

**3-(4-CYCLO-PROPOXYBENZYL)-1-(2,4-DIFLUOROBENZYL)-1
-(1-METHYLPIPERIDIN-4-YL)UREA FOR USE IN THE
TREATMENT OF DISEASES ASSOCIATED WITH THE
SEROTONIN-RECEPTOR 5-HT**

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 63/530,291, filed August 2, 2023, and U.S. Provisional Application No. 63/554,437, filed February 16, 2024, each of which is hereby incorporated by reference in its entirety.

FIELD

[0002] Provided herein are compositions containing 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, as an active ingredient for treatment of diseases and conditions, particularly diseases and conditions associated with the serotonin receptor 5-HT.

BACKGROUND

[0003] Serotonin, or 5-hydroxytryptamine (5-HT), plays a significant role in the functioning of the mammalian body. In the central nervous system, serotonin is an important neurotransmitter and neuromodulator that is implicated in such diverse behaviors and responses as sleeping, eating, locomotion, perceiving pain, learning and memory, sexual behavior, controlling body temperature and blood pressure. In the spinal column, serotonin plays an important role in the control systems of the afferent peripheral nociceptors (Moullignier, *Rev. Neurol.* 150:3-15, (1994)). Peripheral functions in the cardiovascular, hematological and gastrointestinal systems have also been ascribed to serotonin. Serotonin has been found to mediate a variety of contractile, secretory, and electrophysiologic effects including vascular and nonvascular smooth muscle contraction, and platelet aggregation. (Fuller, *Biology of Serotonergic Transmission*, 1982; Boullin, *Serotonin in Mental Abnormalities* 1:316 (1978); Barchas, et al., *Serotonin and Behavior*, (1973)).

[0004] Serotonin may be an important component in various types of pathological conditions such as certain psychiatric disorders (depression, aggressiveness, panic attacks, obsessive compulsive disorders, psychosis, schizophrenia, suicidal tendency), certain neuro-degenerative disorders (Alzheimer-type dementia, Parkinsonism, Huntington's chorea), anorexia, bulimia, disorders associated with alcoholism, cerebral vascular accidents, and migraine (Meltzer,

Neuropsychopharmacology, 21:106S-115S (1999); Barnes & Sharp, *Neuropharmacology*, 38:1083-1152 (1999); Glennon, *Neurosci. Biobehavioral Rev.*, 14:35 (1990)).

[0005] Given the broad distribution of serotonin within the body, it is understandable that tremendous interest in drugs that affect serotonergic systems exists (Gershon, et al., *The Peripheral Actions of 5-Hydroxytryptamine*, 246 (1989); Saxena, et al., *J. Cardiovascular Pharmacol.* 15: Supp. 7 (1990)). Serotonin receptors are members of a large human gene family of membrane-spanning proteins that function as transducers of intercellular communication. They exist on the surface of various cell types, including neurons and platelets, where, upon their activation by either their endogenous ligand serotonin or exogenously administered drugs, they change their conformational structure and subsequently interact with downstream mediators of cellular signaling. Many of these receptors, including the 5-HT_{2A} subclass, are G-protein coupled receptors (GPCRs) that signal by activating guanine nucleotide binding proteins (G-proteins), resulting in the generation, or inhibition of, second messenger molecules such as cyclic AMP, inositol phosphates, and diacylglycerol. These second messengers then modulate the function of a variety of intracellular enzymes, including kinases and ion channels, which ultimately affect cellular excitability and function.

[0006] The effects of serotonin are mediated by at least fourteen genetically distinct 5-HT receptor subtypes. Each subtype, which is assigned to one of seven families (5-HT₁ through 5-HT₇), displays a unique distribution, preference for various ligands, and functional correlate(s).

[0007] The 5-HT_{2A} receptor subtype (also referred to as subclass) is widely yet discretely expressed in the human brain, including many cortical, limbic, and forebrain regions postulated to be involved in the modulation of higher cognitive and affective functions. This receptor subtype is also expressed on mature platelets where it mediates, in part, platelet aggregation, one of the initial steps in the process of vascular thrombosis.

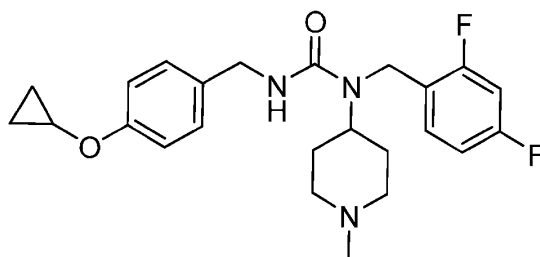
[0008] Antipsychotic drugs have been shown to interact with a large number of central monoaminergic neurotransmitter receptors, including dopaminergic, serotonergic, adrenergic, muscarinic, and histaminergic receptors. It is likely that the therapeutic and adverse effects of these drugs are mediated by distinct receptor subtypes. The high degree of genetic and pharmacological homology between these receptor subtypes has hampered the development of subtype-selective compounds, as well as the determination of the normal physiologic or pathophysiologic role of

any particular receptor subtype. Thus there is a need to develop drugs that are selective for individual receptor classes and subclasses amongst monoaminergic neurotransmitter receptors.

[0009] The prevailing theory for the mechanism of action of antipsychotic drugs involves antagonism of dopamine D2 receptors. Unfortunately, it is likely that antagonism of dopamine D2 receptors also mediates the extrapyramidal side effects as well as some additional undesired effects of antipsychotic therapies such as a worsening of depression symptoms, anhedonia and impairment of cognitive processes. Antagonism of 5-HT2A receptors is an alternate molecular mechanism for drugs with antipsychotic efficacy, possibly through antagonism of heightened or exaggerated signal transduction through serotonergic systems. 5-HT2A antagonists are therefore good candidates for treating psychosis without extrapyramidal side effects or other undesired effects associated with blockade of dopamine D₂ receptors.

[0010] Traditionally, GPCRs such as the 5-HT2A receptor have been assumed to exist in a quiescent state unless activated by the binding of an agonist (a drug that activates a receptor). It is now appreciated that many, if not most, of the GPCR monoamine receptors, including serotonin receptors, can exist in a partially activated state in the absence of their endogenous agonists. This increased basal activity (constitutive activity) can be inhibited by compounds called inverse agonists. Both agonists and inverse agonists possess intrinsic activity at a receptor, in that they alone can activate or inactivate these molecules, respectively. In contrast, classic or neutral antagonists compete against agonists and inverse agonists for access to the receptor, but do not possess the intrinsic ability to inhibit elevated basal or constitutive receptor responses.

[0011] The compound 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea:



which can also be named as *N*-3-(4-cyclopropoxybenzyl)-*N'*-(2,4-difluorobenzyl)-*N'*-(1-methylpiperidin-4-yl)urea or *N'*-[[4-(cyclopropyloxy)phenyl]methyl]-*N'*-[(2,4-difluorophenyl)-

methyl]-N-(1-methyl-4-piperidiny)urea, has been shown to have activity towards the serotonin receptor in mammals. This compound and its synthesis are disclosed in U.S. Patent No. 11,345,693, as is the hemitartrate salt thereof.

[0012] There is therefore a need for pharmaceutical compositions containing this compound, or a salt or salt hydrate thereof, in amounts effective for treating a disease or condition affecting mammals, such as diseases or conditions involving the serotonin receptor.

SUMMARY

[0013] Provided herein are pharmaceutical compositions containing from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof, and one or more pharmaceutically acceptable excipients.

[0014] Also provided herein are methods for treating a disease or condition in a mammalian patient, such as a human, comprising administering to that patient from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof, and one or more pharmaceutically acceptable excipients, wherein the disease is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Athereosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder

(TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAI1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's

disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

[0015] Also provided herein are methods for suppressing the activity of serotonin receptor 5-HT_{2A} in a mammalian patient, such as a human, comprising administering to that patient from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof, and one or more pharmaceutically acceptable excipients.

DETAILED DESCRIPTION

Definitions

[0016] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art. All patents, applications, published applications and other publications referenced herein are incorporated by reference in their entirety. In the event that there are multiple possible definitions for a term herein, those in this section prevail unless stated otherwise.

[0017] As used herein, "tautomer" and "tautomeric" refer to alternate forms of a compound disclosed herein that differ in the position of a proton. Non-limiting examples include enol-keto and imine-enamine tautomers, or the tautomeric forms of heteroaryl groups containing a ring atom

attached to both a ring -NH- moiety and a ring =N- moiety such as pyrazoles, imidazoles, benzimidazoles, triazoles, and tetrazoles.

[0018] It is understood that isotopes may be present in the compounds described herein. Each chemical element as represented in a compound structure may include any isotope of said element. For example, in a compound described herein a hydrogen atom can be any isotope of hydrogen, including but not limited to hydrogen-1 (protium) and hydrogen-2 (deuterium). Thus, reference herein to a compound encompasses all potential isotopic forms unless the context clearly dictates otherwise.

[0019] As used herein, “pharmaceutically acceptable salt” refers to a salt of a compound that does not abrogate the biological activity and properties of the compound. Pharmaceutical salts can be obtained by reaction of a compound disclosed herein with an acid or base. Base-formed salts include, without limitation, ammonium salt (NH_4^+); alkali metal, such as, without limitation, sodium or potassium, salts; alkaline earth, such as, without limitation, calcium or magnesium, salts; salts of organic bases such as, without limitation, dicyclohexylamine, piperidine, piperazine, methylpiperazine, N-methyl-D-glucamine, diethylamine, ethylenediamine, tris(hydroxymethyl)methylamine; and salts with the amino group of amino acids such as, without limitation, arginine and lysine. Useful acid-based salts include, without limitation, acetates, adipates, aspartates, ascorbates, benzoates, butyrates, caprate, caproate, caprylate, camsylates, citrates, decanoates, formates, fumarates, gluconates, glutarate, glycolates, hexanoates, laurates, lactates, maleates, nitrates, oleates, oxalates, octanoates, propanoates, palmitates, phosphates, sebacates, succinates, stearates, sulfates, sulfonates, such as methanesulfonates, ethanesulfonates, p-toluenesulfonates, salicylates, tartrates, and tosylates.

[0053] Acid addition salts can be formed by mixing a solution of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea with a solution of a pharmaceutically acceptable non-toxic acid such as hydrochloric acid, fumaric acid, maleic acid, succinic acid, acetic acid, citric acid, tartaric acid, carbonic acid, phosphoric acid, oxalic acid, dichloroacetic acid, or the like. Basic salts can be formed by mixing a solution of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea with a solution of a pharmaceutically acceptable non-toxic base such as sodium hydroxide, potassium hydroxide, choline hydroxide, sodium carbonate and the like. Suitable pharmaceutically

acceptable salts can be composed of a compound with one or more counterions, *e.g.*, a dichloride, or with a fraction of a counterion, *e.g.*, a hemitartrate.

[0020] Pharmaceutically acceptable solvates and hydrates are complexes of a compound with one or more solvent or water molecules, or a fraction thereof, for example from 1 to about 100, or 1 to about 10, or 1 to about 2, 3 or 4, solvent or water molecules, or, alternatively, $\frac{1}{4}$ to $\frac{1}{2}$ of a solvent or water molecule, *e.g.* monohydrate.

[0021] As used herein, to “modulate” the activity of a receptor means either to activate it, *i.e.*, to increase its cellular function over the base level measured in the particular environment in which it is found, or deactivate it, *i.e.*, decrease its cellular function to less than the measured base level in the environment in which it is found and/or render it unable to perform its cellular function at all, even in the presence of a natural binding partner. A natural binding partner is an endogenous molecule that is an agonist for the receptor.

[0022] As used herein, a “subject” refers to an animal that is the object of treatment, observation and/or experiment. “Animal” includes cold- and warm-blooded vertebrates and invertebrates such as birds, fish, shellfish, reptiles and, in particular, mammals. “Mammal” includes, without limitation, mice; rats; rabbits; guinea pigs; dogs; cats; sheep; goats; cows; horses; primates, such as monkeys, chimpanzees, and apes, and, in particular, humans.

[0023] As used herein, a “patient” refers to a subject that is being treated by a medical professional such as an M.D. or a D.V.M. to attempt to cure, or at least ameliorate the effects of, a particular disease or condition or to prevent the disease or condition from occurring in the first place.

[0024] As used herein, a “pharmaceutically acceptable excipient” refers to an inert substance that is added to a pharmaceutical composition to provide, without limitation, bulk, consistency, stability, binding ability, lubrication, disintegrating ability, etc., to the composition and that does not abrogate the biological activity and properties of the active ingredient.

[0025] As used herein, a “receptor” is intended to include any molecule present inside or on the surface of a cell that may affect cellular physiology when it is inhibited or stimulated by a ligand. Typically, a receptor comprises an extracellular domain with ligand-binding properties, a transmembrane domain that anchors the receptor in the cell membrane, and a cytoplasmic domain that generates a cellular signal in response to ligand binding (“signal transduction”). A receptor

also includes any intracellular molecule that in response to ligation generates a signal. A receptor also includes any molecule having the characteristic structure of a receptor, but with no identifiable ligand. In addition, a receptor includes a truncated, modified, mutated receptor, or any molecule comprising partial or all of the sequences of a receptor.

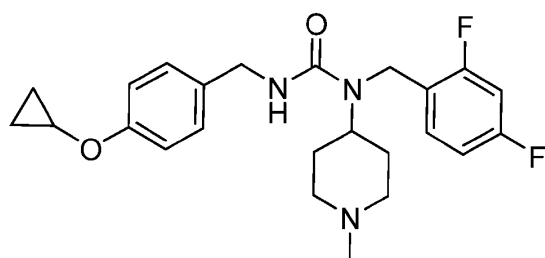
[0026] As is known by those skilled in the art, steady-state concentration (C_{ss}) is defined as the time during which the concentration remains stable or consistent when the drug is given repeatedly. Hence, as used herein, " $C_{max,ss}$ " refers to the maximum stable or consistent concentration observed following administration.

[0027] When used herein, "prevent/preventing" should not be construed to mean that a condition and/or a disease never might occur again after use of a compound or pharmaceutical composition according to embodiments disclosed herein to achieve prevention. Further, the term should neither be construed to mean that a condition not might occur, at least to some extent, after such use to prevent said condition. Rather, "prevent/preventing" is intended to mean that the condition to be prevented, if occurring despite such use, will be less severe than without such use.

[0028] As used herein, the term "about" includes the recited number ± 0.5 of the last digit thereof. Thus, "about 1" means 0.5 to 1.5 and "about 0.1" means 0.05 to 0.15.

Compositions and Methods

[0029] Some embodiments relates to compositions and methods wherein the compound is 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea:

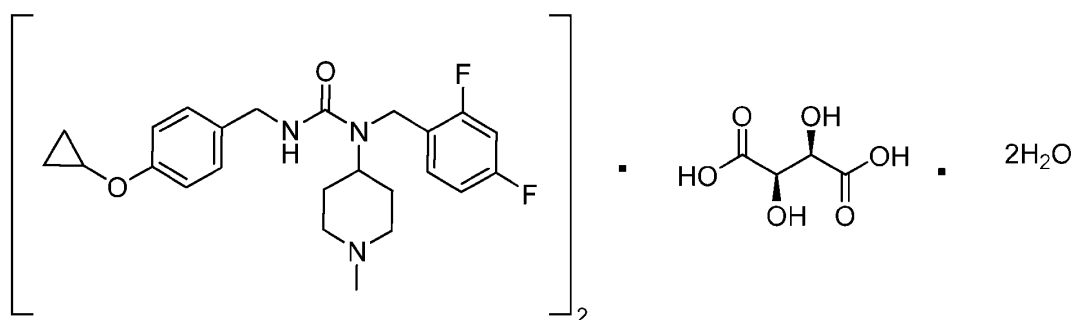


or a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0030] This compound can also be named as *N*-3-(4-cyclopropoxybenzyl)-*N'*-(2,4-difluorobenzyl)-*N'*-(1-methylpiperidin-4-yl)urea or *N'*-[[4-(cyclopropyloxy)phenyl]methyl]-*N*-[(2,4-difluorophenyl)-methyl]-*N*-(1-methyl-4-piperidinyl)urea.

[0031] A pharmaceutically acceptable salt thereof of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea is a tartrate salt, *e.g.*, a hemitartrate salt. The name of the hemitartrate salt is *e.g.* named (3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, (2*R*,3*R*)-2,3-dihydroxybutanedioate (2:1) or Urea, *N*-3-(4-cyclopropoxybenzyl)-*N'*-(2,4-difluorobenzyl)-*N'*-(1-methylpiperidin-4-yl)-, (2*R*,3*R*)-2,3-dihydroxybutanedioate (2:1).

[0032] In some embodiments, (3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, (2*R*,3*R*)-2,3-dihydroxybutanedioate is:



[0033] Some embodiments disclosed herein relate to pharmaceutical compositions containing from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof, and one or more pharmaceutically acceptable excipients.

[0034] According to some embodiments, the pharmaceutical compositions contain about 15 mg to about 85 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0035] According to some embodiments, the pharmaceutical compositions contain about 20 mg to about 80 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0036] According to some embodiments, the pharmaceutical compositions contain about 25 mg to about 75 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-

methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0037] According to some embodiments, the pharmaceutical compositions contain about 25 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0038] According to some embodiments, the pharmaceutical compositions contain about 20 mg to about 40 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0039] According to some embodiments, the pharmaceutical compositions contain about 25 mg to about 35 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0040] According to some embodiments, the pharmaceutical compositions contain about 50 mg to about 70 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0041] According to some embodiments, the pharmaceutical compositions contain about 55 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt or salt hydrate thereof.

[0042] According to some embodiments, the pharmaceutical compositions contain about 10 mg, about 12.5 mg, about 15 mg, about 17.5 mg, about 20 mg, about 22.5 mg, about 25 mg, about 27.5 mg, about 30 mg, about 32.5 mg, about 35 mg, about 37.5 mg, about 40 mg, about 42.5 mg, about 45 mg, about 47.5 mg, about 50 mg, about 52.5 mg, about 55 mg, about 57.5 mg, about 60 mg, about 62.5 mg, about 65 mg, about 67.5 mg, about 70 mg, about 72.5 mg, about 75 mg, about 77.5 mg, about 80 mg, about 82.5 mg, about 85 mg, about 87.5 mg, or about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)-urea,

or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0043] According to certain embodiments, the pharmaceutical compositions contain about 20 mg, about 22.5 mg, about 25 mg, about 27.5 mg, about 30 mg, about 32.5 mg, about 35 mg, about 37.5 mg, or about 40 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0044] According to some embodiments, the pharmaceutical compositions contain about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0045] According to some embodiments, the pharmaceutical compositions contain about 50 mg, about 52.5 mg, about 55 mg, about 57.5 mg, about 60 mg, about 62.5 mg, about 65 mg, about 67.5 mg, or about 70 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0046] According to some embodiments, the pharmaceutical compositions contain about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0047] According to some embodiments, an active ingredient is a salt of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea. Suitable salts include both pharmaceutically acceptable acid addition salts and pharmaceutically acceptable basic addition salts. Examples of pharmaceutically acceptable salts are acid addition salts, e.g. pharmaceutically acceptable salts are tartrates, such as hemitartrates.

[0048] According to some embodiments, an active ingredient is a solvate or hydrate of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, e.g. a hydrate thereof, and e.g. a monohydrate or a hemihydrate.

[0049] According to some embodiments, an active ingredient is a salt hydrate of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea.

[0050] Suitable salt hydrates include both pharmaceutically acceptable acid addition salts and pharmaceutically acceptable basic addition salts. Examples of pharmaceutically acceptable salt hydrates are tartrate hydrates, additional examples of pharmaceutically acceptable salt hydrates are hemitartrate hemihydrates and/or hemitartrate monohydrates.

[0051] According to some embodiments, an active ingredient is a hemitartrate hydrate of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea.

[0052] According to some embodiments, an active ingredient is a hemitartrate monohydrate of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea.

[0053] Suitable routes of administration for the pharmaceutical compositions may, for example, include oral, rectal, transmucosal, topical, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intravenous, intramedullary injections, as well as intrathecal, direct intraventricular, intraperitoneal, intranasal, or intraocular injections. The compounds can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills, transdermal (including electrotransport) patches, and the like, for prolonged and/or timed, pulsed administration at a predetermined rate. For example, the pharmaceutical compositions are formulated for oral administration.

[0054] The pharmaceutical compositions of the present disclosure may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, and/or tableting processes.

[0055] Pharmaceutical compositions for use as described herein thus may be formulated in conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Proper formulation is dependent upon the route of administration chosen. Any of the well-known techniques, carriers, and excipients may be used as suitable and as understood in the art, *e.g.*, as found in *Remington's Pharmaceutical Sciences*.

[0056] Pharmaceutical compositions for oral administration can be formulated readily by combining the requisite amount of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methyl-piperidin-4-yl)urea, or a salt or salt hydrate thereof, with one or more pharmaceutically acceptable excipients well known in the art. Such excipients enable the pharmaceutical compositions of the disclosure to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a mammalian patient being treated.

[0057] According to some embodiments, the pharmaceutical compositions are formulated for administration to a human subject, *e.g.*, an adult human (*i.e.*, a human over 12 years of age). According to some embodiments, the pharmaceutical compositions are formulated for oral administration to a human subject, *e.g.*, an adult human.

[0058] According to some embodiments, the pharmaceutical compositions are formulated for administration to a human subject, *e.g.*, an adult human, once per day. According to other embodiments, the pharmaceutical compositions are formulated for administration to a human subject, *e.g.*, an adult human, more than once per day, *e.g.*, twice a day, three times a day, etc.

[0059] According to some embodiments, the pharmaceutical compositions are formulated for oral administration to a human subject, *e.g.*, an adult human, once per day. According to other embodiments, the pharmaceutical compositions are formulated for oral administration to a human subject, *e.g.*, an adult human, more than once per day.

[0060] Population pharmacokinetic studies, including determination of peak plasma concentrations (C_{max}), are described in U.S. Department of Health and Human Services, Food and Drug Administration Guidance for Industry “Population Pharmacokinetics” (July 2019) and “Exposure-Response Relationships—Study Design, Data Analysis, and Regulatory Applications” (2003). These documents can be found at: <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>. Steady state (ss) values can be obtained following multiple administrations of a substance.

[0061] When administered orally to an adult human, some embodiments of the pharmaceutical compositions disclosed herein results in a mean $C_{max,ss}$ of at least 10 ng/mL, at least about 20 ng/mL, at least about 30 ng/mL, at least about 40 ng/mL, at least about 50 ng/mL, at least about 60 ng/mL, at least about 70 ng/mL, at least about 80 ng/mL, at least about 90 ng/mL, at least about

100 ng/mL, at least about 110 ng/mL, at least about 120 ng/mL, at least about 130 ng/mL, at least about 140 ng/mL, at least about 150 ng/mL, at least about 160 ng/mL, at least about 170 ng/mL, at least about 180 ng/mL, at least about 190 ng/mL, at least about 200 ng/mL, at least 210 ng/mL, at least 220 ng/mL, at least 230 ng/mL, at least 240 ng/mL, and at least 250 ng/mL.

[0062] When administered orally to an adult human, some embodiments of the pharmaceutical compositions disclosed herein result in a mean $C_{max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL, about 30 ng/mL to about 180 ng/mL, about 40 ng/mL to about 170 ng/mL, about 50 ng/mL to about 150 ng/mL, and about 60 ng/mL to about 140 ng/mL.

[0063] When administered orally to an adult human, some embodiments of the pharmaceutical compositions disclosed herein result in a mean $C_{max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL. Other embodiments of the pharmaceutical compositions disclosed herein result in a mean $C_{max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL when administered orally to an adult human.

[0064] Some embodiments disclosed herein relate to methods for treating a disease or condition in a mammalian patient, such as a human, comprising administering to that patient an embodiment of the pharmaceutical compositions disclosed herein, wherein the disease is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Athereosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia

(FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAI1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, e.g. manifested by hallucinations and/or delusions, Psychoses associated with neurodegenerative disorders e.g. manifested by hallucinations and/or delusions, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of

schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

[0065] Some embodiments disclosed herein relate to methods for treating a disease or condition in a mammalian patient, such as a human, comprising administering to that patient an embodiment of the pharmaceutical compositions disclosed herein, wherein the disease is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), e.g. manifested by hallucinations and/or delusions, Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), e.g. manifested by hallucinations and/or delusions, Dementia related psychosis, e.g. manifested by hallucinations and/or delusions, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

[0066] Some embodiments disclosed herein relate to methods for treating a disease or condition in a mammalian patient, such as a human, comprising administering to that patient an embodiment of the pharmaceutical compositions disclosed herein, wherein the disease is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis

(ADP), e.g. manifested by hallucinations and/or delusions, Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), e.g. manifested by hallucinations and/or delusions, Dementia related psychosis, .g. manifested by hallucinations and/or delusions, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, major depressive disorder (MDD), and treatment resistant depression.

[0067] Some embodiments disclosed herein relate to methods for suppressing the activity of the serotonin receptor 5-HT_{2A} in a mammalian subject, such as a human, comprising administering to that subject an embodiment of the pharmaceutical compositions disclosed herein.

[0068] An embodiment of the present disclosure relates to a method of treating PTSD in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0069] Another embodiment of the present disclosure relates to a method of treating PTSD in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0070] Another embodiment of the present disclosure relates to a method of treating PTSD in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0071] Another embodiment of the present disclosure relates to a method of treating Autism in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0072] Another embodiment of the present disclosure relates to a method of treating Autism in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent

amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0073] Another embodiment of the present disclosure relates to a method of treating Autism in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0074] Another embodiment of the present disclosure relates to a method of treating generalized anxiety disorder in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0075] Another embodiment of the present disclosure relates to a method of treating generalized anxiety disorder in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)-urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0076] Another embodiment of the present disclosure relates to a method of treating generalized anxiety disorder in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)-urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0077] Another embodiment of the present disclosure relates to a method of treating All-cause treatment resistant anxiety in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0078] Another embodiment of the present disclosure relates to a method of treating All-cause treatment resistant anxiety in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0079] Another embodiment of the present disclosure relates to a method of treating All-cause treatment resistant anxiety in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0080] Another embodiment of the present disclosure relates to a method of treating Panic disorder in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0081] Another embodiment of the present disclosure relates to a method of treating Panic disorder in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0082] Another embodiment of the present disclosure relates to a method of treating Panic disorder in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0083] Another embodiment of the present disclosure relates to a method of treating Alzheimer's disease psychosis in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0084] Another embodiment of the present disclosure relates to a method of treating Alzheimer's disease psychosis in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0085] Another embodiment of the present disclosure relates to a method of treating Alzheimer's disease psychosis in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or

about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0086] Another embodiment of the present disclosure relates to a method of treating Lewy body dementia in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0087] Another embodiment of the present disclosure relates to a method of treating Lewy body dementia in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0088] Another embodiment of the present disclosure relates to a method of treating Lewy body dementia in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0089] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease dementia in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0090] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease dementia in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0091] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease dementia in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0092] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease psychosis in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0093] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease psychosis in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0094] Another embodiment of the present disclosure relates to a method of treating Parkinson's disease psychosis in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0095] Another embodiment of the present disclosure relates to a method of treating Dementia related psychosis in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0096] Another embodiment of the present disclosure relates to a method of treating Dementia related psychosis in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0097] Another embodiment of the present disclosure relates to a method of treating Dementia related psychosis in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[0098] Another embodiment of the present disclosure relates to a method of treating vascular dementia in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[0099] Another embodiment of the present disclosure relates to a method of treating vascular dementia in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00100] Another embodiment of the present disclosure relates to a method of treating vascular dementia in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00101] Another embodiment of the present disclosure relates to a method of treating frontotemporal dementia in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00102] Another embodiment of the present disclosure relates to a method of treating frontotemporal dementia in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00103] Another embodiment of the present disclosure relates to a method of treating frontotemporal dementia in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00104] Another embodiment of the present disclosure relates to a method of treating negative symptoms in schizophrenia in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00105] Another embodiment of the present disclosure relates to a method of treating negative symptoms in schizophrenia in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-

4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00106] Another embodiment of the present disclosure relates to a method of treating negative symptoms in schizophrenia in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00107] Another embodiment of the present disclosure relates to a method of treating PDD in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00108] Another embodiment of the present disclosure relates to a method of treating PDD in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00109] Another embodiment of the present disclosure relates to a method of treating PDD in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00110] Another embodiment of the present disclosure relates to a method of treating ADD in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00111] Another embodiment of the present disclosure relates to a method of treating ADD in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00112] Another embodiment of the present disclosure relates to a method of treating ADD in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00113] Another embodiment of the present disclosure relates to a method of treating Depression in mild cognitive impairment in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00114] Another embodiment of the present disclosure relates to a method of treating Depression in mild cognitive impairment in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00115] Another embodiment of the present disclosure relates to a method of treating Depression in mild cognitive impairment in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00116] Another embodiment of the present disclosure relates to a method of treating MDD in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

[00117] Another embodiment of the present disclosure relates to a method of treating MDD in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00118] Another embodiment of the present disclosure relates to a method of treating MDD in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent

amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00119] Another embodiment of the present disclosure relates to a method of treating treatment resistant depression in a human comprising administering to that human a pharmaceutical composition according to one of the embodiments or claims disclosed herein.

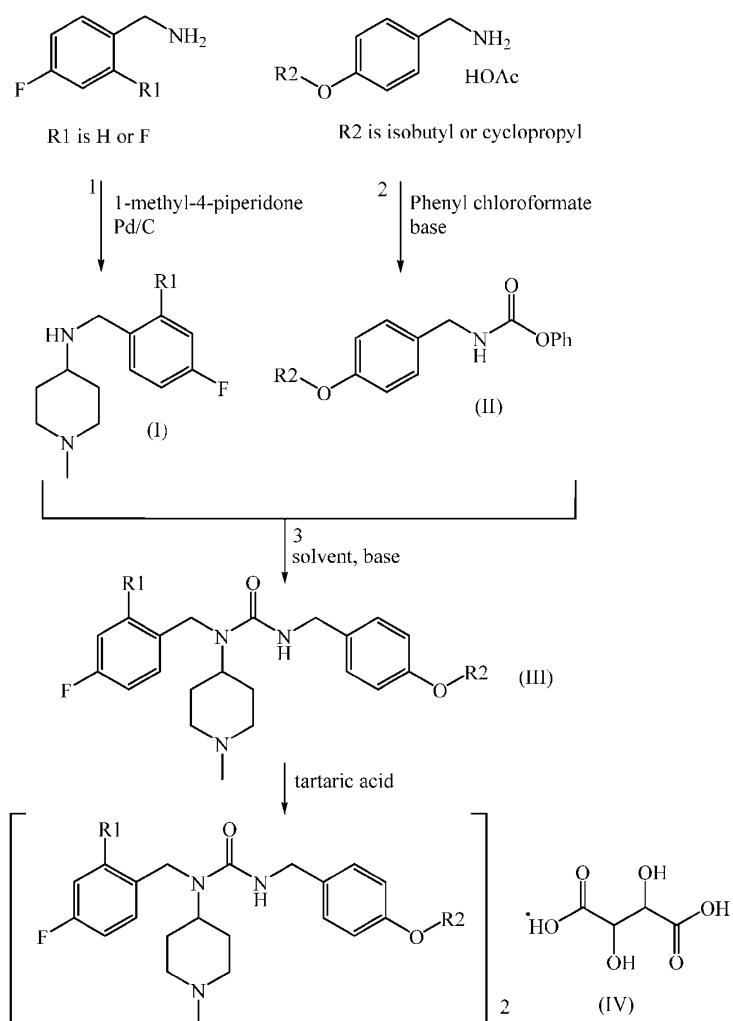
[00120] Another embodiment of the present disclosure relates to a method of treating treatment resistant depression in a human comprising administering to that human about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00121] Another embodiment of the present disclosure relates to a method of treating treatment resistant depression in a human comprising administering to that human about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

Synthesis

[00122] Method for manufacturing a selective 5-HT_{2A} receptor inverse agonist

[00123] Pimavanserin and 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea may be synthesized according to the following general scheme



[00124] Reaction 1 consists of reductive amination of 1-methyl-4-piperidone (NMP) with the applicable benzylamine to produce *N*-(2-[R1]-4-difluorobenzyl)-1-methylpiperidin-4-amine, for example using palladium on carbon in ethanol or methanol is heated under hydrogen atmosphere and subsequently filtered to give compound (I) as a solution.

[00125] Reaction 2 consists of a reaction of a 4-alkoxybenzylamine acetate with phenyl chloroformate and a base such as potassium carbonate (K_2CO_3) in a suitable solvent such as a mixture of toluene and water to give compound (II).

[00126] Reaction 3 is the reaction of (I) and (II) in a suitable solvent, *e.g.*, methanol, toluene, or 2-methyl tetrahydrofuran, in the presence of a suitable base, *e.g.*, triethylamine or potassium carbonate. Except when methanol is used as solvent, the solvent of compound (I) is replaced by another solvent such as toluene.

[00127] The reaction is followed by washing with an alkaline aqueous solution, *e.g.*, a sodium hydroxide solution, and water, and concentration followed by addition of ethyl acetate and heptane and crystallization to give 3-(4-alkoxybenzyl)-1-(2-[R1]-4-fluorobenzyl)-1-(1-methylpiperidin-4-yl)urea.

[00128] The free base (III) of pimavanserine or 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea can be converted to a tartrate salt by adding compound (III) to a mixture of methyl ethyl ketone and methanol in the presence of L-tartaric acid, followed by crystallization using methyl ethyl ketone and water to obtain compound (IV).

[00129] Alternatively, the tartrate salt may be directly obtained by adding L-tartaric acid to compound (III) in methyl ethyl ketone and water. Compound (IV) may then be made into a hydrate by heating compound (IV) in methyl ethyl ketone and water, followed by cooling and seeding to give a pimavanserine tartrate hydrate or 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea hemitartrate hydrate.

[00130] The description set forth above is provided to give those of ordinary skill in the art with a complete disclosure and description of how to make and use the various embodiments claimed below and are not intended to limit the scope of what is disclosed herein. Modifications that are obvious to persons of skill in the art are intended to be within the scope of the following claims. All publications, patents, and patent applications cited in this specification are incorporated herein by reference as if each such publication, patent or patent application were specifically and individually indicated to be incorporated herein by reference.

[00131] In the interest of completeness, embodiments of the invention are set forth in the following numbered clauses.

[00132] Clause 1. A pharmaceutical composition comprising from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or

pharmaceutically acceptable salt hydrate thereof, as an active ingredient and one or more pharmaceutically acceptable excipients.

[00133] Clause 2. A pharmaceutical composition for the treatment of diseases and conditions associated with the serotonin receptor 5-HT, comprising from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, as an active ingredient and one or more pharmaceutically acceptable excipients.

[00134] Clause 3. The pharmaceutical composition of clause 1 or 2, wherein the composition comprises about 15 mg to about 85 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00135] Clause 4. The pharmaceutical composition of any one of clauses 1-3, wherein the composition comprises about 20 mg to about 80 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00136] Clause 5. The pharmaceutical composition of any one of clauses 1-4, wherein the composition comprises about 25 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00137] Clause 6. The pharmaceutical composition of any one of clauses 1-5, wherein the composition comprises about 25 mg to about 35 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00138] Clause 7. The pharmaceutical composition of any one of clauses 1-6, wherein the composition comprises about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00139] Clause 8. The pharmaceutical composition of any one of clauses 1-5, wherein the composition comprises about 55 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-

[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00140] Clause 9. The pharmaceutical composition of any one of clauses 1-5, wherein the composition comprises about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

[00141] Clause 10. The pharmaceutical composition of any one of clauses 1-9, wherein the active ingredient comprises 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)-urea hemitartrate.

[00142] Clause 11. The pharmaceutical composition any one of clauses 1-9, wherein the active ingredient comprises 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)-urea hemitartrate monohydrate.

[00143] Clause 12. The pharmaceutical composition of any one of clauses 1-11, wherein the composition is formulated for oral administration.

[00144] Clause 13. The pharmaceutical composition of any one of clauses 1-12, wherein the composition is formulated for administration to a human.

[00145] Clause 14. The pharmaceutical composition of any one of clauses 1-13, wherein the composition is formulated for administration to a human once per day.

[00146] Clause 15. The pharmaceutical composition of any one of clauses 1-13, wherein the composition is formulated for administration to a human in multiple doses per day.

[00147] Clause 16. The pharmaceutical composition of any one of clauses 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.

[00148] Clause 17. The pharmaceutical composition of any one of clauses 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.

[00149] Clause 18. The pharmaceutical composition of any one of clauses 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.

[00150] Clause 19. The pharmaceutical composition of any one of clauses 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ of about 68 ng/mL.

[00151] Clause 20. The pharmaceutical composition of any one of clauses 1-15, wherein oral administration of to a human results in a mean $C_{max,ss}$ of about 133 ng/mL.

[00152] Clause 21. The pharmaceutical composition of any one of clauses 1-20, wherein the human is an adult human.

[00153] Clause 22. The pharmaceutical composition of any one of clauses 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Atherosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrasidal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm

mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatitis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBA1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

[00154] Clause 23. The pharmaceutical composition of any one of clauses 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

[00155] Clause 24. The pharmaceutical composition of any one of clauses 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

[00156] Clause 25. The pharmaceutical composition of any one of clauses 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is Alzheimer's disease psychosis (ADP).

[00157] Clause 26. The pharmaceutical composition of any one of clauses 1-25, wherein the composition is formulated as a capsule or a tablet.

[00158] Clause 27. A method of treating a disease or condition comprising administering to a mammalian patient in need thereof from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or

about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate.

[00159] Clause 28. The method of clause 27, wherein the disease or condition is associated with the serotonin receptor 5-HT.

[00160] Clause 29. The method of clauses 27 or 28, wherein about 15 mg to about 85 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00161] Clause 30. The method of any one of clauses 27-29, wherein about 20 mg to about 80 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00162] Clause 31. The method of any one of clauses 27-29, wherein about 25 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00163] Clause 32. The method of any one of clauses 27-29, wherein about 25 mg to about 35 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00164] Clause 33. The method of any one of clauses 27-29, wherein about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00165] Clause 34. The method of any one of clauses 27-29, wherein about 55 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00166] Clause 35. The method of any one of clauses 27-29, wherein about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or

about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00167] Clause 36. The method of any one of clauses 27-35, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea hemitartrate is administered.

[00168] Clause 37. The method of any one of clauses 27-35, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea hemitartrate monohydrate is administered.

[00169] Clause 38. The method of any one of clauses 27-37, wherein administration is oral.

[00170] Clause 39. The method of any one of clauses 27-38, wherein administration is once per day.

[00171] Clause 40. The method of any one of clauses 27-38, wherein administration is more than once per day.

[00172] Clause 41. The method of any one of clauses 27-40, wherein the mammalian patient is a human.

[00173] Clause 42. The method of any one of clauses 27-41, wherein the disease or condition is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Athereosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes

mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatitis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBA1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction

associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

[00174] Clause 43. The method of any one of clauses 27-41, wherein the disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

[00175] Clause 44. The method of any one of clauses 27-41, wherein the disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

[00176] Clause 45. The method of any one of clauses 27-44, wherein oral administration to a human in need thereof results in a mean $C_{max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.

[00177] Clause 46. The method of any one of clauses 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.

[00178] Clause 47. The method of any one of clauses 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.

[00179] Clause 48. The method of any one of clauses 27-44, wherein oral administration of to an adult human in need thereof results in a mean $C_{max,ss}$ of about 68 ng/mL.

[00180] Clause 49. The method of any one of claims 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{max,ss}$ of about 133 ng/mL.

[00181] Clause 50. The method of any one of clauses 41-49, wherein the human is an adult human.

[00182] Clause 51. The method of any one of clauses 27-50, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered in the form of a capsule or a tablet.

[00183] Clause 52. The method of any one of clauses 27-51, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate, is administered in combination with one or more pharmaceutically acceptable excipients.

[00184] Clause 53. A method of modulating the activity of serotonin receptor 5-HT_{2A} comprising administering to a mammalian subject in need thereof from about 10 mg to about 90 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate.

[00185] Clause 54. The method of clause 53, wherein the activity of serotonin receptor 5-HT_{2A} is suppressed.

[00186] Clause 55. The method of clauses 53 or 54, wherein about 15 mg to about 85 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00187] Clause 56. The method of any one of clauses 53-55, wherein about 20 mg to about 80 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00188] Clause 57. The method of any one of clauses 53-56, wherein about 25 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00189] Clause 58. The method of any one of clauses 53-57, wherein about 25 mg to about 35 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00190] Clause 59. The method of any one of clauses 53-58, wherein about 30 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00191] Clause 60. The method of any one of clauses 53-57, wherein about 55 mg to about 65 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00192] Clause 61. The method of any one of clauses 53-57 and 60, wherein about 60 mg of 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

[00193] Clause 62. The method of any one of clauses 53-61, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea hemitartrate is administered.

[00194] Clause 63. The method of any one of clauses 53-62, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)methyl]-1-(1-methylpiperidin-4-yl)urea hemitartrate monohydrate is administered.

[00195] Clause 64. The method of any one of clauses 53-63, wherein administration is oral.

[00196] Clause 65. The method of any one of clauses 53-64, wherein administration is once per day.

[00197] Clause 66. The method of any one of clauses 53-64, wherein administration is more than once per day.

[00198] Clause 67. The method of any one of clauses 53-66, wherein the mammalian patient is a human.

[00199] Clause 68. The method of any one of clauses 53-67, wherein the mammalian patient is an adult human.

[00200] Clause 69. The method of any one of clauses 53-68, wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Athereosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimalid disorder, Fibromyalgia, Frailty, Friedrich's

Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatitis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAl)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura,

Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

[00201] Clause 70. The method of any one of clauses 53-69, wherein wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

[00202] Clause 71. The method of any one of clauses 53-69, wherein wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

[00203] Clause 72. The method of any one of clauses 53-69, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.

[00204] Clause 73. The method of any one of clauses 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.

[00205] Clause 74. The method of any one of clauses 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.

[00206] Clause 75. The method of any one of clauses 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ of about 68 ng/mL.

[00207] Clause 76. The method of any one of clauses 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ of about 133 ng/mL.

[00208] Clause 77. The method of any one of clauses 53-71, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered in the form of a capsule or a tablet.

[00209] Clause 78. The method of any one of clauses 53-71, wherein 3-[(1-cyclopropoxyphenyl)-methyl]-1-[(2,4-difluorophenyl)-methyl]-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate, is administered in combination with one or more pharmaceutically acceptable excipients.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising from about 10 mg to about 90 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, as an active ingredient and one or more pharmaceutically acceptable excipients.
2. A pharmaceutical composition for the treatment of diseases and conditions associated with the serotonin receptor 5-HT, comprising from about 10 mg to about 90 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, as an active ingredient and one or more pharmaceutically acceptable excipients.
3. The pharmaceutical composition of claim 1 or 2, wherein the composition comprises about 15 mg to about 85 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.
4. The pharmaceutical composition of any one of claims 1-3, wherein the composition comprises about 20 mg to about 80 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.
5. The pharmaceutical composition of any one of claims 1-4, wherein the composition comprises about 25 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

6. The pharmaceutical composition of any one of claims 1-5, wherein the composition comprises about 25 mg to about 35 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

7. The pharmaceutical composition of any one of claims 1-6, wherein the composition comprises about 30 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

8. The pharmaceutical composition of any one of claims 1-5, wherein the composition comprises about 55 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

9. The pharmaceutical composition of any one of claims 1-5, wherein the composition comprises about 60 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof.

10. The pharmaceutical composition of any one of claims 1-9, wherein the active ingredient comprises 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate.

11. The pharmaceutical composition any one of claims 1-9, wherein the active ingredient comprises 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate monohydrate.

12. The pharmaceutical composition of any one of claims 1-11, wherein the composition is formulated for oral administration.
13. The pharmaceutical composition of any one of claims 1-12, wherein the composition is formulated for administration to a human.
14. The pharmaceutical composition of any one of claims 1-13, wherein the composition is formulated for administration to a human once per day.
15. The pharmaceutical composition of any one of claims 1-13, wherein the composition is formulated for administration to a human in multiple doses per day.
16. The pharmaceutical composition of any one of claims 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.
17. The pharmaceutical composition of any one of claims 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.
18. The pharmaceutical composition of any one of claims 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.
19. The pharmaceutical composition of any one of claims 1-15, wherein oral administration of to a human results in a mean $C_{\max,ss}$ of about 68 ng/mL.

20. The pharmaceutical composition of any one of claims 1-15, wherein oral administration of to a human results in a mean $C_{max,ss}$ of about 133 ng/mL.
21. The pharmaceutical composition of any one of claims 1-20, wherein the human is an adult human.
22. The pharmaceutical composition of any one of claims 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Atherosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrmidal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura,

Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatitis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAl1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma,

glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

23. The pharmaceutical composition of any one of claims 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

24. The pharmaceutical composition of any one of claims 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

25. The pharmaceutical composition of any one of claims 2-21, wherein the disease or condition associated with the serotonin receptor 5-HT is Alzheimer's disease psychosis (ADP).

26. The pharmaceutical composition of any one of claims 1-25, wherein the composition is formulated as a capsule or a tablet.

27. A method of treating a disease or condition comprising administering to a mammalian patient in need thereof from about 10 mg to about 90 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate.

28. The method of claim 27, wherein the disease or condition is associated with the serotonin receptor 5-HT.

29. The method of claims 27 or 28, wherein about 15 mg to about 85 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

30. The method of any one of claims 27-29, wherein about 20 mg to about 80 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

31. The method of any one of claims 27-29, wherein about 25 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

32. The method of any one of claims 27-29, wherein about 25 mg to about 35 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

33. The method of any one of claims 27-29, wherein about 30 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

34. The method of any one of claims 27-29, wherein about 55 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

35. The method of any one of claims 27-29, wherein about 60 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

36. The method of any one of claims 27-35, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate is administered.

37. The method of any one of claims 27-35, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate monohydrate is administered.

38. The method of any one of claims 27-37, wherein administration is oral.

39. The method of any one of claims 27-38, wherein administration is once per day.
40. The method of any one of claims 27-38, wherein administration is more than once per day.
41. The method of any one of claims 27-40, wherein the mammalian patient is a human.
42. The method of any one of claims 27-41, wherein the disease or condition is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Atherosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Straussler-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination,

Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAI1)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness,

vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

43. The method of any one of claims 27-41, wherein the disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

44. The method of any one of claims 27-41, wherein the disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

45. The method of any one of claims 27-44, wherein oral administration to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.
46. The method of any one of claims 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.
47. The method of any one of claims 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.
48. The method of any one of claims 27-44, wherein oral administration of to an adult human in need thereof results in a mean $C_{\max,ss}$ of about 68 ng/mL.
49. The method of any one of claims 27-44, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ of about 133 ng/mL.
50. The method of any one of claims 41-49, wherein the human is an adult human.
51. The method of any one of claims 27-50, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered in the form of a capsule or a tablet.
52. The method of any one of claims 27-51, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate, is administered in combination with one or more pharmaceutically acceptable excipients.

53. A method of modulating the activity of serotonin receptor 5-HT_{2A} comprising administering to a mammalian subject in need thereof from about 10 mg to about 90 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate.

54. The method of claim 53, wherein the activity of serotonin receptor 5-HT_{2A} is suppressed.

55. The method of claim 53 or 54, wherein about 15 mg to about 85 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

56. The method of any one of claims 53-55, wherein about 20 mg to about 80 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

57. The method of any one of claims 53-56, wherein about 25 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

58. The method of any one of claims 53-57, wherein about 25 mg to about 35 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an

equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

59. The method of any one of claims 53-58, wherein about 30 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

60. The method of any one of claims 53-57, wherein about 55 mg to about 65 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

61. The method of any one of claims 53-57 or 60, wherein about 60 mg of 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered.

62. The method of any one of claims 53-61, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate is administered.

63. The method of any one of claims 53-62, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea hemitartrate monohydrate is administered.

64. The method of any one of claims 53-63, wherein administration is oral.

65. The method of any one of claims 53-64, wherein administration is once per day.
66. The method of any one of claims 53-64, wherein administration is more than once per day.
67. The method of any one of claims 53-66, wherein the mammalian patient is a human.
68. The method of any one of claims 53-67, wherein the mammalian patient is an adult human.
69. The method of any one of claims 53-68, wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of Abnormal hormonal activity, Alzheimer's disease, Alzheimer's disease dementia, Alzheimer's disease psychosis, Addiction (alcohol, cocaine, methamphetamine, nicotine, and/or opioid), Addison's disease, ADHD, Alzheimer's disease psychosis, Affective disorders, Aggressiveness, Agitation, Akathisia, Alcohol addiction, Alcohol withdrawal, Amenorrhea, Amyotrophic lateral sclerosis, Anhedonia, Anorexia, Anti-NMDAR encephalitis, Anxiety, Appetite disorders, Asthma, Atherosclerosis, Autism, Behavioral disorders, Behavioral disturbances associated with dementia, Binge eating disorder associated with impulse control disorder (ICD), Bipolar disorder, Blindness, Borderline disorder, Borderline personality disorder, Bradykinesia, Bulimia, Buying associated with ICD, Cardiac arrhythmia, Cerebral vascular accidents, Charles Bonnet disease, Chemotherapy-induced emesis, Childhood autism, Chronic pain, Chronic insomnia, Chronic kidney disease, cocaine addiction, Cognitive disorders, craniofacial pain, temporomandibular joint (TMJ) / temporomandibular disorder (TMD), Cushing's disease, Delusion, Dementia, Dementia with Lewy Body or Lewy Body dementia, dementia and psychosis associated with Creutzfeld-Jakob disease (CJD), Gerstmann-Strausser-Schenker disease (GSSD) and fatal familial insomnia (FFI), Depression, Diabetes mellitus (non-insulin dependent), Diabetic peripheral neuropathy, Drug addiction, Double vision, Down's syndrome, Dyskinesia, Dysthymia, Dystonia, Ejaculatory problem, Emphysema, Epilepsy, Extrapyrimal disorder, Fibromyalgia, Frailty, Friedrich's Ataxia, Frontotemporal Dementia, Gambling associated with ICD, Galactorrhea, General anxiety

disorder, Glaucoma, hallucinations associated with or arising from psychedelic drug usage, Hair loss or thinning, Hallucination, Headache, Hemorrhoids, Huntington's disease, Hyperprolactinemia, Hypertension, Hypersexuality associated with ICD, Hypotension, Hypoglutamateriga disorders, Impulse control disorder, Idiopathic thrombocytopenic purpura, Impotence, Incontinence, Increased intraocular pressure, Infertility, Inflammatory pain, Insomnia, Ischemia, Ischemic stroke, Lewy body disease (LBD), Learning disorders, Libido (decreased), Loss of libido, Low male fertility, Low sperm mobility, Lupus, Machado-Joseph disease, Major depression, Mania, Menopausal symptoms, Metabolic syndrome, methamphetamine addiction, Migraine, mild cognitive impairment (MCI), morphine addiction, Motor tics, Multi-infarct dementia, Multiple sclerosis, Multiplex development disorder, Myocardial infarction, Myoclonus, Neuropathic pain, Neurodegenerative disorder, Neuropsychiatric disease, Nicotine addiction, Non motor symptoms of Parkinson's disease selected from dementia, depression, apathy, hallucinations, dribbling saliva (sialorrhea), constipation, pain, genitourinary problems, Non-alcoholic Fatty Liver disease, and sleep disorders, Obsessive compulsive disorder, On/off phenomena, Opioid addiction, Osteoporosis, Pancreatitis, Panic attacks, Parkinson-like disorders including Machado-Joseph disease, Pantothenate kinase-associated neurodegeneration (PKAN)/Neurodegeneration with brain iron accumulation 1 (NBAl)/Hallervorden-Spatz disease, and Wilson's disease, Parkinson's disease, Parkinson's disease dementia, Parkinson's disease psychosis, Periodic limb movement during sleep (PLMS), Peripheral vascular disease, Borderline Personality disorder, Pituitary tumor, Postherpetic neuralgia, Progressive Supranuclear Palsy, Prion disease including Creutzfeld-Jakob disease (CJD), Gerstmann-Straussler-Schenker disease (GSSD) and fatal familial insomnia (FFI), Postpartum depression, Postpartum psychosis, Prolactinoma, Pseudobulbar affect (PBA), Psychomotor slowing, Psychosis, Psychoses associated with neurodegenerative disorders, Psychosomatic disorders, Psychotic depression, post-traumatic stress disorder (PTSD), Raynaud's disease, Reflex sympathetic dystrophy, Restless legs syndrome, Retinal disease, Schizoaffective disorders, Schizophrenia, negative symptoms of schizophrenia, cognitive impairment associated with schizophrenia, Sepsis, Serotonin syndrome, Sexual dysfunction, Sexual dysfunction associated with antidepressant use, Sleep apnea, Sleep disorders, Sleep maintenance insomnia, social anxiety disorder, Spinal injury, Spinocerebellar Atrophy, Suicidal tendency, Thrombosis, Thrombotic stroke, Thrombotic thrombocytopenic purpura, Tinnitus, Tiredness, Tourette's syndrome, Transient insomnia, Traumatic brain injury, Treatment-

resistant depression, Treatment-resistant schizophrenia, Tremor, Vaginal dryness, Vascular disease, Vasospasm Wakefulness, vascular dementia, Hallucinations associated with Parkinson's disease, Delusions associated with Parkinson's disease; Hallucinations associated with Alzheimer's disease, Delusions associated with Alzheimer's disease; cancer, brain cancer, glioma, glioblastoma, Pancreatic cancer, Skin cancer, Hypoactive sexual desire disorder, adult type 2 diabetes mellitus with Parkinson's disease or dementia and Liver fibrosis.

70. The method of any one of claims 53-69, wherein wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Insomnia secondary to PTSD, Insomnia secondary to neurodegenerative disorders, Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, major depressive disorder (MDD)/treatment resistant depression, Obsessive compulsive disorder, Bipolar Depression, ADHD, Substance use disorder (Alcohol, Nicotine, Opioids, Cocaine, methamphetamine), and Down's syndrome.

71. The method of any one of claims 53-69, wherein wherein the activity of serotonin receptor 5-HT_{2A} is associated with a disease or condition is selected from the group consisting of post-traumatic stress disorder (PTSD), Autism, Autism Spectrum disorders, Asberger's Syndrome, generalized anxiety disorder (GAD), All-cause treatment resistant anxiety, Panic disorder, Alzheimer's disease psychosis (ADP), Lewy body dementia, Parkinson's disease dementia, Parkinson's disease psychosis (PDP), Dementia related psychosis, vascular dementia, frontotemporal dementia, negative symptoms schizophrenia, Parkinson's disease Depression (PDD), Alzheimer's disease Depression (ADD), Depression in mild cognitive impairment, Insomnia in mild cognitive impairment, and major depressive disorder (MDD)/treatment resistant depression.

72. The method of any one of claims 53-69, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 20 ng/mL to about 250 ng/mL.

73. The method of any one of claims 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 30 ng/mL to about 90 ng/mL.

74. The method of any one of claims 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ in the range of about 100 ng/mL to about 180 ng/mL.

75. The method of any one of claims 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ of about 68 ng/mL.

76. The method of any one of claims 53-71, wherein oral administration of to a human in need thereof results in a mean $C_{\max,ss}$ of about 133 ng/mL.

77. The method of any one of claims 53-71, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate thereof, is administered in the form of a capsule or a tablet.

78. The method of any one of claims 53-71, wherein 3-(4-cyclopropoxybenzyl)-1-(2,4-difluorobenzyl)-1-(1-methylpiperidin-4-yl)urea, or about an equivalent amount of a pharmaceutically acceptable salt and/or pharmaceutically acceptable salt hydrate, is administered in combination with one or more pharmaceutically acceptable excipients.