

INHIBITORS OF SOLUTE CARRIER FAMILY 6A MEMBER 19 (SLC6A19) AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 63/535,282 filed on August 29, 2023, and U.S. Provisional Application No. 63/572,752 filed on April 1, 2024, each of which is hereby incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Solute carrier family 6A member 19 (SLC6A19), also known as B0AT1, is a sodium-dependent neutral amino acid (NAA) transporter that is predominantly expressed on the apical membranes of renal and intestinal epithelial cells (Fairweather *et al. J. Biol. Chem* (2015) 290, 24308-24325). In the intestines, surface expression of SLC6A19 is dependent on the chaperone protein ACE2, for amino acid uptake (Singer *et al Am. J. Physiol. Gastrointest. Liver Physiol* (2012) 303, G686-G695). In the kidneys, SLC6A19 requires TMEM27 for surface expression to reabsorb amino acids (Verrey *et al. Arch. Eur. J. Physiol.* (2009) 458, 53-60).

[0003] Phenylketonuria (PKU) is caused by mutations in the enzyme phenylalanine hydroxylase (PAH), the key enzyme in the metabolism of phenylalanine (Phe) to tyrosine (Tyr), both of which are NAA. PKU patients have toxic buildup of Phe in the blood and other tissues, leading to neurologic alterations (Scriver C.R *Hum. Mutat.* (2007) 28, 831-843). Treatment options for PKU include severely limiting protein intake, which has poor compliance, and the 2 FDA-approved drugs, Palynziq and Kuvan, both of which are limited to a subset of patients; significant unmet medical need still remain (Strisciuglio *et. al. Metabolites* (2014) 4, 1007-1017; Gentile *et. al. Mol. Genet. and Metab.* (2010) 99, S64-S67). Because the symptoms of PKU are a result of systemic buildup of Phe, inhibition of SLC6A19 to limit the intestinal absorption of Phe and its reuptake in the kidneys can be a viable approach to treating PKU. Indeed, loss of SLC6A19 in a mouse model of PKU significantly increased the excretion of Phe in urine and dramatically reduced plasma Phe and normalized neurotransmitter levels (Belanger *et al. JCI Insight* (2018) 3, e121762).

[0004] The prevalence of chronic kidney disease (CKD) is rapidly increasing and an estimated 15% of the US adult population have CKD (CDC 2021). An association of loss-of-function splice (c.1173+2T>G) (Sveinbjornsson G. *et al. Hum. Mol. Genet.* (2014) 23, 6935-6943) and missense (D173N) variants in SLC6A19 with protection from CKD has been reported (Sinnott-Amstrong N. *et al. Nat. Genet.* (2021) 53, 185-194).

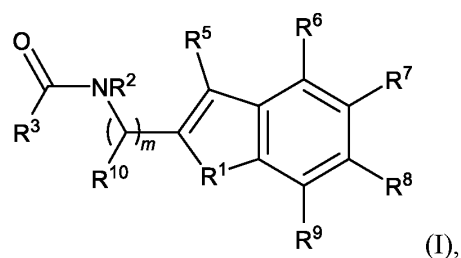
[0005] Metabolic syndrome, and related diseases such as diabetes, is a global epidemic with an estimated one third of US adults having metabolic syndrome (Saklayen M. *Curr Hypertens Rep* (2018) 20, 12). Mice with deletion of SLC6A19 have a number of improved metabolic outcomes, including resistance to weight gain on a high-fat diet, improved glucose tolerance and insulin sensitivity, and increased energy expenditure (Jiang *et al. Mol. Metab.* (2015) 4, 406-417). These positive outcomes are likely due to increased secretion of FGF21 and GLP-1, two hormones that play important roles in regulating energy metabolism, (Geng *et al. Nat Rev Endo.* (2020) 16, 654-667; Baggio *et al. Mol Metab* (2021) 46). Inhibiting SLC6A19, therefore, may be an effective approach to treat metabolic diseases.

[0006] In humans, SLC6A19 biallelic loss of function results in a rare disease called Hartnup disorder, which is predominantly asymptomatic in patients with adequate nutrition (Seow *et al. Nat. Genet.* (2004) 36, 1003-1007. Azmanov *et al. Hum. Mutat.* (2008) 29, 1217-1221). Since the NAA tryptophan is essential for the synthesis of nicotinamide, Harnup patients may develop niacin deficiency and its associated symptoms, which include dermatitis, photosensitivity, and psychosis, but these symptoms are well-controlled with niacin supplementation (Hashmi *et al. StatPearls* (2021)). Similarly, mice with complete loss of SLC6A19 are viable and fertile (Jiang *et al. Mol. Metab.* (2015) 4, 406-417). Thus, inhibition of SLC6A19 is believed to be a viable therapeutic approach.

[0007] There remains a need for therapies to treat such diseases/disorders.

BRIEF SUMMARY OF THE INVENTION

[0008] In one aspect, provided herein is a compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and
the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-;

each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN, and

the C_{1-6} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo;

R^6 and R^9 are each independently H or halo;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a},

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

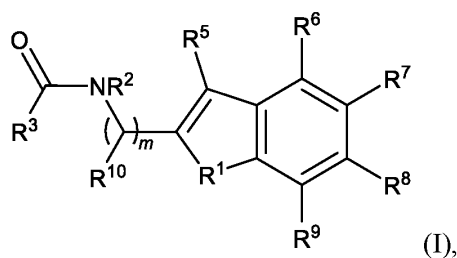
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b},

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}, and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0009] In some embodiments of a compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

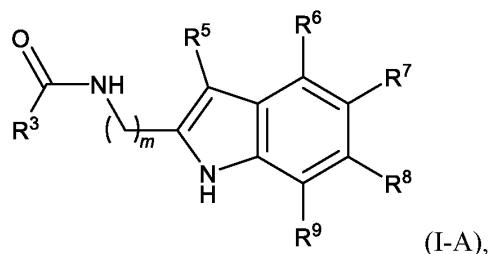
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}, and

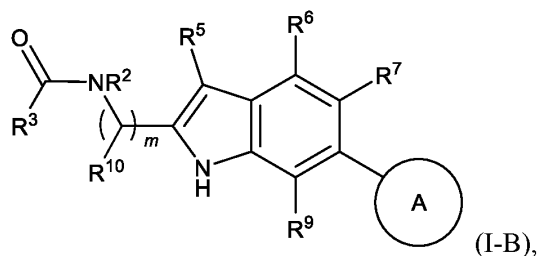
R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0010] In one aspect, provided herein is a compound of formula (I-A):



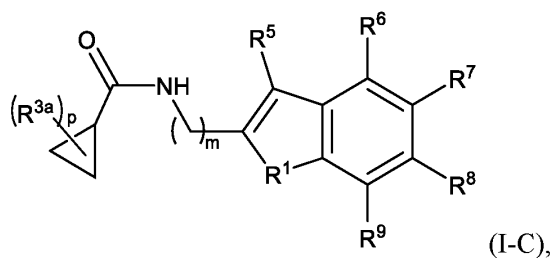
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0011] In one aspect, provided herein is a compound of formula (I-B):



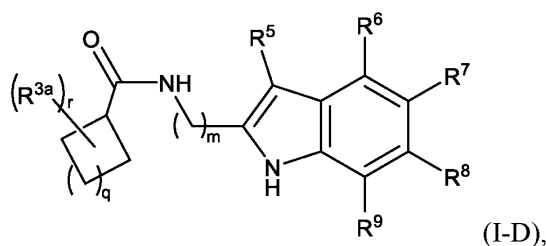
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^2 , R^3 , R^5 , R^6 , R^7 , R^9 , R^{10} and ring A are as defined elsewhere herein.

[0012] In one aspect, provided herein is a compound of formula (I-C):



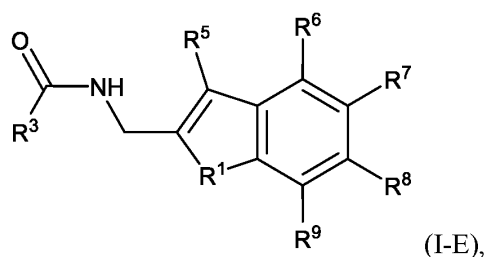
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , p , R^{3a} , R^1 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0013] In one aspect, provided herein is a compound of formula (I-D):



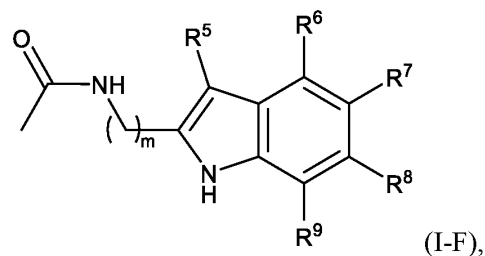
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , q , r , R^{3a} , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0014] In one aspect, provided is a compound of formula (I-E):



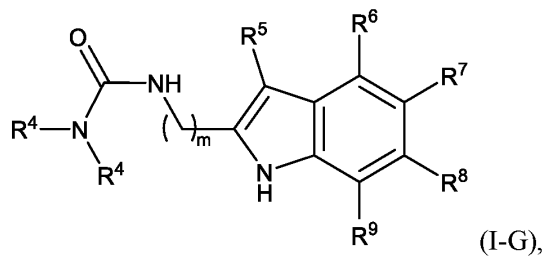
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^1 , R^3 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0015] In one aspect, provided herein is a compound of formula (I-F):



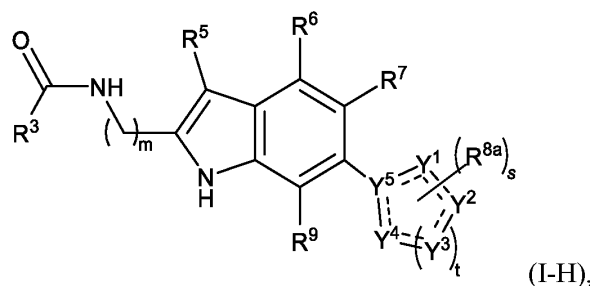
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0016] In one aspect, provided herein is a compound of formula (I-G):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^4 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0017] In one aspect, provided herein is a compound of formula (I-H):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , s , t , R^3 , R^5 , R^6 , R^7 , R^9 , R^{8a} , Y^1 , Y^2 , Y^3 , Y^4 , and Y^5 are as defined elsewhere herein.

[0018] In one aspect, provided herein is a pharmaceutical composition, comprising (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and (ii) one or more pharmaceutically acceptable excipients.

[0019] In one aspect, provided herein is a method of modulating SLC6A19 in a cell, comprising exposing the cell to (i) an effective amount of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients.

[0020] In one aspect, provided herein is a method of inhibiting SLC6A19 in a cell, comprising exposing the cell to (i) an effective amount of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients.

[0021] In one aspect, provided herein is a method of modulating SLC6A19 in a cell of an individual in need thereof, comprising administering to the individual an effective amount of (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients.

[0022] In one aspect, provided herein is a method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual an effective amount of (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients.

[0023] In another variation, provided herein is a method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients. In some embodiments, a therapeutically effective amount of the compound or pharmaceutical composition is administered.

[0024] In one aspect, provided herein is a kit, comprising (i) an effective amount of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, and (ii)

instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

[0025] In another variation, provided herein is a kit, comprising (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof. In some embodiments, the kit comprises a therapeutically effective amount of the compound or pharmaceutical composition.

[0026] In some aspects, provided herein are methods of preparing a compound of formula (I), or any embodiment or variation thereof, such as a compound of formula (I), (I-A), (I-A1), (I-A2), (I-A3), (I-A4), (I-A5), (I-A6), (I-B), (I-C), (I-C1), (I-C2), (I-C3), (I-C4), (I-D), (I-D1), (I-E), (I-F), (I-G), or (I-H), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

DETAILED DESCRIPTION OF THE INVENTION

[0027] “Individual” refers to mammals and includes humans and non-human mammals. Examples of individuals include, but are not limited to, mice, rats, hamsters, guinea pigs, pigs, rabbits, cats, dogs, goats, sheep, cows, and humans. In some embodiments, individual refers to a human.

[0028] As used herein, “about” a parameter or value includes and describes that parameter or value per se. For example, “about X” includes and describes X per se.

[0029] “Treatment” or “treating” is an approach for obtaining beneficial or desired results including clinical results. Beneficial or desired results may include one or more of the following: decreasing one or more symptom resulting from the disease or condition; diminishing the extent of the disease or condition; slowing or arresting the development of one or more symptom associated with the disease or condition (*e.g.*, stabilizing the disease or condition, preventing or delaying the worsening or progression of the disease or condition); and relieving the disease, such as by causing the regression of clinical symptoms (*e.g.*,

ameliorating the disease state, enhancing the effect of another medication, delaying the progression of the disease, increasing the quality of life, and/or prolonging survival).

[0030] As used herein, “delaying” development of a disease or condition means to defer, hinder, slow, retard, stabilize and/or postpone development of the disease or condition. This delay can be of varying lengths of time, depending on the history of the disease and/or individual being treated. As is evident to one skilled in the art, a sufficient or significant delay can, in effect, encompass prevention, in that the individual does not develop the disease or condition.

[0031] As used herein, the term “therapeutically effective amount” or “effective amount” intends such amount of a compound of the disclosure or a pharmaceutically salt thereof sufficient to effect treatment when administered to an individual. As is understood in the art, an effective amount may be in one or more doses, *e.g.*, a single dose or multiple doses may be required to achieve the desired treatment endpoint. An effective amount may be considered in the context of administering one or more therapeutic agents, and a single agent may be considered to be given in an effective amount if, in conjunction with one or more other agents, a desirable or beneficial result may be or is achieved.

[0032] As used herein, “unit dosage form” refers to physically discrete units, suitable as unit dosages, each unit containing a predetermined quantity of active ingredient, or compound, which may be in a pharmaceutically acceptable carrier.

[0033] As used herein, by “pharmaceutically acceptable” is meant a material that is not biologically or otherwise undesirable, *e.g.*, the material may be incorporated into a pharmaceutical composition administered to an individual without causing significant undesirable biological effects.

[0034] The term “alkyl”, as used herein, refers to an unbranched or branched saturated univalent hydrocarbon chain. As used herein, alkyl has 1-20 carbons (*i.e.*, C₁₋₂₀alkyl), 1-16 carbons (*i.e.*, C₁₋₁₆alkyl), 1-12 carbons (*i.e.*, C₁₋₁₂alkyl), 1-10 carbons (*i.e.*, C₁₋₁₀alkyl), 1-8 carbons (*i.e.*, C₁₋₈alkyl), 1-6 carbons (*i.e.*, C₁₋₆alkyl), 1-4 carbons (*i.e.*, C₁₋₄alkyl), or 1-3 carbons (*i.e.*, C₁₋₃alkyl). Examples of alkyl groups include, but are not limited to, methyl, ethyl, propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl, *tert*-butyl, pentyl, 2-pentyl, *iso*-pentyl, *neo*-pentyl, hexyl, 2-hexyl, 3-hexyl, and 3-methylpentyl. When an alkyl residue having a specific number of carbons is named by chemical name or molecular formula, all positional

isomers having that number of carbon atoms may be encompassed—for example, “butyl” includes *n*-butyl, *sec*-butyl, *iso*-butyl, and *tert*-butyl; and “propyl” includes *n*-propyl and *iso*-propyl. Certain commonly used alternative names may be used and will be understood by those of ordinary skill in the art. For instance, a divalent group, such as a divalent “alkyl” group, may be referred to as an “alkylene”.

[0035] The term “alkenyl”, as used herein, refers to a branched or unbranched univalent hydrocarbon chain comprising at least one carbon-carbon double bond. As used herein, alkenyl has 2-20 carbons (*i.e.*, C₂₋₂₀alkenyl), 2-16 carbons (*i.e.*, C₂₋₁₆alkenyl), 2-12 carbons (*i.e.*, C₂₋₁₂alkenyl), 2-10 carbons (*i.e.*, C₂₋₁₀alkenyl), 2-8 carbons (*i.e.*, C₂₋₈alkenyl), 2-6 carbons (*i.e.*, C₂₋₆alkenyl), 2-4 carbons (*i.e.*, C₂₋₄alkenyl), or 2-3 carbons (*i.e.*, C₂₋₃alkenyl). Examples of alkenyl include, but are not limited to, ethenyl, prop-1-enyl, prop-2-enyl, 1,2-butadienyl, and 1,3-butadienyl. When an alkenyl residue having a specific number of carbons is named by chemical name or molecular formula, all positional isomers having that number of carbon atoms may be encompassed—for example, “propenyl” includes prop-1-enyl and prop-2-enyl. Certain commonly used alternative names may be used and will be understood by those of ordinary skill in the art. For instance, a divalent group, such as a divalent “alkenyl” group, may be referred to as an “alkenylene”.

[0036] The term “alkynyl”, as used herein, refers to a branched or unbranched univalent hydrocarbon chain comprising at least one carbon-carbon triple bond. As used herein, alkynyl has 2-20 carbons (*i.e.*, C₂₋₂₀alkynyl), 2-16 carbons (*i.e.*, C₂₋₁₆alkynyl), 2-12 carbons (*i.e.*, C₂₋₁₂alkynyl), 2-10 carbons (*i.e.*, C₂₋₁₀alkynyl), 2-8 carbons (*i.e.*, C₂₋₈alkynyl), 2-6 carbons (*i.e.*, C₂₋₆alkynyl), 2-4 carbons (*i.e.*, C₂₋₄alkynyl), or 2-3 carbons (*i.e.*, C₂₋₃alkynyl). Examples of alkynyl include, but are not limited to, ethynyl, prop-1-ynyl, prop-2-ynyl, but-1-ynyl, but-2-ynyl, and but-3-ynyl. When an alkynyl residue having a specific number of carbons is named by chemical name or molecular formula, all positional isomers having that number of carbon atoms may be encompassed—for example, “propynyl” includes prop-1-ynyl and prop-2-ynyl. Certain commonly used alternative names may be used and will be understood by those of ordinary skill in the art. For instance, a divalent group, such as a divalent “alkynyl” group, may be referred to as an “alkynylene”.

[0037] The term “alkoxy”, as used herein, refers to an -O-alkyl moiety. Examples of alkoxy groups include, but are not limited to, methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *tert*-butoxy, *sec*-butoxy, *n*-pentoxy, *n*-hexoxy, and 1,2-dimethylbutoxy.

[0038] The term “aryl”, as used herein, refers to a fully unsaturated carbocyclic ring moiety. The term “aryl” encompasses monocyclic and polycyclic fused-ring moieties. As used herein, aryl encompasses ring moieties comprising, for example, 6 to 20 annular carbon atoms (*i.e.*, C₆₋₂₀aryl), 6 to 16 annular carbon atoms (*i.e.*, C₆₋₁₆aryl), 6 to 12 annular carbon atoms (*i.e.*, C₆₋₁₂aryl), or 6 to 10 annular carbon atoms (*i.e.*, C₆₋₁₀aryl). Examples of aryl moieties include, but are not limited to, phenyl, naphthyl, fluorenyl, and anthryl.

[0039] The term “cycloalkyl”, as used herein, refers to a saturated or partially unsaturated carbocyclic ring moiety. The term “cycloalkyl” encompasses monocyclic and polycyclic ring moieties, wherein the polycyclic moieties may be fused, branched, or spiro. Cycloalkyl includes cycloalkenyl groups, wherein the ring moiety comprises at least one annular double bond. Cycloalkyl includes any polycyclic carbocyclic ring moiety comprising at least one non-aromatic ring, regardless of the point of attachment to the remainder of the molecule. As used herein, cycloalkyl includes rings comprising, for example, 3 to 20 annular carbon atoms (*i.e.*, a C₃₋₂₀cycloalkyl), 3 to 16 annular carbon atoms (*i.e.*, a C₃₋₁₆cycloalkyl), 3 to 12 annular carbon atoms (*i.e.*, a C₃₋₁₂cycloalkyl), 3 to 10 annular carbon atoms (*i.e.*, a C₃₋₁₀cycloalkyl), 3 to 8 annular carbon atoms (*i.e.*, a C₃₋₈cycloalkyl), 3 to 6 annular carbon atoms (*i.e.*, a C₃₋₆cycloalkyl), or 3 to 5 annular carbon atoms (*i.e.*, a C₃₋₅cycloalkyl). Monocyclic cycloalkyl ring moieties include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic groups include, for example, bicyclo[2.2.1]heptanyl, bicyclo[2.2.2]octanyl, adamantyl, norbornyl, decalanyl, 7,7-dimethyl -bicyclo [2.2.1]heptanyl, and the like. Still further, cycloalkyl also includes spiro cycloalkyl ring moieties, for example, spiro[2.5]octanyl, spiro[4.5]decanyl, or spiro [5.5]undecanyl.

[0040] The term “halo”, as used herein, refers to atoms occupying groups VIIA of The Periodic Table and includes fluorine (fluoro), chlorine (chloro), bromine (bromo), and iodine (iodo). Additionally, terms such as “haloalkyl” are meant to include monohaloalkyl and polyhaloalkyl. For example, the term “C1-C4 haloalkyl” is mean to include trifluoromethyl, 2,2,2-trifluoroethyl, 4-chlorobutyl, 3-bromopropyl, difluoromethyl, and the like.

[0041] The term “heteroaryl”, as used herein, refers to an aromatic (fully unsaturated) ring moiety that comprises one or more annular heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur. The term “heteroaryl” includes both monocyclic and polycyclic fused-ring moieties. As used herein, a heteroaryl comprises, for example, 5 to 20 annular atoms (*i.e.*, a 5-20 membered heteroaryl), 5 to 16 annular atoms (*i.e.*, a 5-16 membered heteroaryl), 5 to 12 annular atoms (*i.e.*, a 5-12 membered heteroaryl), 5 to 10 annular atoms (*i.e.*, a 5-10 membered heteroaryl), 5 to 8 annular atoms (*i.e.*, a 5-8 membered heteroaryl), or 5 to 6 annular atoms (*i.e.*, a 5-6 membered heteroaryl). Any monocyclic or polycyclic aromatic ring moiety comprising one or more annular heteroatoms is considered a heteroaryl, regardless of the point of attachment to the remainder of the molecule (*i.e.*, the heteroaryl moiety may be attached to the remainder of the molecule through any annular carbon or any annular heteroatom of the heteroaryl moiety). Examples of heteroaryl groups include, but are not limited to, acridinyl, benzimidazolyl, benzothiazolyl, benzindolyl, benzofuranyl, benzothiazolyl, benzothiadiazolyl, benzonaphthofuranyl, benzoxazolyl, benzothienyl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridyl, carbazolyl, cinnolinyl, dibenzofuranyl, dibenzothiophenyl, furanyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, isoquinolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 1-oxidopyridinyl, 1-oxidopyrimidinyl, 1-oxidopyrazinyl, 1-oxidopyridazinyl, phenazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinazoliny, quinoxaliny, quinoliny, quinuclidiny, isoquinoliny, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, and triazinyl. Examples of the fused-heteroaryl rings include, but are not limited to, benzo[d]thiazolyl, quinoliny, isoquinoliny, benzo[b]thiophenyl, indazolyl, benzo[d]imidazolyl, pyrazolo[1,5-a]pyridinyl, and imidazo[1,5-a]pyridinyl, wherein the heteroaryl can be bound *via* either ring of the fused system.

[0042] The term “heterocyclyl”, as used herein, refers to a saturated or partially unsaturated cyclic moiety that encompasses one or more annular heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur. The term “heterocyclyl” includes both monocyclic and polycyclic ring moieties, wherein the polycyclic ring moieties may be fused, bridged, or spiro. Any non-aromatic monocyclic or polycyclic ring moiety comprising at least one annular heteroatom is considered a heterocyclyl, regardless of the point of

attachment to the remainder of the molecule (*i.e.*, the heterocyclyl moiety may be attached to the remainder of the molecule through any annular carbon or any annular heteroatom of the heterocyclyl moiety). Further, the term heterocyclyl is intended to encompass any polycyclic ring moiety comprising at least one annular heteroatom wherein the polycyclic ring moiety comprises at least one non-aromatic ring, regardless of the point of attachment to the remainder of the molecule. As used herein, a heterocyclyl comprises, for example, 3 to 20 annular atoms (*i.e.*, a 3-20 membered heterocyclyl), 3 to 16 annular atoms (*i.e.*, a 3-16 membered heterocyclyl), 3 to 12 annular atoms (*i.e.*, a 3-12 membered heterocyclyl), 3 to 10 annular atoms (*i.e.*, a 3-10 membered heterocyclyl), 3 to 8 annular atoms (*i.e.*, a 3-8 membered heterocyclyl), 3 to 6 annular atoms (*i.e.*, a 3-6 membered heterocyclyl), 3 to 5 annular atoms (*i.e.*, a 3-5 membered heterocyclyl), 5 to 8 annular atoms (*i.e.*, a 5-8 membered heterocyclyl), or 5 to 6 annular atoms (*i.e.*, a 5-6 membered heterocyclyl). Examples of heterocyclyl groups include, *e.g.*, azetidiny, azepiny, benzodioxoly, benzo[b][1,4]dioxepiny, 1,4-benzodioxany, benzopyrany, benzodioxiny, benzopyranony, benzofuranony, dioxolany, dihydropyrany, hydropyrany, thienyl[1,3]dithianyl, decahydroisoquinolyl, furanony, imidazoliny, imidazolidiny, indoliny, indoliziny, isoindoliny, isothiazolidiny, isoxazolidiny, morpholiny, octahydroindolyl, octahydroisoindolyl, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolidiny, oxazolidiny, oxirany, oxetany, phenothiaziny, phenoxaziny, piperidiny, piperaziny, 4-piperidony, pyrrolidiny, pyrazolidiny, quinuclidiny, thiazolidiny, tetrahydrofuryl, tetrahydropyrany, trithianyl, tetrahydroquinoliny, thiophenyl (*i.e.*, thienyl), thiomorpholiny, thiamorpholiny, 1-oxo-thiomorpholiny, and 1,1-dioxo-thiomorpholiny. Examples of spiro heterocyclyl rings include, but are not limited to, bicyclic and tricyclic ring systems, such as oxabicyclo[2.2.2]octany, 2-oxa-7-azaspiro[3.5]nonany, 2-oxa-6-azaspiro[3.4]octany, and 6-oxa-1-azaspiro[3.3]heptany. Examples of fused heterocyclyl rings include, but are not limited to, 1,2,3,4-tetrahydroisoquinoliny, 4,5,6,7-tetrahydrothieno[2,3-c]pyridiny, indoliny, and isoindoliny, where the heterocyclyl can be bound via either ring of the fused system.

[0043] The term “oxo”, as used herein, refers to a =O moiety.

[0044] The terms “optional” and “optionally”, as used herein, mean that the subsequently described event or circumstance may or may not occur and that the description includes

instances where the event or circumstance occurs and instances where it does not.

Accordingly, the term “optionally substituted” infers that any one or more (*e.g.*, 1, 2, 1 to 5, 1 to 3, 1 to 2, etc.) hydrogen atoms on the designated atom or moiety or group may be replaced or not replaced by an atom or moiety or group other than hydrogen. By way of illustration and not limitation, the phrase “methyl optionally substituted with one or more chloro” encompasses -CH₃, -CH₂Cl, -CHCl₂, and -CCl₃ moieties.

[0045] It is understood that aspects and embodiments described herein as “comprising” include “consisting of” and “consisting essentially of” embodiments.

[0046] The term “pharmaceutically acceptable salt”, as used herein, of a given compound refers to salts that retain the biological effectiveness and properties of the given compound and which are not biologically or otherwise undesirable. “Pharmaceutically acceptable salts” include, for example, salts with inorganic acids, and salts with an organic acid. In addition, if the compounds described herein are obtained as an acid addition salt, the free base can be obtained by basifying a solution of the acid salt. Conversely, if the product is a free base, an addition salt, particularly a pharmaceutically acceptable addition salt, may be produced by dissolving the free base in a suitable organic solvent and treating the solution with an acid, in accordance with conventional procedures for preparing acid addition salts from base compounds. *See, e.g., Handbook of Pharmaceutical Salts Properties, Selection, and Use*, International Union of Pure and Applied Chemistry, John Wiley & Sons (2008), which is incorporated herein by reference in its entirety. Those skilled in the art will recognize various synthetic methodologies that may be used to prepare nontoxic pharmaceutically acceptable addition salts. Pharmaceutically acceptable acid addition salts may be prepared from inorganic or organic acids. Salts derived from inorganic acids include, *e.g.*, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Salts derived from organic acids include, *e.g.*, acetic acid, propionic acid, gluconic acid, glycolic acid, pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluene-sulfonic acid, salicylic acid, trifluoroacetic acid, and the like. Likewise, pharmaceutically acceptable base addition salts can be prepared from inorganic or organic bases. Salts derived from inorganic bases include, by way of example only, sodium, potassium, lithium, aluminum, ammonium, calcium, and magnesium salts. Salts derived

from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines. Specific examples of suitable amines include, by way of example only, isopropylamine, trimethyl amine, diethyl amine, tri(*iso*-propyl) amine, tri(*n*-propyl) amine, ethanolamine, 2-dimethylaminoethanol, piperazine, piperidine, morpholine, N-ethylpiperidine, and the like.

[0047] Isotopically labeled forms of the compounds depicted herein may be prepared.

Isotopically labeled compounds have structures depicted herein, except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into the disclosed compounds include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, chlorine, and iodine, such as ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{31}P , ^{32}P , ^{35}S , ^{18}F , ^{36}Cl , ^{123}I , and ^{125}I , respectively. In some embodiments, a compound of formula (I) is provided wherein one or more hydrogen is replaced by deuterium or tritium.

[0048] Some of the compounds provided herein may exist as tautomers. Tautomers are in equilibrium with one another. By way of illustration, amide containing compounds may exist in equilibrium with imidic acid tautomers. Regardless of which tautomer is shown and regardless of the nature of the equilibrium among tautomers, the compounds of this disclosure are understood by one of ordinary skill in the art to comprise both amide and imidic acid tautomers. Thus, for example, amide-containing compounds are understood to include their imidic acid tautomers. Likewise, imidic-acid containing compounds are understood to include their amide tautomers.

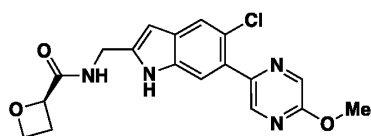
[0049] Also provided herein are prodrugs of the compounds depicted herein, or a pharmaceutically acceptable salt thereof. Prodrugs are compounds that may be administered to an individual and release, *in vivo*, a compound depicted herein as the parent drug compound. It is understood that prodrugs may be prepared by modifying a functional group on a parent drug compound in such a way that the modification is cleaved *in vitro* or *in vivo* to release the parent drug compound. See, e.g., Rautio, J., Kumpulainen, H., Heimbach, T. et al. Prodrugs: design and clinical applications. *Nat Rev Drug Discov* 7, 255–270 (2008), which is incorporated herein by reference, in its entirety.

[0050] The compounds of the present disclosure, or their pharmaceutically acceptable salts, may include an asymmetric center and may thus give rise to enantiomers, diastereomers, and

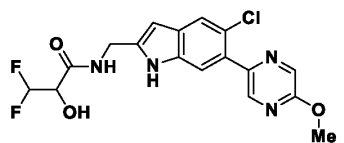
other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (*R*)- or (*S*)- (or as (*D*)- or (*L*)- for amino acids). The present disclosure is meant to include all such possible isomers, as well as their racemic and optically pure forms and mixtures thereof in any ratio. Optically active (+) and (-), (*R*)- and (*S*)-, or (*D*)- and (*L*)- isomers may be prepared using chiral synthons or chiral reagents, or may be resolved using conventional techniques, for example, chromatography and/or fractional crystallization. Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or the resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC), and chiral supercritical fluid chromatography (SFC). When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, unless specified otherwise, it is intended that the present disclosure includes both *E* and *Z* geometric isomers. Likewise, *cis*- and *trans*- are used in their conventional sense to describe relative spatial relationships.

[0051] A “stereoisomer” refers to a compound made up of the same atoms bonded by the same bonds, but having different three-dimensional structures, which are not interchangeable. The present disclosure contemplates various stereoisomers, or mixtures thereof, and includes “enantiomers,” which refers to two stereoisomers whose structures are non-superimposable mirror images of one another. “Diastereomers” are stereoisomers that have at least two asymmetric atoms, but which are not mirror images of each other.

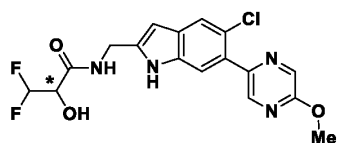
[0052] Where enantiomeric and/or diastereomeric forms exist of a given structure with two stereocenters, wedged and/or dashed bonds indicate the composition is made up of predominantly a single isomer of known relative and absolute stereochemistry, *e.g.*,



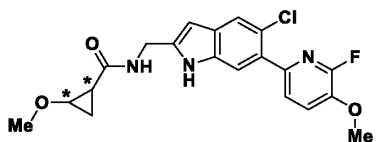
[0053] Where enantiomeric and/or diastereomeric forms exist of a given structure, flat bonds indicate that all stereoisomeric forms of the depicted structure may be present, *e.g.*,



[0054] Where enantiomeric and/or diastereomeric forms exist of a given structure, the composition is made up of at least 90%, by weight, an asterisk indicates a single enantiomer or diastereomer with unknown relative or absolute stereochemistry, e.g.,

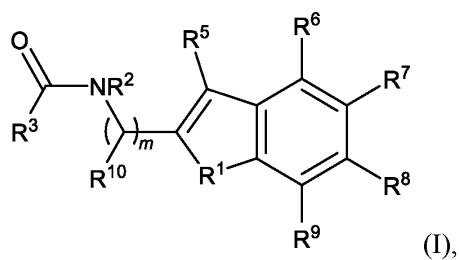


[0055] Where a given structure has potential for cis and trans configuration, and the composition is made up of at least 90%, by weight, astrisks (*) indicate single unknown cis or trans configuration, e.g.,



COMPOUNDS

[0056] In one aspect, provided herein is a compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R³ is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R⁴)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and
the 4-10 membered heteroaryl of R³ is optionally substituted with one or more R^{3x},

provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;

each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

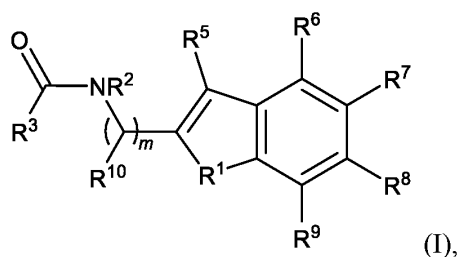
R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b};
 R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}; and
 R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.
[0057] In some embodiments of a compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};
 each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein
 the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or
 both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0058] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 2;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₃alkyl, C₁₋₃alkoxy, C₃₋₆cycloalkyl, -N(R⁴)₂, 4-6 membered heteroaryl, or 4-6 membered heterocyclyl, wherein

the C₁₋₃alkyl, C₁₋₃alkoxy, C₃₋₆cycloalkyl, or 4-6 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and

the 4-6 membered heteroaryl of R³ is optionally substituted with one or more R^{3x};

provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;
each R⁴ is independently H, C₁₋₃alkyl, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, or C₃₋₆cycloalkyl, wherein

the C₁₋₃alkyl, or C₃₋₆cycloalkyl of R⁴ is optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₃alkyl, C₁₋₃alkoxy, C₃₋₆cycloalkyl or C₁₋₃haloalkyl, wherein

the C₁₋₃alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₃alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein

the C₁₋₃alkyl, C₁₋₃alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₃alkyl, C₁₋₃alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₃alkyl, C₁₋₃alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b};

R^{3x} is OH, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₃alkyl, C₁₋₃alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ; and R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy.

[0059] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 2;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C₁₋₃alkyl, C₁₋₃haloalkyl, C₃₋₆cycloalkyl, -N(R^4)₂, or 4-6 membered heterocyclyl, wherein

the C₁₋₃alkyl, C₁₋₃haloalkyl, C₃₋₆cycloalkyl, or 4-6 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R^4 is independently H, C₁₋₃alkyl, C₁₋₃haloalkyl, or C₃₋₆cycloalkyl, wherein the C₁₋₃alkyl, C₁₋₃haloalkyl, or C₃₋₆cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-6 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₃₋₆cycloalkyl or C₁₋₃haloalkyl, wherein

the C₁₋₃alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl, -O- C_{1-3} haloalkyl, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

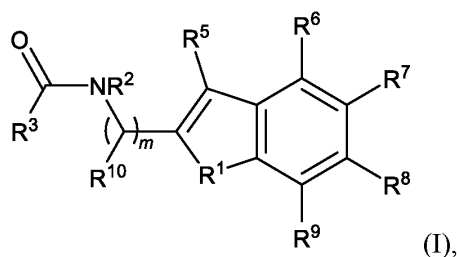
the C_{1-3} alkyl, C_{1-3} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C_{1-3} alkyl, C_{1-3} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C_{1-3} alkyl, C_{1-3} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy.

[0060] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R^1 is -NH-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, -N(R^4)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and

the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ;

each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b};

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}; and R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0061] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}; each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

R^{3a}, R^{4a}, and R^{8a} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0062] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H or C₁₋₆alkyl, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, or C₁₋₆alkoxy, or C₁₋₆haloalkyl;

R⁶ and R⁹ are each independently H or halo;

R⁸ is 3-10 membered heterocyclyl or 5-10 membered heteroaryl, wherein

the 3-10 membered heterocyclyl or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and R^{3b}, R^{4b}, and R^{8b} are each independently D or halo.

[0063] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}; each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},
 the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and
 the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and
 R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0064] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 2;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R⁴)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and

the 4-10 membered heteroaryl of R³ is optionally substituted with one or more R^{3x}

provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;

each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl;

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, or C₁₋₆alkoxy, or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is 3-10 membered heterocyclyl or 5-10 membered heteroaryl, wherein

the 3-10 membered heterocyclyl or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R^{10} is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ;

R^{3x} is C₁₋₆alkyl; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, or halo.

[0065] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 2;

R^1 is -NH-;

R^2 is H;

R^3 is C₁₋₃alkyl, C₁₋₃haloalkyl, C₃₋₆cycloalkyl, -N(R^4)₂, or 4-6 membered heterocyclyl, wherein

the C₁₋₃alkyl, C₁₋₃haloalkyl, C₃₋₆cycloalkyl, or 4-6 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R^4 is independently H, C₁₋₃alkyl, C₁₋₃haloalkyl, or C₃₋₆cycloalkyl, wherein

the C₁₋₃alkyl, C₁₋₃haloalkyl, or C₃₋₆cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-6 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₃₋₆cycloalkyl or C₁₋₃haloalkyl, wherein

the C₁₋₃alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₆cycloalkyl, C₆₋₁₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0066] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

R^{3a}, R^{4a}, and R^{8a} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0067] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing,

m is an integer from 1 to 4;

R¹ is -NH-;

R² is H;

R³ is C₁₋₆alkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

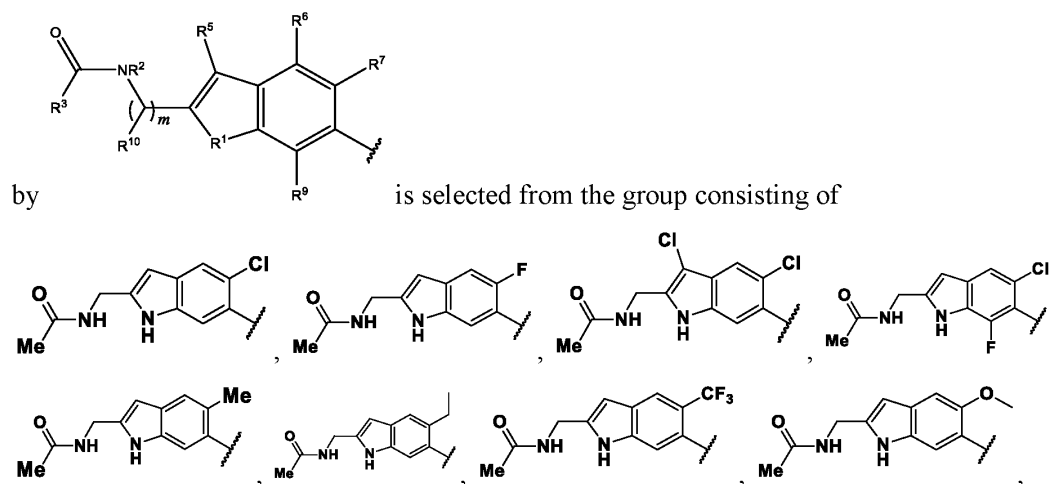
the C₁₋₆alkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

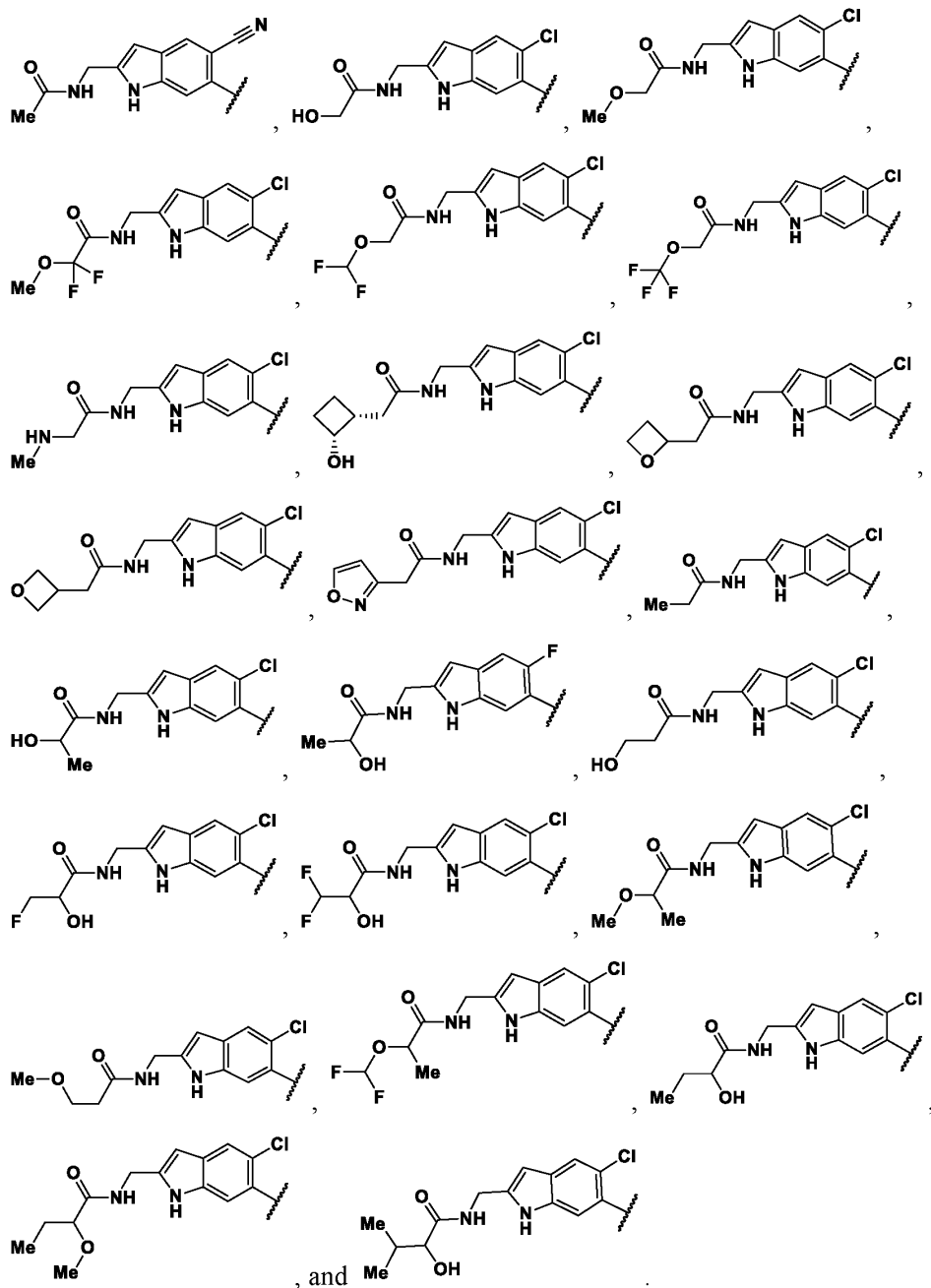
each R⁴ is independently H or C₁₋₆alkyl, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

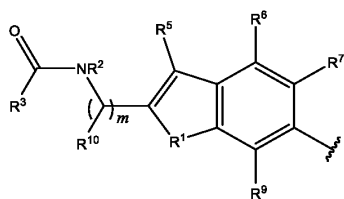
R^5 and R^7 are each independently H, halo, C₁₋₆alkyl, or C₁₋₆alkoxy, or C₁₋₆haloalkyl;
 R^6 and R^9 are each independently H or halo;
 R^8 is 3-10 membered heterocyclyl or 5-10 membered heteroaryl, wherein
 the 3-10 membered heterocyclyl or 5-10 membered heteroaryl of R^8 is
 optionally substituted with one or more R^{8a} ;
 R^{10} is H;
 R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein
 the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is
 optionally substituted with one or more R^{3b} ,
 the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is
 optionally substituted with one or more R^{4b} , and
 the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is
 optionally substituted with one or more R^{8b} ; and
 R^{3a} , R^{4a} , and R^{8a} are each independently D or halo.

[0068] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



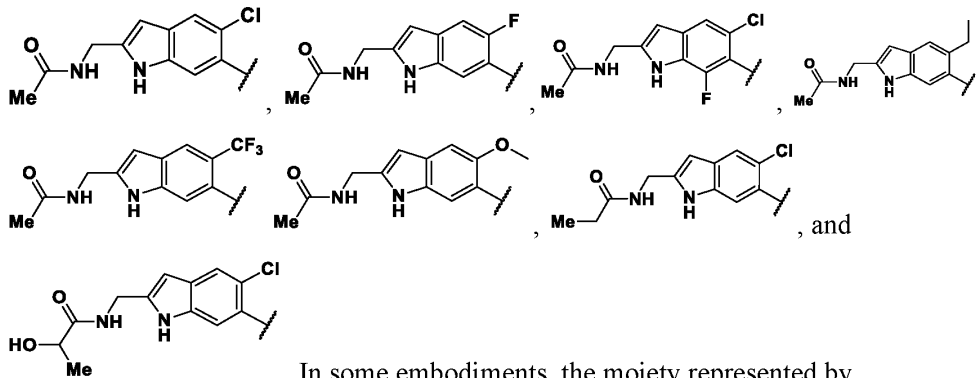


[0069] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

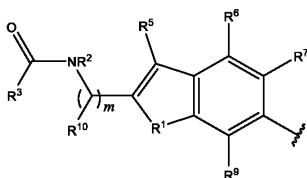


by

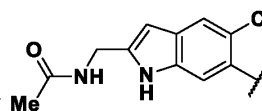
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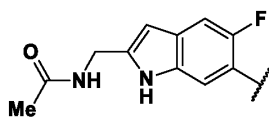
. In some embodiments, the moiety represented by



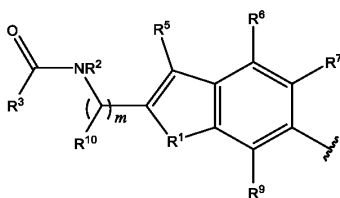
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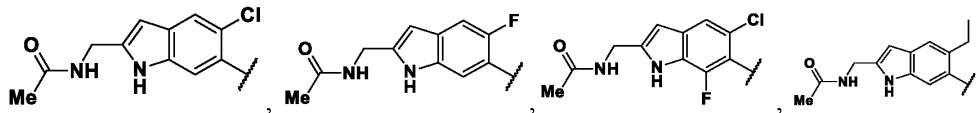
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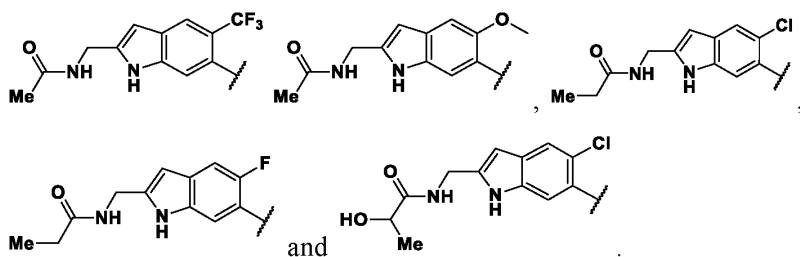


. In some embodiments, the moiety represented by

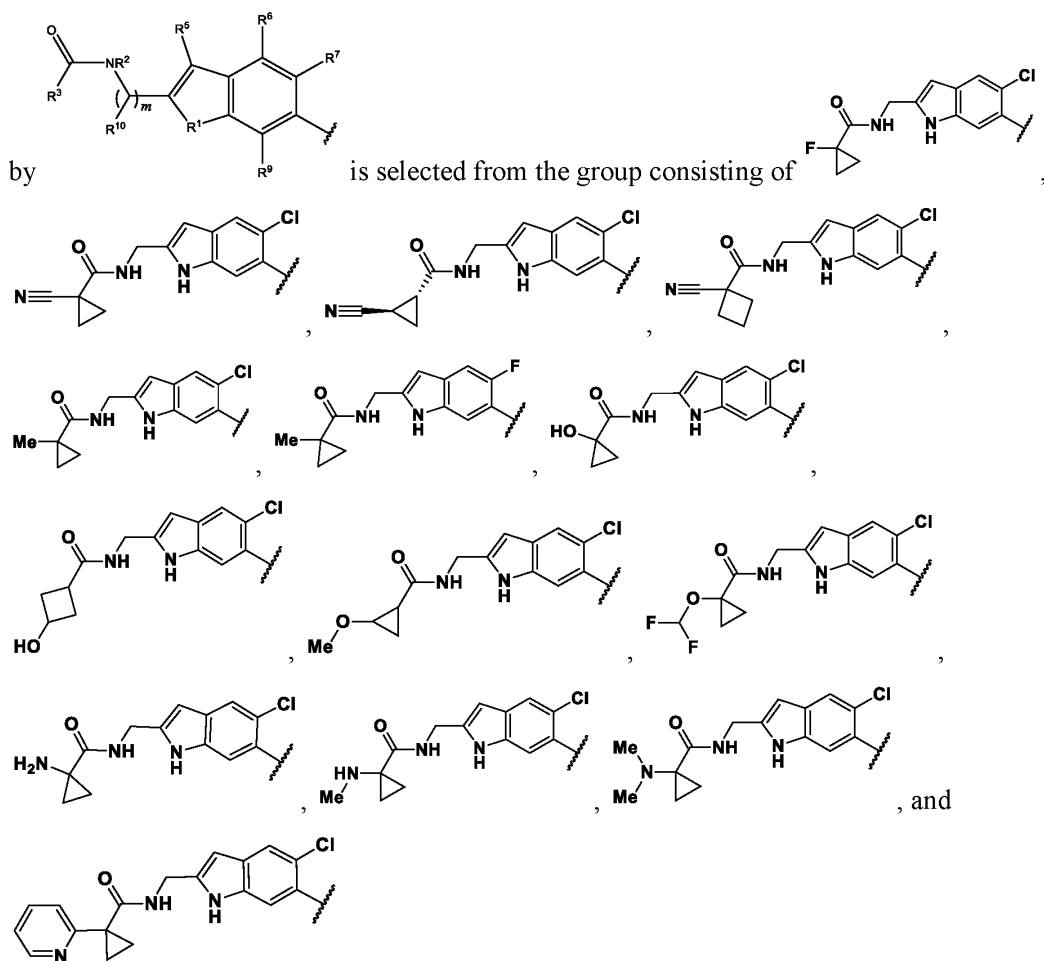


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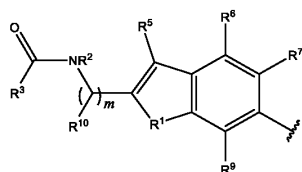




[0070] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

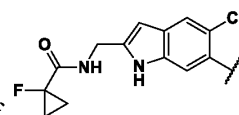


[0071] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

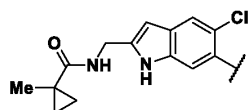


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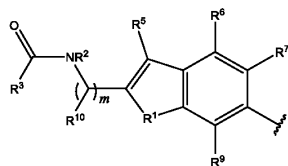
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and

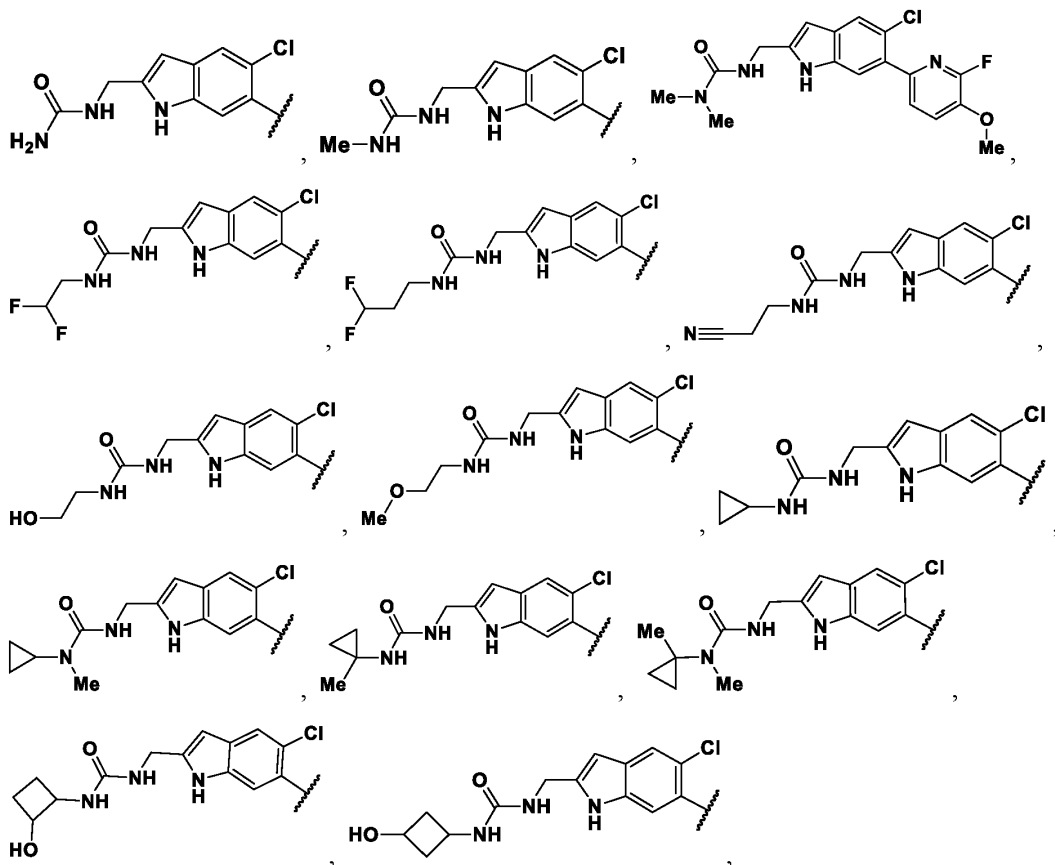


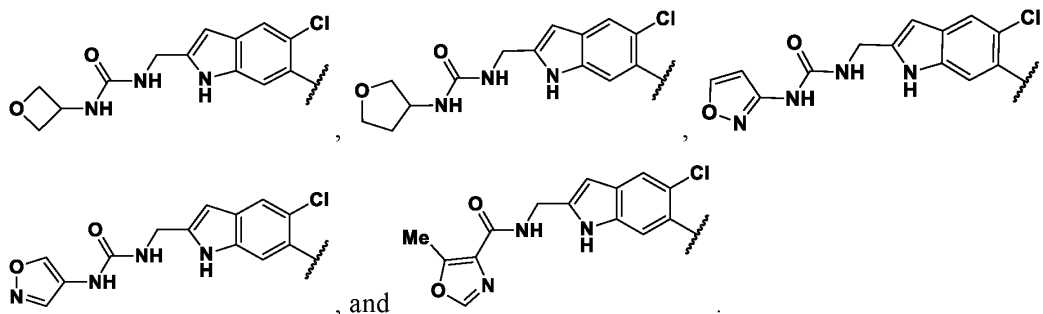
[0072] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



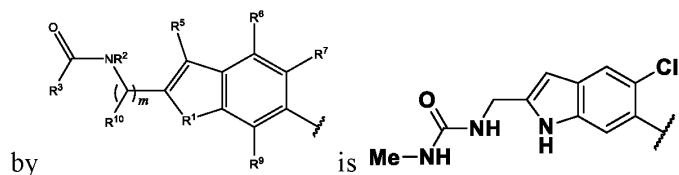
by

is selected from the group consisting of

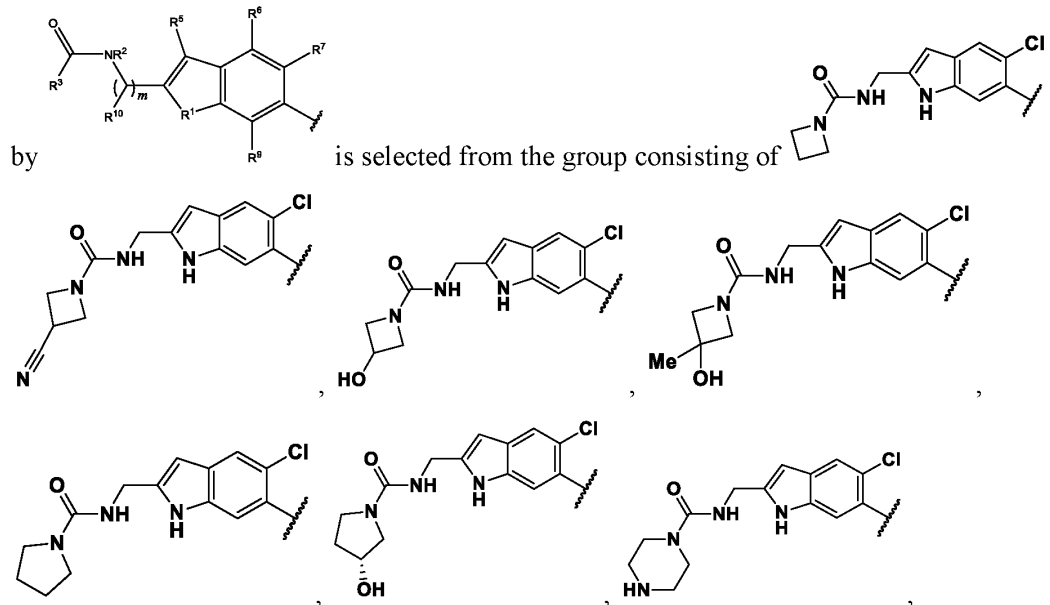


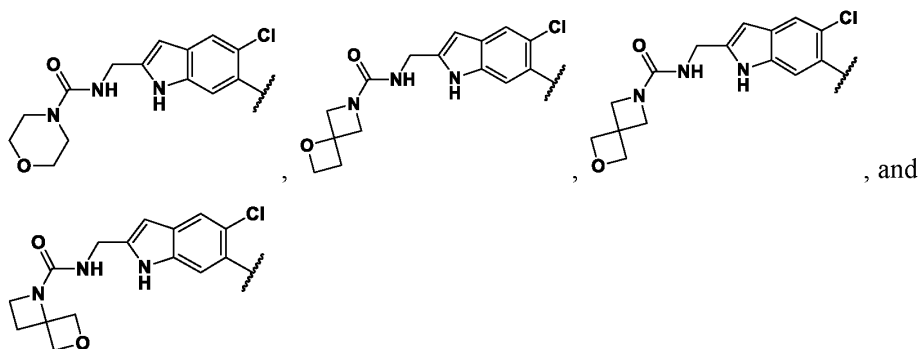


[0073] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

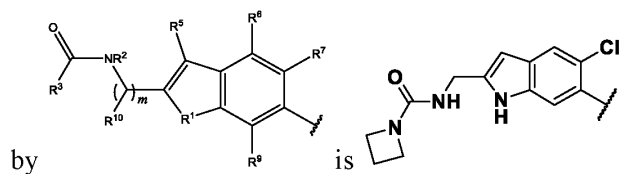


[0074] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

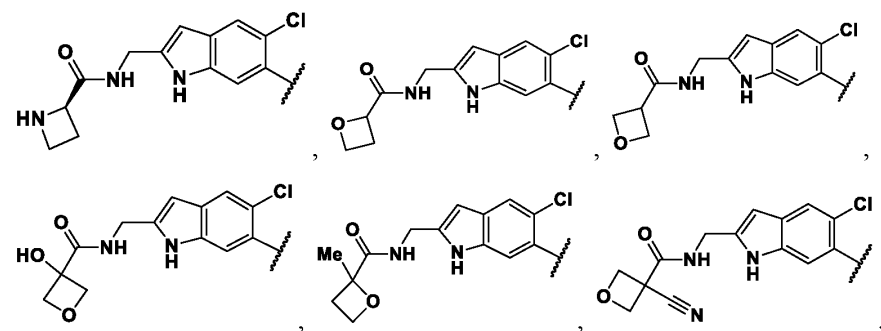
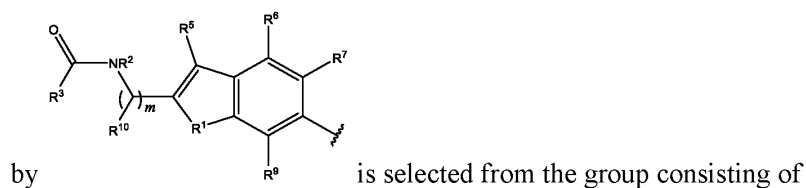


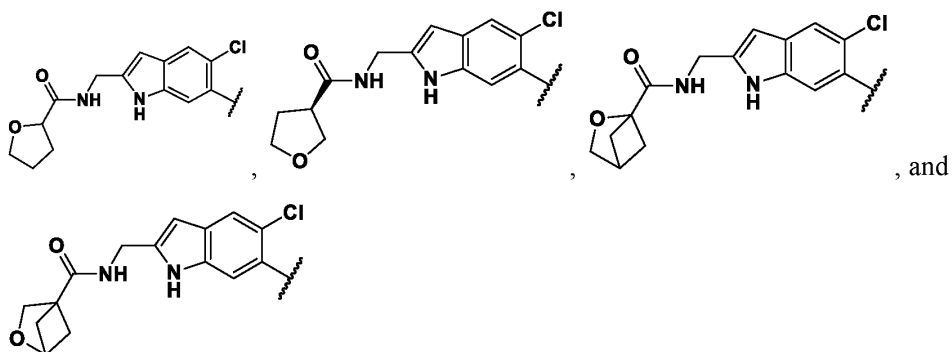


[0075] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

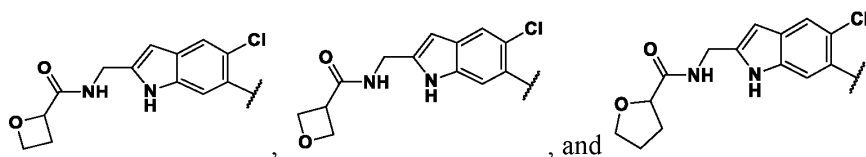
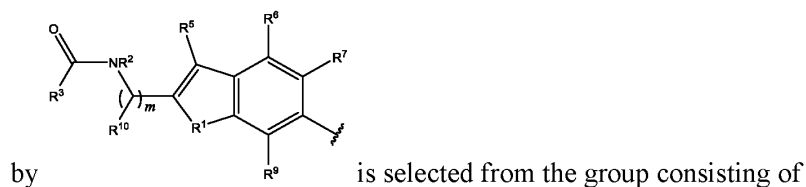


[0076] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

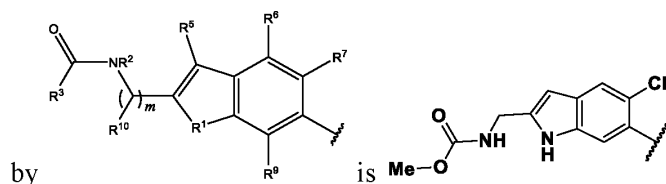




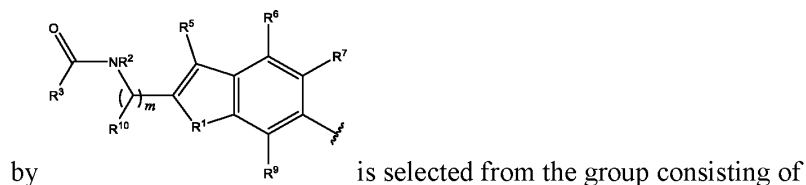
[0077] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

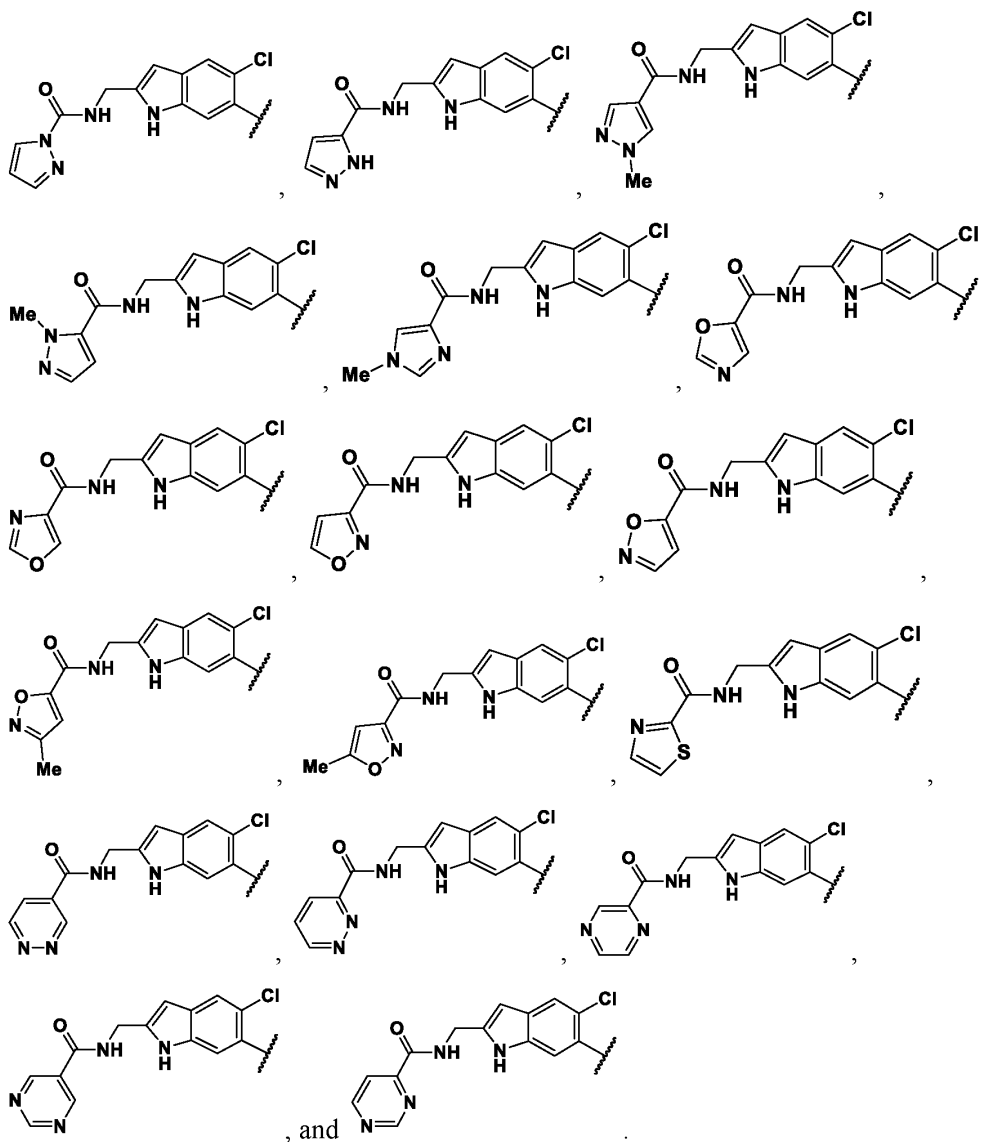


[0078] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

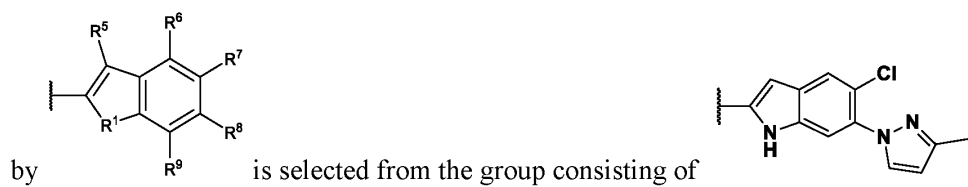


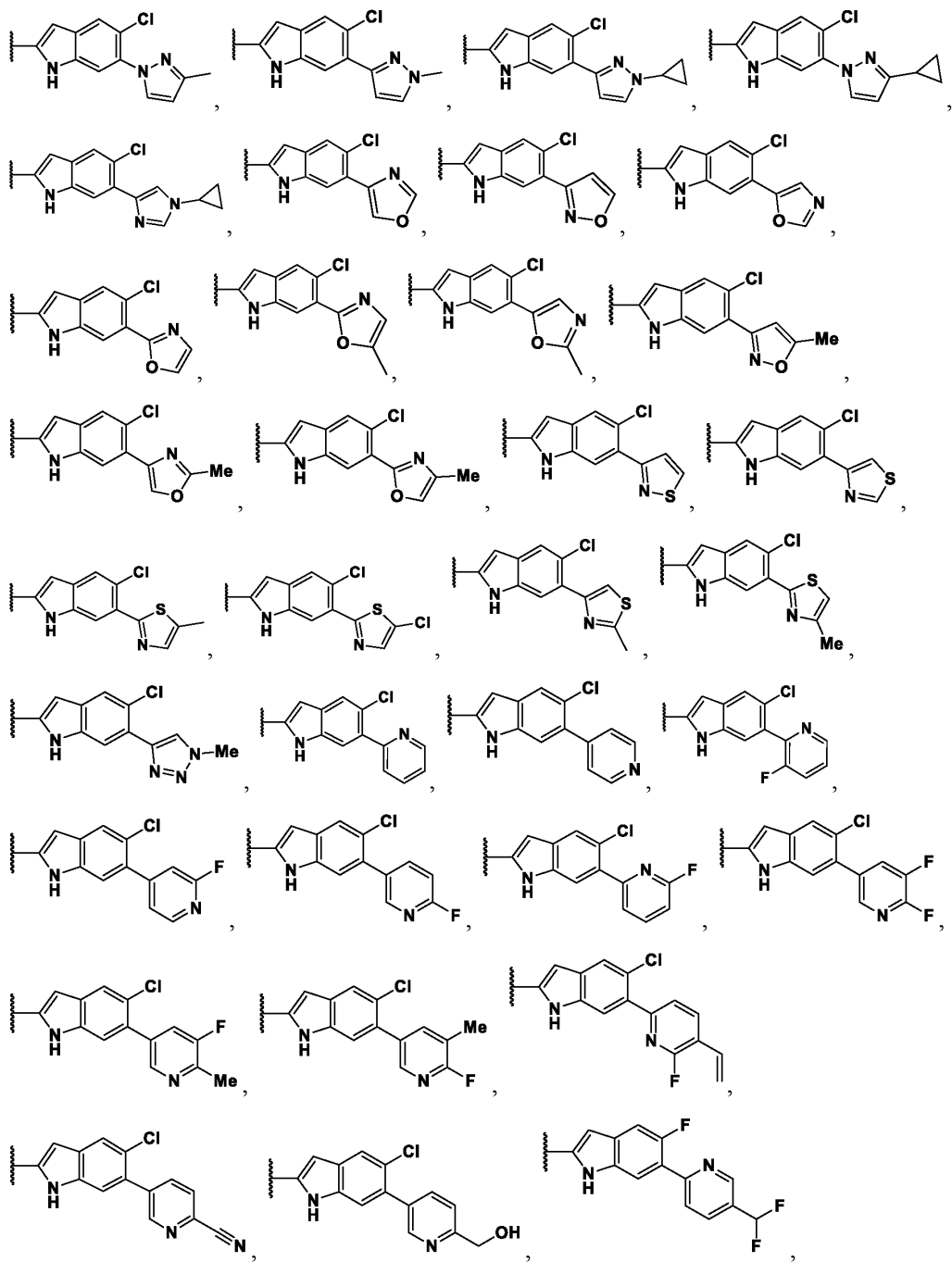
[0079] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

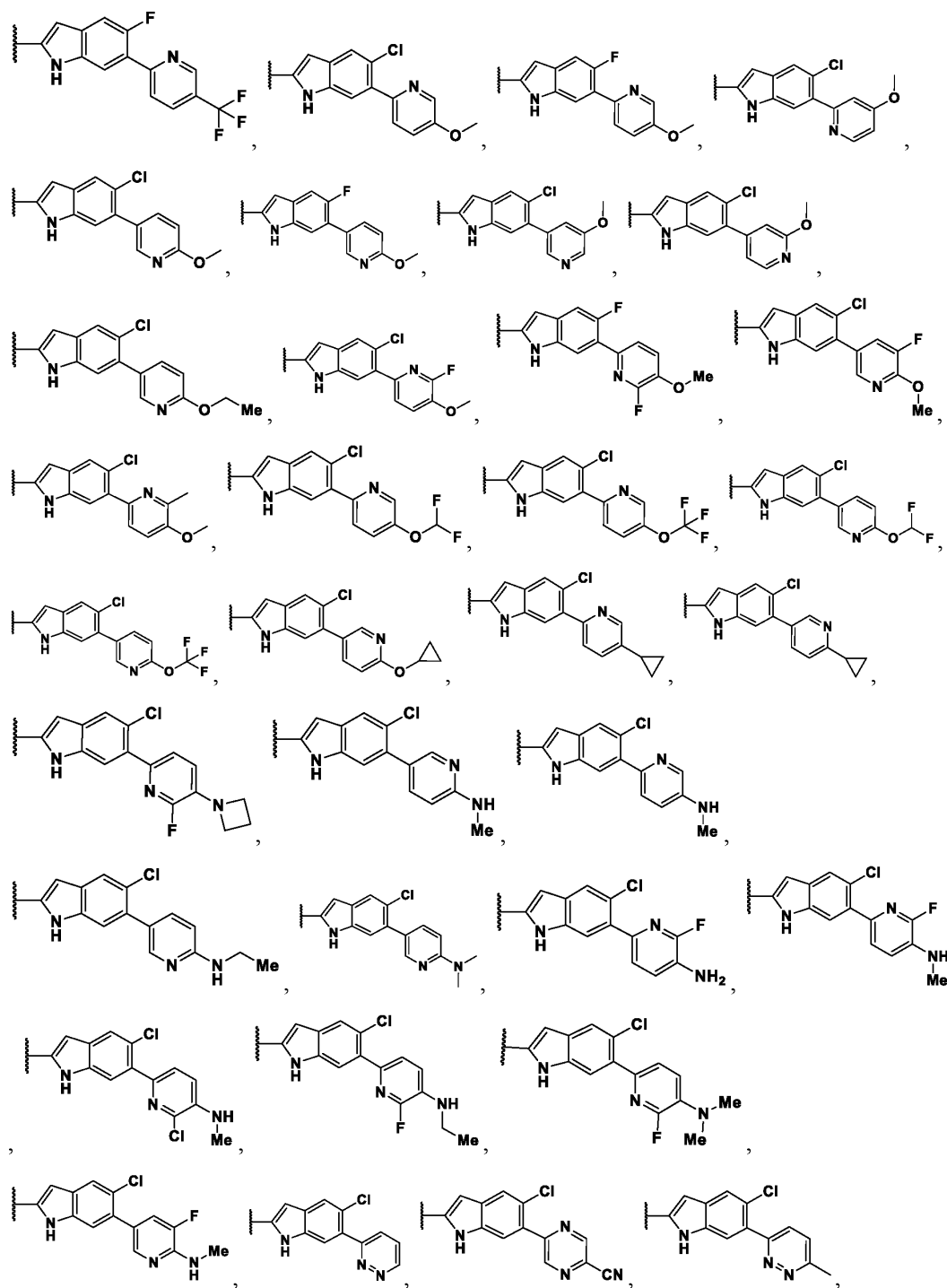


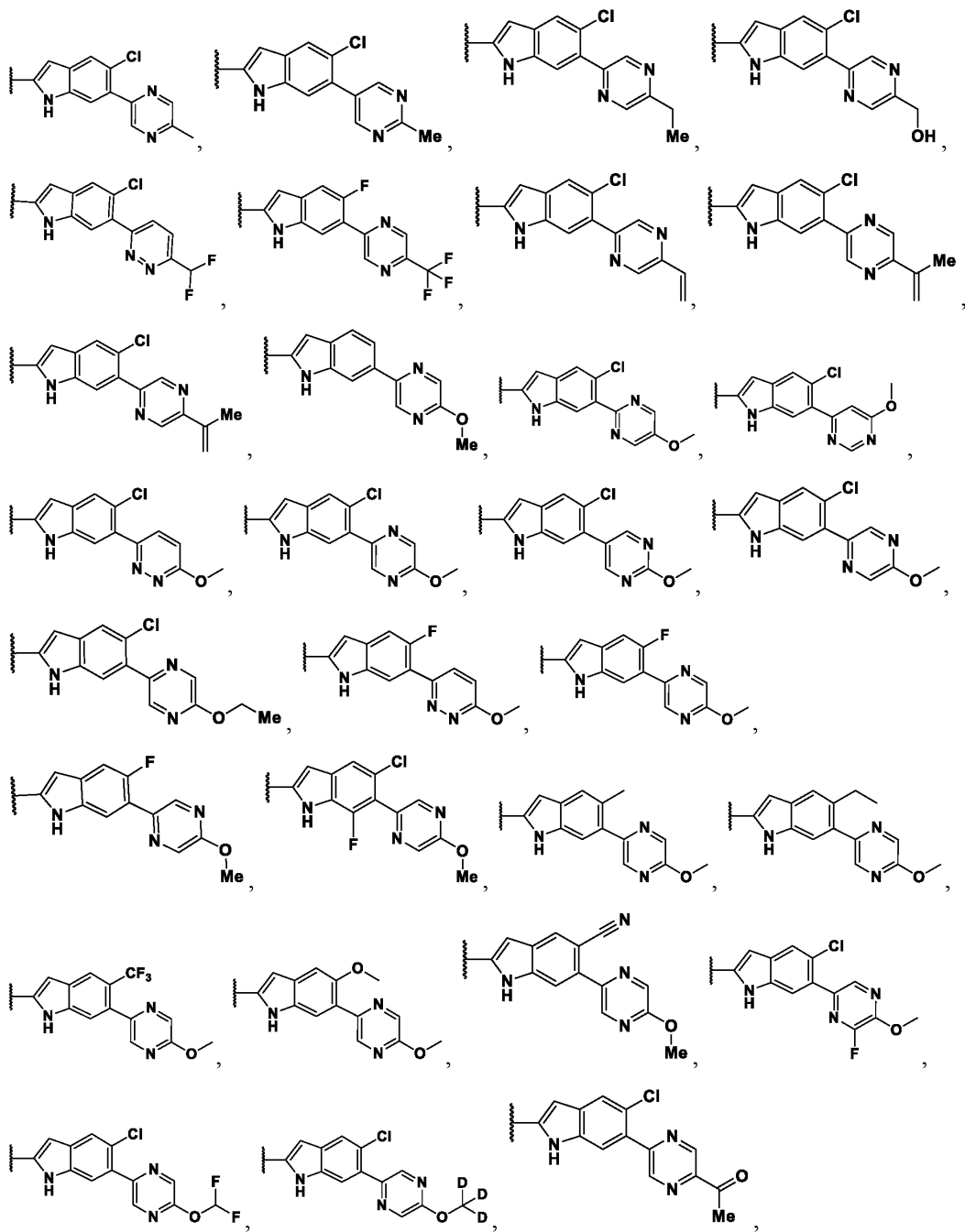


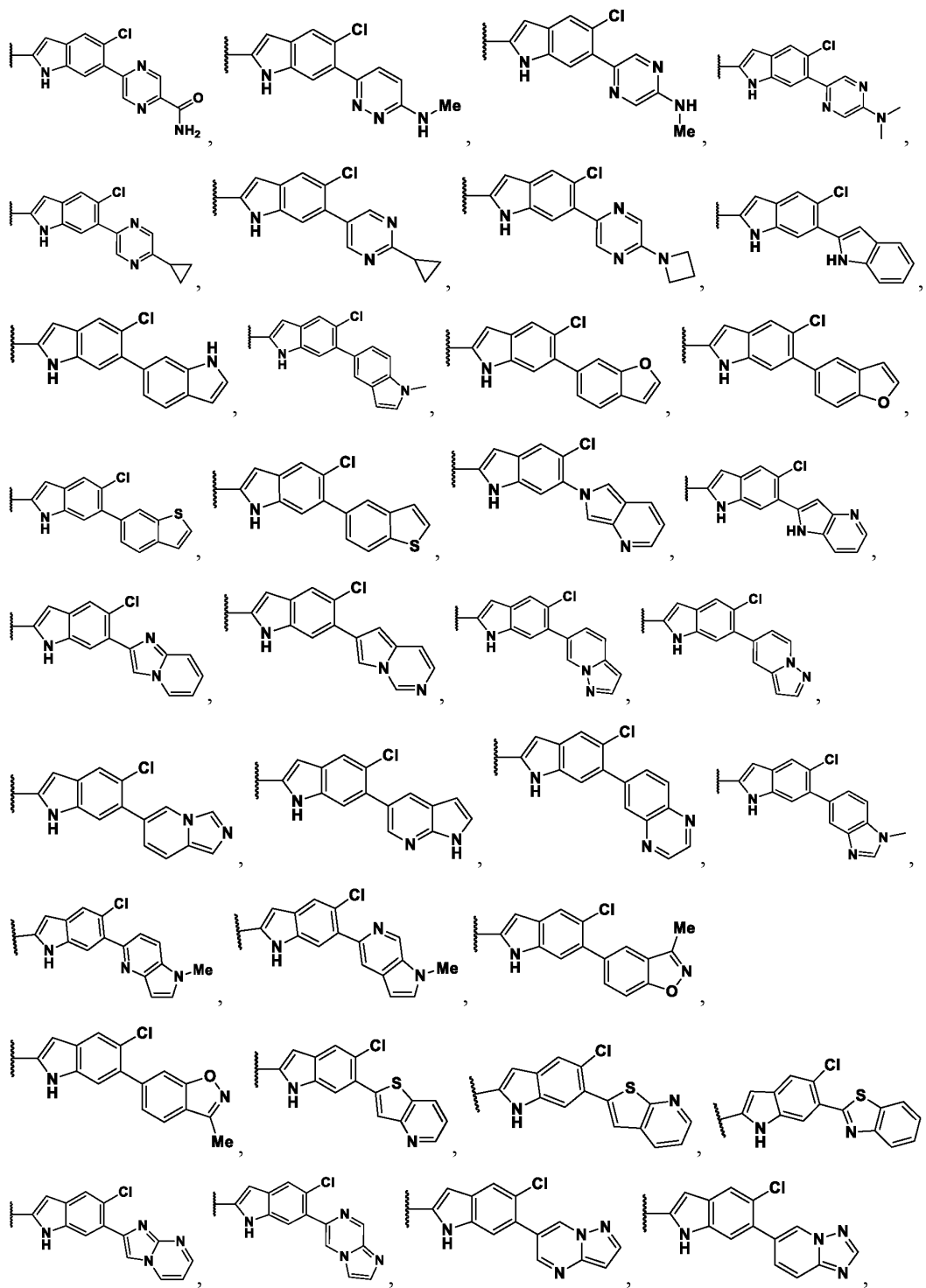
[0080] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

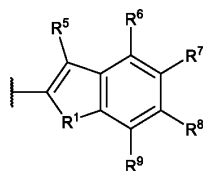
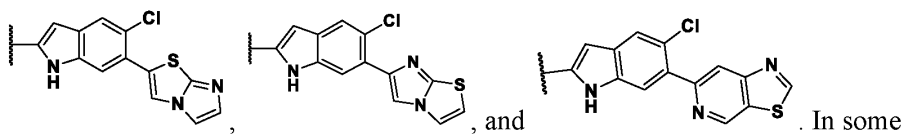








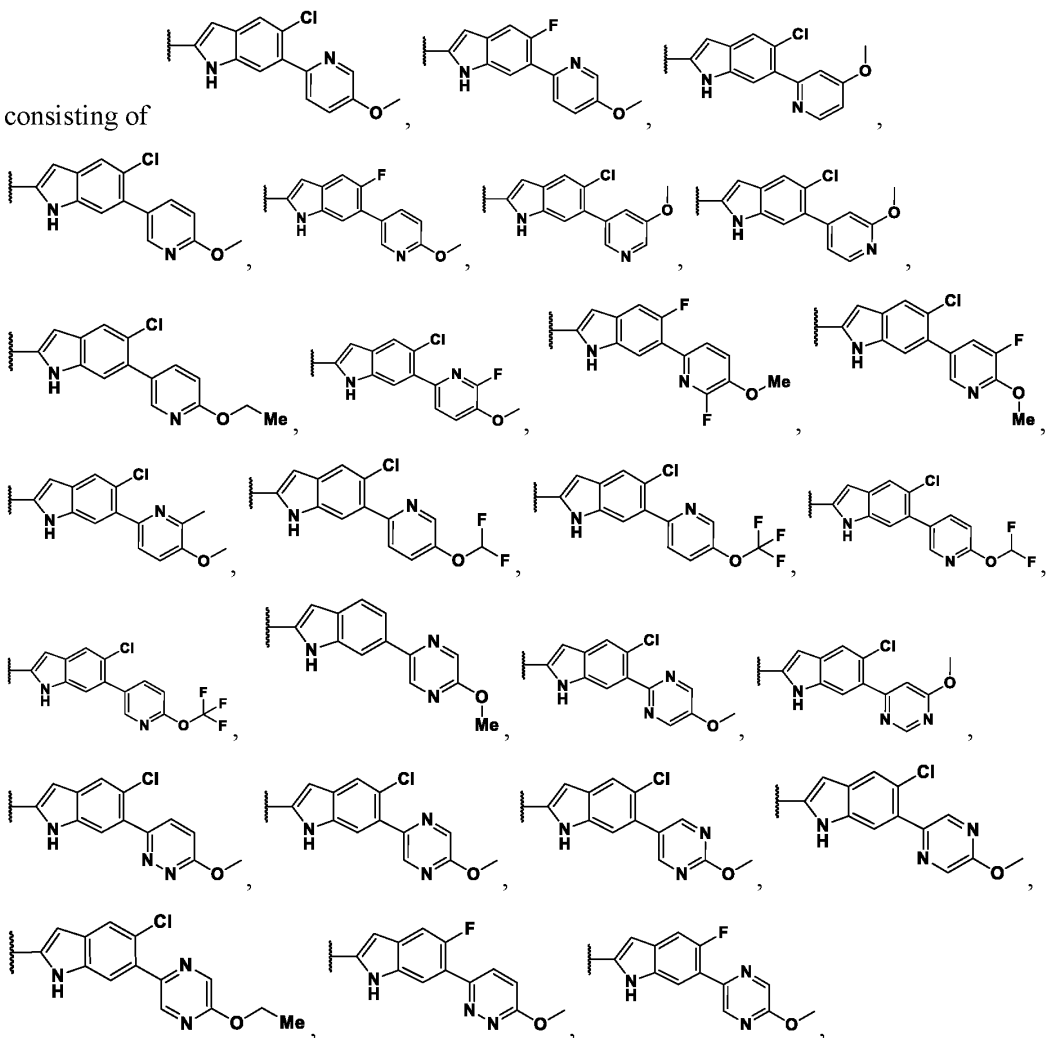


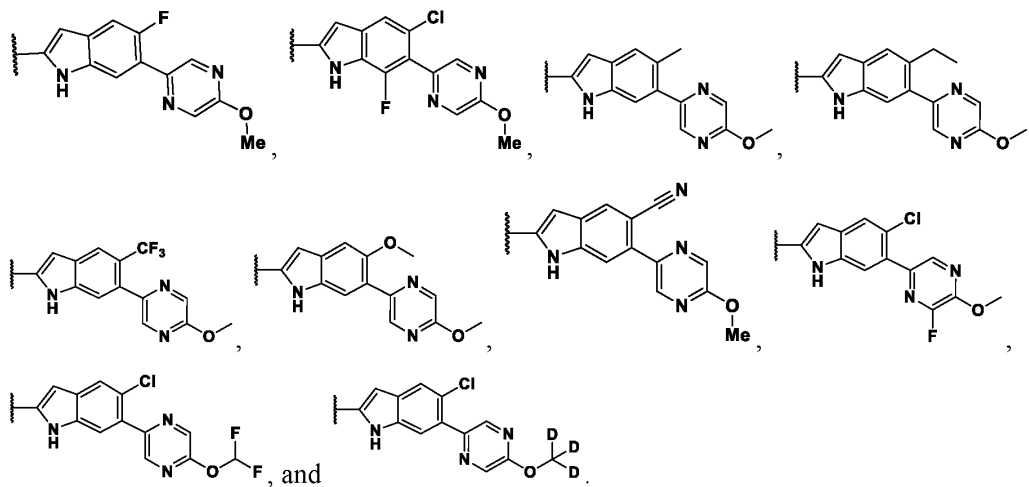


embodiments, the moiety represented by

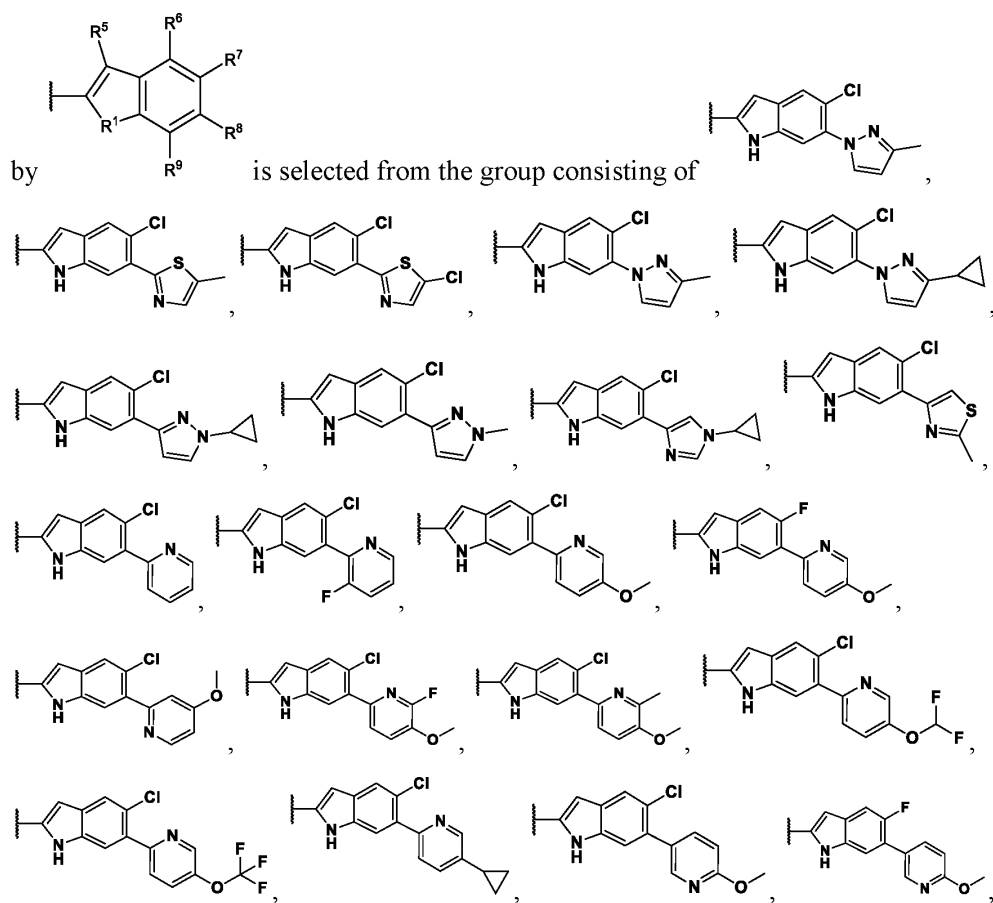
is selected from the group

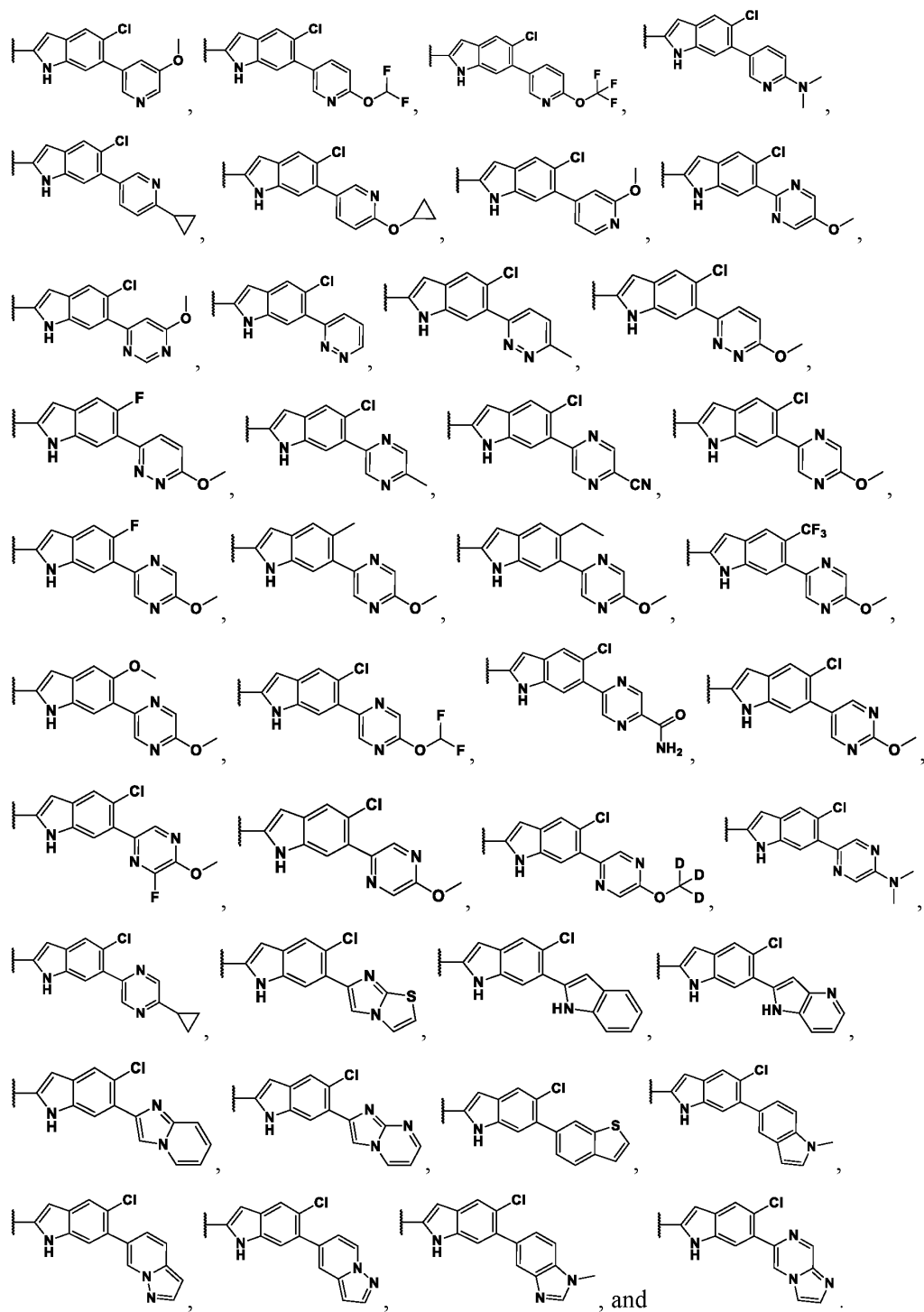
consisting of



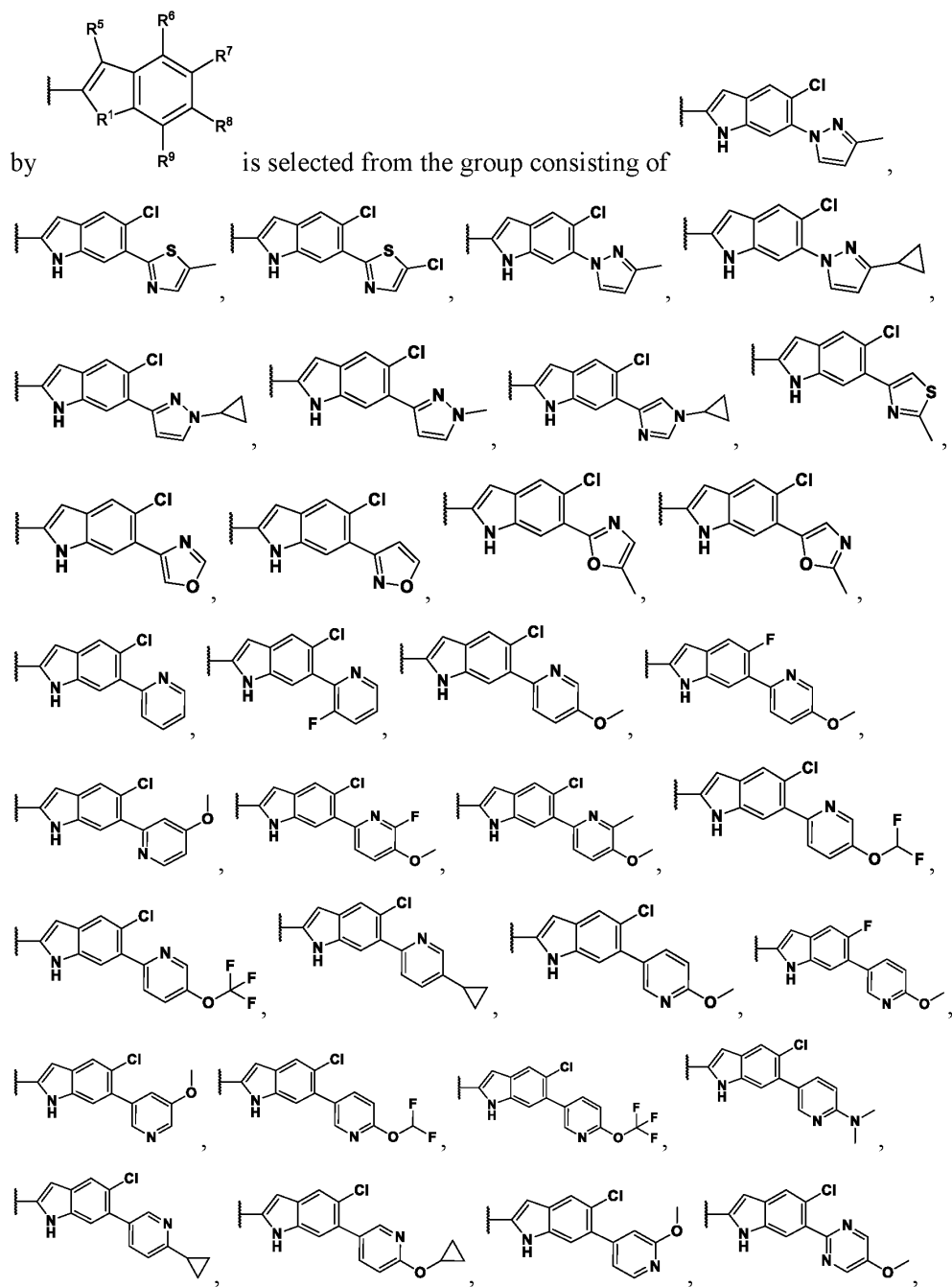


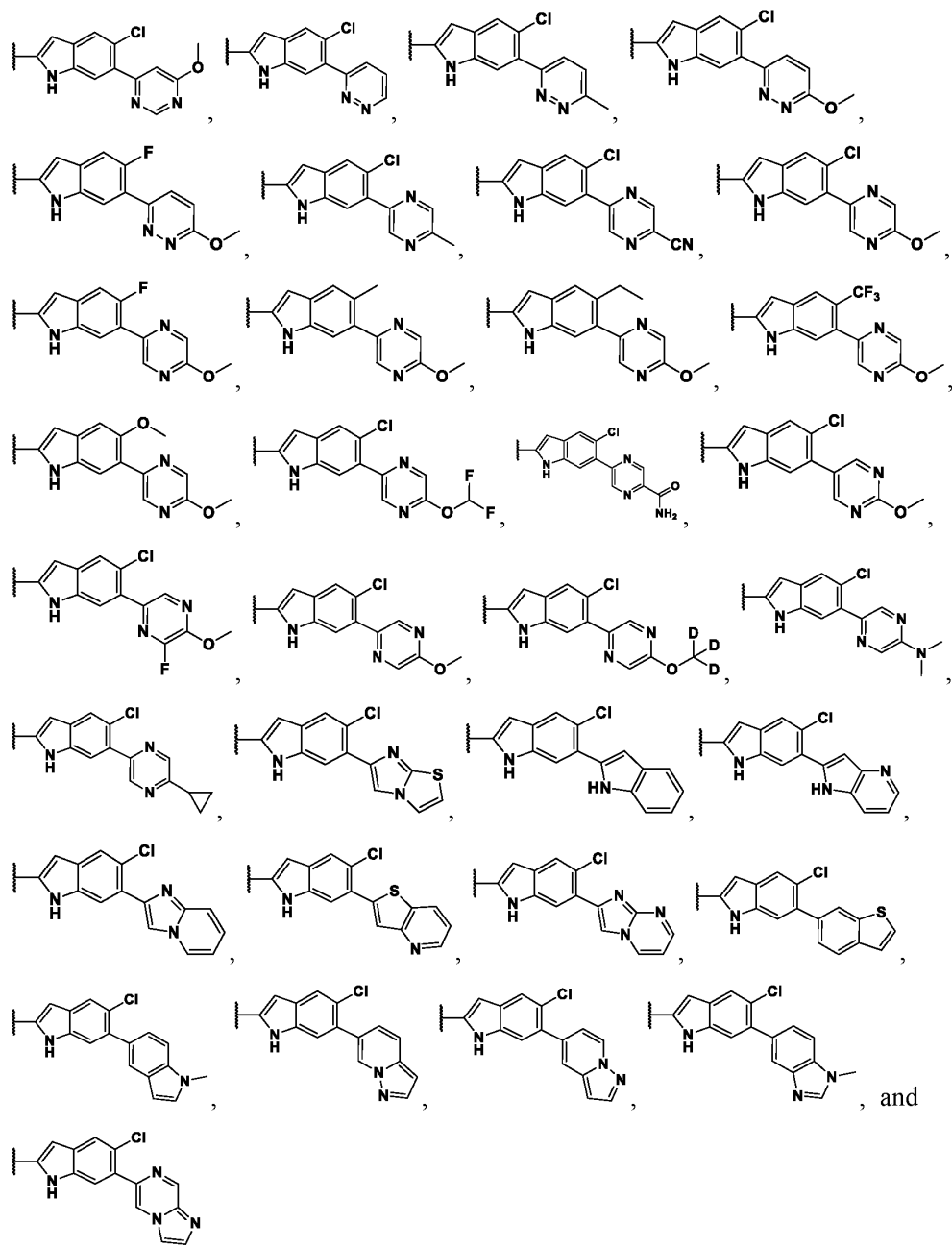
[0081] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



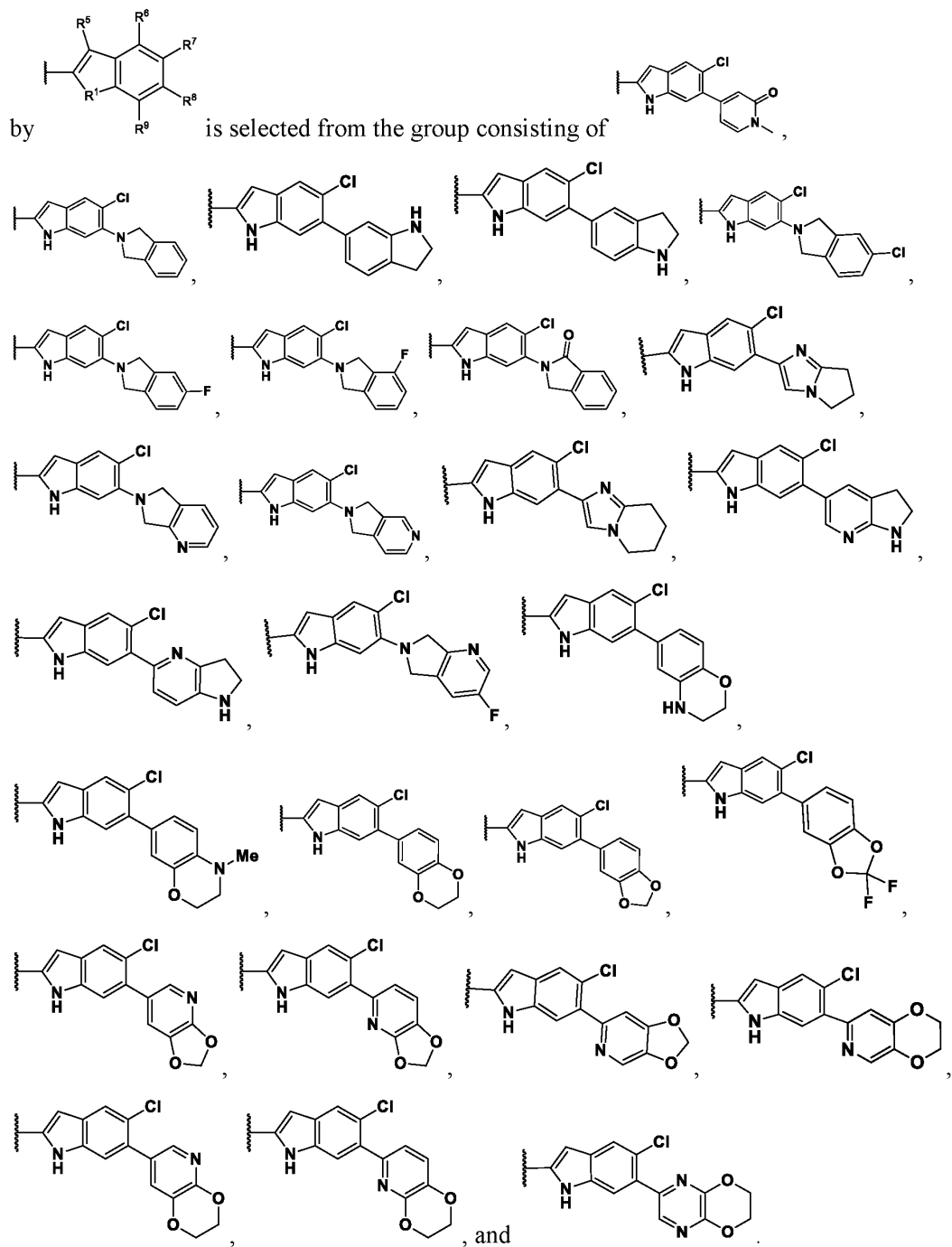


[0082] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented

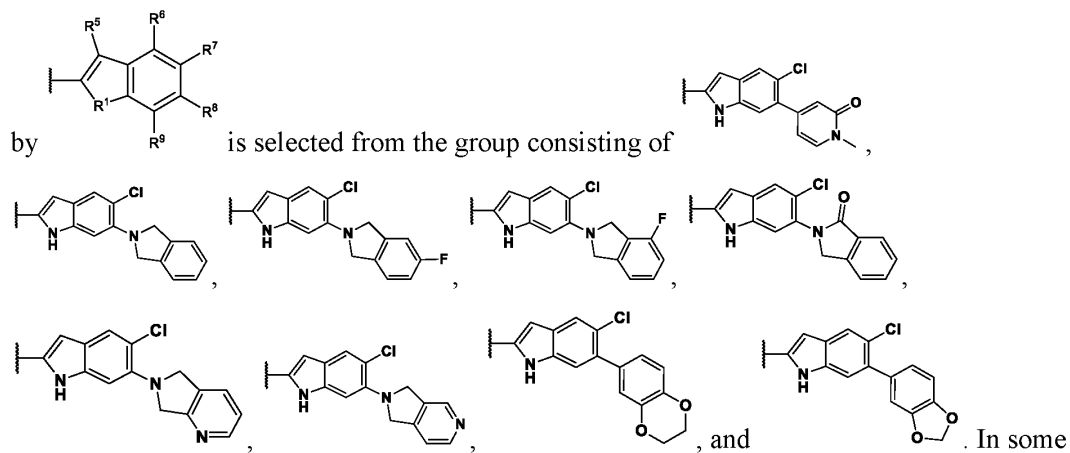


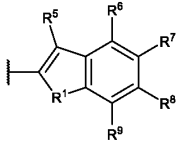


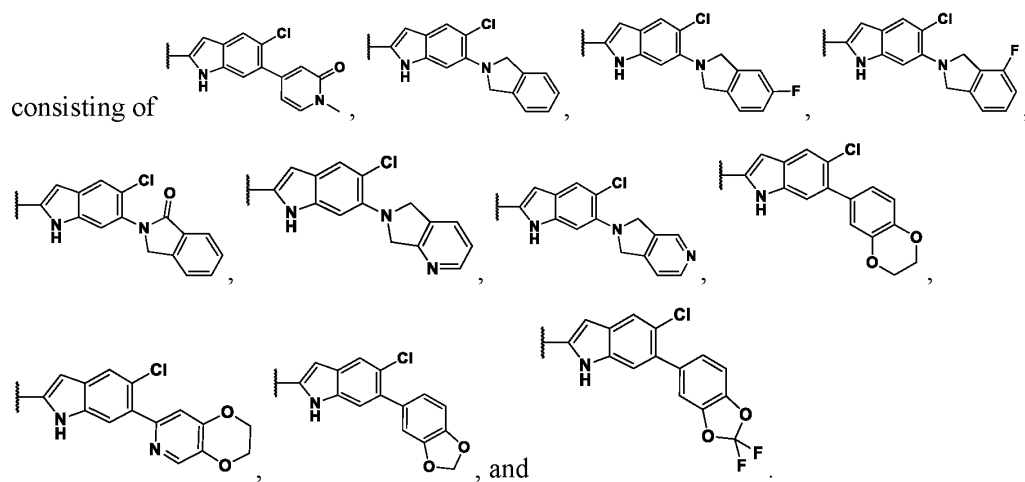
[0083] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



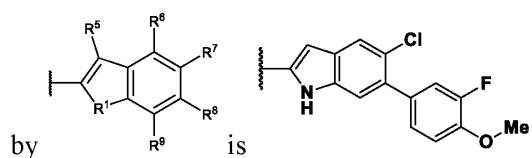
[0084] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



embodiments, the moiety represented by  is selected from the group

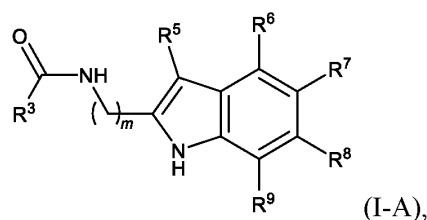


[0085] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the moiety represented



[0086] In some embodiments of a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^1 is -NH-, -O-, or -S-. In some embodiments, R^1 is -O-. In some embodiments, R^1 is -S-. In some embodiments, R^1 is -NH-.

[0087] In one aspect, provided herein is a compound of formula (I), such as a compound of formula (I-A):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

[0088] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, m is an integer from 1-4. In some embodiments, m is an integer from 1-2. In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments, m is 3. In some embodiments, m is 4.

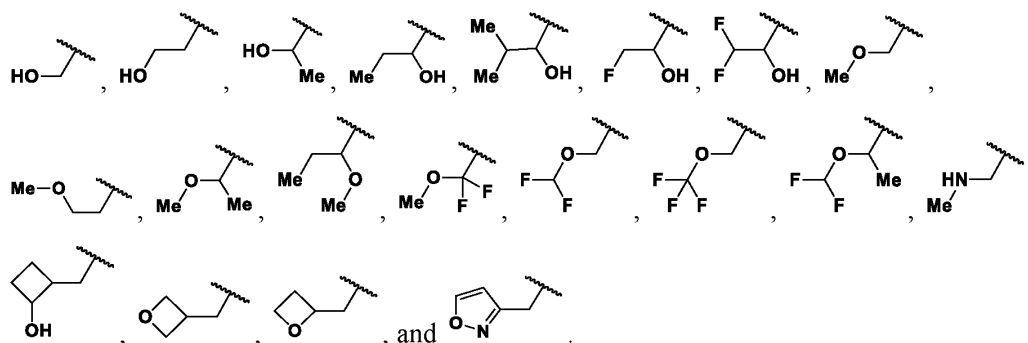
[0089] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} , provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-. In some embodiments, R^3 is C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl, $-N(R^4)_2$, 4-6 membered heteroaryl, or 4-6 membered heterocyclyl, wherein the C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl, or 4-6 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and the 4-6 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} , provided that when R^3 is 4-6 membered heteroaryl, R^1 is -NH-.

[0090] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, $-N(R^4)_2$, or 4-10 membered heterocyclyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} . In some embodiments, R^3 is C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, $-N(R^4)_2$, or 4-6 membered heterocyclyl, wherein the C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, or 4-6 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} . In some embodiments, R^3 is C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, $-N(R^4)_2$, or 4-6 membered heterocyclyl.

[0091] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is C_{1-6} alkyl, optionally substituted with one or more R^{3a} . In some embodiments, R^3 is C_{1-3} alkyl. In some embodiments, R^3 is methyl, ethyl, or isopropyl. In some embodiments, R^3 is methyl. In some embodiments, R^3 is ethyl. In some embodiments, R^3 is isopropyl.

[0092] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is C_{1-6} alkyl, optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, $-NH_2$, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)_2$, $-C(O)C_{1-6}alkyl$, $-C(O)NH_2$, $-C(O)NH(C_{1-6}alkyl)$, $-C(O)N(C_{1-6}alkyl)_2$, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or $-O-C_{3-10}$ cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is C_{1-3} alkyl, optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{2-4} alkenyl, C_{1-3} alkoxy, $-NH_2$, $-NH(C_{1-3}alkyl)$, $-N(C_{1-3}alkyl)_2$, $-C(O)C_{1-3}alkyl$, $-C(O)NH_2$, $-C(O)NH(C_{1-3}alkyl)$, $-C(O)N(C_{1-3}alkyl)_2$, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or $-O-C_{3-6}$ cycloalkyl, wherein the C_{1-3} alkyl, C_{1-3} alkoxy, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or $-O-C_{3-6}$ cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^3 is C_{1-3} alkyl, optionally substituted with one or more R^{3a} ; R^{3a} is -OH, halo, C_{1-6} alkyl, C_{1-6} alkoxy, $-NH_2$, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)_2$, $-C(O)C_{1-6}alkyl$, $-C(O)NH_2$, $-C(O)NH(C_{1-6}alkyl)$, $-C(O)N(C_{1-6}alkyl)_2$, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or $-O-C_{3-10}$ cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy.

alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkoxy or C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}, and R^{3b} is -OH, or halo. In some embodiments, R³ is selected from the group consisting of

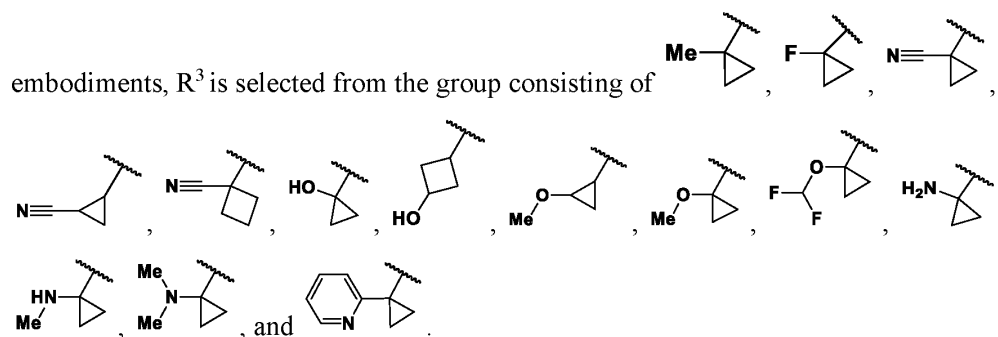


[0093] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R³ is C₁₋₆alkyl, optionally substituted with one or more R^{3a}; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}; and each R^{3b} is, independently at each occurrence, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R³ is C₁₋₃alkyl, optionally substituted with one or more R^{3a}; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}; and each R^{3b} is, independently at each occurrence, D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy. In some embodiments, R³ is C₁₋₃alkyl, optionally substituted with one or more R^{3a}; and R^{3a} is -OH. In

some embodiments, R³ is 

[0094] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R³ is C₃₋₁₀.

cycloalkyl, optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is C_{3-6} cycloalkyl, optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{2-4} alkenyl, C_{1-3} alkoxy, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O) C_{1-3} alkyl, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl, wherein the C_{1-3} alkyl, C_{1-3} alkoxy, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^3 is C_{3-10} cycloalkyl, optionally substituted with one or more R^{3a} ; R^{3a} is -OH, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, or 4-10 membered heteroaryl, wherein the C_{1-6} alkoxy of R^{3a} is optionally substituted with one or more R^{3b} ; and R^{3b} is halo. In some



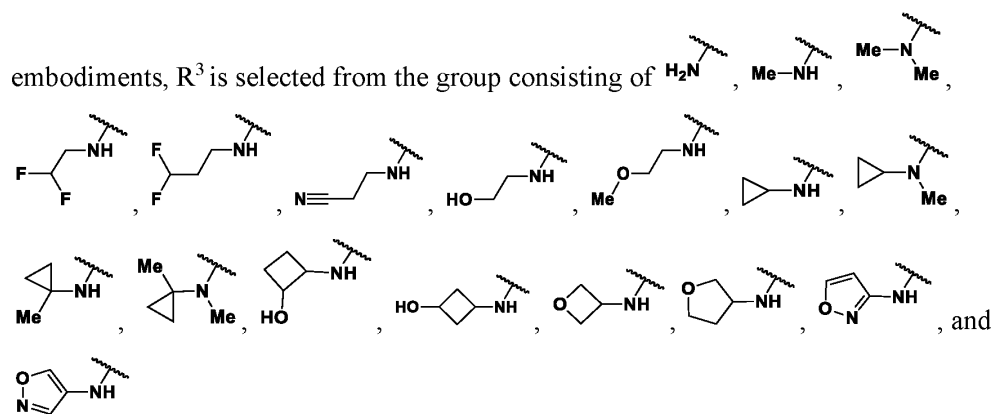
[0095] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is C_{3-10} cycloalkyl optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3a} is optionally substituted with

one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl, -O- C_{1-3} haloalkyl, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-6 membered heterocyclyl C_{3-6} cycloalkyl, or -O- C_{3-6} cylcoalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is, independently at each occurrence, D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} , and R^{3a} is halo or C_{1-3} alkyl. In some embodiments, R^3 is C_{3-6} cycloalkyl optionally substituted with one or more halo or C_{1-3} alkyl. In some embodiments, R^3 is cyclopropyl, optionally substituted

with one or more C_{1-3} alkyl. In some embodiments, R^3 is . In some embodiments, R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} , and R^{3a} is halo. In some embodiments, R^3 is C_{3-6} cycloalkyl optionally substituted with one or more Br, Cl, I, or F. In some embodiments, R^3 is cyclopropyl, optionally substituted with one or more Br, Cl, I, or F.

In some embodiments, R^3 is . In some embodiments, R^3 is selected from the group consisting of  and . In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is -N(R^4)₂, and each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ; R^{4a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cylcoalkyl of R^{4a} is optionally substituted with one or more R^{4b} ; and each R^{4b} is, independently at each occurrence, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is -N(R^4)₂, and

each R^4 is independently H, C_{1-3} alkyl, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, or C_{3-6} cycloalkyl, wherein the C_{1-3} alkyl, or C_{3-6} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ; R^{4a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{2-4} alkenyl, C_{1-3} alkoxy, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O) C_{1-3} alkyl, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl, wherein the C_{1-3} alkyl, C_{1-3} alkoxy, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} ; and each R^{4b} is, independently at each occurrence, D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^3 is -N(R^4)₂, and each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl of R^4 is optionally substituted with one or more R^{4a} ; R^{4a} is, independently at each occurrence, -OH, -CN, halo, C_{1-6} alkyl, or C_{1-6} alkoxy. In some



[0096] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is -N(R^4)₂, and each R^4 is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl. In some embodiments, R^3 is -N(R^4)₂, and each R^4 is independently H, C_{1-3} alkyl, C_{1-3} haloalkyl, or C_{3-6} cycloalkyl. In some embodiments, R^3 is -N(R^4)₂, and each R^4 is independently H or C_{1-3} alkyl.

[0097] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is -N(R^4)₂, and both R^4 are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a} ; R^{4a} is independently -

OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}; and each R^{4b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R³ is -N(R⁴)₂, and both R⁴ are taken together with the N atom to which they are attached to form a 4-6 membered heterocyclyl optionally substituted with one or more R^{4a}, R^{4a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl of R^{4a} is optionally substituted with one or more R^b; and each R^b is, independently at each occurrence, D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy. In some embodiments, R³ is -N(R⁴)₂, and both R⁴ are taken together with the N atom to which they

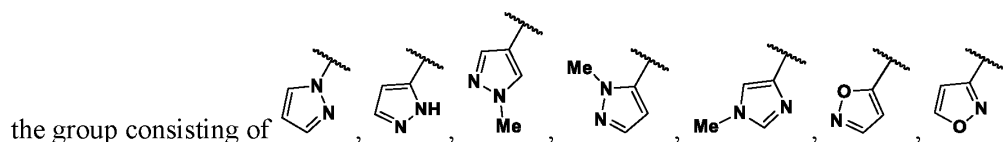
are attached to form a 4-6 membered heterocyclyl. In some embodiments, R³ is .

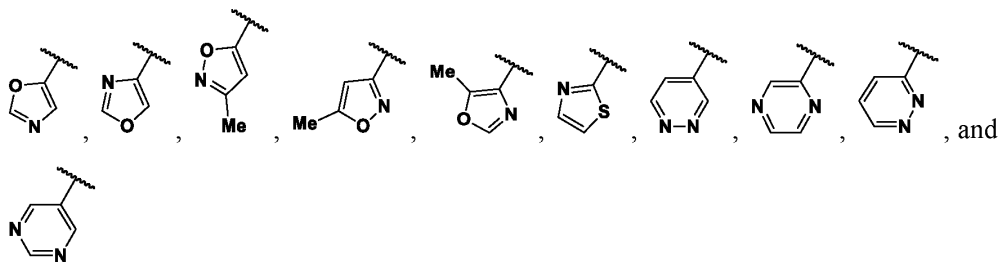
[0098] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R³ is 4-10 membered heterocyclyl optionally substituted with one or more R^{3a}, R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}; and each R^{3b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R³ is 4-6 membered heterocyclyl, optionally substituted with one or more R^{3a}, R^{3a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}; and each R^{3b} is independently D, -OH, halo, C₁₋

alkoxy, optionally substituted with one or more R^{3a} ; R^{3a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ; and each R^{3b} is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is C_{1-3} alkoxy. In some embodiments, R^3 is



[0101] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^3 is 4-10 membered heteroaryl optionally substituted with one or more R^{3x} ; R^{3x} is, independently at each occurrence, -OH, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ; and each R^{3b} is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^3 is 4-6 membered heteroaryl, optionally substituted with one or more R^{3x} ; R^{3x} is independently -OH, -CN, halo, C_{1-3} alkyl, C_{2-4} alkenyl, C_{1-3} alkoxy, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O) C_{1-3} alkyl, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-6 membered heterocyclyl C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ; and each R^{3b} is independently D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^3 is 4-10 membered heteroaryl optionally substituted with one or more R^{3x} ; R^{3x} is, independently at each occurrence, C_{1-6} alkyl. In some embodiments, R^3 is selected from





[0102] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^5 and R^7 are each independently H, halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more halo, or CN, and the C_{1-6} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo. In some embodiments, R^5 and R^7 are each independently H, halo, -CN, C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl or C_{1-3} haloalkyl, wherein the C_{1-3} alkyl of R^5 and R^7 are each independently optionally substituted with one or more halo, or CN, and the C_{1-3} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo. In some embodiments, R^5 and R^7 are each independently H, halo, -CN, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl, and the C_{1-3} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo. In some embodiments, R^5 and R^7 are each independently H. In some embodiments, one of R^5 and R^7 is H, and the other of R^5 and R^7 is independently halo, -CN, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl.

[0103] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^5 and R^7 are each independently H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more halo, or CN. In some embodiments, R^5 and R^7 are each independently H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl or C_{1-3} haloalkyl, wherein the C_{1-3} alkyl of R^5 and R^7 are each independently optionally substituted with one or more halo, or CN. In some embodiments, R^5 and R^7 are each independently H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl. In some embodiments, R^5 and R^7 are each independently H. In some embodiments, one of R^5 and R^7 is H, and the other of R^5 and R^7 is independently halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl.

[0104] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^6 and R^9 are each independently H, or halo. In some embodiments, R^6 and R^9 are each independently H, F, or Cl. In some embodiments, R^6 and R^9 are each independently H. In some embodiments, R^6 and R^9 are each independently halo. In some embodiments, R^6 and R^9 are each independently F, or Cl. In some embodiments, one of R^6 and R^9 is H, and the other of R^6 and R^9 is halo. In some embodiments, one of R^6 and R^9 is H, and the other of R^6 and R^9 is F, or Cl.

[0105] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^8 is C₃₋₁₀-cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-20 membered heteroaryl, wherein each R^8 is optionally substituted with one or more R^{8a} ; R^{8a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} , and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R^8 is C₃₋₆cycloalkyl, C₆₋₁₂aryl, 3-6 membered heterocyclyl, or 5-10 membered heteroaryl, wherein each R^8 is optionally substituted with one or more R^{8a} ; R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} , and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy.

[0106] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^8 is C₃₋₁₀-cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-20 membered heteroaryl, wherein each R^8 is optionally substituted with one or more R^{8a} ; R^{8a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋

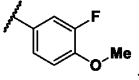
alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is C₃₋₆cycloalkyl, C₆₋₁₂aryl, 3-6 membered heterocyclyl, or 5-10 membered heteroaryl, wherein each R⁸ is optionally substituted with one or more R^{8a}; R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is, independently at each occurrence, D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy.

[0107] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R⁸ is C₃₋₁₀cycloalkyl. In some embodiments, R⁸ is C₃₋₁₀cycloalkyl, optionally substituted with one or more R^{8a}, R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is C₃₋₆cycloalkyl, optionally substituted with one or more R^{8a}; R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy.

[0108] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R⁸ is C₃₋₁₀cycloalkyl. In some embodiments, R⁸ is C₃₋₁₀cycloalkyl, optionally substituted with one or more R^{8a}, R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -

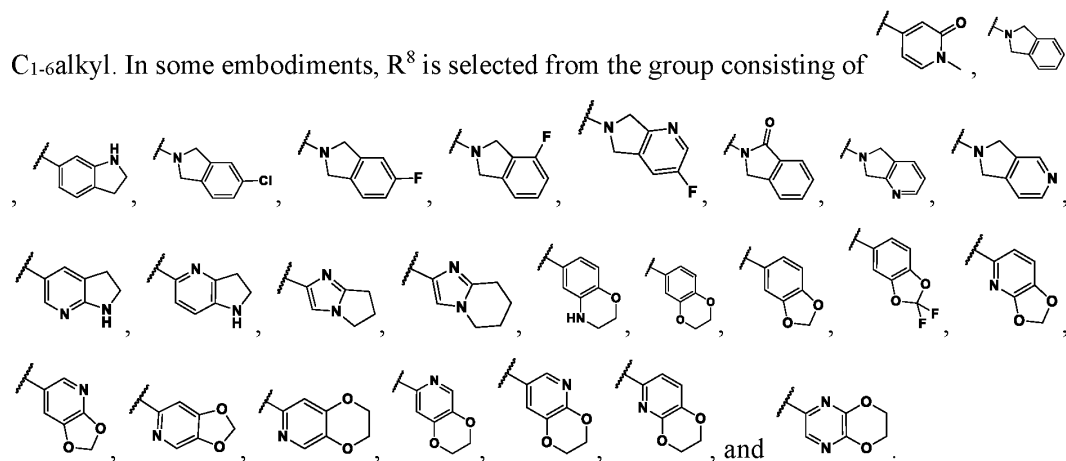
C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^b is, independently at each occurrence, D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is C₃₋₆cycloalkyl.

[0109] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R⁸ is C₆₋₁₂aryl. In some embodiments, R⁸ is C₆₋₁₂aryl, optionally substituted with one or more R^{8a}, R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is C₆₋₁₀aryl, optionally substituted with one or more R^{8a}, R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋

3alkoxy. In some embodiments, R⁸ is .

[0110] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R⁸ is C₆₋₁₂aryl. In some embodiments, R⁸ is C₆₋₁₂aryl, optionally substituted with one or more R^{8a}, R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^b is, independently at each occurrence, D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is C₃₋₆cycloalkyl.

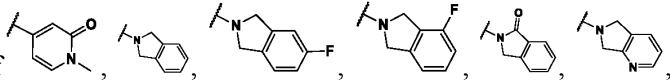
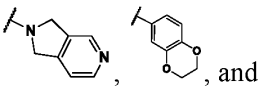
[0111] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^8 is 3-10 membered heterocyclyl. In some embodiments, R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} , R^{8a} is independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl or C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and each R^{8b} is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} , R^{8a} is independently -OH, oxo, -CN, halo, C_{1-3} alkyl, C_{2-4} alkenyl, C_{1-3} alkoxy, -NH₂, -NH(C_{1-3} alkyl), -N(C_{1-3} alkyl)₂, -C(O) C_{1-3} alkyl, -C(O)NH₂, -C(O)NH(C_{1-3} alkyl), -C(O)N(C_{1-3} alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-6 membered heterocyclyl C_{3-6} cycloalkyl, or -O- C_{3-6} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and each R^{8b} is independently D, -OH, halo, C_{1-3} alkyl or C_{1-3} alkoxy. In some embodiments, R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} , R^{8a} is independently oxo, halo, or

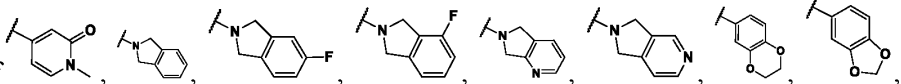
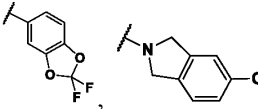
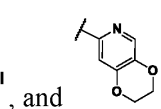


[0112] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^8 is 3-10 membered heterocyclyl. In some embodiments, R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} , R^{8a} is, independently at each occurrence, -OH, oxo, -CN,

halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is, independently at each occurrence, D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

[0113] In some embodiments, R⁸ is 3-6 membered heterocyclyl. In some embodiments, R⁸ is 3-6 membered heterocyclyl, optionally substituted with one or more R^{8a}; R^{8a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy. In some embodiments, R⁸ is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a}; and R^{8a} is, independently at each occurrence, halo or C₁₋₃alkyl. In some embodiments, R⁸ is selected

from the group consisting of , , and . In some embodiments, R⁸ is selected from the group

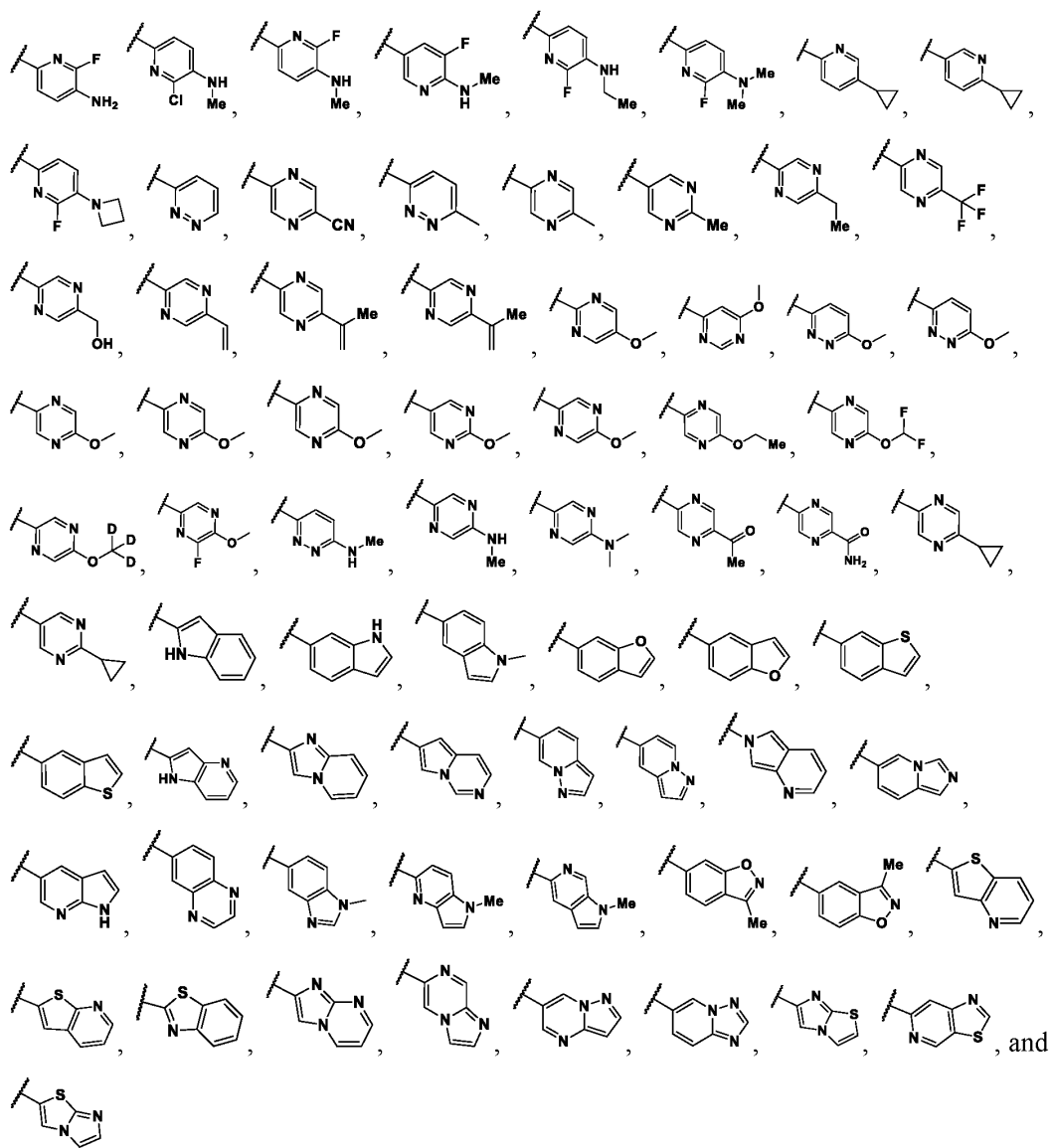
consisting of , , and . In some embodiments of a compound of formula (I), or

(I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R⁸ is 3-10 membered heteroaryl. In some embodiments, R⁸ is 3-10 membered heteroaryl, optionally substituted with one or more R^{8a}; R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋

alkoxy, 4-10 membered heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is 3-10 membered heteroaryl, optionally substituted with one or more R^{8a}; R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₂₋₄alkenyl, C₁₋₃alkoxy, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)C₁₋₃alkyl, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heteroaryl, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy. In some embodiments, R⁸ is 3-10 membered heteroaryl, optionally substituted with one or more R^{8a}, R^{8a} is independently -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, or C₁₋₆alkoxy, of R^{8a} is optionally substituted with one or more R^{8b}, and each R^{8b} is independently D, -OH, or halo. In some embodiments, R⁸ is selected from the

group consisting of

Chemical structures representing various pyridine and pyrrole derivatives, including substituted pyridines and pyrroles, and their corresponding chemical structures.

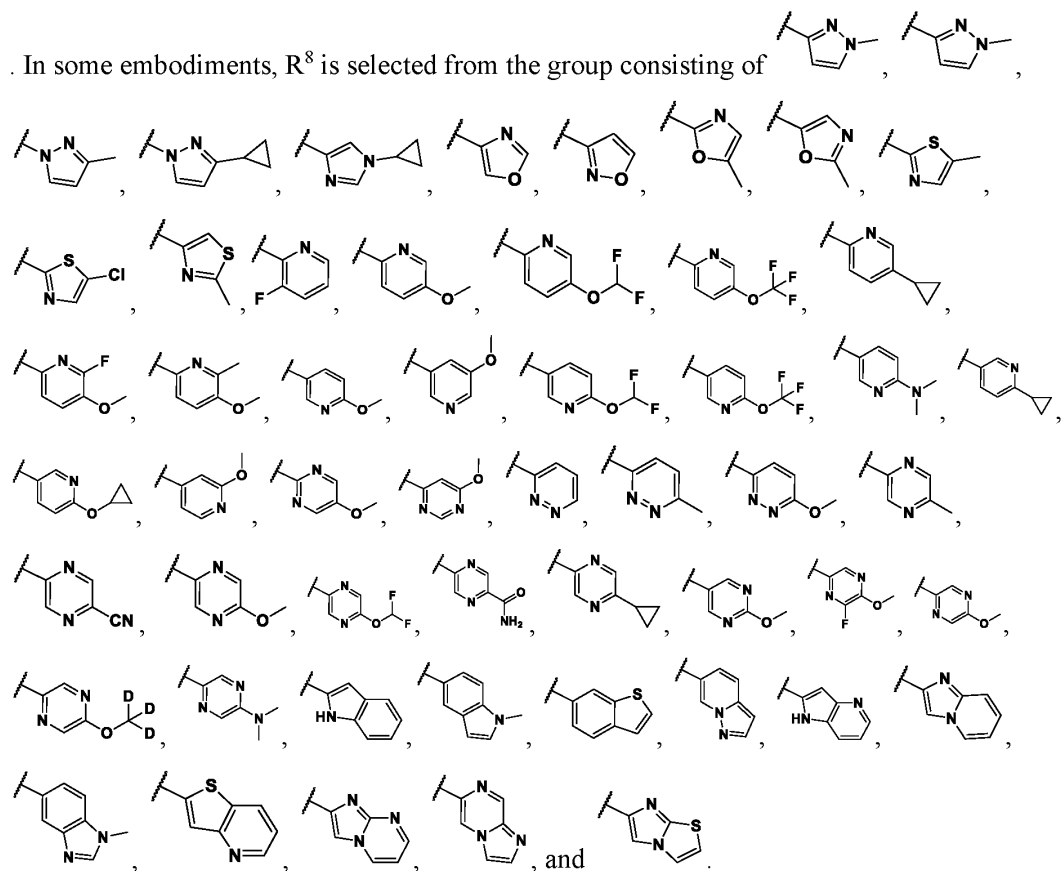


[0114] In some embodiments of a compound of formula (I), or (I-A), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^8 is 5-20 membered heteroaryl. In some embodiments, R^8 is 5-20 membered heteroaryl, optionally substituted with one or more R^{8a} , R^{8a} is, independently at each occurrence, -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered

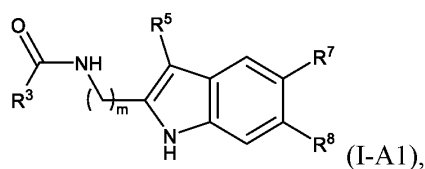
heterocyclyl or C₃₋₁₀cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy. In some embodiments, R⁸ is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a}; R^{8a} is, independently at each occurrence, -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₃alkyl), -C(O)N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, C₃₋₆cycloalkyl, or -O-C₃₋₆cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-6 membered heterocyclyl C₃₋₆cycloalkyl, or -O-C₃₋₆cylcoalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is independently D, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy. In some embodiments, R⁸ is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a}; R^{8a} is, independently at each occurrence, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, -C(O)NH₂, or C₃₋₆cycloalkyl, wherein the C₁₋₆alkoxy, of R^{8a} is optionally substituted with one or more R^{8b}; and each R^{8b} is, independently at each occurrence, D, or halo. In some

embodiments, R⁸ is selected from the group consisting of

and

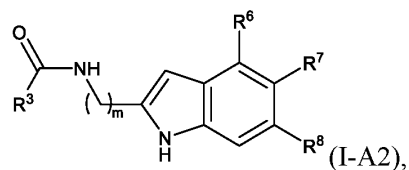


[0115] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A1):



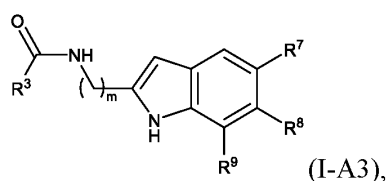
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^5 , R^7 , and R^8 , are as defined for a compound of formula (I).

[0116] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^6 , R^7 , and R^8 are as defined for a compound of formula (I).

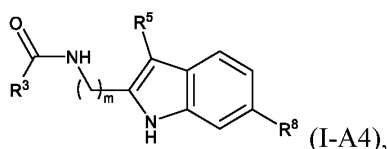
[0117] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^6 , R^7 , and R^8 are as defined for a compound of formula (I).

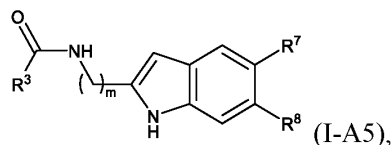
[0118] In some embodiments of a compound of formula (I), or (I-A), such as a compound of formula (I-A3), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^7 is H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein the C_{1-6} alkyl of R^7 is optionally substituted with one or more halo, or CN; and R^9 is H, or halo. In some embodiments, R^7 is H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl or C_{1-3} haloalkyl, wherein the C_{1-3} alkyl of R^7 is optionally substituted with one or more halo, or CN; and R^9 is H, or halo. In some embodiments R^7 is H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl; and R^9 is H, or halo. In some embodiments, R^7 is H; and R^9 is H, or halo. In some embodiments, R^7 is halo; and R^9 is halo.

[0119] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A4):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , R^5 , and R^8 , are as defined for a compound of formula (I).

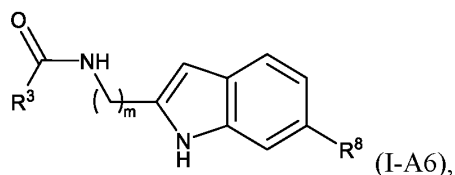
[0120] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A5):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , and R^7 , are as defined for a compound of formula (I).

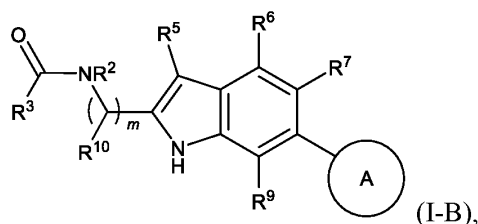
[0121] In some embodiments of a compound of formula (I), or (I-A), such as a compound of formula (I-A5), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^7 is H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein the C_{1-6} alkyl of R^7 is optionally substituted with one or more halo, or CN. In some embodiments, R^7 is H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl or C_{1-3} haloalkyl, wherein the C_{1-3} alkyl of R^7 is optionally substituted with one or more halo, or CN. In some embodiments, R^7 is H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl. In some embodiments, R^7 is halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl. In some embodiments, R^7 is halo. In some embodiments, R^7 is F. In some embodiments, R^7 is Cl. In some embodiments, R^7 is C_{1-6} alkyl. In some embodiments, R^7 is C_{1-3} alkyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is ethyl. In some embodiments, R^7 is isopropyl. In some embodiments, R^7 is C_{1-6} alkoxy. In some embodiments, R^7 is C_{1-3} alkoxy. In some embodiments, R^7 is methoxy. In some embodiments R^7 is C_{1-6} haloalkyl. In some embodiments, R^7 is C_{1-3} haloalkyl. In some embodiments, R^7 is CF_3 .

[0122] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-A6):



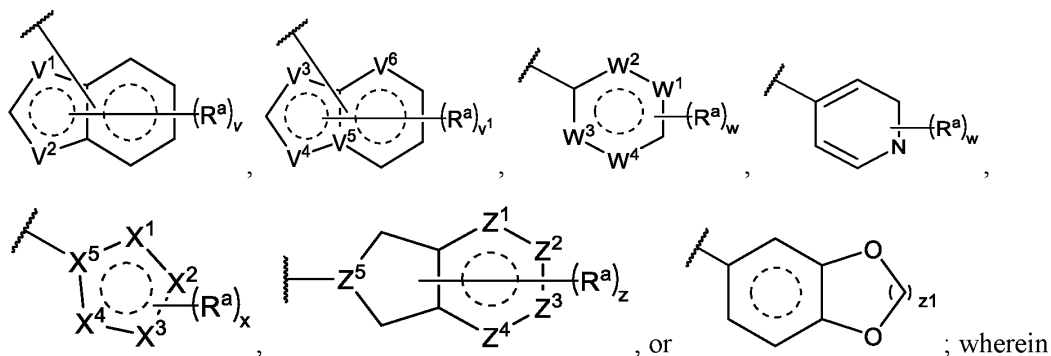
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^3 , and R^8 are as defined for a compound of formula (I).

[0123] In one aspect, provided herein is a compound of formula (I), such as a compound of formula (I-B):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^2 , R^3 , R^5 , R^6 , R^7 , R^9 , and R^{10} are as defined for a compound of formula (I); and ring A is 5-10 membered heteroaryl or 5-10 membered heterocyclyl optionally substituted with one or more R^a ; each R^a is, independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^a is optionally substituted with one or more R^b ; and each R^b is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy. In some embodiments, R^2 , R^3 , R^5 , R^6 , R^7 , R^9 , and R^{10} are as defined for a compound of formula (I); and ring A is a C_{6-20} aryl, 5-10 membered heteroaryl, or 5-10 membered heterocyclyl optionally substituted with one or more R^a ; each R^a is, independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^a is optionally substituted with one or more R^b ; and each R^b is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy.

[0124] In some embodiments of a compound of formula (I-B), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, ring A is



V¹, V², V³, V⁴, V⁵, and V⁶ are each independently -N-, -NH-, -S-, -O-, or -CH-;

W¹, W², W³, W⁴, and W⁵ are each independently -N-, or -CH-;

X¹, X², X³, X⁴ and X⁵ are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z¹, Z², Z³, Z⁴ and Z⁵ are each independently -N-, -S-, -O-, -CH-, or -CH₂-;

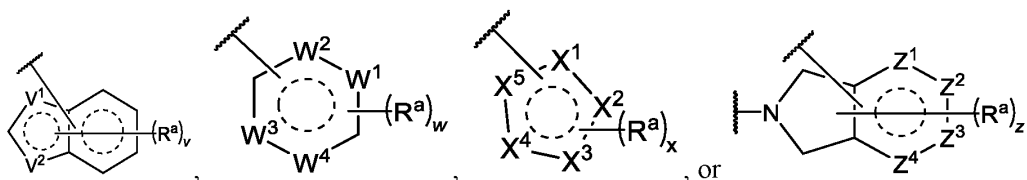
v and v¹ are each independently an integer from 0-7;

w is an integer from 0-6;

x is an integer from 0-5; and

z and z¹ are each independently an integer from 0-8.

[0125] In some embodiments of a compound of formula (I-B), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, ring A is



wherein

V¹ and V² are each independently -N-, -NH-, -S-, -O-, or -CH-;

W¹, W², W³ and W⁴ are each independently -N-, or -CH-;

X¹, X², X³, X⁴ and X⁵ are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z¹, Z², Z³ and Z⁴ are each independently -N-, -S-, -O-, or -CH-;

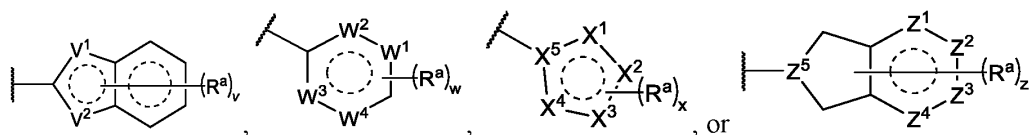
v is an integer from 0-7;

w is an integer from 0-6;

x is an integer from 0-5; and

z is an integer from 0-8.

[0126] In some embodiments of a compound of formula (I-B), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, ring A is



wherein

V^1 and V^2 are each independently -N-, -NH-, -S-, -O-, or -CH-;

W^1 , W^2 , W^3 and W^4 are each independently -N-, or -CH-;

X^1 , X^2 , X^3 , X^4 and X^5 are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z^1 , Z^2 , Z^3 , Z^4 and Z^5 are each independently -N-, -S-, -O-, -CH-, or -CH₂-;

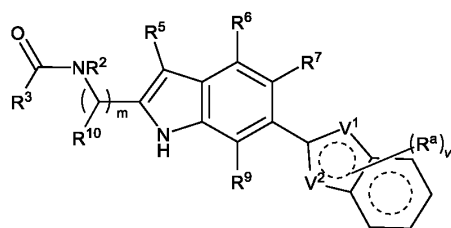
v is an integer from 0-7;

w is an integer from 0-6;

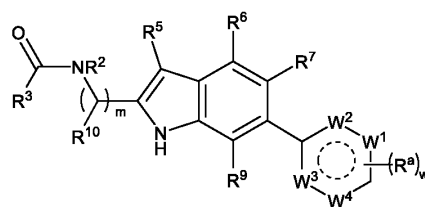
x is an integer from 0-5; and

z is an integer from 0-8.

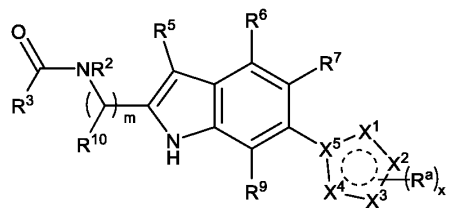
[0127] In some embodiments of a compound of formula (I), (I-A), or (I-B), or a stereoisomer or tautomer thereof, the compound is a compound of formula:



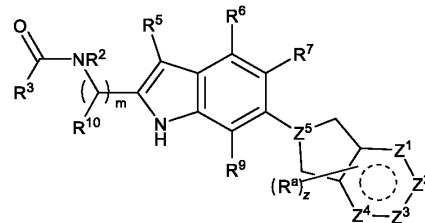
(I-B1),



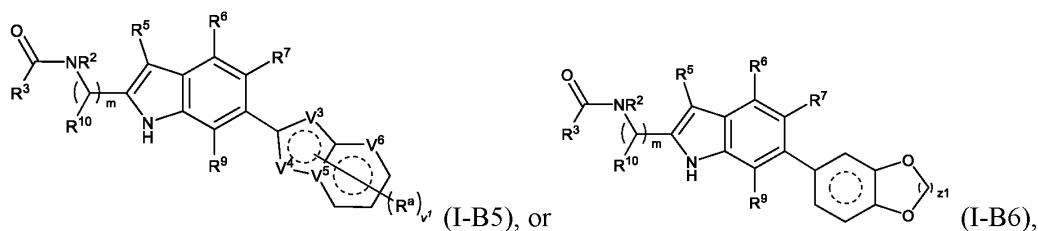
(I-B2),



(I-B3),



(I-B4),



wherein

V^1 , V^2 , V^3 , V^4 , V^5 , and V^6 are each independently -N-, -NH-, -S-, -O-, or -CH-;

W^1 , W^2 , W^3 , W^4 , and W^5 are each independently -N-, or -CH-;

X^1 , X^2 , X^3 , X^4 and X^5 are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z^1 , Z^2 , Z^3 , Z^4 and Z^5 are each independently -N-, -S-, -O-, -CH-, or -CH₂-;

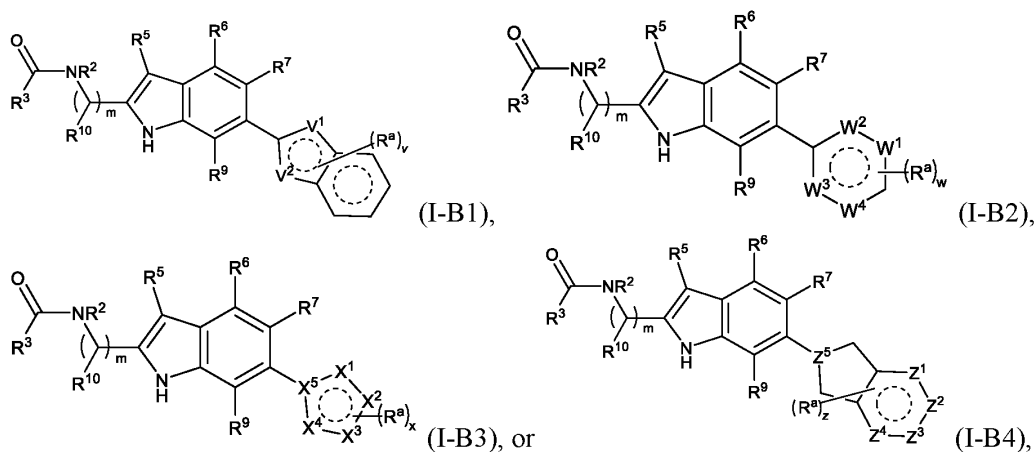
v and v^1 are each independently an integer from 0-7;

w is an integer from 0-6;

x is an integer from 0-5; and

z and z^1 are each independently an integer from 0-8. In some embodiments, the compound is a compound of formula (I-B1). In some embodiments, the compound is a compound of formula (I-B2). In some embodiments, the compound is a compound of formula (I-B3). In some embodiments, the compound is a compound of formula (I-B4). In some embodiments, the compound is a compound of formula (I-B5). In some embodiments, the compound is a compound of formula (I-B6).

[0128] In some embodiments of a compound of formula (I), (I-A), or (I-B), or a stereoisomer or tautomer thereof, the compound is a compound of formula:



wherein

V^1 and V^2 are each independently -N-, -NH-, -S-, -O-, or -CH-;

W^1 , W^2 , W^3 and W^4 are each independently -N-, or -CH-;

X^1 , X^2 , X^3 , X^4 and X^5 are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z^1 , Z^2 , Z^3 and Z^4 are each independently -N-, -S-, -O-, or -CH-;

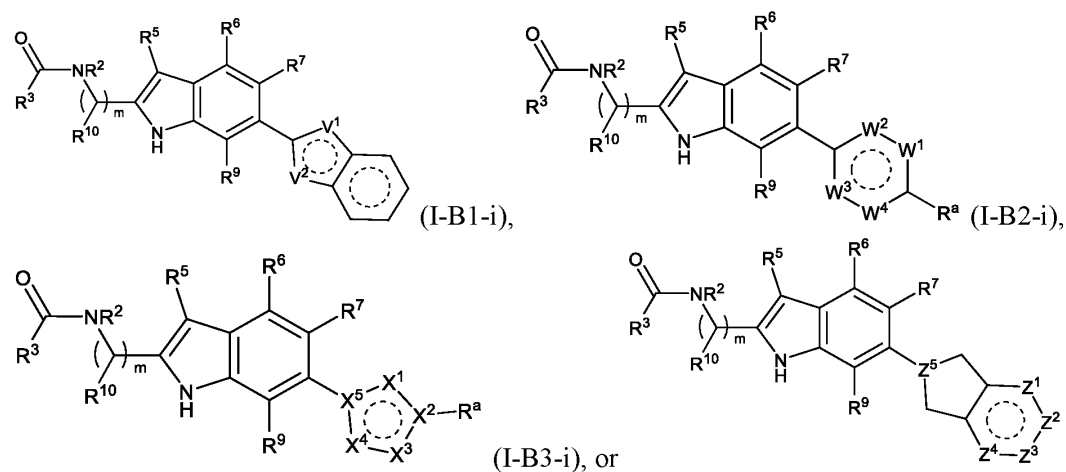
v is an integer from 0-7;

w is an integer from 0-6;

x is an integer from 0-5; and

z is an integer from 0-8. In some embodiments, the compound is a compound of formula (I-B1). In some embodiments, the compound is a compound of formula (I-B2). In some embodiments, the compound is a compound of formula (I-B3). In some embodiments, the compound is a compound of formula (I-B4).

[0129] In some embodiments of a compound of formula (I), (I-A), or (I-B), or a stereoisomer or tautomer thereof, the compound is a compound of formula:



(I-B4-i), wherein

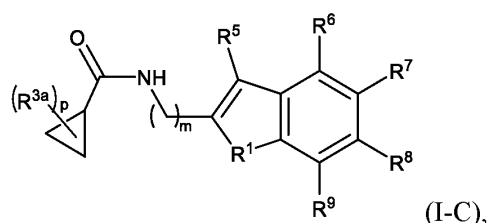
V^1 and V^2 are each independently -N-, -NH-, -S-, -O-, or -CH-;

W^1 , W^2 , W^3 and W^4 are each independently -N-, or -CH-;

X^1 , X^2 , X^3 , X^4 and X^5 are each independently -N-, -NH-, -S-, -O-, -CH-, or -CH₂-;

Z^1 , Z^2 , Z^3 and Z^4 are each independently -N-, -S-, -O-, or -CH-. In some embodiments, the compound is a compound of formula (I-B1-i). In some embodiments, the compound is a compound of formula (I-B2-i). In some embodiments, the compound is a compound of formula (I-B3-i). In some embodiments, the compound is a compound of formula (I-B4-i).

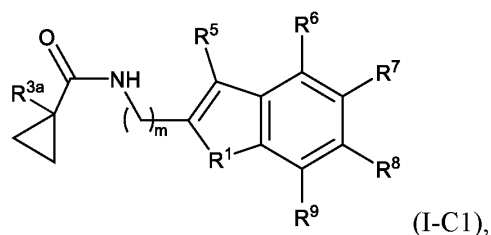
[0130] In one aspect, provided herein is a compound of formula (I), such as a compound of formula (I-C):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , p , R^{3a} , R^1 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I); and p is an integer from 0 to 5.

[0131] In some embodiments of a compound of formula (I), such as a compound of formula (I-C), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, p is 0 or 1. In some embodiments, p is 0. In some embodiments, p is 1.

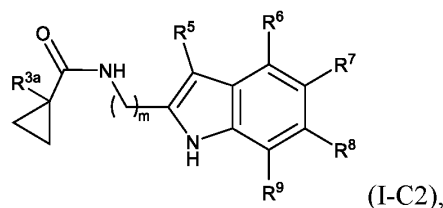
[0132] In one aspect, provided herein is a compound of formula (I), or (I-C), such as a compound of formula (I-C1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^{3a} , R^1 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

[0133] In some embodiments of a compound of formula (I), or (I-C), such as a compound of formula (I-C1), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^1 is -NH-.

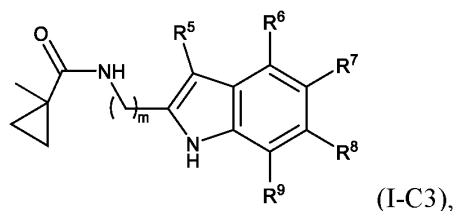
[0134] In one aspect, provided herein is a compound of formula (I), (I-A), or (I-C), such as a compound of formula (I-C2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^{3a} , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I). In some embodiments of a compound of formula (I), (I-A), or (I-C), such as a compound of formula (I-C2), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, R^{3a} is halo or C_{1-6} alkyl. In some embodiments, R^{3a} is halo or C_{1-3} alkyl. In some embodiments, R^{3a} is C_{1-3} alkyl. In some embodiments, R^{3a} is CH_3 . In some embodiments, R^{3a} is halo. In some embodiments, R^{3a} is Br, Cl, F, or I. In some embodiments, R^{3a} is F.

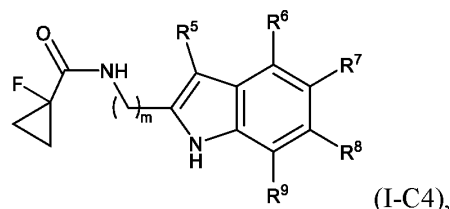
[0135] In some embodiments of a compound of formula (I), (I-A), or (I-C), such as a compound of formula (I-C2), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, X is -O-, and R^{3a} is C_{1-6} alkyl. In some embodiments, X is -O-, and R^{3a} is C_{1-3} alkyl. In some embodiments, X is -O-, and R^{3a} is methyl.

[0136] In one aspect, provided herein is a compound of formula (I-C3):



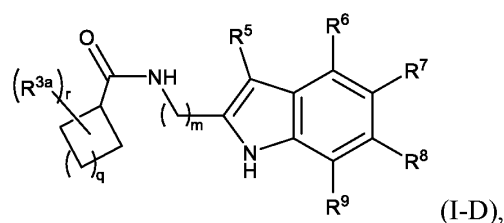
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

[0137] In one aspect, provided herein is a compound of formula (I-C4):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

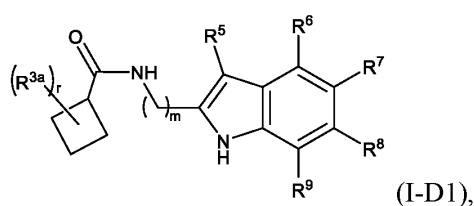
[0138] In one aspect, provided herein is a compound of formula (I), or (I-A), such as a compound of formula (I-D):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , q , r , R^{3a} , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I); q is an integer from 1-7; and r is an integer from 0-18.

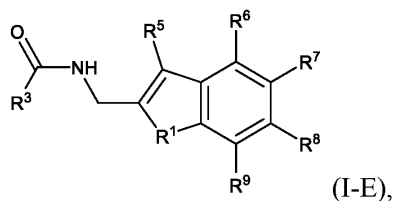
[0139] In some embodiments of a compound of formula (I), such as a compound of formula (I-D), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, q is an integer from 1 to 3. In some embodiments, q is 1. In some embodiments, q is 2. In some embodiments, q is 3.

[0140] In one aspect, provided herein is a compound of formula (I), (I-A), or (I-D), such as a compound of formula (I-D1):



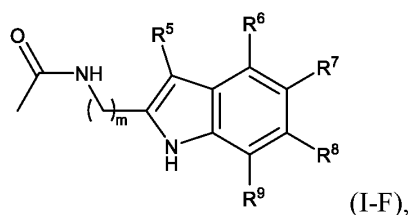
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , r , R^{3a} , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I); and r is an integer from 0 to 6.

[0141] In one aspect, provided is a compound of formula (I), such as a compound of formula (I-E):



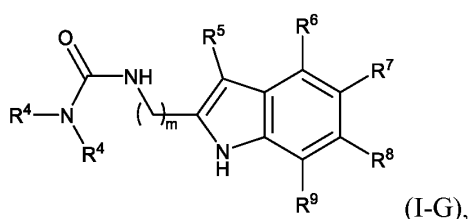
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^1 , R^3 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined elsewhere herein.

[0142] In one aspect, provided herein is a compound of formula (I-F):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

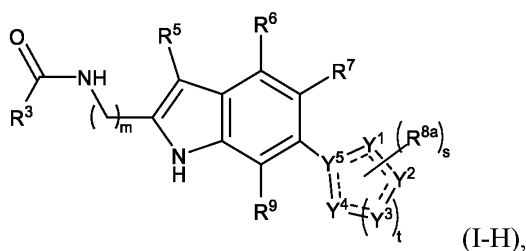
[0143] In one aspect, provided herein is a compound of formula (I-G):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , R^4 , R^5 , R^6 , R^7 , R^8 , and R^9 are as defined for a compound of formula (I).

[0144] In some embodiments of a compound of formula (I), such as a compound of formula (I-G), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, each R^4 is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl. In some embodiments, each R^4 is independently H, C_{1-3} alkyl, C_{1-3} haloalkyl, or C_{3-6} cycloalkyl. In some embodiments, each R^4 is independently H, or C_{1-3} alkyl. In some embodiments, one R^4 is H and the other R^4 is C_{1-3} alkyl. In some embodiments, one R^4 is H and the other R^4 is methyl.

[0145] In one aspect, provided herein is a compound of formula (I-H):



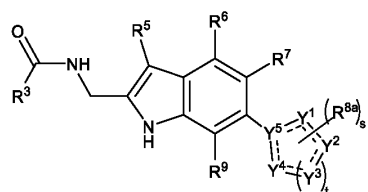
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m , s , t , R^3 , R^5 , R^6 , R^7 , R^9 , R^{8a} , Y^1 , Y^2 , Y^3 , Y^4 , and Y^5 are as defined for a

compound of formula (I); Y^1 , Y^2 , Y^3 , Y^4 , and Y^5 , are each independently -C-, -CH-, -CH₂-, -N-, -NH-, -S-, or -O-; s is an integer from 0-6; t is 1 or 2; and ----- represents a single or double bond. In some embodiments of formula (I-H), t is 1. In some embodiments of formula (I-H), t is 2. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is aryl or heteroaryl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is aryl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is C₆aryl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is heteroaryl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is 6-membered heteroaryl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is pyridyl or pyrazinyl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is pyridyl. In some embodiments of formula (I-H), the ring bearing Y^1 through Y^5 , is pyrazinyl.

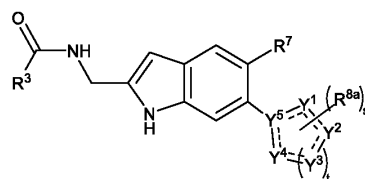
[0146] In some embodiments of a compound of formula (I), such as a compound of formula (I-H), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, m is an integer from 1 to 2; n is an integer from 0 to 2; X is -O-, -S-, -C(R^{12a})(R^{12b})-, -N(H)-, or -N(C₁₋₆alkyl)-; R³ is C₁₋₃alkyl, C₁₋₃haloalkyl, C₃₋₆cycloalkyl, -N(R⁴)₂, or 4-6 membered heterocyclyl, wherein each R³ is optionally substituted with one or more R^{3a}; each R⁴ is independently H, C₁₋₃alkyl, C₁₋₃haloalkyl, or C₃₋₆cycloalkyl, or both R⁴ are taken together with the N atom to which they are attached to form a 4-6 membered heterocyclyl optionally substituted with one or more R^{4a}; R⁵ and R⁷ are each independently H, halo, C₁₋₃alkyl, C₃₋₆cycloalkyl or C₁₋₃haloalkyl, wherein the C₁₋₃alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more halo or CN; R⁶ and R⁹ are each independently H, or halo; R^{11a} and R^{11b} are each independently H or C₁₋₃alkyl, one of R^{11a} and R^{11b} is H or C₁₋₆alkyl, and the other of R^{11a} and R^{11b} is taken together with one of R^{12a} or R^{12b} to form a C₃₋₁₀cycloalkyl; R^{12a} and R^{12b} are each independently, H, or C₁₋₃alkyl, or one of R^{12a} and R^{12b} is H, or C₁₋₃alkyl, and the other of R^{12a} and R^{12b} is taken together with R^{11a} or R^{11b} to form a C₃₋₆cycloalkyl; each R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃haloalkyl, -O-C₁₋₃haloalkyl, -NH₂, -NH(C₁₋₃alkyl), -N(C₁₋₃alkyl)₂, 4-6 membered heterocyclyl, or C₃₋₆cycloalkyl, wherein the C₁₋₃alkyl, C₁₋₃alkoxy, 4-6 membered heterocyclyl or C₃₋₆cylcoalkyl of R^a is optionally substituted with one or more R^{8b}; and each R^{8b} is, independently at each occurrence, -OH, halo, C₁₋₃alkyl or C₁₋₃alkoxy; Y^1 , Y^2 , Y^3 , Y^4 ,

and Y^5 , are each independently -C-, -CH-, -CH₂-, -N-, -NH-, -S-, or -O-; s is an integer from 0-6; t is 1 or 2; and ----- represents a single or double bond.

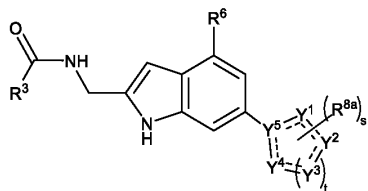
[0147] In some embodiments of a compound of formula (I), such as a compound of formula (I-H), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the compound is compound of formula:



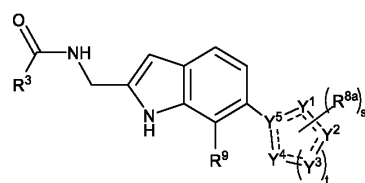
(I-H-a-i),



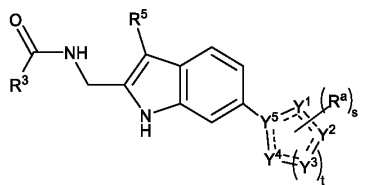
(I-H-a-ii),



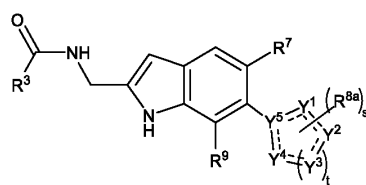
(I-H-a-iii),



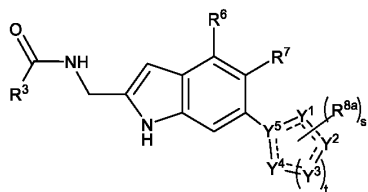
(I-H-a-iv),



(I-H-a-v),

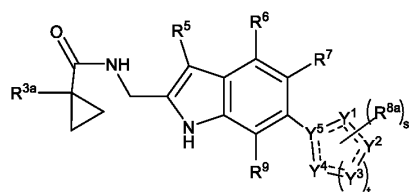


, or

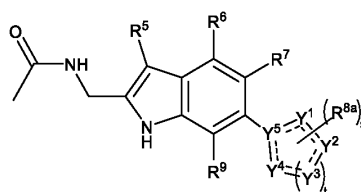
(I-H-a-vi). In some embodiments t is 0. In some

embodiments, t is 1.

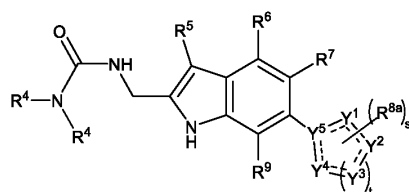
[0148] In some embodiments of a compound of formula (I), such as a compound of formula (I-H), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the compound is compound of formula:



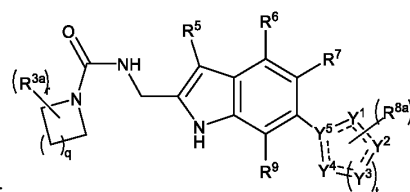
(I-H-b-i),



(I-H-b-ii),



(I-H-b-iii), or



(I-H-

b-iv), wherein q is an integer from 1-7; and r is an integer from 0-18. In some embodiments t is 0. In some embodiments, t is 1. In some embodiments, t is 1, and Y^5 is -C-. In some embodiments, t is 1, Y^5 is -C-, any one of Y^1 , Y^2 , Y^3 , and Y^4 is -N-, -NH-, -S-, or -O- and the others of Y^1 , Y^2 , Y^3 , and Y^4 are each independently -C-, -CH-, or -CH₂-. In some embodiments, t is 1, Y^5 is -C-, any two of Y^1 , Y^2 , Y^3 , and Y^4 is -N-, -NH-, -S-, or -O- and the others of Y^1 , Y^2 , Y^3 , and Y^4 are each independently -C-, -CH-, or -CH₂-.

[0149] In some embodiments of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the compound, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, is selected from Table 1. In some embodiments of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the compound, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, is selected from compounds 1-83 of Table 1. In some embodiments of a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, the compound, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, is selected from compounds 1-90 of Table 1.

[0150] Compound Names included in Table 1 and for all intermediates and compounds were generated using ChemDraw[®] Professional software version 17.1.1.0 or Collaborative Drug Discovery Inc. (CDD) CDD Vault update #3.

[0151] A Knime workflow was created to retrieve structures from an internal ChemAxon Compound Registry, generate the canonical smiles using RDKit Canon SMILES node, remove the stereochemistry using ChemAxon/Infocom MolConverter node, and name the structure using ChemAxon/Infocom Naming node. The following denotes the version of the Knime Analytics Platform and extensions utilized in the workflow:

Knime Analytics Platform 4.2.2

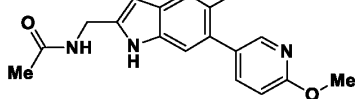
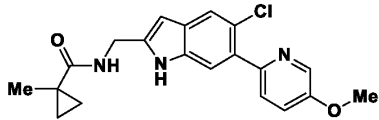
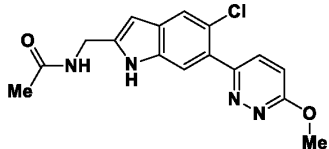
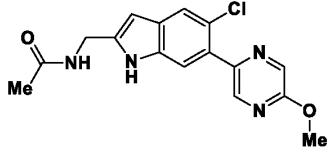
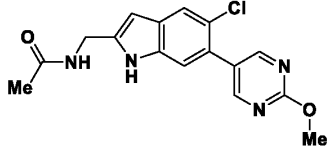
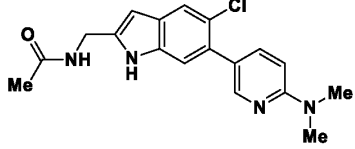
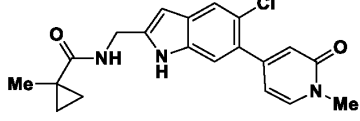
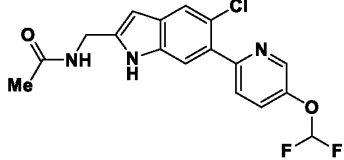
RDKit Knime Integration 4.0.1.v202006261025 (this extension includes the RDKit Canon SMILES node)

ChemAxon/Infocom Marvin Extensions Feature 4.3.0v202100 (this extension includes the MolConverter node)

ChemAxon/Infocom JChem Extensions Feature 4.3.0v202100 (this extension includes the Naming node)

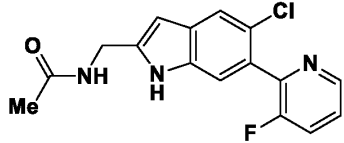
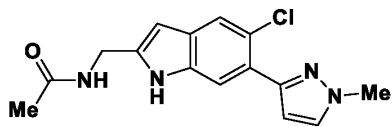
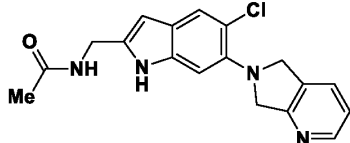
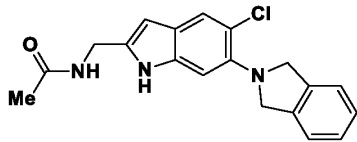
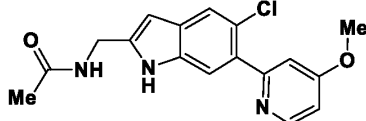
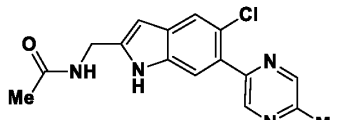
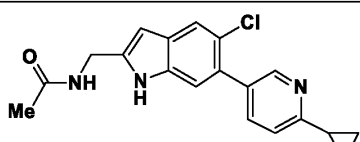
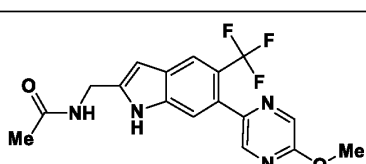
Table 1

Cmpd No.	Structure	IUPAC name
1		<i>N</i> -((5-chloro-6-(6-methoxypyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide
2		<i>N</i> -((5-chloro-6-(1 <i>H</i> -pyrrolo[3,2- <i>b</i>]pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide
3		<i>N</i> -((5'-chloro-1 <i>H</i> ,1' <i>H</i> -[2,6'-biindol]-2'-yl)methyl)-1-methylcyclopropane-1-carboxamide
4		<i>N</i> -((5-chloro-6-(5-methoxypyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

5		<i>N</i> -((5-chloro-6-(6-methoxypyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
6		<i>N</i> -((5-chloro-6-(5-methoxypyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide
7		<i>N</i> -((5-chloro-6-(6-methoxypyridazin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
8		<i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
9		<i>N</i> -((5-chloro-6-(2-methoxypyrimidin-5-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
10		<i>N</i> -((5-chloro-6-(6-(dimethylamino)pyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
11		<i>N</i> -((5-chloro-6-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide
12		<i>N</i> -((5-chloro-6-(5-(difluoromethoxy)pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

13		<i>N</i> -((5-chloro-6-(5-(trifluoromethoxy)pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
14		<i>N</i> -((5-chloro-6-(pyrazolo[1,5- <i>a</i>]pyridin-5-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
15		<i>N</i> -((5-chloro-6-(pyrazolo[1,5- <i>a</i>]pyridin-6-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
16		<i>N</i> -((5-fluoro-6-(6-methoxypyridazin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
17		<i>N</i> -((5-fluoro-6-(5-methoxypyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
18		(<i>S</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-2-hydroxypropanamide
19		<i>N</i> -((5-fluoro-6-(6-methoxypyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
20		(<i>R</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-2-hydroxypropanamide

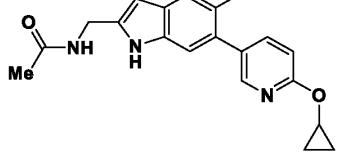
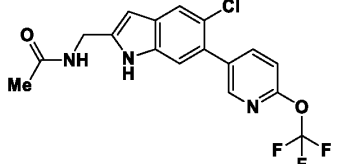
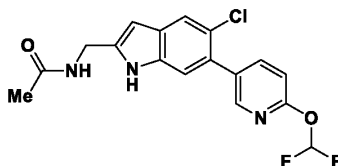
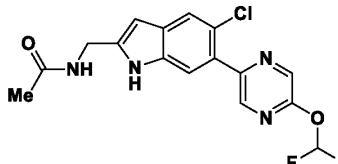
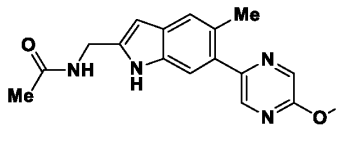
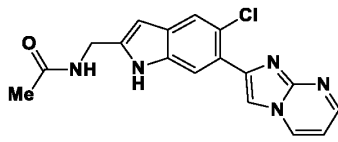
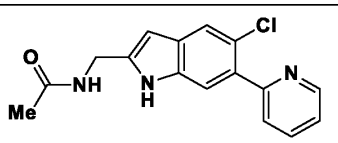
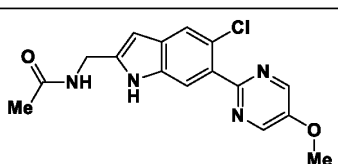
21		<i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)oxetane-3-carboxamide
22		<i>N</i> -((5-fluoro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
23		(<i>S</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)tetrahydrofuran-2-carboxamide
24		(<i>S</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)tetrahydrofuran-3-carboxamide
25		<i>N</i> -((5-chloro-6-(5-cyclopropylpyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
26		<i>N</i> -{[5-chloro-6-(5-cyclopropyl-2-pyridyl)-2-indolyl]methyl}acetamide
27		(<i>S</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)oxetane-2-carboxamide
28		(<i>R</i>)- <i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)oxetane-2-carboxamide

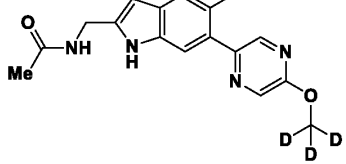
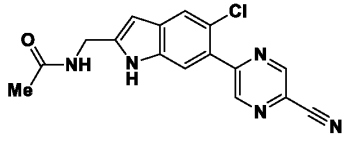
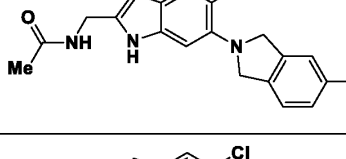
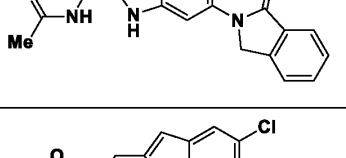
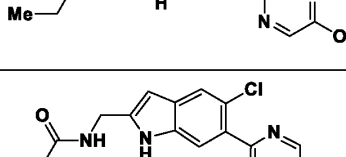
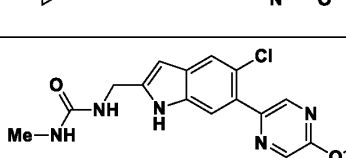
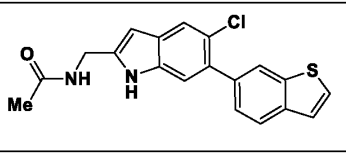
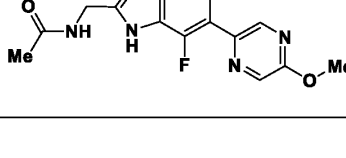
29		<i>N</i> -((5-chloro-6-(3-fluoropyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
30		<i>N</i> -((5-chloro-6-(1-methyl-1 <i>H</i> -pyrazol-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
31		<i>N</i> -((5-chloro-6-(5,7-dihydro-6 <i>H</i> -pyrrolo[3,4- <i>b</i>]pyridin-6-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
32		<i>N</i> -((5-chloro-6-(isindolin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
33		<i>N</i> -((5-chloro-6-(4-methoxypyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
34		<i>N</i> -((5-chloro-6-(5-methylpyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
35		<i>N</i> -((5-chloro-6-(6-cyclopropylpyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
36		<i>N</i> -((6-(5-methoxypyrazin-2-yl)-5-(trifluoromethyl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

37		<i>N</i> -((5-chloro-6-(5-methoxypyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
38		<i>N</i> -((5-chloro-6-(2-methoxypyridin-4-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
39		<i>N</i> -((5-methoxy-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
40		<i>N</i> -((5-chloro-6-(5-methylthiazol-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
41		5-(2-(acetamidomethyl)-5-chloro-1 <i>H</i> -indol-6-yl)pyrazine-2-carboxamide
42		<i>N</i> -((5-chloro-6-(imidazo[1,2- <i>a</i>]pyrazin-6-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
43		<i>N</i> -((5-chloro-6-(5-fluoroisoindolin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
44		<i>N</i> -((5-chloro-6-(5-chlorothiazol-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
45		<i>N</i> -((5-chloro-6-(4-fluoroisoindolin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

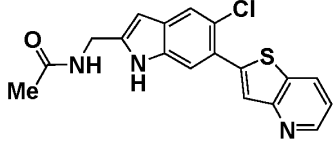
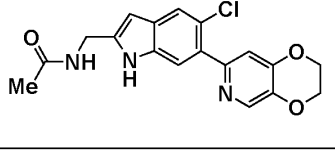
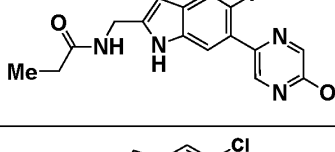
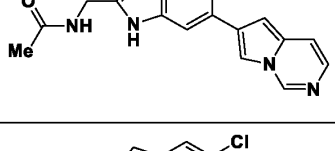
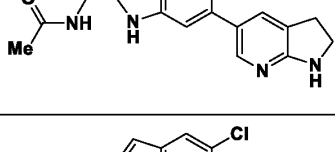
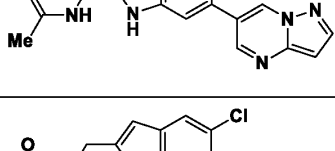
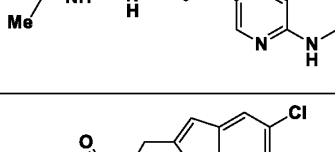
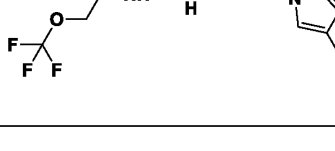
46		<i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide
47		<i>N</i> -((5-chloro-6-(1,3-dihydro-2 <i>H</i> -pyrrolo[3,4- <i>c</i>]pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
48		<i>N</i> -((5-chloro-6-(3-methyl-1 <i>H</i> -pyrazol-1-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
49		<i>N</i> -((5-chloro-6-(imidazo[2,1- <i>b</i>]thiazol-6-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
50		<i>N</i> -((5-chloro-6-(3-cyclopropyl-1 <i>H</i> -pyrazol-1-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
51		<i>N</i> -((5-chloro-6-(5-methoxy-6-methylpyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
52		<i>N</i> -((5-chloro-6-(1-methyl-1 <i>H</i> -benzo[<i>d</i>]imidazol-5-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
53		<i>N</i> -((5'-chloro-1-methyl-1 <i>H</i> ,1' <i>H</i> -[5,6'-biindol]-2'-yl)methyl)acetamide

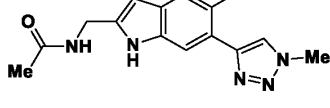
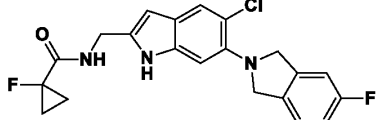
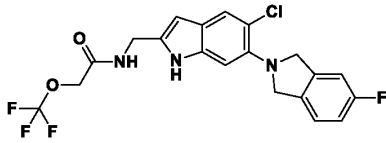
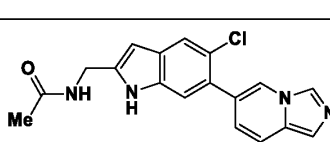
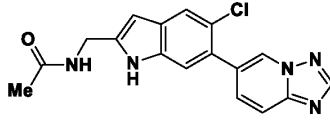
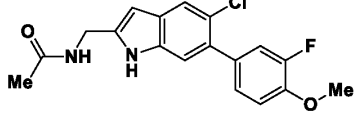
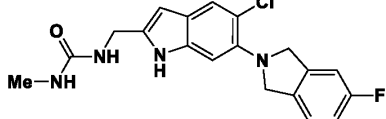
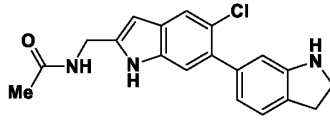
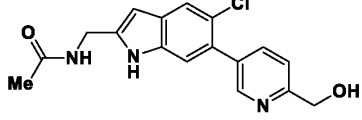
54		<i>N</i> -((5-chloro-6-(2,3-dihydrobenzo[<i>b</i>][1,4]dioxin-6-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
55		<i>N</i> -((5-chloro-6-(2,2-difluorobenzo[<i>d</i>][1,3]dioxol-5-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
56		<i>N</i> -((6-(benzo[<i>d</i>][1,3]dioxol-5-yl)-5-chloro-1 <i>H</i> -indol-2-yl)methyl)acetamide
57		<i>N</i> -((5-chloro-6-(imidazo[1,2- <i>a</i>]pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
58		<i>N</i> -((5-chloro-6-(1-cyclopropyl-1 <i>H</i> -imidazol-4-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
59		<i>N</i> -((5-ethyl-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
60		<i>N</i> -((5-chloro-6-(6-methoxypyrimidin-4-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
61		<i>N</i> -((5-chloro-6-(5-(dimethylamino)pyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

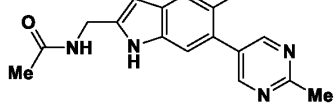
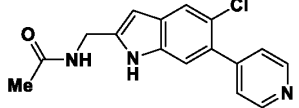
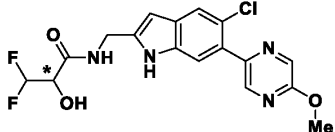
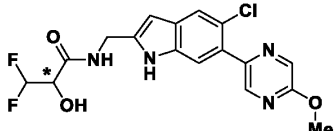
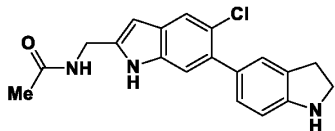
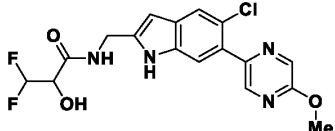
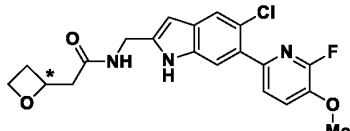
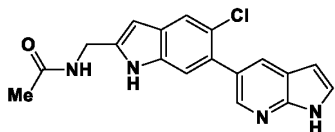
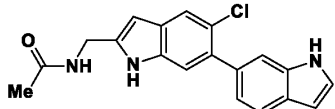
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63		<i>N</i> -((5-chloro-6-(6-(trifluoromethoxy)pyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
64		<i>N</i> -((5-chloro-6-(6-(difluoromethoxy)pyridin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
65		<i>N</i> -((5-chloro-6-(5-(difluoromethoxy)pyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
66		<i>N</i> -((6-(5-methoxypyrazin-2-yl)-5-methyl-1 <i>H</i> -indol-2-yl)methyl)acetamide
67		<i>N</i> -((5-chloro-6-(imidazo[1,2- <i>a</i>]pyrimidin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
68		<i>N</i> -((5-chloro-6-(pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
69		<i>N</i> -((5-chloro-6-(5-methoxypyrimidin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

70		<i>N</i> -((5-chloro-6-(5-(methoxy- <i>d</i> 3)pyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
71		<i>N</i> -((5-chloro-6-(5-cyanopyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
72		<i>N</i> -((5-chloro-6-(5-chloroisindolin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
73		<i>N</i> -((5-chloro-6-(1-oxoisindolin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
74		<i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)propionamide
75		<i>N</i> -((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-1-fluorocyclopropane-1-carboxamide
76		1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)-3-methylurea
77		<i>N</i> -((6-(benzo[<i>b</i>]thiophen-6-yl)-5-chloro-1 <i>H</i> -indol-2-yl)methyl)acetamide
78		<i>N</i> -((5-chloro-7-fluoro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

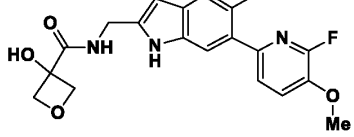
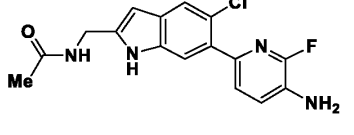
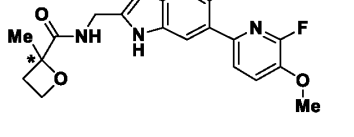
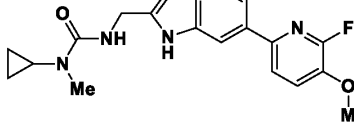
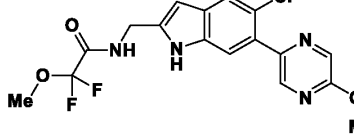
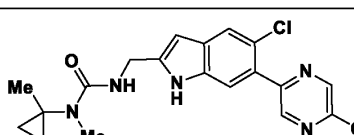
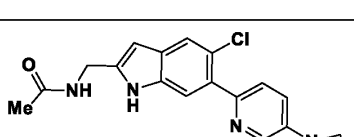
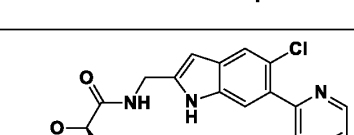
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80		<i>N</i> -((5-chloro-6-(2-methylthiazol-4-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
81		<i>N</i> -((5-chloro-6-(pyridazin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
82		<i>N</i> -((5-chloro-6-(6-methylpyridazin-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
83		<i>N</i> -((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
84		<i>N</i> -((5-chloro-6-(oxazol-4-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
85		<i>N</i> -((5-chloro-6-(isoxazol-3-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
86		<i>N</i> -((5-chloro-6-(5-methyloxazol-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
87		<i>N</i> -((5-chloro-6-(2-methyloxazol-5-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide

88		<i>N</i> -((5-chloro-6-(thieno[3,2- <i>b</i>]pyridin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
89		<i>N</i> -((5-chloro-6-(2,3-dihydro-[1,4]dioxino[2,3- <i>c</i>]pyridin-7-yl)-1 <i>H</i> -indol-2-yl)methyl)acetamide
90		<i>N</i> -((5-fluoro-6-(5-methoxypyrazin-2-yl)-1 <i>H</i> -indol-2-yl)methyl)propionamide
91		<i>N</i> -{[6-(3 <i>a</i> ,5-diaza-2-indenyl)-5-chloro-2-indolyl]methyl}acetamide
92		<i>N</i> -{[5-chloro-6-(1,7-diaza-5-indanyl)-2-indolyl]methyl}acetamide
93		<i>N</i> -{[6-(1,4,7 <i>a</i> -triaza-6-indenyl)-5-chloro-2-indolyl]methyl}acetamide
94		<i>N</i> -({5-chloro-6-[6-(ethylamino)-3-pyridyl]-2-indolyl}methyl)acetamide
95		<i>N</i> -{[5-chloro-6-(2,4-diaza-2 <i>H</i> -inden-2-yl)-2-indolyl]methyl}trifluoromethoxyacetamide

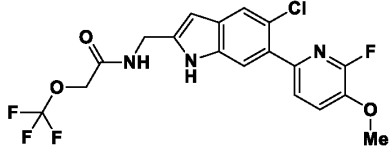
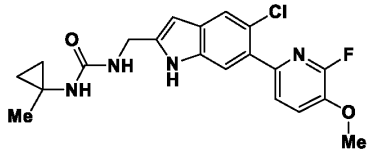
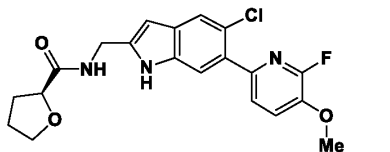
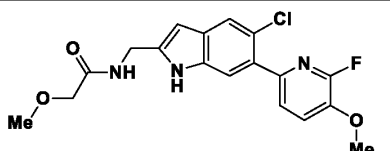
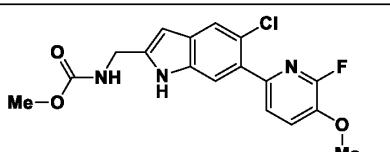
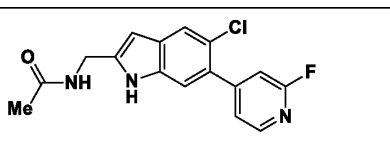
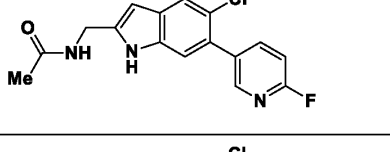
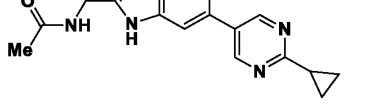
96		N-([5-chloro-6-(1-methyl-1H-1,2,3-triazol-4-yl)-2-indolyl]methyl)acetamide
97		N-([5-chloro-6-(5-fluoro-2-isindoliny)]-2-indolyl]methyl)1-fluorocyclopropanecarboxamide
98		N-([5-chloro-6-(5-fluoro-2-isindoliny)]-2-indolyl]methyl)trifluoromethoxyacetamide
99		N-([6-(2,3a-diaza-5-indenyl)-5-chloro-2-indolyl]methyl)acetamide
100		N-([6-(1,3,3a-triaza-5-indenyl)-5-chloro-2-indolyl]methyl)acetamide
101		N-([5-chloro-6-(3-fluoro-4-methoxyphenyl)-2-indolyl]methyl)acetamide
102		1-([5-chloro-6-(5-fluoro-2-isindoliny)]-2-indolyl]methyl)-3-methylurea
103		N-([5-chloro-6-(6-indoliny)]-2-indolyl]methyl)acetamide
104		N-([5-chloro-6-[6-(hydroxymethyl)-3-pyridyl]-2-indolyl]methyl)acetamide

105		N-([5-chloro-6-(2-methyl-5-pyrimidinyl)-2-indolyl]methyl)acetamide
106		N-([5-chloro-6-(4-pyridyl)-2-indolyl]methyl)acetamide
107		<i>N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3,3-difluorolactamide
108		<i>N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3,3-difluorolactamide
109		N-([5-chloro-6-(5-indolinyl)-2-indolyl]methyl)acetamide
110		<i>N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3,3-difluorolactamide
111		<i>N</i> -([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-2-oxetanylacetamide
112		N-([5-chloro-6-(1,7-diaza-1H-inden-5-yl)-2-indolyl]methyl)acetamide
113		N-[(5-chloro-1H,1'H-6,6'-biindolyl-2-yl)methyl]acetamide

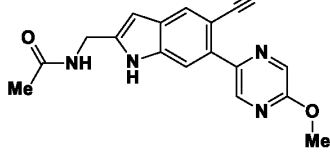
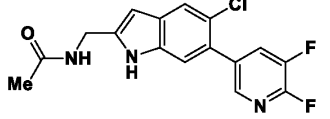
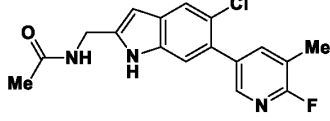
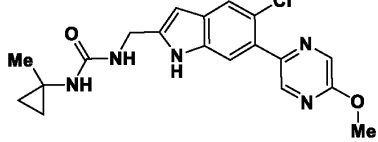
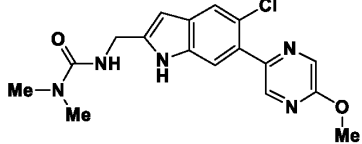
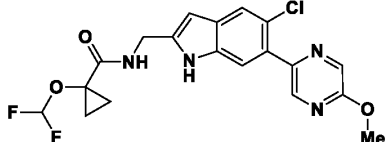
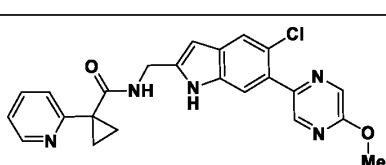
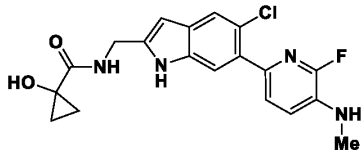
114		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 2-oxetanylacetamide
115		<i>N</i> -{[5-chloro-6-(6-cyano-3-pyridyl)-2-indolyl]methyl}acetamide
116		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}[(<i>R</i> or <i>S</i>)-2-oxetanyl]acetamide
117		<i>N</i> -{[5-chloro-6-(6-ethoxy-3-pyridyl)-2-indolyl]methyl}acetamide
118		<i>Trans-N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 2-methoxycyclopropanecarboxamide
119		<i>Trans-N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(1 <i>R</i> or 1 <i>S</i> , 2 <i>R</i> or 2 <i>S</i>)-2-methoxycyclopropanecarboxamide
120		<i>Trans-N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(1 <i>S</i> or 1 <i>R</i> , 2 <i>S</i> or 2 <i>R</i>)-2-methoxycyclopropanecarboxamide
121		1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}urea

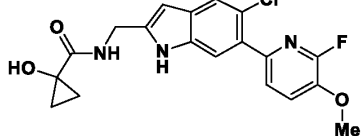
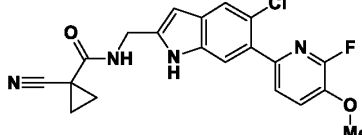
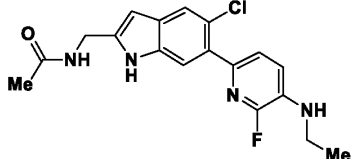
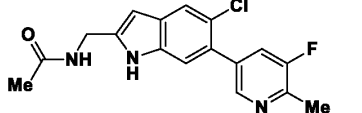
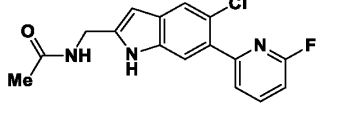
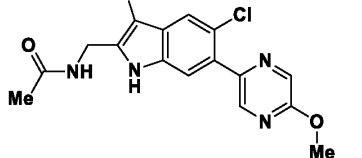
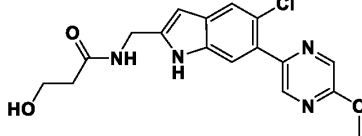
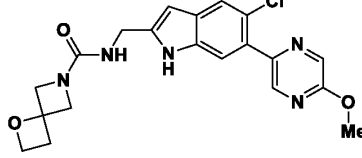
122		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide
123		N-{[6-(5-amino-6-fluoro-2-pyridyl)-5-chloro-2-indolyl]methyl}acetamide
124		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(<i>R</i> or <i>S</i>)-2-methyl-2-oxetanecarboxamide
125		3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea
126		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}difluoromethoxyacetamide
127		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea
128		N-({6-[5-(1-azetidiny)-6-fluoro-2-pyridyl]-5-chloro-2-indolyl}methyl)acetamide
129		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(<i>R</i>)-2-difluoromethoxypropionamide

130		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea
131		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(<i>S</i> or <i>R</i>)-2-methyl-2-oxetanecarboxamide
132		3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea
133		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(<i>S</i>)-2-difluoromethoxypropionamide
134		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-4-morpholinecarboxamide
135		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}3-methoxypropionamide
136		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-(dimethylamino)cyclopropanecarboxamide
137		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-methoxycyclopropanecarboxamide

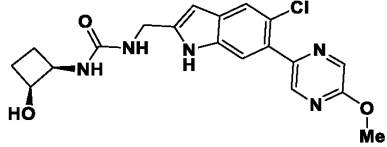
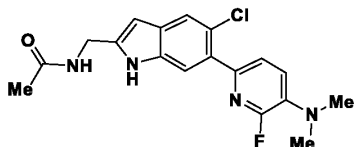
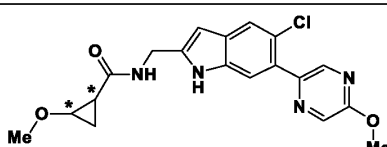
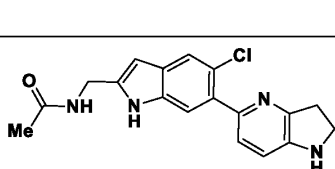
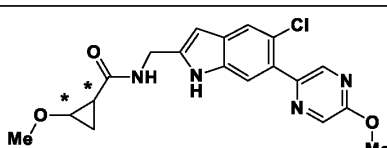
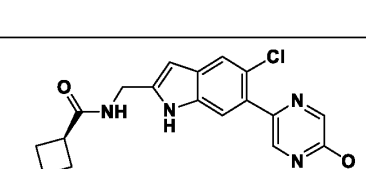
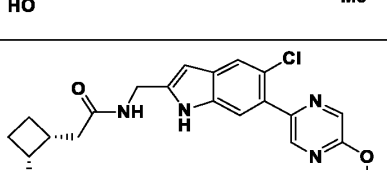
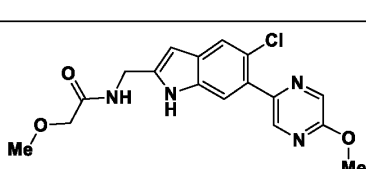
138		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}trifluoromethoxyacetamide
139		3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea
140		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(S)-perhydro-2-furamide
141		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}methoxyacetamide
142		methyl {[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}carbamate
143		N-{[5-chloro-6-(2-fluoro-4-pyridyl)-2-indolyl]methyl}acetamide
144		N-{[5-chloro-6-(6-fluoro-3-pyridyl)-2-indolyl]methyl}acetamide
145		N-{[5-chloro-6-(2-cyclopropyl-5-pyrimidinyl)-2-indolyl]methyl}acetamide

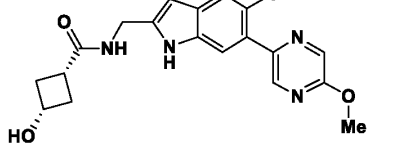
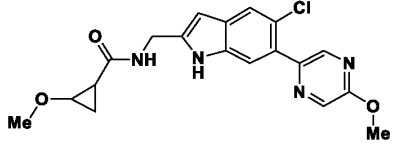
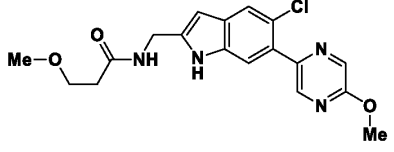
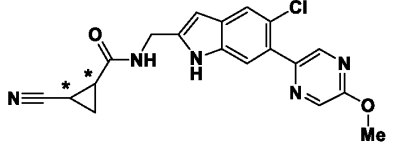
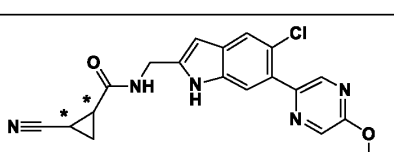
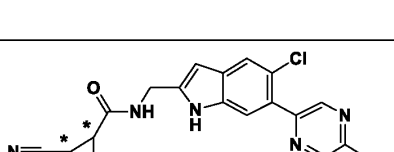
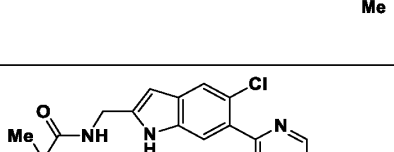
146		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(<i>R</i>)-2-methoxypropionamide
147		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(<i>S</i> or <i>R</i>)-2-methoxybutyramide
148		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(<i>R</i> or <i>S</i>)-2-methoxybutyramide
149		methyl {[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} carbamate
150		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 1-(methylamino)cyclopropanecarboxamide
151		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(<i>R</i> or <i>S</i>)-2-methoxybutyramide
152		<i>N</i> -{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(<i>S</i>)-2-methoxypropionamide
153		3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1,1-dimethylurea

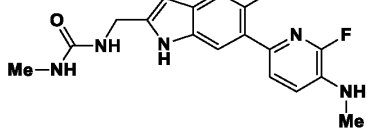
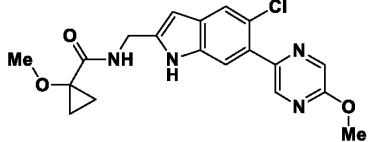
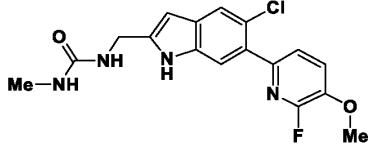
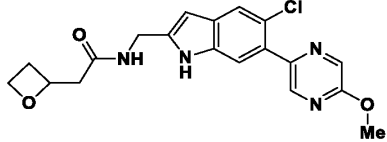
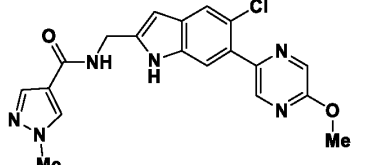
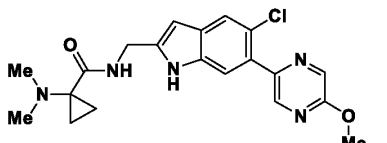
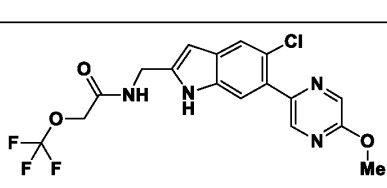
154		N-{[5-cyano-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide
155		N-{[5-chloro-6-(5,6-difluoro-3-pyridyl)-2-indolyl]methyl}acetamide
156		N-{[5-chloro-6-(6-fluoro-5-methyl-3-pyridyl)-2-indolyl]methyl}acetamide
157		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea
158		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,1-dimethylurea
159		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-difluoromethoxycyclopropanecarboxamide
160		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-(2-pyridyl)cyclopropanecarboxamide
161		N-({5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl)1-hydroxycyclopropanecarboxamide

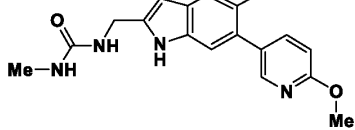
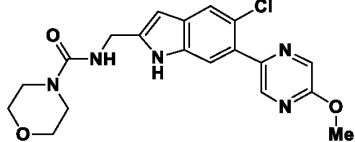
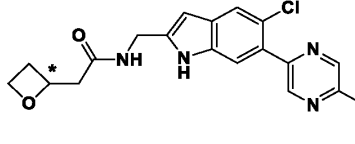
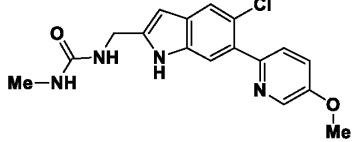
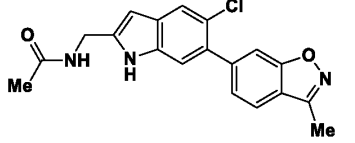
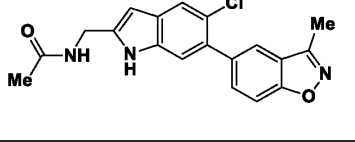
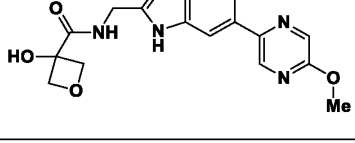
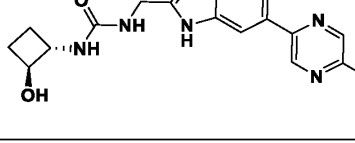
162		N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-1-hydroxycyclopropanecarboxamide
163		N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-1-cyanocyclopropanecarboxamide
164		N-([5-chloro-6-[5-(ethylamino)-6-fluoro-2-pyridyl]-2-indolyl]methyl)acetamide
165		N-([5-chloro-6-(5-fluoro-6-methyl-3-pyridyl)-2-indolyl]methyl)acetamide
166		N-([5-chloro-6-(6-fluoro-2-pyridyl)-2-indolyl]methyl)acetamide
167		N-([3,5-dichloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)acetamide
168		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3-hydroxypropionamide
169		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1-oxa-6-aza-6-spiro[3.3]heptanecarboxamide

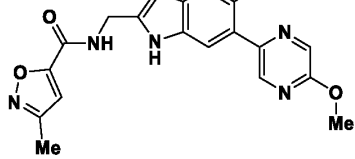
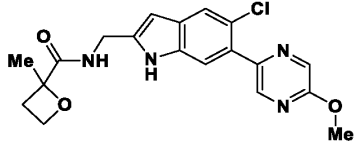
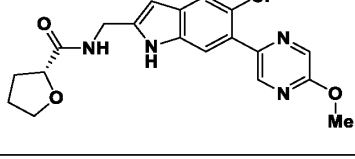
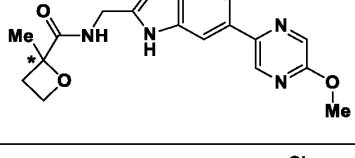
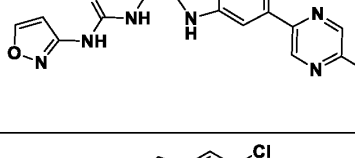
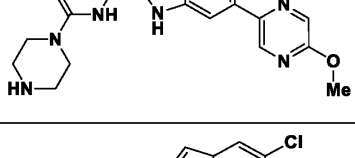
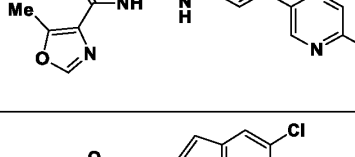
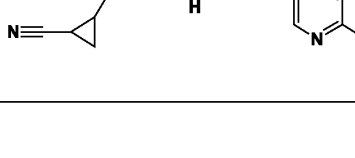
170		N-({5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl) 1-aminocyclopropanecarboxamide
171		N-({5-chloro-6-[6-chloro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl)acetamide
172		N-({5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl)-6-oxa-1-aza-1-spiro[3.3]heptanecarboxamide
173		N-({5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl)-1-azetidinecarboxamide
174		N-({5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl)-2-oxa-6-aza-6-spiro[3.3]heptanecarboxamide
175		N-({6-[5-(1-azetidiny)-2-pyrazinyl]-5-chloro-2-indolyl}methyl)acetamide
176		N-({5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl)-3-hydroxy-1-azetidinecarboxamide
177		N-({5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl)[(R or S)-2-oxetanyl]acetamide

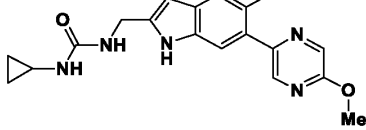
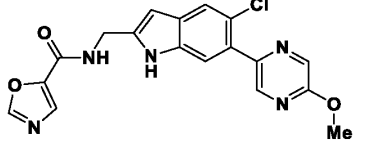
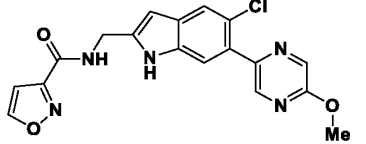
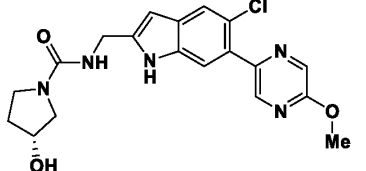
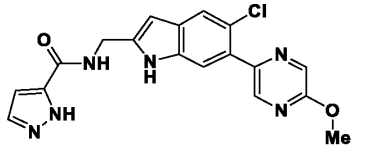
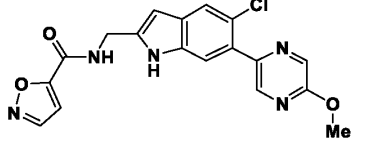
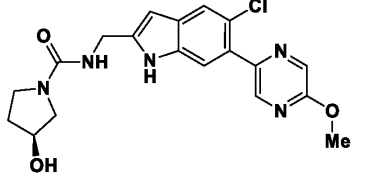
178		(1S,2R)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol
179		N-({5-chloro-6-[5-(dimethylamino)-6-fluoro-2-pyridyl]-2-indolyl}methyl)acetamide
180		<i>Trans</i> -N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1R or 1S,2R or 2S)-2-methoxycyclopropanecarboxamide
181		N-{[5-chloro-6-(1,4-diaza-5-indanyl)-2-indolyl]methyl}acetamide
182		<i>Trans</i> -N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1S or 1R,2S or 2R)-2-methoxycyclopropanecarboxamide
183		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1r,3r)-3-hydroxycyclobutanecarboxamide
184		(1R,2S)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol
185		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}methoxyacetamide

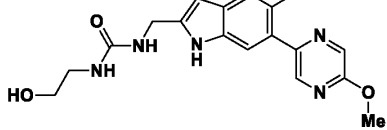
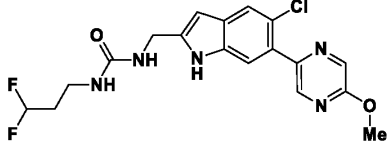
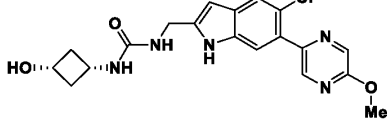
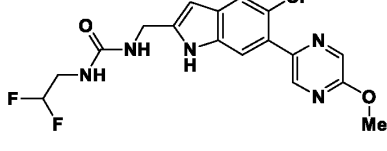
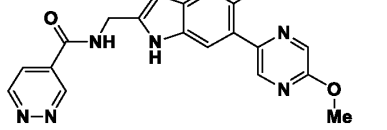
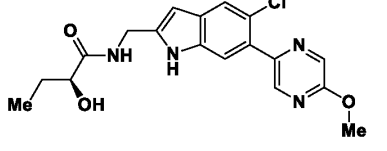
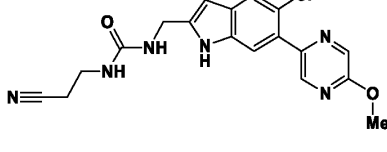
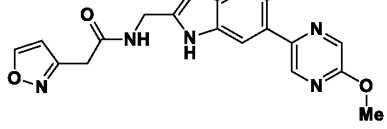
186		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)(1s,3s)-3-hydroxycyclobutanecarboxamide
187		<i>Trans-N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-methoxycyclopropanecarboxamide
188		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3-methoxypropionamide
189		<i>cis-N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-methoxycyclopropanecarboxamide
190		<i>Trans-N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-cyanocyclopropanecarboxamide
191		<i>Trans-N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-cyanocyclopropanecarboxamide
192		<i>N</i> -([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-methyl-2-oxetanecarboxamide

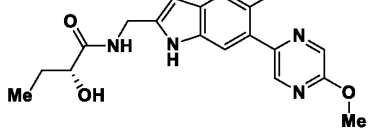
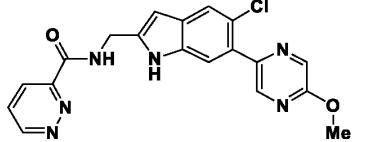
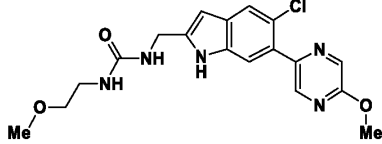
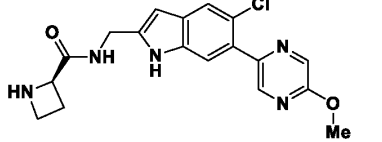
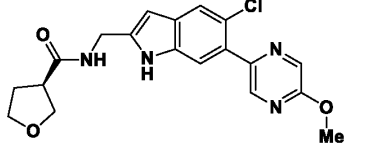
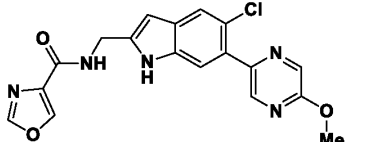
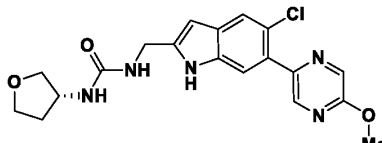
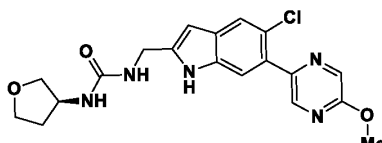
193		6-{5-chloro-2-[(3-methylureido)methyl]-6-indolyl}-2-fluoro-3-(methylamino)pyridine
194		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-methoxycyclopropanecarboxamide
195		1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea
196		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(2-oxetanyl)acetamide
197		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-4-pyrazolecarboxamide
198		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-(dimethylamino)cyclopropanecarboxamide
199		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} trifluoromethoxyacetamide

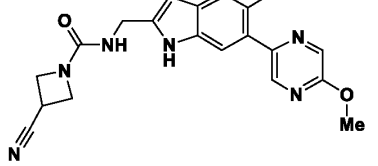
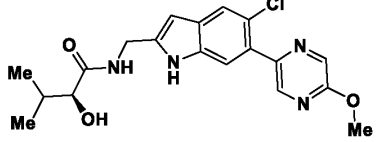
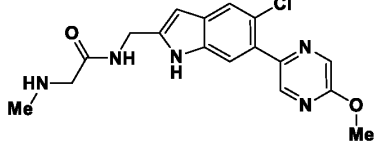
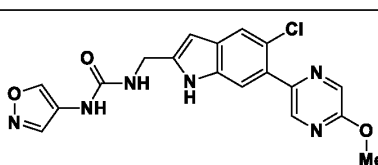
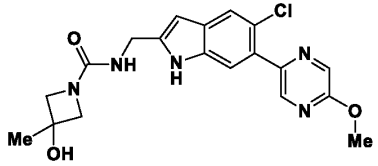
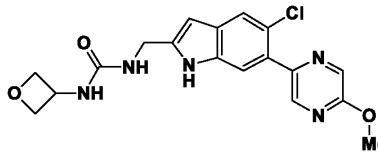
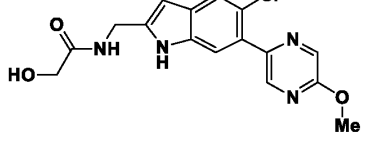
200		1-{[5-chloro-6-(6-methoxy-3-pyridyl)-2-indolyl]methyl}-3-methylurea
201		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-morpholinecarboxamide
202		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}[(S or R)-2-oxetanyl]acetamide
203		1-{[5-chloro-6-(5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea
204		N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-6-yl)-2-indolyl]methyl}acetamide
205		N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-5-yl)-2-indolyl]methyl}acetamide
206		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide
207		(1S,2S)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol

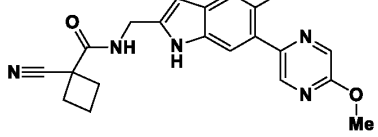
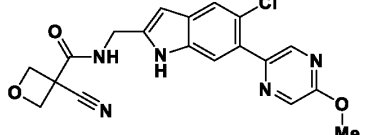
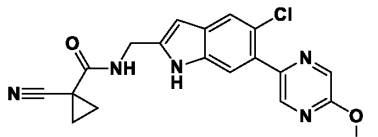
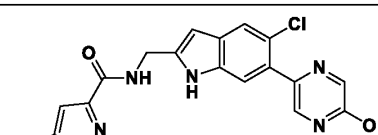
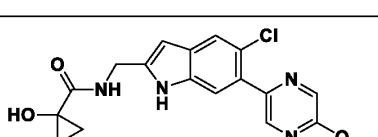
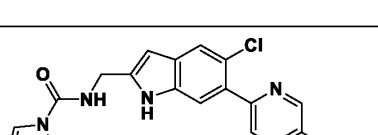
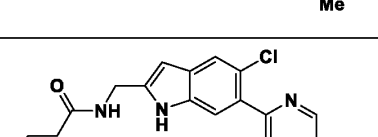
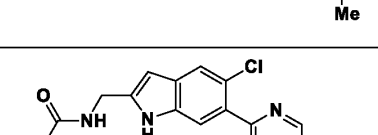
208		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-methyl-5-isoxazolecarboxamide
209		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-methyl-2-oxetanecarboxamide
210		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-perhydro-2-furamide
211		<i>N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(<i>R</i> or <i>S</i>)-2-methyl-2-oxetanecarboxamide
212		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-isoxazolyl)urea
213		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-piperazinecarboxamide
214		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-methyl-1,3-oxazole-4-carboxamide
215		<i>Trans-N</i> -{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(2-cyanocyclopropanecarboxamide

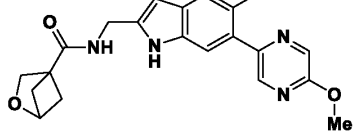
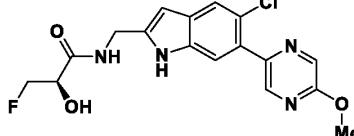
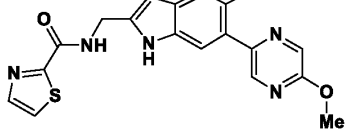
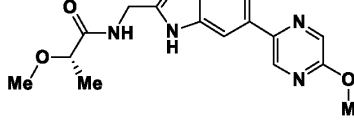
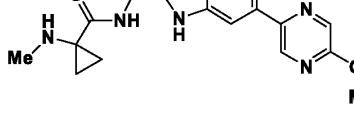
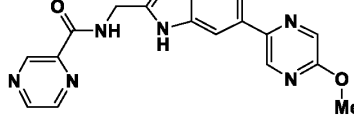
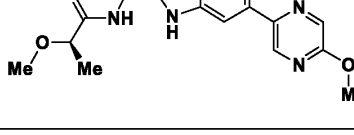
216		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropylurea
217		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-5-carboxamide
218		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-isoxazolecarboxamide
219		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-3-hydroxy-1-pyrrolidinecarboxamide
220		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-pyrazolecarboxamide
221		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-isoxazolecarboxamide
222		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(S)-3-hydroxy-1-pyrrolidinecarboxamide

223		2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)ethanol
224		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3,3-difluoropropyl)urea
225		(1s,3s)-3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol
226		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2,2-difluoroethyl)urea
227		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-pyridinecarboxamide
228		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(S)-2-hydroxybutyramide
229		3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)propiononitrile
230		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(3-isoxazolyl)acetamide

231		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-2-hydroxybutyramide
232		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-pyridinecarboxamide
233		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2-methoxyethyl)urea
234		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-2-azetidinecarboxamide
235		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-perhydro-3-furamide
236		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-4-carboxamide
237		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-[(R)-perhydro-3-furyl]urea
238		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-[(S)-perhydro-3-furyl]urea

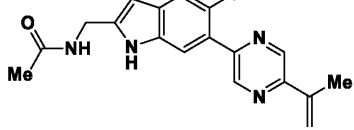
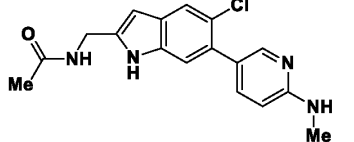
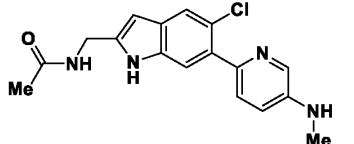
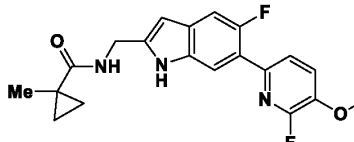
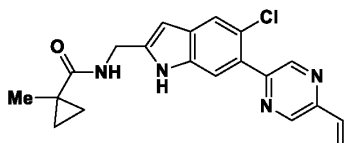
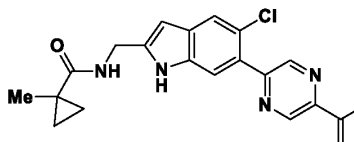
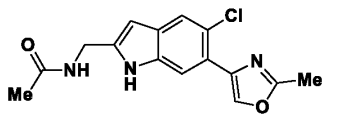
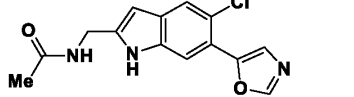
239		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-cyano-1-azetidinecarboxamide
240		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-2-hydroxy-3-methylbutyramide
241		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(methylamino)acetamide
242		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(4-isoxazolyl)urea
243		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-methyl-1-azetidinecarboxamide
244		3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-oxetanyl)urea
245		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}glycolamide

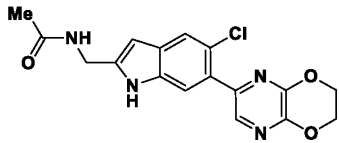
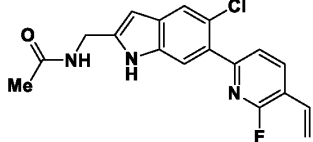
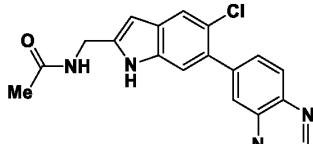
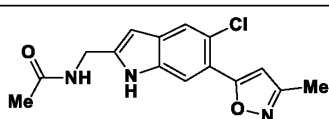
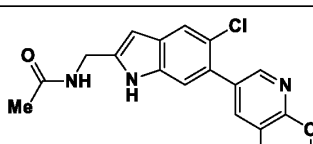
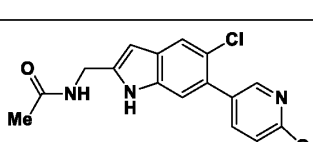
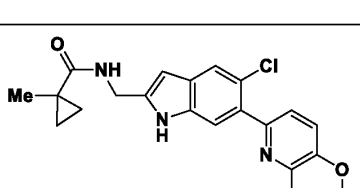
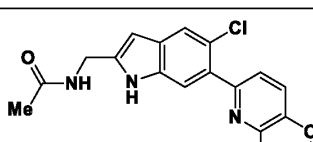
246		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-cyanocyclobutanecarboxamide
247		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 3-cyano-3-oxetanecarboxamide
248		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-cyanocyclopropanecarboxamide
249		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 5-methyl-3-isoxazolecarboxamide
250		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-hydroxycyclopropanecarboxamide
251		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-pyrazolecarboxamide
252		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} (S)-3-fluorolactamide
253		N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 2-oxabicyclo[2.1.1]hexane-1-carboxamide

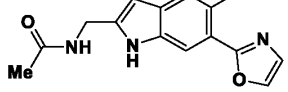
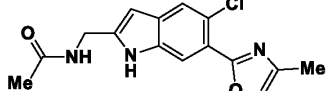
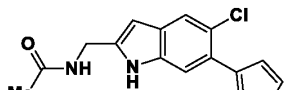
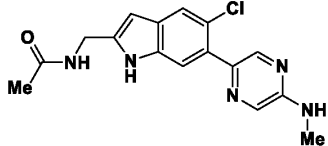
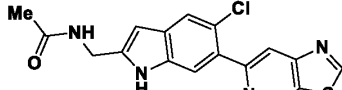
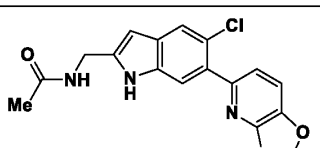
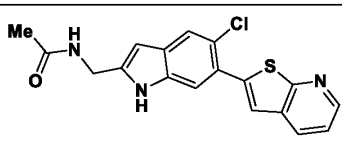
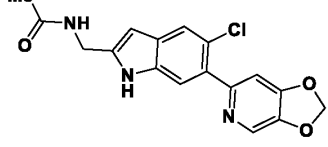
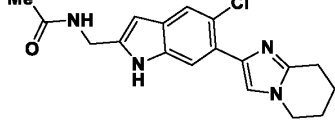
254		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-oxabicyclo[2.1.1]hexane-4-carboxamide
255		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-(R)-3-fluorolactamide
256		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1,3-thiazole-2-carboxamide
257		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-(S)-2-methoxypropionamide
258		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1-(methylamino)cyclopropanecarboxamide
259		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-pyrazinecarboxamide
260		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-(R)-2-methoxypropionamide

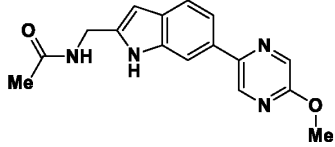
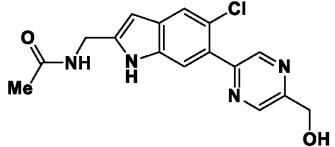
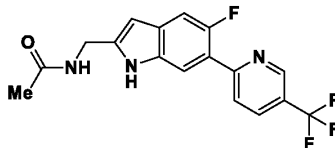
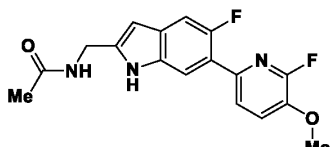
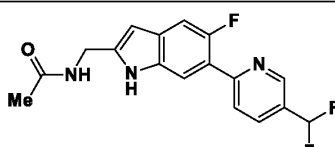
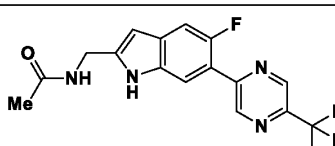
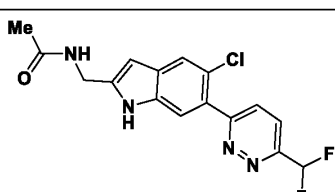
261		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-5-pyrimidinecarboxamide
262		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-4-pyrimidinecarboxamide
263		N-([5-chloro-6-(6-fluoro-5-(methylamino)-2-pyridyl)-2-indolyl]methyl)acetamide
264		1-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)urea
265		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1-methyl-5-pyrazolecarboxamide
266		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)difluoromethoxyacetamide
267		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1-methyl-4-imidazolecarboxamide
268		N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)(3-oxetanyl)acetamide

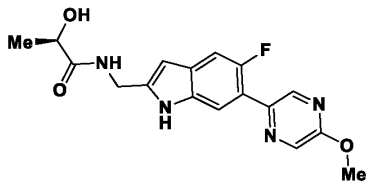
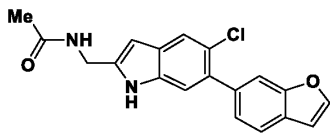
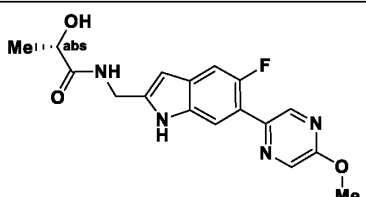
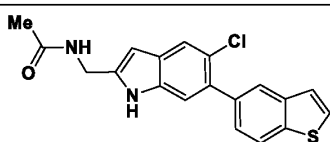
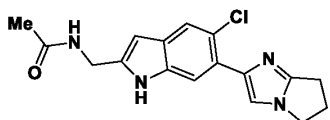
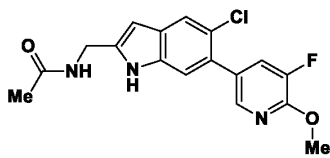
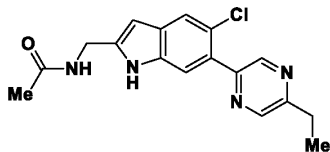
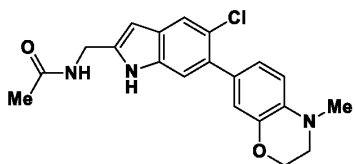
269		N-({5-chloro-6-[6-(methylamino)-3-pyridazinyl]-2-indolyl}methyl)acetamide
270		N-({5-chloro-6-[5-fluoro-6-(methylamino)-3-pyridyl]-2-indolyl}methyl)acetamide
271		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-azetidinecarboxamide
272		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-pyrrolidinecarboxamide
273		N-{[6-(5-acetyl-2-pyrazinyl)-5-chloro-2-indolyl]methyl}acetamide
274		N-{[5-chloro-6-(2,4-diaza-2-indanyl)-2-indolyl]methyl}-1-pyrrolidinecarboxamide
275		N-{[5-chloro-6-(5-methyl-3-isoxazolyl)-2-indolyl]methyl}acetamide
276		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(R)-perhydro-2-furamide

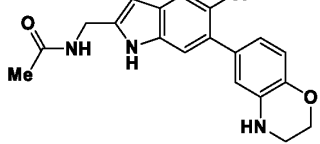
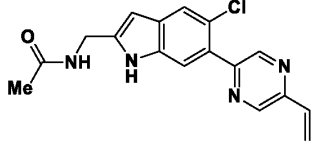
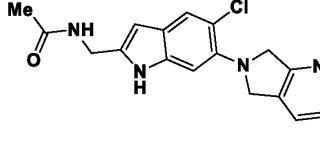
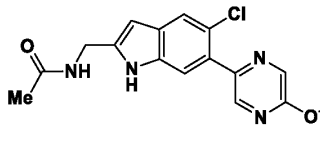
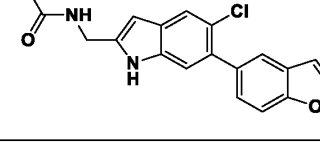
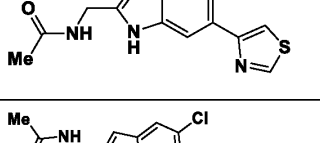
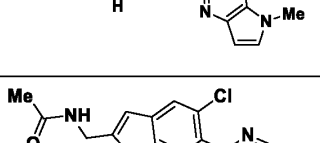
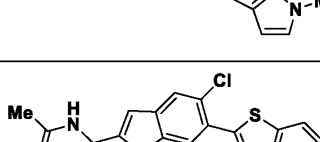
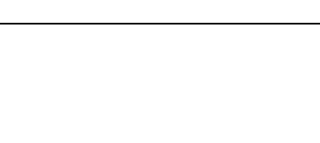
277		N-([5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl]methyl)acetamide
278		N-([5-chloro-6-[6-(methylamino)-3-pyridyl]-2-indolyl]methyl)acetamide
279		N-([5-chloro-6-[5-(methylamino)-2-pyridyl]-2-indolyl]methyl)acetamide
280		N-([5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-1-methylcyclopropanecarboxamide
281		N-([5-chloro-6-(5-vinyl-2-pyrazinyl)-2-indolyl]methyl)-1-methylcyclopropanecarboxamide
282		N-([5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl]methyl)-1-methylcyclopropanecarboxamide
283		N-([5-chloro-6-(2-methyl-1,3-oxazol-4-yl)-2-indolyl]methyl)acetamide
284		N-([5-chloro-6-(1,3-oxazol-5-yl)-2-indolyl]methyl)acetamide

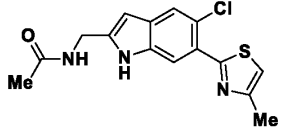
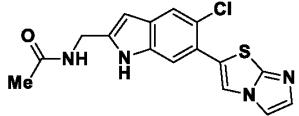
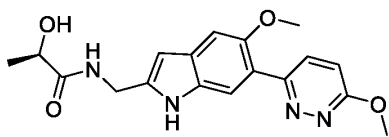
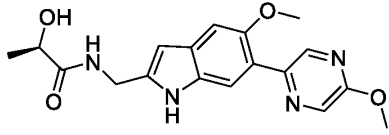
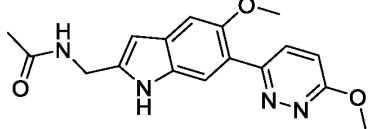
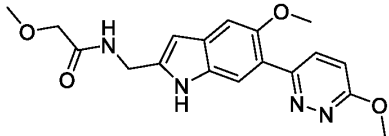
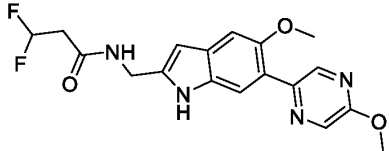
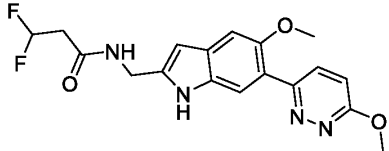
285		N-{[5-chloro-6-(1,4-dioxo-5,8-diaza-2,3-dihydro-6-naphthyl)-2-indolyl]methyl}acetamide
286		N-{[5-chloro-6-(6-fluoro-5-vinyl-2-pyridyl)-2-indolyl]methyl}acetamide
287		N-{[5-chloro-6-(6-quinoxaliny)-2-indolyl]methyl}acetamide
288		N-{[5-chloro-6-(3-methyl-5-isoxazolyl)-2-indolyl]methyl}acetamide
289		N-{[5-chloro-6-(1,4-dioxo-5-aza-2,3-dihydro-7-naphthyl)-2-indolyl]methyl}acetamide
290		N-{[5-chloro-6-(1,3-dioxo-4-aza-6-indanyl)-2-indolyl]methyl}acetamide
291		N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-methylcyclopropanecarboxamide
292		N-{[5-chloro-6-(1,4-dioxo-5-aza-2,3-dihydro-6-naphthyl)-2-indolyl]methyl}acetamide

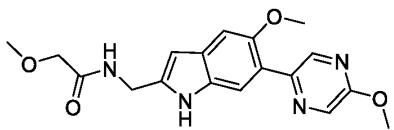
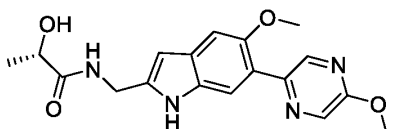
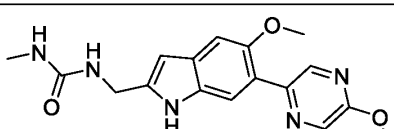
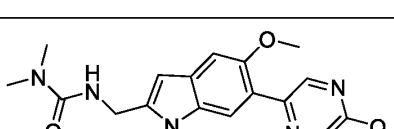
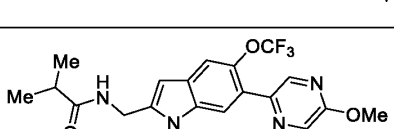
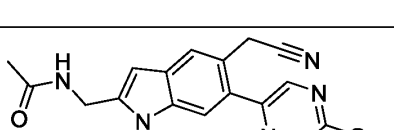
293		N-([5-chloro-6-(1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide
294		N-([5-chloro-6-(4-methyl-1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide
295		N-([5-chloro-6-(3-isothiazolyl)-2-indolyl]methyl)acetamide
296		N-([5-chloro-6-[5-(methylamino)-2-pyrazinyl]-2-indolyl]methyl)acetamide
297		N-([5-chloro-6-(3-thia-1,5-diaza-6-indenyl)-2-indolyl]methyl)acetamide
298		N-([5-chloro-6-(1,3-dioxo-4-aza-5-indanyl)-2-indolyl]methyl)acetamide
299		N-([5-chloro-6-(1-thia-7-aza-2-indenyl)-2-indolyl]methyl)acetamide
300		N-([5-chloro-6-(1,3-dioxo-5-aza-6-indanyl)-2-indolyl]methyl)acetamide
301		N-([6-(1,3a-diaza-4,5,6,7-tetrahydro-2-indenyl)-5-chloro-2-indolyl]methyl)acetamide

302		N-([6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)acetamide
303		N-([5-chloro-6-[5-(hydroxymethyl)-2-pyrazinyl]-2-indolyl]methyl)acetamide
304		N-([5-fluoro-6-[5-(trifluoromethyl)-2-pyridyl]-2-indolyl]methyl)acetamide
305		N-([5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)acetamide
306		N-([6-[5-(difluoromethyl)-2-pyridyl]-5-fluoro-2-indolyl]methyl)acetamide
307		N-([5-fluoro-6-[5-(trifluoromethyl)-2-pyrazinyl]-2-indolyl]methyl)acetamide
308		N-([5-chloro-6-[6-(difluoromethyl)-3-pyridazinyl]-2-indolyl]methyl)acetamide

309		N-{[5-fluoro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-lactamide
310		N-{[6-(1-benzofuran-6-yl)-5-chloro-2-indolyl]methyl}acetamide
311		N-{[5-fluoro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-lactamide
312		N-{[6-(1-benzothiophen-5-yl)-5-chloro-2-indolyl]methyl}acetamide
313		N-{[5-chloro-6-(1,4-diazabicyclo[3.3.0]octa-2,4-dien-3-yl)-2-indolyl]methyl}acetamide
314		N-{[5-chloro-6-(5-fluoro-6-methoxy-3-pyridyl)-2-indolyl]methyl}acetamide
315		N-{[5-chloro-6-(5-ethyl-2-pyrazinyl)-2-indolyl]methyl}acetamide
316		N-{[5-chloro-6-(4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl)-2-indolyl]methyl}acetamide

317		N-{[5-chloro-6-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-2-indolyl]methyl}acetamide
318		N-{[5-chloro-6-(5-vinyl-2-pyrazinyl)-2-indolyl]methyl}acetamide
319		N-{[5-chloro-6-(6-fluoro-2,4-diaza-2-indanyl)-2-indolyl]methyl}acetamide
320		N-{[5-chloro-6-(5-ethoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide
321		N-{[6-(1-benzofuran-5-yl)-5-chloro-2-indolyl]methyl}acetamide
322		N-{[5-chloro-6-(1,3-thiazol-4-yl)-2-indolyl]methyl}acetamide
323		N-{[5-chloro-6-(1-methyl-1,4-diaza-1H-inden-5-yl)-2-indolyl]methyl}acetamide
324		N-{[5-chloro-6-(1-methyl-1,6-diaza-1H-inden-5-yl)-2-indolyl]methyl}acetamide
325		N-{[6-(1,3-benzothiazol-2-yl)-5-chloro-2-indolyl]methyl}acetamide

326		N-{[5-chloro-6-(4-methyl-1,3-thiazol-2-yl)-2-indolyl]methyl}acetamide
327		N-{[5-chloro-6-(4-thia-1,6-diazabicyclo[3.3.0]octa-2,5,7-trien-3-yl)-2-indolyl]methyl}acetamide
328		N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}(R)-lactamide
329		N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-lactamide
330		N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}acetamide
331		N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}methoxyacetamide
332		N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}3,3-difluoropropionamide
333		N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}3,3-difluoropropionamide

334		N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}methoxyacetamide
335		N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-lactamide
336		1-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-methylurea
337		3-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,1-dimethylurea
338		N-{[6-(5-methoxy-2-pyrazinyl)-5-trifluoromethoxy-2-indolyl]methyl}2-methylpropionamide
339		N-{[5-(cyanomethyl)-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide

[0152] In some embodiments, provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from the group consisting of:

N-((5-chloro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;

N-((5-chloro-6-(1H-pyrrolo[3,2-b]pyridin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;

N-((5'-chloro-1H,1'H-[2,6'-biindol]-2'-yl)methyl)-1-methylcyclopropane-1-carboxamide;

N-((5-chloro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(6-methoxypyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2-methoxypyrimidin-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(dimethylamino)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(5-(difluoromethoxy)pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(trifluoromethoxy)pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyrazolo[1,5-a]pyridin-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyrazolo[1,5-a]pyridin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-fluoro-6-(6-methoxypyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-fluoro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-2-hydroxypropanamide;
N-((5-fluoro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)oxetane-3-carboxamide;
N-((5-fluoro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)tetrahydrofuran-2-carboxamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)tetrahydrofuran-3-carboxamide;
N-((5-chloro-6-(5-cyclopropylpyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)oxetane-2-carboxamide;
N-((5-chloro-6-(3-fluoropyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-1H-pyrazol-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5,7-dihydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(isoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-chloro-6-(4-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methylpyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-cyclopropylpyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(5-methoxypyrazin-2-yl)-5-(trifluoromethyl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2-methoxypyridin-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-methoxy-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methylthiazol-2-yl)-1H-indol-2-yl)methyl)acetamide;
5-(2-(acetamidomethyl)-5-chloro-1H-indol-6-yl)pyrazine-2-carboxamide;
N-((5-chloro-6-(imidazo[1,2-a]pyrazin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-fluoroisoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-chlorothiazol-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(4-fluoroisoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(1,3-dihydro-2H-pyrrolo[3,4-c]pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(3-methyl-1H-pyrazol-1-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[2,1-b]thiazol-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(3-cyclopropyl-1H-pyrazol-1-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxy-6-methylpyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-1H-benzo[d]imidazol-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5'-chloro-1-methyl-1H,1'H-[5,6'-biindol]-2'-yl)methyl)acetamide;
N-((5-chloro-6-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(benzo[d][1,3]dioxol-5-yl)-5-chloro-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[1,2-a]pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-cyclopropyl-1H-imidazol-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-ethyl-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-methoxypyrimidin-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(dimethylamino)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-chloro-6-(6-cyclopropoxy)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(trifluoromethoxy)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(difluoromethoxy)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(difluoromethoxy)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(5-methoxypyrazin-2-yl)-5-methyl-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[1,2-a]pyrimidin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrimidin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(methoxy-d3)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-cyanopyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-chloroisindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-oxoisindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)propionamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-1-fluorocyclopropane-1-carboxamide;
1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-3-methylurea;
N-((6-(benzo[b]thiophen-6-yl)-5-chloro-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-7-fluoro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)azetidine-1-carboxamide;
N-((5-chloro-6-(2-methylthiazol-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-methylpyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-{{6-(3a,5-diaza-2-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,7-diaza-5-indanyl)-2-indolyl}methyl}acetamide;
N-{{6-(1,4,7a-triaza-6-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[6-(ethylamino)-3-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(2,4-diaza-2H-inden-2-yl)-2-indolyl}methyl}trifluoromethoxyacetamide;
N-{{5-chloro-6-(1-methyl-1H-1,2,3-triazol-4-yl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-fluoro-2-isindolynyl)-2-indolyl}methyl}trifluoromethoxyacetamide;

N-{[5-chloro-6-(5-fluoro-2-isoindoliny)-2-indolyl]methyl} 1-fluorocyclopropanecarboxamide;
N-{[6-(2,3a-diaza-5-indenyl)-5-chloro-2-indolyl]methyl} acetamide;
N-{[6-(1,3,3a-triaza-5-indenyl)-5-chloro-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(3-fluoro-4-methoxyphenyl)-2-indolyl]methyl} acetamide;
1-{[5-chloro-6-(5-fluoro-2-isoindoliny)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(6-indoliny)-2-indolyl]methyl} acetamide;
N-({5-chloro-6-[6-(hydroxymethyl)-3-pyridyl]-2-indolyl}methyl)acetamide;
N-{[5-chloro-6-(2-methyl-5-pyrimidinyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(4-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(5-indoliny)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 3,3-difluorolactamide;
N-{[5-chloro-6-(1,7-diaza-1H-inden-5-yl)-2-indolyl]methyl} acetamide;
N-[(5-chloro-1H,1'H-6,6'-biindolyl-2-yl)methyl]acetamide;
N-{[5-chloro-6-(6-cyano-3-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(2-oxetanyl)acetamide;
N-{[5-chloro-6-(6-ethoxy-3-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 2-methoxycyclopropanecarboxamide;
1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} urea;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide;
N-{[6-(5-amino-6-fluoro-2-pyridyl)-5-chloro-2-indolyl]methyl} acetamide;
3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} difluoromethoxyacetamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea;
N-({6-[5-(1-azetidiny)-6-fluoro-2-pyridyl]-5-chloro-2-indolyl}methyl)acetamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-2-methyl-2-oxetanecarboxamide;

3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}2-difluoromethoxypropionamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-4-morpholinecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}3-methoxypropionamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-(dimethylamino)cyclopropanecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-methoxycyclopropanecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}trifluoromethoxyacetamide;

3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}methoxyacetamide;

methyl {[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}carbamate;

N-{[5-chloro-6-(2-fluoro-4-pyridyl)-2-indolyl]methyl}acetamide;

N-{[5-chloro-6-(6-fluoro-3-pyridyl)-2-indolyl]methyl}acetamide;

N-{[5-chloro-6-(2-cyclopropyl-5-pyrimidinyl)-2-indolyl]methyl}acetamide;

methyl {[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}carbamate;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}1-(methylamino)cyclopropanecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}2-methoxypropionamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}2-methoxybutyramide;

N-{[5-cyano-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide;

3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1,1-dimethylurea;

N-{[5-chloro-6-(5,6-difluoro-3-pyridyl)-2-indolyl]methyl}acetamide;

N-{[5-chloro-6-(6-fluoro-5-methyl-3-pyridyl)-2-indolyl]methyl}acetamide;

3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea;

3-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-1,1-dimethylurea;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}1-difluoromethoxycyclopropanecarboxamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}1-(2-pyridyl)cyclopropanecarboxamide;
N-{{5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl}1-hydroxycyclopropanecarboxamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}1-hydroxycyclopropanecarboxamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}1-cyanocyclopropanecarboxamide;
N-{{5-chloro-6-[5-(ethylamino)-6-fluoro-2-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-fluoro-6-methyl-3-pyridyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(6-fluoro-2-pyridyl)-2-indolyl}methyl}acetamide;
N-{{3,5-dichloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}3-hydroxypropionamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-1-oxa-6-aza-6-spiro[3.3]heptanecarboxamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}1-aminocyclopropanecarboxamide;
N-{{5-chloro-6-[6-chloro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-6-oxa-1-aza-1-spiro[3.3]heptanecarboxamide;
N-{{5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl}-1-azetidinecarboxamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-2-oxa-6-aza-6-spiro[3.3]heptanecarboxamide;
N-{{6-[5-(1-azetidyl)-2-pyrazinyl]-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-3-hydroxy-1-azetidinecarboxamide;
N-{{5-chloro-6-[5-(dimethylamino)-6-fluoro-2-pyridyl]-2-indolyl}methyl}acetamide;

N-{[5-chloro-6-(1,4-diaza-5-indanyl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}methoxyacetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}3-hydroxycyclobutanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}2-methoxycyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}3-methoxypropionamide;
6-{5-chloro-2-[(3-methylureido)methyl]-6-indolyl}-2-fluoro-3-(methylamino)pyridine;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-methoxycyclopropanecarboxamide;
1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-4-pyrazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-(dimethylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}trifluoromethoxyacetamide;
1-{[5-chloro-6-(6-methoxy-3-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-morpholinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(2-oxetanyl)acetamide;
1-{[5-chloro-6-(5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-5-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-isoxazolecarboxamide;
3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2,2-difluoroethyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-pyridazinecarboxamide;
3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)propiononitrile;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(3-isoxazolyl)acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}2-hydroxybutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-pyridazinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2-methoxyethyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-azetidinecarboxamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-perhydro-3-furamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-4-carboxamide;
1-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-(perhydro-3-furyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-cyano-1-azetidinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-hydroxy-3-methylbutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(methylamino)acetamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(4-isoxazolyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-methyl-1-azetidinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-oxetanyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}glycolamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyanocyclobutanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-cyano-3-oxetanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyanocyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-methyl-3-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-hydroxycyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-pyrazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-oxabicyclo[2.1.1]hexane-1-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-oxabicyclo[2.1.1]hexane-4-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-fluorolactamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-thiazole-2-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(methylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-pyrazinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-methoxypropionamide;

N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-5-pyrimidinecarboxamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-4-pyrimidinecarboxamide;
N-{{5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl}acetamide;
1-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}urea;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-1-methyl-5-pyrazolecarboxamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}difluoromethoxyacetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}(3-oxetanyl)acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-1-methyl-4-imidazolecarboxamide;
N-{{5-chloro-6-[6-(methylamino)-3-pyridazinyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[5-fluoro-6-(methylamino)-3-pyridyl]-2-indolyl}methyl}acetamide;
N-{{6-(5-acetyl-2-pyrazinyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(2,4-diaza-2-indanyl)-2-indolyl}methyl}-1-pyrrolidinecarboxamide;
N-{{5-chloro-6-(5-methyl-3-isoxazolyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}-perhydro-2-furamide;
N-{{5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[6-(methylamino)-3-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[5-(methylamino)-2-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}1-methylcyclopropanecarboxamide;
N-{{5-chloro-6-(5-vinyl-2-pyrazinyl)-2-indolyl}methyl}1-methylcyclopropanecarboxamide;
N-{{5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl}methyl}1-methylcyclopropanecarboxamide;
N-{{5-chloro-6-(2-methyl-1,3-oxazol-4-yl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,3-oxazol-5-yl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,4-dioxa-5,8-diaza-2,3-dihydro-6-naphthyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(6-quinoxaliny)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(6-fluoro-5-vinyl-2-pyridyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,4-dioxa-5-aza-2,3-dihydro-7-naphthyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,3-dioxa-4-aza-6-indanyl)-2-indolyl}methyl}acetamide;

N-({5-chloro-6-[5-(methylamino)-2-pyrazinyl]-2-indolyl}methyl)acetamide;
N-([5-chloro-6-(1,4-dioxo-5-aza-2,3-dihydro-6-naphthyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(4-methyl-1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(3-isothiazolyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(3-thia-1,5-diaza-6-indenyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-dioxo-4-aza-5-indanyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1-thia-7-aza-2-indenyl)-2-indolyl]methyl)acetamide;
N-([6-(1,3a-diaza-4,5,6,7-tetrahydro-2-indenyl)-5-chloro-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-dioxo-5-aza-6-indanyl)-2-indolyl]methyl)acetamide;
N-([6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-({5-chloro-6-[5-(hydroxymethyl)-2-pyrazinyl]-2-indolyl}methyl)acetamide;
N-({5-fluoro-6-[5-(trifluoromethyl)-2-pyridyl]-2-indolyl}methyl)acetamide;
N-([5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)acetamide;
N-({6-[5-(difluoromethyl)-2-pyridyl]-5-fluoro-2-indolyl}methyl)acetamide;
N-({5-fluoro-6-[5-(trifluoromethyl)-2-pyrazinyl]-2-indolyl}methyl)acetamide;
N-({5-chloro-6-[6-(difluoromethyl)-3-pyridazinyl]-2-indolyl}methyl)acetamide;
N-([6-(1-benzofuran-6-yl)-5-chloro-2-indolyl]methyl)acetamide;
N-([5-fluoro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)lactamide;
N-([6-(1-benzothiophen-5-yl)-5-chloro-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,4-diazabicyclo[3.3.0]octa-2,4-dien-3-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-fluoro-6-methoxy-3-pyridyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-ethyl-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-vinyl-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-fluoro-2,4-diaza-2-indanyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-ethoxy-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-([6-(1-benzofuran-5-yl)-5-chloro-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-thiazol-4-yl)-2-indolyl]methyl)acetamide;

N-{[5-chloro-6-(1-methyl-1,4-diaza-1H-inden-5-yl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(1-methyl-1,6-diaza-1H-inden-5-yl)-2-indolyl]methyl}acetamide;
N-{[6-(1,3-benzothiazol-2-yl)-5-chloro-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(4-methyl-1,3-thiazol-2-yl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(4-thia-1,6-diazabicyclo[3.3.0]octa-2,5,7-trien-3-yl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(3-methyl-5-isoxazolyl)-2-indolyl]methyl}acetamide;
2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-perhydro-2-furamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-methyl-2-oxetanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}2-cyanocyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-1-pyrrolidinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3,3-difluoropropyl)urea;
2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)ethanol;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-pyrazolecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-methyl-1,3-oxazole-4-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-piperazinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-isoxazolyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-methyl-5-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide;
N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-5-yl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-6-yl)-2-indolyl]methyl}acetamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-methylcyclopropanecarboxamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-pyrrolidinecarboxamide; and
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-azetidinecarboxamide;
N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}lactamide;
N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}lactamide;
N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}acetamide;
N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}methoxyacetamide;
N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}3,3-difluoropropionamide;
N-{[5-methoxy-6-(6-methoxy-3-pyridazinyl)-2-indolyl]methyl}3,3-difluoropropionamide;
N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}methoxyacetamide;
N-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}lactamide;
1-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-methylurea;
3-{[5-methoxy-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,1-dimethylurea;
N-{[5-chloro-6-(5-cyclopropyl-2-pyridyl)-2-indolyl]methyl}acetamide;
N-{[6-(5-methoxy-2-pyrazinyl)-5-trifluoromethoxy-2-indolyl]methyl}2-methylpropionamide; and
N-{[5-(cyanomethyl)-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide,
or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

[0153] In some embodiments, provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from the group consisting of:

N-((5-chloro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(1H-pyrrolo[3,2-b]pyridin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5'-chloro-1H,1'H-[2,6'-biindol]-2'-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-chloro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(6-methoxypyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2-methoxypyrimidin-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(dimethylamino)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(5-(difluoromethoxy)pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(trifluoromethoxy)pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyrazolo[1,5-a]pyridin-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyrazolo[1,5-a]pyridin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-fluoro-6-(6-methoxypyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-fluoro-6-(5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
(S)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-2-hydroxypropanamide;
N-((5-fluoro-6-(6-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
(R)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-2-hydroxypropanamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)oxetane-3-carboxamide;
N-((5-fluoro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
(S)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)tetrahydrofuran-2-carboxamide;
(S)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)tetrahydrofuran-3-carboxamide;
N-((5-chloro-6-(5-cyclopropylpyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
(S)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)oxetane-2-carboxamide;
(R)-N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)oxetane-2-carboxamide;
N-((5-chloro-6-(3-fluoropyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-1H-pyrazol-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5,7-dihydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-chloro-6-(isoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(4-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methylpyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-cyclopropylpyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(5-methoxypyrazin-2-yl)-5-(trifluoromethyl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2-methoxypyridin-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-methoxy-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methylthiazol-2-yl)-1H-indol-2-yl)methyl)acetamide;
5-(2-(acetamidomethyl)-5-chloro-1H-indol-6-yl)pyrazine-2-carboxamide;
N-((5-chloro-6-(imidazo[1,2-a]pyrazin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-fluoroisoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-chlorothiazol-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(4-fluoroisoindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-1-methylcyclopropane-1-carboxamide;
N-((5-chloro-6-(1,3-dihydro-2H-pyrrolo[3,4-c]pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(3-methyl-1H-pyrazol-1-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[2,1-b]thiazol-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(3-cyclopropyl-1H-pyrazol-1-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxy-6-methylpyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-methyl-1H-benzo[d]imidazol-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5'-chloro-1-methyl-1H,1'H-[5,6'-biindol]-2'-yl)methyl)acetamide;
N-((5-chloro-6-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(benzo[d][1,3]dioxol-5-yl)-5-chloro-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[1,2-a]pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-cyclopropyl-1H-imidazol-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-ethyl-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-methoxypyrimidin-4-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-chloro-6-(5-(dimethylamino)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-cyclopropoxypyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(trifluoromethoxy)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-(difluoromethoxy)pyridin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(difluoromethoxy)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((6-(5-methoxypyrazin-2-yl)-5-methyl-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(imidazo[1,2-a]pyrimidin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrimidin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-(methoxy-d3)pyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-cyanopyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-chloroisindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(1-oxoisindolin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)propionamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-1-fluorocyclopropane-1-carboxamide;
1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-3-methylurea;
N-((6-(benzo[b]thiophen-6-yl)-5-chloro-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-7-fluoro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)azetidine-1-carboxamide;
N-((5-chloro-6-(2-methylthiazol-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(pyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-methylpyridazin-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(oxazol-4-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(isoxazol-3-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(5-methyloxazol-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2-methyloxazol-5-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(thieno[3,2-b]pyridin-2-yl)-1H-indol-2-yl)methyl)acetamide;
N-((5-chloro-6-(2,3-dihydro-[1,4]dioxino[2,3-c]pyridin-7-yl)-1H-indol-2-yl)methyl)acetamide;

N-((5-fluoro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)propionamide;
N-{{6-(3a,5-diaza-2-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(1,7-diaza-5-indanyl)-2-indolyl}methyl}acetamide;
N-{{6-(1,4,7a-triaza-6-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[6-(ethylamino)-3-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(2,4-diaza-2H-inden-2-yl)-2-indolyl}methyl}trifluoromethoxyacetamide;
N-{{5-chloro-6-(1-methyl-1H-1,2,3-triazol-4-yl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-fluoro-2-isoindolyl)-2-indolyl}methyl}1-fluorocyclopropanecarboxamide;
N-{{5-chloro-6-(5-fluoro-2-isoindolyl)-2-indolyl}methyl}trifluoromethoxyacetamide;
N-{{6-(2,3a-diaza-5-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{6-(1,3,3a-triaza-5-indenyl)-5-chloro-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(3-fluoro-4-methoxyphenyl)-2-indolyl}methyl}acetamide;
1-{{5-chloro-6-(5-fluoro-2-isoindolyl)-2-indolyl}methyl}-3-methylurea;
N-{{5-chloro-6-(6-indolyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-[6-(hydroxymethyl)-3-pyridyl]-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(2-methyl-5-pyrimidinyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(4-pyridyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}(S)-3,3-difluorolactamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}(R)-3,3-difluorolactamide;
N-{{5-chloro-6-(5-indolyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl}methyl}-3,3-difluorolactamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}[(S)-2-oxetanyl]acetamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}[(R)-2-oxetanyl]acetamide;
N-{{5-chloro-6-(1,7-diaza-1H-inden-5-yl)-2-indolyl}methyl}acetamide;
N-[(5-chloro-1H,1'H-6,6'-biindolyl-2-yl)methyl]acetamide;
N-{{5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl}methyl}2-oxetanyl]acetamide;
N-{{5-chloro-6-(6-cyano-3-pyridyl)-2-indolyl}methyl}acetamide;
N-{{5-chloro-6-(6-ethoxy-3-pyridyl)-2-indolyl}methyl}acetamide;

Trans-N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 2-methoxycyclopropanecarboxamide;

Trans-N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(1R,2R)-2-methoxycyclopropanecarboxamide;

Trans-N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}(1S,2S)-2-methoxycyclopropanecarboxamide;

1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}urea;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide;

N-{[6-(5-amino-6-fluoro-2-pyridyl)-5-chloro-2-indolyl]methyl}acetamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(R)-2-methyl-2-oxetanecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(S)-2-methyl-2-oxetanecarboxamide;

3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}difluoromethoxyacetamide;

3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea;

N-({6-[5-(1-azetidynyl)-6-fluoro-2-pyridyl]-5-chloro-2-indolyl}methyl)acetamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-2-difluoromethoxypropionamide;

3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropyl-1-methylurea;

3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-methyl-1-(1-methylcyclopropyl)urea;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-2-difluoromethoxypropionamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-4-morpholinecarboxamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}3-methoxypropionamide;

N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 1-(dimethylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 1-methoxycyclopropanecarboxamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} trifluoromethoxyacetamide;
3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-(S)-perhydro-2-furamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} methoxyacetamide;
methyl {[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} carbamate;
N-{[5-chloro-6-(2-fluoro-4-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(6-fluoro-3-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(2-cyclopropyl-5-pyrimidinyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} (R)-2-methoxypropionamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} (S)-2-methoxybutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} (R)-2-methoxybutyramide;
methyl {[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} carbamate;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} 1-(methylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} (R)-2-methoxybutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} (S)-2-methoxybutyramide;
N-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl} (S)-2-methoxypropionamide;
3-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-1,1-dimethylurea;
N-{[5-cyano-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(5,6-difluoro-3-pyridyl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(6-fluoro-5-methyl-3-pyridyl)-2-indolyl]methyl} acetamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(1-methylcyclopropyl)urea;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,1-dimethylurea;

N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)1-difluoromethoxycyclopropanecarboxamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)1-(2-pyridyl)cyclopropanecarboxamide;
N-([5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl]methyl)1-hydroxycyclopropanecarboxamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)1-hydroxycyclopropanecarboxamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)1-cyanocyclopropanecarboxamide;
N-([5-chloro-6-[5-(ethylamino)-6-fluoro-2-pyridyl]-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-fluoro-6-methyl-3-pyridyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-fluoro-2-pyridyl)-2-indolyl]methyl)acetamide;
N-([3,5-dichloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)3-hydroxypropionamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-1-oxa-6-aza-6-spiro[3.3]heptanecarboxamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)1-aminocyclopropanecarboxamide;
N-([5-chloro-6-[6-chloro-5-(methylamino)-2-pyridyl]-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-6-oxa-1-aza-1-spiro[3.3]heptanecarboxamide;
N-([5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl]methyl)-1-azetidinecarboxamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-2-oxa-6-aza-6-spiro[3.3]heptanecarboxamide;
N-([6-[5-(1-azetidyl)-2-pyrazinyl]-5-chloro-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)-3-hydroxy-1-azetidinecarboxamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)[(R)-2-oxetanyl]acetamide;
N-([5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl)[(S)-2-oxetanyl]acetamide;

(1S,2R)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
N-({5-chloro-6-[5-(dimethylamino)-6-fluoro-2-pyridyl]-2-indolyl}methyl)acetamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1R,2R)-2-methoxycyclopropanecarboxamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1S,2S)-2-methoxycyclopropanecarboxamide;
N-{[5-chloro-6-(1,4-diaza-5-indanyl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1r,3r)-3-hydroxycyclobutanecarboxamide;
(1R,2S)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}methoxyacetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1s,3s)-3-hydroxycyclobutanecarboxamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(-2-methoxycyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}3-methoxypropionamide;
cis-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1R,2S)-2-methoxycyclopropanecarboxamide;
cis-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1S,2R)-2-methoxycyclopropanecarboxamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1R,2R)-2-cyanocyclopropanecarboxamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(1S,2S)-2-cyanocyclopropanecarboxamide;
6-{5-chloro-2-[(3-methylureido)methyl]-6-indolyl}-2-fluoro-3-(methylamino)pyridine;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-methoxycyclopropanecarboxamide;
1-{[5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(2-oxetanyl)acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-4-pyrazolecarboxamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-(dimethylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} trifluoromethoxyacetamide;
1-{[5-chloro-6-(6-methoxy-3-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-morpholinecarboxamide;
1-{[5-chloro-6-(5-methoxy-2-pyridyl)-2-indolyl]methyl}-3-methylurea;
N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-6-yl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(3-methyl-1,2-benzisoxazol-5-yl)-2-indolyl]methyl} acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-oxetanecarboxamide;
(1S,2S)-2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-methyl-5-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-methyl-2-oxetanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-perhydro-2-furamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-2-methyl-2-oxetanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(S)-2-methyl-2-oxetanecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-isoxazolyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-piperazinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-methyl-1,3-oxazole-4-carboxamide;
Trans-N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(2-cyanocyclopropanecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-cyclopropylurea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-5-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-3-hydroxy-1-pyrrolidinecarboxamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-pyrazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(S)-3-hydroxy-1-pyrrolidinecarboxamide;
2-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)ethanol;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3,3-difluoropropyl)urea;
(1s,3s)-3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)cyclobutanol;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2,2-difluoroethyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-pyridazinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-2-hydroxybutyramide;
3-(3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}ureido)propiononitrile;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(3-isoxazolyl)acetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-2-hydroxybutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-pyridazinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(2-methoxyethyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-2-azetidinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-(R)-perhydro-3-furamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-oxazole-4-carboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-[(R)-perhydro-3-furyl]urea;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-[(S)-perhydro-3-furyl]urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-cyano-1-azetidinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-2-hydroxy-3-methylbutyramide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(methylamino)acetamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(4-isoxazolyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-hydroxy-3-methyl-1-azetidinecarboxamide;
3-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-(3-oxetanyl)urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}glycolamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}1-cyanocyclobutanecarboxamide;

N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-3-cyano-3-oxetanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-cyanocyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-methyl-3-isoxazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-hydroxycyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-pyrazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-3-fluorolactamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-oxabicyclo[2.1.1]hexane-1-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-oxabicyclo[2.1.1]hexane-4-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-3-fluorolactamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1,3-thiazole-2-carboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(S)-2-methoxypropionamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl} 1-(methylamino)cyclopropanecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-2-pyrazinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-2-methoxypropionamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-5-pyrimidinecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-4-pyrimidinecarboxamide;
N-({5-chloro-6-[6-fluoro-5-(methylamino)-2-pyridyl]-2-indolyl}methyl)acetamide;
1-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}urea;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-5-pyrazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}difluoromethoxyacetamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}-1-methyl-4-imidazolecarboxamide;
N-{[5-chloro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(3-oxetanyl)acetamide;
N-({5-chloro-6-[6-(methylamino)-3-pyridazinyl]-2-indolyl}methyl)acetamide;

N-({5-chloro-6-[5-fluoro-6-(methylamino)-3-pyridyl]-2-indolyl}methyl)acetamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-1-azetidinecarboxamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-1-pyrrolidinecarboxamide;
N-([6-(5-acetyl-2-pyrazinyl)-5-chloro-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(2,4-diaza-2-indanyl)-2-indolyl]methyl)-1-pyrrolidinecarboxamide;
N-([5-chloro-6-(5-methyl-3-isoxazolyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)-(R)-perhydro-2-furamide;
N-([5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl]methyl)acetamide;
N-({5-chloro-6-[6-(methylamino)-3-pyridyl]-2-indolyl}methyl)acetamide;
N-({5-chloro-6-[5-(methylamino)-2-pyridyl]-2-indolyl}methyl)acetamide;
N-([5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)1-methylcyclopropanecarboxamide;
N-([5-chloro-6-(5-vinyl-2-pyrazinyl)-2-indolyl]methyl)1-methylcyclopropanecarboxamide;
N-([5-chloro-6-(5-isopropenyl-2-pyrazinyl)-2-indolyl]methyl)1-methylcyclopropanecarboxamide;
N-([5-chloro-6-(2-methyl-1,3-oxazol-4-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-oxazol-5-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,4-dioxo-5,8-diaza-2,3-dihydro-6-naphthyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-fluoro-5-vinyl-2-pyridyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-quinoxaliny)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(3-methyl-5-isoxazolyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,4-dioxo-5-aza-2,3-dihydro-7-naphthyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-dioxo-4-aza-6-indanyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl)1-methylcyclopropanecarboxamide;
N-([5-chloro-6-(1,4-dioxo-5-aza-2,3-dihydro-6-naphthyl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(4-methyl-1,3-oxazol-2-yl)-2-indolyl]methyl)acetamide;
N-([5-chloro-6-(3-isothiazolyl)-2-indolyl]methyl)acetamide;
N-({5-chloro-6-[5-(methylamino)-2-pyrazinyl]-2-indolyl}methyl)acetamide;

N-{[5-chloro-6-(3-thia-1,5-diaza-6-indenyl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(1,3-dioxo-4-aza-5-indanyl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(1-thia-7-aza-2-indenyl)-2-indolyl]methyl}acetamide;
N-{[5-chloro-6-(1,3-dioxo-5-aza-6-indanyl)-2-indolyl]methyl}acetamide;
N-{[6-(1,3a-diaza-4,5,6,7-tetrahydro-2-indenyl)-5-chloro-2-indolyl]methyl}acetamide;
N-{[6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}acetamide;
N-({5-chloro-6-[5-(hydroxymethyl)-2-pyrazinyl]-2-indolyl}methyl)acetamide;
N-({5-fluoro-6-[5-(trifluoromethyl)-2-pyridyl]-2-indolyl}methyl)acetamide;
N-{[5-fluoro-6-(6-fluoro-5-methoxy-2-pyridyl)-2-indolyl]methyl}acetamide;
N-({6-[5-(difluoromethyl)-2-pyridyl]-5-fluoro-2-indolyl}methyl)acetamide;
N-({5-fluoro-6-[5-(trifluoromethyl)-2-pyrazinyl]-2-indolyl}methyl)acetamide;
N-{[5-chloro-6-(5-cyclopropyl-2-pyridyl)-2-indolyl]methyl}acetamide;
N-({5-chloro-6-[6-(difluoromethyl)-3-pyridazinyl]-2-indolyl}methyl)acetamide; and
N-{[5-fluoro-6-(5-methoxy-2-pyrazinyl)-2-indolyl]methyl}(R)-lactamide;
or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

METHODS OF TREATMENT

[0154] Provided herein is a method of modulating SLC6A19 in a cell, comprising exposing the cell to (i) an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients.

[0155] Provided herein is a method of inhibiting SLC6A19 in a cell, comprising exposing the cell to (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a

pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients. In some embodiments, the individual is a human.

[0156] Provided herein is a method of reducing systemic amino acid levels in an individual in need thereof, comprising administering to the individual (i) an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients. In some embodiments, the amino acid is phenylalanine, tyrosine, glutamine, or glycine. In some embodiments, the systemic phenylalanine, tyrosine, glutamine, or glycine level in the individual is reduced upon treatment. In some embodiments, the phenylalanine, tyrosine, glutamine, or glycine level is reduced at least 10%, at least 20%, at least 30% or at least 50% upon administration of the compound.

[0157] Provided herein is a method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual (i) an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition, comprising an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, or metabolic diseases. In some embodiments, the SLC6A19-mediated disease,

disorder, or condition is phenylketonuria (PKU). In some embodiments, the SLC6A19-mediated disease, disorder, or condition is chronic kidney disease (CKD). In some embodiments, the SLC6A19-mediated disease, disorder, or condition is a metabolic disease. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is metabolic syndrome. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is associated with abnormal levels of amino acids. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase.

[0158] Provided herein is a method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or (ii) a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, or metabolic diseases. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is phenylketonuria (PKU). In some embodiments, the SLC6A19-mediated disease, disorder, or condition is chronic kidney disease (CKD). In some embodiments, the SLC6A19-mediated disease, disorder, or condition is a metabolic disease. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is metabolic syndrome. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is associated with abnormal levels of amino acids. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is associated with

a genetic defect in phenylalanine hydroxylase. In some embodiments, the individual is a human.

[0159] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in modulating SLC6A19 in a cell.

[0160] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in inhibiting SLC6A19 in a cell.

[0161] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof.

[0162] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

[0163] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or

any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in the manufacture of a medicament, for use in modulating SLC6A19 in a cell.

[0164] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in the manufacture of a medicament, for use in inhibiting SLC6A19 in a cell.

[0165] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in the manufacture of a medicament, for use in reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof.

[0166] Provided herein is a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients, for use in treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

[0167] In some embodiments, the compounds provided herein inhibit SLC6A19 at a concentration of less than 10 μM , less than 1 μM , less than 0.5 μM , less than 0.1 μM , less than 0.010 μM , or less than 0.001 μM . In some embodiments, the compounds provided herein inhibit SLC6A19 at a concentration of 1-10 μM , 0.01 to 1 μM , or 0.01 to 10 μM .

[0168] In some embodiments, the compounds have an IC₅₀ of less than 10 nM, less than 10 μM, less than 1 μM, less than 0.5 μM, or less than 0.1 μM. In some embodiments, the compounds provided herein have an IC₅₀ of 1 to 10 nM, 1 to 10 μM, 0.01 to 1 μM, 0.01 to 10 μM, 0.001 to 0.01 μM or 0.001 to 0.010 μM.

[0169] In some embodiments, the individual receiving treatment is a juvenile human or an infant. In some embodiments, the individual is less than 10 years old, less than 9 years old, less than 8 years old, less than 7 years old, less than 6 years old, less than 5 years old, less than 4 years old, less than 3 years old, less than 2 years old, or less than one year old. In some embodiments, the individual is a human.

[0170] In some embodiments, the individual has abnormal levels of amino acids. In some embodiments, the SLC6A19-mediated disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase. In some embodiments, the individual is a human.

[0171] In some embodiments of the foregoing, the administration is oral administration.

KITS

[0172] The present disclosure further provides kits for carrying out the methods disclosed herein. The kits may comprise a compound or pharmaceutically acceptable salt thereof as described herein and suitable packaging. The kits may comprise one or more containers comprising any compound described herein. In one aspect, a kit includes a compound of the disclosure or a pharmaceutically acceptable salt thereof, and a label and/or instructions for use of the compound in the treatment of a disease or disorder described herein. The kits may comprise a unit dosage form of the compound.

[0173] Provided herein are kits, comprising (i) an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof. Also provided herein are kits, comprising (i) a pharmaceutical composition comprising an effective amount of a compound of formula (I) or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients; and (ii) instructions

for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof. In some embodiments, the individual is a human.

[0174] Provided herein are kits, comprising (i) a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof. Also provided herein are kits, comprising (i) a pharmaceutical composition comprising a compound of formula (I), or any variation or embodiment thereof, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and one or more pharmaceutically acceptable excipients; and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof. In some embodiments, the individual is a human.

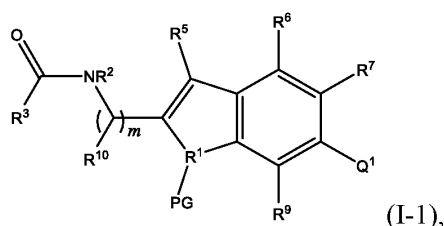
[0175] Articles of manufacture are also provided, wherein the article of manufacture comprises a compound of formula (I) or any variation or embodiment thereof, as described elsewhere herein, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, in a suitable container. Also provided herein are articles of manufacture, comprising a pharmaceutical composition comprising a compound of formula (I) or any variation or embodiment thereof, as described elsewhere herein, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, in a suitable container. The container may be a vial, jar, ampoule, preloaded syringe, or intravenous bag.

METHODS OF PREPARING

[0176] The present disclosure further provides processes for preparing the compounds of present invention. In some aspects, provided herein are processes of preparing a compound of (I), (I-A), (I-A1), (I-A2), (I-A3), (I-A4), (I-A5), (I-A6), (I-B), (I-B1), (I-B2), (I-B3), (I-B4), (I-C), (I-C1), (I-C2), (I-C3), (I-C4), (I-D), (I-D1), (I-E), (I-F), (I-G), or (I-H), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

[0177] In some embodiments, a process for preparing a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (I-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^1 is halo;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^1 is -N-, -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and
the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-;

each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN, and

the C_{1-6} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo;

R^6 and R^9 are each independently H or halo;

R^{10} is H;

R^{3a} and R^{4a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

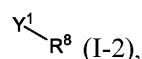
R^{3x} is -OH, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ;

and

R^{3b} and R^{4b} are each independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

with a compound of formula (I-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^1 is a boronic acid or boronic ester;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of

R^8 is optionally substituted with one or more R^{8a} ,

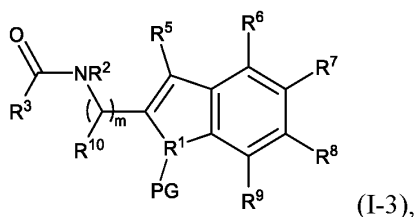
each R^{8a} is independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -

C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b};
and

each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R⁴)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and

the 4-10 membered heteroaryl of R³ is optionally substituted with one or more R^{3x},

provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;

each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a},

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b};

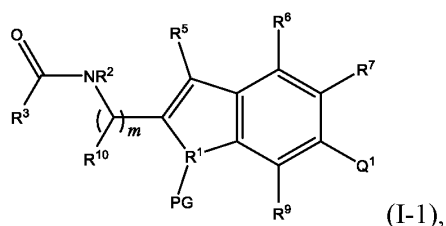
and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

[0178] In some embodiments, a process for preparing a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (I-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^1 is halo;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^1 is -N-, -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, $-N(R^4)_2$, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R^4 is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^{10} is H;

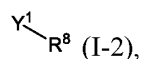
R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; with a compound of formula (I-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^1 is a boronic acid or boronic ester;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

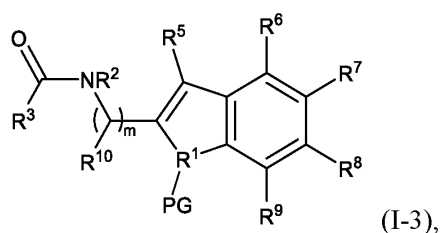
the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ,

each R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a},

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a},

R¹⁰ is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

[0179] In some embodiments, the protecting group is absent.

[0180] In some embodiments, the protecting group is a sulfonyl group. In some embodiments, the protecting group is SO₂Ph. In some embodiments, the protecting group is SO₂Ph(CH₃).

[0181] In some embodiments, the compound of formula (I-1) is an aryl halide, and the compound of formula (I-2) is a boronic ester or a boronic acid. In some embodiments the boronic ester is a pinacol boronate. In some embodiments the reaction is a Suzuki coupling. In some embodiments, the coupling reagent comprises a catalyst. In some embodiments, the catalyst is Pd(dppf)Cl₂·CH₂Cl₂, Pd(PPh₃)₄, chloro[(di(1-adamantyl)-N-butylphosphine)-2-(2-aminobiphenyl)]palladium(II), or [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane.

[0182] In some embodiments, the coupling reagent further comprises a base. In some embodiments, the base is potassium carbonate, cesium carbonate, or sodium carbonate.

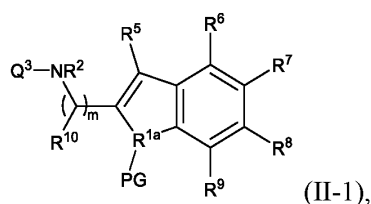
[0183] In some embodiments, the coupling reagent comprises one or more reagents selected from the group consisting of a palladium catalyst, a phosphine ligand, and a base.

[0184] In some embodiments, the deprotecting agent comprises an acid. In some embodiments the acid is HCl, TFA, or barbituric acid.

[0185] In some embodiments, the deprotecting agent comprises a base. In some embodiments the base is potassium carbonate.

[0186] In some embodiments, a process for preparing a compound of formula (I) or (I'), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (II-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^3 is H;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^{1a} is -N-, -NH-, -O-, or -S-;

R^2 is H;

each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O-

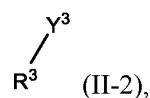
C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O-

C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ;

R^{4b} , and R^{8b} are each independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

with a compound of formula (II-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^3 is -C(O)OH, or -C(O)-halo;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, -N(R^4)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered

heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and

the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -N- or -NH-; and

each R^{3a} is independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -

NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -

C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl,

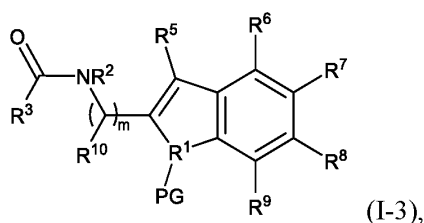
or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O-

C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ;

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ; and each R^{3b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R^4)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and

the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-;

each R^4 is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b};

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

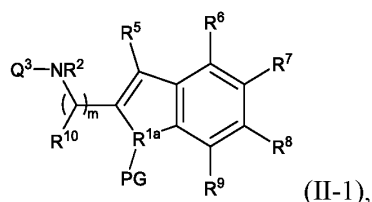
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}, and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

[0187] In some embodiments, a process for preparing a compound of formula (I) or (I'), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (II-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^3 is H;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^{1a} is -N-, -NH-, -O-, or -S-;

R^2 is H;

each R^4 is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

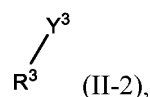
R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{4b} , and R^{8b} are each independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

with a compound of formula (II-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^3 is -C(O)OH, or -C(O)-halo;

R^3 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, -N(R^4)₂, or 4-10 membered heterocyclyl, wherein

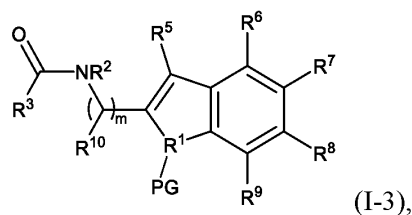
the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and

each R^{3a} is independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

each R^{3b} is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

[0188] In some embodiments, the protecting group is absent.

[0189] In some embodiments, the protecting group is a sulfonyl group. In some embodiments, the protecting group is SO₂Ph. In some embodiments, the protecting group is SO₂Ph(CH₃).

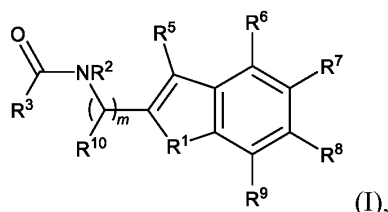
[0190] In some embodiments, the deprotecting agent comprises an acid. In some embodiments the acid is HCl, TFA, or barbituric acid.

[0191] In some embodiments, the deprotecting agent comprises a base. In some embodiments the base is potassium carbonate

[0192] In some embodiments, the compound of formula (II-1) is an amine, and the compound of formula (II-2) is a carboxylic acid. In some embodiments, the coupling reagent comprises HATU. In some embodiments, the coupling reagent further comprises a base. In some embodiments, the base is a tertiary amine. In some embodiments the base is DIEA. In some embodiments, the coupling reagent comprises EDCI, HOBt and a tertiary amine base such as DIEA or N-methylimidazole. In some embodiments, the coupling reagent comprises chloro-N,N,N',N'-tetramethylformamidinium hexafluorophosphate and N-methylimidazole.

ENUMERATED EMBODIMENTS

[0193] Embodiment 1. A compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R^4)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R^4 is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

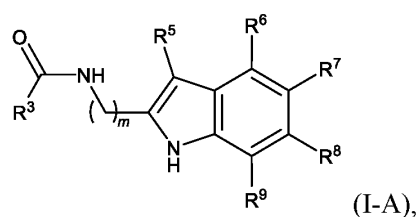
the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

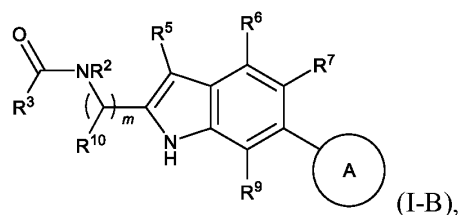
R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy.

[0194] Embodiment 2. The compound of Embodiment 1, wherein the compound is a compound of formula (I-A):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

[0195] Embodiment 3. The compound of Embodiment 1 or 2, wherein the compound is a compound of formula (I-B):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein: ring A is 5-10 membered heteroaryl or 5-10 membered heterocyclyl,

wherein the 5-10 membered heteroaryl or 5-10 membered heterocyclyl are each optionally substituted with one or more R^a .

[0196] Embodiment 4. The compound of any of Embodiments 1-3, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m is an integer from 1-2.

[0197] Embodiment 5. The compound of any of Embodiments 1-4, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein m is 1.

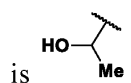
[0198] Embodiment 6. The compound of any of Embodiments 1-5, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, $-N(R^4)_2$, or 4-6 membered heterocyclyl, wherein each R^3 is optionally substituted with one or more R^{3a} .

[0199] Embodiment 7. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{1-3} alkyl.

[0200] Embodiment 8. The compound of any of Embodiments 1-7, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is methyl.

[0201] Embodiment 9. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{1-3} alkyl, optionally substituted with one or more R^{3a} .

[0202] Embodiment 10. The compound of any of Embodiments 1-6, or 9, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3



[0203] Embodiment 11. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} .

[0204] Embodiment 12. The compound of any of Embodiments 1-6, or 11, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{3-6} cycloalkyl optionally substituted with one or more halo or C_{1-3} alkyl.

[0205] Embodiment 13. The compound of any of Embodiments 1-6, or 11-12, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the

foregoing, wherein R^3 is selected from the group consisting of  and .

[0206] Embodiment 14. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is $-N(R^4)_2$, wherein each R^4 is independently H, or C_{1-3} alkyl.

[0207] Embodiment 15. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is 4-6 membered heterocyclyl, optionally substituted with one or more R^{3a} .

[0208] Embodiment 16. The compound of any of Embodiments 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is $-N(R^4)_2$, wherein both R^4 are taken together with the N atom to which they are attached to form a 4-6 membered heterocyclyl optionally substituted with one or more R^{3a} .

[0209] Embodiment 17. The compound of any of Embodiments 1-6, or 16, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3

is .

[0210] Embodiment 18. The compound of any of Embodiments 1-6 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is 4-6 membered heterocyclyl optionally substituted with one or more R^{3a} .

[0211] Embodiment 19. The compound of any of Embodiments 1-6, or 18, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3

is selected from the group consisting of , , and .

[0212] Embodiment 20. The compound of any of Embodiments 1-19, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^5 and R^7 are each independently H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl or C_{1-3} haloalkyl, wherein the C_{1-3} alkyl of R^5 and R^7 are each independently optionally substituted with one or more halo, or CN.

[0213] Embodiment 21. The compound of any of Embodiments 1-20, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^5 and R^7 are each independently H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl.

[0214] Embodiment 22. The compound of any of Embodiments 1-21, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^5 and R^7 are each independently H.

[0215] Embodiment 23. The compound of any of Embodiments 1-21, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein one of R^5 and R^7 is H, and the other of R^5 and R^7 is independently halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl.

[0216] Embodiment 24. The compound of any of Embodiments 1-23, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^6 and R^9 are each independently H, or halo.

[0217] Embodiment 25. The compound of any of Embodiments 1-24, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^6 and R^9 are each independently H, F, or Cl.

[0218] Embodiment 26. The compound of any of Embodiments 1-25, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^6 and R^9 are each independently H.

[0219] Embodiment 27. The compound of any of Embodiments 1-25, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein one of R^6 and R^9 is H, and the other of R^6 and R^9 is F, or Cl.

[0220] Embodiment 28. The compound of any of Embodiments 1-27, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} .

[0221] Embodiment 29. The compound of any of Embodiments 1-28, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is

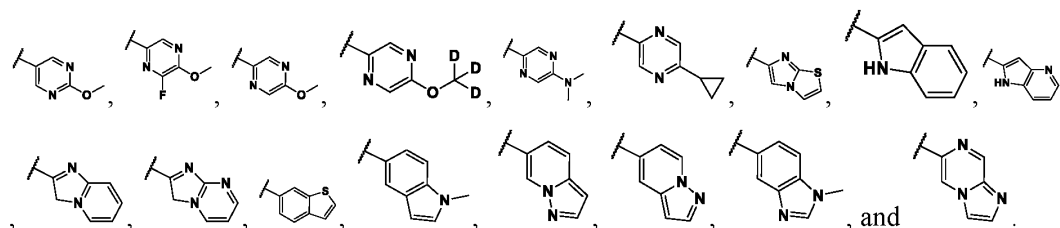
selected from the group consisting of , , , , , , , , and .

[0222] Embodiment 30. The compound of any of Embodiments 1-27, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R⁸ is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a}.

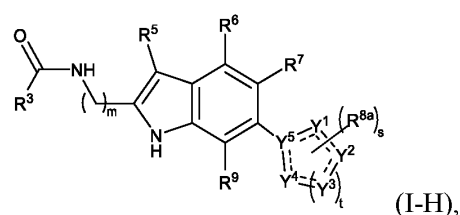
[0223] Embodiment 31. The compound of any of Embodiments 1-27, or 30, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R⁸ is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a}, wherein each R^{8a} is independently -CN, halo, C₁₋₃alkyl, C₁₋₃alkoxy, -C(O)NH₂, or C₃₋₆cycloalkyl, wherein the C₁₋₆alkoxy, of R^{8a} is optionally substituted with one or more R^{8b}, and each R^{8b} is independently D, or halo.

[0224] Embodiment 32. The compound of any of Embodiments 1-27, or 30-31, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the

[illegible]

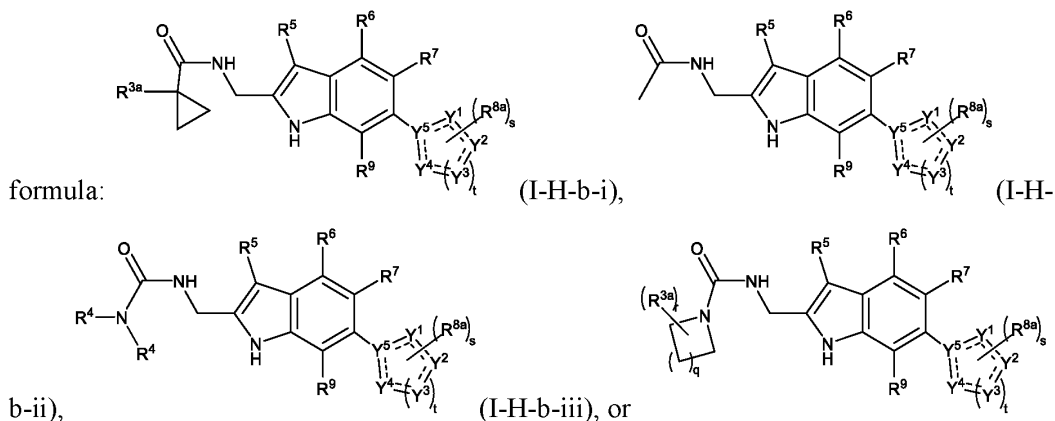


[0225] Embodiment 33. The compound of any of Embodiments 1-27, or 30-32, wherein the compound is of formula (I-H):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein s is an integer from 0-6; t is 1 or 2; and ----- represents a single or double bond.

[0226] Embodiment 34. The compound of Embodiment 33, wherein the compound is of

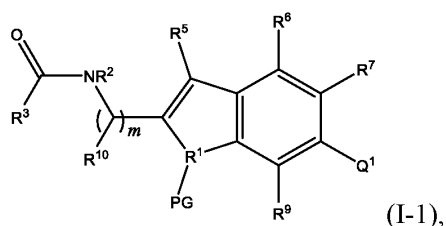


(I-H-b-iv), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

[0227] Embodiment 35. The compound of Embodiment 1, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from Compounds 1-83 of Table 1.

[0228] Embodiment 36. A process for preparing a compound of formula (I), as defined in any of Embodiments 1-35 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (I-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^1 is halo;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^1 is -N-, -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, $-N(R^4)_2$, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R^4 is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} , or

both R^4 are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^{10} is H;

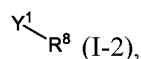
R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; with a compound of formula (I-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^1 is a boronic acid or boronic ester;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

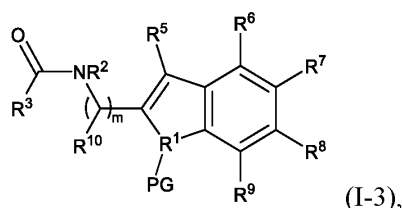
the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ,

each R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R¹ is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

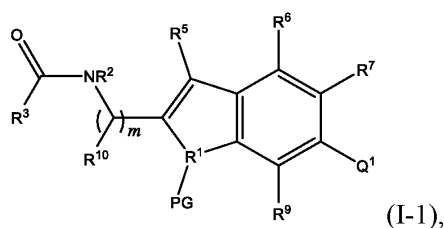
R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

[0229] Embodiment 37. The process of Embodiment 35, wherein the coupling reagent comprises a palladium catalyst, a phosphine ligand, and/or base.

[0230] Embodiment 38. A process for preparing a compound of formula (I), as defined in any of Embodiments 1-35 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (I-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

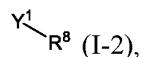
Q^1 is halo;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^1 is -N-, -NH-, -O-, or -S-;

R^2 is H;
 R^3 is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R⁴)₂, or 4-10 membered heterocyclyl,
 wherein
 the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is
 optionally substituted with one or more R^{3a};
 each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein
 the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or
 more R^{4a}, or
 both R⁴ are taken together with the N atom to which they are attached to form a 4-10
 membered heterocyclyl optionally substituted with one or more R^{4a};
 R^5 and R^7 are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or
 C₁₋₆haloalkyl, wherein
 the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -
 CN;
 R^6 and R^9 are each independently H or halo;
 R^{10} is H;
 R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆
 haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆
 alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀
 cycloalkyl, wherein
 the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl
 of R^{3a} is optionally substituted with one or more R^{3b};
 the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl
 of R^{4a} is optionally substituted with one or more R^{4b}, and
 the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl
 of R^{8a} is optionally substituted with one or more R^{8b}, and
 R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;
 with a compound of formula (I-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^1 is a boronic acid or boronic ester;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

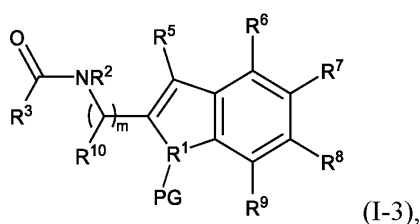
the C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ,

each R^{8a} is independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O- C_{1-6} haloalkyl, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ; and

each R^{8b} is independently D, -OH, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, -N(R^4)₂, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} ;

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein
the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally
substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10
membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or
C₁₋₆haloalkyl, wherein
the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally
substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered
heteroaryl, wherein
the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10
membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;
followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent;
to provide a compound of formula (I).

[0231] Embodiment 39. The process of any of Embodiments 36-38, wherein the protecting group is a sulfonyl group.

[0232] Embodiment 40. The process of any of Embodiments 36-39, wherein the deprotecting agent comprises a base.

[0233] Embodiment 41. A pharmaceutical composition comprising (i) a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and (ii) one or more pharmaceutically acceptable excipients.

[0234] Embodiment 42. A method of modulating SLC6A19 in a cell, comprising exposing the cell to a composition comprising a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of Embodiment 41.

[0235] Embodiment 43. A method of inhibiting SLC6A19 in a cell, comprising exposing the cell to a composition comprising a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of Embodiment 41.

[0236] Embodiment 44. A method of reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof, comprising administering to the individual a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of Embodiment 41.

[0237] Embodiment 45. A method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of Embodiment 41.

[0238] Embodiment 46. The method of Embodiment 45, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders.

[0239] Embodiment 47. The method of Embodiment 45 or 46, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, and metabolic diseases.

[0240] Embodiment 48. The method of Embodiment 45, wherein the disease, disorder, or condition is associated with abnormal levels of amino acids.

[0241] Embodiment 49. The method of Embodiment 45 or 46, wherein the disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase.

[0242] Embodiment 50. The method of any of Embodiments 45-49, wherein the individual is human.

[0243] Embodiment 51. The method of any one of Embodiments 45-50 wherein a therapeutically effective amount of the compound is administered.

[0244] Embodiment 52. A kit, comprising (i) a compound of any of Embodiments 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of Embodiment 41, and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

[0245] Embodiment 53. The kit of Embodiment 52, wherein the disease, disorder, or condition is associated with abnormal levels of amino acids.

[0246] Embodiment 54. The kit of Embodiment 52 or 53, wherein the disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase.

[0247] Embodiment 55. The kit of Embodiment 52 or 53, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders.

[0248] Embodiment 56. The kit of Embodiment any of Embodiments 52-55, wherein the individual has a genetic defect in phenylalanine hydroxylase.

EXAMPLES

[0252] The following synthetic reaction schemes, which are detailed in the Schemes and Examples, are merely illustrative of some of the methods by which the compounds of the present disclosure, or an embodiment or aspect thereof, can be synthesized. Various modifications to these synthetic reaction schemes can be made, as will be apparent to those of ordinary skill in the art.

[0253] The starting materials and the intermediates of the synthetic reaction schemes can be isolated and purified if desired using conventional techniques, including, but not limited to, filtration, distillation, crystallization, chromatography, and the like. Such materials can be characterized using conventional means, including physical constants and spectral data.

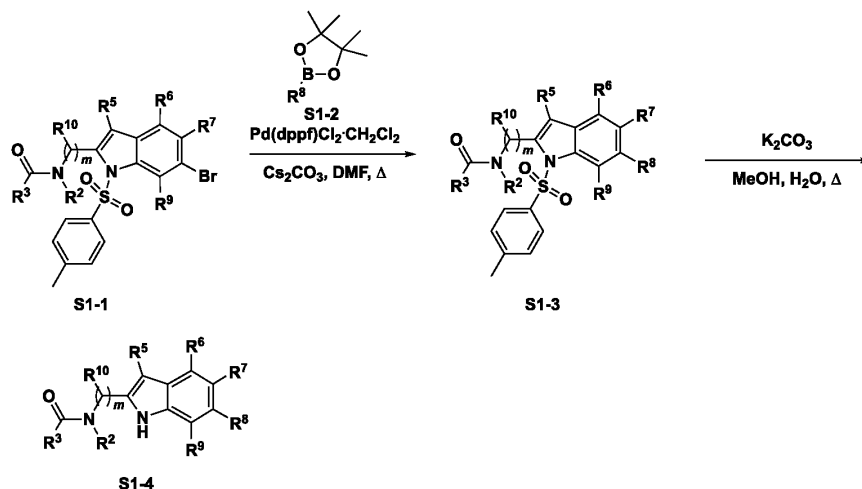
[0254] Although certain exemplary embodiments are depicted and described herein, the compounds of the present disclosure, or any variation or embodiment thereof, may be prepared using appropriate starting materials according to the methods described generally herein and/or by methods available to one of ordinary skill in the art.

Synthetic Examples

[0255] As depicted in the Schemes and Examples below, in certain exemplary embodiments, compounds of formula (I), or any variation or embodiment thereof, as described elsewhere herein, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, are prepared according to the general procedures. The general methods below, and other methods known to synthetic chemists of ordinary skill in the art, can be applied to all formulae, variations, embodiments, and species described herein.

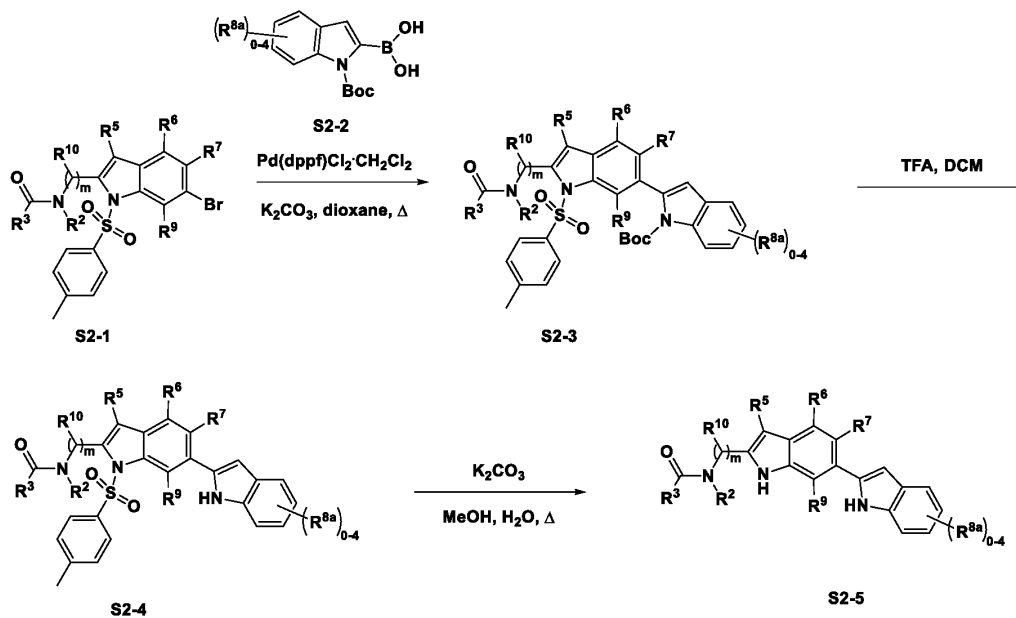
[0256] In some embodiments, provided herein is a process for preparing a compound of formula (I), or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing according to any of Scheme 1-Scheme 8.

*Schemes***Scheme 1**

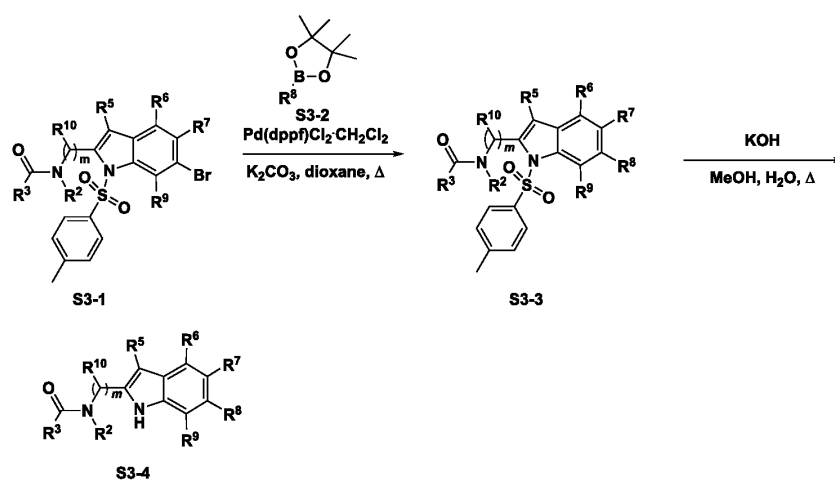


[0257] Compounds of formula **S1-4** can be prepared according to **Scheme 1**. Suzuki coupling of **S1-1** with pinacol boronate **S1-2** in the presence of a palladium catalyst such as [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane complex, an inorganic base such as cesium carbonate in hot DMF gives **S1-3**. Removal of the indole N-sulfonyl protecting group can be accomplished on heating with a base such as potassium carbonate in aqueous methanol to give compounds of formula **S1-4**.

Scheme 2

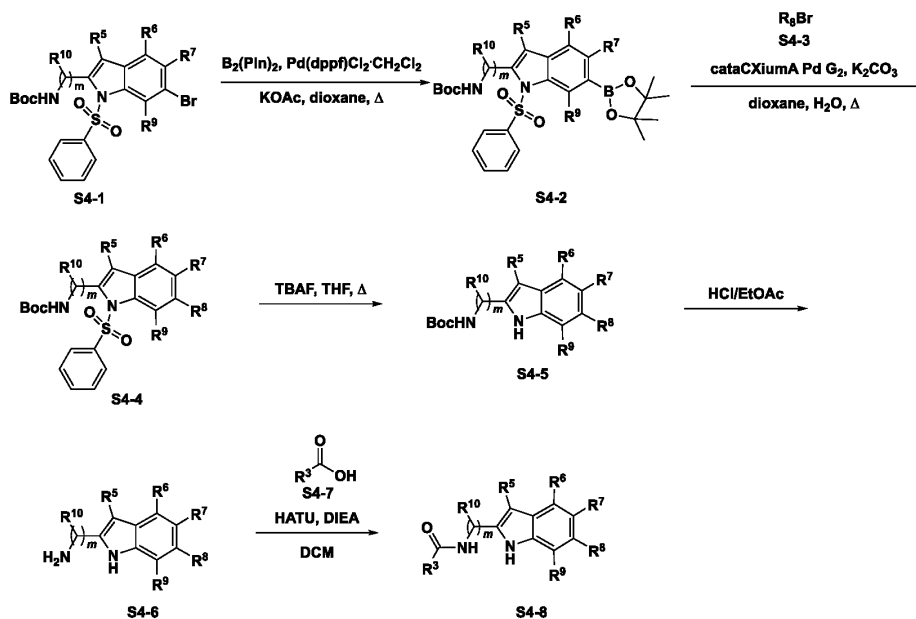


[0258] Compounds of formula **S2-5** can be prepared according to **Scheme 2**. Suzuki coupling of **S2-1** with a boronic acid such as **S2-2** in the presence of a palladium catalyst such as [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane complex, an inorganic base such as potassium carbonate in hot dioxane gives **S2-3**. Treatment with a protic acid such as TFA in a solvent such as DCM gives **S2-4**. Removal of the indole N-sulfonyl protecting group can be accomplished on heating with a base such as potassium carbonate in aqueous methanol to give compounds of formula **S2-5**.

Scheme 3

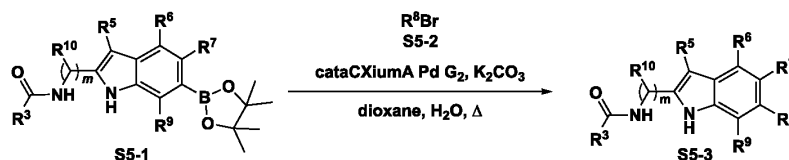
[0259] Compounds of formula **S3-4** can be prepared according to **Scheme 3**. Suzuki coupling of **S3-1** with pinacol boronate **S3-2** in the presence of a palladium catalyst such as [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane complex, an inorganic base such as potassium carbonate in hot dioxane gives **S3-3**. Removal of the indole N-sulfonyl protecting group can be accomplished on heating with a base such as potassium hydroxide in aqueous methanol to give compounds of formula **S3-4**.

Scheme 4



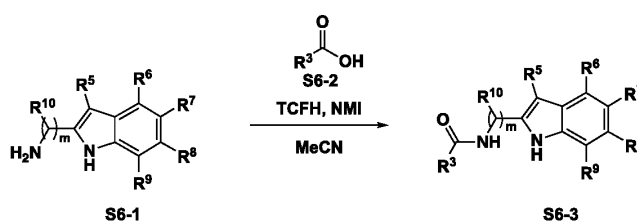
[0260] Compounds of formula **S4-7** can be prepared according to **Scheme 7**. Palladium catalyzed borylation of **S4-1** with Bis(pinacolato)diboron with a palladium catalyst such as [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) dichloromethane complex, an inorganic base such as potassium acetate in hot dioxane gives **S4-2**. Suzuki coupling of **S4-2** occurs upon heating an aryl or heteroaryl halide such as **S4-3** with a palladium catalyst such as chloro[(di(1-adamantyl)-N-butylphosphine)-2-(2-aminobiphenyl)]palladium(II), an inorganic base such as potassium carbonate in aqueous dioxane to give **S4-4**. Removal of the indole N-sulfonyl protecting group can be accomplished on heating with TBAF in THF to give **S4-5**. Removal of the N-Boc group upon treatment with a protic acid such as HCl in EtOAc gives **S4-6**. Coupling of **S4-6** with acid **S4-7** in the presence of HATU and DIEA in a solvent such as DCM gives compounds of formula **S4-8**.

Scheme 5



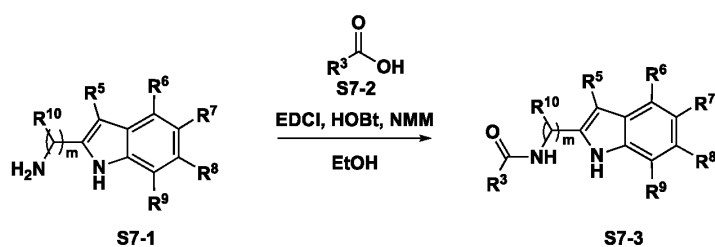
[0261] Compounds of formula **S5-3** can be prepared according to **Scheme 5**. Suzuki coupling of **S5-1** an aryl or heteroaryl halide such as **S5-2** occurs upon heating a palladium catalyst such as chloro[(di(1-adamantyl)-N-butylphosphine)-2-(2-aminobiphenyl)]palladium(II), an inorganic base such as potassium carbonate in hot aqueous dioxane to give **S5-3**.

Scheme 6



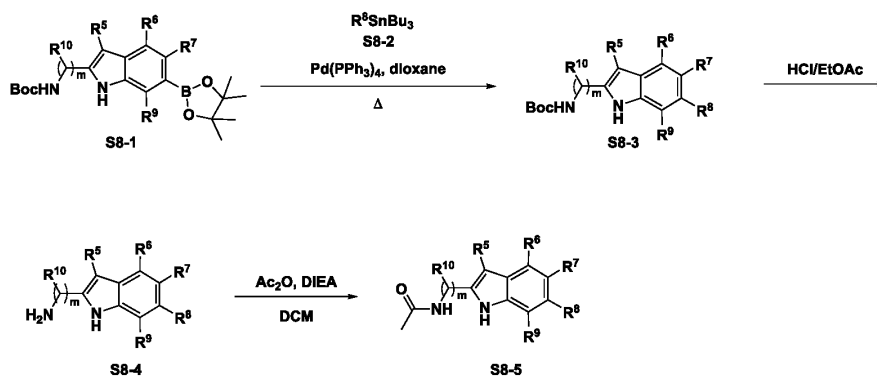
[0262] Compounds of formula **S6-3** may be prepared according to **Scheme 6**. Coupling of **S6-1** with carboxylic acid **S6-2** occurs in the presence of chloro-N,N,N',N'-tetramethylformamidinium hexafluorophosphate and N-methylimidazole in a solvent such as acetonitrile to give compounds of formula **S6-3**.

Scheme 7



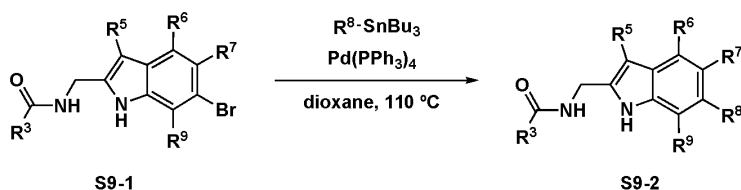
[0263] Compounds of formula **S7-3** may be prepared according to **Scheme 7**. Coupling of **S7-1** with carboxylic acid **S7-2** occurs in the presence of EDCI, HOBT, and N-methylimidazole in a solvent such as ethanol to give compounds of formula **S7-3**.

Scheme 8



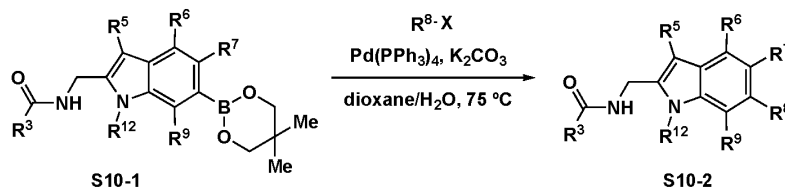
[0264] Compounds of formula **S8-5** may be prepared according to **Scheme 8**. Stille coupling of **S8-1** with an aryl or heteroaryltributyl stannane such as **S8-2** with a catalyst such as Tetrakis(triphenylphosphine)palladium(0) occurs upon heating in a solvent such as dioxane to give **S8-3**. Removal of the N-Boc protecting group upon treatment with HCl in a solvent such as EtOAc gives **S8-4**. Reaction with acetic anhydride and DIEA in a solvent such as DCM gives compounds of formula **S8-5**.

Scheme 9



[0265] Compounds of formula **S9-2** may be prepared according to **Scheme 9**. Stille coupling of compounds of the formula **S9-1** with an aryl or heteroaryltributyl stannane in the presence of a catalyst such as tetrakis(triphenylphosphine)palladium(0) occurs upon heating in a solvent such as dioxane to give compounds of the formula **S9-2**.

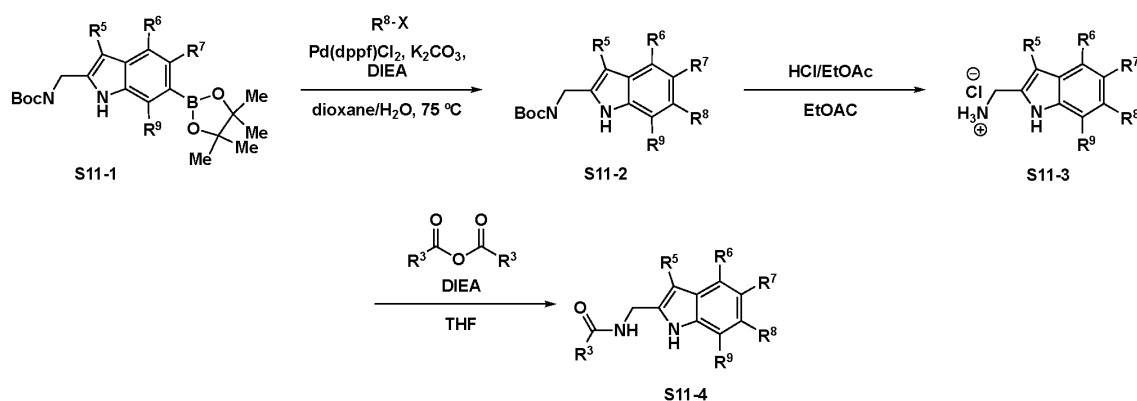
Scheme 10



[0266] Compounds of formula **S10-2** may be prepared according to **Scheme 10**. Suzuki coupling of a compound of the formula **S10-1**, in which R¹² may be hydrogen or a protecting

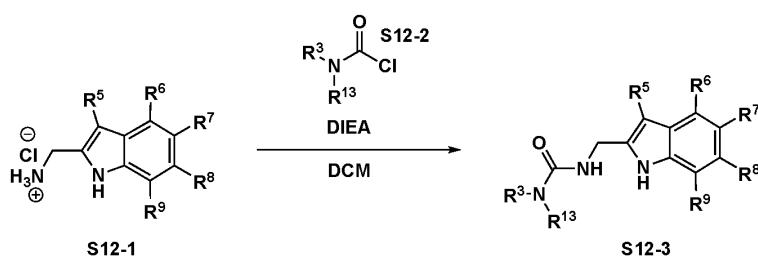
group such as phenylsulfonyl, with an aryl or heteroaryl halide in the presence of a catalyst such tetrakis(triphenylphosphine)palladium(0) and a base such as K_2CO_3 occurs upon heating in a mixed solvent system such as dioxane/water to give compounds of the formula **S10-2**, which may or may not require additional deprotection or functional group manipulation under standard conditions.

Scheme 11



[0267] Compounds of formula **S11-4** may be prepared according to **Scheme 11**. Suzuki coupling of a compound of the formula **S11-1** with an aryl or heteroaryl halide in the presence of a catalyst such $Pd(dppf)Cl_2$ and a base such as K_2CO_3 occurs upon heating in a mixed solvent system such as dioxane/water to give compounds of the formula **S11-2**. Deprotection of the amino group using reagents such as HCl in $EtOAc$ gives compounds of the formula **S11-3**. Acylation of the free amino group using an acylating agent such as a carboxylic acid anhydride gives compounds of the formula **S11-4**.

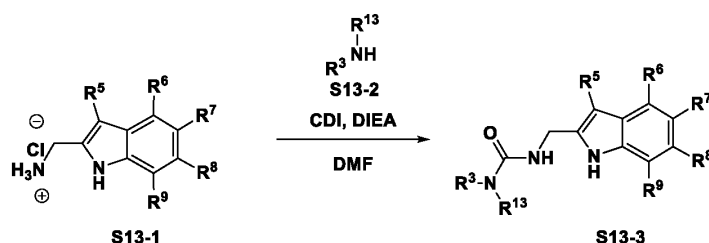
Scheme 12



[0268] Compounds of formula **S12-2** may be prepared according to **Scheme 12**. Reaction of compounds of the formula **S12-1** using a reagent such as **S12-2**, in which R^3 and R^{13} may be individually alkyl or hydrogen or in which R^3 and R^{13} may be cyclized to form a ring, in the

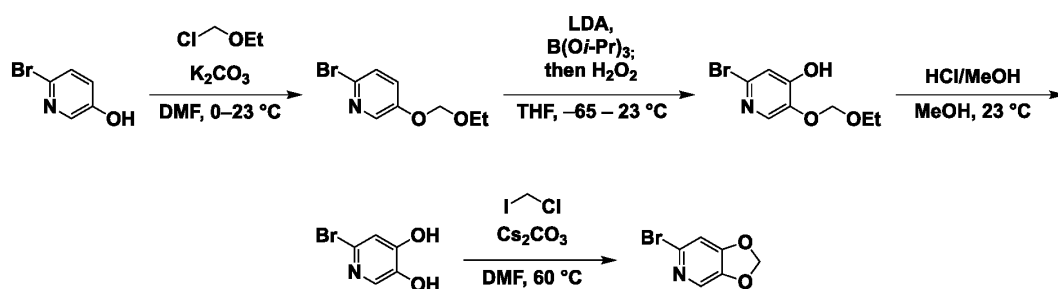
presence of a base such as DIEA in a solvent such as DCM gives compounds of the formula **S12-3**.

Scheme 13



[0269] Compounds of formula **S13-3** may be prepared according to **Scheme 13**. Reaction of compounds of the formula **S13-1** using a reagent such as **S13-2**, in which R³ and R¹³ may be individually alkyl or hydrogen or in which R³ and R¹³ may be cyclized to form a ring, in the presence of CDI and a base such as DIEA in a solvent such as DMF gives compounds of the formula **S13-3**.

Intermediate A-1: Synthesis of 6-bromo-[1,3]dioxolo[4,5-*c*]pyridine



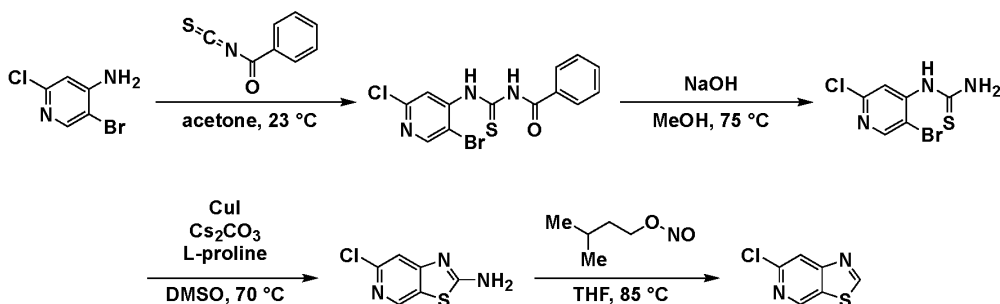
[0270] Step a: To a solution of 6-bromopyridin-3-ol (1.00 g, 5.75 mmol, 1.00 eq) in DMF (4 mL) at 0 °C was added K₂CO₃ (1.59 g, 11.5 mmol, 2.0 eq) and (chloromethoxy)ethane (815 mg, 8.62 mmol, 1.50 eq) dropwise. The reaction was allowed to warm to room temperature. After 6 h, the reaction mixture was quenched by the addition of H₂O (15 mL). The resulting mixture was then extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography to give 2-bromo-5-(ethoxymethoxy)pyridine. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₈H₁₀BrNO₂: 232.0; found: 232.1.

[0271] Step b: To a solution of 2-bromo-5-(ethoxymethoxy)pyridine (1.00 g, 4.31 mmol, 1.00 eq) in anhydrous THF (10 mL) at -65°C was added 2 M LDA in THF (2.37 mL, 4.74 mmol, 1.10 eq) dropwise. After 1 h at -65°C , a THF (5 mL) solution of triisopropyl borate (891 mg, 4.74 mmol, 1.10 eq) was added dropwise. The reaction was warmed to -15°C . After 3 h, 30 wt% H_2O_2 (977 mg, 8.62 mmol, 2.00 eq) was added dropwise. The reaction was then warmed to room temperature. After 1.5 h, the reaction was quenched by the addition of H_2O (15 mL). The resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated aqueous Na_2SO_3 (2 x 20 mL), brine (20 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 2-bromo-5-(ethoxymethoxy)pyridin-4-ol. LC-MS (ESI) m/z: $[\text{M} + \text{H}]^+$ calcd for $\text{C}_8\text{H}_{10}\text{BrNO}_3$: 248.0; found: 248.1.

[0272] Step c: To a solution of 2-bromo-5-(ethoxymethoxy)pyridin-4-ol (510 mg, 2.1 mmol, 1.00 eq) in MeOH (3.0 mL) was added 4 M HCl in MeOH (5 mL, 20.0 mmol, 10.0 eq). After 2 h, the reaction mixture was concentrated under reduced pressure to give 6-bromopyridine-3,4-diol hydrochloride. LC-MS (ESI) m/z: $[\text{M} + \text{H}]^+$ calcd for $\text{C}_5\text{H}_4\text{BrNO}_2$: 190.0; found: 189.8.

[0273] Step d: To a solution of 6-bromopyridine-3,4-diol hydrochloride (450 mg, 1.99 mmol, 1.00 eq) in DMF (15.0 mL) was added Cs_2CO_3 (971 mg, 2.98 mmol, 1.50 eq) and chloriodomethane (526 mg, 2.98, 1.50 eq). The reaction mixture was then warmed to 60°C . After 2 h, the reaction was cooled to room temperature and quenched by the addition of H_2O (10 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (3 x 10 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography to give 6-bromo-[1,3]dioxolo[4,5-c]pyridine. LC-MS (ESI) m/z: $[\text{M} + \text{H}]^+$ calcd for $\text{C}_6\text{H}_4\text{BrNO}_2$: 201.9; found: 202.1.

Intermediate A-2: Synthesis of 6-chlorothiazolo[5,4-c]pyridine



[0274] Step a: To a solution of 5-bromo-2-chloropyridin-4-amine (4.0 g, 19.3 mmol, 1.00 eq) in acetone (40 mL) was added benzoyl isothiocyanate (9.44 g, 57.8 mmol, 3.0 eq) dropwise. After 16 h, the reaction mixture was then concentrated under reduced pressure. The resultant residue was triturated with *n*-heptane (3 mL) for 20 minutes then collected by vacuum filtration to give *N*-((5-bromo-2-chloropyridin-4-yl)carbamothioyl)benzamide.

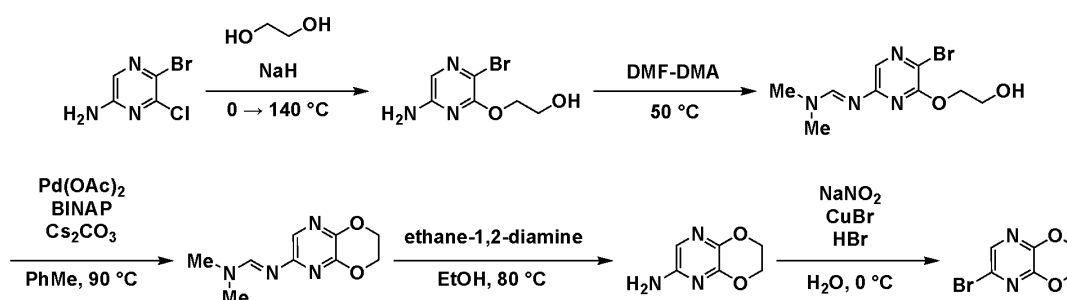
[0275] Step b: To a solution of *N*-((5-bromo-2-chloropyridin-4-yl)carbamothioyl)benzamide (6.00 g, 16.2 mmol, 1.00 eq), in MeOH (60 mL) was added 6 M aqueous sodium hydroxide (5.4 mL, 32.4 mmol, 2.0 eq). The reaction was then warmed to 75 °C. After 4 h, the reaction was cooled to room temperature and quenched by the addition of saturated aqueous NH₄Cl (20 mL). The resulting precipitate was collected by vacuum filtration. The filter cake was washed with H₂O (2 x 20 mL) and DCM (20 mL). The filter cake was then dried under reduced pressure to give 1-(5-bromo-2-chloropyridin-4-yl)thiourea. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₆H₅BrClN₃S: 265.9; found: 266.1.

[0276] Step c: To a solution of 1-(5-bromo-2-chloropyridin-4-yl)thiourea (1.00 g, 3.75 mmol, 1.00 eq) in DMSO (5.0 mL) was added L-proline (863 mg, 7.50 mmol, 2.0 eq), Cs₂CO₃ (2.44 g, 7.5 mmol, 2.0 eq), and CuI (71.5 mg, 0.38, 0.1 eq). The reaction mixture was then warmed to 70 °C. After 2 h, the reaction was cooled to room temperature and quenched by being poured into H₂O (10 mL). The resulting precipitate was collected by vacuum filtration. The filter cake was washed with H₂O (10 mL) then dried under reduced pressure to give 6-chlorothiazolo[5,4-c]pyridin-2-amine. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₆H₄ClN₃S: 186.0; found: 185.8.

[0277] Step d: To a solution of 6-chlorothiazolo[5,4-c]pyridin-2-amine (600 mg, 3.23 mmol, 1.00 eq) in THF (6.0 mL) was added isopentyl nitrite (1.89 g, 16.2 mmol, 5.00 eq). The reaction mixture was then warmed to 85 °C. After 4 h, the reaction was cooled to room

temperature and quenched by being poured into H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 6-chlorothiazolo[5,4-c]pyridine. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₆H₃ClN₂S: 171.0; found: 171.2.

Intermediate A-3: Synthesis of 6-bromo-2,3-dihydro-[1,4]dioxino[2,3-b]pyrazine



[0278] Step a: To a solution of ethane-1,2-diol (63 mL) at 0 °C was added 60% sodium hydride (3.84 g, 95.9 mmol, 2.00 eq) portionwise. After 30 minutes, 5-bromo-6-chloropyrazin-2-amine (10.0 g, 47.9 mmol, 1.00 eq) was added portionwise. The reaction mixture was then warmed to 140 °C. After 1 h, the reaction mixture was cooled to room temperature and quenched by the addition of ice water (50.0 mL). The resulting mixture was then extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was triturated with EtOAc (12 mL) for 10 minutes. The solid was collected by vacuum filtration and dried under reduced pressure to give 2-((6-bromo-4-iodopyridin-3-yl)oxy)ethan-1-ol. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₆H₈BrN₃O₂: 234.0; found: 234.2.

[0279] Step b: A solution of 2-((6-bromo-4-iodopyridin-3-yl)oxy)ethan-1-ol (4.10 g, 17.5 mmol, 1.00 eq), in (dimethoxymethyl)dimethylamine (12 mL) was warmed to 50 °C. After 1 h, the reaction was cooled to room temperature and quenched by the addition of ice water (25 mL). The resulting mixture was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with EtOAc

(15 mL) for 10 minutes. The solid was collected by vacuum filtration and dried under reduced pressure to give (*E*)-*N*-(5-bromo-6-(2-hydroxyethoxy)pyrazin-2-yl)-*N,N*-dimethylformimidamide. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₉H₁₃BrN₄O₂: 289.0; found: 288.8.

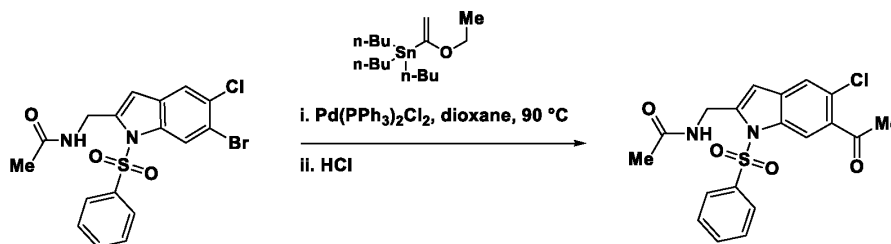
[0280] Step c: (*E*)-*N*-(5-bromo-6-(2-hydroxyethoxy)pyrazin-2-yl)-*N,N*-dimethylformimidamide (3.10 g, 10.7 mmol, 1.00 eq) in toluene (310 mL) was added Cs₂CO₃ (10.4 g, 32.1 mmol, 3.00 eq), Pd(OAc)₂ (240 mg, 1.1 mmol, 0.1 eq), and BINAP (1.34 g, 2.14, 0.20 eq). The sealed reaction vessel was evacuated and refilled with nitrogen three times and then warmed to 90 °C. After 16 h, the reaction mixture was cooled to room temperature and quenched by being poured into H₂O (30 mL). The resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography and prep-HPLC to give (*E*)-*N*-(2,3-dihydro-[1,4]dioxino[2,3-*b*]pyrazin-6-yl)-*N,N*-dimethylformimidamide. LC-MS (ESI) *m/z*: [M + 2H]⁺ calcd for C₉H₁₂N₄O₂: 209.1; found: 209.1.

[0281] Step d: (*E*)-*N*-(2,3-dihydro-[1,4]dioxino[2,3-*b*]pyrazin-6-yl)-*N,N*-dimethylformimidamide (1.2 g, 2.88 mmol, 1.00 eq) in EtOH (12 mL) was added ethane-1,2-diamine (380 mg, 6.32 mmol, 2.19 eq) dropwise. The reaction was then warmed to 80 °C. After 12 h, the reaction was cooled to room temperature and quenched by being poured into H₂O (20 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give 2,3-dihydro-[1,4]dioxino[2,3-*b*]pyrazin-6-amine. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₆H₇N₃O₂: 154.1; found: 154.0.

[0282] Step e: To a solution of 2,3-dihydro-[1,4]dioxino[2,3-*b*]pyrazin-6-amine (190 mg, 1.24 mmol, 1.00 eq) in H₂O (1 mL) at 0 °C was added 40% aqueous HBr (1 mL, 7.37 mmol, 5.9 eq) and a solution of NaNO₂ (128 mg, 1.86 mmol, 1.5 eq) in H₂O (0.5 mL). After 5 minutes, CuBr (355 mg, 2.48 mmol, 2.00 eq) was added in one portion. After 1 h, the reaction was warmed to room temperature and quenched by being poured into H₂O (2 mL). The resulting mixture was extracted with EtOAc (3 x 3 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated

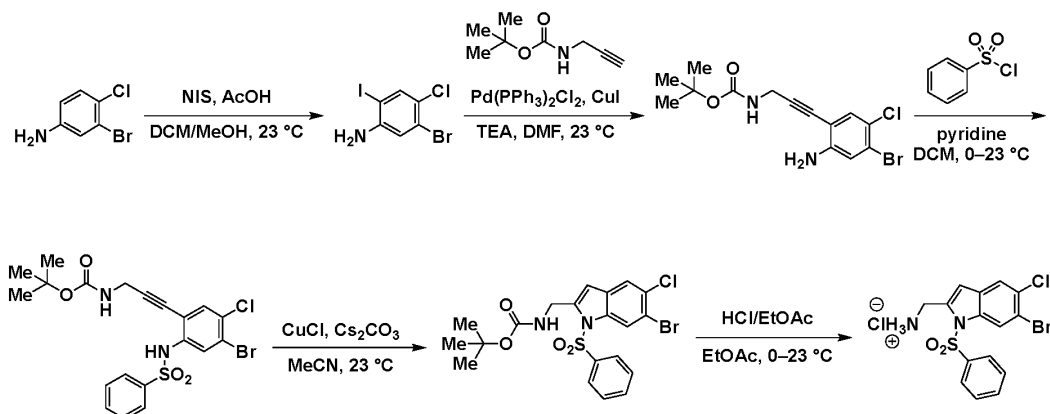
under reduced pressure. The crude residue obtained was purified by prep-HPLC to give 6-bromo-2,3-dihydro-[1,4]dioxino[2,3-b]pyrazine. LC-MS (ESI) m/z : $[M + H]^+$ calcd for $C_6H_5BrN_2O_2$: 217.0; found: 217.2.

Intermediate A-4: Synthesis of *N*-((6-acetyl-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide



[0283] Step a: A mixture of *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (1.50 g, 3.40 mmol, 1.00 eq) and tributyl(1-ethoxyvinyl)stannane (2.45 g, 6.79 mmol, 2.00 eq) in dioxane (10 mL) was degassed and purged with N_2 three times followed by the addition of $Pd(PPh_3)_2Cl_2$ (238 mg, 339 μ mol, 0.10 eq). The reaction mixture was then warmed to 90 °C and stirred for 16 h. The reaction mixture was then cooled to 23 °C and quenched by addition of aqueous HCl (1 M, 5 mL). The resulting mixture was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine (3 x 15 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with MTBE (10 mL) at 23 °C for 30 min to give *N*-((6-acetyl-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): m/z : $[M + H]^+$ calculated for $C_{19}H_{17}ClN_2O_4S$: 405.1; found 405.1.

Intermediate A-5: Synthesis of *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)- λ^5 -chloranimine



[0284] Step a: Four reactions were carried out in parallel. To a solution of 3-bromo-4-chloroaniline (50.0 g, 242.0 mmol, 1.00 eq) in DCM (270.0 mL) was added acetic acid (41.6 mL, 726.0 mmol, 3.0 eq) in a single portion followed by a solution of NIS (76.3 g, 339.0 mmol, 1.40 eq.) in MeOH (270 mL) dropwise over 1 h. After 5 h, the four reactions were combined for work up. The reaction mixture was quenched by the addition of H₂O (2.0 L). The resulting mixture was then extracted with EtOAc (3 x 2.0 L). The combined organic layers were washed with brine (3 x 1.0 L), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 5-bromo-4-chloro-2-iodoaniline. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₆H₄BrClIN: 331.8; found: 331.9.

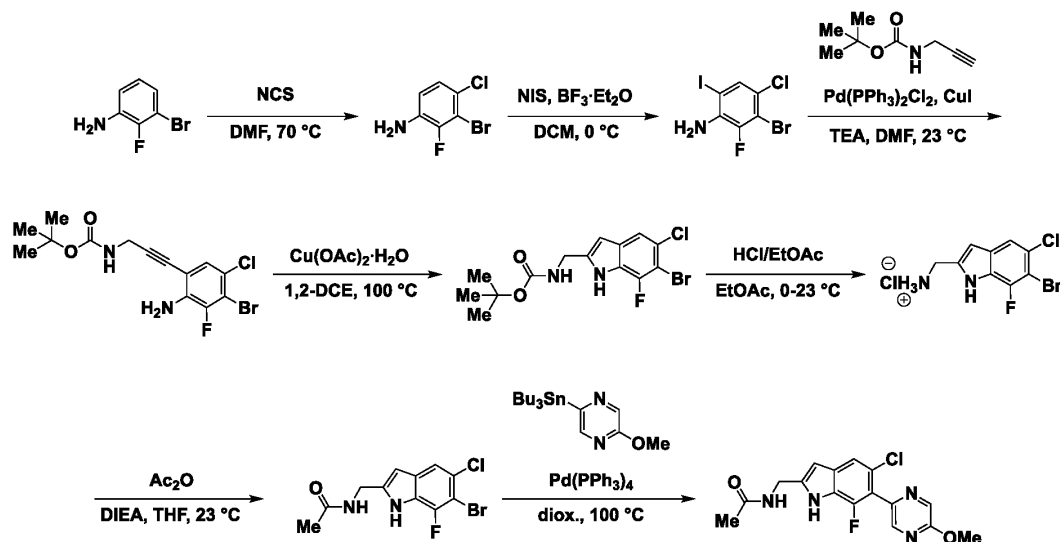
[0285] Step b: To a solution of 5-bromo-4-chloro-2-iodoaniline (118.0 g, 355.0 mmol, 1.00 eq) in DMF (1.0 L) was added *tert*-butyl prop-2-yn-1-ylcarbamate (55.1 g, 355 mmol, 1.0 eq), TEA (247 mL, 1.78 mol, 5.00 eq), CuI (13.5 g, 71.0 mmol, 0.20 eq), and bis(triphenylphosphine)palladium(II) dichloride (7.5 g, 10.7 mmol, 0.03 eq). The sealed reaction vessel was evacuated and refilled with nitrogen three times. After 2 h at room temperature, the reaction was quenched by pouring into ice water (2.0 L). The resulting mixture was extracted with EtOAc (3 x 1.0 L). The combined organic layers were washed with brine (3 x 1.0 L), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl (3-(2-amino-4-bromo-5-chlorophenyl)prop-2-yn-1-yl)carbamate. LC-MS (ESI) m/z: [M – C₄H₉ + 2H]⁺ calcd for C₁₄H₁₆BrClN₂O₂: 303.0; found: 302.8.

[0286] Step c: To a solution of *tert*-butyl (3-(2-amino-4-bromo-5-chlorophenyl)prop-2-yn-1-yl)carbamate (110.0 g, 305 mmol, 1.00 eq), in DCM (1.0 L) at 0 °C was added pyridine (49.4 mL, 611.0 mmol, 2.0 eq) in a single portion followed by benzenesulfonyl chloride (39.0 mL, 305 mmol, 1.00 eq) dropwise. The reaction was then allowed to warm to room temperature. After 1 h, the reaction mixture was quenched by pouring it into ice water (2.0 L). The resulting biphasic mixture was extracted with EtOAc (3 x 1.0 L). The combined organic layers were washed with brine (3 x 1.0 L), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give *tert*-butyl (3-(4-bromo-5-chloro-2-(phenylsulfonamido)phenyl)prop-2-yn-1-yl)carbamate, which was used without further purification. LC-MS (ESI) m/z: [M + Na]⁺ calcd for C₂₀H₂₀BrClN₂O₄S: 521.0; found: 521.0.

[0287] Step d: To a solution of *tert*-butyl (3-(4-bromo-5-chloro-2-(phenylsulfonamido)phenyl)prop-2-yn-1-yl)carbamate (150.0 g, 300.0 mmol, 1.00 eq) in MeCN (1.5 L) was added CuCl (4.46 g, 45.0 mmol, 0.15 eq) and Cs₂CO₃ (14.7 g, 45.0 mmol, 0.15 eq.). The sealed reaction vessel was evacuated and refilled with nitrogen three times. After 3 h at room temperature, the reaction was quenched by being poured into ice water (2.0 L). The resulting biphasic mixture was extracted with EtOAc (3 x 1.0 L). The combined organic layers were washed with brine (3 x 1.0 L), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give *tert*-butyl ((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate, which was used without any further purification. LC-MS (ESI) m/z: [M – C₄H₉ + 2H]⁺ calcd for C₂₀H₂₀BrClFN₂O₄S: 442.9; found: 443.1.

[0288] Step e: To a solution of *tert*-butyl ((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate (59.0 g, 118.0 mmol, 1.00 eq) in EtOAc (10 mL) at 0 °C was added 4 M HCl in EtOAc (500 mL, 2.0 mol, 16.9 eq) portionwise. The reaction was then allowed to warm to room temperature. After 1 h, the reaction mixture was concentrated under reduced pressure to give *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)-λ⁵-chloranimine, which was used without further purification. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₁₅H₁₂BrClN₂O₂S: 398.9; found: 399.1.

Example S-1: Synthesis of *N*-((5-chloro-7-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 78)



[0289] Step a: To a solution of 3-bromo-2-fluoroaniline (14.0 g, 73.7 mmol, 1.00 eq) in DMF (70.0 mL) was added 1-chloropyrrolidine-2,5-dione (10.3 g, 77.3 mmol, 1.05 eq). After the addition, the reaction was warmed to 70 °C and stirred for 1 h. The reaction was then cooled to 0 °C and quenched by the addition of H₂O (100 mL). The resulting mixture was then extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give 3-bromo-4-chloro-2-fluoroaniline, which was used without further purification.

[0290] Step b: To a solution of 3-bromo-4-chloro-2-fluoroaniline (15.0 g, 66.8 mmol, 1.00 eq), in DCM (80 mL) at 0 °C was added 1-iodopyrrolidine-2,5-dione (22.5 g, 100.0 mmol, 1.50 eq) and BF₃·Et₂O (9.48 g, 66.8 mmol, 1.00 eq). After 1h, the reaction mixture was quenched with water (100 mL) and then warmed to room temperature. The resulting biphasic mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 3-bromo-4-chloro-2-fluoro-6-iodoaniline.

[0291] Step c: To a solution of 3-bromo-4-chloro-2-fluoro-6-iodoaniline (6.90 g, 19.6 mmol, 1.00 eq) in DMF (70 mL) was added *tert*-butyl prop-2-yn-1-ylcarbamate (3.67 g, 23.6 mmol, 1.20 eq), TEA (9.96 g, 98.4 mmol, 5.00 eq), CuI (750 mg, 3.94 mmol, 0.20 eq), and bis(triphenylphosphine)palladium(II) dichloride (1.38 g, 1.97 mmol, 0.10 eq). The sealed

reaction vessel was evacuated and refilled with nitrogen 3 times. After 1 h at room temperature, the reaction was quenched with water (30 mL). The resulting mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl (3-(2-amino-4-bromo-5-chloro-3-fluorophenyl)prop-2-yn-1-yl)carbamate. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₁₄H₁₆BrClFN₂O₂: 377.0; found: 377.1.

[0292] Step d: To a solution of *tert*-butyl (3-(2-amino-4-bromo-5-chloro-3-fluorophenyl)prop-2-yn-1-yl)carbamate (5.90 g, 15.6 mmol, 1.00 eq) in 1,2-DCE (60 mL) was added Cu(OAc)₂•H₂O (1.56 mmol, 7.81 mL, 0.50 eq). The reaction mixture was then warmed to 100 °C. After 3 h, the reaction was cooled to room temperature and quenched by being poured into H₂O (40 mL). The biphasic solution was then extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (2 x 50 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl ((6-bromo-5-chloro-7-fluoro-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI) m/z: [M – C₄H₉ + 2H]⁺ calcd for C₁₄H₁₆BrClFN₂O₂: 320.9; found: 321.0.

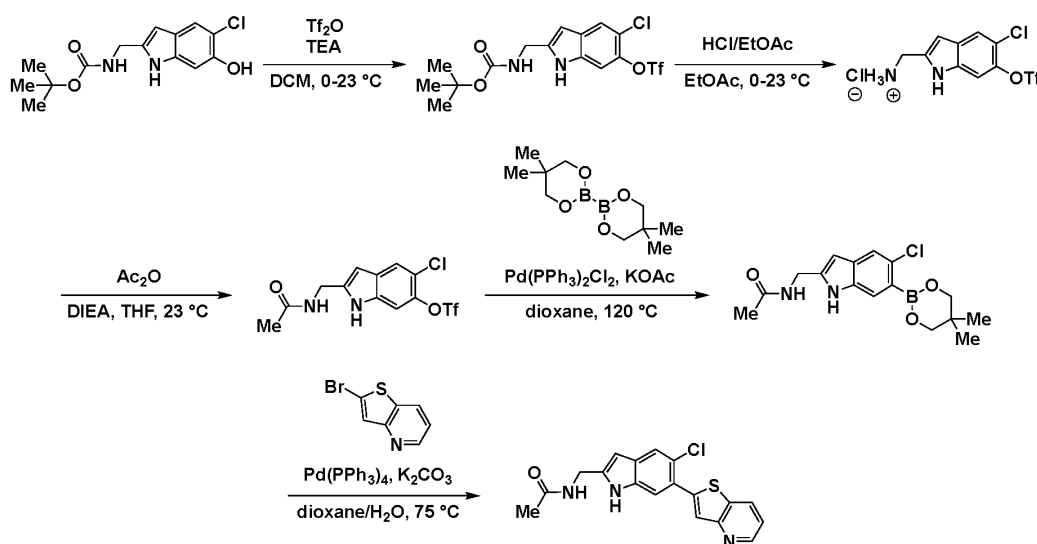
[0293] Step e: To a solution of *tert*-butyl ((6-bromo-5-chloro-7-fluoro-1*H*-indol-2-yl)methyl)carbamate (2.00 g, 5.30 mmol, 1.00 eq) in EtOAc (10 mL) at 0 °C was added 4 M HCl in EtOAc solution (20 mL, 80.00 mmol, 15.10 eq) dropwise. The reaction was then allowed to warm to room temperature. After 1 h, the reaction mixture was concentrated under reduced pressure to give (6-bromo-5-chloro-7-fluoro-1*H*-indol-2-yl)methanamine hydrochloride, which was used without further purification. LC-MS (ESI) m/z: [M – NH₂]⁺ calcd for C₉H₈BrClFN₂: 259.9; found: 260.0.

[0294] Step f: To a solution of (6-bromo-5-chloro-7-fluoro-1*H*-indol-2-yl)methanamine hydrochloride (1.60 g, 5.10 mmol, 1.00 eq) in THF (16 mL) was added DIEA (1.32 g, 10.1 mmol, 2.00 eq) and acetic anhydride (728 mg, 7.13 mmol, 1.40 eq) dropwise. After 1 h, the reaction was quenched by being poured into H₂O (10 mL). The reaction mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography to give *N*-((6-bromo-5-chloro-7-

fluoro-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₁H₁₀BrClFN₂O: 319.0; found: 319.0.

[0295] Step g: Two reactions were carried out in parallel. To a solution of *N*-((6-bromo-5-chloro-7-fluoro-1*H*-indol-2-yl)methyl)acetamide (640 mg, 1.13 mmol, 1.00 eq) in dioxane (2.0 mL) was added 2-methoxy-5-(tributylstannyl)pyrazine (640 mg, 1.25 mmol, 2.00 eq) and Pd(PPh₃)₄ (145.0 mg, 0.13 mmol, 0.20 eq). The sealed reaction vessel was evacuated and refilled with nitrogen 3 times and then was warmed to 100 °C. After 1 h, the reactions were cooled to room temperature, combined, and poured into H₂O (3 mL). The mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with brine (2 x 5 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography to give *N*-((5-chloro-7-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (DMSO 400 MHz) δ ppm 11.81 (s, 1H), 8.46 (s, 1H), 8.38 (t, *J* = 5.4 Hz, 1H), 8.35 (s, 1H), 7.55 (s, 1H), 6.40 (d, *J* = 3.2 Hz, 1H), 4.42 (d, *J* = 5.6 Hz, 2H), 3.98 (s, 3H), 1.90 (s, 3H). LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₆H₁₅ClFN₄O₂: 349.1; found: 349.2.

Example S-2: Synthesis of *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 88)



[0296] Step a: To a solution of *tert*-butyl ((5-chloro-6-hydroxy-1*H*-indol-2-yl)methyl)carbamate (150 g, 505.0 mmol, 1.00 eq) in DCM (1.50 L) at 0 °C was added triethylamine (61.3 g, 606.0 mmol, 1.20 eq) and triflic anhydride (156.0 g, 556 mmol, 1.10 eq). The reaction was then allowed to warm to room temperature. After 1 h, the reaction mixture was quenched by the addition of H₂O (1.0 L). The resulting mixture was then extracted with EtOAc (3 x 500 mL). The combined organic layers were washed with brine (500 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with MTBE (80 mL) for 30 minutes then collected by vacuum filtration to give 2-(((*tert*-butoxycarbonyl)amino)methyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate LC-MS (ESI) m/z: [M – C₄H₉ + 2H]⁺ calcd for C₁₅H₁₇ClF₃N₂O₅S: 373.0; found: 373.1.

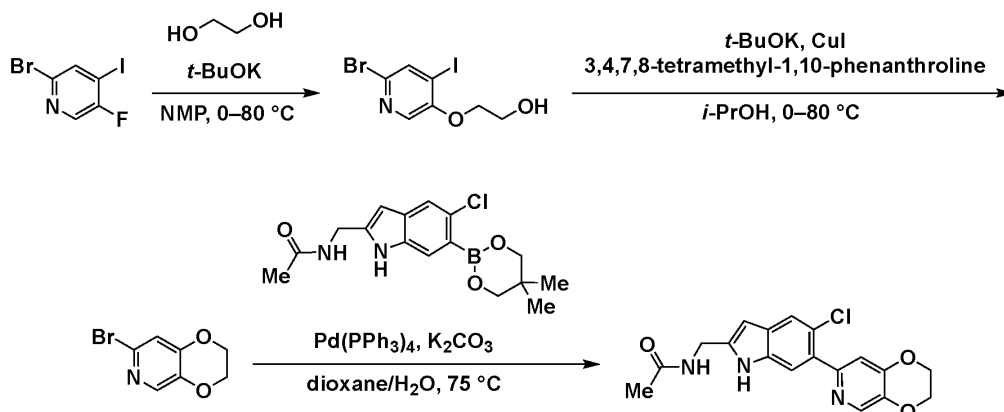
[0297] Step b: Three reactions were carried out in parallel. To a solution of 2-(((*tert*-butoxycarbonyl)amino)methyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate (75.0 g, 174 mmol, 1.00 eq), in EtOAc (75 mL) at 0 °C was added 4M HCl in EtOAc (375 mL, 1.5 mol, 8.62 eq) dropwise. The reaction was then allowed to warm to room temperature. After 2 h, the three reactions were combined and concentrated under reduced pressure to give 2-(((λ⁵-chloraneylidene)amino)methyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate hydrochloride which was used without further purification. LC-MS (ESI) m/z: [M – NH₂]⁺ calcd for C₁₀H₈ClF₃N₂O₃S: 312.0; found: 312.2.

[0298] Step c: Three reactions were carried out in parallel. To a solution of 2-(((λ⁵-chloraneylidene)amino)methyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate hydrochloride (63.8 g, 174 mmol, 1.00 eq) in THF (575 mL) was added DIEA (45.2 g, 349 mmol, 2.00 eq) and a solution of acetic anhydride (25.0 g, 244 mmol, 1.40 eq) in THF (64 mL) dropwise. After 1 h, the reactions were combined and quenched by the addition of H₂O (1.0 L). The solution was then extracted with EtOAc (3 x 500 mL). The combined organic layers were washed with brine (1.0 L), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with petroleum ether/MTBE (1:1, 958 mL) for 30 minutes then collected by vacuum filtration to give 2-(acetamidomethyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate. LC-MS (ESI) m/z: [M + H]⁺ calcd for C₁₂H₁₀ClF₃N₂O₄S: 371.0; found: 371.1.

[0299] Step d: To a solution of 2-(acetamidomethyl)-5-chloro-1*H*-indol-6-yl trifluoromethanesulfonate (70 g, 188 mmol, 1.00 eq) in dioxane (700 mL) was added 5,5,5',5'-tetramethyl-2,2'-bi(1,3,2-dioxaborinane) (127 g, 566 mmol, 3.00 eq), potassium acetate (40.7 g, 415 mmol, 2.20 eq), and Pd(PPh₃)₂Cl₂ (13.2 g, 18.8 mmol, 0.1 eq). The sealed reaction vessel was evacuated and refilled with nitrogen three times and then warmed to 120 °C. After 1 h, the reaction was cooled to room temperature, filtered to remove solids, and concentrated under reduced pressure. The crude residue containing *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1*H*-indol-2-yl)methyl)acetamide was used without further purification.

[0300] Step e: To a solution of *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1*H*-indol-2-yl)methyl)acetamide (100 mg, 0.3 mmol, 1.00 eq) in dioxane/H₂O (5:1, 2.4 mL) was added K₂CO₃ (123 mg, 0.9 mmol, 3.0 eq), 2-bromothieno[3,2-*b*]pyridine (63.9 mg, 298 μmol, 1.00 eq), and Pd(PPh₃)₄ (34.5 mg, 29.8 μmol, 0.10 eq). The sealed reaction vessel was evacuated and refilled with nitrogen three times and then warmed to 75 °C. After 1 h, the reaction mixture was cooled to room temperature and quenched by the addition of H₂O (5.0 mL). The solution was extracted with EtOAc (3 x 1.0 mL). The combined organic layers were washed with brine (1.0 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by prep-HPLC to give *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (DMSO 400 MHz) δ ppm 11.30 (s, 1H), 8.67 (d, *J* = 4.4 Hz, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.42 (t, *J* = 5.2 Hz, 1H), 7.72 (d, *J* = 4.0 Hz, 2H), 7.66 (s, 1H), 7.40 -7.38 (m, 1H), 6.33 (s, 1H), 4.42 (d, *J* = 5.6 Hz, 2H), 1.91 (s, 3H). LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₈H₁₄ClN₃OS: 356.1; found: 356.1.

Example S-3: Synthesis of *N*-((5-chloro-6-(2,3-dihydro-[1,4]dioxino[2,3-*c*]pyridin-7-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 89)



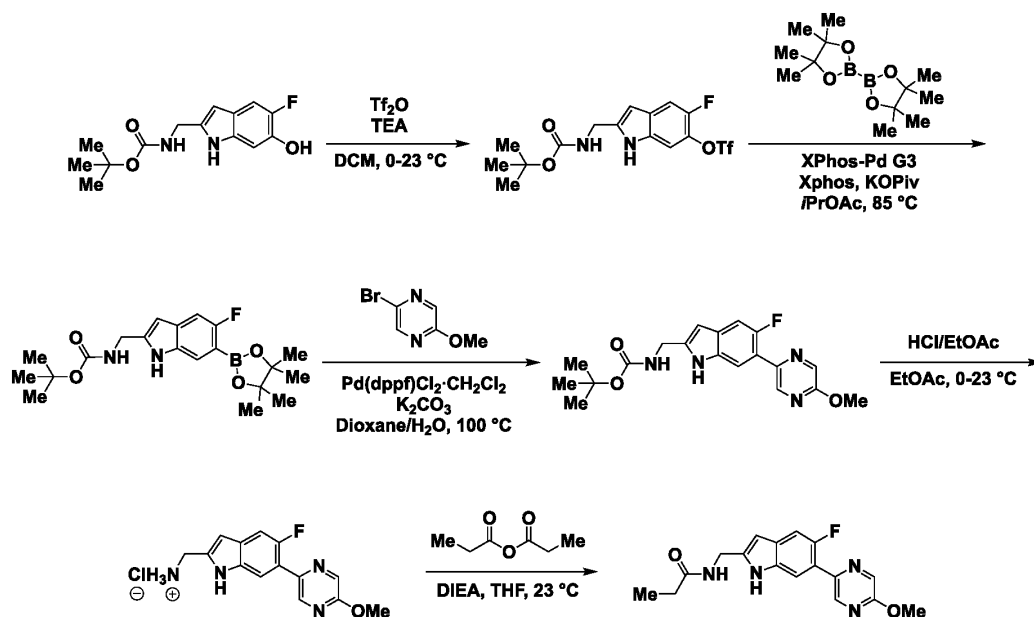
[0301] Step a: To a solution of 2-bromo-5-fluoro-4-iodopyridine (10.0 g, 33.1 mmol, 1.00 eq) in NMP (120 mL) at 0 °C was added ethane-1,2-diol (9.87 g, 159 mmol, 4.8 eq) and *t*-BuOK (4.09 g, 36.4 mmol, 1.10 eq). The reaction was then warmed to 80 °C. After 1 h, the reaction mixture was cooled to room temperature and quenched by the addition of H₂O (50.0 mL). The resulting mixture was then extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine (3 x 50 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 2-((6-bromo-4-iodopyridin-3-yl)oxy)ethan-1-ol. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₇H₇BrINO₂: 343.9; found: 344.0.

[0302] Step b: To a solution of 2-((6-bromo-4-iodopyridin-3-yl)oxy)ethan-1-ol (4.00 g, 11.6 mmol, 1.00 eq), in *i*-PrOH (40 mL) at 0 °C was added 3,4,7,8-tetramethyl-1,10-phenanthroline (27.5 mg, 0.12 mmol, 0.01 eq), CuI (22.2 mg, 0.12 mmol, 0.01 eq), and *t*-BuOK (4.09 g, 36.4 mmol, 1.10 eq) in one portion. The reaction was then warmed to 80 °C. After 1 h, the reaction was cooled to room temperature and quenched by the addition of H₂O (20 mL). The resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (3 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give 7-bromo-2,3-dihydro-[1,4]dioxino[2,3-*c*]pyridine. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₇H₆BrNO: 216.0; found: 215.8.

[0303] Step c: To a solution of *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1*H*-indol-2-yl)methyl)acetamide (100 mg, 0.3 mmol, 1.00 eq) in dioxane/H₂O (5:1, 1.2 mL) was added 7-bromo-2,3-dihydro-[1,4]dioxino[2,3-*c*]pyridine (127 g, 566 mmol, 3.00 eq),

potassium carbonate (124 mg, 0.9 mmol, 3.0 eq), and $\text{Pd}(\text{PPh}_3)_4$ (34.5 mg, 0.03 mmol, 0.1 eq). The sealed reaction vessel was then evacuated and refilled with nitrogen three times and then warmed to 75 °C. After 1 h, the reaction was cooled to room temperature and quenched by the addition of H_2O (5 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (3 x 10 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give *N*-((5-chloro-6-(2,3-dihydro-[1,4]dioxino[2,3-*c*]pyridin-7-yl)-1*H*-indol-2-yl)methyl)acetamide ^1H NMR (DMSO 400 MHz) δ ppm 11.16 (s, 1H), 8.39 (t, J = 5.6 Hz, 1H), 8.19 (s, 1H), 7.57 (s, 1H), 7.46 (s, 1H), 7.11 (s, 1H), 6.28 (s, 1H), 4.40 (d, J = 5.6 Hz, 4H), 4.36 (d, J = 4.8 Hz, 2H), 1.89 (s, 3H). . LC-MS (ESI) m/z : $[\text{M} + 2\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{16}\text{ClN}_3\text{O}_3$: 358.1; found: 358.2.

Example S-4: Synthesis of *N*-((5-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)propionamide (Compound 90)



[0304] Step a: To a solution of *tert*-butyl ((5-fluoro-6-hydroxy-1*H*-indol-2-yl)methyl)carbamate (10.0 g, 35.6 mmol, 1.00 eq) in DCM (100 mL) at 0 °C was added TEA (4.33 g, 42.8 mmol, 1.2 eq) and Tf_2O (11.0 g, 39.2 mmol, 1.10) dropwise. The reaction was allowed to warm to room temperature. After 1 h, the reaction mixture was quenched by being

poured into H₂O (100 mL). The resulting mixture was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with *n*-heptane (100 mL) for 30 minutes. The solid was collected by vacuum filtration to give 2-(((*tert*-butoxycarbonyl)amino)methyl)-5-fluoro-1*H*-indol-6-yl trifluoromethanesulfonate. LC-MS (ESI) *m/z*: [M – C₄H₉ + 2H]⁺ calcd for C₁₅H₁₆F₄N₂O₅S: 357.0; found: 357.2.

[0305] Step b: To a solution of 2-(((*tert*-butoxycarbonyl)amino)methyl)-5-fluoro-1*H*-indol-6-yl trifluoromethanesulfonate (2.00 g, 4.9 mmol, 1.00 eq) in *i*-PrOAc (10 mL) was added bis(pinacolato)diboron (1.48 g, 5.82 mmol, 1.20 eq), KO_tiv (1.50 g, 10.6 mmol, 2.20 eq), XPhos (462 mg, 1.0 mmol, 0.20), and XPhos-Pd G3 (410 mg, 0.49 mmol, 0.10 eq). The sealed reaction vessel was then evacuated and refilled with nitrogen three times and then heated to 85 °C. After 12 h, the reaction was cooled to room temperature and filtered. The filtrate was then concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl ((5-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₂₀H₂₈BrFN₂O₄: 391.2; found: 391.4.

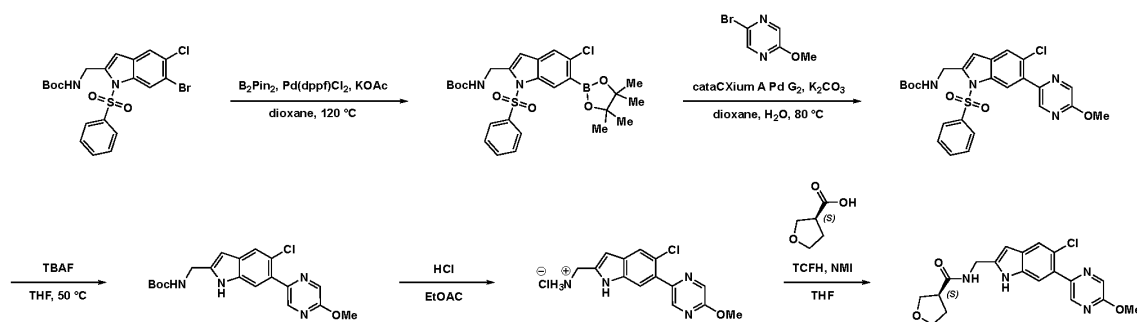
[0306] Step c: To a solution of *tert*-butyl ((5-fluoro-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)carbamate (1.80 g, 3.7 mmol, 1.00 eq) in dioxane/H₂O (5:1, 24 mL) was added 2-bromo-5-methoxypyrazine (697 mg, 3.7 mmol, 1.0 eq), K₂CO₃ (1.53 g, 11.0 mmol, 3.0 eq), and Pd(dppf)Cl₂•CH₂Cl₂ (301 mg, 0.37 mmol, 0.10 eq). The sealed reaction vessel was then evacuated and refilled with nitrogen three times and then warmed to 100 °C. After 2 h, the reaction mixture was cooled to room temperature and quenched by pouring the reaction mixture into H₂O (20 mL). The resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl ((5-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₉H₂₁FN₄O₃: 373.2; found: 373.2.

[0307] Step d: To a solution of *tert*-butyl ((5-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamate (800 mg, 2.15 mmol, 1.00 eq) in EtOAc (4 mL) at 0 °C was added 4 M HCl in EtOAc (10 mL, 40.00 mmol, 18.6 eq) dropwise. The reaction mixture was then

warmed to 23 °C. After 2 h, the reaction mixture was concentrated under reduced pressure to give (5-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanamine hydrochloride, which was used without further purification. LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₄H₁₃FN₄O: 273.1; found: 273.0.

[0308] Step e: To a solution of (5-fluoro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanamine hydrochloride (100 mg, 0.32 mmol, 1.00 eq) in THF (2.0 mL) was added DIEA (125 mg, 0.97 mmol, 3.00 eq) and propionic anhydride (50.6 mg, 0.39 mmol, 1.2 eq) dropwise. After 1 h, the reaction was quenched by the addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (2 x 5 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)propionamide. ¹H NMR (DMSO 400 MHz) δ ppm 11.18 (s, 1H), 8.57 (s, 1H), 8.44 (s, 1H), 8.33 (t, *J* = 5.2 Hz, 1H), 7.82 (d, *J* = 6.4 Hz, 1H), 7.35 (d, *J* = 12.4 Hz, 1H), 6.29 (s, 1H), 4.41 (d, *J* = 5.6 Hz, 2H), 3.96 (s, 3H), 2.20 - 2.14 (m, 2H), 1.03 (t, *J* = 7.4 Hz, 3H). LC-MS (ESI) *m/z*: [M + H]⁺ calcd for C₁₇H₁₇FN₄O: 329.1; found: 329.2.

Example S-5: Synthesis of (*S*)-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)tetrahydrofuran-3-carboxamide (Compound 24)



[0309] Step a: A mixture of (*tert*-butyl ((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate (3.0 g, 6.0 mmol, 1.00 eq), B₂Pin₂ (4.57 g, 18.0 mmol, 3.0 mmol), and KOAc (1.30 g, 13.2 mmol, 2.20 eq) in dioxane (30 mL) was degassed and purged with N₂. Pd(PPh₃)₂Cl₂ (490 mg, 600 μmol, 0.1 eq) was then added under N₂ and the resulting mixture was warmed to 120 °C. The reaction mixture stirred for 1 h at 120 °C, cooled to 23 °C and

filtered through Celite. The filtrate was concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *tert*-butyl ((5-chloro-1-(phenylsulfonyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI): *m/z*: [M + Na]⁺ calculated for C₂₆H₃₂BClN₂O₆S: 569.2; found 569.3.

[0310] Step b: To a mixture of *tert*-butyl ((5-chloro-1-(phenylsulfonyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)carbamate (3.50 g, 5.12 mmol, 1.00 eq), 2-bromo-5-methoxy-pyrazine (1.02 g, 5.38 mmol, 1.05 eq), and K₂CO₃ (2.1 g, 29.8 mmol, 3.00 eq) were added dioxane (2 mL) and H₂O (0.4 mL). The reaction mixture was then degassed and purged with N₂. CataCXium A Pd G₂ (1.71 g, 2.56 mmol, 0.5 eq) was then added under N₂, and the resulting mixture was warmed to 80 °C and stirred for 1 h. The reaction was then cooled to room temperature and quenched by addition of H₂O (10 mL). The resulting mixture was extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The crude residue obtained was purified by column chromatography to give *tert*-butyl ((5-chloro-6-(5-methoxypyrazin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₅H₂₅ClN₄O₅S: 529.2; found 529.3.

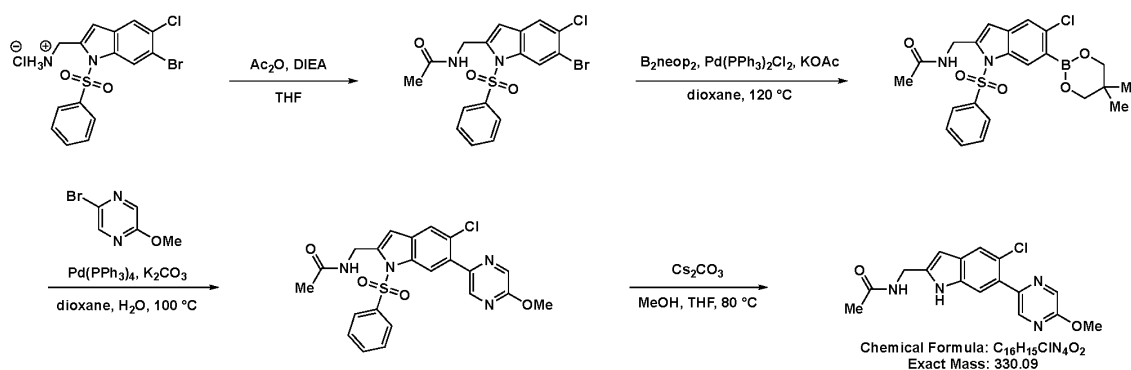
[0311] Step c: To a solution of *tert*-butyl ((5-chloro-6-(5-methoxypyrazin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate (2.7 g, 5.10 mmol, 1.00 eq) in THF (27 mL) was added TBAF (13.3 g, 51.0 mmol, 10 eq). The resulting mixture was warmed to 50 °C and stirred for 1 h. The reaction was then cooled to 23 °C and quenched by addition of H₂O (10 mL). The resulting mixture was extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with saturated aqueous NH₄Cl (5 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give *tert*-butyl ((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₉H₂₁ClN₄O₃: 389.1; found 389.0.

[0312] Step d: To a solution of *tert*-butyl ((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamate (1.8 g, 4.60 mmol, 1.00 eq) in EtOAc (2 mL) was added HCl (4 M in

EtOAc, 20 mL, 80 mmol, 17.3 eq). The resulting mixture was stirred at 23 °C for 1 h. The reaction mixture was then concentrated under reduced pressure to give (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanaminium chloride. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₄H₁₃ClN₄O: 289.1; found 289.0.

[0313] Step e: To a mixture of (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanaminium chloride (110 mg, 380 μmol, 1.00 eq) and (3*S*)-tetrahydrofuran-3-carboxylic acid (53.0 mg, 457 μmol, 1.20 eq) in THF (1 mL) was added NMI (156 mg, 1.90 mmol, 5.0 eq). The reaction mixture was then cooled to 0 °C, and TCFH (160 mg, 571 μmol, 1.50 eq) was added. The resulting mixture was warmed to 23 °C and stirred for 1 h. The reaction mixture was then quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give (*S*)-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)tetrahydrofuran-3-carboxamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.26 (s, 1 H), 8.52 – 8.49 (t, *J* = 5.6 Hz, 1 H), 8.45 (s, 1 H), 8.41 (d, *J* = 1.2 Hz, 1 H), 7.65 (s, 1 H), 7.52 (s, 1 H), 6.31 (d, *J* = 0.8 Hz, 1 H), 4.44 (d, *J* = 5.6 Hz, 2 H), 3.97 (s, 3 H), 3.93 – 3.85 (m, 1 H), 3.79 – 3.72 (m, 1 H), 3.70 – 3.66 (m, 2 H), 3.03 – 2.99 (m, 1 H), 2.05 – 2.00 (m, 2 H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₉H₁₉ClN₄O₃: 387.1; found 387.2.

Example S-6: Synthesis of *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 8)



[0314] Step a: To a solution of (6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methanaminium chloride (6.0 g, 15.0 mmol, 1.00 eq) in THF (60 mL) at 0 °C under N₂ were added DIEA (3.88 g, 30.0 mmol, 2.00 eq) and Ac₂O (2.15 g, 21.0 mmol, 1.40 eq). The resulting mixture was warmed to 23 °C and stirred for 1 h. The reaction mixture was then quenched by addition of H₂O (50 mL). The resulting mixture was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (60 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with EtOAc (60 mL) for 30 min at 23 °C. The mixture was then filtered to give *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): m/z: [M + H]⁺ calculated for C₁₇H₁₄BrClN₂O₃S: 440.9; found 441.0.

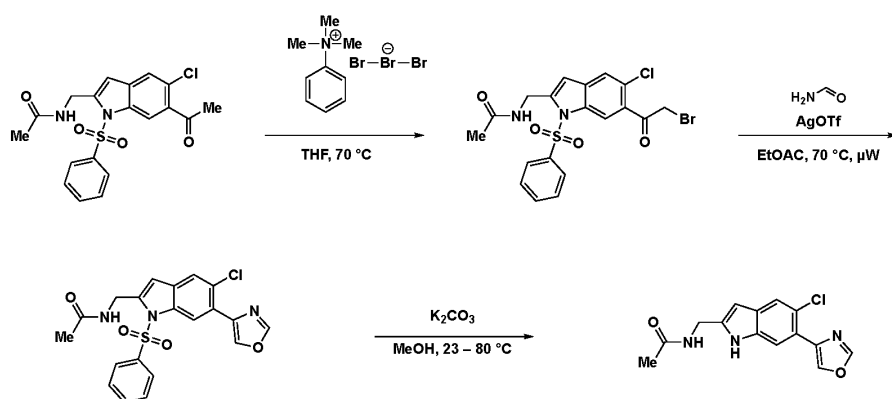
[0315] Step b: A mixture of *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (6.00g, 13.5 mmol, 1.00 eq), B₂neop₂ (30.6 g, 135 mmol, 10.0 eq), and KOAc (2.9 g, 29.8 mmol, 2.20 eq) in dioxane (60 mL) was degassed and purged with N₂. Pd(PPh₃)₂Cl₂ (1.43 g, 2.04 mmol, 0.15 eq) was added, and the resulting mixture was warmed to 120 °C and stirred for 1 h. The reaction was then cooled to room temperature and filtered through Celite. The filter cake was washed with EtOAc (50 mL), and the filtrate was concentrated under reduced pressure. The crude residue obtained was purified by column chromatography to give *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): m/z: [M + Na]⁺ calculated for C₂₂H₂₄BClN₂O₅S: 497.1; found 497.2.

[0316] Step c: In two parallel reactions, separate mixtures of *N*-((5-chloro-6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (2.60 g, 5.48 mmol, 1.00 eq), 2-bromo-5-methoxypyrazine (108 mg, 1.27 mmol, 5.00 eq), and K₂CO₃ (2.27 g, 16.4 mmol, 3.00 eq) in dioxane (26 mL) and H₂O (5 mL) were degassed and purged with N₂. Pd(PPh₃)₄ (1.27 g, 1.10 mmol, 0.20 eq) was then added in one portion. The reaction mixtures were further degassed and purged with N₂. The resulting mixture was warmed to 100 °C and stirred for 1 h. The reactions were then cooled to room temperature, and the two reactions were combined. The resulting mixture was quenched by addition of H₂O (20 mL). The resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The crude residue obtained was

trituted with MTBE (10 mL) at 23 °C for 30 min. The resulting solid was then filtered to give *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₂H₁₉ClN₄O₄S: 471.1; found 471.1.

[0317] Step d: To a solution of *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (2.9 g, 6.16 mmol, 1.00 eq) in THF (20 mL) and MeOH (20 mL) was added Cs₂CO₃ (6.0 g, 18.4 mmol, 3.0 eq). The resulting mixture was warmed to 80 °C and stirred for 1 h. The reaction was then cooled to room temperature and quenched by addition of H₂O (30 mL). The resulting mixture was extracted with EtOAc (2 x 30 mL). The combined organic extracts were washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude residue was recrystallized from EtOH (20 mL) to give *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.25 (s, 1 H), 8.45 (s, 1 H), 8.41 – 8.40 (m, 2H), 7.65 (s, 1 H), 7.52 (s, 1 H), 6.31 (s, 1 H), 4.41 (d, *J* = 5.6 Hz, 2 H), 3.97 (s, 3 H), 1.90 (m, 3 H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₆H₁₅ClN₄O₂: 331.1; found 331.1.

Example S-7: Synthesis of *N*-((5-chloro-6-(oxazol-4-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 84)



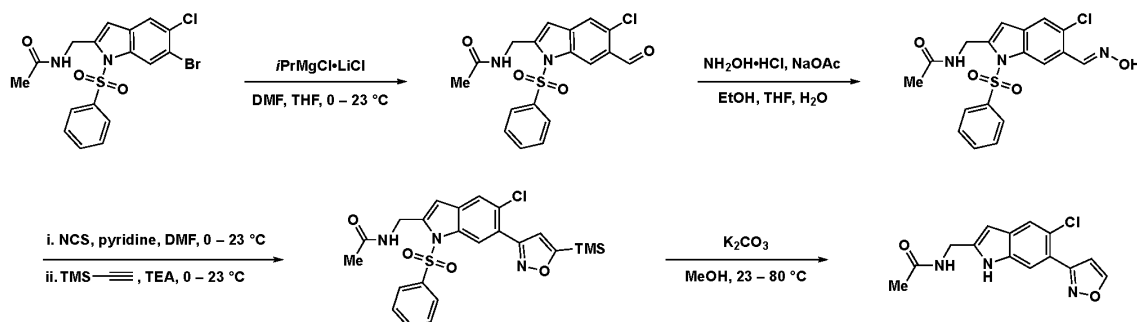
[0318] Step a: To a solution of *N*-((6-acetyl-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (500 mg, 1.23 mmol, 1.00 eq) in THF (5 mL) under N₂ was added

phenyltrimethylammonium tribromide (511 mg, 1.36 mmol, 1.10 eq). The resulting mixture was warmed to 70 °C and stirred for 1 h. The reaction mixture was then cooled to 23 °C and quenched by addition of H₂O (15 mL). The resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with brine (3 x 30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give *N*-((6-(2-bromoacetyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₉H₁₆BrClN₂O₄S: 483.0; found 483.2.

[0319] Step b: A mixture of *N*-((6-(2-bromoacetyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (200 mg, 413 μmol, 1.00 eq), AgOTf (159 mg, 620 μmol, 1.50 eq), and formamide (27.0 mg, 620 μmol, 1.50 eq) in EtOAc (3 mL) was sealed in a microwave vial. The mixture was warmed to 70 °C under microwave for 30 min. The reaction was then cooled to room temperature and quenched with the addition of H₂O (5 mL). The resulting biphasic mixture was extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine (3 x 5 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-TLC to give *N*-((5-chloro-6-(oxazol-4-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₀H₁₆ClN₃O₄S: 430.0; found 430.0.

[0320] Step c: To a solution of *N*-((5-chloro-6-(oxazol-4-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (160 mg, 372 μmol, 1.00 eq) in MeOH (2 mL) was added K₂CO₃ (103 mg, 744 μmol, 2.0 eq). The resulting mixture was warmed to 80 °C and stirred for 2 h. The reaction was then cooled to 23 °C and quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (3 x 10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude residue was purified by prep-HPLC to give *N*-((5-chloro-6-(oxazol-4-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.25 (s, 1H), 8.57 (s, 1H), 8.49 (s, 1H), 8.41 (t, *J* = 4.4 Hz, 1H), 8.03 (s, 1H), 7.62 (s, 1H), 6.27 (s, 1H), 4.40 (d, *J* = 5.6 Hz, 2H), 1.91 (s, 3H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₄H₁₂ClN₃O₂: 290.1; found 290.1.

Example S-8: Synthesis of *N*-((5-chloro-6-(oxazol-4-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 85)



[0321] Step a: To a solution of *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (3.00 g, 6.79 mmol, 1.00 eq) in THF (9 mL) at 0 °C was added *i*PrMgCl·LiCl (1.3 M in THF, 20.9 mL, 27.2 mmol, 4.0 eq). The resulting mixture was warmed to 23 °C and stirred for 1 h. The reaction mixture was cooled to 0 °C, and DMF (4.96 g, 67.9 mmol, 10.0 eq) was added dropwise. The reaction mixture was warmed to 23 °C and stirred for 1 h. The reaction mixture was then quenched by addition of saturated aqueous NH₄Cl (20 mL). The resulting mixture was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with petroleum ether (10 mL) and EtOAc (2 mL) at 23 °C for 20 min to give *N*-((5-chloro-6-formyl-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide.

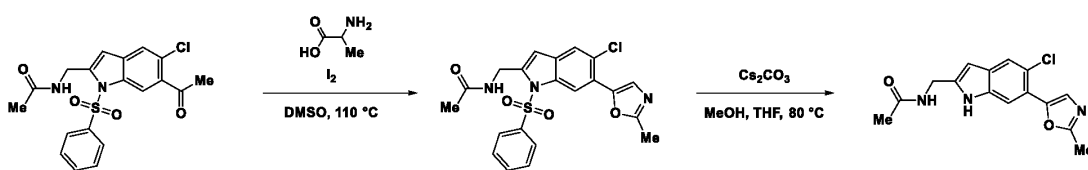
[0322] Step b: To a solution of *N*-((5-chloro-6-formyl-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (1.80 g, 4.61 mmol, 1.00 eq) in EtOH (4 mL), H₂O (4 mL) and THF (10 mL) were added hydroxylamine hydrochloride (480 mg, 6.91 mmol, 1.50 eq) and NaOAc (755 mg, 9.21 mmol, 2.00 eq). The resulting mixture was stirred at 23 °C for 3 h. The reaction mixture was then quenched by the addition of H₂O (10 mL). The resulting biphasic mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give *N*-((5-chloro-6-((hydroxyimino)methyl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₈H₁₆ClN₃O₄S: 406.0; found 406.0.

[0323] Step c: To a solution of *N*-((5-chloro-6-formyl-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (300 mg, 739 μmol, 1.00 eq) in DMF (5 mL) at 0 °C were added NCS (118 mg, 887 μmol, 1.20 eq) and pyridine (3.63 mg, 45.8 μmol, 0.06 eq). The resulting mixture was warmed to 23 °C and stirred for 12 h. The reaction mixture was then cooled to 0

°C. Trimethylsilylacetylene (123 mg, 1.26 mmol, 1.70 eq) and triethylamine (78.5 mg, 776 μ mol, 1.05 eq) were then added, and the reaction was warmed to 23 °C for 3 h. The reaction was then quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude residue was purified by column chromatography to give *N*-((5-chloro-1-(phenylsulfonyl)-6-(5-(trimethylsilyl)isoxazol-3-yl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₃H₂₄ClN₃O₄SSi: 502.1; found 502.2.

[0324] Step d: To a solution of *N*-((5-chloro-1-(phenylsulfonyl)-6-(5-(trimethylsilyl)isoxazol-3-yl)-1*H*-indol-2-yl)methyl)acetamide (200 mg, 398 μ mol, 1.00 eq) in MeOH (2 mL) was added K₂CO₃ (110 mg, 796 μ mol, 2.0 eq). The resulting mixture was warmed to 80 °C and stirred for 1 h. The reaction was then cooled to 23 °C and quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude residue was purified by prep-HPLC to give *N*-((5-chloro-6-(oxazol-4-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.32 (s, 1H), 9.01 (d, *J* = 2.0 Hz, 1H), 8.42 (t, *J* = 5.6 Hz, 1H), 7.69 (s, 1H), 7.62 (s, 1H), 6.94 (s, 1H), 6.33 (s, 1H), 4.42 (d, *J* = 5.6 Hz, 2H), 1.90 (s, 3H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₄H₁₂ClN₃O₂: 290.1; found 290.1.

Example S-9: Synthesis of *N*-((5-chloro-6-(2-methyloxazol-5-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 87)

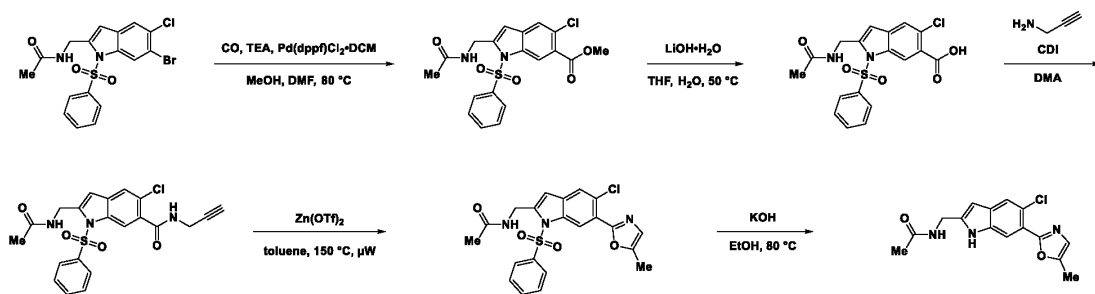


[0325] Step a: A mixture of *N*-((6-acetyl-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (3.00 g, 6.79 mmol, 1.00 eq) and I₂ (501 mg, 1.98 mmol, 2.00 eq) in DMSO (4 mL) was degassed and purged with N₂. The reaction mixture was then warmed to 110 °C and stirred for 1 h, followed by addition of 2-aminopropanoic acid (176 mg, 1.98 mmol, 2.0 eq) at 110 °C. The resulting mixture was stirred at 110 °C for 1 h. The reaction

mixture was cooled to 23 °C and quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained triturated with MTBE (1 mL) at 23 °C for 30 min to give *N*-((5-chloro-6-(2-methyloxazol-5-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₁H₁₈ClN₃O₄S: 444.1; found 444.2.

[0326] Step b: To a solution of *N*-((5-chloro-6-(2-methyloxazol-5-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (200 mg, 450 μmol, 1.00 eq) in MeOH (0.5 mL) and THF (0.5 mL) was added Cs₂CO₃ (440 mg, 1.35 mmol, 3.0 eq). The resulting mixture was warmed to 80 °C and stirred for 2 h. The reaction was then cooled to 23 °C and quenched by addition of H₂O (2 mL). The resulting mixture was extracted with EtOAc (3 x 2 mL). The combined organic extracts were washed with brine (2 x 2 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting crude residue was purified by prep-HPLC to give *N*-((5-chloro-6-(2-methyloxazol-5-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.25 (s, 1H), 8.41 (t, *J* = 5.6 Hz, 1H), 7.71 (s, 1H), 7.65 (s, 1H), 7.48 (s, 1H), 6.28 (s, 1H), 4.41 (d, *J* = 5.6 Hz, 2H), 2.50 (s, 3H), 1.89 (s, 3H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₅H₁₄ClN₃O₂: 304.0; found 304.0.

Example S-10: Synthesis of *N*-((5-chloro-6-(5-methyloxazol-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 86)



[0327] Step a: To a solution of *N*-((6-bromo-5-chloro-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (2.3 g, 5.21 mmol, 1.00 eq) in MeOH (30 mL) and DMF (6 mL) was added TEA (737 mg, 7.29 mmol, 1.40 eq). The reaction mixture was then degassed and purged with CO three times. Pd(PPh₃)₂Cl₂·DCM (425 mg, 520 μmol, 0.1 eq) was then added,

and the resulting reaction mixture was warmed to 80 °C and stirred for 16 h under CO (50 psi). The reaction mixture was then cooled to 23 °C and quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (2 x 20 mL). The combined organic extracts were washed with brine (40 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with MTBE (30 mL) at 23 °C for 10 min. The mixture was then filtered to give methyl 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indole-6-carboxylate. LC-MS (ESI): m/z: [M + H]⁺ calculated for C₁₉H₁₇ClN₂O₅S: 421.1; found 421.0.

[0328] Step b: To a solution of methyl 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indole-6-carboxylate (2.1 g, 3.74 mmol, 1.00 eq) in THF (20 mL) and H₂O (10 mL) was added LiOH•H₂O (314 mg, 7.48 mmol, 2.0 mmol). The resulting mixture was warmed to 50 °C and stirred for 5 h. The reaction was then cooled to 23 °C and quenched with H₂O (2 mL). The resulting mixture was washed with EtOAc (2 x 10 mL). The aqueous layer was adjusted to pH = 1 with aqueous HCl (1 M, 2 mL). The aqueous layer was then extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indole-6-carboxylic acid. LC-MS (ESI): m/z: [M + H]⁺ calculated for C₁₈H₁₅ClN₂O₅S: 407.1; found 407.2.

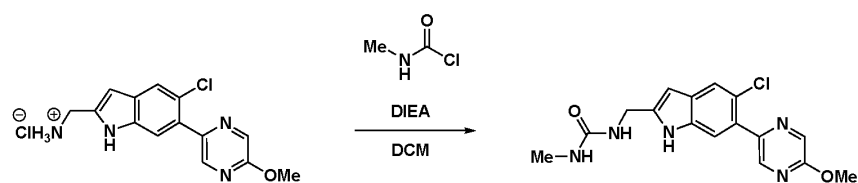
[0329] Step c: To a solution of 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-1*H*-indole-6-carboxylic acid (1.20 g, 1.47 mmol, 1.00 eq) in DMA (15 mL) was added CDI (358 mg, 2.21 mmol, 1.50 eq). The resulting mixture was stirred at 23 °C for 30 min. Prop-2-yn-1-amine (243 mg, 4.42 mmol, 3.00 eq) was then added and the reaction was stirred at 23 °C for 30 min. The reaction was then quenched by addition of H₂O (5 mL). The resulting mixture was extracted with EtOAc (2 x 20 mL). The combined organic extracts were washed with brine (40 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was triturated with EtOAc (10 mL) at 23 °C for 30 min. The resulting solid was then filtered to give 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-*N*-(prop-2-yn-1-yl)-1*H*-indole-6-carboxamide. LC-MS (ESI): m/z: [M + H]⁺ calculated for C₂₁H₁₈ClN₃O₄S: 444.1; found 444.1.

[0330] Step d: In three parallel reactions, mixtures of 2-(acetamidomethyl)-5-chloro-1-(phenylsulfonyl)-*N*-(prop-2-yn-1-yl)-1*H*-indole-6-carboxamide (100 mg, 225 μmol, 1.00 eq)

and $\text{Zn}(\text{OTf})_2$ (16.3 mg, 45.0 μmol , 0.20 eq) in toluene (3 mL) were sealed in microwave vials. The resulting mixtures were warmed to 150 °C under microwave for 1 h. The reaction mixtures were then cooled to 23 °C and the three reaction mixtures were combined. The resulting mixture was quenched by addition of H_2O (2 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The resulting crude residue was purified by column chromatography to give *N*-((5-chloro-6-(5-methyloxazol-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): m/z : $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{21}\text{H}_{18}\text{ClN}_3\text{O}_4\text{S}$: 444.1; found 444.0.

[0331] Step e: To a solution *N*-((5-chloro-6-(5-methyloxazol-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)acetamide (200 mg, 450 μmol , 1.00 eq) in EtOH (1 mL) was added KOH (50.5 mg, 901 μmol , 2.0 eq). The resulting mixture was warmed to 80 °C and stirred for 1 h. The reaction was then cooled to room temperature and quenched with H_2O (2 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (40 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to give *N*-((5-chloro-6-(5-methyloxazol-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.34 (s, 1H), 8.42 (t, $J = 5.6$ Hz, 1H), 7.84 (s, 1H), 7.65 (s, 1H), 6.99 (s, 1H), 6.32 (s, 1H), 4.41 (d, $J = 5.6$ Hz, 2H), 2.38 (s, 3H), 1.90 (s, 3H). LC-MS (ESI): m/z : $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{15}\text{H}_{14}\text{ClN}_3\text{O}_2$: 304.1; found 304.1.

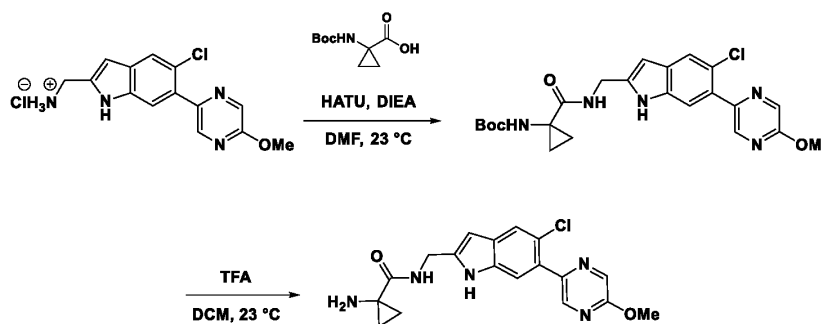
Example S-11: Synthesis of 1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-methylurea (Compound 76)



[0332] Step a: To a solution of (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanaminium chloride (80.0 mg, 246 μmol , 1.0 eq) in DCM (1.00 mL) were added DIEA (95.3 mg, 738 μmol , 3.0 eq) and *N*-methylcarbamoyl chloride (34.5 mg, 369 μmol , 1.5 eq) dropwise. The reaction mixture was then stirred at 20 °C for 1 h. The reaction mixture

was then quenched with H₂O (10 mL) at 23 °C, and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue obtained was purified by prep-HPLC to give 1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-methylurea. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.19 (s, 1H), 8.44 (s, 1H), 8.40 (s, 1H), 7.63 (s, 1H), 7.52 (s, 1H), 6.40 (t, *J* = 6.0 Hz, 1H), 6.27 (s, 1H), 5.90 (d, *J* = 4.4 Hz, 1H), 4.35 (d, *J* = 5.6 Hz, 2H), 3.97 (s, 3H), 2.59 (d, *J* = 4.8 Hz, 3H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₆H₁₆ClN₅O₂: 346.1; found 346.2.

Example S-12: Synthesis of 1-amino-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)cyclopropane-1-carboxamide (Compound 170)

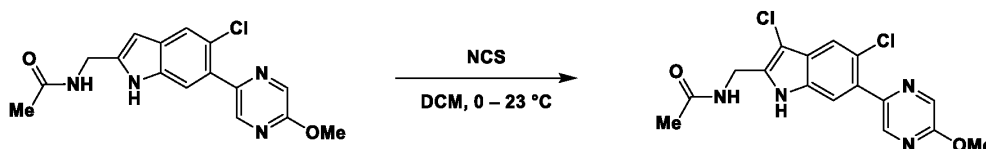


[0333] Step a. To a solution of 1-((*tert*-butoxycarbonyl)amino)cyclopropane-1-carboxylic acid (185 mg, 922 μmol, 1.50 eq) in DMF (2 mL) was added HATU (350 mg, 922 μmol, 1.50 eq). The reaction mixture was stirred at 23 °C for 0.5 h. Then, (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanaminium chloride (200 mg, 615 μmol, 1.00 eq) and DIEA (238 mg, 1.85 mmol, 3.00 eq) were added and the reaction mixture was stirred at 23 °C for 1 h. The reaction mixture was quenched by addition of H₂O (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC to give *tert*-butyl (1-(((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamoyl)cyclopropyl)carbamate. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₃H₂₆ClN₅O₄: 472.17; found 472.2.

[0334] Step b. To a solution of *tert*-butyl (1-(((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamoyl)cyclopropyl)carbamate (100 mg, 212 μmol, 1.00 eq) in DCM (2 mL)

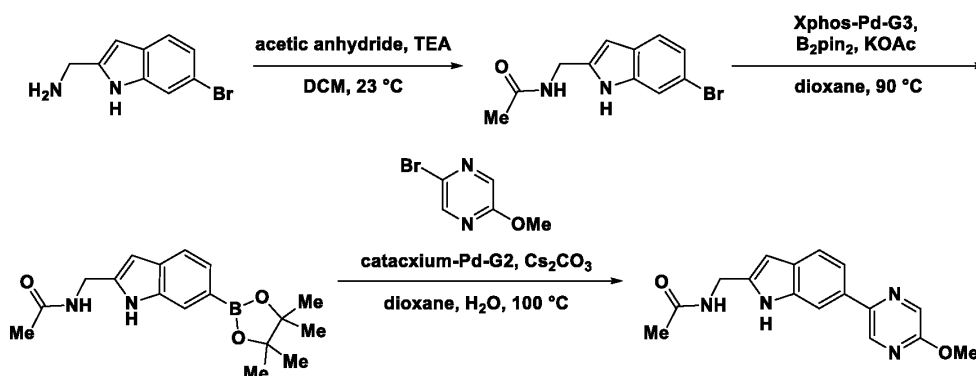
was added TFA (0.5 mL) in one portion. The reaction mixture was stirred at 23 °C for 1 h. The reaction mixture was concentrated under reduced pressure and then diluted with EtOAc (2 mL). The organic layer was washed with saturated aqueous NaHCO₃ solution (2 x 2 mL) and then concentrated under reduced pressure. The residue was purified by prep-HPLC to give 1-amino-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)cyclopropane-1-carboxamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.24 (s, 1H), 8.57 (t, *J* = 6.0 Hz, 1H), 8.44 (s, 1H), 8.41 (s, 1H), 7.65 (s, 1H), 7.53 (s, 1H), 6.31 (s, 1H), 4.46 (d, *J* = 5.6 Hz, 2H), 3.97 (s, 3H), 2.35 – 2.32 (m, 2H), 1.10 – 1.08 (m, 2H), 0.78 – 0.76 (m, 2H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₈H₁₈ClN₅O₂: 372.12; found 372.1.

Example S-13: Synthesis of *N*-((3,5-dichloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 167)



[0335] Step a. To a solution of *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide (40 mg, 0.12 mmol, 1.00 eq) in DCM (0.6 mL) at 0 °C was added *N*-chlorosuccinimide (8.1 mg, 0.06 mmol, 0.5 eq). The reaction mixture warmed to room temperature and stirred for 16 h. The reaction mixture was then quenched with saturated aqueous ammonium chloride (0.5 mL). The aqueous phase was extracted with EtOAc (3 x 0.5 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by prep- to give *N*-((3,5-dichloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 11.64 (s, 1H), 8.49 – 8.44 (m, 2H), 8.42 (d, *J* = 1.5 Hz, 1H), 7.60 (s, 1H), 7.57 (s, 1H), 4.44 (d, *J* = 5.5 Hz, 2H), 3.98 (s, 3H), 1.89 (s, 3H). LC-MS (ESI) *m/z*: [M + H]⁺ calculated for C₁₆H₁₄Cl₂N₄O₂: 365.1; found: 365.2.

Example S-14: Synthesis of *N*-((6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide (Compound 302)



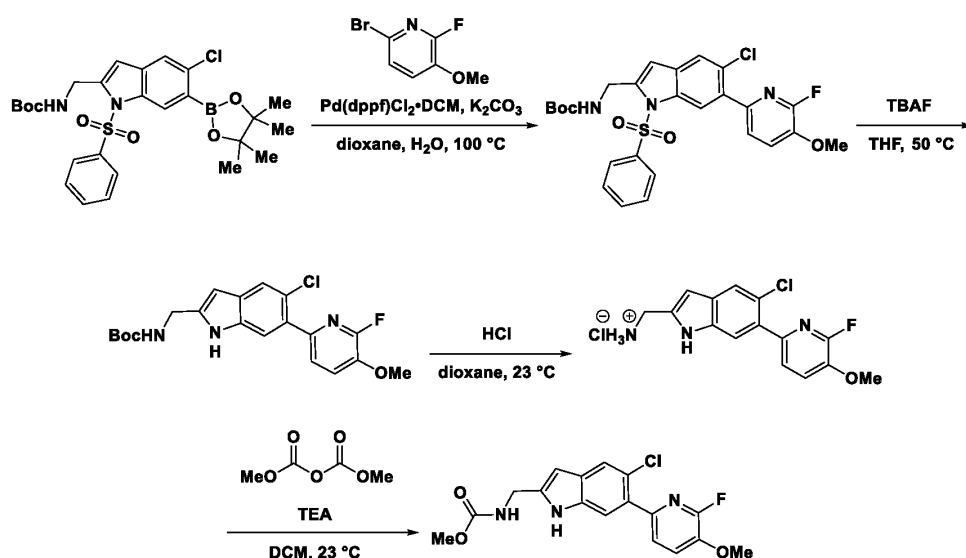
[0336] Step a. To a solution of (6-bromo-1*H*-indol-2-yl)methanamine (440 mg, 2.0 mmol, 1.0 eq) in DCM (7 mL) was added triethylamine (0.82 mL, 5.9 mmol, 3.0 eq) and then acetic anhydride (0.37 mL, 3.9 mmol, 2.0 eq) dropwise at 23 °C. The solution was stirred for 1 h at 23 °C. The solution was then poured onto dry silica and purified by column chromatography to give *N*-((6-bromo-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₁H₁₂BrN₂O: 267.01; found 266.9.

[0337] Step b. A mixture of *N*-((6-bromo-1*H*-indol-2-yl)methyl)acetamide (440 mg, 1.6 mmol, 1.0 eq), bispinacolatodiboron (840 mg, 3.3 mmol, 2.0 eq), potassium acetate (320 mg, 3.3 mmol, 2.0 eq), and Xphos-Pd-G3 (70 mg, 0.08 mmol, 0.05 eq) was dissolved in dioxane (8 mL). The reaction mixture was warmed to 90 °C and stirred for 2 h. The reaction mixture was cooled to room temperature and quenched with H₂O (30 mL). The resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic extracts were concentrated under reduced pressure to give a residue. The resulting crude residue was purified by column chromatography to give *N*-((6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)acetamide. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₇H₂₄BN₂O₃: 315.19; found 315.2.

[0338] Step c. To a solution of *N*-((6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)acetamide (55 mg, 0.18 mmol, 1.0 eq) in dioxane (0.44 mL) and water (0.1 mL) was added 2-bromo-5-methoxypyrazine (40 mg, 0.21 mmol, 1.2 eq), cesium carbonate (86 mg, 0.26 mmol, 1.5 eq), and catacxium-Pd-G2 (6 mg, 0.009 mmol, 0.05 eq). The reaction mixture was degassed and sparged with N₂ for 10 min. The reaction mixture was warmed to 90 °C and stirred for 1 h. The reaction mixture was cooled to room temperature and was then

diluted with DMSO (3 mL). The mixture was filtered, and the filtrate was purified by prep-HPLC to give *N*-((6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)acetamide. ¹H NMR (500 MHz, DMSO-*d*₆) δ 11.03 (s, 1H), 8.68 (d, *J* = 1.5 Hz, 1H), 8.33 – 8.27 (m, 2H), 7.92 (s, 1H), 7.57 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 6.25 – 6.21 (m, 1H), 4.34 (d, *J* = 5.6 Hz, 2H), 1.83 (s, 3H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₆H₁₇N₄O₂: 297.13; found 297.0.

Example S-15: Synthesis of methyl *N*-((5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-1*H*-indol-2-yl)methyl)carbamate (Compound 142)



[0339] Step a. To a solution of *tert*-butyl ((5-chloro-1-(phenylsulfonyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-2-yl)methyl)carbamate (14.0 g, 25.6 mmol, 1.00 eq) in dioxane (112 mL) was added 6-bromo-2-fluoro-3-methoxypyridine (5.27 g, 25.6 mmol, 1.00 eq) in one portion. Then, a solution of K₂CO₃ (10.6 g, 76.8 mmol, 3.00 eq) in H₂O (28 mL) was added dropwise. The mixture was degassed and purged with N₂ three times, and then Pd(dppf)Cl₂·CH₂Cl₂ (2.09 g, 2.56 mmol, 0.10 eq) was added in one portion. The reaction mixture was degassed and purged with N₂ three times and stirred at 100 °C for 1 h. The reaction mixture was then cooled to room temperature, diluted with H₂O (100 mL) and extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine (2 x 20 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a

residue. The residue was triturated with petroleum ether and methyl *tert*-butyl ether (50 mL, V/V = 1/1) at 23 °C for 30 min and then filtered. The filter cake was collected to give *tert*-butyl ((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₆H₂₆ClFN₃O₅S: 546.13; found 546.2.

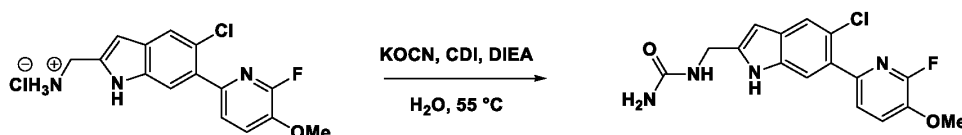
[0340] Step b. To a solution of *tert*-butyl ((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1-(phenylsulfonyl)-1*H*-indol-2-yl)methyl)carbamate (14.3 g, 26.3 mmol, 1.00 eq) in THF (143 mL) was added TBAF (1 M in THF, 131 mL, 5.00 eq) dropwise at 23 °C. The reaction mixture was warmed to 50 °C and stirred for 1 h. The reaction mixture was then cooled to room temperature, washed with saturated aqueous NH₄Cl solution (6 x 50 mL) and brine (2 x 50 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The resulting crude residue was purified by column chromatography to give *tert*-butyl ((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1*H*-indol-2-yl)methyl)carbamate. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₂₀H₂₂ClFN₃O₃: 406.13; found 406.1.

[0341] Step c. To a solution *tert*-butyl ((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1*H*-indol-2-yl)methyl)carbamate (12.0 g, 29.5 mmol, 1.00 eq) in dioxane (12 mL) was added HCl (4 M in dioxane, 120 mL) dropwise. The reaction mixture was then stirred at 23 °C for 30 min. The reaction mixture was then concentrated under reduced pressure to give (5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1*H*-indol-2-yl)methanamine hydrochloride, which was used for next step directly without further purification. LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₅H₁₄ClFN₃O: 306.08; found 306.1.

[0342] Step d. To a solution of (5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-1*H*-indol-2-yl)methanamine hydrochloride (100 mg, 292 μmol, 1.00 eq) in DCM (1 mL) was added TEA (147 mg, 1.46 mmol, 5.00 eq) and methoxycarbonyl methyl carbonate (43.1 mg, 321 μmol, 1.10 eq) dropwise, the reaction mixture was stirred at 23 °C for 1 h. The reaction mixture was then poured into H₂O (10 mL) and stirred for 5 min. The aqueous phase was then extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (2 x 10 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The crude residue was purified by prep-HPLC to give methyl *N*-((5-chloro-6-(6-fluoro-5-methoxy-2-pyridyl)-1*H*-indol-2-yl)methyl)carbamate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.20 (s, 1H), 7.74 – 7.70 (m, 2 H), 7.61 (s, 1 H), 7.55 (d, *J* = 8.4 Hz, 1 H), 7.49 (s, 1

H), 6.27 (s, 1 H), 4.35 (d, $J = 5.6$ Hz, 2 H), 3.93 (s, 3 H), 3.58 (s, 3H). LC-MS (ESI): m/z : $[M + H]^+$ calculated for $C_{17}H_{16}ClFN_3O_3$: 364.09; found 363.9.

Example S-16: Synthesis of 1-((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)urea (Compound 121)



[0343] Step a. To a solution of (5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1H-indol-2-yl)methanamine hydrochloride (150 mg, 0.44 mmol, 1.00 eq) in H_2O (2.0 mL) was added potassium cyanate (39.1 mg, 0.48 mmol, 1.10 eq). The reaction mixture was then warmed to 55 °C. After 16 hours the reaction mixture was cooled to 23 °C, poured into water (10 mL), and stirred for an additional 5 minutes. The aqueous solution was then extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (2 x 10 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to give a residue. The resulting crude residue was purified by prep-HPLC to give 1-((5-chloro-6-(6-fluoro-5-methoxypyridin-2-yl)-1H-indol-2-yl)methyl)urea. 1H NMR (400 MHz, $DMSO-d_6$) δ 11.17 (s, 1H), 7.74 – 7.70 (m, 1 H), 7.61 (s, 1 H), 7.55 (d, $J = 8.0$ Hz, 1 H), 7.49 (s, 1 H), 6.43 (t, $J = 6.0$ Hz, 1 H), 6.26 (s, 1 H), 5.61 (s, 2 H), 4.33 (t, $J = 6.0$ Hz, 2 H), 3.93 (s, 3 H). LC-MS (ESI) m/z : $[M + H]^+$ calculated for $C_{16}H_{14}ClFN_4O_2$: 349.1; found: 349.1.

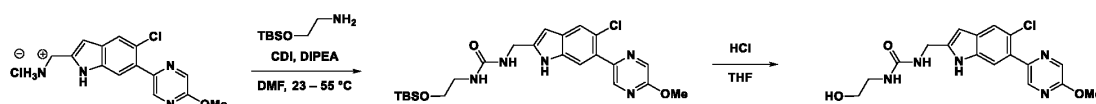
Example S-17: Synthesis of 3-((5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methyl)-1-cyclopropyl-1-methylurea (Compound 130)



[0344] Step a. To a solution of (5-chloro-6-(5-methoxypyrazin-2-yl)-1H-indol-2-yl)methanamine hydrochloride (120 mg, 0.37 mmol, 1.00 eq) in DMF (1.2 mL) was added CDI (120 mg, 0.37 mmol, 1.00 eq). After 30 minutes *N*-methylcyclopropanamine (52.4 mg, 0.74 mmol, 2.00 eq) was added in one portion and the resulting reaction mixture was stirred for 1 h at 23 °C. The reaction mixture was then quenched by addition of H_2O (5 mL). The

mixture was then extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The crude residue was purified by prep-HPLC to give 3-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-1-cyclopropyl-1-methylurea. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.13 (s, 1H), 8.44 – 8.40 (m, 2H), 7.63 (s, 1H), 7.54 (s, 1H), 6.82 (t, *J* = 5.6 Hz, 1H), 6.26 (s, 1H), 4.42 (d, *J* = 6.0 Hz, 2H), 3.97 (s, 3H), 2.78 (s, 3H), 2.47 – 2.46 (m, 1H), 0.82 – 0.77 (m, 2H), 0.65 – 0.62 (m, 2H). LC-MS (ESI) *m/z*: [M + H]⁺ calculated for C₁₉H₂₀ClN₅O₂: 386.1; found: 386.0.

Example S-18: Synthesis of 1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-(2-hydroxyethyl)urea (Compound 223)

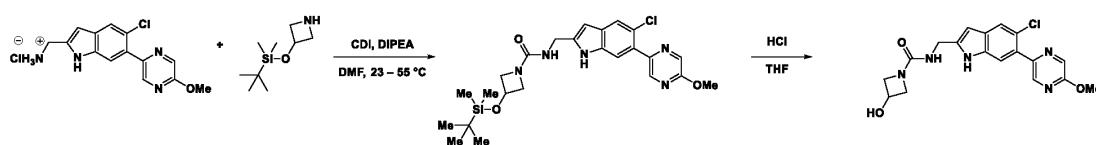


[0345] Step a. To a solution of (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanamine hydrochloride (150 mg, 0.46 mmol, 1.00 eq) in DMF (1.0 mL) was added DIEA (179 mg, 1.38 mmol, 3.00 eq) and CDI (112 mg, 0.69 mmol, 1.50 eq). After 30 minutes 2-[*tert*-butyl(dimethyl)silyl] oxyethanamine (121 mg, 692 μmol, 1.50 eq) was added in one portion. The reaction mixture was then warmed to 55 °C and stirred for 12 h. The reaction mixture was then cooled to room temperature and quenched by addition of H₂O (10 mL). The mixture was extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with brine (2 x 20 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give 1-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-3-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)urea which was used without further purification. LC-MS (ESI) *m/z*: [M + H]⁺ calculated for C₂₃H₃₂ClN₅O₃Si: 490.2; found: 490.2.

[0346] Step b: To a solution of 1-[2-[*tert*-butyl(dimethyl) silyl] oxyethyl]-3- [[5-chloro-6-(5-methoxypyrazin -2-yl)-1*H*-indol-2-yl] methyl] urea (226 mg, 416 μmol, 1.00 eq) in THF (4 mL) was added aqueous HCl (2 M, 1.0 mL, 4.33 eq) in one portion. After 10 minutes at 23 °C the reaction mixture pH was adjusted to 7–8 with saturated aqueous NaHCO₃. The resulting mixture was extracted with EtOAc (5 mL). The organic extracts were concentrated

under reduced pressure to give a residue. The crude residue was purified by prep-HPLC to give 1-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-(2-hydroxyethyl)urea. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.21 (s, 1H), 8.44 – 8.41 (m, 2H), 7.64 (s, 1H), 7.52 (s, 1H), 6.47 (t, *J* = 5.6 Hz, 1H), 6.27 (s, 1H), 6.07 (t, *J* = 5.6 Hz, 1H), 4.67 (t, *J* = 4.8 Hz, 1H), 4.36 (d, *J* = 5.6 Hz, 2H), 3.97 (s, 3H), 3.42 – 3.38 (m, 2H), 3.13 – 3.09 (m, 2H). LC-MS (ESI) *m/z*: [M + H]⁺ calculated for C₁₇H₁₈ClN₅O₃: 376.1; found: 376.1.

Example S-19: *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-hydroxyazetidine-1-carboxamide (Compound 176)

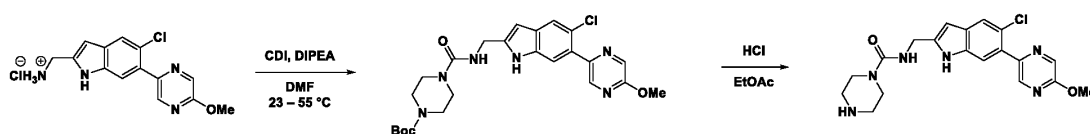


[0347] Step a. To a mixture of (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanamine (200 mg, 615 μmol, 1.10 eq, HCl salt) and DIPEA (109 mg, 839 μmol, 1.50 eq) in DMF (0.5 mL) was added CDI (90.7 mg, 559 μmol, 1.00 eq) in one portion. The reaction mixture was stirred at 23 °C for 0.5 h. Then, 3-((*tert*-butyldimethylsilyl)oxy)azetidine (419 mg, 2.24 mmol, 4.00 eq) in DMF (0.5 mL) was added in one portion. The reaction mixture was then warmed to 55 °C and stirred for 12 h. The reaction mixture was then cooled to room temperature, quenched by addition of H₂O (10 mL), and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (3 x 10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give 3-((*tert*-butyldimethylsilyl)oxy)-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)azetidine-1-carboxamide, which was used directly in next step without further purification.

[0348] Step b. To a solution of 3-((*tert*-butyldimethylsilyl)oxy)-*N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)azetidine-1-carboxamide (280 mg, 558 μmol, 1.00 eq) in THF (1 mL) was added aqueous HCl (2 M, 6.0 mL) dropwise at 23 °C. The reaction mixture was then stirred at 23 °C for 0.5 h. The reaction mixture was basified with saturated aqueous NaHCO₃ to pH = 7, then extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (3 x 10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The crude residue was purified by

reverse phase chromatography to give *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)-3-hydroxyazetidine-1-carboxamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.14 (s, 1H), 8.44 (d, *J* = 1.6 Hz, 1H), 8.41 (s, 1H), 7.63 (s, 1H), 7.53 (s, 1H), 6.87 (t, *J* = 5.6 Hz, 1H), 6.27 (s, 1H), 5.57 (d, *J* = 6.0 Hz, 1H), 4.44 – 4.36 (m, 1H), 4.34 (d, *J* = 5.6 Hz, 2H), 4.02 – 3.97 (m, 2H), 3.97 (s, 3H), 3.62 – 3.59 (m, 2H). LC-MS (ESI) *m/z*: [M + H]⁺ calculated for C₁₈H₁₉ClN₅O₃: 388.12; found: 388.2.

Example S-20: Synthesis of *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)piperazine-1-carboxamide (Compound 213)



[0349] Step a. To a mixture of (5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methanamine hydrochloride (100 mg, 308 μmol, 1.10 eq) and DIPEA (54.2 mg, 419 μmol, 1.50 eq) in DMF (0.5 mL) was added CDI (45.3 mg, 280 μmol, 1.00 eq) in one portion at 23 °C. The reaction mixture was then stirred at 23 °C for 0.5 h. Then, *tert*-butyl piperazine-1-carboxylate (52.1 mg, 280 μmol, 1.00 eq) in DMF (0.5 mL) was added in one portion at 23 °C. The reaction mixture was then heated to 55 °C and stirred for 12 h. The reaction mixture was then cooled to room temperature, quenched by addition of H₂O (5 mL), and extracted with EtOAc (3 x 8 mL). The combined organic extracts were washed with aqueous HCl (2 M, 2 x 5 mL), washed with brine (3 x 10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give *tert*-butyl 4-(((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamoyl)piperazine-1-carboxylate which was used for next step directly without of further purification.

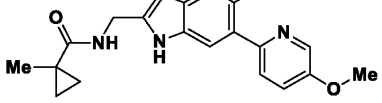
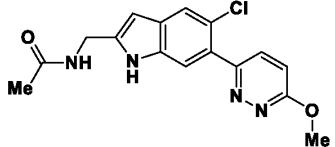
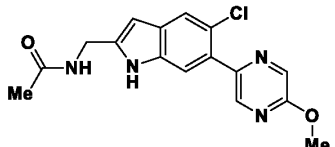
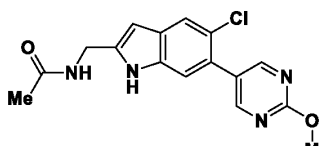
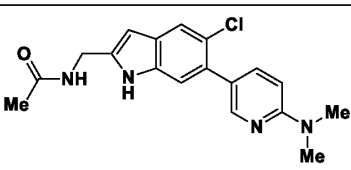
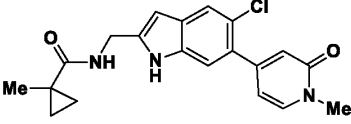
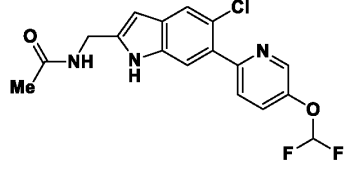
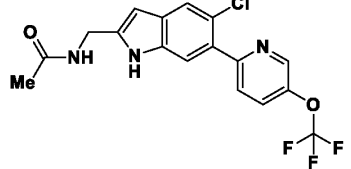
[0350] Step b. To a solution of *tert*-butyl 4-(((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl)methyl)carbamoyl)piperazine-1-carboxylate (147 mg, 293 μmol, 1.00 eq) in EtOAc (0.1 mL) was added HCl (4 M in EtOAc, 3 mL) in one portion at 23 °C. The reaction mixture was then stirred at 23 °C for 1 h. The reaction mixture was then concentrated under reduced pressure to give a residue. The resulting residue was dissolved in H₂O and adjusted to pH = 7 – 8 with saturated aqueous NaHCO₃ solution. The resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were concentrated under reduced

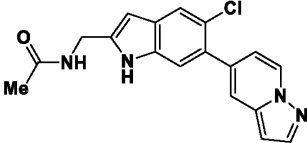
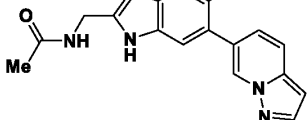
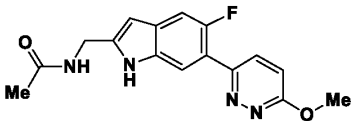
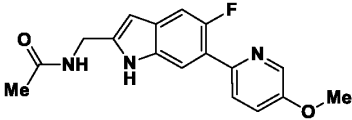
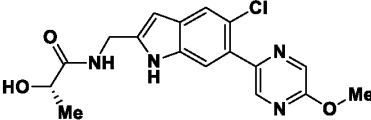
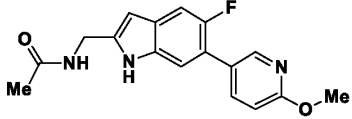
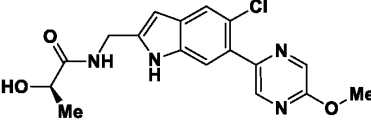
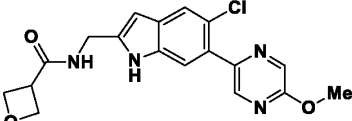
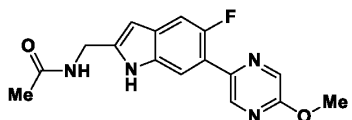
pressure to give a residue. The resulting residue was purified by prep-HPLC to give *N*-((5-chloro-6-(5-methoxypyrazin-2-yl)-1*H*-indol-2-yl) methyl) piperazine-1-carboxamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.25 (s, 1H), 8.44 (d, *J* = 1.2 Hz, 1H), 8.41 (d, *J* = 1.2 Hz, 1H), 7.63 (s, 1H), 7.54 (s, 1H), 7.08 (t, *J* = 5.6 Hz, 1H), 6.26 (s, 1H), 4.38 (d, *J* = 5.6 Hz, 2H), 3.97 (s, 3H), 3.32 – 3.25 (m, 4H), 3.26 – 3.21 (m, 1H), 2.63 (t, *J* = 4.8 Hz, 4H). LC-MS (ESI): *m/z*: [M + H]⁺ calculated for C₁₉H₂₂ClN₆O₂: 401.14; found 401.0.

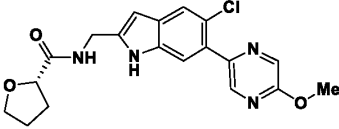
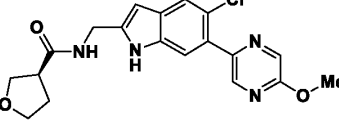
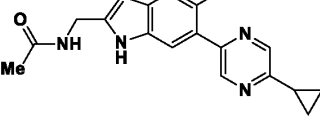
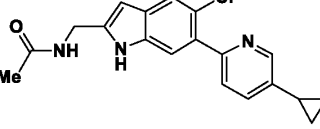
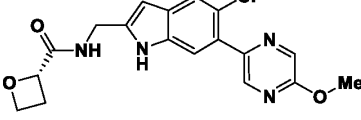
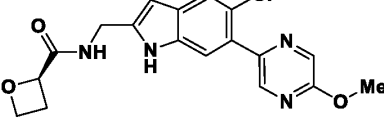
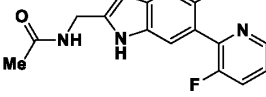
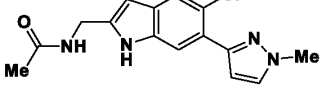
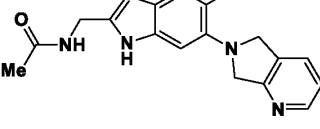
[0351] The following compounds in Table T-1 were synthesized using procedures similar to Examples S-1 through S-20 using the appropriate starting materials.

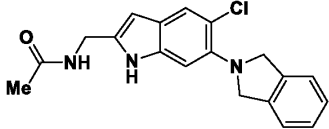
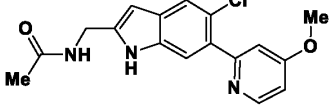
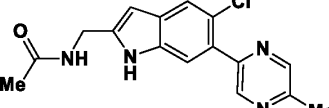
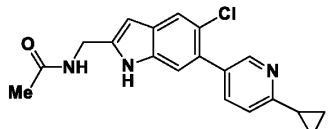
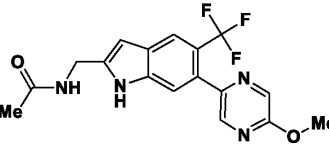
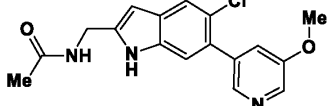
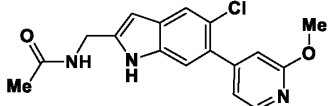
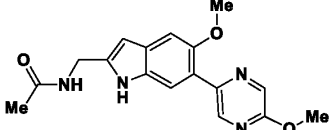
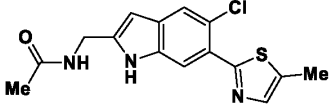
Table T-1

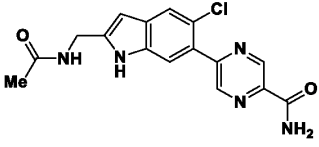
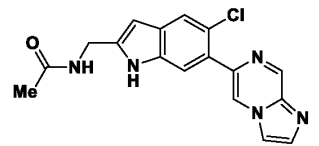
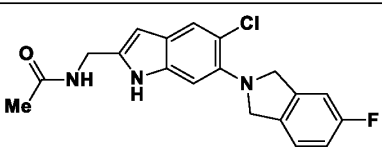
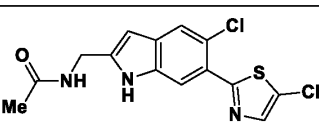
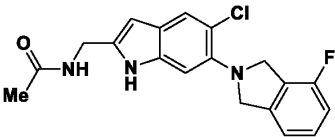
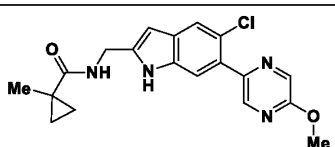
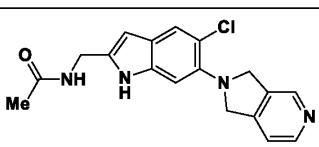
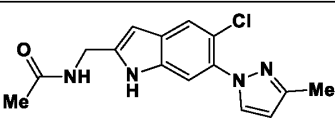
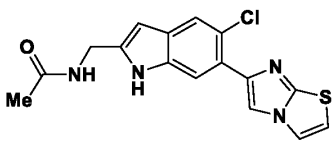
Cmpd No.	Structure	LCMS Exact Mass	LCMS Observed <i>m/z</i> [M+H] ⁺
1		369.12	369.9
2		378.12	379.2
3		377.13	378.2
4		329.09	330.2
5		329.09	330.0

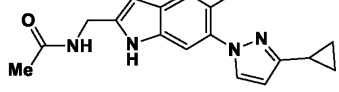
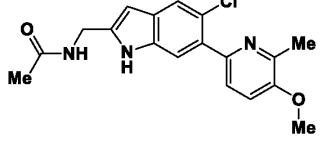
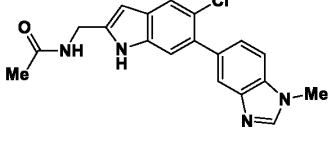
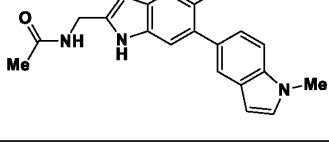
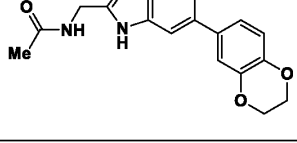
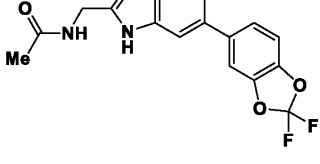
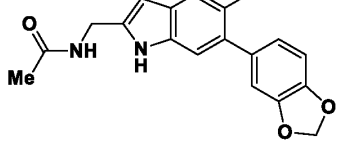
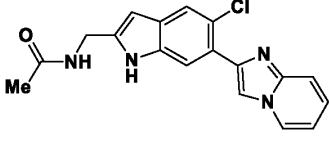
6		369.12	370.0
7		330.09	331.2
8		330.09	331.1
9		330.09	331.2
10		342.12	343.2
11		369.12	370.2
12		365.07	366.1
13		383.06	384.1

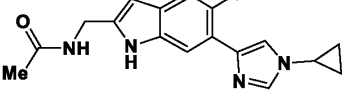
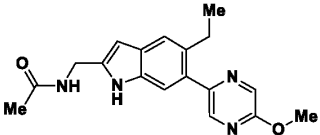
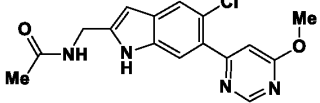
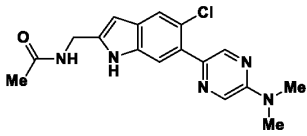
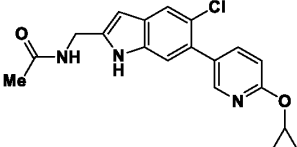
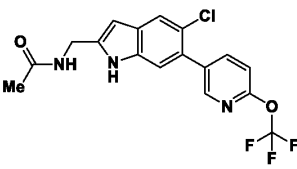
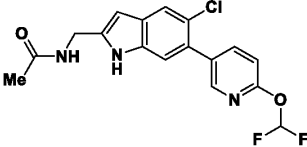
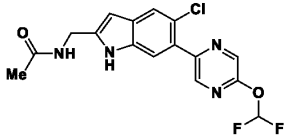
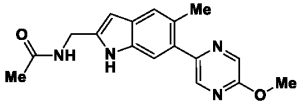
14		338.09	339.1
15		338.09	339.1
16		314.12	315.2
17		313.12	314.3
18		360.10	361.1
19		313.12	314.2
20		360.10	361.1
21		372.10	373.1
22		314.12	315.2

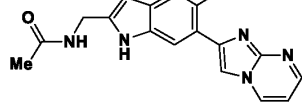
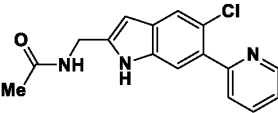
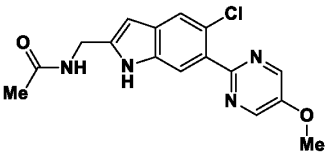
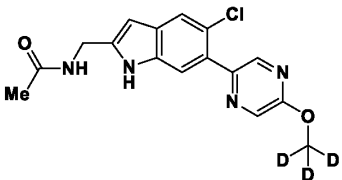
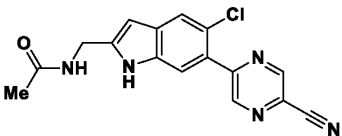
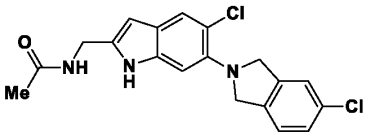
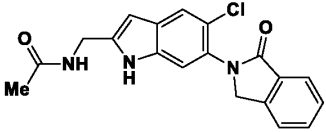
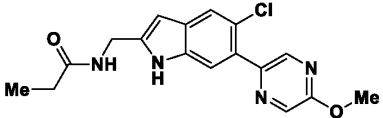
23		386.11	387.2
24		386.11	387.2
25		340.11	341.2
26		339.11	340.2
27		372.10	373.1
28		372.10	373.2
29		317.07	318.0
30		302.09	303.0
31		340.11	340.1

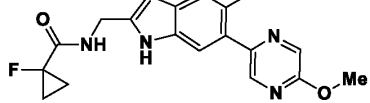
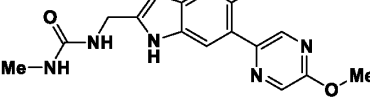
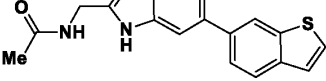
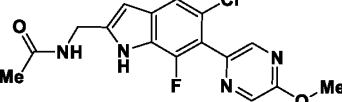
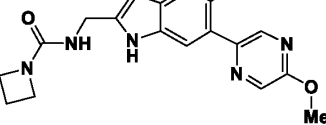
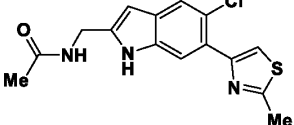
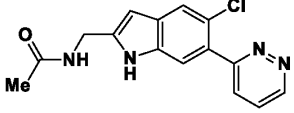
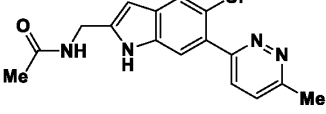
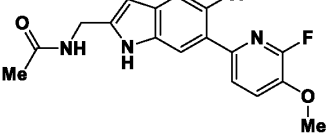
32		339.11	341.1
33		329.09	330.2
34		314.09	315.2
35		339.11	340.2
36		364.11	365.0
37		329.09	330.1
38		329.09	330.2
39		326.14	327.1
40		319.05	320.0

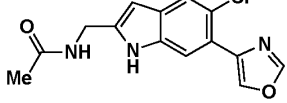
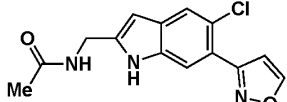
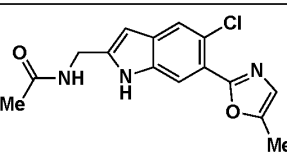
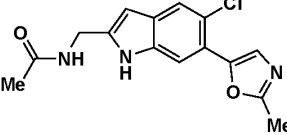
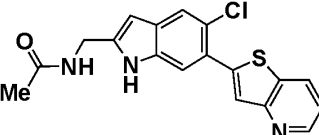
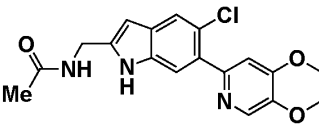
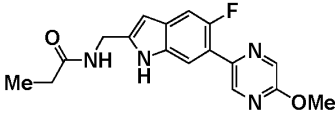
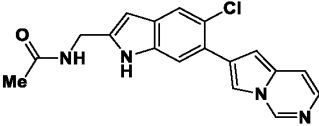
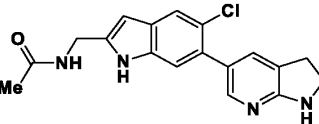
41		343.08	344.04
42		339.09	340.2
43		357.10	358.2
44		339.0	339.9
45		357.10	358.3
46		370.12	371.1
47		340.11	341.2
48		302.09	303.1
49		344.05	345.1

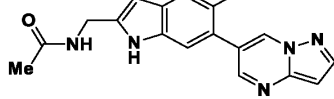
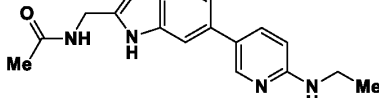
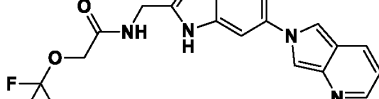
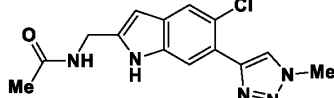
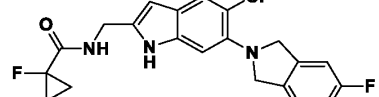
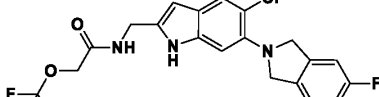
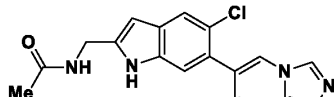
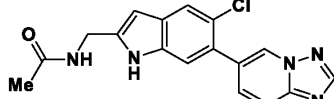
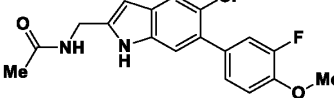
50		328.11	329.1
51		343.11	344.07
52		352.11	353.2
53		351.11	352.2
54		356.09	357.2
55		378.06	379.1
56		342.07	343.1
57		338.09	339.0

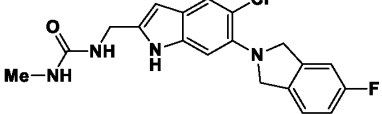
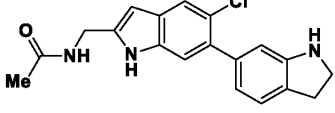
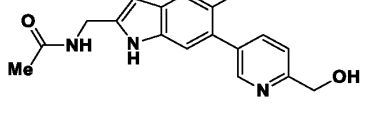
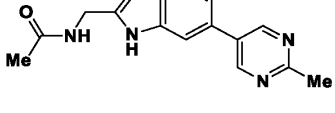
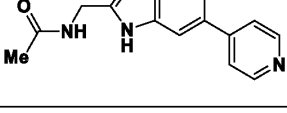
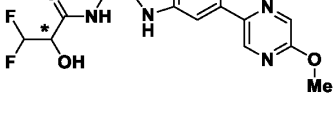
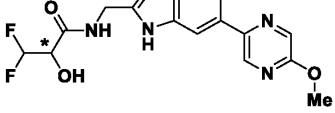
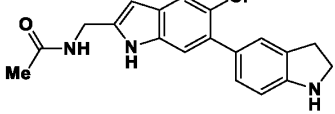
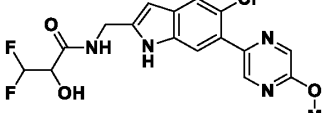
58		328.11	329.0
59		324.16	325.1
60		330.09	331.2
61		343.12	344.2
62		355.11	356.2
63		383.06	384.2
64		365.07	366.2
65		366.07	367.0
66		310.14	311.2

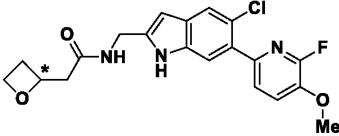
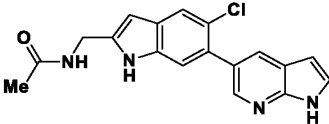
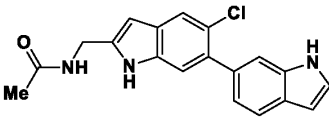
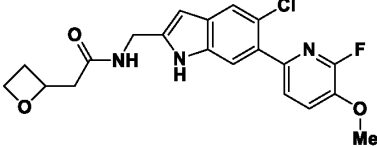
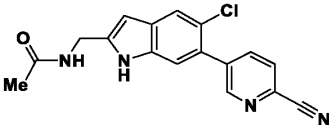
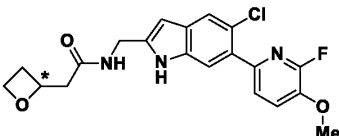
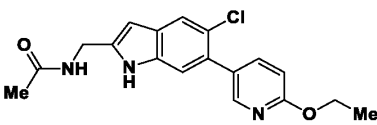
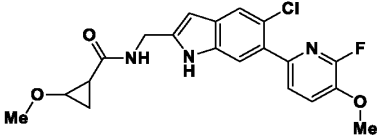
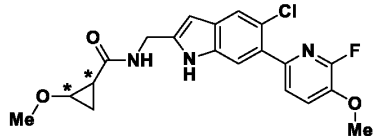
67		339.09	340.1
68		299.08	300.0
69		330.09	331.1
70		333.11	334.1
71		325.07	326.3
72		373.07	374.1
73		353.09	354.2
74		344.10	345.1

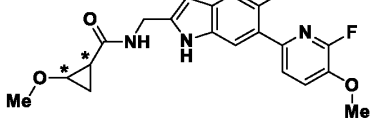
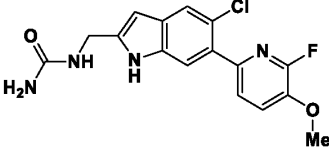
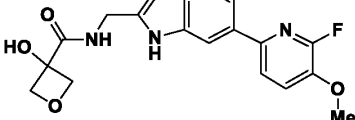
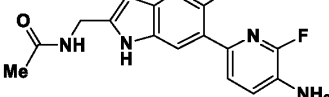
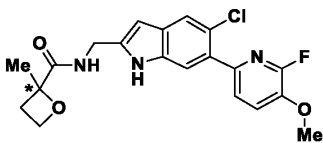
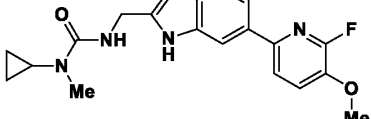
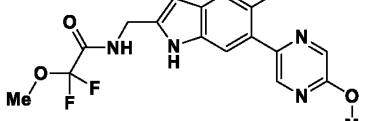
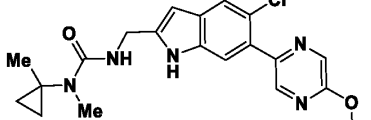
75		374.09	375.2
76		345.10	346.2
77		354.06	355.0
78		348.08	349.2
79		371.11	372.2
80		319.05	320.0
81		300.08	301.1
82		314.09	315.1
83		347.08	348.15

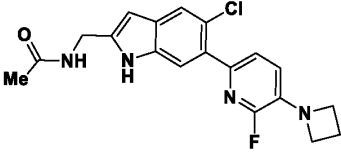
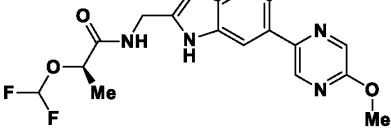
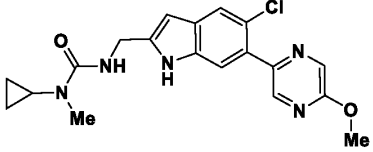
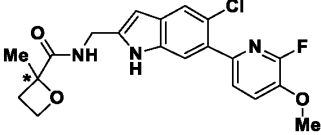
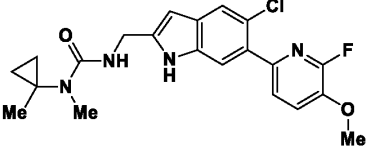
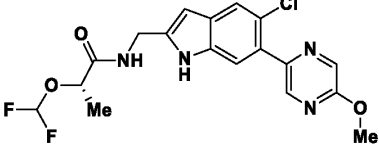
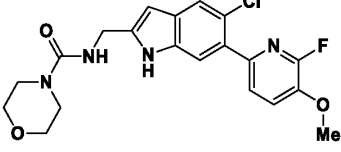
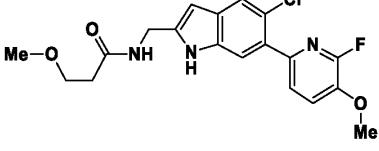
84		289.06	290.1
85		289.06	290.1
86		303.08	304.1
87		303.08	304.0
88		355.05	356.1
89		357.09	358.2
90		328.13	329.2
91		338.09	339.1
92		340.11	341.2

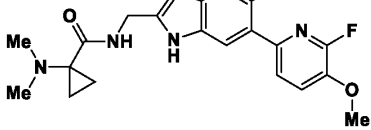
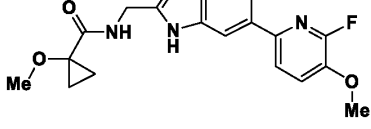
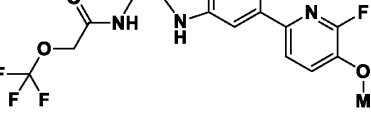
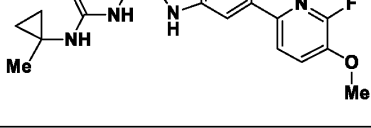
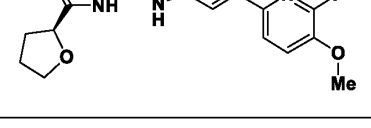
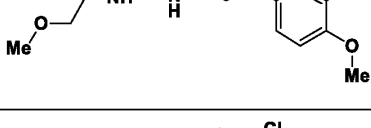
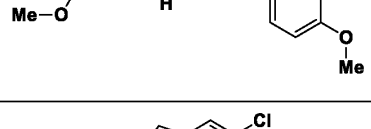
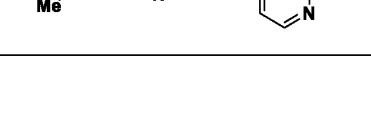
93		339.09	340.1
94		342.12	343.1
95		422.08	423.1
96		303.09	304.1
97		401.11	402.1
98		441.09	442.1
99		338.09	339.1
100		339.09	340.1
101		346.09	347.0

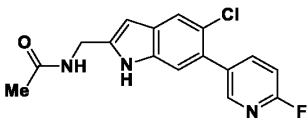
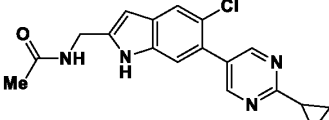
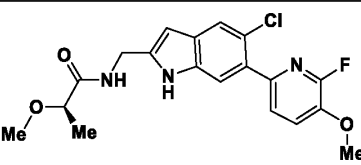
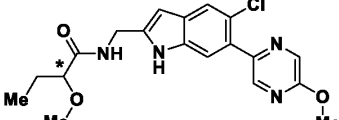
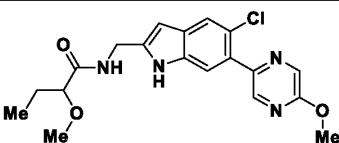
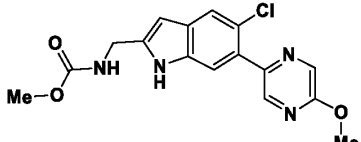
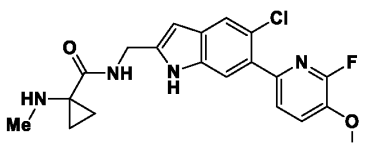
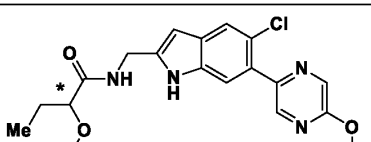
102		372.12	373.1
103		339.11	340.1
104		329.09	330.1
105		314.09	315.1
106		299.08	300.0
107		396.08	397.1
108		396.08	397.1
109		339.11	340.1
110		396.08	397.1

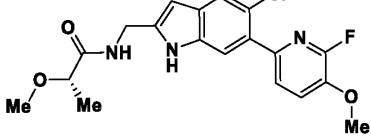
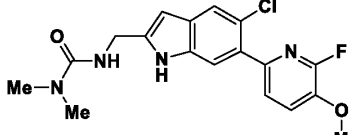
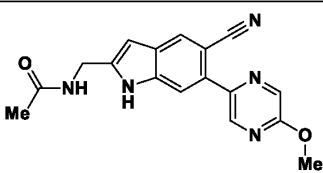
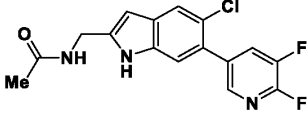
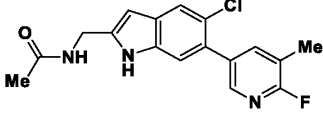
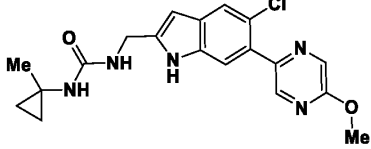
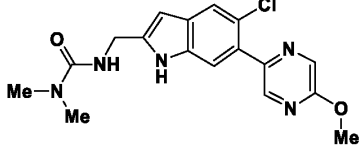
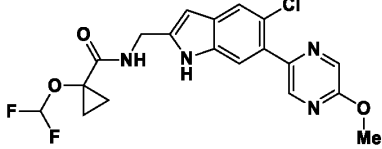
111		403.11	404.1
112		338.09	339.1
113		337.10	338.1
114		403.11	404.1
115		324.08	325.1
116		403.11	404.1
117		343.11	344.1
118		403.11	404.1
119		403.11	404.1

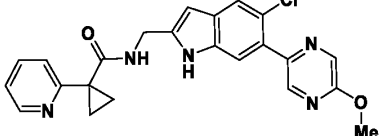
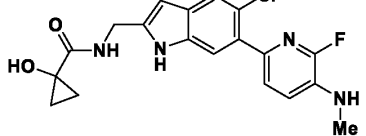
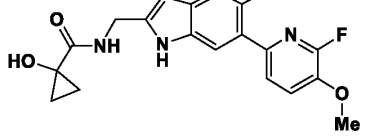
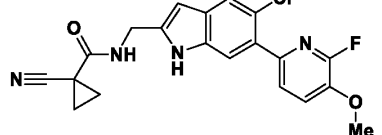
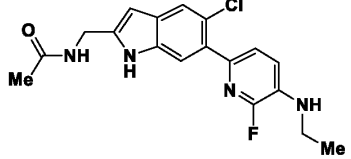
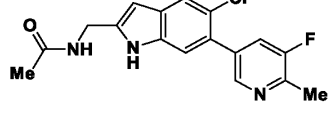
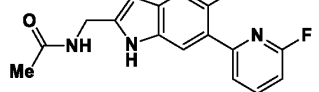
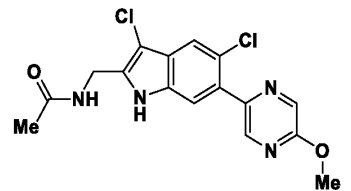
120		403.11	404.1
121		348.08	349.1
122		405.09	406.1
123		332.08	333.1
124		403.11	404.1
125		402.13	403.2
126		396.08	397.1
127		399.15	400.1

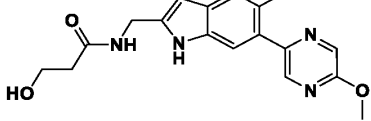
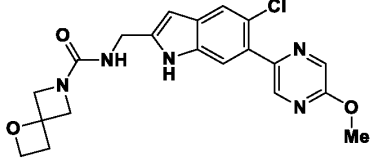
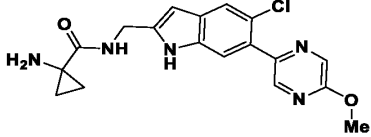
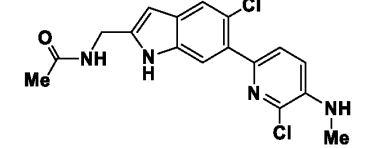
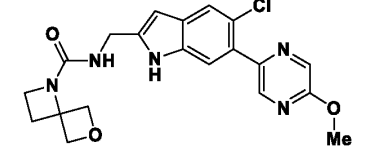
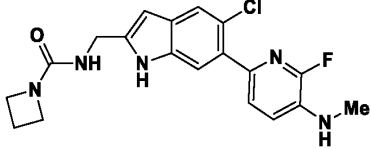
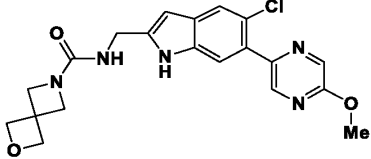
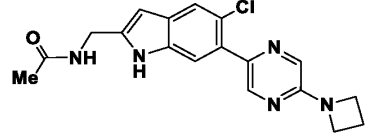
128		372.12	373.0
129		410.10	411.1
130		385.13	386.0
131		403.11	404.1
132		416.14	417.1
133		410.10	411.1
134		418.12	419.0
135		391.11	392.1

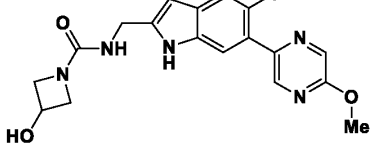
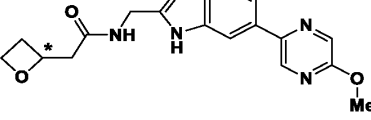
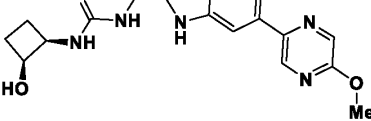
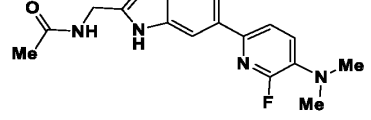
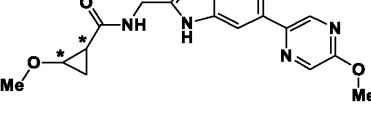
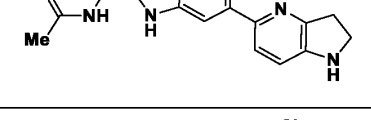
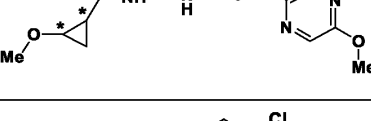
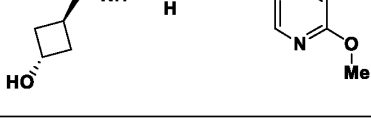
136		416.14	417.1
137		403.11	404.1
138		431.07	432.0
139		402.13	403.1
140		403.11	404.0
141		377.09	378.1
142		363.08	363.9
143		317.07	318.1

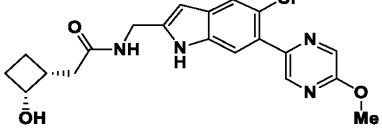
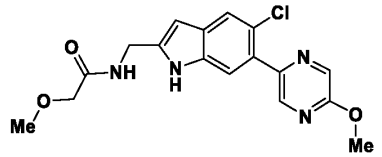
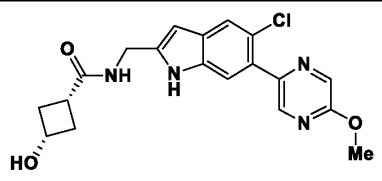
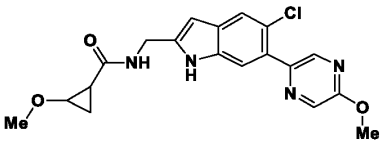
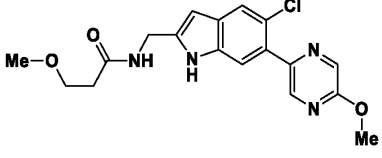
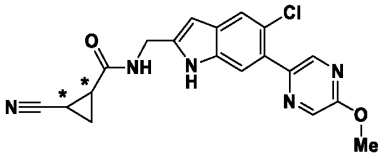
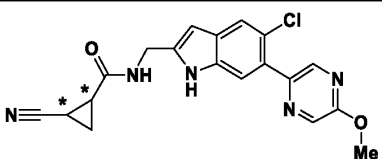
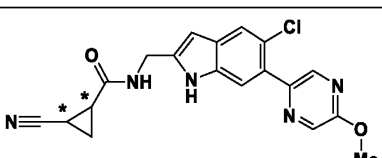
144		317.07	318.1
145		340.11	341.2
146		391.11	392.1
147		388.13	389.0
148		388.13	389.1
149		346.08	347.1
150		402.13	403.2
151		388.13	389.0

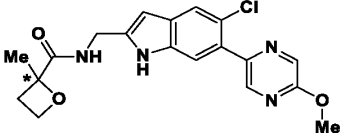
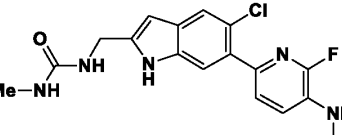
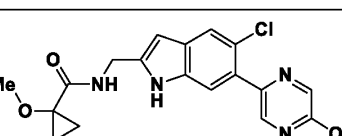
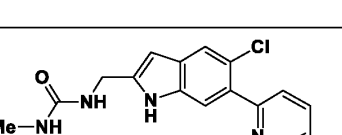
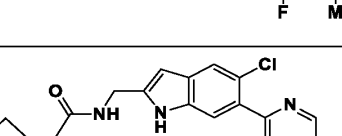
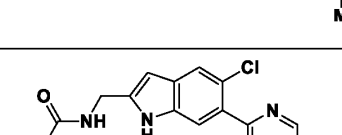
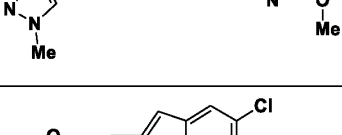
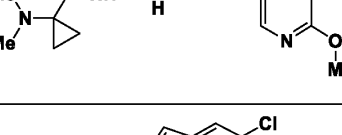
152		391.11	392.1
153		376.11	377.1
154		321.12	322.0
155		335.06	336.1
156		331.09	332.2
157		385.13	386.1
158		359.11	360.0
159		422.10	423.0

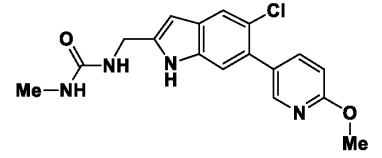
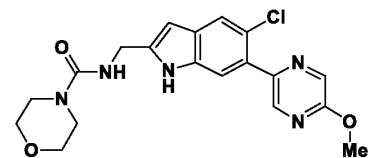
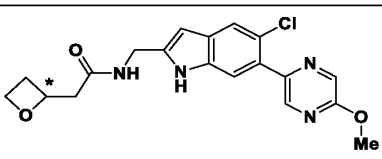
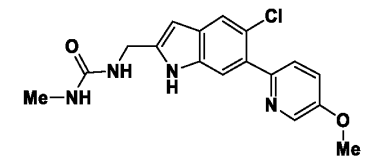
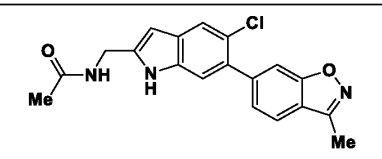
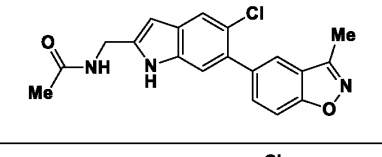
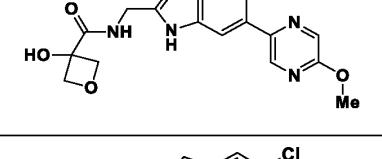
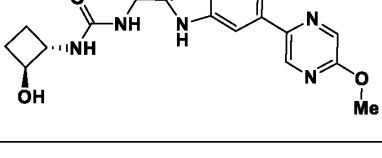
160		433.13	434.1
161		388.11	389.0
162		389.09	390.1
163		398.09	399.1
164		360.12	361.0
165		331.09	332.2
166		317.07	318.1
167		364.05	365.2

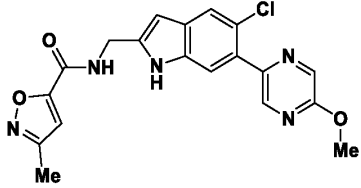
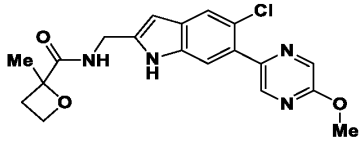
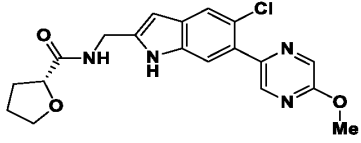
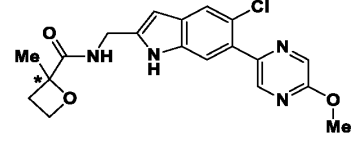
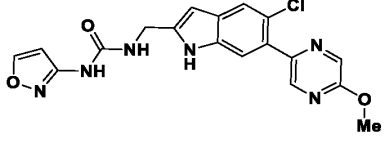
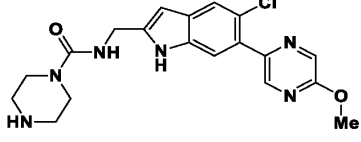
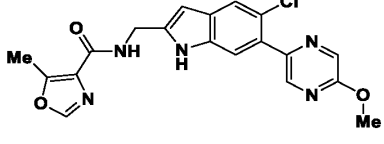
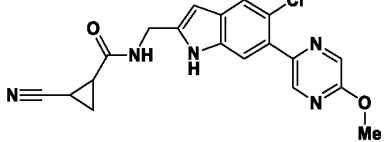
168		360.10	361.1
169		413.13	414.2
170		371.11	372.1
171		362.07	362.9
172		413.13	414.0
173		387.13	388.1
174		413.13	414.1
175		355.12	356.0

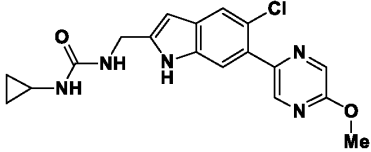
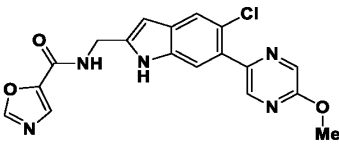
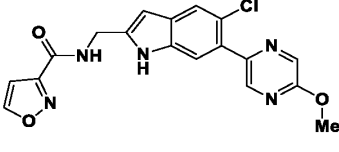
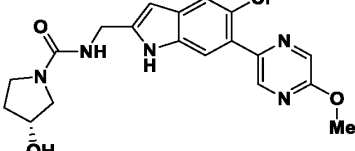
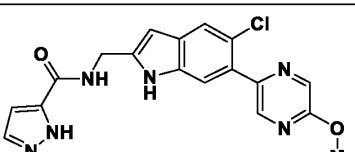
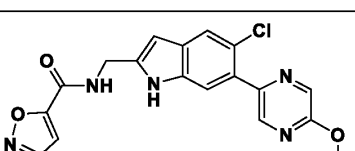
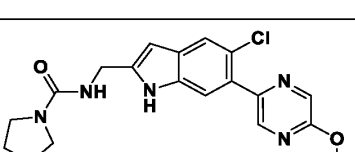
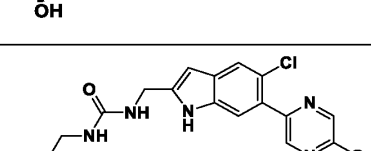
176		387.11	388.2
177		386.11	387.0
178		401.13	402.1
179		360.12	361.0
180		386.11	387.0
181		340.11	341.1
182		386.11	387.0
183		386.11	387.1

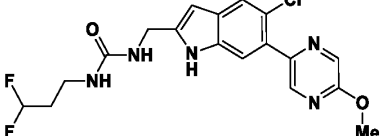
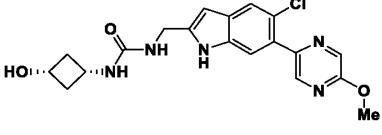
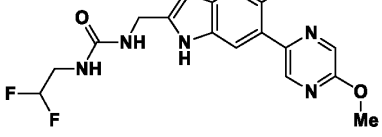
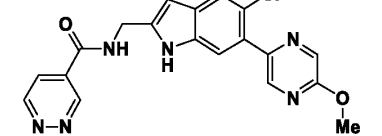
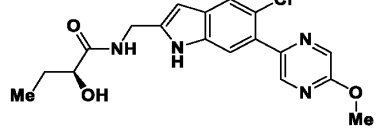
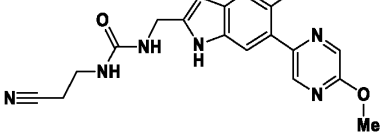
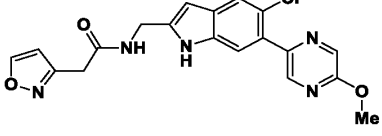
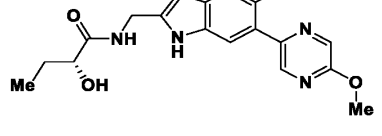
184		401.13	402.1
185		360.10	361.1
186		386.11	387.1
187		386.11	387.0
188		374.11	375.2
189		381.10	382.1
190		381.10	382.0
191		381.10	382.0

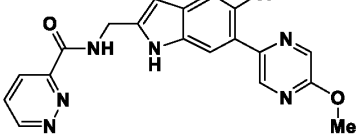
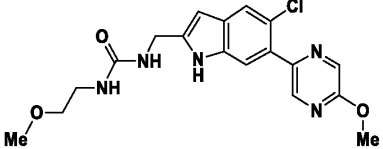
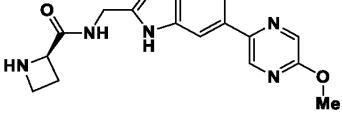
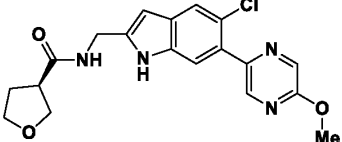
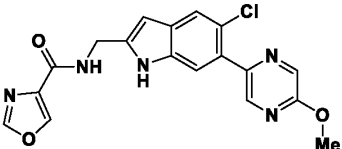
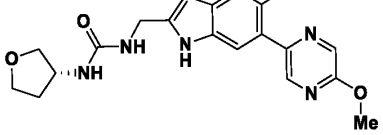
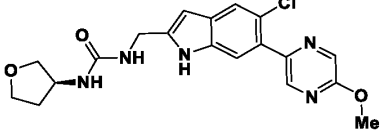
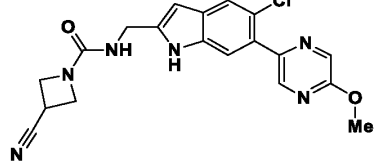
192		386.11	387.1
193		361.11	362.1
194		386.11	387.1
195		362.09	363.1
196		386.11	387.0
197		396.11	397.1
198		399.15	400.2
199		414.07	415.0

200		344.10	345.2
201		401.13	402.1
202		386.11	387.0
203		344.10	345.1
204		353.09	354.2
205		353.09	354.2
206		388.09	389.1
207		401.13	402.1

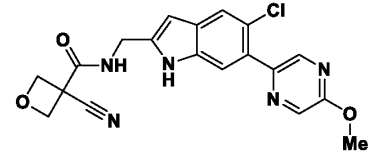
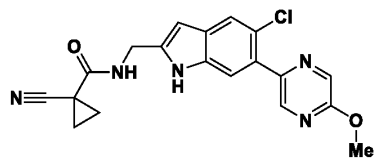
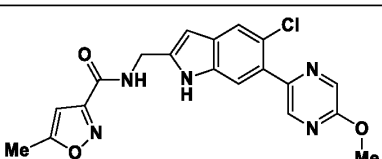
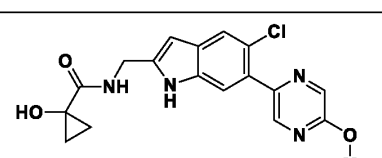
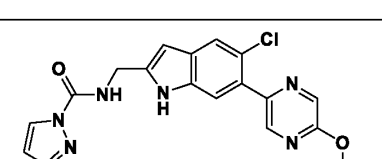
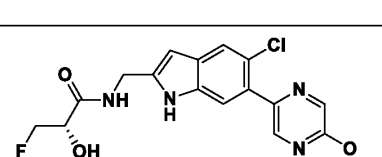
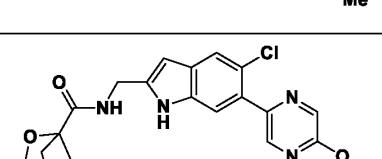
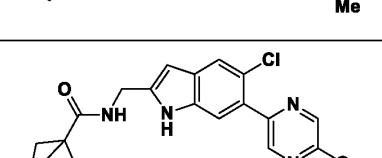
208		397.09	398.0
209		386.11	387.0
210		386.11	387.1
211		386.11	387.1
212		398.09	399.0
213		400.14	401.0
214		397.09	398.0
215		381.10	382.0

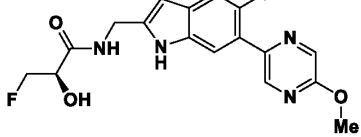
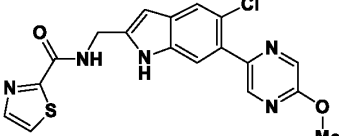
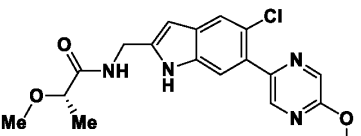
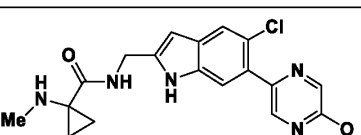
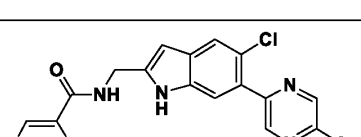
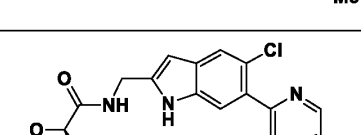
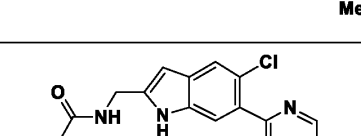
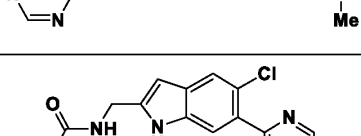
216		371.11	372.1
217		383.08	384.2
218		383.08	384.2
219		401.13	402.0
220		382.09	383.0
221		383.08	384.1
222		401.13	401.9
223		375.11	376.1

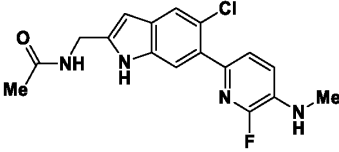
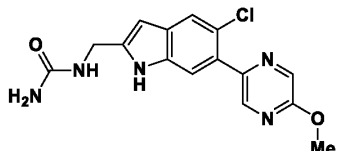
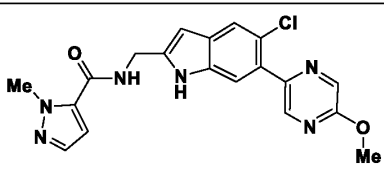
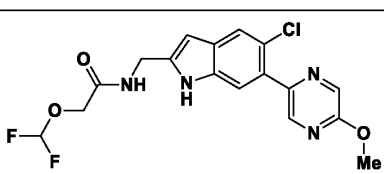
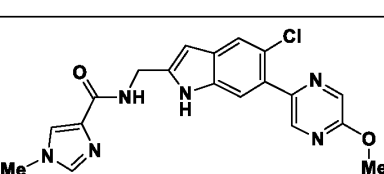
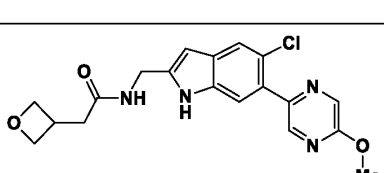
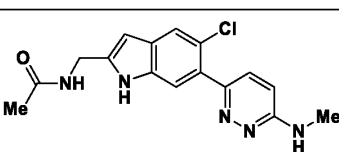
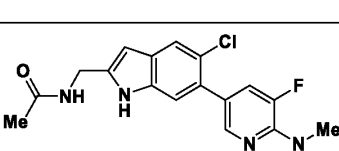
224		409.11	410.0
225		401.13	402.1
226		395.10	396.1
227		394.09	395.1
228		374.11	375.1
229		384.11	385.1
230		397.09	398.1
231		374.11	375.1

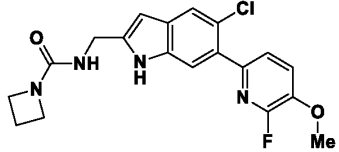
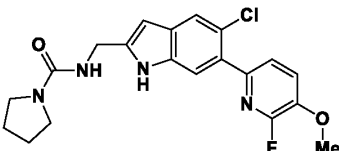
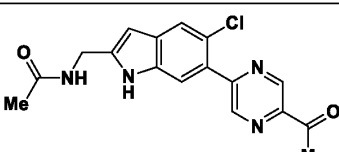
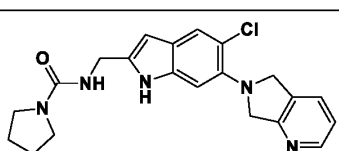
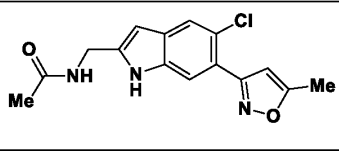
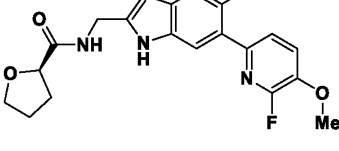
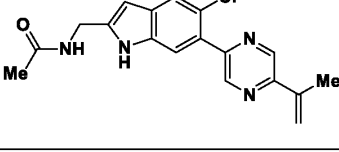
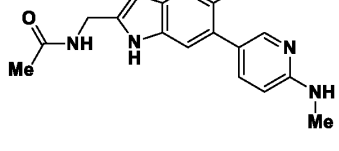
232		394.09	395.1
233		389.13	390.0
234		371.11	372.2
235		386.11	387.2
236		383.08	384.2
237		401.13	402.1
238		401.13	402.1
239		396.11	397.0

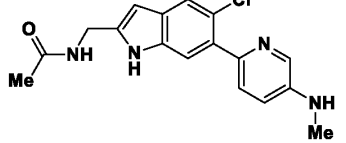
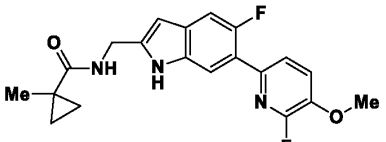
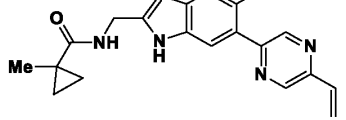
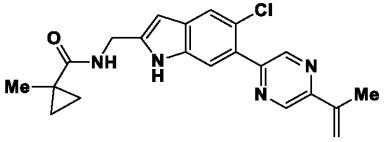
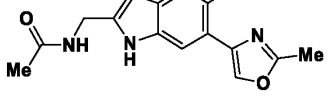
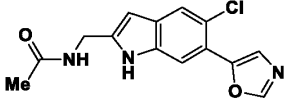
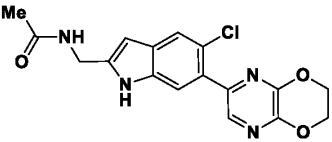
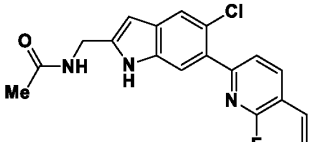
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241		359.11	360.0
242		398.09	399.1
243		401.13	402.1
244		387.11	388.0
245		346.08	347.1
246		395.11	396.2

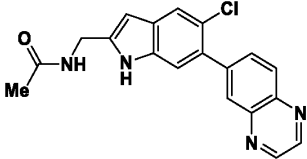
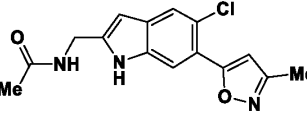
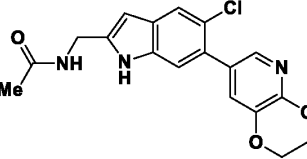
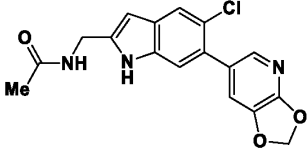
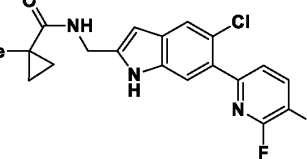
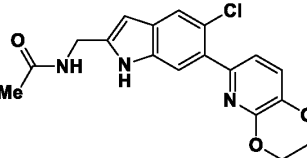
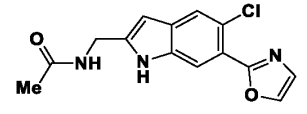
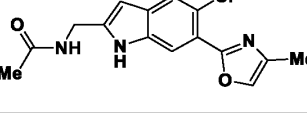
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248		381.10	382.1
249		397.09	398.2
250		372.10	373.1
251		382.09	383.2
252		378.09	379.1
253		398.11	399.2
254		398.11	399.2

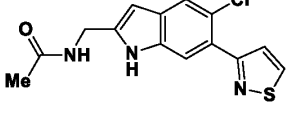
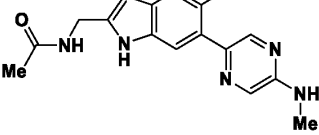
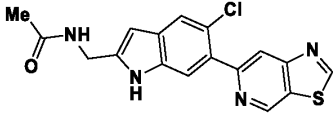
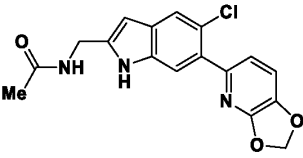
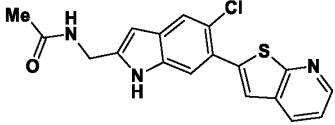
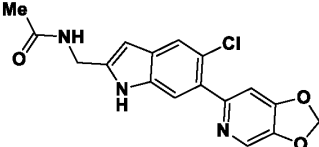
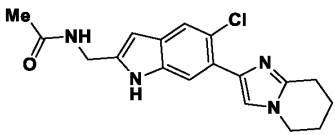
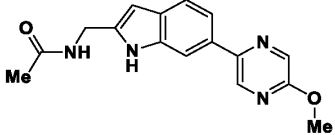
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256		399.06	400.0
257		374.11	375.1
258		385.13	386.2
259		394.09	395.1
260		374.11	375.1
261		394.09	395.1
262		394.09	395.1

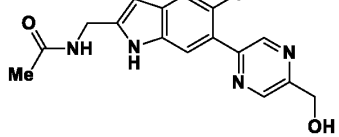
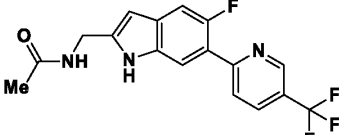
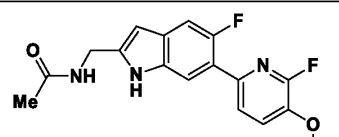
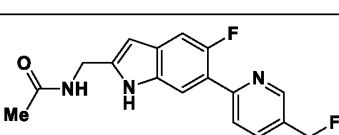
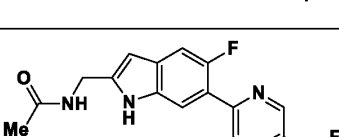
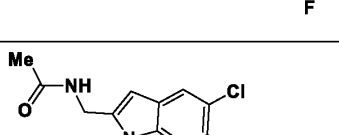
263		346.10	347.2
264		331.08	332.0
265		396.11	397.1
266		396.08	397.0
267		396.11	397.0
268		386.11	387.0
269		329.10	330.0
270		346.10	347.0

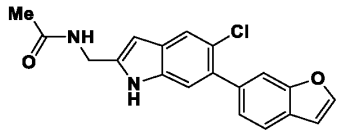
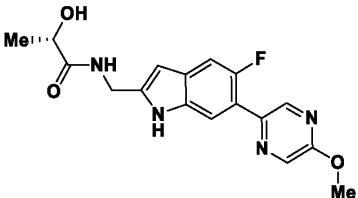
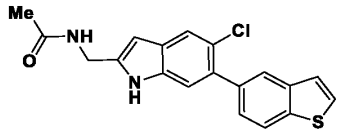
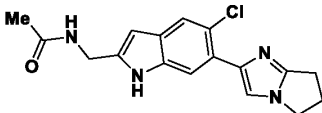
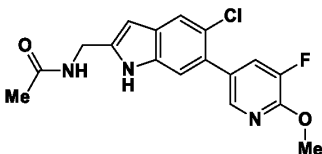
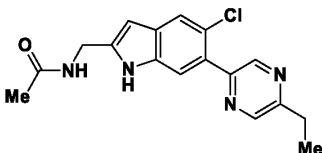
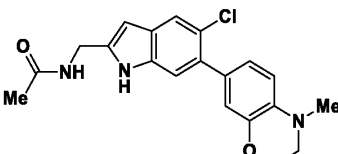
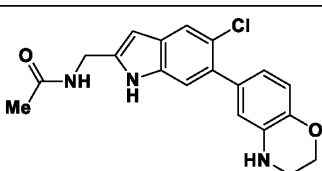
271		388.11	389.1, 389.2
272		402.13	403.1
273		342.09	343.0
274		395.15	396.1
275		303.08	304.0
276		403.11	404.1
277		340.11	341.04
278		328.11	329.02

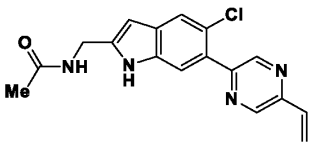
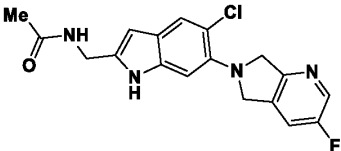
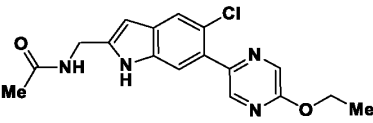
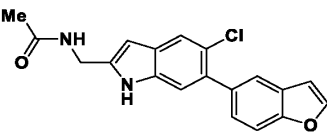
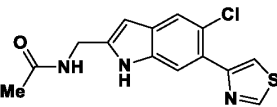
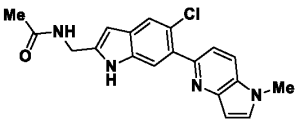
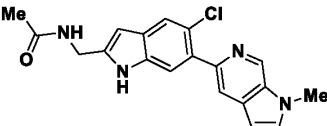
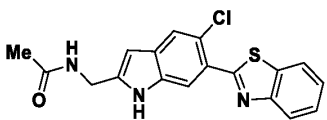
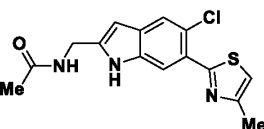
279		328.11	329.02
280		371.14	372.2
281		366.12	367.1
282		380.14	381.1
283		303.08	304.1
284		289.06	290.2
285		358.08	359.0
286		343.09	344.0

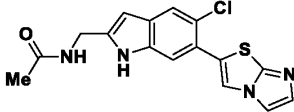
287		350.09	351.1
288		303.08	304.0
289		357.09	358.1
290		343.07	344.0
291		387.12	388.1
292		357.09	358.2
293		289.06	290.1
294		303.08	304.1

295		305.04	306.1
296		329.10	330.0
297		356.05	357.2
298		343.07	344.1
299		355.05	356.1
300		343.07	344.1
301		342.12	343.2
302		296.13	297.0

303		330.09	331.0
304		351.10	352.0
305		331.11	332.1
306		333.11	334.0
307		352.09	353.0
308		350.07	350.9
309		344.13	345.1

310		338.08	339.2
311		344.13	345.2
312		354.06	355.2
313		328.11	329.1
314		347.08	348.03
315		328.11	329.0
316		369.12	370.2
317		355.11	356.2

318		326.09	327.0
319		358.10	359.0
320		344.10	345.1
321		338.08	339.2
322		305.04	306.1
323		352.11	353.0
324		352.11	353.2
325		355.05	356.0
326		319.05	320.1

327		344.05	345.1
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Biological Examples

Example B-1

[0352] CHO cells with doxycycline-inducible expression of human SLC6A19 and TMEM27 were maintained in T150 cell culture treated flasks using cell culture media, which consisted of 1x DMEM/F12 (Gibco, 11330057), 10% Tet System-Approved FBS (Gibco, A4736401), 100U/mL Penicillin-Streptomycin (Gibco, 15140122), 1x GlutaMAX™ Supplement (Gibco, 35050061), 1mM Sodium Pyruvate (Gibco, 11360070), 1.1mg/mL Sodium Bicarbonate (Gibco, 25080094), 5μg/mL Blasticidin (InvivoGen, ant-bl-1), 150μg/mL Hygromycin B Gold (InvivoGen, ant-hg-5), and 500μg/mL G418 (Sigma-Aldrich, G8168-100mL). In preparation for the assay, this media was aspirated and 5mL of TrypLE™ Express Enzyme (Gibco, 12605010) was added to each flask to initiate cell dissociation. The flasks were then incubated (humidified, 37°C with 5% CO₂) for 2 minutes. After incubation, 10mL of pre-warmed cell culture media was added to each flask. The cell suspension was collected and centrifuged for 5 minutes at 200xg. The supernatant was aspirated and the pellet was resuspended in 5mL pre-warmed cell culture media. The resuspended cells were counted using the Countess Cell Counting Chamber (Invitrogen) and the cell concentration of the suspension was readjusted to 1 million live cells/mL using pre-warmed cell culture media. 25uL/well (25,000 cells/well) of readjusted cell suspension was dispensed into Poly-D-Lysine 384-well white/clear plates (Corning, 354660) using a MultiDrop Combi (Thermo Electron Corp). To induce expression of Human SLC6A19 and TMEM27, 25uL/well of cell culture media containing 2μg/mL doxycycline was added to the first 23 columns of each plate resulting in a final concentration of 1μg/mL doxycycline. 25μL/well of cell culture media was added to the last column of each plate, to act as negative control wells for Human SLC6A19 and TMEM27 expression. Assay plates were then incubated (humidified, 37°C with 5% CO₂) for 18 hours. After incubation, the media was aspirated and the wells were washed 4 times with pre-warmed HBSS (Sigma-Aldrich, H8264-1L) using an Apricot S-

Pipette S2 (Apricot Designs), such that 5uL/well HBSS was remaining at the end of each wash. 10uL/well of test compound, a positive control compound to define 0% activity (i.e., 100% inhibition), or DMSO diluted in HBSS (Sigma-Aldrich, H8264-1L) was then added into each well using the Apricot S-Pipette S2 (Apricot Designs). At this step, the final in-well DMSO concentration in the assay plate is 0.5%. All compounds were plated in a duplicate 8-point dilution series that consisted of 3-fold dilutions. The plates were incubated with compound (humidified, 37°C with 5% CO₂) for 1 hour. Afterwards, 15uL/well of 3.2mM hot:cold leucine solution (1:15000 ratio of L-[3,4,5-³H(N)] Leucine (Perkin Elmer, NET460001MC) to L-Leucine (Sigma-Aldrich, L8912-25G) diluted with HBSS (Sigma-Aldrich, H8264-1L)) was added using the Vialflo 384 (Integra), for a final concentration of 1.6mM hot:cold leucine solution. The plates were then incubated (humidified, 37°C with 5% CO₂) for 20 minutes to conduct the uptake reaction. Immediately after the incubation, the plates were washed 4 times with HBSS (Sigma-Aldrich, H8264-1L) using the ELx405 Microplate Washer (Biotek) to terminate the uptake reaction. After the washes, 50uL/well Ultima Gold Scintillation Cocktail (Perkin Elmer, 6013326) was added to each well using the Vialflo 384 (Integra). The plates were then incubated (humidified, 37°C with 5% CO₂) on a plate shaker at 200rpm for 2 hours. After incubation, the plates were removed from the shaker and kept at room temperature for 15 minutes.

[0353] Liquid scintillation analysis was performed using the MicroBeta2 Microplate Counter (Perkin Elmer). Activity (%) was derived by normalizing the average of positive control compound treated wells to 0% and the average of DMSO (negative control) wells to 100%. Collaborative Drug Discovery software was used for graphing data.

Table B1

Cmpd #	SLC6A19_Radioligand Uptake Assay IC50 (μM)	Cmpd #	SLC6A19_Radioligand Uptake Assay IC50 (μM)	Cmpd #	SLC6A19_Radioligand Uptake Assay IC50 (μM)
1	0.296	4	0.181	7	0.231
2	0.627	5	0.207	8	0.118
3	0.798	6	0.366	9	0.705

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
10	0.296
11	2.95
12	0.138
13	0.264
14	0.301
15	0.209
16	0.699
17	0.093
18	0.346
19	0.562
20	0.399
21	0.964
22	0.119
23	0.728
24	0.549
25	0.24
26	0.22
27	0.151
28	0.13

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
29	> 9.77
30	1.26
31	0.144
32	0.157
33	> 9.12
34	0.403
35	0.338
36	0.274
37	2.76
38	1.57
39	0.185
40	0.789
41	3.22
42	3.86
43	0.292
44	0.878
45	0.23
46	0.31
47	1.18
48	0.988

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
49	0.255
50	5.75
51	2.67
52	0.686
53	0.623
54	0.213
55	> 4.21
56	0.302
57	0.134
58	3.8
59	0.259
60	1.14
61	0.579
62	4.3
63	1.87
64	0.636
65	0.206
66	0.318
67	0.824

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
68	0.812
69	0.621
70	0.13
71	0.906
72	1.63
73	1.56
74	0.121
75	0.163
76	0.229
77	1.05
78	1.28
79	0.417
80	0.859
81	3.1
82	0.687
83	0.117
84	3.52
85	1.5
86	2.02
87	1.39

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
88	0.414
89	2.49
90	0.121
91	0.408
92	2.32
93	0.841
94	1.52
95	0.952
96	2.36
97	0.542
98	0.615
99	4.74
100	2.61
101	0.458
102	0.553
103	0.512
104	2.48
105	2.96
106	1.06
107	1.9
108	2.69
109	0.718

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
110	> 9.92
111	0.678
112	1.21
113	0.82
114	0.585
115	1.9
116	0.382
117	0.672
118	0.542
119	0.491
120	0.573
121	0.344
122	0.635
123	0.35
124	0.314
125	0.344
126	0.328
127	0.679
128	1.29
129	0.708
130	0.527
131	1.16

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
132	0.508
133	0.9
134	1.17
135	0.376
136	0.468
137	0.265
138	0.289
139	0.57
140	0.283
141	0.0887
142	0.138
143	0.866
144	0.685
145	0.933
146	0.309
147	0.924
148	0.772
149	0.207
150	0.381
151	0.388
152	0.174
153	0.323

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
154	1.25
155	2
156	> 6.55
157	0.633
158	0.213
159	0.431
160	1.29
161	0.279
162	0.323
163	0.174
164	0.45
165	1.55
166	0.673
167	0.492
168	2.53
169	3.4
170	0.607
171	1.48
172	7.26
173	0.704
174	5.24
175	7.5

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
176	5.77
177	0.634
178	3.71
179	0.274
180	0.566
181	2.35
182	0.464
183	1.84
184	> 8.74
185	0.124
186	> 6.72
187	0.502
188	0.84
189	6.22
190	3.97
191	1.25
192	2.7
193	0.147
194	0.239
195	0.128
196	1.05
197	1.71

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
198	0.73
199	0.323
200	0.196
201	0.61
202	2.72
203	0.183
204	1.69
205	0.587
206	0.716
207	> 5.56
208	1.29
209	1.27
210	0.191
211	0.712
212	2.34
213	> 6.31
214	1.11
215	1.52
216	0.231
217	0.821
218	0.414
219	2.5

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
220	> 8.27
221	0.395
222	3.77
223	3.9
224	0.454
225	1.98
226	0.294
227	2.6
228	1.4
229	> 8.70
230	3.26
231	1.65
232	> 8.03
233	2.82
234	> 8.76
235	0.784
236	0.846
237	3.73
238	2.61
239	2.29
240	> 6.38
241	2.34

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
242	> 6.35
243	3.66
244	0.809
245	0.762
246	0.748
247	0.768
248	1.1
249	0.912
250	0.306
251	0.63
252	0.672
253	0.557
254	1.65
255	1.4
256	0.62
257	0.21
258	0.274
259	1.8
260	0.793
261	0.523
262	2.19
263	0.198

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
264	0.395
265	0.5
266	0.253
267	1.94
268	0.227
269	1.72
270	1.6
271	0.350
272	0.344
273	> 10.0
274	0.505
275	0.201
276	0.189
277	0.305
278	0.472
279	0.533
280	0.336
281	0.416
282	0.529
283	0.903
284	3.11
285	> 5.75

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
286	0.162
287	0.39
288	0.164
289	1.1
290	0.544
291	0.191
292	0.904
293	2.91
294	0.361
295	0.382
296	0.904
297	0.203
298	0.326
299	0.441
300	0.424
301	> 5.94
302	1.2
303	> 5.85
304	0.322
305	0.17
306	0.382
307	0.506

Cmpd #	SLC6A19_ Radioligand Uptake Assay IC50 (μM)
308	0.363
309	2.99
310	0.424
311	1.96
312	1.12
313	> 7.82
314	0.934
315	0.408
316	6
317	0.926
318	0.097
319	0.148
320	0.407
321	0.357
322	0.863
323	0.95
324	3.96
325	0.601
326	> 6.75
327	> 4.41

Example B-2

[0354] Assay ready vials of CHO cells with doxycycline inducible expression of human SLC6A19 and TMEM27 are thawed, plated in T175 flasks containing DMEM/F12 media, 10% FBS, 1% Penicillin-Streptomycin, 1x UltraGlutamate, 1mM Sodium Pyruvate, Sodium Bicarbonate (7.5mL of 7.5% solution in 500mL media final), 5µg/mL Blasticidin, 150µg/mL Hygromycin B Gold, and 500µg/mL G418, and incubated (humidified, 37°C with 5% CO₂) for 48 hours. Media is then removed, flasks are washed with 20mL of DPBS, and 5mL of TrypLE™ Express is added to each flask to initiate cell dissociation. After 5 minutes, 10mL of cell culture media is added to each flask and mixed. The cell suspension is collected and centrifuged for 5 minutes at 200xg. The supernatant is removed, and the pellet is resuspended in 10mL of cell culture media. Resuspended cells are counted using a Vi-Cell. 30µL/well (20,000 cells/well) of cell suspension is added to Poly-D-Lysine 384-well black/clear plates. Plates are incubated (humidified, 37°C with 5% CO₂) for 24 hours. To induce expression of human SLC6A19 and TMEM27, 10µL of assay culture media containing 4µg/mL doxycycline is added to each well. Assay plates are then incubated (humidified, 37°C with 5% CO₂) overnight. After incubation, the media is removed, and wells are washed 3 times with 40µL of warmed DPBS. Next, 10µL of warmed assay buffer (137mM NaCl, 5mM KCl, 1 mM CaCl₂, 1mM MgCl₂, 10mM HEPES, 10mM glucose, pH 7.2) is added to each well. 10µL/well of test compound or positive control compound to define 0% activity (i.e., 100% inhibition), is then added into each well. All compounds are plated in a duplicate 10-point dilution series that consisted of 2-fold dilutions. The plates are incubated (humidified, 37°C with 5% CO₂) with compound for 20 minutes. Afterwards, 20µL/well of 2mM 13C₆, 15N-l-isoleucine is added to each well and plates are incubated again (humidified, 37°C with 5% CO₂) for another 20 minutes. Assay buffer is then removed, and plates are washed. 70µL/well of stop solution (75% acetonitrile, 25% HPLC grade water, 250nM l-leucine-1-¹³C (RapidFire standard)) is added to each well. The plates are sealed and then placed in a -20°C freezer for 20 minutes. The plates are thawed at room temperature for 20 minutes and then centrifuged for 20 minutes at 3000 rpm. Using an ABSciex API4000 mass spectrometer, processed samples are loaded onto the graphitic carbon SPE-column. The time for aspiration, load/wash, elution and re-equilibration time is 600, 1500, 3000 and 500 milliseconds, respectively. Peak areas are calculated using RapidFire Integrator software.

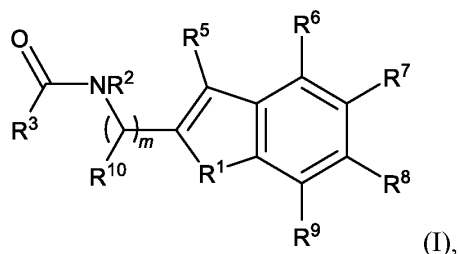
[0355] All publications, patent applications, patents, and other references mentioned herein are expressly incorporated by reference in their entireties, to the same extent as if each were incorporated by reference individually.

[0356] It is to be understood that, while the disclosure has been described in conjunction with the above embodiments, the foregoing description and examples are intended to illustrate and not limit the scope of the disclosure. Other aspects, advantages and modifications within the scope of the disclosure will be apparent to those skilled in the art to which the disclosure pertains.

CLAIMS

What is claimed is:

1. A compound of formula (I):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R⁴)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and

the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-;

each R^4 is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo;

R^6 and R^9 are each independently H or halo;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein
the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;
 R^{10} is H;
 R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ;
 R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} ; and
 R^{3b} , R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

2. The compound of claim 1, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

m is an integer from 1 to 4;
 R^1 is -NH-, -O-, or -S-;
 R^2 is H;
 R^3 is C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, -N(R^4)₂, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a};

each R⁴ is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆haloalkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}, or

both R⁴ are taken together with the N atom to which they are attached to form a 4-10 membered heterocyclyl optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

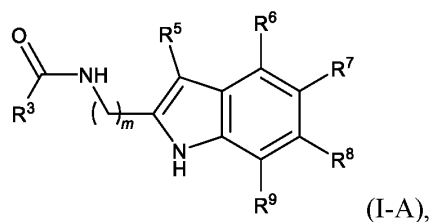
R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b}; and

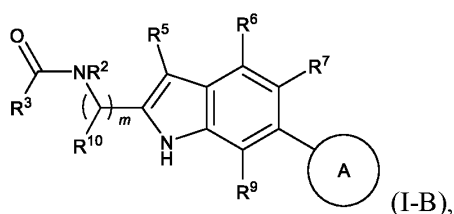
R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy.

3. The compound of claim 1, wherein the compound is a compound of formula (I-A):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing.

4. The compound of any of claims 1-3, wherein the compound is a compound of formula (I-B):



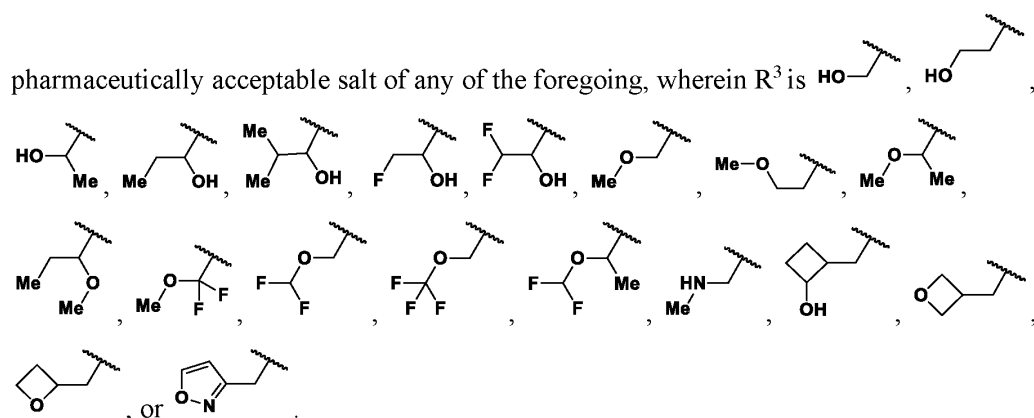
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

ring A is C₆₋₂₀aryl, 5-10 membered heteroaryl, or 5-10 membered heterocyclyl, wherein the C₆₋₂₀aryl, 5-10 membered heteroaryl, or 5-10 membered heterocyclyl are each optionally substituted with one or more R^a.

5. The compound of any of claims 1-4, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein *m* is an integer from 1-2.
6. The compound of any of claims 1-4, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein *m* is 1.
7. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R³ is C₁₋₃alkyl.
8. The compound of any of claims 1-7, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R³ is methyl.

9. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{1-3} alkyl, optionally substituted with one or more R^{3a} .

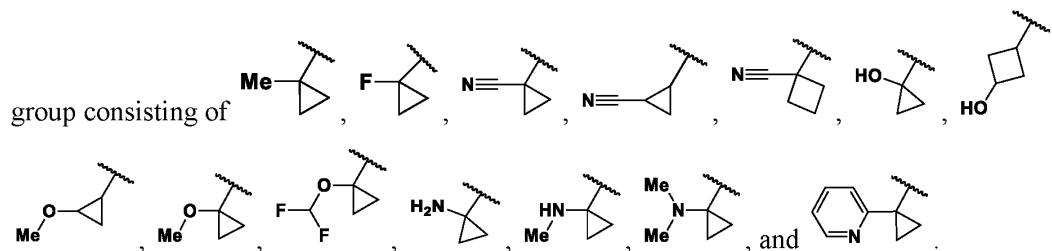
10. The compound of any of claims 1-6, or 9, or a stereoisomer or tautomer thereof, or a



11. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} .

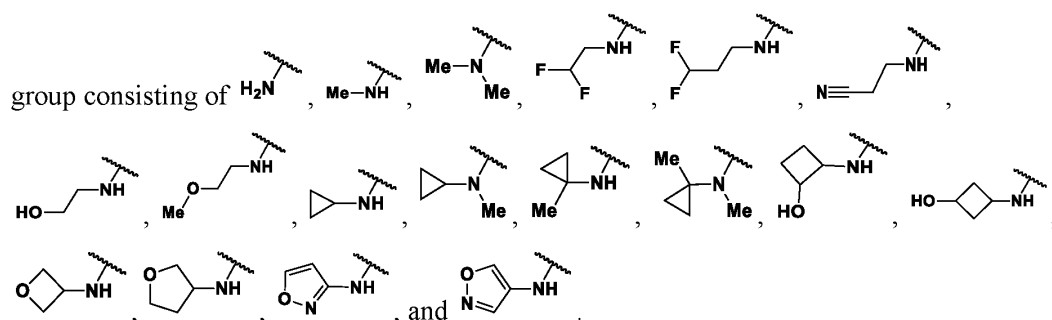
12. The compound of any of claims 1-6, or 11, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{3-6} cycloalkyl optionally substituted with one or more R^{3a} ; R^{3a} is -OH, -CN, halo, C_{1-6} alkyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, or 4-10 membered heteroaryl, wherein the C_{1-6} alkoxy of R^{3a} is optionally substituted with one or more R^{3b} ; and R^{3b} is halo.

13. The compound of any of claims 1-6, or 11-12, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is selected from the



14. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is $-N(R^4)_2$, wherein each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein the C_{1-6} alkyl of R^4 is optionally substituted with one or more R^{4a} , R^{4a} is, independently at each occurrence, -OH, -CN, halo, C_{1-6} alkyl, or C_{1-6} alkoxy.

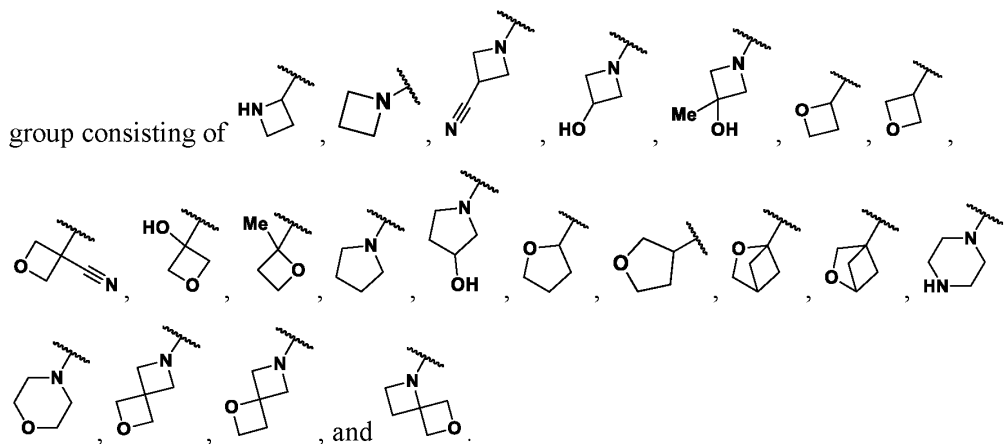
15. The compound of any of claims 1-6 and 14, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is selected from the



16. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is 4-6 membered heterocyclyl, optionally substituted with one or more R^{3a} .

17. The compound of any of claims 1-6 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is 4-10 membered heterocyclyl optionally substituted with one or more R^{3a} , R^{3a} is, independently at each occurrence, -OH, -CN, or C_{1-6} alkyl.

18. The compound of any of claims 1-6, and 17, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is selected from the

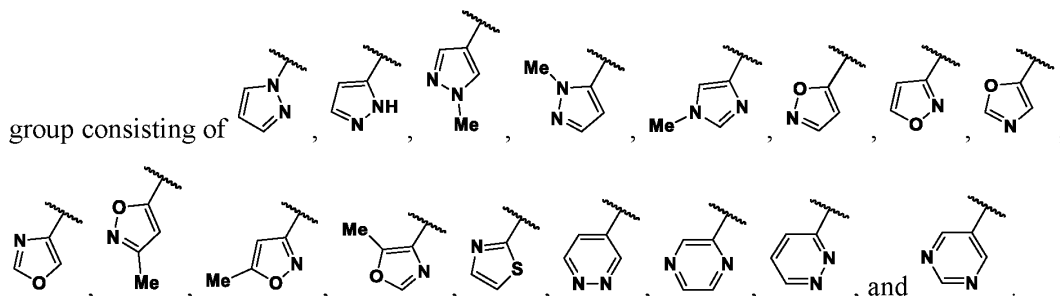


19. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is C_{1-3} alkoxy.

20. The compound of any of claims 1-6, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is methoxy.

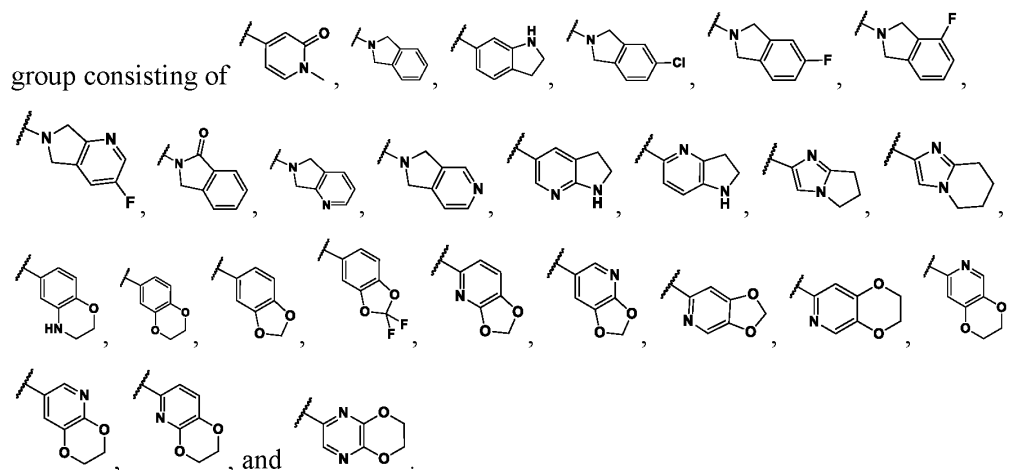
21. The compound of any of claims 1-6 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 4-10 membered heteroaryl optionally substituted with one or more R^{3x} ; R^{3x} is, independently at each occurrence, C_{1-6} alkyl.

22. The compound of any of claims 1-6, and 21, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is selected from the



23. The compound of any of claims 1-22, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^5 and R^7 are each independently H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, or C_{1-3} haloalkyl.
24. The compound of any of claims 1-23, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^5 and R^7 are each independently H.
25. The compound of any of claims 1-23, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein one of R^5 and R^7 is H, and the other of R^5 and R^7 is halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein
- the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN, and
- the C_{1-6} alkoxy of R^5 and R^7 are each independently optionally substituted with one or more halo.
26. The compound of any of claims 1-25, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^6 and R^9 are each independently H.
27. The compound of any of claims 1-25, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein one of R^6 and R^9 is H, and the other of R^6 and R^9 is F, or Cl.
28. The compound of any of claims 1-27, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is 3-10 membered heterocyclyl, optionally substituted with one or more R^{8a} .

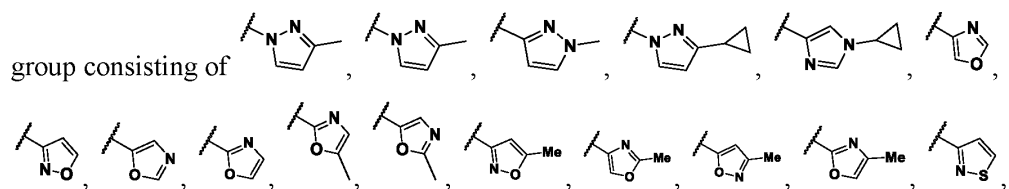
29. The compound of any of claims 1-28, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is selected from the

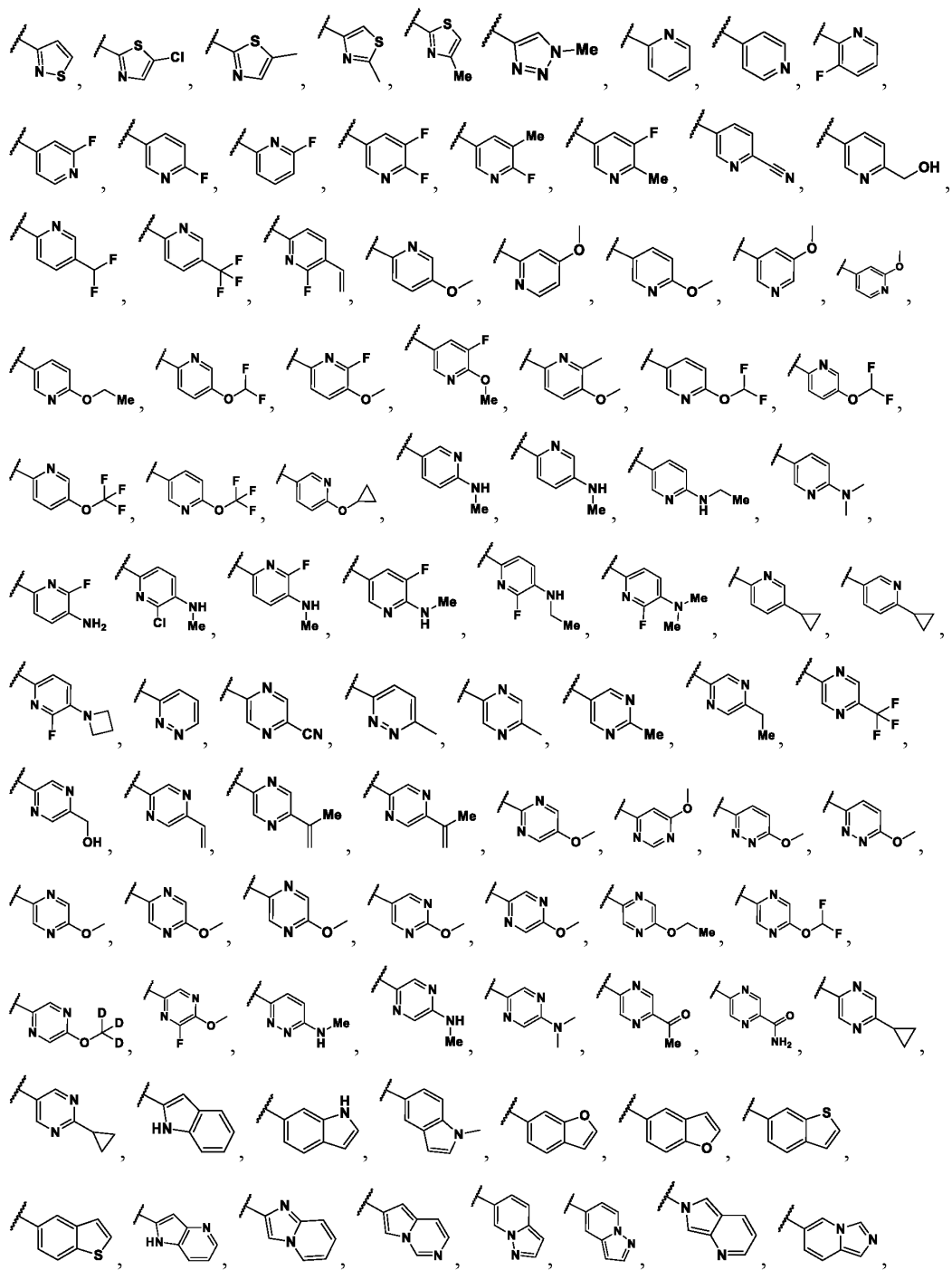


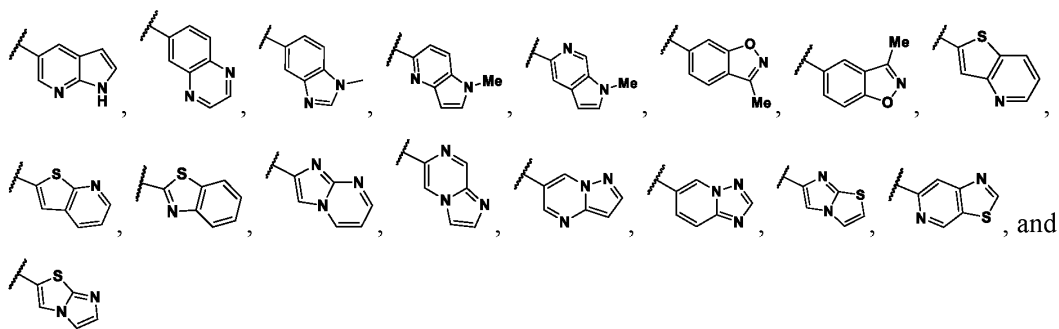
30. The compound of any of claims 1-27, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a} .

31. The compound of any of claims 1-27, or 30, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is 5-10 membered heteroaryl, optionally substituted with one or more R^{8a} , wherein each R^{8a} is independently -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, $-NH_2$, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)_2$, $-C(O)C_{1-6}alkyl$, $-C(O)NH_2$, $-C(O)NH(C_{1-6}alkyl)$, $-C(O)N(C_{1-6}alkyl)_2$, C_{3-10} cycloalkyl, or $-O-C_{3-10}$ cycloalkyl, wherein the C_{1-6} alkyl, or C_{1-6} alkoxy, of R^{8a} is optionally substituted with one or more R^{8b} ; and each R^{8b} is independently D, $-OH$, or halo.

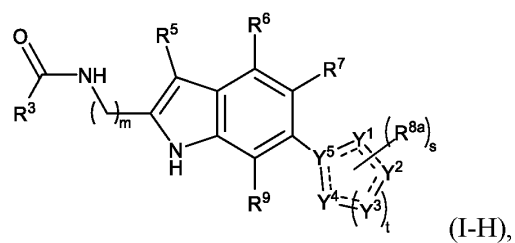
32. The compound of any of claims 1-27, or 30-31, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein R^8 is selected from the







33. The compound of any of claims 1-27, or 30-32, wherein the compound is of formula (I-H):



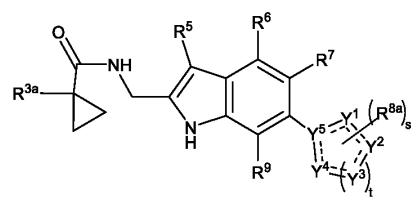
or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein

s is an integer from 0-6;

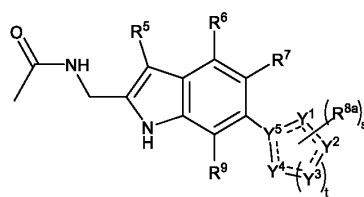
t is 1 or 2; and

— represents a single or double bond.

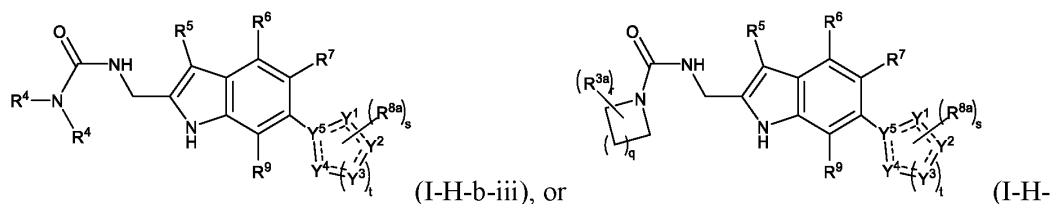
34. The compound of claim 33, wherein the compound is of formula:



(I-H-b-i),



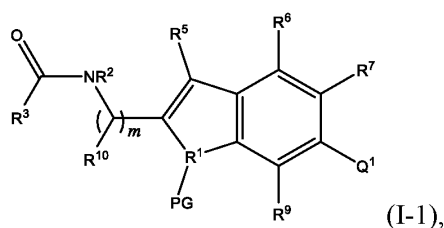
(I-H-b-ii),



35. The compound of claim 1, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from Compounds 1-339 of Table 1.

36. A process for preparing a compound of formula (I), as defined in any of claims 1-35 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (I-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q^1 is halo;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^1 is -N-, -NH-, -O-, or -S-;

R^2 is H;

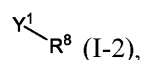
R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and the 4-10 membered heteroaryl of R³ is optionally substituted with one or more R^{3x}, provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;

each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a}; R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo; R¹⁰ is H; R^{3a} and R^{4a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b}, the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}; and

R^{3b} and R^{4b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;
with a compound of formula (I-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^1 is a boronic acid or boronic ester;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

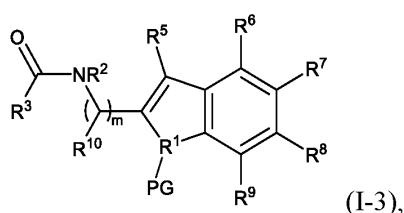
the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

each R^{8a} is independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ;
and

each R^{8b} is independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R² is H;

R³ is C₁₋₆alkyl, C₁₋₃alkoxy, C₃₋₁₀cycloalkyl, -N(R⁴)₂, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl, or 4-10 membered heterocyclyl of R³ is optionally substituted with one or more R^{3a}, and
the 4-10 membered heteroaryl of R³ is optionally substituted with one or more R^{3x},

provided that when R³ is 4-10 membered heteroaryl, R¹ is -NH-;
each R⁴ is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R⁴ is optionally substituted with one or more R^{4a};

R⁵ and R⁷ are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R⁵ and R⁷ are each independently optionally substituted with one or more -CN, and

the C₁₋₆alkoxy of R⁵ and R⁷ are each independently optionally substituted with one or more halo;

R⁶ and R⁹ are each independently H or halo;

R⁸ is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R⁸ is optionally substituted with one or more R^{8a};

R¹⁰ is H;

R^{3a}, R^{4a}, and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b},

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

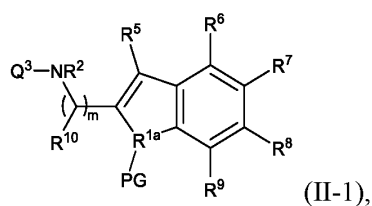
the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}; and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,
(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

37. The process of claim 35, wherein the coupling reagent comprises a palladium catalyst, a phosphine ligand, and/or base.

38. A process for preparing a compound of formula (I), as defined in any of claims 1-35 or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, comprises:

(a) reacting a compound of formula (II-1):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Q³ is H;

PG is absent, or a protecting group;

m is an integer from 1 to 4;

R^{1a} is -N-, -NH-, -O-, or -S-;

R^2 is H;

each R^4 is independently H, C₁₋₆alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, or C₃₋₁₀cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₁₀cycloalkyl or C₁₋₆haloalkyl, wherein

the C₁₋₆alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C₃₋₁₀cycloalkyl, C₆₋₂₀aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

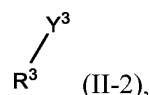
R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)C₁₋₆alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b} , and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b} ;

R^{4b} , and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy;

with a compound of formula (II-2):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

Y^3 is $-C(O)OH$, or $-C(O)$ -halo;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is $-N-$ or $-NH-$; and each R^{3a} is independently $-OH$, oxo, $-CN$, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, $-NH_2$, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)_2$, $-C(O)C_{1-6}alkyl$, $-C(O)NH_2$, $-C(O)NH(C_{1-6}alkyl)$, $-C(O)N(C_{1-6}alkyl)_2$, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or $-O-C_{3-10}$ cycloalkyl, wherein

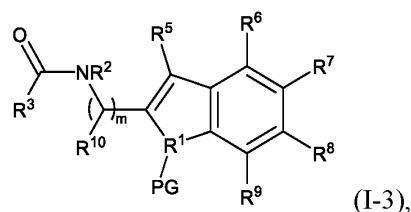
the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or $-O-C_{3-10}$ cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

R^{3x} is $-OH$, $-CN$, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, $-O-C_{1-6}$ haloalkyl, $-NH_2$, $-NH(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)_2$, $-C(O)NH_2$, $-C(O)NH(C_{1-6}alkyl)$, $-C(O)N(C_{1-6}alkyl)_2$, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or $-O-C_{3-10}$ cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or $-O-C_{3-10}$ cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b} , and

each R^{3b} is independently D , $-OH$, halo, C_{1-6} alkyl or C_{1-6} alkoxy;

in the presence of a coupling reagent, to provide a compound of formula (I-3):



or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

PG is absent or a protecting group;

m is an integer from 1 to 4;

R^1 is -NH-, -O-, or -S-;

R^2 is H;

R^3 is C_{1-6} alkyl, C_{1-3} alkoxy, C_{3-10} cycloalkyl, $-N(R^4)_2$, 4-10 membered heteroaryl, or 4-10 membered heterocyclyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl, or 4-10 membered heterocyclyl of R^3 is optionally substituted with one or more R^{3a} , and
the 4-10 membered heteroaryl of R^3 is optionally substituted with one or more R^{3x} ,

provided that when R^3 is 4-10 membered heteroaryl, R^1 is -NH-;

each R^4 is independently H, C_{1-6} alkyl, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, or C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, or C_{3-10} cycloalkyl of R^4 is optionally substituted with one or more R^{4a} ;

R^5 and R^7 are each independently H, halo, -CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-10} cycloalkyl or C_{1-6} haloalkyl, wherein

the C_{1-6} alkyl of R^5 and R^7 are each independently optionally substituted with one or more -CN;

R^6 and R^9 are each independently H or halo;

R^8 is C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl, wherein

the C_{3-10} cycloalkyl, C_{6-20} aryl, 3-10 membered heterocyclyl, or 5-10 membered heteroaryl of R^8 is optionally substituted with one or more R^{8a} ;

R^{10} is H;

R^{3a} , R^{4a} , and R^{8a} are each independently -OH, oxo, -CN, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, -NH₂, -NH(C_{1-6} alkyl), -N(C_{1-6} alkyl)₂, -C(O) C_{1-6} alkyl, -C(O)NH₂, -C(O)NH(C_{1-6} alkyl), -C(O)N(C_{1-6} alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl, or -O- C_{3-10} cycloalkyl, wherein

the C_{1-6} alkyl, C_{1-6} alkoxy, 4-10 membered heterocyclyl, C_{3-10} cycloalkyl or -O- C_{3-10} cycloalkyl of R^{3a} is optionally substituted with one or more R^{3b} ,

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{4a} is optionally substituted with one or more R^{4b}, and

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-C₃₋₁₀cycloalkyl of R^{8a} is optionally substituted with one or more R^{8b},

R^{3x} is -OH, -CN, halo, C₁₋₆alkyl, C₂₋₆alkenyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, -O-C₁₋₆haloalkyl, -NH₂, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)₂, -C(O)NH₂, -C(O)NH(C₁₋₆alkyl), -C(O)N(C₁₋₆alkyl)₂, 4-10 membered heteroaryl, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl, or -O-C₃₋₁₀cycloalkyl, wherein

the C₁₋₆alkyl, C₁₋₆alkoxy, 4-10 membered heterocyclyl, C₃₋₁₀cycloalkyl or -O-

C₃₋₁₀cycloalkyl of R^{3x} is optionally substituted with one or more R^{3b}, and

R^{3b}, R^{4b}, and R^{8b} are each independently D, -OH, halo, C₁₋₆alkyl or C₁₋₆alkoxy; followed by,

(b) optionally contacting the compound of formula (I-3) with a deprotecting agent; to provide a compound of formula (I).

39. The process of any of claims 36-38, wherein the protecting group is a sulfonyl group.

40. The process of any of claims 36-39, wherein the deprotecting agent comprises a base.

41. A pharmaceutical composition comprising (i) a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, and (ii) one or more pharmaceutically acceptable excipients.

42. A method of modulating SLC6A19 in a cell, comprising exposing the cell to a composition comprising a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of claim 41.

43. A method of inhibiting SLC6A19 in a cell, comprising exposing the cell to a composition comprising a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of claim 41.

44. A method of reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof, comprising administering to the individual a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of claim 41.
45. A method of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof, comprising administering to the individual a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of claim 41.
46. The method of claim 45, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders.
47. The method of claim 45 or 46, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, and metabolic diseases.
48. The method of any of claims 45-47, wherein the disease, disorder, or condition is chronic kidney disease (CKD).
49. The method of claim 45, wherein the disease, disorder, or condition is associated with abnormal levels of amino acids.
50. The method of claim 45 or 46, wherein the disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase.
51. The method of any of claims 45-50, wherein the individual is human.

52. The method of any one of claims 45-51 wherein a therapeutically effective amount of the compound is administered.

53. A kit, comprising (i) a compound of any of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or the pharmaceutical composition of claim 41, and (ii) instructions for use in treating an SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

54. The kit of claim 53, wherein the disease, disorder, or condition is associated with abnormal levels of amino acids.

55. The kit of claim 53 or 54, wherein the disease, disorder, or condition is associated with a genetic defect in phenylalanine hydroxylase.

56. The kit of claim 53 or 54, wherein the disease, disorder, or condition is selected from the group consisting of phenylketonuria (PKU), chronic kidney disease (CKD), metabolic syndrome, metabolic diseases, hyperphenylalaninemia, tyrosinemia (Type I, II, or III), nonketotic hyperglycinemia, isovaleric acidemia, methylmalonic acidemia, propionic acidemia, maple syrup urine disease, DNAJC12 deficiency, urea cycle disorders, hyperammonemia, diabetes, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, obesity related disorders, and neurodevelopmental and autism-spectrum disorders.

57. The kit of claim any of claims 53-56, wherein the individual has a genetic defect in phenylalanine hydroxylase.

58. A compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, for use in modulating SLC6A19 in a cell.

59. A compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, for use in inhibiting SLC6A19 in a cell.

60. A compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, for use in reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof.

61. A compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, for use in of treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.

62. Use of a compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, in the manufacture of a medicament, for use in modulating SLC6A19 in a cell.

63. Use of a compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, in the manufacture of a medicament, for use in inhibiting SLC6A19 in a cell.

64. Use of a compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, in the manufacture of a medicament, for use in reducing systemic phenylalanine, tyrosine, glutamine, or glycine levels in an individual in need thereof.

65. Use of a compound of any one of claims 1-35, or a stereoisomer or tautomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, or a pharmaceutical composition of claim 41, in the manufacture of a medicament, for use in treating a SLC6A19-mediated disease, disorder, or condition in an individual in need thereof.