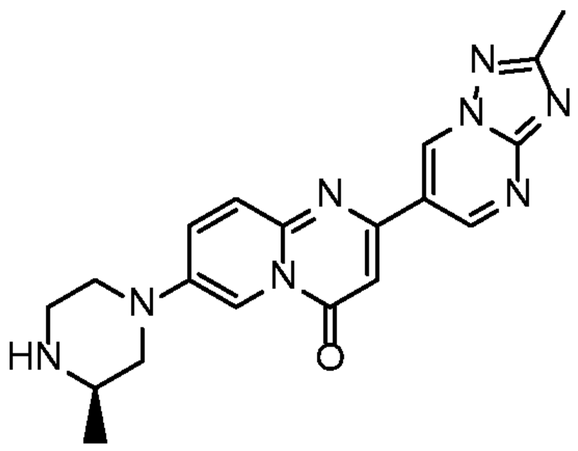

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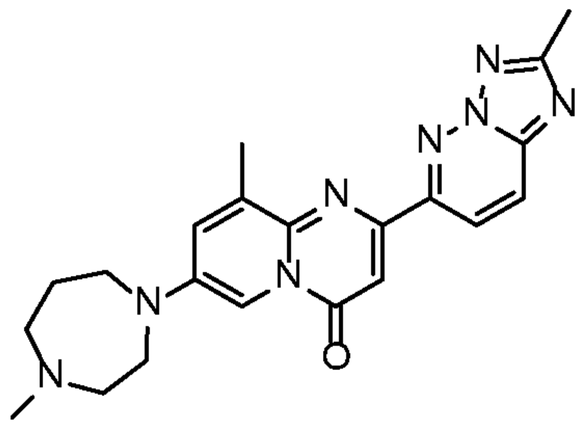

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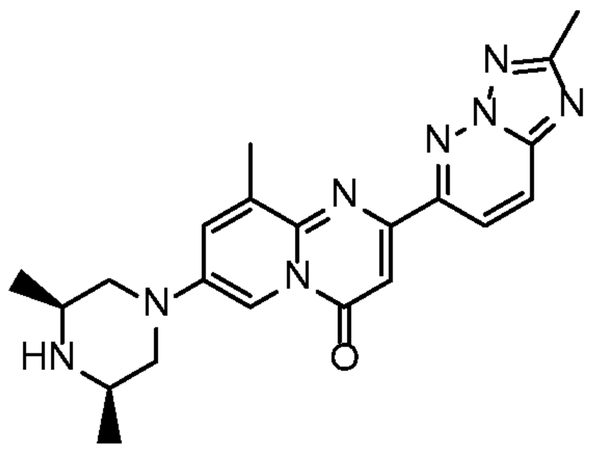

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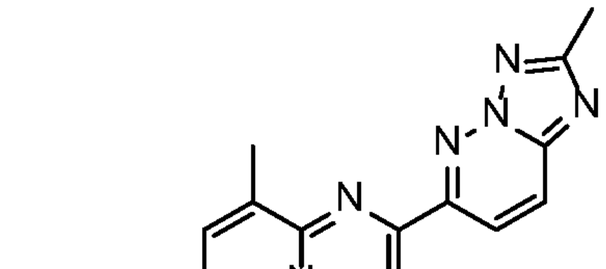

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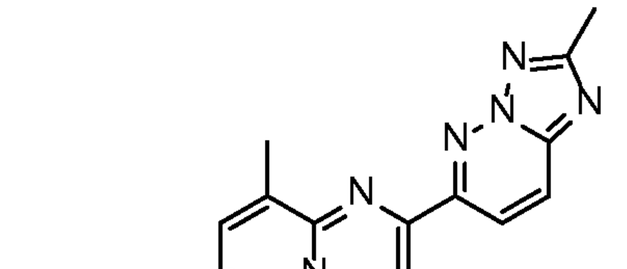

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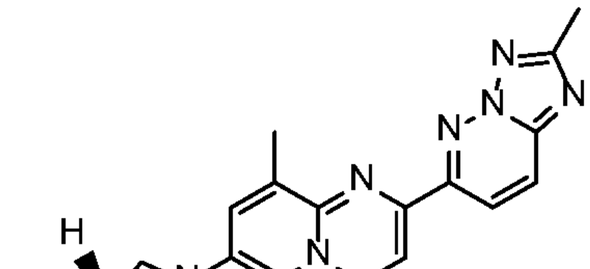

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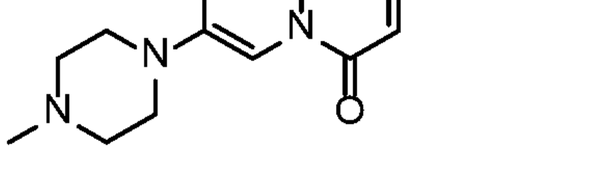

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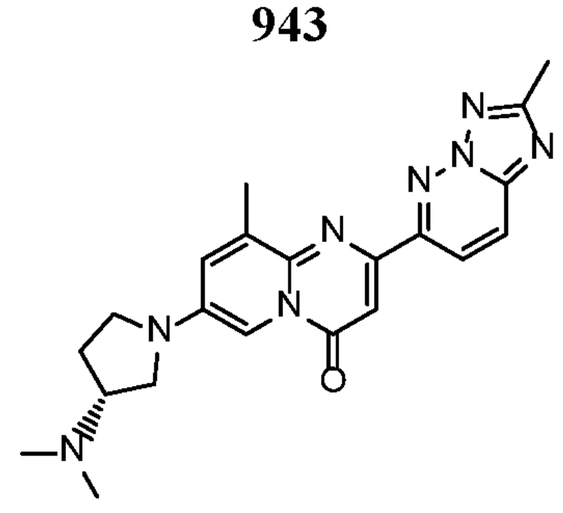

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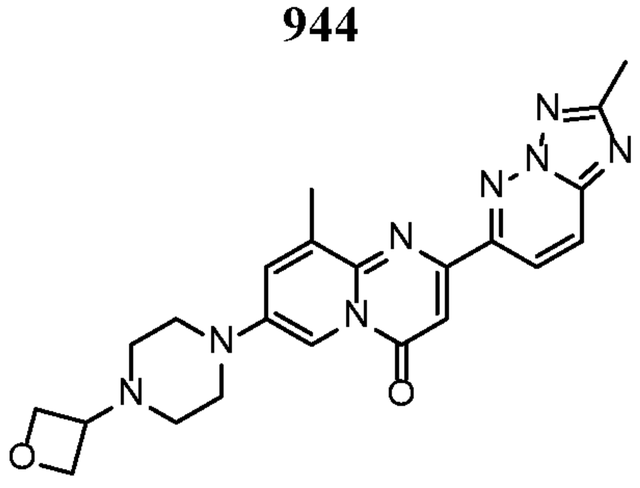

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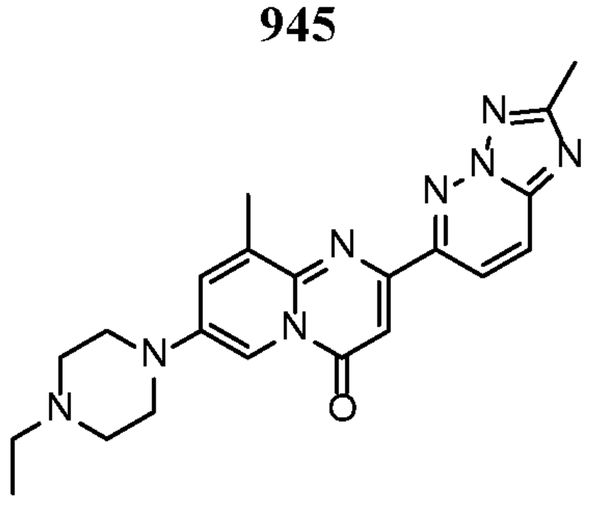

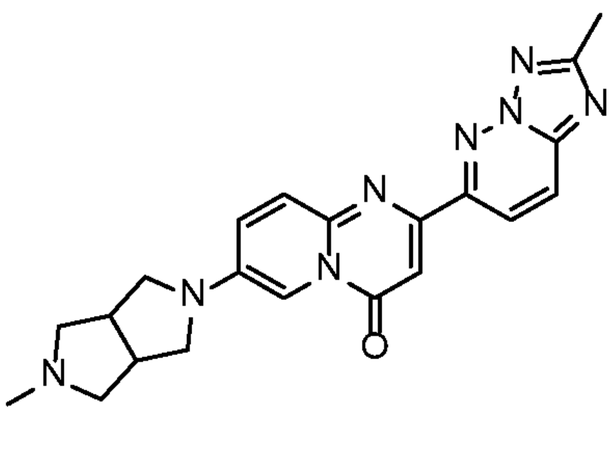

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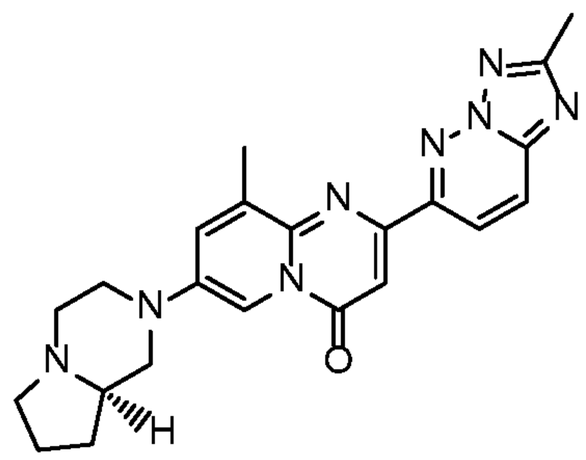

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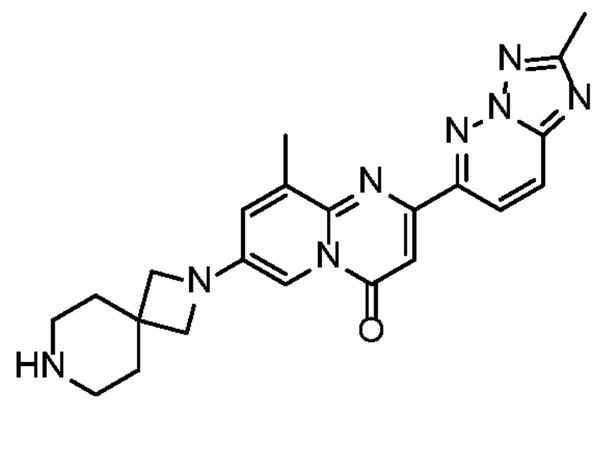

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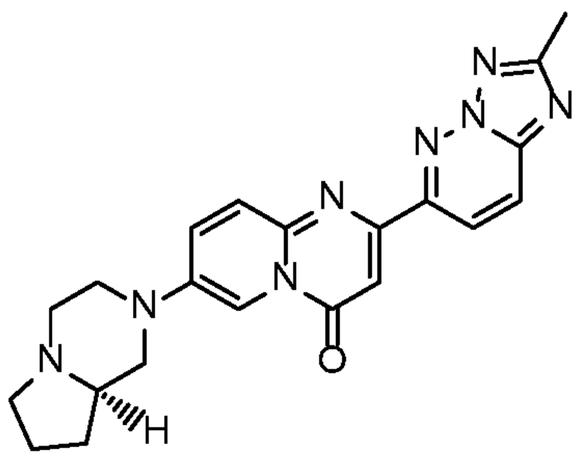

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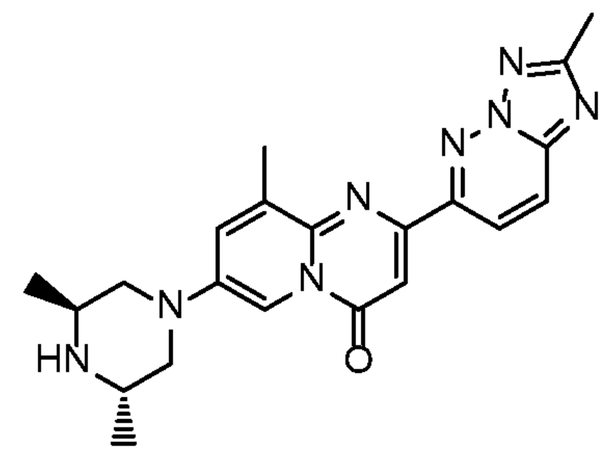

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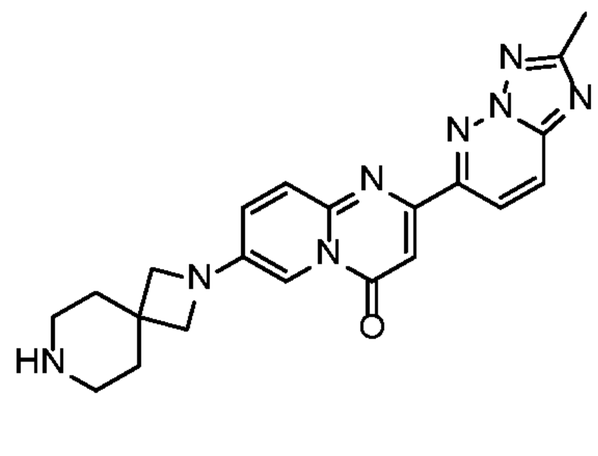

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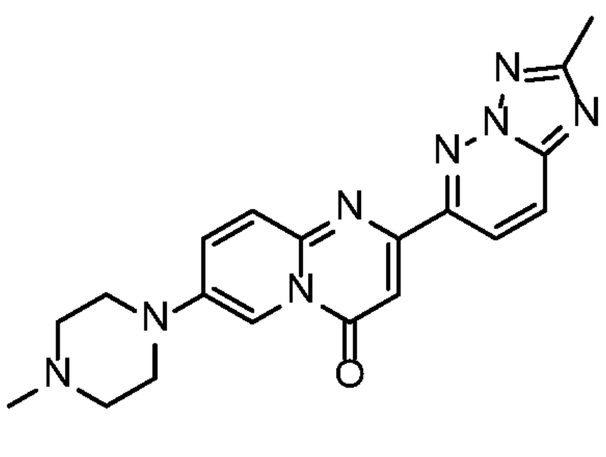

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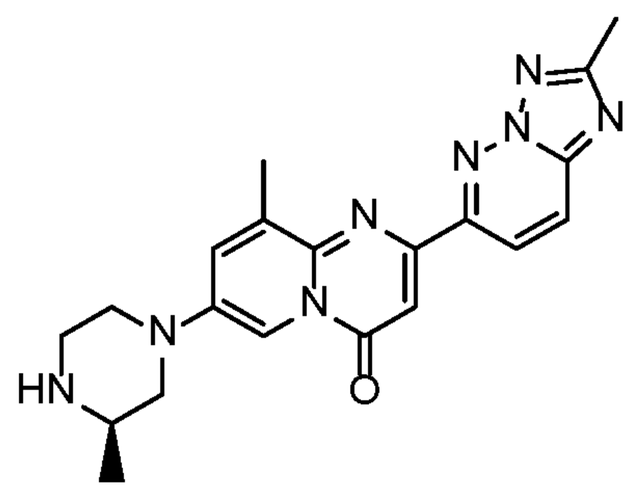

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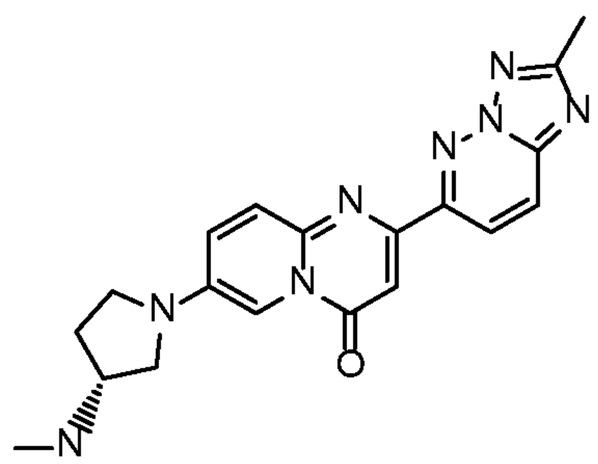

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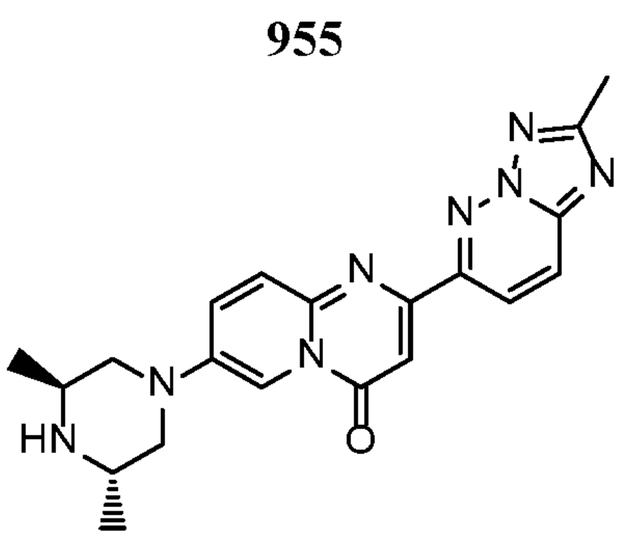

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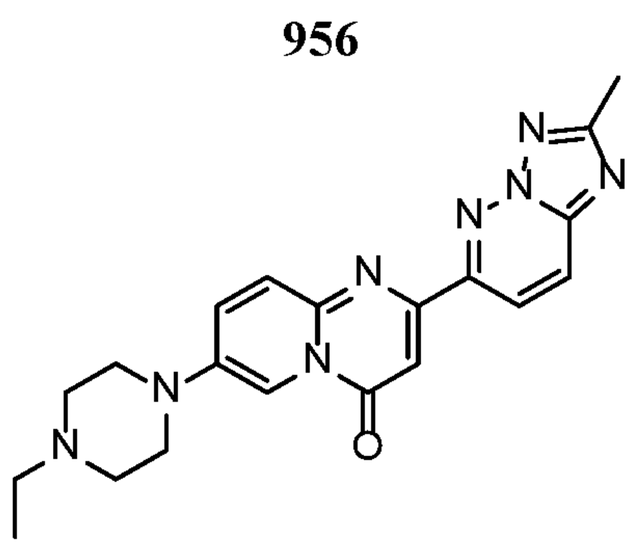

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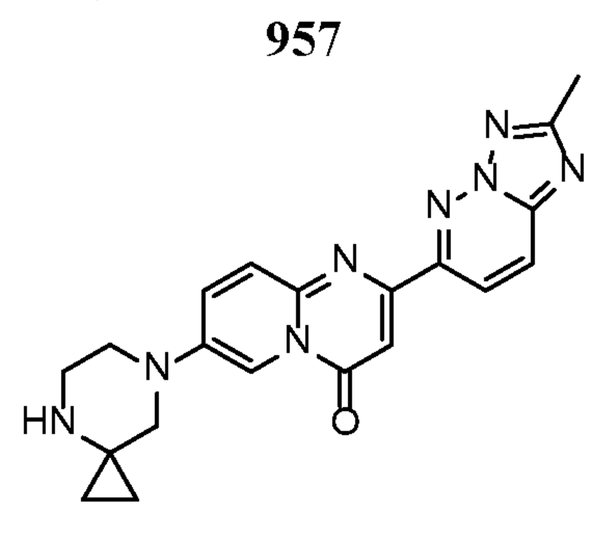

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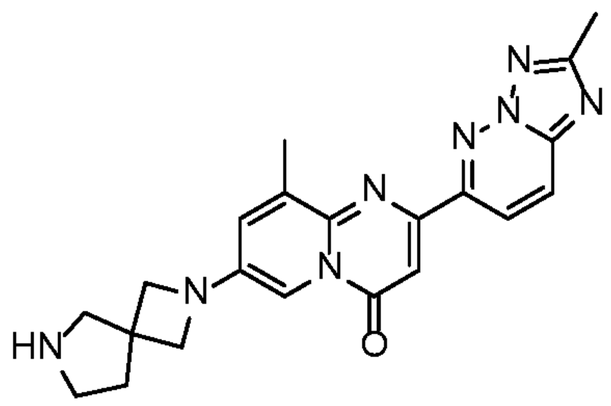
963, or



964

wherein the form of the compound is selected from the group consisting of a salt, prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

An aspect of the use of the compound of Formula (I) or a form thereof is a compound selected from the group consisting of (where compound number (#[1]) indicates that a salt form of the compound was isolated):

Cpd	Name
801	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[4-(2-hydroxyethyl)piperazin-1-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
802	2-(imidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
803	2-(4-fluoro-2-methyl-1,3-benzoxazol-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
804	7-(2,7-diazaspiro[3.5]non-7-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
805	7-(4-methylpiperazin-1-yl)-2-(2-methyl[1,2,4]triazolo[1,5-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
806	7-(4-methylpiperazin-1-yl)-2-[2-methyl-8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
807	2-methyl-6-[7-(4-methylpiperazin-1-yl)-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]imidazo[1,2-a]pyridine-8-carbonitrile
808	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
809	7-(4,7-diazaspiro[2.5]oct-7-yl)-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
810	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(1-methylpiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
811	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-(4-hydroxypiperidin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
812	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
813	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aR)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
814	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
815	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
816	2-(8-fluoro-2-methylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
817	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-(4-ethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
818	2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
819	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(4-ethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
820	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-[(8aS)-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
821	2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
822	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(4-ethyl-6-methylpyrazolo[1,5-a]pyrazin-2-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
827	7-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
828	7-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-2-(2,8-dimethylimidazo[1,2-a]pyridin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
835	2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-7-[(3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl]-4H-pyrido[1,2-a]pyrimidin-4-one
878	2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
879	(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
880	(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
881	(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
882	(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
883	(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
884	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
885	(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
886	(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
887	7-(1,4-diazepan-1-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
888	(S)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
889	(R)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
890	7-(1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
891	7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
892	(S)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
893	(S)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
894	(R)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
895	(R)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
896	2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
897	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
898	(R)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
899	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
900	7-(3,3-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
901	(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
902	(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
903	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
904	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
905	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
906	2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
907	(S)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
908	(S)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
909	7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
910	(S)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
911	(R)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
912	7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
913	7-(3,3-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
914	9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
915	7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
916	(R)-7-(3-ethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
917	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
918	7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
919	(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
920	7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
921	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
922	7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
923	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
924	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
925	7-(3,6-diazabicyclo[3.2.0]heptan-3-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
926	7-(4-(azetidin-3-yl)piperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
927	7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
928	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-(pyrrolidin-1-ylmethyl)piperidin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
929	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
930	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-(oxetan-3-yl)piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
931	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
932	(S)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
933	(R)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
934	(S)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
935	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
936	7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
937	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
938	7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
939	2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
940	(R)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
941	9-methyl-7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
942	7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
943	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
944	7-(3,3-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
945	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-((3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
946	(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
947	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-(oxetan-3-yl)piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
948	7-(4-ethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
949	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
950	(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
951	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
952	(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
953	7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
954[1]	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
955	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
956	(R)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
957	(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
958	7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
959	7-(4-ethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

Cpd	Name
960	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
961	(S)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
962	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one
963	7-((3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-2(3H)-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one, or
964	9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,6-diazaspiro[3.4]octan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

wherein the form of the compound is selected from the group consisting of a salt, prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

Another aspect of the present description includes a method of use of a compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound of Formula (I) or a form thereof to the subject.

Another aspect of the present description includes a use of the compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound of Formula (I) or a form thereof to the subject.

Another aspect of the present description includes a use of the compound salt of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound salt of Formula (I) or a form thereof to the subject.

Another aspect of the present description includes a method of use of a compound salt of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound salt of Formula (I) thereof to the subject, wherein the compound salt is selected from the group consisting of:

Cpd	Name
954	2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one trifluoroacetic acid

wherein the form of the compound salt is selected from the group consisting of a prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

CHEMICAL DEFINITIONS

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.

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

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

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

As used herein, the term "C_{1-8}alkoxy" generally refers to saturated hydrocarbon radicals having from one to eight carbon atoms in a straight or branched chain configuration of the formula: -O-C_{1-8}alkyl, including, but not limited to, methoxy, ethoxy, n-propoxy, isopropoxy,

n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentoxy, n-hexoxy and the like. In some aspects, C_{1-8}alkoxy includes, but is not limited to, C_{1-6}alkoxy, C_{1-4}alkoxy and the like. A C_{1-8}alkoxy radical is optionally substituted with substituent species as described herein where allowed by available valences.

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

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.

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, thienyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxazolyl, 1,3-thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, indolyl, indazolyl, indolizinyl, isoindolyl, benzofuranyl, benzothienyl, benzoimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 1,3-diazinyl, 1,2-diazinyl, 1,2-diazolyl, 1,4-diazanaphthalenyl, acridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, 6*H*-thieno[2,3-*b*]pyrrolyl, thieno[3,2-*c*]pyridinyl, thieno[2,3-*d*]pyrimidinyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, 1*H*-pyrrolo[2,3-*c*]pyridinyl, 1*H*-pyrrolo[3,2-*b*]pyridinyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrazolo[1,5-*a*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, pyrazolo[4,3-b]pyridinyl, pyrazolo[3,4-*c*]pyridinyl, imidazo[1,2-*a*]pyridinyl, 3*H*-imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl,

[1,3]oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, [1,2,4]triazolo[1,5-a]pyrimidinyl, [1,2,4]triazolo[1,5-b]pyridazinyl, pyrido[1,2-a]pyrimidinyl or pyrido[1,2-a]pyrimidinone 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.

In certain aspects, the nomenclature for a heteroaryl radical may differ, such as in non-limiting examples where furanyl may also be referred to as furyl, thienyl may also be referred to as thiophenyl, pyridinyl may also be referred to as pyridyl, benzothienyl may also be referred to as benzothiophenyl and 1,3-benzoxazolyl may also be referred to as 1,3-benzooxazolyl.

In certain other aspects, the term for a heteroaryl radical may also include other regioisomers, such as in non-limiting examples where the term pyrrolyl may also include 2*H*-pyrrolyl, 3*H*-pyrrolyl and the like, the term pyrazolyl may also include 1*H*-pyrazolyl and the like, the term imidazolyl may also include 1*H*-imidazolyl and the like, the term triazolyl may also include 1*H*-1,2,3-triazolyl and the like, the term oxadiazolyl may also include 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl and the like, the term tetrazolyl may also include 1*H*-tetrazolyl, 2*H*-tetrazolyl and the like, the term indolyl may also include 1*H*-indolyl and the like, the term indazolyl may also include 1*H*-indazolyl, 2*H*-indazolyl and the like, the term benzoimidazolyl may also include 1*H*-benzoimidazolyl and the term purinyl may also include 9*H*-purinyl and the like.

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

(3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl,
(3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl,
1,3,3a,4,6,6a-hexahydropyrrolo[3,4-*c*]pyrrolyl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl,
(3a*R*,6a*R*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl,
octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl,
(4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
(8a*S*)-3,4,6,7,8,8a-hexahydro-1*H*-pyrrolo[1,2-*a*]pyrazinyl,
(8a*R*)-3,4,6,7,8,8a-hexahydro-1*H*-pyrrolo[1,2-*a*]pyrazinyl,
(8a*S*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-*a*]pyrazinyl,
(8a*R*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-*a*]pyrazinyl,
(8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,
hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, octahydro-2*H*-pyrido[1,2-*a*]pyrazinyl,
(3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-(3H)-yl, 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,
3,6-diazabicyclo[3.2.0]heptyl, 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,
4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.4]octyl, 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.

In certain aspects, the nomenclature for a heterocyclyl radical may differ, such as in non-limiting examples where 1,3-benzodioxolyl may also be referred to as benzo[*d*][1,3]dioxolyl;
2,3-dihydro-1,4-benzodioxinyl may also be referred to as 2,3-dihydrobenzo[*b*][1,4]dioxinyl;
2,6-diazaspiro[3.3]heptyl may also be referred to as 2,6-diazaspiro[3.3]heptanyl;
4,7-diazaspiro[2.5]octyl may also be referred to as 4,7-diazaspiro[2.5]octanyl;
2,7-diazaspiro[3.5]nonyl may also be referred to as 2,7-diazaspiro[3.5]nonanyl; and, the like.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

As used herein, the term "substituent" means positional variables on the atoms of a core molecule that are substituted at a designated atom position, replacing one or more hydrogens on the designated atom, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. A person of ordinary skill in the art should note that any carbon as well as heteroatom with valences that appear 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. In certain instances one or more substituents having a double bond (e.g., "oxo" or "=O") as the point of attachment may be described, shown or listed herein within a substituent group, wherein the structure may only show a single bond as

the point of attachment to the core structure of Formula (I). A person of ordinary skill in the art would understand that, while only a single bond is shown, a double bond is intended for those substituents.

As used herein, the term "and the like," with reference to the definitions of chemical terms provided herein, means that variations in chemical structures that could be expected by one skilled in the art include, without limitation, isomers (including chain, branching or positional structural isomers), hydration of ring systems (including saturation or partial unsaturation of monocyclic, bicyclic or polycyclic ring structures) and all other variations where allowed by available valences which result in a stable compound.

For the purposes of this description, where one or more substituent variables for a compound of Formula (I) or a form thereof 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.

As used herein, the terms "independently selected," or "each selected" refer to functional variables in a substituent list that may occur more than once on the structure of Formula (I), the pattern of substitution at each occurrence is independent of the pattern at any other occurrence. Further, the use of a generic substituent variable on any formula or structure for a compound described herein is understood to include the replacement of the generic substituent with species substituents that are included within the particular genus, *e.g.*, aryl may be replaced with phenyl or naphthalenyl and the like, and that the resulting compound is to be included within the scope of the compounds described herein.

As used herein, the terms "each instance of" or "in each instance, when present," when used preceding a phrase such as "…C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-C_{1-4}alkyl, aryl, aryl-C_{1-4}alkyl, heteroaryl, heteroaryl-C_{1-4}alkyl, heterocyclyl and heterocyclyl-C_{1-4}alkyl," are intended to refer to the C_{3-14}cycloalkyl, aryl, heteroaryl and heterocyclyl ring systems when each are present either alone or as a substituent.

As used herein, the term "optionally substituted" means optional substitution with the specified substituent variables, groups, radicals or moieties.

COMPOUND FORMS

As used herein, the term "form" means a compound of Formula (I) having a form selected from the group consisting of a free acid, free base, prodrug, salt, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

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

In certain aspects described herein, the form of the compound of Formula (I) is a salt thereof.

In certain aspects described herein, the form of the compound of Formula (I) is an isotopologue thereof.

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

In certain aspects described herein, the form of the compound of Formula (I) is a tautomer thereof.

In certain aspects described herein, the form of the compound of Formula (I) is a pharmaceutically acceptable form.

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

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 characterized by standard analytical techniques described herein or well known to the skilled artisan.

As used herein, the term "protected" means that a functional group in a compound of Formula (I) or a form thereof 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. Such functional groups include hydroxy, phenol, amino and carboxylic acid. Suitable

protecting groups for hydroxy or phenol include trialkylsilyl or diarylalkylsilyl (e.g., t-butyldimethylsilyl, t-butyldiphenylsilyl or trimethylsilyl), tetrahydropyranyl, benzyl, substituted benzyl, methyl, methoxymethanol, and the like. Suitable protecting groups for amino, amidino and guanidino include t-butoxycarbonyl, benzyloxycarbonyl, and the like. Suitable protecting groups for carboxylic acid include alkyl, aryl or arylalkyl esters. In certain instances, the protecting group may also be a polymer resin, such as a Wang resin or a 2-chlorotrityl-chloride resin. Protecting groups may be added or removed in accordance with standard techniques, which are well-known to those skilled in the art and as described herein. It will also be appreciated by those skilled in the art, although such protected derivatives of compounds described herein may not possess pharmacological activity as such, they may be administered to a subject and thereafter metabolized in the body to form compounds described herein which are pharmacologically active. Such derivatives may therefore be described as "prodrugs". All prodrugs of compounds described herein are included within the scope of the use described herein.

As used herein, the term “prodrug” means a form of an instant compound (*e.g.*, a drug precursor) that is transformed *in vivo* to yield an 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 T. Higuchi and W. Stella, “Pro-drugs as Novel Delivery Systems,” Vol. 14 of the A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

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 a hydroxyl functional group, a prodrug form can be prepared by replacing the hydrogen atom of the hydroxyl with another functional group such as alkyl, alkylcarbonyl or a phosphonate ester and the like. In another example, when a compound of Formula (I) or a form thereof contains an amine functional group, a prodrug form can be prepared by replacing one or more amine hydrogen atoms with a functional group such as alkyl or substituted carbonyl. 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 and 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 as a prodrug.

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.

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

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

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) or a form thereof herein is understood to include reference to salt forms 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) or a form thereof contains both a basic moiety, such as, without limitation an amine moiety, 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.

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 the Formula (I) may be formed, for example, by reacting a compound of Formula (I) or a form thereof with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Pharmaceutically acceptable salts include one or more salts of acidic or basic groups present in compounds described herein. Aspects of acid addition salts include, and are not limited to, acetate, ascorbate, benzoate, benzenesulfonate, bisulfate, bitartrate, borate, bromide, butyrate, chloride, citrate, camphorate, camphorsulfonate, ethanesulfonate, formate, fumarate, gentisinate, gluconate, glucaronate, glutamate, iodide, isonicotinate, lactate, maleate, methanesulfonate, naphthalenesulfonate, nitrate, oxalate, pamoate, pantothenate, phosphate, propionate, saccharate, salicylate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate (also known as tosylate), trifluoroacetate salts and the like. Certain aspects of acid addition salts include chloride, dichloride, trichloride, bromide, acetate, formate or trifluoroacetate salts.

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

Suitable basic salts include, but are not limited to, aluminum, ammonium, calcium, lithium, magnesium, potassium, sodium and zinc salts.

All such acid salts and base salts are intended to be included within the scope of pharmaceutically acceptable salts as described herein. In addition, all such acid and base salts are considered equivalent to the free forms of the corresponding compounds for purposes of this description.

Compounds of Formula (I) and forms thereof may further exist in a tautomeric form. All such tautomeric forms are contemplated and intended to be included within the scope of the compounds of Formula (I) or a form thereof as described herein.

The compounds of Formula (I) or a form thereof may contain asymmetric or chiral centers, and, therefore, 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.

The compounds 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 aspect, the compounds described herein are (*S*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*S*) isomer. In another aspect, the compounds 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 described herein may also exist as a (*R,R*), (*R,S*), (*S,R*) or (*S,S*) isomer, as defined by *IUPAC* Nomenclature Recommendations.

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.

In one aspect of the description, a compound of Formula (I) or a form thereof is a substantially pure (*S*) enantiomer form 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%.

In one aspect of the description, a compound of Formula (I) or a form thereof is a substantially pure (*R*) enantiomer form 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%.

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, or about 80/20.

In addition, the present description embraces all geometric and positional isomers. For example, if a compound of Formula (I) or a form thereof 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. 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. 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 as part of this description.

All stereoisomers (for example, geometric isomers, optical isomers and the like) of the present compounds (including those of the salts, solvates, esters and prodrugs of the compounds as well as the salts, solvates and esters of the prodrugs), such as those 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, and diastereomeric forms, are contemplated within the scope of this description, as are positional isomers (such as, for example, 4-pyridyl and 3-pyridyl). Individual stereoisomers of the compounds described herein may, for example, be substantially free of other isomers, or may be present in a racemic mixture, as described supra.

The use of the terms "salt", "solvate", "ester", "prodrug" and the like, is intended to equally apply to the salt, solvate, ester and prodrug of enantiomers, stereoisomers, rotamers, tautomers, positional isomers, racemates or isotopologues of the instant compounds.

The term "isotopologue" refers to isotopically-enriched compounds described herein 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 ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{35}Cl and ^{36}Cl, respectively, each of which are also within the scope of this description.

Certain isotopically-enriched compounds described herein (*e.g.*, those labeled with ^{3}H and ^{14}C) are useful in compound and/or substrate tissue distribution assays. Tritiated (*i.e.*, ^{3}H) and carbon-14 (*i.e.*, ^{14}C) isotopes are particularly preferred for their ease of preparation and

detectability. Further, substitution with heavier isotopes such as deuterium (*i.e.*, ^{2}H) 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.

Polymorphic crystalline and amorphous forms of the compounds of Formula (I) and of the salts, solvates, hydrates, esters and prodrugs of the compounds of Formula (I) are further intended to be included in the present description.

COMPOUND USES

The present description relates to a method or use of a compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound or a form thereof to the subject.

The present description also relates to a method of use of the compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof.

The present description further relates to use of the compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof.

The present description further relates to use of the compound of Formula (I) or a form thereof having activity toward HD.

The present description further relates to use of the compound of Formula (I) or a form thereof in a combination therapy to provide additive or synergistic activity, thus enabling the development of a combination product for treating or ameliorating HD.

In addition to monotherapeutic use, the instant compounds are useful in a combination therapy with current standard of agents, having additive or synergistic activity with one or more known agents.

A combination therapy comprising compounds described herein in combination with one or more known drugs may be used to treat HD regardless of whether HD is responsive to the known drug.

Aspects of the present description include the use of a compound of Formula (I) or a form thereof in a combination therapy for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound of Formula (I) or a form thereof and an effective amount of one or more agent(s).

Aspects of the present description include the use of a compound of Formula (I) or a form thereof in a combination therapy for treating or ameliorating HD in a subject in need thereof

comprising, administering an effective amount of the compound of Formula (I) or a form thereof and an effective amount of one or more agent(s).

In an aspect of a use or method provided herein, compounds of Formula (I) or a form thereof used in combination with one or more additional agents can be administered to a subject or contacted with a subject or patient cell(s) prior to, concurrently with, or subsequent to administering to the subject or patient or contacting the cell with an additional agent(s). A compound(s) of Formula (I) or a form thereof and an additional agent(s) can be administered to a subject or contacted with a cell in single composition or different compositions. In a specific aspect, a compound(s) of Formula (I) or a form thereof is used in combination with gene therapy to inhibit HTT expression (using, *e.g.*, viral delivery vectors) or the administration of another small molecule HTT inhibitor. In another specific aspect, a compound(s) of Formula (I) or a form thereof are used in combination with cell replacement using differentiated non-mutant HTT stem cells. In another specific aspect, a compound(s) of Formula (I) or a form thereof are used in combination with cell replacement using differentiated HTT stem cells.

In one aspect, provided herein is the use of compounds of Formula (I) or a form thereof in combination with supportive standard of care therapies, including palliative care.

An aspect of the present description includes the use of a compound of Formula (I) or a form thereof in the preparation of a kit comprising the compound of Formula (I) or a form thereof and instructions for administering an effective amount of the compound of Formula (I) or a form thereof and an effective amount of one or more agent(s) in a combination therapy for treating or ameliorating HD in a subject in need thereof.

Accordingly, the present description relates to use of a compound of Formula (I) or a form thereof for treating or ameliorating HD. In accordance with the use of the present description, compounds that are useful in selectively treating or ameliorating HD, have been identified and use of these compounds for treating or ameliorating HD has been provided.

One aspect of the use of the present description relates to use of a compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound of Formula (I) or a form thereof to the subject.

One aspect of the use of the present description relates to a method of use of a compound of Formula (I) or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound to the subject.

An aspect of the use of the present description relates to use of a compound of Formula (I) or a form thereof in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the medicament to the subject.

An aspect of the use of the present description relates to use of a compound of Formula (I) or a form thereof in the preparation of a kit comprising the compound of Formula (I) or a form thereof and instructions for administering the compound for treating or ameliorating HD in a subject in need thereof.

In one respect, for each of such aspects, the subject is treatment naive. In another respect, for each of such aspects, the subject is not treatment naive.

As used herein, the phrases "a method or use for a compound for treating or ameliorating HD (Huntington's Disease)," "a method of use for a compound for treating or ameliorating HD" or "a use for a compound for treating or ameliorating HD" coextensively refer to a plurality of potential uses of a compound which would be known to those of skill in the art including, without limitation: (i) a method of use of a compound for treating or ameliorating HD; (ii) a use of a compound for treating or ameliorating HD; (iii) a use of a compound in the preparation of a medicament for treating or ameliorating HD; (iv) a use of a compound in the preparation of a pharmaceutical composition for treating or ameliorating HD; (iv) a use of a compound in the preparation of a kit for treating or ameliorating HD; and, the like.

As used herein, the term "treating" refers to: (i) preventing a disease, disorder or condition from occurring in a subject that may be predisposed to the disease, disorder and/or condition but has not yet been diagnosed as having the disease, disorder and/or condition; (ii) inhibiting a disease, disorder or condition, *i.e.*, arresting the development thereof; and/or (iii) relieving a disease, disorder or condition, *i.e.*, causing regression of the disease, disorder and/or condition.

As used herein, the term "subject" refers to an animal or any living organism having sensation and the power of voluntary movement, and which requires oxygen and organic food. Nonlimiting examples include members of the human, primate, equine, porcine, bovine, murine, rattus, canine and feline specie. In some aspects, the subject is a mammal or a warm-blooded

vertebrate animal. In other aspects, the subject is a human. As used herein, the term “patient” may be used interchangeably with “subject” and “human”.

As used herein, the terms “effective amount” or "therapeutically effective amount" mean an amount of compound of Formula (I) or a form, composition or medicament thereof effective in inhibiting the above-noted diseases and thus producing the desired therapeutic, ameliorative, inhibitory or preventative effect in a subject in need thereof.

The dose administered to achieve an effective target plasma concentration may also be administered based upon the weight of the subject or patient. Doses administered on a weight basis may be in the range of about 0.001 mg/kg/day to about 3500 mg/kg/day, or about 0.001 mg/kg/day to about 3000 mg/kg/day, or about 0.001 mg/kg/day to about 2500 mg/kg/day, or about 0.001 mg/kg/day to about 2000 mg/kg/day, or about 0.001 mg/kg/day to about 1500 mg/kg/day, or about 0.001 mg/kg/day to about 1000 mg/kg/day, or about 0.001 mg/kg/day to about 500 mg/kg/day, or about 0.001 mg/kg/day to about 250 mg/kg/day, or about 0.001 mg/kg/day to about 100 mg/kg/day, or about 0.001 mg/kg/day to about 75 mg/kg/day, or about 0.001 mg/kg/day to about 50 mg/kg/day, or about 0.001 mg/kg/day to about 40 mg/kg/day, or about 0.001 mg/kg/day to about 30 mg/kg/day, or about 0.001 mg/kg/day to about 20 mg/kg/day, or about 0.001 mg/kg/day to about 10 mg/kg/day, or about 0.01 mg/kg/day to about 2000 mg/kg/day, or about 0.01 mg/kg/day to about 1500 mg/kg/day, or about 0.01 mg/kg/day to about 1000 mg/kg/day, or about 0.01 mg/kg/day to about 600 mg/kg/day, or about 0.01 mg/kg/day to about 500 mg/kg/day, or about 0.01 mg/kg/day to about 300 mg/kg/day, or about 0.015 mg/kg/day to about 200 mg/kg/day, or about 0.02 mg/kg/day to about 100 mg/kg/day, or about 0.025 mg/kg/day to about 100 mg/kg/day, or about 0.03 mg/kg/day to about 100 mg/kg/day, wherein said amount is orally administered once (once in approximately a 24 hour period), twice (once in approximately a 12 hour period) or thrice (once in approximately an 8 hour period) daily according to subject weight.

In certain aspects, the effective amount will be in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day, or about 0.01 mg/kg/day to about 500 mg/kg/day, or about 0.1 mg to about 500 mg/kg/day, or about 1.0 mg/day to about 500 mg/kg/day, in single, divided, or a continuous dose for a patient or subject having a weight in a range of between about 40 to about 200 kg (which dose may be adjusted for patients or subjects above or below this range,

particularly children under 40 kg). The typical adult subject is expected to have a median weight in a range of about 70 kg.

In another aspect, where daily doses are adjusted based upon the weight of the subject or patient, compounds described herein may be formulated for delivery at about 0.02, 0.025, 0.03, 0.05, 0.06, 0.075, 0.08, 0.09, 0.10, 0.20, 0.25, 0.30, 0.50, 0.60, 0.75, 0.80, 0.90, 1.0, 1.10, 1.20, 1.25, 1.50, 1.75, 2.0, 3.0, 5.0, 10, 20, 30, 40, 50, 100, 150, 200, 250, 300, 400 or 500 mg/kg/day. Daily doses adjusted based upon the weight of the subject or patient may be administered as a single, divided, or continuous dose. In aspects where a dose of compound is given more than once per day, the dose may be administered twice, thrice, or more times per day.

Within the scope of the present description, the "effective amount" of a compound of Formula (I) or a form thereof for use in the manufacture of a medicament, for use in the preparation of a pharmaceutical kit or in a method of use for treating or ameliorating HD in a subject in need thereof is intended to include an amount in a range of from about 0.001 mg/kg/day to about 3500 mg/kg/day, or about 0.001 mg/kg/day to about 3000 mg/kg/day, or about 0.001 mg/kg/day to about 2500 mg/kg/day, or about 0.001 mg/kg/day to about 2000 mg/kg/day, or about 0.001 mg/kg/day to about 1500 mg/kg/day, or about 0.001 mg/kg/day to about 1000 mg/kg/day, or about 0.001 mg/kg/day to about 500 mg/kg/day, or about 0.001 mg/kg/day to about 250 mg/kg/day, or about 0.001 mg/kg/day to about 100 mg/kg/day, or about 0.001 mg/kg/day to about 75 mg/kg/day, or about 0.001 mg/kg/day to about 50 mg/kg/day, or about 0.001 mg/kg/day to about 40 mg/kg/day, or about 0.001 mg/kg/day to about 30 mg/kg/day, or about 0.001 mg/kg/day to about 20 mg/kg/day, or about 0.001 mg/kg/day to about 10 mg/kg/day, or about 0.01 mg/kg/day to about 2000 mg/kg/day, or about 0.01 mg/kg/day to about 1500 mg/kg/day, or about 0.01 mg/kg/day to about 1000 mg/kg/day, or about 0.01 mg/kg/day to about 600 mg/kg/day, or about 0.01 mg/kg/day to about 500 mg/kg/day, or about 0.01 mg/kg/day to about 300 mg/kg/day, or about 0.015 mg/kg/day to about 200 mg/kg/day, or about 0.02 mg/kg/day to about 100 mg/kg/day, or about 0.025 mg/kg/day to about 100 mg/kg/day, or about 0.03 mg/kg/day to about 100 mg/kg/day, wherein said amount is administered once (once in approximately a 24 hour period; i.e., "q.d."), twice (once in approximately a 12 hour period; i.e., "b.i.d." or "q.12h"), thrice (once in approximately an 8 hour period; i.e., "t.i.d." or "q.8h"), or four times (once in approximately a 6 hour period; i.e., "q.d.s.", "q.i.d." or "q.6h") daily according to subject weight.

Such amounts may further include an amount in a range of from about 0.001 mg to about 3500 mg administered daily; 0.001 mg to about 3000 mg administered daily; 0.001 mg to about 2500 mg administered daily; 0.001 mg to about 2000 mg administered daily; 0.001 mg to about 1500 mg administered daily; 0.001 mg to about 1000 mg administered daily; 0.001 mg to about 500 mg administered daily; 0.001 mg to about 250 mg administered daily; 1.0 mg to about 3500 mg administered daily; 1.0 mg to about 1500 mg administered daily; 1.0 mg to about 1000 mg administered daily; 10.0 mg to about 600 mg administered daily; 0.5 mg to about 2000 mg administered daily; or, an amount in a range of from about 5.0 mg to about 300 mg administered daily.

For example, the effective amount may be the amount required to treat HD in a subject or, more specifically, in a human. The effective amount for a subject will depend upon various factors, including the subject's body weight, size and health. Effective amounts for a given patient can be determined by routine experimentation that is within the skill and judgment of the clinician.

For any compound, the effective amount can be estimated initially either in cell culture assays or in relevant animal models, such as a mouse, chimpanzee, marmoset or tamarin animal model. Relevant animal models may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, ED_{50} (the dose therapeutically effective in 50% of the population) and LD_{50} (the dose lethal to 50% of the population). The dose ratio between therapeutic and toxic effects is therapeutic index, and can be expressed as the ratio, LD_{50}/ED_{50}. In some aspects, the effective amount is such that a large therapeutic index is achieved. In further aspects, the dosage is within a range of circulating concentrations that include an ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed, sensitivity of the patient, and the route of administration.

More specifically, the concentration-biological effect relationships observed with regard to a compound of Formula (I) or a form thereof indicate a target plasma concentration ranging from approximately 0.001 μg/mL to approximately 50 μg/mL, from approximately 0.01 μg/mL to approximately 20 μg/mL, from approximately 0.05 μg/mL to approximately 10 μg/mL, or from

approximately 0.1 μg/mL to approximately 5 μg/mL. To achieve such plasma concentrations, the compounds described herein may be administered at doses that vary, such as, for example, without limitation, from 0.1 ng to 10,000 mg, depending upon the route of administration in single, divided, or continuous doses for a patient weighing between about 10 to about 100 kg (which dose may be adjusted for patients within this weight range, particularly for children under 40 kg).

The exact dosage will be determined by the practitioner, in light of factors related to the subject. Dosage and administration may be adjusted to provide sufficient levels of the active agent(s) or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, general health of the subject, ethnicity, age, weight, gender, diet, time of day and frequency of administration, drug combination(s), reaction sensitivities, experience with other therapies, and tolerance/response to therapy. Long-acting pharmaceutical compositions may be administered every 2, 3 or 4 days, once every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

The compounds and compositions described herein may be administered to the subject via any drug delivery route known in the art. Nonlimiting examples include oral, ocular, rectal, buccal, topical, nasal, sublingual, transdermal, subcutaneous, intramuscular, intraveneous (bolus and infusion), intracerebral, and pulmonary routes of administration.

In one aspect, provided herein are methods for modulating the amount of HTT (huntingtin protein), comprising contacting a human cell with a compound of Formula (I) or a form thereof. In a specific aspect, provided herein are methods for modulating the amount of HTT, comprising contacting a human cell with a compound of Formula (I) or a form thereof that modulates the expression of HTT. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I).

In a specific aspect, provided herein is a method for enhancing the inhibition of mutant HTT transcribed from the Htt gene, comprising contacting a human cell with a compound of

Formula (I) or a form thereof. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of wild-type "normal" HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I).

In another aspect, provided herein is a method for modulating the inhibition of mutant HTT transcribed from the Htt gene, comprising administering to a non-human animal model for HD a compound of Formula (I) or a form thereof. In a specific aspect, provided herein is a method for modulating the inhibition of mutant HTT transcribed from the Htt gene, comprising administering to a non-human animal model for HD a compound of Formula (I) or a form thereof. In a specific aspect, the compound is a form of the compound of Formula (I).

In another aspect, provided herein is a method for decreasing the amount of mutant HTT, comprising contacting a human cell with a compound of Formula (I) or a form thereof. In a specific aspect, provided herein is a method for decreasing the amount of mutant HTT, comprising contacting a human cell with a compound of Formula (I) that inhibits the transcription of mutant *HTT* (huntingtin mRNA) from the Htt gene. In another specific aspect, provided herein is a method for decreasing the amount of HTT, comprising contacting a human cell with a compound of Formula (I) that inhibits the expression of mutant HTT transcribed from the Htt gene. The human cell can be contacted with a compound of Formula (I) or a form thereof *in vitro*, or *in vivo*, *e.g.*, in a non-human animal or in a human. In a specific aspect, the human cell is from or in a human. In another specific aspect, the human cell is from or in a human with HD. In another specific aspect, the human cell is from or in a human with HD, caused by a CAG repeat in the Htt gene, resulting in a loss of HTT expression and/or function. In another aspect, the human cell is from a human with HD. In another aspect, the human cell is in a human with HD. In one aspect, the compound is a form of the compound of Formula (I).

In certain aspects, treating or ameliorating HD with a compound of Formula (I) or a form thereof (alone or in combination with an additional agent) has a therapeutic effect and/or beneficial effect. In a specific aspect, treating HD with a compound of Formula (I) or a form

thereof (alone or in combination with an additional agent) results in one, two or more of the following effects: (i) reduces or ameliorates the severity of HD; (ii) delays onset of HD; (iii) inhibits the progression of HD; (iv) reduces hospitalization of a subject; (v) reduces hospitalization length for a subject; (vi) increases the survival of a subject; (vii) improves the quality of life for a subject; (viii) reduces the number of symptoms associated with HD; (ix) reduces or ameliorates the severity of a symptom(s) associated with HD; (x) reduces the duration of a symptom associated with HD; (xi) prevents the recurrence of a symptom associated with HD; (xii) inhibits the development or onset of a symptom of HD; and/or (xiii) inhibits of the progression of a symptom associated with HD.

METABOLITES

Also included within the scope of the present description are the use of *in vivo* metabolic products of the compounds described herein. Such products may result, for example, from the oxidation, reduction, hydrolysis, amidation, esterification and the like of the administered compound, primarily due to enzymatic processes. Accordingly, the description includes the use of compounds produced by a process comprising contacting a compound described herein with a mammalian tissue or a mammal for a period of time sufficient to yield a metabolic product thereof.

Such products typically are identified by preparing a radio-labeled isotopologue (*e.g.*, ^{14}C or ^{3}H) of a compound described herein, administering the radio-labeled compound in a detectable dose (*e.g.*, greater than about 0.5 mg/kg) to a mammal such as a rat, mouse, guinea pig, dog, monkey or human, allowing sufficient time for metabolism to occur (typically about 30 seconds to about 30 hours), and identifying the metabolic conversion products from urine, bile, blood or other biological samples. The conversion products are easily isolated since they are "radiolabeled" by virtue of being isotopically-enriched (others are isolated by the use of antibodies capable of binding epitopes surviving in the metabolite). The metabolite structures are determined in conventional fashion, *e.g.*, by MS or NMR analysis. In general, analysis of metabolites may be done in the same way as conventional drug metabolism studies well-known to those skilled in the art. The conversion products, so long as they are not otherwise found *in vivo*, are useful in diagnostic assays for therapeutic dosing of the compounds described herein even if they possess no biological activity of their own.

PHARMACEUTICAL COMPOSITIONS

Aspects of the present description include the use of a compound of Formula (I) or a form thereof in a pharmaceutical composition for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the compound of Formula (I) or a form thereof in admixture with one or more pharmaceutically acceptable excipient(s).

An aspect of the present description includes the use of a pharmaceutical composition of the compound of Formula (I) or a form thereof in the preparation of a kit comprising the pharmaceutical composition of the compound of Formula (I) or a form thereof and instructions for administering the compound for treating or ameliorating HD in a subject in need thereof.

As used herein, the term "composition" means a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts.

The pharmaceutical composition may be formulated to achieve a physiologically compatible pH, ranging from about pH 3 to about pH 11. In some aspects, the pharmaceutical composition is formulated to achieve a pH of from about pH 3 to about pH 7. In other aspects, the pharmaceutical composition is formulated to achieve a pH of from about pH 5 to about pH 8.

The term "pharmaceutically acceptable excipient" refers to an excipient for administration of a pharmaceutical agent, such as the compounds described herein. The term refers to any pharmaceutical excipient that may be administered without undue toxicity. Pharmaceutically acceptable excipients may be determined in part by the particular composition being administered, as well as by the particular mode of administration and/or dosage form. Nonlimiting examples of pharmaceutically acceptable excipients include carriers, solvents, stabilizers, adjuvants, diluents, *etc.* Accordingly, there exists a wide variety of suitable formulations of pharmaceutical compositions for the instant compounds described herein (*see*, *e.g.*, Remington's Pharmaceutical Sciences).

Suitable excipients may be carrier molecules that include large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and inactive antibodies. Other exemplary excipients include antioxidants such as ascorbic acid; chelating agents such as EDTA; carbohydrates such as dextrin, hydroxyalkylcellulose, hydroxyalkylmethylcellulose (*e.g.*, hydroxypropylmethylcellulose, also known as HPMC), stearic acid; liquids such as oils, water, saline, glycerol and ethanol; wetting or

emulsifying agents; pH buffering substances; and the like. Liposomes are also included within the definition of pharmaceutically acceptable excipients.

The pharmaceutical compositions described herein may be formulated in any form suitable for the intended use described herein. Suitable formulations for oral administration include solids, liquid solutions, emulsions and suspensions, while suitable inhalable formulations for pulmonary administration include liquids and powders. Alternative formulations include syrups, creams, ointments, tablets, and lyophilized solids which can be reconstituted with a physiologically compatible solvent prior to administration.

When intended for oral use for example, tablets, troches, lozenges, aqueous or oil suspensions, non-aqueous solutions, dispersible powders or granules (including micronized particles or nanoparticles), emulsions, hard or soft capsules, syrups or elixirs may be prepared. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions, and such compositions may contain one or more agents including sweetening agents, flavoring agents, coloring agents, and preserving agents, in order to provide a palatable preparation.

Pharmaceutically acceptable excipients suitable for use in conjunction with tablets include, for example, inert diluents, such as celluloses, calcium or sodium carbonate, lactose, calcium or sodium phosphate; disintegrating agents, such as croscarmellose sodium, cross-linked povidone, maize starch, or alginic acid; binding agents, such as povidone, starch, gelatin or acacia; and lubricating agents, such as magnesium stearate, stearic acid, or talc. Tablets may be uncoated or may be coated by known techniques including microencapsulation to delay disintegration and adsorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate alone or with a wax may be employed.

Formulations for oral use may be also presented as hard gelatin capsules where the active ingredient is mixed with an inert solid diluent, for example celluloses, lactose, calcium phosphate, or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with non-aqueous or oil medium, such as glycerin, propylene glycol, polyethylene glycol, peanut oil, liquid paraffin, or olive oil.

In other aspects, pharmaceutical compositions described herein may be formulated as suspensions comprising a compound of Formula (I) or a form thereof in admixture with one or

more pharmaceutically acceptable excipient(s) suitable for the manufacture of a suspension. In yet other aspects, pharmaceutical compositions described herein may be formulated as dispersible powders and granules suitable for preparation of a suspension by the addition of one or more excipient(s).

Excipients suitable for use in connection with suspensions include suspending agents, such as sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcelluose, sodium alginate, polyvinylpyrrolidone, gum tragacanth, gum acacia, dispersing or wetting agents such as a naturally occurring phosphatide (*e.g.*, lecithin), a condensation product of an alkylene oxide with a fatty acid (*e.g.*, polyoxyethylene stearate), a condensation product of ethylene oxide with a long chain aliphatic alcohol (*e.g.*, heptadecaethyleneoxycethanol), a condensation product of ethylene oxide with a partial ester derived from a fatty acid and a hexitol anhydride (*e.g.*, polyoxyethylene sorbitan monooleate); and thickening agents, such as carbomer, beeswax, hard paraffin, or cetyl alcohol. The suspensions may also contain one or more preservatives such as acetic acid, methyl and/or n-propyl p-hydroxy-benzoate; one or more coloring agents; one or more flavoring agents; and one or more sweetening agents such as sucrose or saccharin.

The pharmaceutical compositions described herein may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, such as olive oil or arachis oil, a mineral oil, such as liquid paraffin, or a mixture of these. Suitable emulsifying agents include naturally-occurring gums, such as gum acacia and gum tragacanth; naturally occurring phosphatides, such as soybean lecithin, esters or partial esters derived from fatty acids; hexitol anhydrides, such as sorbitan monooleate; and condensation products of these partial esters with ethylene oxide, such as polyoxyethylene sorbitan monooleate. The emulsion may also contain sweetening and flavoring agents. Syrups and elixirs may be formulated with sweetening agents, such as glycerol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, a flavoring or a coloring agent.

Additionally, the pharmaceutical compositions described herein may be in the form of a sterile injectable preparation, such as a sterile injectable aqueous emulsion or oleaginous suspension. Such emulsion or suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, such as a solution in 1,2-propanediol. The

sterile injectable preparation may also be prepared as a lyophilized powder. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile fixed oils may be employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or di-glycerides. In addition, fatty acids such as oleic acid may likewise be used in the preparation of injectables.

The compounds described herein may be substantially insoluble in water and sparingly soluble in most pharmaceutically acceptable protic solvents and vegetable oils, but generally soluble in medium-chain fatty acids (*e.g.*, caprylic and capric acids) or triglycerides and in propylene glycol esters of medium-chain fatty acids. Thus, contemplated in the description are compounds which have been modified by substitutions or additions of chemical or biochemical moieties which make them more suitable for delivery (*e.g.*, increase solubility, bioactivity, palatability, decrease adverse reactions, *etc.*), for example by esterification, glycosylation, PEGylation, etc.

In some aspects, the compound described herein is formulated for oral administration in a lipid-based composition suitable for low solubility compounds. Lipid-based formulations can generally enhance the oral bioavailability of such compounds. As such, pharmaceutical compositions described herein may comprise a effective amount of a compound of Formula (I) or a form thereof, together with at least one pharmaceutically acceptable excipient selected from medium chain fatty acids or propylene glycol esters thereof (*e.g.*, propylene glycol esters of edible fatty acids such as caprylic and capric fatty acids) and pharmaceutically acceptable surfactants, such as polysorbate 20 or 80 (also referred to as Tween® 20 or Tween® 80, respectively) or polyoxyl 40 hydrogenated castor oil.

In other aspects, the bioavailability of low solubility compounds may be enhanced using particle size optimization techniques including the preparation of nanoparticles or nanosuspensions using techniques known to those skilled in the art. The compound forms present in such preparations include amorphous, partially amorphous, partially crystalline or crystalline forms.

In alternative aspects, the pharmaceutical composition may further comprise one or more aqueous solubility enhancer(s), such as a cyclodextrin. Nonlimiting examples of cyclodextrin include hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of α-, β-,

and γ-cyclodextrin, and hydroxypropyl-β-cyclodextrin (HPBC). In some aspects, the pharmaceutical composition further comprises HPBC in a range of from about 0.1% to about 20%, from about 1% to about 15%, or from about 2.5% to about 10%. The amount of solubility enhancer employed may depend on the amount of the compound in the composition.

PREPARATION OF COMPOUNDS

Compounds of Formula (I) can be prepared using reagents and methods known in the art, including the methods provided in International Application No. PCT/EP2015/060343, filed on May 11, 2015, and published as International Publication No. WO 2015/173181 on November 19, 2015; and, International Application No. PCT/EP2016/060952, filed on May 17, 2016, and published as International Publication No. WO 2016/184832 on November 24, 2016, the entire contents of each of which are incorporated herein by reference.

BIOLOGICAL EXAMPLES

The following *in vitro* biological examples demonstrate the usefulness of the compounds of the present description for treating Huntington's disease.

To describe in more detail and assist in understanding the present description, the following non-limiting biological examples are offered to more fully illustrate the scope of the description and are not to be construed as specifically limiting the scope thereof. Such variations of the present description that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the present description and as hereinafter claimed.

Compounds of Formula (I) were tested using the Meso Scale Discovery (MSD) Assay provided in International Application No. PCT/US2016/066042, filed on December 11, 2016 and claiming priority to United States Provisional Application U.S. 62/265,652 filed on December 10, 2015, and published as International Publication No. WO 2017/100726 on June 15, 2017, the entire contents of which are incorporated herein by reference.

The Endogenous Huntingtin Protein assay used in Example 1 was developed using the ELISA-based MSD electrochemiluminescence assay platform.

Example 1

Endogenous Huntingtin Protein Assay

Meso Scale Discovery (MSD) 96-well or 384-well plates were coated overnight at 4°C with MW1 (expanded polyglutamine) or MAB2166 monoclonal antibody (for capture) at a concentration of 1 μg/mL in PBS (30 μL per well). Plates were then washed three times with 300 μL wash buffer (0.05% Tween-20 in PBS) and blocked (100 μL blocking buffer; 5% BSA in PBS) for 4-5 hours at room temperature with rotational shaking and then washed three times with wash buffer.

Samples (25 μL) were transferred to the antibody-coated MSD plate and incubated overnight at 4°C. After removal of the lysates, the plate was washed three times with wash buffer, and 25 μL of #5656S (Cell signaling; rabbit monoclonal) secondary antibody (diluted to 0.25 μg/mL in 0.05% Tween-20 in blocking buffer) was added to each well and incubated with shaking for 1Hour at room temperature. Following incubation with the secondary antibody, the wells were rinsed with wash buffer after which 25 μL of goat anti-rabbit SULFO TAG secondary detection antibody (required aspect of the MSD system) (diluted to 0.25 μg/mL in 0.05% Tween-20 in blocking buffer) was added to each well and incubated with shaking for 1 hour at room temperature. After rinsing three times with wash buffer, 150 μL of read buffer T with surfactant (MSD) were added to each empty well, and the plate was imaged on a SI 6000 imager (MSD) according to manufacturers' instructions provided for 96- or 384-well plates. The resulting IC_{50} values (μM) for compounds tested are shown in Table 1.

Representative compounds tested in the assay described herein had the following IC_{50} values:

Compound	IC_{50}
886	*****
899	****
905	**

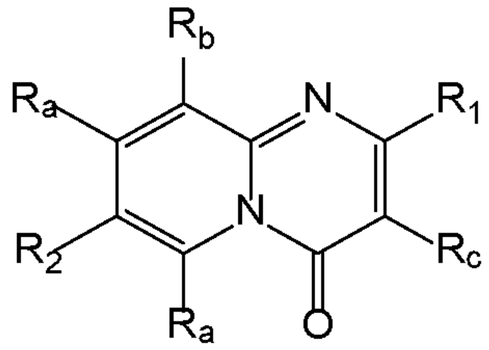
As shown above, an IC_{50} value between > 3 μM and ≤ 33 μM is indicated by a single star (*), an IC_{50} value between > 1 μM and ≤ 3 μM is indicated by two stars (**), an IC_{50} value between > 0.5 μM and ≤ 1 μM is indicated by three stars (***), an IC_{50} value between > 0.1 μM and ≤ 0.5 μM is indicated by four stars (****) and an IC_{50} value of ≤ 0.1 μM is indicated by five stars (*****).

Without regard to whether a document cited herein was specifically and individually indicated as being incorporated by reference, all documents referred to herein are incorporated by reference into the present application for any and all purposes to the same extent as if each individual reference was fully set forth herein.

Having now fully described the subject matter of the claims, it will be understood by those having ordinary skill in the art that the same can be performed within a wide range of equivalents without affecting the scope of the subject matter or aspects described herein. It is intended that the appended claims be interpreted to include all such equivalents.

What is claimed is:

1. A method of use of a compound for treating or ameliorating HD (Huntington's Disease) in a subject in need thereof comprising administering to the subject an effective amount of a compound of Formula (I):



(I)

or a form thereof, wherein:

R_1 is heterocyclyl optionally substituted with one, two or three R_3 substituents and optionally, with one additional R_4 substituent; or, optionally substituted with one, two, three or four R_3 substituents;

R_2 is heteroaryl optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent;

R_a is, in each instance, independently selected from hydrogen, halogen or $C_{1\text{-}8}$alkyl;

R_b and R_c are, in each instance, independently selected from hydrogen, halogenb or $C_{1\text{-}8}$alkyl;

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

R_4 is $C_{3\text{-}14}$cycloalkyl, $C_{3\text{-}14}$cycloalkyl-$C_{1\text{-}8}$alkyl, $C_{3\text{-}14}$cycloalkyl-amino, aryl-$C_{1\text{-}8}$alkyl, aryl-$C_{1\text{-}8}$alkoxy-carbonyl, aryl-sulfonyloxy-$C_{1\text{-}8}$alkyl, heterocyclyl or

heterocyclyl-C_{1-8}alkyl; wherein, each instance of C_{3-14}cycloalkyl, aryl and heterocyclyl is optionally substituted with one, two or three R_5 substituents;

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

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

R_7 is C_{3-14}cycloalkyl, C_{3-14}cycloalkyl-oxy, aryl, heterocyclyl or heteroaryl; and,

wherein the form of the compound is selected from the group consisting of a salt, prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

2. The method of claim 2, wherein R_1 is heterocyclyl selected from azetidinyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, piperazinyl, 1,4-diazepanyl, 3,6-dihydropyridinyl, 1,2,5,6-tetrahydropyridinyl, 1,2,3,6-tetrahydropyridinyl, hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, (3a*R*,6a*R*)-hexahydropyrrolo[3,4-*b*]pyrrol-(1*H*)-yl, hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, (3a*S*,6a*S*)-hexahydropyrrolo[3,4-*b*]pyrrol-(2*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, (3a*R*,6a*S*)-hexahydropyrrolo[3,4-*c*]pyrrol-(1*H*)-yl, 1,3,3a,4,6,6a-hexahydropyrrolo[3,4-*c*]pyrrolyl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*R*,7a*R*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, (4a*S*,7a*S*)-octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, hexahydropyrrolo[1,2-*a*]pyrazin-(2*H*)-one, hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (7*R*,8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*R*)-hexahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, (8a*S*)-3,4,6,7,8,8a-hexahydro-1*H*-pyrrolo[1,2-a]pyrazinyl, (8a*R*)-3,4,6,7,8,8a-hexahydro-1*H*-pyrrolo[1,2-a]pyrazinyl, (8a*S*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (8a*R*)-1,3,4,6,7,8-hexahydropyrrolo[1,2-a]pyrazinyl, (8a*S*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl,

(8a*R*)-octahydropyrrolo[1,2-*a*]pyrazin-(1*H*)-yl, octahydro-2H-pyrido[1,2-*a*]pyrazinyl, (3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-(3H)-yl, 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, 3,6-diazabicyclo[3.2.0]heptyl, 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, 4,7-diazaspiro[2.5]octyl, 2,6-diazaspiro[3.4]octyl, 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 one, two or three R_3 substituents and optionally, with one additional R_4 substituents; or, optionally, with one, two, three or four R_3 substituents.

3. The method of claim 4, wherein R_2 is heteroaryl selected from thienyl, 1*H*-pyrazolyl, 1*H*-imidazolyl, 1,3-thiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, pyridinyl, pyrimidinyl, 1*H*-indolyl, 2*H*-indolyl, 1*H*-indazolyl, 2*H*-indazolyl, indolizinyl, benzofuranyl, benzothienyl, 1*H*-benzimidazolyl, 1,3-benzothiazolyl, 1,3-benzoxazolyl, 9*H*-purinyl, quinazolinyl, quinoxalinyl, 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, pyrazolo[4,3-b]pyridinyl, pyrazolo[3,4-*c*]pyridinyl, imidazo[1,2-*a*]pyridinyl, 3*H*-imidazo[4,5-*b*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[2,1-*b*][1,3]thiazolyl, imidazo[2,1-*b*][1,3,4]thiadiazolyl, [1,3]oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, [1,2,4]triazolo[1,5-a]pyrimidinyl, [1,2,4]triazolo[1,5-b]pyridazinyl, pyrido[1,2-a]pyrimidinyl or pyrido[1,2-a]pyrimidinone; wherein, each instance of heteroaryl is optionally substituted with one, two or three R_6 substituents and optionally, with one additional R_7 substituent.

4. A method of use of a compound or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound selected from the group consisting of:

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

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

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

2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(1,4-diazepan-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(8a-methylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-(3,3-dimethylpiperazin-1-yl)-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-9-methyl-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2,8-dimethylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-7-([1,3'-bipyrrolidin]-1'-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(3-ethylpiperazin-1-yl)-2-(2-methylimidazo[1,2-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,6-diazabicyclo[3.2.0]heptan-3-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-(azetidin-3-yl)piperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-(pyrrolidin-1-ylmethyl)piperidin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-(oxetan-3-yl)piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-7-(4-methyl-1,4-diazepan-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3R,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(3,3-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-((3aR,6aS)-5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-(oxetan-3-yl)piperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(R)-7-(3-(dimethylamino)pyrrolidin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3S,5S)-3,5-dimethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-(4-ethylpiperazin-1-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(4,7-diazaspiro[2.5]octan-7-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

(S)-9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(3-methylpiperazin-1-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

7-((3aR,4aR,7aS)-hexahydro-1H-cyclobuta[1,2-c:1,4-c']dipyrrol-2(3H)-yl)-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-4H-pyrido[1,2-a]pyrimidin-4-one, or

9-methyl-2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,6-diazaspiro[3.4]octan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one

wherein the form of the compound is selected from the group consisting of a salt, prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

5. A method of use of a compound salt or a form thereof for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of a compound salt selected from the group consisting of:

2-(2-methyl-[1,2,4]triazolo[1,5-b]pyridazin-6-yl)-7-(2,7-diazaspiro[3.5]nonan-2-yl)-4H-pyrido[1,2-a]pyrimidin-4-one trifluoroacetic acid

wherein the form of the compound salt is selected from the group consisting of a prodrug, hydrate, solvate, clathrate, isotopologue, racemate, enantiomer, diastereomer, stereoisomer, polymorph and tautomer form thereof.

6. The method of any of claims 1, 4 or 5, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

7. A use of the compound of any of claims 1, 4 or 5 for treating or ameliorating HD in a subject in need thereof comprising, administering to the subject an effective amount of the compound.

8. The use of claim 7, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

9. A use of the compound of any of claims 1, 4 or 5 in the manufacture of a medicament for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the medicament to the subject.

10. The use of claim 9, wherein the effective amount of the compound in the medicament is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

11. A use of the compound of any of claims 1, 4 or 5 in admixture with one or more pharmaceutically acceptable excipient(s) in a pharmaceutical composition for treating or ameliorating HD in a subject in need thereof comprising, administering an effective amount of the pharmaceutical composition to the subject.

12. The use of claim 11, wherein the effective amount of the compound in the pharmaceutical composition is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.