COMBINATION THERAPIES INCLUDING METAL CHANNEL ACTIVATORS AND NMDA RECEPTOR ANTAGONISTS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This International Patent Application claims priority to United States Provisional Patent Application No. 63/402,416, filed August 30, 2022, which is incorporated by reference in its entirety herein.

TECHNICAL FIELD

[0002] The present invention relates to combination therapies for treatment of various medical conditions. Specifically, the present invention relates to a combination of a metal channer activator and N-methyl-D-aspartate (NMDA) receptor antagonists for treatment of neurological and neurodegenerative disorders.

BACKGROUND

[0003] Metal channel activators (openers) are associated with a wide range of physiological functions including the regulation of the electrical properties of excitable cells. Metal channels control the follow of metal ions such as Potassium (K^+) and Sodium (Na^+) across a cell membrane. A primary function of these channels in the brain is to regulate the neuronal action potential. Several neurologic disorders are potentially due to dysregulation of metal channels.

[0004] Potassium (K^+) channels, present on the plasma membranes of most cell types, are the most diverse class of all ion channels. Potassium channels of the Kv7 family of voltage-gated potassium (K^+) channels are of particular therapeutic interest due to their importance in neurological conditions such as excitability disorders including Amyotrophic lateral sclerosis (ALS). There are five members of the Kv7 family of voltage-gated potassium (K^+) channels, including Kv7.1, Kv7.2, Kv7.3, Kv7.4, and Kv7.5.

[0005] Metal channel activators have been reported to be useful for treatment of various neurological and neurodegenerative disorders. Thus far, only one metal channel activator, Retigabine, has been FDA approved. Retigabine is used as anticonvulsant for the treatment of epilepsy. Further Kv7 channel activators have been proposed for the treatment of many conditions including substance abuse and mood disorders (Vigil FA, Carver CM, Shapiro MS. Pharmacological Manipulation of K v 7 Channels as a New Therapeutic Tool for

Multiple Brain Disorders. Front Physiol. 2020 Jun 19;11:688. doi: 10.3389/fphys.2020.00688). There remains a need, however, for new therapies utilizing Kv7. One solution is combining metal channel activators with other therapeutic agents to significantly improve treatment outcomes.

[0006] NDMA receptor antagonists target the NDMA receptor, a receptor which allows calcium efflux in the presence of glutamate or glycine when neurons are depolarized. NDMA receptor antagonists prevent calcium efflux and have been used as anesthetics. Recent research, primarily focused on Ketamine, has revealed an unexpected antidepressant effect. Lanicemine has been developed as an alternative antidepressant to Ketamine with reduced side effects but has not successfully treated depression as a single agent in randomized controlled trials.

[0007] Described herein are compositions and methods for combination therapies of Kv7 openers with NMDA receptor antagonists. The combination therapies have treatment capabilities greater than Kv7 openers or NMDA receptor antagonists alone, and may be particularly useful for depressive disorders. Pharmaceutical compositions combining these agents may also be useful for treatment of a pain and neurological or neurodegenerative diseases. These two agents target distinct molecular targets associated with depressive disorders, pain disorders, neurological diseases and neurodegenerative disorders. Specifically, the Kv7 channel opener reduces excitability, and NMDA receptor antagonists reduce efflux of cations such as calcium. We have found that combining Kv7 opener and an NMDA receptor antagonist will yield improved treatment outcomes as described herein.

SUMMARY

[0008] The present invention is directed to combination therapies including a metal channel activator and an NMDA receptor antagonist.

[0009] In an embodiment, provided is a pharmaceutical composition including a metal channel activator and an NMDA receptor antagonist.

[0010] In another embodiment, provided is a method of treating a depressive disorder, including administering the pharmaceutical composition.

[0011] In another embodiment, provided is a method of treating a neurological or neurodegenerative disorder, including administering the pharmaceutical composition.

[0012] In another embodiment, provided is a method of treating a pain disorder, including administering the pharmaceutical composition.

DETAILED DESCRIPTION

[0013] The following detailed description is provided to aid those skilled in the art in practicing the present invention. Exemplary embodiments will hereinafter be described in detail. However, these embodiments are only exemplary, and the present disclosure is not limited thereto but rather is defined by the scope of the appended claims. Those of ordinary skill in the art may make modifications and variations in the embodiments described herein without departing from the spirit or scope of the present disclosure.

[0014] Accordingly, the embodiments are merely described below, by referring to structures and schemes, to explain aspects of the present description. As used herein, the term "and/or" includes any and all combinations of one or more of the associated listed items. The term "or" means "and/or." Expressions such as "at least one of," when preceding a list of elements, modify the entire list of elements and do not modify the individual elements of the list.

[0015] It will be understood that, although the terms first, second, third etc. may be used herein to describe various elements, components, regions, layers, and/or sections, these elements, components, regions, layers, and/or sections should not be limited by these terms. These terms are only used to distinguish one element, component, region, layer, or section from another element, component, region, layer, or section. Thus, a first element, component, region, layer, or section discussed below could be termed a second element, component, region, layer, or section without departing from the teachings of the present embodiments.

[0016] It is understood that the terms "comprises" and/or "comprising," or "includes" and/or "including" when used in this specification, specify the presence of stated features, regions, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, regions, integers, steps, operations, elements, components, and/or groups thereof.

[0017] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure

belongs. The terminology used in the description is for describing particular embodiments only and is not intended to be limiting. It will be further understood that the terms, such as those defined in commonly used dictionaries, should be interpreted as having a meaning that is consistent with their meaning in the context of the relevant art and the present disclosure, and will not be interpreted in an idealized or overly formal sense unless expressly so defined herein.

[0018] As used in this application, except as otherwise expressly provided herein, each of the following terms shall have the meaning set forth below. Additional definitions are set forth throughout the application. In instances where a term is not specifically defined herein, that term is given an art-recognized meaning by those of ordinary skill applying that term in context to its use in describing the present invention.

[0019] The articles "a" and "an" refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article unless the context clearly indicates otherwise. By way of example, "an element" means one element or more than one element.

[0020] As used herein, when specific definition is not otherwise provided, the term "substituted" refers to a group substituted with deuterium, a halogen (-F, -Cl, -Br, -I), a hydroxy group (-OH), an amino group ($-NH_2$), a carboxyl group ($-CO_2H$), a substituted or unsubstituted C1-C10 amine group, a nitro group ($-NO_2$), a C1-C10 alkyl group, a C3-C10 cycloalkyl group, a C6-C12 aryl group, a C1-C10 alkoxy group, a C1 to C10 trifluoroalkyl group such as a trifluoromethyl group ($-CF_3$) and the like, or a cyano group (-CN) instead of at least one hydrogen of a substituting group or compound.

[0021] Additional aspects will be set forth in part in the description which follows and, in part, will be apparent from the description.

[0022] As used herein, “modulator”, “modulators”, and “modulating”, when describing compounds, describe compounds that may enact their effect through a number of mechanisms of action including but not limited to: binding to the active site of a protein, binding to a region of the protein away from the active site, causing relocalization of a protein, inducing degradation of a protein, inducing stabilization of a protein, causing a conformational change in a protein, decreasing the activation threshold for a protein, increasing the activation threshold for a protein, altering posttranslational modifications for a protein, reducing the transcription of a gene, increasing the transcription of a gene, reducing the translation of an mRNA transcript, increasing the translation of an mRNA transcript,

disrupting an interaction between two proteins, and stabilizing an interaction between two proteins; wherein the protein may be the target of modulation or an intermediary protein which is associated with modulation of the target protein. Modulators of the targets described herein (i.e., Kv7 and NMDA receptor) may each or both be small molecule compounds, proteins, antibody fragments or antibodies, or any other construct effecting modulation. It should be appreciated that an NMDA receptor antagonist is a type of modulator of the NMDA receptor.

[0023] As used herein, "NMDA receptor antagonist" or alternatively "NMDA modulator" means any compound (small molecule, peptide, etc.) effecting modulation or desired change in biological activity of the NMDA receptor. In various embodiments, NMDA receptor antagonists may target particular portions of an NMDA receptor, such as GluN1 (alternatively NR1) or GluN2 (alternatively NR2) subunits, or additionally or alternatively GluN3 subunits. In an embodiment, NMDA receptor antagonist target GluN1 subunits, in some cases selectively. In an embodiment, NMDA receptor antagonists target one or more GluN2 subtypes GluN2A, GluN2B, GluN2C, and/or GluN2D, in some cases selectively. In some embodiments, NMDA receptor antagonists may target one or more GluN3 subtypes GluN3A, GluN3B, and/or GluN3C, in some cases selectively. In some embodiments, NMDA receptor antagonists may target an allosteric site. In some embodiments, NMDA receptor antagonists may include partial agonists which exert dual (agonist/antagonist) effects on NMDA receptors. In certain embodiments, NMDA receptor antagonists may include agents which have a target other than the NMDA receptor which result in an NMDA receptor antagonist-like physiologic effect.

[0024] As used herein, "neurological disease" refers to a disease or disorder which affects the brain and/or nerves found elsewhere in the body. Such neurologic diseases may include: Absence of the Septum Pellucidum, Acid Lipase Disease, Acute Disseminated Encephalomyelitis, Adrenoleukodystrophy, Agenesis of the Corpus Callosum, Agnosia, Aicardi Syndrome, Aicardi-Goutieres Syndrome, Alexander Disease, Alpers' Disease, Alternating Hemiplegia, Alzheimer's Disease, Amyotrophic Lateral Sclerosis (ALS), Anencephaly, Angelman Syndrome, Antiphospholipid Syndrome, Aphasia, Apraxia, Arachnoid Cysts, Arachnoiditis, Arteriovenous Malformation, Asperger Syndrome, Ataxia Telangiectasia, Ataxias and Cerebellar or Spinocerebellar Degeneration, Atrial Fibrillation and Stroke, Attention Deficit-Hyperactivity Disorder, Autism Spectrum Disorder, Back Pain, Barth Syndrome, Batten Disease, Behcet's Disease, Bell's Palsy, Benign Essential Blepharospasm, Binswanger's Disease, Brachial Plexus Injuries, Brain and Spinal Tumors,

Brown-Sequard Syndrome, CADASIL, Canavan Disease, Carpal Tunnel Syndrome, Central Cord Syndrome, Central Pain Syndrome, Central Pontine Myelinolysis, Cephalic Disorders, Cerebellar Degeneration, Cerebellar Hypoplasia, Cerebral Aneurysms, Cerebral Arteriosclerosis, Cerebral Atrophy, Cerebral Cavernous Malformation, Cerebral Hypoxia, Cerebral Palsy, Cerebro-Oculo-Facio-Skeletal Syndrome (COFS), Charcot-Marie-Tooth Disease, Chiari Malformation, Chorea, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Pain, Coffin Lowry Syndrome, Colpocephaly, Coma, Complex Regional Pain Syndrome, Congenital Myasthenia, Congenital Myopathy, Corticobasal Degeneration, Craniosynostosis, Creutzfeldt-Jakob Disease, Cushing's Syndrome, Dandy-Walker Syndrome, Deep Brain Stimulation for Movement Disorders, Dementia, Dementia With Lewy Bodies, Dermatomyositis, Developmental Dyspraxia, Diabetic Neuropathy, Dravet Syndrome, Dysautonomia, Dysgraphia, Dyslexia, Dyssynergia Cerebellaris Myoclonica, Dystonia, Empty Sella Syndrome, Encephalitis Lethargica, Encephaloceles, Encephalopathy, Epilepsy, Erb-Duchenne and Dejerine-Klumpke Palsies, Essential Tremor, Fabry Disease, Fahr's Syndrome, Familial Periodic Paralyses, Farber's Disease, Febrile Seizures, Fibromuscular Dysplasia, Foot Drop, Friedreich Ataxia, Frontotemporal Dementia, Functional Neurologic Disorder, Gaucher Disease, Generalized Gangliosidoses, Gerstmann's Syndrome, Gerstmann-Straussler-Scheinker Disease, Giant Axonal Neuropathy, Glossopharyngeal Neuralgia, Guillain-Barré Syndrome, Headache, Hemicrania Continua, Hemifacial Spasm, Hereditary Neuropathies, Hereditary Spastic Paraplegia, Herpes Zoster Oticus, Holmes-Adie Syndrome, Holoprosencephaly, Huntington's Disease, Hydranencephaly, Hydrocephalus, Hydromyelia, Hypersomnia, Hypertonia, Hypotonia, Inclusion Body Myositis, Incontinentia Pigmenti, Infantile Neuroaxonal Dystrophy, Infantile Refsum Disease, Infantile Spasms, Inflammatory Myopathies, Iniencephaly, Isaacs' Syndrome, Joubert Syndrome, Kearns-Sayre Syndrome, Kennedy's Disease, Kleine-Levin Syndrome, Klippel-Feil Syndrome, Klippel-Trenaunay Syndrome (KTS), Klüver-Bucy Syndrome, Krabbe Disease, Kuru, Lambert-Eaton Myasthenic Syndrome, Landau-Kleffner Syndrome, Learning Disabilities, Leigh's Disease, Lennox-Gastaut Syndrome, Lesch-Nyhan Syndrome, Leukodystrophy, Lipid Storage Diseases, Lipoid Proteinosis, Lissencephaly, Locked-In Syndrome, Machado-Joseph Disease and Spinocerebellar Ataxia, Megalencephaly, Melkersson-Rosenthal Syndrome, Meningitis and Encephalitis, Menkes Disease, Meralgia Paresthetica, Metachromatic Leukodystrophy, Microcephaly, Migraine, Miller Fisher Syndrome, Mitochondrial Myopathies, Moebius Syndrome, Monomelic Amyotrophy, Motor Neuron Diseases, Moyamoya Disease, Mucolipidoses,

Mucopolysaccharidoses, Multi-Infarct Dementia, Multifocal Motor Neuropathy, Multiple Sclerosis, Multiple System Atrophy, Multiple System Atrophy with Orthostatic Hypotension, Muscular Dystrophy, Myasthenia Gravis, Myoclonus, Myopathy, Myotonia, Myotonia Congenita, Narcolepsy, Neuroacanthocytosis, Neurodegeneration with Brain Iron Accumulation, Neurofibromatosis, Neuroleptic Malignant Syndrome, Neurological Complications of AIDS, Neurological Complications of Lyme Disease, Neurological Consequences of Cytomegalovirus Infection, Neurological Sequelae Of Lupus, Neuromyelitis Optica, Neuronal Migration Disorders, Neurosarcoidosis, Neurosyphilis, Neurotoxicity, Niemann-Pick Disease, Normal Pressure Hydrocephalus, Occipital Neuralgia, Ohtahara Syndrome, Olivopontocerebellar Atrophy, Opsoclonus Myoclonus, Orthostatic Hypotension, Paraneoplastic Syndromes, Paresthesia, Parkinson's Disease, Paroxysmal Choreoathetosis, Paroxysmal Hemicrania, Parry-Romberg Syndrome, Pelizaeus-Merzbacher Disease, Peripheral Neuropathy, Periventricular Leukomalacia, Pervasive Developmental Disorders, Pinched Nerve, Piriformis Syndrome, Pituitary Tumors, Polymyositis, Pompe Disease, Porencephaly, Post-Polio Syndrome, Postural Tachycardia Syndrome, Primary Lateral Sclerosis, Progressive Multifocal Leukoencephalopathy, Progressive Supranuclear Palsy, Prosopagnosia, Pseudotumor Cerebri, Rasmussen's Encephalitis, Refsum Disease, Repetitive Motion Disorders, Restless Legs Syndrome, Rett Syndrome, Reye's Syndrome, Sandhoff Disease, Schilder's Disease, Schizencephaly, Septo-Optic Dysplasia, Shaken Baby Syndrome, Shingles, Sjögren's Syndrome, Sleep Apnea, Sotos Syndrome, Spasticity, Spina Bifida, Spinal Cord Infarction, Spinal Cord Injury, Spinal Muscular Atrophy, Stiff-Person Syndrome, Striatonigral Degeneration, Stroke, Sturge-Weber Syndrome, Subacute Sclerosing Panencephalitis, SUNCT Headache, Swallowing Disorders, Sydenham Chorea, Syncope, Syringomyelia, Tabes Dorsalis, Tardive Dyskinesia, Tarlov Cysts, Tay-Sachs Disease, Tethered Spinal Cord Syndrome, Thoracic Outlet Syndrome, Thyrotoxic Myopathy, Todd's Paralysis, Tourette Syndrome, Transient Ischemic Attack, Transmissible Spongiform Encephalopathies, Transverse Myelitis, Traumatic Brain Injury, Tremor, Trigeminal Neuralgia, Tropical Spastic Paraparesis, Troyer Syndrome, Tuberous Sclerosis, Vasculitis Syndromes of the Central and Peripheral Nervous Systems, Von Hippel-Lindau Disease (VHL), Wallenberg's Syndrome, Wernicke-Korsakoff Syndrome, Whiplash, Whipple's Disease, Williams Syndrome, Wilson Disease, and Zellweger Syndrome.

[0025] As used herein, the term “metal channel activator” is construed to include both metal channel activator and pharmaceutically acceptable salt thereof.

[0026] As used herein, the term “NMDA receptor antagonist” or “NMDA modulator” is construed to include both NMDA receptor antagonist and pharmaceutically acceptable salt thereof.

[0027] As used herein, the term “AUC” is the definite integral of the concentration of a drug in blood, cerebrospinal fluid, target organ, or any other physiologically relevant site after a dose is given as a function of time. AUC in this context is used to measure the total exposure to the drug across time. AUC can be evaluated over a definite time interval or estimated based on the integral drug concentrations measured over a time interval extrapolated to infinite time.

[0028] As used herein, the term “Cmax” is the highest concentration of a drug in the blood, cerebrospinal fluid, target organ, or any other physiologically relevant site after a dose is given.

[0029] As used herein, the term “Tmax” is the time taken after administration for a drug to reach its highest concentration in the blood, cerebrospinal fluid, target organ, or any other physiologically relevant site after a dose is given.

[0030] As used herein, the term “proteinopathies” refers to diseases characterized by an accumulation or aggregation of a single protein, or multiple proteins. Proteinopathies include but are not limited to: Creutzfeldt–Jakob disease and other prion diseases, Alzheimer's disease, Parkinson's disease, amyloidosis, multiple system atrophy, Amyotrophic lateral sclerosis (ALS), Frontotemporal Lobar Degeneration, and Lewy Body Dementia.

[0031] Additional aspects will be set forth in part of the description which follows and, in part, will be apparent from the description.

[0032] In the formulas set forth below, it is set out with substituents and definitions, and it should be clear to the reader that substituents and definitions are numbered (e.g., R1, R2, Y, etc.) and are intended to apply within a given formula. Numberings that are repeated across formulas are intentional and should be each read within the context of each particular formula.

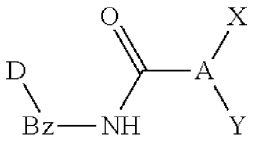
METAL CHANNEL ACTIVATOR

[0033] Examples of metal channel activators including Kv7 channel activators are disclosed in Formulas 1 – 171, the “Further embodiments” section, and in the corresponding referenced applications.

Formula 1

[0034] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 1. Such compounds are described in US Patent No 9,481,653, issued November 1, 2016, and corresponding to US Application No. 14/853,815 filed September 14, 2015; and US Publication No 20210188782A1, published June 24, 2021, and corresponding to US Application No. 17/127,231 filed December 18, 2020; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 1, these references incorporated by reference herein control.

[0035] In an embodiment, the Kv7 channel activator is a compound according to formula 1:



Formula 1

,

wherein D is optionally substituted C_{3-6} carbocyclyl, optionally substituted C_{2-5} heterocyclyl, isopropyl, or t-butyl; Bz is optionally substituted benzoimidazol-1,2-diyl; A is C_{1-8} alkyl; X is F; and Y is H, F, Cl, Br, I, or a moiety having a molecular weight of 15 Da to 300 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0036] In further embodiments, D is optionally substituted cyclobutyl, optionally substituted phenyl, optionally substituted isoxazolyl, optionally substituted pyridinyl, isopropyl, or t-butyl.

[0037] In further embodiments, D is optionally substituted cyclobutyl, optionally substituted phenyl, optionally substituted isoxazolyl, optionally substituted pyridinyl, isopropyl, or t-butyl, wherein each substituent of D and Y, if present, independently has a molecular weight of 15 Da to 200 Da and consists of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0038] In another embodiment, the Kv7 channel activator is a compound according to formula 1 wherein, D is optionally substituted C_{3-6} carbocyclyl, optionally substituted C_{2-5} heterocyclyl, isopropyl, or t-butyl; Bz is optionally substituted benzoimidazol-1,2-diyl; A is C_{1-8} alkyl; X is H, F, CF_3, optionally substituted phenyl, or optionally substituted pyridinyl; and Y is H, F, Cl, Br, I, or a moiety having a molecular weight of 15 Da to 300 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0039] In further embodiments, D is optionally substituted cyclobutyl, optionally substituted phenyl, optionally substituted isoxazolyl, optionally substituted pyridinyl, isopropyl, or t-butyl.

[0040] In further embodiments, each substituent of D, X, and Y, if present, independently has a molecular weight of 15 Da to 200 Da and consists of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0041] In further embodiments, R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl.

[0042] In further embodiments, X is optionally substituted phenyl.

[0043] In further embodiments, X is CF_3.

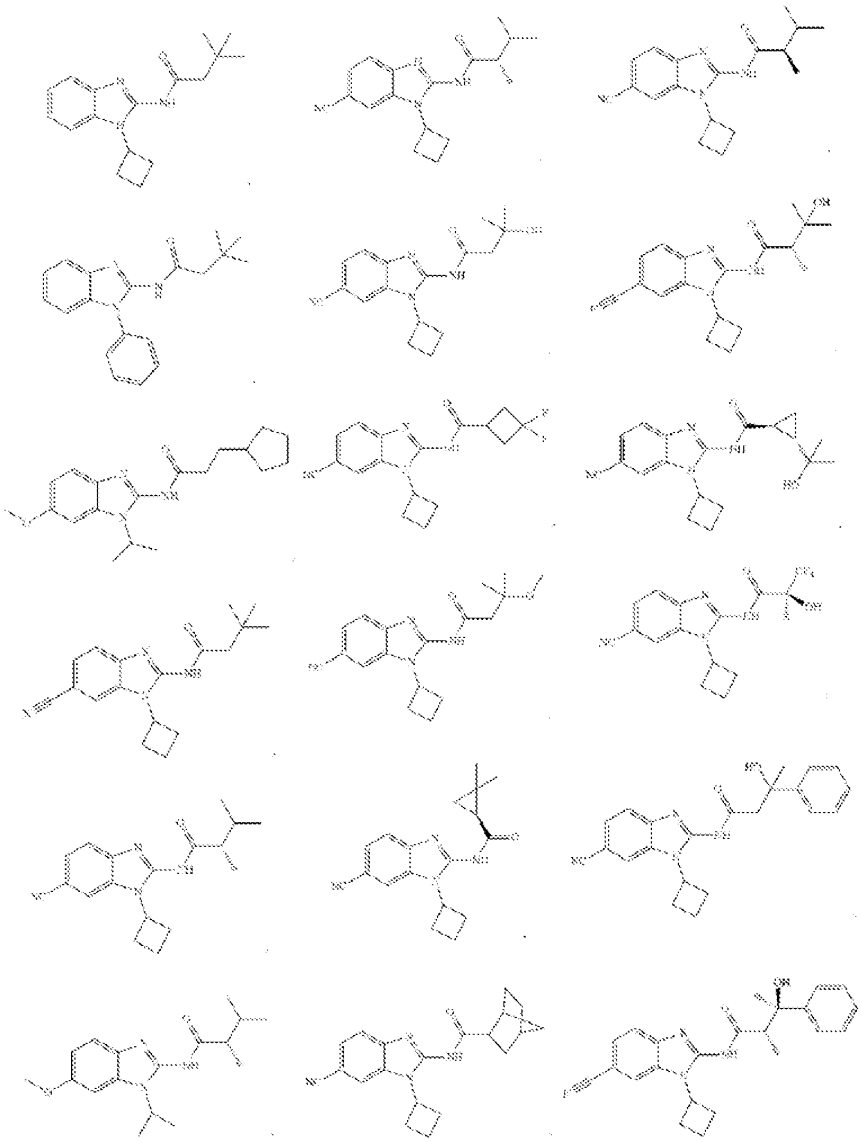
[0044] In further embodiments, X is optionally substituted pyridinyl.

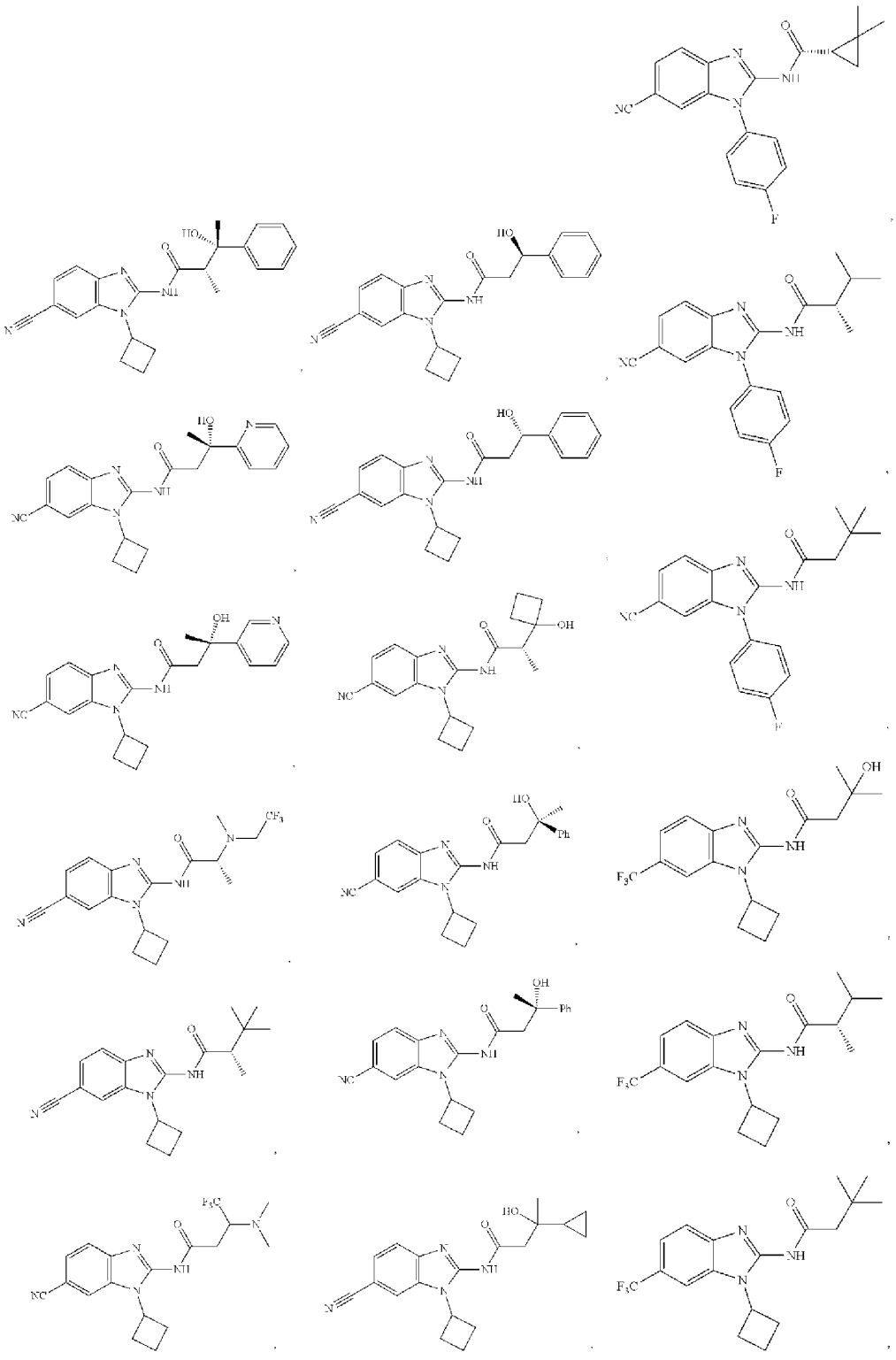
[0045] In further embodiments, X is H.

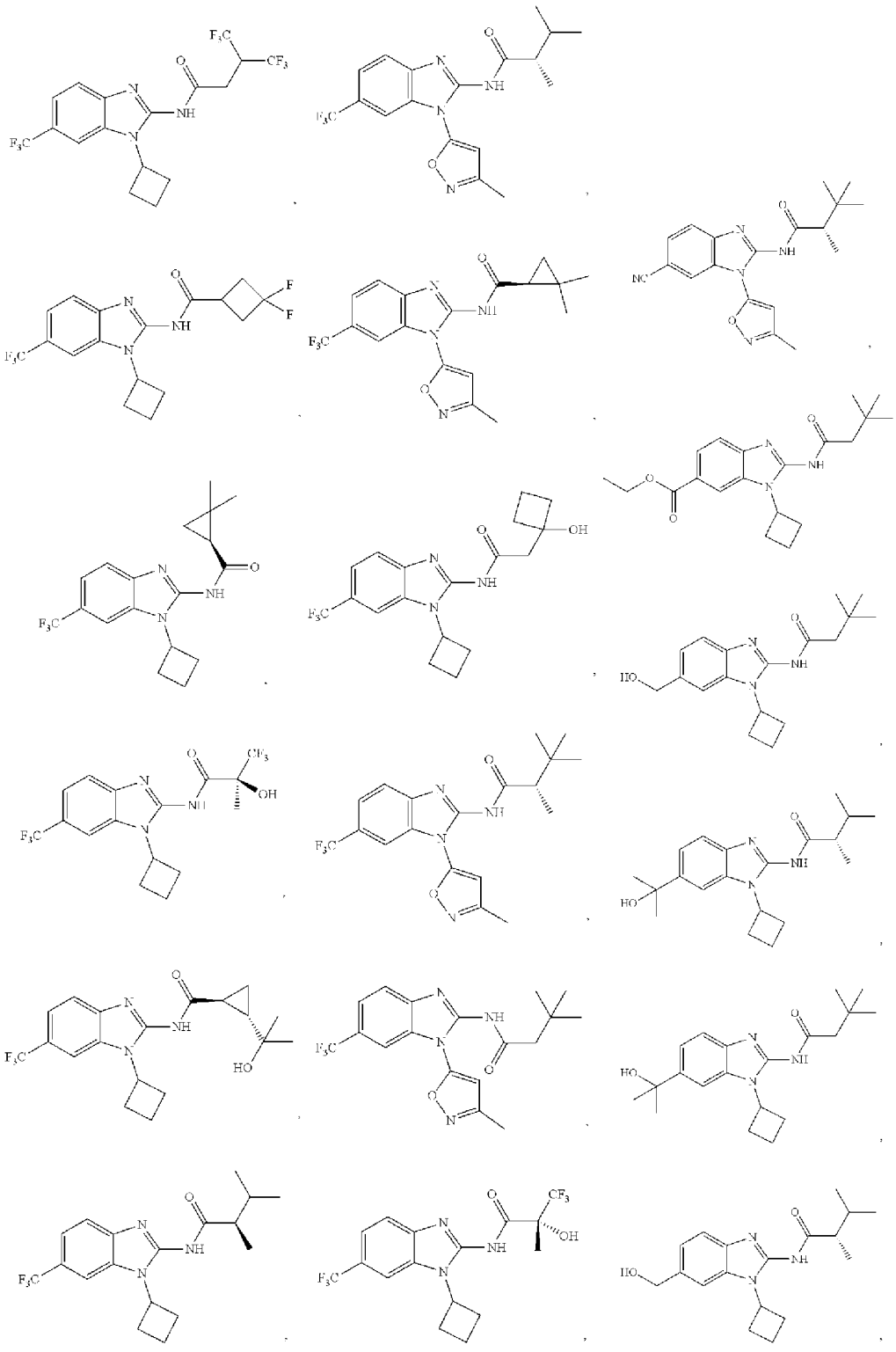
[0046] In further embodiments, Y is H.

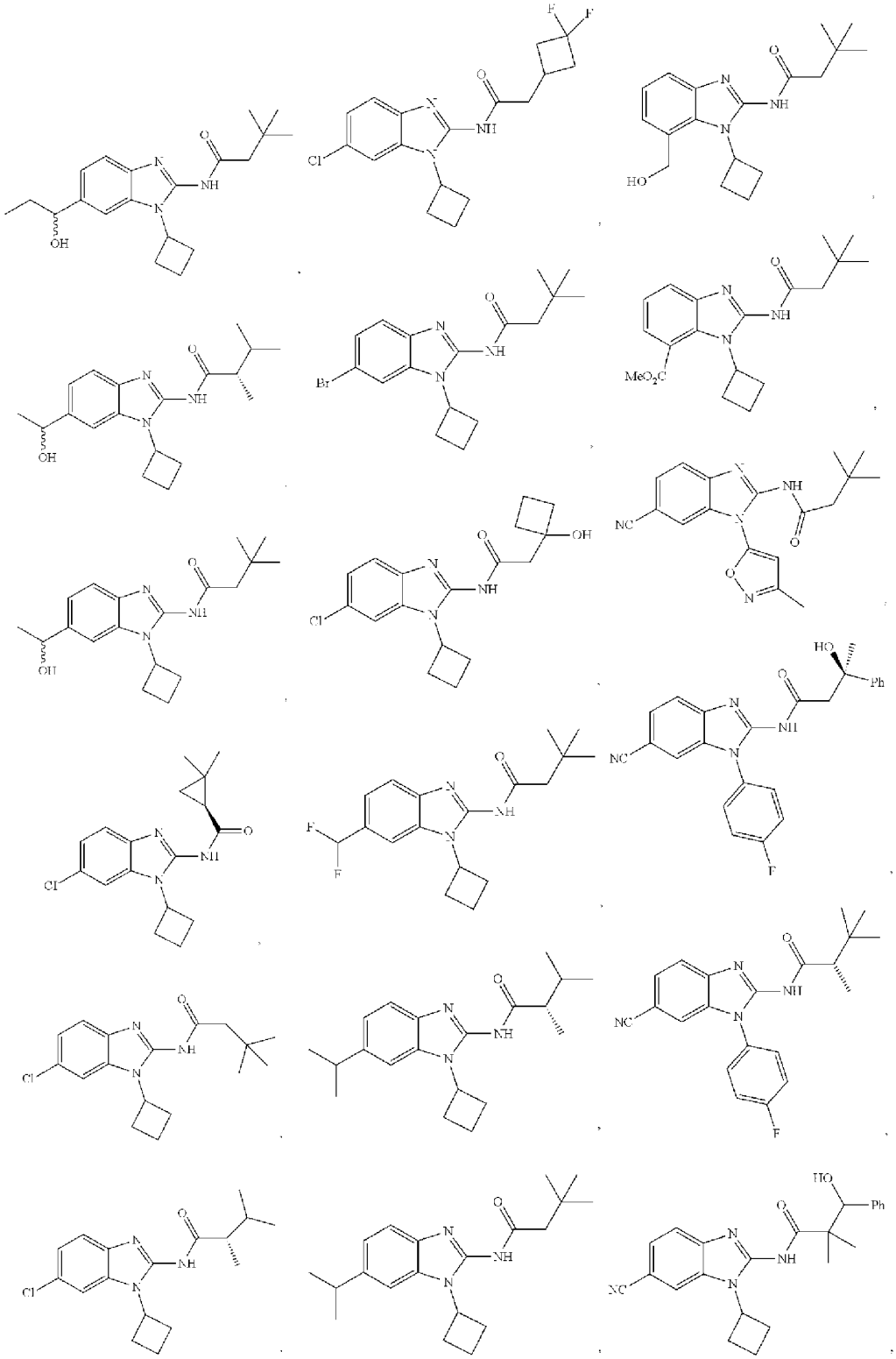
[0047] In further embodiments, Y is OH.

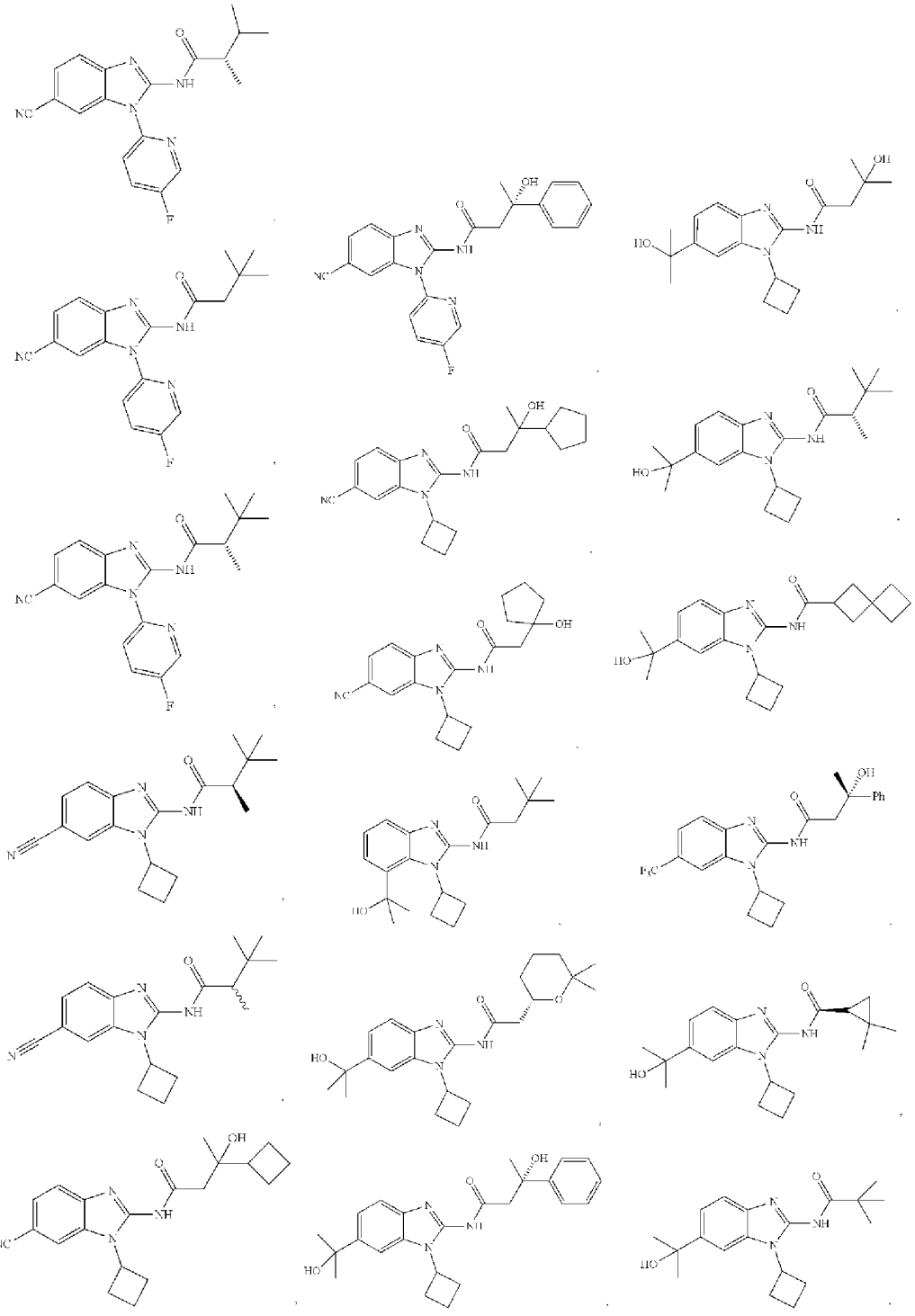
[0048] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:

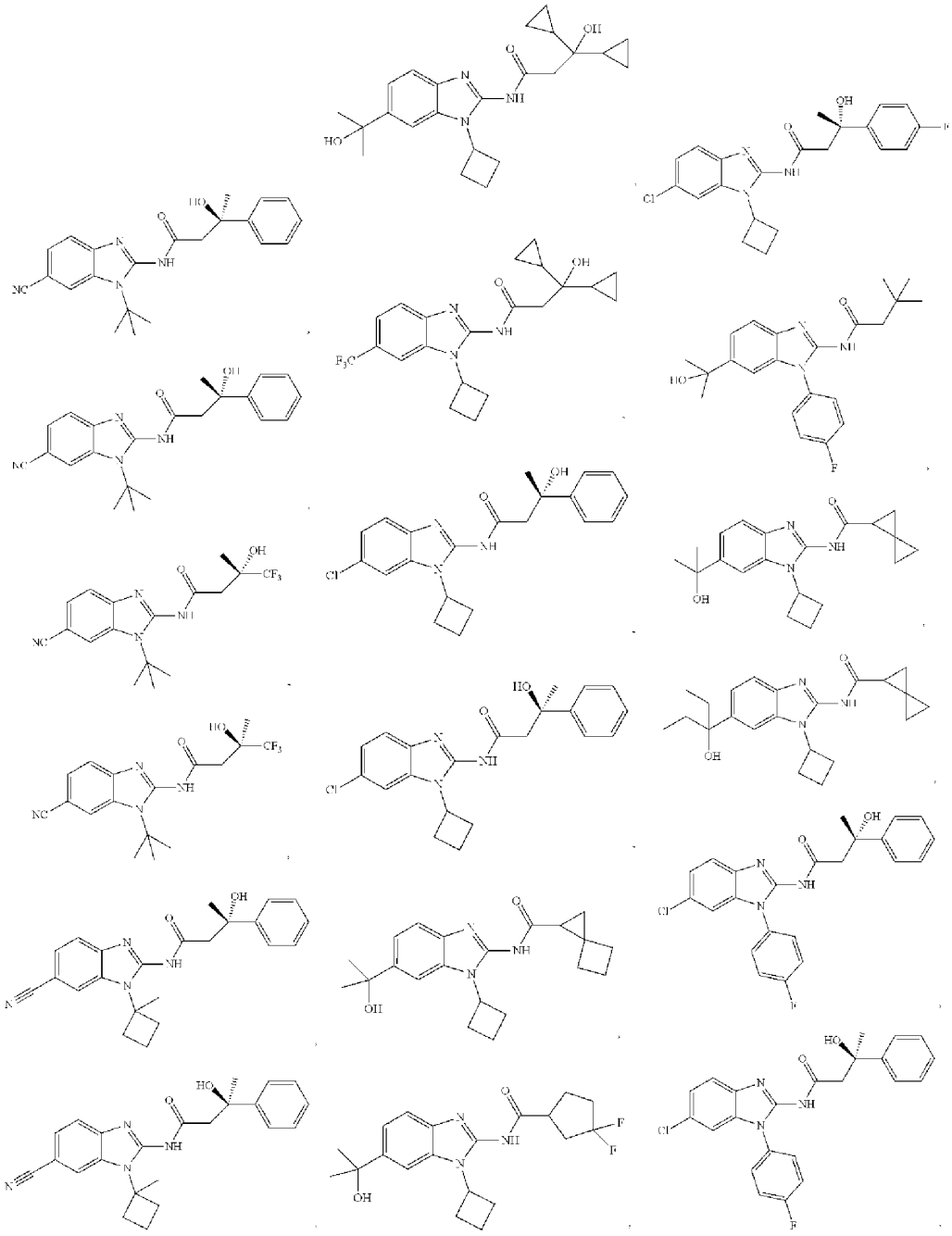


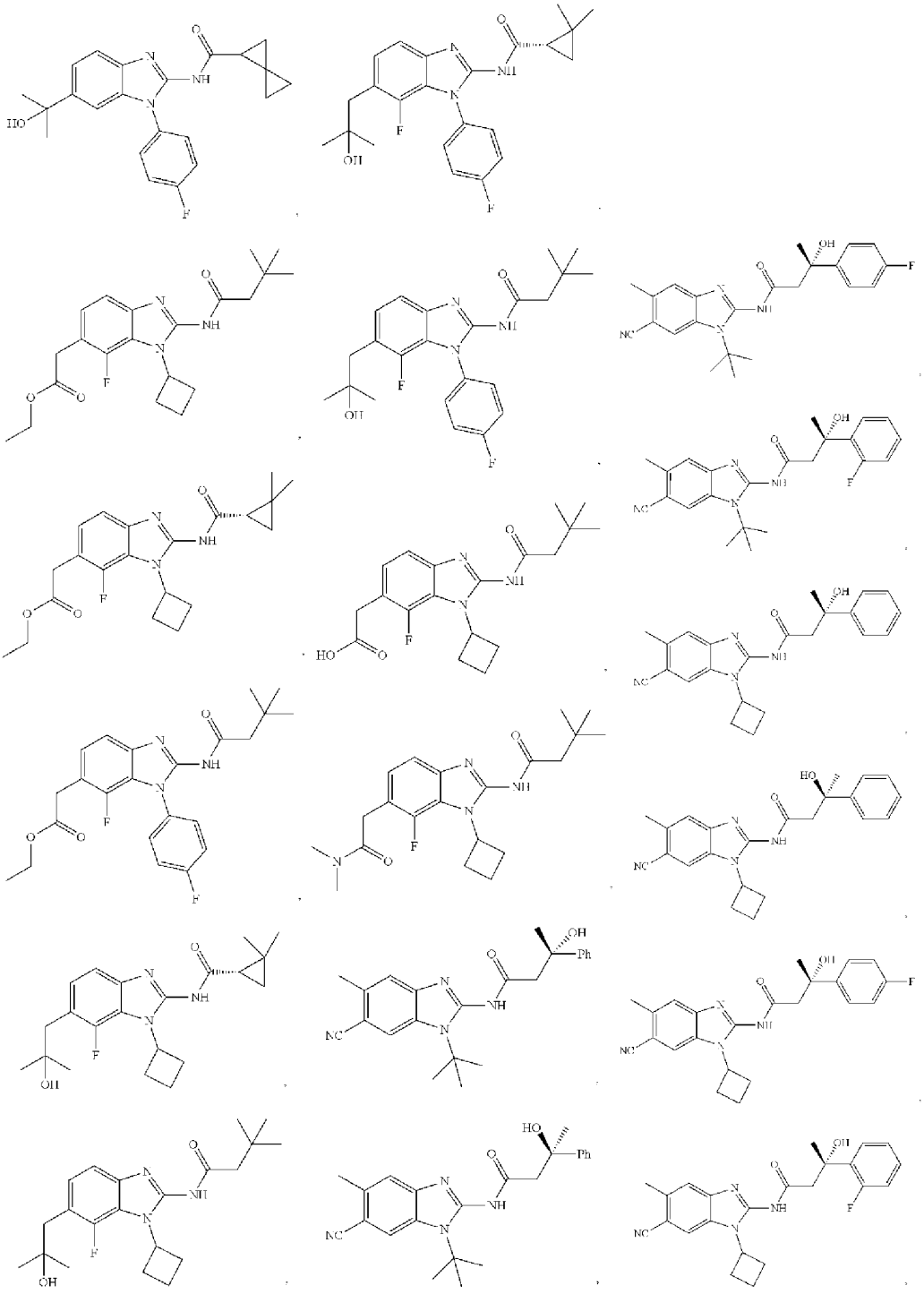


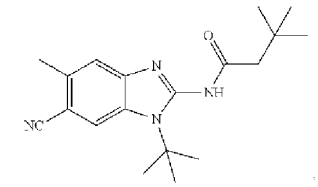


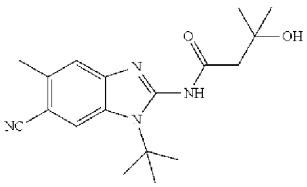


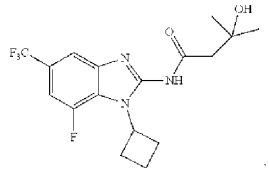


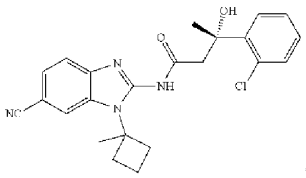


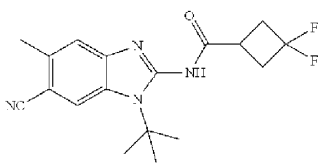


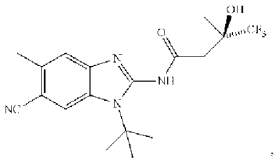


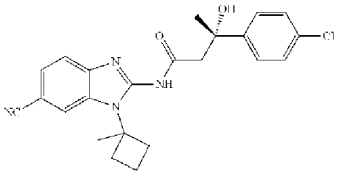


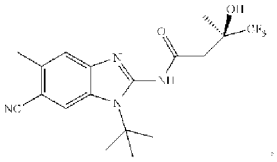


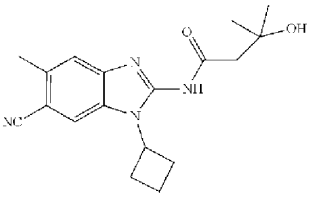


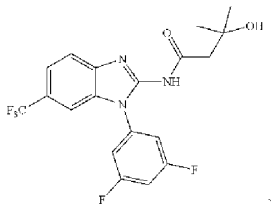


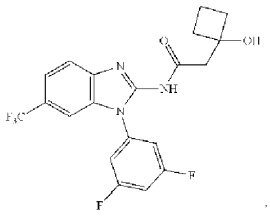


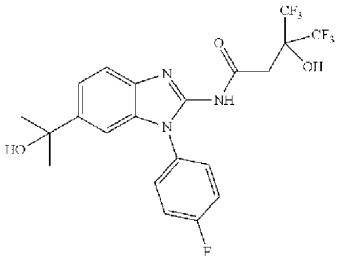


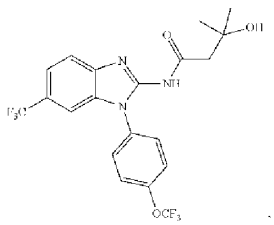


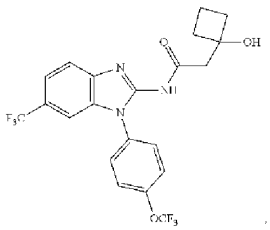


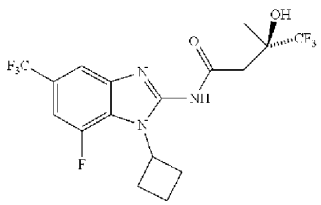


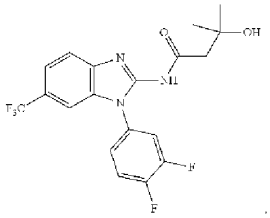


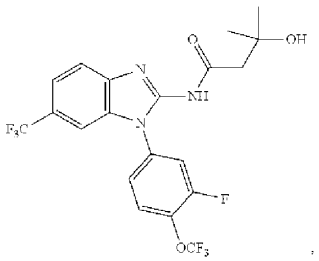




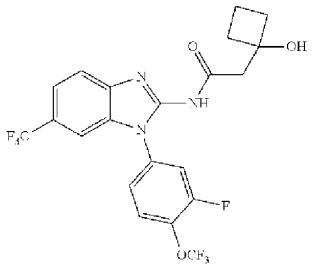








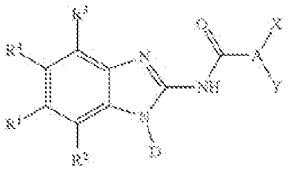
, or



Formula 2

[0049] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 2. Such compounds are described in US Patent No. 9,481,653 issued November 1, 2016 and corresponding to US Application No. US14/853,815 filed September 14, 2015; US Patent No. 9,914,708, issued March 13, 2018 and corresponding to US Application No. 15/339,590 filed October, 31; US patent No 10,385,025, issued August 20, 2019 and corresponding to US Application No. 15/879,792 filed January 25, 2018; US Patent No. 10,906,877 issued on February 2, 2021 and corresponding to US Application No. 16/460,449 filed July 2, 2019; US Patent No. 10,851,067 issued on December 1, 2020 and corresponding to US Application No. 16/358,642 filed March 19, 2019; US Patent No. 11,261,162 issued on March 1, 2022 and corresponding to US Application No. 17/077,068 filed October 22, 2020; US Publication No. 20210188782A1, published June 24, 2021 and corresponding to US Application No. 17/127,231 filed December 18, 2020; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 2, these references incorporated by reference herein control.

[0050] In an embodiment, the Kv7 channel activator is a compound according to formula 2:



Formula 2

,

wherein D is optionally substituted cyclobutyl, optionally substituted phenyl, optionally substituted isoxazolyl, optionally substituted pyridinyl, isopropyl, or t-butyl; A is C_{2-8} alkyl; X is H, F, CF_3 optionally substituted phenyl, or optionally substituted pyridinyl; Y is H, F, Cl, Br, I, or a moiety having a molecular weight of 15 Da to 300 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; R^1 is F, Cl, Br, CN, OCH_3, CHF_2, CF_3, C_{1-4} —CO_2-alkyl, C_{1-4} alkyl, —CH_2CO_2H, —$CH_2CO_2CH_2CH_3$ or —$CH_2CON(CH_3)_2$, or C_{1-5} hydroxyalkyl; and R^2, R^3, and R^4 are independently H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0051] In further embodiments, Y is H, F, CF_3, OH, C_{1-5} O-alkyl, C_{0-6} alkylamino, optionally substituted tetrahydropyranyl, or C_{0-6} fluoroalkylamino.

[0052] In further embodiments R^1 is Cl, Br, —OCH_3, —CN, —CF_3, —CH_2OH, —$COOCH_2CH_3$, —$C(CH_3)_2OH$, —$CHOHCH_2CH_3$, —$CHOHCH_3$, —CHF_2, —$CH(CH_3)_2$, —$C(CH_2CH_3)_2OH$, —$CH_2COOCH_2CH_3$, —$CH_2C(CH_3)_2OH$, —CH_2COOH, or —$CH_2CON(CH_3)_2$.

[0053] In further embodiments, R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$.

[0054] In further embodiments, R^3 is H.

[0055] In further embodiments, R^4 is H, —CH_3, or —CF_3.

[0056] In further embodiments, R^1 is Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl.

[0057] In further embodiments, X is optionally substituted phenyl.

[0058] In further embodiments, X is CF_3.

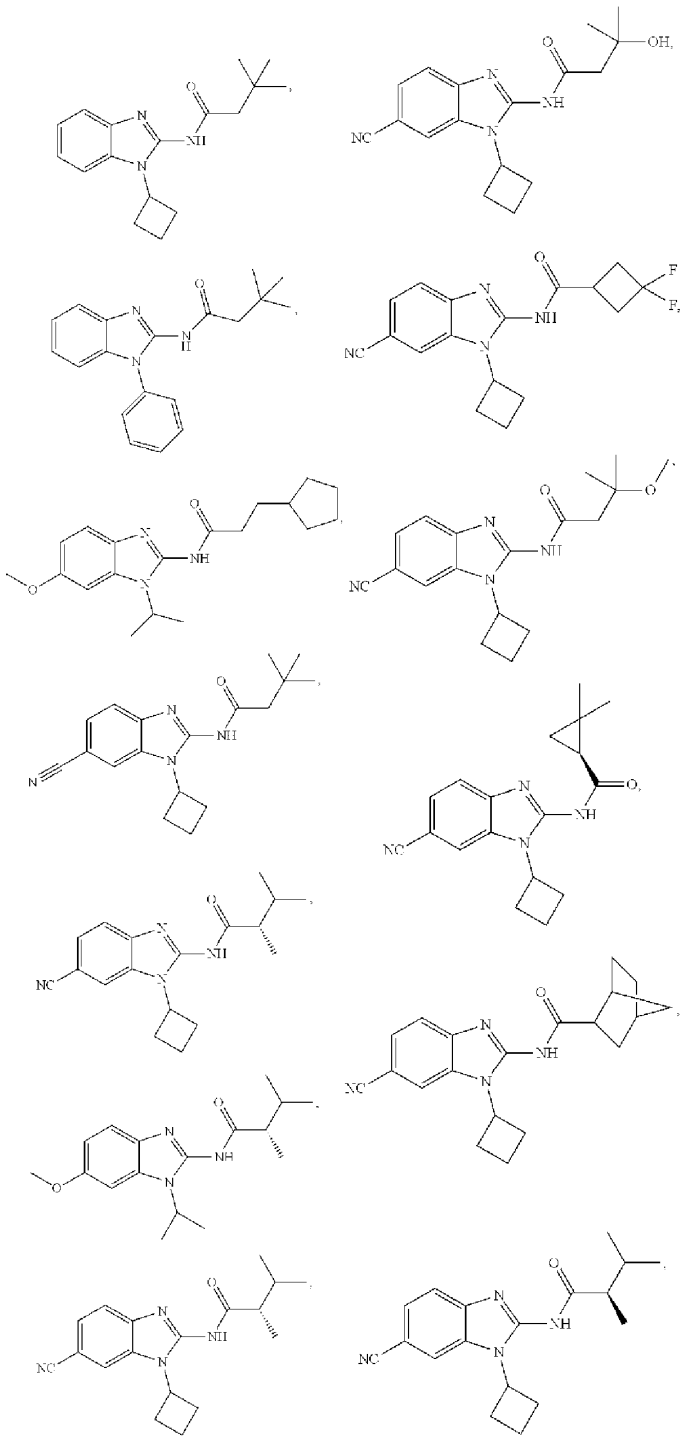
[0059] In further embodiments, X is optionally substituted pyridinyl.

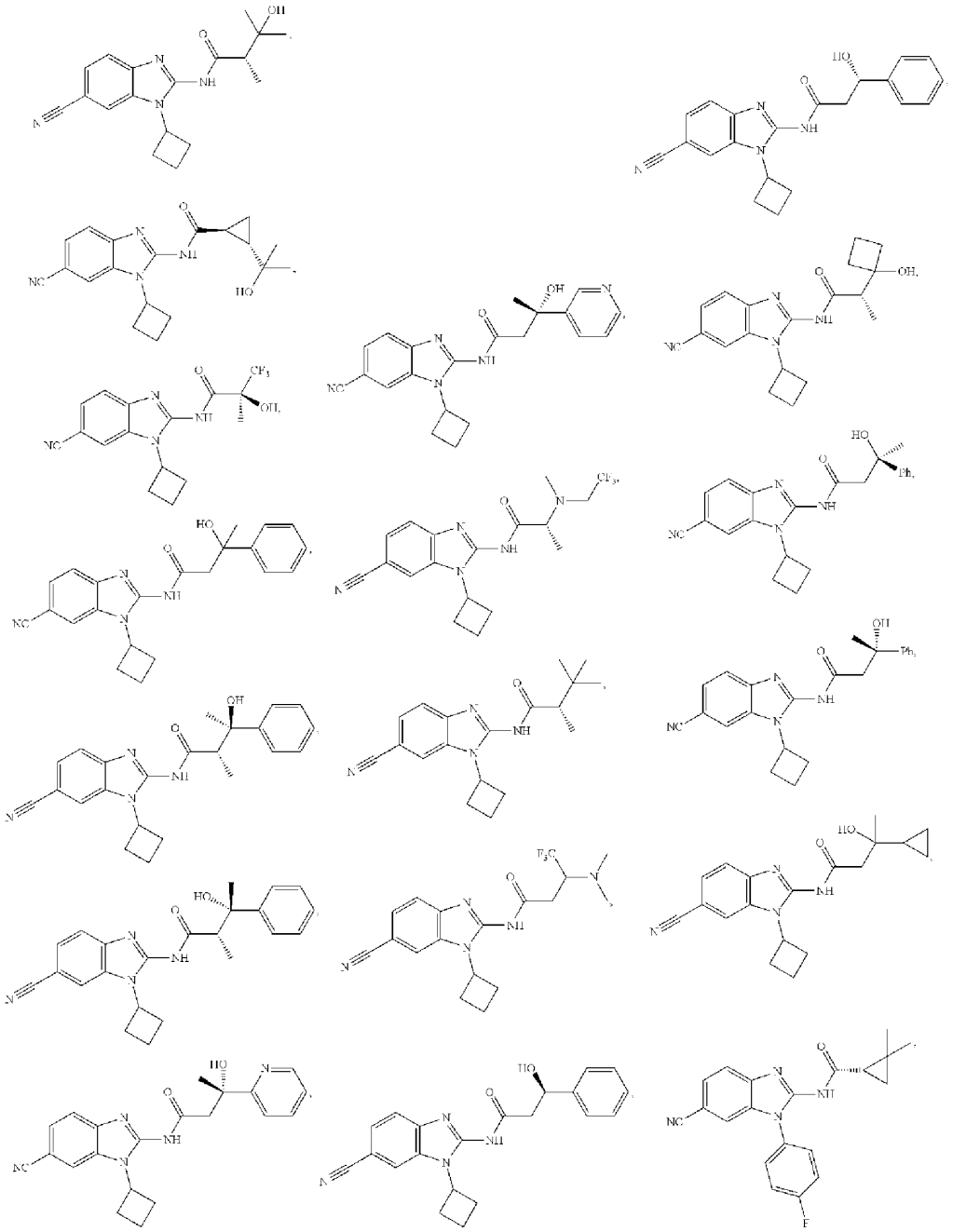
[0060] In further embodiments, X is H.

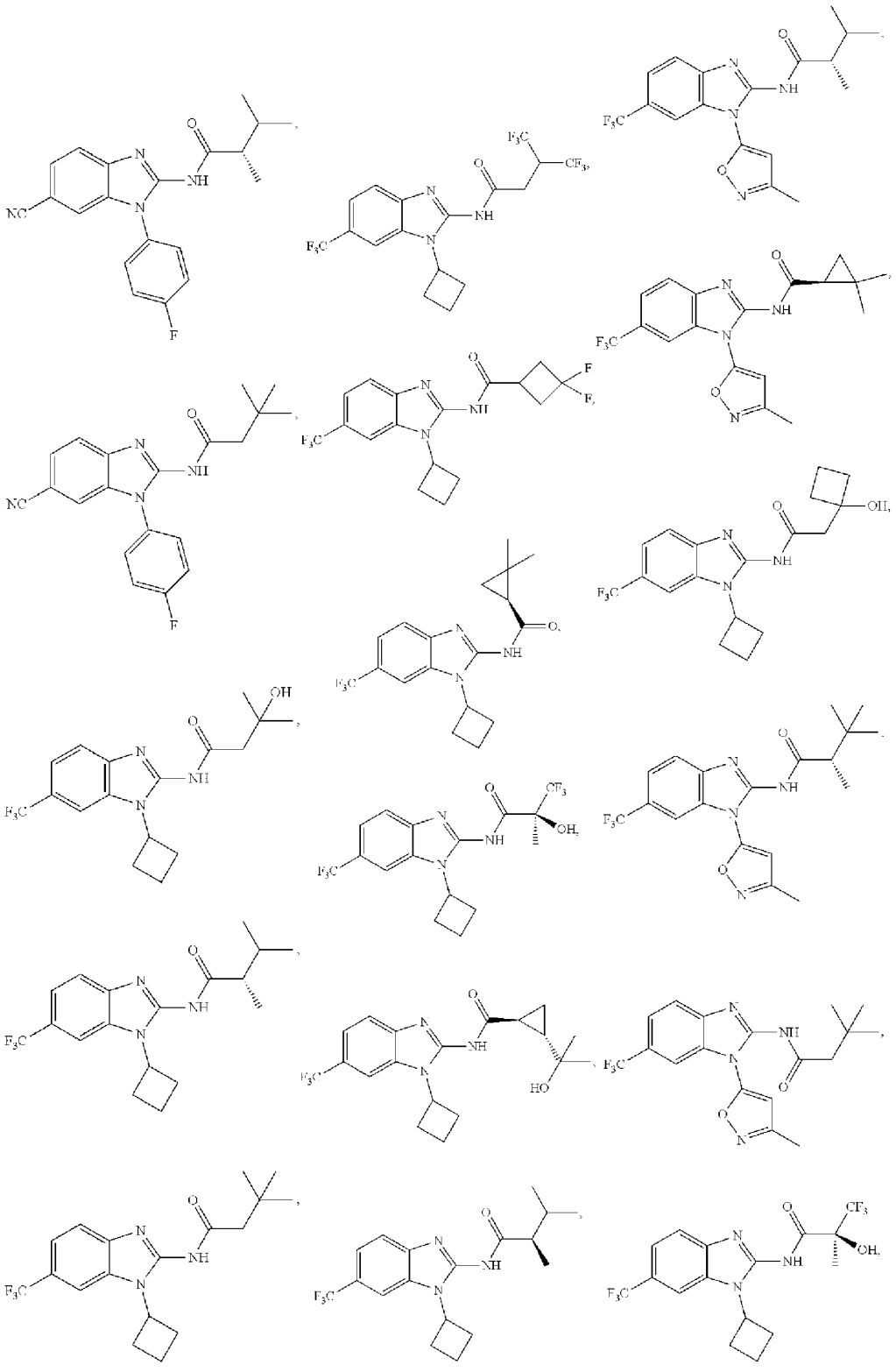
[0061] In further embodiments, Y is H.

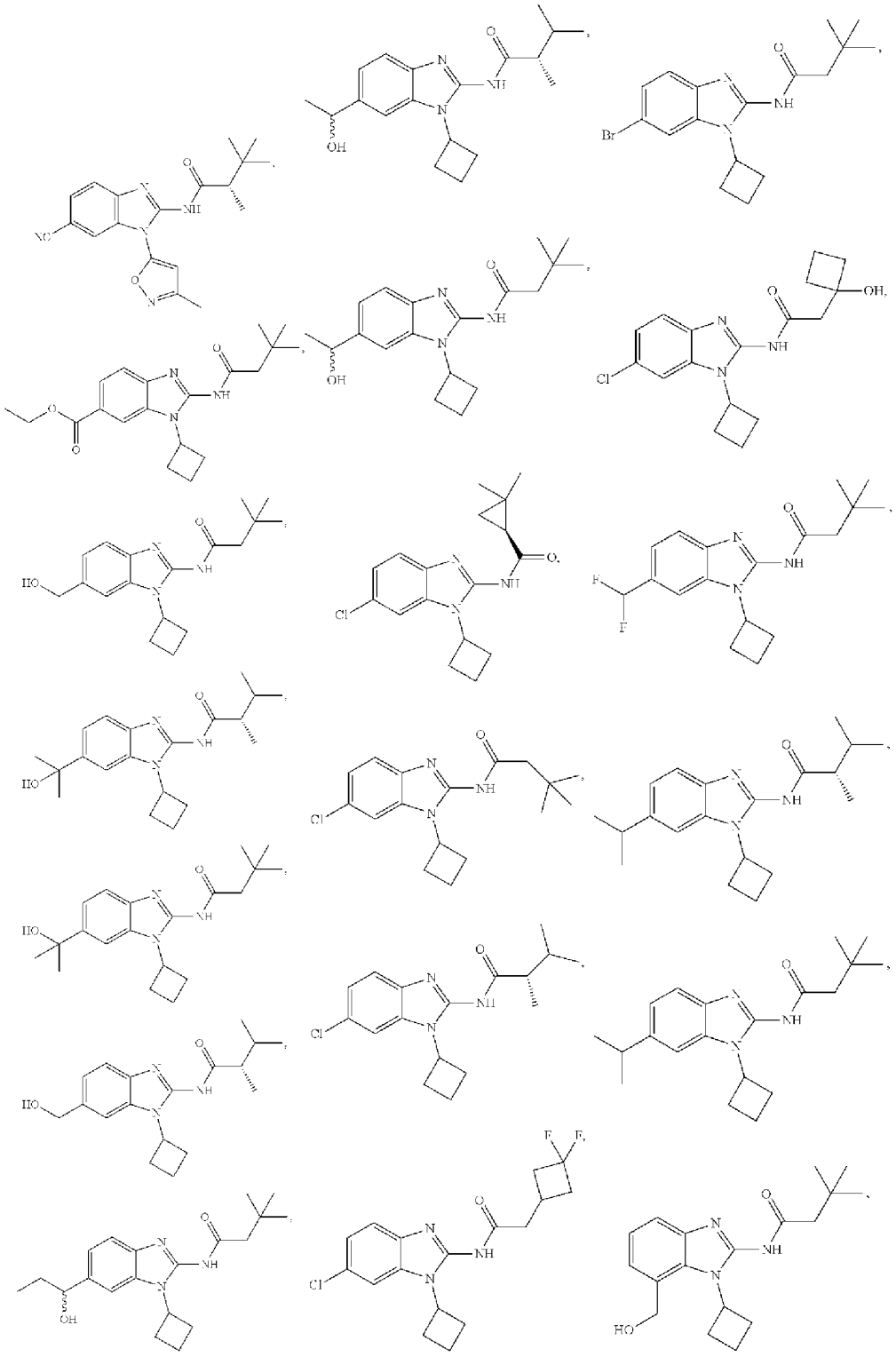
[0062] In further embodiments, Y is OH.

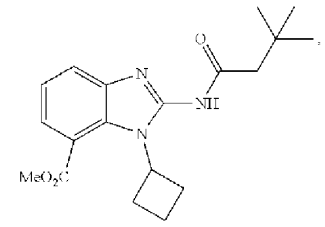
[0063] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:

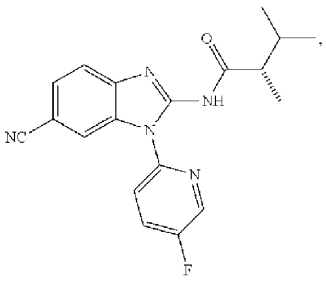


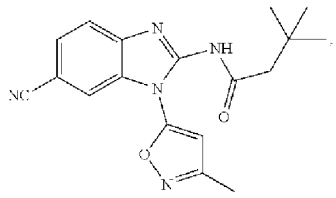


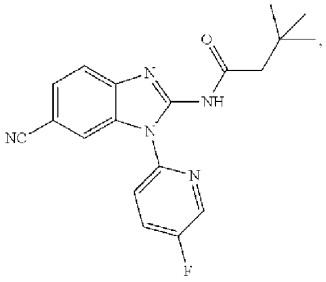


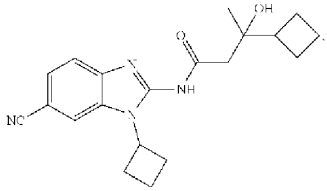


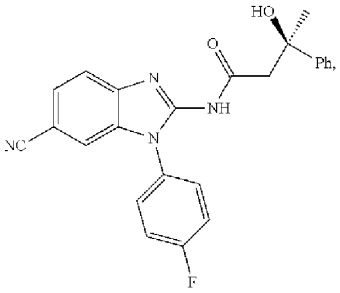


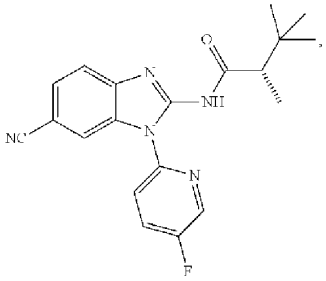


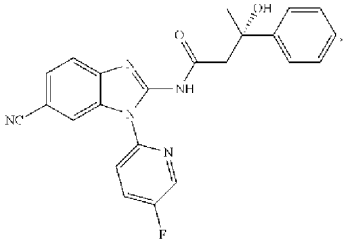


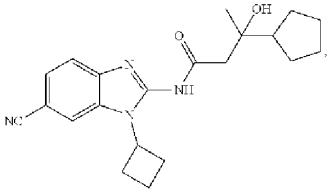


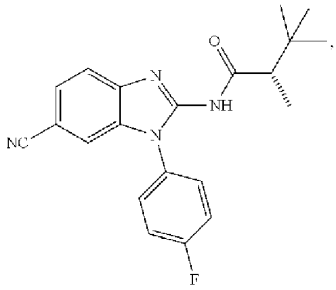


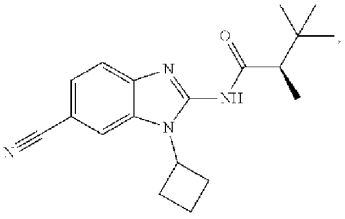


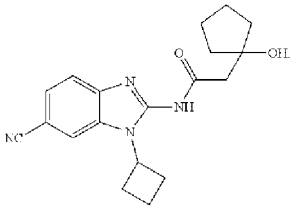


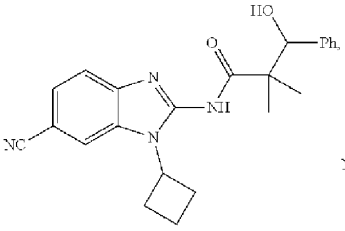


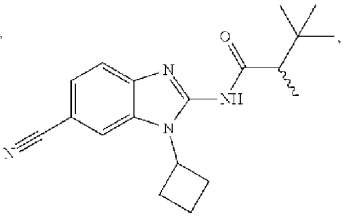


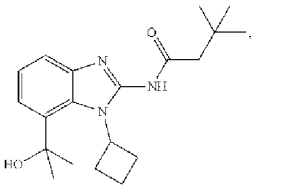


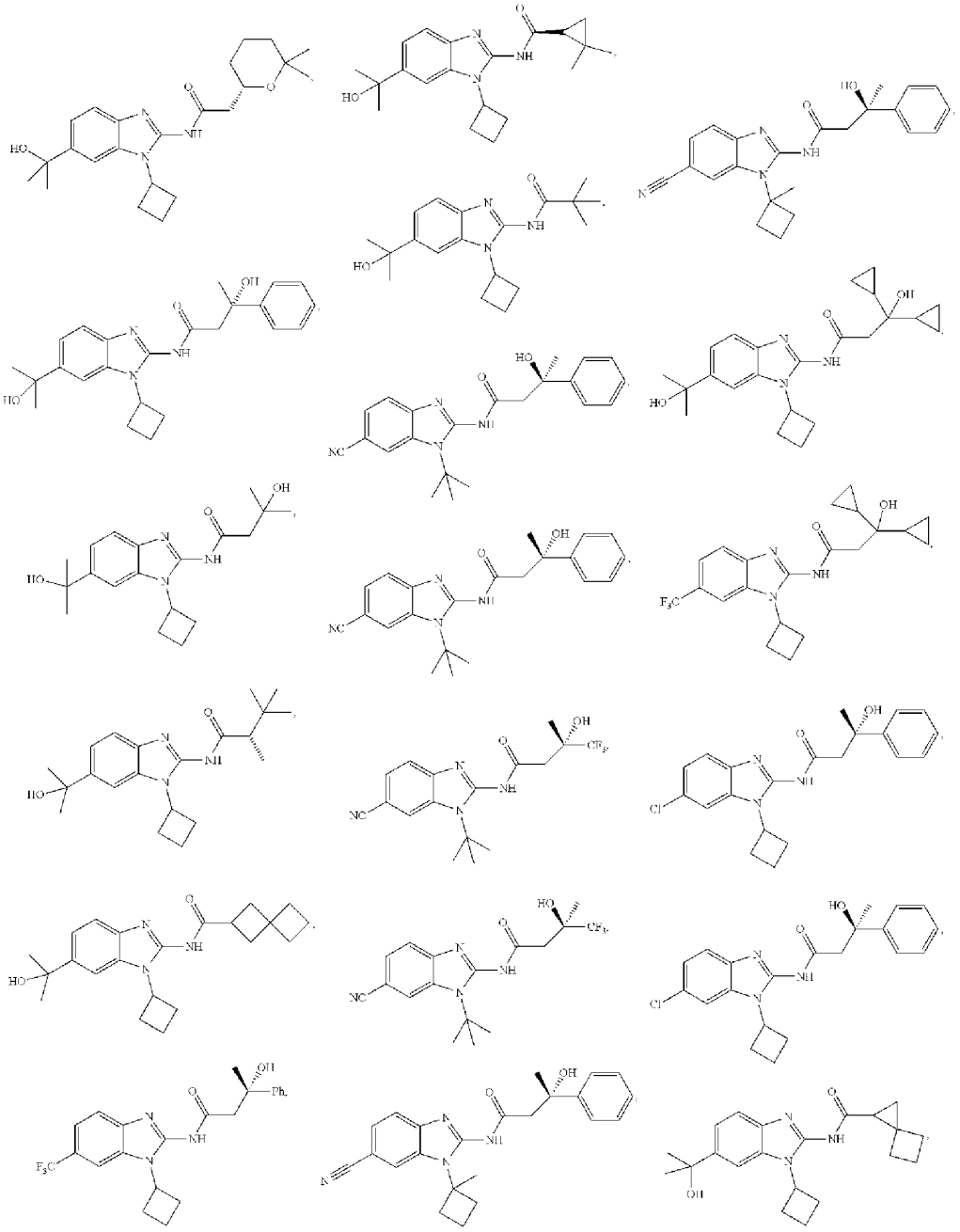


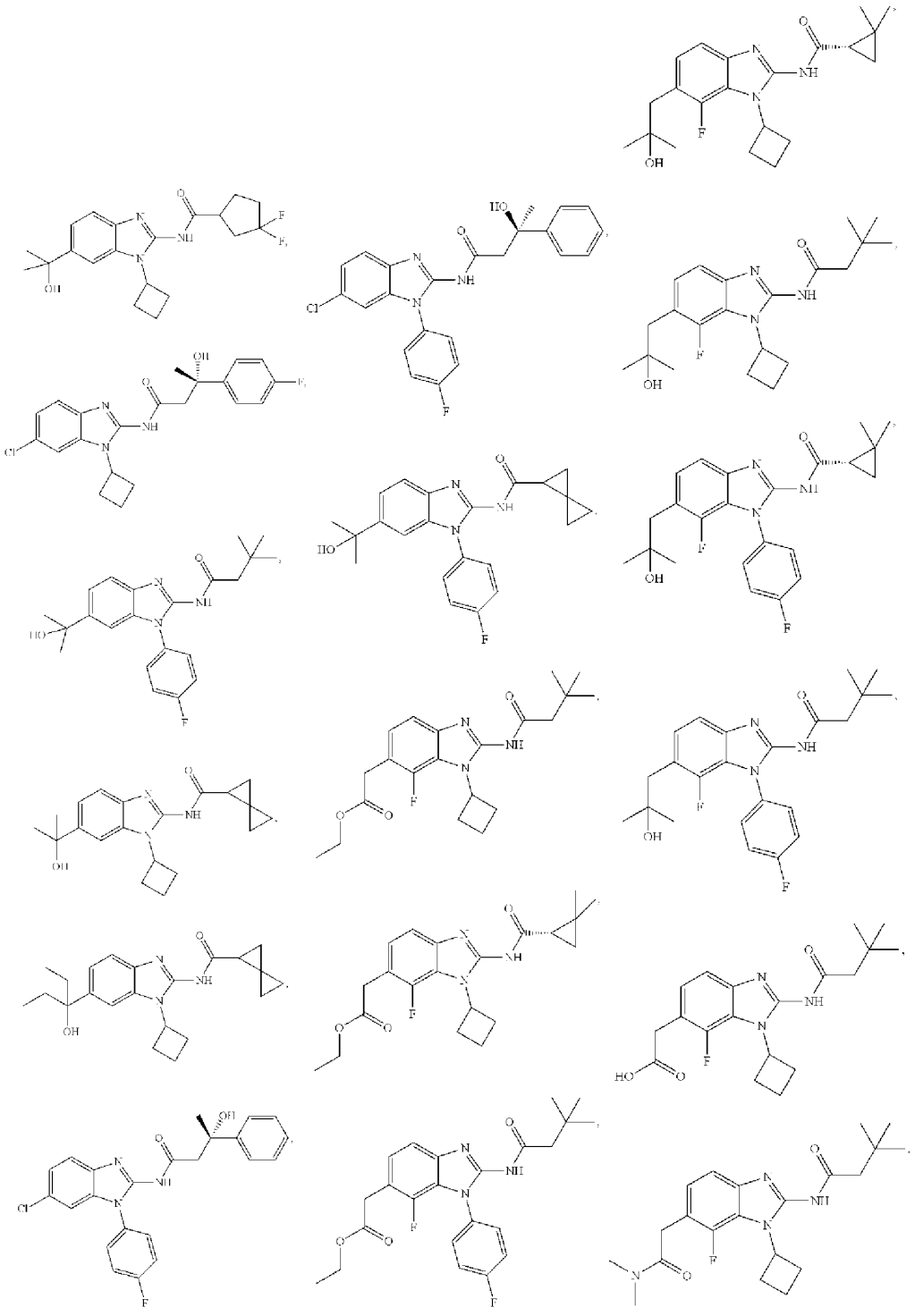


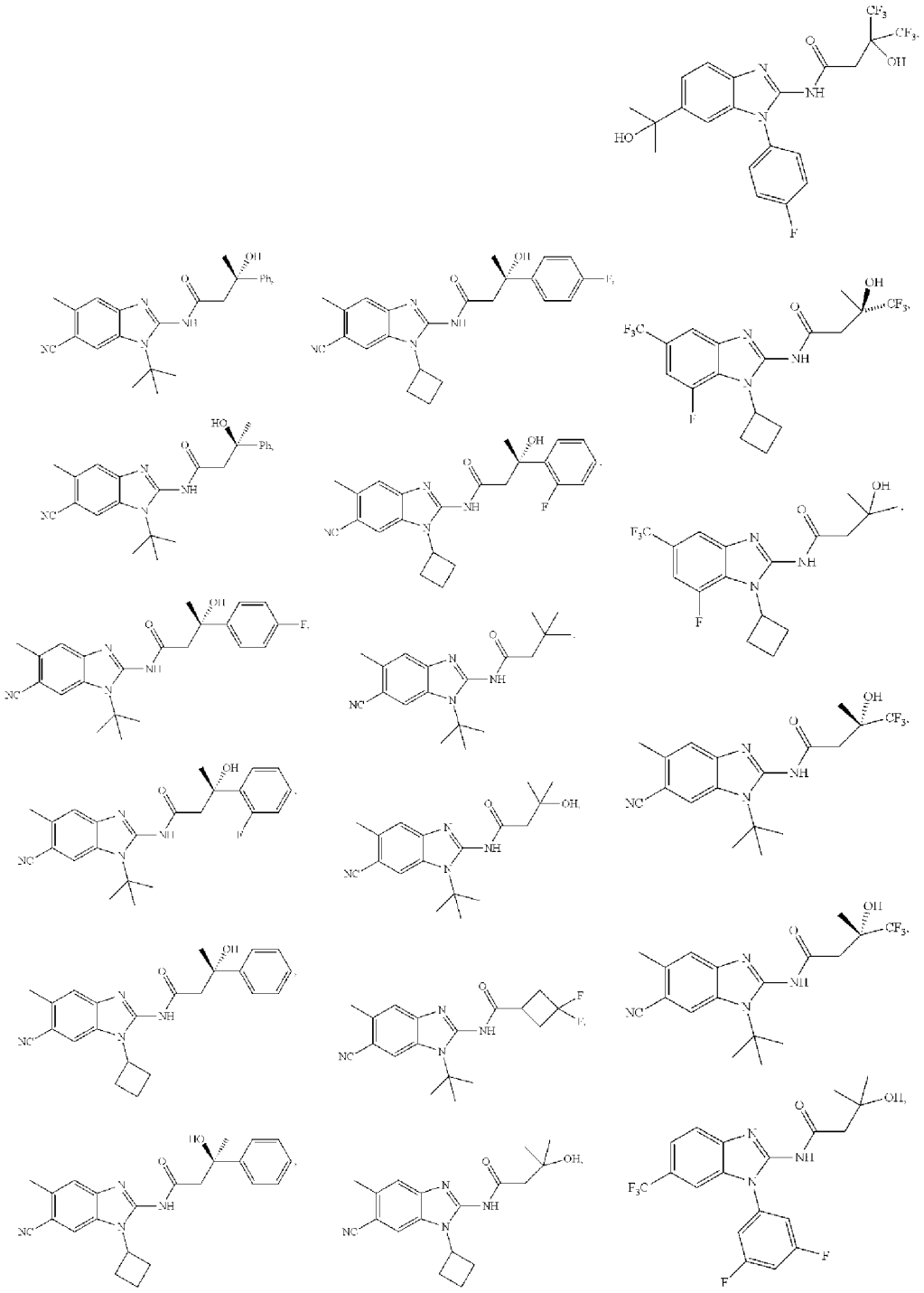


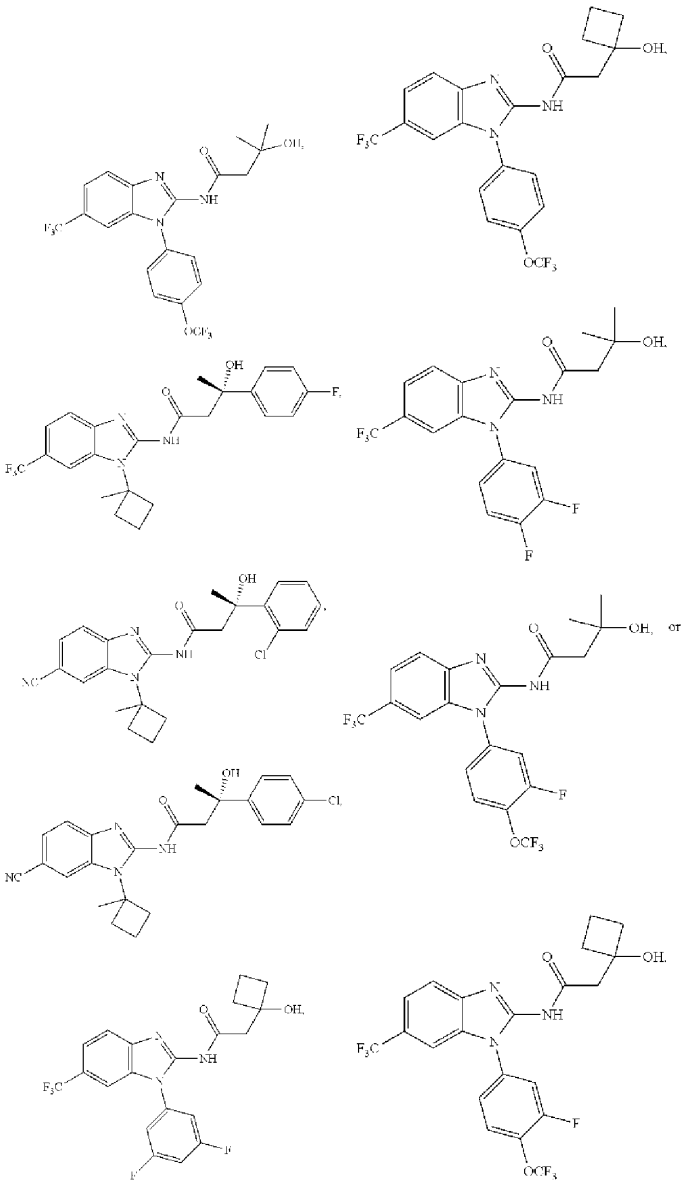












[0064] In further embodiments, the Kv7 channel activator is a compound according to formula 2 wherein, D is optionally substituted cyclobutyl, or t-butyl; A is $C_{2\text{-}8}$ alkyl; X is H, CF_3, or optionally substituted phenyl; Y is H or OH; R^1 is CN or $C_{1\text{-}4}$ hydroxyalkyl; and R^2, R^3, and R^4 are independently H, or F.

[0065] In further embodiments, R^1 is CN, —$C(CH_3)_2OH$, or —$CH_2C(CH_3)_2OH$.

[0066] In further embodiments, R^2 is F.

[0067] In further embodiments, R^3 is H.

[0068] In further embodiments, R^4 is H.

[0069] In further embodiments, R^1 is CN.

[0070] In further embodiments, R^1 is C_{1-4} hydroxyalkyl.

[0071] In further embodiments, X is optionally substituted phenyl.

[0072] In further embodiments, X is CF_3.

[0073] In further embodiments, X is H.

[0074] In further embodiments, Y is H.

[0075] In further embodiments, Y is OH.

[0076] In further embodiments, the Kv7 channel activator is a compound according to formula 2 wherein, D is cyclobutyl; A is C_{1-8} alkyl; X is CF_3; Y is H; R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; and R^4 is H, —CH_3, or —CF_3;

or

D is optionally substituted cyclobutyl; A is C_{1-8} alkyl; X is CF_3; Y is H; R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H; and R^4 is H, —CH_3, or —CF_3;

or

D is t-butyl; A is C_{1-8} alkyl; X is H; Y is H; R^1 is Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; and R^4 is H, —CH_3, or —CF_3 ;

or

D is t-butyl; A is C_{1-8} alkyl; X is CF_3; Y is H; R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; and R^4 is H, —CH_3, or —CF_3;

or

D is cyclobutyl; A is C_{1-8} alkyl; X is H; Y is methyl(2,2,2-trifluoroethyl)amino; R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H; and R^4 is H, —CH_3, or —CF_3;

or

D is cyclobutyl; A is C_{1-8} alkyl; X is CF_3; Y is dimethylamino; R^1 is H, Cl, Br, CN, OCH_3, CF_3, —$CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$; R^3 is H; and R^4 is H, —CH_3, or —CF_3;

or

D is optionally substituted cyclobutyl, optionally substituted phenyl, or optionally substituted C_{2-5} alkyl, wherein the optional substituents are selected from —CH_3 and F; A is C_1 alkyl; X is substituted cyclobutyl, wherein the substituent is F; Y is H; R^1 is selected from H, C_3 hydroxyalkyl, CN, F, or Cl; R^2 is selected from H, CN, F, Br, or —OCF_3; R^3 is selected from H, F, or —OCH_3; R^4 is H or F; and wherein when X is substituted with 2 fluorine atoms, the fluorine atoms are not geminal; or a pharmaceutically acceptable salt thereof;

[0077] In an embodiment, the Kv7 channel activator is a compound according to formula 2. Wherein, R^1, R^2, R^3, and R^4 are independently H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br.

[0078] In further embodiments, Y is H, F, CF_3, OH, C_{1-5} O-alkyl, C_{0-6} alkylamino, optionally substituted tetrahydropyranyl, or C_{0-6} fluoroalkylamino.

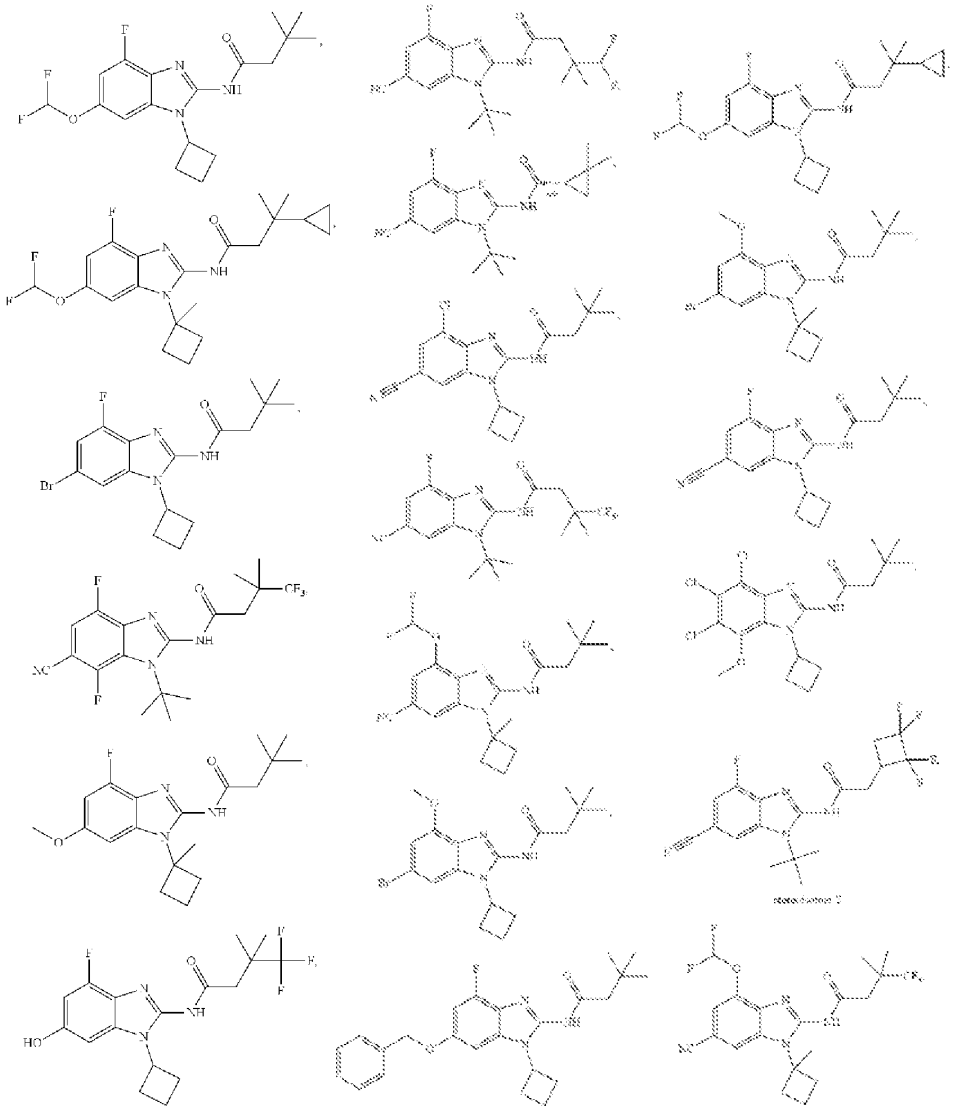
[0079] In further embodiments, R^1 is H, Cl, Br, —OCH_3, —CN, —CF_3, —CH_2OH, —$COOCH_2CH_3$, —$C(CH_3)_2OH$, —$CHOHCH_2CH_3$, —$CHOHCH_3$, —CHF_2, —$CH(CH_3)_2$, —$C(CH_2CH_3)OH$, —$CH_2COOCH_2CH_3$, —$CH_2C(CH_3)_2OH$, —CH_2COOH, or —$CH_2CON(CH_3)_2$.

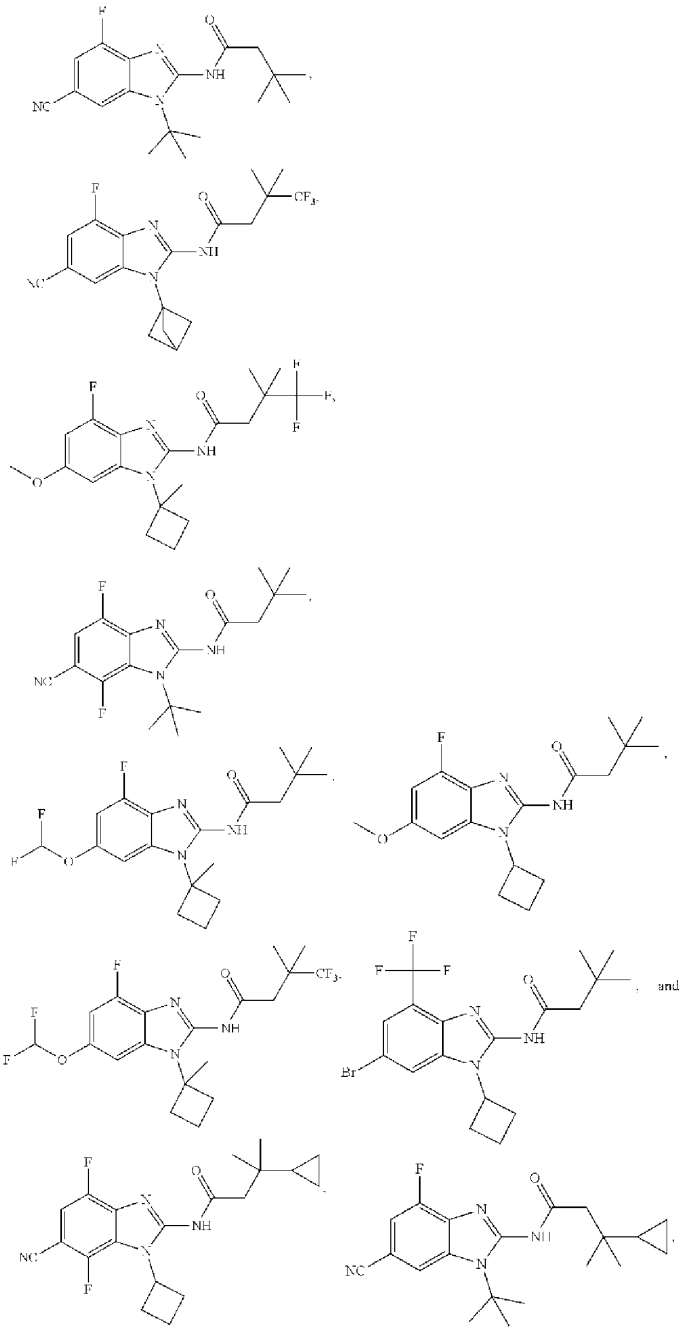
[0080] In further embodiments, R^2 is H, F, —CH_2OH, —CO_2Me, or —$C(CH_3)_2OH$.

[0081] In further embodiments, R^3 is H.

[0082] In further embodiments, R^4 is H, —CH_3, or —CF_3.

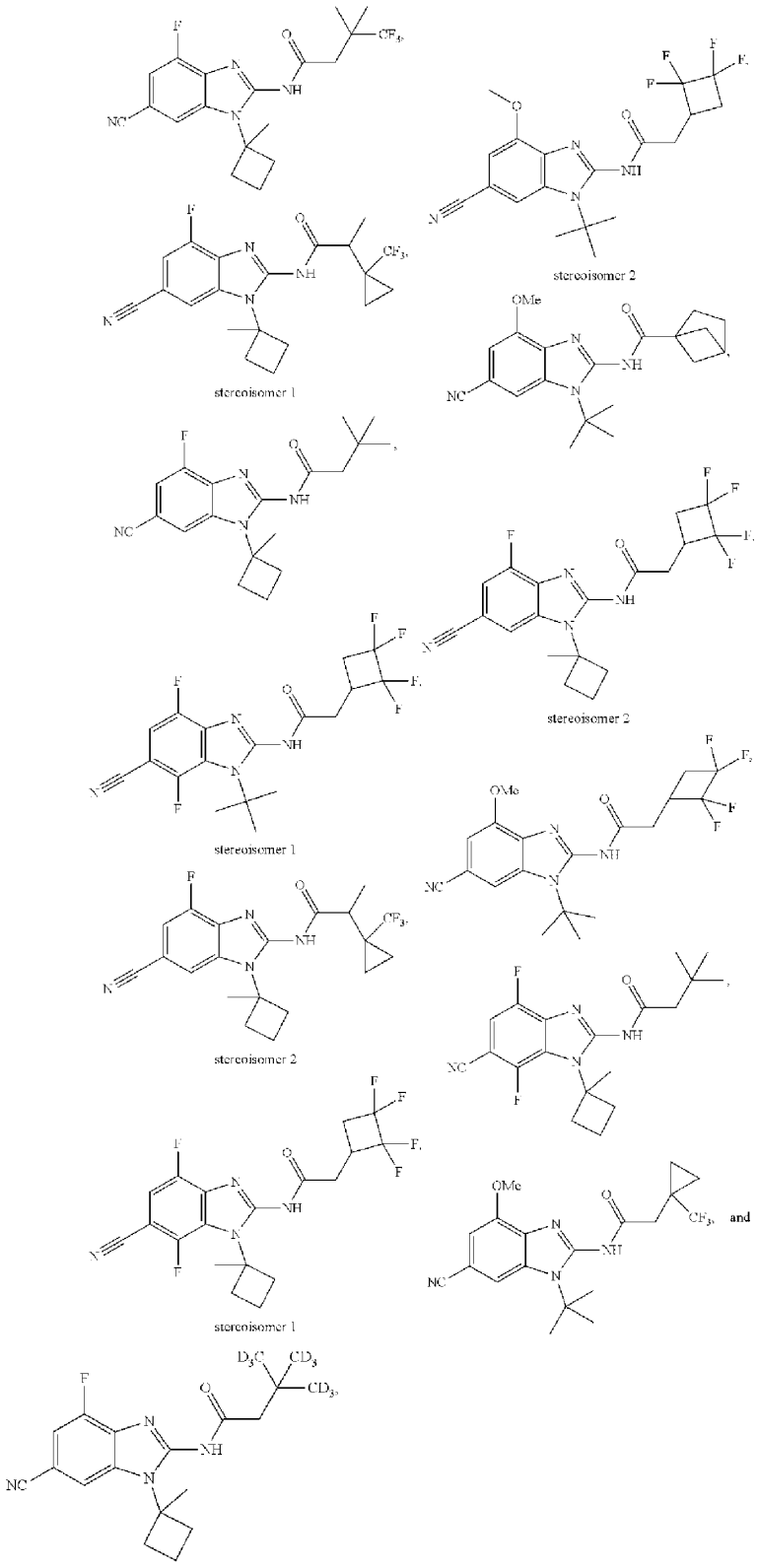
[0083] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:





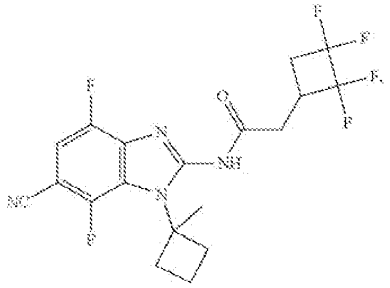
or a pharmaceutically acceptable salt thereof.

[0084] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:

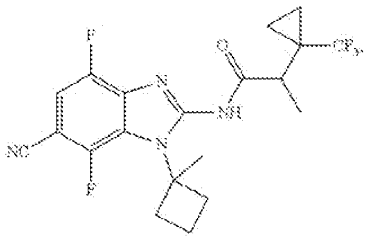


or a pharmaceutically acceptable salt thereof.

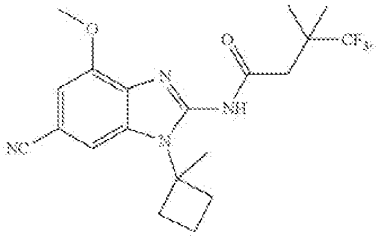
[0085] In further embodiments the Kv7 channel activator is a compound selected from the group consisting of:

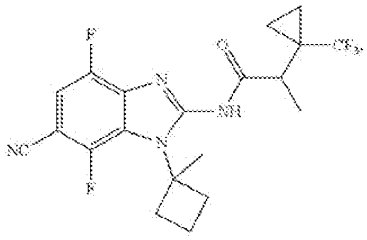


stereoisomer 2

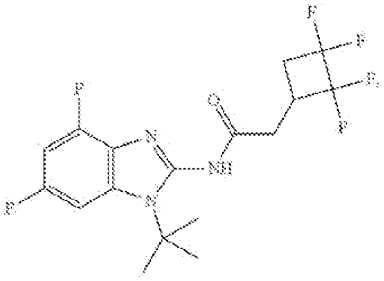


stereoisomer 2

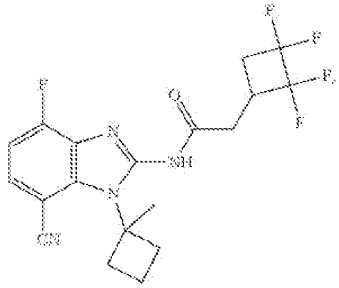




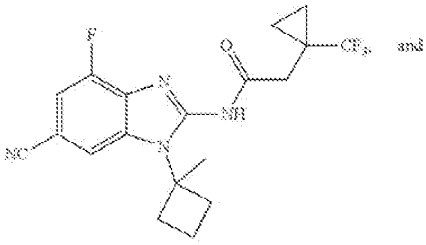
stereoisomer 1



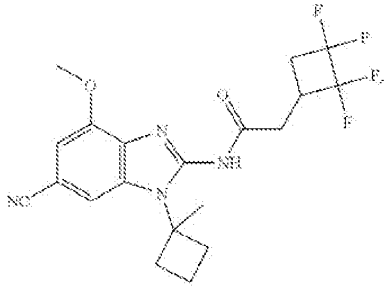
stereoisomer 2



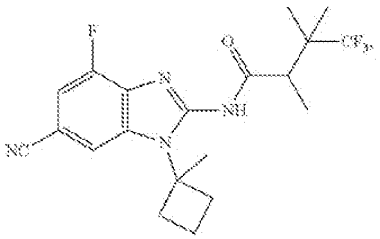
stereoisomer 2



and



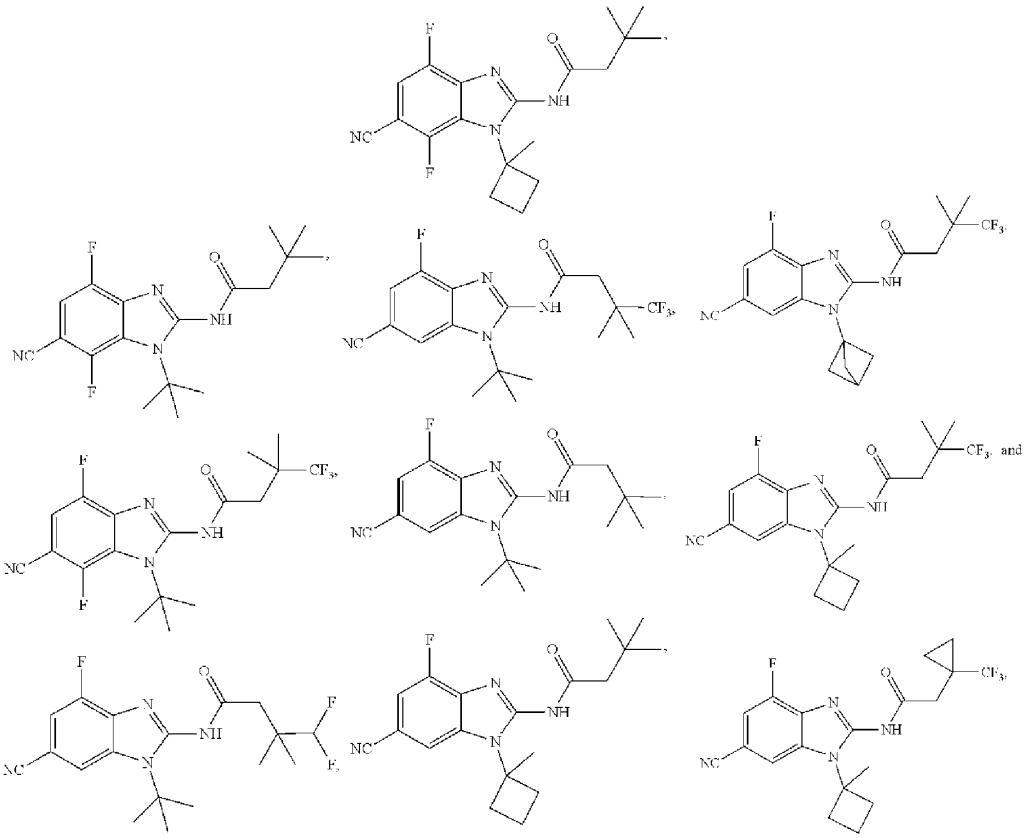
stereoisomer 2



stereoisomer 1

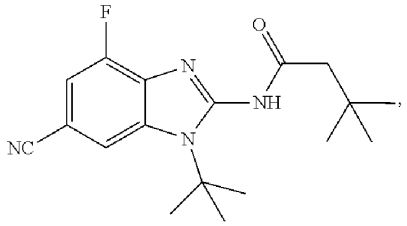
or a pharmaceutically acceptable salt thereof.

[0086] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:



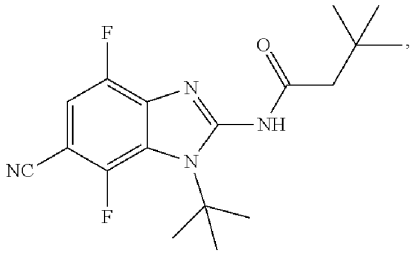
or a pharmaceutically acceptable salt thereof.

[0087] In further embodiments, the compound is:



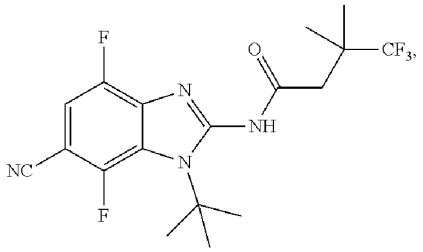
or a pharmaceutically acceptable salt thereof.

[0088] In further embodiments, the compound is:



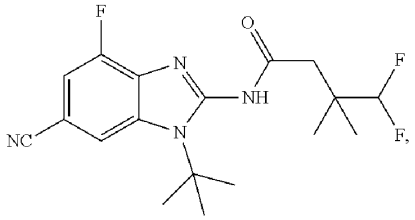
or a pharmaceutically acceptable salt thereof.

[0089] In further embodiments, the compound is:



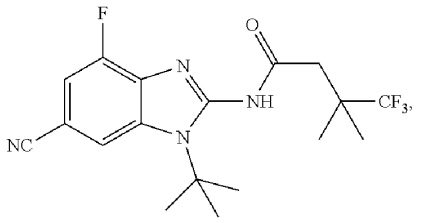
or a pharmaceutically acceptable salt thereof.

[0090] In further embodiments, the compound is:



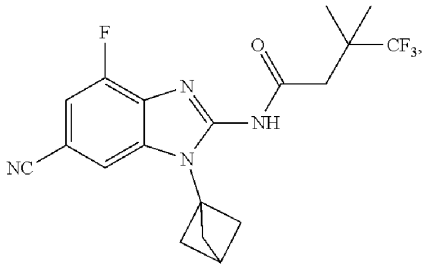
or a pharmaceutically acceptable salt thereof.

[0091] In further embodiments, the compound is:



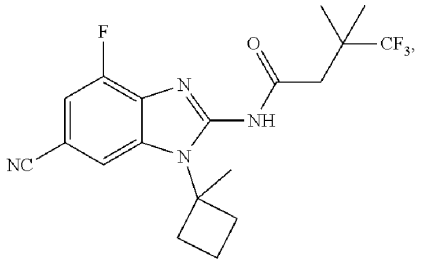
or a pharmaceutically acceptable salt thereof.

[0092] In further embodiments, the compound is:



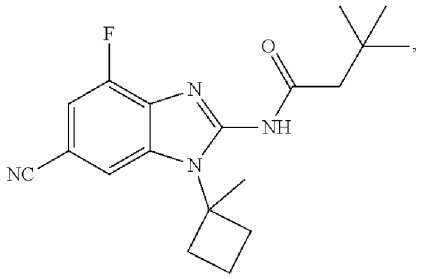
or a pharmaceutically acceptable salt thereof.

[0093] In further embodiments, the compound is:



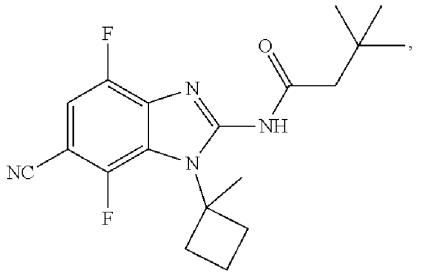
or a pharmaceutically acceptable salt thereof.

[0094] In further embodiments, the compound is:



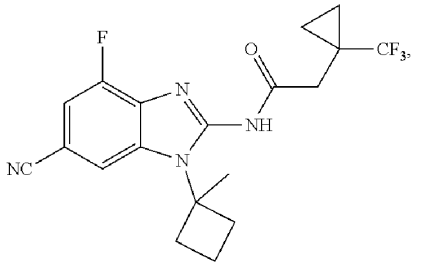
or a pharmaceutically acceptable salt thereof.

[0095] In further embodiments, the compound is:



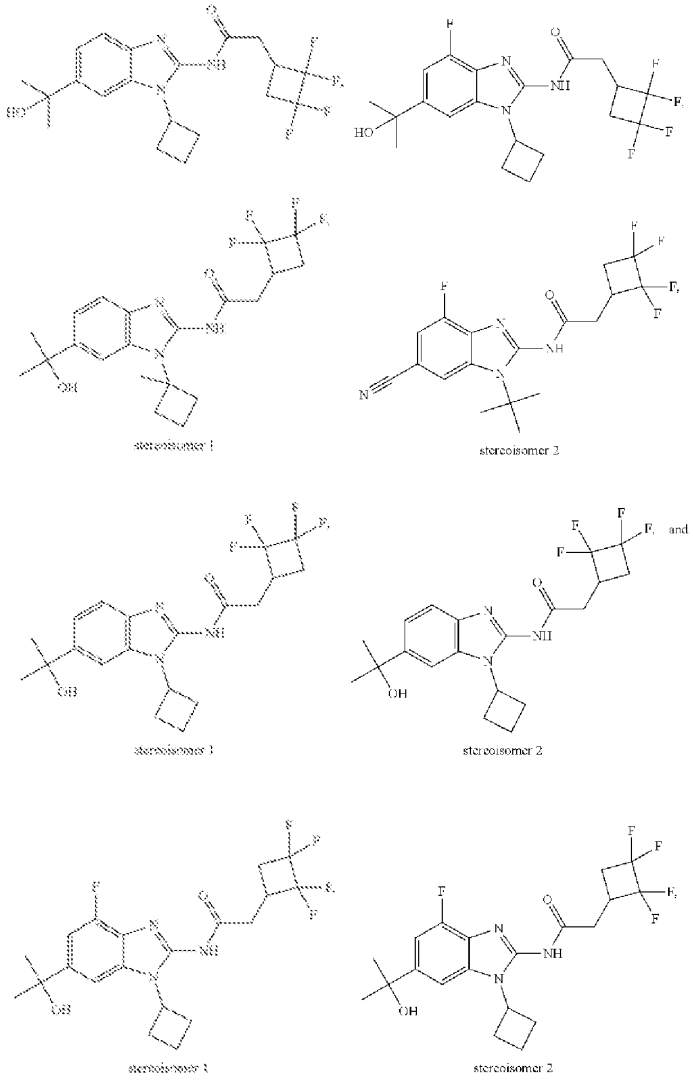
or a pharmaceutically acceptable salt thereof.

[0096] In further embodiments, the compound is:



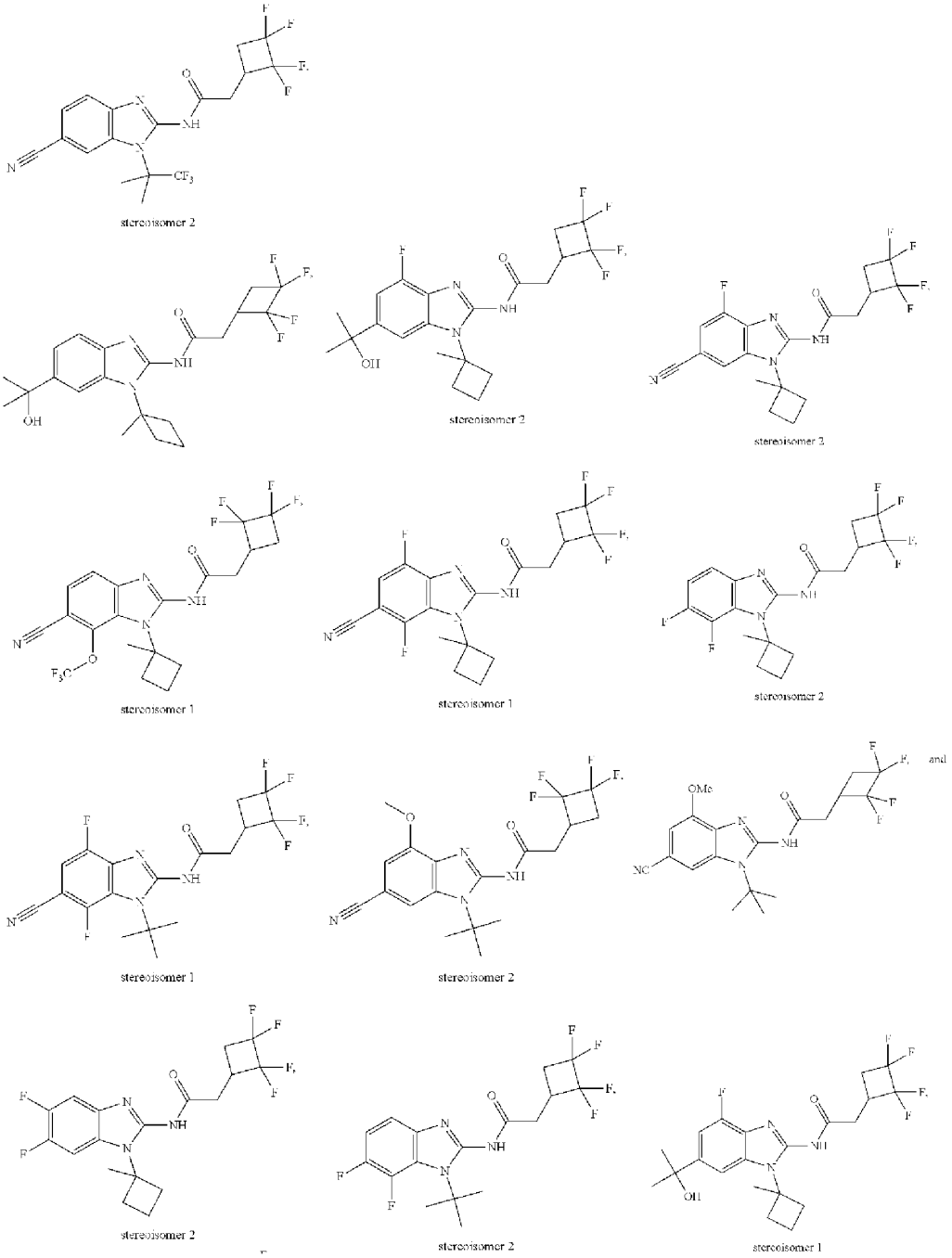
or a pharmaceutically acceptable salt thereof.

[0097] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:



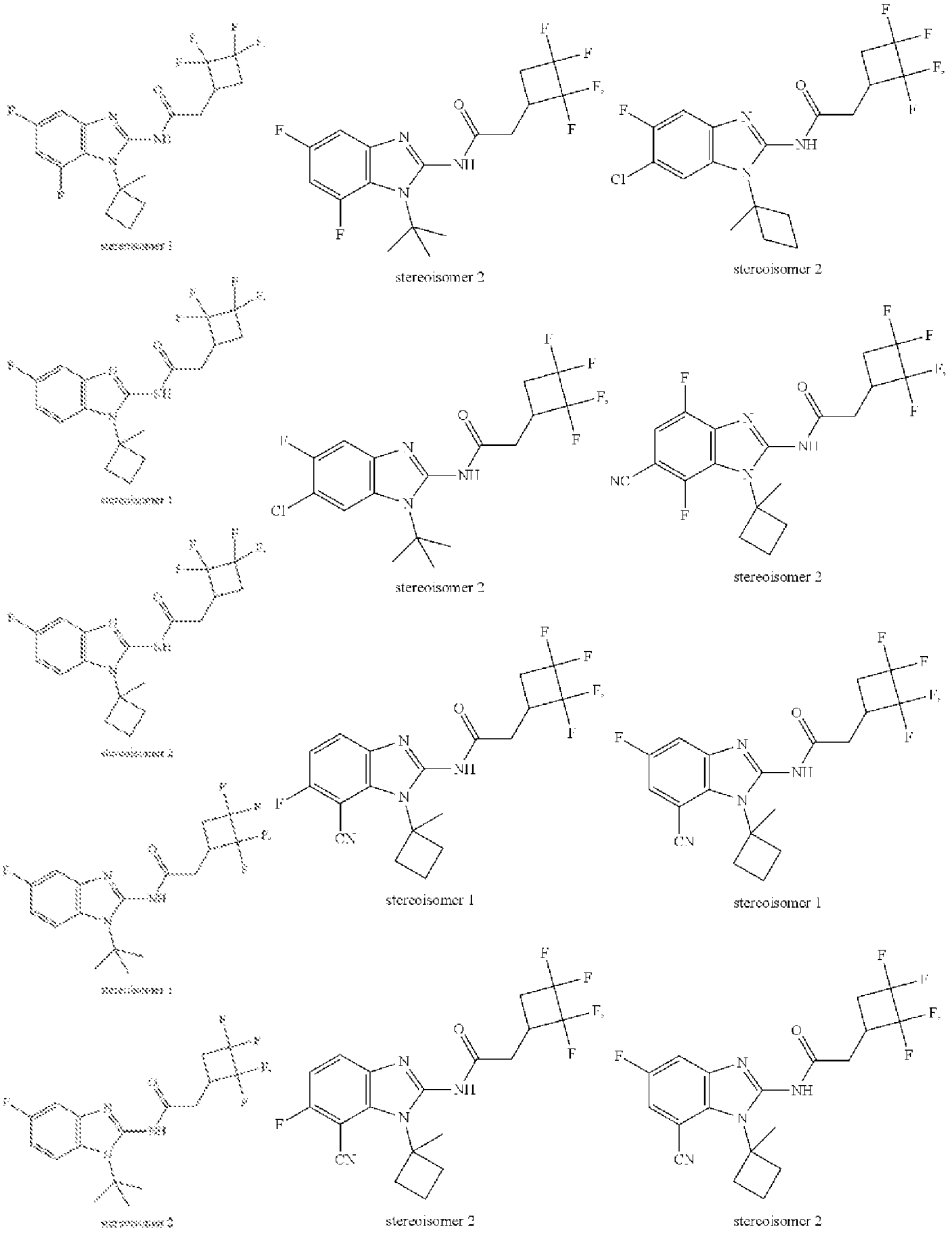
or a pharmaceutically acceptable salt thereof.

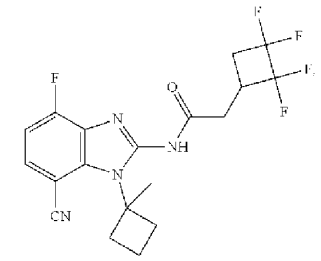
[0098] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:

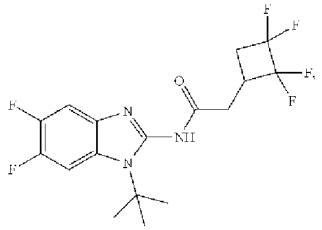


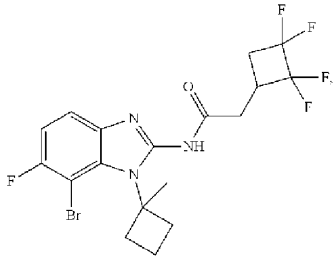
or a pharmaceutically acceptable salt thereof.

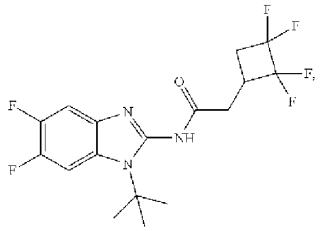
[0099] In further embodiments, the Kv7 channel activator is a compound selected from the group consisting of:

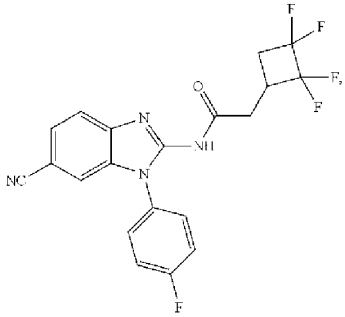

stereoisomer 2
stereoisomer 2
stereoisomer 2
stereoisomer 2
stereoisomer 1
stereoisomer 1
stereoisomer 2
stereoisomer 2

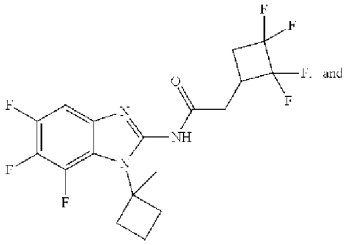

stereoisomer 2

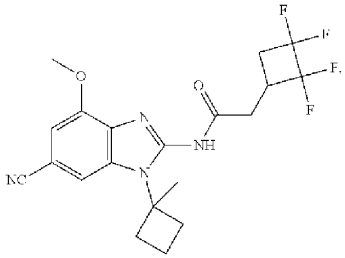

stereoisomer 2

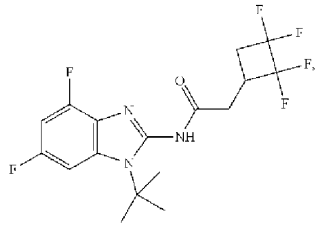

stereoisomer 1


stereoisomer 1

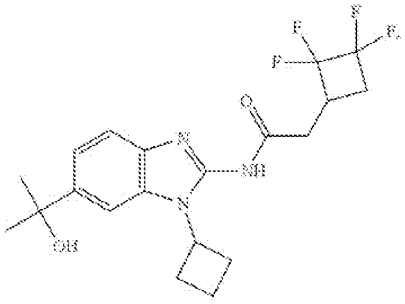

stereoisomer 2


stereoisomer 2


stereoisomer 2


stereoisomer 2

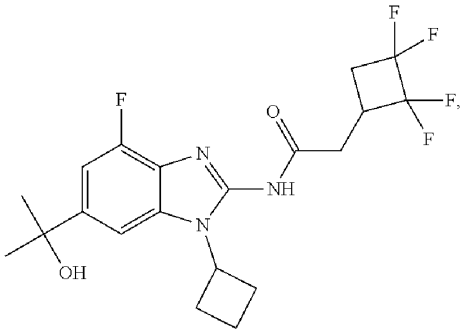
[0100] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

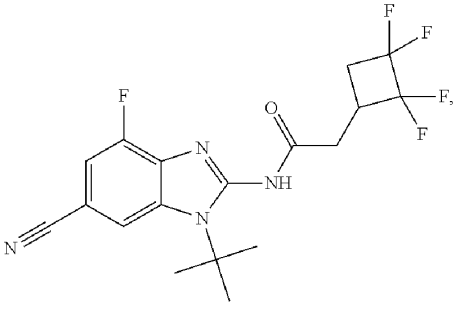
[0101] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

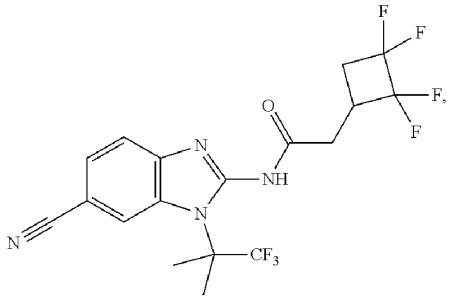
[0102] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

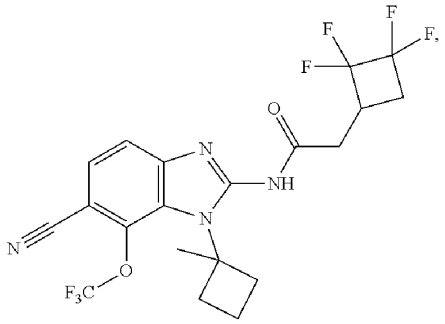
[0103] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

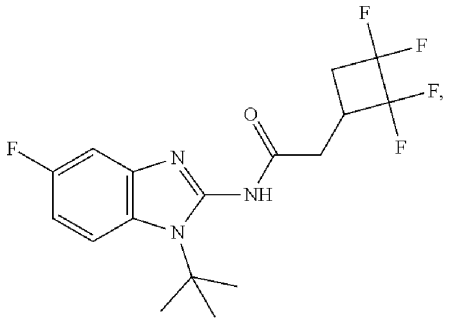
[0104] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

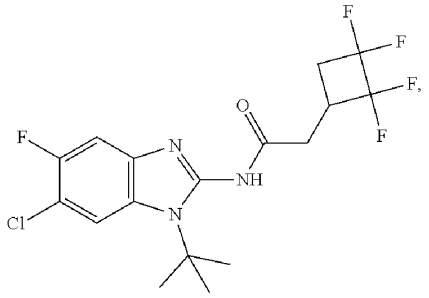
[0105] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

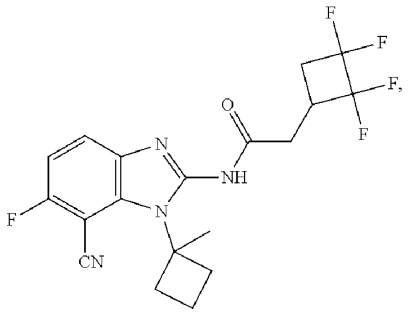
[0106] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

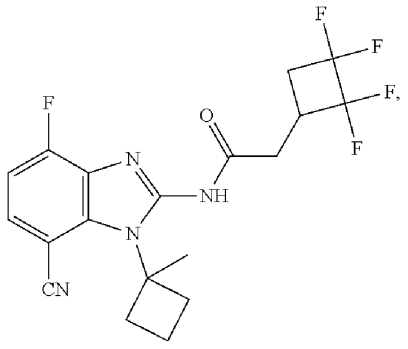
[0107] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

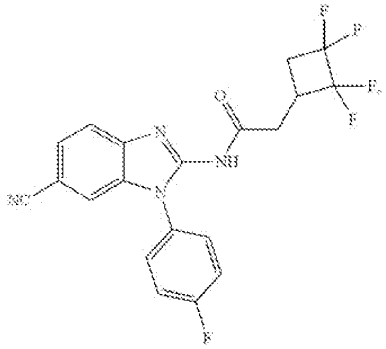
[0108] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

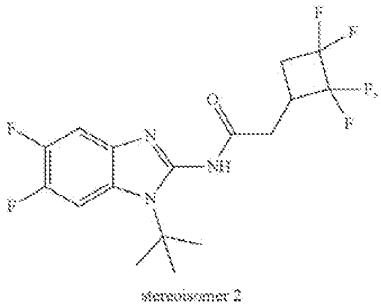
[0109] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

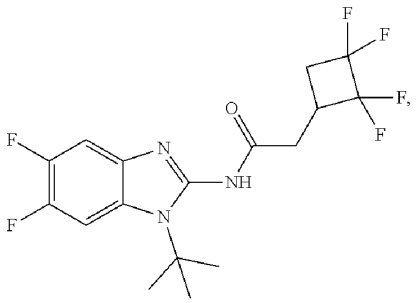
[0110] In further embodiments, the compound is:



stereoisomer 2

or a pharmaceutically acceptable salt thereof.

[0111] In further embodiments, the compound is:



stereoisomer 1

or a pharmaceutically acceptable salt thereof.

[0112] In an embodiment of Formula 2, D is optionally substituted cyclobutyl, or t-butyl; A is C_{2-8} alkyl, X is H, CF_3, or optionally substituted phenyl, Y is H or OH, R^1 is CN or C_{1-4} hydroxyalkyl; and R^2, R^3, and R^4 are independently H, or F. In a further embodiment, R^1 is CN, $-C(CH_3)_2OH$, or $-CH_2C(CH_3)_2OH$. In a further embodiment, R^2 is F. In a further embodiment, R^3 is H. In a further embodiment, R^4 is H. In a further embodiment, R^1 is CN. In a further embodiment, R^1 is C_{1-4} hydroxyalkyl. In a further embodiment, X is optionally

substituted phenyl. In a further embodiment, X is CF_3. In a further embodiment, X is H. In a further embodiment, Y is H. In a further embodiment, Y is OH.

[0113] In an embodiment of Formula 2, D is cyclobutyl; A is C_{1-8} alkyl, X is CF_3, Y is H, R^1 is H, Cl, Br, CN, OCH_3, CF_3, $-CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, $-CH_2OH$, $-CO_2Me$, or $-C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl or B; and R^4 is H, $-CH_3$, or $-CF_3$.

[0114] In an embodiment of Formula 2, D is optionally substituted cyclobutyl, A is C_{1-8} alkyl, X is CH_3, Y is H, R^1 is H, Cl, Br, CN, OCH_3, CF_3, $-CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, $-CH_2OH$, $-CO_2Me$, or $-C(CH_3)_2OH$; R^3 is H; and R^4 is H, $-CH_3$, or $-CF_3$.

[0115] In an embodiment of Formula 2, D is t-butyl; A is C_{1-8} alkyl; X is H; Y is H; R^1 is Cl, Br, CN, OCH_3, CF_3, $-CO_2CH_2CH_3$, C_{1-4}alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, $-CH_2OH$, $-CO_2Me$, or $-C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; and R^4 is H, $-CH_3$, or $-CF_3$.

[0116] In an embodiment of Formula 2, D is t-butyl; A is C_{1-8} alkyl; X is CF_3; Y is H; R^1 is H, Cl, Br, CN, OCH_3, CF_3, $-CO_2CH_2CH_3$, C_{1-4}alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, $-CH_2OH$, $-CO_2Me$, or $-C(CH_3)_2OH$; R^3 is H, F, Cl, Br, I, or a substituent having a molecular weight of 15 Da to 200 Da and consisting of 2 to 5 chemical elements, wherein the chemical elements are independently C, H, O, N, S, F, Cl, or Br; and R^4 is H, CH_3, or CF_3.

[0117] In an embodiment of Formula 2, D is cyclobutyl; A is C_{1-8} alkyl; X is H; Y is methyl(2,2,2-trifluoroethyl)amino; R^1 is H, Cl, Br, CN, OCH_3, CF_3, $-CO_2CH_2CH_3$, C_{1-4} alkyl, or C_{1-4} hydroxyalkyl; R^2 is H, F, $-CH_2OH$, $-CO_2Me$, or $-CH(CH_3)_2OH$; R^3 is H; and R^4 is H, $-CH_3$, or $-CF_3$.

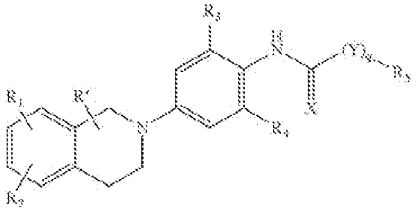
[0118] In an embodiment of Formula 2, D is optionally substituted cyclobutyl, optionally substituted phenyl, or optionally substituted C_{2-5} alkyl, wherein the optional substituents are selected from $-CH_3$ and F; A is C_1 alkyl, X is substituted cyclobutyl, wherein the substituent is F; Y is H; R^1 is selected from H, C_3 hydroxyalkyl, CN, F, or Cl; R^2 is selected from H, CN, F, Br, or $-OCF_3$; R^3 is selected from H, F, or $-OCH_3$; R^4 is H or F; and wherein when X is substituted with 2 fluorine atoms, the fluorine atoms are not geminal; or a pharmaceutically acceptable salt thereof.

Formula 3

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 3. Such compounds are described in US Patent No. 8,293,911 issued on October 23, 2012 and corresponding to US Application No. 11/894,877 filed August 22, 2007; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 3, this reference incorporated by reference herein controls.

[0119] In an embodiment, the Kv7 channel activator is a compound according to formula 3:

Formula 3



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wherein, R_1 and R_2, vary independently, and are selected from the group consisting of H, CN, halogen, CH_2CN, OH, CH_2F, CHF_2, CF_3, CF_2CF_3, C_1-C_6 alkyl, $C(=O)C_1$-C_6 alkyl; $NH—C_1$-C_6 alkyl; $N(C_1$-C_6 alkyl)-C_1-C_6 alkyl, $NHC(=O)C_1$-C_6 alkyl, $C(=O)N(CH_3)_2$, $C(=O)N(Et)_2$, $C(=O)NH_2$, $C(=O)NH—C_1$-C_6alkyl, SO_2NH_2, $NHSO_2—C_1$-C_6 alkyl; $C(=O)OC_1$-C_6 alkyl, $OC(=O)C_1$-C_6 alkyl, OC_1-C_6 alkyl, SC_1-C_6 alkyl, C_3-C_6 cycloalkyl, $(CH_2)_mC_3$-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, $(CH_2)_mC_3$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CH_2)_m$thienyl, $(CH_2)_m$imidazolyl, $(CH_2)_m$pyrazyl, $(CH_2)_m$oxazolyl, $(CH_2)_m$isoxazolyl, $(CH_2)_m$thiazolyl, $(CH_2)_m$isothiazolyl, $(CH_2)_m$phenyl, $(CH_2)_m$pyrrolyl, $(CH_2)_m$pyridyl, and $(CH_2)_m$pyrimidyl, Wherein m=zero, 1, or 2; Ar is a 5- to 10-member mono- or bicyclic aromatic group, optionally containing 1-4 ring heteroatoms selected independently from N, O, and S; or R_1 and R_2, together with the ring carbon atoms to which they are attached, form a 5- or 6-member fused ring; wherein said fused ring may be saturated, unsaturated, or aromatic, and said fused ring optionally contains one or two heteroatoms selected independently from the group consisting of O, N, and S; R′ is selected from the group consisting of H, halogen, phenyl, 2-(N,N-dimethylamino)ethyl, CF_3, OC_1-C_3 alkyl and C_1-C_3 alkyl; R_3 and R_4 vary independently, and are selected from the group consisting of H, CN, halogen, CF_3, OCF_3, OC_1-C_3 alkyl, and C_1-C_3 alkyl; X is O or S; Y is O or S; q=1 or zero; and R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, $CR_6=CH—C_3$-C_6 cycloalkyl, $CH=CR_6—C_3$-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl,

C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_6)_wCH_2Ar$, wherein w=zero, 1, 2, or 3; Ar is a 5- to 10-member mono- or bicyclic aromatic group, optionally containing 1-4 ring heteroatoms selected independently from the group consisting of N, O, and S; and R_6 is selected from the group consisting of H or C_1-C_3 alkyl; where all cycloalkyl and cycloalkenyl optionally contain one or two ring heteroatoms selected independently from N, O, and S; wherein all alkyl, cycloalkyl, alkenyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, alkynyl, aryl, and heteroaryl groups in R_1, R_2, R′, R_3, R_4, R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of C_1-C_3 alkyl, halogen, OH, OEt, OMe, CN, CH_2F, OCF_3, and CF_3; and wherein, additionally, all cycloalkyl and heterocycloalkyl groups are optionally substituted with a carbonyl group.

[0120] In further embodiments, R_1 and R_2, vary independently, and are selected from the group consisting of H, halogen, CF_3, C_1-C_6 alkyl, C(=O)C_1-C_6 alkyl, C(=O)OC_1-C_6 alkyl, OC(=O)C_1-C_6 alkyl, OC_1-C_6 alkyl, SCH_3, C_3-C_6 cycloalkyl, $(CH_2)_mC_3$-C_6 cycloalkyl, phenyl, pyridyl, pyrrolyl, thienyl, $(CH_2)_m$phenyl, $(CH_2)_m$pyrrolyl, and $(CH_2)_m$pyridyl; wherein said cycloalkyl groups optionally contain one or two heteroatoms selected independently from the group consisting of O, N, and S; wherein said alkyl, cycloalkyl, phenyl, pyrrolyl, and pyridyl groups are optionally substituted with one or two groups selected, independently, from halogen, methyl, ethyl, or trifluoromethyl; and wherein m is zero, 1, or 2; R′ is selected from the group consisting of H, halogen, phenyl, 2-(N,N-dimethylamino)ethyl, CF_3, OC_1-C_3 alkyl and C_1-C_3 alkyl; R_3 and R_4 vary independently, and are selected from the group consisting of H, halogen, CF_3, OCF_3, OC_1-C_3 alkyl, and C_1-C_3 alkyl; X is O or S; Y is O or S; q=1 or 0; R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, CR_6=CH—C_3-C_6 cycloalkyl, CH=CR_6—C_3-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_7)_wCH_2Ar$; wherein w=0-3; Ar is selected from the group consisting of phenyl, pyrimidyl, or pyridyl, and a 5-member heteroaromatic ring; wherein said heteroaromatic ring contains 1 or 2 ring heteroatoms selected independently from the group consisting of N, O, and S; and R_6 is selected from the group consisting of H and methyl; wherein all cycloalkyl and cycloalkenyl groups in R_5 optionally contain one or two ring heteroatoms selected independently from the group consisting of N, O, and S; and wherein all alkyl, cycloalkyl, alkenyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, alkynyl, aryl, and heteroaryl groups in R_1, R_2, R_3, R_4,

R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of C_1-C_3 alkyl, halogen, OEt, OMe, and trifluoromethyl.

[0121] In further embodiments, R_1 and R_2, vary independently, and are selected from the group consisting of H, halogen, CF_3, C_1-C_6 alkyl, $C(=O)C_1$-C_6 alkyl, $C(=O)OC_1$-C_6 alkyl, $OC(=O)C_1$-C_6 alkyl, OC_1-C_6 alkyl, SCH_3, $(CH_2)_m$cyclopropyl, $(CH_2)_m$cyclobutyl, $(CH_2)_m$cyclopentyl, $(CH_2)_m$cyclohexyl, $(CH_2)_m$oxazolyl, $(CH_2)_m$isoxazolyl, $(CH_2)_m$thiazolyl, $(CH_2)_m$isothiazolyl, $(CH_2)_m$phenyl, $(CH_2)_m$pyrrolyl, $(CH_2)_m$pyridyl, and $(CH_2)_m$pyrimidyl; wherein said cyclopentyl and said cyclohexyl groups optionally contain one or two ring heteroatoms selected independently from the group consisting of O, N, and S; wherein said alkyl, cycloalkyl, phenyl, pyrrolyl, and pyridyl groups are optionally substituted with one or two groups selected, independently, from the group consisting of halogen, CH_3, ethyl, and CF_3; and m is zero, 1, or 2; R′ is selected from the group consisting of H, halogen, CF_3, and C_1-C_3 alkyl; R_3 and R_4 vary independently, and are selected from the group consisting of H, halogen, CF_3, OCF_3, OC_1-C_3 alkyl, and C_1-C_3 alkyl; X is O or S; Y is O; q=1 or 0; R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, CR_6=CH—C_3-C_6 cycloalkyl, CH=CR_6—C_3-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_6)_wCH_2Ar$; wherein w=0-3, Ar is selected from the group consisting of phenyl, pyridyl, and a 5-member heteroaromatic ring, wherein said heteroaromatic ring contains 1 or 2 ring heteroatoms selected independently from the group consisting of N, O, and S; R_6 is H or methyl; wherein all cycloalkyl and cycloalkenyl groups optionally contain one or two ring heteroatoms selected independently from the group consisting of N, O, and S; and wherein all alkyl, cycloalkyl, alkenyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, alkynyl, aryl, and heteroaryl groups in R_1, R_2, R_3, R_4, R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of C_1-C_3 alkyl, halogen, OMe, OEt, and CF_3.

[0122] In further embodiments, R_1 and R_2, vary independently, and are selected from the group consisting of H, halogen, CF_3, OC_1-C_3 alkyl, C_1-C_6 alkyl, $C(=O)OC_1$-C_3 alkyl, $OC(=O)C_1$-C_3 alkyl, and $C(=O)C_1$-C_3 alkyl; R′ is selected from the group consisting of H, F, CH_3, and ethyl; R_3 and R_4 vary independently, and are selected from the group consisting of H, F, Cl, CF_3, OCF_3, OC_1-C_3 alkyl, and C_1-C_3 alkyl; and R_5 is C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, or $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, or $(CHR_6)_wCH_2Ar$.

[0123] In further embodiments, R_2 is H or F; R′ is H; R_3 is selected from the group consisting of H, CH_3, OCH_3, CF_3, OCF_3, and Cl; R_4 is selected from the group consisting of CH_3, OCH_3, CF_3, OCF_3, and Cl; and R_5 is C_3-C_6 alkyl or $(CH_2)_wC_3$-C_6 cycloalkyl.

[0124] In further embodiments, R_1 is halogen or CF_3; R_2 is H or F; R′ is H; R_3 and R_4 vary independently, and are selected from the group consisting of H, CH_3, OCH_3, CF_3, OCF_3, or Cl; and R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, CR_6=CH—C_3-C_6 cycloalkyl, CH=CR_6—C_3-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_6)_wCH_2Ar$.

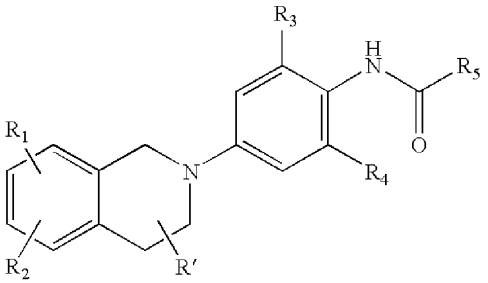
[0125] In further embodiments, R_1 is halogen or CF_3; R_2 is H or F; R′ is H; R_3 and R_4 vary independently, and are selected from the group consisting of H, CH_3, OCH_3, CF_3, OCF_3, or Cl; and R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, CR_6=CH—C_3-C_6 cycloalkyl, CH=CR_6—C_3-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_6)_wCH_2Ar$.

Formula 4

[0126] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 4. Such compounds are described in US Patent No. 8,293,911 issued on October 23, 2012 and corresponding to US Application No. 11/894,877; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 4, this reference incorporated by reference herein controls.

[0127] In an embodiment, the Kv7 channel activator is a compound according to formula 4:

Formula 4



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wherein, R_1 is selected from the group consisting of H, halogen, CN, CH_2CN, CF_3, C_1-C_6 alkyl, OCH_3, (C=O)OCH_3, O(C=O)CH_3, OCF_3, $(CH_2)_mC_3$-C_6 cycloalkyl, phenyl, and

pyridyl; R_2 is selected from the group consisting of H, F, OCH_3, CH_3, and CF_3; R_3 and R_4 vary independently, and are selected from the group consisting of H, F, Cl, CF_3, OCF_3, OC_1-C_3 alkyl, or C_1-C_3 alkyl; and R_5 is selected from the group consisting of C_1-C_6 alkyl, $(CHR_6)_wC_3$-C_6 cycloalkyl, $(CHR_6)_wCH_2C_3$-C_6 cycloalkyl, $CH_2(CHR_6)_wC_3$-C_6 cycloalkyl, CR_6═CH—C_3-C_6 cycloalkyl, CH═CR_6—C_3-C_6 cycloalkyl, $(CHR_6)_wC_5$-C_6 cycloalkenyl, $CH_2(CHR_6)_wC_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, Ar, $(CHR_6)_wAr$, $CH_2(CHR_6)_wAr$, and $(CHR_6)_wCH_2Ar$, wherein w=0-3; Ar is phenyl, furyl, pyrrolyl, oxazolyl, thiazolyl, thienyl, or pyridyl; and R_6 is C_1-C_3 alkyl; wherein all alkyl, cycloalkyl, aryl, and heteroaryl groups in R_1, R_2, R_3, R_4, R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of C_1-C_3 alkyl, halogen, OCH_3, OCH_2CH_3, CN, and CF_3.

[0128] In other embodiments, R_1 is selected from the group consisting of H, F, Cl, Br, CF_3, C_1-C_6 alkyl, OCH_3, CH_2OCH_3, $CH_2CH_2OCH_3$, $CH_2OCH_2CH_3$, and OCH_2CH_3; R′ is selected from the group consisting of H, CH_3, CH_2CH_3, or halogen; R_3 and R_4 vary independently, and are selected from the group consisting of H, F, Cl, CF_3, OCF_3, OCH_3, and CH_3; and R_5 is selected from the group consisting of C_1-C_6 alkyl, CH_2C_3-C_6 cycloalkyl, $CH_2CH_2C_3$-C_6 cycloalkyl, CH═CH—C_3-C_6 cycloalkyl, CH═CH—C_5-C_6 cycloalkenyl, CH_2C_5-C_6 cycloalkenyl, $CH_2CH_2C_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, and $(CH_2)_wAr$; wherein w=1 or 2; Ar is selected from the group consisting of phenyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, furyl, thienyl, pyrrolyl, and pyridyl; wherein all alkyl, cycloalkyl, aryl, and heteroaryl groups in R_1, R_2, R_3, R_4, R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of CH_3, halogen, OCH_3, OCH_2CH_3, CN, and CF_3.

[0129] In other embodiments, R_1 is selected from the group consisting of H, F, Cl, Br, CF_3, C_1-C_6 alkyl, OCH_3, CH_2OCH_3, $CH_2CH_2OCH_3$, $CH_2OCH_2CH_3$, and OCH_2CH_3; R′ is selected from the group consisting of H, CH_3, CH_2CH_3, or halogen; R_3 and R_4 vary independently, and are selected from the group consisting of H, F, Cl, CF_3, OCF_3, OCH_3, and CH_3; and R_5 is selected from the group consisting of C_1-C_6 alkyl, CH_2C_3-C_6 cycloalkyl, $CH_2CH_2C_3$-C_6 cycloalkyl, CH═CH—C_3-C_6 cycloalkyl, CH═CH—C_5-C_6 cycloalkenyl, CH_2C_5-C_6 cycloalkenyl, $CH_2CH_2C_5$-C_6 cycloalkenyl, C_2-C_6 alkenyl, and $(CH_2)_wAr$; wherein w=1 or 2; Ar is selected from the group consisting of phenyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, furyl, thienyl, pyrrolyl, and pyridyl; wherein all alkyl, cycloalkyl, aryl, and heteroaryl groups in R_1, R_2, R_3, R_4, R_5, R_6, and Ar are optionally substituted with one or two substituents selected independently from the group consisting of CH_3, halogen, OCH_3,

OCH_2CH_3, CN, and CF_3. Wherein, R_1 is selected from the group consisting of F, CF_3, Cl, CH_3, CH_2CH_3, SCH_3, OCH_3, CH_2OCH_3, $CH_2OCH_2CH_3$, OCF_3, phenyl, thienyl, and H; R_2 is selected from the group consisting of H, F, Cl, and OCH_3; R′ is selected from the group consisting of H, F, CH_2CH_3, and CH_3; R_3 and R_4 vary independently, and are selected from the group consisting of H, Cl, CH_3, CF_3, OCH_3, and OCF_3; and R_5 is selected from the group consisting of C_4-C_6 alkyl, $(CH_2)_wAr$, and $(CH_2)_wC_5$-C_6 cycloalkyl; wherein w is 1, 2, or 3.

[0130] In other embodiments, R_1 is selected from the group consisting of F, CF_3, Cl, CH_3, OCH_3, CH_2OCH_3, and H; R_2 is selected from the group consisting of H, F, CH_3, and Cl; R′ is H; R_3 is selected from the group consisting of H, Cl, CH_3, CF_3, OCH_3, and OCF_3; R_4 is selected from the group consisting of Cl, OCH_3, and CH_3; and R_5 is C_4-C_6 alkyl or 2-cyclopentyl ethyl.

[0131] In other embodiments, R_3 and R_4 are both CH_3 or both OCH_3; and R_5 is C_5-C_6 alkyl.

[0132] In other embodiments, R′ and R_2 are H; R_3 and R_4 are both methyl; and R_5 is C_5-C_6 alkyl or $(CH_2)_wC_5$-C_6 cycloalkyl; wherein w is 1, 2, or 3.

[0133] In other embodiments, the compound is selected from the group consisting of: N-(2-chloro-4-(3,4-dihydroisoquinolin-2(1H)-yl)-6-(trifluoromethyl)phenyl)-3,3-dimethylbutanamide; N-(4-(3,4-dihydroisoquinolin-2(1H)-yl)-2,6-dimethylphenyl)-3,3-dimethylbutanamide; N-(2-chloro-4-(3,4-dihydroisoquinolin-2(1H)-yl)-6-(trifluoromethyl)phenyl)-3-cyclopentylpropanamide; N-(2-chloro-4-(6-fluoro-3,4-dihydroisoquinolin-2(1H)-yl)-6-(trifluoromethylphenyl)-3,3-dimethylbutanamide; N-[2-chloro-4-(3,4-dihydro-1H-isoquinolin-2-yl)-6-methyl phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-6-trifluoromethyl phenyl]-3-cyclopentylpropionamide; N-[2,6-dimethyl-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethylbutanamide; N-[2-chloro-6-trifluoromethyl-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(6-chloro-3,4-dihydro-1H-isoquinolin-2-yl)-6-trifluoromethyl phenyl]-3,3-dimethylbutanamide; N-[4-(6-chloro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide; N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(7-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-6-trifluoromethyl-phenyl]-3,3-dimethylbutanamide; N-[4-(7-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-6-methylphenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(7-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-6-methylphenyl]-3,3-dimethylbutanamide; N-[2-chloro-6-methyl-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-

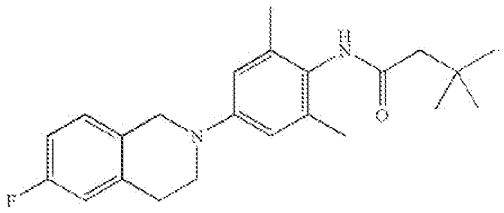
dimethylbutanamide; N-[2-chloro-4-(6-chloro-3,4-dihydro-1H-isoquinolin-2-yl)-6-methyl-phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethylbutanamide; N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2-methyl-phenyl]-3,3-dimethylbutanamide; N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2-trifluoromethylphenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethylbutanamide; N-[4-(7-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2-trifluoromethyl-phenyl]-3,3-dimethylbutanamide; 3,3-dimethyl-N-[2-trifluoromethyl-4-(7-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]butanamide; N-[4-(6-methoxy-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide; N-[4-(3,4-dihydro-1H-isoquinolin-2-yl)-2-methoxy-6-methyl-phenyl]-3,3-dimethylbutanamide; N-[2-chloro-4-(3,4-dihydro-1H-isoquinolin-2-yl)-6-trifluoromethoxy-phenyl]-3,3-dimethylbutanamide; N-[4-(3,4-dihydro-M-isoquinolin-2-yl)-2,6-dimethoxy-phenyl]-3,3-dimethylbutanamide; N-[2,6-dimethyl-4-(7-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethyl butanamide; N-[2,6-Dimethyl-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethyl-thiobutanamide; [2,6-Dimethyl-4-(6-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-carbamic acid ethyl ester; and N-[2,6-Dimethyl-4-(7-trifluoromethyl-3,4-dihydro-1H-isoquinolin-2-yl)-phenyl]-3,3-dimethyl butanamide.

Formula 5

In another embodiment, the Kv7 channel activator may be selected from one of the following compounds. Such compounds are described in US Patent No. 8,993,593 issued on March 31, 2015 and corresponding to US Application No. 12/698,070 filed February 1, 2010; US Publication No. US20220265634A1, published August 25, 2022 and corresponding to US Application No. 17/668,340 filed February 9, 2022;which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 5, these references incorporated by reference herein control.

[0134] In an embodiment, the Kv7 channel activator is a compound according to formula 5:

Formula 5

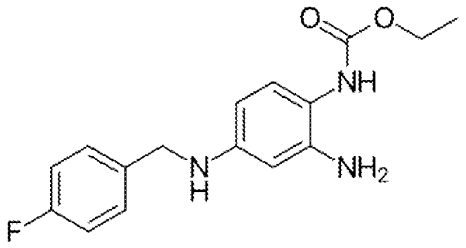


,

optionally wherein the compound is substituted at any position.

Formula 6

[0135] In another embodiment, the Kv7 channel activator may be the following compound (ezogabine, also known as retigabine) or a pharmaceutically acceptable salt thereof. Ezogabine is a compound according to formula 6: In the case of any conflict of terminology in the context of Formula 6, these references incorporated by reference herein control.



Formula 6

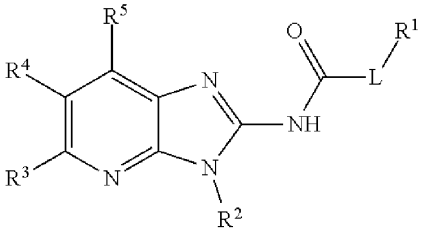
,

or, optionally, wherein the compound is substituted at any position.

Formula 7

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 7. Such compounds are described in US Patent No. 10,526,328 issued on January 7, 2020 and corresponding to US Application No. 16/124,853 filed September 7, 2018; US Patent No. 10,106,536 issued on October 23, 2018 and corresponding to US Application No. 15/591,844 filed on May 10, 2017; US Patent No. 9,650,376 issued on May 16, 2017, and corresponding to US Application No. 14/776,271 filed March 17, 2014;; US Publication No. US20220060208A1, published February 24, 2022 and corresponding to US Application No. 17/277,145 filed January 14, 2019; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 7, these references incorporated by reference herein control.

[0136] In an embodiment, the Kv7 channel activator is a compound according to formula 7:



Formula 7

,

wherein, L is CH_2; R^1 is optionally substituted cyclic C_3H_5, wherein the optional substituent of R^1 is CF_3; R^2 is optionally substituted cyclobutyl; R^3 is optionally substituted C_3 alkyl, wherein the optional substituent of R^3 is OH; R^4 is H; and R^5 is H;

or

wherein, L is CH_2; R^1 is optionally substituted C_2 alkyl, wherein the optional substituents of R^1 are independently CF_3 or CH_3; R^2 is optionally substituted cyclobutyl; R^3 is optionally substituted C_3 alkyl, wherein the optional substituent of R^3 is OH; R^4 is H; and R^5 is H;

or

wherein, wherein L is CH_2, CF_2, $CHCH_3$, CH_2CH_2, C_3H_6, CH_2O, C_2H_4O, or C_3H_6O with the O of CH_2O, C_2H_4O, or C_3H_6O bonded with R^1; wherein R^1 is optionally substituted $C_{1\text{-}2}$ alkyl, optionally substituted $C_{5\text{-}10}$ cycloalkyl, optionally substituted $C_{1\text{-}12}$ —O-alkyl, optionally substituted $C_{6\text{-}10}$ aryl, optionally substituted $C_{6\text{-}10}$ —O-aryl, or optionally substituted $C_{2\text{-}9}$ heterocyclyl, wherein the optional substituents of R^1 are independently R^A, F, Cl, CN, OR^A, CF_3, NR^AR^B, COR^A, CO_2R^A, $OCOR^A$, NR^ACOR^B, $CONR^AR^B$, wherein R^A and R^B are independently H or $C_{1\text{-}12}$ alkyl; wherein R^2 is optionally substituted $C_{2\text{-}4}$ acyclic alkyl, optionally substituted cyclobutyl, optionally substituted $C_{6\text{-}10}$ aryl, or optionally substituted $C_{2\text{-}9}$ heterocyclyl, wherein the optional substituents of R^2 are independently F, Cl, Br, I, CN, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ —O-alkyl, $C_{1\text{-}6}$ alkylamine, $C_{1\text{-}6}$ aminoalkyl, $C_{1\text{-}6}$ aminoacyl, $C_{1\text{-}6}$ alkylthio, or $C_{1\text{-}6}$ alkylsulfonyl; wherein R^3, R^4, and R^5 are independently H, F, Cl, Br, I, CN, optionally substituted $C_{1\text{-}12}$ alkyl, optionally substituted $C_{1\text{-}12}$ —O-alkyl, optionally substituted $C_{2\text{-}9}$ heterocyclyl, optionally substituted $C_{6\text{-}10}$ aryl, optionally substituted $C_{2\text{-}9}$ —O-heterocyclyl, optionally substituted $C_{6\text{-}10}$ O-aryl, optionally substituted $C_{1\text{-}12}$ acylamino, optionally substituted $C_{1\text{-}12}$ aminoacyl, or optionally substituted $C_{1\text{-}12}$ aminoalkyl, wherein the optional substituents of R^3, R^4, or R^5 are independently F, Cl, Br, I, CN, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ —O-alkyl, $C_{1\text{-}6}$ alkylamine, $C_{1\text{-}6}$ aminoalkyl, $C_{1\text{-}6}$ aminoacyl, $C_{1\text{-}6}$ acylamino, $C_{1\text{-}6}$ alkylthio, or $C_{1\text{-}6}$ alkylsulfonyl.

[0137] In further embodiments, R^2 is optionally substituted C_4H_9, optionally substituted cyclobutyl, optionally substituted $C_{6\text{-}10}$ aryl, or optionally substituted $C_{2\text{-}9}$ heterocyclyl.

[0138] In further embodiments, R^2 is optionally substituted C_4H_9, or optionally substituted cyclobutyl.

[0139] In further embodiments, R^2 is optionally substituted phenyl, or optionally substituted $C_{2\text{-}9}$ heterocyclyl.

[0140] In further embodiments, R^1 is optionally substituted phenyl.

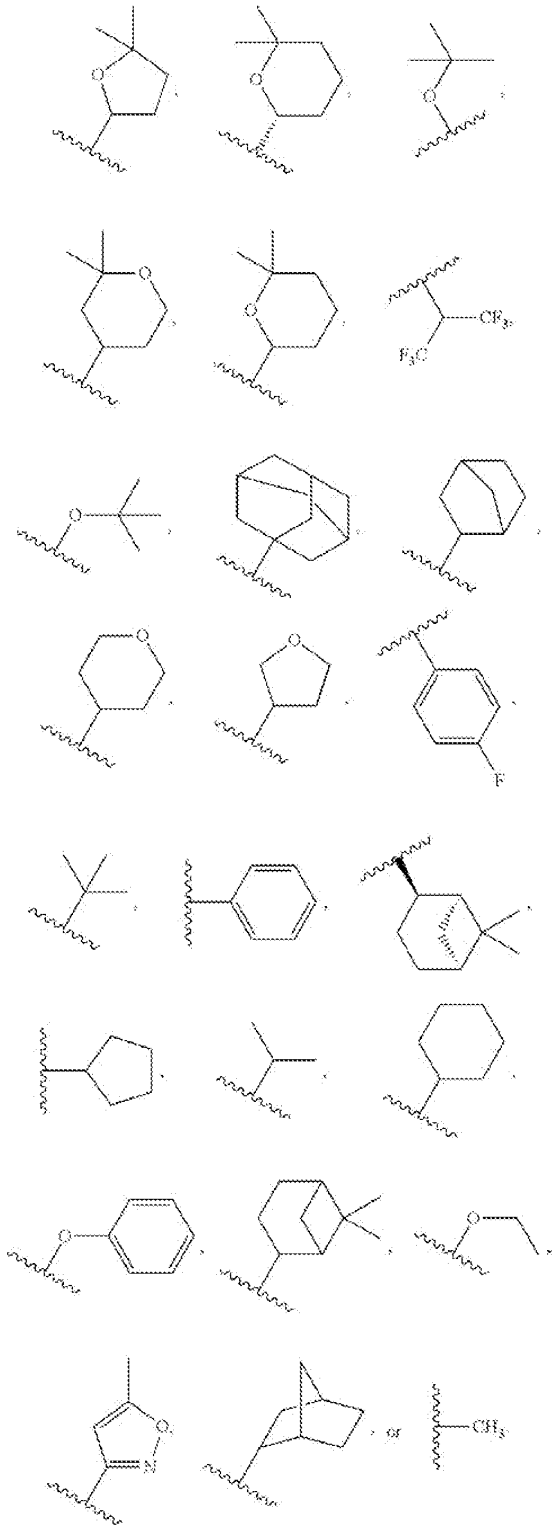
[0141] In further embodiments, R^1 is optionally substituted phenyl.

[0142] In further embodiments, R^1 is optionally substituted cyclopentyl or optionally substituted cyclohexyl.

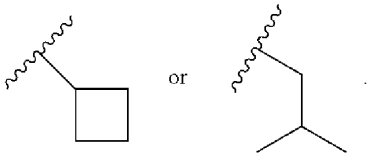
[0143] In further embodiments, R^1 is C_{2-4} —O-alkyl.

[0144] In further embodiments, R^1 is optionally substituted tetrahydrofuranyl or optionally substituted tetrahydro-2H-pyranyl.

[0145] In further embodiments, R^1 is selected from the group consisting of:

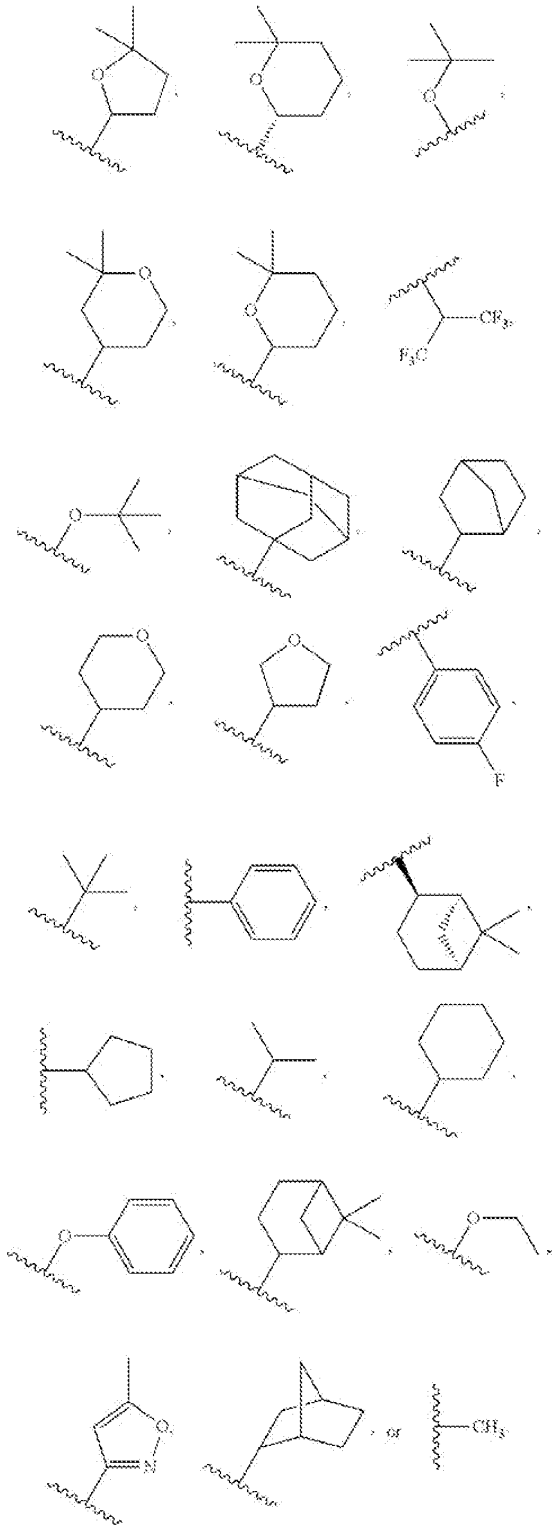


[0146] In further embodiments, R^2 is selected from the group consisting of:



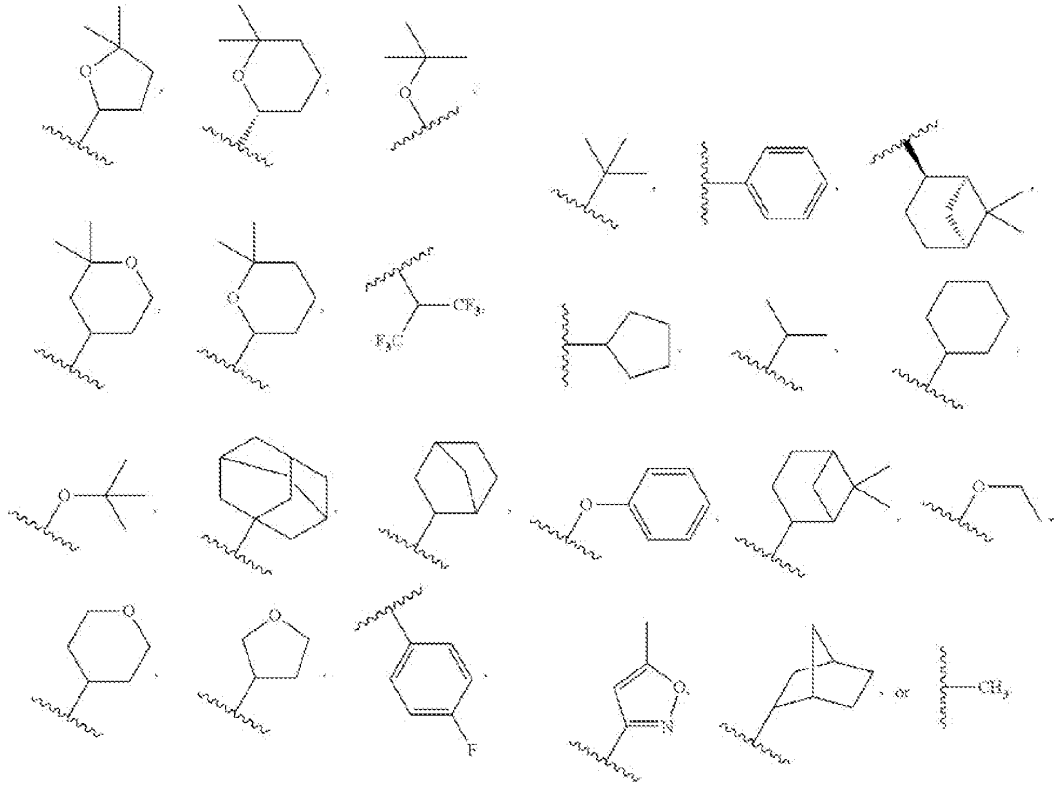
[0147] In further embodiments, R^3 is CF_3, Cl, CN, OCH_3, or H.

[0148] In further embodiments, R^1 is selected from the group consisting of:

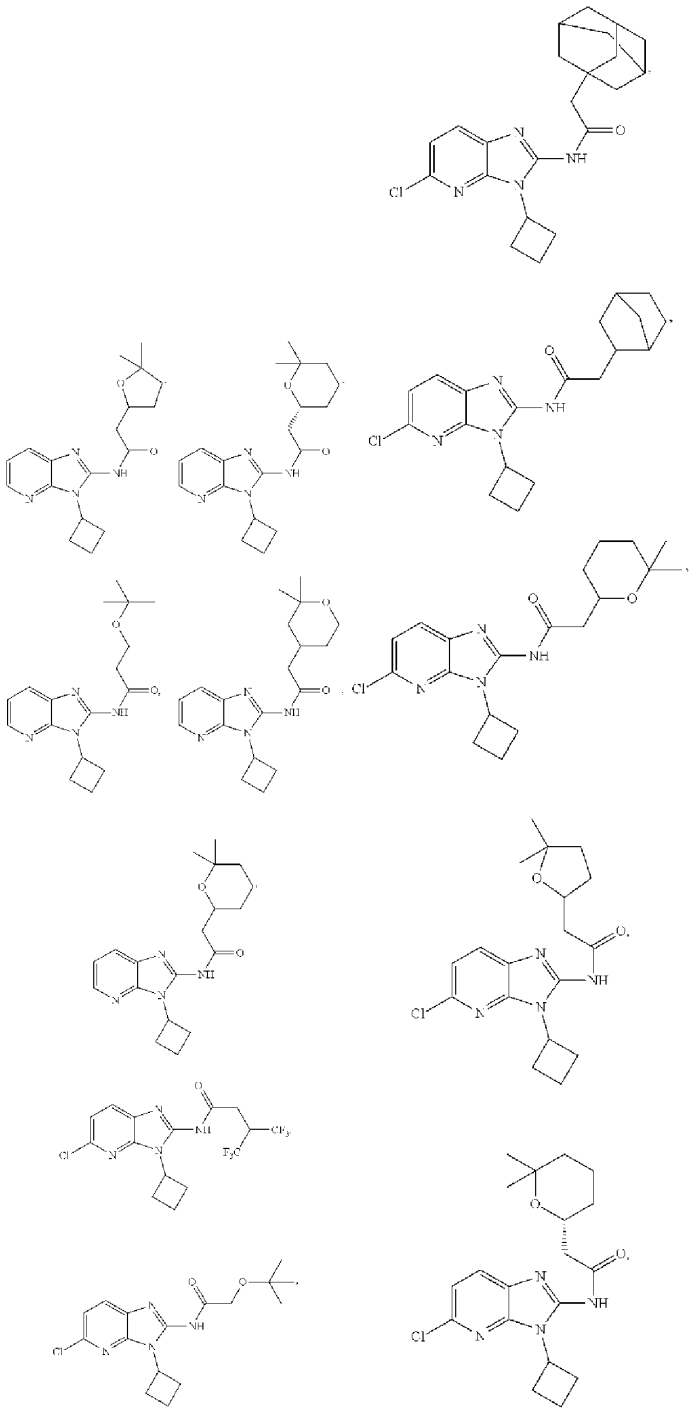


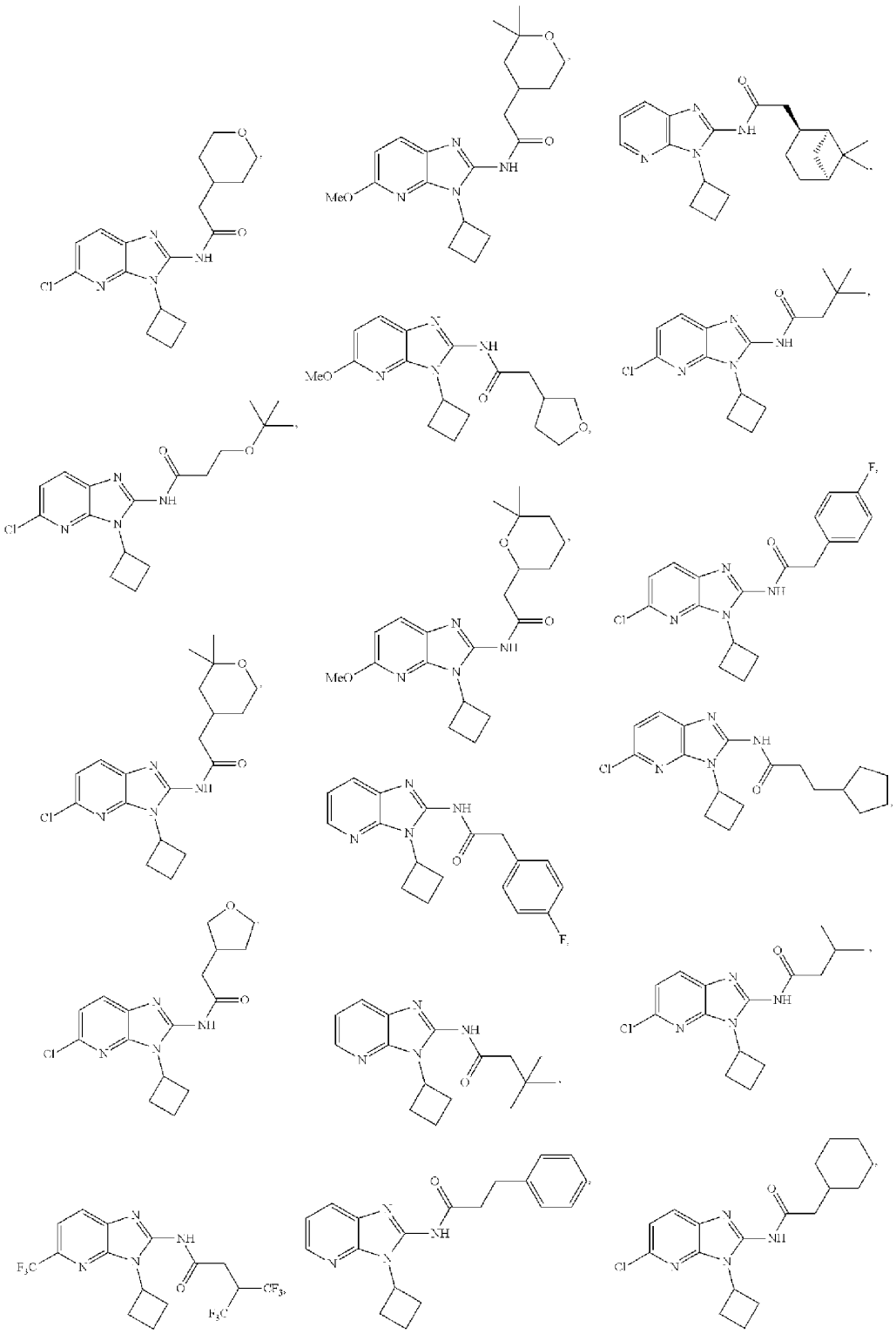
[0149] In further embodiments, R^4 is CH_3, CF_3, Cl, or H.

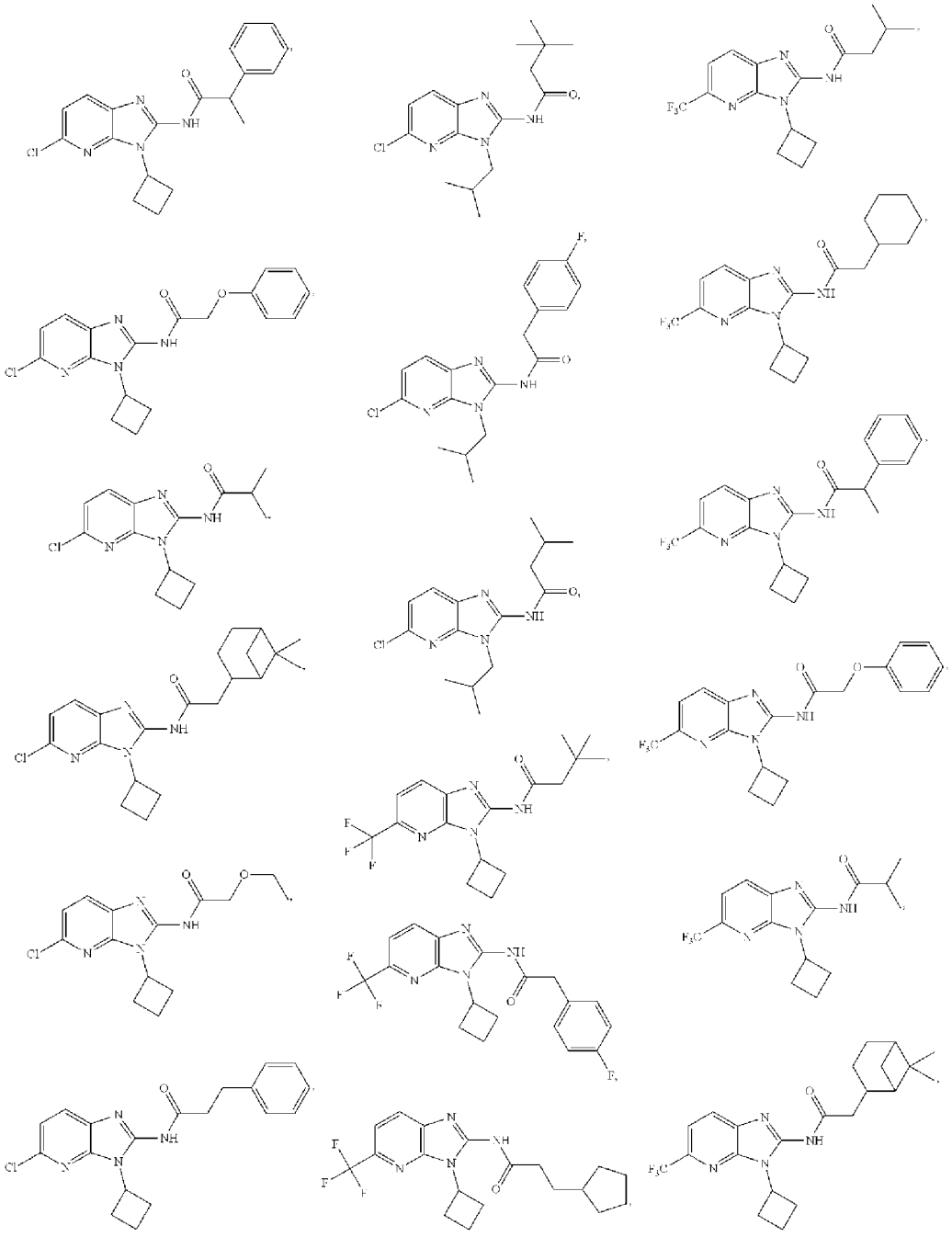
[0150] In further embodiments, R^2 is selected from the group consisting of:

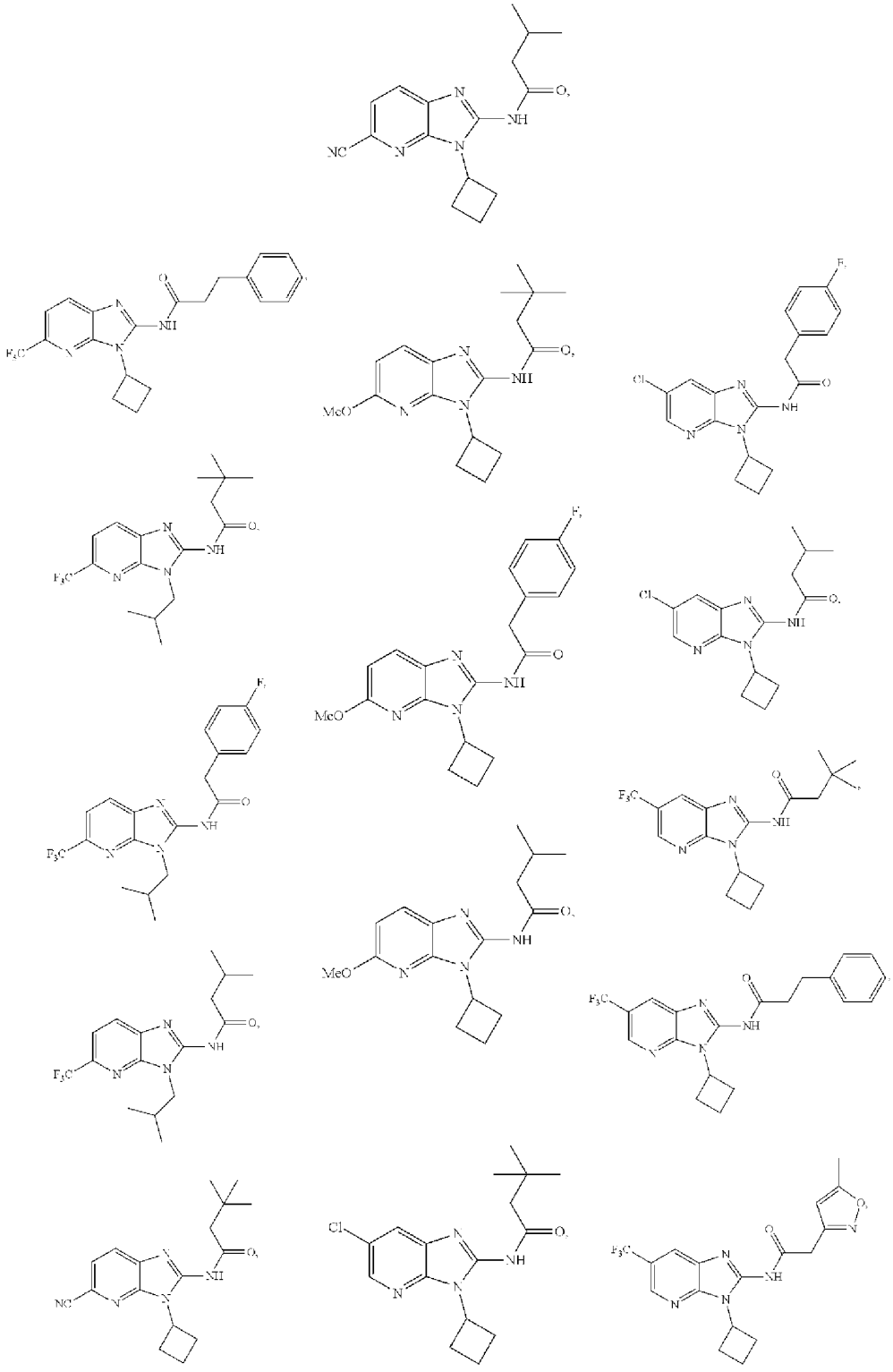


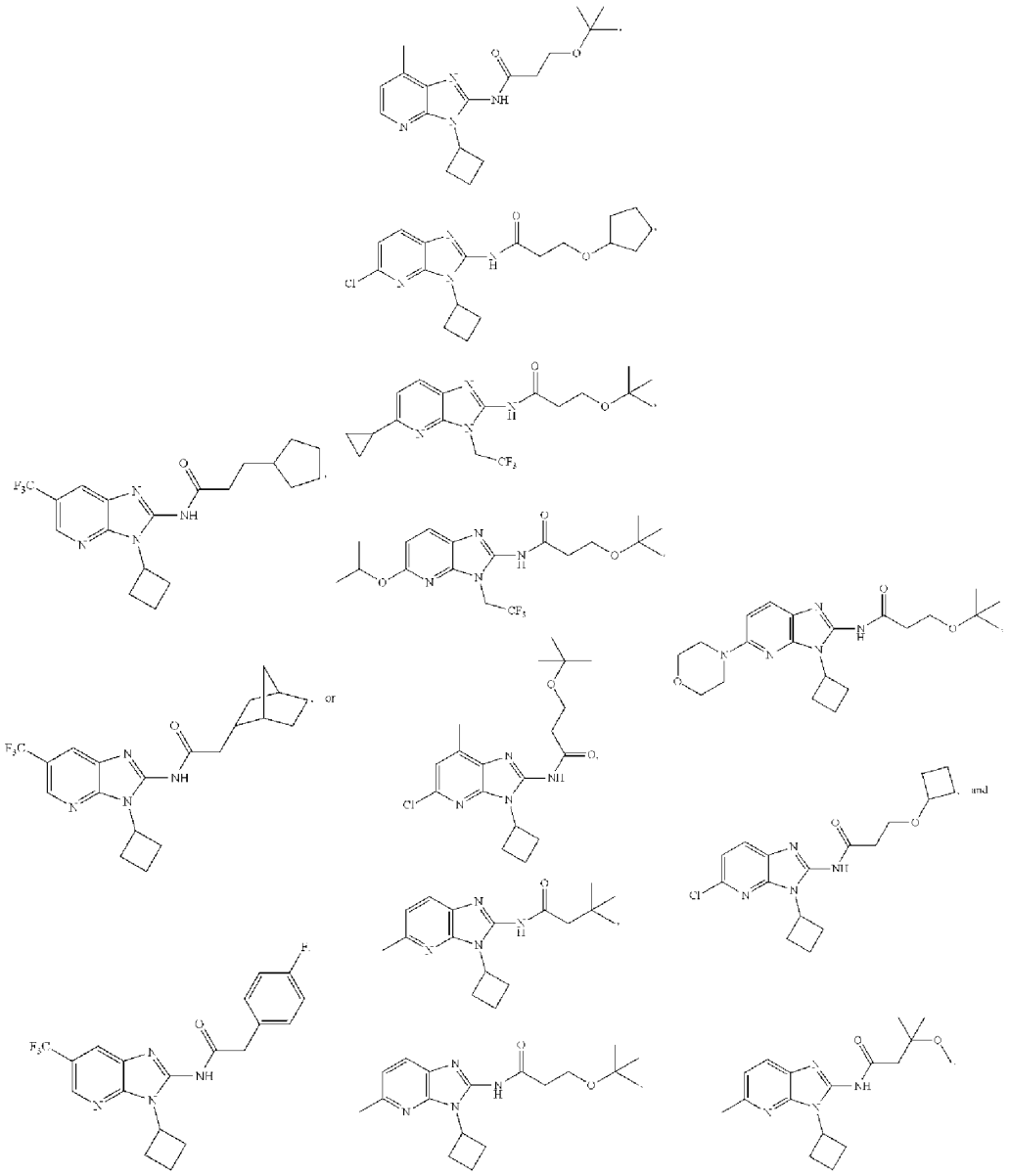
[0151] In further embodiments, the Kv7 channel activator is selected from the group consisting of:



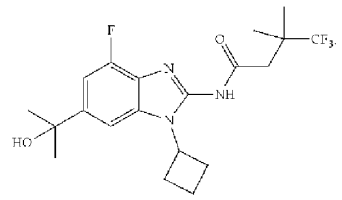


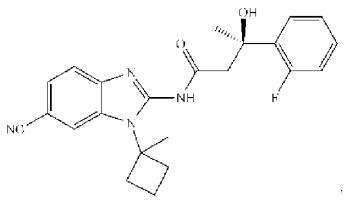


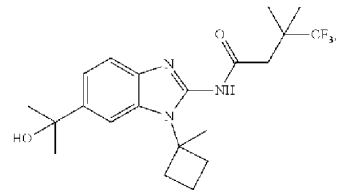


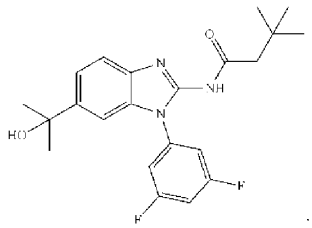


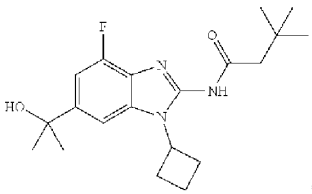
[0152] In further embodiments, the Kv7 channel activator is selected from the group consisting of:

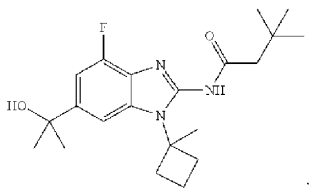


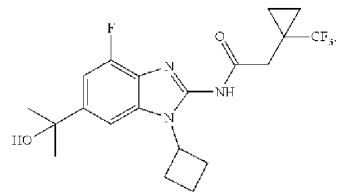


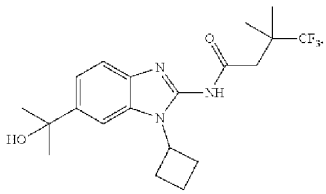


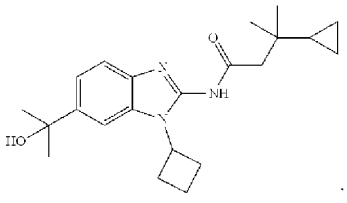


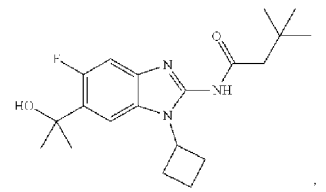


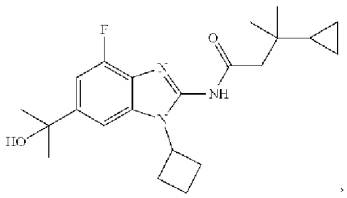


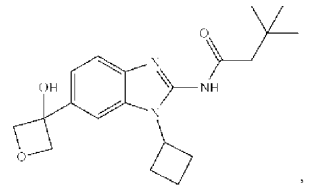


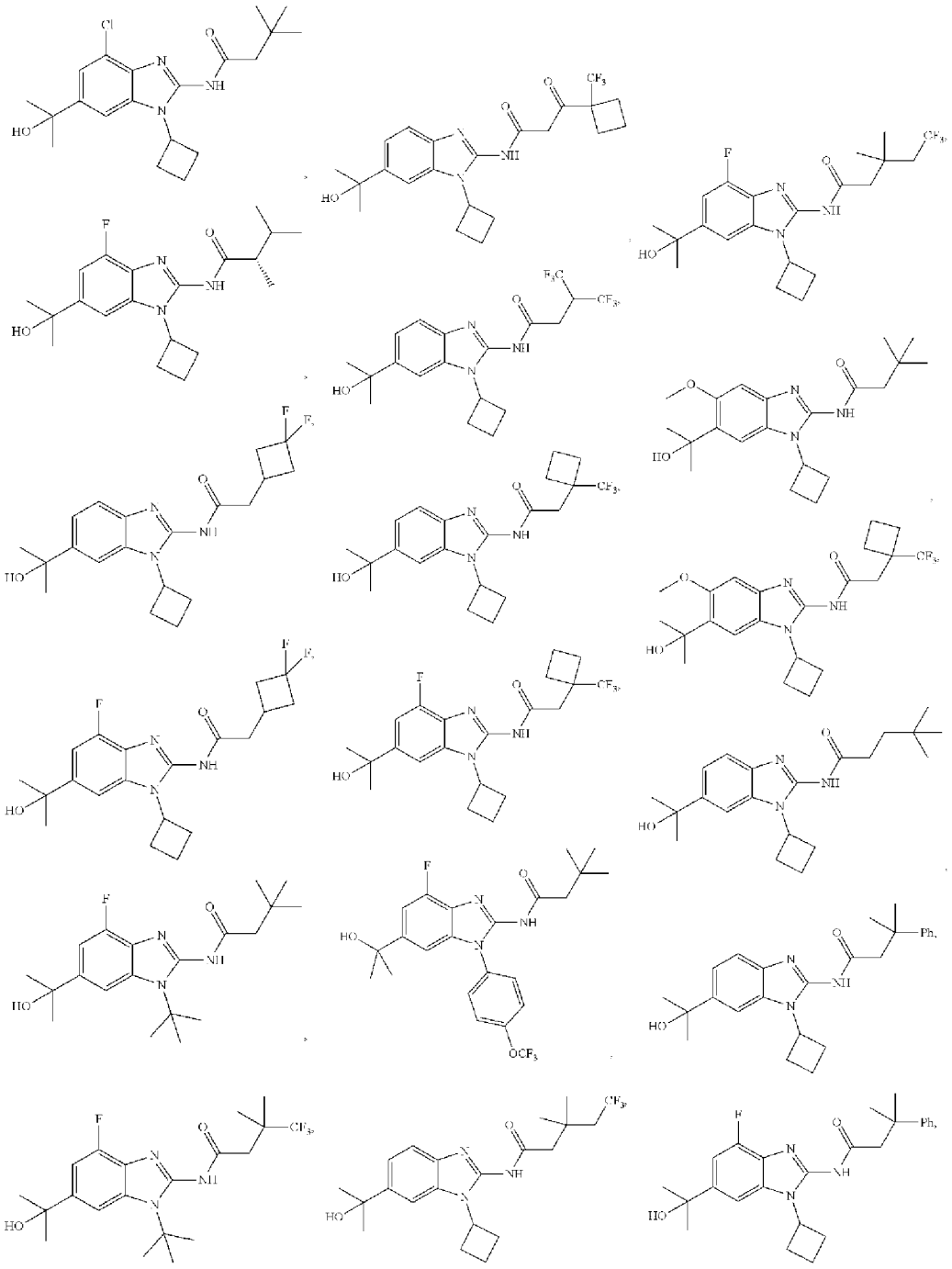


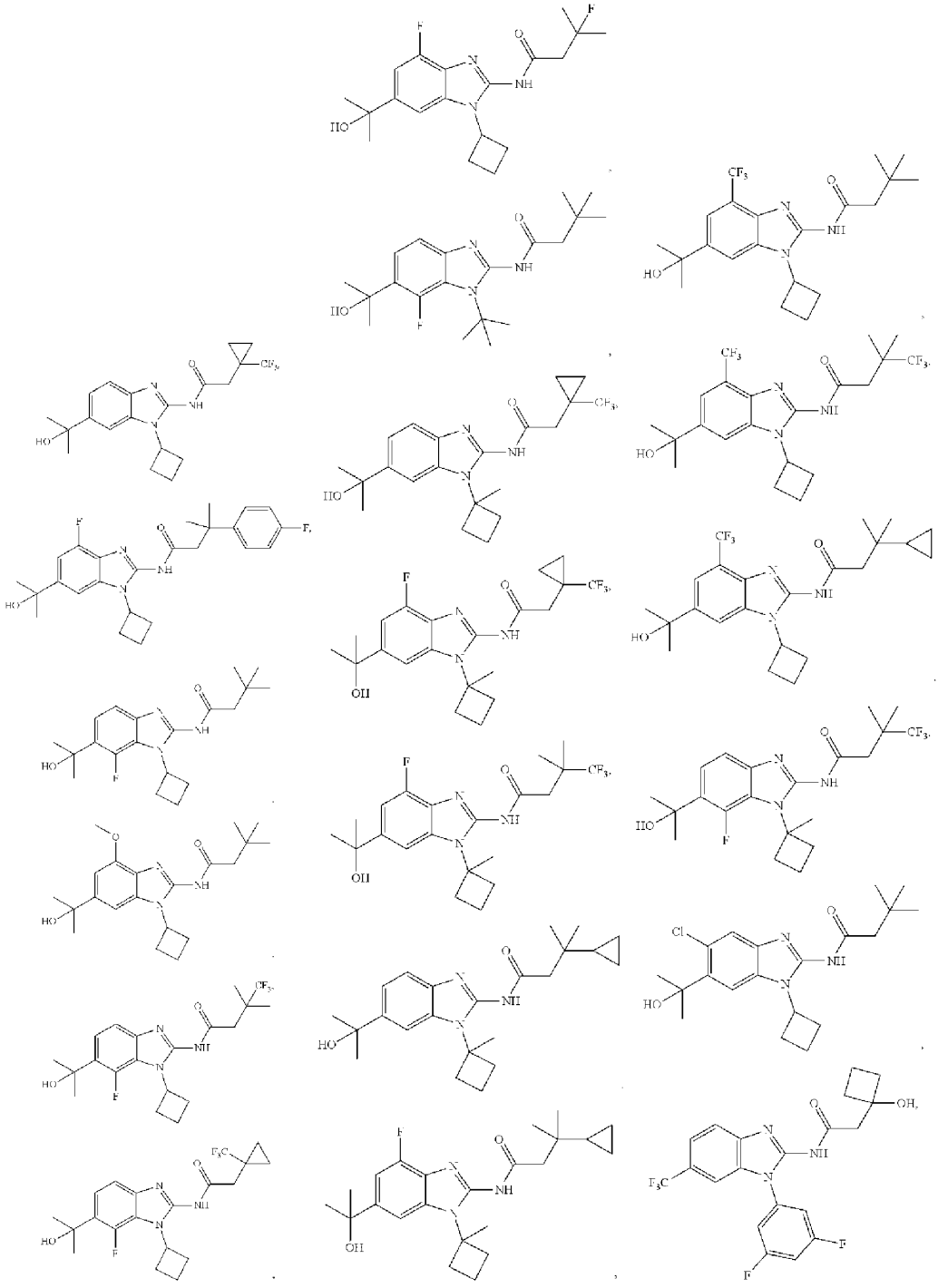


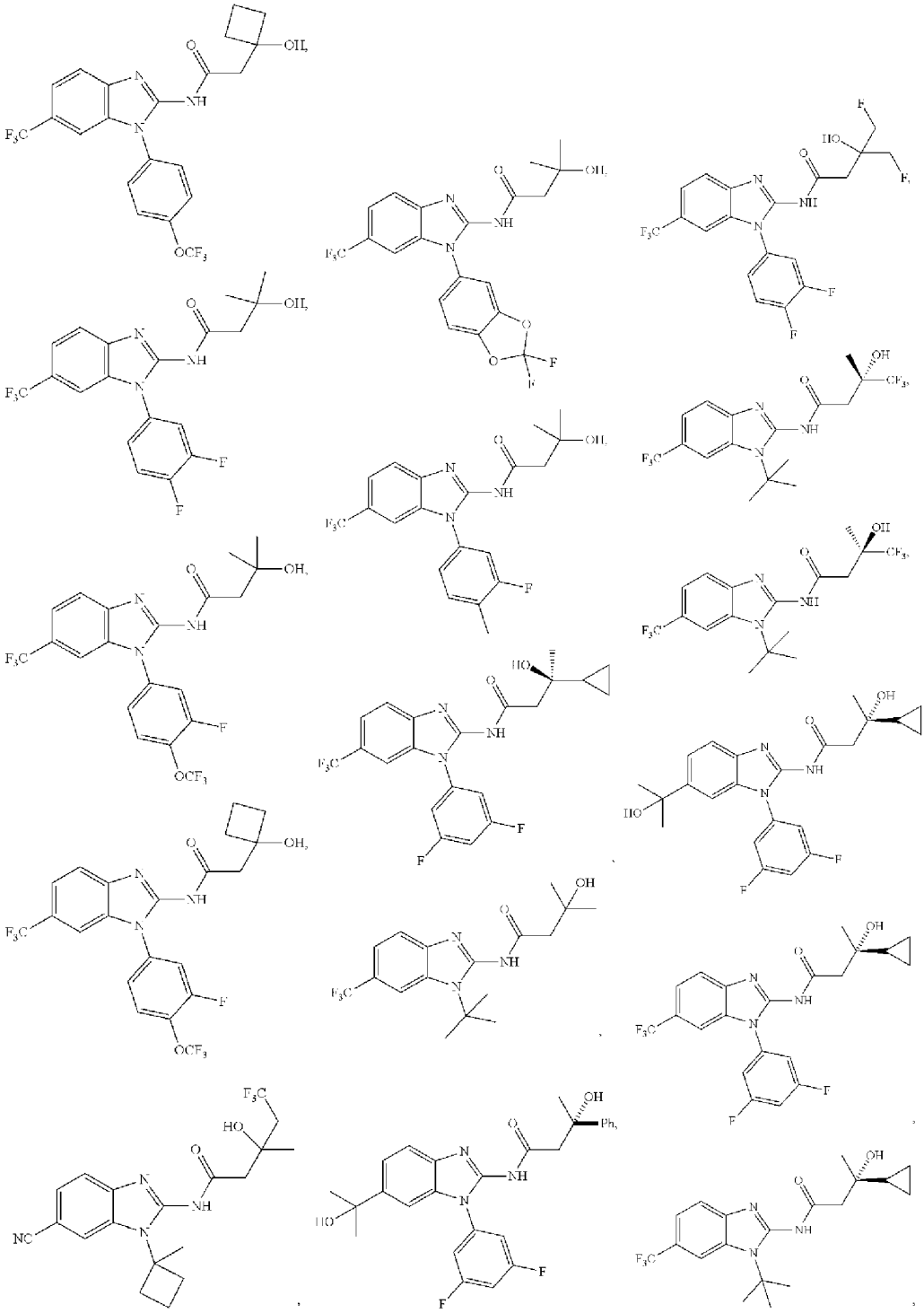


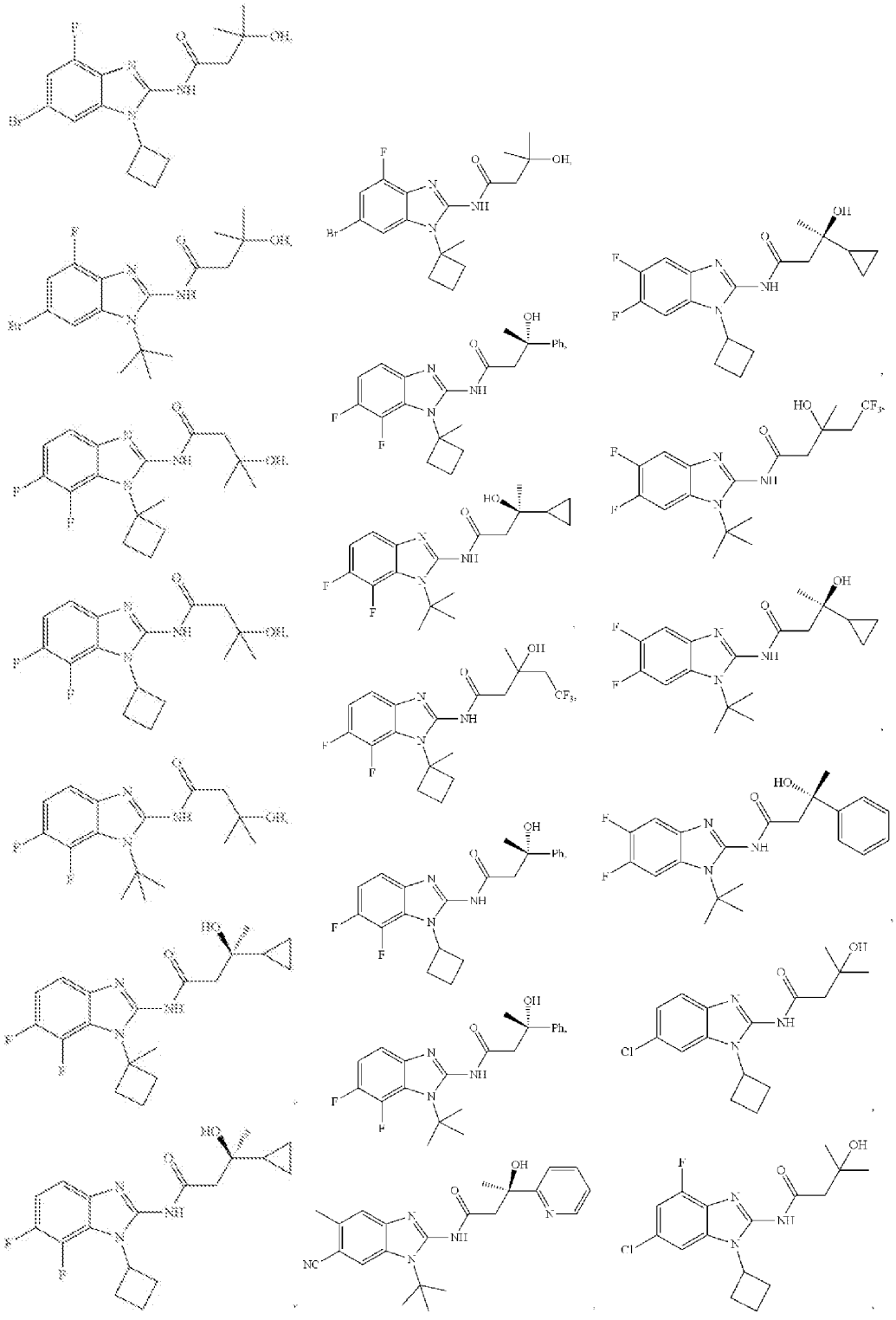


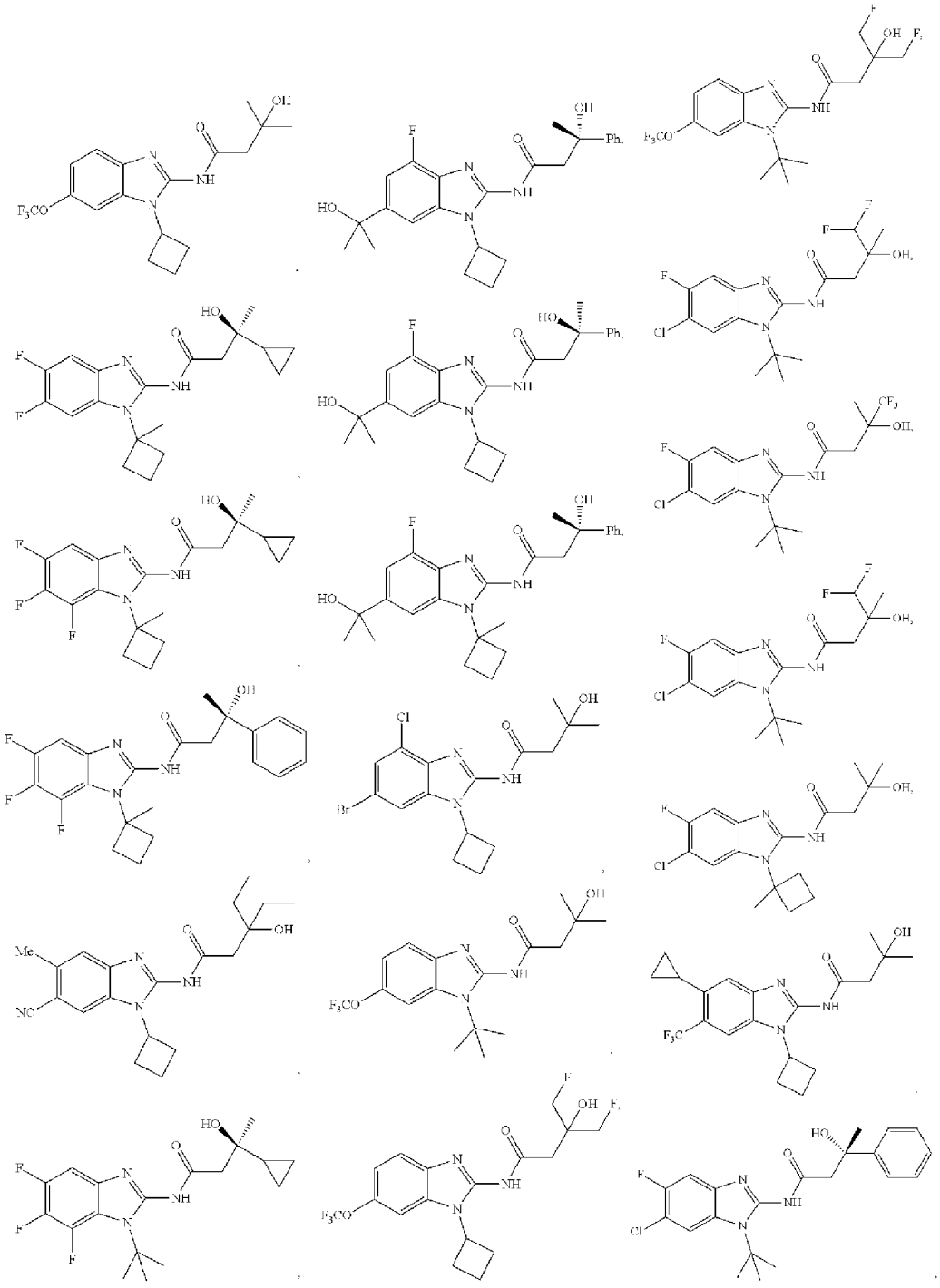


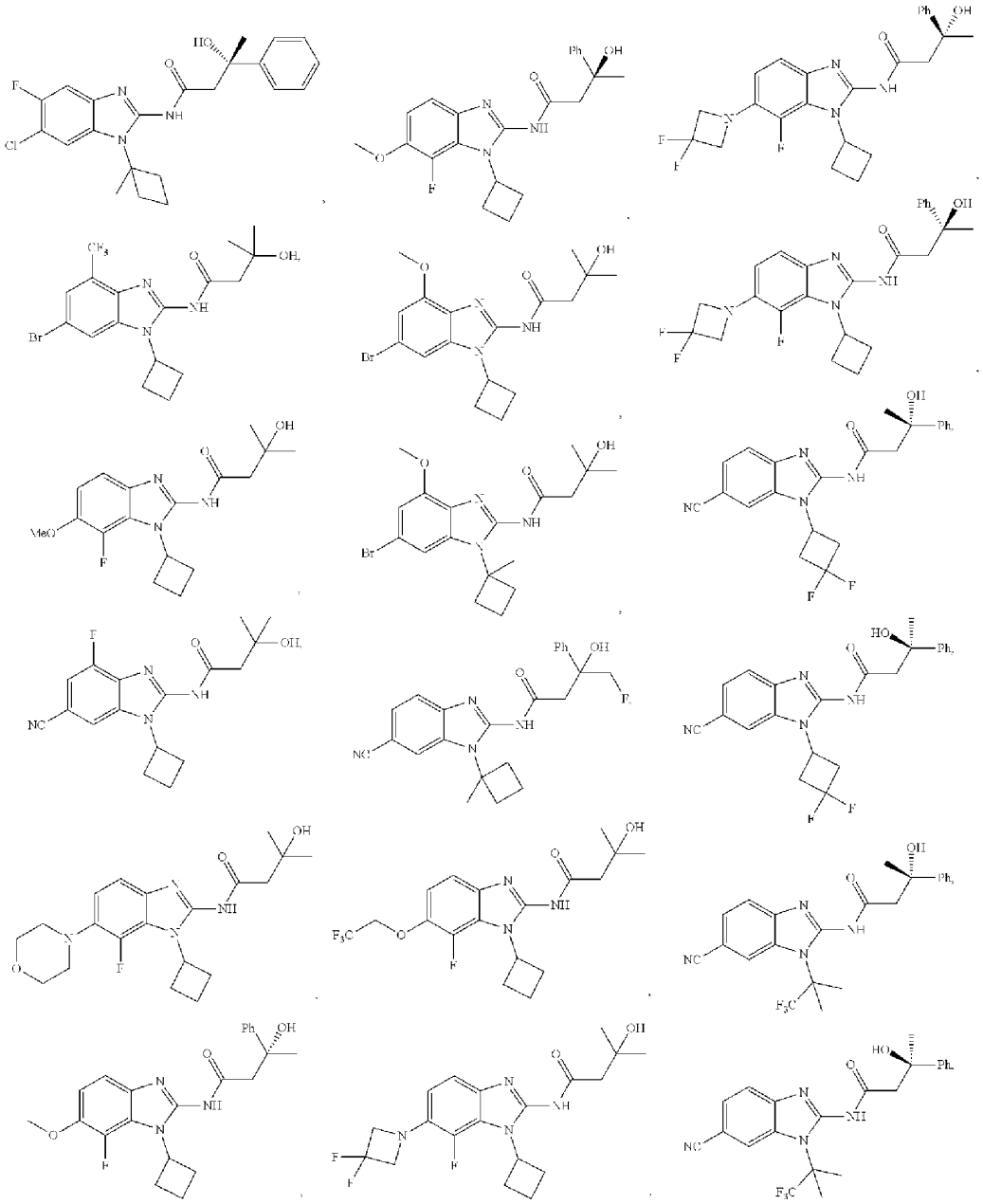


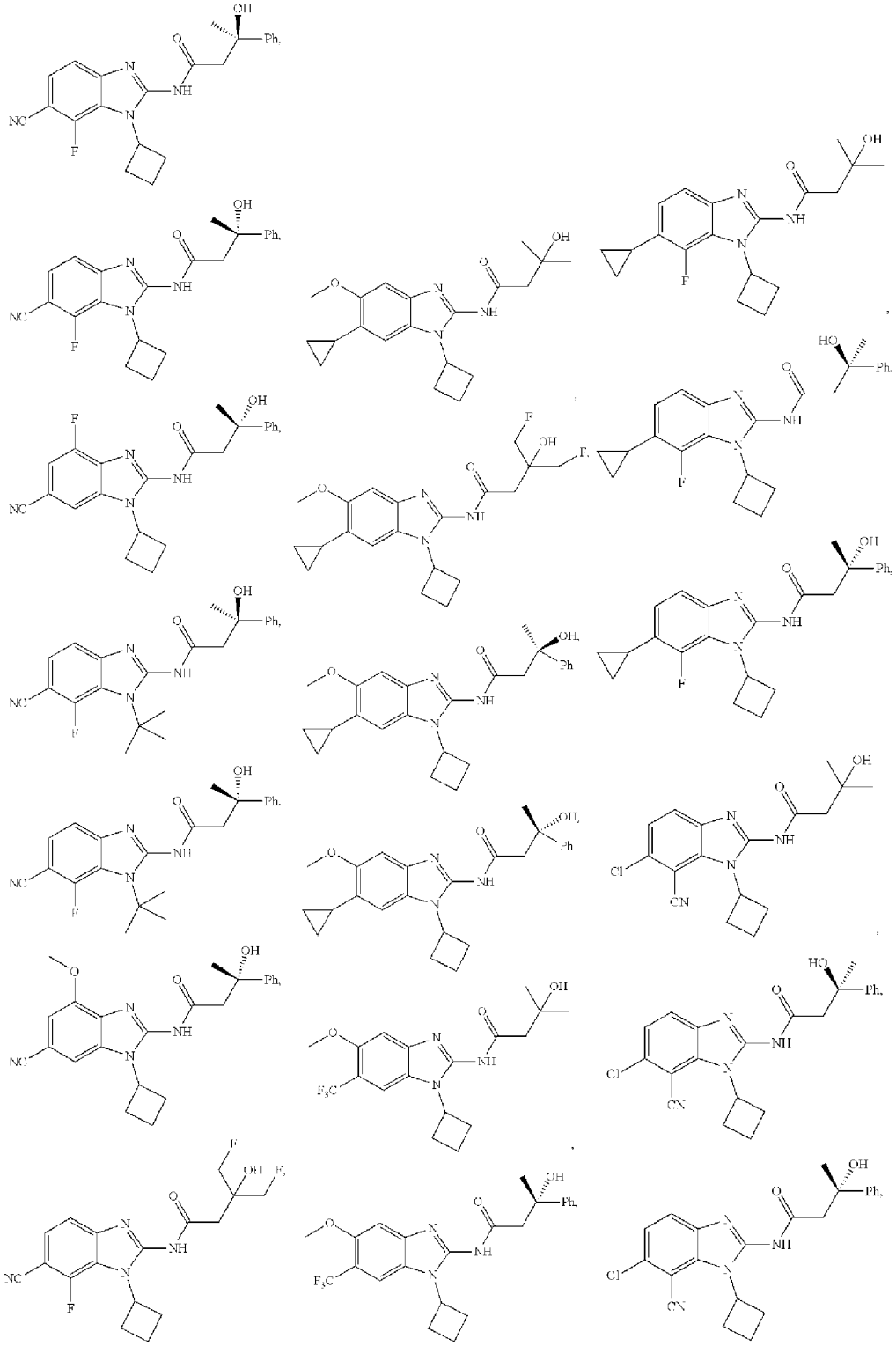


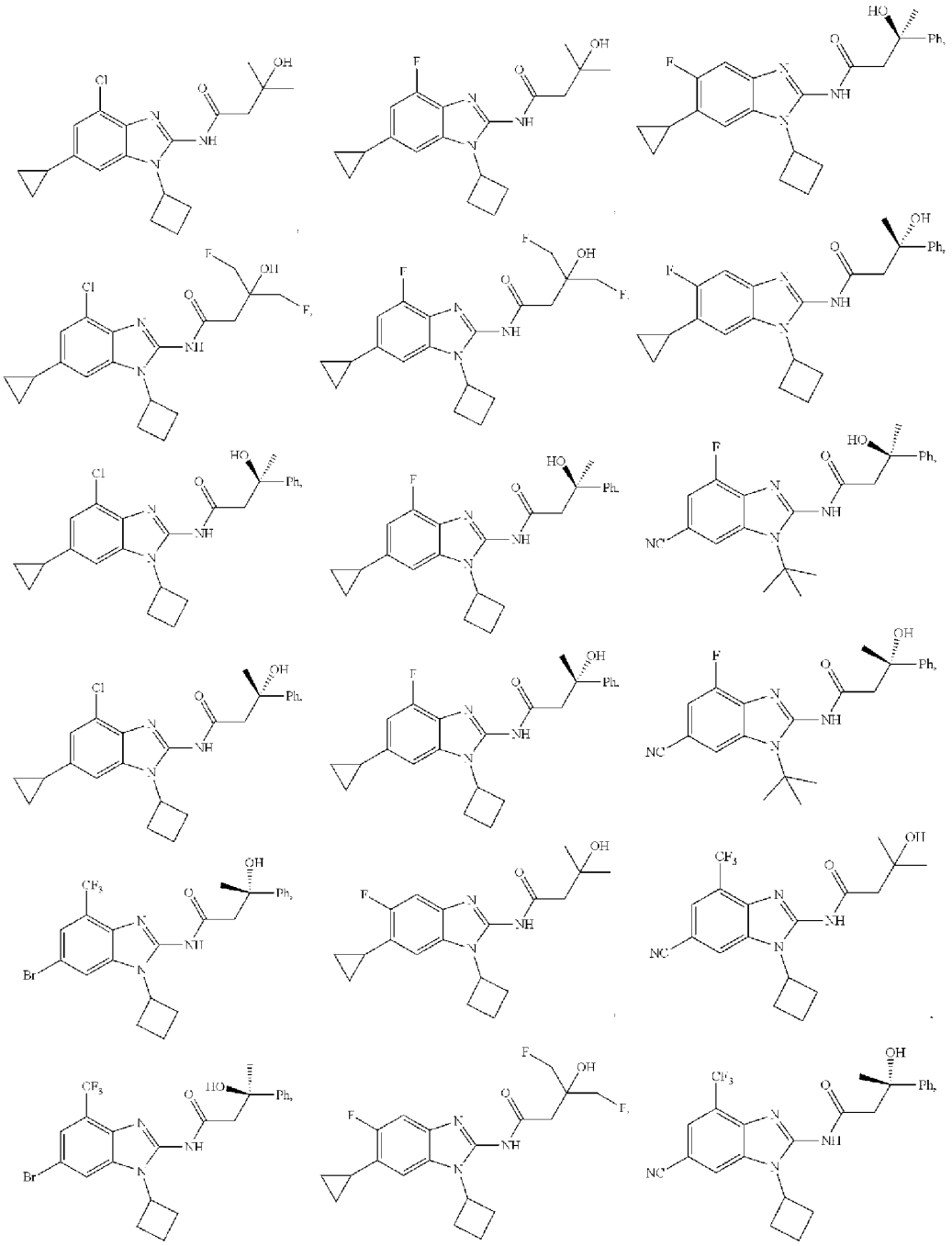


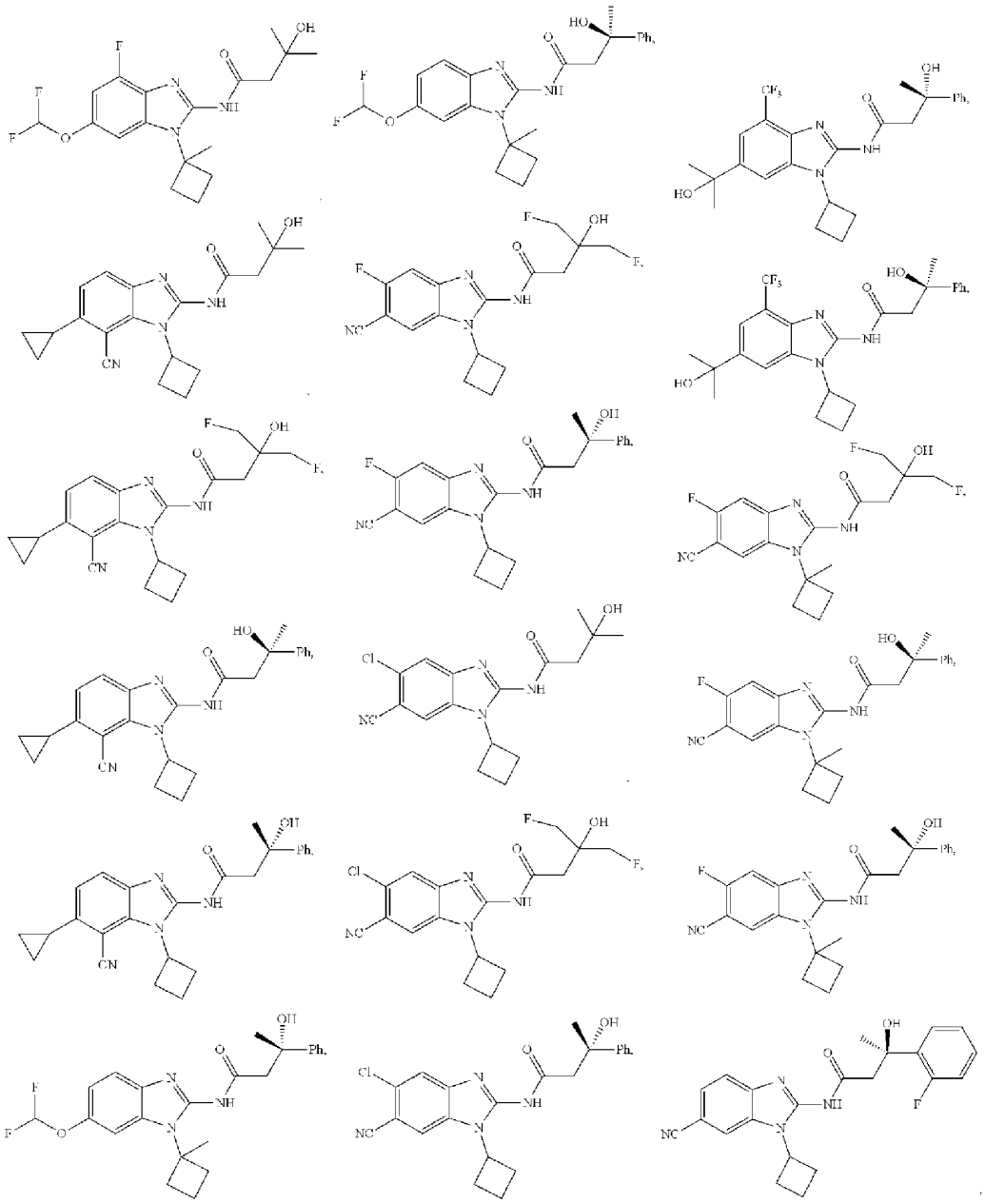


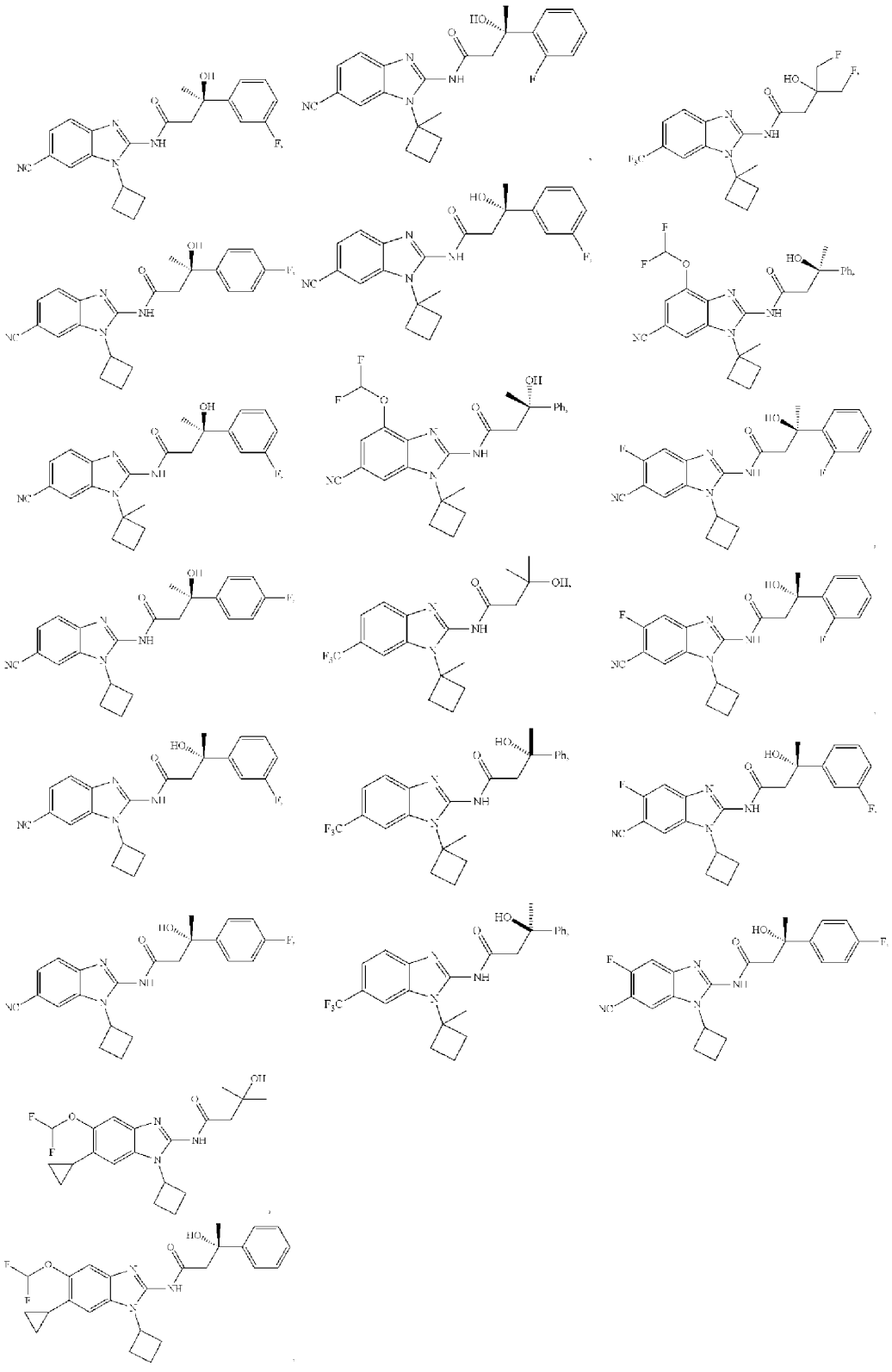










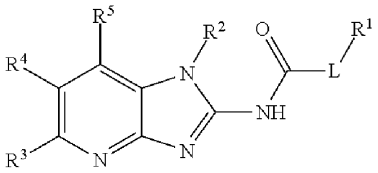


Formula 8

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 8. Such compounds are described in US Patent No. 9,650,376, published on February 4, 2014 and corresponding to US Application No. 14/776,271 filed March 17, 2014; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 8, this reference incorporated by reference herein controls.

[0153] In an embodiment, the Kv7 channel activator is a compound according to formula 8:

Formula 8



,

wherein, L is CH_2, CF_2, $CHCH_3$, CH_2CH_2, C_3H_6, CH_2O, C_2H_4O, or C_3H_6O with the O of CH_2O, C_2H_4O, or C_3H_6O bonded with R^1; wherein R^1 is optionally substituted C_{1-2} alkyl, optionally substituted C_{5-10} cycloalkyl, optionally substituted C_{1-12} —O-alkyl, optionally substituted C_{6-10} aryl, optionally substituted C_{6-10} —O-aryl, or optionally substituted C_{2-9} heterocyclyl, wherein the optional substituents of R^1 are independently R^A, F, Cl, CN, OR^A, CF_3, NR^AR^B, COR^A, CO_2R^A, $OCOR^A$, NR^ACOR^B, $CONR^AR^B$, wherein R^A and R^B are independently H or C_{1-12} alkyl; wherein R^2 is optionally substituted C_{2-4} acyclic alkyl, optionally substituted cyclobutyl, optionally substituted C_{6-10} aryl, or optionally substituted C_{2-9} heterocyclyl, wherein the optional substituents of R^2 are independently F, Cl, Br, I, CN, C_{1-6} alkyl, C_{1-6} —O-alkyl, C_{1-6} alkylamine, C_{1-6} aminoalkyl, C_{1-6} aminoacyl, C_{1-6} alkylthio, or C_{1-6} alkylsulfonyl; wherein R^3, R^4, and R^5 are independently H, F, Cl, Br, I, CN, optionally substituted C_{1-12} alkyl, optionally substituted C_{1-12} —O-alkyl, optionally substituted C_{2-9} heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted C_{2-9} —O-heterocyclyl, optionally substituted C_{6-10} O-aryl, optionally substituted C_{1-12} acylamino, optionally substituted C_{1-12} aminoacyl, or optionally substituted C_{1-12} aminoalkyl, wherein the optional substituents of R^3, R^4, or R^5 are independently F, Cl, Br, I, CN, C_{1-6} alkyl, C_{1-6} —O-alkyl, C_{1-6} alkylamine, C_{1-6} aminoalkyl, C_{1-6} aminoacyl, C_{1-6} acylamino, C_{1-6} alkylthio, or C_{1-6} alkylsulfonyl.

[0154] In further embodiments, R^2 is optionally substituted C_4H_9, optionally substituted cyclobutyl, optionally substituted C_{6-10} aryl, or optionally substituted C_{2-9} heterocyclyl.

[0155] In further embodiments, R^2 is optionally substituted C_4H_9, or optionally substituted cyclobutyl.

[0156] In further embodiments, R^2 is optionally substituted phenyl, or optionally substituted C_{2-9} heterocyclyl.

[0157] In further embodiments, R^1 is optionally substituted phenyl.

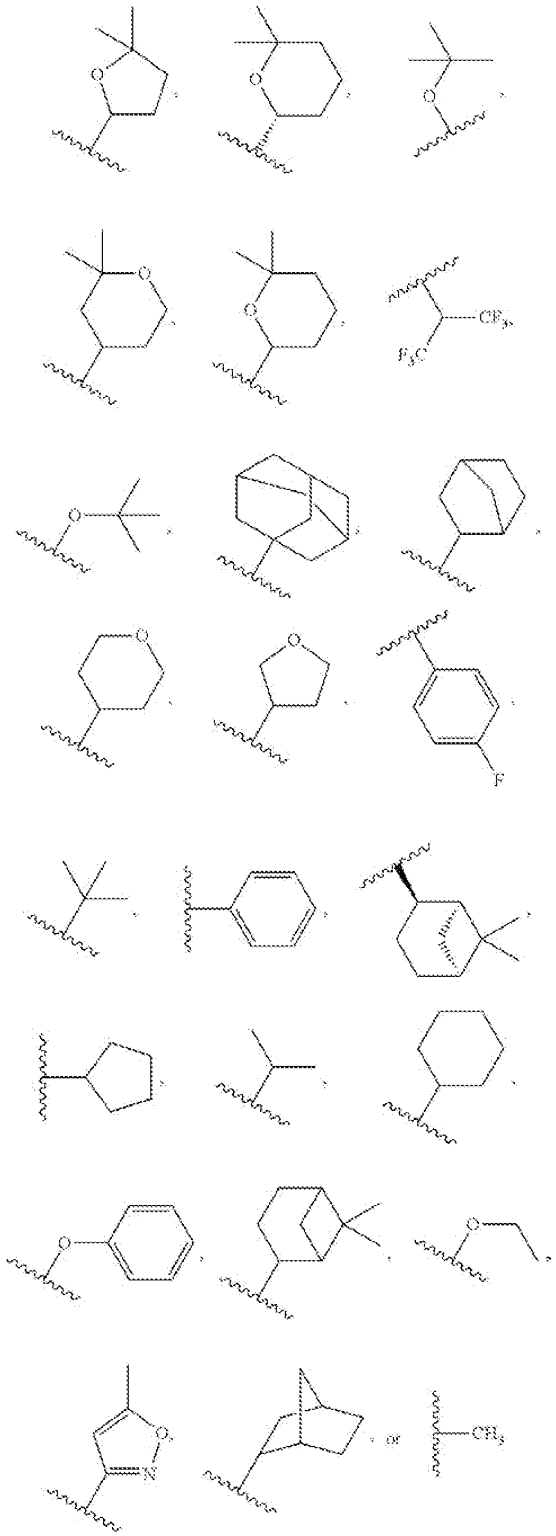
[0158] In further embodiments, R^1 is optionally substituted phenyl.

[0159] In further embodiments, R^1 is optionally substituted cyclopentyl or optionally substituted cyclohexyl.

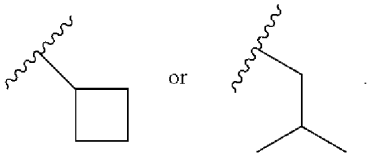
[0160] In further embodiments, R^1 is C_{2-4} —O-alkyl.

[0161] In further embodiments, R^1 is optionally substituted tetrahydrofuranyl or optionally substituted tetrahydro-2H-pyranyl.

[0162] In further embodiments, R^1 is selected from the group consisting of:

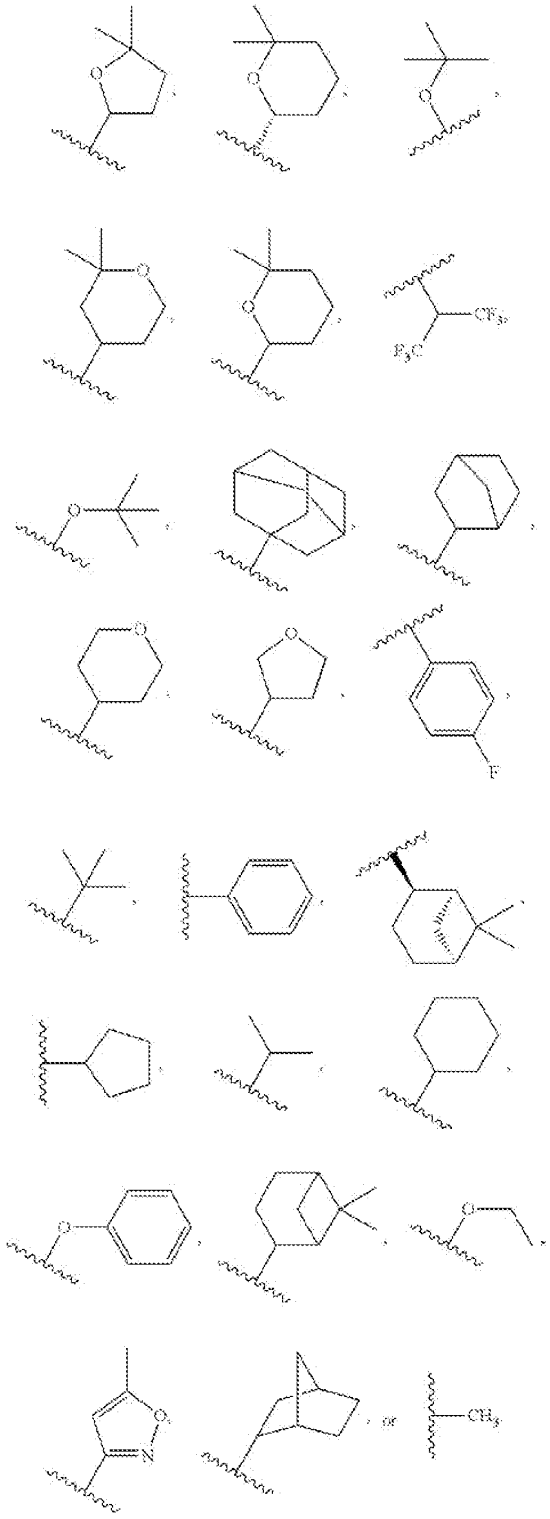


[0163] In further embodiments, R^2 is selected from the group consisting of:



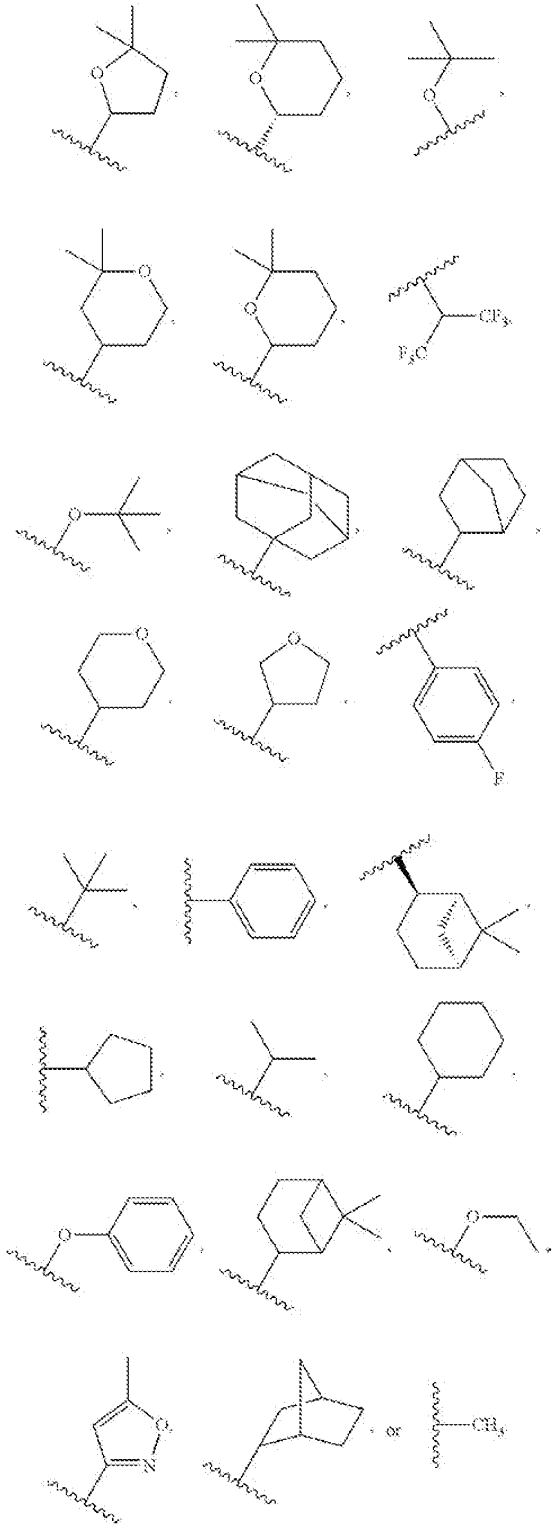
[0164] In further embodiments, R^3 is CF_3, Cl, CN, OCH_3, or H.

[0165] In further embodiments, R^1 is selected from the group consisting of:



[0166] In further embodiments, R^4 is CH_3, CF_3, Cl, or H.

[0167] In further embodiments, R^2 is selected from the group consisting of:

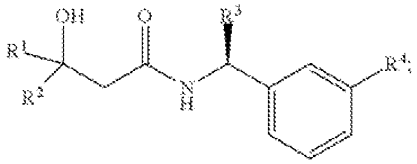


Formula 9

[0168] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 9. Such compounds are described in International Publication No. WO2021023616A1, published February 11, 2021 and corresponding to International Application No. PCT/EP2020/071514 filed July 30, 2020; International Publication No. WO2019161877A1, published August 29, 2019 and corresponding to International Application No. PCT/EP2018/054057 filed February 20, 2018; US Publication No. US20220280455A1, published September 8, 2022 and corresponding to US Application No. 17/631,762 filed July 30, 2020; US Publication No. US20210032196A1, published February 4, 2021 and corresponding to US Application No. 16/943,872 filed July 30, 2020; US Publication No. US20210032196A1, published February 4, 2021 and corresponding to US Application No. 16/943,872 filed July 30, 2020;, , which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 9, these references incorporated by reference herein control.

[0169] In an embodiment, the Kv7 channel activator is a compound according to formula 9:

Formula 9



wherein, R1 is selected from the group consisting of C_1-C_6 alkyl, CF_3, CH_2CF_3, CF_2CHF_2, C_3-C_8 cycloalkyl, wherein said C_3-C_8 cycloalkyl may be substituted with 1 or 2 substituents selected from the group consisting of C_1-C_3 alkyl, F, CHF_2 and CF_3; and R2 is H, C_1-C_6 alkyl or CF_3; or R1 and R2 combine to form C_3-C_5 cycloalkyl optionally substituted with 1 or 2 F, CHF_2 or CF_3; and R3 is C_1-C_3 alkyl or CH_2O—$C_{1\text{-}3}$ alkyl, said C_1-C_3 alkyl or CH_2O—C_1-C_3 is alkyl substituted with C≡N, 3 F or C_3-C_5 cycloalkyl; R4 is selected from the group consisting of OCF_3, or $OCHF_2$

[0170] In further embodiments, R4 is OCF_3 or $OCHF_2$.

[0171] In further embodiments, R3 is selected from the group consisting of CH_2—O—CF_3, CH_2—O— cyclopropyl, CH_2—C≡N.

[0172] In further embodiments R1 is C_3-C_4 cycloalkyl optionally substituted with 1 or 2 C_1-C_3 alkyl, F, CHF_2 or CF_3.

[0173] In further embodiments, R1 and R2 combine to form cyclobutyl optionally substituted with 1 or 2 F and R4 is OCF_3 or $OCHF_2$.

[0174] In further embodiments, the Kv7 channel activator is selected from the group consisting of: (S)—N—((R)-2-cyclopropoxy-1-(3-(difluoromethoxy) phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((R)-1-(3-(difluoromethoxy)phenyl)-2-(trifluoromethoxy)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((R)-1-(3-(trifluoromethoxy)phenyl)-2-(trifluoromethoxy)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((S)-2-cyano-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((S)-3-cyano-1-(3-(trifluoromethoxy)phenyl) propyl)-3-hydroxy-4,4-dimethylpentanamide; (R)—N-(2-cyclopropoxy-1-(3-(trifluoromethoxy) phenyl)ethyl)-2-(3,3-difluoro-1-hydroxycyclobutyl)acetamide; (R)—N-(2-cyclopropoxy-1-(3-(difluoromethoxy) phenyl)ethyl)-2-(3,3-difluoro-1-hydroxycyclobutyl)acetamide; (R)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(1-(3-(difluoromethoxy)phenyl)-2-(trifluoromethoxy)ethyl)acetamide; and (S)—N-(2-cyano-1-(3-(trifluoromethoxy) phenyl)ethyl)-2-(3,3-difluoro-1-hydroxycyclobutyl)acetamide or a pharmaceutically acceptable salt of any of these compounds.

[0175] In further embodiments, the Kv7 channel activator is selected from the group consisting of (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (S)-3-hydroxy-4,4-dimethyl-N—((S)-1-(3-(2,2,2-trifluoroethoxy)phenyl)ethyl) pentanamide; (R)-3-hydroxy-4,4-dimethyl-N—((S)-1-(3-(2,2,2-trifluoroethoxy) phenyl)ethyl)pentanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3-(1-(trifluoro-methyl)cyclopropyl)propanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3-(1-(trifluoro-methyl)cyclopropyl)propanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-hydroxy-3-(1-(trifluoromethyl)cyclopropyl)propanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl) ethyl)-3-hydroxy-3-(1-(trifluoromethyl)cyclopropyl) propanamide; (R)-3-(3,3-difluorocyclobutyl)-N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxypropanamide; (S)-3-(3,3-difluorocyclobutyl)-N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxypropanamide; (R)-3-(3,3-difluorocyclobutyl)-N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl) ethyl)-3-hydroxypropanamide; (S)-3-(3,3-difluorocyclobutyl)-N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-hydroxypropanamide; (S)-3-(3,3-difluorocyclobutyl)-N—((S)-1-(3-(difluoromethoxy)phenyl)butyl)-3-hydroxypropanamide; (R)-3-(3,3-difluorocyclobutyl)-N—((S)-1-(3-(difluoromethoxy) phenyl)butyl)-3-hydroxypropanamide;

(S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-(1-ethylcyclopropyl)-3-hydroxypropanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl) ethyl)-3-(1-ethylcyclopropyl)-3-hydroxypropanamide; (S)—N—((S)-1-(3-(difluoromethoxy)phenyl)butyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((S)-1-(3-(difluoromethoxy)phenyl)-4,4-difluorobutyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((S)-1-(3-(difluoromethoxy)phenyl)-3,3-difluoropropyl)-3-hydroxy-4,4-dimethylpentanamide; (S)—N—((S)-1-(3-(difluoromethoxy) phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (R)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl) ethyl)acetamide; (R)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl)ethyl)acetamide; (S)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(1-(3-(difluoromethoxy)phenyl)butyl)acetamide; (S)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(1-(3-(difluoromethoxy)phenyl)-4,4-difluorobutyl)acetamide; (S)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(1-(3-(trifluoromethoxy) phenyl)propyl)acetamide; (S)—N-(3,3-difluoro-1-(3-(trifluoromethoxy)phenyl)propyl)-2-(3,3-difluoro-1-hydroxycyclobutyl)acetamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-4,4-dimethylpentanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-(1-fluorocyclopropyl)-3-hydroxybutanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl) ethyl)-3-(1-fluorocyclopropyl)-3-hydroxybutanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-(1-fluorocyclopropyl)-3-hydroxybutanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl) ethyl)-3-(1-fluorocyclopropyl)-3-hydroxybutanamide; (R)-3-cyclopropyl-N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl) ethyl)-3-hydroxybutanamide; (S)-3-cyclopropyl-N—((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy) phenyl)ethyl)-3-hydroxybutanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-5,5,5-trifluoro-3-hydroxy-3-methylpentanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-5,5,5-trifluoro-3-hydroxy-3-methylpentanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3,5-dimethylhexanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3,5-dimethylhexanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3,4-dimethylpentanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxy-3,4-dimethylpentanamide; (S)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-(3,3-dimethylcyclobutyl)-3-

hydroxypropanamide; (R)—N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-(3,3-dimethylcyclobutyl)-3-hydroxypropanamide; (S)-3-cyclopentyl-N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxypropanamide; (R)-3-cyclopentyl-N—((R)-2-(difluoromethoxy)-1-(3-(difluoromethoxy)phenyl)ethyl)-3-hydroxypropanamide; (R)-3-(1-fluorocyclopropyl)-3-hydroxy-N—((R)-2-methoxy-1-(3-(trifluoromethoxy)phenyl)ethyl)butanamide; and (S)-3-(1-fluorocyclopropyl)-3-hydroxy-N—((R)-2-methoxy-1-(3-(trifluoromethoxy)phenyl)ethyl)butanamide; or a pharmaceutically acceptable salt of any of these compounds.

[0176] In further embodiments, the Kv7 channel activator is a compound according to formula 8 wherein R^1 is selected from the group consisting of C_1-C_6 alkyl, CF_3, CH_2CF_3, CF_2CHF_2, C_3-C_8 cycloalkyl, wherein said C_3-C_8 cycloalkyl may be substituted with 1 or 2 F, CHF_2 or CF_3, and R^2 is H, C_1-C_6 alkyl or CF_3; or R^1 and R^2 combine to form C_3-C_5 cycloalkyl optionally substituted with 1 or 2 F, CHF_2 or CF_3; R^3 is C_1-C_3 alkyl or CH_2O—$C_{1\text{-}3}$ alkyl, said C_1-C_3 alkyl or CH_2O—$C_{1\text{-}3}$ alkyl may optionally be substituted with 1 or 2 F; and R^4 is selected from the group consisting of OCF_3, OCH_2CF_3 or $OCHF_2$.

[0177] In further embodiments, R^4 is OCF_3 or $OCHF_2$.

[0178] In further embodiments, R^2 is H or CH_3.

[0179] In further embodiments, R^3 is CH_2O—$C_{1\text{-}3}$ alkyl.

[0180] In further embodiments, R^1 is C_3-C_4 cycloalkyl optionally substituted with 1 or 2 F, CHF_2 or CF_3.

[0181] In further embodiments, R^1 is t-butyl and R^2 is H and R^4 is OCF_3, OCH_2CF_3, $OCHF_2$ or CF_3.

[0182] In further embodiments, R^1 and R^2 combine to form cyclobutyl optionally substituted with 1 or 2 F and R^4 is OCF_3, OCH_2CF_3, $OCHF_2$ or CF_3.

[0183] In further embodiments, the Kv7 channel activator is selected from the group consisting of: (S)-3-hydroxy-4,4-dimethyl-N-[(1S)-1-[3-(trifluoromethoxy)phenyl]ethyl]pentanamide, (R)-3-hydroxy-4,4-dimethyl-N-[(1S)-1-[3-(trifluoromethoxy)phenyl]ethyl]pentanamide, (S)-3-hydroxy-4,4-dimethyl-N-((S)-1-(3-(2,2,2- trifluoroethoxy)phenyl) ethyl)pentanamide, (R)-3-hydroxy-4,4-dimethyl-N-((S)-1-(3-(2,2,2- trifluoroethoxy)phenyl) ethyl)pentanamide, (S)-N-((S)-1-(3-(difluoromethoxy)phenyl)ethyl)-3- hydroxy-4,4-dimethylpentanamide, (R)-N-((S)-1-(3-(difluoromethoxy)phenyl)ethyl)-3- hydroxy-4,4-dimethylpentanamide, (S)-3-hydroxy-4,4-dimthyl-N-((S)-1-(3- (trifluoromethyl)phenyl)ethyl)pentanamide (R)-3-hydroxy-4,4-

dimethyl-N-((S)-1-(3- (trifluoromethyl)phenyl)ethyl)pentanamide, (S)-3-hydroxy-4,4-dimethyl-N-((S)-1-(3- (trifluoromethoxy)phenyl)propyl)pentanamide, (R)-3-hydroxy-4,4-dimethyl-N-((S)-1-(3- (trifluoromethoxy)phenyl)propyl)pentanamide, (S)-3-(3,3-difluorocyclobutyl)-3-hydroxy-N-((S)- 1-(3-(trifluoromethoxy)phenyl)ethyl)propanamide, (R)-3-(3,3-difluorocyclobutyl)-3-hydroxy-N-((S)- 1-(3-(trifluoromethoxy)phenyl)ethyl)propanamide, (S)-3-hydroxy-4-methyl-N-((S)-1-(3-(2,2,2-trifluoroethoxy)phenyl)ethyl)pentanamide, (R)-3-hydroxy-4-methyl-N-((S)-1-(3-(2,2,2-trifluoroethoxy)phenyl)ethyl)pentanamide, (S)-3-(1-(difluoromethyl)cyclopropyl)-3-hydroxy-N-((S)-1-(3-(trifluoro- methoxy)phenyl)ethyl)propanamide, (R)-3-(1-(difluoromethyl)cyclopropyl)-3-hydroxy- N-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)propanamide, (R)-3-hydroxy-N-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-(1- (trifluoromethyl)cyclopropyl)propanamide, (S)-3-hydroxy-N-((S)-1-(3- (trifluoromethoxy)phenyl)ethyl)-3-(1-(trifluoromethyl)cyclopropyl)propanamide, (S)- 3-hydroxy-4-methyl-N-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)pentanamide, (R)-3-hydroxy-4-methyl-N-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)pentanamide, N-((R)-2-(difluoromethoxy)-1-(3-(trifluoromethoxy)phenyl)ethyl)-3-(R)-hydroxy- 4,4-dimethylpentanamide, N-((R)-2-(difluoromethoxy)-1-(3- (trifluoromethoxy) phenyl)ethyl)-3-(S)-hydroxy- 4,4-dimethylpentanamide, (S)-3-hydroxy-N-((R)-2-methoxy-1-(3-(trifluoromethoxy)phenyl)ethyl)-4,4- dimethylpentanamide, (R)-3-hydroxy-N-((R)-2-methoxy-1-(3-(trifluoromethoxy) phenyl)ethyl)- 4,4-dimethylpentanamide, (S)-2-(3,3-difluoro-1-hydroxycyclobutyl)-N-(1-(3- (trifluoromethoxy)phenyl)ethyl)acetamide, (S)-2-(1-hydroxycyclobutyl)-N-(1-(3-(2,2,2- trifluoroethoxy)phenyl)ethyl)acetamide, (3R)-3-hydroxy-4-methyl-N-[(1S)-1-[3-(2,2,2- trifluoroethoxy)phenyl]ethyl]-3-(trifluoromethyl)pentanamide, (3S)-3-hydroxy-4-methyl-N-[(1S)-1-[3-(2,2,2-trifluoroethoxy)phenyl]ethyl]-3- (trifluoromethyl)pentanamide, 4,4,4-Trifluoro-3-hydroxy-N-[(1S)-1-[3- (trifluoromethoxy)phenyl]ethyl]-3- (trifluoromethyl)butanamide, (R)-4,4,5,5-tetrafluoro-3-hydroxy-3-methyl-N- ((S)-1-(3- (trifluoromethoxy)phenyl)ethyl)pentanamide, (S)-4,4,5,5-tetrafluoro-3-hydroxy-3-methyl-N- ((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)pentanamide, (R)-5,5,5-trifluoro-3-hydroxy-3-methyl-N-((S)-1- (3-(trifluoromethoxy)phenyl)ethyl)pentanamide, (S)-5,5,5-trifluoro-3-hydroxy-3-methyl-N-((S)-1- (3-(trifluoro methoxy)phenyl)ethyl)pentanamide, (R)-3-(1-fluorocyclopropyl)-3-hydroxy-N-((S)-1- (3-(trifluoromethoxy)phenyl)ethyl)butanamide, (S)-3-(1-fluorocyclopropyl)-3-hydroxy-N-((S)-1- (3-(trifluoro-methoxy)phenyl)ethyl)butanamide,

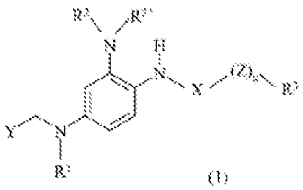
(R)-2-(1-hydroxycyclopentyl)-N-(2-methoxy-1-(3-(trifluoromethoxy)phenyl)ethyl)acetamide, (R)-3-cyclopropyl-3-hydroxy-N-((S)-1-(3-(2,2,2-trifluoroethoxy)phenyl)ethyl)butanamide, (S)-3-cyclopropyl-3-hydroxy-N-((S)-1-(3-(2,2,2-trifluoroethoxy)phenyl)ethyl)butanamide, (R)-4,4,4-trifluoro-3-hydroxy-3-methyl-N-((S)-1-(3-(2,2,2- trifluoroethoxy)phenyl)ethyl)butanamide, and (S)-4,4,4-trifluoro-3-hydroxy-3-methyl-N-((S)-1- (3-(2,2,2-trifluoroethoxy)phenyl)ethyl)butanamide or a pharmaceutically acceptable salt of any of these compounds.

Formula 10

[0184] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 10. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2009, and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; International Publication No. WO2004058739A1, published July 15, 2004 and corresponding to International Application No. PCT/DK2003/000906 filed December 18, 2003; US patent No. 7,368,472 issued May 6, 2008 and corresponding to US Application No. 10/540,075 filed December 18, 2003; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 8, these references incorporated by reference herein control.

[0185] In an embodiment, the Kv7 channel activator is a compound according to formula 10:

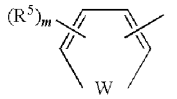
Formula 10



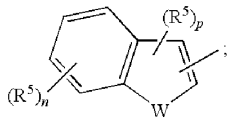
(I) ,

wherein R^1 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-Cycloalk(en)yl; R^2 and $R^{2'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; R^3 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{3-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, aryl-C_{3-8}-cycloalk(en)yl, $NR^{10}R^{10'}$—C_{1-4}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-

Cycloalk(en)yl and hydroxy-C_{3-8}-cycloalk(en)yl; wherein: R^{10} and $R^{10'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{10} and $R^{10'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; X is CO or SO_2; Z is O or NR^4, wherein: R^4 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; or R^3 and R^4 together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms, and the ring formed by R^3 and R^4 and the nitrogen atom is optionally substituted with one or more substituents independently selected from C_{1-6}-alk(en/yn)yl, aryl and aryl-C_{1-6}-alk(en/yn)yl; q is 0 or 1; and Y represents a heteroaryl of one of the following formulas:



or

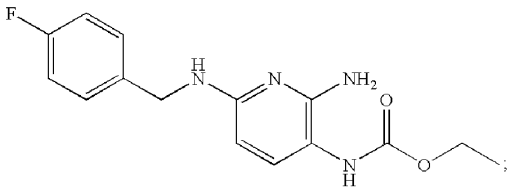


;

wherein: W is O or S; m is 0, 1, 2 or 3; n is 0, 1, 2, 3 or 4; p is 0 or 1; and each R^5 is independently selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, halogen, halo-C_{1-6}-alk(en/yn)yl, alk(en/yn)yloxy, —CO—$NR^6R^{6'}$, cyano, nitro, —$NR^7R^{4'}$, —S—R^8, —SO_2R^8, and SO_2OR^8; wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and aryl; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and acyl; and R^8 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{1-6}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and $NR^9R^{9'}$; wherein: R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or a pharmaceutically acceptable salt thereof.

[0186] In further embodiments, the Kv7 channel activator is selected from the group consisting of: {2-Amino-4-[(5-chloro-thiophen-2-ylmethyl)-methyl-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-methyl-thiophen-2-ylmethyl)-methyl-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-bromo-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(6-chloro-3-methoxy-benzo[b]thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {(2-Amino-4-[(benzo[b]thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-methyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-bromo-3-methoxy-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-phenyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(3-chloro-thiophen-2-ylmethyl-amino]-phenyl}-carbamic acid ethyl ester; (2-Amino-4-{[4-(4-chloro-benzenesulfonyl)-3-methyl-thiophen-2-ylmethyl]-amino}-phenyl)-carbamic acid ethyl ester; {2-Amino-4-[(3-methyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-fluoro-benzofuran-3-ylmethyl)-amino]phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-bromo-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-ethyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(thiophen-3-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-chloro-thiophen-2-ylmethyl)-ethyl-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(benzo[b]thiophen-3-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-dimethyl-amino-benzo[b]thiophen-3-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-dimethyl-amino-3-methyl-benzo[b]thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(5-fluoro-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(benzo[b]thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {2-Amino-4-[(benzo[b]thiophen-3-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; N-{2-Amino-4-[(5-chloro-thiophen-2-ylmethyl)amino]phenyl}-2-(4-fluoro-phenyl)-acetamide; N-{2-Amino-4-[(5-chloro-thiophen-2-ylmethyl)amino]phenyl}-3,3-dimethyl-butyramide; and pharmaceutically acceptable salts thereof.

[0187] In further embodiments, the Kv7 channel activator is a compound according to the formula:

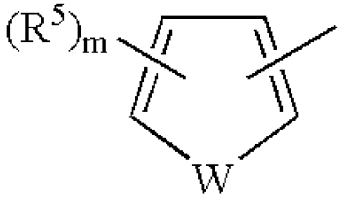


or a pharmaceutically acceptable salt thereof.

[0188] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 2-Cyclopentyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide; N-(4,6-Dimethyl-2-morpholin-4-yl-pyrimidin-5-yl)-2-(4-fluoro-phenyl)-acetamide; Hexanoic acid (2,6-difluoro-4-morpholin-4-yl-phenyl)-amide; 2-Cyclopentyl-N-(4,6-dimethyl-2-morpholin-4-yl-pyrimidin-5-yl)-acetamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-propionamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-3,3-dimethyl-butyramide; [2-Amino-4-(2,4,6-trimethyl-benzylamino)-phenyl]-carbamic acid ethyl ester; 2-Cyclopentyl-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; and pharmaceutically acceptable salts thereof.

[0189] In further embodiments, the Kv7 channel activator is a compound according to formula 10 wherein: R^1 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; R^2 and $R^{2'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; R^3 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, aryl-C_{3-8}-cycloalk(en)yl, $NR^{10}R^{10'}$—C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl and hydroxy-C_{3-8}-cycloalk(en)yl, wherein: R^{10} and $R^{10'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, or R^{10} and $R^{10'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; X is CO or SO_2; Z is O

or NR^4, wherein: R^4 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; or R^3 and R^4 together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms, the ring formed by R^3 and R^4 and the nitrogen atom is optionally substituted with one or more substituents independently selected from C_{1-6}-alk(en/yn)yl, aryl and aryl-C_{1-6}-alk(en/yn)yl; q is 0 or 1; and Y represents a heteroaryl of formula:



,

wherein: W is S; m is 0, 1, 2 or 3; n is 0, 1, 2, 3 or 4; p is 0 or 1; and each R^5 is independently selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, halogen, halo-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, —CO—$NR^6R^{6'}$, cyano, nitro, —$NR^7R^{7'}$, —S—R^8, —SO_2R^8, and SO_2OR^8, wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and aryl; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and acyl; and R^8 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and —$NR^9R^{9'}$, wherein: R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or a pharmaceutically acceptable salt thereof.

[0190] In further embodiments, R^1 is selected from the group consisting of hydrogen and C_{1-6}-alk(en/yn)yl.

[0191] In further embodiments, at least one of the substituents R^2 and $R^{2'}$ is a hydrogen atom.

[0192] In further embodiments both R^2 and $R^{2'}$ are hydrogen atoms.

[0193] In further embodiments, X is CO.

[0194] In further embodiments, q is 0.

[0195] In further embodiments, q is 1 and Z is an oxygen atom.

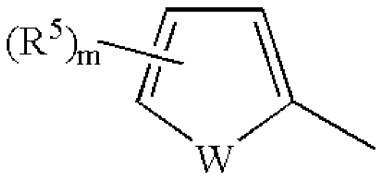
[0196] In further embodiments, R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl and aryl-C_{1-6}-alk(en/yn)yl.

[0197] In further embodiments, R^3 is C_{1-6}-alk(en/yn)yl.

[0198] In further embodiments, R^3 is aryl-C_{1-6}-alk(en/yn)yl.

[0199] In further embodiments, W is a sulfur atom.

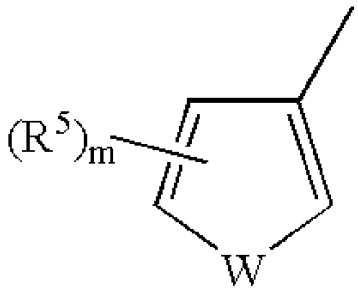
[0200] In further embodiments, Y is of formula:



,

wherein: W is S; m is 0, 1, 2 or 3; n is 0, 1, 2, 3 or 4; p is 0 or 1; and each R^5 is independently selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, halogen, halo-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, —CO—$NR^6R^{6'}$, cyano, nitro, —$NR^7R^{7'}$, —S—R^8, —SO_2R^8, and SO_2OR^8, wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and aryl; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and acyl; and R^8 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and —$NR^9R^{9'}$, wherein: R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl.

[0201] In further embodiments, Y is of formula:



,

wherein: W is S; m is 0, 1, 2 or 3; n is 0, 1, 2, 3 or 4; p is 0 or 1; and each R^5 is independently selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, aryl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl-C_{1-6}-alk(en/yn)yl, acyl, halogen, halo-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, —CO—$NR^6R^{6'}$, cyano, nitro, —$NR^7R^{7'}$, —S—R^8, —SO_2R^8, and SO_2OR^8, wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and aryl; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and acyl; and R^8 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl and —$NR^9R^{9'}$, wherein: R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl.

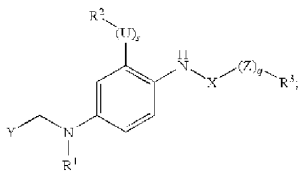
Formula 11

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 11. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2009, and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; International Publication No. WO2004058739A1, published July 15, 2004 and corresponding to International Application No. PCT/DK2003/000906 filed December 18, 2003; US patent No. 7,368,472 issued May 6, 2008 and corresponding to US Application No. 10/540,075 filed December 18, 2003; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; International Publication No. WO2004082677A1, published September 30, 2004 and corresponding to International Application No. PCT/DK2004/000186 filed March 18, 2004; International

Publication No. WO2004080950A1, published or issued September 23, 2004 and corresponding to International Application No. PCT/DK2004/000162 filed March 12, 2004; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 11, these references incorporated by reference herein control.

[0202] In an embodiment, the Kv7 channel activator is a compound according to formula 11:

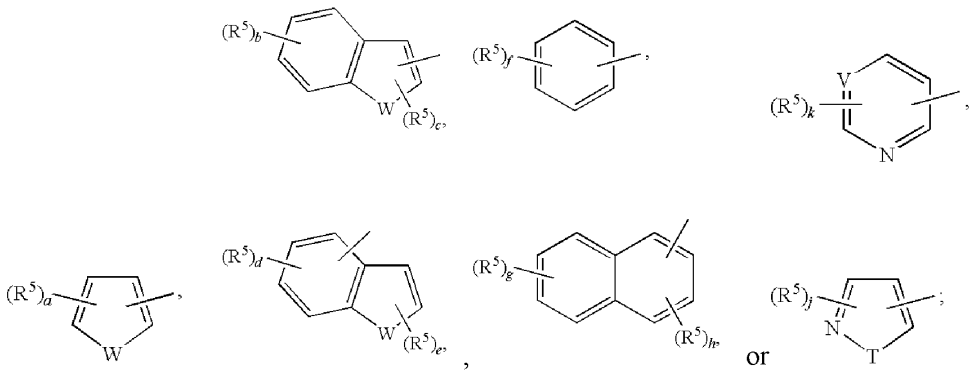
Formula 11



wherein: s is 0 or 1; U is O, S, SO_2, SO_2NR^{11}, CO—O or $CONR^{11}$; wherein: R^{11} is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^2 and R^{11} together with the nitrogen atom to which R^{11} is attached form a 5-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; q is 0 or 1; X is CO or SO_2; with the proviso when X is SO_2, then q is 0; Z is O or S; R^1 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; R^2 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl and $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{10} and $R^{10'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yl; or R^{10} and $R^{10'}$ together with the nitrogen atom to which they are attached form a 5-8 membered saturated or unsaturated ring that optionally

contains 1, 2 or 3 further heteroatoms; and provided that: when R^2 is halogen or cyano, then s is 0; and when s is l and R^2 is a hydrogen atom or acyl, then U is O or S; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar-heterocycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, Ar—C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-heterocycloalk(en)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycl oal k(en)yl-C_{1-6}-alk(en/yn)yl oxy-carbonyl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-heterocycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-heterocycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl-Ar, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-heterocycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, cyano-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl, acyl-C_{3-8}-cycloalk(en)yl, acyl-heterocycloalk(en)yl, acyl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, $NR^{12}R^{12'}$, optionally substituted $NR^{12}R^{12'}$—C_{1-6}-alk(en/yn)yl, optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl, and optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{12} and $R^{12'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar-heterocycloalk(en)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar-oxy-heterocycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yr)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{12} and $R^{12'}$ together with the nitrogen atom to which

they are attached form a 5-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; provided that: when R^3 is $NR^{12}R^{12'}$, then q is 0; and Y represents a group of the following formulas:



wherein: the line represents a bond attaching the group represented by Y to the carbon atom; W is O or S; V is N, C or CH; T is N, NH or O; a is 0, 1, 2 or 3; b is 0, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is 0, 1, 2, 3, 4 or 5; g is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; j is 0, 1 or 2; k is 0, 1, 2 or 3; and each R^5 is independently selected from the group consisting of a C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar-oxy, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, C_{1-6}-alk(en/yn)yloxy-carbonyl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —CO—$NR^6R^{6'}$, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, $NR^7R^{7'}$, S—R^8 and SO_2R^8; or two adjacent R^5 together with the aromatic group form a 5-8 membered ring that optionally contains one or two heteroatoms; wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, heterocycloalk(en)yl-C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, heterocycloalk(en)yl-Ar and acyl; or R^7 and $R^{7'}$ together with the nitrogen atom to which they are attached form a 5-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycl oal

k(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}- alk(en/yn)yl, Ar and —$NR^9R^{9'}$; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or a pharmaceutically acceptable salt thereof.

[0203] In further embodiments, the Kv7 channel activator is selected from the group consisting of: {4-[(Benzofuran-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid ethyl ester; {4-[(Benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid ethyl ester; {2-Methyl-4-[(5-phenyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; [4-(4-Isopropyl-benzylamino)-2-methylphenyl]-carbamic acid ethyl ester; [4-(4-Fluoro-benzylamino)-2-methylphenyl]-carbamic acid propyl ester; (4-{[4-(4-Chloro-benzenesulfonyl)-3-methyl-thiophen-2-ylmethyl]-amino}-2-methylphenyl)-carbamic acid propyl ester; {4-[(5-Methyl-thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {4-[(Benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {2-Methyl-4-[(5-phenyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; [4-(4-Isopropyl-benzylamino)-2-methylphenyl]-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid ethyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid ethyl ester; {4-[(Benzo[b]thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid ethyl ester; [2-Chloro-4-(4-isopropyl-benzylamino)-phenyl]-carbamic acid ethyl ester; [2-Chloro-4-(4-fluoro-benzylamino)-phenyl]-carbamic acid propyl ester; 2-Chloro-4-{[4-(4-chloro-benzenesulfonyl)-3-methyl-thiophen-2-ylmethyl]-amino)-phenyl}-carbamic acid propyl ester; {4-[(5-Methyl-thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid propyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(Benzo[b]thiophen-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid propyl ester; {4-[(Benzofuran-2-ylmethyl)-amino]-2-chlorophenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-cyanophenyl}-carbamic acid ethyl ester; {4-[(Benzo[b]thiophen-2-ylmethyl)-amino]-2-methoxyphenyl}-carbamic acid methyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-methoxyphenyl}-carbamic acid isopropyl ester; {4-[(4-Fluoro-benzyl)-(methyl)amino]-2-methoxyphenyl}-carbamic acid propyl ester; [4-(Benzo[b]thiophen-2-ylmethyl-(methyl)amino)-2-methoxy-phenyl]-carbamic acid propyl

ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methoxy-phenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-methoxy-phenyl}-carbamic acid propyl ester; {2-Methoxy-4-[methyl-(5-methyl-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(4-Fluorobenzyl)-(methyl)-amino]-2-isopropoxyphenyl}-carbamic acid ethyl ester; [4-(3-Fluorobenzylamino)-2-methoxyphenyl]-carbamic acid ethyl ester; [4-(4-Isopropylbenzylamino)-2-methoxyphenyl]-carbamic acid ethyl ester; {2-Methoxy-4-[(3-methylthiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid ethyl ester; [4-(2,4-Difluorobenzylamino)-2-methoxyphenyl]-carbamic acid ethyl ester; [2-Cyclopentyloxy-4-(4-methoxybenzylamino)-phenyl]-carbamic acid ethylester; [2-Cyclopentyloxy-4-(3-fluoro-2-methylbenzylamino)-phenyl]-carbamic acid ethyl ester; [4-(3-Fluoro-2-methylbenzylamino)-2-phenethyloxyphenyl]-carbamic acid ethyl ester; [2-Benzyloxy-4-(3-fluoro-2-methylbenzylamino)-phenyl]carbamic acid ethyl ester; [2-Benzyloxy-4-(4-methylsulfanylbenzylamino)-phenyl]-carbamic acid ethyl ester; {4-[(Benzo[b]thiophen-3-ylmethyl)-amino]-2-cyclopentyloxyphenyl}-carbamic acid ethyl ester; [4-(3-Fluoro-2-methylbenzylamino)-2-isopropoxyphenyl]-carbamic acid ethyl ester; [2-Benzyloxy-4-(3-methoxybenzylamino)-phenyl]-carbamic acid ethyl ester; {4-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-2-isopropoxyphenyl}-carbamic acid ethyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; [2-Cyano-4-(4-isopropylbenzylamino)-phenyl]-carbamic acid ethyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl phenyl}-carbamic acid propyl ester; {4-[(4-Isopropylbenzyl)-(methyl)amino]-2-methyl phenyl}-carbamic acid propyl ester; {2-Methyl-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-carbamic acid propyl ester; {2-Methyl-4-[methyl-(4-methylsulfanyl-benzyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(4-tert-Butyl-benzyl)-(methyl)amino]-2-chlorophenyl}-carbamic acid ethyl ester; {2-Chloro-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-carbamic acid ethyl ester; {2-Chloro-4-[methyl-(4-methylsulfanyl-benzyl)-amino]-phenyl}-carbamic acid ethyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-chlorophenyl}-carbamic acid propyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid propyl ester; {4-[(4-tert-Butyl-benzyl)-(methyl)amino]-2-chlorophenyl}-carbamic acid propyl ester; {2-Chloro-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[(4-Isopropyl-benzyl)-(methyl)amino]-2-

trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[(4-tert-Butyl-benzyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[Methyl-(4-trifluoromethyl-benzyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[Methyl-(4-methylsulfanyl-benzyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[(4-Isopropyl-benzyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[(4-tert-Butyl-benzyl)-(methyl)amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[Methyl-(4-trifluoromethyl-benzyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[Methyl-(4-methylsulfanyl-benzyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-(methyl)amino]-2-cyanophenyl}-carbamic acid propyl ester; {4-[(4-tert-Butyl-benzyl)-(methyl)amino]-2-cyanophenyl}-carbamic acid propyl ester; {2-Cyano-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-carbamic acid propyl ester; {2-Bromo-4-[(5-bromo-thiophen-2-ylmethyl)-(methyl)amino]phenyl}-carbamic acid propyl ester; {2-Bromo-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid propyl ester; {2-Bromo-4-[(4-isopropylbenzyl)-(methyl)amino]-phenyl}-carbamic acid propyl ester; {2-Bromo-4-[(4-tert-butyl-benzyl)-(methyl)amino]-phenyl}-carbamic acid propyl ester; {2-Bromo-4-[methyl-(4-trifluoromethyl-benzyl-amino]-phenyl}-carbamic acid propyl ester; [2-Iodo-4-(4-isopropyl-benzylamino)-phenyl]-carbamic acid propyl ester; [4-(4-tert-Butyl-benzylamino)-2-iodophenyl]-carbamic acid propyl ester; [2-Iodo-4-(4-trifluoromethyl-benzylamino)-phenyl]-carbamic acid propyl ester; [2-Iodo-4-(4-methylsulfanyl-benzylamino)-phenyl]-carbamic acid propyl ester; {2-Iodo-4-[4-(4-methylpiperazin-1-yl)-benzylamino]-phenyl}-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethylyamino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid ethyl ester; [4-(4-tert-Butyl-benzylamino)-2-trifluoromethyl-phenyl]-carbamic acid ethyl ester; [4-(4-Methylsulfanyl-benzylamino)-2-trifluoromethyl-phenyl]-carbamic acid ethyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-trifluoromethyl-phenyl}-carbamic acid propyl ester; [4-(4-Isopropylbenzylamino)-2-trifluoromethyl-phenyl]-carbamic acid propyl ester; [4-(4-tert-Butyl-benzylamino)-2-trifluoromethyl-phenyl]-carbamic acid propyl ester; [2-Trifluoromethyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-carbamic acid propyl ester; [4-(4-Dimethylamino-benzylamino)-2-trifluoromethyl-phenyl]-carbamic acid propyl ester; [4-(4-Methylsulfanyl-benzylamino)-2-trifluoromethyl-phenyl]-carbamic acid propyl ester; {4-[(5-Bromo-thiophen-2-ylmethyl)-

amino]-2-cyanophenyl}-carbamic acid propyl ester; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-cyanophenyl}-carbamic acid propyl ester; [2-Cyano-4-(4-trifluoromethyl-benzylamino)-phenyl]-carbamic acid propyl ester; {2-Bromo-4-[(5-bromo-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {2-Bromo-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; [2-Bromo-4-(4-isopropylbenzylamino)-phenyl]-carbamic acid propyl ester; [2-Bromo-4-(4-tert-butyl-benzylamino)-phenyl]-carbamic acid propyl ester; [2-Bromo-4-(4-trifluoromethyl-benzylamino)-phenyl]carbamic acid propyl ester; [2-Bromo-4-(4-methylsulfanyl-benzylamino)-phenyl]-carbamic acid propyl ester; N-{4-[(5-Bromo-thiophen-2-ylmethyl)-amino]-2-methoxyphenyl}-butyramide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-methoxyphenyl}-butyramide; N-[4-(4-Isopropylbenzylamino)-2-methoxyphenyl]-butyramide; N-[4-(4-tert-Butyl-benzylamino)-2-methoxyphenyl]-butyramide; N-[2-Methoxy-4-(4-trifluoromethyl-benzylamino)-phenyl]-butyramide; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-furan-2-yl-phenyl}-carbamic acid propyl ester; [2-Furan-2-yl-4-(4-isopropylbenzylamino)-phenyl]-carbamic acid propyl ester; [5-(4-Fluorobenzylamino)-biphenyl-2-yl]-carbamic acid propyl ester; {5-[(5-Chloro-thiophen-2-ylmethyl)-amino]-biphenyl-2-yl}-carbamic acid propyl ester; [5-(4-Isopropylbenzylamino)-biphenyl-2-yl]-carbamic acid propyl ester; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-phenylacetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-3,3-dimethylbutyramide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-3-phenylpropionamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-butyramide; Pentanoic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-amide; Cyclopropanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-amide; Cyclobutanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-amide; Cyclopentanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-amide; Cyclohexanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-amide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-thiophen-2-yl-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-(3-methoxy-phenyl)-acetamide, N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl)-2-(4-chloro-phenyl}-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-(4-methoxy-phenyl)-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl)-2-(4-fluoro-phenyl}-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-

2-ylmethyl)-(methyl)amino]-phenyl}-3-cyclohexylpropionamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2,2-dimethylpropionamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-phenoxyacetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-phenyl acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-3,3-dimethylbutyramide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-butyramide; Pentanoic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide;Cyclopropanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide; Cyclobutanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide; Cyclopentanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]phenyl}-amide; Cyclohexanecarboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-thiophen-2-yl-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-(3-methoxyphenyl)-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-(4-chlorophenyl)-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-(4-methoxyphenyl)-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2-(4-fluorophenyl)-acetamide; 2,3-Dihydro-benzo[1,4]dioxine-6-carboxyl acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide; 2,3-Dihydro-benzofuran-5-carboxylic acid {2-chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-amide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-3-cyclohexylpropionamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-2,2-dimethylpropionamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-2-phenyl acetamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-3,3-dimethylbutyramide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-3-phenylpropionamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-butyramide; 2,2,2-Trichloro-N-{4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-acetamide; Cyclopropanecarboxylic acid {4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl-phenyl}-amide; Cyclobutanecarboxylic acid {4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-amide; Cyclopentanecarboxylic acid {4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl phenyl}-amide; Cyclohexanecarboxylic acid {4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-amide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-2-thiophen-2-yl-acetamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-2-(3-methoxyphenyl)-acetamide; N-{4-[(5-

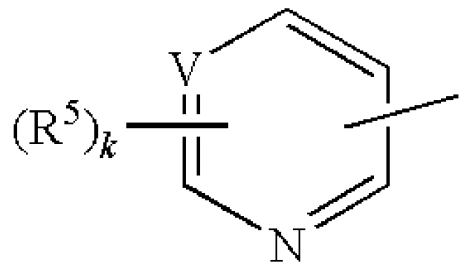
Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl phenyl}-malonamic acid methyl ester; 2-(4-Chlorophenyl)-N-{4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-acetamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl phenyl}-2-(4-methoxyphenyl)-acetamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methyl phenyl}-2-(4-fluorophenyl)-acetamide; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-3-cyclohexylpropionamide; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid phenyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid benzyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid isobutyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid butyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid hexyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid 4-nitrobenzyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid but-3-enyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid but-2-ynyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid 2,2-dimethylpropyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid 2-chlorobenzyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid 3-chloropropyl ester; {2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-carbamic acid 2-benzyloxyethyl ester; 3-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-1-methyl-1-propyl-urea; 1-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-3-(2-fluorophenyl)-urea; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2,2,2-trifluoroacetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-phenyl}-2,2,2-trifluoroacetamide; N-{5-[(5-Chloro-thiophen-2-ylmethyl)-amino]-4′-dimethylamino-biphenyl-2-yl}-2-(4-fluorophenyl)-acetamide; N-{2-Chloro-4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-(4-chlorophenyl)-acetamide; [4-(3-Fluoro-4-trifluoromethyl-benzylamino)-2-methylphenyl]-carbamic acid ethyl ester; 2-(4-Fluorophenyl)-N-{2-methyl-4-[(6-p-tolyloxypyridin-3-ylmethyl)-amino]-phenyl}-acetamide; N-[2-Methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-butyramide; 2-(4-Fluorophenyl)-N-{2-methyl-4-[6-trifluoromethylpyridin-3-ylmethyl)-amino]-phenyl}-acetamide; Pentanoic acid {4-[(5-chloro-thiophen-2-ylmethyl)-(methyl)amino]-2-methylphenyl}-amide; 3,3-Dimethyl-N-{2-methyl-4-[(6-p-tolyloxypyridin-3-ylmethyl)-amino]-phenyl}-butyramide; [2-Methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-carbamic acid ethyl ester; N-{2-Chloro-4-[(5-chloro-

thiophen-2-ylmethyl)-(methyl)amino]-phenyl}-2-(4-chlorophenyl)-propionamide; [4-(4-Chloro-benzylamino)-2-methylphenyl]-carbamic acid ethyl ester; {4-[(6-Methoxy-benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; {4-[(5=Chloro-thiophen-2-ylmethyl)-amino]-2-quinolin-3-yl-phenyl}-carbamic acid ethyl ester; {4-[(5-Dimethylamino-3-methyl-benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; 3,3-Dimethyl-N-{2-methyl-4-[(6-trifluoromethylpyridin-3-ylmethyl)-amino]-phenyl}-butyramide; N-(4-{[6-(4-Cyanophenoxy)-pyridin-3-ylmethyl]-amino}-2-methylphenyl)-2-(4-fluorophenyl)-acetamide; {2-Benzyloxy-4-[(4-fluorobenzyl)-(methyl)amino]-phenyl}-thiocarbamic acid S-ethyl ester; {2-Cyclopentyloxy-4-[(4-fluorobenzyl)-(methyl)amino]-phenyl}-thiocarbamic acid S-ethyl ester; N-{4-[(6-Chloropyridin-3-ylmethyl)-amino]-2-methylphenyl}-2-(4-fluorophenyl)-acetamide; {4-[(7-Dimethylamino-benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid propyl ester; 1-{2-Cyclopentyloxy-4-[(4-fluorobenzyl)-(methyl)amino]-phenyl}-3-ethyl-urea; 2-Amino-4-methyl-pentanoic acid [2-methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-amide; {4-[(6-Methoxy-benzo[b]thiophen-2-ylmethyl)-amino]-2-methylphenyl}-carbamic acid ethyl ester; 2-Amino-4-methyl-pentanoic acid [2-methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-amide; 2-(4-Fluorophenyl)-N-{2-methyl-4-[(4-methyl-2-phenylpyrimidin-5-ylmethyl)-amino]-phenyl}-acetamide, 3,3-Dimethyl-N-{2-methyl-4-[(2-phenylpyrimidin-5-ylmethyl)-amino]-phenyl}-butyramide; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-pyridin-3-yl-phenyl}-carbamic acid ethyl ester; 1-Amino-cyclopropanecarboxylic acid [2-methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-amide; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-pyridin-4-yl-phenyl}-carbamic acid ethyl ester; N-[2-Methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-2-piperidin-1-yl-acetamide; N-(4-{[5-(4-Chlorophenoxy)-1,3-dimethyl-1H-pyrazol-4-ylmethyl]-amino}-2-methylphenyl)-2,2-dimethylpropionamide; 2,2-Dimethyl-N-{2-methyl-4-[(6-phenoxypyridin-3-ylmethyl)-amino]-phenyl}-propionamide; N-[2-Methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-2-pyrrolidin-1-yl-acetamide; [4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-(6-methoxypyridin-3-yl)-phenyl]-carbamic acid ethyl ester; 4-[(3-Methyl-4-propoxycarbonylamino-phenyl amino)-methyl]-benzoic acid methyl ester; N-[2-Methyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-2-morpholin-4-yl-acetamide; 2,2-Dimethyl-N-{2-methyl-4-[(3-methyl-5-phenylisoxazol-4-ylmethyl)-amino]-phenyl}-propionamide; {4-[(5-Chloro-thiophen-2-ylmethyl-amino]-2-iodophenyl}-carbamic acid ethyl ester; N-{4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2-iodophenyl}-2-(4-fluorophenyl)-acetamide; {4-[(5-

Chloro-thiophen-2-ylmethyl)-amino]-2-quinolin-5-yl-phenyl}-carbamic acid ethyl ester; and pharmaceutically acceptable salts thereof.

[0204] In further embodiments, the Kv7 channel activator is a compound according to formula 11, wherein: s is 0 or 1; U is O, S, SO_2, $SONR^{11}$, or $CONR^{11}$; wherein: R^{11} is hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, or C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^2 and R^{11} taken together with the nitrogen atom form a 5-8 membered saturated or unsaturated ring, which optionally contains 1, 2 or 3 further heteroatoms; q is 0 or 1; X is CO or SO_2; with the proviso that q is 0 when X is SO_2; Z is O or S; R^1 is hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo -C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en) yl or cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; R^2 is hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk (en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk (en)yl, halo -C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl or $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{10} and $R^{10'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl or cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{10} and $R^{10'}$ taken together with the nitrogen atom form a 5-8 membered saturated or unsaturated ring, which optionally contains 1, 2 or 3 further heteroatoms; with the proviso that: when R^2 is halogen or cyano, then s is 0; and when s is 1 and R^2 is a hydrogen atom or acyl, then U is O or S; R^3 is C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-heterocycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy -carbonyl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy

-heterocycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl -C_{3-8}-cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo -C_{3-8}-cycloalk(en)yl, halo-heterocycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo -C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-heterocycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl -C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, cyano-C_{1-6}-alk(en/yn)yl -heterocycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl, acyl-C_{3-8}-cycloalk(en)yl, acyl-heterocycloalk(en)yl, acyl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, $NR^{12}R^{12'}$, optionally substituted $NR^{12}R^{12'}$-C_{1-6}-alk(en/yn)yl, optionally substituted $NR^{12}R^{12'}$-C_{3-8}-alk(en/yn)yl, or optionally substituted $NR^{12}R^{12'}$-C_{3-8}-alk(en/yn)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{12} and $R^{12'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar-heterocycloalk(en)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar-oxy -heterocycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, or cyano -C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{12} and $R^{12'}$ taken together with the nitrogen atom form a 5-8 membered saturated or unsaturated ring, which optionally contains 1, 2 or 3 further heteroatoms; with the proviso that when R^3 is $NR^{12}R^{12'}$ then q is 0; and Y is a group of formula:



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wherein: "|" represents a bond attaching the group represented by Y to the carbon atom; V is C or CH; and k is 0, 1, 2 or 3; and each R^5 is independently C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk (en)yl, C_{3-8}-cycloalk(en) yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk (en)yl-C_{1-6}-alk(en/yn)yl , Ar-oxy, Ar-oxy-C_{1-6}alk(en/yn)yl, Ar-oxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk (en/yn)yl -heterocycloalk(en)yl, Ar-oxy-C_{3-8}-

cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, C_{1-6}-alk (en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, C_{1-6}-alk(en/yn)yloxy-carbonyl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —CO—$NR^6R^{6'}$, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk (en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, $NR^7R^{7'}$, S—R^8 or SO_2R^8; or two adjacent R^5 groups taken together with the aromatic group form a 5-8 membered ring, which optionally contains one or two heteroatoms; wherein: R^6 and $R^{6'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl or Ar; R^7 and $R^{7'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, heterocycloalk(en)yl-C_{1-6}-alk (en/yn)yl, heterocycloalk(en)yl-C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk (en/yn)yl, heterocycloalk(en)yl-Ar or acyl; or R^7 and $R^{7'}$ taken together with the nitrogen atom form a 5-8 membered saturated or unsaturated ring which optionally contains 1, 2 or 3 further heteroatoms; and R^8 is hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar or —$NR^9R^{9'}$; wherein: R^9 and $R^{9'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl or C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or salts thereof.

[0205] In further embodiments, R^1 is C_{1-6}-alk(en/yn)yl or a hydrogen atom.

[0206] In further embodiments, s is 0.

[0207] In further embodiments, s is 1.

[0208] In further embodiments, U is an oxygen atom.

[0209] In further embodiments, R^2 is hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, halogen, halo-C_{1-6}-alk(en/yn)yl or cyano; with the provisos that when R^2 is halogen or cyano, then s is 0; and when s is 1 and R^2 is a hydrogen atom, then U is O or S.

[0210] In further embodiments, Z is an oxygen atom.

[0211] In further embodiments, Z is a sulfur atom.

[0212] In further embodiments, q is 0.

[0213] In further embodiments, q is 1.

[0214] In further embodiments, X is CO.

[0215] In further embodiments, R^3 is C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, heterocycloalk (en)yl-C_{1-6}-alk(en/yn)yl, heterocycloalk(en)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar-oxy-C_{1-6}-alk (en/yn)yl, Ar—C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, halo-C_{1-}

$_{6}$-alk(en/yn)yl, $NR^{12}R^{12'}$, optionally substituted $NR^{12}R^{12'}$—C_{1-6}-alk(en/yn)yl, or optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl.

[0216] In further embodiments, R^{12} and $R^{12'}$ are each independently hydrogen, C_{1-6}-alk(en/yn)yl or Ar.

[0217] In further embodiments, V is CH.

[0218] In further embodiments, each R^5 is independently C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, Ar, C_{1-6}-alk(en/yn)yloxy, Ar-oxy, C_{1-6}-alk(en/yn)yloxy-carbonyl, halogen, halo-C_{1-6}-alk(en/yn)yl, $NR^7R^{7'}$, S—R^8 or SO_2R^8; or two adjacent R^5 groups taken together with the aromatic group form a 5-8 membered ring, which optionally contains one or two heteroatoms.

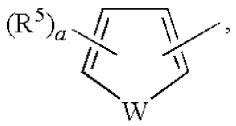
[0219] In further embodiments, both R^7 and $R^{7'}$ are C_{1-6}-alk(en/yn)yl.

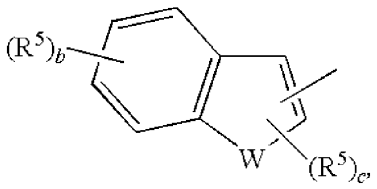
[0220] In further embodiments, R^8 is C_{1-6}-alk(en/yn)yl or Ar.

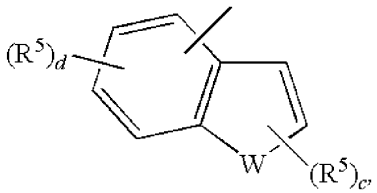
[0221] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 2-(4-Fluorophenyl)-N-{2-methyl-4-[(6-p-tolyloxypyridin-3-ylmethyl)-amino]-phenyl}-acetamide; 2-(4-Fluorophenyl)-N-{2-methyl-4-[(6-trifluoromethylpyridin-3-ylmethyl)-amino]-phenyl}-acetamide; 3,3-Dimethyl-N-{2-methyl-4-[(6-p-tolyloxypyridin-3-ylmethyl)-amino]-phenyl }-butyramide; 3,3-Dimethyl-N-{2-methyl-4-[(6-trifluoromethylpyridin-3-ylmethyl)-amino]-phenyl}-butyramide; N-(4-{[6-(4-Cyanophenoxy)-pyridin-3-ylmethyl]-amino}-2-methylphenyl)-2-(4-fluorophenyl) -acetamide; N-{4-[(6-Chloropyridin-3-ylmethyl)-amino]-2-methylphenyl}-2-(4-fluorophenyl)-acetamide; or 2,2-Dimethyl-N-{2-methyl-4-[(6-phenoxypyridin-3-ylmethyl)-amino]-phenyl }-proprionamide; or a salt thereof.

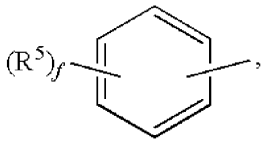
[0222] In further embodiments, the Kv7 channel activator is a compound according to formula 11 wherein: U is O, S or $NR^{2'}$; s is 0 or 1; X is CO or SO_2; Z is O, S or NR^4; wherein R^4 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; q is 0 or 1; R^1 and $R^{1'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; R^2 is selected from the group consisting of hydrogen, halogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and cyano; provided that: when R^2 is halogen or cyano, then s is 0; and when s is 1 and U is $NR^{2'}$, then $R^{2'}$ is selected

from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; or R^2 and $R^{2'}$ together form a 5-8 membered saturated or unsaturated ring that optionally contains one further heteroatom; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; and Y represents a group of the following formulas:

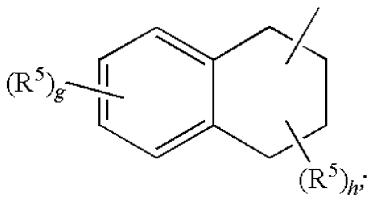








or



wherein: the line represents a bond attaching the group represented by Y to the nitrogen atom; W is O or S; a is 0, 1, 2 or 3; b is 0, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is 0, 1, 2, 3, 4 or 5; g is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; and each R^5 is independently selected from the group consisting of a C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, Ar, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yl, acyl, C_{1-6}-alk(an/en/yn)yloxy, halogen, halo-C_{1-6}-alk(en/yn)yl, —CO—$NR^6R^{6'}$, cyano, nitro, —$NR^7R^{7'}$, —S—R^8 and SO_2OR^8; or two adjacent R^5 substituents together with the aromatic group form a 5-8 membered saturated or unsaturated ring that optionally contains one or two heteroatoms; wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and acyl; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and —$NR^9R^{9'}$; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; with the provisos that; when R^5 is SO_2OR^8 then R^8 is not —$NR^9R^{9'}$; and when R^5 is SO_2R^8, then R^8 is not a hydrogen atom; or a pharmaceutically acceptable salt thereof; with the proviso that the compound of formula I is not: N-[4-[[(4-aminophenyl)amino]methyl]phenyl]-acetamide; N-[4-[[(4-amino-2-methylphenyl)amino]methyl]phenyl]-acetamide; N-[4-[[(4-amino-3-methylphenyl)amino]methyl]phenyl]-acetamide; 2-[[[4-(acetylamino)phenyl]methyl]amino]-5-chloro-N-(5-chloro-2-pyridinyl)- benzamide; N- [4- [[(3 ,4, 5-trimethoxyphenyl)amino]methyl]phenyl] -acetamide; N-[4-[[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2- naphthalenyl)amino]methyl]phenyl]-acetamide; N-[4-[[[3-(lH-imidazol-l-ylmethyl)phenyl]amino]methyl]phenyl]- acetamide; N-[4-[[[2-(lH-imidazol-l-ylmethyl)phenyl]amino]methyl]phenyl]-acetamide; N-[4-[[(4-amino-3,5-dichlorophenyl)amino]methyl]phenyl]- acetamide; N-[4-[[(2,4-diamino-6-quinazolinyl)amino]methyl]phenyl]- acetamide; or N-[4-[[(2,4-diamino-6-quinazolinyl)amino]methyl]phenyl]- acetamide.

[0223] In further embodiments, R^1 and $R^{1'}$ are independently selected from the group consisting of hydrogen and C_{1-6}-alk(en/yn)yl.

[0224] In further embodiments, at least one of R^1 and $R^{1'}$ is a hydrogen atom.

In further embodiments, s is 1.

[0225] In further embodiments, s is 0.

[0226] In further embodiments, R^2 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, Ar and halogen, provided that when R is halogen, then s is 0.

[0227] In further embodiments, U is $NR^{2'}$ and at least one of R and $R^{2'}$ is a hydrogen atom.

[0228] In further embodiments, both R^2 and R^2 are hydrogen atoms.

[0229] In further embodiments, X is CO.

[0230] In further embodiments, q is 0.

[0231] In further embodiments, q is 1.

[0232] In further embodiments, Z is an oxygen atom.

[0233] In further embodiments, R^3 is C_{1-6}- alk(en/yn)yl.

[0234] In further embodiments, each R^5 is independently selected from the group consisting of a C_{1-6}-alk(en yn)yl, C_{3-8}- cycloalk(en)yl, Ar, cyano, halogen, halo-C_{1-6}-alk(en/yn)yl and C_{1-6}- alk(an/en/yn)yloxy or two adjacent substituents together form a 5-8 membered saturated or unsaturated ring which optionally contains one or two heteroatoms.

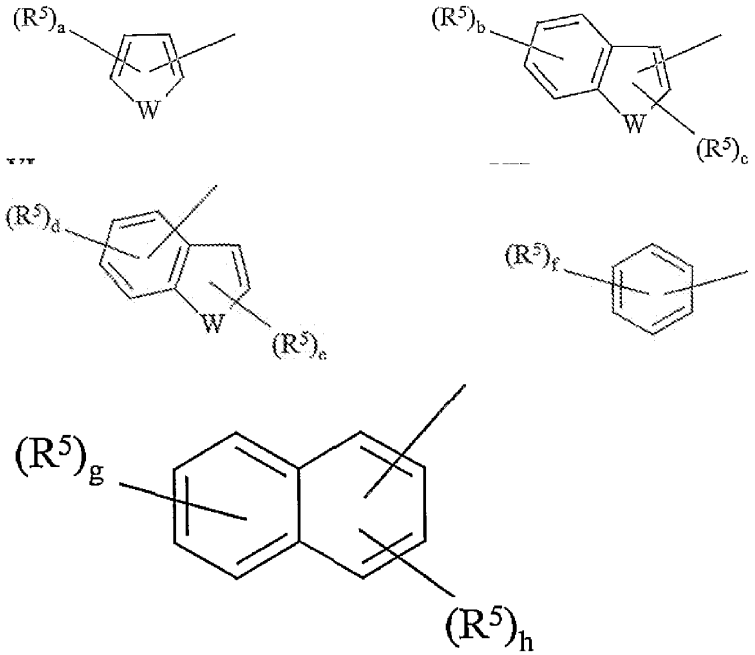
[0235] In further embodiments, the Kv7 channel activator is selected from the group consisting of: {2-Amino-4-[(4-tert-butyl phenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; (2-Amino-4-phenylaminomethyl-phenyl)-carbamic acid ethyl ester; [2-Amino-4-(aphthalene-2-ylaminomethyl)-phenyl]carbamic acid ethyl ester; [2-Amino-4-(p-tolylamino-methyl)-phenyl]carbamic acid ethyl ester; {2-Amino-4-[(4-trifluoromethylphenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-chlorophenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(3-fluorophenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-fluorophenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(2-fluorophenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; [2-Amino-4-(biphenyl-4-ylaminomethyl)-phenyl]-carbamic acid ethyl ester; {2-Amino-4-[(2,4-difluorophenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-methoxyphenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-cyclohexylphenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; [2-Amino-4-(indan-5-ylaminomethyl-phenyl]-carbamic acid ethyl ester; {2-Amino-4-[(4-isopropylphenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-butylphenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; {2-Amino-4-[(4-chloro-3-fluorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(2,4-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(2,3-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3,5-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3,4-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3-

trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3-fluoro-4-trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3,4-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(4-cyanophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(4-fluoro-3-trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3-chloro-4-methylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[(3-chlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; [2-Amino-4-(m-tolylaminomethyl)phenyl]carbamic acid ethyl ester; {2-Amino-4-[1-(4-chlorophenylamino)ethyl]phenyl}carbamic acid ethyl ester; {2-Amino-4-[1-(4-trifluoromethylphenylamino)ethyl]phenyl}carbamic acid ethyl ester; N-{2-Amino-4-[(3-fluorophenylamino)methyl]phenyl}-2,2-dimethylpropionamide; {4-[(4-Chlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {4-[(4-Trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {4-[(4-Chlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {4-[(4-Fluorophenylamino)methyl]-2-methylphenyl}carbamic acid ethyl ester; {4-[(4-Chlorophenylamino)methyl]-2-methylphenyl}carbamic acid ethyl ester; {2-Methyl-4-[(4-trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {4-[(3,4-Difluorophenylamino)methyl]-2-methylphenyl}carbamic acid ethyl ester; {4-[(3-Fluorophenylamino)methyl]-2-methylphenyl}carbamic acid ethyl ester; {2-Chloro-4-[(4-chlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Chloro-4-[(4-trifluoromethyl-phenylamino)-methyl]phenyl}-carbamic acid ethyl ester; {2-Chloro-4-[(4-fluorophenylamino)methyl]phenyl}-carbamic acid ethyl ester; {2-Chloro-4-[(3-fluorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Chloro-4-[(3,4-dichlorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {2-Chloro-4-[(4-chloro-3-fluorophenylamino)methyl]phenyl}carbamic acid ethyl ester; {4-[(4-Chlorophenylamino)methyl]-2-fluorophenyl}carbamic acid ethyl ester; {4-[(4-Chloro-3-fluorophenylamino)methyl]-2-fluorophenyl}carbamic acid ethyl ester; {2-Fluoro-4-[(4-trifluoromethylphenylamino)methyl]phenyl}carbamic acid ethyl ester; {4′-Dimethylamino-5-[(3-fluorophenylamino)methyl]biphenyl-2-yl}carbamic acid ethyl ester; {4′-Dimethylamino-5-[(4-trifluoromethylphenylamino)methyl]biphenyl-2-yl}carbamic acid ethyl ester; {4′-Chloro-5-[(3-fluorophenylamino)methyl]biphenyl-2-yl}carbamic acid ethyl ester; {4′-Chloro-5-[(4-trifluoromethylphenylamino)methyl]biphenyl-2-yl}carbamic acid ethyl ester; N-{4-[(4-chlorophenylamino)methyl]phenyl}butyramide; N-{4-[(3,4-dichlorophenylamino)methyl]phenyl}butyramide; N-{4-[(4-chloro-3-

fluorophenylamino)methyl]phenyl}butyramide; N-{4-[(4-fluoro-phenylamino)methyl]-2-methyl phenyl}butyramide; N-{4-[(3-fluorophenylamino)methyl]-2-methylphenyl}butyramide; N-{4-[(4-chlorophenylamino)methyl]-2-methylphenyl}butyramide; N-{4-[(3,4-dichlorophenylamino)methyl]-2-methylphenyl}butyramide; N-{4-[(4-chloro-3-fluorophenylamino)methyl]-2-methyl phenyl}butyramide; N-{2-chloro-4-[(4-trifluoromethylphenylamino)methyl]phenyl}butyramide; N-{2-chloro-4-[(4-fluorophenylamino)methyl]phenyl}butyramide; N-{2-chloro-4-[(3-fluorophenylamino)methyl]phenyl}butyramide; N-{2-chloro-4-[(4-chlorophenylamino)methyl]phenyl}butyramide; N-{2-chloro-4-[(3,4-dichlorophenylamino)methyl]phenyl}butyramide; N-{2-chloro-4-[(4-chloro-3-fluorophenylamino)methyl]phenyl}butyramide; N-{2-fluoro-4-[(3-fluorophenylamino)methyl]phenyl}butyramide; N-{4-[(4-chlorophenylamino)methyl]-2-fluorophenyl}butyramide; N-{2-fluoro-4-[(4-trifluoromethylphenylamino)methyl]phenyl}butyramide; N-{-4-[(3,4-dichlorophenylamino)methyl]-2-fluorophenyl}butyramide; N-{4-[(4-chloro-3-fluorophenylamino)methyl]-2-fluorophenyl}butyramide; and pharmaceutically acceptable salts thereof.

[0236] In further embodiments, the Kv7 channel activator is a compound according to formula 11 wherein: U is O, S or C s is O or 1; X is CO or SO_2; Z is O, S or NR. , wherein R^4 is selected from the group consisting of hydrogen, Cι-6-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; q is O or 1; R^1 and $R^{1'}$ are independently selected from the group consisting of hydrogen, $C_{\cdot\cdot 6}$-alk(en/yn)yl, C3-8-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-Cι-6-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; R is selected from the group consisting of hydrogen, halogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-Cι-6-alk(en/yn)yl, Ar, Ar-C_{1-6}-alk(en/yn)yl, Ar-C_{3-8}-cycloalk(en)yl, acyl, hydroxy-Cι-6-alk(en/yn)yl, hydroxy- C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and cyano; provided that when R^2 is halogen or cyano then s is 0; when s is 1 and U is $NR^{2'}$ then $R^{2'}$ is selected from the group consisting of hydrogen, C_{1-6}-alk(en yn)yl, C $_{-8}$-cycloalk(en)yl, C_{3-8}-cycloallc(en)yl-Cι-6- alk(en/yn)yl, Ar, Ar-C_{1-6}-alk(en/yn)yl, Ar-C_{3-8}-cycloalk(en)yl, acyl, hydroxy- $_{\cdot\cdot 6}$-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; or R^2 and $R^{2'}$ together form a 5-8 membered saturated or unsaturated ring

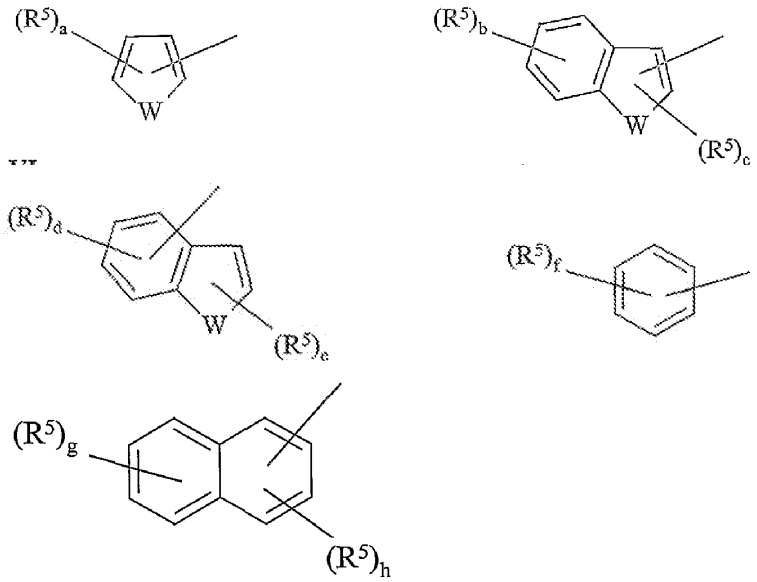
which optionally contains one further heteroatom; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar-C_{1-6}-alk(en/yn)yl, Ar-C_{3-8}- cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-Cj. $_6$-alk(en/yn)yl and halo-C_{3-8}-cycloalk(en)yl; and Y is selected from groups according to a formula selected from the group consisting of:



wherein: the line represents a bond attaching the group represented by Y to the nitrogen atom; W is O or S; a is 0, 1, 2 or 3; b is O, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is O, 1, 2, 3, 4 or 5; g is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; and each R^5 is independently selected from the group consisting of a C_{1-6}- alk(en yn)yl, C_{3-8}-cycloalk(en)yl, Ar, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en yn)yl, Ar- C_{1-6}-alk(en/yn)yl, acyl, C_{1-6}-alk(an/en/yn)yloxy, halogen, halo-C_{1-6}-alk(en/yn)yl, -CO-$NR^6R^{6'}$, cyano, nitro, -$NR^7R^{7'}$, -S-R^8, -SO_2R^8 and SO_2OR^8, or two substituents together form a 5-8 membered saturated or unsaturated ring which optionally contains one or two heteroatoms; R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, $C_{\backslash. 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, $C_{\backslash. 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and acyl; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}- cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and -$NR^9R^{9'}$; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C $_6$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; with the provisos

that when R^5 is SO_2OR^8 then R^8 is not $-NR^9R^{9'}$ and when R^5 is SO_2R^8 , then R^8 is not a hydrogen atom; or salts thereof; with the proviso that the compound of formula I is not: 2-[[[4-(acetylamino)phenyl]methyl]amino]-5-chloro-N-(5-chloro-2-pyridinyl)- benzamide; N-[4-[[(3,4,5-trimethoxyphenyl)amino]methyl]phenyl]-acetamide; N-[4-[[(5,6,7,8-tetrahydiO-5,5,8,8-tetramethyl-2- naphthalenyl)amino]methyljρhenyl]-acetamide; N- [4- [[[3 -(1 H-imidazol- 1 -ylmethyl)phenyl]amino]methyl]phenyl] - acetamide; N-[4-[[[2-(lH-imidazol-l-ylmethyl)phenyl]amino]methyl]phenyl]-acetamide; N-[4-[[[4-(IH-imidazol- 1 -ylmethyl)phenyl]amino]methyl]phenyl]- acetamide; N-[4-[[(4-amino-3,5-dichlorophenyl)ammo]methyl]phenyl]- acetamide; N-[4-[[(2,4-diamino-6-quinazolinyl)amino]methyl]phenyl]- acetamide; or N-[4-[[(2,4-diamino-6-quinazolinyl)amino]methyl]phenyl]- acetamide.

[0237] In further embodiments, the Kv7 channel activator is a compound according to formula 11 wherein: wherein U is O, S or NR^2 s is O or 1; X is CO or SO_2; Z is O, S or NR , wherein R is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_3-s-cycloaUc(en)yl-$C_{ι-6}$-alk(en/yn)yl, hydroxy-$C_{ι-6}$-alk(en/yn)yl and hydroxy-C_{3-8}-cycloalk(en)yl; q is O or 1; 1 1 ' R and R are independently selected from the group consisting of hydrogen, $C_{ι\_\ 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-$C_{1.6}$-alk(en/yn)yl, acyl, hydroxy-$C_{ι-6}$-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-$C_{1\_.6}$-alk(en/yn)yl and halo-$C_{3.8}$-cycloalk(en)yl; R is selected from the group consisting of hydrogen, halogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-$C_{ι-6}$-alk(en yn)yl, Ar, Ar-$C_{ι-6}$- alk(en yn)yl, Ar-C_{3-8}-cycloalk(en)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy- C_{3-8}-cycloalk(en)yl, halo-$C_{ι-6}$-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and cyano; provided that when R^2 is halogen or cyano then s is 0; when s is 1 and U is NR^2 then $R^{2'}$ is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C $_{-8}$-cycloalk(en)yl, C $_{.8}$-cycloalk(en)yl-C_{1-6}- alk(en/yn)yl, Ar, Ar-C_{1-6}-alk(en/yn)yl, Ar-$C_{3.8}$-cycloalk(en)yl, acyl, hydroxy-C^ $_6$-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl and halo-C_{3-8}- cycloalk(en)yl; or R and R together form a 5-8 membered saturated or unsaturated ring which optionally contains one further heteroatom; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en yn)yl, Ar, Ar-C_{1-6}-alk(en/yn)yl, Ar-C_{3-8}- cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, halo-Ci- $_6$-alk(en yn)yl and halo-C_{3-}s-cycloalk(en)yl; and Y is selected from groups according to a formula selected from the group consisting of:



[0238] wherein, the line represents a bond attaching the group represented by Y to the nitrogen atom; W is O or S; a is 0, 1, 2 or 3; h is 0, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is O, 1, 2, 3, 4 or 5; is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; and each R^5 is independently selected from the group consisting of a C_{1-6}- alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, Ar, Cs-s-cycloall^ei^yl-Ci-e-all^en/^yl, Ar- C_{1-6}-alk(en/yn)yl, acyl, C_{1-6}-alk(an/en/yn)yloxy, halogen, halo-C_{1-6}-alk(en/yn)yl, -CO-$NR^6R^{6'}$, cyano, nitro, -$NR^7R^{7'}$, -S-R^8, -SO_2R^8 and SO_2OR^8, or two substituents together form a 5-8 membered saturated or unsaturated ring which optionally contains one or two heteroatoms; R^6 and R^6 are independently selected from the group consisting of hydrogen, $C_{\backslash.\ 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, $C_{j.\ 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, Cs-s-cycloall^en l- -e-all^en/yn l, Ar and acyl; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and -NR^9R^9 ; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, $Q._{\ 6}$-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en yn)yl; with the provisos that when R^5 is SO_2OR^8 then R^8 is not -$NR^9R^{9'}$ and when R^5 is SO_2R^8 , then R^s is not a hydrogen atom; or salts thereof for increasing ion flow in a potassium channel of a mammal such as a human.

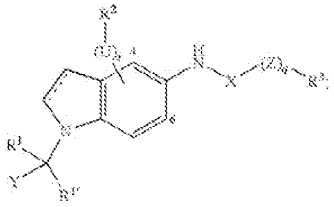
Formula 12

[0239] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 12. Such compounds are described in

International Publication No. WO2009015667A1, published February 5, 2009, and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; International Publication No. WO2004096767A1, published November 11, 2004 and corresponding to International Application No. PCT/DK2004/000283 filed April 23, 2004; US Publication No. US20060264496A1 published November 23, 2006 and corresponding to US Application No. 10/551,738 filed April 23, 2003; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 12, these references incorporated by reference herein control.

[0240] In an embodiment, the Kv7 channel activator is a compound according to formula 12:

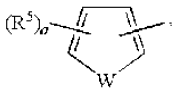
Formula 12

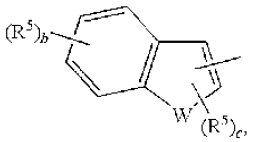


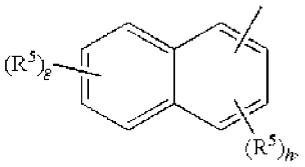
wherein, the dotted line represents an optional bond; R^1 and $R^{1'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^1 and $R^{1'}$ together with the carbon atom to which they are attached form a 3-8 membered saturated or unsaturated ring that optionally contains 1 or 2 heteroatoms; s is 0 or 1; U is O, NR^{11}, S, SO_2, SO_2NR^{11}, CO—O or CO—NR^{11}; wherein: R^{11} is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycl oal k(en)yl, and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^2 and $R^{2'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; R^2 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-

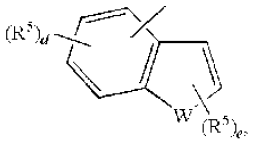
alk(en/yn)yl, —NO_2, $NR^{10}R^{10'}$—C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl and $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{10} and $R^{10'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-Cl—6-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{10} and $R^{10'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; with the proviso that; when R^2 is NO_2, halogen or cyano, then s is 0; and when R^2, R^2 is a hydrogen atom or acyl and s is 1, then U is NR^{11}, O or S; wherein the group —$(U)_s$—R^2 is linked to position 4 or 6 of the indole or indoline; q is 0 or 1; Z is O or S; X is CO or SO_2; with the proviso that when q is 0, then X is SO_2; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar-heterocycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, Ar—C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-heterocycloalk(en)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-heterocycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-heterocycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl-Ar, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-heterocycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, cyano-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl, acyl-C_{3-8}-cycloalk(en)yl, acyl-heterocycloalk(en)yl, acyl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, —$NR^{12}R^{12'}$, optionally substituted $NR^{12}R^{12'}$—C_{1-6}-alk(en/yn)yl,

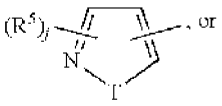
optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl, and optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein: R^{12} and $R^{12'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^{12} and $R^{12'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring that optionally contains 1, 2 or 3 further heteroatoms; with the proviso that when R^3 is $NR^{12}R^{12'}$, then q is 0; and Y represents a group of formula from the group:

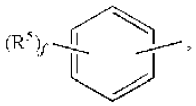


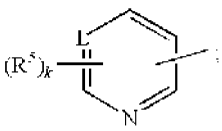












wherein: the line represents a bond attaching the group represented by Y to the carbon atom; W is O or S; T is N, NE or O; L is N, C or CH; a is 0, 1, 2 or 3; b is 0, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is 0, 1, 2, 3, 4 or 5; g is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; j is 0, 1, 2 or 3; with the provisos that: when T is a nitrogen atom, then j is 0, 1, 2 or 3; and when T

is NH or an oxygen atom, then j is 0, 1 or 2; k is 0, 1, 2, 3 or 4; and each R^5 is independently selected from the group consisting of a C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar-thio, Ar-oxy, acyl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —CO—$NR^6R^{6'}$, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —$NR^7R^{7'}$, —S—R^8 and —SO_2R^8; or two adjacent R^5 substituents together with the aromatic group to which they are attached form a 4-8 membered ring that optionally contains one or two heteroatoms; wherein: R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and acyl; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and —$NR^9R^{9'}$; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; provided that when R^8 is —$NR^9R^{9'}$, then R^5 is not —S—R^8, or a pharmaceutically acceptable salt thereof. with the proviso that the compound of formula I is not: N-[1-(phenylmethyl)-1H-indol-5-yl]-Methanesulfonamide; N-[1-[(4-fluorophenyl)methyl]-1H-indol-5-yl]-Methanesulfonamide; N-[2,3-dihydro-1-(phenylmethyl)-1H-indol-5-yl]-Methanesulfonamide; N-[1-(phenylmethyl)-1H-indol-5-yl]-N′-4-quinolinyl-Urea; N-[1-(phenylmethyl)-1H-indol-5-yl]-N′-4-quinolinyl-Urea; or 1-(1-benzyl-5-indolinyl)-3-phenyl-Urea; or salts thereof.

[0241] In further embodiments, least one of R^1 or $R^{1'}$ is a hydrogen atom.

[0242] In further embodiments, R^1 and $R^{1'}$ are hydrogen atoms.

[0243] In further embodiments, s is 0.

[0244] In further embodiments, s is 1.

[0245] In further embodiments, R^2 is a hydrogen atom.

[0246] In further embodiments, R^2 is NO_2 or a halogen atom.

[0247] In further embodiments, U is NR^{11}.

[0248] In further embodiments, R^{11} is a hydrogen atom.

[0249] In further embodiments, X is CO.

[0250] In further embodiments, X is SO_2.

[0251] In further embodiments, q is 0.

[0252] In further embodiments, q is 1.

[0253] In further embodiments, Z is an oxygen atom.

[0254] In further embodiments, R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl and —$NR^{12}R^{12'}$; with the proviso that when R^3 is $NR^{12}R^{12'}$ then q is 0.

[0255] In further embodiments, R^3 is $NR^{12}R^{12'}$, q is 0 and R^{12} and $R^{12'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, Ar and Ar—C_{1-6}-alk(en/yn)yl, or R^{12} and $R^{12'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring which optionally contains 1, 2 or 3 further heteroatoms.

[0256] In further embodiments, each R^5 is independently selected from the group consisting of C_{1-6}-alk(en/yn)yl, Ar, Ar-thio, Ar-oxy, halogen and halo-C_{1-6}-alk(en/yn)yl or two adjacent R^5 together with the aromatic group to which they are attached form a 4-8 membered ring which optionally contains one or two heteroatoms.

[0257] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[4-Chloro-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[4-Chloro-1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; [1-(4-Fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-carbamic acid propyl ester; N-[1-(4-Fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-C-phenyl-methanesulfonamide; 4-Fluoro-N-[1-(4-fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-benzamide; N-[1-(4-Fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(4-Fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-2-thiophen-2-ylacetamide; N-[1-(4-Fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; 3-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-1,1-diisopropylurea; Morpholine-4-carboxylic acid [1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-amide; Pyrrolidine-1-carboxylic acid [1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-amide; [1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-carbamic acid 2-benzyloxyethyl ester; 3-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-1-methyl-1-propylurea; [1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-carbamic acid tert-butyl ester; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-C-phenyl-methanesulfonamide; Butane-1-sulfonic acid [1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-amide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-4-fluorobenzamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-

5-yl]-2,2-dimethylpropionamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-phenoxyacetamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; Cyclopentanecarboxylic acid [1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-amide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-thiophen-2-ylacetamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-isonicotinamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-4-dimethylaminobenzamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-6-trifluoromethylnicotinamide; 1-tert-Butyl-3-[1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-urea; 1-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3-ethyl urea; 1-Benzyl-3-[1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-urea; 1-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3-phenethyl urea; 1-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3-thiophen-2-ylurea; 1-[1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3-thiophen-3-ylurea; [1-(5-Chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-carbamic acid propyl ester; 2,2-Dimethyl-N-[6-nitro-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-propionamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-6-nitro-2,3-dihydro-1H-indol-5-yl]-2,2-dimethylpropionamide; 2-(4-Fluorophenyl)-N-[6-nitro-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-6-nitro-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-[1-(5-Chlorothiophen-2-ylmethyl)-6-nitro-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[6-Amino-1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[6-Amino-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-2,2-dimethylpropionamide; N-[6-Amino-1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2,2-dimethylpropionamide; N-[6-Amino-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-[6-Amino-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide, N-[6-Amino-1-(4-fluorobenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[6-Amino-1-(3-fluoro-4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(5-Chlorothiophen-2-ylmethyl)-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[6-Bromo-1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[6-Bromo-1-(5-chlorothiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(4-Chlorobenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; 3,3-Dimethyl-N-[1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-

yl]-butyramide; N-[1-(4-Isopropylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(3-Fluoro-4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(6-Chlorobenzo[1,3]dioxol-5-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide, N-[1-(3,5-Dimethyl-1-phenyl-1H-pyrazol-4-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-[1-(2-Chloro-5-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; N-{1-[5-(4-Chlorophenoxy)-1,3-dimethyl-1H-pyrazol-4-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-3,3-dimethylbutyramide; 3,3-Dimethyl-N-[1-(6-p-tolyloxy-pyridin-3-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; N-{1-[6-(4-Chlorophenyl sulfanyl)-pyridin-3-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-3,3-dimethylbutyramide, N-{1-[6-(4-Cyanophenoxy)-pyridin-3-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-3,3-dimethylbutyramide; 3,3-Dimethyl-N-[1-(6-trifluoromethylpyridin-3-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; 3,3-Dimethyl-N-[1-(3-methyl-benzo[b]thiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; N-[1-(6-Fluoro-4H-benzo[1,3]dioxin-8-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-3,3-dimethylbutyramide; 3,3-Dimethyl-N-[1-(6-phenoxypyridin-3-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; 3,3-Dimethyl-N-[1-(3-methyl-5-phenyl-isoxazol-4-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide, N-(1-Benzo[b]thiophen-2-ylmethyl-2,3-dihydro-1H-indol-5-yl)-3,3-dimethylbutyramide; N-{1-[1-(4-Fluorophenyl)-5-methyl-1H-pyrazol-4-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-3,3-dimethylbutyramide; 3,3-Dimethyl-N-[1-(5-methyl thiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; 3,3-Dimethyl-N-[1-(4-pyrrol-1-yl-benzyl)-2,3-dihydro-1H-indol-5-yl]-butyramide; N-[1-(4-Chlorobenzyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; 2-(4-Fluorophenyl)-N-[1-(4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; 2-(4-Fluorophenyl)-N-[1-(4-isopropylbenzyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; 2-(4-Fluorophenyl)-N-[1-(3-fluoro-4-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; N-[1-(6-Chlorobenzo[1,3]dioxol-5-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-[1-(3,5-Dimethyl-1-phenyl-1H-pyrazol-4-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-[1-(2-Chloro-5-trifluoromethylbenzyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; N-{1-[5-(4-Chlorophenoxy)-1,3-dimethyl-1H-pyrazol-4-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-2-(4-fluorophenyl)-acetamide; N-{1-[6-(4-Cyanophenoxy)-pyridin-3-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-2-(4-fluorophenyl)-acetamide; 2-(4-Fluorophenyl)-N-[1-(3-methyl-benzo[b]thiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; N-[1-(6-Fluoro-4H-benzo[1,3]dioxin-8-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-2-(4-fluorophenyl)-acetamide; 2-(4-Fluorophenyl)-N-[1-(6-phenoxypyridin-3-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-

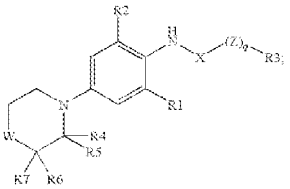
acetamide; N-(1-Benzo[b]thiophen-2-ylmethyl-2,3-dihydro-1H-indol-5-yl)-2-(4-fluorophenyl)-acetamide; 2-(4-Fluorophenyl)-N-{1-[1-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-ylmethyl]-2,3-dihydro-1H-indol-5-yl}-acetamide; 2-(4-Fluorophenyl)-N-[1-(5-methylthiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; 2-(4-Fluorophenyl)-N-[1-(4-pyrrol-1-yl-benzyl)-2,3-dihydro-1H-indol-5-yl]-acetamide; and pharmaceutically acceptable salts thereof.

Formula 13

[0258] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 13. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2009, and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 13, these references incorporated by reference herein control.

[0259] In an embodiment, the Kv7 channel activator is a compound according to formula 13.

Formula 13



wherein: q is 0 or 1; W is O or S; X is CO; Z is O; R1 is selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy; R2 is selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, optionally substituted phenyl and optionally substituted pyridyl; wherein the phenyl and pyridyl are optionally substituted with one or more substituents independently being halogen, C_{1-6}-alk(en/yr)yl, C_{3-8}-cycloalk(en)yl or C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; R3 is selected from the group consisting of C_{1-10}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl,

Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; and each of R4, R5, R6 and R7 is independently selected from the group consisting of hydrogen and Ar; as the free base or a salt thereof.

[0260] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-2-(4-fluoro-phenyl)-acetamide; 2-Cyclopentyl-N-(2-bromo-6-trifluoromethyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-3-cyclopentyl-propionamide; N-(2-Chloro-6-cyano-4-morpholin-4-yl-phenyl)-3-cyclohexyl-propionamide; 2-Cyclopentyl-N-(2,6-dimethyl-4-thiomorpholin-4-yl-phenyl)-acetamide; 2-Cyclopentyl-N-[2,6-dimethyl-4-(2-phenyl-morpholin-4-yl)-phenyl]-acetamide; 2-Cyclopentyl-N-[2,6-dimethyl-4-(2-phenyl-thiomorpholin-4-yl)-phenyl]-acetamide; 2-Cyclopentyl-N-[2,6-dimethyl-4-(3-pyridin-3-yl-thiomorpholin-4-yl)-phenyl]-acetamide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[2-(4-trifluoromethyl-phenyl)-thiomorpholin-4-yl]-phenyl}-acetamide; N-{4-[2-(2-Chloro-phenyl)-thiomorpholin-4-yl]-2,6-dimethyl-phenyl}-2-cyclopentyl-acetamide; 2-Bicyclo[2.2.1]hept-2-yl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 2-Cyclohexyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 3-(3,4-Difluoro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-propionamide; 2-Cyclopentyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; (2,6-Dimethyl-4-morpholin-4-yl-phenyl)-carbamic acid butyl ester; 2-(4-Chloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 2,3-Dihydro-benzofuran-2-carboxylic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 3-Cyclohexyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-propionamide; 3-Cyclopentyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-propionamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-(4-fluoro-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-thiophen-2-yl-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide; Hexanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 2-Cycloheptyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; (2,6-Dimethyl-4-morpholin-4-yl-phenyl)-carbamic acid benzyl ester; (2,6-Dimethyl-4-morpholin-4-yl-phenyl)-carbamic acid 2-chloro-benzyl ester; 3,5,5-Trimethyl-hexanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; Octanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; Heptanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-phenyl-acetamide; 2-(3,4-Dichloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 2-(4-Allyloxy-3-chloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-(3-trifluoromethyl-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-naphthalen-2-yl-acetamide; 3-(3-

Chloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-propionamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-(3,4-dimethyl-phenyl)-acetamide; 2-(3-Bromo-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 2-(3-Chloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-p-tolyl-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-m-tolyl-acetamide; 2-(3,4-Difluoro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2,6-Dimethyl-4-morpholin-4-yl-phenyl)-2-(3-fluoro-phenyl)-acetamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-3-cyclohexyl-propionamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-2-(3-fluoro-phenyl)-acetamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-propionamide; N-(2-Bromo-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-butyramide; N-(2-Chloro-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-2-(3-fluoro-phenyl)-acetamide; N-(2-Chloro-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-2-cyclopentyl-acetamide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[2-(4-trifluoromethyl-phenyl)-morpholin-4-yl]-phenyl}-acetamide; N-{4-[2-(2-Chloro-phenyl)-morpholin-4-yl]-2,6-dimethyl-phenyl}-2-cyclopentyl-acetamide; 2-Cyclopentyl-N-{4-[2-(4-fluoro-phenyl)-morpholin-4-yl]-2,6-dimethyl-phenyl}-acetamide; 2-(2-Chloro-phenyl)-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; Pentanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 4-Methyl-pentanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 2-Cyclopent-2-enyl-N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-acetamide; 5-Methyl-hexanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 3-Methyl-pentanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; Hex-5-enoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 3-Ethyl-pentanoic acid (2,6-dimethyl-4-morpholin-4-yl-phenyl)-amide; 2-Cyclopentyl-N-(4-morpholin-4-yl-2-pyridin-3-yl-6-trifluoromethyl-phenyl)-acetamide; 2-Cyclopentyl-N-(5-morpholin-4-yl-3-trifluoromethyl-biphenyl-2-yl)-acetamide; 2-Cyclopentyl-N-(4′-fluoro-5-morpholin-4-yl-3-trifluoromethyl-biphenyl-2-yl)-acetamide; 2-Cyclopentyl-N-(4′-methyl-5-morpholin-4-yl-3-trifluoromethyl-biphenyl-2-yl)-acetamide, 2-Cyclopentyl-N-(3′-methyl-5-morpholin-4-yl-3-trifluoromethyl-biphenyl-2-yl)-acetamide; 2-Cyclopentyl-N-(3′,4′-difluoro-5-morpholin-4-yl-3-trifluoromethyl-biphenyl-2-yl)-acetamide; 2-(4-Fluoro-phenyl)-N-(4-morpholin-4-yl-2-pyridin-3-yl-6-trifluoromethyl-phenyl)-acetamide; 2-Cyclopentyl-N-(2,6-diethyl-4-morpholin-4-yl-phenyl)-acetamide; 2-Cyclopentyl-N-(2,6-diisopropyl-4-morpholin-4-yl-phenyl)-acetamide; 2-Cyclopentyl-N-(2,6-difluoro-4-morpholin-4-yl-phenyl)-acetamide; Hexanoic acid (2,6-difluoro-4-morpholin-4-yl-phenyl)-amide; N-(2,6-Difluoro-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide; N-(2,6-Difluoro-4-morpholin-4-yl-phenyl)-2-(3-fluoro-phenyl)-acetamide; 2-Cyclopent-2-enyl-N-(2,6-difluoro-4-morpholin-4-yl-phenyl)-

acetamide; 2-Bicyclo[2.2.1]hept-2-yl-N-(2,6-difluoro-4-morpholin-4-yl-phenyl)-acetamide; 2-Bicyclo[2.2.1]hept-2-yl-N-(2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-acetamide; 5-Methyl-pentanoic acid (2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-amide; 5-Methyl-hexanoic acid (2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-amide; 2-Cyclopent-2-enyl-N-(2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-acetamide; 2-Cyclopentyl-N-(2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-acetamide; Hexanoic acid (2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-amide; 3,3-Dimethyl-N-(2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-butyramide; 2-(3,4-Difluoro-phenyl)-N-(2-methyl-4-morpholin-4-yl-6-trifluoromethyl-phenyl)-acetamide; Hexanoic acid (2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-amide; 2-Cyclopentyl-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; N-(2-Methoxy-6-methyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide; 2-(3,4-Difluoro-phenyl)-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; 2-Cyclopent-2-enyl-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; 2-(3-Fluoro-phenyl)-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; 2-Bicyclo[2.2.1]hept-2-yl-N-(2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-acetamide; 4-Methyl-pentanoic acid (2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-amide; 5-Methyl-Hexanoic acid (2-methoxy-6-methyl-4-morpholin-4-yl-phenyl)-amide; N-(2-Chloro-6-methyl-4-morpholin-4-yl-phenyl)-2-(3-fluoro-phenyl)-acetamide; and N-(2-Chloro-6-methyl-4-morpholin-4-yl-phenyl)-2-cyclopentyl-acetamide; as the free base or a pharmaceutically acceptable salt thereof.

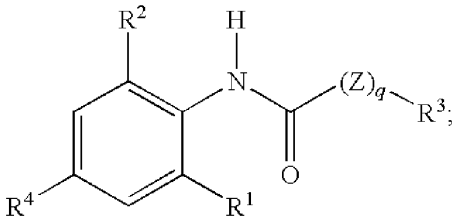
Formula 14

[0261] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 14. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2008 and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; International Publication No. WO2006029623A1, published March 23, 2006 and corresponding to International Application No. PCT/DK2005/000560 filed September 2, 2005; US Patent No. 7,601,870, issued October 13, 2009 and corresponding to US Application No. 11/312,664 filed December 20, 2005; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein.

In the case of any conflict of terminology in the context of Formula 14, these references incorporated by reference herein control.

[0262] In an embodiment, the Kv7 channel activator is a compound according to formula 14:

Formula 14



wherein, Z is O or S; q is 0 or 1; each of R^1 and R^2 is independently selected from the group consisting of halogen, cyano, amino, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl, Aryl, Heteroaryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, and C_{3-8}-heterocycloalk(en)yloxy; R^3 is selected from the group consisting of C_{1-8}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Heteroaryl-C alk(en/yn)yl, Heteroaryl-C_{3-8}-cycloalk(en)yl, Heteroaryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, amino-C_{1-6}-alk(en/yn)yl, amino-C_{3-8}-cycloalk(en)yl, amino-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; and R^4 is selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl, Aryl, Heteroaryl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, NR^5R^6 and R^7NH—C_{1-6}-alk(en/yn)yl; wherein: R^5 and R^6 are independently selected from the group consisting of hydrogen, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Heteroaryl-C_{1-6}-alk(en/yn)yl, Heteroaryl-C_{3-8}-cycloalk(en)yl and Heteroaryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, with the proviso that R^5 and R^6 are not hydrogen at the same time; and R^7 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl,

Aryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl and Heteroaryl; or a pharmaceutically acceptable salt thereof.

[0263] In further embodiments, the Kv7 channel activator is selected from the group consisting of: Hexanoic acid (4-bromo-2,6-dimethyl-phenyl)-amide; N-(4-Bromo-2,6-dimethyl-phenyl)-2-(4-fluoro-phenyl)-acetamide; N-(2-Bromo-4,6-dimethyl-phenyl)-2-(4-fluoro-phenyl)-acetamide; N-(2-Bromo-4,6-dimethyl-phenyl)-3,3-dimethyl-butyramide; N-(2-Bromo-4,6-dimethyl-phenyl)-2-cyclopentyl-acetamide; N-(2-Bromo-4,6-dichloro-phenyl)-3,3-dimethyl-butyramide; N-(2-Bromo-4,6-dichloro-phenyl)-2-(4-fluoro-phenyl)-acetamide; N-(2-Bromo-4,6-dichloro-phenyl)-2-cyclopentyl-acetamide; Heptanoic acid (4-bromo-2,6-dimethyl-phenyl)-amide; Cyclohexanecarboxylic acid (4-bromo-2,6-dimethyl-phenyl)-amide; N-(4-Bromo-2,6-dimethyl-phenyl)-2-thiophen-2-yl-acetamide; 2-Phenyl-cyclopropanecarboxylic acid (4-bromo-2,6-dimethyl-phenyl)-amide; N-(4-Bromo-2,6-dimethyl-phenyl)-2-(4-chloro-phenyl)-acetamide; Pentanoic acid (4-bromo-2,6-dimethyl-phenyl)-amide; Octanoic acid (4-bromo-2,6-dimethyl-phenyl)-amide; N-(4-Bromo-2,6-dimethyl-phenyl)-2-cyclopentyl-acetamide; 2-Bicyclo[2.2.1]kept-2-yl-N-(2,4-difluoro-6-morpholin-4-yl-phenyl)-acetamide; (S)-2-Amino-N-{2,6-dimethyl-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-3- methyl-butyramide; (S)-2-Amino-4-methyl-pentanoic acid {2,6-dimethyl-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-amide; (4-Bromo-2,6-dimethyl-phenyl)-carbamic acid ethyl ester; (4-Bromo-2,6-dimethyl-phenyl)-carbamic acid propyl ester; N-(2-Amino-4-bromo-6-methyl-phenyl)-3,3-dimethyl-butyramide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[2-(4-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-phenyl}-acetamide; N-(4-Azepan-1-yl-2,6-dimethyl-phenyl)-2-cyclopentyl-acetamide; 2-Cyclopentyl-N-(2,6-dimethyl-4-pyrrol-1-yl-phenyl)-acetamide; N-(3′-Amino-3,5-dimethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(4′-Dimethylamino-3,5-dimethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(2,4-Dimethyl-6-quinolin-3-yl-phenyl)-2-(4-fluoro-phenyl)-acetamide; 2-(4-Fluoro-phenyl)-N-(4′-hydroxy-3′-methoxy-3,5-dimethyl-biphenyl-2-yl)-acetamide; 2-(4-Fluoro-phenyl)-N-(3′-hydroxy-3,5-dimethyl-biphenyl-2-yl)-acetamide; 2-(4-Fluoro-phenyl)-N-(2′-methanesulfonylamino-3,5-dimethyl-biphenyl-2-yl)-acetamide; N-(4′-Isopropyl-3,5-dimethyl-biphenyl-2-yl)-3,3-dimethyl-butyramide; 2-Cyclopentyl-N-(3,5-dimethyl-biphenyl-2-yl)-acetamide; N-(4′-Fluoro-3,5-dimethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(3,5-Dimethyl-3′,5′-bis-trifluoromethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(3′-Acetylamino-3,5-dimethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; 2-(4-Fluoro-phenyl)-N-(2′-methoxy-3,5-dimethyl-biphenyl-2-yl)-acetamide; N-

(3,5-Dimethyl-4′-vinyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(3′-Cyano-3,5-dimethyl-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-(3,5-Dimethyl-3′-trifluoromethoxy-biphenyl-2-yl)-2-(4-fluoro-phenyl)-acetamide; N-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-4,6-dimethyl-phenyl]-2-(4-fluoro-phenyl)-acetamide; N-[2,4-Dimethyl-6-(2,2,5-trimethyl-2,3-dihydro-benzofuran-7-yl)-phenyl]-2-(4-fluoro-phenyl)-acetamide; N-[2,6-Dimethyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-acetamide; N-{2,6-Dimethyl-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-acetamide; {4-[(5-Chloro-thiophen-2-ylmethyl)-amino]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; [4-(4-Fluoro-benzylamino)-2,6-dimethyl-phenyl]-carbamic acid propyl ester; [2,6-Dimethyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-carbamic acid propyl ester; [4-(3-Fluoro-4-trifluoromethyl-benzylamino)-2,6-dimethyl-phenyl]-carbamic acid propyl ester; {2,6-Dimethyl-4-[(4-methyl-2-phenyl-pyrimidin-5-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {2,6-Dimethyl-4-[(6-p-tolyloxy-pyridin-3-ylmethyl)-amino]-phenyl}-carbamic acid propyl ester; {4-[(6-Methoxy-pyridin-3-ylmethyl)-amino]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; {4-[(3-Fluoro-4-trifluoromethyl-benzyl)-methyl-amino]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; 2-Cyclopentyl-N-[2,6-dimethyl-4-(4-trifluoromethyl-benzylamino)-phenyl]-acetamide 2-Cyclopentyl-N-{2,6-dimethyl-4-[methyl-(4-trifluoromethyl-benzyl)-amino]-phenyl}-acetamide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[(6-trifluoromethyl-pyridin-3-ylmethyl)-amino]-phenyl}-acetamide; N-{2,6-Dimethyl-4-[(6-trifluoromethyl-pyridin-3-ylmethyl)-amino]-phenyl}-3,3-dimethyl-butyramide; N-{2-Bromo-4-[(5-chloro-thiophen-2-ylmethyl)-amino]-6-trifluoromethyl-phenyl}-3-cyclohexyl-propionamide; {4-[(3-Fluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-carbamic acid ethyl ester; {2,6-Dimethyl-4-[(4-trifluoromethyl-phenylamino)-methyl]-phenyl}-carbamic acid ethyl ester; 2-Cyclopentyl-N-{4-[(3-fluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-acetamide; N-{4-[(3-Chloro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-2-cyclopentyl-acetamide; 2-Cyclopentyl-N-{4-[(3-methoxy-phenylamino)-methyl]-2,6-dimethyl-phenyl}-acetamide; N-{4-[(4-Chloro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-2-cyclopentyl-acetamide; 2-Cyclopentyl-N-{4-[(3,4-difluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-acetamide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[(4-trifluoromethyl-phenylamino)-methyl]-phenyl}-acetamide; 2-Cyclopentyl-N-[2,6-dimethyl-4-(p-tolylamino-methyl)-phenyl]-acetamide; 2-Cyclopentyl-N-{2,6-dimethyl-4-[(3-trifluoromethyl-phenylamino)-methyl]-phenyl}-acetamide; 2-Cyclopentyl-N-{-4-[(3,5-difluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-acetamide; {4-[(4-Fluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; {4-[(4-Chloro-phenylamino)-

methyl]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; {2,6-Dimethyl-4-[(4-trifluoromethyl-phenylamino)-methyl]-phenyl}-carbamic acid propyl ester; {4-[(3,5-Difluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; {4-[(3-Fluoro-phenylamino)-methyl]-2,6-dimethyl-phenyl}-carbamic acid propyl ester; N-(4-Bromo-2-methyl-6-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide; {4-[(4-Methoxyphenylamino)-methyl]-2,6-dimethylphenyl}-carbamic acid propyl ester; (R)-2-Amino-4-methylpentanoic acid [2,6-dimethyl-4-(4-trifluoromethylbenzylamino)-phenyl]-amide; Pentanoic acid (4-[(4-chlorophenylamino)-methyl]-2,6-dimethylphenyl)-amide; 2-(4-Chlorophenyl)-N-[4-(4-chlorophenylamino)-methyl]-2,6-dimethyl phenyl)-acetamide; {2,6-Dimethyl-4-[(4-trifluoromethylphenylamino)-methyl]-phenyl}-carbamic acid 2-methoxyethyl ester; N-{4-[(5-Chloro-pyridin-2-ylamino)-methyl]-2,6-dimethylphenyl}-2-cyclopentylacetamide; 2-Cyclopentyl-N-{4-[(2,6-dichloro-pyridin-4-ylamino)-methyl]-2,6-dimethylphenyl}-acetamide; N-{2-Chloro-6-methyl-4-[(6-trifluoromethyl-pyridin-3-ylmethyl)-amino]-phenyl}-2-(3-fluoro-phenyl)-acetamide; N-[2-Chloro-6-trifluoromethyl-4-(4-trifluoromethylbenzylamino)-phenyl]-2-cyclopentylacetamide; [2-Amino-6-methyl-4-(4-trifluoromethylbenzylamino)-phenyl]-carbamic acid ethyl ester; 3,3-Dimethyl-N-{2-methyl-6-morpholin-4-yl-4-(4-trifluoromethylbenzylamino)-phenyl}-butyramide; 2-Cyclopentyl-N-{2,6-dichloro-4-[(4-fluoro-phenylamino)-methyl]-phenyl}-acetamide; 2-Cyclopentyl-N-{2,6-dichloro-4-[(5-trifluoromethylpyridin-2-ylamino)-methyl]-phenyl}-acetamide; and pharmaceutically acceptable salts thereof.

[0264] In further embodiments, Z is O or S; q is 0; R^1 and R^2 are each independently selected from the group consisting of halogen, cyano, amino, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy; R^3 is selected from the group consisting of C_{1-8}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, amino-C_{1-6}-alk(en/yn)yl, amino-C_{3-8}-cycloalk(en)yl, amino-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; and R^4 is selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-

alk(en/yn)yl, NR^5R^6 and R^7NH—C_{1-6}-alk(en/yn)yl; wherein: R^5 and R^6 are each independently selected from the group consisting of hydrogen, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, and C_{3-8}-cycloalk(en)yl-C_{1-6}alk(en/yn)yl, with the proviso that R^5 and R^6 can not both be hydrogen; and R^7 is selected from the group consisting of C_{1-6}-alk(en/yn)yl; C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, and Aryl-C_{3-8}-cycloalk(en)yl; with the proviso that the compound of formula I is not N-(4-Bromo-2,6-dimethyl-phenyl)-2-cyclopentyl-acetamide; or a pharmaceutically acceptable salt thereof.

[0265] In further embodiments, R^1 and R^2 are each independently selected from the group consisting of halogen, amino, C_{1-6}-alk(en/yn)yl, Aryl, and halo-C_{1-6}-alk(en/yn)yl.

[0266] In further embodiments, R^3 is selected from the group consisting of C_{1-8}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, and amino-C_{1-6}-alk(en/yn)yl.

[0267] In further embodiments, R^4 is selected from the group consisting of halogen, C_{1-6}-alk(en/yn)yl, NR^5R^6 and R^7NH—C_{1-6}-alk(en/yn)yl, wherein R^5, R^6 and R^7 are as previously defined.

[0268] In further embodiments, R^4 is NR^5R^6, wherein R^5 and R^6 are independently selected from the group consisting of hydrogen, Aryl-C_{1-6}-alk(en/yn)yl, and C_{1-6}-alk(en/yn)yl, with the proviso that R^5 and R^6 cannot both be hydrogen.

[0269] In further embodiments, R^4 is R^7NH—C_{1-6}-alk(en/yn)yl, wherein R^7 is Aryl.

[0270] In further embodiments, any Aryl is optionally substituted with one or more substituents independently selected from the group consisting of amino, halogen, cyano, C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, hydroxy, C_{1-6}-alk(en/yn)yloxy, halo-C_{1-6}-alk(en/yn)yloxy, di-(C_{1-6}-alk(en/yn)yl)amino, C_{1-6}-alk(en/yn)yl-CO—NH— and C_{1-6}-alk(en/yn)yl-sulfonamide; or two adjacent substituents may together with the Aryl group to which they are attached form a 4-8 membered ring, which is optionally substituted with one or more C_{1-6}-alk(en/yn)yl groups.

[0271] In further embodiments, the Kv7 channel activator is a compound according to formula 14, wherein: Z is O or S; q is 0; R^1 and R^2 are each independently selected from the group consisting of halogen, cyano, amino, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy; R^3 is selected from the group consisting of C_{1-8}-

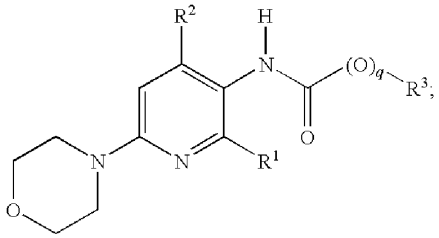
alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, amino-C_{1-6}-alk(en/yn)yl, amino-C_{3-8}-cycloalk(en)yl, amino-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; and R^4 is selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, NR^5R^6 and R^7NH—C_{1-6}-alk(en/yn)yl; wherein: R^5 and R^6 are each independently selected from the group consisting of hydrogen, Aryl-C_{1-6}-alk(en/yn)yl, Aryl-C_{3-8}-cycloalk(en)yl, Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, with the proviso that R^5 and R^6 cannot both be hydrogen; and R^7 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Aryl-C_{1-6}-alk(en/yn)yl, and Aryl-C_{3-8}-cycloalk(en)yl; with the proviso that the compound of formula I is not N-(4-Bromo-2,6-dimethyl-phenyl)-2-cyclopentyl-acetamide; or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier or diluent.

Formula 15

[0272] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 15. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2009 and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; International Publication No. WO2006092143A1, published September 8, 2006 and corresponding to International Application No. PCT/DK2006/000123 filed March 2, 2006; US Patent No. 7,812,020, issued October 12, 2010 and corresponding to US Application No. 11/817,340 filed March 2, 2006; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 15, these references incorporated by reference herein control.

[0273] In an embodiment, the Kv7 channel activator is a compound according to formula 15:

Formula 15



wherein, q is 0 or 1; each of R^1 and R^2 is independently selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy; and R^3 is selected from the group consisting of C_{1-8}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, optionally substituted Aryl-C_{1-6}-alk(en/yn)yl, optionally substituted Aryl-C_{3-8}-cycloalk(en)yl, optionally substituted Aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Heteroaryl-C_{1-6}-alk(en/yn)yl, Heteroaryl-C_{3-8}-cycloalk(en)yl, Heteroaryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, NR^4R^5—C_{1-6}-alk(en/yn)yl, NR^4R^5—C_{3-8}-cycloalk(en)yl NR^4R^5—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein each of R^4 and R^5 is independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; as the free base or a pharmaceutically acceptable salt thereof.

[0274] In further embodiments, the Kv7 channel activator is selected from the group consisting of: (2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-carbamic acid benzyl ester; (2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-carbamic acid 2-chloro-benzyl ester; 2-(4-Chloro-phenyl)-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 2-Phenyl-cyclopropanecarboxylic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-thiophen-2-yl-acetamide; 3-Cyclohexyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-propionamide; (2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-carbamic acid isobutyl ester; 3-(3-Chloro-phenyl)-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-propionamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(3,5-dimethyl-phenyl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-3-p-tolyl-propionamide; 2-(3-Chloro-phenyl)-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-

acetamide; 2-(3,4-Dichloro-phenyl)-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-thiophen-3-yl-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-p-tolyl-acetamide; 2-(3-Bromo-phenyl)-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(3-trifluoromethyl-phenyl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-phenyl-acetamide; 3,5,5-Trimethyl-hexanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; Octanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-naphthalen-2-yl-acetamide; Heptanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(3,4-dimethyl-phenyl)-acetamide; 2-Cyclohex-1-enyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(4-methoxy-3-methyl-phenyl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(4-methoxy-phenyl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-3-(4-methoxy-phenyl)-propionamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-m-tolyl-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(4-fluoro-phenyl)-acetamide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-3,3-dimethyl-butyramide; N-(2,4-Dimethyl-6-morpholin-4-yl-pyridin-3-yl)-2-(3-fluoro-phenyl)-acetamide; 2-Bicyclo[2.2.1]kept-2-yl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 4-Methyl-pentanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; 2-Cyclopent-2-enyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 2-Cyclohexyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 5-Methyl-hexanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; 2-Cyclopentyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-acetamide; 3-Cyclopentyl-N-(2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-propionamide; Hexanoic acid (2,4-dimethyl-6-morpholin-4-yl-pyridin-3-yl)-amide; N-(4-Chloro-2-methoxy-6-morpholin-4-yl-pyridin-3-yl)-2-cyclopentylacetamide; N-(2-Chloro-4-methoxy-6-morpholin-4-yl-pyridin-3-yl)-2-cyclopentylacetamide; N-(2-Chloro-4-methoxy-6-morpholin-4-yl-pyridin-3-yl)-3,3-dimethylbutyramide; N-(4-Chloro-2-methoxy-6-morpholin-4-yl-pyridin-3-yl)-3,3-dimethylbutyramide; N-(4-Chloro-2-methoxy-6-morpholin-4-yl-pyridin-3-yl)-propionamide; and pharmaceutically acceptable salts thereof.

[0275] In further embodiments, q is 0 or 1; R^1 and R^2 each is independently selected from the group consisting of halogen, cyano, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy and C_{3-8}-

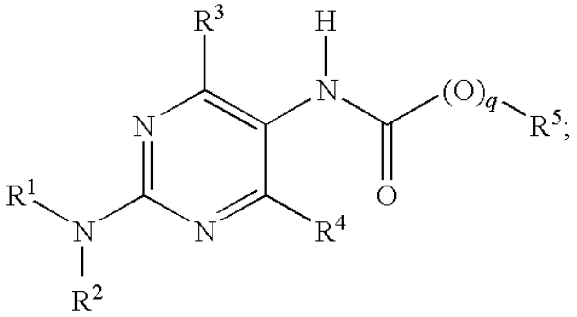
cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy; and R^3 is selected from the group consisting of C_{1-8}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, optionally substituted aryl-C_{1-6}-alk(en/yn)yl, optionally substituted aryl-C_{3-8}-cycloalk(en)yl, optionally substituted aryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-heterocycloalk(en)yl-C_{1-6}-alk(en/yn)yl, heteroaryl-C_{1-6}-alk(en/yn)yl, heteroaryl-C_{3-8}-cycloalk(en)yl, heteroaryl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, NR^4R^5—C_{1-6}-alk(en/yn)yl, NR^4R^5—C_{3-8}-cycloalk(en)yl, NR^4R^5—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, wherein: R^4 and R^5 each is independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl.

Formula 16

[0276] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 16. Such compounds are described in International Publication No. WO2009015667A1, published February 5, 2009 and corresponding to International Application No. PCT/DK2008/050191 filed July 31, 2008; US Publication No. US20100256145A1, published October 7, 2010 and corresponding to US Application No. 12/671,505 filed July 31, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 16, these references incorporated by reference herein control.

[0277] In an embodiment, the Kv7 channel activator is a compound according to formula 16:

Formula 16



wherein: q is 0 or 1; R^1 and R^2 are independently selected from the group consisting of hydrogen and optionally substituted aryl-C_{1-6}-alk(en/yn)yl, provided that R^1 and R^2 are not both hydrogen; or R^1 and R^2 together with the nitrogen to which they are attached form a 5 to 7 membered ring optionally containing a further heteroatom; R^2 and R^4 are independently selected from hydrogen, halogen, cyano, amino, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, halo-C_{1-6}-alk(en/yn)yloxy, halo-C_{3-8}-cycloalk(en)yloxy and halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, provided that R^3 and R^4 are not both hydrogen; and R^5 is selected from the group consisting of C_{1-10}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, optionally substituted aryl-C_{1-6}-alk(en/yn)yl and optionally substituted aryl; as the free base or a pharmaceutically acceptable salt thereof.

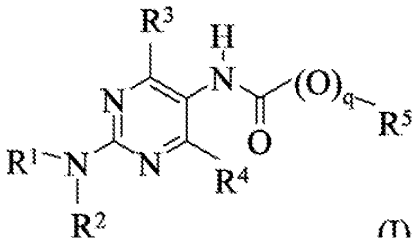
[0278] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-cyclopentylacetamide; N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-3,3-dimethylbutyramide; N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-(4-fluorophenyl)-acetamide; Hexanoic acid [4-amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-amide; N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-(3-chlorophenyl)-acetamide; 2-Cyclopentyl-N-(4,6-dimethyl-2-morpholin-4-yl-pyrimidin-5-yl)-acetamide; N-(4,6-Dimethyl-2-morpholin-4-yl-pyrimidin-5-yl)-3,3-dimethylbutyramide; N-(4,6-Dimethyl-2-morpholin-4-ylpyrimidin-5-yl)-2-(4-fluorophenyl)-acetamide; 2-(3,4-Difluorophenyl)-N-(4,6-dimethyl-2-morpholin-4-ylpyrimidin-5-yl)-acetamide; N-(4,6-Dimethyl-2-morpholin-4-ylpyrimidin-5-yl)-2-(3-fluorophenyl)-acetamide; and Hexanoic acid (4,6-dimethyl-2-morpholin-4-ylpyrimidin-5-yl)-amide; as the free base or a pharmaceutically acceptable salt thereof.

Formula 17

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 17. Such compounds are described in International Publication No. WO2007065449A1, published June 14, 2007 and corresponding to International Application No. PCT/DK2006/050039 filed September 7, 2006; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 17, this reference incorporated by reference herein controls.

[0279] In an embodiment, the Kv7 channel activator is a compound according to formula 17:

Formula 17



(I)

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wherein: q is 0 or 1; R^1 and R^2 are independently selected from the group consisting of hydrogen and optionally substituted aryl-C_{1-6}-alk(en/yn)yl, provided that R^1 and R^2 are not both hydrogen, or R^1 and R^2 together with the nitrogen to which they are attached form a 5 to 7 membered ring optionally containing a further heteroatom;R^3 and R^4 are independently selected from hydrogen, halogen, cyano, amino, C_{1-6}- alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, halo-C_{1-6}-alk(en/yn)yloxy, halo-C_{3-8}-cycloalk(en)yloxy and halo-C_{3-8}-cycloalk(en)yl- C_{1-6}-alk(en/yn)yloxy, provided that R^3 and R^4 are not both hydrogen;R^5 is selected from the group consisting of C_{1-10}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}- alk(en/yn)yl, optionally substituted aryl-C_{1-6}-alk(en/yn)yl and optionally substituted aryl; as the free base or salts thereof.

[0280] In further embodiments, q is 0.

[0281] In further embodiments, q is 1.

[0282] In further embodiments, R^1 and R^2 are independently selected from hydrogen and optionally substituted aryl-C_{1-6}-alk(en/yn)yl, provided that R^1 and R^2 are not both hydrogen.

[0283] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached form a 5 to 7 membered ring optionally containing a further hetero atom.

[0284] In further embodiments, said further hetero atom is oxygen.

[0285] In further embodiments, said ring is a 6 membered ring.

[0286] In further embodiments, said ring is a morpholine ring.

[0287] In further embodiments, R^3 and R^4 are independently selected from amino and C_{1-6}-alk(en/yn)yl, preferably methyl.

[0288] In further embodiments, R^5 is selected from the group consisting of C_{1-10}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, optionally substituted aryl-C_{1-6}-alk(en/yn)yl and optionally substituted aryl.

[0289] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-cyclopentylacetamide, N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-

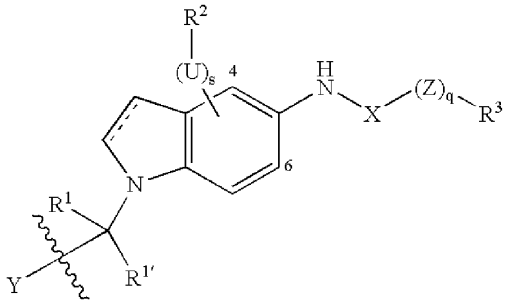
yl]-3,3- dimethylbutyramide, N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-(4- fluorophenyl)-acetamide, Hexanoic acid [4-amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]- amide, N-[4-Amino-6-methyl-2-(4-trifluoromethylbenzylamino)-pyrimidin-5-yl]-2-(3- chlorophenyl)-acetamide, 2-Cyclopentyl-N-(4,6-dimethyl-2-moφholin-4-yl-pyrimidin-5-yl)-acetamide, N-(4,6-Dimethyl-2-moφholin-4-yl-pyrimidin-5-yl)-3,3-dimethylbutyramide, N-(4,6-Dimethyl-2-moφholin-4-ylpyrimidin-5-yl)-2-(4-fluorophenyl)-acetamide, 2-(3,4-Difluorophenyl)-N-(4,6-dimethyl-2-morpholin-4-ylpyrimidin-5-yl)-acetamide, N-(4,6-Dimethyl-2-moφholin-4-ylpyrimidin-5-yl)-2-(3-fluorophenyl)-acetamide and Hexanoic acid (4,6-dimethyl-2-moφholin-4-ylpyrimidin-5-yl)-amide; as the free base or a salt thereof.

Formula 18

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 18. Such compounds are described in International Publication No. WO2004096767A1, published November 11, 2004 and corresponding to International Application No. PCT/DK2004/000283 filed April 23, 2004; US Publication No. US20060264496A1, published November 23, 2006 and corresponding to US Application No. 10/551,783 filed April 23, 2004; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 18, these references incorporated by reference herein control.

[0290] In an embodiment, the Kv7 channel activator is a compound according to formula 18:

Formula 18

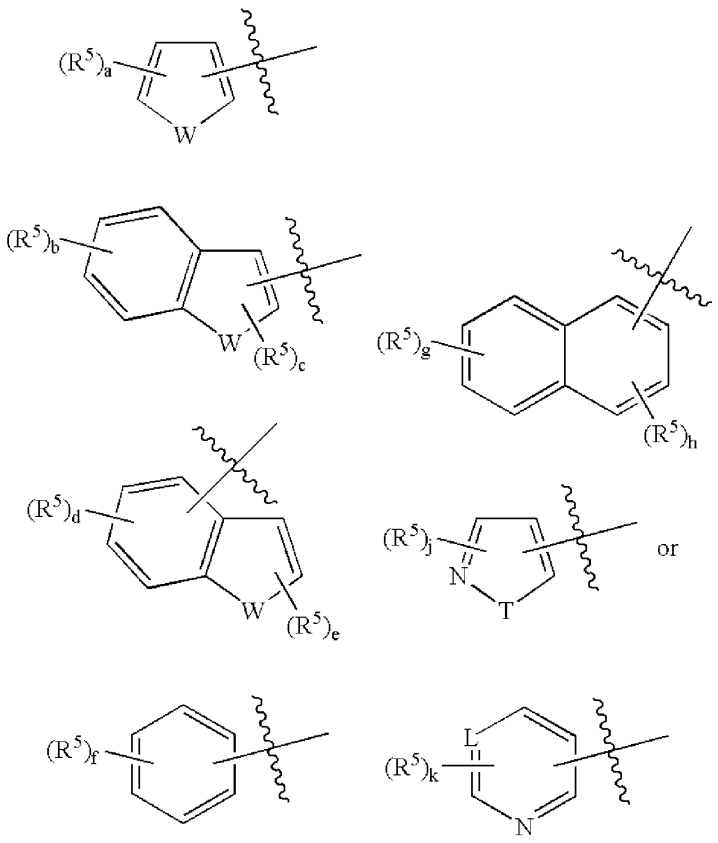


,

wherein, the dotted line represents an optional bond; R^1 and $R^{1'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-}

$_{8}$-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^1 and $R^{1'}$ together with the carbon atom to which they are attached form a 3-8 membered saturated or unsaturated ring which optionally contains 1 or 2 heteroatoms; s is 0 or 1; U is O, NR^{11}, S, SO_2, SO_2NR^{11}, CO—O or CO—NR^{11}; wherein R^{11} is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; or R^2 and R^{11} together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring which optionally contains 1, 2 or 3 further heteroatoms; R^2 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —NO_2, $NR^{10}R^{10'}$—C_{1-6}-alk(en/yn)yl, $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl and $NR^{10}R^{10'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein R^{10} and $R^{10'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, or R^{10} and $R^{10'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring which optionally contains 1, 2 or 3 further heteroatoms; with the proviso that when R^2 is NO_2, halogen or cyano then s is 0; and with the proviso that when R^2 is a hydrogen atom or acyl and s is 1 then U is NR^{11}, O or S; wherein the group —$(U)_s$—R^2 is linked to position 4 or 6 of the indole or indoline; q is 0 or 1; Z is O or S; X is CO or SO_2; with the proviso that q is 0 when X is SO_2; R^3 is selected from the group consisting of C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, heterocycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar-heterocycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, Ar—C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-C_{3-8}-cycloalk(en)yl, C_{1-6}-alk(en/yn)yloxy-heterocycloalk(en)yl, Ar-oxy-C_{1-6}-alk(en/yn)yl, Ar—C_{1-6}-alk(en/yn)yloxy-C_{1-6}-alk(en/yn)yl, C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yloxy-carbonyl-C_{1-6}-

alk(en/yn)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy-carbonyl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-heterocycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, hydroxy-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-heterocycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, halo-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-Ar, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl-Ar, halo-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl-Ar, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-heterocycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, cyano-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl, acyl-C_{3-8}-cycloalk(en)yl, acyl-heterocycloalk(en)yl, acyl-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, acyl-C_{1-6}-alk(en/yn)yl-C_{3-8}-cycloalk(en)yl, acyl-C_{1-6}-alk(en/yn)yl-heterocycloalk(en)yl and —$NR^{12}R^{12'}$, optionally substituted $NR^{12}R^{12'}$—C_{1-6}-alk(en/yn)yl, optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl, optionally substituted $NR^{12}R^{12'}$—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; wherein R^{12} and $R^{12'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar—C_{3-8}-cycloalk(en)yl, Ar—C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, hydroxy-C_{1-6}-alk(en/yn)yl, hydroxy-C_{3-8}-cycloalk(en)yl, hydroxy-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl and cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, or R^{12} and $R^{12'}$ together with the nitrogen atom to which they are attached form a 4-8 membered saturated or unsaturated ring which optionally contains 1, 2 or 3 further heteroatoms; with the proviso that when R^3 is $NR^{12}R^{12'}$ then q is 0; and Y is selected from the groups according to the following formulas:



wherein, W is O or S; T is N, NH or O; L is N, C or CH; a is 0, 1, 2 or 3; b is 0, 1, 2, 3 or 4; c is 0 or 1; d is 0, 1, 2 or 3; e is 0, 1 or 2; f is 0, 1, 2, 3, 4 or 5; g is 0, 1, 2, 3 or 4; h is 0, 1, 2 or 3; j is 0, 1, 2 or 3; with the proviso that when T is a nitrogen atom then j is 0, 1, 2 or 3; and when T is NH or an oxygen atom then j is 0, 1 or 2; k is 0, 1, 2, 3 or 4; and each R^5 is independently selected from the group consisting of a C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar, Ar—C_{1-6}-alk(en/yn)yl, Ar-thio, Ar-oxy, acyl, C_{1-6}-alk(en/yn)yloxy, C_{3-8}-cycloalk(en)yloxy, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yloxy, halogen, halo-C_{1-6}-alk(en/yn)yl, halo-C_{3-8}-cycloalk(en)yl, halo-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —CO—$NR^6R^{6'}$, cyano, cyano-C_{1-6}-alk(en/yn)yl, cyano-C_{3-8}-cycloalk(en)yl, cyano-C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, —$NR^7R^{7'}$, —S—R^8 and —SO_2R^8, or two adjacent R^5 together with the aromatic group to which they are attached form a 4-8 membered ring which optionally contains one or two heteroatoms; R^6 and $R^{6'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl and Ar; R^7 and $R^{7'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar

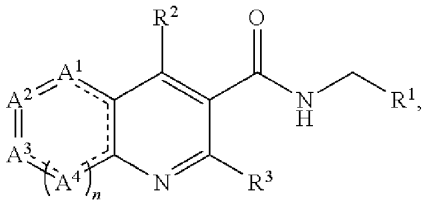
and acyl; and R^8 is selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, Ar and —$NR^9R^{9'}$; wherein R^9 and $R^{9'}$ are independently selected from the group consisting of hydrogen, C_{1-6}-alk(en/yn)yl, C_{3-8}-cycloalk(en)yl and C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl; provided that when R^8 is —$NR^9R^{9'}$ then R^5 is not —S—R^8; or salts thereof.

Formula 19

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 19. Such compounds are described in US Patent No. 9,248,122, issued February 2, 2016 and corresponding to US Application No. 14/091,395 filed November 27, 2013; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 19, this reference incorporated by reference herein controls.

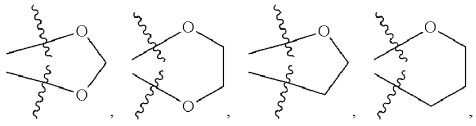
[0291] In an embodiment, the Kv7 channel activator is a compound according to formula 19:

Formula 19



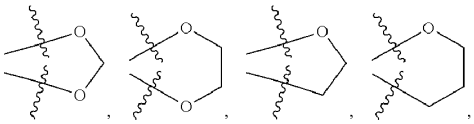
wherein, A^1, A^2 and A^3 independently of each other represent CR^4, N, O, S or $N(CH_3)$, A^4 represents CR^4 or N, and n denotes 0 or 1, with the proviso, that at least one of A^1, A^2, A^3 and A^4 does not represent CR^4, and with the proviso, that if n denotes 0, then precisely one of A^1, A^2 and A^3 represents O, S or $N(CH_3)$, or if n denotes 1, then A^1, A^2 and A^3 independently of each other represent CR^4 or N, R^1 represents C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C(=O)—NH—C_{1-4}-aliphatic residue, C(=O)—N(C_{1-4}-aliphatic residue)$_2$, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, S—C_{1-4}-aliphatic

residue, $S(=O)_2$—C_{1-4}-aliphatic residue, $S(=O)_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted;
R^3 represents C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, or denotes S—R^5, O—R^6 or $N(R^7R^8)$, wherein R^5 and R^6 in each case represent C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; with the proviso, that if R^5 or R^6 denote a 3 to 10 membered heterocycloaliphatic residue, than the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, R^7 represents C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; with the proviso that if R^7 denotes 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom; and R^8 denotes C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; or R^7 and R^8 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted; and each R^4 independently represents H, F; Cl; Br; I; CN; CF_3; CHF_2; CH_2F; OCF_3; $OCHF_2$; OCH_2F; SCF_3; O—C_{1-4}-aliphatic residue, C_{1-4}-aliphatic residue or $S(=O)_2$—C_{1-4}-aliphatic residue; in which an “aliphatic group” and “aliphatic residue” may in each case be branched or unbranched, saturated or unsaturated, in which a “cycloaliphatic residue” and a “heterocycloaliphatic residue” may in each case be saturated or unsaturated, in which “mono- or polysubstituted” with respect to an “aliphatic group”, an “aliphatic residue”, a “cycloaliphatic residue” and a “heterocycloaliphatic residue” relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, $NH(C_{1-4}$-aliphatic residue), $N(C_{1-4}$-aliphatic residue)$_2$, NH—C(=O)—

C_{1-4}aliphatic residue, N(C_{1-4}aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, NH—S(=O)$_2$—C_{1-4} aliphatic residue, N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, S(=O)$_2$—C_{1-4}-aliphatic residue, S(=O)$_2$—O—C_{1-4}-aliphatic residue, S(=O)$_2$—NH(C_{1-4}-aliphatic residue), S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CF_3, CHO, COOH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, C(=O)NH_2, a C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in which “mono- or polysubstituted” with respect to “aryl” and a “heteroaryl” relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,  , NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, NH—C(=O)—C_{1-4}-aliphatic residue, N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, NH—S(=O)$_2$—C_{1-4} aliphatic residue, N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, S(=O)$_2$—C_{1-4}-aliphatic residue, S(=O)$_2$—O—C_{1-4}-aliphatic residue, S(=O)$_2$—NH(C_{1-4}-aliphatic residue), S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CF_3, C(=O)H, C(=O)OH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)NH_2, C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in the form of an individual single stereoisomer or a mixture of the stereoisomers in any mixing ratio, and/or in the form of a free compound, a solvate and/or a physiologically acceptable salt.

[0292] In further embodiments, A^1, A^2 and A^3 independently of each other represent CR^4, N, O, S or N(CH_3), A^4 represents CR^4 or N, and n denotes 0 or 1, with the proviso, that at least one of A^1, A^2, A^3 and A^4 does not represent CR^4, and with the proviso, that if n denotes 0, then precisely one of A^1, A^2 and A^3 represents O, S or N(CH_3), or if n denotes 1, then A^1, A^2 and A^3 independently of each other represent CR^4 or N, R^1 denotes C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case

may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—OH, C_{3-8}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-8}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, O_{3-8}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,



, benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the aryl or the heteroaryl residue may in each case be optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; C_{1-4}-aliphatic residue, S—C_{1-4}-aliphatic residue, O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue,

Or

C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, R^3 denotes C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue,

Or

denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-

aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH,

Or

denotes S—R^5, O—R^6 or N(R^7R^8), wherein R^5 and R^6 in each case represent C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, or in each case represent C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—OH, C_{3-8}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-8}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-8}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent

selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, on the condition that if R^5 or R^6 denote a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a O_{1-0}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom,

and/or

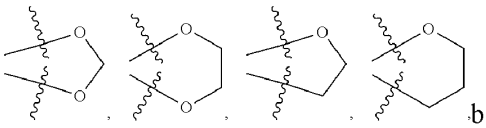
R^8 denotes C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, $NH(C_{1-4}$-aliphatic residue), $N(C_{1-4}$-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue,

Or

R^7 and R^8 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, $NH(C_{1-4}$-aliphatic residue), $N(C_{1-4}$-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue,wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue,

And/or

wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, $NH(C_{1-4}$-aliphatic residue), $N(C_{1-4}$-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^7 and R^8 together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, $NH(C_{1-4}$-aliphatic residue), $N(C_{1-4}$-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and

oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)—OH, and each R^4 independently represents H, F, Cl, Br, I, CN, CF_3, CHF_2, CH_2F, OCF_3, $OCHF_2$, OCH_2F, SCF_3, O—C_{1-4}-aliphatic residue, C_{1-4}-aliphatic residue or S(=O)$_2$—C_{1-4}-aliphatic residue.

In further embodiments, n denotes 1 and A^1 represents N, A^2 represents CR^4, A^3 represents CR^4 and A^4 represents CR^4; or n denotes 1 and A^1 represents CR^4, A^2 represents N, A^3 represents CR^4 and A^4 represents CR^4; or n denotes 1 and A^1 represents CR^4, A^2 represents CR^4, A^3 represents N and A^4 represents CR^4; or n denotes 1 and A^1 represents CR^4, A^2 represents CR^4, A^3 represents CR^4 and A^4 represents N; or n denotes 1 and A^1 represents N, A^2 represents N, A^3 represents CR^4 and A^4 represents CR^4; or n denotes 1 and A^1 represents N, A^2 represents CR^4, A^3 represents N and A^4 represents CR^4; or n denotes 1 and A^1 represents N, A^2 represents CR^4, A^3 represents CR^4 and A^4 represents N; or n denotes 1 and A^1 represents CR^4, A^2 represents N, A^3 represents N and A^4 represents CR^4; or n denotes 1 and A^1 represents CR^4, A^2 represents N, A^3 represents CR^4 and A^4 represents N; or n denotes 1 and A^1 represents CR^4, A^2 represents CR^4, A^3 represents N and A^4 represents N; or n denotes 0 and A^1 represents CR^4, A^2 represents CR^4, and A^3 represents S; or n denotes 0 and A^1 represents N, A^2 represents CR^4, and A^3 represents S; or n denotes 0 and A^1 represents S, A^2 represents CR^4 and A^3 represents CR^4; or n denotes 0 and A^1 represents S, A^2 represents CR^4 and A^3 represents N.

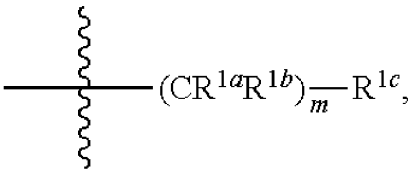
[0293] In further embodiments, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; C_{1-4}-aliphatic residue, S—C_{1-4}-aliphatic residue or O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least

one substituent selected from the group consisting of F, Cl, Br, I, =O, OH and O—C_{1-4}-aliphatic residue.

[0294] In further embodiments, R^2 represents C_{1-4}-aliphatic residue.

[0295] In further embodiments, each R^4 independently represents H; F; Cl; Br; CN; CF_3; OCF_3; CH_3, OCH_3 or $S(=O)_2CH_3$.

[0296] In further embodiments, R^1 represents the partial structure:



wherein, m denotes 0, 1, or 2, R^{1a} and R^{1b} each independently of one another represent H, F, Cl, Br, I, O—C_{1-4}-aliphatic residue or C_{1-4}-aliphatic residue, R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected

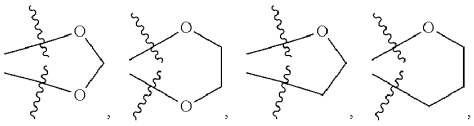
from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3 C_{1-4}-aliphatic residue and C(=O)OH.

[0297] In further embodiments, m denotes 1 or 2, R^{1a} and R^{1b} represent H, R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or m denotes 0 and R^{1c} denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, C_{1-4}-aliphatic residue and C(=O)OH.

[0298] In further embodiments, R^3 denotes a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, (=O)—O—C_{1-4}-aliphatic residue, S—C_{1-4}-aliphatic residue, CF_3, CN and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-7}-cycloaliphatic residue or the 3 to 7 membered

heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, or R^3 denotes S—R^5 or O—R^6, wherein R^5 and R^6 in each case denote C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, CF_3 and C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and O—C_{1-4}-aliphatic residue, or in each case denote C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may be linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN and C_{1-4}-aliphatic residue, on the condition that if R^5 or R^6 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, or R^3 denotes N(R^7R^8), wherein R^7 denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may in each case be linked, via a C_{1-4}-aliphatic group, which in turn may be

unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, on the condition that if R^7 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, and R^8 denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or R^7 and R^8 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^7 and R^8 together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, ON, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6} cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,



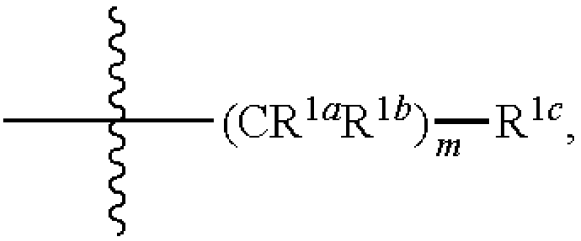
benzyl, phenyl, thienyl, and pyridyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SCF_3, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH.

[0299] In further embodiments, R^3 denotes C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with OH or O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, or R^3 denotes S—R^5 or O—R^6, wherein R^5 and R^6 in each case denote C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or in each case denote C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue in each case may be linked via an unsubstituted C_{1-4}-aliphatic group, on the condition that if R^5 or R^6 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, or R^3 denotes N(R^7R^8), wherein R^7 denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or

mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue is in each case linked via a unsubstituted C_{1-4}-aliphatic group, on the condition that if R^7 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, and R^8 denotes unsubstituted C_{1-4}-aliphatic residue, or R^7 and R^8 form together with the nitrogen atom connecting them a 3 to 7 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the 3 to 7 membered heterocycloaliphatic residue formed by R^7 and R^8 together with the nitrogen atom connecting them may optionally be condensed with phenyl or pyridyl, wherein the phenyl or pyridyl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, benzyl, phenyl, and pyridyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OCH_3, OCF_3, OCH_2CH_2OH, $OCH_2CH_2OCH_3$, SCF_3, CF_3 and C_{1-4}-aliphatic residue.

[0300] In further embodiments, A^1, A^2 and A^3 independently of each other represent CR^4, N, O, S or $N(CH_3)$, A^4 represents CR^4 or N, and n denotes 0 or 1, with the proviso, that at least one of A^1, A^2, A^3 and A^4 does not represent CR^4, and with the proviso, that if n denotes 0, then precisely one of A^1, A^2 and A^3 represents O, S or $N(CH_3)$, or if n denotes 1, then A^1,

A^2 and A^3 independently of each other represent CR^4 or N, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2, R^{1a} and R^{1b} each independently of one another represent H, F, Cl, O—C_{1-4}-aliphatic residue or C_{1-4}-aliphatic residue, R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, C_{1-10}—C_{1-4} aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, C_{1-10}—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3 C_{1-4}-aliphatic residue and C(=O)OH,
R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; C_{1-4}-aliphatic residue, S—C_{1-4}-aliphatic residue or O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from

the group consisting of F, Cl, =O, OH and O—C_{1-4}-aliphatic residue, R^3 denotes C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with OH or O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, or R^3 denotes S—R^5 or O—R^6, wherein R^5 and R^6 in each case denote C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or in each case denote C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue in each case may be linked via an unsubstituted C_{1-4}-aliphatic group, on the condition that if R^5 or R^6 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, or R^3 denotes $N(R^7R^8)$, wherein R^7 denotes C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3 and C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, C(=O)—O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic

residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue is in each case linked via an unsubstituted C_{1-4}-aliphatic group, on the condition that if R^7 denotes 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, and R^8 denotes unsubstituted C_{1-4}-aliphatic residue, or R^7 and R^8 form together with the nitrogen atom connecting them a 3 to 7 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the 3 to 7 membered heterocycloaliphatic residue formed by R^7 and R^8 together with the nitrogen atom connecting them may optionally be condensed with phenyl or pyridyl, wherein the phenyl or pyridyl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, benzyl, phenyl, and pyridyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OCH_3, OCF_3, OCH_2CH_2OH, O $CH_2CH_2OCH_3$, SH, SCF_3, CF_3 and C_{1-4}-aliphatic residue; and each R^4 independently represents H, F, Cl, Br, CN, CF_3, OCF_3, CH_3, OCH_3 or $S(=O)_2CH_3$.

[0301] In further embodiments, the Kv7 channel activator is selected from the group consisting of:1 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-[1,5]naphthyridine-3-carboxylic acid amide; 2 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-[1,5]naphthyridine-3-carboxylic acid amide; 3-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-[1,6]naphthyridine-3-carboxylic acid amide; 4 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-[1,6]naphthyridine-3-carboxylic acid amide; 5 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-[1,7]naphthyridine-3-carboxylic acid amide; 6-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-[1,7]naphthyridine-3-carboxylic acid amide; 7 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-[1,8]naphthyridine-3-

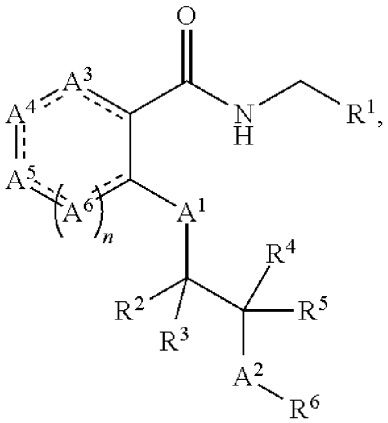
carboxylic acid amide; 8 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-[1,8]naphthyridine-3-carboxylic acid amide; 9 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,8]naphthyridine-3-carboxylic acid amide; 10 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,8]naphthyridine-3-carboxylic acid amide; 11 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,6]naphthyridine-3-carboxylic acid amide; 12 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,6]naphthyridine-3-carboxylic acid amide; 13 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,5]naphthyridine-3-carboxylic acid amide; 14 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-[1,5]naphthyridine-3-carboxylic acid amide; 15 5-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-7-methyl-thieno[3,2-b]pyridine-6-carboxylic acid amide; 16 6-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-thieno[2,3-b]pyridine-5-carboxylic acid amide; 17 5-Ethoxy-N-[(3-fluorophenyl)-methyl]-7-methyl-2-(trifluoromethyl)-thieno[3,2-b]pyridine-6-carboxylic acid amide; 18 6-Ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-2-(trifluoromethyl)-thieno[2,3-b]pyridine-5-carboxylic acid amide; in the form of a free compound, a solvate and/or a physiologically acceptable salt.

Formula 20

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 20. Such compounds are described in US Patent No. 9,284,286 issued March 15, 2016 and corresponding to US Application No. 14/091.373 filed November 27, 2013; International Publication No. WO2014082737A1, published June 5, 2014 and corresponding to International Application No. PCT/EP2013/003572 filed November 27, 2013; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 20, these references incorporated by reference herein control.

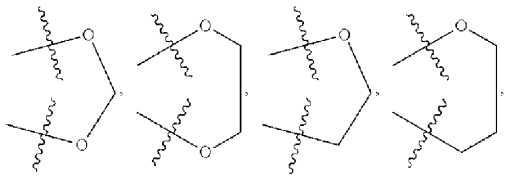
[0302] In an embodiment, the Kv7 channel activator is a compound according to formula 20:

Formula 20



wherein: A^1 represents $CR^{10}R^{11}$ or S; A^2 represents $CR^{12}R^{13}$, C(=O), O, S, S(=O) or $S(=O)_2$; A^3, A^4 and A^5 independently of each other represent CR^7, N, O, S or NR^8, A^6 represents CR^7 or N, and n denotes 0 or 1, with the proviso, that if n denotes 0, then precisely one of A^3, A^4 and A^5 represents O, S or NR^8, or if n denotes 1, then A^3, A^4 and A^5 independently of each other represent CR^7 or N; and with the proviso, that if n denotes 1 and A^3, A^4 and A^5 each represent CR^7, then A^6 does not represent N; R^1 represents C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2, R^3; R^4, R^5, R^{10}, R^{11}, R^{12} and R^{13} each independently of another represent H; F; Cl; Br; I; NO_2; CF_3; CN; OH; OCF_3; SH; SCF_3; C_{1-10}-aliphatic residue, O—C_{1-10}-aliphatic residue or S—C_{1-10}-aliphatic residue, in each case saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted; or C_{3-10}-cycloaliphatic residue, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted; or R^2 and R^3 or R^4 and R^5 or R^{10} and R^{11} or R^{12} and R^{13} or R^2 and R^{11} or R^2 and R^4 or R^2 and R^{13} or R^4 and R^{13} or R^4 and R^{11} or R^{12} and R^{13}, together with the carbon atom(s) joining them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated, unsubstituted or mono- or poly-substituted; wherein the remaining substituents R^2, R^3; R^4; R^5; R^{10}, R^{11}, R^{12} and R^{13} in each case have the meaning given above; R^6 represents a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated, unsubstituted or mono- or poly-substituted; or represents an aryl or a heteroaryl, in each case unsubstituted or mono- or poly-substituted; each R^7 independently of each other

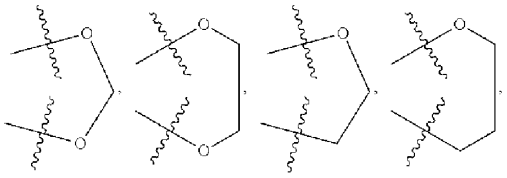
represents H, F; Cl; CN; CF_3; CHF_2; CH_2F; OCF_3; $OCHF_2$; OCH_2F; SCF_3; O—C_{1-4}-aliphatic residue, C_{1-4}-aliphatic residue or $S(=O)_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted; and R^8 represents H or a C_{1-4}-aliphatic residue, wherein the aliphatic residue may be saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted; in which an "aliphatic group" and "aliphatic residue" may in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" may in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group", an "aliphatic residue", a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, NH—C(=O)—C_{1-4}aliphatic residue, N(C_{1-4}-aliphatic residue)-C(=O)—C_{1-4}-aliphatic residue, NH—$S(=O)_2$—C_{1-4}-aliphatic residue, N(C_{1-4}-aliphatic residue)-$S(=O)_2$—C_{1-4}-aliphatic residue, =O, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, $S(=O)_2$—C_{1-4}-aliphatic residue, $S(=O)_2$—O—C_{1-4}-aliphatic residue, $S(=O)_2$—NH(C_{1-4}-aliphatic residue), $S(=O)_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CF_3, CHO, COOH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, $C(=O)NH_2$, a C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,



NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, NH—C(=O)—C_{1-4}-aliphatic residue, N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, NH—$S(=O)_2$—C_{1-4} aliphatic residue, N(C_{1-4} aliphatic residue)-$S(=O)_2$—C_{1-4} aliphatic residue, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, $S(=O)_2$—C_{1-4}-aliphatic residue, $S(=O)_2$—O—C_{1-4}-aliphatic residue, $S(=O)_2$—NH(C_{1-4}-aliphatic residue), $S(=O)_2$—N(C_{1-4}-

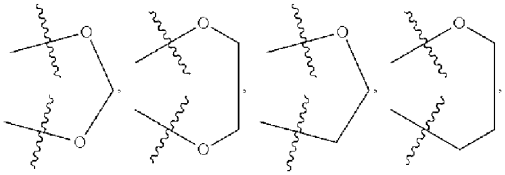
aliphatic residue)$_2$, CN, CF_3, C(=O)H, C(=O)OH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)NH_2, C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in the form of an individual single stereoisomer or a mixture of the stereoisomers in any mixing ratio, and/or in the form of a free compound, a solvate and/or a physiologically acceptable salt.

[0303] In further embodiments, A^1 represents $CR^{10}R^{11}$ or S; A^2 represents $CR^{12}R^{13}$, C(=O), O, S, S(=O) or S(=O)$_2$; A^3, A^4 and A^5 independently of each other represent CR^7, N, O, S or NR^8, A^6 represents CR^7 or N, and n denotes 0 or 1, with the proviso, that if n denotes 0, then precisely one of A^3, A^4 and A^5 represents O, S or NR^8, or if n denotes 1, then A^3, A^4 and A^5 independently of each other represent CR^7 or N; and with the proviso, that if n denotes 1 and A^3, A^4 and A^5 each represent CR^7, then A^6 does not represent N; R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6}-cycloaliphatic residue and a 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case be optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent

selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6} cycloaliphatic residue, 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the aryl or the heteroaryl residue may in each case be optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, R^2, R^3, R^5, R^{10}, R^{11}, R^{12} and R^{13} each independently of the others represents H; F; Cl; Br; I; NO_2; CF_3; CN; OH; OCF_3; SH; SCF_3; C_{1-4}-aliphatic residue, O—C_{1-4}-aliphatic residue or S—C_{1-4}-aliphatic residue, in each case saturated or unsaturated, branched or unbranched, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least

one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, or a C_{3-10}-cycloaliphatic residue, saturated or unsaturated, branched or unbranched, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or R^2 and R^3 or R^4 and R^5 or R^{10} and R^{11} or R^{12} and R^{13} or R^2 and R^{11} or R^2 and R^4 or R^2 and R^{13} or R^4 and R^{13} or R^4 and R^{11} or R^{12} and R^{13}, together with the carbon atom(s) joining them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated and in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the remaining substituents R^2, R^3, R^4, R^5, R^{10}, R^{11}, R^{12} and R^{13} in each case have the meaning given above; R^6 represents a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated and in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue,

CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or represents an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or

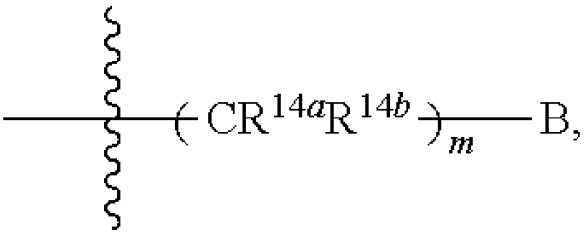
polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the aryl or the heteroaryl residue may in each case be optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, each R^7 independently of each other represents H, F; Cl; CN; CF_3; CHF_2; CH_2F; OCF_3; $OCHF_2$; OCH_2F; SCF_3; a O—C_{1-4}-aliphatic residue, a C_{1-4}-aliphatic residue or a S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue. and R^8 represents H or C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and O—C_{1-4}-aliphatic residue.

[0304] In further embodiments, A^1 represents S; and A^2 represents S, S(=O)$_2$ or $CR^{12}R^{13}$, wherein R^{12} and R^{13} both represent H or both represent F.

[0305] In further embodiments, n denotes 1 and A^3 represents CR^7, A^4 represents CR^7, A^5 represents CR^7 and A^6 represents CR^7; or n denotes 1 and A^3 represents N, A^4 represents CR^7, A^5 represents CR^7 and A^6 represents CR^7; or n denotes 1 and A^3 represents CR^7, A^4 represents N, A^5 represents CR^7 and A^6 represents CR^7; or n denotes 1 and A^3 represents CR^7, A^4 represents CR^7, A^5 represents N and A^6 represents CR^7; or n denotes 1 and A^3 represents N, A^4 represents N, A^5 represents CR^7 and A^6 represents CR^7; or n denotes 1 and A^3 represents N, A^4 represents CR^7, A^5 represents N and A^6 represents CR^7; or n denotes 1 and A^3 represents N, A^4 represents CR^7, A^5 represents CR^7 and A^6 represents N; or n denotes 1 and A^3 represents CR^7, A^4 represents N, A^5 represents CR^7 and A^6 represents N; or n denotes 1 and A^3 represents CR^7, A^4 represents N, A^5 represents N and A^6 represents CR^7; or n denotes 1 and A^3 represents CR^7, A^4 represents CR^7, A^5 represents N and A^6 represents N; or n denotes 0 and A^3 represents S, A^4 represents CR^7 and A^5 represents CR^7; or n denotes 0 and A^3 represents S, A^4 represents CR^7 and A^5 represents N; or n denotes 0 and A^3 represents O, A^4 represents CR^7 and A^5 represents CR^7, or n denotes 0 and A^3 represents O, A^4 represents CR^7 and A^5 represents N; or n denotes 0 and A^3 represents CR^7, A^4 represents CR^7 and A^5 represents S; or n denotes 0 and A^3 represents N, A^4 represents CR^7 and A^5 represents S; or

n denotes 0 and A^3 represents CR^7, A^4 represents CR^7 and A^5 represents O; or n denotes 0 and A^3 represents N, A^4 represents CR^7 and A^5 represents O.

[0306] In further embodiments, R^1 represents the partial structure:



wherein: R^{14a} and R^{14b} each independently of the other represent H; F; Cl; Br; CF_3; CN; OH; OCF_3; NH_2; C_{1-4}-aliphatic residue, O—C_{1-4}-aliphatic residue, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, in each case saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, OH and OCF_3; or independently represent C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, C_{1-4}-aliphatic residue, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$; m represents 0, 1, 2 or 3; Y represents O or NR^{15}, wherein R^{15} represents H or C_{1-4}-aliphatic residue, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, C_{1-4}-aliphatic residue, OH, O—C_{1-4}-aliphatic residue, OCF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$; or C_{3-10}-cycloaliphatic residue, saturated or unsaturated, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, C_{1-4}-aliphatic residue, OH, O—C_{1-4}-aliphatic residue, OCF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$; o represents 0 or 1, B represents C_{1-8}-aliphatic residue, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, CN, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, C(=O)OH, CF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$; or C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case saturated or

unsaturated, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, C(=O)—OH, CF_3, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$ and SCF_3; or aryl or heteroaryl, in each case unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, NO_2, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, C(=O)OH, CF_3, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, S—C_{1-4}-aliphatic residue, SCF_3, benzyl, phenyl, pyridyl and thienyl, wherein benzyl, phenyl, pyridyl, thienyl can in each case be unsubstituted or mono- or poly-substituted by one or more substituents selected independently of one another from the group consisting of F, Cl, Br, NO_2, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, C(=O)—OH, CF_3, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, S—C_{1-4}-aliphatic residue and SCF_3.

[0307] In further embodiments, R^{14a} and R^{14b} each independently of the other represents H; F; Cl; CH_3; CH_2CH_3; $(CH_2)_2CH_3$; $CH(CH_3)_2$; $(CH_2)_3CH_3$; $CH(CH)_3CH_2CH_3$; $C(CH_3)_3$; OH; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$ or $O(CH_2)_2OH$; m represents 0, 1 or 2 and represents 0 and B represents CH_3; CH_2CH_3; $(CH_2)_2CH_3$; $CH(CH_3)_2$; $(CH_2)_3CH_3$; $CH(CH_3)CH_2CH_3$; $C(CH_3)_3$; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; cycloheptyl; adamantyl; bicyclo[2.2.1]heptyl; bicyclo[2.2.2]octyl; phenyl, pyridyl or thienyl, in each case unsubstituted or mono-, di- or tri-substituted by one, two or three substituents each selected independently of one another from the group consisting of F, Cl, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, CF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$.

[0308] In further embodiments, R^2; R^3; R^4; R^5; R^{10}, R^{11}, R^{12} and R^{13} each independently of the others represents H; F; Cl; CF_3; CN; OH; OCF_3; SCF_3; CH_3; CH_2CH_3; $(CH_2)_2CH_3$; $CH(CH_3)_2$; $(CH_2)_3CH_3$; $CH(CH)_3CH_2CH_3$; $C(CH_3)_3$; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$; $O(CH_2)_2OH$; SCH_3; SCH_2CH_3; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; or R^2 and R^3 or R^4 and R^5 or R^{10} and R^{11} or R^{12} and R^{13} or R^2 and R^{11} or R^2 and R^4 or R^2 and R^{13} or R^4 and R^{13} or R^4 and R^{11} or R^{12} and R^{13}, together with the carbon atom(s) joining them, form a cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, in each case unsubstituted; wherein the remaining substituents R^2, R^3; R^4; R^5; R^{10}, R^{11}, R^{12} and R^{13} in each case have the meaning given above.

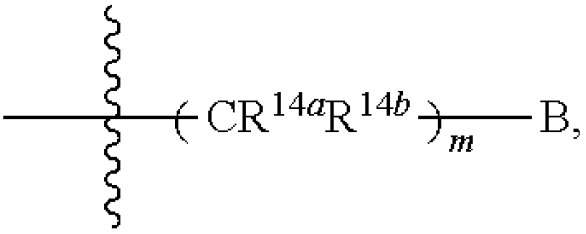
[0309] In further embodiments, each R^7 represents H, F; Cl; CN; CF_3; CHF_2; CH_2F; OCF_3; $OCHF_2$; OCH_2F; SCF_3; CH_3; CH_2CH_3; $CH_2CH_2CH_3$; $CH(CH_3)_2$; $OH_2CH_2CH_2CH_3$;

$CH(CH)_3CH_2CH_3$; $CH_2CH(CH_3)_2$; $O(CH_3)_3$; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$; $O(CH_2)_2OH$; $S(=O)_2CH_3$ $S(=O)_2CH_2CH_3$ $S(=O)_2CH(CH_3)_2$ or $S(=O)_2CH_2CH_2CH_3$; and R^8 represents H or CH_3 or CH_2CH_3 or $CH(CH_3)_2$.

[0310] In further embodiments, R^6 represents a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case saturated or unsaturated, unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, I, NO_2, CN, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, CF_3, SH, S—C_{1-4}-aliphatic residue and SCF_3; or an aryl or a heteroaryl, in each case unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, I, NO_2, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, CF_3, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, SH, S—C_{1-4}-aliphatic residue and SCF_3.

[0311] In further embodiments, R^6 represents phenyl, pyridyl or thienyl, in each case unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, CN, OH, O—C_{1-4}-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, CF_3 and SCF_3.

[0312] In further embodiments, A^1 represents S; and A^2 represents S, $S(=O)_2$ or $CR^{12}R^{13}$, wherein R^{12} and R^{13} both represent H or both represent F; and R^1 represents the partial structure:



wherein: R^{14a} and R^{14b} each independently of the other represents H; F; Cl; CH_3; CH_2CH_3; $(CH_2)_2CH_3$; $CH(CH_3)_2$; $(OH_2)_3CH_3$; $CH(CH)_3CH_2CH_3$; $C(CH_3)_3$; OH; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$; or $O(CH_2)_2OH$; m represents 0, 1 or 2 and B represents phenyl or naphthyl or pyridyl or thienyl, in each case unsubstituted or mono- or di- or tri-substituted by one, two or three substituents each selected independently of one another from the group consisting of F, Cl, CN, OH, O-$_{1-4}$-aliphatic residue, OCF_3, C_{1-4}-aliphatic residue, C(=O)—OH, CF_3, NH_2, NH(C_{1-4}-aliphatic residue) and N(C_{1-4}-aliphatic residue)$_2$; R^2, R^3, R^4; R^5, R^{10}, R^{11}, R^{12} and R^{13}

each independently of the others represent H; F; Cl; Br; I; NO_2; CF_3; CN; OH; OCF_3; SH; SCF_3; CH_3; CH_2CH_3; $CH_2CH_2CH_3$; $CH(CH_3)_2$; $CH_2CH_2CH_2CH_3$; $CH(CH)_3CH_2CH_3$; $CH_2CH(CH_3)_2$; $C(CH_3)_3$; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$; $O(CH_2)_2OH$; SCH_3; SCH_2CH_3; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; or R^2 and R^3 or R^4 and R^5 or R^{10} and R^{11} or R^{12} and R^{13} or R^2 and R^{11} or R^2 and R^4 or R^2 and R^{13} or R^4 and R^{13} or R^4 and R^{11} or R^{12} and R^{13}, together with the carbon atom(s) joining them, form a cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, in each case unsubstituted; wherein the remaining substituents R^2, R^3; R^4; R^5; R^{10}, R^{11}, R^{12} and R^{13} in each case have the meaning given above; R^6 represents phenyl, in each case unsubstituted or mono- or poly-substituted by one or more substituents each selected independently of one another from the group consisting of F, Cl, Br, I, CN, OH, OCH_3, OCH_2CH_3, OCF_3, CH_3, CH_2CH_3, $CH(CH_3)_2$ and CF_3; each R^7 represents H, F; CI; CN; CF_3; CHF_2; CH_2F; OCF_3; $OCHF_2$; OCH_2F; SCF_3; CH_3; CH_2CH_3; $CH_2CH_2CH_3$; $CH(CH_3)_2$; $CH_2CH_2CH_2CH_3$; $CH(CH)_3CH_2CH_3$; $CH_2CH(CH_3)_2$; $C(CH_3)_3$; OCH_3; OCH_2CH_3; $O(CH_2)_2OCH_3$; $O(CH_2)_2OH$; $S(=O)_2CH_3$ $S(=O)_2CH_2CH_3$, $S(=O)_2CH(CH_3)_2$ or $S(=O)_2CH_2CH_2CH_3$; and R^8 represents H or CH_3 or CH_2CH_3 or $CH(CH_3)_2$.

[0313] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 1 2-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-benzamide; 2 N-(3,3-Dimethyl-butyl)-2-[3-(4-fluorophenyl)-propylsulfanyl]-benzamide; 3 3-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyridine-2-carboxylic acid amide; 4 3-[2-(Benzenesulfonyl)-ethylsulfanyl]-N-(thiophen-2-yl-methyl)-pyridine-2-carboxylic acid amide; 5 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyridine-3-carboxylic acid amide; 6 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-[(4-fluorophenyl)-methyl]-pyridine-3-carboxylic acid amide; 7 3-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyridine-4-carboxylic acid amide; 8 3-[2-(Benzenesulfonyl)-ethylsulfanyl]-N-(thiophen-2-yl-methyl)-pyridine-4-carboxylic acid amide; 9 3-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyrazine-2-carboxylic acid amide; 10 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyrimidine-5-carboxylic acid amide; 11 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-[(4-fluorophenyl)-methyl]-pyrimidine-5-carboxylic acid amide; 12 3-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-(3-methyl-butyl)-pyridazine-4-carboxylic acid amide; 13 3-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-[(4-fluorophenyl)-methyl]-pyridazine-4-carboxylic acid amide; 14 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-[(4-fluorophenyl)-methyl]-thiazole-5-carboxylic acid amide; 15 4-[[3,3-Difluoro-3-(4-fluorophenyl)-propyl]sulfanyl]-N-[(4-

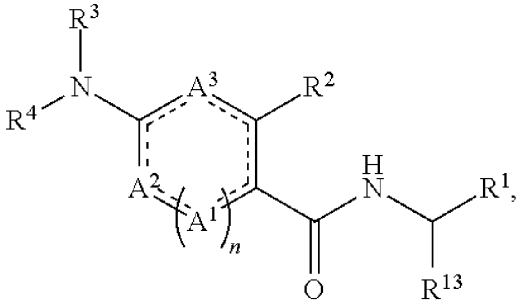
fluorophenyl)-methyl]-2-methyl-thiazole-5-carboxylic acid amide; in the form of a free compound, a solvate and/or a physiologically acceptable salt.

Formula 21

[0314] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds. Such compounds are described in US Publication No. US20140148454A1, published May 29, 2014 and corresponding to US Application No. 14/091,378 filed November 27, 2013; International Publication No. WO2014082739A1, published June 5, 2014 and corresponding to International Application No. PCT/EP2013/003574 filed November 27, 2013; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 21, these references incorporated by reference herein control.

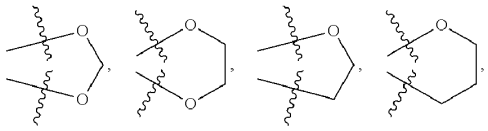
[0315] In an embodiment, the Kv7 channel activator is a compound according to formula 21:

Formula 21



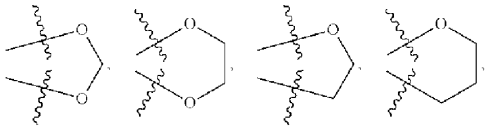
wherein, A^1 represents CR^5 or N; A^2 represents CR^6, N, O, S or NR^7; A^3 represents CR^8 or N, and n denotes 0 or 1, on the condition, that if n denotes 0, then A^2 represents O, S or NR^7, or if n denotes 1, then A^2 represents CR^6 or N, wherein R^5 is selected from F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; R^6 is selected from H, F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; R^7 represents $C_{1\text{-}4}$-aliphatic residue or $C_{3\text{-}5}$-cycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; R^8 is selected from H, F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; with the proviso, that, if n denotes 1, then at least one of A^1, A^2 and A^3 denotes N, with the proviso, that if n denotes 1 and A^3 denotes N, then A^1 and/or A^2 denotes N, and with the proviso, that if n denotes 1 and A^2 denotes N and A^1 denotes CR^5 and A^3 denotes CR^8, then R^5 denotes F, Cl, CH_3, CF_3, CHF_2 or CH_2F; R^{13} represents H or $C_{1\text{-}4}$-aliphatic residue, R^1 represents $C_{1\text{-}10}$-aliphatic residue, unsubstituted or mono- or polysubstituted; or $C_{3\text{-}10}$-cycloaliphatic residue or 3 to 10 membered

heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; or aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted, or denotes S—R^9, O—R^{10} or N($R^{11}R^{12}$), wherein R^9 and R^{10} in each case represent C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; with the proviso, that if R^9 or R^{10} denote a 3 to 7 membered heterocycloaliphatic residue, than the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, R^{11} represents C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; C_{3-6}-cycloaliphatic residue or a 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; with the proviso that if R^{11} denotes a 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom; and R^{12} denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; or R^{11} and R^{12} form together with the nitrogen atom connecting them a 3 to 7 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted;
R^3 represents C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; or C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; or aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^3 denotes a 3 to 10 membered heterocycloaliphatic residue or a heteroaryl, the 3 to 10 membered heterocycloaliphatic residue or the heteroaryl is linked via a carbon atom; and R^4 denotes H or C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; or R^3 and R^4 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted; in which an “aliphatic group” and “aliphatic residue” may in each case be branched or

unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" may in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group", an "aliphatic residue", a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, NH—C(=O)—C_{1-4}-aliphatic residue, N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, NH—S(=O)$_2$—C_{1-4} aliphatic residue, N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, S(=O)$_2$—C_{1-4}-aliphatic residue, S(=O)$_2$—O—C_{1-4}-aliphatic residue, S(=O)$_2$—NH(C_{1-4}-aliphatic residue), S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CF_3, CHO, COOH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, C(=O)NH_2, a C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,  NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, NH—C(=O)—C_{1-4}-aliphatic residue, N(C_{1-4} aliphatic residue)-O(=O)—C_{1-4} aliphatic residue, NH—S(=O)$_2$—C_{1-4} aliphatic residue, N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, O—C_{1-4}-aliphatic residue, O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, S(=O)$_2$—C_{1-4}-aliphatic residue, S(=O)$_2$—O—C_{1-4}-aliphatic residue, S(=O)$_2$—NH(C_{1-4}-aliphatic residue), S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CF_3, C(=O)H, C(=O)OH, C_{1-4}-aliphatic residue, C(=O)—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)NH_2, C(=O)—NH(C_{1-4}-aliphatic residue) and C(=O)—N(C_{1-4}-aliphatic residue)$_2$; in the form of an individual single stereoisomer or a mixture of the stereoisomers in any mixing ratio, and/or in the form of a free compound, a solvate and/or a physiologically acceptable salt.

[0316] In further embodiments, A^1 represents CR^5 or N; A^2 represents CR^6, N, O, S or NR^7; A^3 represents CR^8 or N, and n denotes 0 or 1, on the condition, that if n denotes 0, then A^2 represents O, S or NR^7, or if n denotes 1, then A^2 represents CR^6 or N, wherein R^5 is selected from F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; R^6 is selected from H, F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; R^7 represents C_{1-4}-aliphatic residue or C_{3-5}-cycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, R^8 is selected from H, F, Cl, Br, CN, CH_3, CF_3, CHF_2, CH_2F, OCH_3, C_2H_5, SCH_3, OCF_3, $OCHF_2$ or OCH_2F; with the proviso, that, if n denotes 1, then at least one of A^1, A^2 and A^3 denotes N, with the proviso, that if n denotes 1 and A^3 denotes N, then A^1 and/or A^2 denotes N, and with the proviso, that if n denotes 1 and A^2 denotes N and A^1 denotes CR^5 and A^3 denotes CR^8, then R^5 denotes F, Cl, CH_3, CF_3, CHF_2 or CH_2F; R^{13} represents H or C_{1-4}-aliphatic residue, R^1 denotes C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from

the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,

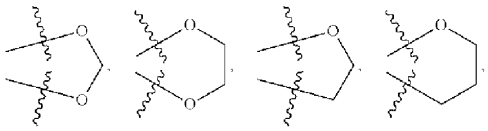


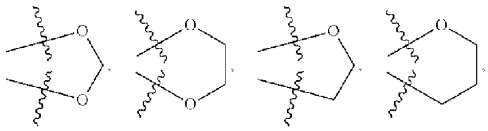
benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)—OCH_3 and C(=O)—OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4}-aliphatic residue), an N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the aryl or the heteroaryl residue may in each case be optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, R^2 denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, or denotes S—R^9, O—R^{10} or N($R^{11}R^{12}$); wherein R^9 and R^{10} in each case represent C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or in each case represent C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocyclo-aliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue,

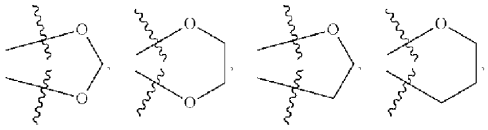
wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), an N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, on the condition that if R^9 or R^{10} denote a 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, R^{11} denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes C_{3-6}-cycloaliphatic residue or 3 to 7 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue, and a 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3,

S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, on the condition that if R^{11} denotes a 3 to 7 membered heterocycloaliphatic residue, the 3 to 7 membered heterocycloaliphatic residue is linked via a carbon atom, and R^{12} denotes C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}aliphatic residue, or R^{11} and R^{12} form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^{11} and R^{12} together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3,

CN, C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—OCH_3 and C(=O)—OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, R^3 denotes C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)—O—C_{1-4}-aliphatic residue, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and

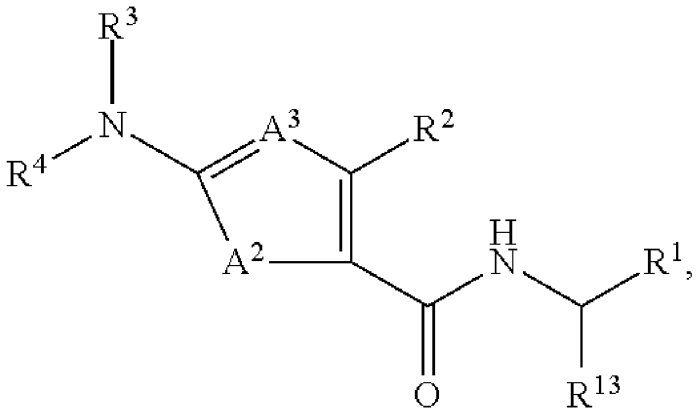
unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, on the condition that if R^3 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), an N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—

C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the aryl or the heteroaryl residue may in each case be optionally linked via a C_{1-4}-aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN and C(=O)OH, R^4 denotes H or C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or R^3 and R^4 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C_{3-6}-cycloaliphatic residue and 3 to 7 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^3 and R^4 together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue,



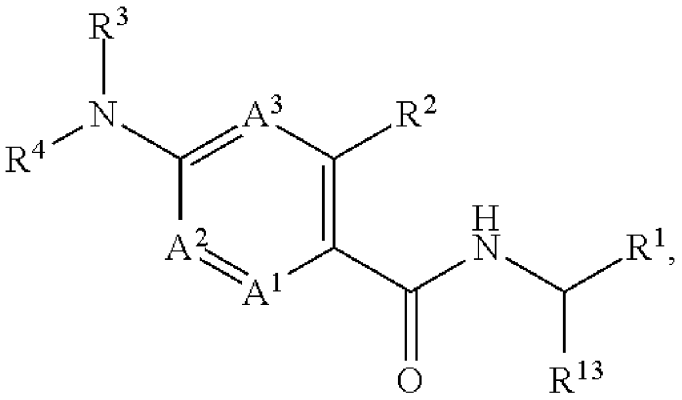
benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^3 and R^4 together with the nitrogen atom connecting them may optionally be condensed with a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, =O, OH, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, O—C_{1-4}-aliphatic residue, OCF_3, OCH_2CH_2OH, OCH_2OCH_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, NH(C_{1-4}-aliphatic residue), N(C_{1-4}-aliphatic residue)$_2$, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, CN, C_{1-4}-aliphatic residue and C(=O)OH.

[0317] In further embodiments, the compound is according to formula 21 wherein n denotes 0 and is according to the formula:



wherein, A^2 represents O and A^3 represents CR^8; or A^2 represents S and A^3 represents CR^8; or A^2 represents NR^7 and A^3 represents CR^8; or A^2 represents O and A^3 represents N; or A^2 represents S and A^3 represents N; or A^2 represents NR^7 and A^3 represents N.

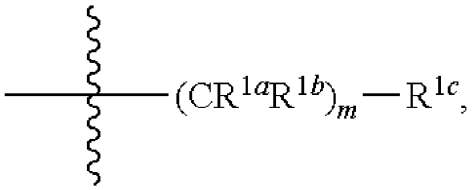
[0318] In further embodiments, the compound is according to formula 21 wherein n denotes 1 and is according to the formula:



wherein: A^1 represents N and A^2 represents CR^6 and A^3 represents CR^8; or A^1 represents CR^5 and A^2 represents N and A^3 represents CR^8; or A^1 represents N and A^2 represents N and A^3 represents CR^8; or A^1 represents N and A^2 represents CR^6 and A^3 represents N; or A^1 represents CR^5 and A^2 represents N and A^3 represents N; or A^1 represents N and A^2 represents N and A^3 represents N.

[0319] In further embodiments, R^5 denotes F, Cl, CH_3, OCH_3 or CH_2CH_3; and/or R^6 denotes H; and/or R^7 denotes CH_3, CH_2CH_3 or cyclopropyl; and/or R^8 denotes H.

[0320] In further embodiments, R^1 represents the partial structure:



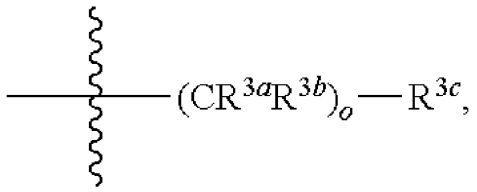
wherein: m denotes 0, 1, or 2, R^{1a} and R^{1b} each independently of one another represent H, F, Cl, Br, I, O—C_{1-4}-aliphatic residue or C_{1-4}-aliphatic residue, R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3C_{1-4}-aliphatic residue and C(=O)OH.

[0321] In further embodiments, m denotes 1 or 2, R^{1a} and R^{1b} represent H, R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at

least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or m denotes 0 and R^{1c} denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3 and C(=O)OC_2H_5, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3C_{1-4}-aliphatic residue and C(=O)OH.

[0322] In further embodiments, R^2 is selected from the group consisting of CH_3, C_2H_5, $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, CH_2-cyclopropyl, OCH_3, OC_2H_5, $OCH_2CH_2CH_3$, $OCH(CH_3)_2$, O-cyclopropyl, SCH_3, SC_2H_5, $SCH_2CH_2CH_3$, $SCH(CH_3)_2$, S-cyclopropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, $N(CH_3)_2$, $N(CH_3)C_2H_5$, $N(CH_3)CH_2CH_2CH_3$, $N(CH_3)CH(CH_3)_2$, $N(CH_3)$-cyclopropyl, $N(C_2H_5)_2$, $N(C_2H_5)CH_2CH_2CH_3$, $N(C_2H_5)CH(CH_3)_2$, $N(C_2H_5)$-cyclopropyl, N-aziridinyl, N-azetidinyl, N-pyrrolidinyl, N-piperidinyl or N-morpholinyl, in each case unsubstituted or mono- or polysubstituted with F, OH and/or OCH_3.

[0323] In further embodiments, R^3 represents the partial structure:

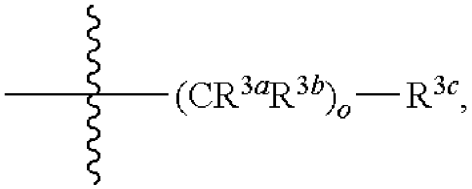


wherein: o denotes 0, 1, 2 or 3, R^{3a} and R^{3b} each independently of one another represent H, F, Cl, Br, I, O—C_{1-4}-aliphatic residue or C_{1-4}-aliphatic residue or together denote =O, and R^{3c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and O—C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic

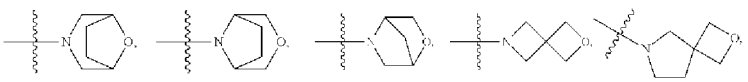
residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)CH_3, C(=O)C_2H_5, C(=O)OCH_3, C(=O)OC_2H_5, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, C_{1-4}-aliphatic residue and C(=O)—OH, and R^4 denotes H or unsubstituted C_{1-4}-aliphatic residue or C_{1-4}-aliphatic residue, monosubstituted with OCH_3, or R^3 and R^4 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, C(=O)OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, C_{1-4}-aliphatic residue, cyclopropyl, cyclobutyl and cyclopentyl, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, CF_3 and O—C_{1-4}-aliphatic residue, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^3 and R^4 together with the nitrogen atom connecting them may optionally be condensed with phenyl or pyridyl, wherein the phenyl or pyridyl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, C_{1-4}-aliphatic residue, C(=O)OH and C_{3-6}-cycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, O—C_{1-4}-aliphatic

residue, OCF_3, SCF_3, S—C_{1-4}-aliphatic residue, CF_3, C_{1-4}-aliphatic residue and C(=O)OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^3 and R^4 together with the nitrogen atom connecting them may optionally be condensed with a C_{3-6}-cycloaliphatic residue, or a 3 to 7 membered heterocycloaliphatic residue, wherein the C_{3-6}-cycloaliphatic residue or the 3 to 7 membered heterocycloaliphatic residue condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, O—C_{1-4}-aliphatic residue, OCF_3, SCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)OH, $C(=O)CH_3$, $C(=O)C_2H_6$, $C(=O)OCH_3$ and $C(=O)OC_2H_6$.

[0324] In further embodiments, R^3 represents the partial structure:



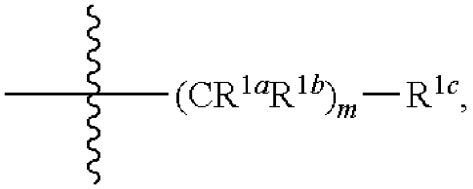
Wherein, o denotes 0, 1, 2 or 3, R^{3a} and R^{3b} each independently of one another represent H, F, CH_3 or OCH_3, or together denote =O, R^{3c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, O—C_{1-4}-aliphatic residue, and CF_3, or denotes cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, pyrrolidinyl, morpholinyl, piperazinyl, piperidinyl or tetrahydropyranyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, and C_{1-4}-aliphatic residue, and R^4 denotes H, CH_3, CH_2CH_3, $CH_2CH_2OCH_3$ or $CH_2CH_2CH_2OCH_3$, or R^3 and R^4 form together with the nitrogen atom connecting them a heteroaliphatic residue, selected from the group consisting of morpholinyl, piperidinyl, pyrrolidinyl, azetidinyl, oxazepanyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, thiomorpholinyl, azepanyl, tetrahydroimidazo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl,



dihydroindolinyl, or dihydroisoindolyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, C(=O)OH, OCH_3,

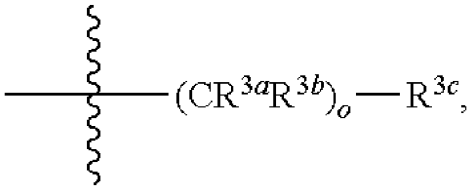
OCH_2CH_3, OCF_3, SCF_3, CF_3, $C(=O)CH_3$, $C(=O)OCH_3$, CH_2CF_3, CH_2OH, CH_2OCH_3, $CH_2CH_2OCH_3$, CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH(CH_3)_2$ and cyclopropyl.

[0325] In further embodiments, A^1 represents CR^5, N; A^2 represents CR^6, N, O, S or NR^7; A^3 represents CR^8 or N, and n denotes 0 or 1, on the condition, that if n denotes 0, then A^2 represents O, S or NR^7, or if n denotes 1, then A^2 represents CR^6 or N, wherein R^5 denotes F, Cl, CH_3, OCH_3 or CH_2CH_3; and/or R^6 denotes H; and/or R^7 denotes CH_3, CH_2CH_3 or cyclopropyl; and/or R^8 denotes H; with the proviso, that, if n denotes 1, then at least one of A^1, A^2 and A^3 denotes N, with the proviso, that if n denotes 1 and A^3 denotes N, then A^1 and/or A^2 denotes N, and with the proviso, that if n denotes 1 and A^2 denotes N and A^1 denotes CR^5 and A^3 denotes CR^8, then R^5 denotes F, Cl, CH_3, CF_3, CHF_2 or CH_2F; R^{13} represents H or CH_3; R^1 represents the partial structure:

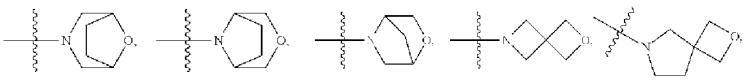


wherein, m denotes 1 or 2, R^{1a} and R^{1b} represent H and R^{1c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or denotes C_{3-10}-cycloaliphatic residue or 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or wherein m denotes 0 and R^{1c} denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, C(=O)—CH_3, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, C_{3-6}-cycloaliphatic residue, 3 to 7 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, C_{1-4}-aliphatic residue, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$ and $C(=O)OC_2H_5$, and wherein the C_{3-6}-cycloaliphatic residue and the 3 to 7 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, CF_3C_{1-4}-aliphatic residue and C(=O)OH; R^2 is

selected from the group consisting of CH_3, C_2H_5, $CH_2CH_2CH_3$, $CH(CH_3)_2$, $CH_2CH_2CH_2CH_3$, $CH_2CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$, $C(CH_3)_3$, CH_2-cyclopropyl, OCH_3, OC_2H_5, $OCH_2CH_2CH_3$, $OCH(CH_3)_2$, O-cyclopropyl, SCH_3, SC_2H_5, $SCH_2CH_2CH_3$, $SCH(CH_3)_2$, S-cyclopropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, $N(CH_3)_2$, $N(CH_3)C_2H_5$, $N(CH_3)CH_2CH_2CH_3$, $N(CH_3)CH(CH_3)_2$, $N(CH_3)$-cyclopropyl, $N(C_2H_5)_2$, $N(C_2H_5)CH_2CH_2CH_3$, $N(C_2H_5)CH(CH_3)_2$, $N(C_2H_5)$-cyclopropyl, N-aziridinyl, N-azetidinyl, N-pyrrolidinyl, N-piperidinyl or N-morpholinyl, in each case unsubstituted or mono- or polysubstituted with F, OH and/or OCH_3; R^3 represents the partial structure:



wherein: denotes 0, 1, 2 or 3, R^{3a} and R^{3b} each independently of one another represent H, F, CH_3 or OCH_3, or together denote =O, R^{3c} denotes C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, O—C_{1-4}-aliphatic residue, and CF_3, or denotes cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, pyrrolidinyl, morpholinyl, piperazinyl, piperidinyl or tetrahydropyranyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, O—C_{1-4}-aliphatic residue, CF_3 and C_{1-4}-aliphatic residue, or denotes aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, OH, O—C_{1-4}-aliphatic residue, OCF_3, CF_3, CN, and C_{1-4}-aliphatic residue, and R^4 denotes H, CH_3, CH_2CH_3, $CH_2CH_2OCH_3$ or $CH_2CH_2CH_2OCH_3$, or R^3 and R^4 form together with the nitrogen atom connecting them a morpholinyl, piperidinyl, pyrrolidinyl, azetidinyl, oxazepanyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, thiomorpholinyl, azepanyl, tetrahydroimidazo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]-pyrazinyl,



dihydroindolinyl, or dihydroisoindolyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, C(=O)OH, OCH_3, OCH_2CH_3, OCF_3, SCF_3, CF_3, C(=O)CH_3, C(=O)OCH_3, CH_2CF_3, CH_2OH, CH_2OCH_3, $CH_2CH_2OCH_3$, CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH(CH_3)_2$ and cyclopropyl.

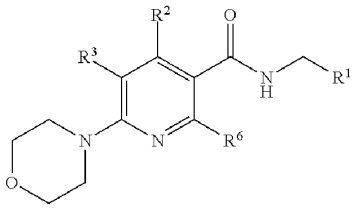
[0326] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[(4-Chlorophenyl)-methyl]-4-ethylsulfanyl-6-methyl-2-morpholin-4-yl-pyrimidine-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4,6-dimethoxy-2-morpholin-4-yl-pyrimidine-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-ethylsulfanyl-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-methyl-6-morpholin-4-yl-4-propyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-ethoxy-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-[(3R)-3-fluoro-pyrrolidin-1-yl]-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-3-isopropyl-5-morpholin-4-yl-pyrazine-2-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-3-isopropyl-5-morpholin-4-yl-pyridine-2-carboxylic acid amide; 4-Isopropyl-2-(methyl-tetrahydro-pyran-4-yl-amino)-N-[1-[3-(trifluoromethyloxy)-phenyl]-ethyl]-thiazole-5-carboxylic acid amide; 4-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-methyl-2-morpholin-4-yl-pyrimidine-5-carboxylic acid amide; 4-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 4-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-ethylsulfanyl-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-ethylsulfanyl-2-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-ethylsulfanyl-2-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-cyclopropyl-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-ethoxy-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-dimethylamino-2-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-3-(1-methyl-propyl)-5-morpholin-4-yl-pyrazine-2-carboxylic acid amide; N-(2-Cyclopentyl-ethyl)-3-(1-methyl-propyl)-5-morpholin-4-yl-pyrazine-2-carboxylic acid amide; 4-Isopropyl-2-[methyl-(tetrahydro-pyran-4-yl-methyl)-amino]-N-[1-[3-(trifluoromethyloxy)-phenyl]-ethyl]-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-(methyl-tetrahydro-pyran-4-yl-amino)-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-[methyl-(tetrahydro-pyran-4-yl-methyl)-amino]-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-morpholin-4-yl-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-piperidin-1-yl-thiazole-5-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-isopropyl-2-piperidin-1-yl-thiazole-5-carboxylic acid

amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-([1,4]oxazepan-4-yl)-thiazole-5-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-isopropyl-2-([1,4]oxazepan-4-yl)-thiazole-5-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-morpholin-4-yl-4-propyl-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-isopropyl-2-morpholin-4-yl-oxazole-5-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-isopropyl-2-morpholin-4-yl-oxazole-5-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-5-isopropyl-3-methyl-2-morpholin-4-yl-3H-imidazole-4-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-5-isopropyl-3-methyl-2-morpholin-4-yl-3H-imidazole-4-carboxylic acid amide; 2-(Methyl-tetrahydro-pyran-4-yl-amino)-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyloxy)-phenyl]-ethyl]-thiazole-5-carboxylic acid amide; 2-(Methyl-tetrahydro-pyran-4-yl-amino)-4-(trifluoromethyl)-N-[[3-(trifluoromethyloxy)-phenyl]-methyl]-thiazole-5-carboxylic acid amide; N-[1-(4-Chlorophenyl)-ethyl]-2-(methyl-tetrahydro-pyran-4-yl-amino)-4-(trifluoromethyl)-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(methyl-tetrahydro-pyran-4-yl-amino)-4-(trifluoromethyl)-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-[methyl-(tetrahydro-pyran-4-yl-methyl)-amino]-4-(trifluoromethyl)-thiazole-5-carboxylic acid amide; 2-Morpholin-4-yl-4-(trifluoromethyl)-N-[[3-(trifluoromethyloxy)-phenyl]-ethyl]-thiazole-5-carboxylic acid amide; 2-Morpholin-4-yl-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyloxy)-phenyl]-ethyl]-thiazole-5-carboxylic acid amide; N-[1-(4-Chlorophenyl)-ethyl]-2-morpholin-4-yl-4-(trifluoromethyl)-thiazole-5-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-morpholin-4-yl-4-(trifluoromethyl)-thiazole-5-carboxylic acid amide; 2-Morpholin-4-yl-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]-ethyl]-thiazole-5-carboxylic acid amide; in the form of a free compound, a solvate and/or a physiologically acceptable salt.

Formula 22

In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 22. Such compounds are described in Patent No. 9,278,103 issued March 8, 2016 and corresponding to US Application No. 14/230,572 filed March 31, 2014; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 22, this reference incorporated by reference herein controls.

[0327] In an embodiment, the Kv7 channel activator is a compound according to formula 22:

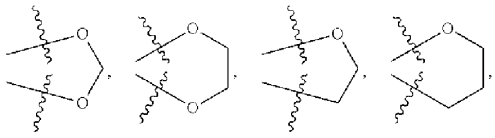


Formula 22

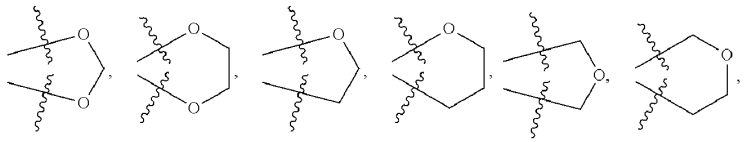
,

wherein, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^6 represents a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or denotes, O—R^8, wherein R^8 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10

membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, in which an "aliphatic group" and an "aliphatic residue" can in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" can in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of

F, Cl, Br, I, NO_2, NH_2,  an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—$S(=O)_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—$NH(C_{1-4}$ aliphatic residue), and a C(=O)—$N(C_{1-4}$ aliphatic residue$)_2$; said compound being in the form of a free compound, the racemate, a mixture of enantiomers, diastereomers, or of enantiomers and diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of a salt of physiologically acceptable acids or bases.

[0328] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a $S(=O)_2$—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—

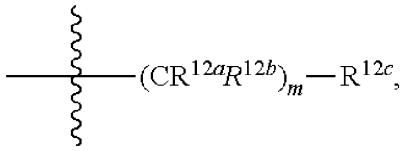
C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH)C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, preferably a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent sleeted from the group consisting of F,

Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, or a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and an O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue, R^6 denotes a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic

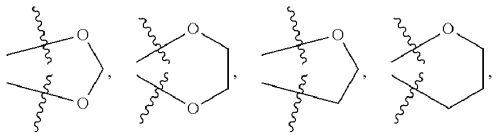
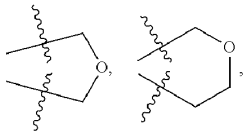
residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue, or R^6 denotes O—R^8, wherein R^8 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic

residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue.

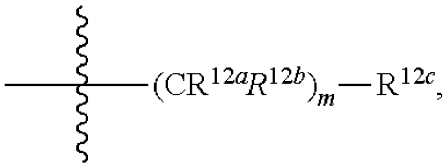
[0329] In further embodiments, R^1 represents the partial structure:



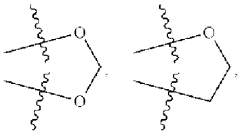
wherein: m denotes 0, 1, 2, 3 or 4, R^{12a} and R^{12b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, and R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a S(=O)$_2$—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at

least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a S(=O)$_2$—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, 

benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0330] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2 or 3, R^{12a} and R^{12b} each independently of one another represent H, F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue or together denote =O, and R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, CN, a S(=O)$_2$—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, OCF_2H, CF_3, CN, a C_{1-4}-aliphatic residue, CH_2—OH, CH_2—OCH_3, S(=O)$_2$—CH_3, SCF_3, NO_2, N(C_{1-4} aliphatic residue)$_2$,



C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, preferably with at least one substituent selected from the group consisting of F, Cl, CH_3, O—CH_3, CF_3 and OCF_3, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue

may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

[0331] In further embodiments, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, or a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl, piperazinyl, 4-methylpiperazinyl, morpholinyl, or piperidinyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl, piperazinyl, 4-methylpiperazinyl, morpholinyl or piperidinyl may in each case be optionally bridged via an C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

[0332] In further embodiments, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, or a S—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4} aliphatic residue.

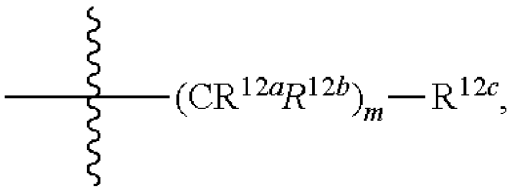
[0333] In further embodiments, R^6 denotes a C_{2-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a C(=O)—O—C_{1-4}-aliphatic residue, a S—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent

selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes O—R^8 wherein R^8 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, CF_3, a C(=O)—O—C_{1-4}-aliphatic residue, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may be bridged via a C_{1-8} aliphatic group, preferably a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, on the condition that if R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

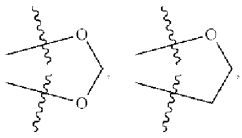
[0334] In further embodiments, R^6 denotes a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic

residue in each case is unsubstituted, or denotes a C_{3-10}-cycloaliphatic residue, or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with OH or an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a unsubstituted C_{1-4} aliphatic group, on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes O—R^8 wherein R^8 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4} aliphatic residue, or in each case denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue in each case may be bridged via an unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 or R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0335] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2, and R^{12a} and R^{12b} each independently of one another represent H, F, OH, CH_3 or OCH_3, or together denote =O, R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, CN, OH, $S(=O)_2—CH_3$, an unsubstituted O—C_{1-4} aliphatic residue, and CF_3, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0 or 2, and R^{12a} and R^{12b} each independently of one another represent H, F, OH, CH_3 or OCH_3; and R^{12c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, OCF_2H, $CH_2—OH$, $CH_2—OCH_3$, $S(=O)_2—CH_3$, SCF_3, NO_2, $N(CH_3)_2$,



CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; methyl; ethyl; n-propyl; iso-propyl; n-butyl; sec.-butyl; tert.-butyl; $CH_2—OH$; $CH_2—O—CH_3$; $CH_2—CH_2—OH$; $CH_2—CH_2—OCH_3$; O-methyl; O-ethyl; O—$(CH_2)_2$—O—CH_3; O—$(CH_2)_2$—OH; S-Methyl; S-Ethyl; cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; methyl; ethyl; n-propyl; iso-propyl; n-butyl; sec.-butyl; tert.-butyl; O-methyl; O-ethyl; O—$(CH_2)_2$—O—CH_3; O—$(CH_2)_2$—OH; S-Methyl; or S-Ethyl, R^6 denotes ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, $CH_2—CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, $CH_2—OCH_3$, $C_2H_4—OCH_3$, $C_3H_6—OCH_3$, cyclopropyl, cyclobutyl, or tetrahydropyranyl, ethenyl or propenyl (—$CH_2CH=CH_2$, —CH=CH—CH_3, —C((=CH_2)—CH_3), in each case unsubstituted, or R^6 denotes O—R^8 wherein R^8 denotes methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, or n-hexyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, N(C_{1-4} aliphatic residue) and an O—C_{1-4}-

aliphatic residue, or in each case denote CH_2-cyclopropyl or oxetanyl, wherein the C_{1-4}-aliphatic residue in each case is unsubstituted.

[0336] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[(3,5-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 9 N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-[(E)-prop-1-enyl]-pyridine-3-carboxylic acid amide; 10 N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; 19 N-[(3-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[3-Fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-[(E)-prop-1-enyl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide 2-Ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-[(2-phenyl-phenyl)-methyl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-[(2-phenyl-phenyl)-methyl]-pyridine-3-carboxylic acid amide; 2-Butoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propoxy-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid

amide; N-[(4-Chlorophenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-(1-methyl-propyl)-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-(1-methyl-propyl)-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-tert-Butyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-tert-Butyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(2-fluoro-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-

Chlorophenyl)-methyl]-2-(2,2-difluoro-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(cyclopropyl-methoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-(2,2-Difluoro-ethoxy)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-(Cyclopropyl-methoxy)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-6-[(3S)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-2-(2-methyl-butyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(1,1-dimethyl-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(2-dimethylaminoethyloxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Isopropyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Isopropyl-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-(oxetan-3-yloxy)-pyridine-3-carboxylic acid amide; 4-Methyl-6-morpholin-4-yl-2-propyl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; 4-Methyl-6-morpholin-4-yl-2-propyl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-4-methyl-6-

morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3,4-difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3,5-difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(2-methoxy-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[4-fluoro-3-(methoxymethyl)-phenyl]-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(3-methoxy-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[3-fluoro-4-(methoxymethyl)-phenyl]-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-(methoxymethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2,4-diisopropyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(2-methoxy-ethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2,4-diethyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; and N-(4,4-Dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-2-tetrahydro-pyran-4-yl-pyridine-3-carboxylic acid amide, respectively in the form of free compounds; racemic mixtures; mixtures of the enantiomers, diastereomers, or enantiomers and diastereomers in any mixing ratio, or an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

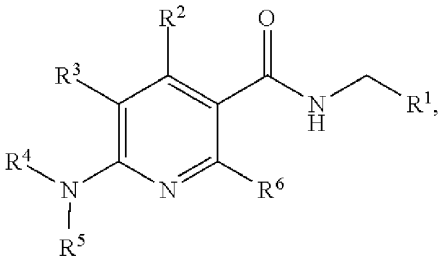
Formula 23

[0337] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 23. Such compounds are described in US Patent No. 9,168,259 issued March 8, 2016 and corresponding to US Application No. 13/449,472 filed April 18, 2012; US Patent No. 8,552,200 issued December 12, 2013 and corresponding to US Application No. 13/276,464 filed October 19, 2011; International Publication No. WO2012052167A1, published April 26, 2012 and corresponding to International Application

No. PCT/EP2011/005265 filed April 26, 2012; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 23, these references incorporated by reference herein control.

[0338] In an embodiment, the Kv7 channel activator is a compound according to formula 23:

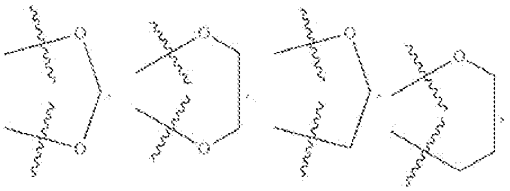
Formula 23



wherein, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^4 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or

polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^4 denotes a 3 to 10 membered heterocycloaliphatic residue or a heteroaryl, the 3 to 10 membered heterocycloaliphatic residue or the heteroaryl is linked via a carbon atom; R^5 denotes H or a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; or R^4 and R^5 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted; R^6 represents a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or denotes S—R^7, O—R^8 or N(R^9R^{10}), wherein R^7 and R^8 in each case represent a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 or R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, R^9 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^9 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom; R^{10} denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; or R^9 and R^{10} form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted; in which an “aliphatic group” and an “aliphatic residue” can in each case be branched or unbranched, saturated or unsaturated, in which a “cycloaliphatic residue” and a “heterocycloaliphatic residue” can in each case be saturated or unsaturated, in which “mono- or polysubstituted” with respect to an “aliphatic group” and an “aliphatic residue” relates, with respect to the corresponding residues or groups, to the substitution of one or more

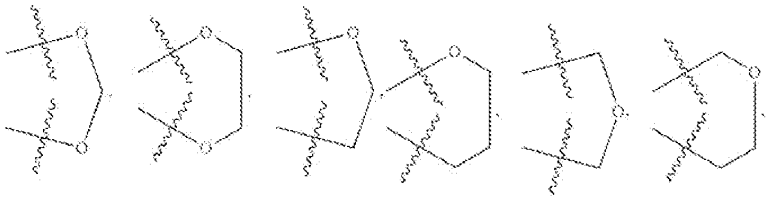
hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,



an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-

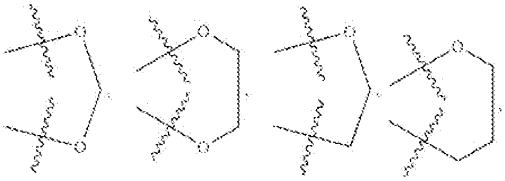
aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; said compound being in the form of a free compound, the racemate, a mixture of enantiomers, diastereomers, or of enantiomers and diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of a salt of physiologically acceptable acids or bases.

[0339] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an

$NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, a $S(=O)_2—C_{1-4}$-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and $C(=O)—O—C_2H_5$, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted $O—C_{1-4}$-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, $O—CH_2—OH$, $O—CH_2—O—CH_3$, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and $C(=O)—O—C_2H_5$, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, preferably a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a $S—C_{1-4}$-aliphatic residue, or a $O—C_{1-4}$-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted $O—C_{1-4}$-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent

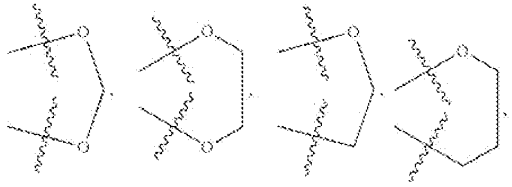
selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and an O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue, R^4 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic

residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C(=O)—O—C_{1-4}-aliphatic residue a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^4 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic

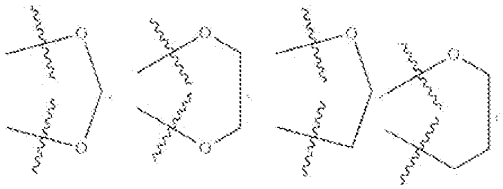
residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, R^5 denotes H or a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or R^4 and R^5 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen

atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and $C(=O)—O—C_2H_5$, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen atom connecting them may optionally be condensed with a C_{3-10} cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, wherein the C_{3-10} cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, =O, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, $O—CH_2—OH$, $O—CH_2—O—CH_3$, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

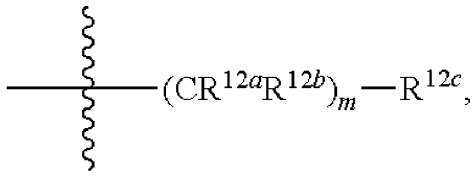
NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, R^6 denotes a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$-aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted $O—C_{1-4}$-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted $O—C_{1-4}$-aliphatic residue, and and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue, or R^6 denotes $S—R^7$, $O—R^8$ or $N(R^9R^{10})$, wherein R^7 and R^8 in each case represent a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$-aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted $O—C_{1-4}$-aliphatic residue, or in each case represent a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F,

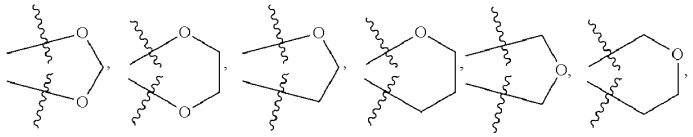
Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 or R^9 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue, R^9 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C(=O)—O—C_{1-4}-aliphatic residue a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected

from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^9 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue, R^{10} denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or R^9 and R^{10} form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-}

$_{4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^9 and R^{10} together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0340] In further embodiments, R^1 represents the partial structure:

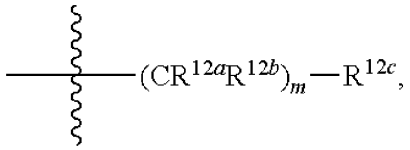


wherein: m denotes 0, 1, 2, 3 or 4, R^{12a} and R^{12b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, and R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a S(=O)$_2$—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a S(=O)$_2$—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, 

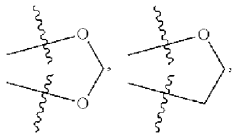
benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an

unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O) —OH.

[0341] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2 or 3, R^{12a} and R^{12b} each independently of one another represent H, F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue or together denote =O, and R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, CN, a S(=O)$_2$—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, OCF_2H, CF_3, CN, a C_{1-4}-aliphatic residue, CH_2—



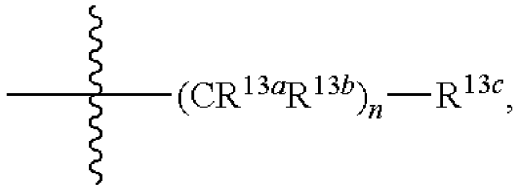
OH, CH_2—OCH_3, $S(=O)_2$—CH_3, SCF_3, NO_2, $N(C_{1\text{-}4}$ aliphatic residue$)_2$, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a $C_{3\text{-}6}$ cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—$C_{1\text{-}4}$ aliphatic residue, OCF_3, CF_3, CN, a $C_{1\text{-}4}$-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, preferably with at least one substituent selected from the group consisting of F, Cl, CH_3, O—CH_3, CF_3 and OCF_3, and wherein the $C_{3\text{-}6}$ cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—$C_{1\text{-}4}$ aliphatic residue, OCF_3, CF_3 a $C_{1\text{-}4}$-aliphatic residue and C(=O)—OH.

[0342] In further embodiments, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a $C_{1\text{-}4}$-aliphatic residue, a S—$C_{1\text{-}4}$-aliphatic residue, or a O—$C_{1\text{-}4}$-aliphatic residue, wherein the $C_{1\text{-}4}$-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted aliphatic residue, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl, piperazinyl, 4-methylpiperazinyl, morpholinyl, or piperidinyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted $C_{1\text{-}4}$-aliphatic residue and an unsubstituted O—$C_{1\text{-}4}$-aliphatic residue, and wherein cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl, piperazinyl, 4-methylpiperazinyl, morpholinyl or piperidinyl may in each case be optionally bridged via an $C_{1\text{-}4}$ aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, an unsubstituted $C_{1\text{-}4}$-aliphatic residue and an unsubstituted aliphatic residue.

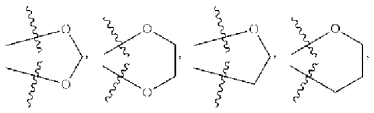
[0343] In further embodiments, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; a $C_{1\text{-}4}$-aliphatic residue, a O—$C_{1\text{-}4}$-aliphatic residue, or a S—$C_{1\text{-}4}$-aliphatic residue, wherein the $C_{1\text{-}4}$ aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted with

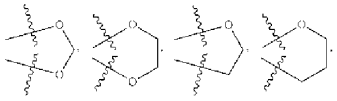
at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue.

[0344] In further embodiments, R^4 represents the partial structure:

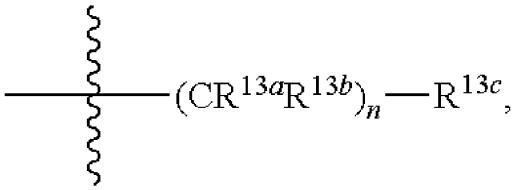


wherein: n denotes 0, 1, 2, or 3, R^{13a} and R^{13b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, and R^{13c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—

C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, R^5 denotes H or a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or R^4 and R^5 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, C(=O)—OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic

residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  benzyl, phenyl, thienyl, and pyridyl, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen atom connecting them may optionally be condensed with a C_{3-10} cycloaliphatic residue, preferably cyclopropyl, cyclobutyl or cycclopentyl, or a 3 to 10 membered heterocycloaliphatic residue, preferably oxetanyl or oxiranyl, wherein the C_{3-10} cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, =O, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, and C(=O)—OH, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0345] In further embodiments, R^4 represents the partial structure:



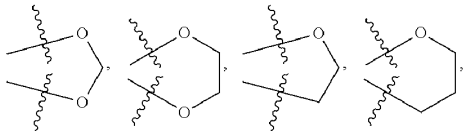
wherein: n denotes 0, 1, 2 or 3, R^{13a} and R^{13b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue or together denote =O, and R^{13c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, preferably with at least one substituent selected from the group consisting of F, Cl, CH_3, O—CH_3, CF_3 and OCF_3, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH, R^5 denotes H or an unsubstituted C_{1-4}-aliphatic residue or a C_{1-4}-aliphatic residue monosubstituted with O-methyl, or R^4 and R^5 form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue,

unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, C(=O)—OH, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, cyclopropyl, cyclobutyl and cyclopentyl, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen atom connecting them may optionally be condensed with phenyl or pyridyl, wherein the phenyl or pyridyl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, a C_{1-4}-aliphatic residue, C(=O)—OH, and a C_{3-6} cycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^4 and R^5 together with the nitrogen atom connecting them may optionally be condensed with a C_{3-6} cycloaliphatic residue, preferably cyclopropyl, cyclobutyl or cyclopentyl, or a 4 to 7 membered heterocycloaliphatic residue, preferably oxetanyl or oxiranyl, wherein the C_{3-6} cycloaliphatic residue or the 4 to 7 membered heterocycloaliphatic residue condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5.

[0346] In further embodiments, R^6 denotes a C_{2-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10

membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a C(=O)—O—C_{1-4}-aliphatic residue, a S—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue. on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes S—R^7 or O—R^8 wherein R^7 and R^8 in each case denote a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, CF_3, a C(=O)—O—C_{1-4}-aliphatic residue, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or in each case denote a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may be bridged via a C_{1-8} aliphatic group, preferably a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, on the condition that if R^7 or R^8 denotes a 3 to 10 membered heterocycloaliphatic

residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes $N(R^9R^{10})$, wherein R^9 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, a C(=O)—O—C_{1-4}-aliphatic residue, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case be bridged, preferably is bridged, via a C_{1-8} aliphatic group, preferably a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, on the condition that if R^9 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, and R^{10} denotes a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or R^9 and R^{10} form together with the nitrogen atom connecting them a 3 to 10 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue,

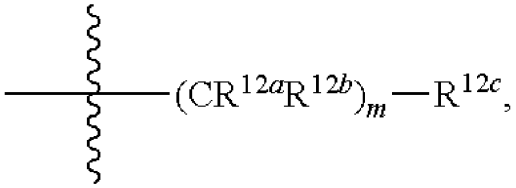
and wherein the 3 to 10 membered heterocycloaliphatic residue formed by R^9 and R^{10} together with the nitrogen atom connecting them may optionally be condensed with aryl or heteroaryl, preferably with phenyl or pyridyl, wherein the aryl or heteroaryl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, residue,  benzyl, phenyl, thienyl, and pyridyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, and C(=O)—OH.

[0347] In further embodiments, R^6 denotes a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case is unsubstituted, or denotes a C_{3-10}-cycloaliphatic residue, or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with OH or an unsubstituted O—C_{1-4}-aliphatic residue. and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a unsubstituted C_{1-4} aliphatic group, on the condition that if R^6 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes S—R^7 or O—R^8 wherein R^7 and R^8 in each case denote a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue,

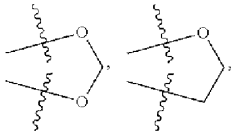
OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or in each case denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue in each case may be bridged via an unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 or R^8 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, or R^6 denotes N(R^9R^{10}), wherein R^9 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue is in each case bridged via a unsubstituted C_{1-8} aliphatic group, preferably an unsubstituted C_{1-4} aliphatic group, on the condition that if R^9 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, and R^{10} denotes an unsubstituted C_{1-4}-aliphatic residue, or R^9 and R^{10} form together with the

nitrogen atom connecting them a 3 to 6 membered heterocycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the 3 to 6 membered heterocycloaliphatic residue formed by R^9 and R^{10} together with the nitrogen atom connecting them may optionally be condensed with phenyl or pyridyl, wherein the phenyl or pyridyl residues condensed in this way can for their part be respectively unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, residue, benzyl, phenyl, and pyridyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OCH_3, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, CF_3, and a C_{1-4}-aliphatic residue.

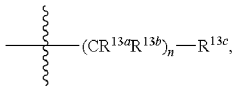
[0348] In further embodiments, R^1 represents the partial structure:

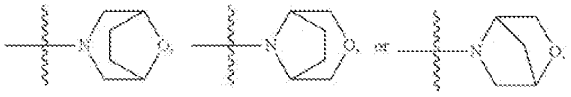


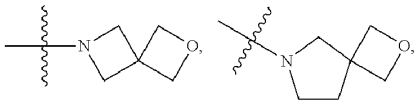
wherein: m is 0, 1 or 2, and R^{12a} and R^{12b} each independently of one another represent H, F, OH, CH_3 or OCH_3, or together denote =O, R^{12c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, CN, OH, S(=O)$_2$—CH_3, an unsubstituted O—C_{1-4} aliphatic residue, and CF_3, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0 or 2, and R^{12a} and R^{12b} each independently of one another represent H, F, OH, CH_3 or OCH_3; and R^{12c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one

substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, OCF_2H, CH_2—OH, CH_2—OCH_3, S(=O)$_2$—CH_3, SCF_3, NO_2, $N(CH_3)_2$,  CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; methyl; ethyl; n-propyl; iso-propyl; n-butyl; sec.-butyl; tert.-butyl; CH_2—OH; CH_2—O—CH_3; CH_2—CH_2—OH; CH_2—CH_2—OCH_3; O-methyl; O-ethyl; O—$(CH_2)_2$—O—CH_3; O—$(CH_2)_2$—OH; S-Methyl; S-Ethyl; cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl, R^3 represents H; F; Cl; Br; I; CN; CF_3; SCF_3; NO_2; OCF_3; methyl; ethyl; n-propyl; iso-propyl; n-butyl; sec.-butyl; tert.-butyl; O-methyl; O-ethyl; O—$(CH_2)_2$—O—CH_3; O—$(CH_2)_2$—OH; S-Methyl; or S-Ethyl, R^4 represents the partial structure (T2)

(T2)



wherein n denotes 0, 1, 2 or 3, R^{13a} and R^{13b} each independently of one another represent H, F, CH_3 or OCH_3, or together denote =O, R^{13c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, an unsubstituted O—C_{1-4} aliphatic residue, and CF_3, or denotes cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, pyrrolidinyl, morpholinyl, piperazinyl, piperidinyl or tetrahydropyranyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, and a C_{1-4}-aliphatic residue, R^5 denotes H, methyl or ethyl, $C_2H_4OCH_3$ or $C_3H_6OCH_3$, or R^4 and R^5 form together with the nitrogen atom connecting them a morpholinyl, piperidinyl, pyrrolidinyl, azetidinyl, oxazepanyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, thiomorpholinyl, azepanyl,  tetrahydroimidazo[1,2-

a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, 
dihydroindolinyl, or dihydroisoindolyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, =O, C(=O)—OH, O-methyl, O-ethyl, OCF_3, SCF_3, CF_3, C(=O)—CH_3, C(=O)—OCH_3, CH_2CF_3, CH_2OH, CH_2—OCH_3, CH_2CH_2—OCH_3, methyl, ethyl, n-propyl, 2-propyl, cyclopropyl, and cyclobutyl, R^6 denotes ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, CH_2—OCH_3, C_2H_4—OCH_3, C_3H_6—OCH_3, cyclopropyl, cyclobutyl, or tetrahydropyranyl, ethenyl or propenyl (—CH_2CH=CH_2, —CH=CH—CH_3, —C((=CH_2)—CH_3), in each case unsubstituted, or R^6 denotes S—R^7 or O—R^8 wherein R^7 and R^8 in each case denote methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, or n-hexyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, N(C_{1-4} aliphatic residue) and an O—C_{1-4}-aliphatic residue, or in each case denote CH_2-cyclopropyl or oxetanyl, wherein the C_{1-4}-aliphatic residue in each case is unsubstituted, or R^6 denotes N(R^9R^{10}), wherein R^9 denotes methyl, C(=O)—CH_3, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, or n-hexyl, R^{10} denotes methyl or ethyl, or R^9 and R^{10} form together with the nitrogen atom connecting them a morpholinyl, piperidinyl, pyrrolidinyl, or azetidinyl, in each case unsubstituted.

[0349] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[(3,5-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(tetrahydro-pyran-2-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(3-methoxy-azetidin-1-yl)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(3-hydroxy-azetidin-1-yl)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(4-fluorophenyl)-methylamino]-4-methyl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-[(E)-prop-1-enyl]-pyridine-3-carboxylic acid amide; N-[(3-

Fluorophenyl)methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-morpholin-4-yl-4-(trifluoromethyl)-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)methyl]-4-methyl-2,6-dimorpholin-4-yl-pyridine-3-carboxylic acid amide; 1-[6-Ethylsulfanyl-5-[(3-fluorophenyl)-methyl-carbamoyl]-4-methyl-pyridin-2-yl]-piperidine-4-carboxylic acid methyl ester; 1-[6-Ethylsulfanyl-5-[(3-fluorophenyl)-methyl-carbamoyl]-4-methyl-pyridin-2-yl]-piperidine-4-carboxylic acid; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(4-hydroxy-piperidin-1-yl)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(4-oxo-piperidin-1-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluoro-2-methoxy-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluoro-2-hydroxy-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)methyl]-4-methyl-6-morpholin-4-yl-2-pyrrolidin-1-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-pyrrolidin-1-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(1,2,3,4-tetrahydro-isoquinolin-2-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[6-(trifluoromethyl)-1,2,3,4-tetrahydro-isoquinolin-2-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)methyl]-4-methyl-6-morpholin-4-yl-2-[(E)-prop-1-enyl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(3-methoxy-pyrrolidin-1-yl)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(4-methyl-piperazin-1-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-piperidin-1-yl-pyridine-3-carboxylic acid amide; 6-Dimethylamino-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-methylamino-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(2-methoxy-ethyl-methyl-amino)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(2-methoxy-ethylamino)-4-methyl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-(isopropylsulfanyl)-4-methyl-6-morpholin-4-yl-

pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-(3-methyl-butyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(Cyclopentyl-methyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(2-Cyclopentyl-ethyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(6-fluoro-pyridin-2-yl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(5-fluoro-pyridin-2-yl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(2,2-Dimethyl-propyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(2-methyl-morpholin-4-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(4-methoxy-piperidin-1-yl)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[(2-phenyl-phenyl)-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[2-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(4-fluorophenyl)-methyl-methyl-amino]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(3-phenyl-propyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-phenethyl-pyridine-3-carboxylic acid amide; N-Benzyl-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-(propylsulfanyl)-pyridine-3-carboxylic acid amide; 2-(Butylsulfanyl)-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-5-fluoro-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[3-(trifluoromethyl)phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(tetrahydro-pyran-4-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-(2-methyl-propylsulfanyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-(2-methoxy-ethylsulfanyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-

carboxylic acid amide; 2-Dimethylamino-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 6-(2,6-Dimethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(2-tetrahydro-pyran-2-yl-ethyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(tetrahydro-pyran-2-yl-methyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(4-methyl-piperidin-1-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[2-(4-fluorophenyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-[[6-Ethylsulfanyl-5-[(3-fluorophenyl)-methyl-carbamoyl]-4-methyl-pyridin-2-yl]-methyl-amino]-acetic acid ethyl ester; 6-(4-Cyclopropyl-piperazin-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 6-(4,4-Dimethyl-piperidin-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethylsulfanyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; N-(Cyclohexyl-methyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(2-methoxy-ethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(3-methoxy-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-(4-methyl-pentyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-Butyl-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-pentyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-fluoro-3-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(2-tert-Butoxy-ethyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-fluoro-2-(4-fluorophenyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-[(2-phenyl-phenyl)-methyl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-

[(2-phenyl-phenyl)-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[3-fluoro-5-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[2-fluoro-3-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[2-fluoro-5-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-([1,4]oxazepan-4-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyloxy)-phenyl]-methyl]pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-([1,4]oxazepan-4-yl)-pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-6-([1,4]oxazepan-4-yl)-pyridine-3-carboxylic acid amide; N-[(2,3-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(2,5-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Cyano-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(2-isopropoxy-ethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(3,3-Dimethyl-butyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(3-Cyclopentyl-propyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(2-Cyclohexyl-ethyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(2,4-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[3-(4-fluorophenyl)-propyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(3-pyridin-2-yl-propyl)-pyridine-3-carboxylic acid amide; 2-Butoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propoxy-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-oxo-azetidin-1-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[3-(3-fluorophenyl)-propyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(3-pyridin-3-yl-propyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(3-pyridin-4-yl-propyl)-pyridine-3-carboxylic acid amide; N-(5,5-Dimethyl-hexyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(pyridin-4-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-

(pyridin-3-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-6-[(4-fluoro-benzoyl)-methyl-amino]-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(pyridin-2-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(pyridin-3-yl-methylamino)-pyridine-3-carboxylic acid amide; 6-(Acetyl-methyl-amino)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Chlorophenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 6-[Bis(2-methoxy-ethyl)-amino]-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-(Ethyl-methyl-amino)-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-(3-methoxy-propyl-methyl-amino)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[3-(2-fluorophenyl)-propyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[[3-(trifluoromethyloxy)-phenyl]-methyl]pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[3-(methoxymethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethoxy-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-(1,3-Benzodioxol-5-yl-methyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[2-fluoro-4-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 6-(Azepan-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-methoxyphenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; (2S)-2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(2-methyl-morpholin-4-yl)-pyridine-3-carboxylic acid amide; (2R)-2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(2-methyl-morpholin-4-yl)-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-(3-Cyclopropyl-propyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[3-fluoro-4-(trifluoromethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-oxo-piperazin-1-yl)-pyridine-3-carboxylic acid amide; 6-(4-Acetyl-piperazin-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Cyano-phenyl)-methyl]-2-

ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-(methoxymethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[3-fluoro-4-(methoxymethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Dimethylaminophenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-fluoro-3-(methoxymethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(4-methyl-3-oxo-piperazin-1-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(6-oxa-2-azaspiro[3.3]heptan-2-yl)-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 4-Methyl-2-methylsulfanyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 4-Methyl-2-methylsulfanyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(6-oxo-2,3,4,7,8,8a-hexahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-oxa-6-azabicyclo[2.2.1]heptan-6-yl)-pyridine-3-carboxylic acid amide; N-(3-Cyano-propyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(p-tolyl-methyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-(3-methylsulfonyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4-Cyano-butyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(m-tolyl-methyl)-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-methoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethoxy-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 6-(2-Ethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-2-methylsulfanyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-pyridin-2-yl-amino)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-pyridin-3-yl-

amino)-pyridine-3-carboxylic acid amide; 2-Dimethylamino-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-(Ethyl-methyl-amino)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-(Ethyl-methyl-amino)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(tetrahydro-pyran-3-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-methylsulfanyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 6-(3-Ethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(3R)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(3S)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Dimethylamino-N-(4,4-dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(ethyl-methyl-amino)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-(Ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-(Ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-methylsulfanyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-(1-methyl-propyl)-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-(1-methyl-propyl)-pyridine-3-carboxylic acid amide; 2-

Cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-pyridin-4-yl-amino)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluoro-3-methyl-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(2-hydroxy-3-phenyl-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-(ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-(ethyl-methyl-amino)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Dimethylamino-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-dimethylamino-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3,5-Dimethyl-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-heptyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 6-Dimethylamino-N-(4,4-dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-6-(2-methoxy-ethyl-methyl-amino)-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-6-(3-methoxy-propyl-methyl-amino)-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-propyl-morpholin-4-yl)-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-hexyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-(methyl-tetrahydro-furan-3-yl-amino)-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-(2-methyl-morpholin-4-yl)-pyridine-3-carboxylic acid amide; 2-tert-Butyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-

methyl-6-(2-oxa-6-azaspiro[3.4]octan-6-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(2R)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(3-hydroxy-3-phenyl-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(2-hydroxy-4-methyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[2-(2-methoxy-ethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(5-hydroxy-4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-[(3-methylsulfonyl-phenyl)-methyl]-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[2-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,6]naphthyridin-6-yl]pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-[[4-(trifluoromethyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; 2-Methoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-N-[[4-(trifluoromethyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[3-(methoxymethyl)-azetidin-1-yl]-4-methyl-pyridine-3-carboxylic acid amide; 6-(2,5-Dimethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Dimethylamino-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-dimethylamino-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[2-(trifluoromethyl)-5,6,7,8-tetrahydro-imidazo[1,2-a]pyrazin-7-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-dimethylamino-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Dimethylamino-N-(4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Dimethylamino-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-

butyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-[(4-methylsulfonyl-phenyl)-methyl]-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-6-[(3R)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluorophenyl)-methyl]-6-[(3S)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-tert-Butyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[4-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyridine-3-carboxylic acid amide; 6-(2,2-Dimethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(2-oxo-propyl)-amino]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-6-[(2R)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-6-[(3R)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethylsulfanyl-6-[(3S)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-tetrahydro-pyran-4-yl-amino)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(4-methoxy-cyclohexyl)-methyl-amino]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[2-(trifluoromethyl)-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-tetrahydro-pyran-3-yl-amino)-pyridine-3-carboxylic acid amide; 6-(3,5-Dimethyl-morpholin-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(3S)-3-(hydroxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(3R)-3-(hydroxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-2-propyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(3-hydroxy-4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Cyano-3-fluoro-phenyl)-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(2-fluoro-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(2,2-difluoro-ethoxy)-4-methyl-6-

morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(cyclopropyl-methoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-(2,2-Difluoro-ethoxy)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-ethoxy-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-[(2S)-2-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-[(2R)-2-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-(Cyclopropyl-methoxy)-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-6-[(3S)-3-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-2-(2-methyl-butyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(1,1-dimethyl-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-ethylsulfanyl-4-methyl-6-(methyl-tetrahydro-pyran-3-yl-amino)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-[(4-nitrophenyl)-methyl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-(2-dimethylaminoethyloxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(4-fluoro-3-methoxy-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(3-hydroxy-4-methyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluoro-4-methoxy-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[[4-(Difluoro-methoxy)-phenyl]-methyl]-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(1,3-Dihydro-isobenzofuran-5-yl-methyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-6-[(2S)-2-(methoxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(2S)-2-(hydroxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(2R)-2-(hydroxymethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 6-(Benzyl-methyl-amino)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-(tetrahydro-furan-2-yl-methyl)-amino]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-

[(3-fluorophenyl)-methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[(3S)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-[methyl-[[4-(trifluoromethyl)-phenyl]-methyl]-amino]-pyridine-3-carboxylic acid amide; 6-(1,1-Dioxo-[1,4]thiazinan-4-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 6-(Azetidin-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(methyl-tetrahydro-furan-3-yl-amino)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(N-methyl-anilino)-pyridine-3-carboxylic acid amide; 6-(2,3-Dihydro-1H-isoindol-2-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(1,2,3,4-tetrahydro-quinolin-1-yl)-pyridine-3-carboxylic acid amide; 6-(2,3-Dihydro-1H-indol-1-yl)-2-ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(2,4,4-trimethyl-pentyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(3-methoxy-cyclohexyl)-methyl-amino]-4-methyl-pyridine-3-carboxylic acid amide; N-(4,4-Difluoro-pentyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Isopropyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-oxo-morpholin-4-yl)-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Isopropyl-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-(oxetan-3-yloxy)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(4-methoxy-4-methyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-(4-fluoro-4-methyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 4-Methyl-6-morpholin-4-yl-2-propyl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; N-[(3,4-Difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-[(3,5-Difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-

carboxylic acid amide; 4-Methyl-6-morpholin-4-yl-2-propyl-N-[[4-(trifluoromethyl)-phenyl]-methyl]-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-2-oxo-pentyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-2-propyl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-(4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-butyl)-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3,4-difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[(3,5-difluoro-phenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-4-methyl-6-morpholin-4-yl-N-[[4-(trifluoromethyl)-phenyl]methyl]-pyridine-3-carboxylic acid amide;N-[(4-Chlorophenyl)-methyl]-2-cyclopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide;2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methoxy-6-morpholin-4-yl-pyridine-3-carboxylic acid amide;N-(4,4-Dimethyl-pentyl)-2-(2-methoxy-ethylsulfanyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide;2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(4-fluorophenyl)-methyl-(3-methoxy-propyl)-amino]-4-methyl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-6-morpholin-4-yl-N-(3,4,4-trimethyl-pentyl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[3-(2-methoxy-ethyl)-morpholin-4-yl]-4-methyl-pyridine-3-carboxylic acid amide; 2-(Acetyl-methyl-amino)-N-[(3-fluorophenyl)-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-6-[(4-fluorophenyl)-methyl-(2-methoxy-ethyl)-amino]-4-methyl-pyridine-3-carboxylic acid amide;2-Ethylsulfanyl-4-methyl-N-[3-(3-methyl-oxetan-3-yl)-propyl]-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pent-2-ynyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-methyl-6-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[(3-fluorophenyl)-methyl]-4-(methoxymethyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-4-methyl-2-(1-methyl-propyl)-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-hexyl)-2-ethylsulfanyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(2-

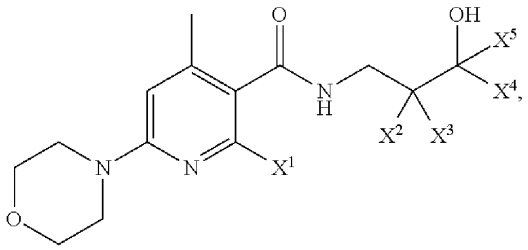
methoxy-ethoxy)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-4-methyl-N-[3-(1-methyl-cyclopropyl)-propyl]-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[4-fluoro-3-(methoxymethyl)-phenyl]-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-fluoro-3-(methoxymethyl)-phenyl]methyl]-4-methyl-6-[(3R)-3-methyl-morpholin-4-yl]-pyridine-3-carboxylic acid amide; 2-Ethylsulfanyl-N-[[4-fluoro-3-(hydroxymethyl)-phenyl]methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(3-methoxy-propyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[3-fluoro-4-(methoxymethyl)-phenyl]-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-2-(methoxymethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2,4-diisopropyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-2-(2-methoxy-ethyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-[(4-Chlorophenyl)-methyl]-2,4-diethyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; and N-(4,4-Dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-2-tetrahydro-pyran-4-yl-pyridine-3-carboxylic acid amide, respectively in the form of free compounds; racemic mixtures; mixtures of the enantiomers, diastereomers, or enantiomers and diastereomers in any mixing ratio, or an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

Formula 24

[0350] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 24. Such compounds are described in US Patent No. 9,168,259 issued March 8, 2016 and corresponding to US Application No. 13/449,472 filed April 18, 2012; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 24, this reference incorporated by reference herein controls.

[0351] In an embodiment, the Kv7 channel activator is a compound according to formula 24:

Formula 24



wherein, X^1 represents a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted, and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; or represents OX^6, wherein X^6 represents a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted; X^2 and X^3 independently of one another represent H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, or X^2 and X^3 and/or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted, and the respective remaining substituents of X^2 and X^3 each independently of one another represent H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic

residue, wherein the C_{1-4} aliphatic residue may be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted, and X^3 represents H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; and X^5 represents H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be unsubstituted or mono- or polysubstituted; or a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted; on the condition that if X^5 denotes a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, in which an "aliphatic group" and an "aliphatic residue" can in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" can in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a N(C_{1-4}-aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, a N(C_{1-4}-aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCH_2F, $OCHF_2$, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, a S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CH_2F, CHF_2, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, CH_2OH, CH_2—OCH_3, C_2H_4—OH, C_2H_4—OCH_3 CH_2—CF_3, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a

"cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a N(C_{1-4}-aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, a N(C_{1-4}-aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCH_2F, $OCHF_2$, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, a S(=O)$_2$—N(C_{1-4}-aliphatic residue)$_2$, CN, CH_2F, CHF_2, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, CH_2OH, CH_2—OCH_3, C_2H_4—OH, C_2H_4—OCH_3 CH_2—CF_3, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; said compound being in the form of a free compound, the racemate, a mixture of enantiomers, diastereomers, or of enantiomers and diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of a salt of physiologically acceptable acids or bases.

[0352] In further embodiments, X^1 represents a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue may optionally be bridged via a C_{1-4} aliphatic group,

which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents OX^6, wherein X^6 represents a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue; wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, X^2 and X^3 independently of one another represent H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; CH_2F; CHF_2; CF_3; or a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—

C_{1-4}-aliphatic residue, a $S(=O)_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or X^2 and X^3 and/or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a $S(=O)_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and the respective remaining substituents of X^2 and X^3 each independently of one another represent H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a $S(=O)_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent

selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and the remaining substituent X^3 represents H; F; Cl; Br; I; CN; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an

unsubstituted O—C_{1-4}-aliphatic residue, and the remaining substituent X^5 represents H; CH_2F; CHF_2; CF_3; OCH_2F; $OCHF_2$; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, on the condition that if X^5 denotes a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue.

[0353] In further embodiments, X^1 represents a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or represents OX^6, wherein X^6 represents a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCH_2F, $OCHF_2$, OCF_3, CH_2F, CHF_2, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue.

[0354] In further embodiments, X^1 represents a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, or represents a C_{3-6}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, or represents OX^6, wherein X^6 represents a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCH_2F, $OCHF_2$, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a S(=O)—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, CN, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted.

[0355] In further embodiments, X^1 represents a C_{2-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represents OX^6, wherein X^6 represents a C_{1-4}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue.

[0356] In further embodiments, X^1 represents ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$,

$C(CH_3)_2(C_2H_5)$, ethenyl or propenyl (—CH_2CH═CH_2, —CH═CH—CH_3, —C(═CH_2)—CH_3), cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl, or represents OX^6, wherein X^6 represents methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2OH, CH_2OCH_3, CH_2CH_2OH, $CH_2CH_2OCH_3$, and $CH(OH)CH_2OH$.

[0357] In further embodiments, X^2 and X^3 independently of one another represent H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, or X^2 and X^3 and/or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent

selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and the respective remaining substituents of X^2 and X^3 each independently of one another represent H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and the remaining substituent X^3 represents H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; OCH_2F; $OCHF_2$; OCF_3; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-

aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and the remaining substituent X^5 represents H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, OCH_2F, $OCHF_2$, OCF_3, and a C_{1-4}-aliphatic residue, on the condition that if X^5 denotes a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted O—C_{1-4}-aliphatic residue.

[0358] In further embodiments, X^2 and X^3 independently of one another represent H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is unsubstituted, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, or X^2 and X^3 and/or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, and the respective remaining substituents of X^2 and X^3 each independently of one another represent H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each unsubstituted, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represent H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is unsubstituted, or represent a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, on the condition that if X^4 and/or X^5 denote(s) a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom, or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, CH_2F, CHF_2, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, and the remaining substituent X^3 represents H; F; Cl; Br; I; CH_2F; CHF_2; CF_3; OH; a C_{1-4}-aliphatic residue, or an O—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue is in each case unsubstituted, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, and the remaining substituent X^5 represents H; CH_2F; CHF_2; CF_3; a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue is unsubstituted, or represents a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted, on the condition that if X^5 denotes a 3 to 6 membered heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom.

[0359] In further embodiments, X^2 and X^3 independently of one another represent H; OH; an unsubstituted C_{1-4}-aliphatic residue, or an unsubstituted O—C_{1-4} aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; CH_2F; CHF_2; CF_3; an unsubstituted C_{1-4}-aliphatic residue, or X^2 and X^3 or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CH_2F, CHF_2, CF_3, an unsubstituted O—C_{1-4}-aliphatic

residue, and an unsubstituted C_{1-4}-aliphatic residue, and the respective remaining substituents of X^2 and X^3 each independently of one another represent H; OH; an unsubstituted C_{1-4}-aliphatic residue, or an unsubstituted O—C_{1-4} aliphatic residue, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represent H; CH_2F; CHF_2; CF_3; an unsubstituted C_{1-4}-aliphatic residue, or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an unsubstituted aliphatic residue, CH_2F, CHF_2, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, and the remaining substituent X^3 represents H; F; Cl; Br; I; OH; an unsubstituted C_{1-4}-aliphatic residue, or an unsubstituted O—C_{1-4} aliphatic residue, and the remaining substituent X^5 represents H; CH_2F; CHF_2; CF_3; an unsubstituted C_{1-4}-aliphatic residue.

[0360] In further embodiments, X^2 and X^3 independently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, OCH_3 or OCH_2CH_3, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, X^4 and X^5 independently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, CH_2F; CHF_2; CF_3; or X^2 and X^3 or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-6}-cycloaliphatic residue selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, CF_3, OCH_3 and OCH_2CH_3, and the respective remaining substituents of X^2 and X^3 each independently of one another represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, OCH_3 or OCH_2CH_3, with the proviso that at least one of X^2 and X^3 denotes H or is linked via a carbon atom, and the respective remaining substituents of X^4 and X^5 each independently of one another represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, CH_2F; CHF_2; CF_3; or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-6}-cycloaliphatic residue selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, unsubstituted or mono- or polysubstituted with at least one

substituent selected from the group consisting of F, Cl, Br, I, OH, methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, CF_3, OCH_3 and OCH_2CH_3, and the respective remaining substituent of X^3 represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, OCH_3 or OCH_2CH_3, and the respective remaining substituent X^5 represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, CH_2—$CH(CH_3)(C_2H_5)$, $C(CH_3)_2(C_2H_5)$, CH_2F; CHF_2; CF_3.

[0361] In further embodiments, X^1 represents ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl, or represents OX^6, wherein X^6 represents methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, or tert.-butyl, X^2 and X^3 in dependently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, or tert.-butyl, X^4 and X^5 independently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, or CF_3; or X^2 and X^3 or X^4 and X^5 in pairs, in each case independently of one another, together with the carbon atom connecting them, form a C_{3-6}-cycloaliphatic residue selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of OH, methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, CH_2F, CHF_2, CF_3, OCH_3 and OCH_2CH_3, and the respective remaining substituents of X^2 and X^3 in dependently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, or tert.-butyl, and the respective remaining substituents of X^4 and X^5 independently of one another represent H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, or CF_3; or X^2 and X^4 together with the carbon atoms connecting them, form a C_{3-6}-cycloaliphatic residue selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of OH, methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, CF_3, OCH_3 and OCH_2CH_3, and X^3 represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, or tert.-butyl, and X^5 represents H; methyl; ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, CH_2F, CHF_2, or CF_3.

[0362] In further embodiments, the Kv7 cannel activator is selected from the group consisting of: 2-Cyclopropyl-N-(3-hydroxy-4,4-dimethyl-pentyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[(1S,2R)-2-hydroxy-cyclohexyl]-

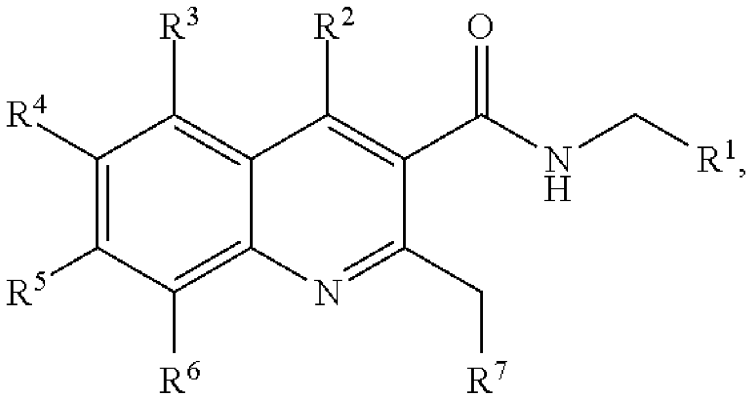
methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-[[(1R,2S)-2-hydroxy-cyclohexyl]-methyl]-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Cyclopropyl-N-([2-hydroxy-cyclopentyl]-methyl)-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; N-(3-Hydroxy-4,4-dimethyl-pentyl)-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; 2-Isopropyl-4-methyl-6-morpholin-4-yl-N-(4,4,4-trifluoro-3-hydroxy-butyl)-pyridine-3-carboxylic acid amide; and N-[[(1S,2R)-2-Hydroxy-cyclohexyl]-methyl]-2-isopropyl-4-methyl-6-morpholin-4-yl-pyridine-3-carboxylic acid amide; optionally in the form of a single stereoisomer or a mixture of stereoisomers, in the form of the free compound and/or a physiologically acceptable salt thereof.

Formula 25

[0363] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 25. Such compounds are described in US Patent No. 8,653,101 issued February 18, 2014 and corresponding to US Application No. 10/992,118 filed November 18, 2005; International Publication No. WO2012025236A1, published March 1, 2012 and corresponding to International Application No. PCT/EP2011/004277 filed August 26, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 25, these references incorporated by reference herein control.

[0364] In an embodiment, the Kv7 channel activator is a compound according to formula 25.

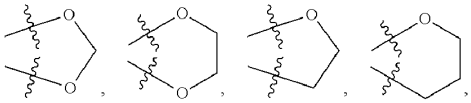
Formula 25



wherein, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally

bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents H; F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-8}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; SCF_3; S(=O)$_2$—OH; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, a N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, or a N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^7 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, in which an “aliphatic group” and “aliphatic residue” can in each case be branched or unbranched, saturated or unsaturated, in which a “cycloaliphatic residue” and a “heterocycloaliphatic residue” can in each case be saturated or unsaturated, in

which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,

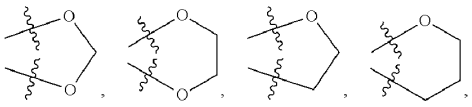


, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue,

a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in the form of the free compounds, the racemate, the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of the salts of physiologically acceptable acids or bases.

[0365] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an

$NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted $O—C_{1-4}$-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an $O—C_{1-4}$ aliphatic residue, OCF_3, $O—CH_2—OH$, $O—CH_2—O—CH_3$, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, $C(=O)—CH_3$, $C(=O)—C_2H_5$, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an $O—C_{1-4}$ aliphatic residue, OCF_3, SH, SCF_3, a $S—C_{1-4}$ aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a $S—C_{1-4}$-aliphatic residue, a $O—C_{1-4}$-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; $C(=O)—NH_2$; $S(=O)_2—OH$; NO_2; a C_{1-4}-aliphatic residue, a $C(=O)—C_{1-4}$ aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-}

$_{4}$ aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, and a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group,

R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-}

$_{4}$ aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0366] In further embodiments, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted aliphatic residue, a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

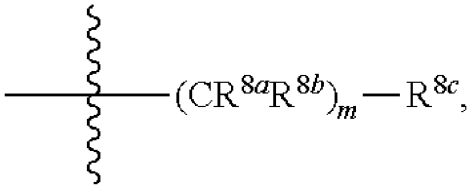
[0367] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group.

[0368] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another are selected from the group consisting of H; F; Cl; Br; I; NO_2; CF_3; CN; OCF_3; SCF_3; a (C=O)—C_{1-4} aliphatic residue, a C_{1-4} aliphatic residue, O—C_{1-4} aliphatic residue, a S—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or

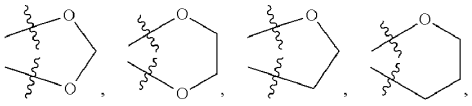
polysubstituted with at least one substituent selected from the group consisting of F, Cl, and O—CH_3.

[0369] In further embodiments, at least one of R^3, R^4, R^5 and R^6 is ≠H.

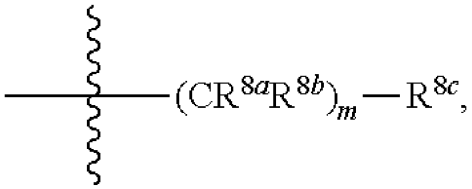
[0370] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, 2, 3 or 4, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic

residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  , benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0371] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

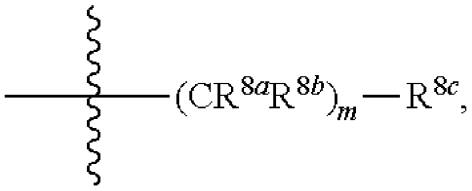
an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

[0372] In further embodiments, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic

residue, CF_3, CN, and a C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue. on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0373] In further embodiments, R^7 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue is bridged via a unsubstituted C_{1-8} aliphatic group.

[0374] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2 and R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10

membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0, R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; and R^{8c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, R^2 is selected from the group consisting of H; F; Cl; CF_3; CH_3; C_2H_5, iso-propyl; cyclopropyl; and O—CH_3; R^3, R^4, R^5 and R^6 are each independently of one another selected from the group consisting of H; F; Cl; Br; CF_3; CN; OCF_3 and NO_2;
R^7 denotes a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case is unsubstituted.

[0375] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-(3,3-dimethyl-butyl)-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-4-methyl-N-(thiophene-2-yl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-(2-hydroxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-isopropoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-isopropoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(3-

fluorophenyl)-methyl]-4-methoxy-7-(trifluoremethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2,4-dimethoxy-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(4-fluorophenyl)-methyl]-4-methoxy-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-6,7-difluoro-N-[(3-fluorophenyl)-methyl]-4-methoxy-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2,4-dimethoxy-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 6,7-difluoro-N-[(3-fluorophenyl)-methyl]-2,4-dimethoxy-quinoline-3-carboxylic acid amide; 7-fluoro-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; N-[(3-fluoro-4-methyl-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(3-fluoro-4-methyl-phenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-methoxy-4-methyl-N-(m-tolyl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-4-methyl-N-(m-tolyl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluoro-3-methyl-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(4-fluoro-3-methyl-phenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-methoxy-4-methyl-N-(p-tolyl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-4-methyl-N-(p-tolyl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-4-methyl-N-(4-methyl-pentyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-methoxy-4-methyl-N-(4-methyl-pentyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-(4,4-dimethyl-pentyl)-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-(4,4-dimethyl-pentyl)-2-ethoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-bromo-2-ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-2-ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-N-[(4-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-2-ethoxy-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-2-ethoxy-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-N-[(4-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; N-[(3-fluoro-2-methoxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluoro-5-methoxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(5-fluoro-2-methoxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-

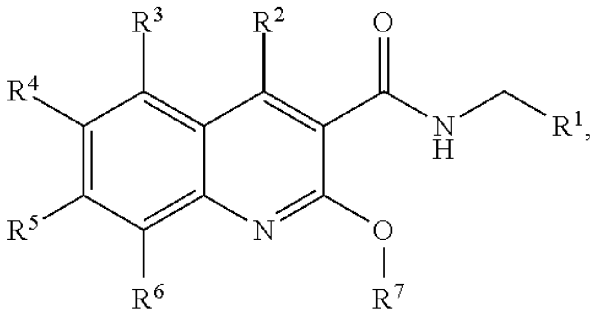
carboxylic acid amide; N-[(3-fluoro-2-hydroxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluoro-5-hydroxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(5-fluoro-2-hydroxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluoro-4-hydroxy-phenyl)-methyl]-2-methoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-fluoro-N-[(4-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide: 5,7-difluoro-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; 6,7-difluoro-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; 7,8-difluoro-N-[(3-fluorophenyl)-methyl]-2-methoxy-4-methyl-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-(2,2,2-trifluoro-ethoxy)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-methoxy-4-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethoxy-N-[(3-fluorophenyl)-methyl]-4-(trifluoromethyl)-quinoline-3-carboxylic acid amide; and N-[(3-fluorophenyl)-methyl]-2-isopropoxy-4-(trifluoromethyl)-quinoline-3-carboxylic acid amide; respectively in the form of the free compounds; the racemate; the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio or of an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

Formula 26

[0376] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 26. Such compounds are described in International Publication No. WO2012025236A1, published March 1, 2012 and corresponding to International Application No. PCT/EP2011/004277 filed August 26, 2011; US Patent No. 9,073,862 issued July 7, 2015 and corresponding to US Application No. 14/098,842 filed November 26, 2013; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 26, these references incorporated by reference herein control.

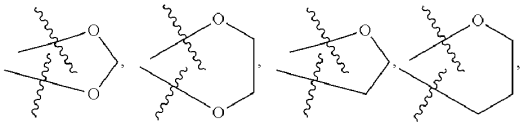
[0377] In an embodiment, the Kv7 channel activator is a compound according to formula 26:

Formula 26

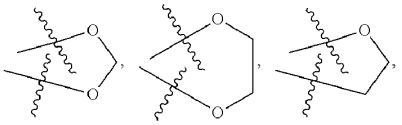
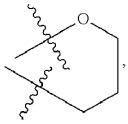


wherein, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents H; F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; SCF_3; S(=O)$_2$—OH; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, a N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, or

a N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^7 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 represents an unsubstituted aliphatic residue, then R^7 does not represent methyl or ethyl, and on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, in which an “aliphatic group” and “aliphatic residue” can in each case be branched or unbranched, saturated or unsaturated, in which a “cycloaliphatic residue” and a “heterocycloaliphatic residue” can in each case be saturated or unsaturated, in which “mono- or polysubstituted” with respect to an “aliphatic group” and an “aliphatic residue” relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which “mono- or polysubstituted” with respect to a “cycloaliphatic residue” and a “heterocycloaliphatic residue” relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO,

COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, 
an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in the form of the free compounds, the racemate, the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of the salts of physiologically acceptable acids or bases.

[0378] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic

residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,  ,  , benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered

heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—$N(C_{1-4}$ aliphatic residue$)_2$, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a $NH(C_{1-4}$ aliphatic residue), a $N(C_{1-4}$ aliphatic residue$)_2$, a NH—C(=O)—C_{1-4} aliphatic residue, and a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—

C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 represents an unsubstituted aliphatic residue, then R^7 does not represent methyl or ethyl, and on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0379] In further embodiments, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered

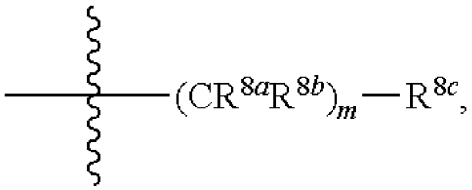
heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

[0380] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; $S(=O)_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a $S(=O)_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group.

[0381] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another are selected from the group consisting of H; F; Cl; Br; I; NO_2; CF_3; CN; OCF_3; SCF_3; a (C=O)—C_{1-4} aliphatic residue, a C_{1-4} aliphatic residue, O—C_{1-4} aliphatic residue, a S—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, and O—CH_3.

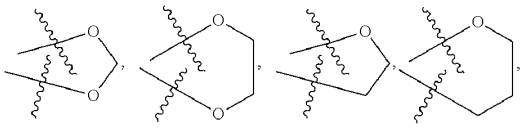
[0382] In further embodiments, at least one of R^3, R^4, R^5 and R^6 is ≠H.

[0383] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, 2, 3 or 4, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic

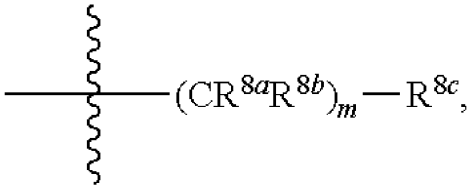
residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6

membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0384] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the

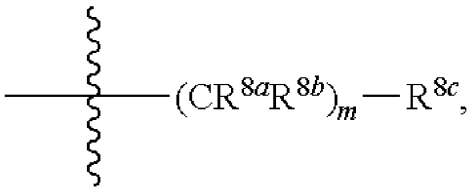
group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

[0385] In further embodiments, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, on the condition that if R^7 represents an unsubstituted aliphatic residue, then R^7 does not represent methyl or ethyl, and on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0386] In further embodiments, R^7 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one

substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue is bridged via a unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 represents an unsubstituted aliphatic residue, then R^7 does not represent methyl or ethyl.

[0387] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2 and R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0, R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; and R^{8c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—

CH_3 and C(=O)—O—C_2H_5, R^2 is selected from the group consisting of H; F; Cl; CF_3; CH_3; C_2H_5, iso-propyl; cyclopropyl; and O—CH_3; R^3, R^4, R^5 and R^6 are each independently of one another selected from the group consisting of H; F; Cl; Br; CF_3; CN; OCF_3 and NO_2;
R^7 denotes a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case is unsubstituted, and on the condition that if R^7 represents an unsubstituted aliphatic residue, then R^7 does not represent methyl or ethyl.

[0388] In further embodiments, the Kv7 channel activator may be selected from the group consisting of:

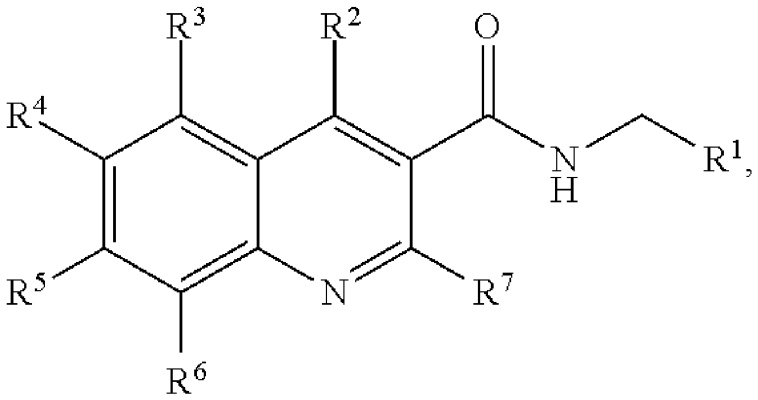
[0389] N-[(3-fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-(2-methoxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-(2-hydroxy-ethoxy)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-isopropoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-isopropoxy-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-(2,2,2-trifluoro-ethoxy)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; and N-[(3-fluorophenyl)-methyl]-2-isopropoxy-4-(trifluoromethyl)-quinoline-3-carboxylic acid amide; respectively in the form of the free compounds; the racemate; the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio or of an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

Formula 27

[0390] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 27. Such compounds are described in International Publication No. WO2012025238A1, published March 1, 2012 and corresponding to International Application No. PCT/EP2011/004279 filed August 26, 2011; US Patent No. 8,445,512 issued May 21, 2013 and corresponding to US Application No. 13/218,556 filed August 26, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 27, these references incorporated by reference herein control.

[0391] In an embodiment, the Kv7 channel activator is a compound according to formula 27:

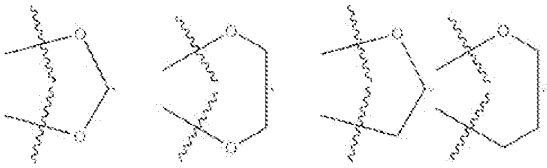
Formula 27



wherein: R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents H; F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-8}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; SCF_3; S(=O)$_2$—OH; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—

$S(=O)_2$—C_{1-4}-aliphatic residue, a N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, or a N(C_{1-4} aliphatic residue)-$S(=O)_2$—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that at least one of R^3, R^4, R^5 and R^6 is ≠H, R^7 represents a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the binding is carried out via a carbon atom of the 3 to 10 membered heterocycloaliphatic residue, in which an "aliphatic group" and "aliphatic residue" can in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" can in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—$S(=O)_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—$S(=O)_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic

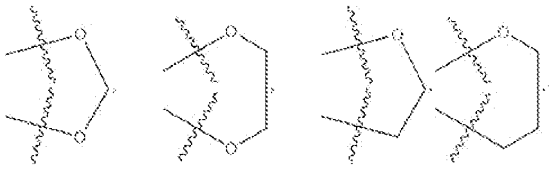
residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,



an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in the form of the free compounds, the racemate, the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of the salts of physiologically acceptable acids or bases.

[0392] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic

residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—O_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—O_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected

from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, and a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group, on the condition that at least one of R^3, R^4, R^5 and R^6 is ≠H, R^7 denotes a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10

membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0393] In further embodiments, R^2 represents H; F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted aliphatic residue, a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the

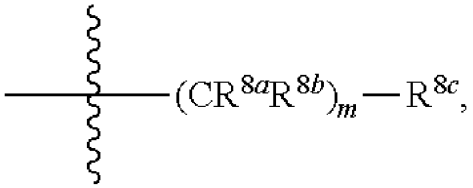
group consisting of F, Cl, Br, I, =O, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

[0394] In further embodiments, R^2 is ≠H.

[0395] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group, on the condition that at least one of R^3, R^4, R^5 and R^6 is ≠H.

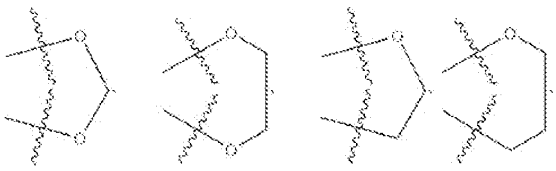
[0396] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another are selected from the group consisting of H; F; Cl; Br; I; NO_2; CF_3; CN; OCF_3; SCF_3; a (C=O)—C_{1-4} aliphatic residue, a C_{1-4} aliphatic residue, O—C_{1-4} aliphatic residue, a S—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, and O—CH_3, on the condition that at least one of R^3, R^4, R^5 and R^6 is ≠H.

[0397] In further embodiments, R^1 represents the partial structure:



[0398] Wherein, m denotes 0, 1, 2, 3 or 4, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-}

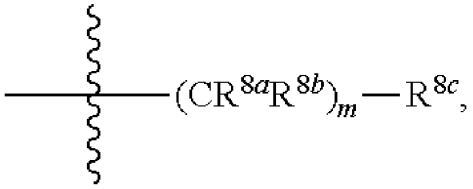
$_{4}$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—O_2H_5, C(=O)—O—CH_3 and C(=O)—O—O_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—O_2H_5, C(=O)—O—CH_3 and C(=O)—O—O_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or

polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0399] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, or 2, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—O_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—O_2H_5, C(=O)—O—CH_3 and C(=O)—O—O_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the

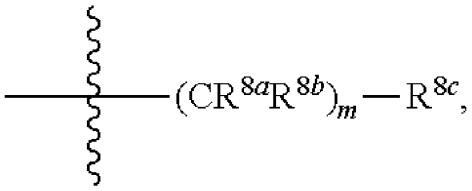
group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

[0400] In further embodiments, R^7 denotes a C_{2-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue. on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0401] In further embodiments, R^7 denotes a C_{2-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue

in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0402] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2 and R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0, R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; and R^{8c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, R^2 is selected from the group consisting of H; F; Cl; CF_3; CH_3; C_2H_5, iso-propyl; cyclopropyl; and O—CH_3; R^3, R^4, R^5 and R^6 are each independently of one another selected from the group consisting of H; F; Cl; Br; CH_3; CF_3; CN; OCF_3 and NO_2; on the condition that at least one of R^3, R^4, R^5 and R^6 is ≠H, R^7 denotes ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, ethenyl or propenyl (—CH_2CH=CH_2, —CH=CH—CH_3, —C(=CH_2)—CH_3), in each case

unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, O—CH_3, CF_3, and $N(CH_3)_2$, or denotes cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, piperidinyl tetrahydrofuranyl, or tetrahydropyranyl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, OH, an O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case is unsubstituted, and wherein cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, piperidinyl tetrahydrofuranyl, or tetrahydropyranyl may in each case be optionally bridged, via an unsubstituted C_{1-4} aliphatic group, on the condition that if R^7 denotes piperidinyl tetrahydrofuranyl, or tetrahydropyranyl, each of these residues is linked via a carbon atom.

[0403] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 4-methyl-2-propyl-N-(thiophene-2-yl-methyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-(cycloheptyl-methyl)-4-methyl-2-propyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-4-methyl-2-propyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-propyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-isopropyl-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-isopropyl-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-cyclopropyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-isopropyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-isopropyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-tert-butyl-N-[(3-fluorophenyl)-methyl]-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-tert-butyl-N-[(4-fluorophenyl)-methyl]-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-(methoxymethyl)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(4-fluorophenyl)-methyl]-2-(methoxymethyl)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-2-(hydroxymethyl)-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-(2,2-dimethyl-propyl)-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-(2,2-dimethyl-propyl)-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-

cyclopentyl-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-cyclopentyl-N-[(4-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-(4,4-dimethyl-pentyl)-4-methyl-2-propyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-[(E)-prop-1-enyl]-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-(2-methyl-prop-1-enyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-bromo-2-ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-2-ethyl-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-2-cyclopropyl-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-2-cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-N-[(3-fluorophenyl)-methyl]-2-isopropyl-4-methyl-quinoline-3-carboxylic acid amide; 7-bromo-N-[(4-fluorophenyl)-methyl]-2-isopropyl-4-methyl-quinoline-3-carboxylic acid amide; 2-(dimethylaminomethyl)-N-[(3-fluorophenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 2-ethyl-N-[(4-fluoro-3-methyl-phenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-cyano-2-ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 2-ethyl-N-[(3-fluoro-4-methyl-phenyl)-methyl]-4-methyl-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-cyano-2-ethyl-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; N-[(3-fluorophenyl)-methyl]-4-methyl-2-(2-methyl-propyl)-7-(trifluoromethyl)-quinoline-3-carboxylic acid amide; 7-cyano-2-cyclopropyl-N-[(3-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-2-cyclopropyl-N-[(4-fluorophenyl)-methyl]-4-methyl-quinoline-3-carboxylic acid amide; 7-cyano-N-[(3-fluorophenyl)-methyl]-2-isopropyl-4-methyl-quinoline-3-carboxylic acid amide; and 7-cyano-N-[(4-fluorophenyl)-methyl]-2-isopropyl-4-methyl-quinoline-3-carboxylic acid amide; respectively in the form of the free compounds; the racemate; the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio or of an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

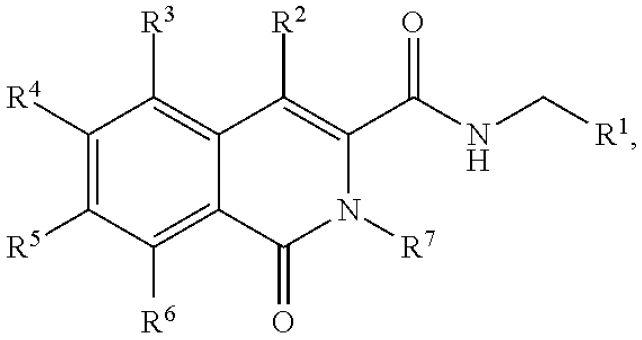
Formula 28

[0404] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 28. Such compounds are described in International Publication No. WO2012028300A1, published March 8,2012 and corresponding to International Application No. PCT/EP2011/004369 filed August 31, 2011;

US Patent No. 8,618,129 issued December 31, 2013 and corresponding to US Application No. 13/222,023 filed August 31, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 28, these references incorporated by reference herein control.

[0405] In an embodiment, the Kv7 channel activator is a compound according to formula 28:

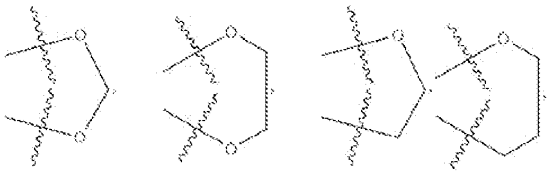
Formula 28



wherein, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted and optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; SCF_3; S(=O)$_2$—OH; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue

may be in each case be unsubstituted or mono- or polysubstituted; a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, a N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, or a N(C_{1-4} aliphatic residue)S(=O)$_2$—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^7 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom, in which an "aliphatic group" and "aliphatic residue" can in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" can in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, OH, =O, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic

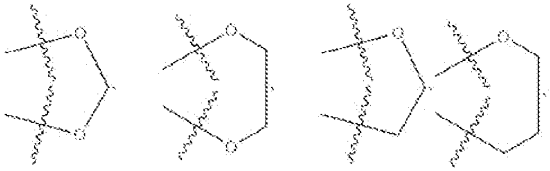
residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,



an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—S(=O)$_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, S(=O)$_2$OH, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, a S(=O)$_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in the form of the free compounds, the racemate, the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of the salts of physiologically acceptable acids or bases.

[0406] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be

unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue may optionally be bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-}

$_4$ aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, and a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic

residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, =O, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0407] In further embodiments, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

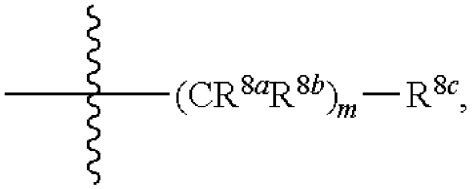
[0408] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—

C_{1-4} aliphatic residue, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group.

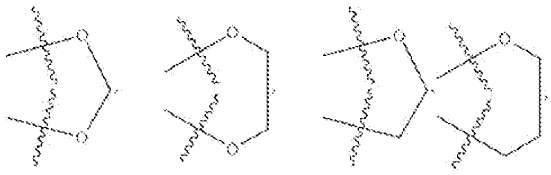
[0409] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another are selected from the group consisting of H; F; Cl; Br; I; NO_2; CF_3; CN; OCF_3; SCF_3; a (C=O)—C_{1-4} aliphatic residue, a C_{1-4} aliphatic residue, O—C_{1-4} aliphatic residue, a S—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, and O—CH_3.

[0410] In further embodiments, at least one of R^3, R^4, R^5 and R^6 is ≠H.

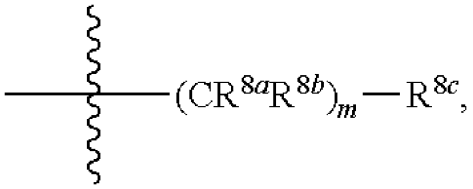
[0411] In further embodiments, R^1 represents the partial structure:



wherein: m denotes 0, 1, 2, 3 or 4, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, or together denote =O, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, =O, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, 
benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0412] In further embodiments, R^1 represents the partial structure



wherein, m denotes 0, 1, or 2, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, in each case may be unsubstituted or mono- or polysubstituted, preferably unsubstituted or mono- or disubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, preferably with at least one substituent selected from the group consisting of F, Cl, CH_3, O—CH_3, CF_3 and OCF_3, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

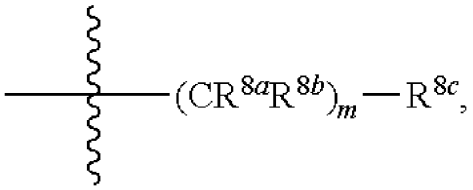
[0413] In further embodiments, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl,

Br, I, NO_2, =O, OH, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue. on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0414] In further embodiments, R^7 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic

residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue in each case may be bridged via an unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0415] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2 and R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0, R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, R^2 is selected from the group consisting of F; Cl; CF_3; CH_3; C_2H_5, iso-propyl; cyclopropyl; and O—CH_3; R^3, R^4, R^5 and R^6 are each independently of one another selected from the group consisting of H; F; Cl; CF_3; CN; OCF_3 and NO_2; R^7 denotes a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a

C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of OH, and an unsubstituted O—C_{1-4}-aliphatic residue.

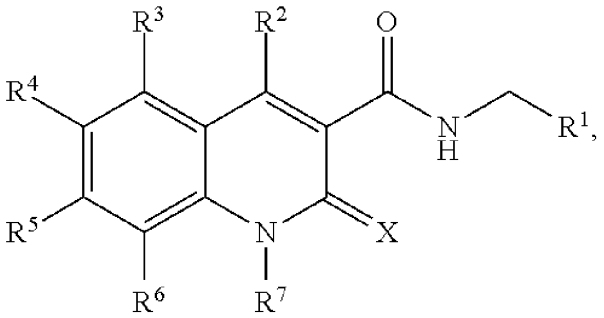
[0416] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-(3-fluorobenzyl)-2,4-dimethyl-1-oxo-7-(trifluoromethyl)-1,2-dihydroisoquinoline-3-carboxamide; N-(3-fluorobenzyl)-4-methyl-1-oxo-2-propyl-7-(trifluoromethyl)-1,2-dihydroisoquinoline-3-carboxamide; 2-ethyl-N-(3-fluorobenzyl)-4-methyl-1-oxo-7-(trifluoromethyl)-1,2-dihydroisoquinoline-3-carboxamide; N-(3-fluorobenzyl)-2-isopropyl-4-methyl-1-oxo-7-(trifluoromethyl)-1,2 dihydroisoquinoline-3-carboxamide; andN-(3-fluorobenzyl)-2-(2-methoxyethyl)-4-methyl-1-oxo-7-(trifluoromethyl)-1,2-dihydroisoquinoline-3-carboxamide; respectively in the form of the free compounds; the racemate; the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio or of an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

Formula 29

[0417] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 29. Such compounds are described in US Patent No. 8,653,102 issued February 18, 2014and corresponding to US Application No. 13/218,579 filed August 26, 2011; International Publication No. PCT/EP2011/004280, published March 1, 2012, and corresponding to International Application No. WO2012025239A1filed August 25, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 29, these references incorporated by reference herein control.

[0418] In an embodiment, the Kv7 channel activator is a compound according to formula 29:

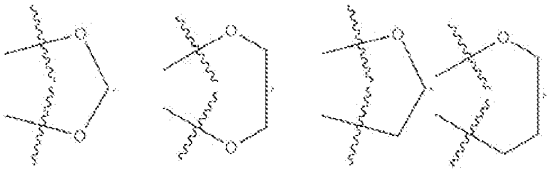
Formula 29



wherein: X denotes O or S, R^1 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic

residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^2 represents F; Cl; Br; I; CN; CF_3; C(=O)H; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; SCF_3; S(=O)$_2$—OH; NO_2; OCF_3; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a S(=O)$_2$—O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, a N(C_{1-4} aliphatic residue)-C(=O)—C_{1-4} aliphatic residue, or a N(C_{1-4} aliphatic residue)-S(=O)$_2$—C_{1-4} aliphatic residue, wherein the C_{1-4} aliphatic residue may in each case be unsubstituted or mono- or polysubstituted; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; R^7 represents a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted; a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted; on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic

residue is linked via a carbon atom, in which an "aliphatic group" and "aliphatic residue" can in each case be branched or unbranched, saturated or unsaturated, in which a "cycloaliphatic residue" and a "heterocycloaliphatic residue" can in each case be saturated or unsaturated, in which "mono- or polysubstituted" with respect to an "aliphatic group" and an "aliphatic residue" relates, with respect to the corresponding residues or groups, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), a NH—C(=O)—C_{1-4} aliphatic residue, a NH—$S(=O)_2$—C_{1-4} aliphatic residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to a "cycloaliphatic residue" and a "heterocycloaliphatic residue" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, a NH—$S(=O)_2$—C_{1-4} aliphatic residue, =O, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, CHO, COOH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; in which "mono- or polysubstituted" with respect to "aryl" and a "heteroaryl" relates, with respect to the corresponding residues, to the substitution of one or more hydrogen atoms each independently of one another by at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2,

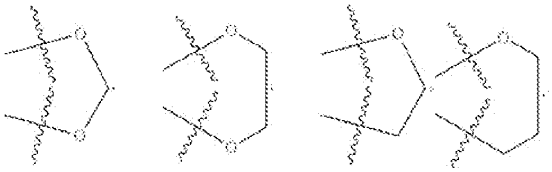


an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, an NH—C(=O)—C_{1-4} aliphatic residue, an NH—$S(=O)_2$—C_{1-4} aliphatic

residue, OH, OCF_3, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, SH, SCF_3, a S—C_{1-4}-aliphatic residue, $S(=O)_2OH$, a $S(=O)_2$—C_{1-4}-aliphatic residue, a $S(=O)_2$—O—C_{1-4}-aliphatic residue, a $S(=O)_2$—NH—C_{1-4}-aliphatic residue, CN, CF_3, C(=O)H, C(=O)OH, a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, a C_{3-6}-cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, aryl, heteroaryl, C(=O)—NH_2, a C(=O)—NH(C_{1-4} aliphatic residue), and a C(=O)—N(C_{1-4} aliphatic residue)$_2$; with the exception of the following compound: 1-ethyl-N-(4-methoxybenzyl)-4-methyl-2-oxo-1,2-dihydroquinoline-3-carboxamide, in the form of the free compounds, the racemate, the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio, or of an individual enantiomer or diastereomer, or in the form of the salts of physiologically acceptable acids or bases.

[0419] In further embodiments, R^1 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), OH, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least

one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, O—CH_2—OH, O—CH_2—O—CH_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), an $N(C_{1-4}$ aliphatic residue$)_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the aryl or the heteroaryl residue may in each case be optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an $NH(C_{1-4}$ aliphatic residue), OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN and C(=O)—OH, X represents O or S; R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4} aliphatic residue may be in each case be unsubstituted or mono- or polysubstituted; a C_{3-}

$_{6}$-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted and in each case optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a C(=O)—NH—C_{1-4} aliphatic residue, a C(=O)—N(C_{1-4} aliphatic residue)$_2$, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, a NH(C_{1-4} aliphatic residue), a N(C_{1-4} aliphatic residue)$_2$, a NH—C(=O)—C_{1-4} aliphatic residue, and a NH—S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), OH, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue and C(=O)—OH, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I,

NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0420] In further embodiments, R^2 represents F; Cl; Br; I; CN; CF_3; NO_2; OCF_3; SCF_3; a C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted aliphatic residue, a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and an unsubstituted aliphatic residue, and wherein the C_{3-6}-cycloaliphatic residue or the 3 to 6 membered heterocycloaliphatic residue may in each case be optionally bridged via a C_{1-4} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an unsubstituted C_{1-4}-aliphatic residue and an unsubstituted O—C_{1-4}-aliphatic residue.

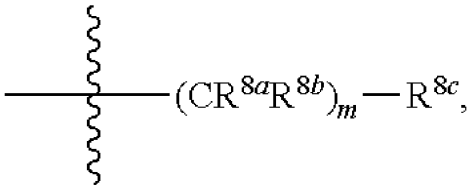
[0421] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another represent H; F; Cl; Br; I; CN; CF_3; OCF_3; SCF_3; C(=O)H; C(=O)—OH; C(=O)—NH_2; S(=O)$_2$—OH; NO_2; a C_{1-4}-aliphatic residue, a C(=O)—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4} aliphatic residue, a O—C_{1-4}-aliphatic residue, a O—C(=O)—C_{1-4}-aliphatic residue, a S—C_{1-4}-aliphatic residue, a S(=O)$_2$—C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, and a O—C_{1-4}-aliphatic residue; a C_{3-6}-cycloaliphatic residue or a 3 to 6 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the

group consisting of F, Cl, Br, I, =O, OH, a C_{1-4}-aliphatic residue and a O—C_{1-4}-aliphatic residue, and in each case optionally bridged via an unsubstituted C_{1-4} aliphatic group.

[0422] In further embodiments, R^3, R^4, R^5 and R^6 each independently of one another are selected from the group consisting of H; F; Cl; Br; I; NO_2; CF_3; CN; OCF_3; SCF_3; a (C=O)—C_{1-4} aliphatic residue, a C_{1-4} aliphatic residue, O—C_{1-4} aliphatic residue, a S—C_{1-4} aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, and O—CH_3.

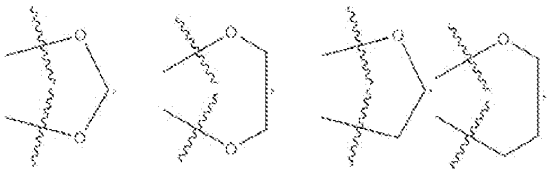
[0423] In further embodiments, at least one of R^3, R^4, R^5 and R^6 is ≠H.

[0424] In further embodiments, R^1 represents the partial structure:



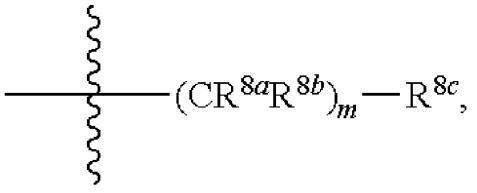
wherein, m denotes 0, 1, 2, 3 or 4, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, NO_2, NH_2, a NH(C_{1-4} aliphatic residue), OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4} aliphatic residue or C(=O)—OH, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, a C_{3-6} cycloaliphatic residue and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-}

$_{4}$ aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue,



benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein benzyl, phenyl, thienyl, pyridyl, furyl, thiazolyl and oxazolyl may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—OH, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, NH_2, an NH(C_{1-4} aliphatic residue), an N(C_{1-4} aliphatic residue)$_2$, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue and C(=O)—OH.

[0425] In further embodiments, R^1 represents the partial structure:



$$(CR^{8a}R^{8b})_m—R^{8c},$$

wherein: m denotes 0, 1, or 2, R^{8a} and R^{8b} each independently of one another represent H, F, Cl, Br, I, an O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue, R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from

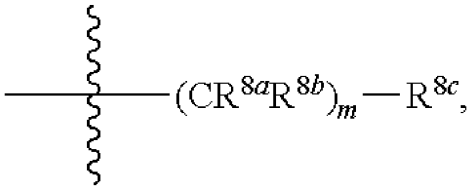
the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an O—C_{1-4} aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, a C_{3-6} cycloaliphatic residue, a 3 to 6 membered heterocycloaliphatic residue, benzyl, phenyl, thienyl or pyridyl, wherein benzyl, phenyl, thienyl and pyridyl, may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, CF_3 a C_{1-4}-aliphatic residue and C(=O)—OH.

[0426] In further embodiments, R^7 denotes a C_{1-10}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, COOH, CF_3, CN, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, CN, a C_{1-4}-aliphatic residue, a C_{3-6} cycloaliphatic residue, and a 3 to 6 membered heterocycloaliphatic residue, wherein the C_{1-4}-aliphatic

residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted O—C_{1-4}-aliphatic residue, and wherein the C_{3-6} cycloaliphatic residue and the 3 to 6 membered heterocycloaliphatic residue may in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue may in each case optionally bridged via a C_{1-8} aliphatic group, which in turn may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, NO_2, OH, an O—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4} aliphatic residue, CF_3, CN, and a C_{1-4}-aliphatic residue. on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0427] In further embodiments, R^7 denotes a C_{1-8}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, COOH, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, CF_3 and an unsubstituted aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, =O, an O—C_{1-4} aliphatic residue, OCF_3, SCF_3, a S—C_{1-4} aliphatic residue, a C(=O)—O—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, OCF_3, CF_3 and an unsubstituted C_{1-4}-aliphatic residue, and wherein the C_{3-10}-cycloaliphatic residue or the 3 to 10 membered heterocycloaliphatic residue in each case may be bridged via an unsubstituted C_{1-8} aliphatic group, on the condition that if R^7 denotes a 3 to 10 membered heterocycloaliphatic residue, the 3 to 10 membered heterocycloaliphatic residue is linked via a carbon atom.

[0428] In further embodiments, R^1 represents the partial structure:



wherein: m is 0, 1 or 2 and R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; R^{8c} denotes a C_{1-4} aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or denotes a C_{3-10}-cycloaliphatic residue or a 3 to 10 membered heterocycloaliphatic residue, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, an unsubstituted O—C_{1-4} aliphatic residue, CF_3, and an unsubstituted C_{1-4}-aliphatic residue, or wherein m is 0, R^{8a} and R^{8b} each independently of one another represent H, F, a O—C_{1-4} aliphatic residue or a C_{1-4} aliphatic residue; and R^{8c} denotes an aryl or heteroaryl, in each case unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3, C(=O)—O—C_2H_5 and phenyl, wherein phenyl may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4} aliphatic residue, OCF_3, CF_3, CN, a C_{1-4}-aliphatic residue, C(=O)—CH_3, C(=O)—C_2H_5, C(=O)—O—CH_3 and C(=O)—O—C_2H_5, X represents O or S; R^2 is selected from the group consisting of F; Cl; Br; CF_3; CH_3; C_2H_5, iso-propyl; cyclopropyl; and O—CH_3; R^3, R^4, R^5 and R^6 are each independently of one another selected from the group consisting of H; F; Cl; Br; CF_3; CN; OCF_3 and NO_2; R^7 denotes a C_{1-6}-aliphatic residue, unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of F, Cl, Br, I, OH, an O—C_{1-4}-aliphatic residue, COOH, a C(=O)—O—C_{1-4}-aliphatic residue, OCF_3, SH, SCF_3, a S—C_{1-4}-aliphatic residue, CF_3, and a C_{1-4}-aliphatic residue, wherein the C_{1-4}-aliphatic residue in each case may be unsubstituted or mono- or polysubstituted with at least one substituent selected from the group consisting of OH, and an unsubstituted O—C_{1-4}-aliphatic residue, or denotes an unsubstituted C_{3-6}-cycloaliphatic residue or an unsubstituted 3 to 6 membered heterocycloaliphatic residue, on the condition that if R^7 denotes a 3 to 6 membered

heterocycloaliphatic residue, the 3 to 6 membered heterocycloaliphatic residue is linked via a carbon atom.

[0429] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-[(3-Fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 1-Butyl-N-[(3-fluorophenyl)-methyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1,4-dimethyl-2-thioxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 1-Ethyl-N-[(3-fluorophenyl)-methyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 1-Ethyl-N-[(4-fluorophenyl)-methyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-oxo-1-propyl-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-1-(3-methyl-butyl)-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-1-(4-methyl-pentyl)-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(3-methoxy-propyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-[2-(2-methoxy-ethoxy)-ethyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 7-Bromo-N-[(3-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Bromo-N-[(4-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Bromo-N-[(3-fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Bromo-N-[(4-fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Cyano-N-[(3-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Cyano-N-[(4-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Cyano-N-[(3-fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-1H-quinoline-3-carboxylic acid amide; 7-Cyano-N-[(4-fluorophenyl)-methyl]-1-(2-methoxy-ethyl)-4-methyl-2-oxo-1H-quinoline-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-1-(2-methoxy-ethyl)-

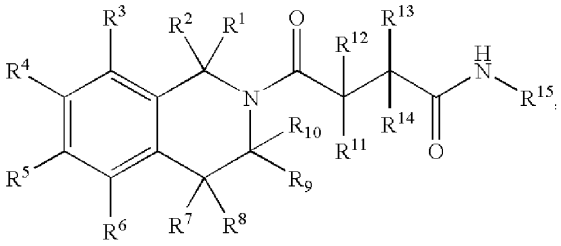
4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-(4,4-Dimethyl-pentyl)-1,4-dimethyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 2-[3-[(3-Fluorophenyl)-methyl-carbamoyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinolin-1-yl]-acetic acid methyl ester; 3-[3-[(3-Fluorophenyl)-methyl-carbamoyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinolin-1-yl]-propionic acid methyl ester; 2-[3-[(3-Fluorophenyl)-methyl-carbamoyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinolin-1-yl]-acetic acid; 3-[3-[(3-Fluorophenyl)-methyl-carbamoyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinolin-1-yl]-propionic acid; N-[(3-Fluorophenyl)-methyl]-1-[1-(methoxymethyl)-propyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-[2-methoxy-1-(methoxymethyl)-ethyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-methoxy-butyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-7-(trifluoromethyloxy)-1H-quinoline-3-carboxylic acid amide; 7-Fluoro-N-[(3-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-methoxy-1-methyl-ethyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(4-Fluorophenyl)-methyl]-1,4-dimethyl-2-thioxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 7-Chloro-N-[(3-fluorophenyl)-methyl]-1,4-dimethyl-2-oxo-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-hydroxy-ethyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; 1-(2-Ethoxy-ethyl)-N-[(3-fluorophenyl)-methyl]-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-isopropyl-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-oxo-1-pentyl-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-methyl-2-oxo-4-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-1-(2-methoxy-propyl)-4-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; N-[(3-Fluorophenyl)-methyl]-4-methyl-2-oxo-1-tetrahydro-pyran-4-yl-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; and N-[(3-Fluorophenyl)-methyl]-4-methoxy-1-methyl-2-oxo-7-(trifluoromethyl)-1H-quinoline-3-carboxylic acid amide; respectively in the form of the free compounds; the racemate; the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers in any mixing ratio or of an individual enantiomer or diastereomer; or in the form of the salts of physiologically acceptable acids or bases.

Formula 30

[0430] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 30. Such compounds are described in International Publication No. WO2010075973A1, published July 8, 2010, and corresponding to International Application No. PCT/EP2009/009040 filed December 16, 2009; US Patent No. 8,367,700 issued February 5, 2013 and corresponding to US Application No. 12/635,800 filed December 11, 2009; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 30, these references incorporated by reference herein control.

[0431] In an embodiment, the Kv7 channel activator is a compound according to formula 30:

Formula 30



,

wherein, R^0 stands for C_{1-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or heteroaryl, each unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{1-8} alkyl-bridged aryl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; R^1 stands for F; Cl; Br; CN; C_{1-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or heteroaryl, each unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; C_{1-8} alkyl-bridged heteroaryl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{1-8} alkyl-bridged aryl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be unbranched, saturated or

unsaturated, unsubstituted; R^2 stands for H; F; Cl; Br; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; or R^1 and R^2 together with the carbon atom binding them as ring member form a C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, each optionally fused to (hetero)aryl, unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each mutually independently denote H; F; Cl; Br; I; NO_2; CF_3; CN; R^0; C(=O)H; $C(=O)R^0$; CO_2H; $C(=O)OR^0$; $CONH_2$; $C(=O)NHR^0$; $C(=O)N(R^0)_2$; OH; OR^0; —O—(C_{1-8} alkyl)-O—; O—C(=O)—R^0; O—C(=O)—O—R^0; O—(C=O)—NH—R^0; O—C(=O)—$N(R^0)_2$; O—$S(=O)_2$—R^0; O—$S(=O)_2OH$; O—$S(=O)_2OR^0$; O—$S(=O)_2NH_2$; O—$S(=O)_2NHR^0$; O—$S(=O)_2N(R^0)_2$; NH_2; NH—R^0; $N(R^0)_2$; NH—C(=O)—R^0; NH—C(=O)—O—R^0; NH—C(=O)—NH_2; NH—C(=O)—NH—R^0; NH—C(=O)—$N(R^0)_2$; NR^0—C(=O)—R^0; NR^0—C(=O)—O—R^0; NR^0—C(=O)—NH_2; NR^0—C(=O)—NH—R^0; NR^0—C(=O)—)—$N(R^0)_2$; NH—$S(=O)_2OH$; NH—$S(=O)_2R^0$; NH—$S(=O)_2OR^0$; NH—$S(=O)_2NH_2$; NH—$S(=O)_2NHR^0$; NH—$S(=O)_2N(R^0)_2$; NR^0—$S(=O)_2OH$; NR^0—$S(=O)_2R^0$; NR^0—$S(=O)_2OR^0$; NR^0—$S(=O)_2NH_2$; NR^0—$S(=O)_2NHR^0$; NR^0—$S(=O)_2N(R^0)_2$; SH; SR^0; $S(=O)R^0$; $S(=O)_2R^0$; $S(=O)_2OH$; $S(=O)_2OR^0$; $S(=O)_2NH_2$; $S(=O)_2NHR^0$; or $S(=O)_2N(R)_2$; R^7, R^8, R^9, R^{10} each mutually independently stand for H; F; Cl; Br; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; R^{11} stands for H; F; Cl; Br; CN; or R^0; R^{12} stands for H; F; Cl; Br; CN; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; R^{13} stands for H; F; Cl; Br; CN; C_{1-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or heteroaryl, each unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{2-8} alkyl-bridged aryl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; R^{14} stands for H; F; Cl; Br; CN; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; or R^{11} and R^{13} together with the carbon atoms binding them as ring members form a C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, optionally fused to (hetero)aryl, unsubstituted or mono- or polysubstituted; or R^{11} and R^{12}; or R^{13} and R^{14},

together with the carbon atoms binding them as ring members form a C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, each optionally fused to (hetero)aryl, unsubstituted or mono- or polysubstituted; R^{15} stands for R^0; wherein "alkyl-substituted", "heteroalkyl-substituted", "heterocyclyl-substituted" and "cycloalkyl-substituted" stand for the substitution of one or more hydrogen atoms, each mutually independently, with F; Cl; Br; I; CN; CF_3; =O; =NH; $=C(NH_2)_2$; NO_2; R^0; C(=O)H; $C(=O)R^0$; CO_2H; $C(=O)OR^0$; $CONH_2$; $C(=O)NHR^0$; $C(=O)N(R^0)_2$; OH; OR^0; O—(C_{1-8} alkyl)-O; O—C(=O)—R^0; O—C(=O)—O—R^0; O—(C=O)—NH—R^0; O—C(=O)—$N(R^0)_2$; O—$S(=O)_2$—R^0; O—$S(=O)_2OH$; O—$S(=O)_2OR^0$; O—$S(=O)_2NH_2$; O—$S(=O)_2NHR^0$; O—$S(=O)_2N(R^0)_2$; NH_2; NH—R^0; $N(R^0)_2$; NH—C(=O)—R^0; NH—C(=O)—O—R^0; NH—C(=O)—NH_2; NH—C(=O)—NH—R^0; NH—C(=O)—$N(R^0)_2$; NR^0—C(=O)—R^0; NR^0—C(=O)—O—R^0; NR^0—C(=O)—NH_2; NR^0—C(=O)—NH—R^0; NR^0—C(=O)—$N(R^0)_2$; NH—$S(=O)_2OH$; NH—$S(=O)_2R^0$; NH—$S(=O)_2OR^0$; NH—$S(=O)_2NH_2$; NH—$S(=O)_2NHR^0$; NH—$S(=O)_2N(R)_2$; NR^0—$S(=O)_2OH$; NR^0—$S(=O)_2R^0$; NR^0—$S(=O)_2OR^0$; NR^0—$S(=O)_2NH_2$; NR^0—$S(=O)_2NHR^0$; NR^0—$S(=O)_2N(R^0)_2$; SH; SR^0; $S(=O)R^0$; $S(=O)_2R^0$; $S(=O)_2OH$; $S(=O)_2OR^0$; $S(=O)_2NH_2$; $S(=O)_2NHR^0$; or $S(=O)_2N(R)_2$; wherein "aryl-substituted" and "heteroaryl-substituted" stand for the substitution of one or more hydrogen atoms, each mutually independently, with F; Cl; Br; I; NO_2; CF_3; CN; R^0; C(=O)H; $C(=O)R^0$; CO_2H; $C(=O)OR^0$; $CONH_2$; $C(=O)NHR^0$; $C(=O)N(R^0)_2$; OH; OR^0; O—(C_{1-8} alkyl)-O; O—C(=O)—R^0; O—C(=O)—O—R^0; O—(C=O)—NH—R^0; O—C(=O)—$N(R^0)_2$; O—$S(=O)_2$—R^0; O—$S(=O)_2OH$; O—$S(=O)_2OR^0$; O—$S(=O)_2NH_2$; O—$S(=O)_2NHR^0$; O—$S(=O)_2N(R^0)_2$; NH_2; NH—R^0; $N(R^0)_2$; NH—C(=O)—R^0; NH—C(=O)—O—R^0; NH—C(=O)—NH_2; NH—C(=O)—NH—R^0; NH—C(=O)—$N(R^0)_2$; NR^0—C(=O)—R^0; NR^0—C(=O)—O—R^0; NR^0—C(=O)—NH_2; NR^0—C(=O)—NH—R^0; NR^0—C(=O)—$N(R^0)_2$; NH—$S(=O)_2OH$; NH—$S(=O)_2R^0$; NH—$S(=O)_2OR^0$; NH—$S(=O)_2NH_2$; NH—$S(=O)_2NHR^0$; NH—$S(=O)_2N(R^0)_2$; NR^0—$S(=O)_2OH$; NR^0—$S(=O)_2R^0$; NR^0—$S(=O)_2OR^0$; NR^0—$S(=O)_2NH_2$; NR^0—$S(=O)_2NHR^0$; NR^0—$S(=O)_2N(R^0)_2$; SH; SR^0; $S(=O)R^0$; $S(=O)_2R^0$; $S(=O)_2OH$; $S(=O)_2OR^0$; $S(=O)_2NH_2$; $S(=O)_2NHR^0$; or $S(=O)_2N(R)_2$; in the form of a free compound or salt of a physiologically compatible acid or base.

[0432] In further embodiments, R^1 stands for C_{1-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or heteroaryl, each unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain

can be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; C_{1-8} alkyl-bridged heteroaryl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{1-8} alkyl-bridged aryl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be unbranched, saturated or unsaturated, unsubstituted; R^2 stands for H; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted.

[0433] In further embodiments, R^3, R^4, R^5 and R^6 each mutually independently denote H; F; Cl; Br; I; NO_2; CF_3; CN; R^0; C(=O)(R^0 or H); C(=O)O(R^0 or H); C(=O)N(R^0 or H)$_2$; OH; OR^0; —O—(C_{1-8} alkyl)-O—; O—(C_{1-8} alkyl)-O—C_{1-8} alkyl; OCF_3; N(R^0 or H)$_2$; N(R^0 or H)—C(=O)—R^0; N(R^0 or H)—C(=O)—N(R^0 or H)$_2$; SH; SCF_3; SR^0; $S(=O)_2R^0$; $S(=O)_2O(R^0$ or H); $S(=O)_2$—N(R^0 or H)$_2$.

[0434] In further embodiments, R^7, R^8, R^9, R^{10} mutually independently stand for H; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted.

[0435] In further embodiments, R^{11} stands for H; F; Cl; Br; CN; C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; phenyl or heteroaryl, each unsubstituted or mono- or polysubstituted; or C_{1-4} alkyl-bridged phenyl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted or mono- or polysubstituted; R^{13} stands for H; F; Cl; Br; CN; C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; phenyl or heteroaryl, each unsubstituted or mono- or polysubstituted; or C_{2-4} alkyl-bridged phenyl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted or mono- or polysubstituted; or R^{11} and R^{13} together with the carbon atoms binding them as ring members form a C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted, optionally fused to phenyl, unsubstituted or mono- or polysubstituted.

[0436] In further embodiments, R^{12} and R^{14} each mutually independently stand for H; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted.

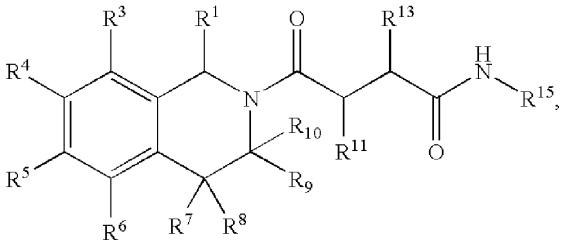
[0437] In further embodiments, R^{15} stands for C_{3-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or

heteroaryl, unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{1-8} alkyl-bridged aryl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted.

Formula 31

[0438] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 31. Such compounds are described in International Publication No. WO2010075973A1, published July 8, 2010, and corresponding to International Application No. PCT/EP2009/009040 filed December 16, 2009; US Patent No. 8,367,700 issued February 5, 2013, and corresponding to US Application No. 12/635,800 filed December 11, 2009; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 31, these references incorporated by reference herein control.

[0439] In an embodiment, the Kv7 channel activator is a compound according to formula 31:

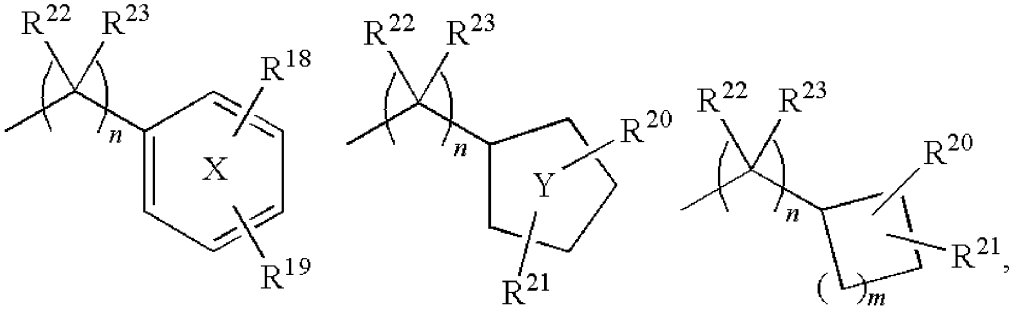


Formula 31

wherein, R^1 stands for C_{1-10} alkyl or C_{2-10} heteroalkyl, each saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted; phenyl or thienyl, each unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged phenyl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be branched or unbranched, saturated or unsaturated, unsubstituted; or C_{1-8} alkyl-bridged thienyl, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can be branched or unbranched, saturated or unsaturated, unsubstituted or mono- or polysubstituted; R^3, R^4, R^5 and R^6 each mutually independently denote H; F; Cl; Br; I; NO_2; CF_3; CN; R^0; C(=O)(R^0 or H); C(=O)O(R^0 or H); C(=O)N(R^0 or H)$_2$; OH; OR^0; O—(C_{1-8} alkyl)-O; O—(C_{1-8} alkyl)-O—C_{1-8} alkyl; N(R^0 or H)$_2$;

$N(R^0 \text{ or } H)—C(=O)—R^0$; $N(R^0 \text{ or } H)—C(=O)—N(R^0 \text{ or } H)_2$; SH; SR^0; $S(=O)_2R^0$; $S(=O)_2O(R^0 \text{ or } H)$; or $S(=O)_2—N(R^0 \text{ or } H)_2$; R^7, R^8, R^9, R^{10} each mutually independently stand for H; or C_{1-4} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; R^{11} and R^{13} each independently stand for H; or C_{1-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; or R^{11} and R^{13} together with the carbon atoms binding them as ring members form a C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; R^{15} stands for C_{3-10} alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or mono- or polysubstituted; C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted; aryl or heteroaryl, unsubstituted or mono- or polysubstituted; C_{1-8} alkyl-bridged C_{3-7} cycloalkyl, saturated or unsaturated, unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted; or C_{1-8} alkyl-bridged aryl or heteroaryl, each unsubstituted or mono- or polysubstituted, wherein the alkyl chain can in each case be branched or unbranched, saturated or unsaturated, unsubstituted, mono- or polysubstituted.

[0440] In further embodiments, R^{15} stands for C_{3-10} alkyl, saturated or unsaturated; branched or unbranched, unsubstituted or mono- or polysubstituted; or is selected from the following substructures:



wherein: n=0, 1, 2, 3, 4, 5, 6, 7 or 8; m=0, 1, 2 or 3; ring X can contain one or two N atoms as ring member(s); ring Y contains at least 1 heteroatom selected from N, O or S and can contain up to 3 heteroatoms mutually independently selected from N, O or S; and/or can contain one or two double bonds; R^{18} and R^{19} mutually independently denote H; F; Cl; Br; I; NO_2; CF_3; CN; R^0; $C(=O)(R^0 \text{ or } H)$; $C(=O)O(R^0 \text{ or } H)$; $C(=O)N(R^0 \text{ or } H)_2$; OH; OR^0; O—(C_{1-8} alkyl)-O; O—(C_{1-8} alkyl)-O—C_{1-8} alkyl; $N(R^0 \text{ or } H)_2$; $N(R^0 \text{ or } H)—C(=O)—R^0$; $N(R^0 \text{ or } H)—C(=O)—N(R^0 \text{ or } H)_2$; SH; SR^0; $S(=O)_2R^0$; $S(=O)_2O(R^0 \text{ or } H)$; or $S(=O)_2—N(R^0 \text{ or }$

H)$_2$H; or R^{18} and R^{19} together with the carbon or nitrogen atoms binding them as ring members form an aryl or heteroaryl fused to the phenyl or heteroaryl ring, each unsubstituted or mono- or polysubstituted; or a C_{3-7} cycloalkyl or heterocyclyl fused to the phenyl or heteroaryl ring, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; R^{20} and R^{21} mutually independently denote H or C_{1-10} alkyl, saturated or unsaturated; branched or unbranched, unsubstituted or mono- or polysubstituted; or C_{3-7} cycloalkyl or heterocyclyl, each saturated or unsaturated, unsubstituted or mono- or polysubstituted; or R^{20} and R^{21} together with the carbon atoms or heteroatoms binding them as ring members form an aryl or heteroaryl fused to ring Y, each unsubstituted or mono- or polysubstituted; R^{22} and R^{23} mutually independently denote H; or C_{1-10} alkyl, saturated or unsaturated; branched or unbranched, unsubstituted.

[0441] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 4-Oxo-4-(1-phenyl-3,4-dihydroisoquinolin-2(1H)-yl)-N-(3-(trifluoromethyl)benzyl)butyric acid amide; 4-(1-Methyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-Oxo-4-(1-thien-2-yl-3,4-dihydroisoquinolin-2(1H)-yl)-N-(3-(trifluoromethyl)benzyl)butyric acid amide; 4-Oxo-4-[1-(4-pyridyl)-3,4-dihydro-1H-isoquinolin-2-yl]-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(7-Fluoro-1-phenyl-3,4-dihydroisoquinolin-2(1H)-yl)-4-oxo-N-(3-(trifluoromethyl)benzyl)butyric acid amide; 4-(5-Fluoro-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[2-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[4-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(4-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(4,4-Dimethyl-1-phenyl-1,3-dihydroisoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(7-Methoxy-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(5-Methoxy-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(3-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; N-(2-Chlorophenyl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-(2,1,3-Benzothiadiazol-4-yl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-(1-Methyl-6-indazolyl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric

acid amide; N-(2-Furylmethyl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-Benzyl-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(2-pyridylmethyl)butyric acid amide; N-[(4-Methoxyphenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-Oxo-N-phenethyl-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(4-pyridylmethyl)butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(3-phenylpropyl)butyric acid amide; N-[2-(1H-Indol-3-yl)ethyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(4-methoxyphenyl)-4-oxobutyric acid amide; N-(2-Chlorophenyl)-4-(5,7-dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; -(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(1-methyl-6-indazolyl)-4-oxobutyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(2-furylmethyl)-4-oxobutyric acid amide; N-Benzyl-4-(5,7-dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide;4 -(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(2-pyridylmethyl)butyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-[(4-methoxyphenyl)methyl]-4-oxobutyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-phenethylbutyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(3-phenylpropyl)butyric acid amide; N-(4-Methoxyphenyl)-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(2-Chlorophenyl)-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(1-Methyl-6-indazolyl)-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(2-Furylmethyl)-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-Benzyl-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; 4-(5-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(2-pyridylmethyl)butyric acid amide; N-[(4-Methoxyphenyl)methyl]-4-(5-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; 4-(5-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-phenethylbutyric acid amide; 4-(5-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(3-phenylpropyl)butyric acid amide; N-(4-Methoxyphenyl)-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(2-Chlorophenyl)-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(1-Methyl-6-indazolyl)-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; N-(2-Furylmethyl)-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid

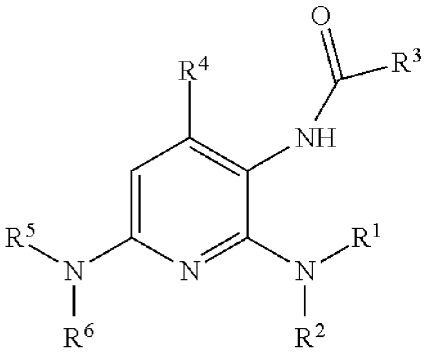
amide; N-Benzyl-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; 4-(7-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(2-pyridylmethyl)butyric acid amide; N-[(4-Methoxyphenyl)methyl]-4-(7-methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxobutyric acid amide; 4-(7-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-phenethylbutyric acid amide; 4-(7-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-(4-pyridylmethyl)butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(2-thienylmethyl)butyric acid amide; N-[(2-Chlorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(2,4-Dichlorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(3,4-Dichlorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-(p-tolylmethyl)butyric acid amide; N-(1,3-Benzodioxol-5-ylmethyl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(3-Fluorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(2-Fluorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(4-Fluorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-[(2,5-Difluorophenyl)methyl]-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; N-(1-Naphthylmethyl)-4-oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)butyric acid amide; 4-(7-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-propylbutyric acid amide; 4-(5-Methyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-propylbutyric acid amide; 4-(5,7-Dimethyl-1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-propylbutyric acid amide; 4-Oxo-4-(1-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-propylbutyric acid amide; 4-Oxo-4-(1-(2-tolyl)-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[3-(trifluoromethyl)-phenyl]methyl]butyric acid amide;4-Oxo-4-(1-(2-tolyl)-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[4-(trifluoromethyl)-phenyl]methyl]butyric acid amide; 4-Oxo-4-(1-(2-tolyl)-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[2-(trifluoromethyl)-phenyl]methyl]butyric acid amide; 4-Oxo-4-(1-(2-tolyl)-6-methyl-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[3-(trifluoromethyl)-phenyl]methyl]butyric acid amide; 4-(1-(2-Methyl-prop-2-yl)-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide; 4-(1-Cyclohexyl-3,4-dihydro-1H-isoquinolin-2-yl)-4-oxo-N-[[3-(trifluoromethyl)-phenyl]methyl]butyric acid amide; and 4-Oxo-4-(1-(2-fluorophenyl)-3,4-dihydro-1H-isoquinolin-2-yl)-N-[[3-(trifluoromethyl)phenyl]methyl]butyric acid amide.

Formula 32

[0442] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 32. Such compounds are described in International Publication No. WO2010037863A1, published April 8, 2010, and corresponding to International Application No. PCT/EP2009/062859 filed October 2, 2009; US Publication No. US20120238547A1, published September 20, 2012 and corresponding to US Application No. 13/394,345 filed September 2, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 32, these references incorporated by reference herein control.

[0443] In an embodiment, the Kv7 channel activator is a compound according to formula 32:

Formula 32



,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, azetidinyl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, azetidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halo and trifluoromethyl; R^3 represents a heterocyclic ring selected from furanyl and pyrrolyl which furanyl and pyrrolyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, C_{1-6}-alkoxy, halo and trifluoromethyl; R^4 represents C_{1-6}-alkyl; and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocyclic ring selected from morpholinyl and 1,4-oxazepanyl.

[0444] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl which is optionally substituted one or more times with halo.

[0445] In further embodiments, R^3 represents furanyl which is optionally substituted with C_{1-6}-alkyl.

[0446] In further embodiments, R^4 represents C_{1-6}-alkyl.

[0447] In further embodiments, R^5 and R^6, together with the nitrogen to which they are attached, represents morpholinyl.

[0448] In further embodiments, the compound is 3-Methyl-furan-2-carboxylic acid [2-((R)-3-fluoro-pyrrolidin-1-yl)-4-methyl-6-[1,4]oxazepan-4-yl-pyridin-3-yl]-amide.

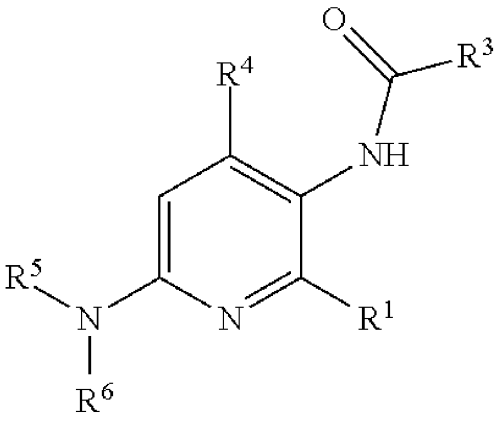
[0449] In further embodiments, the compound is 3-Methyl-furan-2-carboxylic acid [2-((R)-3-fluoro-pyrrolidin-1-yl)-4-methyl-6-morpholin-4-yl-pyridin-3-yl]-amide;

Formula 33

[0450] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 33. Such compounds are described in US Publication No. US20120232058A1, published September 13, 2012, and corresponding to US Application No. 13/394,468 filed September 2, 2010; International Publication No. WO2011026891A1, published March 10, 2011 and corresponding to International Application No. PCT/EP2010/062860 filed September 2, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 33, these references incorporated by reference herein control.

[0451] In an embodiment, the Kv7 channel activator is a compound according to formula 33:

Formula 33



,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents C_{1-6}-alkyl; R^3 represents a heterocyclic ring selected from furanyl and pyrrolyl which furanyl and pyrrolyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, C_{1-6}-alkoxy, halo and trifluoromethyl; R^4 represents C_{1-6}-alkyl; and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocyclic ring selected from morpholinyl and 1,4-oxazepanyl.

[0452] In further embodiments, R^1 represents metyl or iso-propyl.

[0453] In further embodiments, R^3 represents furanyl which is optionally substituted with C_{1-6}-alkyl.

[0454] In further embodiments, R^4 represents C_{1-6}-alkyl.

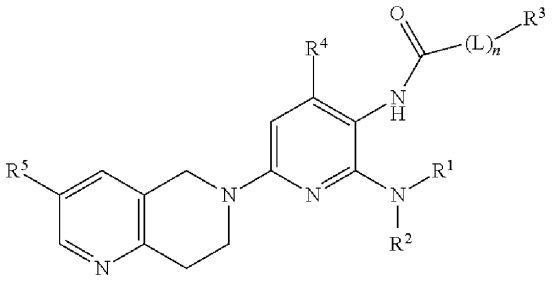
[0455] In further embodiments, R^5 and R^6, together with the nitrogen to which they are attached, represents 1,4-oxazepanyl.

[0456] In further embodiments, the compound is 3-Methyl-furan-2-carboxylic acid(2-isopropyl-4-methyl-6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide; or 3-Methyl-furan-2-carboxylic acid(2,4-dimethyl-6-[1,4]oxazepan-4-yl-pyridin-3-yl)-amide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 34

[0457] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 34. Such compounds are described in International Publication No. WO2010122064A1, published October 28, 2010, and corresponding to International Application No. PCT/EP2010/055284 filed April 21, 2010; US Publication No. US20120115900A1, published May 10, 2012 and corresponding to US Application No. 13/265,273 filed April 21, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 34, these references incorporated by reference herein control.

[0458] In an embodiment, the Kv7 channel activator is a compound according to formula 34:



Formula 34

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halo, hydroxy, amino, C_{1-6}-alkyl, trifluoromethyl, C_{1-6}-

alkoxy, hydroxy-C_{1-6}-alkyl and C_{1-6}-alkoxy-C_1-C_6-alkyl; L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″-CH_2—, and —O—, wherein R′ and R″, independently of each other, represent hydrogen, C_{1-6}-alkyl or halo; n is 0 or 1; R^3 represents C_{1-6}-alkyl, phenyl, pyridyl, furanyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, or C_{3-6}-cycloalkyl, which phenyl, pyridyl, furanyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl and isothiazolyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, C_{3-6}-cycloalkyl, phenyl, C_{1-6}-alkoxy, halo and trifluoromethyl; R^4 represents hydrogen, halo or C_{1-6}-alkyl; and R^5 represents hydrogen or halo.

[0459] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl or piperidinyl, which pyrrolidinyl and piperidinyl is optionally substituted one or more times with halo.

[0460] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl, which pyrrolidinyl is optionally substituted one or more times with halo.

[0461] In further embodiments, L represents —CH_2—.

[0462] In further embodiments, R^3 represents C_{1-6}-alkyl.

[0463] In further embodiments, R^3 represents phenyl, pyridyl, furanyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, or C_{3-6}-cycloalkyl, which phenyl, pyridyl, furanyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl and isothiazolyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl and halo.

[0464] In further embodiments, R^4 represents C_{1-6}-alkyl.

[0465] In further embodiments, R^5 represents hydrogen.

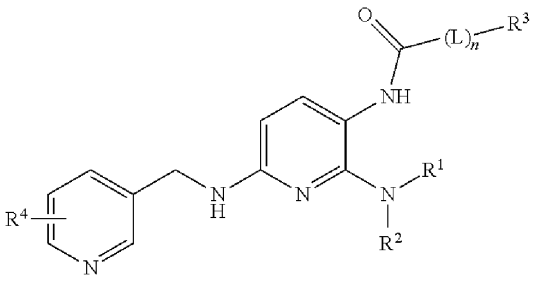
[0466] In further embodiments, the Kv7 channel activator is selected from the group consisting of: 2-(3,5-Difluoro-phenyl)-N-[6-(7,8-dihydro-5H-[1,6]naphthyridin-6-yl)-4-methyl-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide N-[6-(7,8-Dihydro-5H-[1,6]naphthyridin-6-yl)-4-methyl-2-pyrrolidin-1-yl-pyridin-3-yl]-3,3-dimethyl-butyramide; N-[6-(7,8-Dihydro-5H-[1,6]naphthyridin-6-yl)-4-methyl-2-pyrrolidin-1-yl-pyridin-3-yl]-3-fluoro-benzamide; N-[6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-2-[(3R)-3-fluoropyrrolidin-1-yl]-4-methyl-3-pyridyl]-3-methyl-furan-2-carboxamide; 2-(3,5-difluorophenyl)-N-[6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-2-[(3R)-3-fluoropyrrolidin-1-yl]-4-methyl-3-pyridyl]acetamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-3-methyl-furan-2-carboxamide; 2-(3,5-difluorophenyl)-N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]acetamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-1-methyl-

imidazole-2-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-5-methyl-oxazole-4-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-4-methyl-thiazole-5-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-3-methyl-isoxazole-4-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-4-methyl-oxazole-5-carboxamide; 2-cyclopropyl-N-[2-(4,4-difluoro-1-pipridyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]acetamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-5-ethyl-oxazole-4-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-3-methyl-pyridine-2-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-2,5-dimethyl-oxazole-4-carboxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-5-phenyl-oxazole-4-carboxamide; 5-cyclopropyl-N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]oxazole-4-carb oxamide; N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]-5-methyl-isothiazole-4-carboxamide; ethyl N-[2-(4,4-difluoro-1-piperidyl)-6-(7,8-dihydro-5H-1,6-naphthyridin-6-yl)-4-methyl-3-pyridyl]carbamate; N-[6-(3-chloro-7,8-dihydro-5H-1,6-naphthyridin-6-yl)-2-[(3R)-3-fluoropyrrolidin-1-yl]-4,6-dimethyl-1H-pyridin-3-yl]-3,3-dimethyl-butanamide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 35

[0467] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 35. Such compounds are described in US Publication No. US20120059037A1, published March 8, 2012, and corresponding to US Application No. 13/256,893 filed March 11, 2010; International Publication No. WO2010105960A1, published September 23, 2010 and corresponding to International Application No. PCT/EP2010/053072 filed March 11, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 35, these references incorporated by reference herein control.

[0468] In an embodiment, the Kv7 channel activator is a compound according to formula 35:



Formula 35

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent hydrogen, C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl or C_{1-6}-alkoxy-C_{1-6}-alkyl; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halogen, hydroxy, amino, C_{1-6}-alkyl, trifluoromethyl, C_{1-6}-alkoxy, hydroxy-C_{1-6}-alkyl and C_{1-6}-alkoxy-C_{1-6}-alkyl; L represents a linker selected from —CR′R″—, —CH_2—CR′R″— and —CR′R″—CH_2—, wherein R′ and R″, independently of each other, represent hydrogen, C_{1-6}-alkyl or halogen; n is 0, 1; R^3 represents C_{1-6}-alkyl, phenyl or furanyl, which phenyl and furanyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, C_{1-6}-alkoxy, halogen and trifluoromethyl; and R^4 represents hydrogen, halogen or C_{1-6}-alkyl.

[0469] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl, which pyrrolidinyl is optionally substituted one or more times with halogen.

[0470] In further embodiments, L represents —CH_2—, and n is 1.

[0471] In further embodiments, R^3 represents phenyl, which phenyl is optionally substituted one or more times with halogen.

[0472] In further embodiments, R^3 represents C_{1-6}-alkyl.

[0473] In further embodiments, R^4 represents halogen.

[0474] In further embodiments, R^4 represents hydrogen.

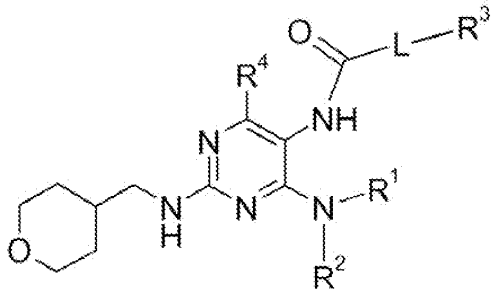
[0475] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-{6-[(6-Chloro-pyridin-3-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-{6-[(pyridin-3-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-acetamide; N-{6-[(6-Chloro-pyridin-3-ylmethyl)-amino]-2-pyrrolidin-1yl-pyridin-3-yl}-3,3-dimethyl-butyramide; or a stereoisomer or a

mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof.

Formula 36

[0476] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 36. Such compounds are described in Patent Cooperation Treaty application No. EP2010/052257 published September 2, 2010, which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 36, these references incorporated by reference herein control.

[0477] In an embodiment, the Kv7 channel activator is a compound according to formula 36:



Formula 36

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent hydrogen, Ci-6-alkyl, hydroxy- C-ι-6-alkyl or Ci-6-alkoxy-Ci-6-alkyl; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1 H-pyrrol-1-yl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halogen, hydroxy, amino, Ci-6-alkyl, trifluoro- methyl, Ci-6-alkoxy, hydroxy-d-6-alkyl and d-6-alkoxy- d-6-alkyl; L represents a linker selected from -CR^1R"-, -CH_2-CR^1R"- and -CR'R"-CH_2-, wherein R' and R", independently of each other, represent hydrogen, d-6-alkyl or halogen; R^3 represents Ci-6-alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, Ci-6-alkoxy, halogen and trifluoromethyl; and R^4 represents H or Ci-6-alkyl.

[0478] In further embodiments, R^1 and R^2, independently of each other, represent Ci-6-alkyl.

[0479] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached, is morpholinyl.

[0480] In further embodiments, L represents -CH_2-.

[0481] In further embodiments, R^3 represents phenyl, which phenyl is optionally substituted one or more times with halogen.

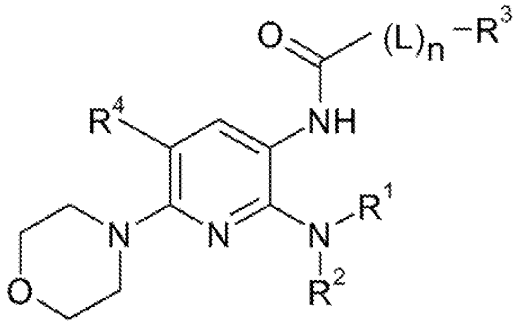
[0482] In further embodiments, R^4 represents methyl.

[0483] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3,5-Difluoro-phenyl)-N-{4-methyl-6-morpholin-4-yl-2-[(tetrahydro-pyran-4- ylmethyl)-amino]-pyrimidin-5-yl}-acetamide; 2-(3,5-Difluoro-phenyl)-N-{4-dimethylamino-6-methyl-2-[(tetrahydro-pyran-4- ylmethyl)-amino]-pyrimidin-5-yl}-acetamide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an /V-oxide thereof.

Formula 37

[0484] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 37. Such compounds are described in International Publication No. WO2010094644A1, published August 26, 2010, and corresponding to International Application No. PCT/EP2010/051839 filed February 15, 2010; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 37, the reference incorporated by reference herein controls.

[0485] In an embodiment, the Kv7 channel activator is a compound according to formula 37:



Formula 37

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent C_{i-6}-alkyl; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1 H-pyrrol-1 -yl, piperidinyl and morpholinyl, which pyrrolidinyl and piperidinyl is optionally substituted one or more times with a substituent selected from the group consisting of halogen, hydroxy, amino, C_{1-6}-alkyl, trifluoromethyl, C_{i-6}-alkoxy, hydroxy-d_{-6}-alkyl and C_{i-6}-alkoxy-C_{i-6}-alkyl; L represents a linker selected from -CR^1R"- and -O-CR'R"-, wherein R' and R", independently of each

other, represent hydrogen, d-$_6$-alkyl or halogen; n is 0 or 1 ; R^3 represents d-$_6$-alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from d-6-alkyl, Ci-6-alkoxy, halogen and trifluoromethyl; and R^4 represents Ci-6-alkyl.

[0486] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl, which pyrrolidinyl is optionally substituted one or more times with halogen.

[0487] In further embodiments, R' and R", independently of each other, represents hydrogen or methyl.

[0488] In further embodiments, R^3 represents phenyl, which phenyl is optionally substituted one or more times with halogen.

[0489] In further embodiments, R^3 represents d-e-alkyl.

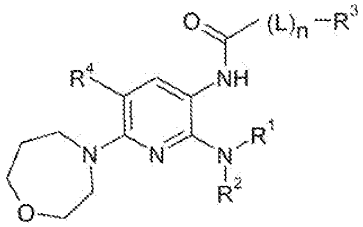
[0490] In further embodiments, R^4 represents methyl.

[0491] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 3,3-Dimethyl-N-(5-methyl-6-morpholin-4-yl-2-pyrrolidin-1-yl-pyridin-3-yl)-butyramide; 2-(3,5-Difluoro-phenyl)-N-(5-methyl-6-morpholin-4-yl-2-pyrrolidin-1-yl-pyridin-3-yl)-acetamide; N-[2-((R)-3-Fluoro-pyrrolidin-1-yl)-5-methyl-6-morpholin-4-yl-pyridin-3-yl]-3,3-dimethylbutyramide; (S)-N-[2-((R)-3-Fluoro-pyrrolidin-1-yl)-5-methyl-6-morpholin-4-yl-pyridin-3-yl]-2-phenylpropionamide;[2-((R)-3-Fluoro-pyrrolidin-1-yl)-5-methyl-6-morpholin-4-yl-pyridin-3-yl]-carbamic acid ethyl ester; (S)-N-[2-((R)-3-Fluoro-pyrrolidin-1-yl)-5-methyl-6-morpholin-4-yl-pyridin-3-yl]-2-methyl-butyramide;or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an /V-oxide thereof.

Formula 38

[0492] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 38. Such compounds are described in International Publication No. WO2010094645A1, published August 26, 2010, and corresponding to International Application No. PCT/EP2010/051840 filed February 15, 2010; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 38, the reference incorporated by reference herein controls.

[0493] In an embodiment, the Kv7 channel activator is a compound according to Formula 38:



Formula 38

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent d-e-alkyl; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1 H-pyrrol-1-yl, piperidinyl, morpholinyl and 1 ,4-oxazepanyl, which pyrrolidinyl and piperidinyl is optionally substituted one or more times with a substituent selected from the group consisting of halogen, hydroxy, amino, d-$_6$-alkyl, trifluoromethyl, d-$_6$-alkoxy, hydroxy-Ci-$_6$-alkyl and Ci-$_6$-alkoxy-Ci-$_6$-alkyl; L represents a linker selected from -CR^{1}R"- and -O-CR'R"-, wherein R' and R", independently of each other, represent hydrogen, Ci-$_6$-alkyl or halogen; n is 0 or 1 ; R^3 represents C_{1-6}-alkyl, phenyl or furanyl, which phenyl and furanyl is optionally substituted one or more times with substituents selected from d-$_6$-alkyl, Ci-$_6$- alkoxy, halogen and trifluoromethyl; and R^4 represents d-$_6$-alkyl.

[0494] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl, which pyrrolidinyl is optionally substituted one or more times with halogen.

[0495] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is 1 ,4-oxazepanyl.

[0496] In further embodiments, L is -CH_2- and n is 1.

[0497] In further embodiments, n is 0.

[0498] In further embodiments, R^3 represents phenyl, which phenyl is optionally substituted one or more times with halogen.

[0499] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3,4-Difluoro-phenyl)-N-[2-((R)-3-fluoro-pyrrolidin-1-yl)-5-methyl-6- [1 ,4]oxazepan-4-yl-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-/V-(5-methyl-2,6-bis-[1 ,4]oxazepan-4-yl-pyridin-3-yl)- acetamide; 3-Fluoro-/V-(5-methyl-6-[1 ,4]oxazepan-4-yl-2-pyrrolidin-1-yl-pyridin-3-yl)- benzamide; 3-methyl-N-[5-methyl-6-(1 ,4-oxazepan-4-yl)-2-pyrrolidin-1-yl-3-pyridyl]furan-2-carboxamide; 2-(3-fluorophenyl)-N-[2-[(3R)-3-fluoropyrrolidin-1-yl]-5-methyl-6-(1 ,4-oxazepan-4- yl)-3-pyridyl]acetamide; or a

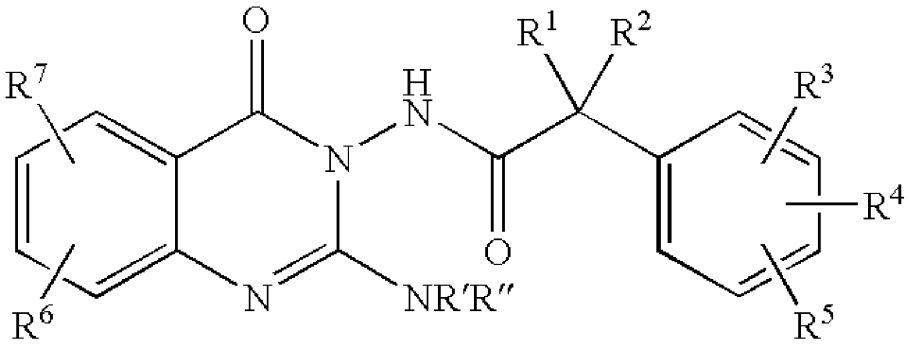
stereoisomer or a mixture of its stereoisomers, or a pharmaceutically- acceptable addition salt thereof, or an /V-oxide thereof.

Formula 39

[0500] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 1. Such compounds are described in International Publication No. WO2008142140A2, published November 27, 2008, and corresponding to International Application No. PCT/EP2008/056322 filed May 22, 2008; US Patent No. 8,178,544 published May 15, 2012 and corresponding to US Application No. 12/601,124 filed May 22, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 39, the reference incorporated by reference herein controls.

[0501] In an embodiment, the Kv7 channel activator is a compound according to Formula 39:

Formula 39



,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents hydrogen, alkyl or halo; and R^2 represents hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxyalkyl, hydroxy, alkoxy, phenyl, phenyl-alkyl, amino, alkyl-carbonyl-amino, cyano or nitro; or R^1 and R^2 together with the carbon atom to which they are attached form a cycloalkyl (spiro) group; or R^1 represents hydrogen; and R^2 together with one of R^3, R^4 and R^5, attached in ortho-position on the aromatic ring, form a $—(CH_2)_n—$ bridge, wherein n is 1, 2 or 3; R^3, R^4 and R^5, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, alkyl-sulfanyl, alkyl-sulfonyl, phenyl, phenoxy, benzoyl, cyano or nitro; or two of R^3, R^4 and R^5, together form a methylenedioxy group; and the remaining of R^3, R^4 and R^5 is as defined above; or two of R^3, R^4 and R^5, together with the phenyl ring to which they are attached, form a naphthyl group; and the remaining of R^3,

R^4 and R^5 is as defined above; or one of R^3, R^4 and R^5, attached in ortho-position on the aromatic ring, and together with R^2 form a —$(CH_2)_n$— bridge, wherein n is 1, 2 or 3; and the remaining of R^3, R^4 and R^5, are as defined above; R^6 and R^7, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, nitro, cyano or phenyl; and R′ and R″, independently of each other, represent alkyl, hydroxy-alkyl, amino-alkyl, cycloalkyl, phenyl-alkyl, phenyl-hydroxyalkyl, N-alkyl-amino-alkyl, N,N-dialkyl-amino-alkyl, alkoxy-alkyl, piperidinyl, N-alkyl-piperidinyl, furanyl-alkyl, pyridinyl-alkyl, pyrazolyl-alkyl, imidazolyl-alkyl, pyrimidinyl, pyrimidinyl substituted with one or two substituents selected from N-alkyl-amino, N,N-dialkyl-amino and phenyl; or R′ and R″, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, thiazolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and homomorpholinyl, which pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and homomorpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of alkyl, alkoxy, alkoxy-alkyl, alkyl-carbonyl-amino, cycloalkyl-carbonyl-amino, hydroxy-alkyl, hydroxy, amino, N-alkyl-amino, N,N-dialkyl-amino, amino-alkyl, N-alkyl-amino-alkyl, N,N-dialkyl-amino-alkyl, carbamoyl-alkyl, N-alkyl-carbamoyl-alkyl, N,N-dialkyl-carbamoyl-alkyl, N-hydroxy-alkyl-carbamoyl, N,N-dialkyl-amino-alkyl-carbamoyl, alkoxy-carbonyl, cyano-alkyl, pyrrolidinyl, pyrrolidinyl-alkyl, piperidinyl, piperidinyl-carbonyl, hydroxy-piperidinyl, hydroxy-piperidinyl-alkyl, hydroxy-piperidinyl-carbonyl, N-alkyl-piperidinyl, piperidinyl-alkyl, N-alkyl-piperidinyl-alkyl, morpholino-alkyl, morpholino-alkyl-carbamoyl, morpholino-carbonyl-alkyl, triazolyl-alkyl, piperazinyl, piperazinyl-alkyl, piperazinyl-carbonyl, N-alkyl-piperazinyl, N-alkyl-piperazinyl-alkyl, N-alkyl-piperazinyl-carbonyl, pyridinyl, pyridinyl-alkyl, and pyridinyl substituted once or twice with alkyl, trifluoromethyl and/or cyano.

[0502] In further embodiments, R^1 represents hydrogen or alkyl; and R^2 represents hydrogen or alkyl.

[0503] In further embodiments, R^3, R^4 and R^5, independently of each other, represent hydrogen, alkyl, halo, haloalkyl, hydroxy, alkoxy, alkyl-sulfanyl, alkyl-sulfonyl, phenyl or phenoxy.

[0504] In further embodiments, R^6 and R^7, independently of each other, represent hydrogen, halo, haloalkyl, hydroxy, alkoxy, or amino.

[0505] In further embodiments, R′ and R″, independently of each other, represent alkyl, hydroxy-alkyl, cycloalkyl, or phenyl-alkyl.

[0506] In further embodiments, R′ and R″, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, thiazolidinyl, piperidinyl, piperazinyl, homopiperazinyl and morpholinyl, which piperazinyl is optionally substituted one or more times with alkyl.

[0507] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3,5-Difluoro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-dimethylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(4-Chloro-phenyl)-N-(2-diethylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-dimethylamino-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; N-(2-Diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(4-methanesulfonyl-phenyl)-acetamide; N-{2-[(2-Methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-2-(4-trifluoromethyl-phenyl)-acetamide; 2-(4-Butoxy-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-acetamide; N-[2-(Benzyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(4-methanesulfonyl-phenyl)-acetamide; 2-(4-Butoxy-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(4-oxo-2-thiazolidin-3-yl-4H-quinazolin-3-yl)-acetamide; N-(2-Diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Bis-trifluoromethyl-phenyl)-N-(4-oxo-2-thiazolidin-3-yl-4H-quinazolin-3-yl)-acetamide; 2-Benzo[1,3]dioxol-5-yl-N-(2-diethylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; N-(2-Diethylamino-4-oxo-4H-quinazolin-3-yl)-2-phenyl-acetamide; or N-[2-(Ethyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-phenyl-acetamide; or a stereoisomer or a mixture of its stereoisomers, a pharmaceutically-acceptable addition salt thereof.

[0508] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3-Fluoro-4-trifluoromethyl-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Bis-trifluoromethyl-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-acetamide; N-[2-(Benzyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-morpholin-4-yl-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(4-Chloro-phenyl)-N-{7-fluoro-2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-acetamide; 2-(4-Chloro-phenyl)-N-(2-morpholin-4-yl-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-{7-fluoro-2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-acetamide; 2-(4-Chloro-phenyl)-N-(2-dimethylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; N-(2-Diethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(4-

Chloro-phenyl)-N-(2-diethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(4-methyl-piperazin-1-yl)-4oxo-4H-quinazolin-3-yl]-acetamide; N-(2-Diethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-5-trifluoromethyl-phenyl)-acetamide; N-[2-(Benzyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-acetamide; 2-(3-Fluoro-5-trifluoromethyl-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-7-trifluoromethyl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-7-trifluoromethyl-4H-quinazolin-3-yl)-acetamide; 2-(3-Fluoro-5-trifluoromethyl-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl}-acetamide; 2-(3,5-Difluoro-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl}-acetamide; N-(6-Butoxy-2-morpholin-4-yl-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(5-Chloro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(5-Chloro-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-7-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-5-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(7-Chloro-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(7-Chloro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(6-Chloro-2-diethylamino-7-fluoro-4-oxo-4H-quinazolin-3yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-5,7-difluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(7-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-(6-Chloro-7-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(5,7-Difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(5,7-Dichloro-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-6,7-difluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(6,7-Difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3-Fluoro-4-trifluoromethyl-phenyl)-N-(2-morpholin-4-yl-4-oxo-4H-quinazolin-3-yl)-acetamide; N-(2-Dimethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; N-(6-Chloro-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Dimethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; N-(6-Fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; 2-(4-Chloro-3-fluoro-phenyl)-N-(6-fluoro-4-oxo-2-

pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(6-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(4-Chloro-3-fluoro-phenyl)-N-(2-dimethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-dimethylamino-6-fluoro-4-oxo-4H-quinazolin-3-yl)-acetamide; N-(5,7-Dichloro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-dimethylamino-5-fluoro-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-dimethylamino-7-fluoro-4-oxo-4H-quinazolin-3-yl)-acetamide; N-(2-Dimethylamino-5-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-5-trifluoromethyl-phenyl)-acetamide; N-(2-Dimethylamino-7-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; 2-(4-Chloro-phenyl)-N-(2-diethylamino-5,7-difluoro-4-oxo-4-quinazolin-3-yl)-acetamide; 2-(4-Chloro-phenyl)-N-(7-fluoro-4-oxo-2-pyrrolidin-1yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[5-fluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-5-fluoro-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[7-fluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(4-Chloro-phenyl)-N-(7-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-propionamide; 2-(4-Chloro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-propionamide; N-(2-Diethylamino-8-fluoro-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(8-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-Naphthalen-2-yl-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-(5,7-Difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,4-difluoro-phenyl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(4-Chloro-phenyl)-N-[2-(ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-Naphthalen-1-yl-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(4-Chloro-phenyl)-N-(5,7-difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-5,7-difluoro-4-oxo-4H-quinazolin-3-yl]-acetamide; N-[5,7-Difluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; N-[5,7-Difluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-(Ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-2-(4-methylsulfanyl-phenyl)-acetamide; 2-(4-Isobutyl-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-propionamide; N-[2-(Ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-2-(4-methoxy-phenyl)-acetamide; N-(7-Fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(4-phenoxy-phenyl)-acetamide;

2-Biphenyl-4-yl-N-(7-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(4-Chloro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-[2-(Ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-2-(4-isopropyl-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(isopropyl-methyl-amino)-4-oxo-4-quinazolin-3-yl]-acetamide; 2-(3,4-Difluoro-phenyl)-N-[2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,4-Difluoro-phenyl)-N-(7-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-(8-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-[2-(isobutyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(isobutyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; 2-(3,4-Difluoro-phenyl)-N-[7-fluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-acetamide; N-(7-Chloro-6-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(2-diisopropylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; N-[2-(Cyclopentyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-(Cyclopentyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-(2-diisopropylamino-4-oxo-4H-quinazolin-3-yl)-acetamide; 2-(3,4-Difluoro-phenyl)-N-(4-oxo-2-piperidin-1-yl-4H-quinazolin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-(4-oxo-2-piperidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-(8-Chloro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-6-hydroxy-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(6,8-Dichloro-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(6-Amino-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(7-Amino-2-diethylamino-4-oxo-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-(7-Amino-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; or a stereoisomer or a mixture of its stereoisomers, a pharmaceutically-acceptable addition salt thereof.

[0509] In further embodiments, 2-(3,5-difluorophenyl)-N-(2-dimethylamino-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof.

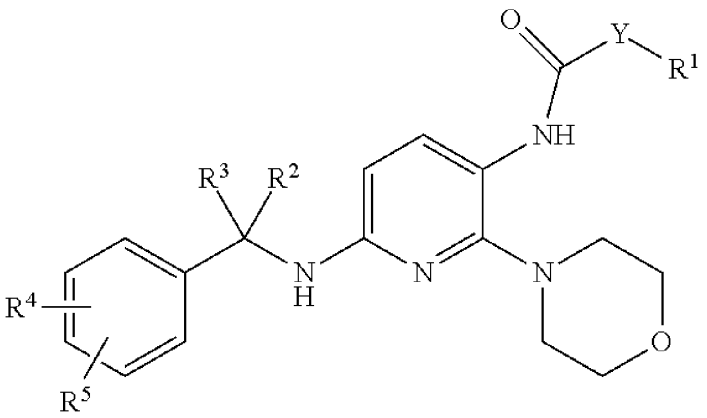
Formula 40

[0510] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 40. Such compounds are described in International Publication No. WO2010060955A1, published June 3, 2010 and corresponding

to International Application No. PCT/EP2009/065890 filed November 26, 2009; US Publication No. US20110312962A1, published December 22, 2011 and corresponding to US Application No. 13/131,218 filed November 26, 2009; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 40, these references incorporated by reference herein control.

[0511] In an embodiment, the Kv7 channel activator is a compound according to Formula 40:

Formula 40



,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof, wherein Y represents —$(CH_2)_n$—, —$(CH_2)_n$—O— or —$(CH_2)_n$—S— wherein n is 0 or 1; R^1 represents C_{1-6}-alkyl, benzo[1,3]dioxolyl, phenyl or pyridyl, which phenyl and pyridyl are optionally substituted one or more times with substituents selected from the group consisting of C_{1-6}-alkyl, halogen, trifluoromethyl, hydroxy, C_{1-6}-alkoxy and trifluoromethoxy; R^2 and R^3, independently of each other, represent hydrogen or C_{1-6}-alkyl; and R^4 and R^5, independently of each other, represent hydrogen, C_{1-6}-alkyl, halogen, trifluoromethyl, hydroxy, C_{1-6}-alkoxy or trifluoromethoxy.

[0512] In further embodiments, Y represents —$(CH_2)_n$—, wherein n is 0 or 1; R^1 represents C_{1-6}-alkyl, benzo[1,3]dioxolyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from the group consisting of C_{1-6}-alkyl, halogen, trifluoromethyl, hydroxy, C_{1-6}-alkoxy and trifluoromethoxy; R^2 and R^3, independently of each other, represent hydrogen or C_{1-6}-alkyl; and R^4 and R^5, independently of each other, represent hydrogen, C_{1-6}-alkyl, halogen, trifluoromethyl, hydroxy, C_{1-6}-alkoxy or trifluoromethoxy.

[0513] In further embodiments, n is 1.

[0514] In further embodiments, R^1 represents phenyl optionally substituted one or more times with substituents selected from the group consisting of C_{1-6}-alkyl, halogen, trifluoromethyl and C_{1-6}-alkoxy.

[0515] In further embodiments, R^2 and R^3 represent hydrogen.

[0516] In further embodiments, R^2 and R^3 represent C_{1-6}-alkyl.

[0517] In further embodiments, R^4 and R^5, independently of each other, represent hydrogen or halogen.

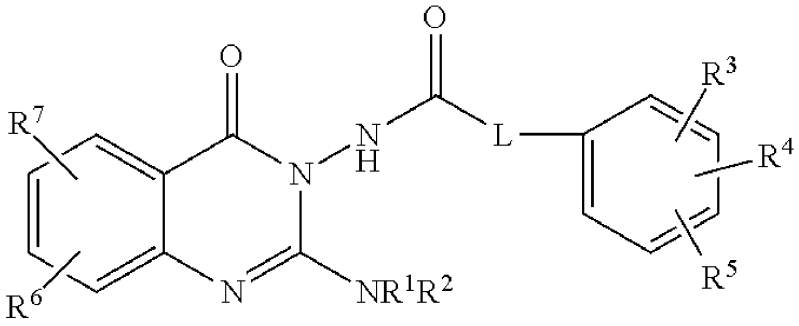
[0518] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3,5-Difluoro-phenyl)-N-[6-(4-fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-{6-[1-(4-fluoro-phenyl)-1-methyl-ethylamino]-2-morpholin-4-yl-pyridin-3-yl}-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-methyl-benzamide; 2-Benzo[1,3]dioxol-5-yl-N-[6-(4-fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-(4-methoxy-phenyl)-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-(3-methoxy-phenyl)-acetamide; 2-(2,4-Dichloro-phenyl)-N-[6-(4-fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-(3-trifluoromethyl-phenyl)-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-(2-fluoro-phenyl)-acetamide; N-[6-(4-Fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-2-(3-fluoro-phenyl)-acetamide; or 2-(4-Chloro-phenyl)-N-[6-(4-fluoro-benzylamino)-2-morpholin-4-yl-pyridin-3-yl]-acetamide, N-[6-[(4-Fluorophenyl)-methylamino]-2-morpholino-3-pyridyl]-2-(4-fluorophenyl)-sulfanyl-acetamide; 2-(3-fluorophenoxy)-N-[6-[(4-fluorophenyl)-methyl amino]-2-morpholino-3-pyridyl]acetamide; 2-(6-chloro-3-pyridyl)-N-[6-[(4-fluorophenyl)-methylamino]-2-morpholino-3-pyridyl]acetamide; 2-fluoro-N-[6-[(4-fluorophenyl)-methylamino]-2-morpholino-3-pyridyl]pyridine-3-carboxamide; a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof.

Formula 41

[0519] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 41. Such compounds are described in US Publication No. US20110269783A1, published November 3, 2011, and corresponding to US Application No. 13/128,015 filed November 6, 2009; International Publication No. WO2010051819A1, published May 14, 2010, and corresponding to International Application No. PCT/DK2009/050293 filed November 6, 2009; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 41, these references incorporated by reference herein control.

[0520] In an embodiment, the Kv7 channel activator is a compound according to Formula 41:

Formula 41



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A stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof, wherein L represents a linker selected from —(CR′R″)$_2$—, —CR′R″—S—, —CR′R″—O— or  wherein R′ and R″, independently of each other, represent hydrogen, C_{1-6}-alkyl or halogen; R^1 and R^2, independently of each other, represent C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl-, C_{1-6}-alkoxy-C_{1-6}-alkyl-, phenyl, phenyl-C_{1-6}-alkyl-, which phenyl is optionally substituted with one or two times with a substituent selected from the group consisting of C_{1-6}-alkoxy, halogen and cyano; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halogen, hydroxy, amino, C_{1-6}-alkyl, trifluoromethyl, C_{1-6}-alkoxy, hydroxy-C_{1-6}-alkyl- and C_{1-6}-alkoxy-C_{1-6}-alkyl-; R^3, R^4 and R^5, independently of each other, represent hydrogen, C_{1-6}-alkyl, halogen, trihalomethyl, hydroxy, C_{1-6}-alkoxy, trifluoromethoxy, amino, cyano or nitro; and R^6 and R^7, independently of each other, represent hydrogen, C_{1-6}-alkyl, halogen, trihalomethyl, hydroxy, C_{1-6}-alkoxy, trifluoromethoxy, amino, nitro, cyano or phenyl.

[0521] In further embodiments, R^1 and R^2, independently of each other, represent C_{1-6}-alkyl, alkoxy-C_{1-6}-alkyl- or phenyl-C_{1-6}-alkyl-.

[0522] In further embodiments, R^1 and R^2, together with the nitrogen to which they are attached, form a pyrrolidinyl ring.

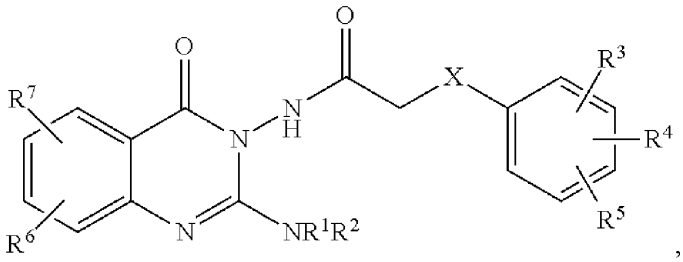
[0523] In further embodiments, R^3, R^4 and R^5, independently of each other, represent hydrogen, C_{1-6}-alkyl or halogen.

[0524] In further embodiments, R^6 and R^7, independently of each other, represent hydrogen or halogen.

[0525] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-(7-Fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-3-(3-fluoro-phenyl)-

propionamide; 3-(3-Fluoro-phenyl)-N-{2-[(2-methoxy-ethyl)-methyl-amino]-4-oxo-4H-quinazolin-3-yl}-propionamide; N-[2-(Benzyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-3-(3-fluoro-phenyl)-propionamide; N-[2-(Benzyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-3-(3,5-difluoro-phenyl)-propionamide; 3-(3-Fluoro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-propionamide; N-(4-Oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-3-phenyl-propionamide; N-(2-Dimethylamino-7-fluoro-4-oxo-4H-quinazolin-3-yl)-3-(3-fluoro-phenyl)-propionamide; N-(4-Oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-phenylsulfanyl-acetamide; N-(4-Oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-2-phenoxy-acetamide; N-(5-Fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-3-(3-fluoro-phenyl)-propionamide; 2-(4-Fluoro-phenylsulfanyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-(5,7-Difluoro-4-oxo-2-pynolidin-1-yl-4H-quinazolin-3-yl)-3-(3-fluoro-phenyl)-propionamide; 2-(4-tert-Butyl-phenylsulfanyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-acetamide; N-[5,7-Difluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-3-(3-fluoro-phenyl)-propionamide; N-(5,7-Difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-3-(3,5-difluoro-phenyl)-propionamide; (S)-N-(5,7-Difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-3-phenyl-butyramide; 3-(4-Chloro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-butyramide; 3-(3-Fluoro-phenyl)-N-(4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-butyramide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid(2-dimethylamino-7-fluoro-4-oxo-4H-quinazolin-3-yl)-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid[5,7-difluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid(5,7-difluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid[2-(ethyl-methyl-amino)-7-fluoro-4-oxo-4H-quinazolin-3-yl]-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid[7-fluoro-2-(isopropyl-methyl-amino)-4-oxo-4H-quinazolin-3-yl]-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid[2-(ethyl-methyl-amino)-5,7-difluoro-4-oxo-4H-quinazolin-3-yl]-amide; cis-2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid(8-fluoro-4-oxo-2-pyrrolidin-1-yl-4H-quinazolin-3-yl)-amide; or a stereoisomer or a mixture of its stereoisomers, a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof.

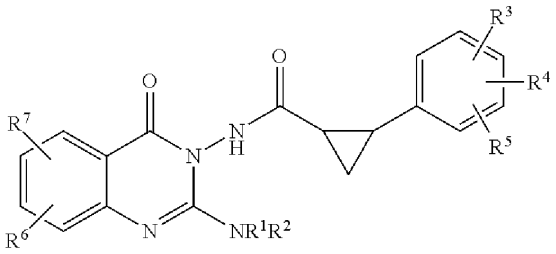
[0526] In further embodiments, the compound is of formula:



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wherein: X represents —CR′R″—, —S—, or —O—, wherein R′ and R″, independently of each other, represent hydrogen, C_{1-6}-alkyl or halogen, and R′, R^2, R^3, R^4, R^5, R^6 and R^7 are as defined above.

[0527] In further embodiments, the compound is of formula:



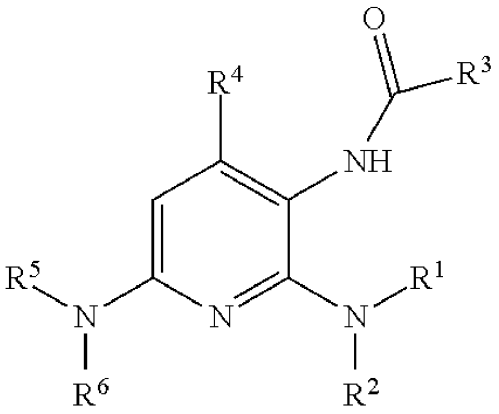
wherein: R^1, R^2, R^3, R^4, R^5, R^6 and R^7 are as defined above.

Formula 42

[0528] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds. Such compounds are described in International Publication No. WO2011026890A1, published March 10, 2011, and corresponding to International Application No. PCT/EP2010/062859 filed September 2, 2010; US Publication No. US20120238547A1, published September 20, 2012, and corresponding to US Application No. 13/394,345 filed September 2, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 42, these references incorporated by reference herein control.

[0529] In an embodiment, the Kv7 channel activator is a compound according to Formula 42:

Formula 42



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a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1H-pyrrol-1-yl, azetidinyl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, azetidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halo and trifluoromethyl; R^3 represents a heterocyclic ring selected from furanyl and pyrrolyl which furanyl and pyrrolyl is optionally substituted one or more times with substituents selected from C_{1-6}-alkyl, C_{1-6}-alkoxy, halo and trifluoromethyl; R^4 represents C_{1-6}-alkyl; and R^5 and R^6, together with the nitrogen to which they are attached, form a heterocyclic ring selected from morpholinyl and 1,4-oxazepanyl.

[0530] In further embodiments, R^1 and R^2 together with the nitrogen to which they are attached is pyrrolidinyl which is optionally substituted one or more times with halo.

[0531] In further embodiments, R^3 represents furanyl which is optionally substituted with C_{1-6}-alkyl.

[0532] In further embodiments, R^4 represents C_{1-6}-alkyl.

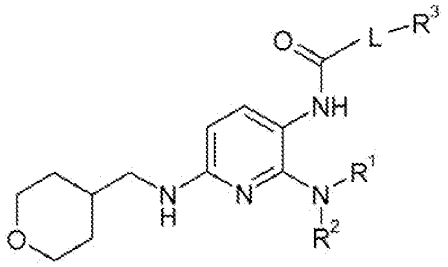
[0533] In further embodiments, R^5 and R^6, together with the nitrogen to which they are attached, represents morpholinyl.

[0534] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 3-Methyl-furan-2-carboxylic acid [2-((R)-3-fluoro-pyrrolidin-1-yl)-4-methyl-6-[1,4]oxazepan-4-yl-pyridin-3-yl]-amide; 3-Methyl-furan-2-carboxylic acid [2-((R)-3-fluoro-pyrrolidin-1-yl)-4-methyl-6-morpholin-4-yl-pyridin-3-yl]-amide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically acceptable addition salt thereof, or an N-oxide thereof.

Formula 43

[0535] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 43. Such compounds are described in International Publication No. WO2010026104A1, published March 11, 2010, and corresponding to International Application No. PCT/EP2009/061125 filed August 28, 2009; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 43, the reference incorporated by reference herein controls.

[0536] In an embodiment, the Kv7 channel activator is a compound according to Formula 43:



Formula 43

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a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent C_{i-6}-alkyl, hydroxy-d-e-alkyl or C_{i-6}- alkoxy-C_{i-6}-alkyl; or R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, 2,5-dihydro-1 H-pyrrol-1 -yl, azetidinyl, thiazolidinyl, piperidinyl, piperazinyl and morpholinyl, which pyrrolidinyl, azetidinyl, piperidinyl, piperazinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halo, hydroxy, amino, C_{i-6}-alkyl, trifluoromethyl, C_{i-6}-alkoxy, hydroxy-C_{i-6}-alkyl and C_{i-6}-alkoxy-C_{i-6}-alkyl; R^3 represents C_{i-6}-alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from C_{i-6}-alkyl, C_{i-6}-alkoxy, halo and trifluoromethyl; and L represents a linker selected from -CR^1R"-, -CH_2-CR^1R"- and -CR^1R^1^CH_2-, wherein R^1 and R", independently of each other, represent hydrogen, C_{i-6}-alkyl or halo.

[0537] In further embodiments, R^1 and R^2, independently of each other, represent C_{i-6}-alkyl.

[0538] In further embodiments, R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring selected from pyrrolidinyl, azetidinyl, piperidinyl and morpholinyl, which pyrrolidinyl, azetidinyl, piperidinyl and morpholinyl is optionally substituted one or more times with a substituent selected from the group consisting of halo, d-e-alkyl and trifluoromethyl.

[0539] In further embodiments, R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring which is pyrrolidinyl optionally substituted one or more times with a substituent selected from the group consisting of halo, d-e-alkyl and trifluoromethyl.

[0540] In further embodiments, R^1 and R^2, together with the nitrogen to which they are attached, form a heterocyclic ring which is piperidinyl optionally substituted one or more times with a substituent selected from the group consisting of halo, d-e-alkyl and trifluoromethyl.

[0541] In further embodiments, R^3 represents te/t-butyl.

[0542] In further embodiments, R^3 represents phenyl, which is optionally substituted one or more times with substituents selected from Ci_{-6}-alkyl, Ci_{-6}-alkoxy, halo and trifluoromethyl.

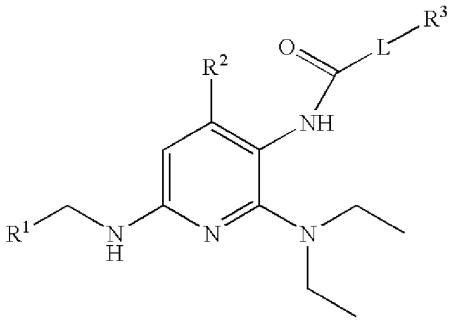
[0543] In further embodiments, L represents $-CH_2-$.

[0544] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(3,5-Difluorophenyl)-N-{2-pyrrolidin-1-yl-6-[(tetrahydro-pyran-4-ylmethyl)-amino]- pyridin-3-yll-acetamide; 3,3-Dimethyl-N-{2-pyrrolidin-1-yl-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yllbutyramide; 2-(3,5-Difluoro-phenyl)-N-{2-morpholin-4-yl-6-[(tetrahydro-pyran-4-ylmethyl)-amino]- pyridin-3-yll-acetamide; 2-(3,5-Difluoro-phenyl)-N-{2-dimethylamino-6-[(tetrahydro-pyran-4-ylmethyl)-amino]- pyridin-3-yll-acetamide; N-{2-Dimethylamino-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-{2-((S)-3-fluoro-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-acetamide; N-{2-((S)-3-Fluoro-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-{2-(3,3-dimethyl-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-acetamide; N-{2-(3,3-Dimethyl-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-3,3-dimethyl-butyramide; N-{2-((R)-3-Fluoro-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-{2-((R)-3-fluoro-pyrrolidin-1-yl)-6-[(tetrahydro-pyran-4-ylmethyl)-amino]-pyridin-3-yll-acetamide; 2-(3,5-Difluoro-phenyl)-N-[6-[(tetrahydro-pyran-4-ylmethyl)-amino]-2-((S)-2-trifluoromethyl-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide; 3,3-Dimethyl-N-[6-[(tetrahydro-pyran-4-ylmethyl)-amino]-2-((S)-2-trifluoromethylpyrrolidin-1-yl)-pyridin-3-yl]-butyramide; or a pharmaceutically-acceptable addition salt thereof.

Formula 44

[0545] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 44. Such compounds are described in International Publication No. WO2010105960A1, published September 23, 2010, and corresponding to International Application No. PCT/EP2010/053072 filed March 11, 2010; US Publication No. US20110003865A1, published January 6, 2011, and corresponding to US Application No. 12/747,394 filed December 10, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 44, these references incorporated by reference herein control.

[0546] In an embodiment, the Kv7 channel activator is a compound according to Formula 44:



Formula 44

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl; R^2 represents hydrogen; R^3 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl; and L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

[0547] In further embodiments, R^1 represents alkyl.

[0548] In further embodiments, R^1 represents phenyl optionally substituted one or more times with substituents selected from alkyl and halo.

[0549] In further embodiments, R^3 represents phenyl, optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl.

[0550] In further embodiments, R^3 represents alkyl.

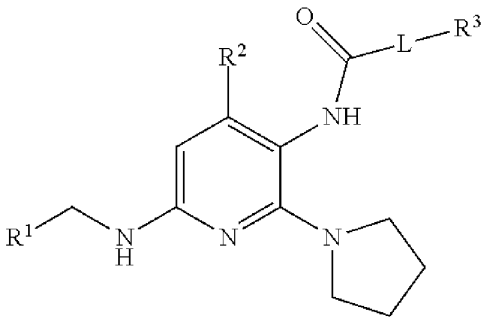
[0551] In further embodiments, L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen or alkyl.

[0552] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; (S)—N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-phenyl-propionamide; N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3-(3-fluoro-phenyl)-propionamide; (R)—N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3-phenyl-butyramide; trans-2-Phenyl-cyclopropanecarboxylic acid [2-diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-amide; N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-phenyl)-acetamide; N-[2-Diethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3,3-dimethyl-butyramide; N-[2-Diethylamino-6-(2,4,6-trimethyl-benzylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-(2-Diethylamino-6-isobutylamino-pyridin-3-yl)-2-(3,5-difluoro-phenyl)-acetamide; N-[2-Diethylamino dimethyl-benzylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-Diethylamino-6-(2,2-dimethyl-propylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 45

[0553] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 45. Such compounds are described in US Publication No. US20110039896A1, published February 17, 2011, and corresponding to US Application No. 12/747,346 filed December 10, 2008; International Publication No. WO2009074593A1, published June 18, 2009, and corresponding to International Application No. PCT/EP2008/067164 filed December 10, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 45, these references incorporated by reference herein control.

[0554] In an embodiment, the Kv7 channel activator is a compound according to Formula 45:



Formula 45

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents alkyl, phenyl, benzo[1,3]dioxolyl or benzo[1,4]dioxinyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, trifluoromethyl, alkoxy, cyano and difluoromethoxy; R^2 represents hydrogen; R^3 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl; and L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

[0555] In further embodiments, R^1 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl; R^2 represents hydrogen; R^3 represents phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl; and L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

[0556] In further embodiments, R^1 represents alkyl.

[0557] In further embodiments, R^1 represents phenyl, benzo[1,3]dioxolyl or benzo[1,4]dioxinyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, trifluoromethyl, alkoxy, cyano and difluoromethoxy.

[0558] In further embodiments, R^3 represents alkyl.

[0559] In further embodiments, R^3 represents phenyl, optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl.

[0560] In further embodiments, L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen or alkyl.

[0561] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-(3-fluoro-4-

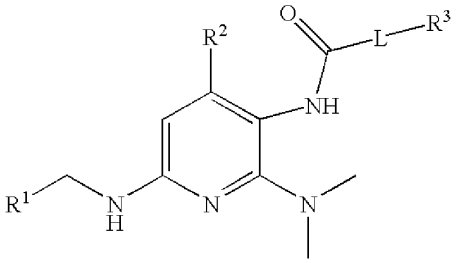
trifluoromethyl-phenyl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[6-(4-fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide; 2-(3,4-Difluoro-phenyl)-N-[6-(4-fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide; (S)-N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-phenyl-propionamide; N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-3-(3-fluoro-phenyl)-propionamide; (R)-N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-3-phenyl-butyramide; (R)-2-Phenyl-cyclopropanecarboxylic acid [6-(4-fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-amide; N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-(3-fluoro-phenyl)-acetamide; N-[6-(4-Fluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-(6-isobutylamino-2-pyrrolidin-1-yl-pyridin-3-yl)-acetamide; 2-(3,5-Difluoro-phenyl)-N-[6-(5-fluoro-2-methyl-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[6-(2,6-dimethyl-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-pyrrolidin-1-yl-6-(4-trifluoromethyl-benzylamino)-pyridin-3-yl]-acetamide; N-{6-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-3,3-dimethyl-butyramide; N-[6-(3,4-Difluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-{6-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-2-(3,5-difluoro-phenyl)-acetamide; N-[6-(4-Cyano-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[6-(3,4-Difluoro-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-[6-(4-methoxy-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-acetamide; N-[6-(4-Difluoromethoxy-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[6-(4-Difluoromethoxy-benzylamino)-2-pyrrolidin-1-yl-pyridin-3-yl]-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-{6-[(2,3-dihydro-benzo[1,4]dioxin-6-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-acetamide; N-{6-[(2,3-Dihydro-benzo[1,4]dioxin-6-ylmethyl)-amino]-2-pyrrolidin-1-yl-pyridin-3-yl}-3,3-dimethyl-butyramide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 46

[0562] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 46. Such compounds are described in International Publication No. WO2009074591A1, published June 18, 2009, and corresponding to International Application No. PCT/EP2008/067161 filed December 10, 2008; US Publication No. US20110003866A1, published December 10, 2008, and

corresponding to US Application No. 12/747,414 filed December 10, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 46, these references incorporated by reference herein control.

[0563] In an embodiment, the Kv7 channel activator is a compound according to Formula 46:



Formula 46

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a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl; R^2 represents hydrogen; R^3 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl; and L represents a linker selected from —CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

[0564] In further embodiments, R^1 represents alkyl.

[0565] In further embodiments, R^1 represents phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl.

[0566] In further embodiments, R^3 represents alkyl.

[0567] In further embodiments, R^3 represents phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl.

[0568] In further embodiments, L represents a linker selected from —CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

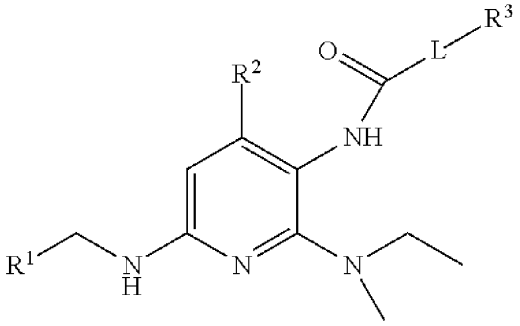
[0569] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; (S)—N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-phenyl-propionamide; N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3-(3-fluoro-phenyl)-propionamide; trans-2-Phenyl-

cyclopropanecarboxylic acid[2-dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-amide; N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-phenyl)-acetamide; N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3,3-dimethyl-butyramide; 2-(3,5-Difluoro-phenyl)-N-[2-dimethylamino-6-(2,4,6-trimethyl-benzylamino)-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-dimethylamino-6-(2,6-dimethyl-benzylamino)-pyridin-3-yl]-acetamide; N-[2-Dimethylamino-6-(5-fluoro-2-methyl-benzylamino)-pyridin-3-yl]-3,3-dimethyl-butyramide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 47

[0570] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 47. Such compounds are described in US Publication No. US20110003867A1, published January 6, 2011, and corresponding to US Application No. 12/747,422 filed December 10, 2008; International Publication No. WO2009074594A1, published June 18, 2009, and corresponding to International Application No. PCT/EP2008/067165 filed December 10, 2008; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 47, these references incorporated by reference herein control.

[0571] In an embodiment, the Kv7 channel activator is a compound according to Formula 47:



Formula 47

,

a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl; R^2 represents hydrogen; R^3 represents alkyl or phenyl, which phenyl is optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl; and L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

[0572] In further embodiments, R^1 represents alkyl.

[0573] In further embodiments, R^1 represents phenyl, optionally substituted one or more times with substituents selected from alkyl, halo and trifluoromethyl.

[0574] In further embodiments, R^3 represents phenyl, optionally substituted one or more times with substituents selected from alkyl, halo, alkoxy and trifluoromethyl.

[0575] In further embodiments, R^3 represents alkyl.

[0576] In further embodiments, L represents a linker selected from —CR′R″—, —CH_2—CR′R″—, —CR′R″—CH_2— and cycloalkyl, wherein R′ and R″, independently of each other, represent hydrogen, alkyl or halo.

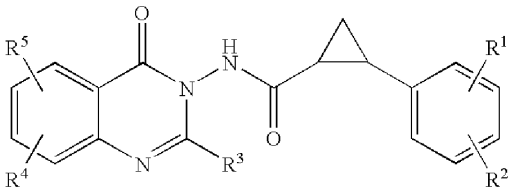
[0577] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-[2-Dimethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,5-difluoro-phenyl)-acetamide; N-[2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3,4-difluoro-phenyl)-acetamide; N-[2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-4-trifluoromethyl-phenyl)-acetamide; N-[2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3-(3-fluoro-phenyl)-propionamide; (R)—N-[2-(Ethyl-methyl-amino)-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3-phenyl-butyramide; trans-2-Phenyl-cyclopropanecarboxylic acid [2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-amide; N-[2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-2-(3-fluoro-phenyl)-acetamide; N-[2-Ethylmethylamino-6-(4-fluoro-benzylamino)-pyridin-3-yl]-3,3-dimethyl-butyramide; pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[6-(2,2-dimethyl-propylamino)-2-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide; 2-(3,5-Difluoro-phenyl)-N-[2-(ethyl-methyl-amino)-6-isobutylamino-pyridin-3-yl]-acetamide; or a stereoisomer or a mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof.

Formula 48

[0578] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 48. Such compounds are described in International Publication No. WO2007104717A1, published September 20, 2007, and corresponding to International Application No. PCT/EP2007/052239 filed March 9, 2007; US Publication No. US20090036473A1, published February 5, 2009, and corresponding to US Application No. 12/278,091 filed March 9, 2007; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 48, these references incorporated by reference herein control.

[0579] In an embodiment, the Kv7 channel activator is a compound according to Formula 48:

Formula 48



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including any of its stereoisomers, or any mixture of its stereoisomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 and R^2, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, baloalkoxy, amino, alkyl-carbonyl-amino, alkyl-sulfonyl, cyano or nitro; R^3 represents alkyl, cycloalkyl or alkoxy; and R^4 and R^5, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, nitro or cyano.

[0580] In further embodiments, R^1 and R^2, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, alkyl-sulfonyl, cyano or nitro.

[0581] In further embodiments, R^3 represents alkyl, cycloalkyl or alkoxy.

[0582] In further embodiments, R^4 and R^5, independently of each other, represent hydrogen, alkyd, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, nitro or cyano.

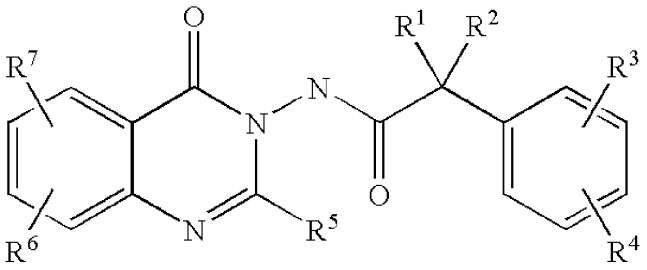
[0583] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(4-Fluoro-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(3-Fluoro-4-methyl-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)- amide; 2-Phenyl-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(4-Chloro-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(^{4}-Fluoro-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-p-Tolyl-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(3-Fluoro-phenyl)-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; or 2-p-Tolyl-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; or a pharmaceutically-acceptable addition salt thereof.

Formula 49

[0584] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 49. Such compounds are described in International Publication No. WO2007057447A1, published May 24, 2007, and corresponding to International Application No. PCT/EP2006/068627 filed November 17, 2006; US Publication No. US20090291973A1, published November 26, 2009, and corresponding to US Application No. 12/085,188 filed November 17, 2006; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 49, these references incorporated by reference herein control.

[0585] In an embodiment, the Kv7 channel activator is a compound according to Formula 49:

Formula 49



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including any of its stereoenantiomers or any mixture of its stereoenantiomers, or a pharmaceutically-acceptable addition salt thereof, or an N-oxide thereof, wherein R^1 represents hydrogen or alkyl; and R^2 represents alkyl, cycloalkyl, halo, haloalkyl, hydroxyalkyl, hydroxy, alkoxy, phenyl, phenylalkyl, amino, alkyl-carbonyl-amino, cyano or nitro; or R^1 and R^2 together with the carbon atom to which they are attached form a cycloalkyl group; or R^1 represents hydrogen; and R^2 together with R^3 attached in ortho-position on the aromatic ring form a —$(CH_2)_n$— bridge, wherein n is 1, 2 or 3; R^3 and R^4, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, alkyl-sulfonyl, phenyl, benzoyl, cyano or nitro; or R^3 and R^4 together form a methylenedioxy group; or R^3 attached in ortho-position on the aromatic ring and together with R^2 form a —$(CH_2)_n$— bridge, wherein n is 1, 2 or 3; and R^4 is as defined above; R^5 represents alkyl, cycloalkyl, alkoxy, alkylthio or phenyl; and R^6 and R^7, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino(acetamido), nitro, cyano or phenyl; provided, however, that if R^1 is hydrogen, R^2 is methyl, R^3 and R^4 represent hydrogen, R^5 is isopropyl, and R^6 and R^7 represent hydrogen, then the compound it is not a quinazoline derivative racemate but the R- or S-enantiomer of the quinazoline derivative.

[0586] In further embodiments, R^1 represents hydrogen or alkyl.

[0587] In further embodiments, R^2 represents alkyl, cycloalkyl, halo, haloalkyl, hydroxyalkyl, hydroxy, alkoxy, phenyl, phenylalkyl, amino, alkyl-carbonyl-amino, cyano or nitro.

[0588] In further embodiments, R^1 represents hydrogen or methyl; and R^2 represents methyl, ethyl, isopropyl, cyclohexyl, fluoro or benzyl.

[0589] In further embodiments, R^1 and R^2 together with the carbon atom to which they are attached form a cycloalkyl group.

[0590] In further embodiments, R^1 represents hydrogen; and R^2 together with R^3 attached in ortho-position on the aromatic ring form a —$(CH_2)_n$— bridge, wherein n is 1, 2 or 3.

[0591] In further embodiments, R^3 and R^4, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino, alkyl-sulfonyl, phenyl, benzoyl, cyano or nitro; or R^3 and R^4 together form a methylenedioxy group.

[0592] In further embodiments, R^3 attached in ortho-position on the aromatic ring and together with R^2 form a —$(CH_2)_n$— bridge, wherein n is 1, 2 or 3; and R^4 is as defined in claim 7.

[0593] In further embodiments, R^5 represents alkyl, cycloalkyl, alkoxy, alkylthio or phenyl.

[0594] In further embodiments, R^6 and R^7, independently of each other, represent hydrogen, alkyl, cycloalkyl, halo, haloalkyl, hydroxy, alkoxy, haloalkoxy, amino, alkyl-carbonyl-amino(acetamido), nitro, cyano or phenyl.

[0595] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-3-methyl-2-phenyl-butyramide; 2-(4-Chloro-phenyl)-N-(2-isopropylsulfanyl-4-oxo-4H-quinazolin-3-yl)-butyramide; 2-(3,5-Difluoro-phenyl)-N-(2-isopropylsulfanyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; N-(2-Ethyl-7-fluoro-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; (S)-N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2,3-diphenyl-propionamide; Bicyclo[4.2.0]octa-1,3,5-triene-7-carboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2-p-tolyl-propionamide; 2-Cyclohexyl-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-acetamide; 2-(3-Benzoyl-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; 1-Phenyl-cyclopropanecarboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; 2-(3,4-Dimethoxy-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; (R)-N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-isobutyramide; 2-(4-Chloro-phenyl)-N-(2-isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; N-(2-Isopropyl-4-

oxo-4H-quinazolin-3-yl)-2-(4-trifluoromethyl-phenyl)-propionamide; 2-(3,4-Dichloro-phenyl)-N-(2-isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; 2-(3-Fluoro-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; 2-(4-Chloro-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; N-(2-Isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-2-(4-trifluoromethyl-phenyl)-propionamide; N-(2-Isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(4-methoxy-phenyl)-propionamide; N-(2-Isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-2-(4-methoxy-phenyl)-propionamide; 2-(3,4-Dichloro-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; 2-(3-Fluoro-4-methyl-phenyl)-N-(2-isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; 2-(3-Fluoro-4-methyl-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; 2-(4-Isobutyl-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; N-(7-Chloro-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-phenyl)-propionamide; N-(6-Chloro-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-phenyl)-propionamide; 2-(4-Fluoro-phenyl)-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-propionamide; N-(5-Chloro-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-phenyl)-propionamide; N-(8-Chloro-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-phenyl)-propionamide; N-(8-Cyano-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-(3-fluoro-phenyl)-propionamide; 7-Methyl-bicyclo[4.2.0]octa-1(6),2,4-triene-7-carboxylic acid (2-isopropyl-4-oxo-4H-quinazolin-3-yl)-amide; N-(2-Isopropylsulfanyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; 2-(4-Chloro-phenyl)-N-(2-isopropylsulfanyl-4-oxo-4H-quinazolin-3-yl)-propionamide; 2-(4-Chloro-phenyl)-N-(2-ethoxy-4-oxo-4H-quinazolin-3-yl)-propionamide; 2-(3,5-Difluoro-phenyl)-N-(2-methylsulfanyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-propionamide; 2-Fluoro-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; (S)-2-Fluoro-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; (R)-2-Fluoro-N-(2-isopropyl-4-oxo-4H-quinazolin-3-yl)-2-phenyl-propionamide; (S)-2-Fluoro-N-(2-isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-2-phenyl-propionamide; or (R)-2-Fluoro-N-(2-isopropyl-4-oxo-7-trifluoromethyl-4H-quinazolin-3-yl)-2-phenyl-propionamide; or an N-oxide thereof, any of its stereoenantiomers or any mixture of its stereoenantiomers, or a pharmaceutically-acceptable addition salt thereof.

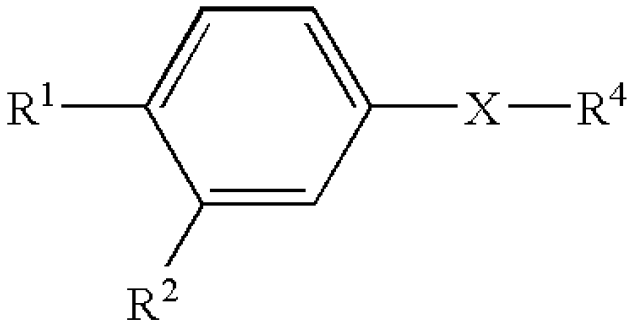
Formula 50

[0596] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 50. Such compounds are described in US Patent No. 7,741,352, issued June 22, 2010, and corresponding to US Application No. 10/546,533

filed March 11, 2004; International Publication No. WO2004080377A2, published September 23, 2004, and corresponding to International Application No. PCT/EP2004/050290 filed March 11, 2004; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 50, these references incorporated by reference herein control.

[0597] In an embodiment, the Kv7 channel activator is a compound according to Formula 50:

Formula 50



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any of its enantiomers or any mixture of its enantiomers, or a prodrug, or a pharmaceutically-acceptable addition salt thereof, wherein R^1 represents —CN; R^2 represents halo, haloalkyl, hydroxyl or alkoxy; X represents, NR″ or NR″CH_2 (read in the stated direction); wherein R″ represents hydrogen; R^4 represents aryl-alkyl, which is substituted one or more times with substituents selected from the group consisting of halo, or methylenedioxy; or R^4 represents a group of formula -Z′-L″-Z″; wherein Z′ and Z″, independently of one another, represent an aryl group, which aryl may be optionally substituted one or more times with halo; and L″ represents a single (covalent) bond, or a linker selected from O or OCH_2, with the proviso that when X represents NR″, then R^4 represents aryl-alkyl and when X represents NR″CH_2, then R^4 represents a group of formula -Z′-L″-Z″.

[0598] In further embodiments, R^4 represents benzyl which is substituted one or two times with halo or one time with methylenedioxy.

[0599] In further embodiments, R^4 represents 4-fluoro-benzyl, 3,4-dichloro-benzyl or benzo[1,3]dioxol-5-ylmethyl.

[0600] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 4-(4-Fluoro-benzylamino)-2-hydroxy-benzonitrile 4-(3,4-Dichloro-benzylamino)-2-hydroxy-benzonitrile or 4-[(Benzo[1,3]dioxol-5-ylmethyl)-amino]-2-hydroxy-benzonitrile; or a pharmaceutically-acceptable addition salt thereof.

[0601] In further embodiments, R^4 represents a group of formula -Z′-L″-Z″; wherein Z′ represents phenyl, or phen-4-yl; which phenyl may optionally be substituted one or two times with halo; and Z″ represent phenyl; which may optionally be substituted one or two times

with halo; and L″ represents a single (covalent) bond, or a linker selected from alkyl, O, or OCH_2.

[0602] In further embodiments, R^4 represents 3-phenoxy-phenyl, 3-benzyloxy-phenyl, or biphenyl-4-yl.

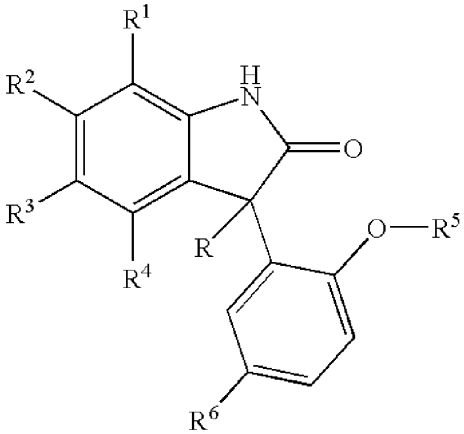
[0603] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-Hydroxy-4-(3-phenoxy-benzylamino)-benzonitrile; 4-(3-Benzyloxy-benzylamino)-2-hydroxy-benzonitrile; or 4-[(Biphenyl-4-ylmethyl)-amino]-2-hydroxy-benzonitrile; or a pharmaceutically-acceptable addition salt thereof.

Formula 51

[0604] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 51. Such compounds are described in US Patent No. 7,741,352, issued June 22, 2010, and corresponding to US Application No. 10/546,533 filed March 11, 2004; International Publication No. WO2004080377A2, published September 23, 2004 and corresponding to International Application No. PCT/EP2004/050290 filed March 11, 2004; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 51, these references incorporated by reference herein control.

[0605] In an embodiment, the Kv7 channel activator is a compound according to Formula 51:

Formula 51



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wherein, R represents hydrogen, halogen or hydroxy. R^1, R^2, R^3 and R^4 independently of each another represent hydrogen, halogen, alkyl, trihalogenmethyl, phenyl, p-methyl-phenyl or p-trihalogenmethyl-phenyl, or R^1 and R^2, R^2 and R^3, or R^3 and R^4 are joined together to form a benzo fused ring, R^5 represents hydrogen or alkyl, and R^6 represents halogen or trihalogenmethyl, or a pharmaceutically-acceptable addition salt thereof.

[0606] In further embodiments, R represents hydrogen, halogen or hydroxy, R^1, R^2, R^3 and R^4 independently of each another represent hydrogen, halogen, alkyl, trihalogenmethyl, phenyl, p-methyl-phenyl or p-trihalogenmethyl-phenyl, and when R^1 and R^4 are hydrogen, then R^2 or R^3 is phenyl, p-methyl-phenyl or p-trihalogenmethyl-phenyl; or R^1 and R^2, R^2 and R^3, or R^3 and R^4 are joined together to form a benzo fused ring, R^5 represents hydrogen or alkyl, and R^6 represents halogen or trihalogenmethyl.

[0607] In further embodiments, R^1, R^3 and R^4 represent hydrogen, and R^2 represents halogen, trihalogenmethyl or phenyl.

[0608] In further embodiments, R^1 and R^2, R^2 and R^3, or R^3 and R^4 are joined together to form a benzo fused ring.

[0609] In further embodiments, R^5 is hydrogen or methyl.

[0610] In further embodiments, R^6 is chlorine.

[0611] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: (+)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-6-(trifluoromethyl)-2H-indol-2-one; (−)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-6-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-6(4-methylphenyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-2H-indol-one; (±)-3-(5-chloro-2-hydroxyphenyl)-4,6-dichloro-1,3-dihydro-2H-indol-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-6-phenyl-2H-indol-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-6-iodo-2H-indol-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-6-trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-6-[4-(trifluoromethyl)-phenyl]-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-2H-benz[e]indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-2H-benz[f]indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-2H-benx[g]indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-6-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-4-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-6-(trifluoromethyl)-2H-indol-2-one; (−)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-hydroxy-6-(trifluoromethyl)-2H-indol-**2**-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-7-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-5-bromo-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-6-iodo-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-4,6-dichloro-1,3-dihydro-3-hydroxy-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-hydroxy-2H-benz[f]indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-4,6-bis-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-

hydroxy-4-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-6-(trifluoromethyl)-2H-indol-2-one; (+)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-6-(trifluoromethyl)-2H-indol-2-one; (−)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-6-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-7-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-4,6-dichloro-1,3-dihydro-3-hydroxy-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-5-bromo-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-6-iodo-2H-indol-2-one; (±)-1,3-dihydro-3-hydroxy-3-[2-hydroxy-5-(trifluoromethyl)-phenyl]-6-(trifluoromethyl)-2H-indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-2H-benz[g]indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-hydroxy-2H-benz[f]indol-2-one; (±)-3-(5-chloro-2-hydroxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3S)-(+)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol-2-one; (3R)-(−)-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2H-indol2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-7-(trifluoromethyl)2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-phenyl-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-6-iodo-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-5-methyl-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-5-bromo-2H-indol-2-one; (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-4,6-bis-(trifluoromethyl)-2H-indol-2-one; or (±)-3-(5-chloro-2-methoxyphenyl)-1,3-dihydro-3-fluoro-7-(trifluoromethyl)-2H-indol-2-one; or a pharmaceutically-acceptable addition salt thereof.

[0612] In further embodiments, R represents hydrogen, halogen or hydroxy, R^1, R^2, R^3 and R^4 independently of each another represent hydrogen, halogen, alkyl, trihalogenmethyl, phenyl, p-methyl-phenyl or p-trihalogenmethyl-phenyl, or R^1 and R^2, R^2 and R^3, or R^3 and R^4 are joined together to form a bezo fused ring, R^5 represents hydrogen or alkyl, and R^6 represents halogen or trihalogenmethyl, or a pharmaceutically-acceptable addition salt thereof, together with at least one pharmaceutically-acceptable carrier or diluent.

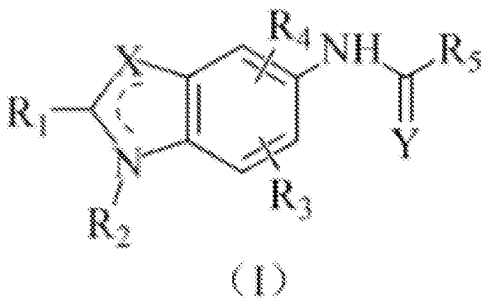
Formula 52

[0613] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 52. Such compounds are described in International Publication No. CN114380731A, published April 22, 2022, and corresponding to International Application No. CN202210226122.7A filed March 9, 2022; which is

incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 52, this reference incorporated by reference herein controls.

[0614] In an embodiment, the Kv7 channel activator is a compound according to Formula 52:

Formula 52



(I)

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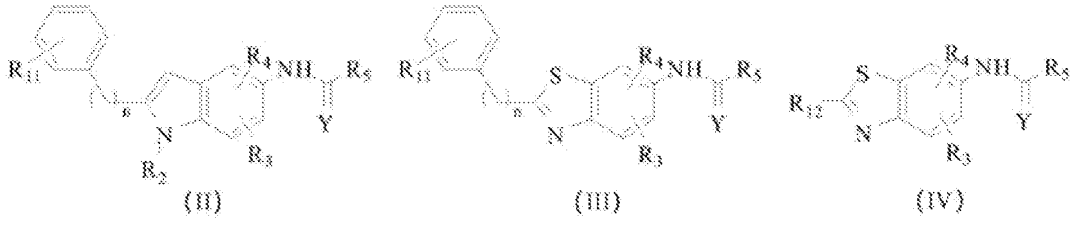
wherein, R_1 is selected from H, halogen, substituted or unsubstituted phenyl, or a substituted or unsubstituted phenylalkyl group, the substituents of said phenyl and phenylalkyl groups each being independently selected from halogen or haloalkyl; X is selected from S or C; R_2 is optionally selected from H, alkyl, alkenyl or alkynyl; R_3 and R_4 each independently selected from H or alkyl; y is selected from O or S; R_5 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, alkoxy or furyl, the substituent of the alkyl is selected from alkoxy, dialkylamino or alkoxycarbonyl, and the substituent of the cycloalkyl is selected from halogen.

[0615] In further embodiments, R_2 is selected from H, C_1-C_3Alkyl radical, C_1-C_3Alkenyl or C_1-C_3Alkynyl.

[0616] In further embodiments, R_3 and R_4 are each independently selected from H or C_1-C_6An alkyl group.

[0617] In further embodiments, R_5 is selected from substituted or unsubstituted C_1-C_6Alkyl, substituted or unsubstituted C_3-C_6Cycloalkyl radical, C_1-C_6Alkoxy or furyl, the substituents of the alkyl or the alkoxy being selected from C_1-C_6Alkoxy, di $(C)_1$-C_4Alkyl) amino or C_1-C_6Alkoxycarbonyl, the substituents of cycloalkyl being selected from halogen.

[0618] In further embodiments, the formula is one of formulas II – IV:



(II) (III) (IV)

wherein, n is more than or equal to 0;$R_{11}$and R_{12} each independently selected from H, halogen or halomethyl; R_2 is selected from H, C_1-C_3Alkyl radical, C_2-C_3Alkenyl or C_2-C_3An alkynyl group; $R_3$and R_4 are independently selected from H or C_1-C_6 alkyl group; y is selected from O or S; R_5 is selected from substituted or unsubstituted C_1-C_6Alkyl, substituted or unsubstituted C_3-C_6Cycloalkyl radical, C_1-C_6Alkoxy or furyl, the substituents of the alkyl being selected from C_1-C_6Alkoxy, di $(C)_1$-C_4Alkyl) amino or C_1-C_6Alkoxycarbonyl, the substituents of cycloalkyl being selected from halogen.

[0619] In further embodiments, n is 0 to 3, R_{11} is selected from H, F or trifluoromethyl, and R_{12} is selected from H, F, Cl or methyl.

[0620] In further embodiments, R_3 is one of H or methyl, and R_4 is other of H or methyl.

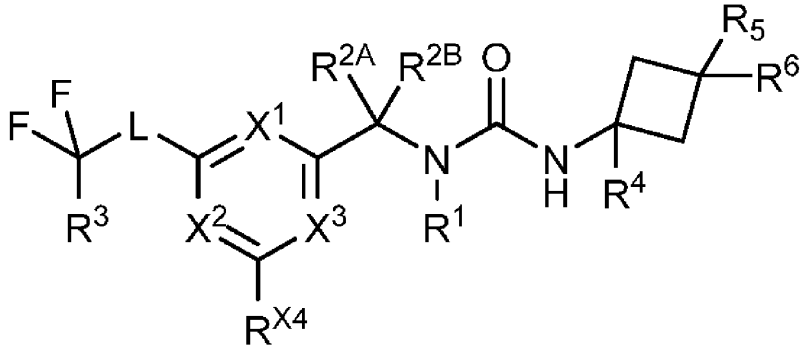
[0621] In further embodiments, R_5 is selected from methyl, ethyl, isopropyl, isobutyl, neopentyl, cyclobutyl, ethoxy, isopropoxy, tert-butoxy or tetrahydrofuranyl.

Formula 53

[0622] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 53. Such compounds are described in International Publication No. WO2021260090A1, published December 30, 2021, and corresponding to International Application No. PCT/EP2021/067288 filed June 24, 2021; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 53, this reference incorporated by reference herein controls.

[0623] In an embodiment, the Kv7 channel activator is a compound according to Formula 53:

Formula 53



,

wherein, X^1 represents nitrogen or CR^{X1}; wherein R^{X1} represents hydrogen, halogen, (C_{1-4})alkyl, or (C_{1-4})alkoxy; X^2 represents nitrogen or CR^{X2}; wherein R^{X2} represents hydrogen, halogen, (C_{1-4})alkyl, or (C_{1-4})alkoxy; X^3 represents nitrogen or CR^{X3}; wherein R^{X3} represents hydrogen, halogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, or hydroxy; R^1 represents hydrogen or methyl;

R^{X4} represents hydrogen, halogen, or (C_{1-4})alkyl; • R^{2A} represents hydrogen; (C_{1-4})alkyl; (C_{2-4})alkenyl; (C_{2-4})alkynyl; (C_{3-6})cycloalkyl; (C_{1-4})fluoroalkyl; (C_{1-4})hydroxyalkyl; (C_{1-4})alkoxy-(C_{1-2})alkyl; (C_{1-2})alkoxy-(C_{1-2})alkoxy-(C_{1-2})alkyl; (C_{1-2})alkyl-S-(C_{1-2})alkyl; (C_{1-2})alkyl-(SO_2)-(C_{1-2})alkyl; cyano; (C_{1-2})cyanoalkyl; H_2N- C(O)-(C_{1-2})alkyl; $(R^{N1})_2N$-(C_{1-2})alkyl or $(R^{N1})_2N$-C(O)-, wherein R^{N1} independently represents hydrogen or (C_{1-2})alkyl; or a 5-membered heteroaryl group containing one to four nitrogen atoms, wherein said 5-membered heteroaryl group is independently unsubstituted or mono-substituted with (C_{1-4})alkyl; and R^{2B} represents hydrogen or methyl; or • R^{2A} and R^{2B} form, together with the carbon atom to which they are attached, a ring of 3- to 6 members, wherein the members needed to complete said ring are each independently selected from -CH_2- and -O- and wherein said ring does not contain more than one -O- member; L represents a direct bond, cycloprop-1,1-diyl, -CHR^L-O-*, -O-CH_2-*, -CH_2-NH-*, -CH_2- $N(CH_3)$-*, -O-, or –(SO_2)-; wherein R^L represents hydrogen, (C_{1-4})alkyl, CH_3-O-CH_2-, or $(CH_3)_2NCH_2$-; wherein the asterisks indicate the bond which is linked to the aromatic carbon atom; R^3 represents hydrogen or fluoro; • R^4 represents hydrogen or (C_{1-4})alkyl; R^5 represents hydrogen, fluoro, or hydroxy; and R^6 represents fluoro or (C_1)fluoroalkyl; or • R^4 and R^5 together represent a bridge selected from -CH_2- and -CH_2CH_2-; and R^6 represents hydrogen, fluoro, (C_1)fluoroalkyl, or (C_{1-4})alkyl; or a salt thereof.

[0624] In further embodiments, X^1 represents CR^{X1}; wherein R^{X1} represents hydrogen or halogen; X^2 represents nitrogen or CH; X^3 represents nitrogen or CH; R^1 represents hydrogen; R^{X4} represents hydrogen, halogen, or (C_{1-4})alkyl; R^{2A} represents hydrogen; (C_{1-4})alkyl; (C_{1-4})fluoroalkyl; (C_{1-4})hydroxyalkyl; or (C_{1-4})alkoxy-(C_{1-2})alkyl; R^{2B} represents hydrogen; L represents a direct bond, -CH_2-O-*, or-O-; wherein the asterisk indicates the bond which is linked to the aromatic carbon atom; R^3 represents hydrogen or fluoro; • R^4 represents hydrogen or (C_{1-4})alkyl; R^5 represents hydrogen, fluoro, or hydroxy; and R^6 represents fluoro or (C_1)fluoroalkyl; or • R^4 and R^5 together represent a bridge selected from -CH_2- and -CH_2CH_2-; and R^6 represents hydrogen, fluoro, (C_1)fluoroalkyl, or (C_{1-4})alkyl; or a salt thereof (meaning a salt of the compound of Formula 53).

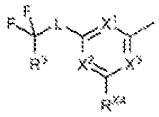
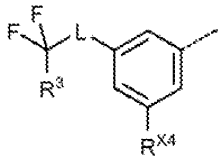
[0625] In further embodiments, R^{2A} represents hydrogen, (C_{1-4})alkyl, (C_{1-4})fluoroalkyl, (C_{1-4})hydroxyalkyl, or methoxymethyl; and R^{2B} represents hydrogen; or a salt thereof.

[0626] In further embodiments, L represents a direct bond; or a salt thereof.

[0627] In further embodiments, R^3 represents fluoro; or a salt thereof.

[0628] In further embodiments, R^{X4} represents hydrogen; or a salt thereof.

[0629] In further embodiments, each of X^1, X^2, and X^3 represents CH; or a salt thereof.

[0630] In further embodiments, the fragment  represents:  ; wherein R^{X4} represents hydrogen or halogen; R^3 represents hydrogen or fluoro; and L represents a direct bond, -CH_2-O-*, or-O-; wherein the asterisk indicates the bond which is linked to the aromatic carbon atom; or • ; wherein X^3 represents nitrogen or CH; R^{X4} represents hydrogen or (C_{1-4})alkyl; R^3 represents hydrogen or fluoro; and L represents -CH_2-O-*, or-O-; wherein the asterisk indicates the bond which is linked to the aromatic carbon atom; or a salt thereof.

[0631] In further embodiments, R^4 represents hydrogen; R^5 represents hydrogen or fluoro; and R^6 represents fluoro, difluoromethyl or trifluoromethyl; or a salt thereof.

[0632] In further embodiments, R^4 and R^5 together represent a -CH_2- bridge; and R^6 represents hydrogen, fluoro, difluoromethyl, or trifluoromethyl; or a salt thereof.

[0633] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 1-(3,3-Difluoro-cyclobutyl)-3-(3-trifluoromethyl-benzyl)-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-[1-(3-trifluoromethoxy-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-[1-(3-trifluoromethoxy-phenyl)-ethyl]-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-[1-(3-trifluoromethoxy-phenyl)-ethyl]-urea; 1-[2,2-Difluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-3-(3-hydroxy-3-trifluoromethyl-cyclobutyl)-urea; 1-(3,3-Difluoro-1-methyl-cyclobutyl)-3-[2,2-difluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-[1-(3-difluoromethoxy-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-[2-hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-[2,2-difluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-[2-methoxy-1-(3-trifluoromethyl-phenyl)-ethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-(2-fluoro-3-trifluoromethyl-benzyl)-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-(3-fluoro-5-trifluoromethyl-benzyl)-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-[3-(2,2,2-trifluoro-ethoxy)-benzyl]-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-[3-(2,2,2-trifluoro-ethoxy)-benzyl]-urea; 1-[3-(2,2,2-Trifluoro-ethoxy)-benzyl]-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethoxy-

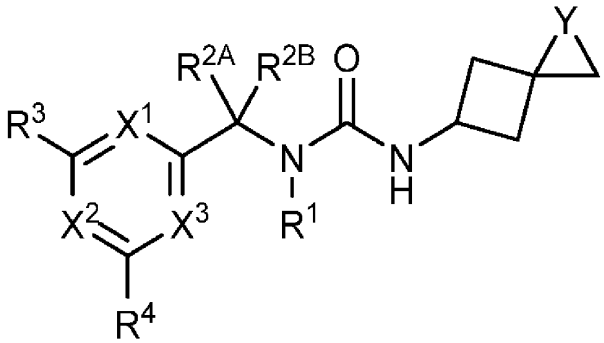
benzyl)-3-(3-fluoro-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethoxy-benzyl)-3-(3-difluoromethyl-cyclobutyl)-urea; 1-(3-Difluoromethoxy-benzyl)-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Trifluoromethoxy-benzyl)-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-(3-trifluoromethoxy-benzyl)-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-(3-trifluoromethoxy-benzyl)-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-(3-trifluoromethoxy-benzyl)-urea; 1-(3-Difluoromethyl-benzyl)-3-(3-difluoromethyl-cyclobutyl)-urea; 1-(3-Difluoromethyl-benzyl)-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-(2-trifluoromethoxy-pyridin-4-ylmethyl)-urea; 1-(2-Trifluoromethoxy-pyridin-4-ylmethyl)-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-{2-methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-urea; 1-{2-Methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-3-(3-trifluoromethyl-cyclobutyl)-urea; 1-[1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-(3-difluoromethyl-cyclobutyl)-urea; 1-{1-[2-Methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-Trifluoromethyl-benzyl)-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-Methyl-bicyclo[1.1.1]pent-1-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-Fluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-Trifluoromethyl-benzyl)-3-(3-trifluoromethyl-cyclobutyl)-urea; 1-(3-Hydroxy-3-trifluoromethyl-cyclobutyl)-3-(3-trifluoromethyl-benzyl)-urea; 1-Bicyclo[1.1.1]pent-1-yl-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea; 1-(3-Fluoro-bicyclo[1.1.1]pent-1-yl)-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea; 1-[2-(2,2,2-Trifluoro-ethoxy)-pyridin-4-ylmethyl]-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)-urea; 1-(3-Difluoromethyl-cyclobutyl)-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea; 1-(3-Difluoromethyl-bicyclo[1.1.1]pent-1-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-Bicyclo[2.1.1]hex-1-yl-3-(3-trifluoromethyl-benzyl)-urea; 1-(3,3-Difluoro-1-methyl-cyclobutyl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(3-(trifluoromethyl)benzyl)-3-((1s,3s)-3-(trifluoromethyl)cyclobutyl)urea; 1-(3-(trifluoromethyl)benzyl)-3-((1r,3r)-3-(trifluoromethyl)cyclobutyl)urea; 1-((1s,3s)-3-(difluoromethyl)cyclobutyl)-3-(3-(trifluoromethyl)benzyl)urea; 1-((1r,3r)-3-(difluoromethyl)cyclobutyl)-3-(3-(trifluoromethyl)benzyl)urea; 1-{(S)-1-[2-Methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-(3-trifluoromethyl-bicyclo[1.1.1]pent-1-yl)- urea; 1-((1r,3r)-3-(difluoromethyl)cyclobutyl)-3-((2-(2,2,2-trifluoroethoxy)pyridin-4-yl)methyl)urea; 1-((1s,3s)-3-(difluoromethyl)cyclobutyl)-3-((2-(2,2,2-

trifluoroethoxy)pyridin-4-yl)methyl)urea; 1-((1s,3R)-3-(difluoromethyl)cyclobutyl)-3-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)urea; and 1-((1r,3S)-3-(difluoromethyl)cyclobutyl)-3-((S)-1-(3-(trifluoromethoxy)phenyl)ethyl)urea; or a salt thereof.

Formula 54

[0634] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 54. Such compounds are described in International Publication No. WO2021219594A1, published November 4, 2021 and corresponding to International Application No. PCT/EP2021/060918 filed April 27, 2021; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 54, this reference incorporated by reference herein controls.

[0635] In an embodiment, the Kv7 channel activator is a compound according to Formula 54:

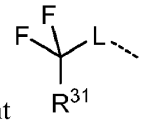


Formula 54

,

wherein, X^1 represents nitrogen or CR^{x1}; wherein R^{X1} represents hydrogen, halogen, (C_{1-4})alkyl, or (C_{1-4})alkoxy;X^2 represents nitrogen or CR^{X2}; wherein R^{X2} represents hydrogen, halogen, (C_{1-4})alkyl, or (C_{1-4})alkoxy; X^3 represents nitrogen or CR^{X3}; wherein R^{X3} represents hydrogen, halogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, or hydroxy;• R^1 represents hydrogen, or methyl; or• R^1 and R^{X1} together represent a $-CH_2CH_2-$ bridge; Y represents $-C(R^{Y1})(R^{Y2})-$, or $*-CH_2-C(R^{Y3})(R^{Y4})-$, wherein the asterisk indicates the bond which is linked to the cyclobutyl ring;R^{Y1} represents hydrogen, or fluoro;R^{Y2} represents hydrogen or fluoro;R^{Y3} represents hydrogen, fluoro or iodo;R^{Y4} represents hydrogen or fluoro; R^{2A} represents hydrogen; (C_{1-4})alkyl; (C_{2-4})alkenyl; (C_{2-4})alkynyl; (C_{3-6})cycloalkyl; (C_{1-4})fluoroalkyl; (C_{1-4})hydroxyalkyl; (C_{1-4})alkoxy-(C_{1-2})alkyl; (C_{1-2})alkoxy-(C_{1-2})alkoxy-(C_{1-2})alkyl; (C_{1-2})alkyl-S-(C_{1-2})alkyl; (C_{1-2})alkyl-(SO_2)-(C_{1-2})alkyl; cyano; (C_{1-2})cyanoalkyl; H_2N- C(O)-(C_{1-2})alkyl; $(R^{N1})_2N$-(C_{1-2})alkyl or $(R^{N1})_2N$-C(O)-, wherein R^{N1} independently represents hydrogen or (C_{1-2})alkyl; or a 5-membered heteroaryl group containing one to four nitrogen atoms, wherein said 5-membered heteroaryl group is independently unsubstituted or mono-substituted with$(C_{1-}$

$_4$)alkyl; and R^{2B} represents hydrogen, or methyl; or R^{2A} and R^{2B} form, together with the carbon atom to which they are attached, a ring of 3- to 6 members, wherein the members needed to complete said ring are each independently selected from -CH_2- and -O- and wherein said ring does not contain more than one -O- member; or R^{2A} and R^{X3} together represent a -CH_2-O-* bridge, wherein the asterisk indicates the bond which is linked to the aromatic carbon atom, andR^{2B} represents hydrogen;R^3 represents -SFs; (C_{1-2})alkyi-S(O)$_2$-; or



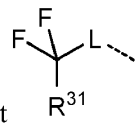
a fragment wherein R^{31} represents hydrogen, or fluoro; and L represents a direct bond, cycloprop-1 ,1-diyl, -CHR^L-O-*, -O-CH_2-*, -CH_2-NH-*, - CH_2-N(CH_3)-*, -O-, or -(SO_2)-; wherein R^L represents hydrogen, (C_{1-})alkyl, CH_3-0-CH_2-, or (CH_3)$_2$NCH_2-; wherein the asterisks indicate the bond which is linked to the aromatic carbon atom; orR^3 and R^{X1} together represent a -O-CF_2-O- bridge; orR^3 and R^{X2} together represent a -O-CF_2-O- bridge; and R^4 represents hydrogen, halogen, or (C_{1-4})alkyl; or a salt thereof.

[0636] In further embodiments, R^1 represents hydrogen; or a salt thereof (meaning a salt of compound of Formula 54).

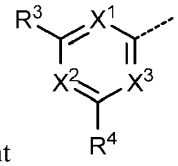
[0637] In further embodiments, R^{Y1}, R^{Y2}, R^{Y3} and R^{Y4} all represent hydrogen; or a salt thereof.

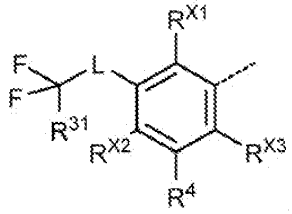
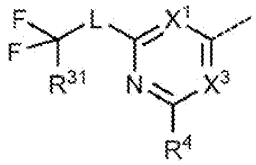
[0638] In further embodiments, R^{2A} represents hydrogen, (C_{1-4})alkyl, (C_{3-6})cycloalkyl, (C_{1-4})fluoroalkyl, (C_{1-4})hydroxyalkyl, (C_{1-4})alkoxy-(C_{1-2})alkyl, (C_{1-2})alkyl-S-(C_{1-2})alkyl, (C_{1-2})alkyl-(SO_2)-(C_{1-2})alkyl, cyano, (C_{1-2})cyanoalkyl, H_2N-C(O)-(C_{1-2})alkyl, (R^{N1})$_2$N-(C_{1-2})alkyl, or (R^{N1})$_2$N-C(O)-, wherein R^{N1} independently represents hydrogen or (C_{1-2})alkyl; and R^{2B} represents hydrogen; or R^{2A} and R^{2B} form, together with the carbon atom to which they are attached, a ring of 3- to 6 members selected from cycloprop-1 ,1-diyl, cyclobut-1 ,1-diyl, oxetane-3,3-diyl and tetrahydropyran-4,4-diyl; or a salt thereof.

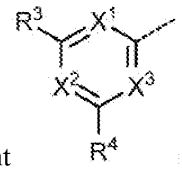
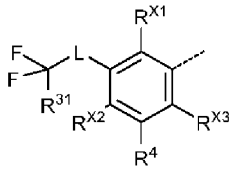
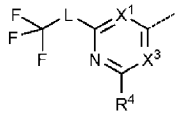
[0639] In further embodiments, R^{2A} represents hydrogen, methyl, or hydroxymethyl; and R^{2B} represents hydrogen; or a salt thereof.

[0640] In further embodiments, R^3 represents a fragment  , where inR^{31} represents hydrogen, or fluoro; and L represents a direct bond, -CHR^L-O-*, -O-CH_2-*, -CH_2-NH-*, -CH_2-N(CH_3)-*, or -O-; wherein R^L represents hydrogen, methyl, CH_3-O-CH_2-, or (CH_3)$_2$NCH_2-; wherein the asterisks indicate the bond which is linked to the aromatic carbon atom; or a salt thereof.

[0641] In further embodiments, R^4 represents hydrogen; or a salt thereof.

[0642] In further embodiments, the fragment  represents:

 ; or  wherein X^3 represents nitrogen and X^1 represents CR^{X1}; X^1 represents nitrogen and X^3 represents CR^{X3}; or X^1 represents CR^{X1} and X^3 represents CR^{X3}; or a salt thereof.

[0643] In further embodiments, the fragment  represents  wherein R^{X1} represents hydrogen, fluoro, chloro, methyl, or methoxy; R^{X2} represents hydrogen; R^{X3} represents hydrogen, fluoro, or chloro; R^4 represents hydrogen, fluoro, chloro, or methyl; R^{31} represents hydrogen, or fluoro; and L represents a direct bond, $-CHR^L-O-^*$, $-CH_2-NH-^*$, $-CH_2-N(CH_3)-^*$, -O-, or  ; wherein R^L represents hydrogen, or methyl; wherein the asterisks indicate the bond which is linked to the aromatic carbon atom; or wherein X^3 represents nitrogen and X^1 represents CR^{X1}; X^1 represents nitrogen and X^3 represents CR^{X3}; or X^1 represents CR^{X1} and X^3 represents CR^{X3}; wherein R^{X1} represents hydrogen, or methoxy; R^{X3} represents hydrogen; R^4 represents hydrogen, or methyl; and L represents $-CHR^L-O-^*$, $-CH_2-NH-^*$, or $-CH_2-N(CH_3)-^*$; wherein R^L represents hydrogen, methyl, CH_3-O-CH_2-, or $(CH_3)_2NCH_2-$; wherein the asterisks indicate the bond which is linked to the aromatic carbon atom; or a salt thereof.

[0644] In further embodiments, X^1 represents CR^{X1}; wherein R^{X1} represents hydrogen; X^2 represents nitrogen or CR^{X2}; wherein R^{X2} represents hydrogen; X^3 represents nitrogen or CR^{X3}; wherein R^{X3} represents hydrogen; R^1 represents hydrogen; Y represents $-CH_2-$, or $-CH_2-CH_2-$; R^{2A} represents hydrogen, or hydroxymethyl;R^{2B} represents hydrogen;

R^3 represents trifluoromethyl or 2,2,2-trifluoroethoxy; and R^4 represents hydrogen; or a salt thereof.

[0645] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 1-Spiro[3.3]hept-2-yl-3-(3-trifluoromethyl-benzyl)-urea;1-Spiro[2.3]hex-5-yl-3-(3-trifluoromethyl-benzyl)-urea;1 -(1 , 1 -Difluoro-spiro[2.3]hex-5-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-((3r,5r)-1,1-Difluoro-spiro[2.3]hex-5-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-((3s,5s)-1 , 1 -Difluoro-spiro[2.3]hex-5-yl)-3-(3-trifluoromethyl-benzyl)-urea; 1-(6,6-Difluoro-spiro[3.3]hept-2-yl)-3-(3-trifluoromethyl-benzyl)-urea;1-[1-(3-Difluoromethoxy-phenyl)-cyclopropyl]-3-spiro[3.3]hept-2-yl-urea;1-(2-Fluoro-3-trifluoromethoxy-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-[2-Methoxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-2-methoxy-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-(5-trifluoromethoxy-2,3-dihydro-benzofuran-3-yl)-urea;1-(2-Fluoro-3-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-(3-Difluoromethoxy-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[3-(2,2,2-trifluoro-ethoxy)-benzyl]-urea;1-(3-Difluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-(2-Fluoro-5-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-(4-Fluoro-3-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-(3-Fluoro-5-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Bromo-5-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Methoxy-5-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Methoxy-3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-(2-Methoxy-3-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-[Cyclopropyl-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-[Cyclopropyl-(3-difluoromethoxy-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-{1-[4-Methyl-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[4-Chloro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[4-Methoxy-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Methyl-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Chloro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Methoxy-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[3-Methyl-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[3-Chloro-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-(1-(3-(pentafluoro-l6-sulfaneyl)phenyl)ethyl)-3-(spiro[3.3]heptan-2-yl)urea;1-(3-(pentafluoro-l6-sulfaneyl)benzyl)-3-(spiro[3.3]heptan-2-yl)urea;1-[1-(3-Methanesulfonyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea; 1-Spiro[3.3]hept-2-yl-3-[3-(1-

trifluoromethyl-cyclopropyl)-benzyl]-urea;1-(2-Hydroxy-5-trifluoromethyl-benzyl)-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Chloro-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Methoxy-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-(3-trifluoromethoxy-benzyl)-urea;1-Spiro[3.3]hept-2-yl-3-(3-trifluoromethanesulfonyl-benzyl)-urea;1-Spiro[3.3]hept-2-yl-3-(3-trifluoromethoxymethyl-benzyl)-urea;1-Spiro[3.3]hept-2-yl-3-[3-(3-trifluoromethyl-phenyl)-oxetan-3-yl]-urea;1-[2-Hydroxy-2-methyl-1-(3-trifluoromethyl-phenyl)-propyl]-3-spiro[3.3]hept-2-yl-urea;1-(2,2-Difluoro-benzo[1,3]dioxol-4-ylmethyl)-3-spiro[3.3]hept-2-yl-urea;1-[1-(2,2-Difluoro-benzo[1,3]dioxol-4-yl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-{2-Dimethylamino-1-[6-(2,2,2-trifluoro-ethoxy)-pyridin-2-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{4-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-tetrahydro-pyran-4-yl}-urea;1-{2-Methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-1-methyl-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-cyclobutyl]-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-1 -methyl-ethyl]-3-spiro[3.3]hept-2-yl-urea; 5-(2,2,2-Trifluoro-ethoxy)-3,4-dihydro-1H-[2,6]naphthyridine-2-carboxylic acid spiro[3.3]hept-2-ylamide; 1-Methoxymethyl-5-(2,2,2-trifluoro-ethoxy)-3,4-dihydro-1 H-isoquinoline-2-carboxylic acid spiro[3.3]hept-2- ylamide;1-[Cyano-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[(1 H-[1 ,2,4]triazol-3-yl)-(3-trifluoromethyl-phenyl)-methyl]-urea;1-[2,2-Difluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[2,2,2-trifluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-[2-Methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-ylmethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-urea;2-(3-Spiro[3.3]hept-2-yl-ureido)-2-(3-trifluoromethyl-phenyl)-acetamide; N-Methyl-2-(3-spiro[3.3]hept-2-yl-ureido)-2-(3-trifluoromethyl-phenyl)-acetamide; 1-[2-Methanesulfonyl-1-(3-trifluoromethoxy-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea; 1-[1-(2,2-Difluoro-benzo[1,3]dioxol-5-yl)-ethyl]-3-spiro[3.3]hept-2-yl-urea; 1-[2-Cyano-1-(3-trifluoromethoxy-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea; 1-[2-Cyano-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-[2-Methanesulfonyl-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[2-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-[2-(2-Methoxy-ethoxy)-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[2-lsopropoxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[3-Ethoxy-1-(3-trifluoromethyl-phenyl)-propyl]-3-

spiro[3.3]hept-2-yl-urea;1-[3-Hydroxy-1-(3-trifluoromethyl-phenyl)-propyl]-3-spiro[3.3]hept-2-yl-urea;1-[3-Methylsulfanyl-1-(3-trifluoromethyl-phenyl)-propyl]-3-spiro[3.3]hept-2-yl-urea;1-[2-Hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-{3-Ethoxy-1 -[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-propyl)-3-spiro[3.3]hept-2-yl-urea;1-{2-Methoxy-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;4-(3-Spiro[3.3]hept-2-yl-ureido)-4-(3-trifluoromethyl-phenyl)-butyramide;1-Spiro[3.3]hept-2-yl-3-[1 -(3-trifluoromethyl-phenyl)-but-3-enyl]-urea;1-[3-Methanesulfonyl-1-(3-trifluoromethyl-phenyl)-propyl]-3-spiro[3.3]hept-2-yl-urea;1-{2-Hydroxy-1-[2-methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{2-Hydroxy-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-[3,3-Difluoro-1-(3-trifluoromethyl-phenyl)-propyl]-3-spiro[3.3]hept-2-yl-urea;1-{3-Hydroxy-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-propyl}-3-spiro[3.3]hept-2-yl-urea;1-[1-(3-Methanesulfonyl-phenyl)-2-methoxy-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-{2-Hydroxy-1-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{3-Hydroxy-1-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-propyl)-3-spiro[3.3]hept-2-yl-urea;1-[Cyano-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{1-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-urea;1-{2-Methoxy-1-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{2-Methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-urea;1-{2-Dimethylamino-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[3-Fluoro-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-(2-trifluoromethoxy-pyridin-4-ylmethyl)-urea;1-Spiro[3.3]hept-2-yl-3-[1-(2-trifluoromethoxy-pyridin-4-yl)-ethyl]-urea; 1-{1-[2-Fluoro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-{1-[2-Huoro-5-(2,2,2-trifluoro- ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-(Spiro[3.3]heptan-2-yl)-3-(1-(2-((1,1,1-trifluoropropan-2-yl)oxy)pyridin-4-yl)ethyl)urea;1-(Spiro[3.3]heptan-2-yl)-3-(1-(3-((1,1,1-trifluoropropan-2-yl)oxy)phenyl)ethyl)urea;1-Spiro[3.3]hept-2-yl-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[6-(2,2,2-trifluoro-1-methoxymethyl-ethoxy)-pyridin-2-ylmethyl]-urea;1-[6-(1-Dimethylaminomethyl-2,2,2-trifluoro-ethoxy)-pyridin-2-ylmethyl]-3-spiro[3.3]hept-2-yl-urea;1-[2-(1-Dimethylaminomethyl-2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[2-(2,2,2-trifluoro-1-methoxymethyl-ethoxy)-pyridin-4-ylmethyl]-urea;1-[5-Methyl-6-(2,2,2-trifluoro-ethoxy)-

pyridin-2-ylmethyl]-3-spiro[3.3]hept-2-yl-urea;1-[4-Methyl-3-(2,2,2-trifluoro-ethoxy)-benzyl]-3-spiro[3.3]hept-2-yl-urea;1-[3-Huoro-5-(2,2,2-trifluoro-1-methyl-ethoxy)-benzyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{1-[3-(2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-cyclopropyl}-urea;1-Spiro[3.3]hept-2-yl-3-[4-(2,2,2-trifluoro-ethoxy)-pyrimidin-2-ylmethyl]-urea;1-{1-[4-Huoro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-[4-Huoro-3-(2,2,2-trifluoro-ethoxy)-benzyl]-3-spiro[3.3]hept-2-yl-urea;1-{2-[Methyl-(2,2,2-trifluoro-ethyl)-amino]-pyridin-4-ylmethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[2-(2,2,2-trifluoro-ethylamino)-pyridin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[4-(2,2,2-trifluoro-1-methyl-ethoxy)-pyridin-2-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[2-(2,2,2-trifluoro-1-methyl-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[1-(3-trifluoromethoxy-phenyl)-ethyl]-urea;1-Spiro[2.3]hex-5-yl-3-[6-(2,2,2-trifluoro-1-methyl-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-[1-(2,2-Difluoro-benzo[1,3]dioxol-4-yl)-ethyl]-3-spiro[2.3]hex-5-yl-urea; 1-{2-Hydroxy-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-{2-Hydroxy-1 -[2-methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-[1-(3-Difluoromethoxy-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-(2-Methoxy-5-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-Spiro[2.3]hex-5-yl-3-[4-(2,2,2-trifluoro-ethoxy)-pyrimidin-2-ylmethyl]-urea;1-(1-(3-(pentafluoro-l6-sulfaneyl)phenyl)ethyl)-3-(spiro[2.3]hexan-5-yl)urea;1-(2-Methoxy-3-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea; 1-{1-[2-Huoro-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-(3-(pentafluoro-l6-sulfaneyl)benzyl)-3-(spiro[2.3]hexan-5-yl)urea;1-{1-[2-Huoro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-{1-[3-Huoro-5-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-[1-(2-Methoxy-3-trifluoromethyl-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-(2-Huoro-3-trifluoromethoxy-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-Spiro[2.3]hex-5-yl-3-{1-[3-(2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-cyclopropyl}-urea;1-[1-(3-Difluoromethoxy-phenyl)-cyclopropyl]-3-spiro[2.3]hex-5-yl-urea;1-[1-(2-Methoxy-5-trifluoromethyl-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-[3-Hydroxy-1-(3-trifluoromethoxy-phenyl)-propyl]-3-spiro[2.3]hex-5-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-Spiro[2.3]hex-5-yl-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-Spiro[2.3]hex-5-yl-3-[1-(3-trifluoromethoxy-phenyl)-ethyl]-urea;1-(3-Huoro-5-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-[2-Hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-Spiro[2.3]hex-5-yl-3-{1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-urea;1-{1-[2-Methyl-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-[2,2-Difluoro-1 -(3-trifluoromethyl-

phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-[2-Methoxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-(4-Huoro-3-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-(2-Huoro-3-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-(2-Chloro-3-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-(2-Huoro-5-trifluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea;1-{1-[5-Methoxy-6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-Spiro[2.3]hex-5-yl-3-(2-trifluoromethoxy-pyridin-4-ylmethyl)-urea;1-{2-Methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-(3-Difluoromethoxy-benzyl)-3-spiro[2.3]hex-5-yl-urea;1 -Spiro [2.3] h ex-5-y I -3-(3-trifIuoromethoxy-benzyI)-urea; 1-Spiro[2.3]hex-5-yl-3-[3-(2,2,2-trifluoro-ethoxy)-benzyl]-urea; 1-(3-Difluoromethyl-benzyl)-3-spiro[2.3]hex-5-yl-urea; 1-Spiro[2.3]hex-5-yl-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea; 1-(6,6-Difluoro-spiro[3.3]hept-2-yl)-3-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-ylmethyl]-urea;1-(6,6-Difluoro-spiro[3.3]hept-2-yl)-3-[1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[(1 H-[1 ,2,3]triazol-4-yl)-(3-trifluoromethyl-phenyl)-methyl]-urea;1-[(1-Methyl-1 H-tetrazol-5-yl)-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-[(2-Methyl-2H-tetrazol-5-yl)-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-[(3-Methyl-3H-[1,2,3]triazol-4-yl)-(3-trifluoromethyl-phenyl)-methyl]-3-spiro[3.3]hept-2-yl-urea;1-[1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-(6-iodo-spiro[3.3]hept-2-yl)-urea;1-[(R)-1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[(S)-1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-{1-[3-((R)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-cyclopropyl}-urea;1-Spiro[3.3]hept-2-yl-3-{1-[3-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-phenyl]-cyclopropyl}-urea;1-Spiro[3.3]hept-2-yl-3-[2-((R)-2,2,2-trifluoro-1-methoxymethyl-ethoxy)-pyridin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[2-((S)-2,2,2-trifluoro-1-methoxymethyl-ethoxy)-pyridin-4-ylmethyl]-urea;1-[(S)-1-(3-Difluoromethoxy-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[(R)-1-(3-Difluoromethoxy-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[(S)-1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-Spiro[3.3]hept-2-yl-3-{(S)-1-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-urea;1-{(S)-1-[4-Fluoro-3-(2,2,2-trifluoro-ethoxy)-phenyl]-ethyl}-3-spiro[3.3]hept-2-yl-urea;1-Spiro[3.3]hept-2-yl-3-[(R)-2,2,2-trifluoro-1-(3-trifluoromethyl-phenyl)-ethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[(R)-(1H-[1,2,4]triazol-3-yl)-(3-trifluoromethyl-phenyl)-methyl]-urea;1-Spiro[3.3]hept-2-yl-3-[2-((R)-2,2,2-trifluoro-1-methyl-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-[2-((S)-2,2,2-trifluoro-1-methyl-ethoxy)-pyrimidin-4-ylmethyl]-urea;1-Spiro[3.3]hept-2-yl-3-{(S)-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-urea;1-Spiro[3.3]hept-2-yl-3-{(R)-1-[6-(2,2,2-trifluoro-ethoxy)-pyrimidin-4-yl]-ethyl}-

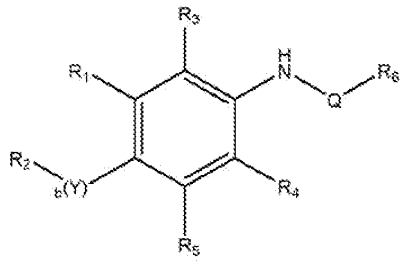
urea;1-[(R)-2-Hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[(S)-2-Hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-[(R)-2-Hydroxy-1-(3-trifluoromethyl-phenyl)-ethyl]-3-spiro[2.3]hex-5-yl-urea;1-[(R)-1-(2-Difluoromethoxy-pyridin-4-yl)-2-methoxy-ethyl]-3-spiro[3.3]hept-2-yl-urea;1-{(R)-2-Methoxy-1-[2-(2,2,2-trifluoro-ethoxy)-pyridin-4-yl]-ethyl}-3-spiro[2.3]hex-5-yl-urea;1-[(S)-1-(2-Difluoromethoxy-pyridin-4-yl)-ethyl]-3-spiro[2.3]hex-5-yl-urea; or 1-[(S)-1-(2-Bromo-5-trifluoromethyl-phenyl)-ethyl]-3-spiro[3.3]hept-2-yl-urea; or a salt thereof.

Formula 55

[0646] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds of Formula 55. Such compounds are described in International Publication No. WO2020157126A1, published August 6, 2020, and corresponding to International Application No. PCT/EP2020/052156 filed January 29, 2020; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 55, this reference incorporated by reference herein controls.

[0647] In an embodiment, the Kv7 channel activator is a compound according to Formula 55:

Formula 55



,

or a tautomer, salt, solvate, stereoisomer or isotope thereof, wherein: Y is selected from: C1-C10 alkylamino, C1-C10 alkyl, C1-C10 alkoxy, C3-C8 cycloalkyl, Cl- C10 alkylcarbonyl, Cl -CIO alkylaminocarbonyl, Cl -CIO alkylthio, aryl, heterocycle, Cl -CIO carbonyl, C1-C10 amide and C1-C10 carboxyl and it is optionally mono-substituted or bi- substituted with a first substituent independently selected from: hydroxyl, amino, thiol, carboxylic acid, amide, carbonyl, halogen, C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 alkylcarbonyl, C1-C6 alkoxy carbonyl, C1-C6 alkylamino, C1-C6 alkylaminocarbonyl, C1-C6 alkyloxy, C1-C6 alkylthio, C2-C8 alkenyl, C5-C7 cycloalkenyl, C2-C8 alkynyl and C5-C10 aryl, any of said first substituents being optionally substituted by one or more second substituents independently selected from: hydroxyl, amino, thiol, carboxylic acid, amide, carbonyl, halogen, C1-C6 alkyl, C3- C6 cycloalkyl, C1-C6 alkylcarbonyl, C1-C6 alkoxy carbonyl, C1-C6 alkylamino, C1-C6 alkylaminocarbonyl, C1-C6 alkyloxy, C1-C6 alkylthio, C2-C8 alkenyl, C5-C7

cycloalkenyl, C2- C8 alkynyl and C5-C10 aryl; b is an integer comprised between 1 and 3;or Y is NH or O and b is 1;R.2 is selected from: an aromatic ring, a cycloalkyl, a heterocycle, a linear or branched saturated alkyl and a linear or branched unsaturated alkyl, any of which optionally bearing in one or more positions at least one substituent independently selected from the group consisting of: OH, NO2, CN, halogen, NH2, C1-C3 haloalkyl, C1-C3 haloalkoxy, C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 alkylcarbonyl, C1-C6 alkoxy carbonyl, C1-C6 alkylamino, C1-C6 dialkylamino, C1-C6 alkylaminocarbonyl, acetamidyl, C1-C6 alkyloxy, C1-C6 alkylthio, C2-C8 alkenyl, C5-C7 cycloalkenyl, C2-C8 alkynyl, C5-C10 aryl, thiol and thiol ether; Ri, R3, R4 and R5 are each independently selected from the group consisting of: H, N¾, OH, halogen, C1-C6 alkyl, C3-C6 cycloalkyl, C1-C6 alkylcarbonyl, C1-C6 alkoxy carbonyl, C1-C6 alkylamino, C2-C6 dialkylamino, C1-C6 alkylaminocarbonyl, C1-C6 alkyloxy, C1-C6 alkylthio, C2-C8 alkenyl, C5-C7 cycloalkenyl, heterocycle, C2-C8 alkynyl and C5-C10 aryl, any of which being optionally substituted by one or more substituents independently selected from: hydroxyl, amine, thiol, carboxyl, carboxylic acid, and halogen; Q is selected from the group consisting of: C=0, SO2, SO, SO2NH, CONH, CSNH, C=NH, CNHNH, and C=S; when Q is C=0 or C=S, R_6 is selected from: linear or branched C3-C30 alkyl, linear or branched C5-C30 arylalkyl, C3-C8 cycloalkyl, linear or branched C2-C4 alkyl substituted by C3-C8 cycloalkyl, linear or branched C3-C10 cycloalkylamino, linear or branched Cl -CIO alkylamino, linear or branched C2-C10 alkenylamino, linear or branched C2-C10 alkynylamino, C5-C10 aryl, linear or branched C7-C15 arylalkylamino, linear or branched C7-C15 arylalkenylamino, linear or branched C7-C15 arylalkynylamino, C2-C30 alkenyl, C2-C30 alkynyl and C1-C30 alkoxyl, any of which being optionally substituted with one or more substituents independently selected from: linear or branched alkyl group, halogen, hydroxyl group, amine group, alkylamine, dialkylamine, thiol, thioether and cycloalkyl; when Q is SO2, SO, SO2NH, CONH, CSNH, C=NH, or CNHNH, R_6 is selected from: linear or branched C1-C30 alkyl, C3-C8 cycloalkyl, linear or branched C1-C30 alkylcarbonyl, linear or branched C1-C30 alkoxycarbonyl, linear or branched C1-C30 alkylamino, linear or branched Cl- C30 alkylaminocarbonyl, linear or branched C1-C30 alkyloxy, linear or branched C1-C30 alkylthio, linear or branched C2-C30 alkenyl, C5-C8 cycloalkenyl, linear or branched C2-C30 alkynyl, heterocycle and aryl, any of which being optionally substituted with one or more substituents independently selected from: halogen, C1-C6 alkyl, oxo and C3-C7 cycloalkyl.

[0648] In further embodiments, b is 1.

[0649] In further embodiments, Q is C=0 or SO2.

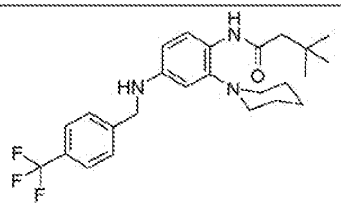
[0650] In further embodiments, Y is Cl -CIO alkylamino, Cl -CIO alkyl or Cl -CIO alkoxy.

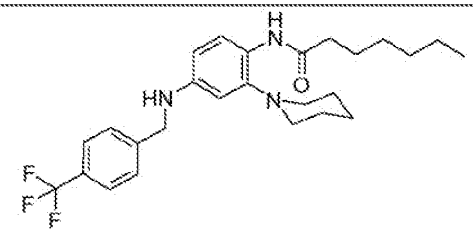
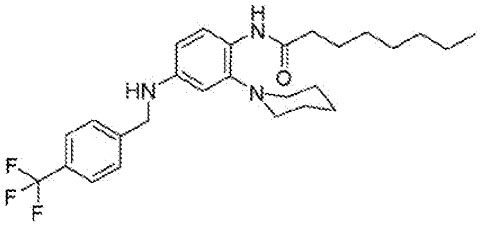
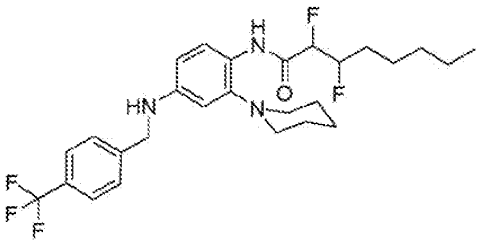
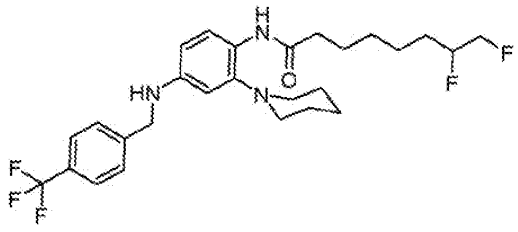
[0651] In further embodiments, R2 is an aromatic ring optionally substituted with one or more substituents independently selected from the group consisting of: OH, NO2, halogen, NH2, C1-C3 haloalkyl, acetamidyl, C1-C6 alkyloxy, C1-C3 haloalkoxy, and C1-C6 alkylcarbonyl.

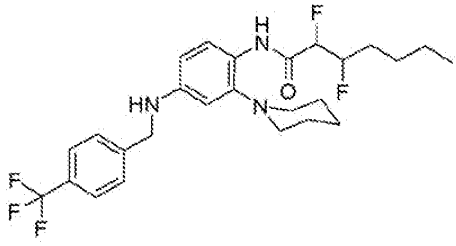
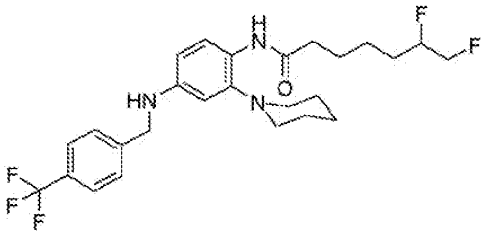
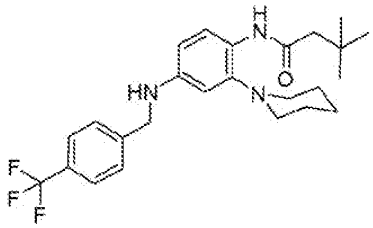
[0652] In further embodiments, Ri, R3, R4 and R5 are each independently: H, C1-C6 alkyl, C3- C6 cycloalkyl, NH_2, NH(C1-C6 alkyl), N(C1-C6 alkyl)2 , azepane, pirrolidine, piperidine, aziridine or halogen.

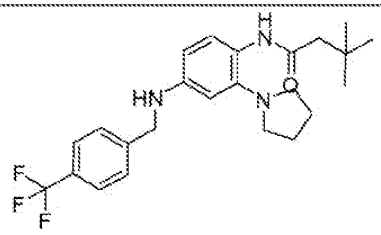
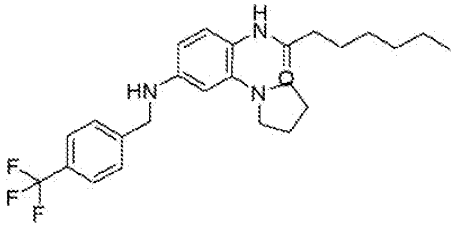
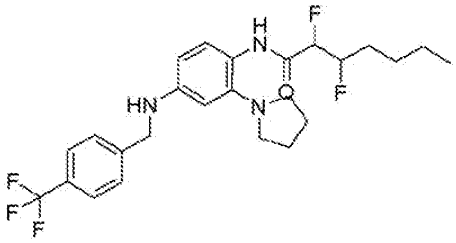
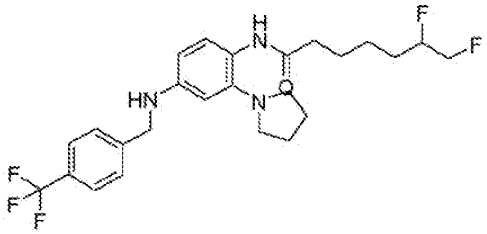
[0653] In further embodiments, when Q is C=0 or C=S, R_6 is selected from: linear or branched C3-C30 alkyl, linear or branched C5-C30 arylalkyl, C3-C8 cycloalkyl, linear or branched C2-C4 alkyl substituted by C3-C8 cycloalkyl, linear or branched C1-C10 alkylamino, linear or branched C7-C15 arylalkylamino, C2- C30 alkenyl, C2-C30 alkynyl and C1-C30 alkoxyl, any of which being optionally substituted with one or more substituents independently selected from: halogen and cycloalkyl; and where Q is $S0_2$, SO, SO2NH, CONH, CSNH, C=NH, or CNHNH, Re is C3-C8 cycloalkyl or aryl and is optionally substituted with one or more C1-C6 alkyl.

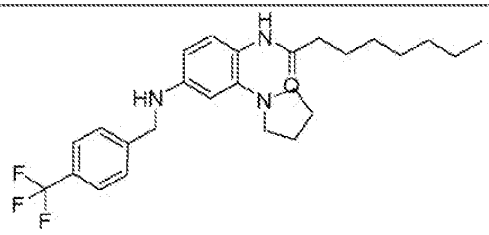
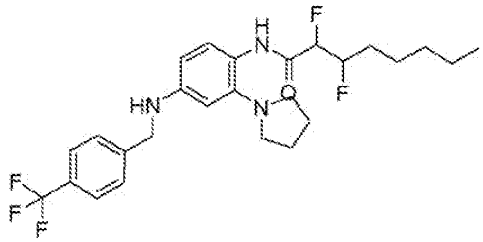
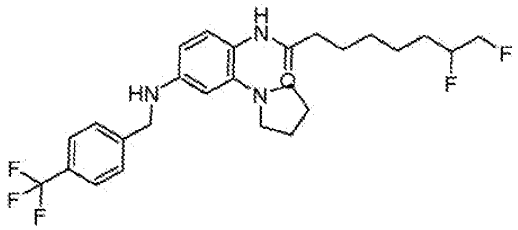
[0654] In further embodiments, the Kv7 Channel activator is selected from the group consisting of those listed in the following table

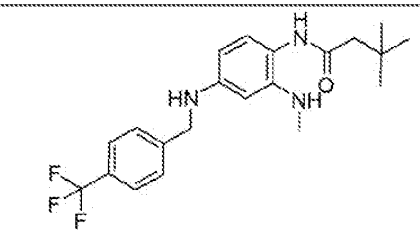
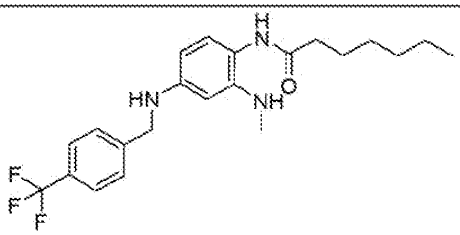
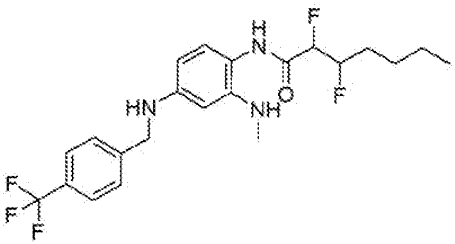
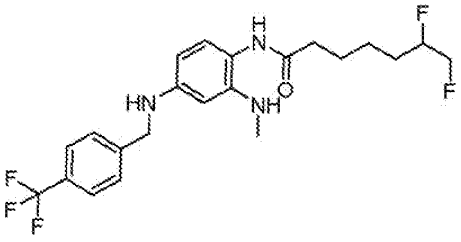
COMPOUND STRUCTURE	COMPOUND NAME
	N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide

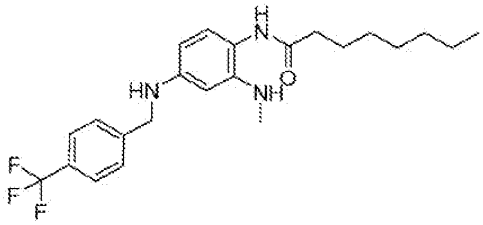
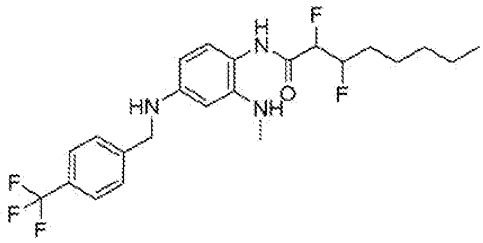
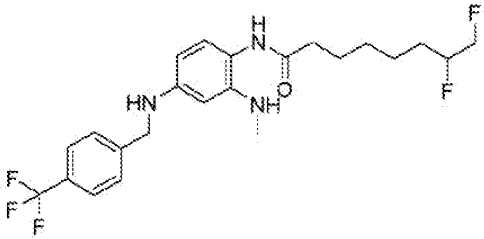
	N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	2,3-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2R,3S)-2,3-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2S,3R)-2,3-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2R,3R)-2,3-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2S,3S)-2,3-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	7,8-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7R)-7,8-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7S)-7,8-difluoro-N-(2-(piperidin-1-yl)-4-((4-

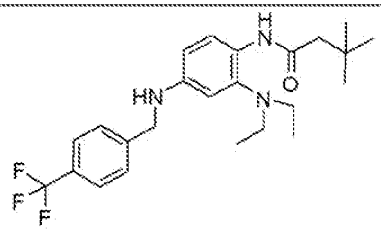
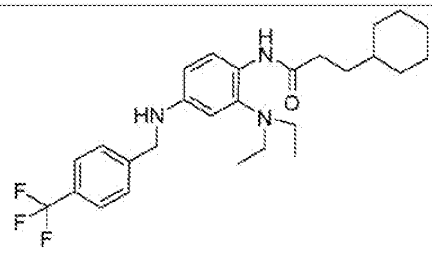
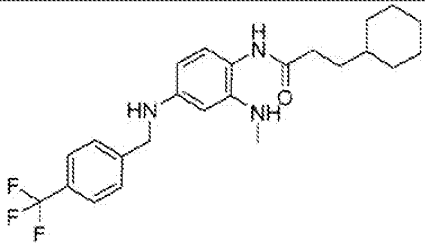
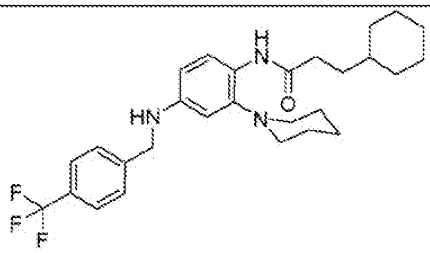
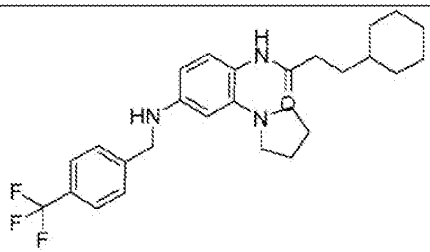
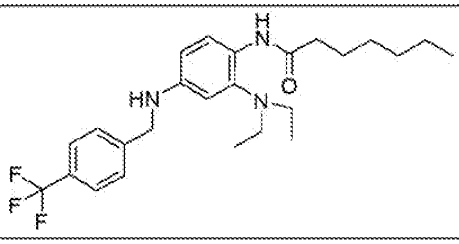
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	6,7-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6R)-6,7-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6S)-6,7-difluoro-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	3,3-dimethyl-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)butanamide

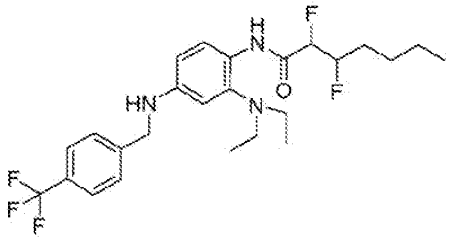
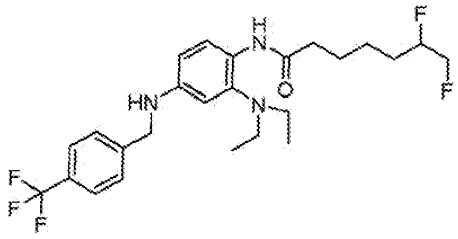
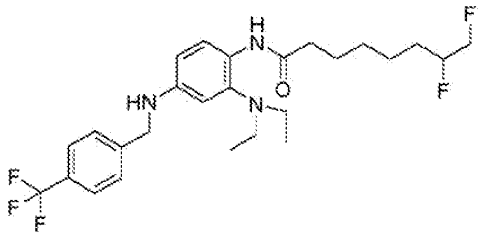
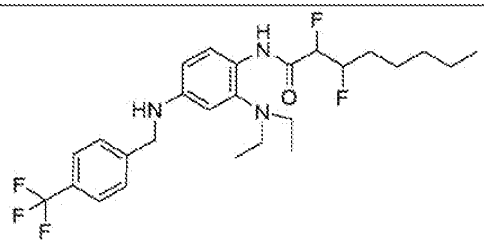
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	6,7-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6R)-6,7-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6S)-6,7-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide

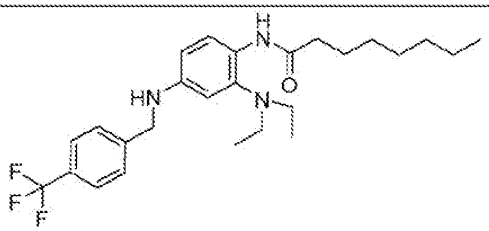
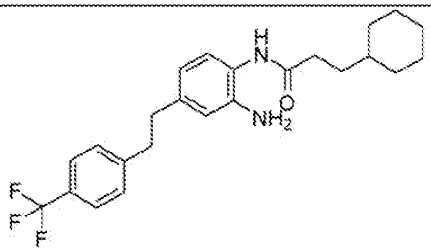
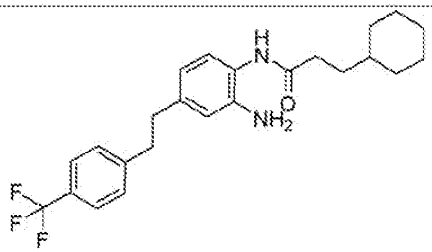
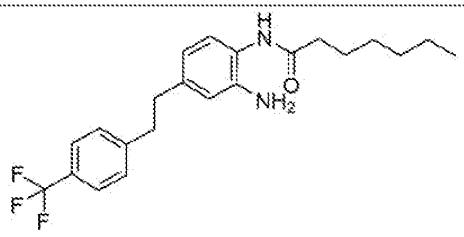
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	7,8-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7R)-7,8-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7S)-7,8-difluoro-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide

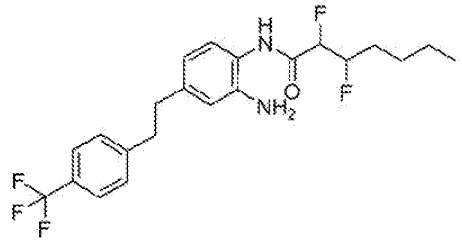
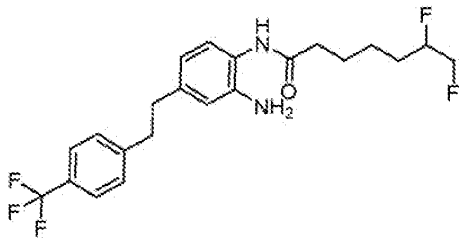
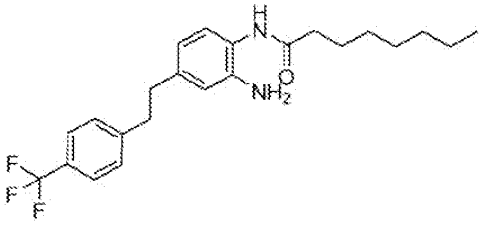
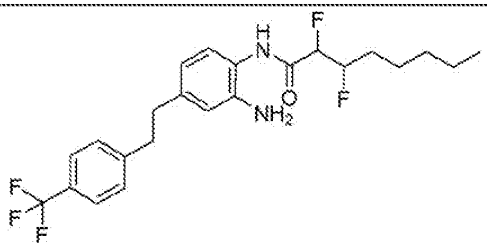
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	2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (2R, 3S)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (2S, 3R)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (2R, 3R)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (2S, 3S)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	6,7-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6R)-6,7-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide (6S)-6,7-difluoro-N-(2-(methylamino)-4-((4-

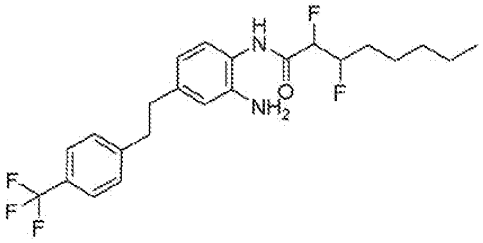
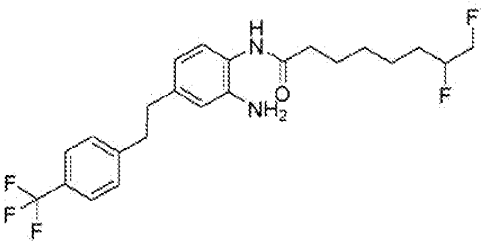
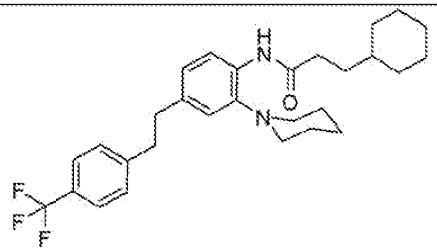
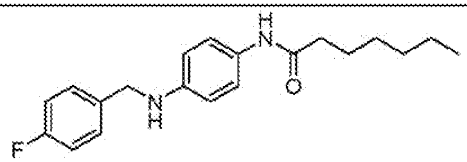
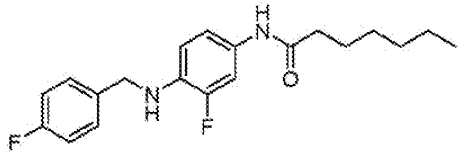
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	2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2R,3S)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2S,3R)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2R,3R)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (2S,3S)-2,3-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	7,8-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7R)-7,8-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide (7S)-7,8-difluoro-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide

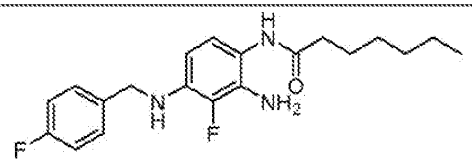
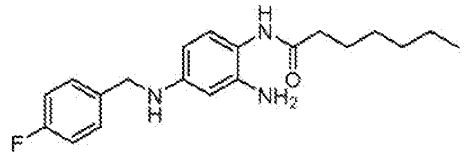
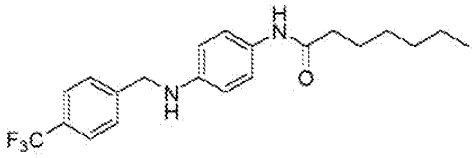
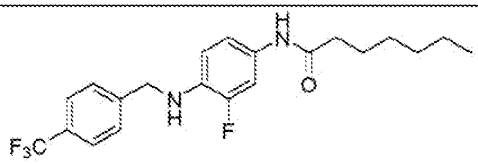
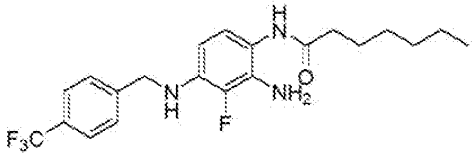
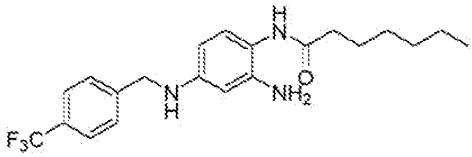
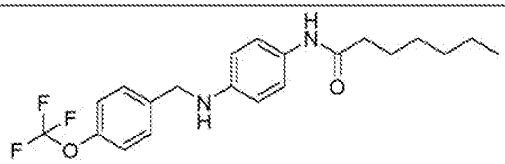
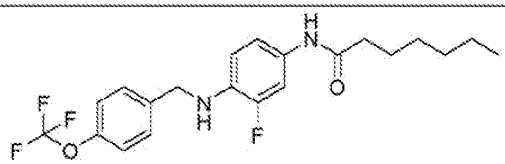
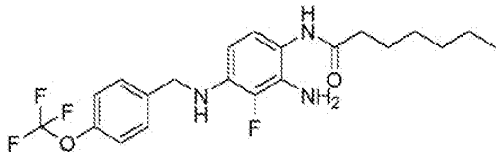
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	3-cyclohexyl-N-(2-(methylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)propanamide
	3-cyclohexyl-N-(2-(piperidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)propanamide
	3-cyclohexyl-N-(2-(pyrrolidin-1-yl)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)propanamide
	N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide

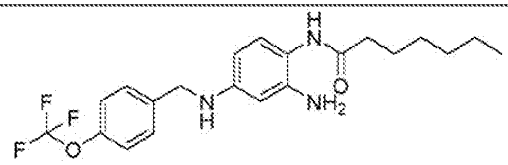
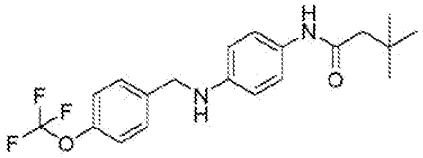
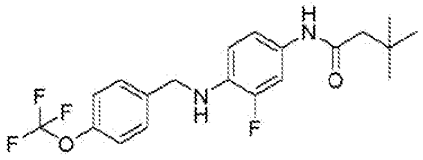
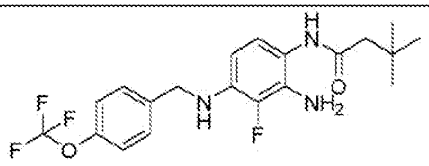
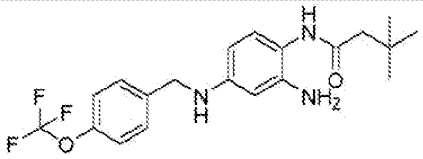
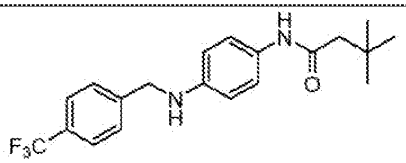
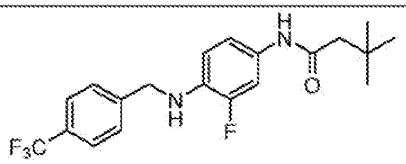
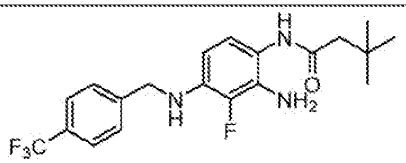
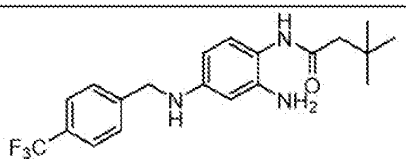
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	N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide (6R)-N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide (6S)-N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide
	N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7R)-N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7S)-N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide
	N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorooctanamide (2R,3S)-N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorooctanamide

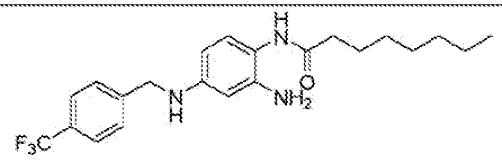
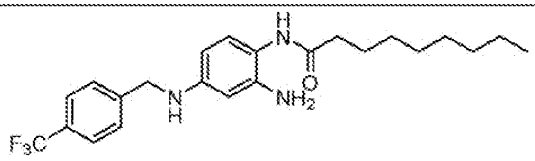
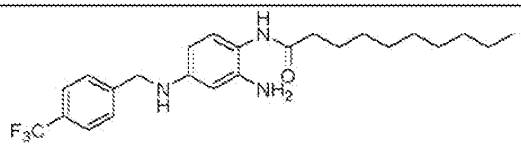
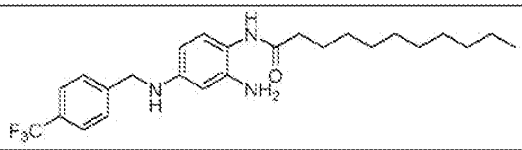
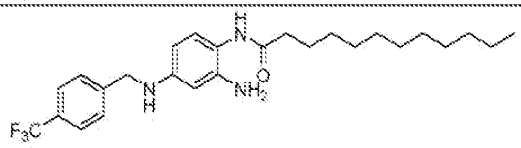
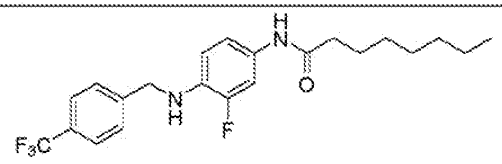
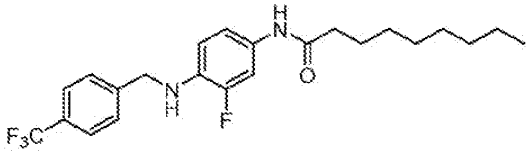
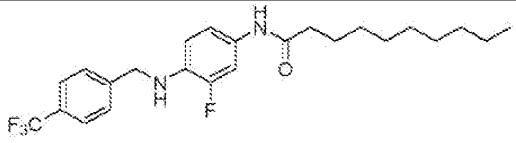
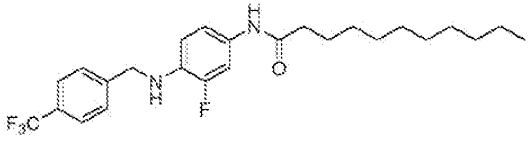
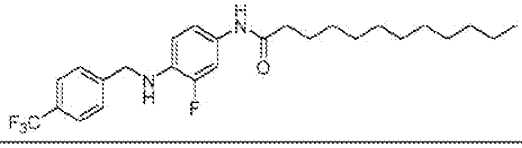
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	N-(2-(diethylamino)-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-3-cyclohexylpropanamide
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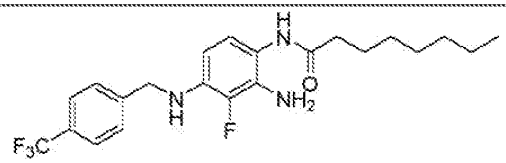
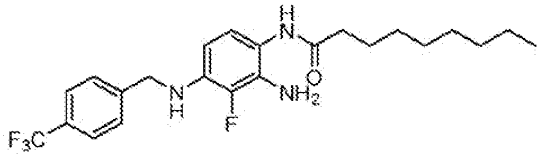
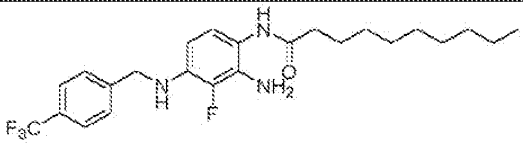
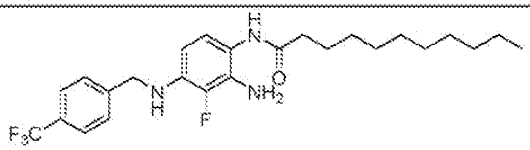
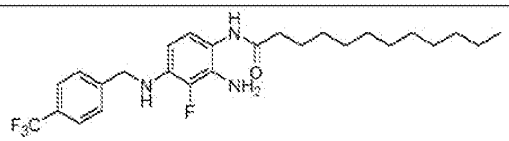
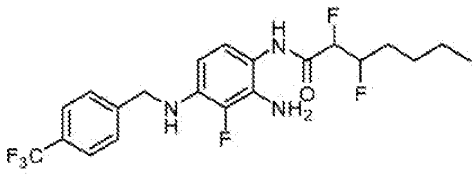
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	N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-6,7-difluoroheptanamide (6R)-N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-6,7-difluoroheptanamide (6S)-N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-6,7-difluoroheptanamide
	N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)octanamide
	N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluorooctanamide

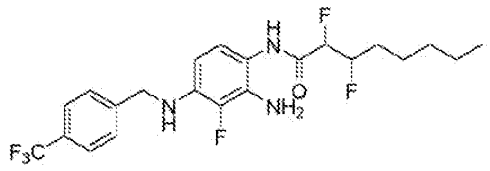
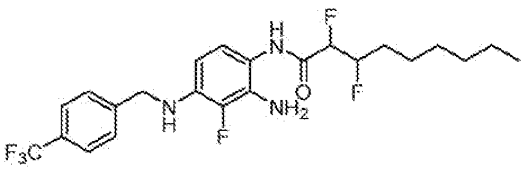
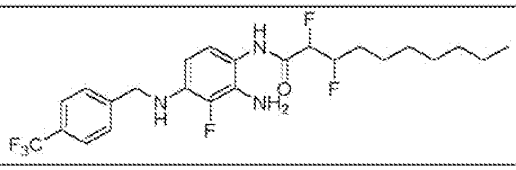
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	N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide (7R)-N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide (7S)-N-(2-amino-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide
	3-cyclohexyl-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)propanamide
	N-(4-((4-fluorobenzyl)amino)phenyl)heptanamide
	N-(3-fluoro-4-((4-fluorobenzyl)amino)phenyl)heptanamide

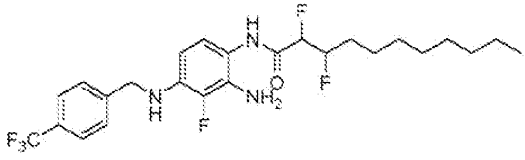
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	N-(2-amino-4-((4-fluorobenzyl)amino)phenyl)heptanamide
	N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(4-((4-(trifluoromethoxy)benzyl)amino)phenyl)heptanamide
	N-(3-fluoro-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)heptanamide
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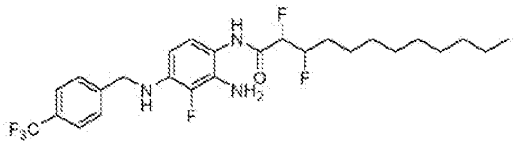
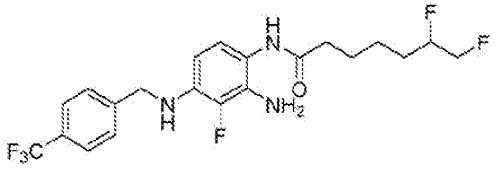
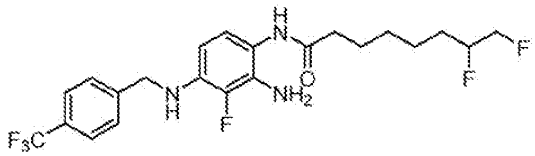
	N-(2-amino-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)heptanamide
	3,3-dimethyl-N-(4-((4-(trifluoromethoxy)benzyl)amino)phenyl)butanamide
	N-(3-fluoro-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	3,3-dimethyl-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)butanamide
	N-(3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide

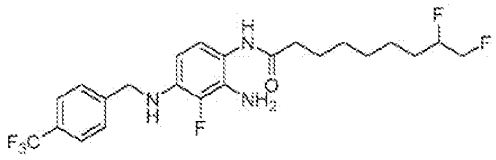
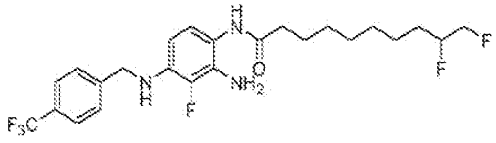
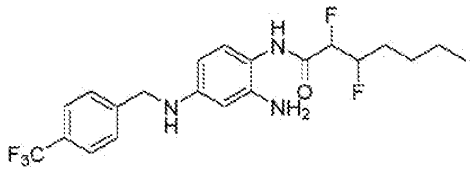
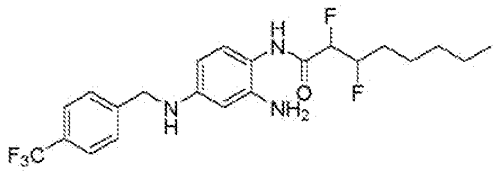
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	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)nonanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)undecanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dodecanamide
	N-(3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	N-(3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)nonanamide
	N-(3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
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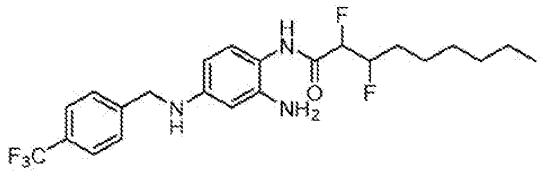
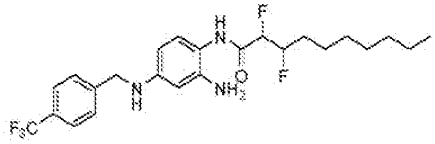
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)nonanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)undecanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dodecanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide racemic mixtures thereof

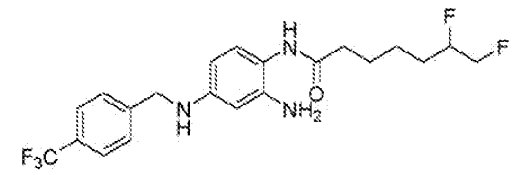
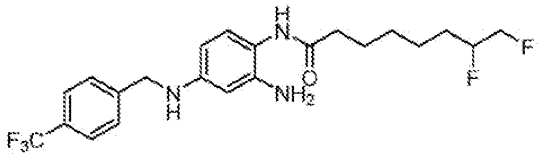
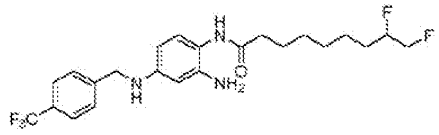
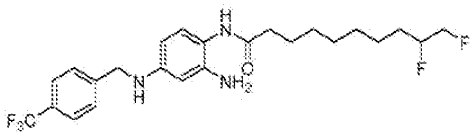
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2R,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2S,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide

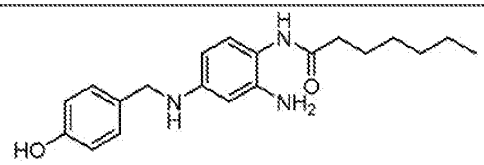
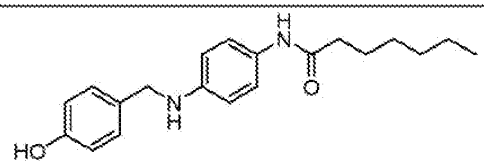
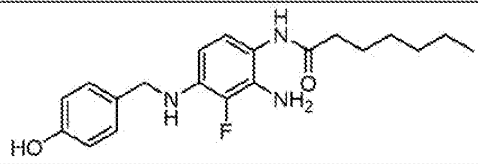
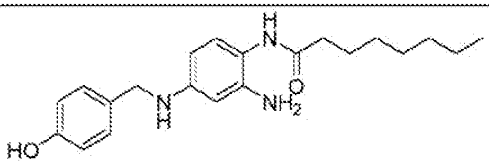
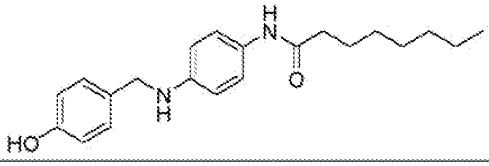
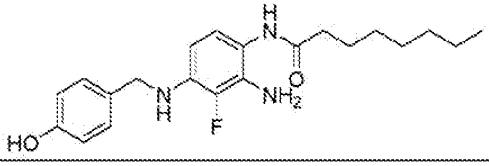
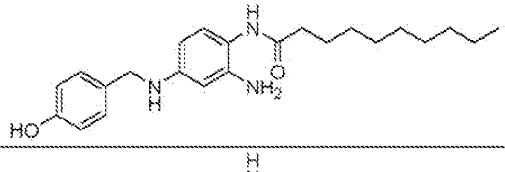
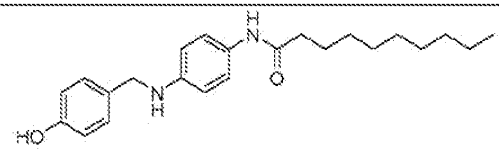
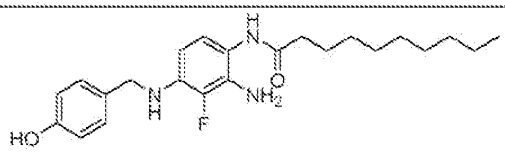
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroundecanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroundecanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroundecanamide (2R,3R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroundecanamide (2S,3S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroundecanamide racemic mixtures thereof

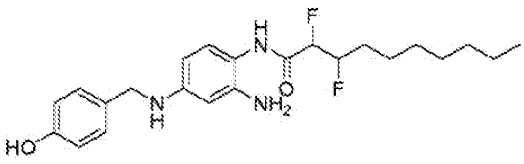
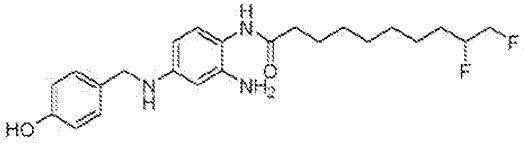
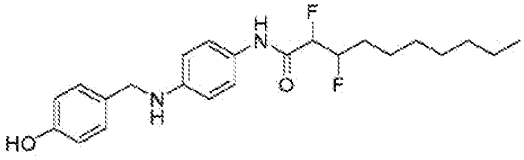
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide (6R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide (6S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluoroheptanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorooctanamide (6R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorooctanamide (6S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorooctanamide

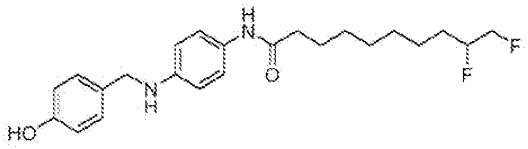
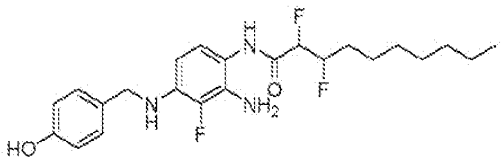
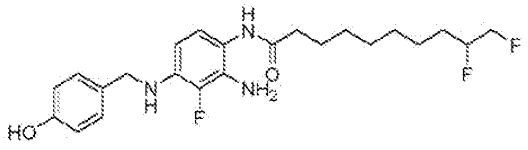
	racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-8,9-difluorononanamide (8R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-8,9-difluorononanamide (8S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-8,9-difluorononanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-9,10-difluorodecanamide (9R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-9,10-difluorodecanamide (9S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-9,10-difluorodecanamide racemic mixtures thereof
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3R)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3R)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide racemic mixtures thereof
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorooctanamide (2R,3S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorooctanamide

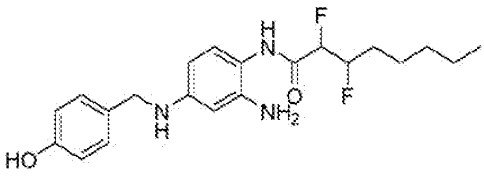
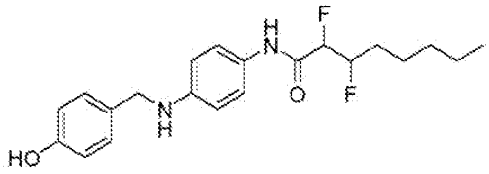
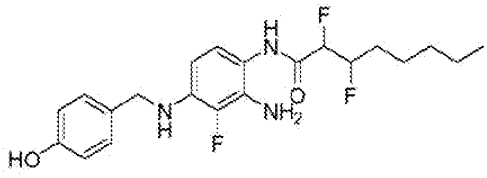
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	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2R,3S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2S,3R)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2R,3R)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide (2S,3S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorononanamide racemic mixtures thereof
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide (2R,3S)- N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide (2S,3R)- N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide (2R,3R)- N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide (2S,3S)- N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluorodecanamide racemic mixtures thereof

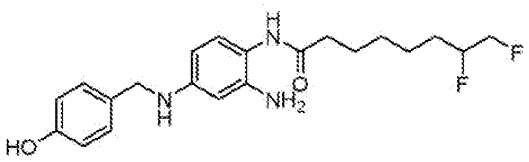
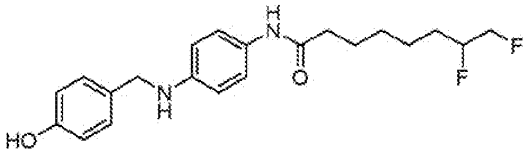
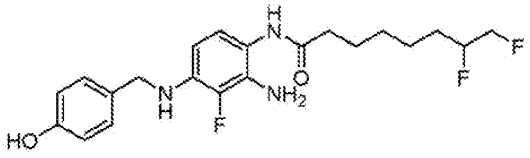
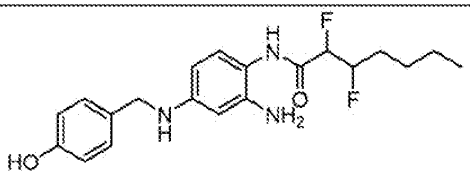
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	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7R)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7S)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorononanamide (6R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorononanamide (6S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorononanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorododecanamide (6R)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorododecanamide (6S)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-6,7-difluorododecanamide racemic mixtures thereof

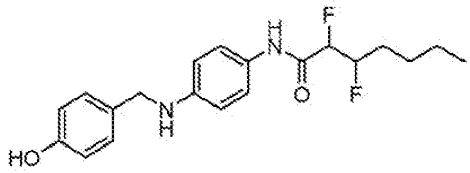
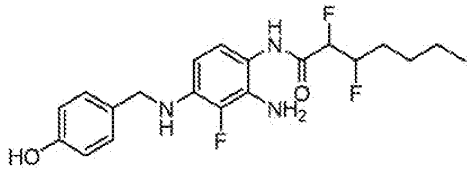
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	N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)heptanamide
	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)octanamide
	N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)octanamide
	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)decanamide
	N-(4-((4-hydroxybenzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)decanamide

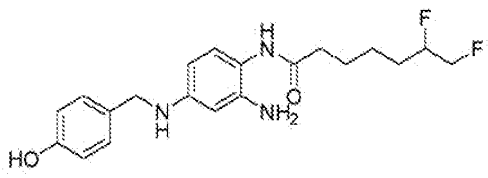
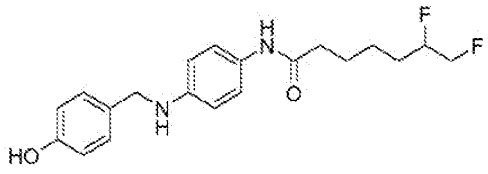
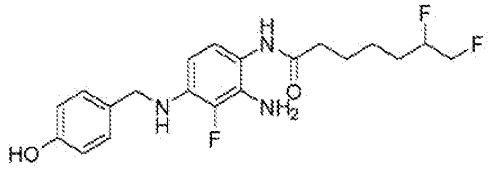
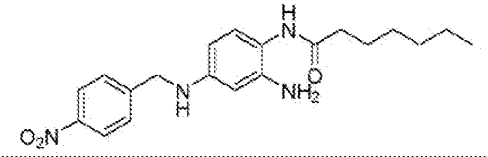
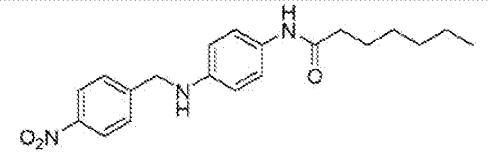
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	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-9,10-difluorodecanamide (9R)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide (9S)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide racemic mixtures thereof
	2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)deca decanamide (2R,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)deca decanamide (2S,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)decanamide (2R,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)deca decanamide (2S,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)decanamide racemic mixtures thereof

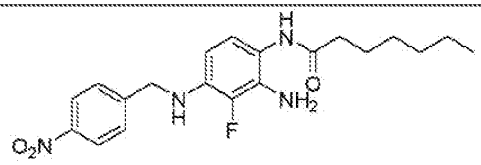
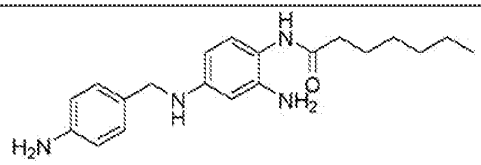
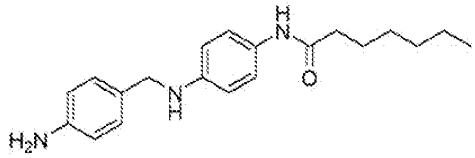
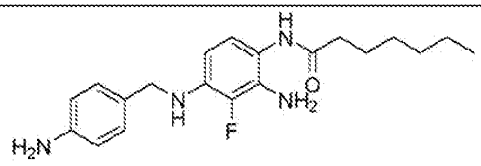
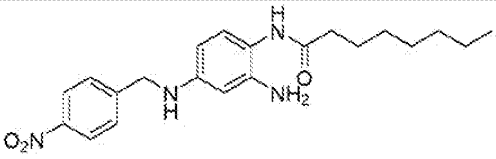
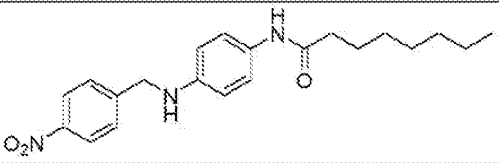
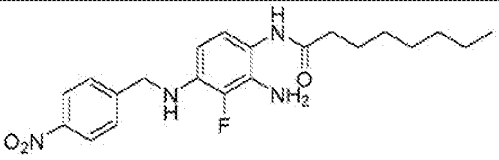
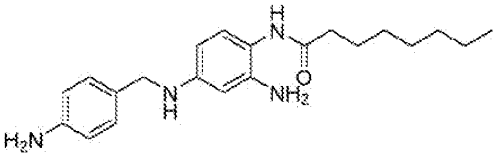
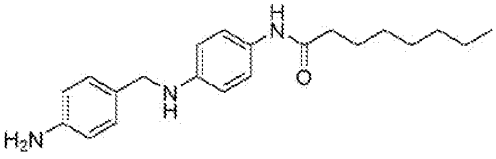
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	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide (2R,3R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide (2S,3S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorodecanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-9,10-difluorodecanamide (9R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-9,10-difluorodecanamide (9S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-9,10-difluorodecanamide racemic mixtures thereof

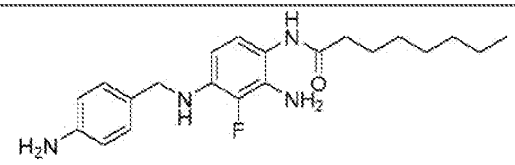
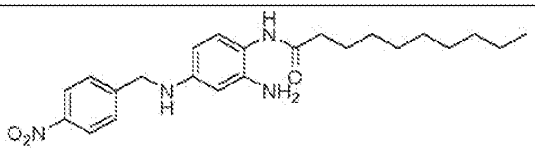
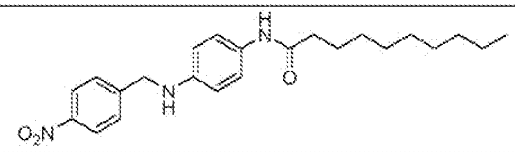
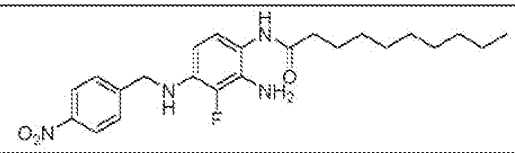
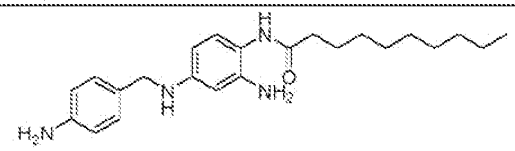
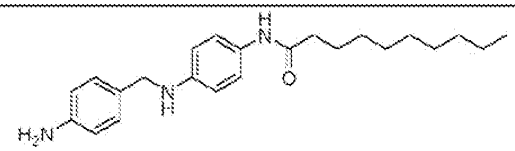
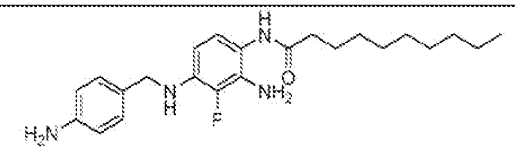
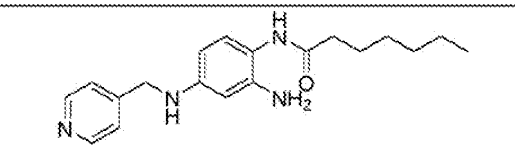
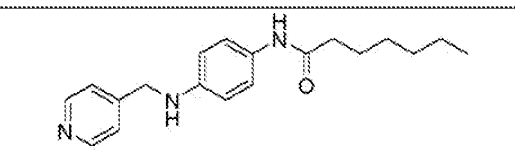
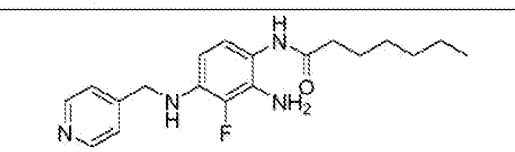
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	2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (2R,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (2S,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (2R,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (2S,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorooctanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorooctanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluorooctanamide

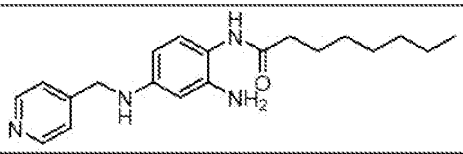
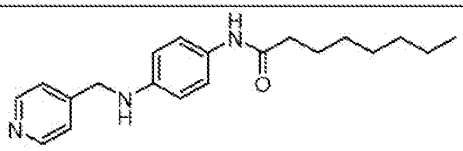
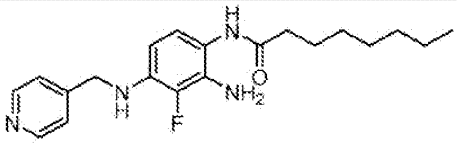
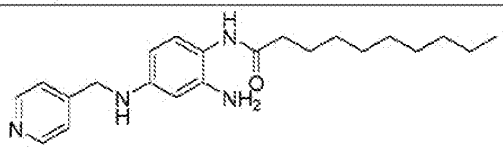
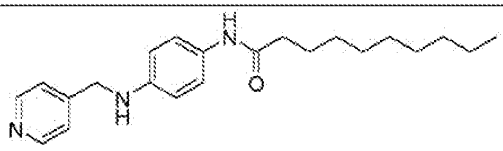
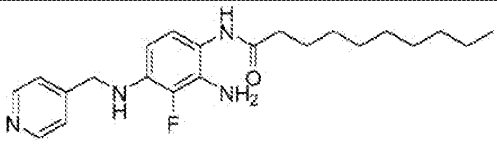
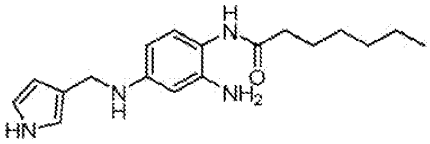
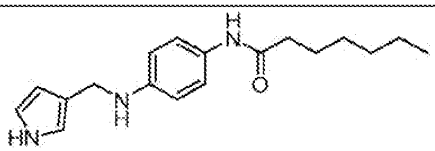
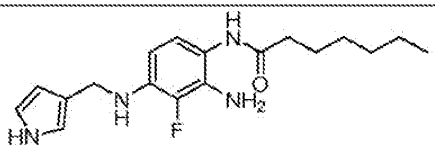
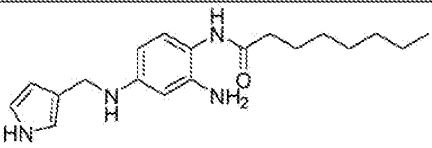
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	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide (7S)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide (7R)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide racemic mixtures thereof
	7,8-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (7R)-7,8-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide (7S)-7,8-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)octanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide (7R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide (7S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-7,8-difluorooctanamide racemic mixtures thereof
	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide

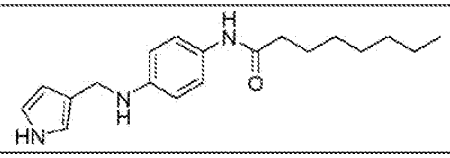
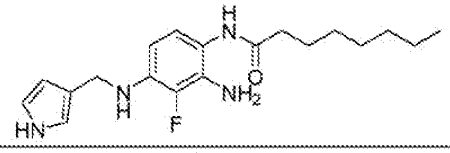
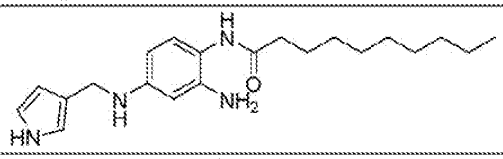
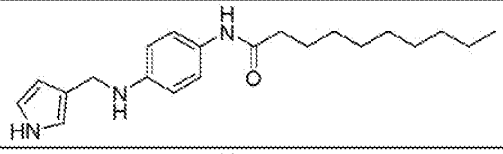
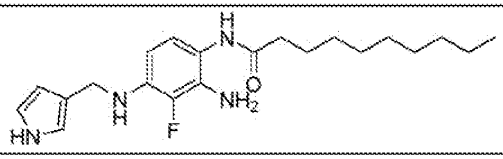
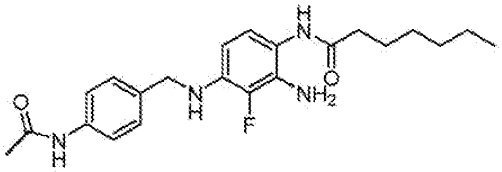
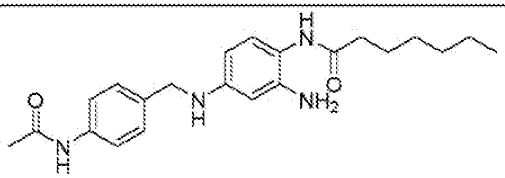
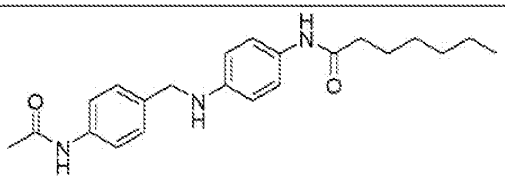
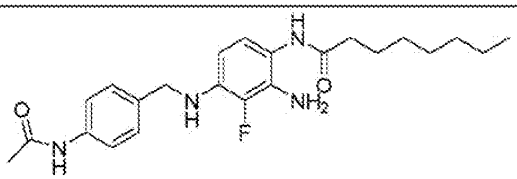
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	2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (2R,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (2S,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (2R,3R)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (2S,3S)-2,3-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide

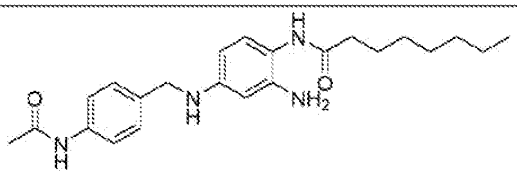
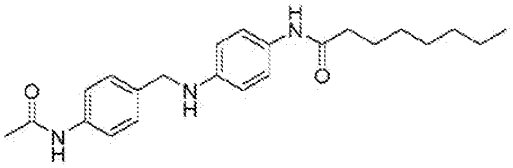
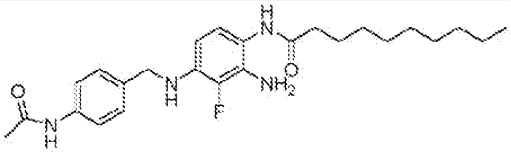
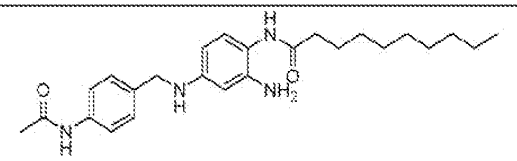
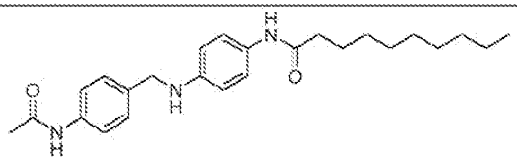
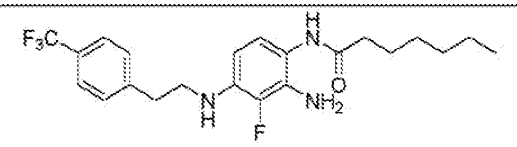
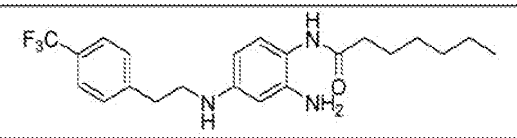
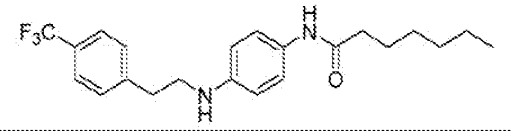
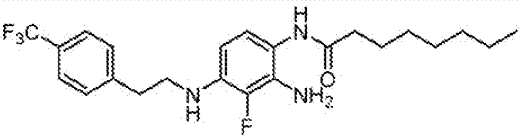
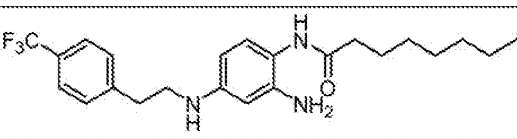
	(2S,3S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-2,3-difluoroheptanamide racemic mixtures thereof
	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide (6R)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide (6S)-N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide racemic mixtures thereof
	6,7-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (6R)-6,7-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide (6S)-6,7-difluoro-N-(4-((4-hydroxybenzyl)amino)phenyl)heptanamide racemic mixtures thereof
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide (6R)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide (6S)-N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)-6,7-difluoroheptanamide racemic mixtures thereof
	N-(2-amino-4-((4-nitrobenzyl)amino)phenyl)heptanamide
	N-(4-((4-nitrobenzyl)amino)phenyl)heptanamide

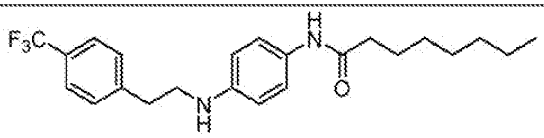
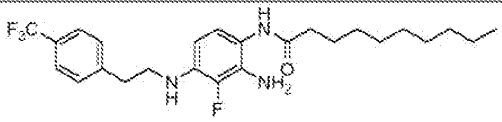
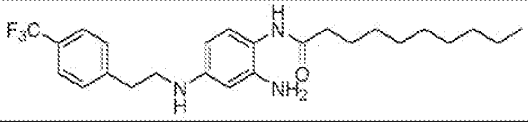
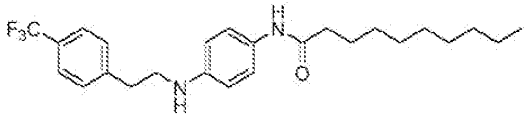
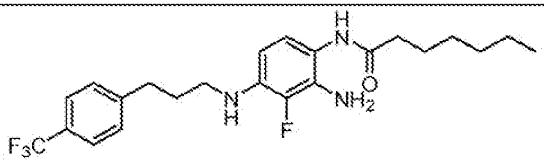
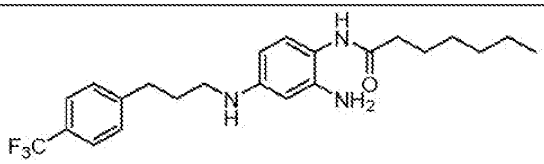
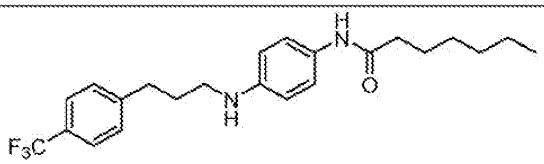
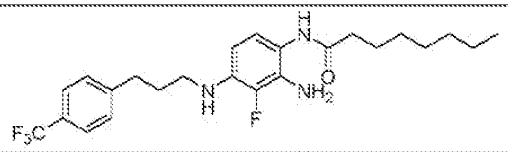
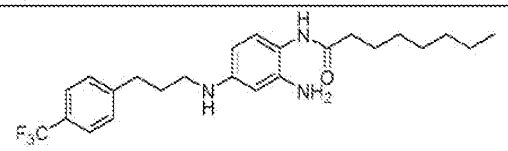
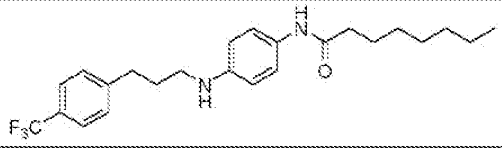
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	N-(2-amino-4-((4-aminobenzyl)amino)phenyl)heptanamide
	N-(4-((4-aminobenzyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-aminobenzyl)amino)phenyl)heptanamide
	N-(2-amino-4-((4-nitrobenzyl)amino)phenyl)octanamide
	N-(4-((4-nitrobenzyl)amino)phenyl)octanamide
	N-(2-amino-3-fluoro-4-((4-nitrobenzyl)amino)phenyl)octanamide
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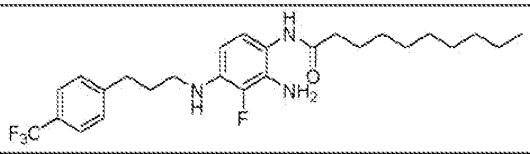
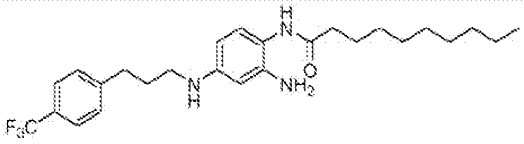
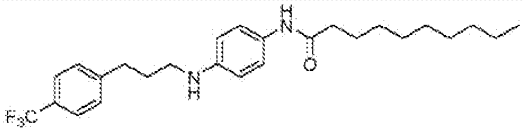
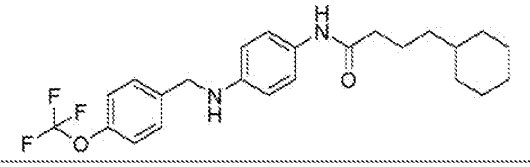
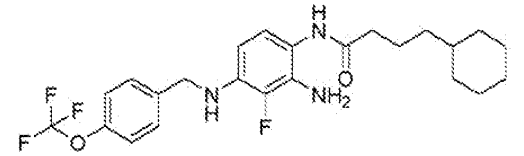
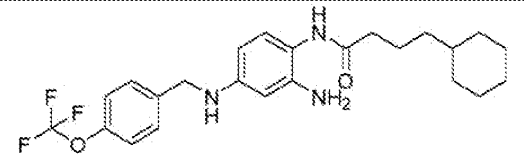
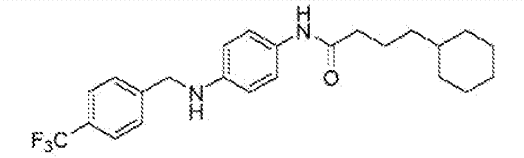
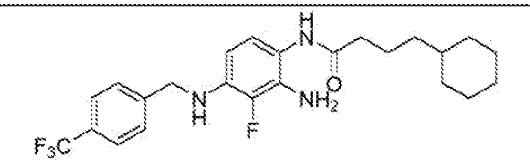
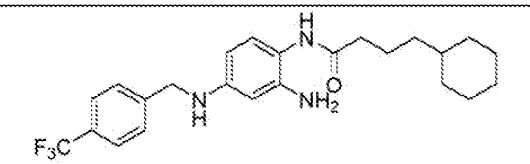
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	N-(2-amino-4-((4-nitrobenzyl)amino)phenyl)decanamide
	N-(4-((4-nitrobenzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-nitrobenzyl)amino)phenyl)decanamide
	N-(2-amino-4-((4-aminobenzyl)amino)phenyl)decanamide
	N-(4-((4-aminobenzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-aminobenzyl)amino)phenyl)decanamide
	N-(2-amino-4-((pyridin-4-ylmethyl)amino)phenyl)heptanamide
	N-(4-((pyridin-4-ylmethyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((pyridin-4-ylmethyl)amino)phenyl)heptanamide

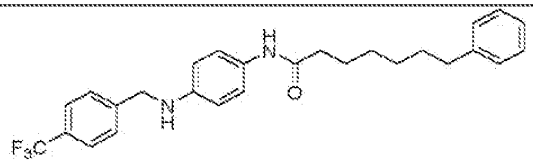
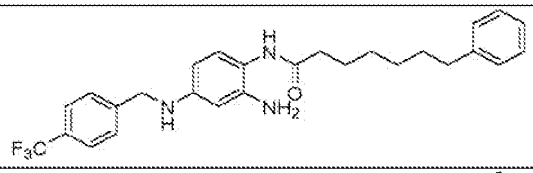
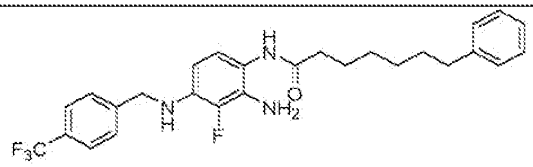
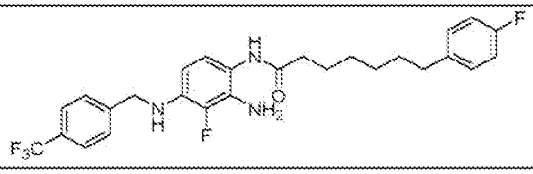
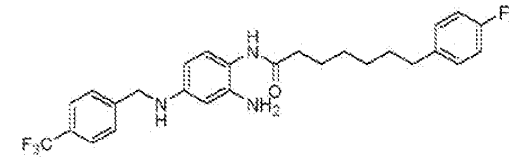
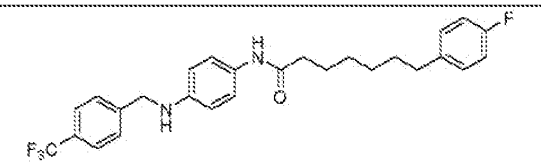
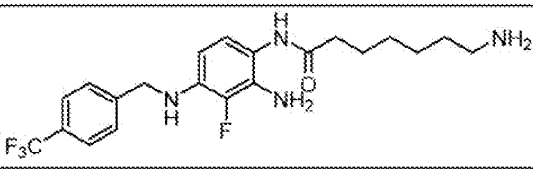
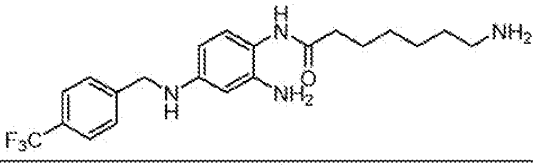
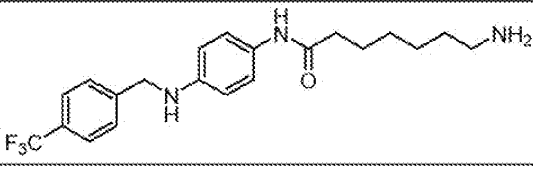
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	N-(2-amino-3-fluoro-4-((pyridin-4-ylmethyl)amino)phenyl)octanamide
	N-(2-amino-4-((pyridin-4-ylmethyl)amino)phenyl)decanamide
	N-(4-((pyridin-4-ylmethyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((pyridin-4-ylmethyl)amino)phenyl)decanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-aminophenyl)heptanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)phenyl)heptanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-amino-3-fluorophenyl)heptanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-aminophenyl)octanamide

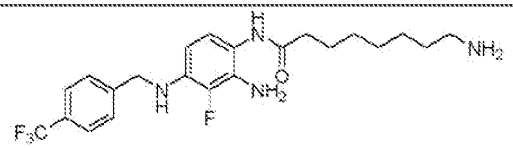
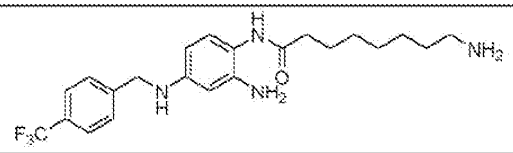
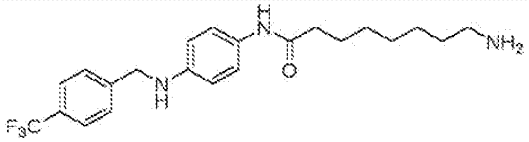
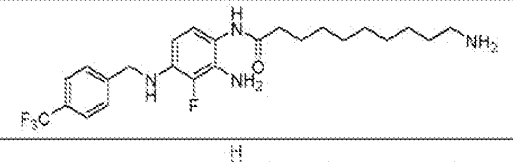
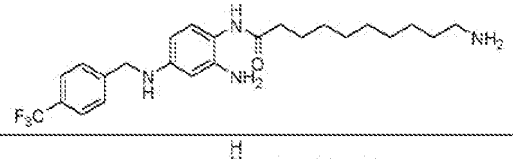
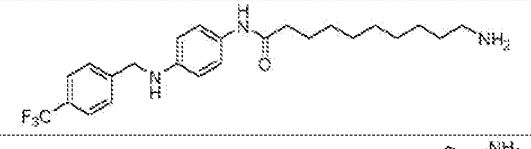
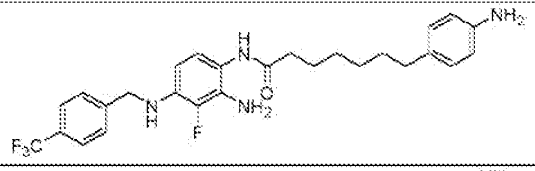
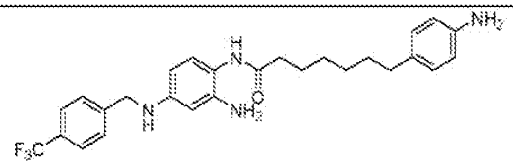
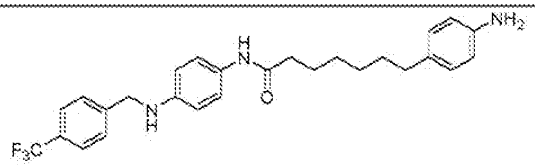
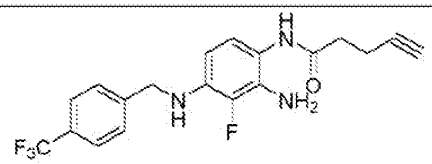
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	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-amino-3-fluorophenyl)octanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-aminophenyl)decanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)phenyl)decanamide
	N-(4-(((1H-pyrrol-3-yl)methyl)amino)-2-amino-3-fluorophenyl)decanamide
	N-(4-((4-acetamidobenzyl)amino)-2-amino-3-fluorophenyl)heptanamide
	N-(4-((4-acetamidobenzyl)amino)-2-aminophenyl)heptanamide
	N-(4-((4-acetamidobenzyl)amino)phenyl)heptanamide
	N-(4-((4-acetamidobenzyl)amino)-2-amino-3-fluorophenyl)octanamide

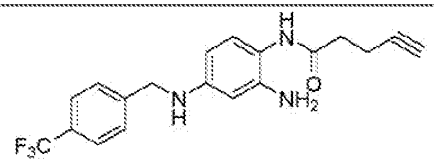
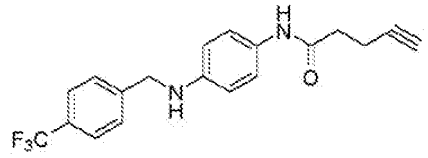
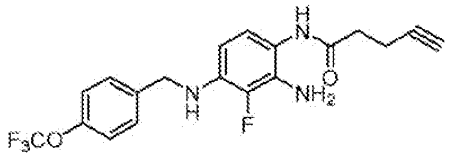
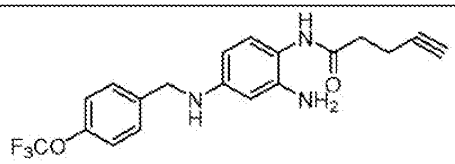
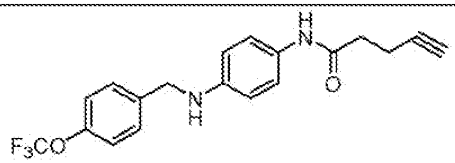
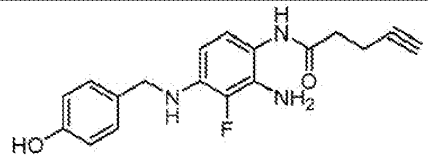
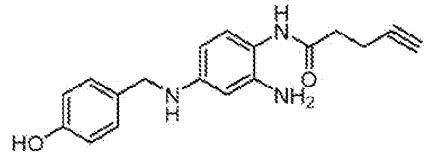
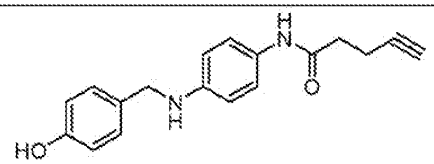
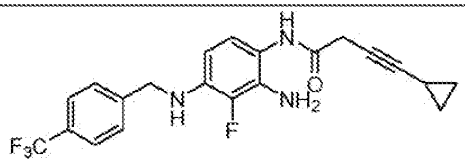
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	N-(4-((4-acetamidobenzyl)amino)phenyl)octanamide
	N-(4-((4-acetamidobenzyl)amino)-2-amino-3-fluorophenyl)decanamide
	N-(4-((4-acetamidobenzyl)amino)-2-aminophenyl)decanamide
	N-(4-((4-acetamidobenzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)phenethyl)amino)phenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)phenethyl)amino)phenyl)heptanamide
	N-(4-((4-(trifluoromethyl)phenethyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)phenethyl)amino)phenyl)octanamide
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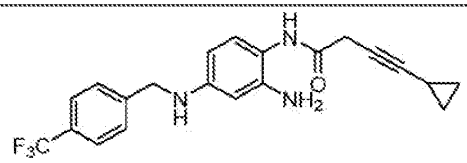
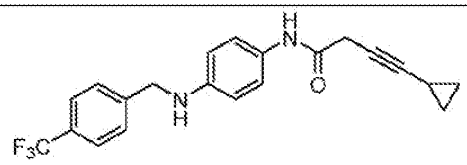
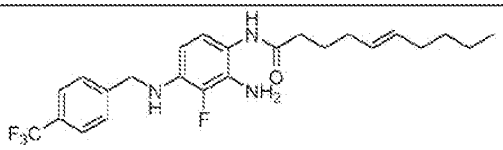
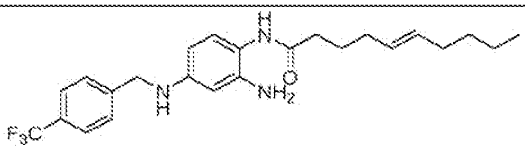
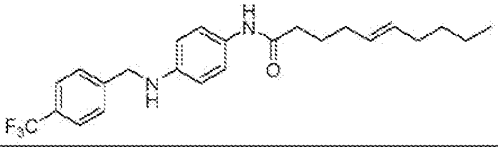
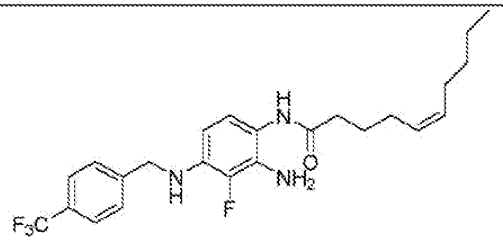
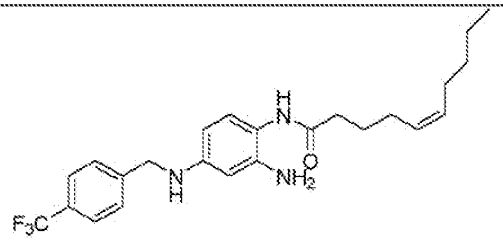
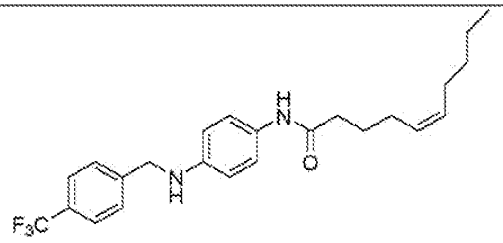
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)phenethyl)amino)phenyl)decanamide
	N-(2-amino-4-((4-(trifluoromethyl)phenethyl)amino)phenyl)decanamide
	N-(4-((4-(trifluoromethyl)phenethyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)heptanamide
	N-(2-amino-4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)heptanamide
	N-(4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)octanamide
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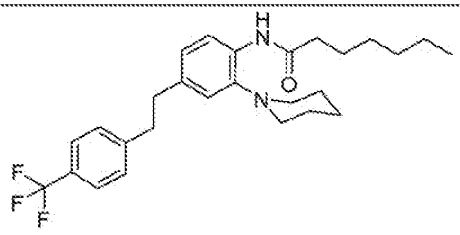
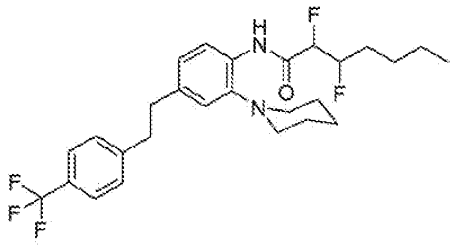
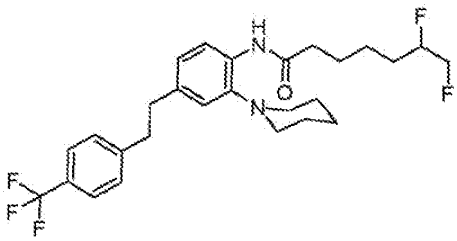
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	N-(2-amino-4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)decanamide
	N-(4-((3-(4-(trifluoromethyl)phenyl)propyl)amino)phenyl)decanamide
	4-cyclohexyl-N-(4-((4-(trifluoromethoxy)benzyl)amino)phenyl)butanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)-4-cyclohexylbutanamide
	N-(2-amino-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)-4-cyclohexylbutanamide
	4-cyclohexyl-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)butanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-4-cyclohexylbutanamide
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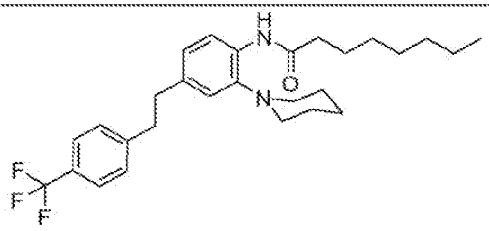
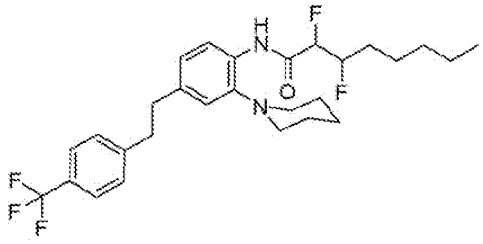
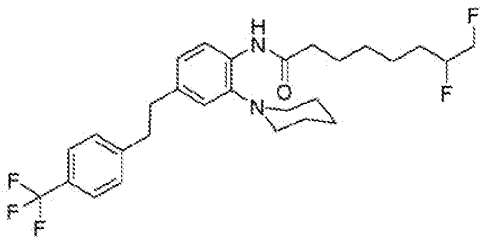
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7-phenylheptanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7-(4-fluorophenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7-(4-fluorophenyl)heptanamide
	7-(4-fluorophenyl)-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	7-amino-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	7-amino-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
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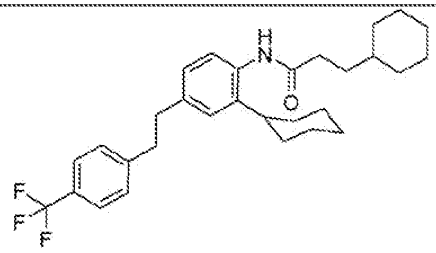
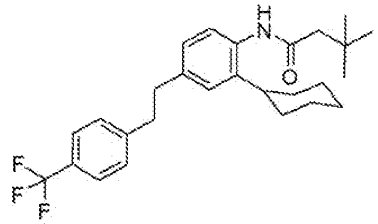
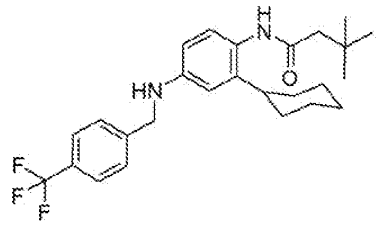
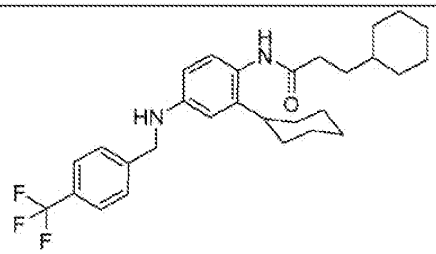
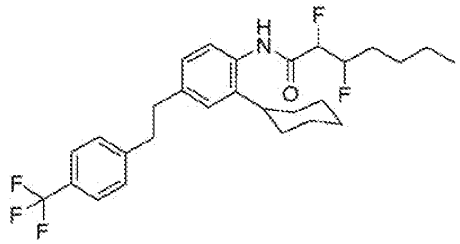
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	8-amino-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	10-amino-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
	10-amino-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
	10-amino-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)decanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7-(4-aminophenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7-(4-aminophenyl)heptanamide
	7-(4-aminophenyl)-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)pent-4-ynamide

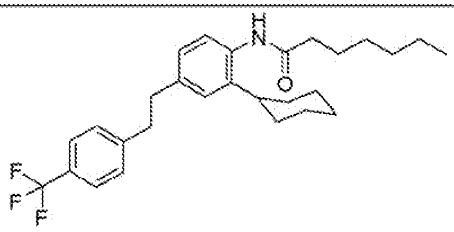
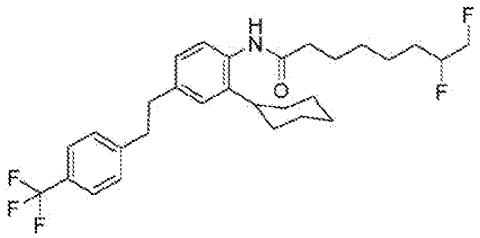
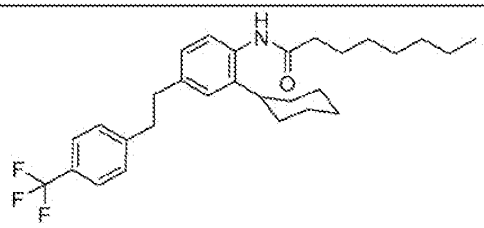
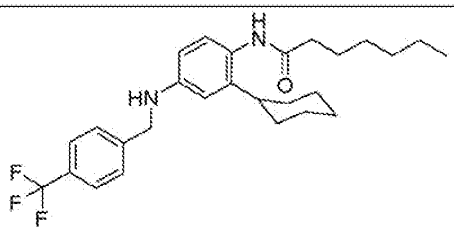
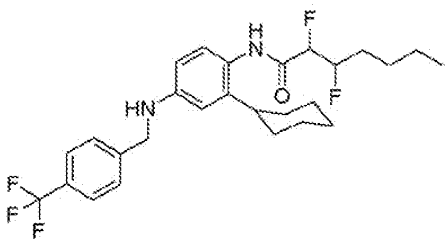
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	N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)pent-4-ynamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)pent-4-ynamide
	N-(2-amino-4-((4-(trifluoromethoxy)benzyl)amino)phenyl)pent-4-ynamide
	N-(4-((4-(trifluoromethoxy)benzyl)amino)phenyl)pent-4-ynamide
	N-(2-amino-3-fluoro-4-((4-hydroxybenzyl)amino)phenyl)pent-4-ynamide
	N-(2-amino-4-((4-hydroxybenzyl)amino)phenyl)pent-4-ynamide
	N-(4-((4-hydroxybenzyl)amino)phenyl)pent-4-ynamide
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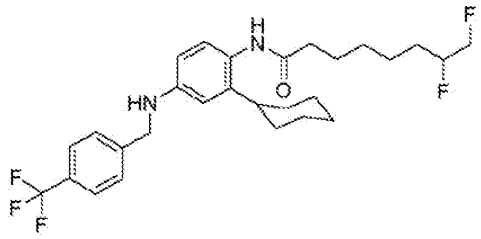
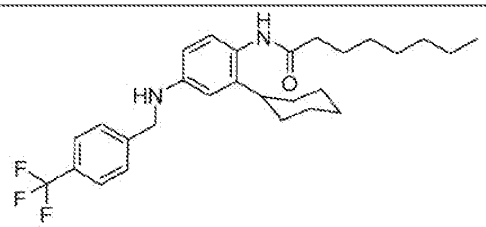
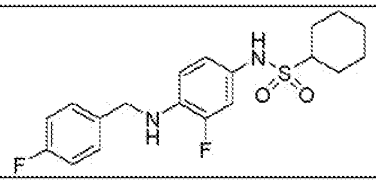
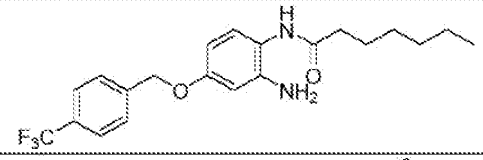
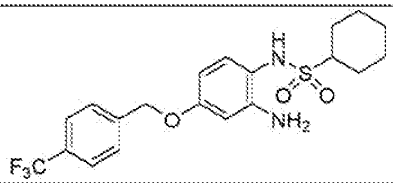
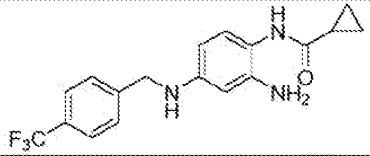
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	(E)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dec-5-enamide
	(E)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dec-5-enamide
	(E)-N-(4-((4-(trifluoromethyl)benzyl)amino)phenyl)dec-5-enamide
	(Z)-N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dec-5-enamide
	(Z)-N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)dec-5-enamide
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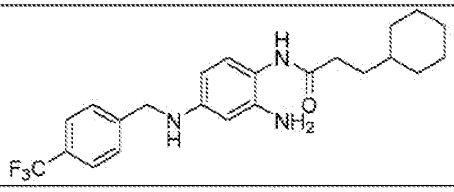
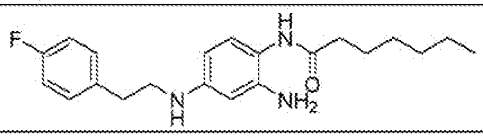
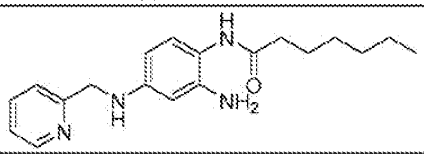
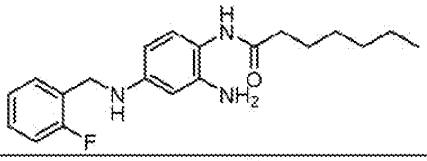
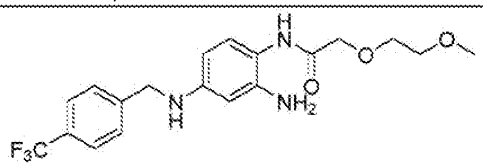
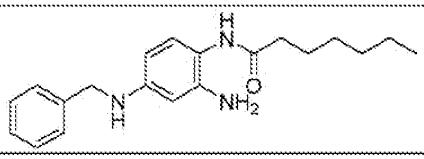
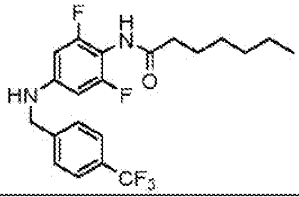
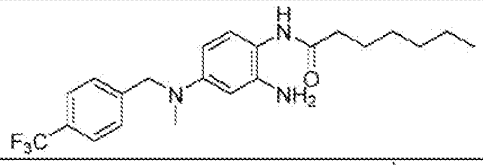
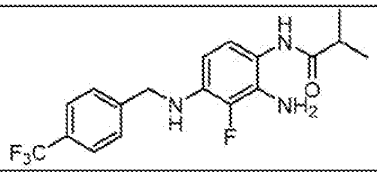
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	6,7-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)heptanamide (6R)-6,7-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)heptanamide (6S)-6,7-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)heptanamide

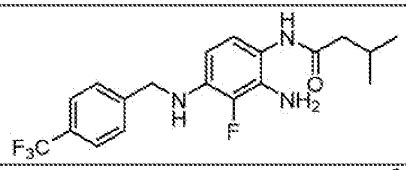
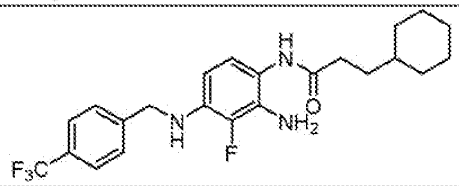
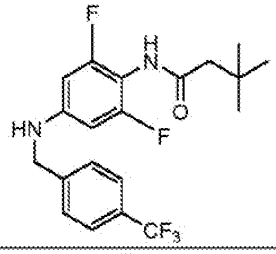
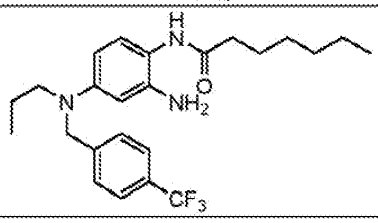
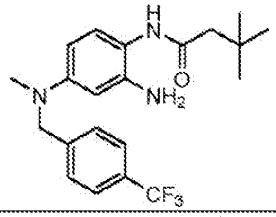
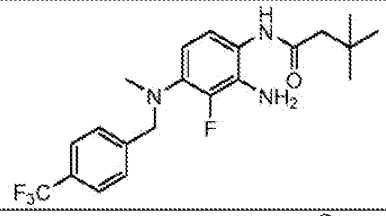
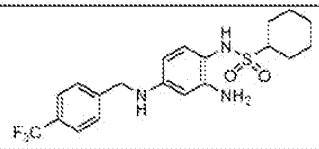
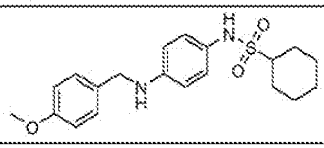
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	7,8-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)octanamide (7R)-7,8-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)octanamide (7S)-7,8-difluoro-N-(2-(piperidin-1-yl)-4-(4-(trifluoromethyl)phenethyl)phenyl)octanamide

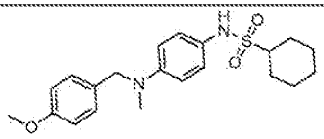
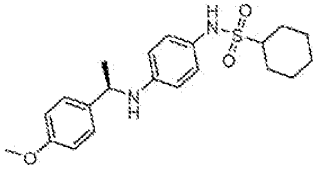
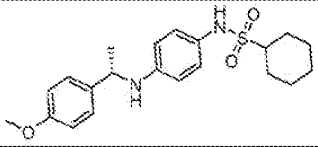
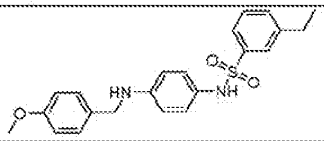
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	N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	3-cyclohexyl-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)propanamide
	N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluoroheptanamide (2R,3S)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluoroheptanamide (2S,3R)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluoroheptanamide (2R,3R)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluoroheptanamide

	(2S,3S)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-2,3-difluoroheptanamide
	N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)heptanamide
	N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide (7R)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide (7S)-N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)-7,8-difluorooctanamide
	N-(2-cyclohexyl-4-(4-(trifluoromethyl)phenethyl)phenyl)octanamide
	N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2R,3S)-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3R)-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide

	(2R,3R)-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide (2S,3S)-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2,3-difluoroheptanamide
	N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7R)-N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide (7S)- N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-7,8-difluorooctanamide
	N-(2-cyclohexyl-4-((4-(trifluoromethyl)benzyl)amino)phenyl)octanamide
	N-(3-fluoro-4-((4-fluorobenzyl)amino)phenyl)cyclohexanesulfonamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)cyclohexanesulfonamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)cyclopropanecarboxamide

	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3-cyclohexylpropanamide
	N-(2-amino-4-((4-fluorophenethyl)amino)phenyl)heptanamide
	N-(2-amino-4-((pyridin-2-ylmethyl)amino)phenyl)heptanamide
	N-(2-amino-4-((2-fluorobenzyl)amino)phenyl)heptanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-2-(2-methoxyethoxy)acetamide
	N-(2-amino-4-(benzylamino)phenyl)heptanamide
	N-(2,6-difluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-4-(methyl(4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)isobutyramide

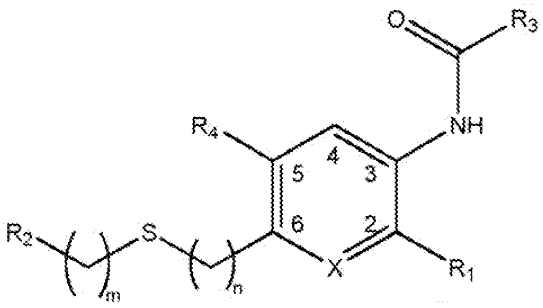
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	N-(2-amino-3-fluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3-cyclohexylpropanamide
	N-(2,6-difluoro-4-((4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-4-(propyl(4-(trifluoromethyl)benzyl)amino)phenyl)heptanamide
	N-(2-amino-4-(methyl(4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-3-fluoro-4-(methyl(4-(trifluoromethyl)benzyl)amino)phenyl)-3,3-dimethylbutanamide
	N-(2-amino-4-((4-(trifluoromethyl)benzyl)amino)phenyl)cyclohexanesulfonamide
	N-(4-((4-methoxybenzyl)amino)phenyl)cyclohexanesulfonamide

	N-(4-((4-methoxybenzyl)(methyl)amino)phenyl) cyclohexanesulfonamide
	(R)-N-(4-((1-(4-methoxyphenyl)ethyl)amino)phenyl) cyclohexanesulfonamide
	(S)-N-(4-((1-(4-methoxyphenyl)ethyl)amino)phenyl) cyclohexanesulfonamide
	3-ethyl-N-(4-((4-methoxybenzyl)amino)phenyl)benzenesulfonamide

Formula 56

[0655] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 56. Such compounds are described in International Publication No. WO2020016297A1, published January 23, 2020, and corresponding to International Application No. PCT/EP2019/069240 filed July 17, 2019; Patent Cooperation Treaty application No. PCT/EP2019/069240 published January 23, 2020, which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of Formula 56, this reference incorporated by reference herein controls.

[0656] In an embodiment, the Kv7 channel activator is a compound according to Formula 56:



Formula 56

,

wherein, R_1 is selected from a branched or unbranched C1 to C5 alkyl group and – $NR_{1a}R_{1b}$ group, where R_{1a} and R_{1b} are selected independently of one another from hydrogen atom and branched or unbranched C1 to C5 alkyl group or with one another and with the nitrogen atom the $NR_{1a}R_{1b}$ group form a C3 to

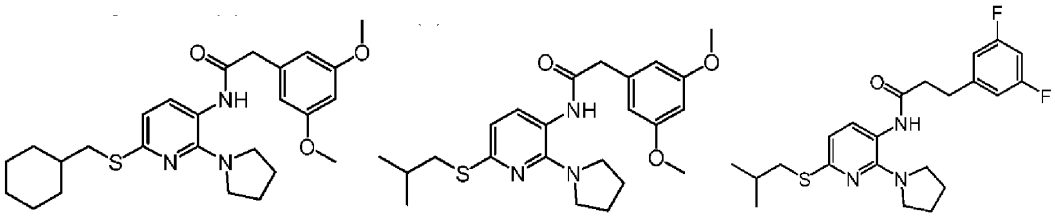
C9 heterocycloalkyl group, the C3 to C9 heterocycloalkyl group each having at least one substituent selected from the hydrogen atom and C1 to C3 alkyl group and optionally in addition to the nitrogen atom of the $NR_{1a}R_{1b}$ - Group has at least one further heteroatom in the cycle; $R_{2\,is}$ selected from the group consisting of branched or unbranched C1 to C10 alkyl group, C3 to C10 cycloalkyl group, C3 to C10 heterocycloalkyl group, at least one hetero atom being selected from nitrogen and oxygen atom, C6 to C12 aryl group; and C5 to C1 1 heteroaryl group, the C1 to C10 alkyl group, C3 to C10 cycloalkyl group, C3 to C10 heterocycloalkyl group, C6 to C12 aryl group, or C5 to C11 heteroaryl group in each case at least one further Substituents R_{2a} , wherein $R_{2a\,is}$ selected from the group consisting of hydrogen atom, halogen atom, branched or unbranched C1 to C3 alkyl group, branched or unbranched (per) halogenated C1 to C3 alkyl group and branched or unbranched C1 to C3 Alkoxy group, and wherein the C3 to C10 cycloalkyl group, C3 to C10 heterocycloalkyl group, C6 to C12 aryl group or C5 to C1 1 heteroaryl group comprises one or more ring systems which are condensed or separated; $R_{3\,is}$ selected from the group consisting of branched or unbranched C1 to C10 alkoxy group; branched or unbranched C1-C10 alkyl group and - $(CH_2)_p$ -C6 to C12 aryl group, which has at least one substituent selected from hydrogen atom, halogen atom and C1 to C3 alkoxy group and wherein the C6 to C12 aryl group has one or comprises several ring systems which are condensed or separated; $R_{4\,is}$ selected from hydrogen, halogen atom and branched or unbranched C1 -C5 alkyl group; X is a nitrogen atom or a -CH group; n is zero or an integer ranging from 1 to 3; m is zero or an integer ranging from 1 to 5; and p is zero or an integer ranging from 1 to 5.

[0657] In further embodiments, n is zero and / or m is 1 and / or X is a nitrogen atom.

[0658] In further embodiments, R_1 is selected from the group consisting of branched or unbranched C1- to C3-alkyl group and - $NR_{1a}R_{1b}$ group, wherein R_{1a} and R_{1b} are independently selected from hydrogen atom and branched or unbranched C1- to C3-alkyl group or with one another and form a C4 to C6 heterocycloalkyl group with the nitrogen atom of the $NR_{1a}R_{1b}$ group, the C4 to C6 heterocycloalkyl group each having at least one substituent selected from the hydrogen atom and C1 to C3 alkyl group and optionally in addition to the nitrogen atom of the $NR_{1a}R_{1b}$ group has at least one further oxygen atom in the cycle; and or $R_{2\,is}$ selected from the group consisting of mono- or difluorophenyl group; CF_3 phenyl group; F_5 S-phenyl group; C4 to C8 cycloalkyl group; branched or unbranched C1 to C5 alkyl group; Biphenyl group; Pyridine group; Piperidine group; Tetrahydropyran group; Dioxolane group and phenyl group, the phenyl group having at least one substituent R_{2a} selected from hydrogen atom and methoxy group; and or $R_{3\,is}$ selected from the group

consisting of ethoxy group, propyl group, tert-butyl group, - $(CH_2)_P$ -phenyl group, which has at least one substituent selected from hydrogen atom, halogen atom and methoxy group and where p is zero or is 1 or 2; and or $R_{4\,is}$ a hydrogen atom , a bromine atom or a methyl group.

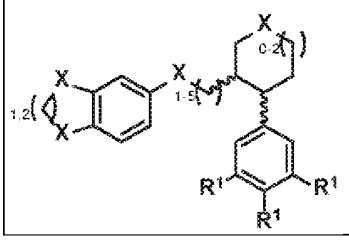
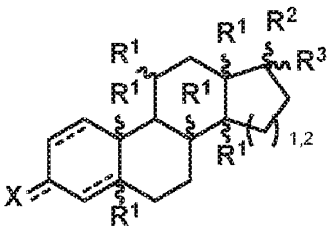
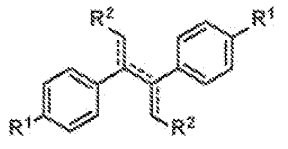
[0659] In further embodiments, the Kv7 channel activator is selected from the group consisting of:

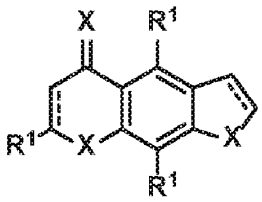
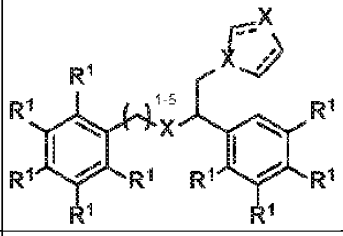
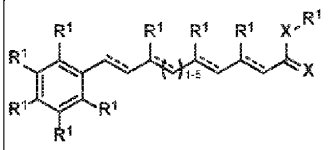
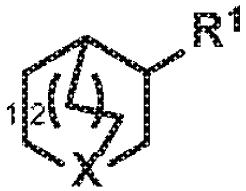
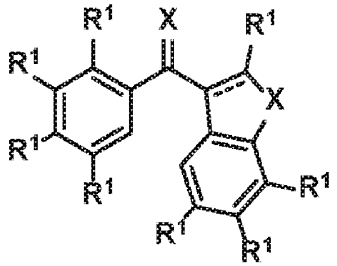
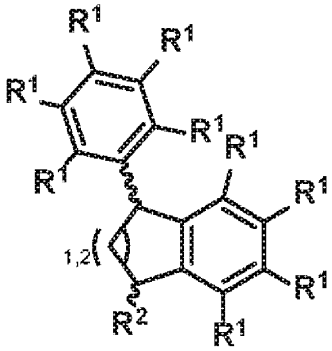
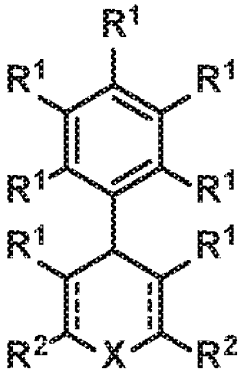
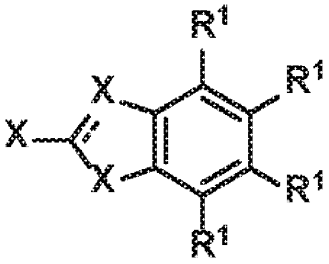
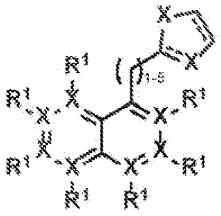


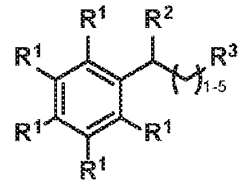
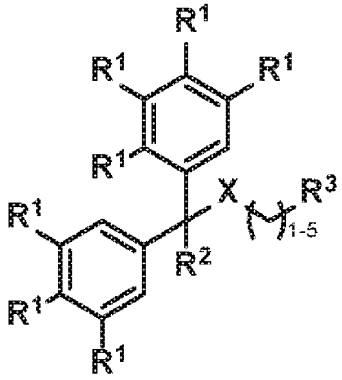
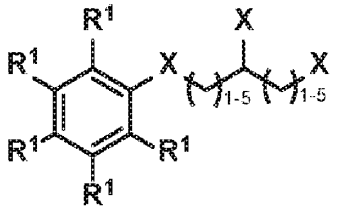
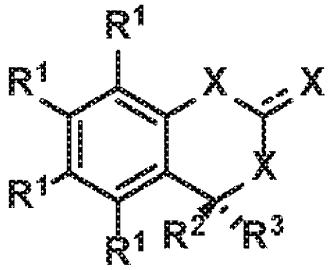
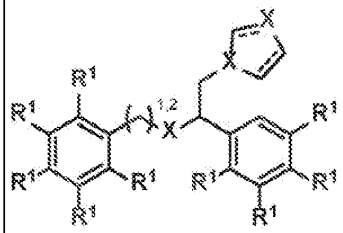
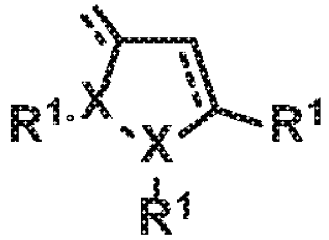
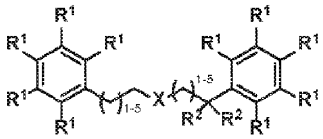
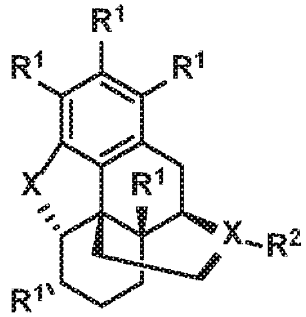
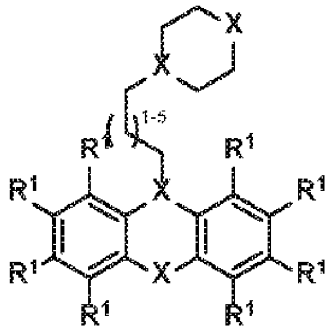
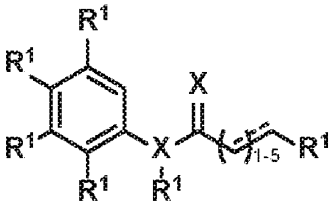
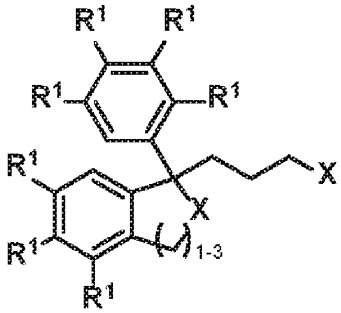
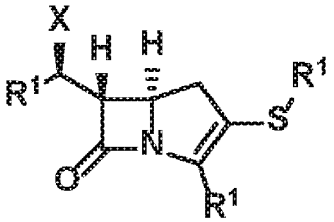
Formulas 57 – 139

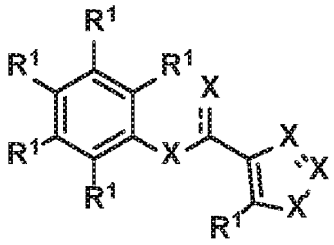
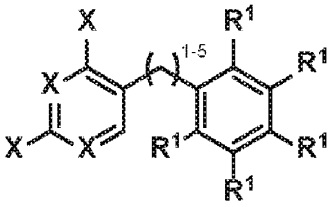
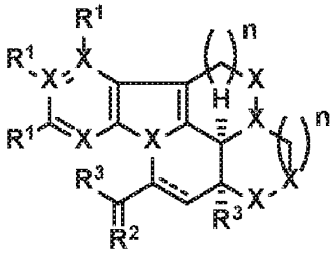
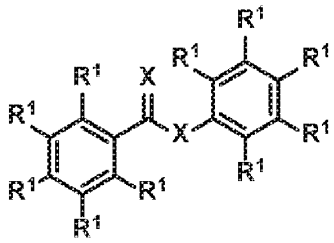
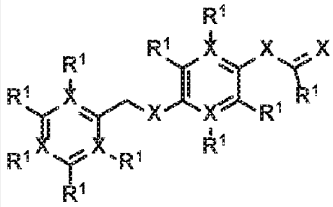
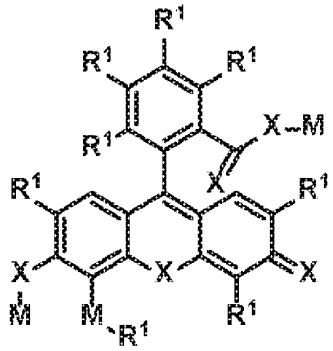
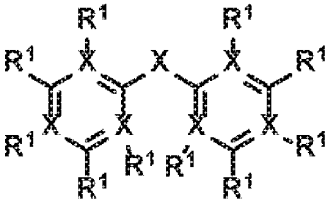
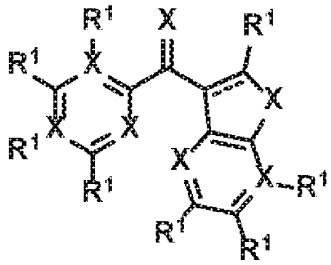
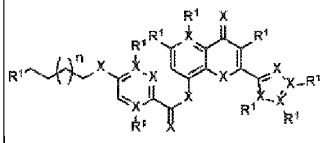
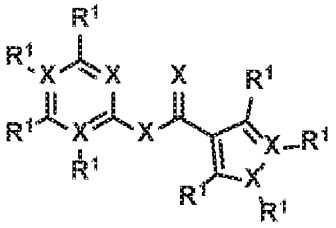
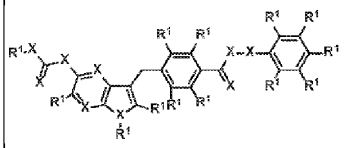
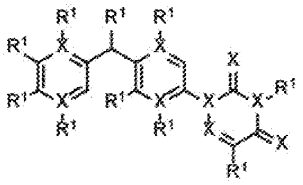
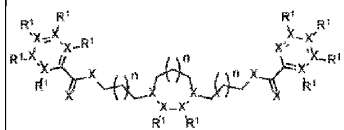
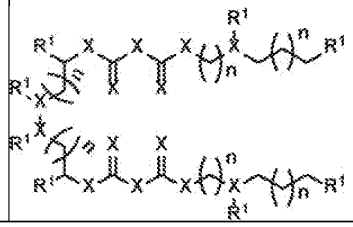
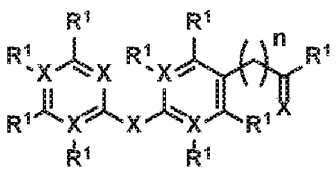
[0660] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds of formulas 57 - 139. Such compounds are described in International Publication No. WO2018204765A1, published November 8, 2018, and corresponding to International Application No. PCT/US2018/031057 filed May 4, 2018; which is incorporated by reference in its entirety herein. In the case of any conflict of terminology in the context of any of Formulas 57 - 139, this reference incorporated by reference herein controls.

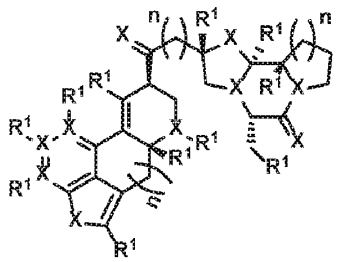
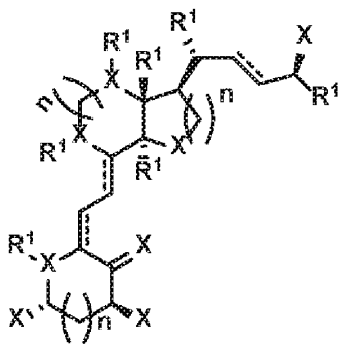
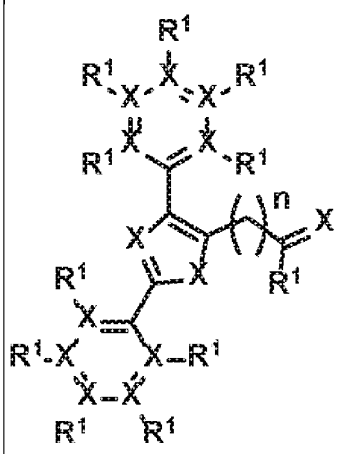
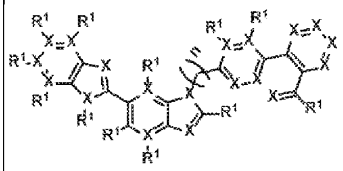
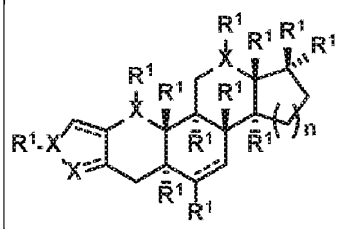
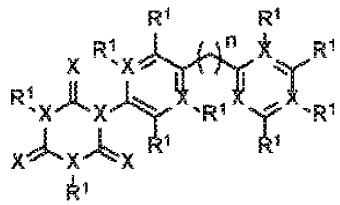
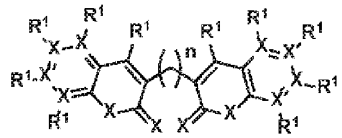
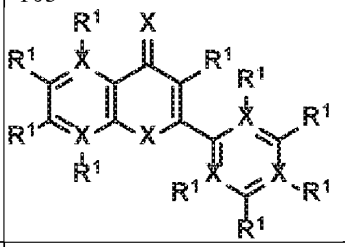
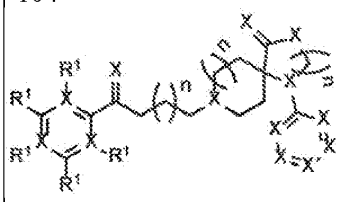
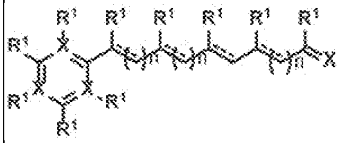
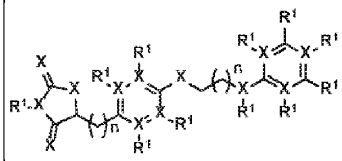
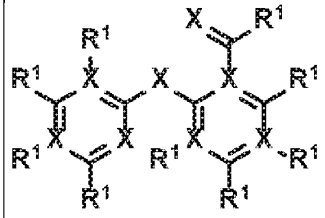
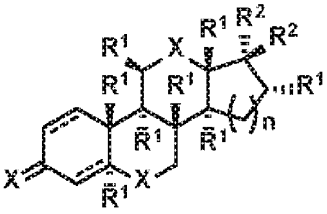
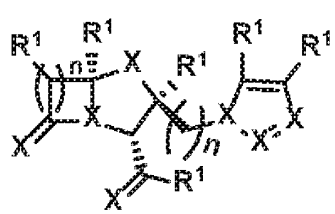
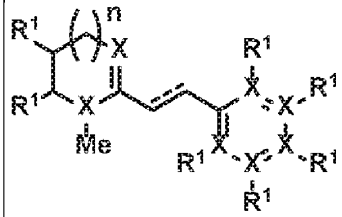
[0661] In an embodiment, the Kv7 channel activator is a compound according to any one of formulas 57 – 139:

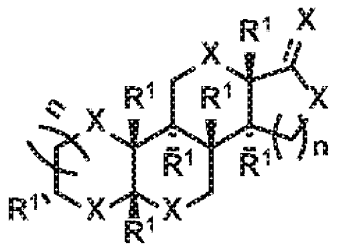
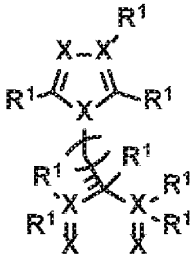
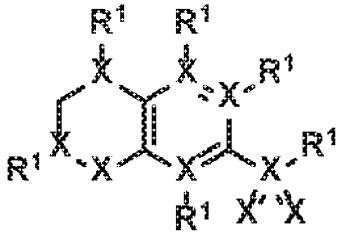
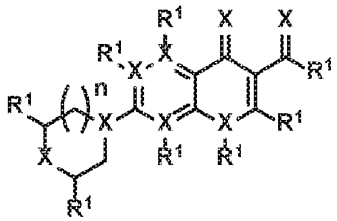
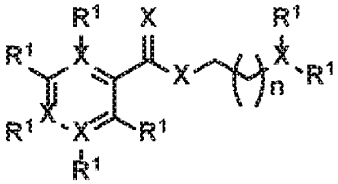
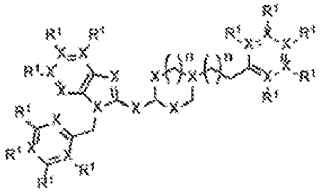
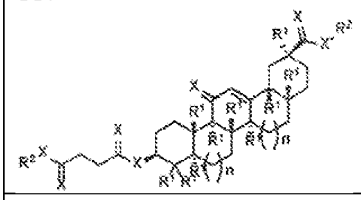
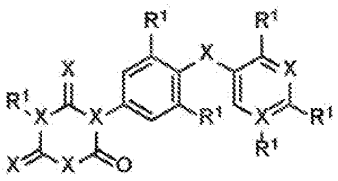
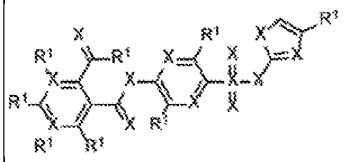
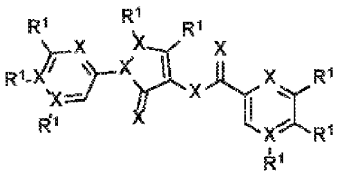
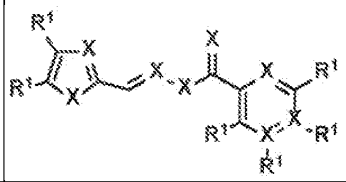
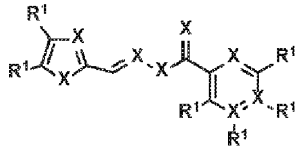
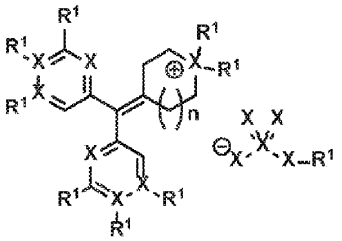
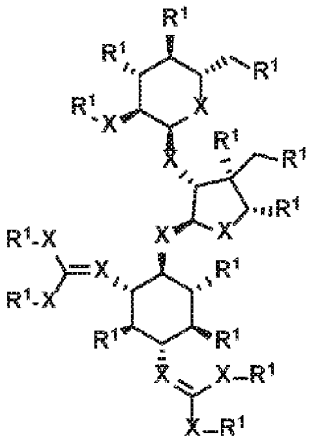
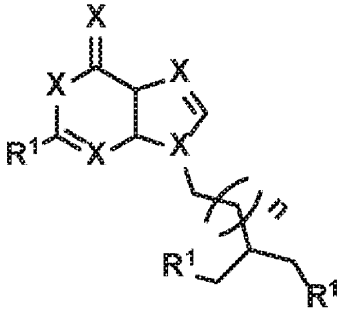
57	58	59
		

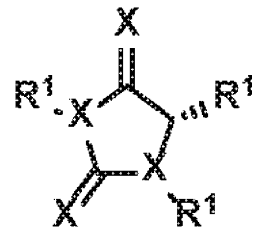
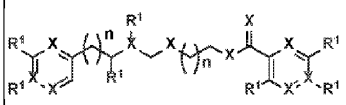
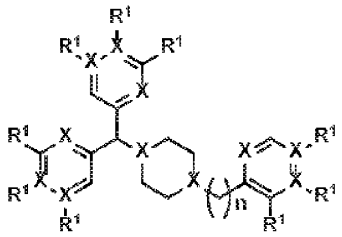
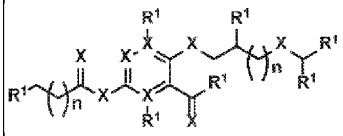
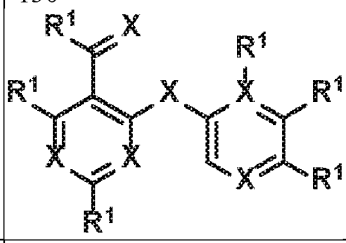
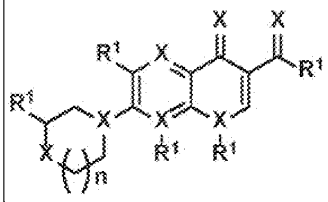
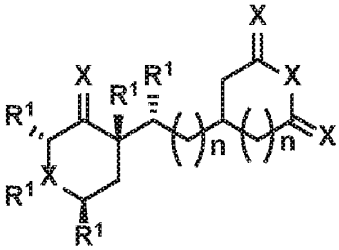
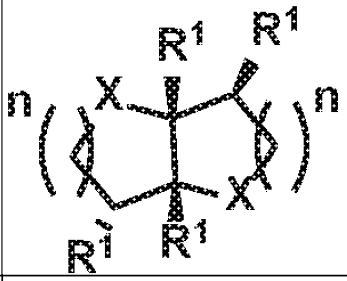
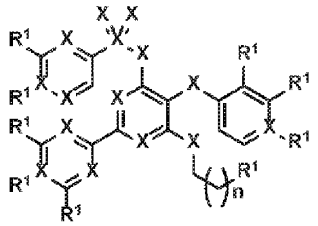
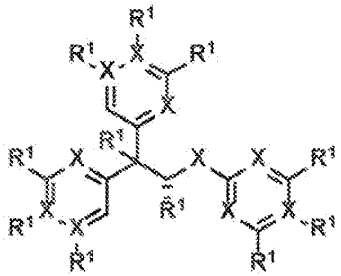
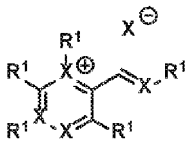
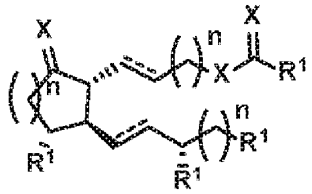
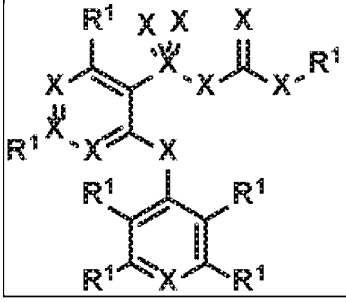
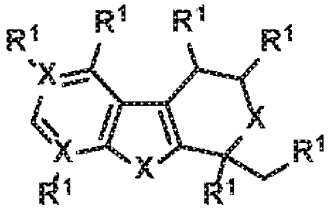
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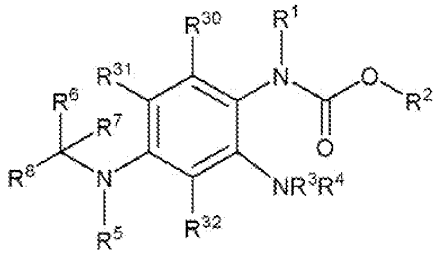
126 	127 	128 
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135 	136 	137 
138 	139 	

wherein (for any of compounds 57 – 139), each and any of $R^{1,}$ $R^{2,}$ and R^3 independently = H, CI, Br, F, I, OH, OAc, CF3, NH2, CN, OC_{1-6} saturated, unsaturated alkyl, cycloalkyl, cycloheteroalkyl, or aryl, SC_{1-6} saturated, unsaturated alkyl, cycloalkyl, cycloheteroalkyl, or aryl, C_{1-6} saturated alkyl, unsaturated alkyl, cycloalkyl, cycloheteroalkyl, CO2H, COC1-8 alkyl unsaturated alkyl, or aryl, $C02C_{1-6}$ saturated, unsaturated alkyl, or aryl, CONH2, $C02NHC_{1-6}$ saturated, unsaturated alkyl or aryl, $C02N(C_{1-6}$ saturated, unsaturated alkyl or aryl)2, NHC_{1-6} saturated, unsaturated alkyl, or cycloalkyl, $N(C_{1-6}$ saturated, unsaturated alkyl, or cycloalkyl)2, or C_{5-7}aryl or heteroaryl; and wherein each X = independently C, CH, CH2, S, SO, SO2, NH, NC_{1-6}saturated, unsaturated alkyl, or cycloalkyl, or O, and wherein each n, where present, is independently = 0-6.

Formula 140

[0662] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 140. Such compounds are described in International Publication No. WO2016077724A1, published May 19, 2016, and corresponding to International Application No. PCT/US2015/060627 filed November 13, 2015; US Patent No. 10,526,280, issued January 7, 2020 and corresponding to US Application No. US10526280B2 filed November 11, 2015; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 140, this reference incorporated by reference herein controls.

[0663] In an embodiment, the Kv7 channel activator is a compound according to Formula 140:



Formula 140

,

wherein, R^1 is H or optionally-substituted alkyl;R^2 is optionally-substituted alkyl;R^3 and R^4 are each independently H or optionally-substituted alkyl;R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl;R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl, or R^6 and R^7 together form a carbocycle;R^8 is optionally-substituted thiazolyl, optionally-substituted thiophenyl, or substituted phenyl, provided that if R^8 is 4-halophenyl, then R^2 is substituted alkyl or branched alkyl or at least one of R^6 or R^7 is not H;

andR^{30}, R^{31} and R^{32} are each independently H, deuterium, halogen, substituted sulfanyl, or optionally-substituted alkoxy.

[0664] In further embodiments, R^1 is H.

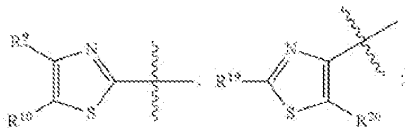
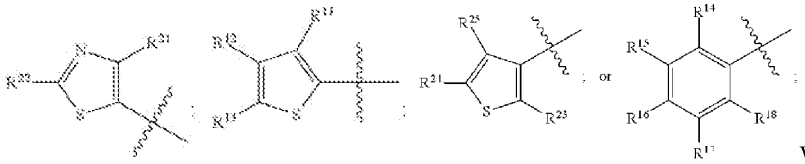
[0665] In further embodiments, R^2 is C_1-C_6 alkyl.

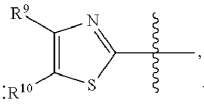
[0666] In further embodiments, R^2 is carbocyclic-substituted alkyl or heterocyclic-substituted alkyl.

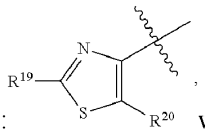
[0667] In further embodiments, R^3 and R^4 are each H.

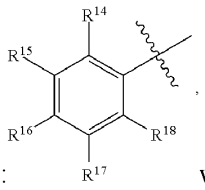
[0668] In further embodiments, R^5 is H.

[0669] In further embodiments, R^6 and R^7 are both H; R^6 and R^7 are both deuterium; R^6 and R^7 together form a cycloalkyl; or at least one of R^6 or R^7 is a substituted alkyl.

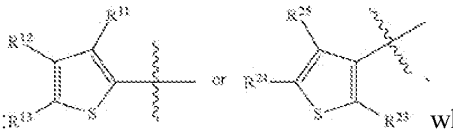
[0670] In further embodiments, R^8 is selected from:   wherein R^9-R^{25} are each independently H, halogen, optionally-substituted sulfanyl, or optionally-substituted alkyl.

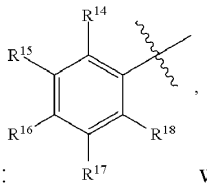
[0671] In further embodiments, R^8 is:  wherein at least one of R^9 or R^{10} is halogen.

[0672] In further embodiments, R^8 is:  wherein at least one of R^{19} or R^{20} is halogen.

[0673] In further embodiments, R^8 is:  wherein at least one of R^{14}-R^{18} is substituted sulfanyl or haloalkyl; or wherein R^{16} is F.

[0674] In further embodiments, at least one of R^{14}-R^{18} is —SF_5 or CF_3.

[0675] In further embodiments, R^8 is:  wherein at least one of R^{11}-R^{13} or R^{23}-R^{25} is substituted sulfanyl.



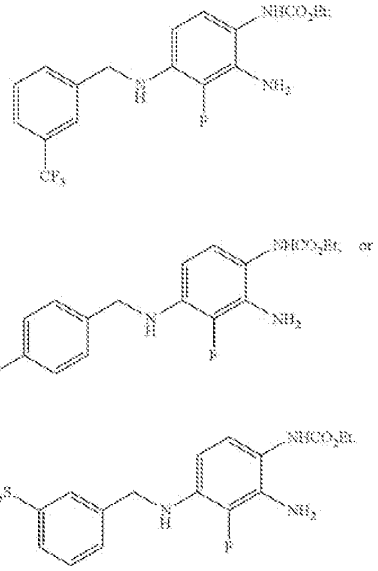
[0676] In further embodiments, R^8 is: wherein at least one of R^{14}-R^{18} is halo-substituted sulfanyl, haloalkyl or halogen.

[0677] In further embodiments, at least one of R^{14}-R^{18} is —SF_5 or —CF_3.

[0678] In further embodiments, R^{15}, R^{16}, or R^{17} is —SF_5 or —CF_3.

[0679] In further embodiments, R^{32} is —F, and $R^{30}$and R^{31} are each H.

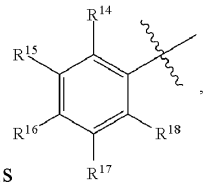
[0680] In further embodiments, the Kv7 Channel activator is selected from the group consisting of:



[0681] In further embodiments, the compound is according to formula 141 wherein: R^1 is H or optionally-substituted alkyl; R^2 is substituted alkyl having one or more hydrogen atoms substituted with a substituent selected from halogen, cycloalkyl, alkoxy, amino, hydroxyl, aryl, alkenyl, or carboxyl; R^3 and R^4 are each independently H or optionally-substituted alkyl; R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl; R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl, or R^6 and R^7 together form a carbocycle; R^8 is optionally-substituted thiazolyl, optionally-substituted thiophenyl, or

substituted phenyl; andR^{30}, R^{31} and R^{32} are each independently H, deuterium, halogen, substituted sulfanyl, or optionally-substituted alkoxy.

[0682] In further embodiments, the compound is according to formula 141 wherein: R^1 is H or optionally-substituted alkyl; R^2 is optionally-substituted alkyl; R^3 and R^4 are each independently H or optionally-substituted alkyl; R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl; R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl, or R^6 and R^7 together form a carbocycle, provided at least one R^6 or R^7 is not H; R^8 is optionally-substituted thiazolyl, optionally-substituted thiophenyl, or substituted phenyl, provided that if R^8 is 4-halophenyl, then R^2 is substituted alkyl or branched alkyl or at least one of R^6 or R^7 is not H; andR^{30}, R^{31} and R^{32} are each independently H, deuterium, halogen, substituted sulfanyl, or optionally-substituted alkoxy.

[0683] In further embodiments, the compound is according to formula 141 wherein: R^1 is H or optionally-substituted alkyl;R^2 is optionally-substituted alkyl;R^3 and R^4 are each independently H or optionally-substituted alkyl;R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl;R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl, or R^6 and R^7 together form a carbocycle;R^8 is  wherein at least one of R^{14}-R^{18} is substituted sulfanyl or haloalkyl; andR^3 and R^{31} are each independently H, deuterium, halogen, substituted sulfanyl, or optionally-substituted alkoxy; andR^{32} is deuterium, halogen, substituted sulfanyl, or optionally-substituted alkoxy.

[0684] In further embodiments, R^{32} is halogen.

[0685] In further embodiments, R^{32} is —F.

[0686] In further embodiments, at least one of R^{14}-R^{18} is halo-substituted sulfanyl.

[0687] In further embodiments, at least one of R^{14}-R^{18} is haloalkyl.

[0688] In further embodiments, at least one of R^{14}-R^{18} is —SF_5.

[0689] In further embodiments, at least one of R^{14}-R^{18} is —CF_3.

[0690] In further embodiments, R^{16} is —SF_5.

[0691] In further embodiments, R^{16} is —CF_3.

[0692] In further embodiments, R^2 is alkyl.

[0693] In further embodiments, R^2 is C_1-C_6 alkyl.

[0694] In further embodiments, R^2 is ethyl.

[0695] In further embodiments, R^3, R^4, R^5, R^6, and R^7 are each H.

[0696] In further embodiments, R^{32} is —F and R^{16} is —CF_3.

[0697] In further embodiments, R^2 is alkyl.

[0698] In further embodiments, $R^3$and R^{31} are each H.

[0699] In further embodiments, R^{15}, R^{16}, or R^{17} is —SF_5 or —CF_3.

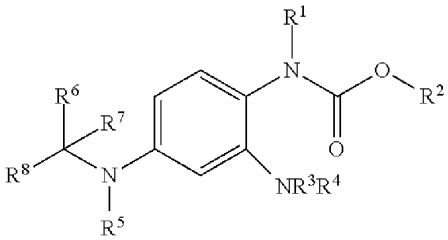
[0700] In further embodiments, R^1, R^1, R^3, R^4, R^5, R^6, and R^7 are each H; R^2 is alkyl; and R^{32} is —F.

Formula 141

[0701] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 141. Such compounds are described in International Publication No. WO2016077724A1, published May 19, 2016, and corresponding to International Application No. PCT/US2015/060627 filed November 13, 2015; US Patent No. 10,526,280, issued January 7, 2020, and corresponding to US Application No. US10526280B2 filed November 11, 2015; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 141, these references incorporated by reference herein control.

[0702] In an embodiment, the Kv7 channel activator is a compound according to Formula 141:

Formula 141



,

wherein, R^1 is H or optionally-substituted alkyl; R^2 is optionally-substituted alkyl; R^3 and R^4 are each independently H or optionally-substituted alkyl; R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl; R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl, or R^6 and R^7 together form a carbocycle; andR^8 is optionally-substituted thiazolyl.

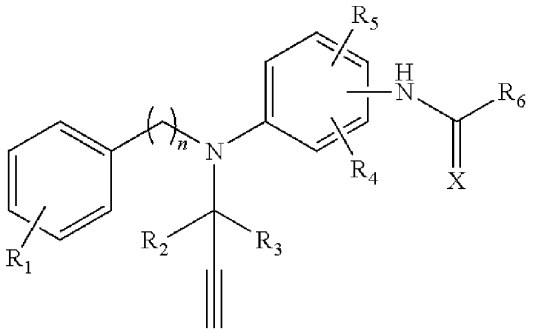
[0703] In further embodiments, the compound is according to formula 142 wherein: R^1 is H or optionally-substituted alkyl; R^2 is optionally-substituted alkyl; R^3 and R^4 are each independently H or optionally-substituted alkyl; R^5 is H, optionally-substituted alkyl, acyl, or alkoxycarbonyl; R^6 and R^7 are each independently H, deuterium, optionally-substituted alkyl,

or R^6 and R^7 together form a carbocycle; and R^8 is substituted thiophenyl, wherein at least one substituent on the thiophenyl is halo-substituted sulfanyl.

Formula 142

[0704] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 142. Such compounds are described in US Patent No. 10,077,245, issued September 18, 2018, and corresponding to US Application No. 15/306,971 filed April 22, 2015; US Patent No. 10,316,008, issued June 11, 2019 and corresponding to US Application No. 15/870,276 filed January 12, 2018; international Publication No. WO2015165352A1, published November 5, 2015 and corresponding to International Application No. PCT/CN2015/077216 filed April 22, 2015; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 142, these references incorporated by reference herein control.

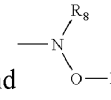
[0705] In an embodiment, the Kv7 channel activator is a compound according to Formula 142:



Formula 142

,

wherein, X is selected from a group consisting of oxygen and sulfur; n is 1, 2 or 3;R_1 is H or halogen;R_2 and R_3 are each independently selected from a group consisting of H, D and C_1-C_3 alkyl; or R_2 and R_3 together with the carbon atom to which they attached form C_3-C_6 saturated ring;R_4 and R_5 are each independently selected from a group consisting of H; halogen; C_1-C_6 alkyl; C_3-C_6 cycloalkyl; cyano; alkoxyl; C_1-C_6 alkyl substituted by hydroxy, amino, C_1-C_4 alkoxy, C_1-C_4 alkylcarbonyl, or halogen; C_1-C_4 alkoxy substituted by halogen; C_1-C_6 alkylcarbonyl; C_1-C_6 alkoxycarbonyl; C_1-C_6 alkylaminocarbonyl; C_2-C_6 alkenyl; and C_2-C_6 alkynyl; provided that R_4 and R_5 are not simultaneously hydrogen; R_6 is selected from a group consisting of C_1-C_6 alkoxy; C_1-C_6 alkylamino; C_1-C_6 alkyl; C_3-C_6 cycloalkyl; C_2-C_6 alkenyl; C_2-C_6 alkynyl; C_6-C_{10} aryl; C_1-C_6 alkyl substituted by halogen, cyano, hydroxy, C_1-C_6 alkoxyl, di(C_1-C_4 alkyl) amino, C_1-C_6 alkylcarbonyl, C_1-C_6 alkylcarbonylamino, or C_1-

C_6 alkoxycarbonyl; C_3-C_6 cycloalkyl substituted by halogen; C_2-C_6 alkenyl substituted by halogen; C_2-C_6 alkynyl substituted by halogen; tetrahydrofuranyl; and  wherein, R_7 and R_8 are each independently selected from a group consisting of C_1-C_4 alkyl.

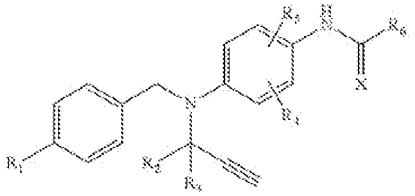
[0706] In further embodiments, R_1 is H or fluorine; R_2 and R_3 are each independently selected from a group consisting of H and D, or R_2 and R_3 together with the carbon atom to which they attached form cyclopropyl; one of R_4 and R_5 is C_1-C_4 alkyl, and the other is H or C_1-C_4 alkyl.

[0707] In further embodiments, one of R_4 and R_5 is methyl, and the other is H or methyl.

Formula 143

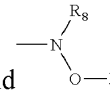
[0708] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 143. Such compounds are described in US Patent No. 10,077,245, issued September 18, 2018, and corresponding to US Application No. 15/306,971 filed April 22, 2015; US Patent No. 10,316,008, issued June 11, 2019 and corresponding to US Application No. 15/870,276 filed January 12, 2018; international Publication No. WO2015165352A1, published November 5, 2015, and corresponding to International Application No. PCT/CN2015/077216 filed April 22, 2015; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 143, these references incorporated by reference herein control.

[0709] In an embodiment, the Kv7 channel activator is a compound according to Formula 143:

 **Formula 143**

,

wherein, X: is selected from a group consisting of oxygen and sulfur;R_1 is H or halogen;R_2 and R_3 are each independently selected from a group consisting of H, D and C_1-C_3 alkyl; or R_2 and R_3 together with the carbon atom to which they attached form C_3-C_6 saturated ring;R_4 and R_5 are each independently selected from a group consisting of H; halogen; C_1-C_6 alkyl; C_3-C_6 cycloalkyl; cyano; C_1-C_4 alkoxyl; C_1-C_6 alkyl substituted by hydroxy, amino, C_1-C_4 alkoxy, C_1-C_4 alkylcarbonyl, or halogen; C_1-C_4 alkoxy substituted by halogen; C_1-C_6 alkylcarbonyl; C_1-C_6 alkoxycarbonyl; C_1-C_6 alkylaminocarbonyl; C_2-C_6 alkenyl; and C_2-C_6 alkynyl; provided that R_4 and R_5 are not simultaneously hydrogen;R_6 is

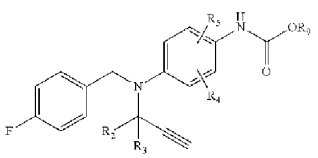
selected from a group consisting of C_1-C_6 alkoxy; C_1-C_6 alkylamino; C_1-C_6 alkyl; C_3-C_6 cycloalkyl; C_2-C_6 alkenyl; C_2-C_6 alkynyl; C_6-C_{10} aryl; C_1-C_6 alkyl substituted by halogen, cyano, hydroxy, C_1-C_6 alkoxyl, di(C_1-C_4 alkyl) amino, C_1-C_6 alkylcarbonyl, C_1-C_6 alkylcarbonylamino, or C_1-C_6 alkoxycarbonyl; C_3-C_6 cycloalkyl substituted by halogen; C_2-C_6 alkenyl substituted by halogen; C_2-C_6 alkynyl substituted by halogen; tetrahydrofuranyl; and  wherein, R_7 and R_8 are each independently selected from a group consisting of C_1-C_4 alkyl.

[0710] In further embodiments, R_1 is H or fluorine; R_2 and R_3 are each independently selected from a group consisting of H and D, or R_2 and R_3 together with the carbon atom to which they attached form cyclopropyl; one of R_4 and R_5 is C_1-C_4 alkyl, and the other is H or C_1-C_4 alkyl.

Formula 144 - 146

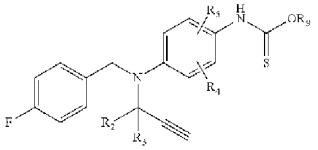
[0711] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to any one of Formulas 144 - 146. Such compounds are described in US Patent No. 10,077,245, issued September 18, 2018, and corresponding to US Application No. 15/306,971 filed April 22, 2015; US Patent No. 10,316,008, issued June 11, 2019, and corresponding to US Application No. 15/870,276 filed January 12, 2018; international Publication No. WO2015165352A1, published November 5, 2015, and corresponding to International Application No. PCT/CN2015/077216 filed April 22, 2015; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formulas 144 - 146, these references incorporated by reference herein control.

[0712] In an embodiment, the Kv7 channel activator is a compound according to a formula from the group consisting of 144, 145, and 146:



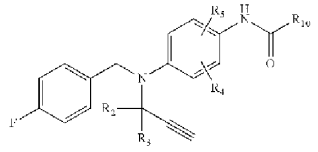
Formula 144

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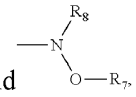
Formula 145

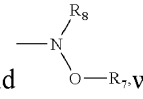
, or

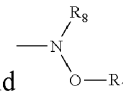


Formula 146

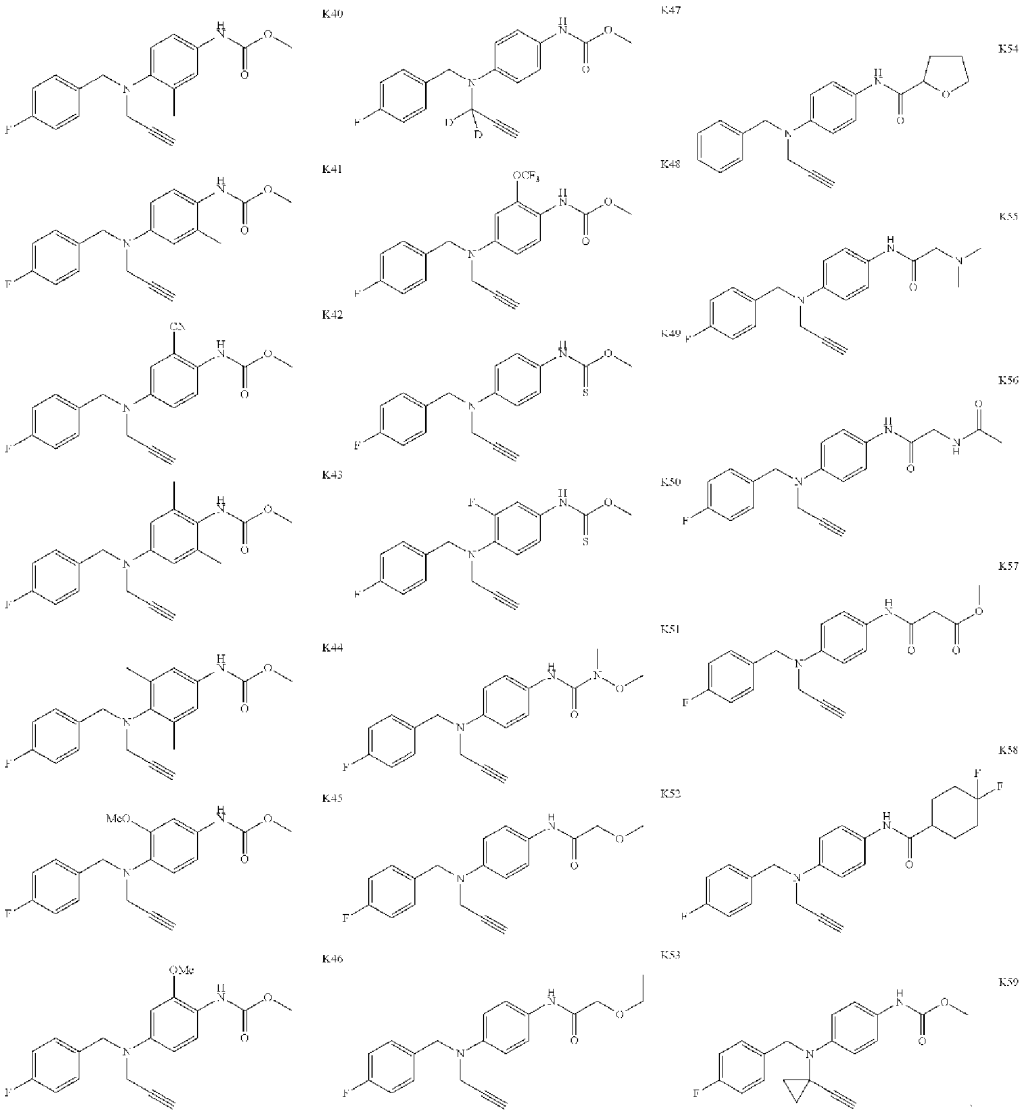
,

wherein, R_2 and R_3 are each independently selected from a group consisting of H, D and C_1-C_3 alkyl; or R_2 and R_3 together with the carbon atom to which they attached form C_3-C_6 saturated ring;R_4 and R_5 are each independently selected from a group consisting of H; C_1-C_6 alkyl; C_1-C_4 alkoxyl; C_1-C_6 alkyl substituted by halogen; C_1-C_4 alkoxy substituted by halogen; provided that R_4 and R_5 are not simultaneously hydrogen;R_9 is selected from a group consisting of C_1-C_6 alkyl and C_3-C_6 cycloalkyl;R_{10} is selected from a group consisting of C_1-C_6 alkyl; C_1-C_6 alkyl substituted by halogen, cyano, hydroxy, C_1-C_6 alkoxyl, di(C_1-C_4 alkyl)amino, C_1-C_6 alkylcarbonyl, C_1-C_6 alkylamido, or C_1-C_6 alkoxycarbonyl; C_3-C_6 cycloalkyl; and C_3-C_6 cycloalkyl substituted by halogen; tetrahydrofuranyl; and  wherein, R_7 and R_8 are each independently selected from a group consisting of C_1-C_4 alkyl.

[0713] In further embodiments, R_2 and R_3 are each independently selected from a group consisting of H and D, or R_2 and R_3 together with the carbon atom to which they attached form cyclopropyl; one of R_4 and R_5 is C_1-C_1 alkyl, and the other is H or C_1-C_4 alkyl;R_9 is selected from a group consisting of C_1-C_6 alkyl and C_3-C_6 cycloalkyl;R_{10} is selected from a group consisting of C_1-C_6 alkyl; C_1-C_6 alkyl substituted by halogen, cyano, hydroxy, C_1-C_6 alkoxyl, di(C_1-C_4 alkyl)amino, C_1-C_6 alkylcarbonyl, C_1-C_6 alkylamido, or C_1-C_6 alkoxycarbonyl; C_3-C_6 cycloalkyl; C_3-C_6 cycloalkyl substituted by halogen; tetrahydrofuranyl; and  wherein, R_7 and R_8 are each independently selected from a group consisting of C_1-C_4 alkyl.

[0714] In further embodiments, R_9 is selected from a group consisting of methyl, ethyl and propyl;R_{10} is selected from a group consisting of C_1-C_3 alkyl; C_1-C_3 alkyl substituted by halogen, cyano, hydroxy, C_1-C_3 alkoxyl, di(C_1-C_3 alkyl)amino, C_1-C_3 alkylcarbonyl, C_1-C_3 alkylamido, or C_1-C_3 alkoxycarbonyl; C_3-C_6 cycloakyl; C_3-C_6 cycloakyl substituted by halogen; tetrahydrofuranyl; and  wherein, R_7 and R_8 are each independently selected from a group consisting of C_1-C_3 alkyl.

[0715] In further embodiments, the Kv7 Channel activator is selected from the group consisting of:

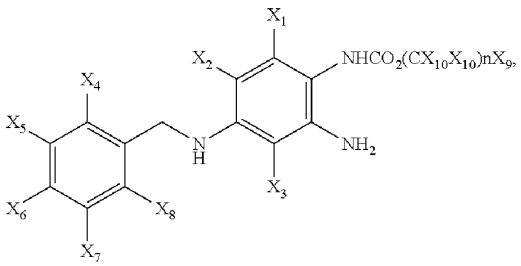


Formula 147

[0716] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 147. Such compounds are described in International Publication No. WO2013165575A1, published November 7, 2013, and corresponding to International Application No. PCT/US2013/030984 filed March 13, 2013; US Patent No. 9,556,114 issued January 31, 2017, and corresponding to US Application No. 14/566,167 filed December 10, 2014; US Publication No. US20170096390A1, published April 6, 2017, and corresponding to US Application No. 15/380,216 filed December 15, 2016; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 147, these references incorporated by reference herein control.

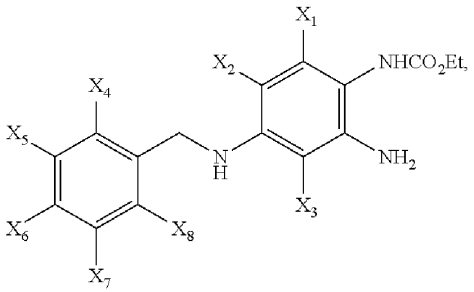
[0717] In an embodiment, the Kv7 channel activator is a compound according to Formula 147:

Formula 147



or a pharmaceutically acceptable salt or solvate thereof, wherein: X_1, X_2, X_3, X_4, X_5, X_6, X_7, and X_8 are each independently selected from hydrogen, deuterium, and F; X_9 and X_{10} are each independently selected from hydrogen and deuterium; and n is 1, 2, or 3, wherein at least one of X_1, X_2, and X_3 is F.

[0718] In further embodiments, the Kv7 channel activator is:

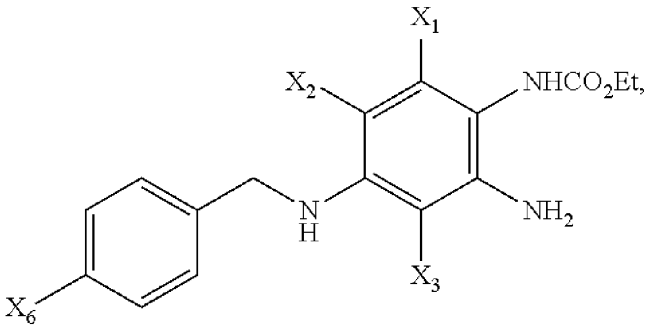


wherein, A is N or C—X_3; X_1, X_2, X_3, X_4, X_5, X_6, X_7, and X_8 are each independently selected from hydrogen, 19F and 18F; and n is 2 or 3, provided that one of X_1, X_2, X_3, X_4, X_5, X_6, X_7, and X_8 is 18F.

[0719] In further embodiments, two of X_1, X_2, X_3, X_4, X_5, X_6, X_7 and X_8 are F.

[0720] In further embodiments, three of X_1, X_2, X_3, X_4, X_5, X_6, X_7 and X_8 are F.

[0721] In further embodiments, the Kv7 channel activator is:



wherein, X_1, X_2, X_3, and X_6 are each independently selected from hydrogen, 18F, and 19F, provided that one of X_1, X_2, X_3, and X_6 is 18F.

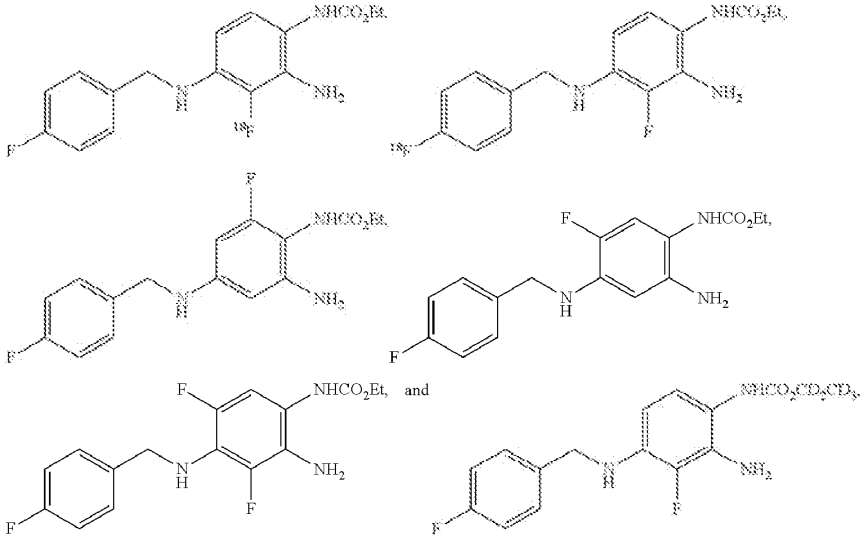
[0722] In further embodiments, X_6 is fluorine and one of X_1, X_2, and X_3 is fluorine.

[0723] In further embodiments, one of X_1, X_2, X_3, and X_6 is 18F.

[0724] In further embodiments, at least one of X_1, X_2, and X_3 is 19F.

[0725] In further embodiments, X_6 is 19F or 18F.

[0726] In further embodiments, the compound is selected from the group consisting of:



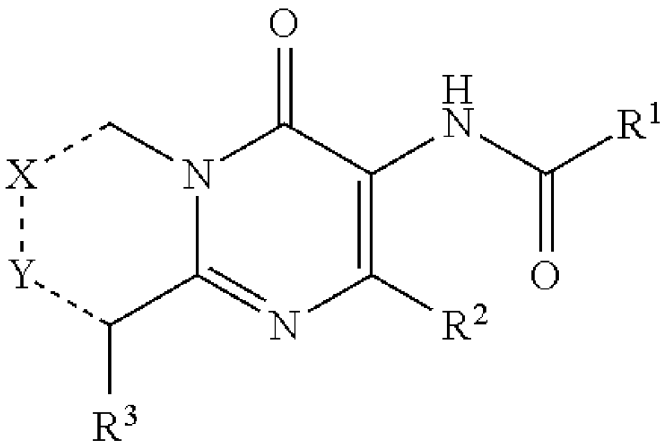
Formula 148

[0727] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 148. Such compounds are described in US Publication No. US20130184294A1, published July 18, 2013, and corresponding to US

Application No. 13/822,669 filed September 7, 2011; International Publication No. WO2012038850A1, published March 29, 2012, and corresponding to International Application No. PCT/IB2011/053917 filed September 7, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 148, these references incorporated by reference herein control.

[0728] In an embodiment, the Kv7 channel activator is a compound according to Formula 148:

Formula 148



,

wherein, R^1 is alkyl, cycloalkyl, wherein alkyl or cycloalkyl may be substituted with one or more halogen, alkoxy, aryl, or aryloxy; R^2 is cycloalkyl or NR^4R^5; R^3 is H, halogen, alkyl, or alkoxy, wherein any alkyl may be substituted with one or more halogen atoms; R^4 and R^5 are independently selected from H, $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl, or —$C_{1\text{-}6}$alkyl-$C_{3\text{-}6}$cycloalkyl, wherein each alkyl or each cycloalkyl may be substituted with one or more halogen, provided that both R^4 and R^5 are not H simultaneously; or R^4 and R^5, together with the N atom to which they are attached, form a heterocycloalkyl;—X—Y— is =CH—CH=, —CH_2—CH_2—, or —CH_2—; or a pharmaceutically acceptable salt thereof.

[0729] In further embodiments, R^1 is $C_{5\text{-}6}$ alkyl; R^2 is NR^4R^5, wherein one of R^4 or R^5 is H and the other is $C_{3\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl, or —$C_{1\text{-}3}$alkyl-$C_{3\text{-}6}$cycloalkyl; R^3 is halogen, alkyl, or alkoxy, wherein any alkyl may be substituted with one or more halogen atoms; —X—Y— is =CH—CH= or —CH_2—CH_2—; or a pharmaceutically acceptable salt thereof.

[0730] In further embodiments, R^1 is —$CH_2C(CH_3)_3$; R^3 is chloro, methyl, trifluoromethyl or 1,1-difluoroethoxy; R^4 is H and R^5 is isopropyl, isobutyl, 1-cyclopropylethyl, cyclobutyl or cyclopentyl; —X—Y— is =CH—CH= or —CH_2—CH_2—; or a pharmaceutically acceptable salt thereof.

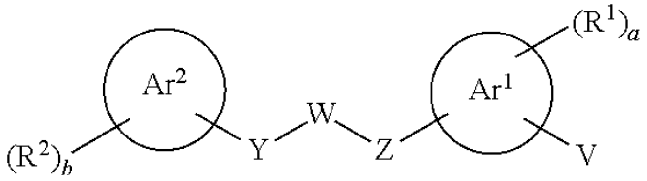
[0731] In further embodiments, R^1 is $C_{5\text{-}6}$ alkyl; R^2 is $C_{3\text{-}6}$cycloalkyl; R^3 is halogen, or alkyl, wherein alkyl may be substituted with one or more halogen atoms; —X—Y— is =CH—CH= or —CH_2—CH_2—; or a pharmaceutically acceptable salt thereof.

[0732] In further embodiments, R^1 is —$CH_2C(CH_3)_3$; R^2 is cyclopropyl; R^3 is chloro, methyl, trifluoromethyl or 1,1-difluoroethoxy; —X—Y— is =CH—CH= or —CH_2—CH_2—; or a pharmaceutically acceptable salt thereof.

Formula 149

[0733] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 149. Such compounds are described in US Patent No. 8,466,201, issued June 18, 2013, and corresponding to US Application No. 12/746,524 filed December 5, 2008; US Patent No. 9,464,052, issued October 11, 2016, and corresponding to US Application No. 13/054,960 filed July 20, 2009; US Patent No. 9,675,567 issued June 13,2017, and corresponding to US Application No. 15/259,064 filed September 8, 2016; US Patent No. 8,466,201 issued June 18, 2013, and corresponding to US Application No. 12/746,524 filed December 5, 2008; International Publication No. WO2009071947A2, published June 11, 2009, and corresponding to International Application No. PCT/GB2008/051158 filed December 5, 2008; International Publication No. WO2010010380A1, published January 28, 2010, and corresponding to International Application No. PCT/GB2009/050887 filed July 20, 2009; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 149, these references incorporated by reference herein control.

[0734] In an embodiment, the Kv7 channel activator is a compound according to Formula 149:



Formula 149

,

wherein, Ar^1 and Ar^2 are each phenyl; are the same or different and each is an aryl group or a heteroaryl group; a is an integer of from 0 to 5;R^1 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups, dialkylamino groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and, where a is greater than 1, each

substituent R^1 may be the same or different; b is an integer of from 0 to 5;R^2 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and where b is greater than 1, each substituent R^2 may be the same or different; V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^3b)X$;W is NR^{4a}; X is a substituent selected from the group consisting of hydroxyalkyl groups, and polyalkylene glycol residues; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and p is an integer of from 0 to 2,and wherein V is substituting said Ar^1 at an ortho position with respect to said Z or said W.

[0735] In further embodiments, a is an integer of from 0 to 3.

[0736] In further embodiments, R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different.

[0737] In further embodiments, b is an integer of from 0 to 4.

[0738] In further embodiments, R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups.

[0739] In further embodiments, R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups.

[0740] In further embodiments, V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of from 0 to 2, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6

carbon atoms, and polyalkylene glycol residues of general formula HO—[(CR ($CR^{6a}R^{6b}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

[0741] In further embodiments, V is a group of formula of ($CR^{3a}R^{3b}$)$_p$$SO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 4 carbon atoms and polyalkylene glycol residues of general formula HO—[($CR^{6a}R^{6b}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{6c}, R^{6d} may be the same or different and each is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms.

[0742] In further embodiments, V is a group of formula of ($CR^{3a}R^{3b}$)$_p$$SO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is a hydroxylalkyl group having from 1 to 4 carbon atoms or a polyalkylene glycol residue of general formula HO—-[($CR^{6a}R^{6b}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is 1 or 2, c3 is an integer of from 1 to 6 and each of R^{6a}, R^{6b}, R^{6c} and R^{6d} is a hydrogen atom.

[0743] In further embodiments, Ar^1 and Ar^2 are each phenyl; a is an integer of from 0 to 3;R^1 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 4;R^2 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl

groups may be the same or different and each has from 1 to 6 carbon atoms, nitro groups, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where b is greater than 1, each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$ and, wherein p is an integer of from 0 to 2,R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms which may optionally be substituted with at least one substituent selected from alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, carbonyl groups, hydroxyl groups and cyano groups, and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, and polyalkylene glycol residues of general formula $HO-[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}—$ wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

[0744] In further embodiments, Ar^1 and Ar^2 are each phenyl; a is 0 or 1;R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to

3;R^2 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, nitro groups, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where b is greater than 1, each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 4 carbon atoms, aryl groups having from 6 to 10 carbon atoms and 5- or 6-membered aromatic heterocyclic groups containing 1 or 2 sulfur atoms, oxygen atoms and/or nitrogen atoms; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 4 carbon atoms and polyalkylene glycol residues of general formula $HO—[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}—$ wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{bc} and R^{6d} may be the same or different and each is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms.

[0745] In further embodiments, Ar^1 and Ar^2 are each phenyl; a is 0 or 1;R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is 0 to 3;R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups; W is a group of formula NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups; Y and Z are each a group of

formula $(CR^{5a}R^{5b})_{n1}$ wherein each n1 is 0; and V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is a hydroxylalkyl group having from 1 to 4 carbon atoms or a polyalkylene glycol residue of general formula $HO—[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}—$ wherein c1 and c2 are the same or different and each is 1 or 2, c3 is an integer of from 1 to 6 and each of R^{6a}, R^{6b}, R^{6c} and R^{6d} is a hydrogen atom.

[0746] In further embodiments, Ar^1 and Ar^2 are each phenyl; a is an integer of from 0 to 3;R^1 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 4;R^2 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, nitro groups, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where b is greater than 1, each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms; and V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$ wherein p is an integer of from 0 to 2, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having

from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, and polyalkylene glycol residues of general formula HO—[($CR^{6a}R^{6c}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

[0747] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 1-[2-(2,6-Dichlorophenylamino)phenyl]-N-[2-(2-hydroxyethoxy)ethyl]-methanesulfonamide,N-[2-(2-hydroxyethoxy)ethyl]-C-[2-(2,4,6-trichlorophenylamino)phenyl]-methanesulfonamide,1-[2-(2,6-dichloro-4-trifluoromethylphenylamino)phenyl]-N-{2-(2-hydroxyethoxy)ethyl]methanesulfonamide,1-[2-(2,6-dichloro-3-methylphenylamino)phenyl]-N-{2-(2-hydroxyethoxy)-ethyl]methanesulfonamide,N-(2-hydroxyethyl)-1-[3-(2,4,6-trichlorophenylamino)phenyl]methane sulphonamide,N-(2-hydroxyethyl)-2-(2,4,6-trichlorophenylamino)benzenesulfonamide,N-(2-hydroxyethyl)-2-(2,6-dichlorophenylamino)benzene sulfonamide,2-(2,6-dichloro-4-trifluoromethylphenylamino)-N-(2-hydroxyethyl)-benzenesulfonamide,2-(2,6-dichloro-3-methylphenylamino)-N-(2-hydroxyethyl)-benzenesulfonamide,2-(2,6-dichloro-4-trifluoromethylphenylamino)-N-[2-(2-hydroxyethoxy)ethyl]-benzenesulfonamide,2-(2,6-dichloro-3-methylphenylamino)-N-[2-(2-hydroxyethoxy)ethyl]-benzenesulfonamide,2-(3,5-dichlorophenylamino)-N-[2-(2-hydroxyethoxy)ethyl]-benzenesulfonamide, andN-[2-(2-hydroxyethoxy)ethyl]-2-(2,4,6-trichlorophenylamino)-benzenesulfonamide, or a pharmacologically acceptable salt or pro-drug thereof.

[0748] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are the same or different and each is an aryl group or a heteroaryl group; a is an integer of from 0 to 5; R^1 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, haloalkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monoalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 5;R^2 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, haloalkoxy groups,

alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monoalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and where b is greater than 1, each substituent R^2 may be the same or different; V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b})CO(X)$, wherein said groups are in the 3- (meta) or 4- (para) position with respect to the substituent Z;W is selected from the group consisting of NR^{4a}, O, S, S=O, SO_2 and $C(R^{4a}R^{4b})_2$;X is a substituent selected from the group consisting of hydroxyalkyl groups, alkoxyalkyl groups, haloalkoxyalkyl groups, aryloxyalkyl groups, polyalkylene glycol residues, carboxyalkyl groups, alkoxycarbonylalkyl groups, haloalkoxycarbonylalkyl groups and aralkyloxycarbonylalkyl groups; Y and Z are the same or different and each is a substituent selected from the group consisting of $(CR^{5a}R^{5b})_{n1}$, C=O, SO_2, $C(=O)NR^{5a}$; $C(=O)NR^{5a}SO_2$ and $C=O(R^{5a}R^{5b})_{n2}$;R^{3a}, R^{3b}, R^{4a}, R^{4b}, R^{5a} and R^{5b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups, cycloalkyl groups, aryl groups and heteroaryl groups;n1 and n2 are the same or different and each is an integer of from 0 to 2; and p is an integer of from 0 to 2.

[0749] In further embodiments, Ar^1 and Ar^2 are the same or different and each is an aryl group having from 5 to 14 carbon atoms or a 5- to 7-membered aromatic heterocyclic group containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms.

[0750] In further embodiments, Ar^1 and Ar^2 are the same or different and each is an aryl group having from 6 to 10 carbon atoms or a 5- or 6-membered aromatic heterocyclic group containing 1 or 2 sulfur atoms, oxygen atoms and/or nitrogen atoms.

[0751] In further embodiments, Ar^1 and Ar^2 are each phenyl.

[0752] In further embodiments, R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, haloalkoxy groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups.

[0753] In further embodiments, W is a group of formula NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups.

[0754] In further embodiments, Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$ wherein each n1 is 0.

[0755] In further embodiments, V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b}CO(X)$, wherein said groups are in the 3- (meta)

or 4- (para) position with respect to the substituent Z, wherein p is an integer of from 0 to 2, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, alkoxyalkyl groups comprising alkyl groups having from 1 to 6 carbon atoms which are substituted by at least one alkoxy group having from 1 to 6 carbon atoms, haloalkoxyalkyl groups comprising alkyl groups having from 1 to 6 carbon atoms which are substituted by at least one haloalkoxy group having from 1 to 6 carbon atoms, aryloxy groups having from 5 to 14 carbon atoms, polyalkylene glycol residues of general formula HO—$[(CR^{6a}R^{6b})_{c1}$—O—$(CR^{6c}R^{6d})_{c2}]_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms, carboxyalkyl groups comprising alkyl groups having from 1 to 6 carbon atoms which are substituted with at least one carboxy group, alkoxycarbonylalkyl groups comprising alkyl groups having from 1 to 6 carbon atoms which are substituted with at least one alkoxycarbonyl group having from 2 to 7 carbon atoms, haloalkoxycarbonylalkyl groups comprising carbonylalkyl groups having from 2 to 7 carbon atoms that are substituted with haloalkoxy groups having from 1 to 6 carbon atoms and aralkyloxycarbonylalkyl groups comprising carbonylalkyl groups having from 2 to 7 carbon atoms which are substituted with at least one aralkyloxy group that comprises an alkyl group having from 1 to 6 carbon atoms that is substituted with an aryl group having from 5 to 14 carbon atoms.

[0756] In further embodiments, V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b})CO(X)$, wherein said groups are in the 3- (meta) or 4- (para) position with respect to the substituent Z, wherein p is an integer of 0 or 1, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 4 carbon atoms, polyalkylene glycol residues of general formula HO—$[(CR^{6a}R^{6b})_{c1}$—O—$(CR^{6c}R^{6d})_{c2}]_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different and each is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms, alkoxyalkyl groups

comprising an alkyl group having from 1 to 4 carbon atoms that is substituted with at least one alkoxy group having from 1 to 4 carbon atoms, carboxyalkyl groups comprising an alkyl group having from 1 to 4 carbon atoms that is substituted with at least one carboxy group, carboxyalkyl groups comprising alkyl groups having from 1 to 4 carbon atoms which are substituted with at least one carboxy group and alkoxycarbonylalkyl groups comprising alkyl groups having from 1 to 4 carbon atoms which are substituted with at least one alkoxycarbonyl group having from 2 to 5 carbon atoms.

[0757] In further embodiments, V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b})CO(X)$, wherein said groups are in the 3- (meta) or 4- (para) position with respect to the substituent Z, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is selected from the group consisting of alkyl groups having 1 or 2 carbon atoms which are substituted with a group selected from hydroxyl groups, methoxy groups, ethoxy groups, carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups.

[0758] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is 0 or 1;R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, haloalkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monoalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, nitro groups, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is 0 to 3; R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, haloalkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups; W is a group of formula NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$ wherein each n1 is 0; and V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b})CO(X)$, wherein said groups are in the 3- (meta) or 4- (para) position with respect to the substituent Z, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is selected from the group consisting of alkyl groups

having 1 or 2 carbon atoms which are substituted with a group selected from hydroxyl groups, methoxy groups, ethoxy groups, carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups.

[0759] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-(2-hydroxyethyl)-2-[3-(2,4,6-trichlorophenylamino)phenyl]acetamide;{2-[5-(3,5-dichlorophenylamino)-2-fluorophenyl]-acetylamino}acetic acid; 2-[4-(2,6-dichloro-4-trifluoromethyl-phenylamino)-phenyl]-N-(2-hydroxyethyl)-acetamide; {2-[4-(3,5-dichlorophenylamino)-phenyl]-acetylamino}acetic acid;N-(2-hydroxy-ethyl)-2-[4-(2,4,6-trichloro-phenylamino)-phenyl]acetamide; 3-(2,6-dichloro-4-trifluoromethyl-phenylamino)-N-(2-hydroxy-ethyl)benzamide; 2-[2-fluoro-5-(2,4,6-trichloro-phenylamino)-phenyl]-N-(2-hydroxy-ethyl)acetamide; 2-[5-(2,6-dichloro-4-trifluoromethyl-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-ethyl)acetamide; 2-[5-(2,6-dichloro-4-trifluoromethoxy-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-ethyl)acetamide; 2-[4-(2,6-dichloro-4-trifluoromethoxy-phenylamino)-phenyl]-N-(2-hydroxy-ethyl)-acetamide; 5-(2,6-dichloro-4-trifluoromethyl-phenylamino)-2-fluoro-N-(2-hydroxy-ethyl)-benzamide; 2-[4-(2,6-dichloro-4-trifluoromethyl-phenylamino)-phenyl]-N-(2-hydroxy-2-methyl-propyl)acetamide; 2-[5-(2,6-dichloro-4-trifluoromethyl-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-2-methyl-propyl)acetamide; and 2-[4-(2,6-dichloro-4-trifluoromethoxy-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-ethyl)propionamide.

[0760] In further embodiments, the compound is according to formula 150 wherein: Ar^1 and Ar^2 are the same or different and each is an aryl group or a heteroaryl group; a is an integer of from 0 to 5; R^1 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, haloalkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monoalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 5; R^2 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, haloalkoxy groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monoalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and where b is greater than 1, each substituent R^2 may be the same or different; V is selected from the group consisting of $(CR^{3a}R^{3b})_pCON(R^{3b})X$ and $(CR^{3a}R^{3b})_pN(R^{3b})CO(X)$, wherein said groups are in the 3- (meta) or 4- (para) position with respect to the substituent Z;

W is selected from the group consisting of NR^{4a}, O, S, S=O, SO_2 and $C(R^{4a}R^{4b})_2$; X is a substituent selected from the group consisting of hydrogen atoms, alkyl groups, hydroxyalkyl groups, alkoxyalkyl groups, haloalkoxyalkyl groups, aryloxyalkyl groups, cycloalkyl groups, aryl groups, heteroaryl groups, polyalkylene glycol residues, aminoalkyl groups, monoalkylaminoalkyl groups, dialkylaminoalkyl groups; alkyl groups that are substituted with groups of formula NR8R9 wherein R8 and R9 together with the nitrogen atom to which they are attached form a saturated or partially unsaturated heterocyclic group which optionally contains at least one more heteroatom selected from nitrogen, oxygen and sulphur atoms (said saturated or partially unsaturated heterocyclic group optionally further being substituted by one or more substituents selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, nitro groups, amino groups, monoalkylamino groups, dialkylamino groups and hydroxyl groups), carboxyalkyl groups, alkoxycarbonylalkyl groups, haloalkoxycarbonylalkyl groups and aralkyloxycarbonylalkyl groups; Y and Z are the same or different and each is a substituent selected from the group consisting of $(CR^{5a}R^{5b})_{n1}$, C=O, SO_2, $C(=O)NR^{5a}$; $C(=O)NR^{5a}SO_2$ and $C=O(R^{5a}R^{5b})_{n2}$;R^{3a}, R^{3b}, R^{4a}, R^{4b}, R^{5a} and R^{5b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups, cycloalkyl groups, aryl groups and heteroaryl groups; n1 and n2 are the same or different and each is an integer of from 0 to 2; and p is an integer of from 0 to 2.

[0761] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is 1; R^1 is halogen; b is an integer of from 0 to 3; R^2 is selected from the group consisting of alkyl having from 1 to 3 carbon atoms, halogen, haloalkyl having from 1 to 3 carbon atoms, alkoxy having from 1 to 3 carbon atoms, haloalkoxy having from 1 to 3 carbon atoms, carboxyl, amino, hydroxyl and cyano, and where b is greater than 1, each substituent R^2 may be the same or different; V is $(CR^{3a}R^{3b})_pCON(R^{3b})X$, wherein said group is in the 3-(meta) or 4-(para) position with respect to the substituent Z;W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen, alkyl having from 1 to 3 carbon atoms and phenyl; X is a substituent selected from the group consisting of hydroxyalkyl having from 1 to 4 carbon atoms, polyalkylene glycol residue of general formula: $HO—[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}$—wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different and each is a hydrogen or an alkyl having from 1 to 4 carbon atoms, alkoxyalkyl comprising an alkyl having from 1 to 4 carbon atoms that is substituted with at least one alkoxy having from 1 to 4 carbon atoms, carboxyalkyl comprising an alkyl

having from 1 to 4 carbon atoms that is substituted with at least one carboxy, carboxyalkyl comprising alkyl having from 1 to 4 carbon atoms which are substituted with at least one carboxy and alkoxycarbonylalkyl comprising alkyl having from 1 to 4 carbon atoms which are substituted with at least one alkoxycarbonyl having from 2 to 5 carbon atoms; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$ wherein each n1 is 0;R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen and alkyl; and p is an integer of from 0 to 2.

[0762] In further embodiments, V is $(CR^{3a}R^{3b})_pCON(R^{3b})X$, wherein said groups is in the 3-(meta) or 4-(para) position with respect to the substituent Z, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is hydrogen, and X is selected from the group consisting of alkyl having 1 or 2 carbon atoms which are substituted with a group selected from hydroxyl groups, methoxy groups, ethoxy groups, carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups.

[0763] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: {2-[5-(3,5-dichlorophenylamino)-2-fluorophenyl]-acetylamino}acetic acid; 2-[5-(2,6-dichloro-4-trifluoromethoxy-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-ethyl)acetamide; 5-(2,6-dichloro-4-trifluoromethyl-phenylamino)-2-fluoro-N-(2-hydroxy-ethyl)-benzamide; 2-[5-(2,6-dichloro-4-trifluoromethyl-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-2-methyl-propyl)acetamide; and 2-[4-(2,6-dichloro-4-trifluoromethoxy-phenylamino)-2-fluoro-phenyl]-N-(2-hydroxy-ethyl)propionamide.

[0764] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; are the same or different and each is an aryl group or a heteroaryl group; a is an integer of from 0 to 5; R^1 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups, dialkylamino groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 5; R^2 is selected from the group consisting of alkyl groups, halogen atoms, haloalkyl groups, alkoxy groups, alkoxycarbonyl groups, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups, dialkylamino groups, nitro groups, acylamino groups, alkoxycarbonylamino groups, alkylsulphonyl groups, alkylsulphonylamino groups and cyano groups and where b is greater than 1, each substituent R^2 may be the same or different; V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^3b)X$;W is NR^{4a};X is a substituent selected from the group consisting of

hydroxyalkyl groups, and polyalkylene glycol residues; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and p is an integer of from 0 to 2,and wherein V is substituting said Ar^1 at an ortho position with respect to said Z or said W. In further embodiments,

[0765] In further embodiments, a is an integer of from 0 to 3.

[0766] In further embodiments, R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different.

[0767] In further embodiments, b is an integer of from 0 to 4.

[0768] In further embodiments, R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups.

[0769] In further embodiments, R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups.

[0770] In further embodiments, V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of from 0 to 2, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, and polyalkylene glycol residues of general formula HO—[(CR $(CR^{6a}R^{6b})_{c1}$—O—$(CR^{6c}R^{6d})_{c2}]_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

[0771] In further embodiments, V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 4 carbon atoms and polyalkylene glycol residues of general formula HO—$[(CR^{6a}R^{6b})_{c1}$—O—$(CR^{6c}R^{6d})_{c2}]_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{6c}, R^{6d} may be the same or different and each is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms.

[0772] In further embodiments, V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is a hydroxylalkyl group having from 1 to 4 carbon atoms or a polyalkylene glycol residue of general formula HO—-$[CR^{6a}R^{6b})_{c1}$—O—$(CR^{6c}R^{6d})_{c2}]_{c3}$— wherein c1 and c2 are the same or different and each is 1 or 2, c3 is an integer of from 1 to 6 and each of R^{6a}, R^{6b}, R^{6c} and R^{6d} is a hydrogen atom.

[0773] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is an integer of from 0 to 3;R^1 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 4;R^2 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, nitro groups, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where b is greater than 1,

each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and V is selected from the group consisting of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$ and, wherein p is an integer of from 0 to 2,R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms which may optionally be substituted with at least one substituent selected from alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, carbonyl groups, hydroxyl groups and cyano groups, and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, and polyalkylene glycol residues of general formula $HO\text{-}[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}—$ wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

[0774] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is 0 or 1;R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 3;R^2 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1

to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, nitro groups, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where b is greater than 1, each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 4 carbon atoms, aryl groups having from 6 to 10 carbon atoms and 5- or 6-membered aromatic heterocyclic groups containing 1 or 2 sulfur atoms, oxygen atoms and/or nitrogen atoms; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$, wherein each n1 is 0; and V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms, and X is a substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 4 carbon atoms and polyalkylene glycol residues of general formula $HO—[(CR^{6a}R^{6b})_{c1}—O—(CR^{6c}R^{6d})_{c2}]_{c3}—$ wherein c1 and c2 are the same or different and each is an integer of from 1 to 3, c3 is an integer of from 1 to 10 and R^{6a}, R^{6b}, R^{bc} and R^{6d} may be the same or different and each is a hydrogen atom or an alkyl group having from 1 to 4 carbon atoms.

[0775] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is 0 or 1; R^1 is selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 4 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 4 carbon atoms, acylamino groups having from 1 to 4 carbon atoms, alkylsulphonyl groups having from 1 to 4 carbon atoms, alkylsulphonylamino groups having from 1 to 4 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is 0 to 3; R^2 is selected from the group consisting of alkyl groups having from 1 to 3 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 3 carbon atoms, alkoxy groups having from 1 to 3 carbon atoms, carboxyl groups, amino groups, hydroxyl groups and cyano groups; W is a group of formula NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 3 carbon atoms and phenyl groups; Y and Z are each a group of formula $(CR^{5a}R^{5b})_{n1}$ wherein each n1 is 0; and V is a group of formula of $(CR^{3a}R^{3b})_pSO_2N(R^{3b})X$, wherein p is an integer of 0 or 1, each of R^{3a} and R^{3b} is a hydrogen atom, and X is a hydroxylalkyl group having from 1 to 4 carbon

atoms or a polyalkylene glycol residue of general formula HO—[($CR^{6a}R^{6b}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is 1 or 2, c3 is an integer of from 1 to 6 and each of R^{6a}, R^{6b}, R^{6c} and R^{6d} is a hydrogen atom.

[0776] In further embodiments, the compound is according to Formula 149 wherein: Ar^1 and Ar^2 are each phenyl; a is an integer of from 0 to 3; R^1 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where a is greater than 1, each substituent R^1 may be the same or different; b is an integer of from 0 to 4; R^2 is selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, halogen atoms, haloalkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, alkoxycarbonyl groups wherein the alkoxy group has from 1 to 6 carbon atoms, carboxyl groups, hydroxyl groups, amino groups, monalkylamino groups wherein the alkyl group has from 1 to 6 carbon atoms, dialkylamino groups wherein the alkyl groups may be the same or different and each has from 1 to 6 carbon atoms, nitro groups, acylamino groups having from 1 to 6 carbon atoms, alkoxycarbonylamino groups wherein the alkoxy group has from 1 to 6 carbon atoms, alkylsulphonyl groups having from 1 to 6 carbon atoms, alkylsulphonylamino groups having from 1 to 6 carbon atoms and cyano groups and, where b is greater than 1, each substituent R^2 may be the same or different; W is NR^{4a}, wherein R^{4a} is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms; and V is selected from the group consisting of ($CR^{3a}R^{3b}$)$_p$$SO_2N(R^{3b})X$ wherein p is an integer of from 0 to 2, R^{3a} and R^{3b} are the same or different and each is selected from the group consisting of hydrogen atoms, alkyl groups having from 1 to 6 carbon atoms, cycloalkyl groups having from 3 to 7 carbon atoms, aryl groups having from 5 to 14 carbon atoms and 5- to 7-membered aromatic heterocyclic groups containing from 1 to 3 sulfur atoms, oxygen atoms and/or nitrogen atoms, and X is a

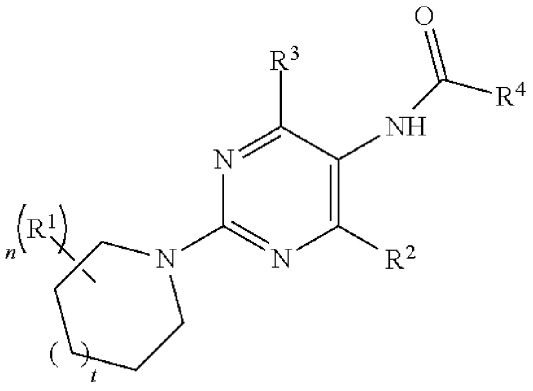
substituent selected from the group consisting of hydroxyalkyl groups having from 1 to 6 carbon atoms, and polyalkylene glycol residues of general formula HO—[($CR^{6a}R^{6c}$)$_{c1}$—O—($CR^{6c}R^{6d}$)$_{c2}$]$_{c3}$— wherein c1 and c2 are the same or different and each is an integer of from 0 to 4, c3 is an integer of from 1 to 20 and R^{6a}, R^{6b}, R^{6c} and R^{6d} may be the same or different from each other and each is a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms.

Formula 150

[0777] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 150. Such compounds are described in International Publication No. WO2012004698A1, published January 12, 2012, and corresponding to International Application No. PCT/IB2011/052686 filed June 20, 2011; US Patent No. 8,883,812, issued November 11, 2014 and corresponding to US Application No. 13/808,355 filed June 20, 2011; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 150, these references incorporated by reference herein control.

[0778] In an embodiment, the Kv7 channel activator is a compound according to Formula 150:

Formula 150



,

wherein, n is an integer of 1 or 2; t is 0 or 1; each R^1 is independently selected from C_{1-3} alkoxy, C_{1-3} alkyl, C_{1-3} alkyl-O—C_{1-3} alkyl; R^2 and R^3 are independently C_{1-3} alkyl, C_{1-3} alkoxy, or C_{3-6}cyloalkyl provided that at least one is C_{1-3} alkoxy; R^4 is C_{1-6} alkyl, C_{1-3} alkyl-C_{3-6}cyloalkyl, C_{3-6} heterocycloalkyl; or a pharmaceutically acceptable salt thereof.

[0779] In further embodiments, R^1, R^2, and R^3 are each C_{1-3} alkoxy; wherein R^4 is C_{4-6} alkyl, and wherein n and t are each 1, or a pharmaceutically acceptable salt thereof.

[0780] In further embodiments, R^1, R^2, and R^3 are each methoxy; R^4 is —CH_2-t-butyl, and n and t are each 1, or a pharmaceutically acceptable salt thereof.

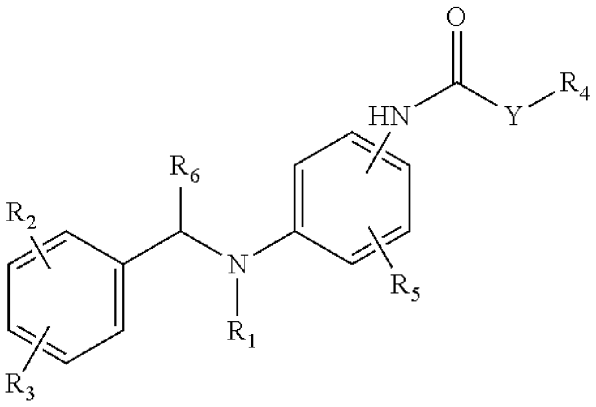
[0781] In further embodiments, the compound is N-(4,6-dimethoxy-2-(4-methoxypiperidin-1-yl)pyrimidin-5-yl)-3,3-dimethylbutanamide, or a pharmaceutically acceptable salt thereof.

Formula 151

[0782] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 151. Such compounds are described in US Patent No. 9,353,048 issued May 31, 2016, and corresponding to US Application No. 14/353,842 filed October 23, 2012; International Publication No. WO2013060097A1, published May 2, 2013, and corresponding to International Application No. PCT/CN2012/001423 filed October 23, 2012; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 152, these references incorporated by reference herein control.

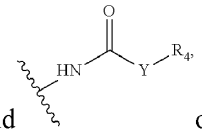
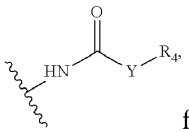
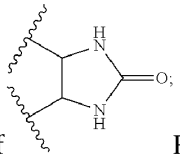
[0783] In an embodiment, the Kv7 channel activator is a compound according to Formula 151:

Formula 151

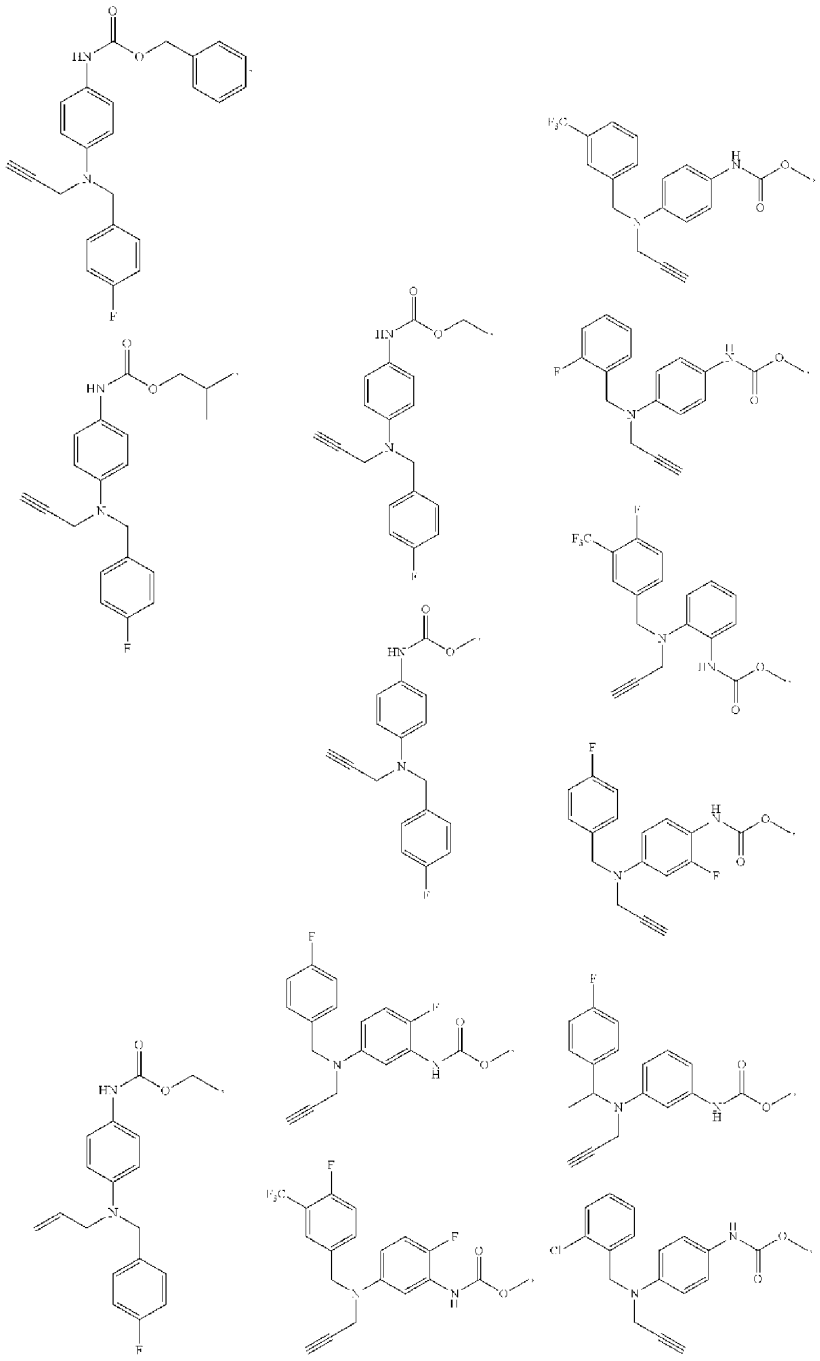


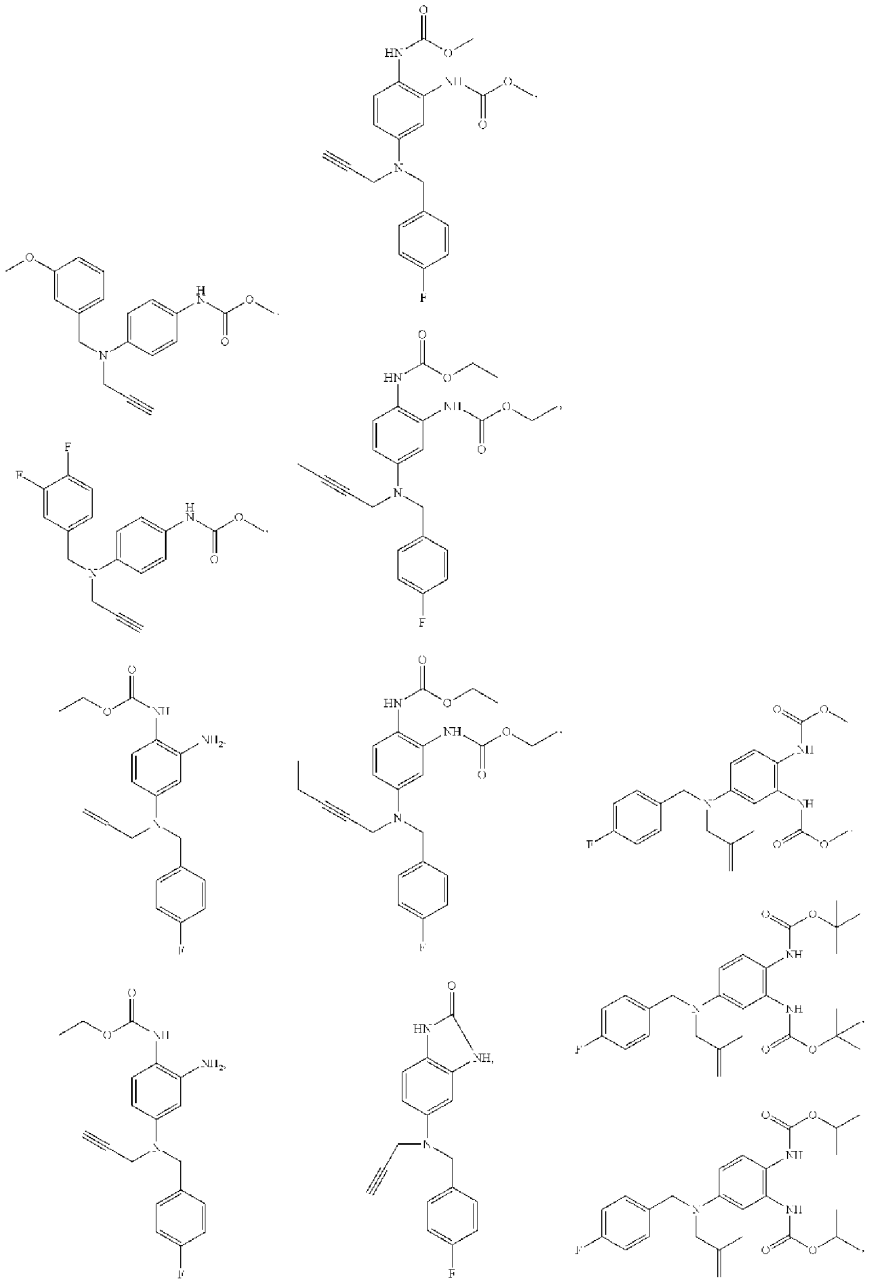
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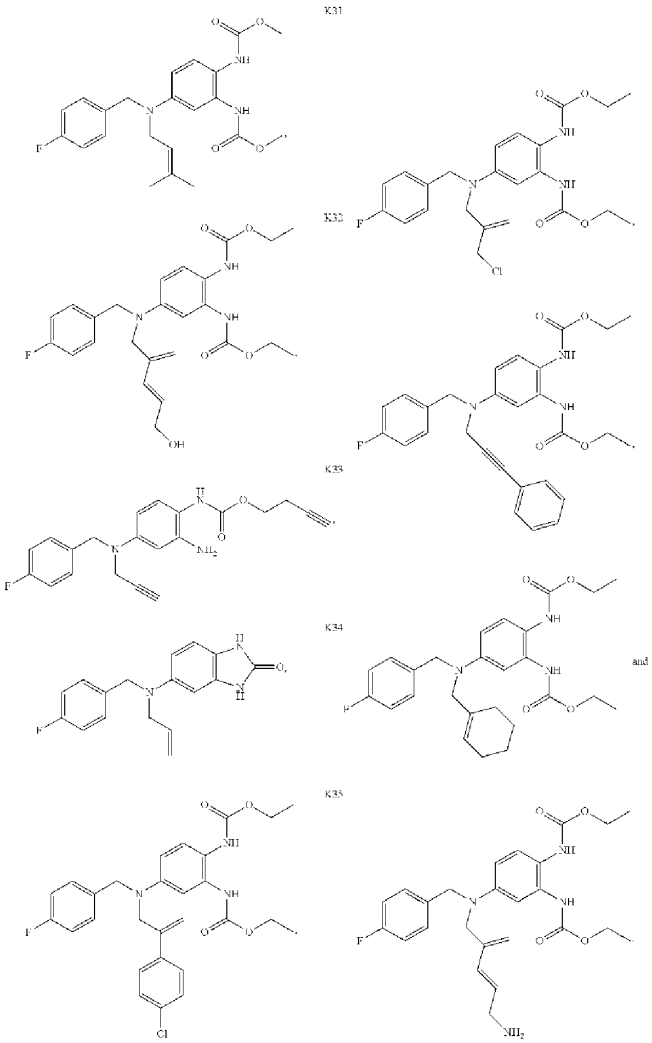
wherein, R_1 is a radical selected from the group consisting of C_2-C_8 alkenyl, C_5-C_7 cycloalkenyl and C_2-C_8 alkynyl; wherein, the C_2-C_8 alkenyl is unsubstituted or optionally substituted by hydroxyl, amino, halogen atom, phenyl or halogenated phenyl; the C_2-C_8 alkynyl is unsubstituted or optionally substituted by hydroxyl, amino, halogen atom, phenyl or halogenated phenyl; R_2 is a radical selected from the group consisting of F, Cl and methoxyl;R_3 is a radical selected from the group consisting of H, halogen atom and trifluoromethyl; Y is not present or Y is O;R_4 is a radical selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl and C_6-C_{10} aryl;R_5 is a radical selected from the

group consisting of H, halogen atom, amino and  or R_5, together with adjacent  forms a fused-ring structure of  R_6 is H or C_1-C_6 alkyl.

[0784] In further embodiments, the Kv7 Channel activator is selected from the group consisting of:





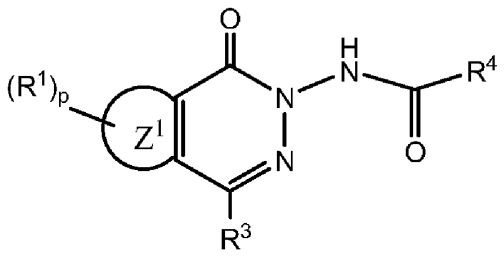


Formula 152

[0785] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 152. In another embodiment, the Kv7 channel activator may be selected from one of the following compounds. Such compounds are described in International Publication No. US20100057224A1, published June 3, 2011, and corresponding to International Application No. PCT/US2010/057224 filed November 18, 2010; US Patent No. 8,629,143 published January 14, 2014, and corresponding to US Application No. 12/949,435 filed November 18, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 152, these references incorporated by reference herein control.

[0786] In an embodiment, the Kv7 channel activator is a compound according to Formula 152:

Formula 152



,

or a pharmaceutically acceptable salt, solvate, prodrug, or salt of a prodrug or solvate thereof, wherein Z is a ring fused with the pyridazine ring, selected from the group consisting of benzo, cycloalkyl, cycloalkenyl, heterocycle, and heteroaryl;R^1 is an optional substituent wherein each occurrence of R^1 is independently G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b,-$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$, or -$(CR^{za}R^{zb})_m$-G^a; p is 0, 1, 2, 3, or 4;R^3 is hydrogen, alkyl, alkenyl, alkynyl, halogen, haloalkyl, -$(CR^{3a}R^{3b})_m$-G^{3a}, or G^{3a}; G^{3a}, at each occurrence, is independently aryl, cycloalkyl, or cycloalkenyl; each of which is optionally substituted;R^4 is alkenyl, alkynyl, haloalkyl, G^{4a}, -$(CR^{4a}R^{4b})_n$-G^{4a}, or alkyl which is optionally substituted with one or two groups independently selected from the group consisting of $S(R^{1a})$, $0(R^{1a})$ and $N(R^{1a})_2$;each occurrence of R^{1a} is independently hydrogen, G^a, -$(CR^{za}R^{zb})_m$-G^a, alkyl, haloalkyl, hydroxyalkyl, or alkoxyalkyl;G^{4a}, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is optionally substituted; G^{3a} and G^{4a}, at each occurrence, are each independently unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-G^a, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-

$N(R^a)COOR^b$, $-(CR^{za}R^{zb})_m-N(R^a)CONR^aR^b$, and $-(CR^{za}R^{zb})_m-N(R^a)SO_2NR^aR^b$;$G^a$, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, $-NO_2$, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-NR^aR^b$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-N(R^a)COOR^b$, $-N(R^a)CONR^aR^b$,$-N(R^a)SO_2NR^aR^b$, $-(CR^{za}R^{zb})_m-CN$, $-(CR^{za}R^{zb})_m-NO_2$, $-(CR^{za}R^{zb})_m-OR^a$,$-(CR^{za}R^{zb})_m-OC(O)R^a$, $-(CR^{za}R^{zb})_m-OC(O)NR^aR^b$, $-(CR^{za}R^{zb})_m-SR^a$, $-(CR^{za}R^{zb})_m-S(O)R^a$,$-(CR^{za}R^{zb})_m-S(O)_2R^a$, $-(CR^{za}R^{zb})_m-S(O)_2NR^aR^b$, $-(CR^{za}R^{zb})_m-C(O)R^a$, $-(CR^{za}R^{zb})_m-C(O)OR^a$, $-(CR^{za}R^{zb})_m-C(O)NR^aR^b$, $-(CR^{za}R^{zb})_m-NR^aR^b$, $-(CR^{za}R^{zb})_m-N(R^a)COOR^b$,$-(CR^{za}R^{zb})_m-N(R^a)CONR^aR^b$, and $-(CR^{za}R^{zb})_m-N(R^a)SO_2NR^aR^b$;$R^{za}$, R^{zb}, R^{3a}, R^{3b}, R^{4a}, and R^{4b}, at each occurrence, are each independently hydrogen, alkyl, halogen, or haloalkyl; R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or haloalkyl; and m and n, at each occurrence, are each independently 1, 2, 3, or 4;with the proviso that when Z^1 is benzo, p is 0 or 4, R^1 is halogen, R^3 is G^{3a}, and G^{3a} is aryl, substituted with 1 or 2 substituents selected from the group consisting of alkyl and unsubstituted aryl, then R^4 is other than unsubstituted aryl, unsubstituted alkyl, or haloalkyl.

[0787] In further embodiments, Z^1 is benzo, heteroaryl, or cycloalkyl.

[0788] In further embodiments, R^3 is alkyl, halogen, haloalkyl, G^{3a}, or $-(CR^{3a}R^{3b})_m-G^{3a}$.

[0789] In further embodiments, R^4 is unsubstituted alkyl, haloalkyl, $-C(R^{4a}R^{4b})_n-G^{4a}$, or alkyl substituted with a $-S(R^{la})$ group.

[0790] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; and R^4 is unsubstituted alkyl, haloalkyl, $-C(R^{4a}R^{4b})_n-G^{4a}$, or alkyl substituted with a $-S(R^{la})$ group.

In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; and R^4 is $-C(R^{4a}R^{4b})_n-G^{4a}$.

[0791] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is $-C(R^{4a}R^{4b})_n-G^{4a}$; and R^3 is alkyl, halogen, haloalkyl, G^{3a}, or $-(CR^{3a}R^{3b})_m-G^{3a}$.

[0792] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is $-C(R^{4a}R^{4b})_n-G^{4a}$;$R^3$ is alkyl, halogen, haloalkyl, G^{3a}, or $-(CR^{3a}R^{3b})_m-G^{3a}$; and$G^{3a}$ is aryl or cycloalkyl.

[0793] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; andR^4 is unsubstituted alkyl or haloalkyl.

[0794] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is unsubstituted alkyl or haloalkyl; and R^3 is alkyl, halogen, haloalkyl, G^{3a}, or $-(CR^{3a}R^{3b})_m-G^{3a}$.

[0795] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is unsubstituted alkyl or haloalkyl; R^3 is alkyl, halogen, haloalkyl, G^{3a}, or $-(CR^{3a}R^{3b})_m-G^{3a}$; and G^{3a} is aryl or cycloalkyl.

[0796] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; and R^4 is alkyl substituted with a -S(R^{la}) group.

[0797] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is alkyl substituted with a -S(R^{la}) group; and R^3 is alkyl, halogen, haloalkyl, G^{3a}, or -$(CR^{3a}R^{3b})_m$-G^{3a}.

[0798] In further embodiments, Z^1 is benzo, cycloalkyl, or heteroaryl; R^4 is alkyl substituted with a -S(R^{la}) group; R^3 is alkyl, halogen, haloalkyl, G^{3a}, or -$(CR^{3a}R^{3b})_m$-G^{3a}; and G^{3a} is aryl or cycloalkyl.

[0799] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(4-chlorophenyl)-N-(4-isopropyl-l-oxophthalazin-2(lH)-yl)acetamide; 2-(1 -adamantyl)-N- [4-(4-bromophenyl)- 1 -oxophthalazin-2(1 H)-yl]acetamide; N-[4-(4-bromophenyl)-l-oxophthalazin-2(lH)-yl]-2-(4-chlorophenyl)acetamide; 2-(4-chlorophenyl)-N-(1 -oxo-4-phenylphthalazin-2(1 H)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(4-isopropyl-l-oxophthalazin-2(lH)-yl)acetamide; 2-(1 -adamantyl)-N-(4-isopropyl- 1 -oxophthalazin-2(1 H)-yl)acetamide; 2-(l-adamantyl)-N-(8-oxo-5-phenylpyrido[2,3-d]pyridazin-7(8H)-yl)acetamide; 2-(l-adamantyl)-N-(4-isopropyl-l-oxo-5,6,7,8-tetrahydro-5,8-ethanophthalazin-2(1 H)-yl)acetamide; 2-(l-adamantyl)-N-(4-oxo-7-phenylthieno[2,3-d]pyridazin-5(4H)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(4-oxo-7-phenylthieno[2,3-d]pyridazin-5(4H)-yl)acetamide; 2-(3,5-difluorophenyl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; 2-(1 -adamantyl)-N-[1 -oxo-4-(trifluoromethyl)phthalazin-2(l H)-yl]acetamide; 2-(4-chlorophenyl)-N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] acetamide; N-(5,8-difluoro-l-oxo-4-phenylphthalazin-2(lH)-yl)-2-(4-fluorophenyl)acetamide; 2-(l-adamantyl)-N-(5,8-difluoro-l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(4-chlorophenyl)-N-(5,8-difluoro-l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(l-adamantyl)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; N-(4-chloro-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; 2-(1 -adamantyl)-N-(4-chloro- 1 -oxophthalazin-2(1 H)-yl)acetamide; N-(4-chloro-l-oxophthalazin-2(lH)-yl)-2-(4-chlorophenyl)acetamide; 2-(4-chlorophenyl)-N-(4-cyclopropyl-l-oxophthalazin-2(lH)-yl)acetamide; N-(4-cyclopropyl-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; 2-(1 -adamantyl)-N-(4-cyclopropyl- 1 -oxophthalazin-2(1 H)-yl)acetamide; 2-(2,3-difluorophenyl)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(4-fluorophenyl)-N-(1 -oxo-4-phenylphthalazin-2(1 H)-yl)acetamide; 2-(2,5-difluorophenyl)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(4-chlorophenyl)-N-(4-methyl- 1 -oxophthalazin-2(1 H)-yl)acetamide; 2-(l-adamantyl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)-yl)acetamide; 2-[(l S,2S,5S)-6,6-

dimethylbicyclo[3.1.1]hept-2-yl]-N-(7-oxo-4-phenylthieno[2,3- d]pyridazin-6(7H)-yl)acetamide; 2-(4-chlorophenyl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)-yl)acetamide; 2-(4-fluorophenyl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)-yl)acetamide; 2-[3,5-dimethyl-l-adamantyl]-N-(4-isopropyl-l-oxophthalazin-2(lH)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(6-fluoro-l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(4-chlorophenyl)-N-(6-fluoro-l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; 2-(1 -adamantyl)-N-(6-fluoro- 1 -oxo-4-phenylphthalazin-2(1 H)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(4-methyl-l-oxophthalazin-2(lH)-yl)acetamide; 2-[l-(4-chlorophenyl)cyclopropyl]-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; 2- [1 -(4-chlorophenyl)cyclobutyl] -N-[1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl]acetamide; 2-(2-naphthyl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; 3-(4-chlorophenyl)-3-methyl-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]butanamide; 2-cyclopentyl-N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] acetamide; 2.2- difluoro-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]-2-phenylacetamide; 2-cyclobutyl-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; N-[1 -oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]-2-[4- (trifluoromethyl)phenyl]acetamide; 2- [4-(dimethylamino)phenyl]-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl] acetamide; 3.3- dimethyl-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]butanamide; 2-[4-(methylsulfonyl)phenyl]-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl] acetamide; N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] -3-phenylpropanamide; N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]-2-(l-phenylcyclopropyl)acetamide; 3- methyl-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]-3-phenylbutanamide; N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]-2-(3-thienyl)acetamide; N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] -2-(2-thienyl)acetamide; 2-(5-chloro-2-thienyl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; 2-(5-methyl-2-thienyl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] -2-phenylacetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl] acetamide; 2-(4-chloro-3-fluorophenyl)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl] acetamide; 2-(3-fluoroadamantan- 1-yl)-N-(4-isopropyl- 1 -oxophthalazin-2(lH)-yl)acetamide; 2-(3-hydroxyadamantan-l-yl)-N-(4-isopropyl-l-oxophthalazin-2(lH)-yl)acetamide; N-(4-tert-butyl-l-oxophthalazin-2(lH)-yl)-2-cyclopentylacetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-(4-tert-butyl-l-oxophthalazin-2(lH)-yl)acetamide; N-(4-tert-butyl- 1 -oxophthalazin-2(1 H)-yl)-3 -methyl-3-phenylbutanamide; N-(4-tert-butyl-l-oxophthalazin-2(lH)-yl)-2-(4-

chlorophenyl)acetamide; 2-[(l S,2S,4R)-bicyclo[2.2.1]hept-2-yl]-N-(4-cyclobutyl-l-oxophthalazin-2(lH)- yl)acetamide; 2-[(l S,2S,4S)-bicyclo[2.2.1]hept-5-en-2-yl]-N-(4-cyclobutyl-l-oxophthalazin-2(lH)- yl)acetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-(4-cyclobutyl-l-oxophthalazin-2(lH)- yl)acetamide; N-(4-cyclobutyl-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; 2-(4-chlorophenyl)-N-(4-cyclobutyl-l-oxophthalazin-2(lH)-yl)acetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-(4-cyclopentyl-l-oxophthalazin-2(lH)-yl)acetamide; 2-(4-chlorophenyl)-N-(4-cyclopentyl-l-oxophthalazin-2(lH)-yl)acetamide; N-(4-cyclopentyl-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-(4-cyclohexyl-l-oxophthalazin-2(lH)- yl)acetamide; 2-(adamantan- 1 -yl)-N-(4-cyclohexyl- 1 -oxophthalazin-2(1 H)-yl)acetamide; 2- (4-chlorophenyl)-N-(4-cyclohexyl-l-oxophthalazin-2(lH)-yl)acetamide; N-(4-cyclohexyl-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; (±)-4-(3- { [(ero-bicyclo[2.2.1]heptan-2-yl)acetyl]amino} -4-oxo-3,4- dihydrophthalazin- 1-yl)benzoic acid; (±)-methyl 4-(3 - { [ero-bicyclo [2.2.1]hept-2-ylacetyl] amino } -4-oxo-3 ,4- dihydrophthalazin- 1 -yl)benzoate; methyl 4-(3- {[(4-chlorophenyl)acetyl]amino}-4-oxo-3,4-dihydrophthalazin-l-yl)benzoate; (±)-4-(3- {[e o-bicyclo[2.2.1]hept-2-ylacetyl]amino}-4-oxo-3,4-dihydrophthalazin-l- yl)-N,N-dimethylbenzamide; 3- methyl-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)-3-phenylbutanamide; 2-(2,4-dichlorophenyl)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; (±)-2-(e o-bicyclo[2.2.1]heptan-2-yl)-N-[4-(4-bromophenyl)-l-oxophthalazin-2(lH)- yl]acetamide; N-[4-(4-bromophenyl)-l-oxophthalazin-2(lH)-yl]-3-methyl-3-phenylbutanamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(l-methylcyclopentyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[l-(trifluoromethyl)cyclopentyl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[(l S,2S,5R)-3,3-difluoro-6,6- dimethylbicyclo[3.1. l]hept-2-yl]acetamide; N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl]-3 -methyl-3 -phenylbutanamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-fluoro-2-phenylacetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-phenylacetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(morpholin-4-yl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(pyridin-3-yl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(pyridin-2-yl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,4-dichlorophenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5-dimethoxyphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5-dimethylphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[3-(trifluoromethoxy)phenyl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[4-

(trifluoromethyl)phenyl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[3-(trifluoromethyl)phenyl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[4-(dimethylamino)phenyl]acetamide; 2-(4-bromophenyl)-N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(3-chlorophenyl)-N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(4-methoxyphenyl)acetamide; N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] -2-(3 -methoxyphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(4-hydroxyphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(4-methylphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(3-methylphenyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-cyclopentylacetamide; N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] -4-methylpentanamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[4-(methylsulfonyl)phenyl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(5-chloro-2-thienyl)acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)- yl]acetamide; 2-(4-chloro-3-fluorophenyl)-N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)- yl]acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-[(l S,2S,5S)-6,6- dimethylbicyclo[3.1. l]hept-2-yl]acetamide; 2-(adamantan- 1 -yl)-N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; 2-(4-chlorophenyl)-N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5-difluorophenyl)acetamide; N-[4-(4-chlorophenyl)- 1 -oxophthalazin-2(l H)-yl]-2-(1 -phenylcyclopentyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2- phenylcyclopropanecarboxamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(2-naphthyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-2-(l-naphthyl)acetamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-4,4,4-trifluorobutanamide; N-[4-(4-chlorophenyl)-l-oxophthalazin-2(lH)-yl]-3,3,3-trifluoropropanamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(3-chlorophenyl)-l-oxophthalazin-2(lH)- yl] acetamide; 2-(adamantan- 1 -yl)-N- [4-(3 -chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; 2-(4-chlorophenyl)-N- [4-(3 -chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; N- [4-(3 -chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl]-2-(3 ,5 -difluorophenyl)acetamide; 2-[(l S,2S,4R)-bicyclo[2.2.1]hept-2-yl]-N-[4-(4-fluorophenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; 2-[(l S,2S,4S)-bicyclo[2.2.1]hept-5-en-2-yl]-N-[4-(4-fluorophenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-fluorophenyl)-l-oxophthalazin-2(lH)- yl] acetamide; 2-(4-chlorophenyl)-N-[4-(4-fluorophenyl)-l-oxophthalazin-2(lH)-yl] acetamide; 2-(3,5-

difluorophenyl)-N-[4-(4-fluorophenyl)-l-oxophthalazin-2(lH)-yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(2,4-difluorophenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; 2-(4-chlorophenyl)-N-[4-(4-methylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(3,5-difluorophenyl)-N-[4-(4-methylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-[(l S,2S,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]-N-[4-(4-methylphenyl)-l- oxophthalazin-2(lH)-yl]acetamide; 2-(adamantan- 1 -yl)-N- [4-(4-methylphenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; N-(4-benzyl- 1 -oxophthalazin-2(1 H)-yl)-2- [1 -(trifluoromethyl)cyclopentyl] acetamide; N-(4-benzyl- 1 -oxophthalazin-2(1 H)-yl)-3-methyl-3 -phenylbutanamide; (±)-N-(4-benzyl-l-oxophthalazin-2(lH)-yl)-2-(e o-bicyclo[2.2.1]hept-2-yl)acetamide; N-(4-benzyl-l-oxophthalazin-2(lH)-yl)-2-(4-chlorophenyl)acetamide; N-(4-benzyl-l-oxophthalazin-2(lH)-yl)-2-(3,5-difluorophenyl)acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-chlorobenzyl)-l-oxophthalazin-2(lH)- yl] acetamide; N-[4-(4-chlorobenzyl)-l-oxophthalazin-2(lH)-yl]-2-(4-chlorophenyl)acetamide; N-[4-(4-chlorobenzyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5-difluorophenyl)acetamide; 2- [(l S,2S,4R)-bicyclo[2.2.1]hept-2-yl]-N-{ l-oxo-4-[4-(trifluoromethyl)phenyl]phthalazin-2(lH)-yl} acetamide; 3- methyl-N- { l-oxo-4-[4-(trifluoromethyl)phenyl]phthalazin-2(lH)-yl}-3- phenylbutanamide; 2-(adamantan-l-yl)-N- { l-oxo-4-[4-(trifluoromethyl)phenyl]phthalazin-2(lH)- yl} acetamide; (±)-2-(exo-bicyclo[2.2.1]hept-2-yl)-N- { 1 -oxo-4-[4- (trifluoromethyl)phenyl]phthalazin-2(lH)-yl} acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-methoxyphenyl)-l-oxophthalazin-2(lH)- yl] acetamide; N-[4-(4-methoxyphenyl)-l-oxophthalazin-2(lH)-yl]-2-(4- methylcyclohexyl)acetamide; 2-(3,5-difluorophenyl)-N-[4-(4-methoxyphenyl)-l-oxophthalazin-2(lH)- yl] acetamide; 2-(adamantan- 1 -yl)-N- [4-(4-methoxyphenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(2,5-dimethylphenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; 2-(adamantan-l-yl)-N-[4-(2,5-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(4-chlorophenyl)-N-[4-(2,5-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(3,5-difluorophenyl)-N-[4-(2,5-dimethylphenyl)-l-oxophthalazin-2(lH)- yl] acetamide; 2-[(l S,2S,4S)-bicyclo[2.2.1]hept-5-en-2-yl]-N-[4-(2,4-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(2,4-dimethylphenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; 2-(4-chlorophenyl)-N-[4-(2,4-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(3,5-difluorophenyl)-N-[4-(2,4-dimethylphenyl)-l-oxophthalazin-2(lH)- yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(3,4-dimethylphenyl)-l-oxophthalazin- 2(1 H)-yl]acetamide; 2-(adamantan-l-yl)-N-[4-(3,4-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(4-chlorophenyl)-N-[4-(3,4-dimethylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(3,5-difluorophenyl)-N-[4-(3,4-

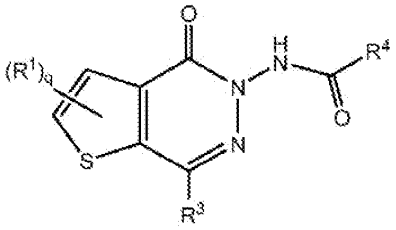
dimethylphenyl)-l-oxophthalazin-2(lH)- yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[l-oxo-4-(2-phenylethyl)phthalazin-2(lH)- yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-isopropylphenyl)-l-oxophthalazin-2(lH)- yl]acetamide; 2-(adamantan-l-yl)-N-[4-(4-isopropylphenyl)-l-oxophthalazin-2(lH)-yl]acetamide; 2-(4-chlorophenyl)-N- [4-(4-isopropylphenyl)- 1 -oxophthalazin-2(1 H)-yl] acetamide; 2-(3,5-difluorophenyl)-N-[4-(4-isopropylphenyl)-l-oxophthalazin-2(lH)- yl] acetamide; (±)-2-(ero-bicyclo[2.2.1]hept-2-yl)-N-[1 -oxo-4-(l -phenylcyclopropyl)phthalazin- 2(1 H)-yl]acetamide; 2-(adamantan- 1 -yl)-N-[4-isopropyl- 1 -oxo-7-(trifluoromethyl)phthalazin-2(1 H)- yl] acetamide; 2-(adamantan- 1 -yl)-N- [7-bromo-4-(4-methoxyphenyl)- 1 -oxophthalazin-2(1 H)- yl] acetamide; 2-(adamantan- 1 -yl)-N- [6-bromo-4-(4-methoxyphenyl)- 1 -oxophthalazin-2(1 H)- yl] acetamide; N-[6-bromo-4-(4-methoxyphenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5-difluorophenyl)acetamide; N-[7-bromo-4-(4-methoxyphenyl)-l-oxophthalazin-2(lH)-yl]-2-(3,5- difluorophenyl)acetamide; 2-(3-bromoadamantan-l-yl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)- yl)acetamide; 2-(3-fluoroadamantan-l-yl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)- yl)acetamide; 2-(3-hydroxyadamantan-l-yl)-N-(7-oxo-4-phenylthieno[2,3-d]pyridazin-6(7H)- yl)acetamide; N-[4-(4-chlorophenyl)-5,8-difluoro-l-oxophthalazin-2(lH)-yl]-2-(3,5- difluorophenyl)acetamide; 2-(4-chlorophenyl)-N- [4-(4-chlorophenyl)-5 , 8-difluoro- 1 -oxophthalazin-2(1 H)- yl]acetamide; 2-(adamantan- l-yl)-N-[4-(4-chlorophenyl)-5,8-difluoro- 1 -oxophthalazin-2(lH)- yl]acetamide; (±)-2-(e o-bicyclo[2.2.1]hept-2-yl)-N-[4-(4-chlorophenyl)-5,8-difluoro-l- oxophthalazin-2(lH)-yl]acetamide; 2-(adamantan-l-yl)-N-(l-oxo-4-phenyl-5,6,7,8-tetrahydrophthalazin-2(lH)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(l-oxo-4-phenyl-5,6,7,8-tetrahydrophthalazin-2(lH)-yl)acetamide; 2-(4-chlorophenyl)-N-(l-oxo-4-phenyl-5,6,7,8-tetrahydrophthalazin-2(lH)-yl)acetamide; 2-(3,5-difluorophenyl)-N-(l-oxo-4-phenyl-l,5,6,7-tetrahydro-2H-cyclopenta[d]pyridazin-2-yl)acetamide; 2-(adamantan-l-yl)-N-(l-oxo-4-phenyl-l,5,6,7-tetrahydro-2H- cyclopenta[d]pyridazin-2-yl)acetamide; 2-(4-chlorophenyl)-N-(l-oxo-4-phenyl-l,5,6,7-tetrahydro-2H-cyclopenta[d]pyridazin- 2-yl)acetamide; 2-(methylthio)-N-[l-oxo-4-(trifluoromethyl)phthalazin-2(lH)-yl]acetamide; 2-(adamantan- 1 -ylthio)-N- [1 -oxo-4-(trifluoromethyl)phthalazin-2(1 H)-yl] acetamide; 2-(adamantan-l-ylthio)-N-(l-oxo-4-phenylphthalazin-2(lH)-yl)acetamide; and 2-(1 ,3 -benzodioxol-5 -yl)-N- [4-(4-chlorophenyl)- 1 -oxophthalazin-2(1 H)-yl]acetamide.

Formula 153

[0800] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 153. Such compounds are described in US Patent No. 8,629,143, issued January 14, 2014, and corresponding to US Application No. US8629143B2 filed November 18, 2010; International Publication No. WO2011066168A1, published June 3, 2011, and corresponding to International Application No. PCT/US2010/057224 filed November 18, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 153, these references incorporated by reference herein control.

[0801] In an embodiment, the Kv7 channel activator is a compound according to Formula 153:

Formula 153



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or a pharmaceutically acceptable salt, solvate, prodrug, or salt of a prodrug or solvate thereof, wherein, R^1 is an optional substituent wherein each occurrence of R^1 is independently G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b,-$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$, or -$(CR^{za}R^{zb})_m$-G^a; p is 0, 1, 2, 3, or 4;R^3 is hydrogen, alkyl, alkenyl, alkynyl, halogen, haloalkyl, -$(CR^{3a}R^{3b})_m$-G^{3a}, or G^{3a}; G^{3a}, at each occurrence, is independently aryl, cycloalkyl, or cycloalkenyl; each of which is optionally substituted;R^4 is alkenyl, alkynyl, haloalkyl, G^{4a}, -$(CR^{4a}R^{4b})_n$-G^{4a}, or alkyl which is optionally substituted with one or two groups independently selected from the group consisting of $S(R^{1a})$, $0(R^{1a})$ and $N(R^{1a})_2$;each occurrence of R^{1a} is independently hydrogen, G^a, -$(CR^{za}R^{zb})_m$-G^a, alkyl, haloalkyl, hydroxyalkyl, or alkoxyalkyl;G^{4a}, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is optionally substituted; G^{3a} and G^{4a}, at each occurrence, are each independently unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of G^a, alkyl, alkenyl, alkynyl, halogen,

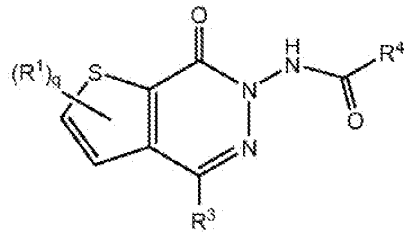
haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-G^a, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$;G^a, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$, -$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$,-$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a,-$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$,-$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$,-$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$;R^{za}, R^{zb}, R^{3a}, R^{3b}, R^{4a}, and R^{4b}, at each occurrence, are each independently hydrogen, alkyl, halogen, or haloalkyl; R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or haloalkyl; and m and n, at each occurrence, are each independently 1, 2, 3, or 4.

Formula 154

[0802] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 154. Such compounds are described in US Patent No. 8,629,143, issued January 14, 2014, and corresponding to US Application No. US8629143B2 filed November 18, 2010; International Publication No. WO2011066168A1, published June 3, 2011, and corresponding to International Application No. PCT/US2010/057224 filed November 18, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 154, these references incorporated by reference herein control.

[0803] In an embodiment, the Kv7 channel activator is a compound according to Formula 154:

Formula 154



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or a pharmaceutically acceptable salt, solvate, prodrug, or salt of a prodrug or solvate thereof, whereinR^1 is an optional substituent wherein each occurrence of R^1 is independently G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b,-$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$, or -$(CR^{za}R^{zb})_m$-G^a; p is 0, 1, 2, 3, or 4;R^3 is hydrogen, alkyl, alkenyl, alkynyl, halogen, haloalkyl, -$(CR^{3a}R^{3b})_m$-G^{3a}, or G^{3a}; G^{3a}, at each occurrence, is independently aryl, cycloalkyl, or cycloalkenyl; each of which is optionally substituted;R^4 is alkenyl, alkynyl, haloalkyl, G^{4a}, -$(CR^{4a}R^{4b})_n$-G^{4a}, or alkyl which is optionally substituted with one or two groups independently selected from the group consisting of $S(R^{1a})$, $0(R^{1a})$ and $N(R^{1a})_2$;each occurrence of R^{1a} is independently hydrogen, G^a, -$(CR^{za}R^{zb})_m$-G^a, alkyl, haloalkyl, hydroxyalkyl, or alkoxyalkyl;G^{4a}, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is optionally substituted; G^{3a} and G^{4a}, at each occurrence, are each independently unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-G^a, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$;G^a, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$,

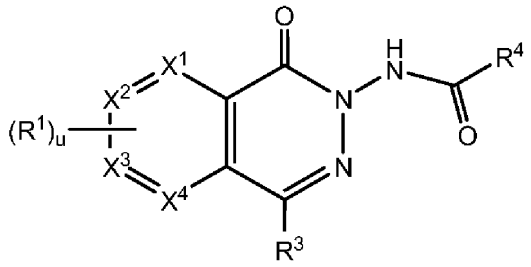
$-NR^aR^b$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-N(R^a)COOR^b$, $-N(R^a)CONR^aR^b$,$-N(R^a)SO_2NR^aR^b$, $-(CR^{za}R^{zb})_m-CN$, $-(CR^{za}R^{zb})_m-NO_2$, $-(CR^{za}R^{zb})_m-OR^a$,$-(CR^{za}R^{zb})_m-OC(O)R^a$, $-(CR^{za}R^{zb})_m-OC(O)NR^aR^b$, $-(CR^{za}R^{zb})_m-SR^a$, $-(CR^{za}R^{zb})_m-S(O)R^a$,$-(CR^{za}R^{zb})_m-S(O)_2R^a$, $-(CR^{za}R^{zb})_m-S(O)_2NR^aR^b$, $-(CR^{za}R^{zb})_m-C(O)R^a$, $-(CR^{za}R^{zb})_m-C(O)OR^a$, $-(CR^{za}R^{zb})_m-C(O)NR^aR^b$, $-(CR^{za}R^{zb})_m-NR^aR^b$, $-(CR^{za}R^{zb})_m-N(R^a)COOR^b$,$-(CR^{za}R^{zb})_m-N(R^a)CONR^aR^b$, and $-(CR^{za}R^{zb})_m-N(R^a)SO_2NR^aR^b$;$R^{za}$, R^{zb}, R^{3a}, R^{3b}, R^{4a}, and R^{4b}, at each occurrence, are each independently hydrogen, alkyl, halogen, or haloalkyl; R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or haloalkyl; and m and n, at each occurrence, are each independently 1, 2, 3, or 4 ; and q is 0, 1, or 2.

Formula 155

[0804] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 155. Such compounds are described in US Patent No. 8,629,143, issued January 14, 2014, and corresponding to US Application No. US8629143B2 filed November 18, 2010; International Publication No. WO2011066168A1, published June 3, 2011, and corresponding to International Application No. PCT/US2010/057224 filed November 18, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 155, these references incorporated by reference herein control.

[0805] In an embodiment, the Kv7 channel activator is a compound according to Formula 155:

Formula 155



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or a pharmaceutically acceptable salt, solvate, prodrug, or salt of a prodrug or solvate thereof, wherein R^1 is an optional substituent wherein each occurrence of R^1 is independently G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, $-NO_2$, $-OR^a$, $-OC(O)R^a$, $-OC(O)NR^aR^b$, $-NR^aR^b$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$,-$N(R^a)COOR^b$, $-N(R^a)CONR^aR^b$, $-N(R^a)SO_2NR^aR^b$, $-(CR^{za}R^{zb})_m-CN$, $-(CR^{za}R^{zb})_m-NO_2$, $-(CR^{za}R^{zb})_m-OR^a$, $-(CR^{za}R^{zb})_m-OC(O)R^a$, $-(CR^{za}R^{zb})_m-OC(O)NR^aR^b$, $-(CR^{za}R^{zb})_m-SR^a$, -

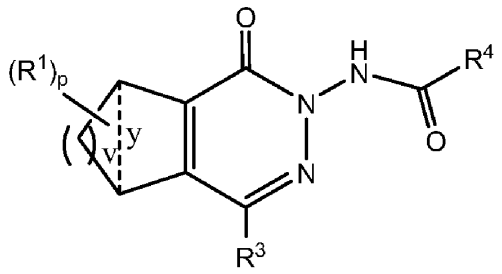
$(CR^{za}R^{zb})_m$-S(O)R^a, -$(CR^{za}R^{zb})_m$-S$(O)_2R^a$, -$(CR^{za}R^{zb})_m$-S$(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-C(O)R^a, -$(CR^{za}R^{zb})_m$-C(O)OR^a, -$(CR^{za}R^{zb})_m$-C(O)NR^aR^b, -$(CR^{za}R^{zb})_m$-NR^aR^b,-$(CR^{za}R^{zb})_m$-N$(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-N$(R^a)CONR^aR^b$, -$(CR^{za}R^{zb})_m$-N$(R^a)SO_2NR^aR^b$, or -$(CR^{za}R^{zb})_m$-G^a; p is 0, 1, 2, 3, or 4;R^3 is hydrogen, alkyl, alkenyl, alkynyl, halogen, haloalkyl, -$(CR^{3a}R^{3b})_m$-G^{3a}, or G^{3a}; G^{3a}, at each occurrence, is independently aryl, cycloalkyl, or cycloalkenyl; each of which is optionally substituted;R^4 is alkenyl, alkynyl, haloalkyl, G^{4a}, -$(CR^{4a}R^{4b})_n$-G^{4a}, or alkyl which is optionally substituted with one or two groups independently selected from the group consisting of S(R^{1a}), 0(R^{1a}) and N$(R^{1a})_2$;each occurrence of R^{1a} is independently hydrogen, G^a, -$(CR^{za}R^{zb})_m$-G^a, alkyl, haloalkyl, hydroxyalkyl, or alkoxyalkyl;G^{4a}, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is optionally substituted; G^{3a} and G^{4a}, at each occurrence, are each independently unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -OC(O)R^a, -OC(O)NR^aR^b, -NR^aR^b, -SR^a, -S(O)R^a, -S$(O)_2R^a$, -S$(O)_2NR^aR^b$, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b,-N$(R^a)COOR^b$, -N$(R^a)CONR^aR^b$, -N$(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-G^a, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-OC(O)R^a, -$(CR^{za}R^{zb})_m$-OC(O)NR^aR^b, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-S(O)R^a, -$(CR^{za}R^{zb})_m$-S$(O)_2R^a$, -$(CR^{za}R^{zb})_m$-S$(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-C(O)R^a, -$(CR^{za}R^{zb})_m$-C(O)OR^a, -$(CR^{za}R^{zb})_m$-C(O)NR^aR^b, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-N$(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-N$(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-N$(R^a)SO_2NR^aR^b$;G^a, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -OC(O)R^a, -OC(O)NR^aR^b, -NR^aR^b, -SR^a, -S(O)R^a, -S$(O)_2R^a$, -S$(O)_2NR^aR^b$, -C(O)R^a, -C(O)OR^a, -C(O)NR^aR^b, -N$(R^a)COOR^b$, -N$(R^a)CONR^aR^b$,-N$(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a,-$(CR^{za}R^{zb})_m$-OC(O)R^a, -$(CR^{za}R^{zb})_m$-OC(O)NR^aR^b, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-S(O)R^a,-$(CR^{za}R^{zb})_m$-S$(O)_2R^a$, -$(CR^{za}R^{zb})_m$-S$(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-C(O)R^a, -$(CR^{za}R^{zb})_m$-C(O)OR^a, -$(CR^{za}R^{zb})_m$-C(O)NR^aR^b, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-N$(R^a)COOR^b$,-$(CR^{za}R^{zb})_m$-N$(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-N$(R^a)SO_2NR^aR^b$;R^{za}, R^{zb}, R^{3a}, R^{3b}, R^{4a}, and R^{4b}, at each occurrence, are each independently hydrogen, alkyl, halogen, or haloalkyl; R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or haloalkyl; and m and n, at each occurrence, are each independently 1, 2, 3, or 4 ; and u is 0, 1, 2, or 3.

Formula 156

[0806] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 156. Such compounds are described in US Patent No. 8,629,143, issued January 14, 2014, and corresponding to US Application No. US8629143B2 filed November 18, 2010; International Publication No. WO2011066168A1, published June 3, 2011, and corresponding to International Application No. PCT/US2010/057224 filed November 18, 2010; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 156, these references incorporated by reference herein control.

[0807] In an embodiment, the Kv7 channel activator is a compound according to Formula 156:

Formula 156



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or a pharmaceutically acceptable salt, solvate, prodrug, or salt of a prodrug or solvate thereof, wherein R^1 is an optional substituent wherein each occurrence of R^1 is independently G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b,-$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$, or -$(CR^{za}R^{zb})_m$-G^a; p is 0, 1, 2, 3, or 4;R^3 is hydrogen, alkyl, alkenyl, alkynyl, halogen, haloalkyl, -$(CR^{3a}R^{3b})_m$-G^{3a}, or G^{3a}; G^{3a}, at each occurrence, is independently aryl, cycloalkyl, or cycloalkenyl; each of which is optionally substituted;R^4 is alkenyl, alkynyl, haloalkyl, G^{4a}, -$(CR^{4a}R^{4b})_n$-G^{4a}, or alkyl which is optionally substituted with one or two groups independently selected from the group consisting of $S(R^{1a})$, $0(R^{1a})$ and $N(R^{1a})_2$;each occurrence of R^{1a} is independently hydrogen, G^a, -$(CR^{za}R^{zb})_m$-G^a, alkyl, haloalkyl, hydroxyalkyl, or alkoxyalkyl;G^{4a}, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is optionally substituted; G^{3a} and G^{4a}, at each

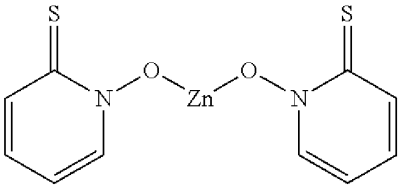
occurrence, are each independently unsubstituted or substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of G^a, alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$,-$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$, -$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-G^a, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a, -$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$, -$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$;G^a, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; each of which is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, halogen, haloalkyl, oxo, -CN, -NO_2, -OR^a, -$OC(O)R^a$, -$OC(O)NR^aR^b$, -NR^aR^b, -SR^a, -$S(O)R^a$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$, -$N(R^a)COOR^b$, -$N(R^a)CONR^aR^b$,-$N(R^a)SO_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-CN, -$(CR^{za}R^{zb})_m$-NO_2, -$(CR^{za}R^{zb})_m$-OR^a,-$(CR^{za}R^{zb})_m$-$OC(O)R^a$, -$(CR^{za}R^{zb})_m$-$OC(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-SR^a, -$(CR^{za}R^{zb})_m$-$S(O)R^a$,-$(CR^{za}R^{zb})_m$-$S(O)_2R^a$, -$(CR^{za}R^{zb})_m$-$S(O)_2NR^aR^b$, -$(CR^{za}R^{zb})_m$-$C(O)R^a$, -$(CR^{za}R^{zb})_m$-$C(O)OR^a$, -$(CR^{za}R^{zb})_m$-$C(O)NR^aR^b$, -$(CR^{za}R^{zb})_m$-NR^aR^b, -$(CR^{za}R^{zb})_m$-$N(R^a)COOR^b$,-$(CR^{za}R^{zb})_m$-$N(R^a)CONR^aR^b$, and -$(CR^{za}R^{zb})_m$-$N(R^a)SO_2NR^aR^b$;R^{za}, R^{zb}, R^{3a}, R^{3b}, R^{4a}, and R^{4b}, at each occurrence, are each independently hydrogen, alkyl, halogen, or haloalkyl; R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or haloalkyl; and m and n, at each occurrence, are each independently 1, 2, 3, or 4 ; v is 1, 2, or 3; and

y is absent, a bond, -CH_2-, or -CH_2CH_2-.

Formula 157

[0808] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 157. Such compounds are described in US Publication No. US20110257146A1, published October 20, 2011, and corresponding to US Application No. 12/223,136 filed January 25, 2007; International Publication No. WO2007087424A2, published August 2, 2007, and corresponding to International Application No. PCT/US2007/002116 filed January 26, 2007; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 157, these references incorporated by reference herein control.

[0809] In an embodiment, the Kv7 channel activator is a compound according to Formula 157:



Formula 157

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[0810] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: zinc-5,7-Diiodo-8-hydroxyquinoline and zinc-8-Hydroxyquinoline.

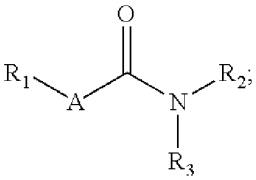
[0811] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: zinc-pyrrolidine dithiocarbamate, zinc-diethyldithiocarbamate, zinc-disulfiram and zinc-dimethyldithiocarbamate.

[0812] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: zinc-vitamin E and zinc-vitamin A.

Formula 158

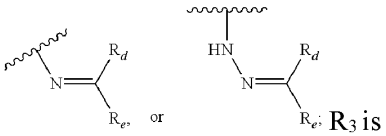
[0813] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 158. Such compounds are described in US Publication No. US20110257146A1, published October 20, 2011, and corresponding to US Application No. 12/223,136 filed January 25, 2007; International Publication No. WO2007087424A2, published August 2, 2007, and corresponding to International Application No. PCT/US2007/002116 filed January 26, 2007; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 158, these references incorporated by reference herein control.

[0814] In an embodiment, the Kv7 channel activator is a compound according to Formula 158:



Formula 158

wherein, A is a bond, CH_2, CHR_b, CH_2S, CHR_bS, CH_2O, CH_2NR_c, or NH; Rb is alkyl; R_c is H or $S(O)_m$-aryl; R_1 is an optionally substituted alkyl, an optionally substituted aryl, an optionally substituted cycloalkyl, or an optionally substituted heteroaryl; R_2 is an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted aryl, an optionally substituted cycloalkyl, an optionally substituted heteroaryl, an optionally

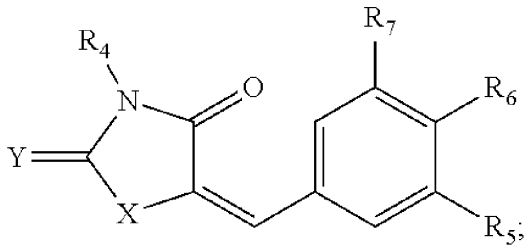
substituted heterocyclic, an optionally substituted aralkyl,  R_3 is H or alkyl; each R_d and R_e is independently an optionally substituted alkyl, an optionally substituted aryl, or R_d and R_e together form an optionally substituted cycloalkyl; and m is 0, 1, or 2.

Formula 159

[0815] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 159. Such compounds are described in US Publication No. US20110257146A1, published October 20, 2011, and corresponding to US Application No. 12/223,136 filed January 25, 2007; International Publication No. WO2007087424A2, published August 2, 2007, and corresponding to International Application No. PCT/US2007/002116 filed January 26, 2007; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 159, these references incorporated by reference herein control.

[0816] In an embodiment, the Kv7 channel activator is a compound according to Formula 159:

Formula 159



wherein, R_4 is H, an optionally substituted alkyl, an optionally substituted alkenyl, alkynyl, allyl, or an optionally substituted aryl; R_5 is H, hal, or hydroxyl; R_6 is H, hal, hydroxyl, NH_2, a mono- or di-substituted amine, or an optionally substituted alkoxy; R_7 is H, hal, hydroxyl, an optionally substituted alkoxy, or nitro; X is S or NR_a; Y is O, S, or NR_a; and each R_a is independently H or an optionally substituted aryl.

[0817] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: N-Benzo[g]quinolin-4-yl-N′-(2-diethylamino-ethyl)-benzene-1,4-diamine; 2-[2-(3,4-Dihydroxy-phenyl)-2-oxo-ethylsulfanyl]-4,6-dimethyl-nicotinonitrile; 2-[2-(4-Methoxy-phenyl)-2-oxo-ethylsulfanyl]-4-(5-methyl-furan-2-yl)-5,6,7,8-tetrahydro-quinoline-3-carbonitrile; 6-Methyl-4-(5-methyl-furan-2-yl)-2-(2-oxo-2-phenyl-ethylsulfanyl)-

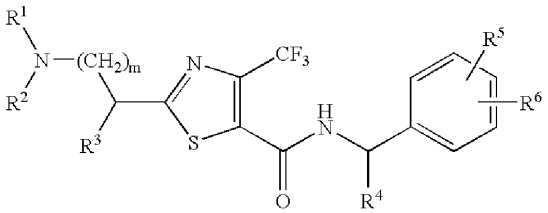
nicotinonitrile; 2-(2-Oxo-2-thiophen-2-yl-ethylsulfanyl)-4-pyridin-4-yl-5,6,7,8-tetrahydro-quinoline-3-carbonitrile; 2-(3,5-Diiodo-2-methoxy-phenyl)-2,3,5,6,7,8-hexahydro-1H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one; 2,2,2-Trifluoro-1-[1-(2,2,2-trifluoro-1-hydroxy-1-trifluoromethyl-ethyl)-1H-pyrrol-2-yl]-ethanone; 1,5-Diphenyl-1H-pyrazole-3-carboxylic acid tert-butylamide; 3-(4-Bromo-phenyl)-5-(3-phenyl-allylidene)-dihydro-pyrimidine-2,4-dione; 2-Amino-7-hydroxy-6-[(2-iodo-phenylimino)-methyl]-4-phenyl-4H-chromene-3-carbonitrile; 3-(1H-Benzoimidazol-2-yl)-6-nitro-chromen-2-ylideneamine; 6-Methoxy-3-(4-nitro-phenyl)-chroman-2-one; 2-(Benzo[1,2,5]thiadiazol-4-yliminomethyl)-benzo[b]thiophen-3-ol; 4-[3-(4-Bromo-phenyl)-3-oxo-propenylamino]-N-(4,6-dimethyl-pyrimidin-2-yl)-benzenesulfonamide; 2-[(5-Nitro-furan-2-ylmethylene)-amino]-benzamide; 2-Benzo[4,5]imidazo[1,2-c]quinazolin-6-yl-phenylamine; Dimethyl-phenyl)-5-(3-phenyl-allylidene)-pyrimidine-2,4,6-trione; 4-(4-Cyclohexyl-phenyl)-thiazol-2-ylamine; or 4-(4-Cyclohexyl-phenyl)-thiazol-2-ylamine.

Formula 160

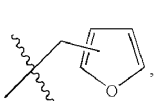
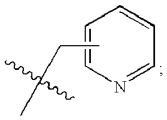
[0818] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 160. Such compounds are described in International Publication No. WO2004060880A1, published July 22, 2004, and corresponding to International Application No. PCT/US2003/039352 filed December 11, 2003; US Patent No. 6,933,308, issued August 23, 2005, and corresponding to US Application No. 10/730,781 filed December 9, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 160, these references incorporated by reference herein control.

[0819] In an embodiment, the Kv7 channel activator is a compound according to Formula 160:

Formula 160



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wherein, R_1 is $C_{1\text{-}6}$alkyl, $C_{3\text{-}7}$cycloalkyl, —$(CH_2)_{1\text{-}4}C_{3\text{-}7}$cycloalkyl, —$(CH_2)_{2\text{-}4}N(C_{1\text{-}6}alkyl)_2$, —$(CH_2)_{2\text{-}4}OC_{1\text{-}6}$alkyl,  or  R^2 is hydrogen, $C_{1\text{-}6}$alkyl, or —

$(CH_2)_{2\text{-}4}OC_{1\text{-}6}$alkyl; or where R^1 and R^2 taken together are —$CH_2CH_2XCH_2CH_2$—, where X is a chemical bond, CH_2, CHOH, NH, NCH_3, $NCOCH_3$, O, or S; R^3 is hydrogen or hydroxy, provided that where R^3 is hydroxy, m is not 0; R^4 is hydrogen, $C_{1\text{-}6}$alkyl, hydroxymethyl, or trifluoromethyl; R^5 is halogen, $C_{1\text{-}6}$alkyl, $C_{1\text{-}2}$perfluoroalkyl, $C_{1\text{-}6}$alkoxy, $C_{1\text{-}2}$perfluoroalkoxy, —$N(R^4)_2$, N-morpholinyl, or pyridyl; R^6 is hydrogen, halogen, or $C_{1\text{-}6}$alkoxy; m is 0 or 1.

[0820] In further embodiments, R^3 is hydrogen and m is 1.

[0821] In further embodiments, R^4 is methyl.

[0822] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-[2-(4-morpholinyl)ethyl]-N-[1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; N-[1-[3-(dimethylamino)phenyl]ethyl]-2-[2-(1-pyrrolidinyl)ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(1-pyrrolidinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[(2-furanylmethyl)methylamino]ethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(2-furanylmethyl)methylamino]ethyl]-N-[1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(1-pyrrolidinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(2-furanylmethyl)methylamino]ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(diethylamino)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(diethylamino)ethyl]-N-[1-[3-(dimethylamino)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[ethyl(4-pyridinylmethyl)amino]ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-(4-thiomorpholinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[[2-(dimethylamino)ethyl]methylamino]ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[[2-(dimethylamino)ethyl]methylamino]ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-(4-methyl-1-piperazinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(1-piperidinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; N-[1-[3-(dimethylamino)phenyl]ethyl]-2-[2-(1-piperidinyl)ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(1-piperidinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-2-[2-(1-piperidinyl)ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(4-hydroxy-1-piperidinyl)ethyl]-N-[1-[3-

(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(4-hydroxy-1-piperidinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[(cyclopropylmethyl)propylamino]ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(cyclopropylmethyl)propylamino]ethyl]-N-[1-[3-(dimethylamino)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(cyclopropylmethyl)propylamino]ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-(diethylamino)ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(1-piperidinyl)ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(1-ethylpropyl)amino]ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(1-ethylpropyl)amino]ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[(2-furanylmethyl)amino]ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(cyclopentylamino)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(cyclopentylamino)ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[bis(2-methoxyethyl)amino]ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[bis(2-methoxyethyl)amino]ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[bis(2-methoxyethyl)amino]ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(4-morpholinyl)ethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; N-[1-[3-(dimethylamino)phenyl]ethyl]-2-[2-(4-thiomorpholinyl)ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[[2-(dimethylamino)ethyl]methylamino]ethyl]-N-[1-[3-(dimethylamino)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; and 2-[2-(4-methyl-1-piperazinyl)ethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide.

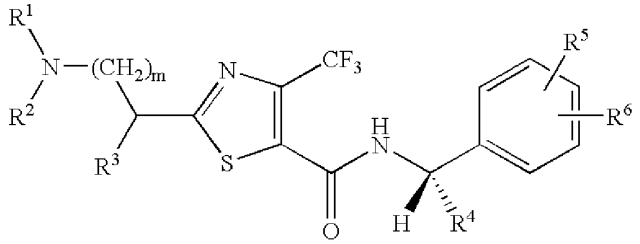
[0823] In further embodiments, R^3 is hydroxy and m is 1.

[0824] In further embodiments, R^4 is methyl.

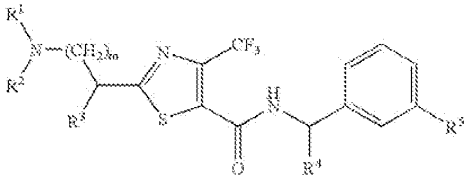
[0825] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-[1-hydroxy-2-(1-piperidinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(1-pyrrolidinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[(2-furanylmethyl)methylamino]-1-hydroxyethyl]-4-(trifluoromethyl)-N-[1-[3-

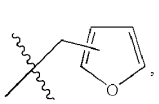
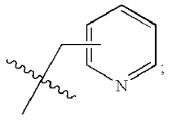
(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[2-[(cyclopropylmethyl)propylamino]-1-hydroxyethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(diethylamino)-1-hydroxyethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-(diethylamino)-1-hydroxyethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(4-morpholinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(4-morpholinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[1-hydroxy-2-(4-methyl-1-piperazinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[1-hydroxy-2-(4-methyl-1-piperazinyl)ethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(4-methyl-1-piperazinyl)ethyl]-N-[(1S)-1-[3-(3-pyridinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(1-piperidinyl)ethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; 2-[1-hydroxy-2-(1-pyrrolidinyl)ethyl]-N-[1-[3-(trifluoromethoxy)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; N-[1-[3-(dimethylamino)phenyl]ethyl]-2-[1-hydroxy-2-(1-pyrrolidinyl)ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[1-hydroxy-2-(1-pyrrolidinyl)ethyl]-N-[(1S)-1-[3-(4-morpholinyl)phenyl]ethyl]-4-(trifluoromethyl)-5-thiazolecarboxamide; 2-[2-[(cyclopropylmethyl)propylamino]-1-hydroxyethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide; and 2-[2-(4-acetyl-1-piperazinyl)-1-hydroxyethyl]-4-(trifluoromethyl)-N-[1-[3-(trifluoromethyl)phenyl]ethyl]-5-thiazolecarboxamide.

[0826] In further embodiments, the compound has a stereochemical configuration according to the formula:



[0827] In further embodiments, the compound is according to the formula:

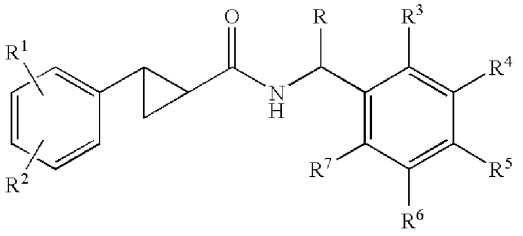


[0828] Wherein, $R^1$is C_{1-6}alkyl, C_{3-7}cycloalkyl, —$(CH_2)_{1-4}C_{3-7}$cycloalkyl, —$(CH_2)_{2-4}N(C_{1-6}$alkyl$)_2$, —$(CH_2)_{2-4}OC_{1-6}$alkyl,  or  R^2 is hydrogen C_{1-6}alkyl, or —$(CH_2)_{2-4}OC_{1-6}$alkyl; or where R^1 and R^2 taken together are —$CH_2CH_2XCH_2CH_2$—, where X is a chemical bond, CH_2, CHOH, NH, NCH_3, $NCOCH_3$, O, or S; R^3 is hydrogen or hydroxy, provided that where R^3 is hydroxy, m is not 0; R^4 is hydrogen, C_{1-6}alkyl, hydroxymethyl, or trifluoromethyl; R^5 is halogen, C_{1-6}alkyl, C_{1-2}perfluoroalkyl, C_{1-6}alkoxy, C_{1-2}perfluoroalkoxy, —$N(R^4)_2$, N-morpholinyl, or pyridyl; and m is 0 or 1; or a pharmaceutically acceptable salt thereof.

Formula 161

[0829] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 161. Such compounds are described in US Patent No. 7,144,881 issued December 5, 2006, and corresponding to US Application No. 10/919,184 filed November 21, 2003; International Publication No. WO2004047738A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037305 filed November 21, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 161, these references incorporated by reference herein control.

[0830] In an embodiment, the Kv7 channel activator is a compound according to Formula 161:



Formula 161

,

wherein, R is C_{1-4} alkyl, CF_3 or hydroxymethyl; R^1 and R^2 are each independently hydrogen, C_{1-4} alkyl, halogen or morpholin-4-yl; R^4 is selected from the group consisting of optionally

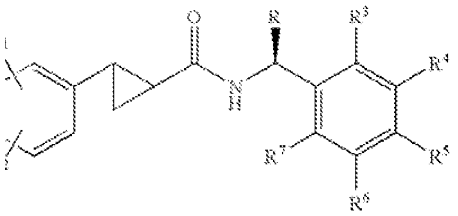
substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl, in which said substituent is independently selected from the group consisting of C_{1-4}alkyl, dimethylamino, hydroxymethyl, chloro and fluoro; R^5 is hydrogen or fluoro; or R^4 and R^5 taken together are —CH=CH—CH=CH— or —CH_2CH_2O—; and R^3, R^6 and R^7 are each independently selected from hydrogen or fluoro.

Formula 162

[0831] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 162. Such compounds are described in US Patent No. 7,144,881 issued December 5, 2006, and corresponding to US Application No. 10/919,184 filed November 21, 2003; International Publication No. WO2004047738A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037305 filed November 21, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 162, these references incorporated by reference herein control.

[0832] In an embodiment, the Kv7 channel activator is a compound according to Formula 162:

Formula 162



,

wherein, R is methyl or hydroxymethyl; R^1 and R^2 are each independently hydrogen, C_{1-4} alkyl, halogen or morpholin-4-yl; R^4 is selected from the group consisting of optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl, in which said substituent is independently selected from the group consisting of C_{1-4}alkyl, dimethylamino, hydroxymethyl, chloro and fluoro; R^5 is hydrogen or fluoro; or R^4 and R^5 taken together are —CH=CH—CH=CH— or —CH_2CH_2O—; and R^3, R^6 and R^7 are each independently selected from hydrogen or fluoro.

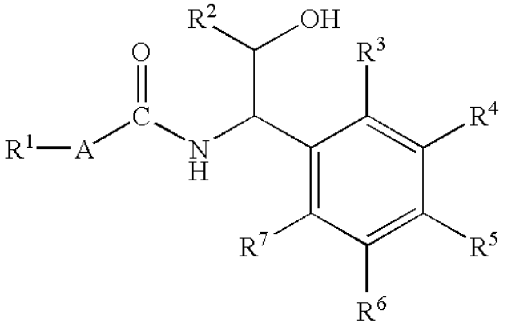
[0833] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-(2-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(2,3-dihydro-benzofuran-5-yl)-ethyl]-amide; 2-(3-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(2,3-dihydro-benzofuran-5-yl)-ethyl]-amide; 2-(4-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(2,3-dihydro-benzofuran-5-yl)-ethyl]-amide; 2-(2-fluoro-phenyl)-cyclopropanecarboxylic acid(2-

hydroxy-1-naphthalen-2-yl-ethyl)-amide; 2-(3-fluoro-phenyl)-cyclopropanecarboxylic acid(2-hydroxy-1-naphthalen-2-yl-ethyl)-amide; 2-(4-fluoro-phenyl)-cyclopropanecarboxylic acid(2-hydroxy-1-naphthalen-2-yl-ethyl)-amide; 2-(2,5-difluoro-phenyl)-cyclopropanecarboxylic acid(2-hydroxy-1-naphthalen-2-yl-ethyl)-amide; 2-(2-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-amide; 2-(3-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-amide; 2-(4-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-amide; 2-(2,5-difluoro-phenyl)-cyclopropanecarboxylic acid[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-amide; 2-(4-fluoro-phenyl)-cyclopropanecarboxylic acid(1-naphthalen-2-yl-ethyl)-amide; 2-(2,5-difluoro-phenyl)-cyclopropanecarboxylic acid(1-naphthalen-2-yl-ethyl)-amide; 2-(4-fluoro-phenyl)-cyclopropanecarboxylic acid{1-[3-(3-dimethylamino-pyrrolidin-1-yl)-phenyl]-ethyll}-amide; 2-(2,5-difluoro-phenyl)-cyclopropanecarboxylic acid{1-[3-(3-dimethylamino-pyrrolidin-1-yl)-phenyl]-ethyl}-amide; 2-(3-fluoro-phenyl)-cyclopropanecarboxylic acid[1-(3-pyridin-3-yl-phenyl)-ethyl]-amide; 2-(2,5-difluoro-phenyl)-cyclopropanecarboxylic acid[1-(3-pyridin-3-yl-phenyl)-ethyl]-amide; (S)-2-phenyl-cyclopropanecarboxylic acid[1-(3-pyridin-3-yl-phenyl)-ethyl]-amide; (S)-2-(3-fluoro-phenyl)-cyclopropanecarboxylic acid{1-[3-(6-fluoro-pyridin-3-yl)-phenyl]-ethyl}-amide; (S)-2-phenyl-cyclopropanecarboxylic acid{1-[3-(2-fluoro-pyridin-3-yl)-phenyl]-ethyl}-amide; and (S)-2-(2-fluoro-phenyl)-cyclopropanecarboxylic acid{1-[3-(2-fluoro-pyridin-3-yl)-phenyl]-ethyl}-amide; or a pharmaceutically acceptable salt thereof.

Formula 163

[0834] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 163. Such compounds are described in International Publication No. WO2004047743A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037348 filed November 21, 2003; US Patent No. 7,045,551 issued May 16, 2006, and corresponding to US Application No. 10/719,465 filed November 21, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 163, these references incorporated by reference herein control.

[0835] In an embodiment, the Kv7 channel activator is a compound according to Formula 163:



Formula 163

,

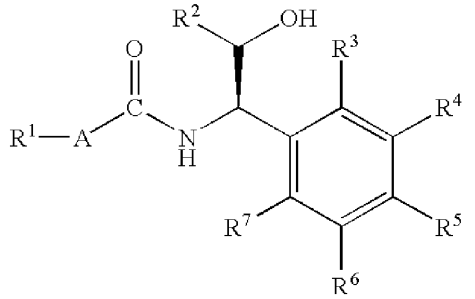
wherein, R^1 is selected from the group consisting of pyridinyl, 3-quinolinyl, 2-thienyl, furanyl, C_{3-6} cycloalkyl and phenyl optionally substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy and nitro; A is —CH=CH— or —$(CH_2)_n$—; R^2 is hydrogen or hydroxymethyl; n is an integer of 0, 1 or 2; R^4 is selected from the group consisting of di(C_{1-4} alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, morpholin-4-ylmethyl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R_5 is hydrogen or fluoro; or R^4 and R^5 taken together is —CH=CH—CH=CH— optionally substituted with a substituent independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl and trifluoromethoxy; and R^3, R^6, and R^7 are each independently hydrogen or fluoro.

Formula 164

[0836] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 164. Such compounds are described in International Publication No. WO2004047743A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037348 filed November 21, 2003; US Patent No. 7,045,551 issued May 16, 2006, and corresponding to US Application No. 10/719,465 filed November 21, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 164, these references incorporated by reference herein control.

[0837] In an embodiment, the Kv7 channel activator is a compound according to Formula 164:

Formula 164



,

wherein, R^1 is selected from the group consisting of pyridinyl, 3-quinolinyl, 2-thienyl, furanyl, C_{3-6} cycloalkyl and phenyl optionally substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy and nitro; A is —CH=CH— or —$(CH_2)_n$—; R^2 is hydrogen; n is an integer of 0, 1 or 2; R^4 is selected from the group consisting of di(C_{1-4} alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, morpholin-4-ylmethyl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R^5 hydrogen or fluoro; or R^4 and R^5 taken together is —CH=CH—CH=CH— optionally substituted with a substituent independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl and trifluoromethoxy; and R^3, R^6, and R^7 are each independently hydrogen or fluoro.

[0838] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: (R)-N-[2-hydroxy-1-(3-morpholin-4-yl-phenyl)-ethyl]-3-phenyl-propionamide; (R)-3-(2-fluoro-phenyl)-N-[2-hydroxy-1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (R)-3-(3-fluoro-phenyl)-N-[2-hydroxy-1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (R)-3-(2,4-difluoro-phenyl)-N-[2-hydroxy-1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (R)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-3-(2-fluoro-phenyl)-acrylamide (R)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-3-(3-fluoro-phenyl)-acrylamide (R)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-3-(4-fluoro-phenyl)-acrylamide (R)-3-(2,4-difluoro-phenyl)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-2-hydroxy-ethyl]-acrylamide (R)-3-(3-fluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-acrylamide; (R)-3-(4-fluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-acrylamide; (R)-3-(2,4-difluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-acrylamide; (R)-3-(3,4-difluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-acrylamide; (R)-4-fluoro-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-benzamide; (R)-2,3-difluoro-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-benzamide; (R)-2,4-difluoro-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-benzamide;

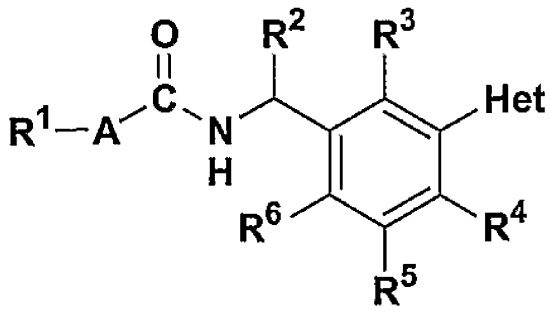
(R)-3,4-difluoro-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-benzamide; (R)-2-(2,4-difluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-acetamide; (R)-3-(2-fluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-propionamide; (R)-3-(3-fluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-propionamide; (R)-3-(4-fluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-propionamide; (R)-3-(2,4-difluoro-phenyl)-N-(2-hydroxy-1-naphthalen-2-yl-ethyl)-propionamide; (R)-3-(2-fluoro-phenyl)-N-[2-hydroxy-1-(7-methoxy-naphthalen-2-yl)-ethyl]-acrylamide; (R)-3-(3-fluoro-phenyl)-N-[2-hydroxy-1-(7-methoxy-naphthalen-2-yl)-ethyl]-acrylamide; (R)-3-(4-fluoro-phenyl)-N-[2-hydroxy-1-(7-methoxy-naphthalen-2-yl)-ethyl]-acrylamide; (R)-3-(2,4-difluoro-phenyl)-N-[2-hydroxy-1-(7-methoxy-naphthalen-2-yl)-ethyl]-acrylamide; (1R, 2S)-N-(2,3-dihydroxy-1-naphthalen-2-yl-propyl)-3-(2-fluoro-phenyl)-acrylamide; (1R, 2S)-3-(2,4-difluoro-phenyl)-N-(2,3-dihydroxy-1-naphthalen-2-yl-propyl)-acrylamide; (1R, 2S)-3-(3,4-difluoro-phenyl)-N-(2,3-dihydroxy-1-naphthalen-2-yl-propyl)-acrylamide; and (1R, 2S)-3-(3,5-difluoro-phenyl)-N-(2,3-dihydroxy-1-naphthalen-2-yl-propyl)-acrylamide; or a pharmaceutically acceptable salt thereof.

Formula 165

[0839] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 165. Such compounds are described in US Patent No. 7,135,472 issued November 14, 2006, and corresponding to US Application No. 10/719,187 filed November 21, 2003; International Publication No. WO2004047744A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037349 filed November 21, 2003; US Patent No. 7,135,472 issued November 14, 2006, and Patent Cooperation Treaty application No. US2003/037349 published June 10, 2004, which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 165, these references incorporated by reference herein control.

[0840] In an embodiment, the Kv7 channel activator is a compound according to Formula 165:

Formula 165



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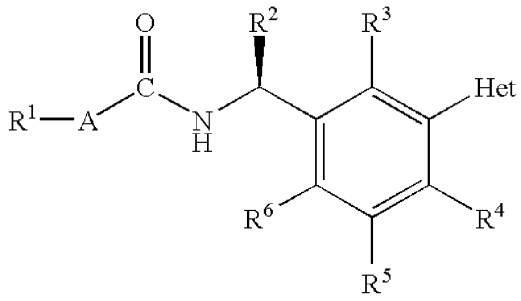
wherein, R^1 is selected from the group consisting of straight or branched chain C_{x_6} alkyl optionally substituted with amino, C alkylamino or di($C_{1.4}$ alkyl) amino, pyridinyl, pyrrodidinyl, piperidinyl, 2-thienyl, furanyl, imidazolyl, indenyl, benzofuran, $C_{3.6}$ cycloalkyl and phenyl optionally substituted with substituent independently selected from the group consisting of halogen, C_M alkyl, C alkoxy, trifluoromethyl, and trifiuoromethoxy; A is -CH=CH-, 1,1 -cyclopropyl, or-$(CH_2)_n$-; R^2 is C_M alkyl, CF_3 or hydroxymethyl; R^3, R^4, R^5 and R^6 each are independently hydrogen or fluoro; n is an integer of 0 to 4, inclusive; Het is selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, thiazolyl, imidazolyl, isoxazolyl, oxazolyl, pyrazolyl and triazolyl optionally substituted with substituents independently selected from the group consisting of C_M alkyl, halogen, amino and dimethylaminomethyl; provided that when Het is pyridinyl, pyrimidinyl or pyrazinyl, then A is not -CH=CH-.

Formula 166

[0841] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 166. Such compounds are described in US Patent No. 7,135,472, issued November 14, 2006, and corresponding to US Application No. 10/719,187 filed November 21, 2003; International Publication No. WO2004047744A2, published June 10, 2004, and corresponding to International Application No. PCT/US2003/037349 filed November 21, 2003; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 166, these references incorporated by reference herein control.

[0842] In an embodiment, the Kv7 channel activator is a compound according to Formula 166:

Formula 166



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wherein, R^1 is selected from the group consisting of straight or branched chain C_{1-6} alkyl optionally substituted with amino, C_{1-4} alkylamino or di(C_{1-4} alkyl) amino, pyridinyl, pyrrodidinyl, piperidinyl, 2-thienyl, furanyl, imidazolyl, indenyl, benzofuran, C_{3-6} cycloalkyl and phenyl optionally substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, and trifluoromethoxy; A is —CH=CH—, 1,1-cyclopropyl, or —$(CH_2)_n$—; R^2 is methyl or hydroxymethyl; R^3, R^4, R^5 and R^6 each are independently hydrogen or fluoro; n is an integer of 0 to 4, inclusive; Het is selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, thiazolyl, imidazolyl, isoxazolyl, oxazolyl, pyrazolyl and triazolyl optionally substituted with substituents independently selected from the group consisting of C_{1-4} alkyl, halogen, amino and dimethylaminomethyl; provided that when Het is pyridinyl, pyrimidinyl or pyrazinyl, then A is not —CH=CH—.

[0843] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: (S)-3-(2-fluoro-phenyl)-N-[1-(3-[1,2,4]triazol-1-yl-phenyl)-ethyl]-acrylamide; (S)-3-(2-fluoro-phenyl)-N-[1-(3-thiazol-2-yl-phenyl)-ethyl]-acrylamide; (S)-3-(2-fluoro-phenyl)-N-[1-(3-pyrazol-1-yl-phenyl)-ethyl]-acrylamide; (S)-3-(2-fluoro-phenyl)-N-[1-(3-imidazol-1-yl-phenyl)-ethyl]-acrylamide; (S)-4-phenyl-N-[1-(3-pyridin-3-yl-phenyl)-ethyl]-butyramide; (S)-N-[1-(3-pyridin-3-yl-phenyl)-ethyl]-benzamide; (S)-1H-imidazole-4-carboxylic acid [1-(3-pyridin-3-yl-phenyl)-ethyl]-amide; (S)-N-[1-(3-imidazol-1-yl-phenyl)-ethyl]-3-phenyl-acrylamide; (S)-N-[1-(3-oxazol-5-yl-phenyl)-ethyl]-3-phenyl-acrylamide; (S)-3-phenyl-N-[1-(3-thiazol-2-yl-phenyl)-ethyl]-acrylamide; (S)-3-phenyl-N-[1-(3-pyrazol-1-yl-phenyl)-ethyl]-acrylamide; and (S)-benzofuran-2-carboxylic acid {1-[3-(6-fluoro-pyridin-3-yl)-phenyl]-ethyl}-amide; or a pharmaceutically acceptable salt thereof.

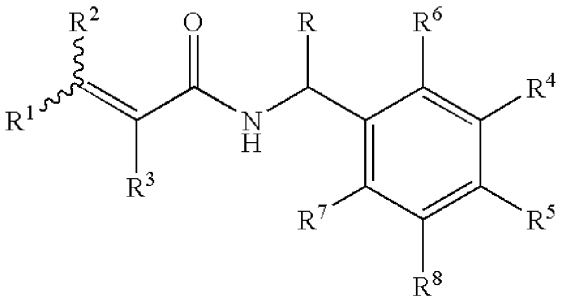
Formula 167

[0844] In an embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 167. Such compounds are described in

International Publication No. WO2002096858A1, published December 5, 2002, and corresponding to International Application No. PCT/US2002/017049 filed May 31, 2002; US Patent No. 6,831,080, issued December 14, 2004, and corresponding to US Application No. 10/160,582 filed May 31, 2002; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 167, these references incorporated by reference herein control.

[0845] In an embodiment, the Kv7 channel activator is a compound according to Formula 167:

Formula 167



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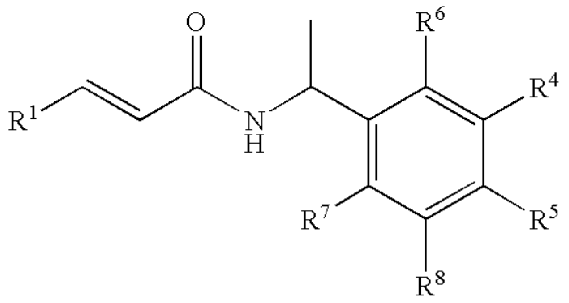
wherein, R is C_{1-4} alkyl or trifluoromethyl; R^1 is selected from the group consisting of pyridinyl, quinolinyl, thienyl, furanyl, 1,4-benzodioxanyl, 1,3-benzodioxolyl, chromanyl, indanyl, biphenylyl, phenyl and substituted phenyl, in which said substituted phenyl is substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy and nitro; R^2 and R^3 are each independently selected from the group consisting of hydrogen, C_{1-4} alkyl and halogen; R^4 is selected from the group consisting of di(C_{1-4} alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C_{1-4}alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R^5 is hydrogen, chloro or fluoro; or R^4 and R^5 taken together are —CH=CH—CH=CH— or —$X(CH_2)_mY$— in which X and Y are each independently selected from the group consisting of CH_2, $(CH_2)_nN(R^9)$— and O, wherein m is 1 or 2; n is 0 or 1; R^6, R^7, and R^8 are each independently selected from hydrogen, chloro and fluoro; and R^9 is selected from the group consisting of hydrogen, C_{1-4} alkyl, hydroxyethyl, C_{1-4} alkoxyethyl, cyclopropylmethyl, —$CO_2(C_{1-4}$alkyl), and —$CH_2CH_2NR^{10}R^{11}$ in which R^{10} and R^{11} are each independently hydrogen or C_{1-4} alkyl.

Formula 168

[0846] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 168. Such compounds are described in International Publication No. WO2002096858A1, published December 5, 2002, and corresponding to International Application No. PCT/US2002/017049 filed May 31, 2002; US Patent No. 6,831,080 issued December 14, 2004, and corresponding to US Application No. 10/160,582 filed May 31, 2002; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 168, these references incorporated by reference herein control.

[0847] In an embodiment, the Kv7 channel activator is a compound according to Formula 168:

Formula 168



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wherein, R^1 is selected from the group consisting of pyridinyl, 3-quinolinyl, 2-thienyl, benzodioxanyl, 1,3-benzodioxol-5-yl, chroman-5-yl, indan-5-yl, 4-biphenylyl, phenyl and substituted phenyl, in which said substituted phenyl is substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C -4 alkoxy, trifluoromethyl, trifluoromethoxy and nitro; R^4 is selected from the group consisting of optionally substituted di(C_{1-4} alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R^5 is hydrogen or fluoro; or R^4 and R^5 taken together are —CH=CH—CH=CH— or —$X(CH_2)_mY$—, in which X and Y are each independently selected from the group consisting of CH_2, $(CH_2)_nN(R^9)$— and O, wherein m is 1 or 2; n is 0 or 1; R^6, R^7, and R^8 are each independently selected from hydrogen, chloro and fluoro; and R^9 is selected from the group consisting of hydrogen, C_{1-4} alkyl, hydroxyethyl, C_{1-4} alkoxyethyl, cyclopropylmethyl, —$CO_2(C_{1-4}$alkyl), and —$CH_2CH_2NR^{10}R^{11}$ in which R^{10} and R^{11} are each independently hydrogen or C_{1-4} alkyl.

[0848] In further embodiments, R^1 is substituted phenyl or 1,3-benzodioxol-5-yl in which said substituted phenyl is substituted with one or two substituents each independently

selected from the group consisting of halogen, C_{1-4} alkyl, and C_{1-4} alkoxy; and R^4 and R^5 taken together are —$X(CH_2)_mY$— in which X and Y are each O, and m is 1.

[0849] In further embodiments, R^1 is selected from the group consisting of substituted phenyl, 1,3-benzodioxol-5-yl, and indan-5-yl in which said substituted phenyl is substituted with one or two substituents each independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy and trifluoromethyl; and R^4 and R^5 taken together are —$X(CH_2)_mY$— in which X is CH_2, Y is O, and m is 1.

[0850] In further embodiments, R^1 is thienyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy, trifluoromethyl and nitro; R^4 is optionally substituted morpholin-4-yl with one or two substituents each independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; and R^5 is hydrogen or fluoro.

[0851] In further embodiments, R^1 is phenyl, fluorophenyl or difluorophenyl.

[0852] In further embodiments, R^1 is substituted phenyl or 1,3-benzodioxol-5-yl in which said substituted phenyl is substituted with one or two substituents each independently selected from halogen or C_{1-4} alkyl; and R^4 and R^5 taken together are —$X(CH_2)_mY$— in which X and Y are O, and m is 2.

[0853] In further embodiments, R^1 is phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from halogen or C_{1-4} alkyl; R^4 and R^5 taken together are —$X(CH_2)_mY$— in which X is $(CH_2)_nN(R^9)$—; Y is CH_2, and m and n are 1; and R^9 is $CO_2(C_{1-4}alkyl)$.

[0854] In further embodiments, R^1 is substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from halogen; R^4 and R^5 taken together are —$X(CH_2)_mY$— in which X is $(CH_2)_nN(R^9)$— and Y is O wherein m is 2 and n is 0; and R^9 is hydrogen, cyclopropylmethyl or C_{1-4}alkyl.

[0855] In further embodiments, R^1 is 3-quinolinyl or pyridinyl; R^4 is trifluoromethoxy; and R^5 is hydrogen.

[0856] In further embodiments, R^1 is substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen or C_{1-4}alkyl; R^4 and R^5 taken together are —$X(CH_2)_mY$—, in which X is CH_2 and Y is $(CH_2)_nN(R^9)$— wherein m is 1 and n is 0; and R^9 is $CO_2(C_{1-4}alkyl)$.

[0857] In further embodiments, R^1 is phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 and R^5 taken

together are —X(CH_2)$_m$Y—, in which X is (CH_2)$_n$N(R^9)— and Y is CH_2 wherein m is 2 and n is 0; and R^9 is hydrogen, C_{1-4}alkyl, acetyl, hydroxyethyl or methoxyethyl.

[0858] In further embodiments, R^1 is phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 and R^5 taken together are —X(CH_2)$_n$Y—, in which X is CH_2 and Y is (CH_2)$_n$N(R^9)— wherein m is 2 and n is 0; and R^9 is hydrogen, C_{1-4}alkyl, acetyl, hydroxyethyl or methoxyethyl.

[0859] In further embodiments, R^1 is pyridinyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 is optionally substituted pyridinyl with one or two substituents each independently selected from C_{1-4} alkyl and halogen; and R^5 is hydrogen or fluoro.

[0860] In further embodiments, R^1 is 1,3-benzodioxol-5-yl; R^4 is di(C_{1-4}alkyl)amino; and R^5 is hydrogen or fluoro.

[0861] In further embodiments, R^1 is phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 is pyrimidinyl; and R^5 is hydrogen or fluoro.

[0862] In further embodiments, R^1 is phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 is pyrazinyl; and R^5 is hydrogen or fluoro.

[0863] In further embodiments, R^1 is thienyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from C_{1-4}alkyl and halogen; R^4 is piperazinyl or 4-methylpiperazinyl; and R^5 is hydrogen or fluoro.

[0864] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: 2-Methyl-3-phenyl-but-2-enoic acid (1-naphthalen-2-ylethyl)-amide; N-(1-Benzo[1,3]dioxol-5-yl-ethyl)-3-(3-methoxy-phenyl)-acrylamide; N-[1-(2,3-Dihydrobenzofuran-5-yl)ethyl]-3-(3-methoxyphenyl)-acrylamide; (S)-3-Phenyl-N-[1-(3-morpholin-4-yl-phenyl)ethyl]acrylamide; 3-(3-Fluorophenyl)-N-[1-(2,3-dihydrobenzo[1,4]dioxin-6-yl)-ethyl]acrylamide; (±)-7-{1-[3-(4-Fluorophenyl)acryloylamino]ethyl}-3,4-dihydro-1H-isoquinoline-2-carboxylic acid methyl ester; 3-(2-Fluorophenyl)-N-[1-(4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)ethyl]-acrylamide; (S)-N-(1-Naphthalen-2-yl-ethyl)-3-phenyl-acrylamide; (S)-3-(4-Fluoro-phenyl)-N-(1-naphthalen-2-yl-ethyl)-acrylamide; (±)-N-(1-Benzo[1,3]dioxol-5-yl-ethyl)-3-(2,4-difluoro-phenyl)-acrylamide; (±)-N-[1-(2,3-Dihydro-benzofuran-5-yl)-ethyl]-3-(2-fluoro-phenyl)-acrylamide; (±)-3-(2,4-Difluoro-phenyl)-N-[1-(2,3-dihydro-benzofuran-5-yl)-ethyl]-acrylamide; (S)-3-(2,4-Difluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide;

(S)-N-[1-(3-(2,6-Dimethyl-morpholin)-4-yl-phenyl)-ethyl]-3-phenyl-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (S)-N-[1-(3-Morpholin-4-yl-phenyl)-ethyl]-3-thiophen-3-yl-acrylamide; (S)-3-(4-Fluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (S)-N-{1-[3-(cis-2,6-Dimethyl-morpholin-4-yl)-phenyl]-ethyl}-3-(4-fluoro-phenyl)-acrylamide; (S)-3-(2,4-Difluoro-phenyl)-N-{1-[3-(cis-2,6-dimethyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(3,4-Difluoro-phenyl)-N-{1-[3-(cis-2,6-dimethyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(2,5-Difluoro-phenyl)-N-{1-[3-(cis-2,6-dimethyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-{1-[3-(2-methyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(3-Fluoro-phenyl)-N-{1-[3-(2-methyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(4-Fluoro-phenyl)-N-{1-[3-(2-methyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-3-(2,4-Difluoro-phenyl)-N-{1-[3-(2-methyl-morpholin-4-yl)-phenyl]-ethyl}-acrylamide; (S)-N-{1-[3-(2-Oxa-5-aza-bicyclo[2.2.1]hept-5-yl)phenyl]ethyl}-3-phenyl-acrylamide; (S)-N-{1-[3-(2-Hydroxymethyl-morpholin-4-yl)-phenyl]-ethyl}-3-phenyl-acrylamide; (±)-N-[1-(3-Morpholin-4-yl-phenyl)-propyl]-3-phenyl-acrylamide; (±)-3-(2,4-Difluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-propyl]-acrylamide; (±)-3-(2-Fluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-propyl]-acrylamide; (±)-3-(3-Fluoro-phenyl)-N-[1-(3-morpholin-4-yl-phenyl)-propyl]-acrylamide; (±)-N-[1-(4-Fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(2-fluoro-phenyl)-acrylamide; (±)-N-[1-(4-Fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(4-fluoro-phenyl)-acrylamide; (±)-3-(2,4-Difluoro-phenyl)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (±)-N-[1-(4-Fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(4-fluoro-phenyl)-acrylamide; (±)-3-(3,4-Difluoro-phenyl)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (±)-3-(2,5-Difluoro-phenyl)-N-[1-(4-fluoro-3-morpholin-4-yl-phenyl)-ethyl]-acrylamide; (±)-N-[1-(4-Fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(3-fluoro-phenyl)-acrylamide; (±)-N-[1-(4-Fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(2-fluoro-phenyl)-acrylamide; (±)-3-(3-Fluoro-phenyl)-N-[1-(1,2,3,4-tetrahydro-quinolin-7-yl)-ethyl]-acrylamide; (±)-3-(4-Fluoro-phenyl)-N-[1-(1,2,3,4-tetrahydro-quinolin-7-yl)ethyl]-acrylamide; (±)-3-(2-Fluoro-phenyl)-N-[1-(1-methyl-1,2,3,4-tetrahydro-quinolin-7-yl)ethyl]acrylamide; (±)-N-{1-[1-(2-Hydroxy-ethyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-ethyl}-3-phenyl-acrylamide; (±)-3-(2,5-Difluoro-phenyl)-N-{1-[1-(2-hydroxy-ethyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-ethyl}-acrylamide; (±)-3-(3,5-Difluoro-phenyl)-N-{1-[1-(2-hydroxy-ethyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-ethyl}-acrylamide; (S)-3-Phenyl-N-[1-(3-pyridyl-phenyl)-ethyl]acrylamide; (S)-(2,4-Difluoro-phenyl)-N-[1-(3-pyridin-3-yl-phenyl)-ethyl]-acrylamide; (S)-3-Phenyl-N-[1-(3-pyridin-4-yl-phenyl)-ethyl]-acrylamide; (S)-N-{1-

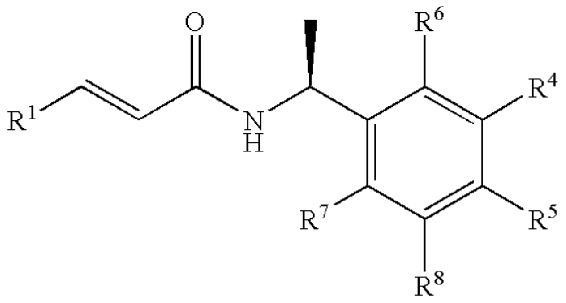
[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-(2-fluoro-phenyl)-acrylamide; (S)-3-Phenyl-N-[1-(3-pyrimidin-5-yl-phenyl)-ethyl]-acrylamide; (S)-3-Phenyl-N-[1-(3-pyridin-2-yl-phenyl)-ethyl]-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-pyridin-2-yl-phenyl)-ethyl]-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-{1-[3-(6-fluoro-pyridin-3-yl)-phenyl]ethyl}-acrylamide; (S)-3-(4-Fluoro-phenyl)-N-{1-[3-(6-fluoro-pyridin-3-yl)-phenyl]-ethyl}-acrylamide; (S)-N-{1-[3-(6-Fluoro-pyridin-3-yl)-phenyl]-ethyl}-3-pyridin-3-yl-acrylamide; (S)-N-{1-[3-(6-Fluoro-pyridin-3-yl)-phenyl]-ethyl}-3-pyridin-4-yl-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-(3-fluoro-phenyl)-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-pyridin-3-yl-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-pyridin-2-yl-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-pyridin-4-yl-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-(2-fluoro-phenyl)-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-(2,4-difluoro-phenyl)-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-(4-fluoro-phenyl)-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-pyridin-3-yl-phenyl)ethyl]acrylamide; (S)-N-{1-[3-(6-Fluoro-pyridin-3-yl)-phenyl]-ethyl}-3-phenyl-acrylamide; (S)-N-{1-[3-(6-Chloro-pyridin-3-yl)-phenyl]-ethyl}-3-phenyl-acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-pyridin-4-yl-phenyl)ethyl]acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-pyrazin-2-yl-phenyl)ethyl]acrylamide; (S)-3-(2-Fluoro-phenyl)-N-[1-(3-pyrimidin-5-yl-phenyl)ethyl]acrylamide; (S)-3-(2-Fluoro-phenyl)-N-{1-[3-(4-methyl-pyridin-3-yl)phenyl]ethyl}acrylamide; (S)-3-(4-Fluorophenyl)-N-{1-[3-(4-methylpiperazin-1-yl)phenyl]ethyl}acrylamide; and (S)-3-(2,3-Difluoro-phenyl)-N-{1-[3-(4-methyl-piperazin-1-yl)-phenyl]-ethyl}-acrylamide; or a pharmaceutically acceptable salt thereof.

Formula 169

[0865] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 169. Such compounds are described in International Publication No. WO2002096858A1, published December 5, 2002, and corresponding to International Application No. PCT/US2002/017049 filed May 31, 2002; US Patent No. 6,831,080, issued December 14, 2004, and corresponding to US Application No. 10/160,582 filed May 31, 2002; which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 169, these references incorporated by reference herein control.

[0866] In an embodiment, the Kv7 channel activator is a compound according to Formula 169:

Formula 169



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wherein, R^1 is selected from the group consisting of pyridinyl, 3-quinolinyl, 2-thienyl, benzodioxanyl, 1,3-benzodioxol-5-yl, chroman-5-yl, indan-5-yl, 4-biphenylyl, phenyl and substituted phenyl, in which said substituted phenyl is substituted with substituent independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl, trifluoromethoxy and nitro; R^4 is selected from the group consisting of optionally substituted di(C_{1-4} alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R^5 is hydrogen or fluoro; or R^4 and R^5 taken together are —CH=CH—CH=CH— or —X$(CH_2)_m$Y—, in which X and Y are each independently selected from the group consisting of CH_2, $(CH_2)_n$N(R^9)— and O, wherein m is 1 or 2; n is 0 or 1; R^6, R^7, and R^8 are each independently selected from hydrogen, chloro and fluoro; and R^9 is selected from the group consisting of hydrogen, C_4 alkyl, hydroxyethyl, C_{1-4} alkoxyethyl, cyclopropylmethyl, —CO_2(C_{1-4}alkyl), and —$CH_2CH_2NR^{10}R^{11}$ in which R^{10} and R^{11} are each independently hydrogen or C_{1-4} alkyl.

[0867] In further embodiments, R^1 is selected from the group consisting of 2-thienyl, chroman-5-yl, 4-biphenylyl, phenyl and substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy and nitro; and R^4 and R^5 taken together are —CH=CH—CH=CH—.

[0868] In further embodiments, R^1 is thienyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy, trifluoromethyl and nitro; R^4 is optionally substituted morpholin-4-yl with one or two substituents each independently selected from the group consisting of C_{1-4} alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; and R^5 is hydrogen or fluoro.

[0869] In further embodiments, R^1 is phenyl, fluorophenyl or difluorophenyl.

[0870] In further embodiments, R^1 is pyridinyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from halogen; R^4 is optionally substituted pyridinyl with one or two substituents each independently selected from C_{1-4} alkyl and halogen; and R^5 is hydrogen or fluoro.

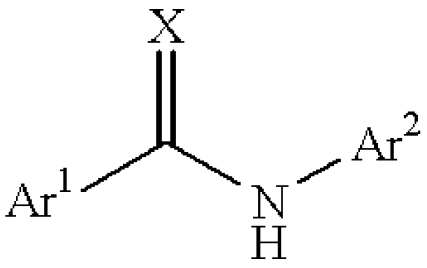
[0871] In further embodiments, R^1 is thienyl, phenyl or substituted phenyl in which said substituted phenyl is substituted with one or two substituents selected from C_{1-4}alkyl and halogen; R^4 is piperazinyl or 4-methylpiperazinyl; and R^5 is hydrogen or fluoro.

Formula 170

[0872] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds according to Formula 170. Such compounds are described in US Patent No. 6,326,385, issued December 4, 2001, and corresponding to US Application No. 09/361,747 filed August 4, 2000; International Publication No. WO2001010381A2, published February 15, 2001, and corresponding to International Application No. PCT/US2000/021309 filed August 4, 2000; US Patent No. 6,326,385 issued December 4, 2001, and Patent Cooperation Treaty application No. US2000/021309 published February 15, 2001, which are incorporated by reference in their entirety herein. In the case of any conflict of terminology in the context of Formula 170, these references incorporated by reference herein control.

[0873] In an embodiment, the Kv7 channel activator is a compound according to Formula 170:

Formula 170



,

wherein, Ar^1 and Ar^2 are each members independently selected from the group consisting of aryl, substituted aryl, heteroaryl and substituted heteroaryl; and X is a member selected from the group consisting of O, S and N—R^1, wherein R^1 is a member selected from the group consisting of H, (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl, substituted aryl(C_1-C_4)alkyl, CN, —C(O)R^2, —OR^3, —C(O)NR^3R^4, and —S(O)$_2$NR^3R^4; wherein R^2 is a member selected from the group consisting of (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl, heteroaryl,

substituted heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl; and R^3 and R^4 are each members independently selected from the group consisting of hydrogen, (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^3 and R^4 can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.

[0874] In further embodiments, Ar^1 is a member selected from the group consisting of phenyl, substituted phenyl, indolyl, substituted indolyl, benzofuranyl, substituted benzofuranyl, furanyl, substituted furanyl, thienyl, substituted thienyl, isothiazolyl, substituted isothiazolyl, pyrazolyl and substituted pyrazolyl.

[0875] In further embodiments, Ar^1 is substituted phenyl, substituted or unsubstituted 2-indolyl and substituted or unsubstituted 2-thienyl.

[0876] In further embodiments, X is O.

[0877] In further embodiments, the Ar^1 substituents are selected from the group consisting of halogen, alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, nitro, cyano, —NHC(O)R^7, —NHR^7, phenyl and substituted phenyl, wherein R^7 is a member selected from hydrogen, (C_1-C_8)alkyl, substituted (C_1-C_8)alkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, substituted heteroalkyl, heterocyclyl, substituted hcterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C_1-C_4)alkyl and substituted aryl(C_1-C_4)alkyl, or R^7 can be combined with the nitrogen to which it is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.

[0878] In further embodiments, Ar^2 is selected from the group consisting of heteroaryl and substituted heteroaryl.

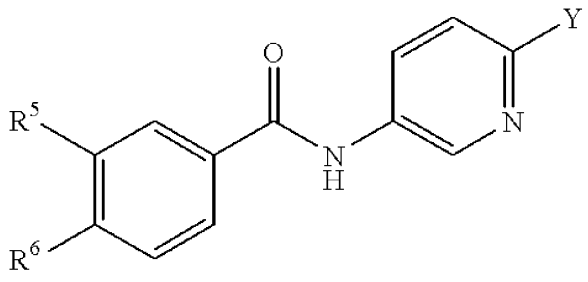
[0879] In further embodiments, Ar^1 is substituted aryl; Ar^2 is heteroaryl or substituted heteroaryl; and X is O.

[0880] In further embodiments, Ar^2 is pyridyl or substituted pyridyl.

[0881] In further embodiments, Ar^2 is selected from the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl.

[0882] In further embodiments, Ar^1 is substituted phenyl.

[0883] In further embodiments, the compound is according to the formula:



,

[0884] wherein, Y is a member selected from the group consisting of halogen, C_1-C_4 alkyl, C_1-C_4 substituted alkyl, —OCH_3 and —OCF_3, and R^5 and R^6 are members independently selected from the group consisting of H, halogen, alkyl, halo(C_1-C_4)alkyl, nitro, cyano and phenyl, with the proviso that both R^5 and R^6 are not H.

[0885] In further embodiments, R^5 and R^6 are members independently selected from the group consisting of H, F, and Cl, with the optional proviso that both R^5 and R^6 are not H.

Further embodiments (Collectively referred to as "Formula 171" for ease of reference in the appended claims. "Formula 171", as recited in the claims, captures any of the below compounds preceding the NMDA receptor antanogists section.)

[0886] In another embodiment, the Kv7 channel activator may be selected from one of the following compounds. Such compounds are described in International Publication No. WO2021055538A1, published March 25, 2021, and corresponding to International Application No. PCT/US2020/051171 filed September 17, 2020; International Publication No. WO2017075222A1, published May 4, 2017, and corresponding to International Application No. PCT/US2016/059128 filed October 27, 2016; International Publication No. WO2021211867A1, published October 21, 2021, and corresponding to International Application No. PCT/US2021/027518 filed April 15, 2021; International Publication No. WO2020092577A1, published May 7, 2020, and corresponding to International Application No. PCT/US2019/058878 filed October 30, 2019; International Publication No. WO2021119018A1, published June 17, 2021, and corresponding to International Application No. PCT/US2020/063,822 filed December 8, 2020; International Publication No. WO2011085351A2, published July 14, 2011, and corresponding to International Application No. PCT/US2011/020784 filed January 11, 2011; US Publication No. US20100286138A1, published November 11, 2010, and corresponding to US Application No. 12/777,935 filed May 11, 2010; US Publication No. US20210262029A1, published August 26, 2021, and corresponding to US Application No. 17/245734 filed April 30, 2021; US Patent No.

11,221,329, issued on January 11, 2022, and corresponding to US Application No. 15/771,857 filed October 27, 2016; which are incorporated by reference in their entirety herein.

[0887] In further embodiments, the compound is selected from the group consisting of N-(l-cyclobutyl-4-fluoro-6-(l- hydroxycyclobutyl)-lH-benzo[d]imidazol-2-yl)-4,4,4-trifluoro-3,3-dimethylbutanamide; N-(l -(tert-butyl)-6-(difluoromethoxy)- 1H- benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N-(6-cyano-l-(l,l,l- trifluoro-2-methylpropan-2-yl)-lH-benzo[d]imidazol-2-yl)-3,3- dimethylbutanamide; N-(l -cyclobutyl -4-fluoro-6-(2-hydroxypropan-2-yl)- 1H- benzo[d]imidazol-2-yl)-2-(l -methyl cyclopropyljacetamide; N-(6-cyano-l- cyclobutyl-4-fluoro-lH-benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N- (l-cyclobutyl-6-fluoro-lH-benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N-(l-(tert-butyl)-6-cyano-4-fluoro-lH-benzo[d]imidazol-2-yl)-3,3- dimethylbutanamide; N-(7-cyano-l-(l-methylcyclobutyl)-lH- benzo[d]imidazol -2 -yl)-3 -cyclopropyl-3 -methylbutanamide; N-(6-chloro-7- cyano-l-cyclobutyl-lH-benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N- (l-cyclobutyl-5-fluoro-lH-benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N-(l-(tert-butyl)-6-cyano-4,7-difluoro-lH-benzo[d]imidazol-2-yl)-3,3- dimethylbutanamide; N-(6-cyano- 1 -cyclobutyl-7-(trifluoromethyl)-lH- benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N-(6-cyano-4,7-difluoro-l- (l-methylcyclobutyl)-lH-benzo[d]imidazol-2-yl)-3,3-dimethylbutanamide; N- (l-(tert-butyl)-5,7-difluoro-lH-benzo[d]imidazol-2-yl)-4,4,4-trifluoro-3,3- dimethylbutanamide; and N-(l-(tert-butyl)-5,6-difluoro-lH-benzo[d]imidazol- 2-yl)-2-(2,2,3,3-tetrafluorocyclobutyl)acetamide.

[0888] In another embodiment, the Kv7 channel activator is selected from the group consisting of N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide in a crystalline form with XRPD reflections at 10.36, 12.67, 28.64 and 29.98 (°2θ) using $CuK_{\alpha 1}$ radiation.; N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide in a crystalline form with XRPD reflections at 8.68, 18.09, 22.60 and 30.62 (°2θ) using $CuK_{\alpha 1}$ radiation.; N-(2,6-dimethyl-4-morpholin-4-yl-phenyl)-3,3-dimethyl-butyramide in a crystalline form with XRPD reflections at 8.63, 22.26, 23.40 and 30.49 (°2θ) using $CuK_{\alpha 1}$ radiation.

[0889] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: Chromanol 293B, MIR-1556, UCL2077, JNJ303, L-735821 (L-7), fenofibrate; and a salt or hydrate thereof.

[0890] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: a Triaminopyridine or one of its derivatives, an Acrylamide, a Benzamide, a

Fenamate, a Dimethoxypyrimidine or one of its derivatives, Oxindole, Celecoxib, zinc pyrithione, ML213, QO58, QO58 lysine, NS1643, Benzbromarone, ZG1732 and ZG2083.

[0891] In further embodiments, the Kv7 Channel activator is selected from the group consisting of: NS15370, P-Retigabine, SF0034 or RL648_81 or any combination thereof.

[0892] In further embodiments, the Kv7 channel activator is selected from the group consisting of: linopirdine, (1,3-Dihydro-1-phenyl-3,3-bis(4-pyridinylmethyl)-2H-indol-2-one) XE991 (10,10-bis(4-pyridinylmethyl)-9(10H)-anthracenone (XE991)), DMP-543 (10,10-bis(2-fluoro-4-pyridinylmethyl)-9(10H)-anthracenone (DMP-543)), ML252 ((S)-2-phenyl-N-(2-(pyrrolidin-1-yl)phenyl)butanamide (ML252)) and UCL2077.

[0893] In further embodiments, the Kv7 channel activator is an analog of flupirtine.

[0894] In further embodiments, the Kv7 channel activator is selected from the group consisting of: N-(2,4,6-trimethylphenyl)bicyclo[2.2.1]heptane-3-carboxamide; N- (2,6-dimethylphenyl)bicyclo[2.2.1]heptane-3-carboxamide; N-(2,5-dimethylphenyl)bicyclo[2.2.1]heptane-3-carboxamide; N-(2-chloro-4,6-dimethylphenyl)pentanamide; N-(2-chloro-4,6-dimethylphenyl)-3,3-dimethylbutanamide; 2-(l -adamantyl)-N-(2,6-difluorophenyl)acetamide; N-(2-bromo-4-methylphenyl)-2-cyclopentylacetamide; N-(2,3-dimethylphenyl)-2-phenylcyclopropane-l-carboxamide; N- (4-methylphenyl)-2-phenylcyclopropane-l -carboxamide; N-(2,4-dimethoxyphenyl)bicyclo[2.2.1]heptane-3-carboxamide; 7-ethyl-l,3-dimethyl-5-(2-oxo-2-piperidin-1 -ylethyl)sulfanylpyrimido[4,5-d]pyrimidine-2,4-dione; 1 ,3-dimethyl-7-(2-methylpropyl)-5-(2-oxo-2-piperidin-l -ylethyl)sulfanylpyrimido[4,5-d]pyrimidine-2,4- dione; l,3-dimethyl-5-[2-(4-methylpiperidin-l-yl)-2-oxoethyl]sulfanyl-7- propylpyrimido[4,5-d]pyrimidine-2,4-dione; 7-ethyl-l ,3-dimethyl-5-[2-(4- methylpiperidin-l-yl)-2-oxoethyl]sulfanylpyriinido[4,5-d]pyrimidine-2,4-dione; 2-(4- chloro-2-methyl-5-pyrrolidin-l -ylsulfonylphenoxy)-N-cyclohexylacetamide; 2-(4-chloro- 2-methyl-5-thiomo holin-4-ylsulfonylphenoxy)-N-cyclohexylacetamide; 1-[1-(1,3- benzodioxol-5-yl)ethyl]-3-cyclohexylurea; l-(l -adamantyl)-3-[l-(l,3-benzodioxol-5- yl)ethyl]urea; 3-(5-bromo-2-hydroxyphenyl)-N-(furan-2-ylmethyl)-3-phenylpropanamide; ethyl 2-benzamido-2-(2,6-dimethylpyran-4-ylidene)acetate; (2,4-dichlorophenyl)methyl 1- benzamido-5-oxopyrrolidine-3-carboxylate; N-[2-cyano-5-(cyanomethylsulfanyl)-4- phenylthiophen-3-yl]-2-phenylacetamide; N-(6-bromo-l,3-diethyl-2-oxobenzimidazol-5- yl)-2-phenylpropanamide; N-(2,5-diethoxy-4-mo holin-4-ylphenyl)-2-phenylacetamide; N-[4-[(5-methylthiophen-2-yl)methylamino]phenyl]butanamide; N-[(2-methylsulfanyl-6- propan-2-ylpyridin-3-yl)methyl]-3-phenylbutanamide; 4-bromo-N-(thiophen-2- ylmethylideneamino)-lH-pyrazole-

5-carboxamide; S-[2-[(6-fiuoro-3-prop-2-ynyl-l ,3- benzothiazol-2-ylidene)amino]-2-oxoethyl] ethanethioate; 1 -cyclohexyl-3-[l -(3,4- dimethylphenyl)ethyl]thiourea; N-[4-methyl-l -oxo-l-(l -phenylethylamino)pentan-2- yljcyclohexanecarboxamide; 5-chloro-2-[(3-methylphenyl)methylsulfonyl]-N-(5-propyl-I , 3,4-thiadiazol-2-yl)pyrimidine-4-carboxamide; 2-benzylsulfonyl-5-chloro-N-(5-propan- 2-yl-l ,3,4-thiadiazol-2-yl)pyrimidine-4-carboxamide; and 4-bromo-N-(furan-2- ylmethylideneamino)-lH-pyrazole-5-carboxamide.

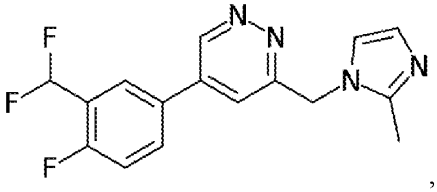
[0895] In further embodiments, the metal channel activator is QRA-244 as described in Dan Elbaum *et al.* "TST-20: QRA-244 a Potent, Selective KCNQ2/3 Opener and a Potential Therapy for Motor System Hyperexcitability induced Disease Progression in ALS patients"; 31st International symposium on ALS/MND; Live Poster Session C, December 11, 2020.

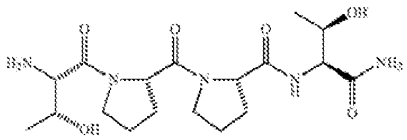
NMDA RECEPTOR ANTAGONISTS

[0896] NMDA receptor antagonists are a class of pharmaceutically active molecules that work to antagonize, or inhibit the action of, the N-Methyl-D-aspartate receptor ($NMDA_R$). Some examples of the NMDA receptor antagonists include ketamine, lanicemine, dextromethorphan (DXM), phencyclidine (PCP), methoxetamine (MXE), and nitrous oxide (N_2O). Several synthetic opioids function additionally as $NMDA_R$-antagonists, such as pethidine, levorphanol, methadone, dextropropoxyphene, tramadol and ketobemidone. As described herein, there are several other NMDA receptor antagonist compounds and classes of NMDA receptor antagonists

[0897] The NMDA receptor is an ionotropic receptor that allows for the transfer of electrical signals between neurons in the brain and in the spinal column. For electrical signals to pass, the NMDA receptor must be open. To remain open, glutamate and glycine must bind to the NMDA receptor. An NMDA receptor that has glycine and glutamate bound to it and has an open ion channel is called "activated."

[0898] Chemicals that deactivate the NMDA receptor are known as NMDA receptor antagonists ($NMDA_R$). $NMDA_R$ antagonists fall into four categories: competitive antagonists, which bind to and block the binding site of the neurotransmitter glutamate; glycine antagonists, which bind to and block the glycine site; noncompetitive antagonists, which inhibit $NMDA_R$ by binding to allosteric sites; and uncompetitive antagonists, which block the ion channel by binding to a site within it.

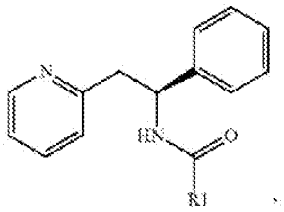
[0899] In an embodiment, the NMDA receptor antagonist is ketamine or a pharmaceutically acceptable salt thereof. In another embodiment, the NMDA receptor antagonist is (S)-1-phenyl-2-(pyridin-2-yl)ethanamine (lanicemine) or a pharmaceutically acceptable salt thereof. In another embodiment, the NMDA receptor antagonist may be a prodrug of ketamine or a pharmaceutically acceptable salt thereof. In another embodiment, the NMDA receptor antagonist may be EVT-101:  , or a pharmaceutically acceptable salt thereof.

[0900] In another embodiment, the NMDA receptor antagonist is rapastinel:  , (S)—N-((2S,3R)-1-amino-3-hydroxy-1-oxobutan-2-yl)-1-((S)-1-((S)-2-amino-3-hydroxypropanoyl)pyrrolidine-2-carbonyl)pyrrolidine-2-carboxamide, (S)—N—((S)-1-amino-3-hydroxy-1-oxopropan-2-yl)-1-((S)-1-((2S,3R)-2-amino-3-hydroxybutanoyl) pyrrolidine-2-carbonyl) pyrrolidine-2-carboxamide, (S)—N—((S)-1-amino-3-hydroxy-1-oxopropan-2-yl)-1-((S)-1-((S)-2-amino-3-hydroxy-propanoyl)-pyrrolidine-2-carbonyl)-pyrrolidine-2-carboxamide, and/or N-((2S,3R)-1-amino-3-hydroxy-1-oxobutan-2-yl)-1-((S)-1-((2S,3R)-2-amino-3-hydroxybutanoyl)-pyrrolidine-2-carbonyl)-2-benzylpyrrolidine-2-carboxamide

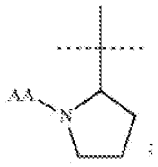
[0901] In another embodiment, the NMDA receptor antagonist may be amantadine or a pharmaceutically acceptable salt thereof. In another embodiment, the NMDA receptor antagonist may be lanicemine. In another embodiment, the NMDA receptor antagonist may be a prodrug of lanicemine.

[0902] In further embodiments, for example, the prodrug of lanicemine may have the following chemical structure:

(I)

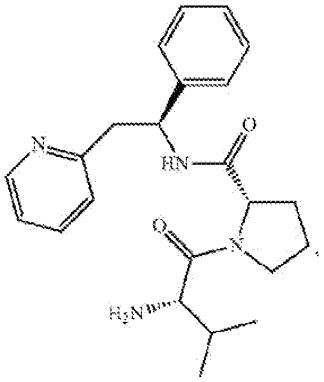


wherein R1 is C_{1-6} alkylC(O)O(C_{1-6}alkoxy), or



AA is a peptide bond-linked natural amino acid;
or a pharmaceutically acceptable salt thereof.

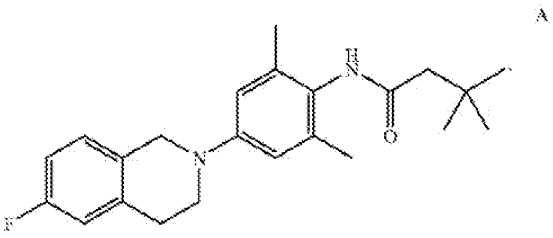
[0903] In further embodiments, the prodrug of lanicemine may have the following structure:



, or a pharmaceutically acceptable salt thereof.

[0904] In further embodiments, pharmaceutical compositions including the following Compound A or a pharmaceutically acceptable salt thereof and an NMDA receptor antagonist or a pharmaceutically acceptable salt thereof:

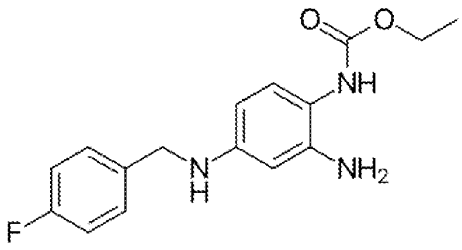
1. Compound A:



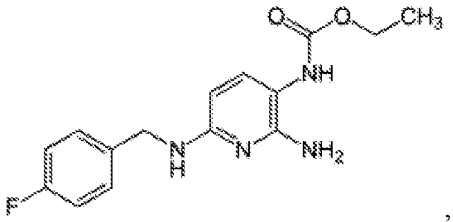
A

[0905] The NMDA receptor antagonist may be selected from ketamine, lanicemine, dextromethorphan (DXM), phencyclidine (PCP), methoxetamine (MXE), and nitrous oxide (N2O).

[0906] In another embodiment, provided is a pharmaceutical composition including the following compound (ezogabine) or a pharmaceutically acceptable salt thereof and an NMDA receptor antagonist or a pharmaceutically acceptable salt thereof:



[0907] In another embodiment, the NMDA receptor antagonist is flupirtine:



, or a pharmaceutically acceptable salt thereof.

[0908] In an embodiment, the NMDA receptor antagonist may be selected from ketamine, lanicemine, dextromethorphan (DXM), phencyclidine (PCP), methoxetamine (MXE), and pharmaceutically acceptable salts and prodrugs thereof, or nitrous oxide (N2O).

[0909] In various embodiments, the NMDA receptor antagonist is one or more of a compound according to Formulas 200 – 260. Pharmaceutical compositions may include one or more metal channel activators according to Formulas 1 – 171 and one or more NMDA receptor antagonist compounds according to Formulas 200-260 described below.

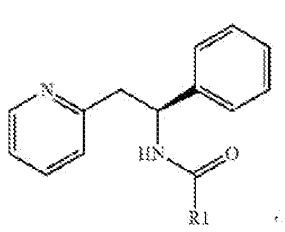
Formula 200

[0910] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 200. Such compounds are described in International Publication No. WO2015/067923, published May 14, 2015, and corresponding to International Application No. PCT/GB2014/053236 filed October 30, 2014, as well as U.S. Patent No. 9,822,075 issued on November 21, 2017; U.S. Patent No. 10,207,994 issued on February 19, 2019; U.S. Patent No. 10,815,199 issued on October 27, 2020, and U.S. Patent

No. 11,358,935 issued on June 14, 2022, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 200, these references incorporated by reference herein control.

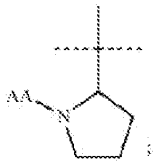
[0911] In an embodiment, the NMDA receptor antagonist is lanicemine, or a prodrug of lanicemine or a pharmaceutically acceptable salt thereof. The prodrug of lanicemine may have the following chemical structure:

Formula 200



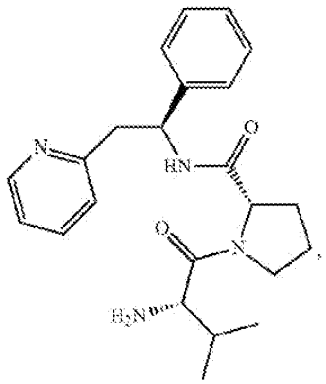
(I)

wherein R1 is C_{1-6} alkylC(O)O(C_{1-6}alkoxy), or



AA is a peptide bond-linked natural amino acid;
or a pharmaceutically acceptable salt thereof.

[0912] In further embodiments, for example, the prodrug of lanicemine may have the following chemical structure:



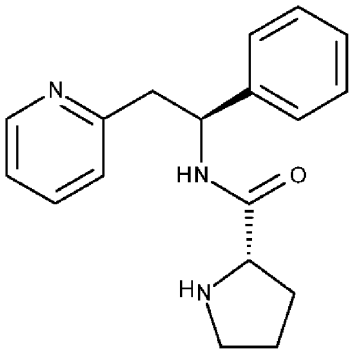
, or a pharmaceutically acceptable salt thereof.

[0913] In further embodiments, the NMDA receptor antagonist is one or more of:

(S)-(l-Phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)methyl isobutyrate;
2-Methyl- 1 -((S)- 1 -phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)propyl isobutyrate;
2-Methyl- 1 -((S)- 1 -phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)propyl isobutyrate diastereomer 1 ;
2-Methyl- 1 -((S)- 1 -phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)propyl isobutyrate diastereomer 2;
1 -((S)- 1 -phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl acetate;
l-((S)-l-phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl acetate diastereomer 1 ; l-((S)-l-phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl acetate diastereomer 2; 1 -((S)- 1 -Phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl isobutyrate;
l-((S)-l-Phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl isobutyrate diastereomer 1 ;
l-((S)-l-Phenyl-2-(pyridin-2-yl)ethylcarbamoyloxy)ethyl isobutyrate diastereomer 2;
(SJ-i-((S)-2-Amino-3-methylbutanoyl)-N-((S)-l-phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide; (S)- 1 -((S)-2,6-Diaminohexanoyl)-N-((S)- 1 -phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2- carboxamide;
(S)-l-((S)-2-Amino-3-(lH-imidazol-4-yl)propanoyl)-N-((S)-l-phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide;
2-((S)-2-((S)-l-((S)-2-Amino-3-(4-hydroxyphenyl)propanoyl)pyrrolidine-2-carboxamido)-2-phenylethyl)pyridine;
2-((S)-2-((S)-l-((S)-2-Amino-3-(lH-indol-3-yl)propanoyl)pyrrolidine-2-carboxamido)-2- phenylethyl)pyridine;
(S)- 1 -((S)-2- Amino-3 -phenylpropanoyl)-N-((S)- 1 -phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide; or,
(S)- 1 -((S)-2- Amino-4-methylpentanoyl)-N-((S)- 1 -phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide;
or a pharmaceutically acceptable salt of any one of the foregoing.

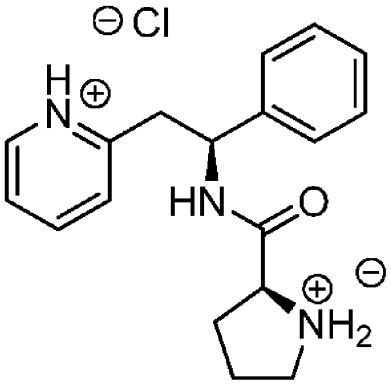
[0914] In further embodiments, the NMDA receptor antagonist is (S)- 1 -((S)-2-amino-3 -methylbutanoyl)-N-((S)- 1 -phenyl-2-(pyridin-2- yl)ethyl)pyrrolidine-2-carboxamide or a pharmaceutically acceptable salt thereof.

[0915] In further embodiments, the NMDA receptor antagonist is:



, or a pharmaceutically acceptable salt thereof.

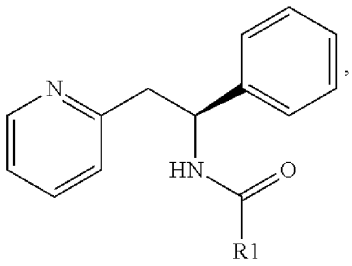
[0916] In further embodiments, the NMDA receptor antagonist is:



.

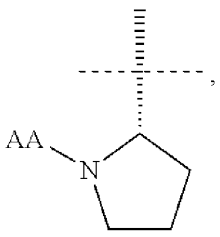
[0917] In further embodiments, the NMDA receptor antagonist is a compound according to:

(I)



,

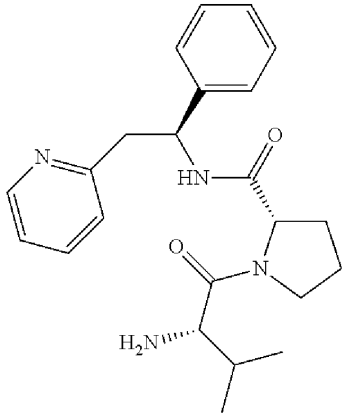
wherein R1 is C1-6 alkylC(O)O(C1-6 alkoxy), or



,

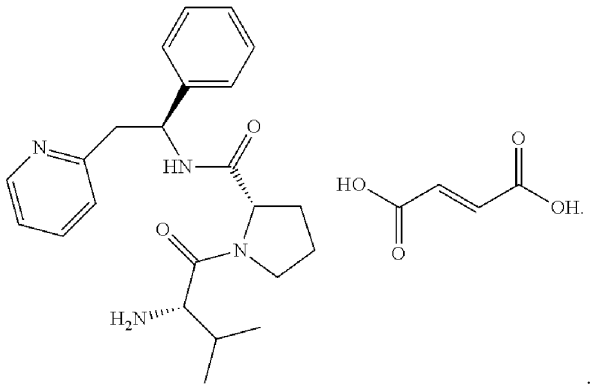
wherein AA is a peptide bond-lined natural amino acid; or a pharmaceutically acceptable salt thereof.

[0918] In further embodiments, the NMDA receptor antagonist is (S)-1-((S)-2-amino-3-methylbutanoyl)-N—((S)-1-phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide dihydrochloride salt:



2HCl.

[0919] In further embodiments, the NMDA receptor antagonist is (S)-1-((S)-2-amino-3-methylbutanoyl)-N—((S)-1-phenyl-2-(pyridin-2-yl)ethyl)pyrrolidine-2-carboxamide fumarate salt:

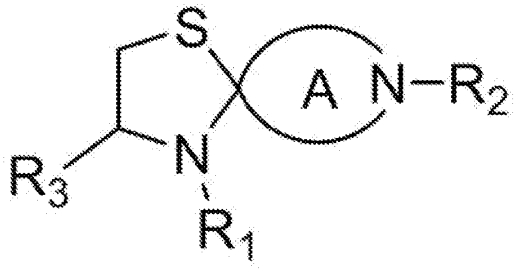


Formula 201

[0920] In an embodiment, the NMDA receptor modulator may be selected from one of the following compounds according to Formula 201. Such compounds are described in International Publication No. WO 2021/228123, published November 18, 2021 and corresponding to PCT/CN2021/093264, filed May 12, 2021, is incorporated by reference in

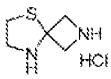
its entirety herein. In the case of any conflict of terminology of Formula 201, these references incorporated by reference herein control.

[0921] In an embodiment, the NMDA receptor modulator is a compound according to Formula 201:

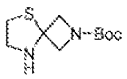


[0922] or a pharmaceutically acceptable salt or ester, stereoisomer, or solvate thereof, wherein, Ring A is 3- to 8-membered aliphatic heterocycle; R_1 is selected from H, C1-C6 alkyl, aryl-C1-C4 alkyl, C2-C6 acyl, -CONRR' and natural amino acid fragments; R2 is selected from H, C1-C6 alkyl, C1-C6 alkoxycarbonyl, C2-C6 acyl, -CONRR' and natural amino acid fragments; R3 is selected from H, cyano, 3- to 8-membered nitrogen-containing aliphatic heterocycle- C1-C4 acyl, C1-C6 alkoxycarbonyl and -CONHR4; R and R' are each independently selected from H and C1-C6 alkyl; R4 is selected from H, C1-C6 alkyl, natural amino acid fragments and carboxylic acid derivatives of the said natural amino acid fragments; optionally, the C1-C6 alkyl, aryl-C1-C4 alkyl, C2-C6 acyl, 3- to 8-membered nitrogen-containing aliphatic heterocycle- C1-C4 acyl, C1-C6 alkoxycarbonyl, -CONRR', -CONHR4 and natural amino acid fragments are each independently substituted by one or more substituents selected from: halogen, amino, hydroxyl, cyano, carboxyl, nitro, C1-C6 alkyl and C1-C6 alkoxy.

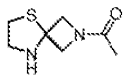
[0923] In further embodiments, the NMDA receptor modulator is selected from:



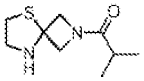
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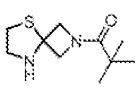
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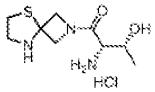
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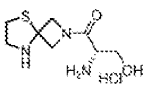
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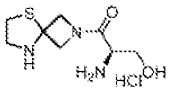
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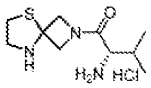
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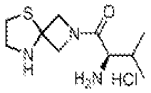
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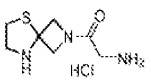
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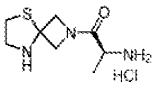
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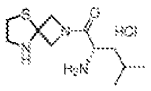
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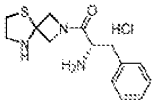
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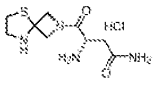
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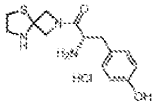
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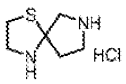
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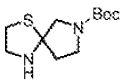
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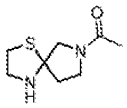
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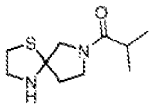
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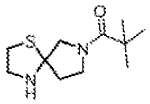
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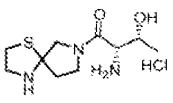
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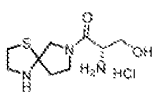
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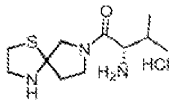
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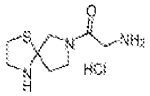
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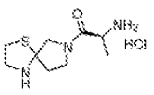
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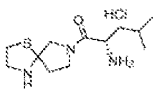
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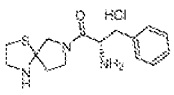
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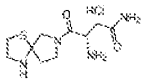
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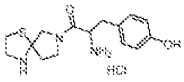
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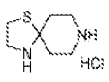
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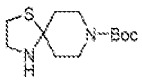
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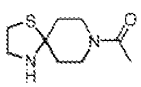
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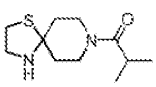
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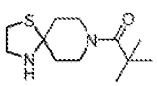
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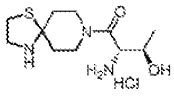
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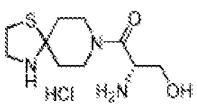
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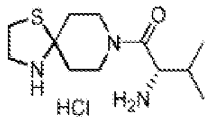
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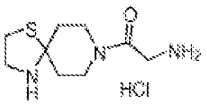
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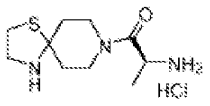
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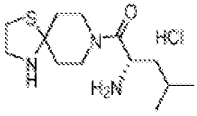
A-036



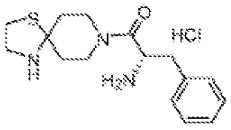
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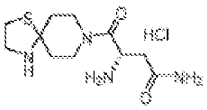
A-038



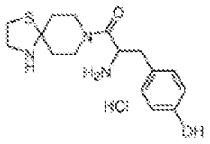
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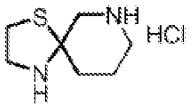
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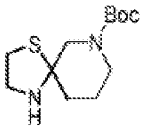
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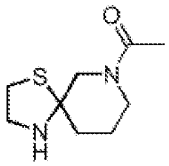
A-042



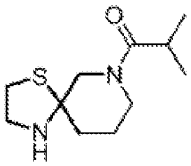
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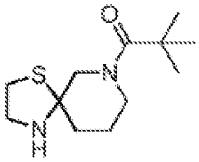
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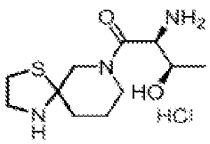
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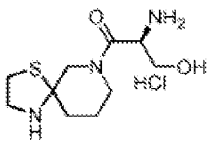
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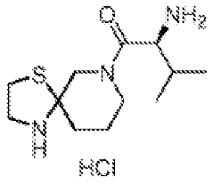
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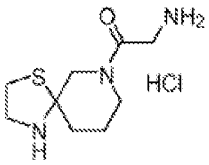
A-048



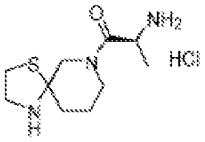
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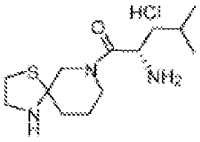
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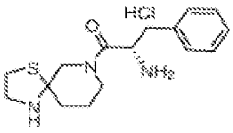
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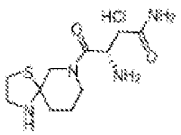
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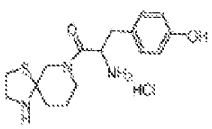
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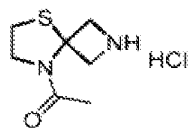
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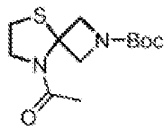
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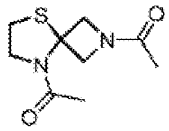
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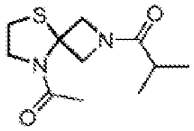
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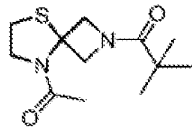
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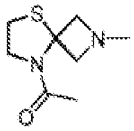
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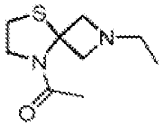
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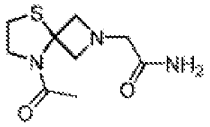
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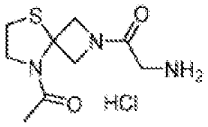
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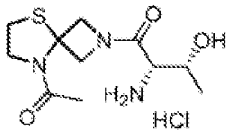
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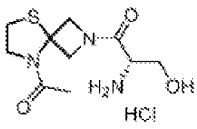
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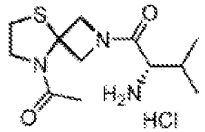
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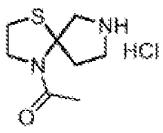
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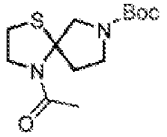
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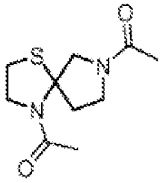
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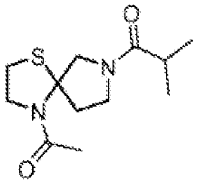
A-069



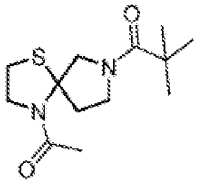
A-070



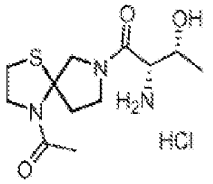
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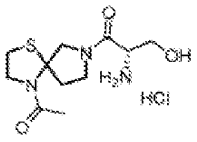
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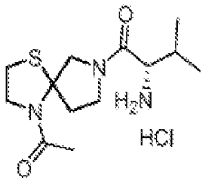
A-073



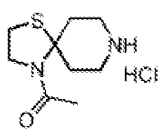
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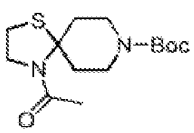
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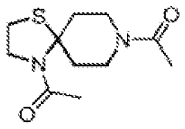
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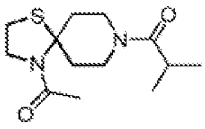
A-077



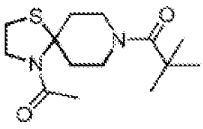
A-078



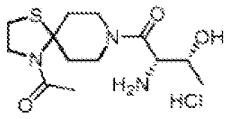
A-079



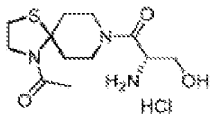
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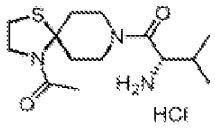
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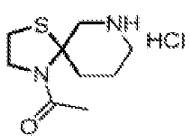
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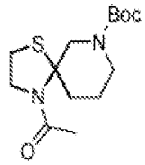
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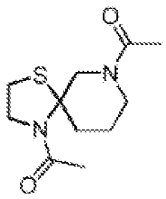
A-084



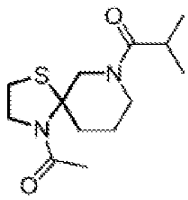
A-085



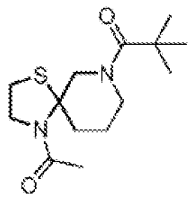
A-086



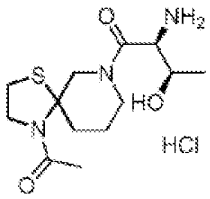
A-087



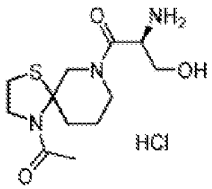
A-088



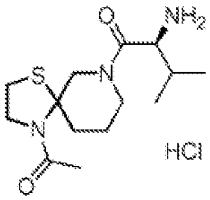
A-089



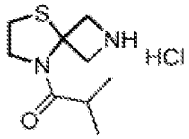
A-090



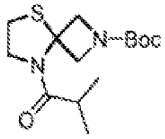
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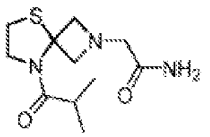
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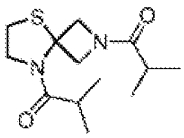
A-093



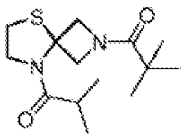
A-094



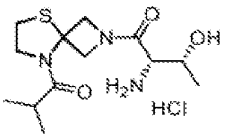
A-095



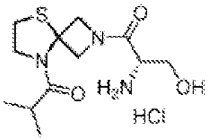
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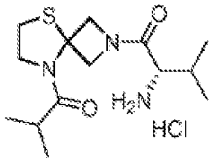
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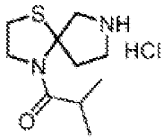
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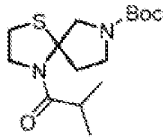
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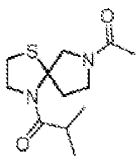
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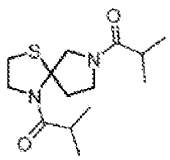
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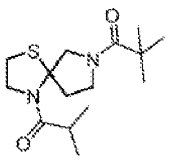
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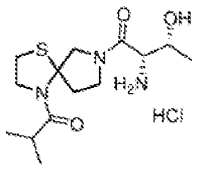
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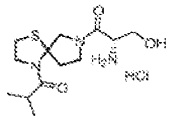
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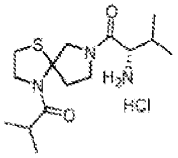
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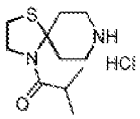
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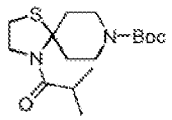
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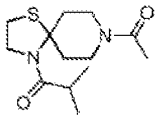
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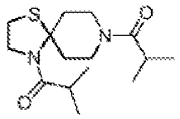
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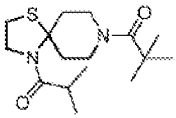
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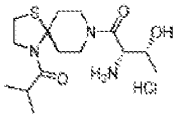
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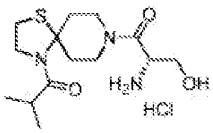
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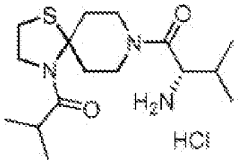
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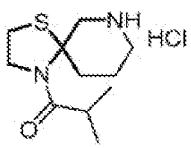
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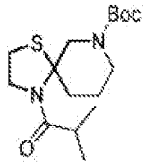
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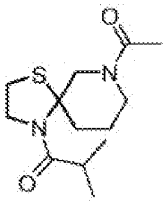
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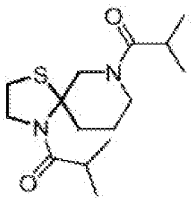
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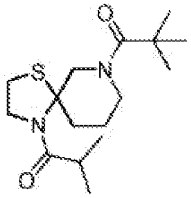
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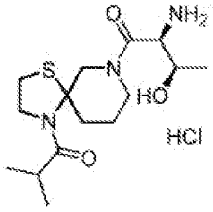
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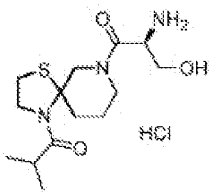
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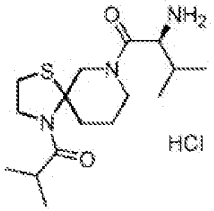
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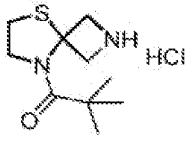
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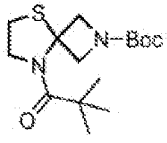
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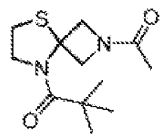
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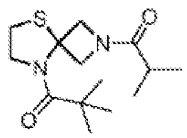
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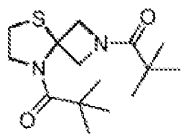
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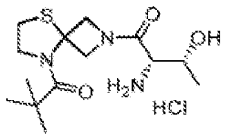
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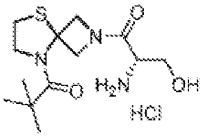
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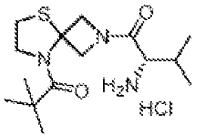
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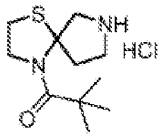
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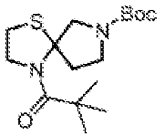
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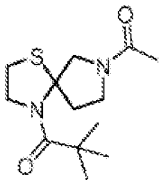
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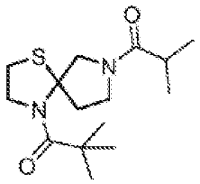
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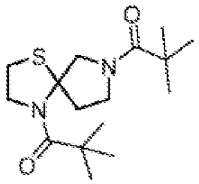
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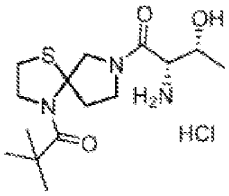
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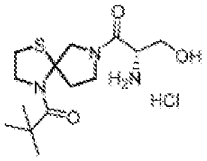
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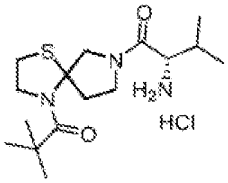
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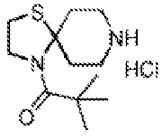
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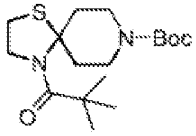
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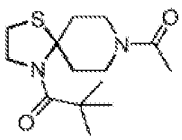
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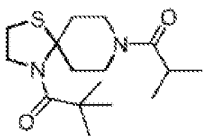
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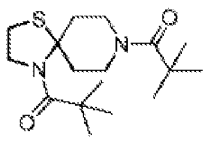
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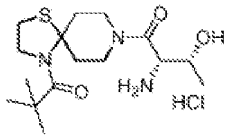
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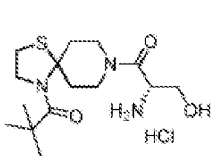
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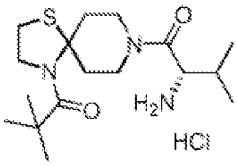
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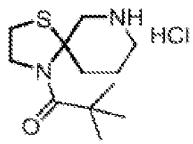
A-146



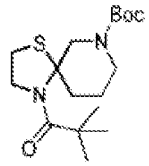
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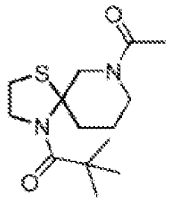
A-148



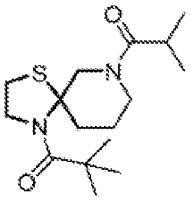
A-149



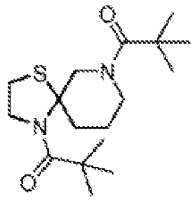
A-150



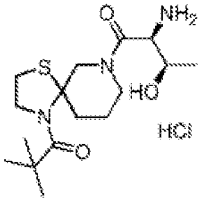
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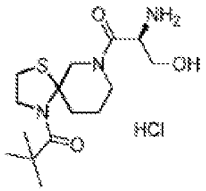
A-152



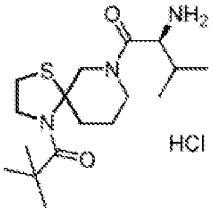
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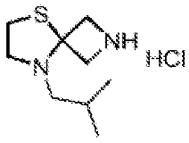
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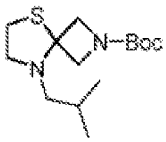
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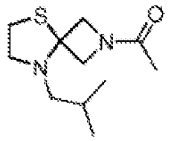
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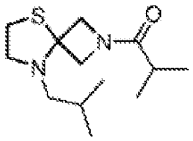
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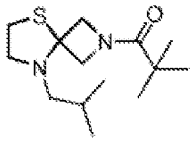
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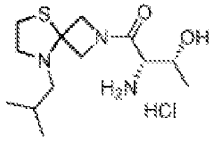
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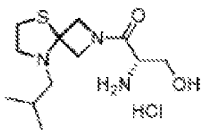
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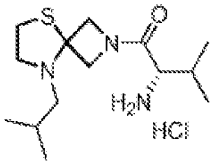
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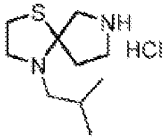
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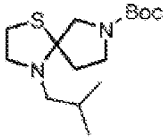
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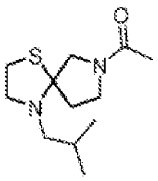
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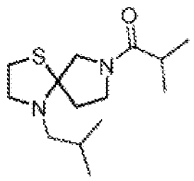
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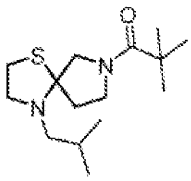
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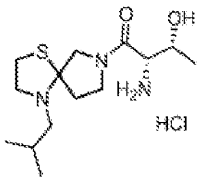
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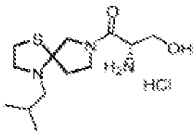
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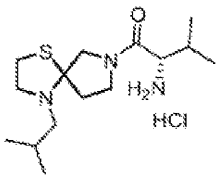
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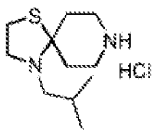
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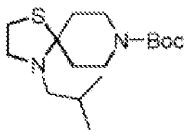
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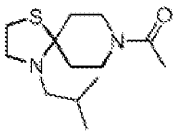
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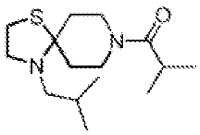
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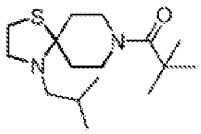
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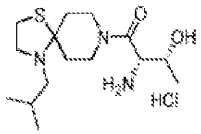
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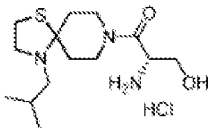
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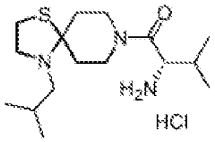
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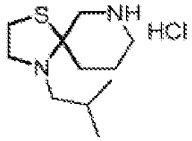
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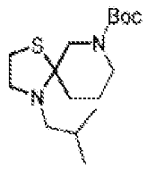
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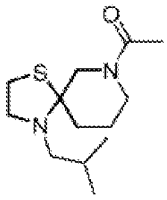
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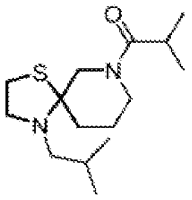
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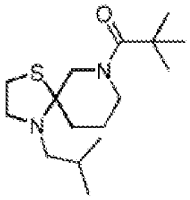
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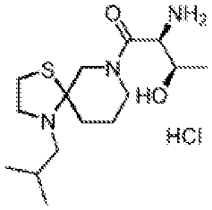
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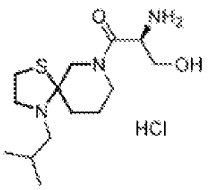
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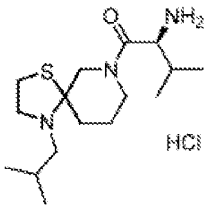
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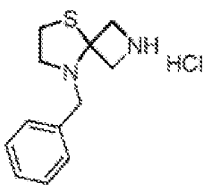
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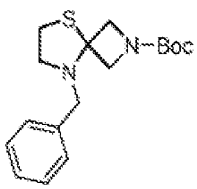
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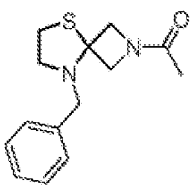
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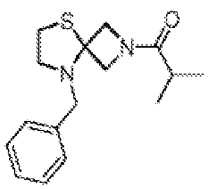
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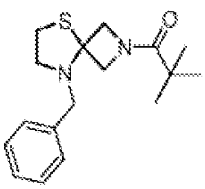
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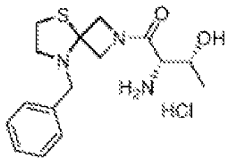
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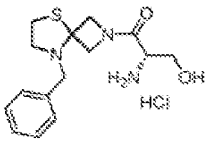
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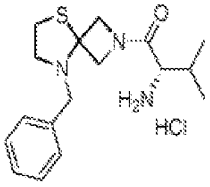
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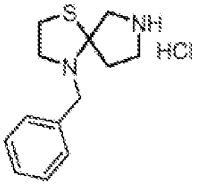
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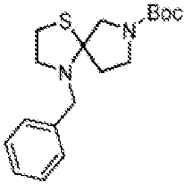
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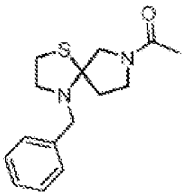
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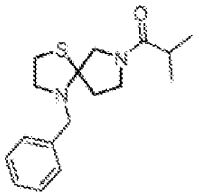
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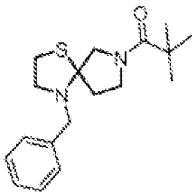
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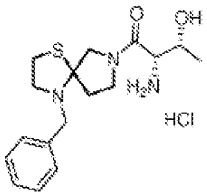
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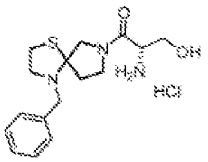
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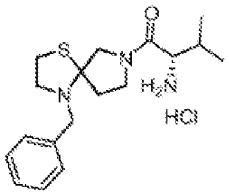
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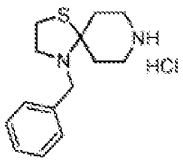
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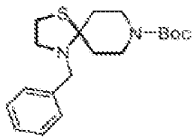
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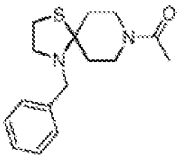
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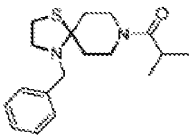
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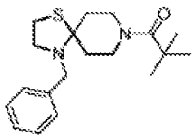
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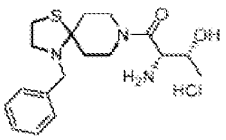
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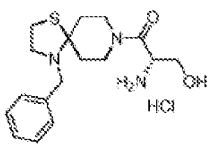
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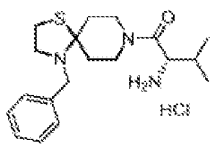
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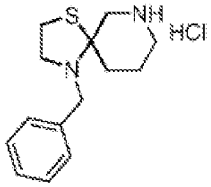
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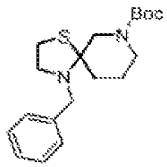
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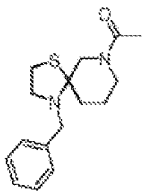
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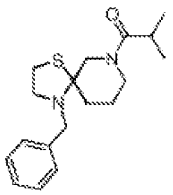
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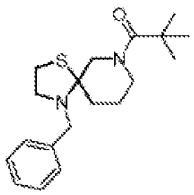
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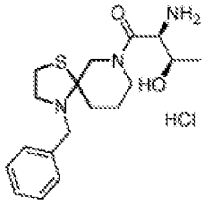
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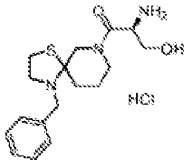
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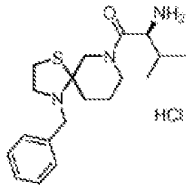
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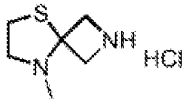
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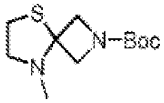
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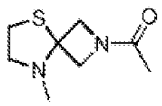
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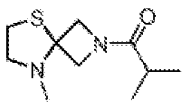
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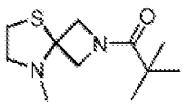
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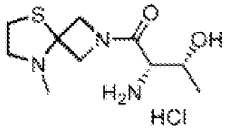
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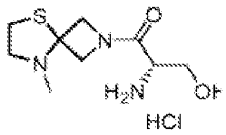
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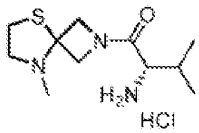
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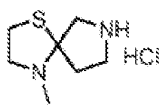
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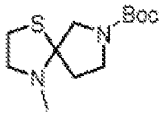
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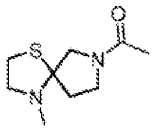
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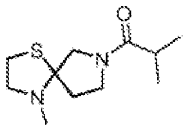
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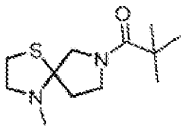
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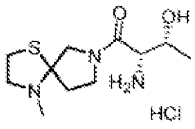
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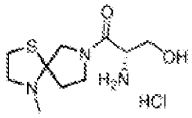
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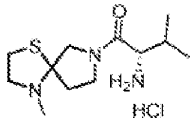
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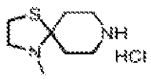
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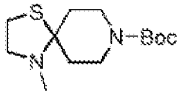
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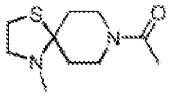
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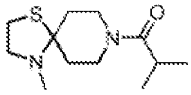
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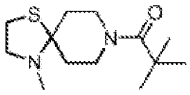
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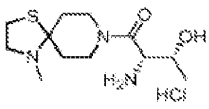
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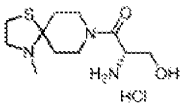
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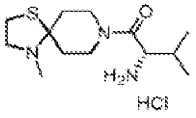
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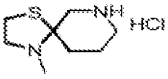
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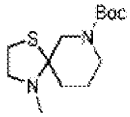
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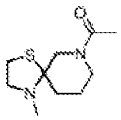
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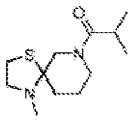
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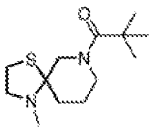
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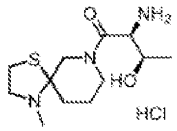
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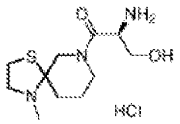
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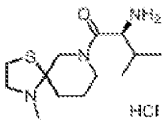
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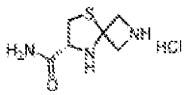
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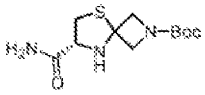
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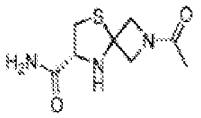
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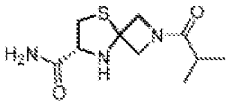
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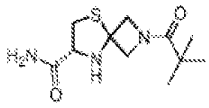
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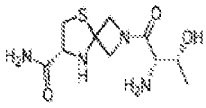
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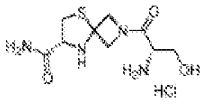
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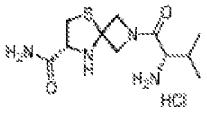
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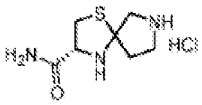
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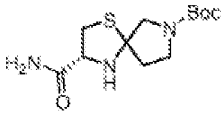
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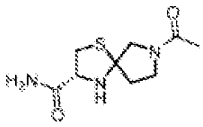
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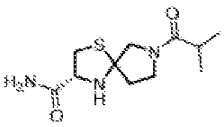
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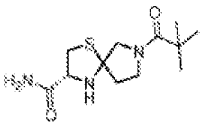
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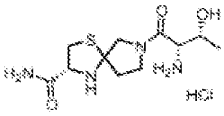
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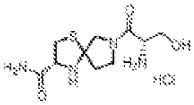
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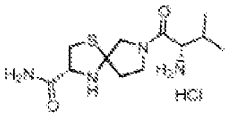
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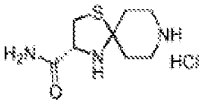
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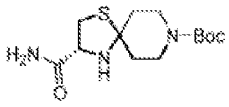
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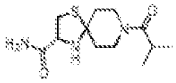
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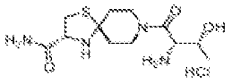
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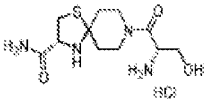
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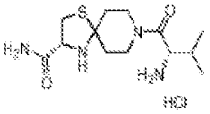
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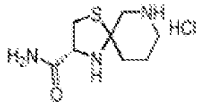
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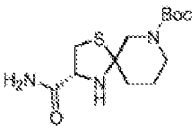
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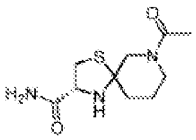
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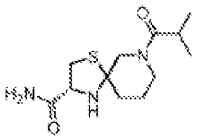
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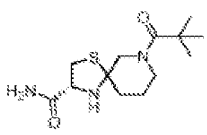
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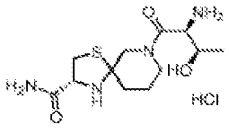
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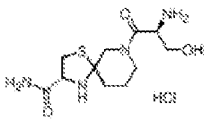
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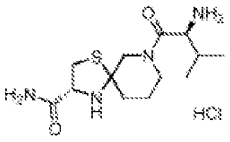
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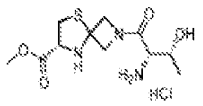
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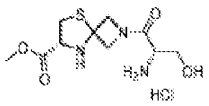
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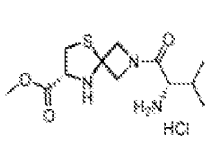
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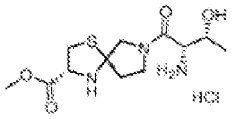
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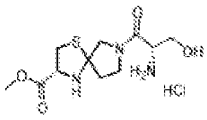
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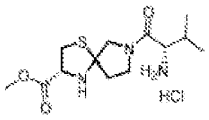
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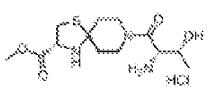
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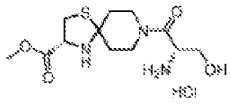
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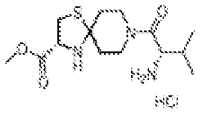
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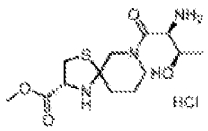
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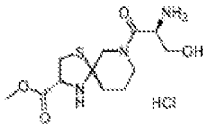
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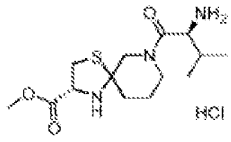
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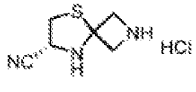
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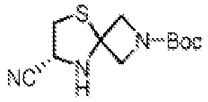
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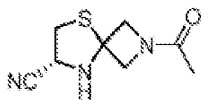
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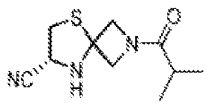
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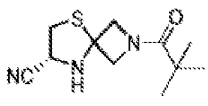
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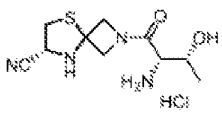
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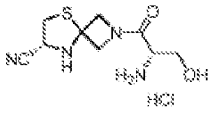
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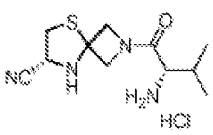
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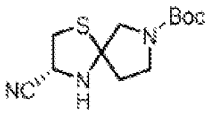
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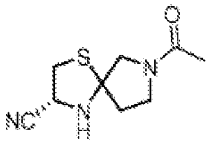
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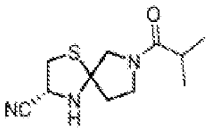
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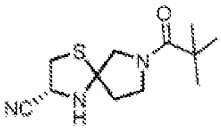
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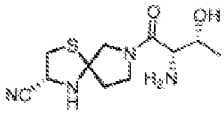
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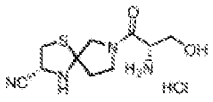
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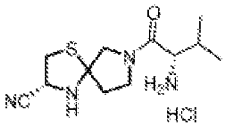
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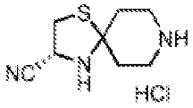
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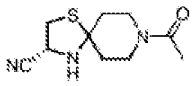
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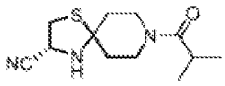
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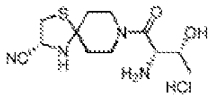
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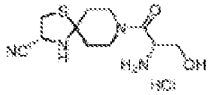
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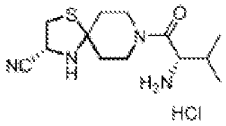
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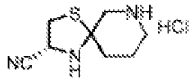
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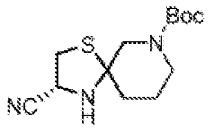
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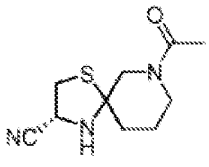
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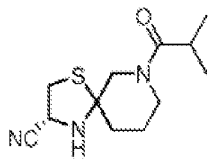
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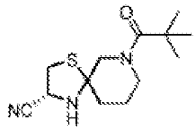
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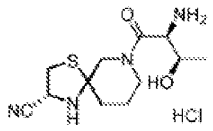
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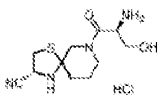
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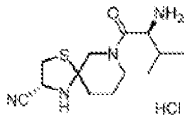
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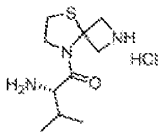
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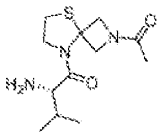
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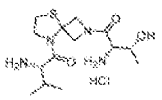
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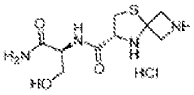
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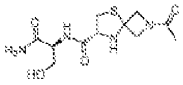
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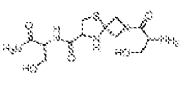
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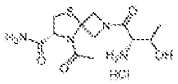
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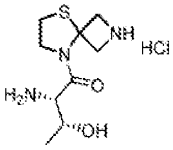
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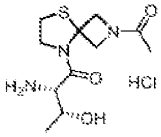
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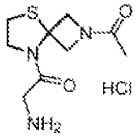
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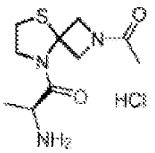
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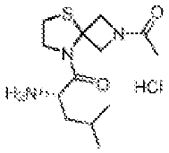
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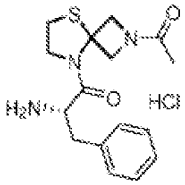
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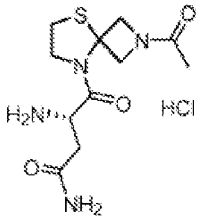
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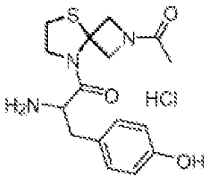
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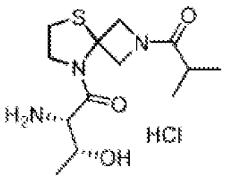
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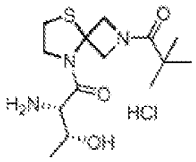
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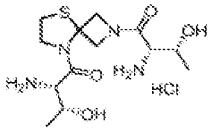
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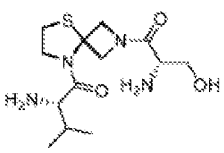
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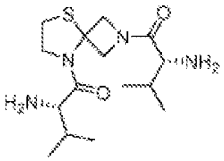
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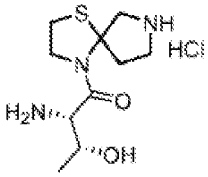
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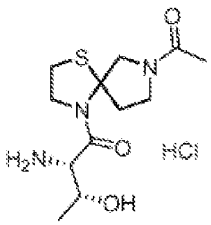
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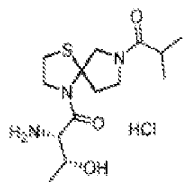
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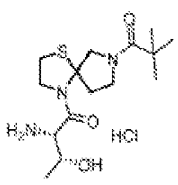
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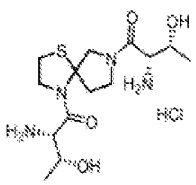
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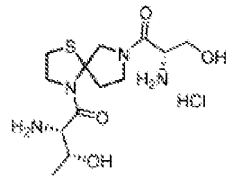
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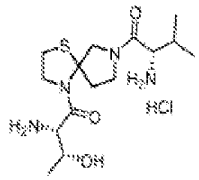
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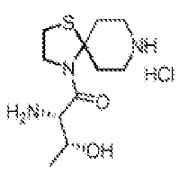
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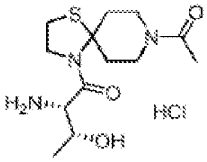
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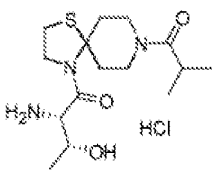
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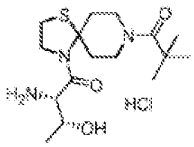
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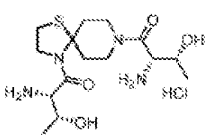
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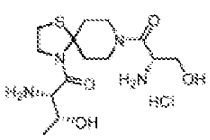
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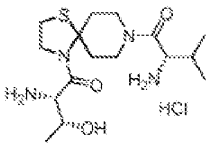
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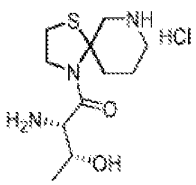
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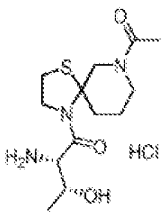
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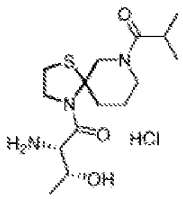
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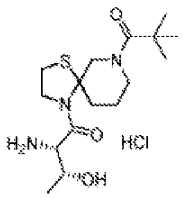
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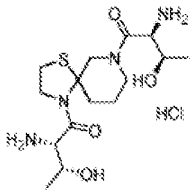
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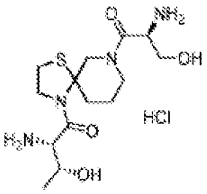
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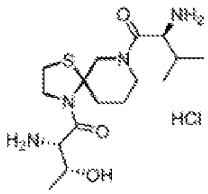
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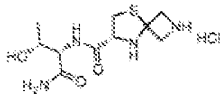
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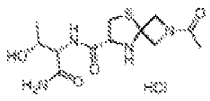
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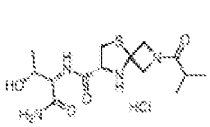
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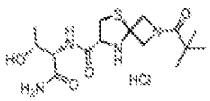
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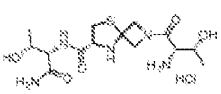
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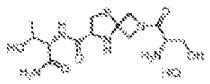
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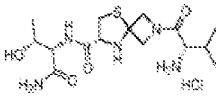
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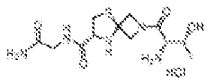
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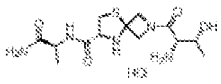
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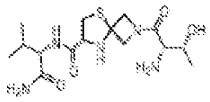
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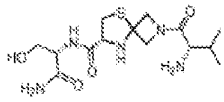
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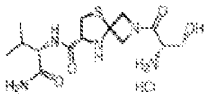
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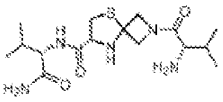
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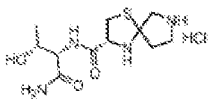
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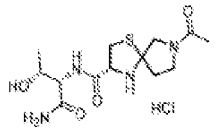
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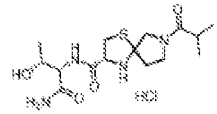
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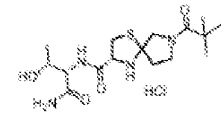
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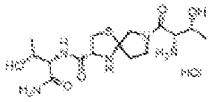
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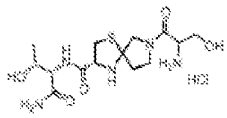
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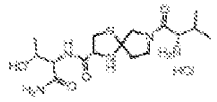
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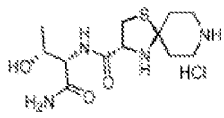
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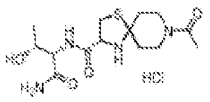
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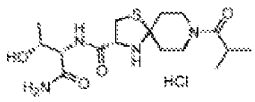
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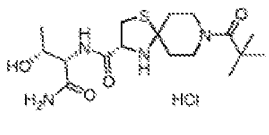
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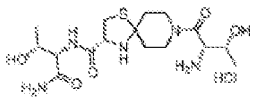
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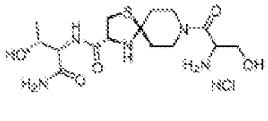
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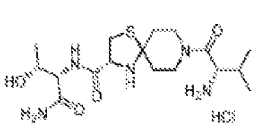
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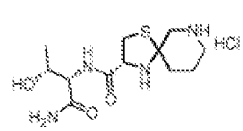
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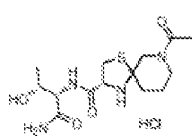
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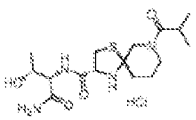
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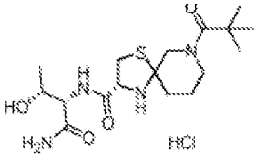
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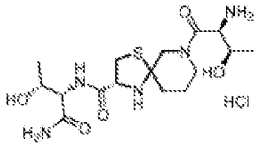
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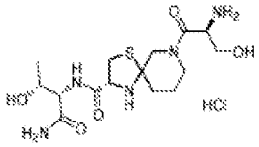
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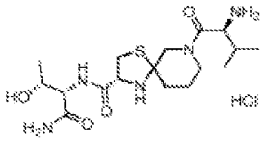
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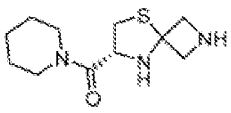
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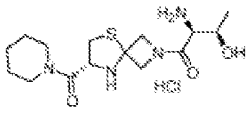
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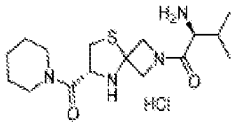
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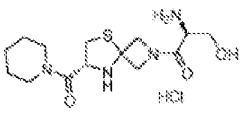
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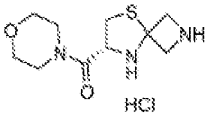
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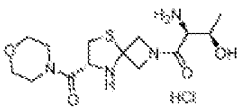
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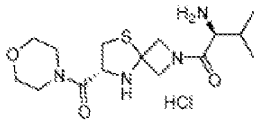
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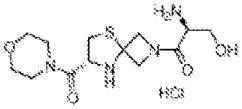
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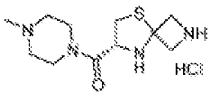
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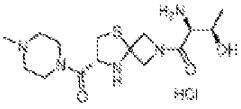
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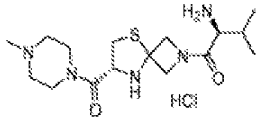
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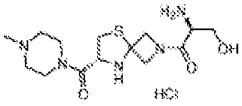
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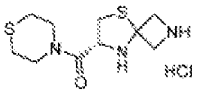
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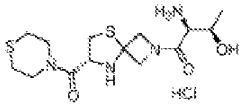
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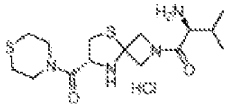
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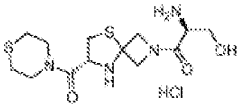
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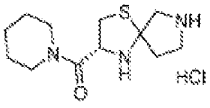
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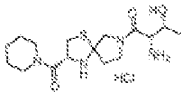
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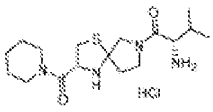
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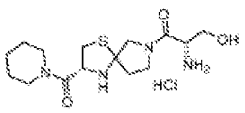
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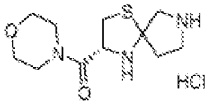
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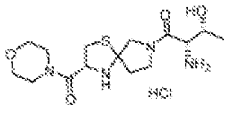
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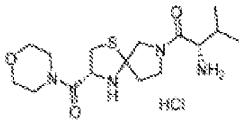
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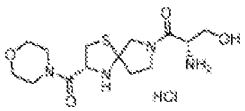
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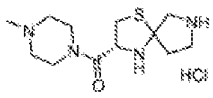
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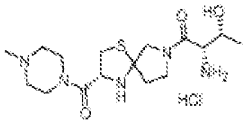
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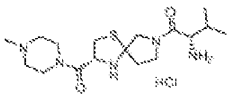
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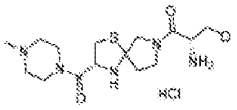
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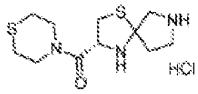
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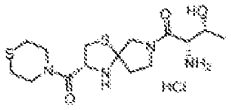
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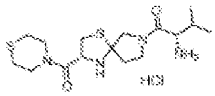
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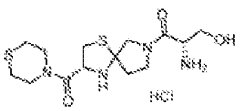
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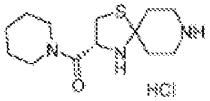
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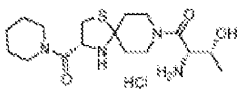
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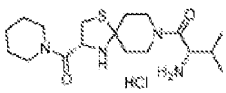
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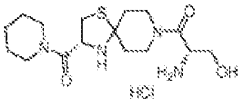
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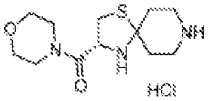
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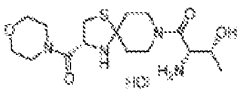
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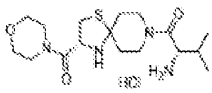
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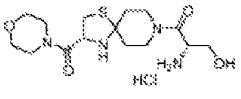
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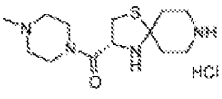
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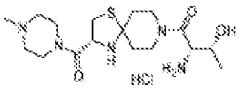
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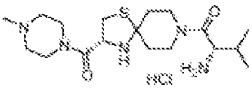
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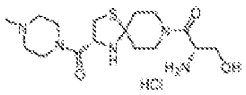
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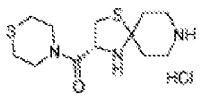
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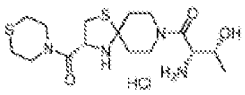
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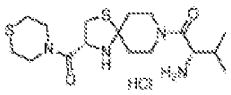
A-447



A-448



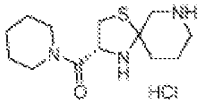
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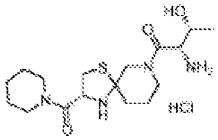
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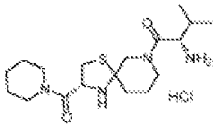
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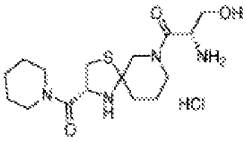
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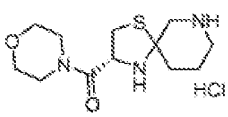
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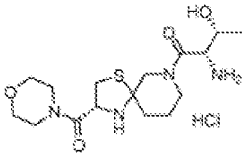
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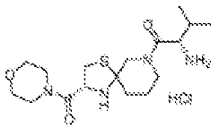
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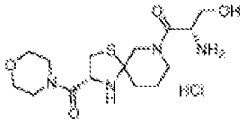
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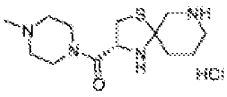
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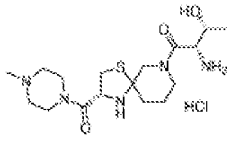
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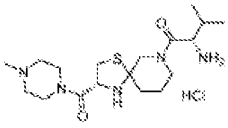
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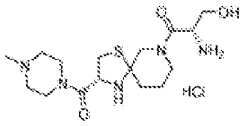
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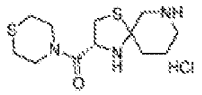
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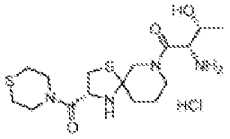
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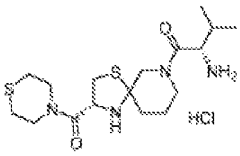
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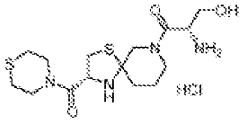
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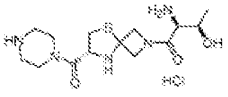
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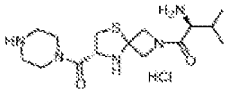
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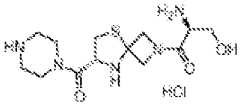
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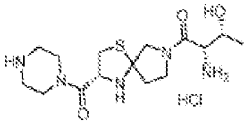
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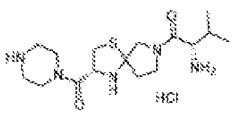
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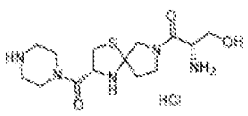
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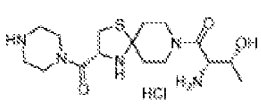
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A-472



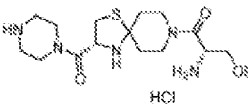
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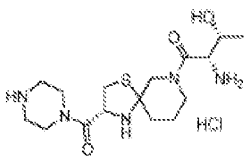
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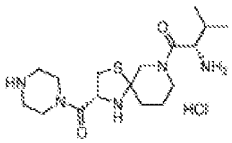
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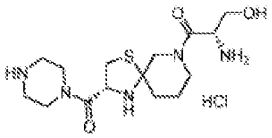
A-476



A-477



A-478



A-479

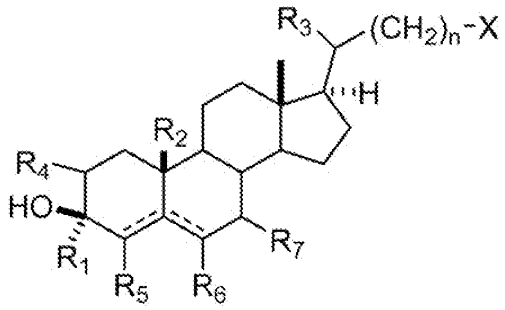
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Formula 202

[0924] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 202. Such compounds are described in International Publication No. WO 2021/080880, published April 29, 2021 and corresponding to PCT/US2020/056171, filed October 16, 2020, which is incorporated by reference in its entirety herein. In the case of any conflict of terminology of Formula 202, these references incorporated by reference herein control.

[0925] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 202:

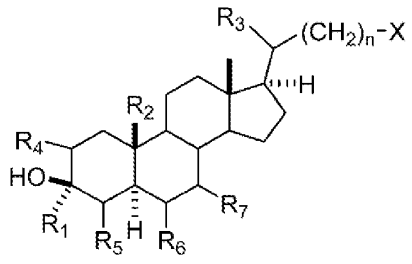
Formula 202



(I)

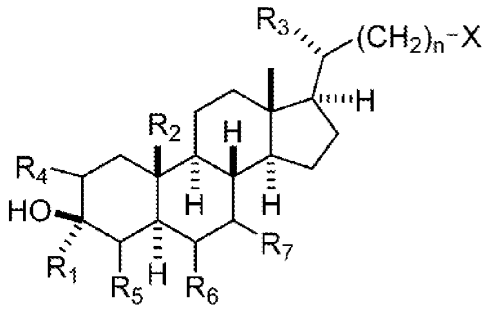
, or a pharmaceutically acceptable salt thereof, wherein R1 is hydrogen, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, or C1 to C6 haloalkyl; R2 is hydrogen, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, C1 to C6 haloalkyl, –CH2O-RA, or –CH2O(C=O)-RB; R3 is hydrogen, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 haloalkyl, –CH2O-RA, or –CH2O(C=O)-RB; each RA is independently C1 to C6 alkyl or C1 to C6 haloalkyl; each RB is independently hydrogen, C1 to C6 alkyl, or C1 to C6 haloalkyl; R4 is hydrogen, hydroxy, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, or C1 to C6 haloalkyl; R5 is hydrogen, hydroxy, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, or C1 to C6 haloalkyl; R6 is hydrogen, hydroxy, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, or C1 to C6 haloalkyl; R7 is hydrogen, hydroxy, C1 to C6 alkyl, C1 to C6 alkenyl, C1 to C6 alkynyl, C1 to C6 alkoxy, or C1 to C6 haloalkyl; X is hydroxy, OSO3H, OSO3-NH4+, SO3H, SO2H, COOH, NH(CH2)m-Y, H2PO4, HPO3R8, C(R9)2COOH, C(R9)2-Y, or other negatively charged group at physiological pH; Y is OSO3H, SO3H, SO2H, COOH, H2PO4, HPO3R8, or other negatively charged group at physiological pH; each R8 is independently hydrogen, C1 to C6 alkyl or C1 to C6 haloalkyl; each R9 is independently hydrogen, C1 to C6 alkyl, C1 to C6 haloalkyl, or halo; m is an integer from 1 to 6; and n is an integer from 1 to 8.

[0926] In further embodiments, the compound according to Formula 202 is:



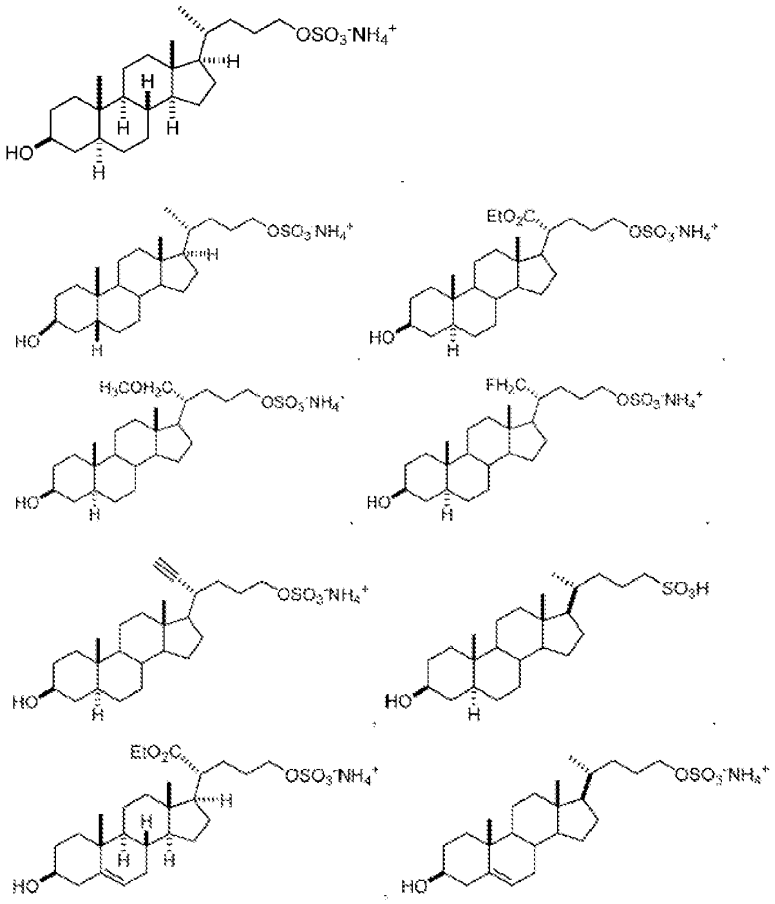
or a pharmaceutically acceptable salt thereof, where R1, R2, R3, R4, R5, R6, R7, and X are as defined above.

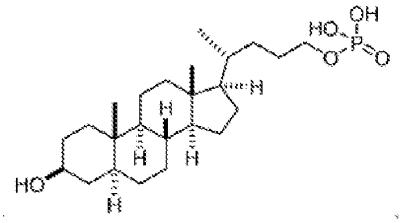
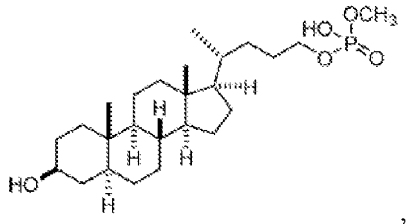
[0927] In further embodiments, the compound according to Formula 202 is:



or a pharmaceutically acceptable salt thereof, where R1, R2, R3, R4, R5, R6, R7, and X are as defined above.

[0928] In further embodiments, the compound according to Formula 202 is selected from:



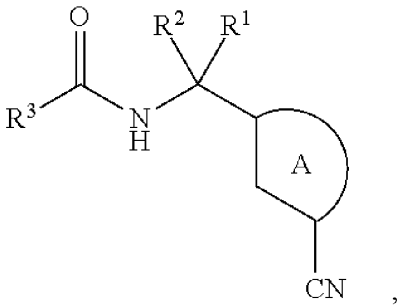
, or pharmaceutically acceptable salts thereof.

Formula 203

[0929] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 203. Such compounds are described in WO2020/153414, published July 30, 2020 and corresponding to PCT/JP2020/002216, filed January 23, 2020, and US20220089525, published March 24, 2022, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 203, these references incorporated by reference herein control.

[0930] In some embodiments, the compound according to Formula 203 is:

Formula 203

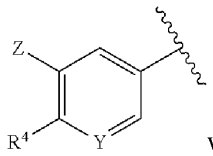


,

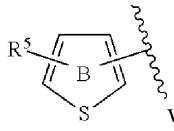
and/or wherein ring A is a 6-membered aromatic ring further substituted by 1 to 4 substituents selected from (1) a C1-3 alkyl group, (2) a C1-3 haloalkyl group, (3) an optionally substituted cyclic group, (4) an optionally substituted C1-6 alkoxy group, and (5) a halogen atom;

R1 and R2 are each independently a hydrogen atom or a C1-3 alkyl group optionally substituted by fluorine atom(s);

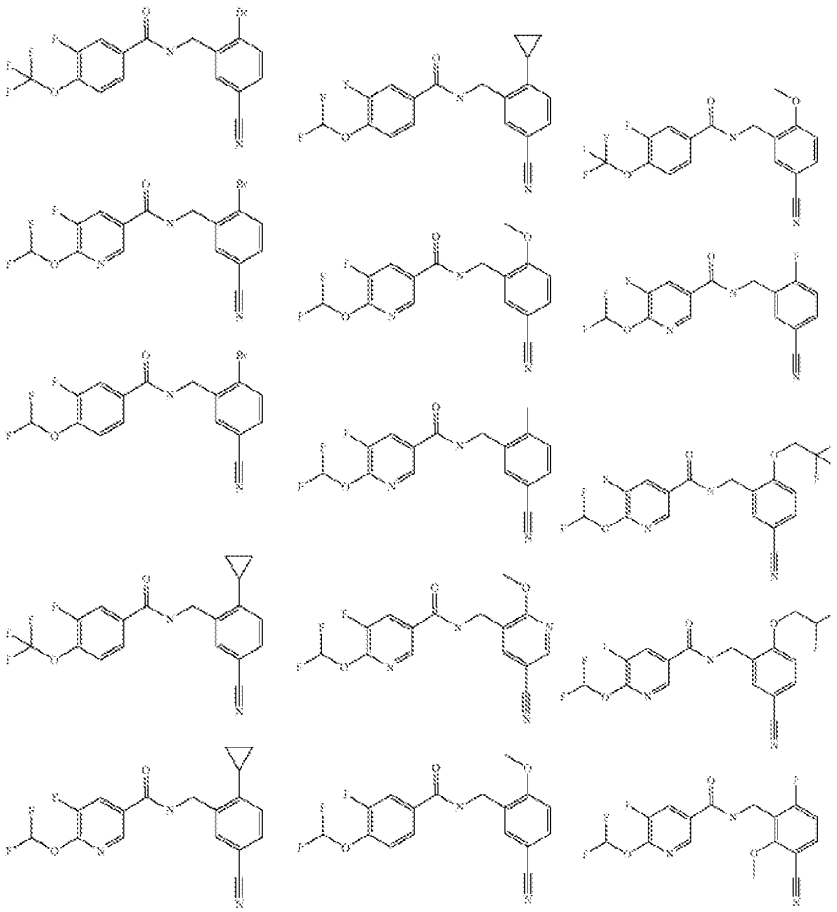
R3 is (1) a group represented by

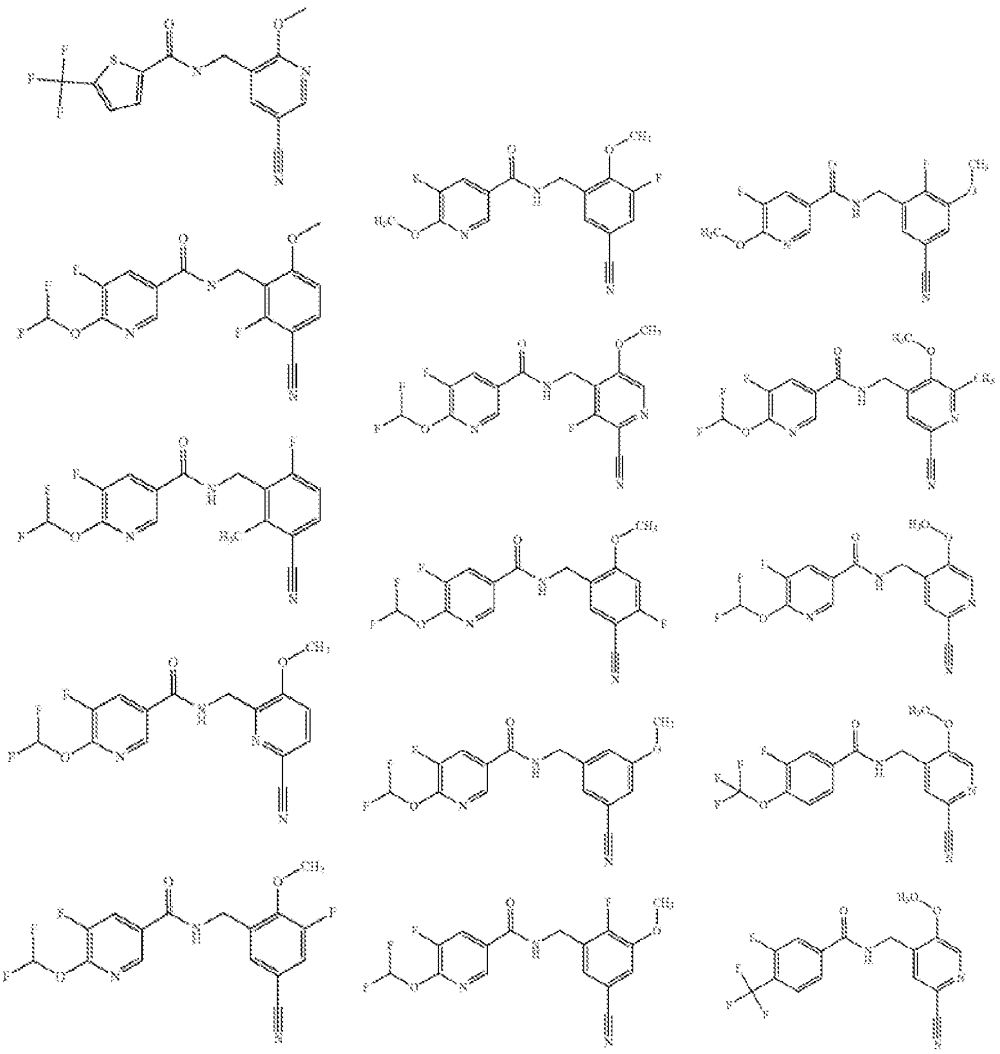


wherein R4 is a substituent selected from (1) a C1-3 haloalkyl group, (2) an optionally substituted C3-7 cycloalkyl group, and (3) an optionally substituted C1-6 alkoxy group, Y is a nitrogen atom or CR6, R6 is a hydrogen atom or a halogen atom, and Z is a hydrogen atom or a halogen atom, or (2) a group represented by



wherein R5 is a substituent selected from (1) a C1-3 haloalkyl group, (2) an optionally substituted C3-7 cycloalkyl group, and (3) an optionally substituted C1-6 alkoxy group, and ring B is a thiophene ring optionally further substituted by one halogen atom, or a salt thereof.



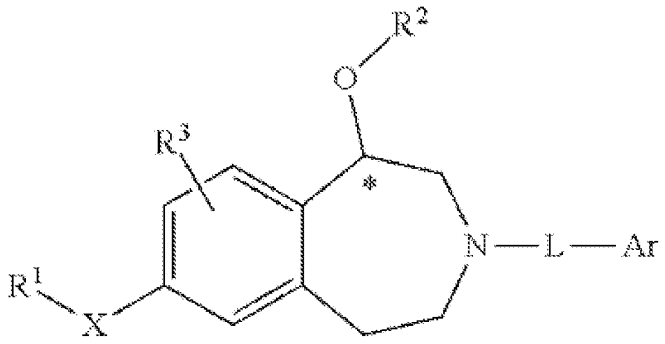


Formula 204

[0931] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 204. Such compounds are described in WO2019/210130, published October 31, 2019, corresponding to PCT/US2019/029285, filed April 26, 2019, and US2021/0094920, published April 1, 2021, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 204, these references incorporated by reference herein control.

[0932] In an embodiment, the NMDA receptor antagonist is:

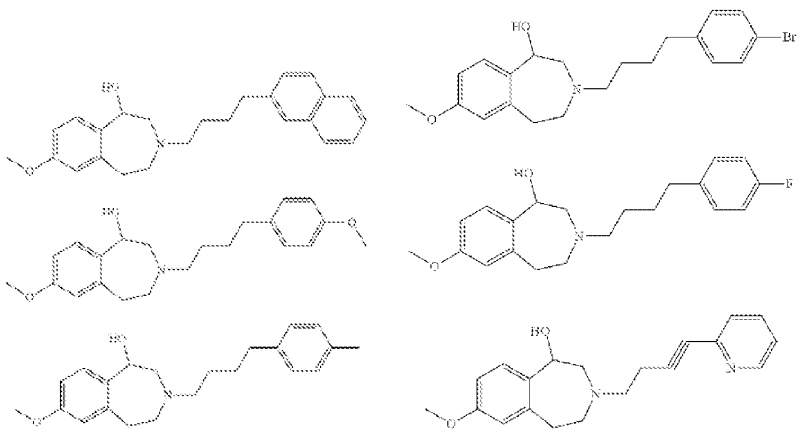
Formula 204

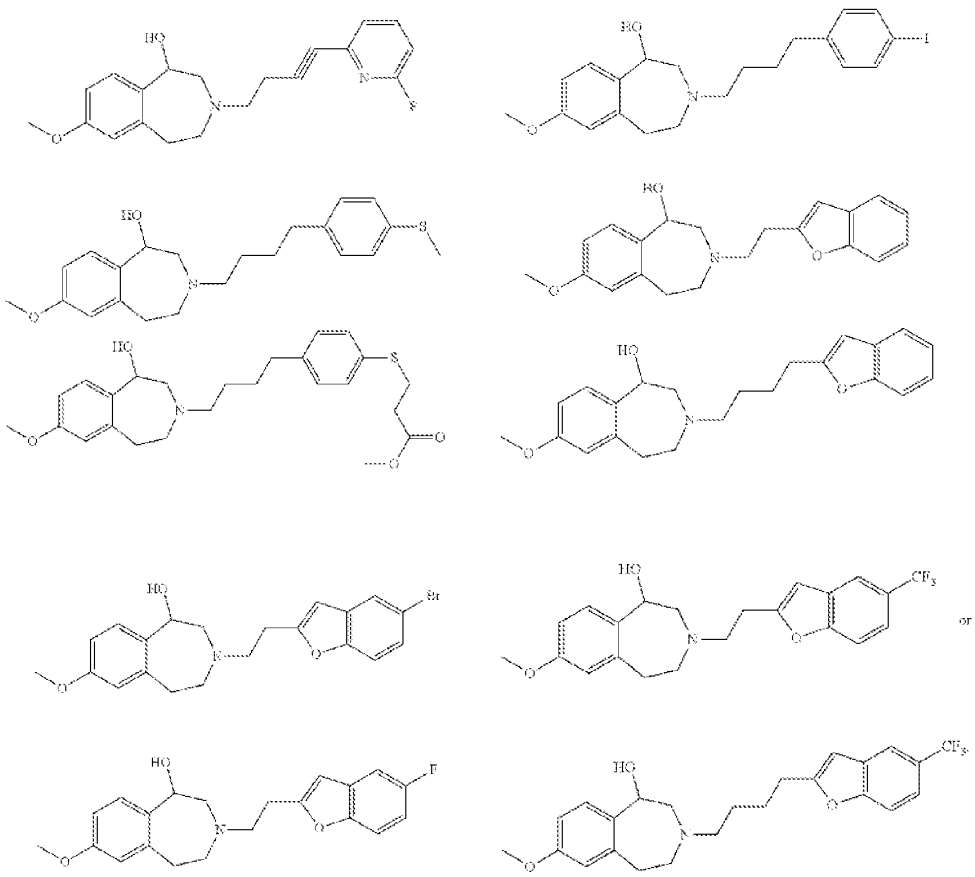


, wherein

X is O or S, specifically O;R1 is H, C1-C6 alkyl, C1-C6 haloalkyl, specifically C1-C3 alkyl, and more specifically methyl; R2 is H, C1-C6 alkyl, C1-C6 haloalkyl, specifically H or C1-C3 alkyl, and more specifically H; R3 is H, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 haloalkyl, C1-C6 haloalkoxy, —OH, halo, —COOH, —CN, —NO2, amino, mono- or di-alkylamino, C2-C6 alkanoyl, C2-C8 cycloalkyl, or heterocycloalkyl, specifically H, C1-C3 alkyl, or C1-C3 haloalkyl, and more specifically H; L is a linking group; and Ar is an aryl or heteroaryl group, each of which is optionally substituted with one, two, or three substituents.

[0933] In further embodiments, the NMDA receptor antagonist is selected from:



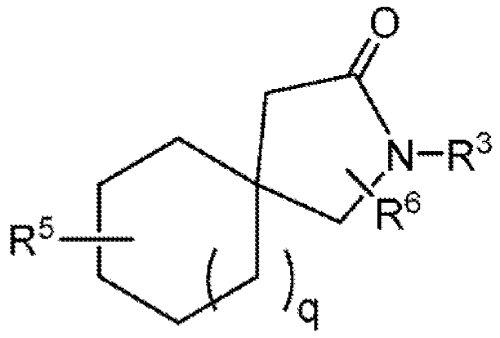


Formula 205

[0934] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 205. Such compounds are described in WO2019/152688, published August 8, 2019 and corresponding to PCT/US2019/016114, filed January 31, 2019, which is incorporated by reference in its entirety herein. In the case of any conflict of terminology of Formula 205, these references incorporated by reference herein control.

[0935] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 205:

Formula 205



or a pharmaceutically acceptable salt and/or a stereoisomer thereof, wherein:

q is 1, 2, 3, or 4;

R5 is independently, for each occurrence, one or more optional substituents selected from the group consisting of C1-C6alkyl, -S(O)$_w$-C1-C3alkyl, -NRaRb, and halogen, wherein C1- C6alkyl is optionally substituted with one, two, or three substitutents each independently selected from Rs;

R6 is one or two optional substituents bound to one or more available ring carbons, and is independently, for each occurrence, selected from the group consisting of C1-C6alkyl, - S(O)$_w$-C1-C3alkyl, -NRaRb, and halogen, wherein C1-C6alkyl is optionally substituted with one, two, or three substitutents each independently selected from Rs;

w is 0, 1, or 2;

R3 is selected from the group consisting of H, phenyl, C1-C6alkyl, -C(O)R31, and -C(O)OR32, wherein C|1-C6, alkyl is optionally substituted with one, two, or three substitutents each independently selected from Rs;

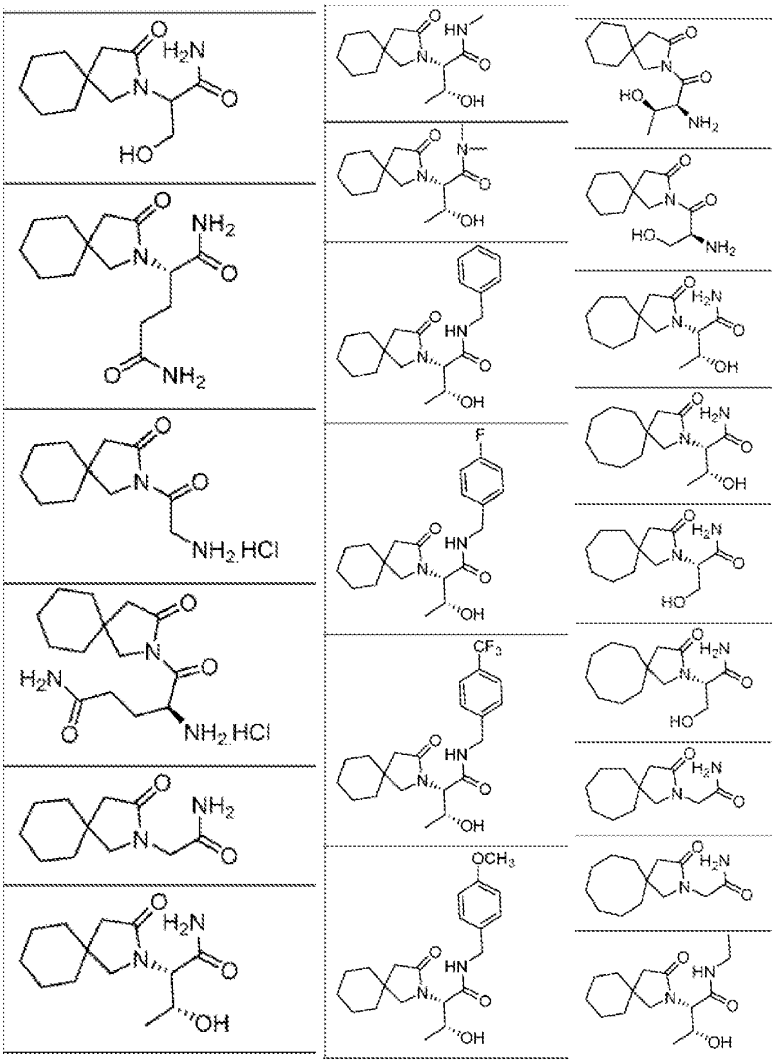
R31 and R32 are each independently selected from the group consisting of H, C1-C6alkyl, -C3-C6cycloalkyl, and phenyl, wherein C1-C6alkyl is optionally substituted with one, two, or three substitutents each independently selected from Rs, and phenyl is optionally substituted with one, two, or three substitutents each independently selected from RT;

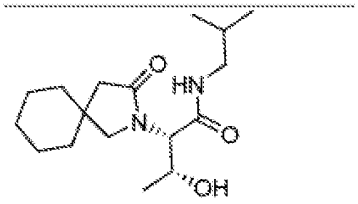
Ra and Rb are independently, for each occurrence, selected from the group consisting of H, phenyl, C1-C4alkyl, -C1-C4alkylene-phenyl, or Ra and Rb taken together with the nitrogen to which they are attached form a 4-6 membered heterocyclic ring, wherein phenyl is optionally substituted with one, two, or three substitutents each

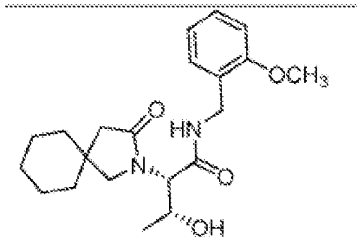
independently selected from hydroxyl, - C1-C3alkoxy, -C1-C3alkyl, and halogen, and C1-C3alkyl is optionally substituted with one, two or three halogens;

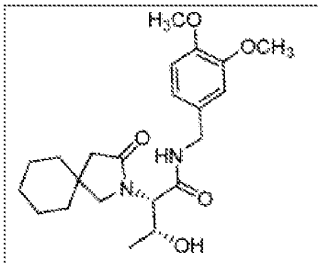
Rs is independently, for each occurrence, selected from the group consisting of -C(O)NRaRb, -NRaRb, hydroxyl, S(O)w-C1-C3alkyl, SH, phenyl and halogen; and RT is independently, for each occurrence, selected from the group consisting of -C1- C6alkyl, hydroxyl, C1-C6alkoxy, and halogen.

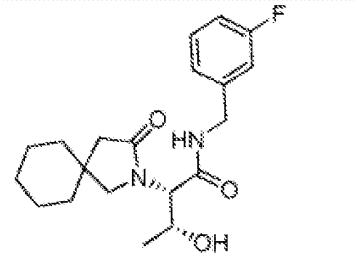
[0936] In further embodiments, the NMDA receptor antagonist is a compound selected from:

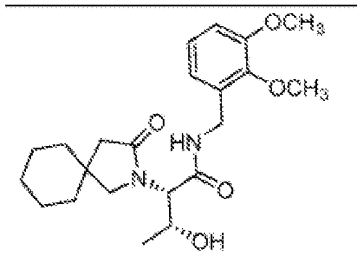


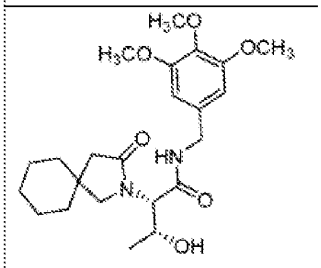


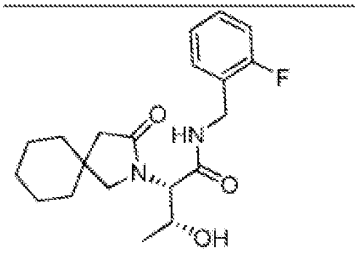


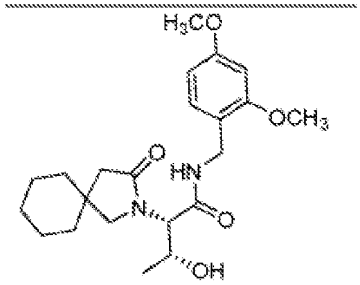


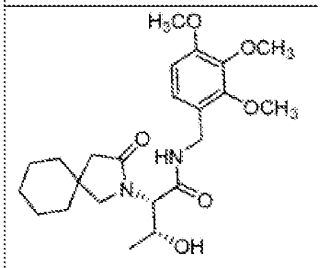


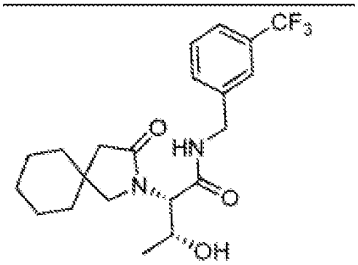


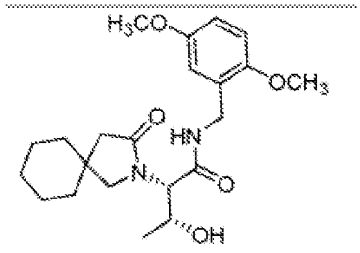


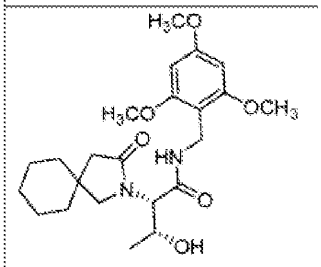


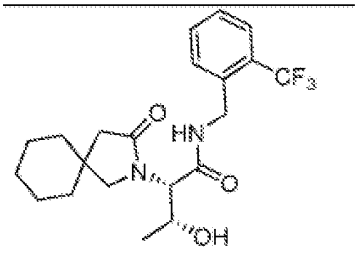


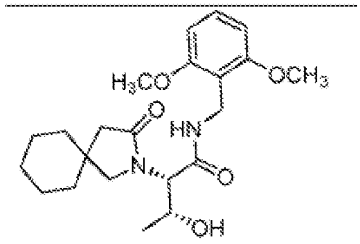


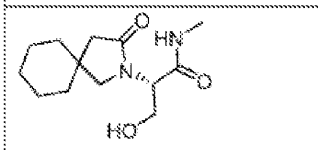


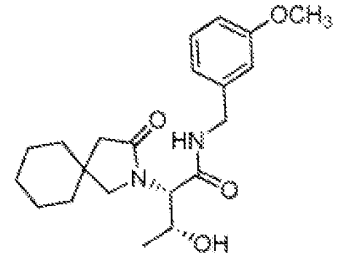


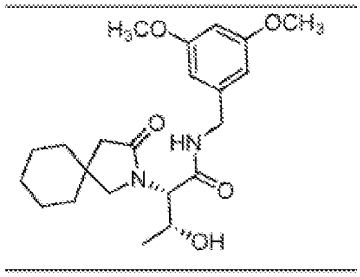


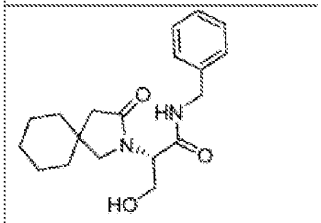


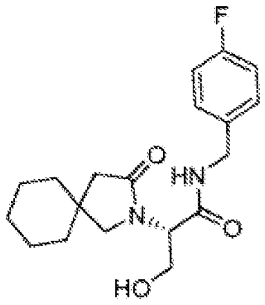












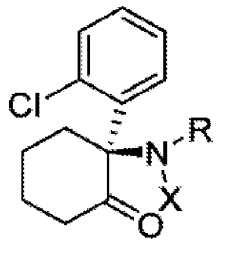
and , including pharmaceutically acceptable salts thereof.

Formula 206

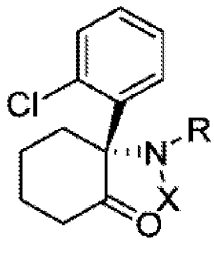
[0937] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 206. Such compounds are described in, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 206, these references incorporated by reference herein control.

[0938] In an embodiment, the NMDA receptor antagonist may be a ketamine prodrug selected from:

Formula 206

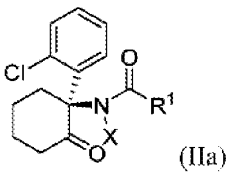


(Ia)

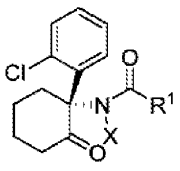


(Ib)

, wherein R is -C (=O) R 1, -C (=O) OR 2, -C (=O) O (CHR 3) OC (=O) R 4 or -CD 3; and X is -CH 3 or -CD 3, including pharmaceutically acceptable salts thereof, or



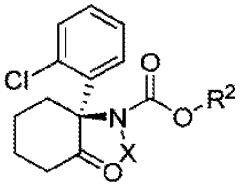
(IIa)

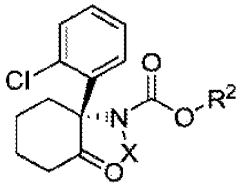


(IIb);

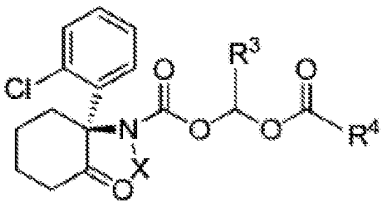
, wherein R 1 is, optionally, substituted or unsubstituted aryl-OH, aryl-NH 2, alkenyl-OH, alkenyl-NH 2, alkyl-NH 2, alkyl-OH,

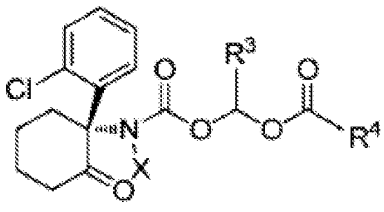
carbocyclyl or heterocyclyl containing one or more N or O; and X is -CH 3 or -CD 3, including pharmaceutically acceptable salts thereof, or


(IIIa)


(IIIb)

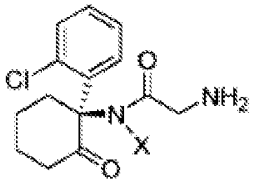
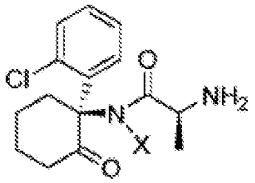
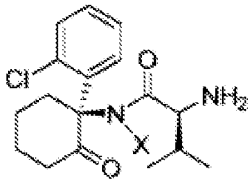
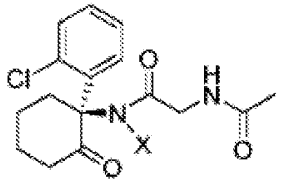
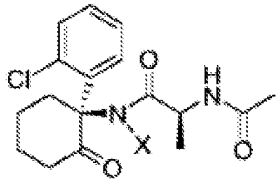
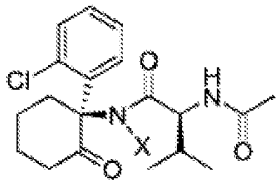
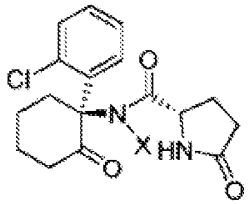
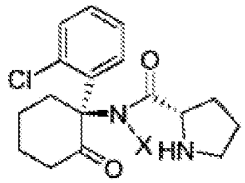
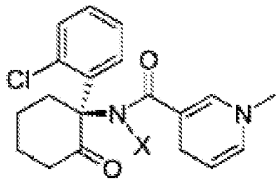
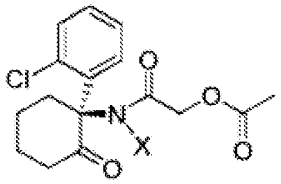
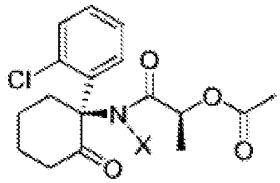
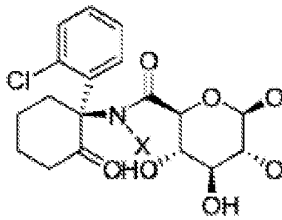
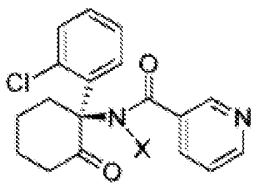
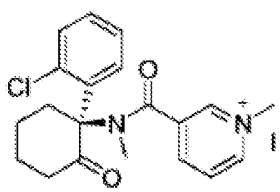
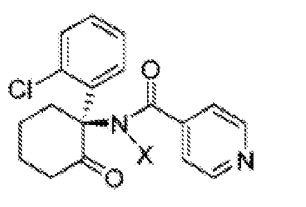
wherein R2 is optionally substituted or unsubstituted alkyl, aryl, carbocyclyl or heterocyclyl containing one or more O; and X is -CH 3 or -CD 3, including pharmaceutically acceptable salts thereof, or

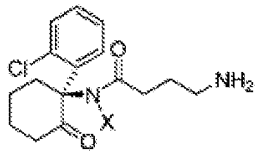
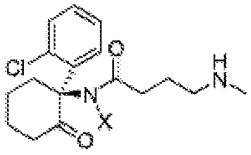
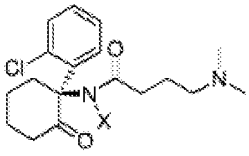
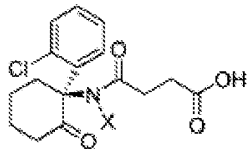
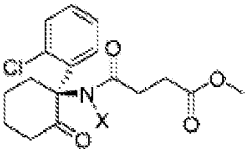
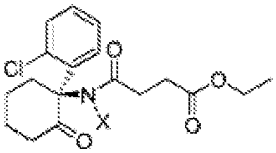
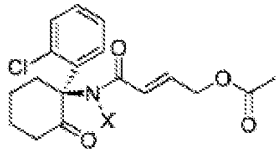
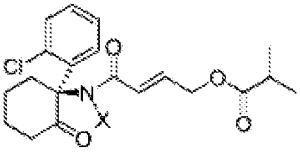
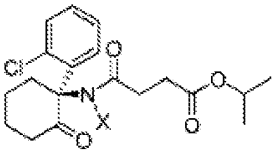
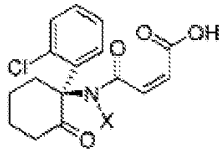
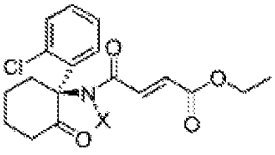
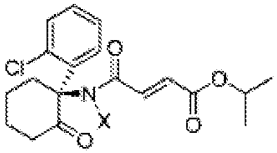
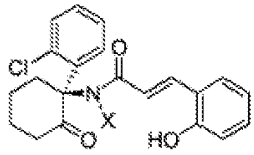
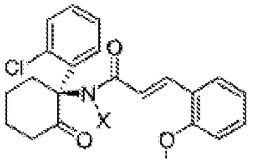
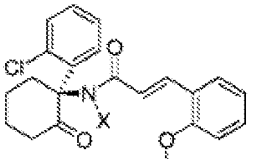
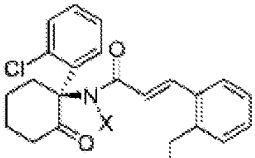
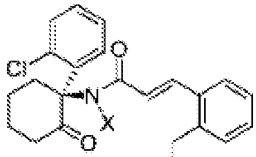
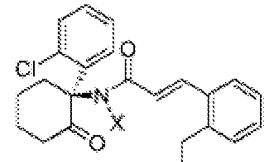

(IVa)

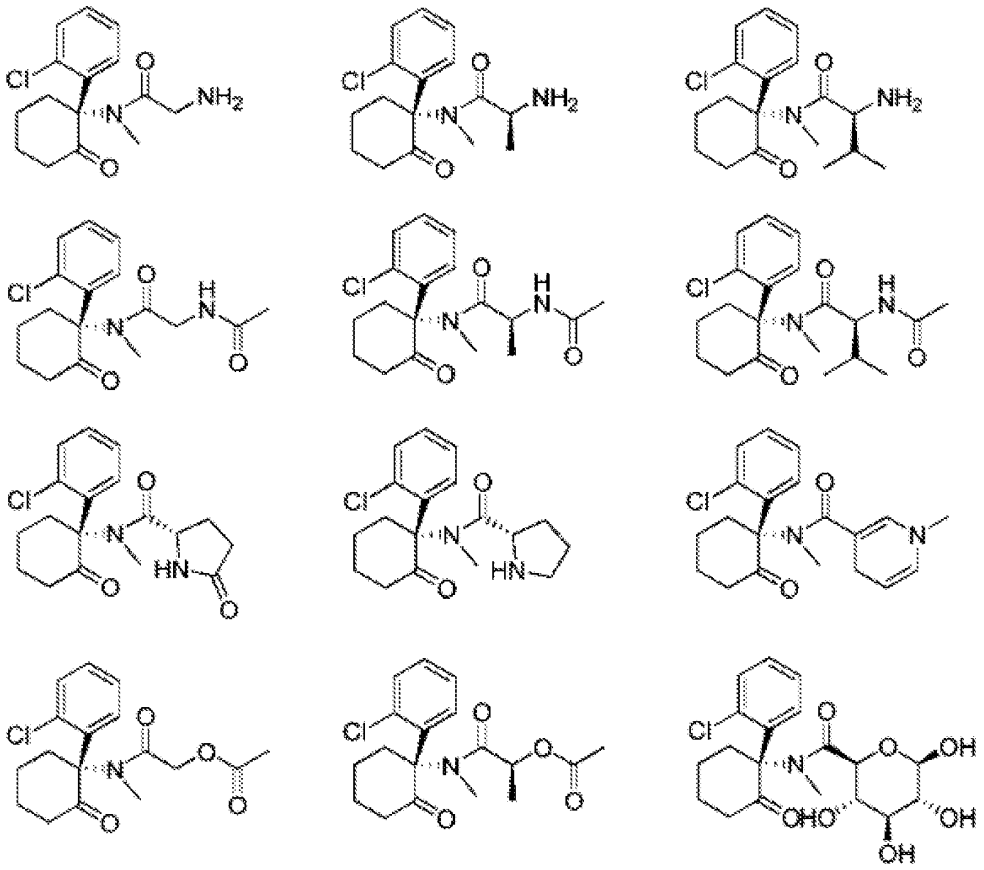

(IVb),

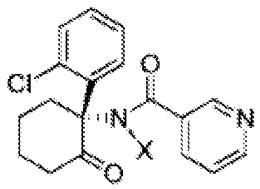
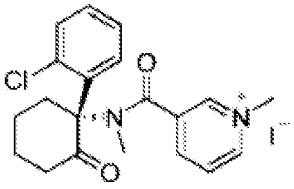
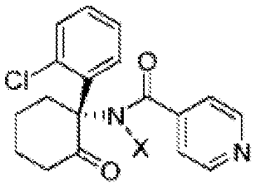
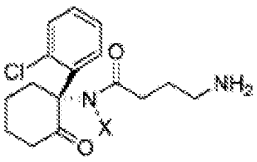
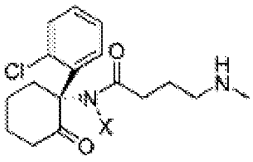
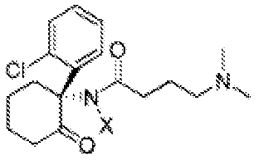
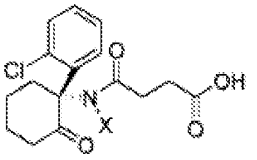
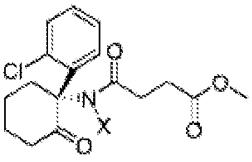
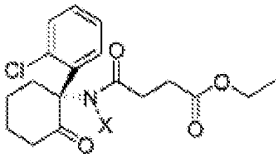
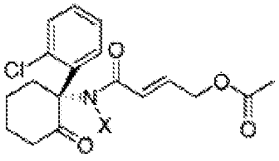
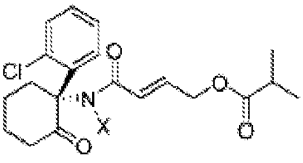
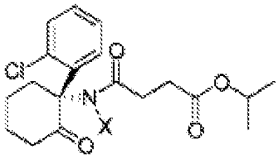
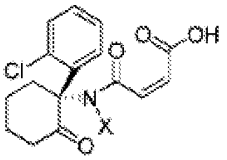
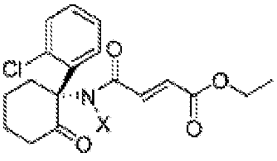
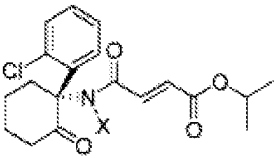
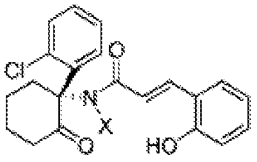
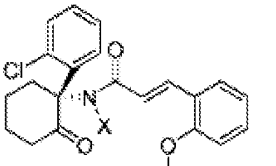
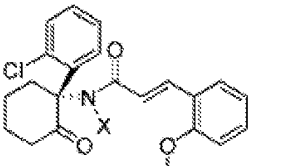
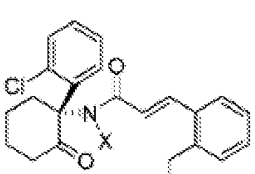
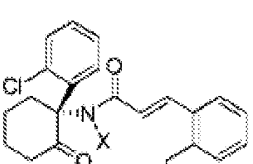
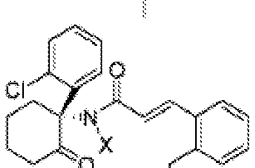
, wherein R4 is independently substituted or unsubstituted alkyl, aryl, azaaryl, carbocyclyl or heterocyclyl containing one or more O or N, while R3 is H or substituted or unsubstituted alkyl; and X is -CH 3 or -CD 3, including pharmaceutically acceptable salts thereof.

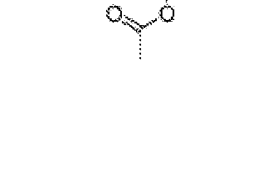
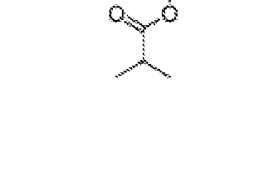
[0939] In further embodiments, the NMDA receptor antagonist is a compound selected from:

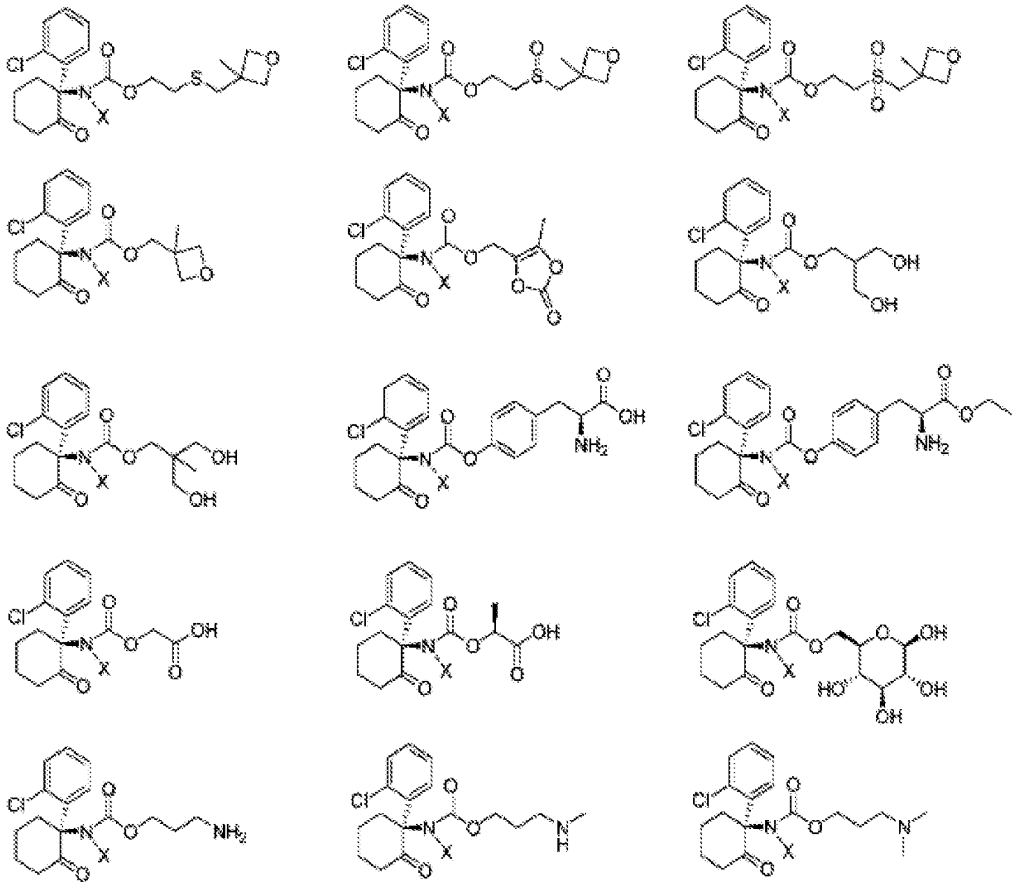


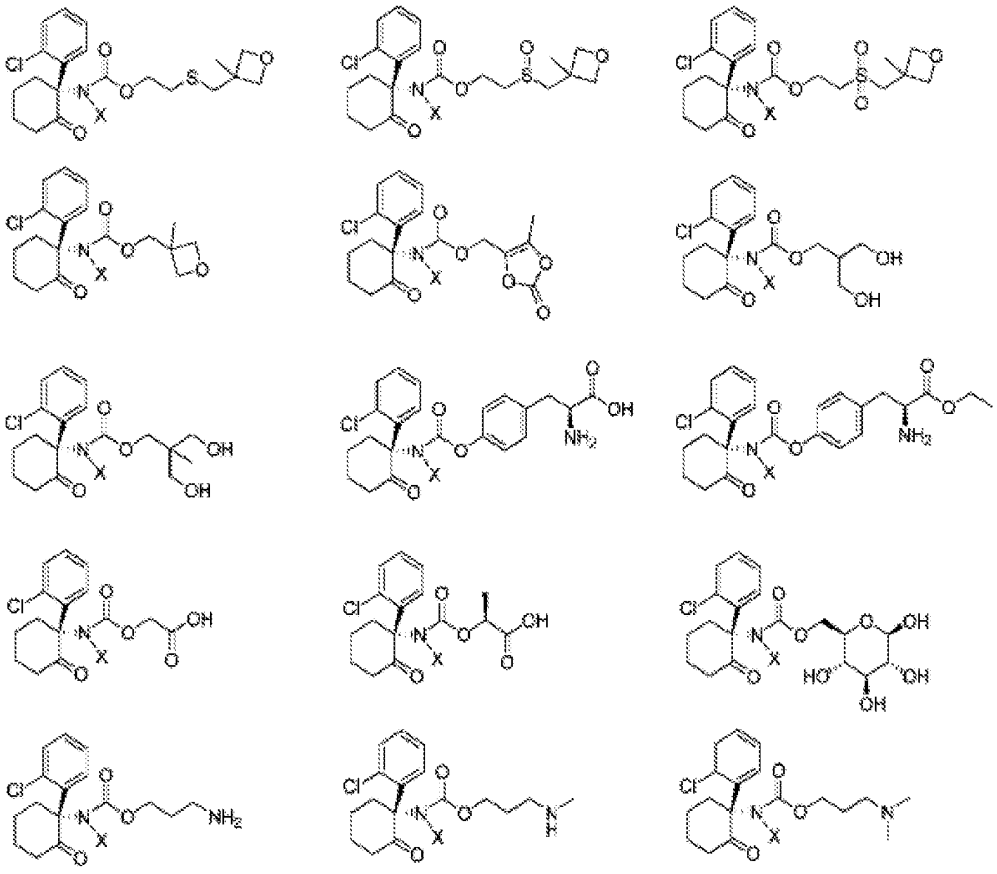






















, Wherein X is -CH3 or -CD3, including pharmaceutically acceptable salts thereof.

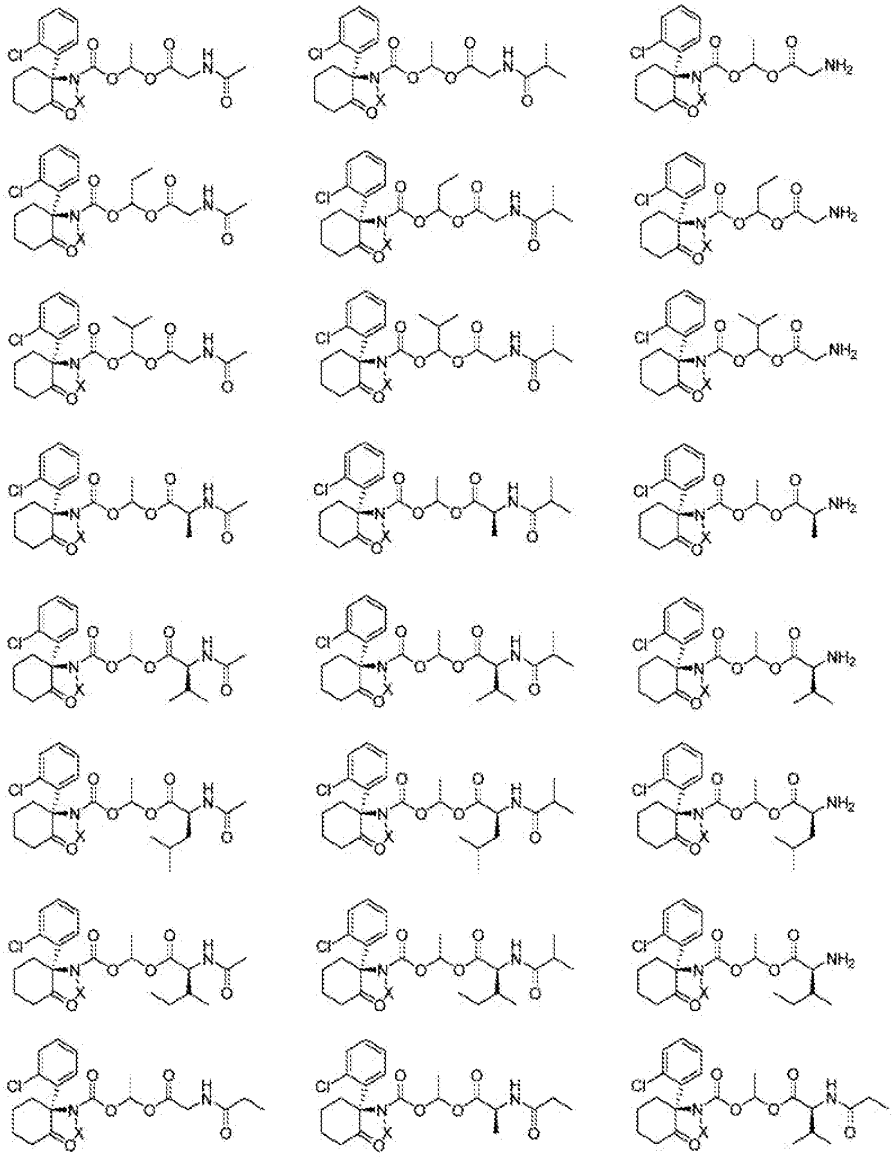
[0940] In further embodiments, the NMDA receptor antagonist is a compound selected from:

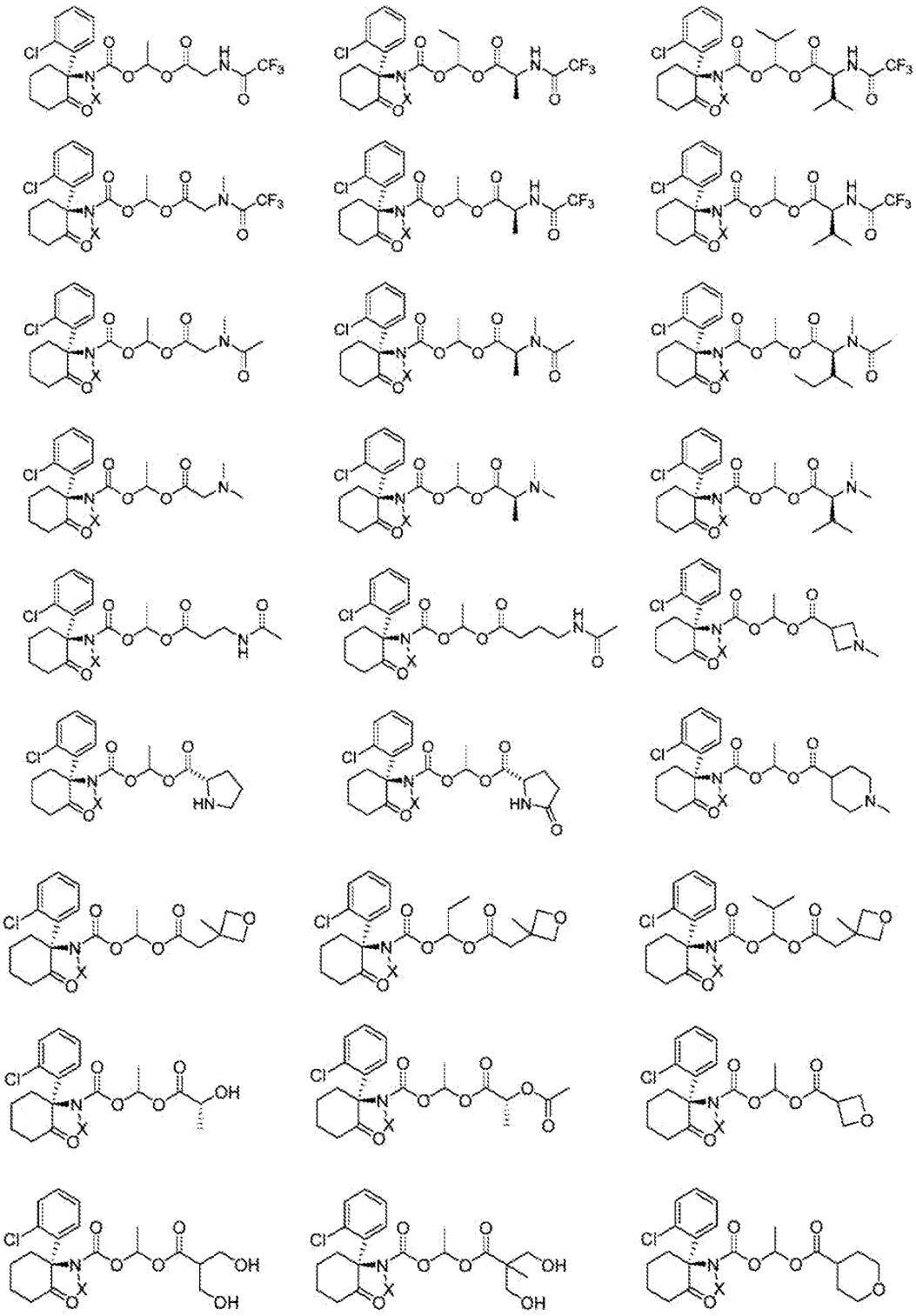


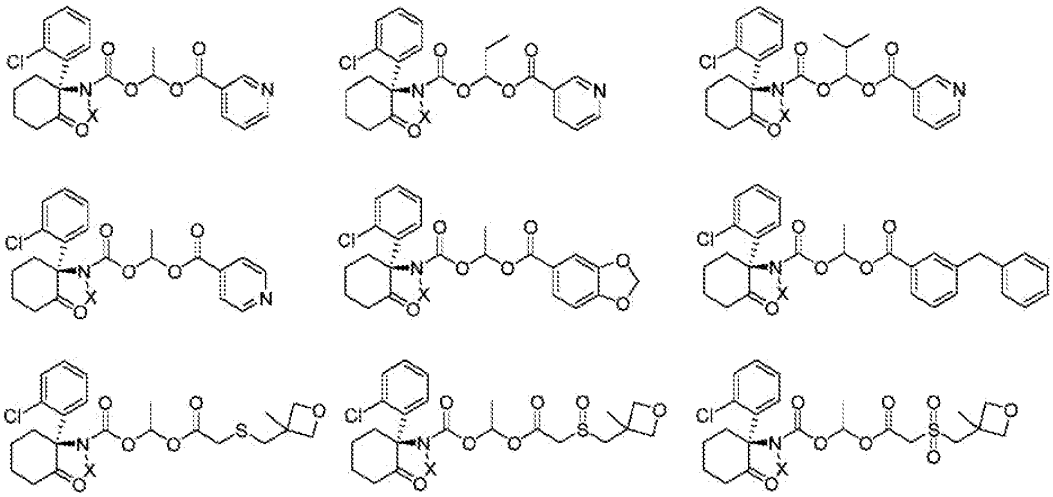


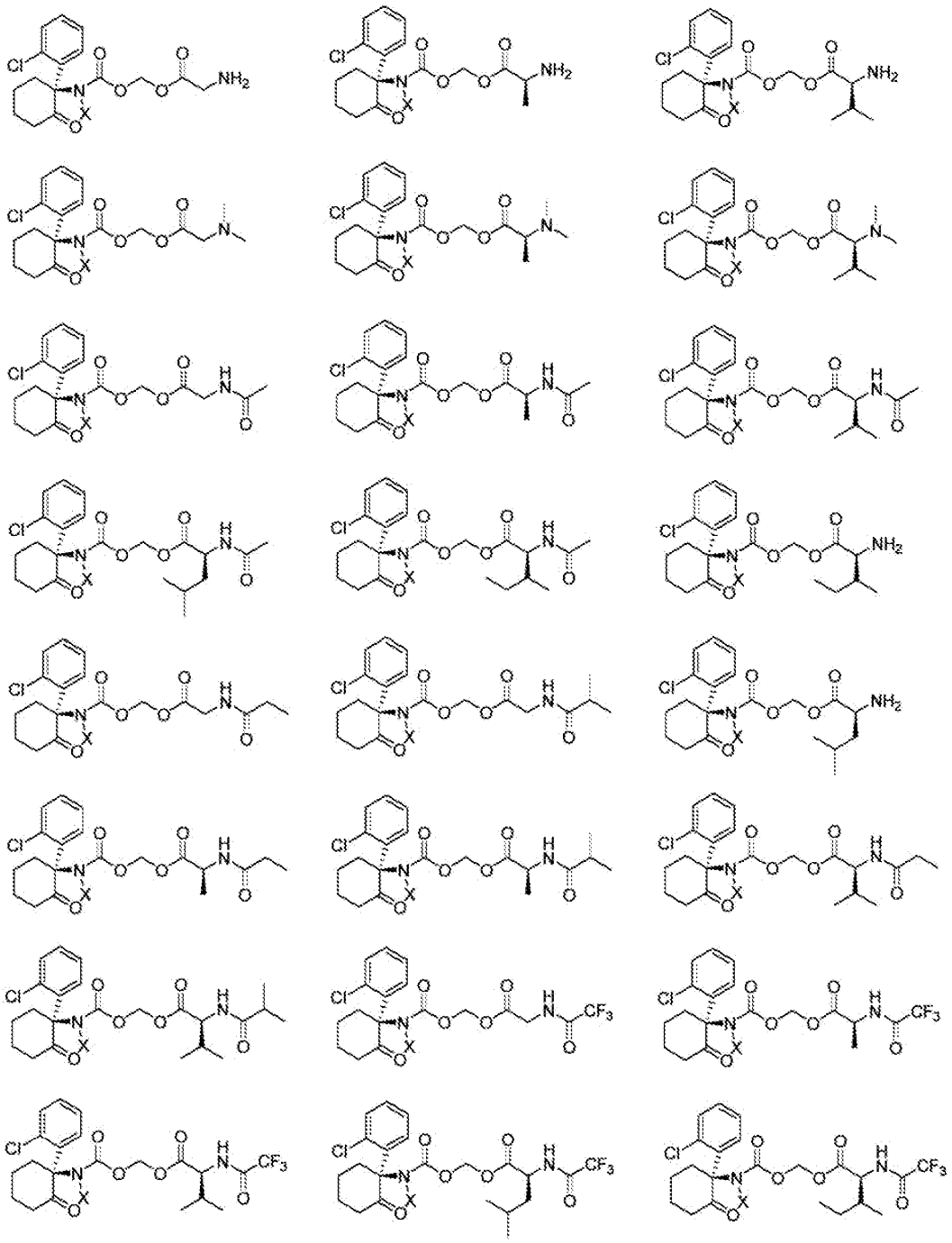
, including pharmaceutically acceptable salts thereof

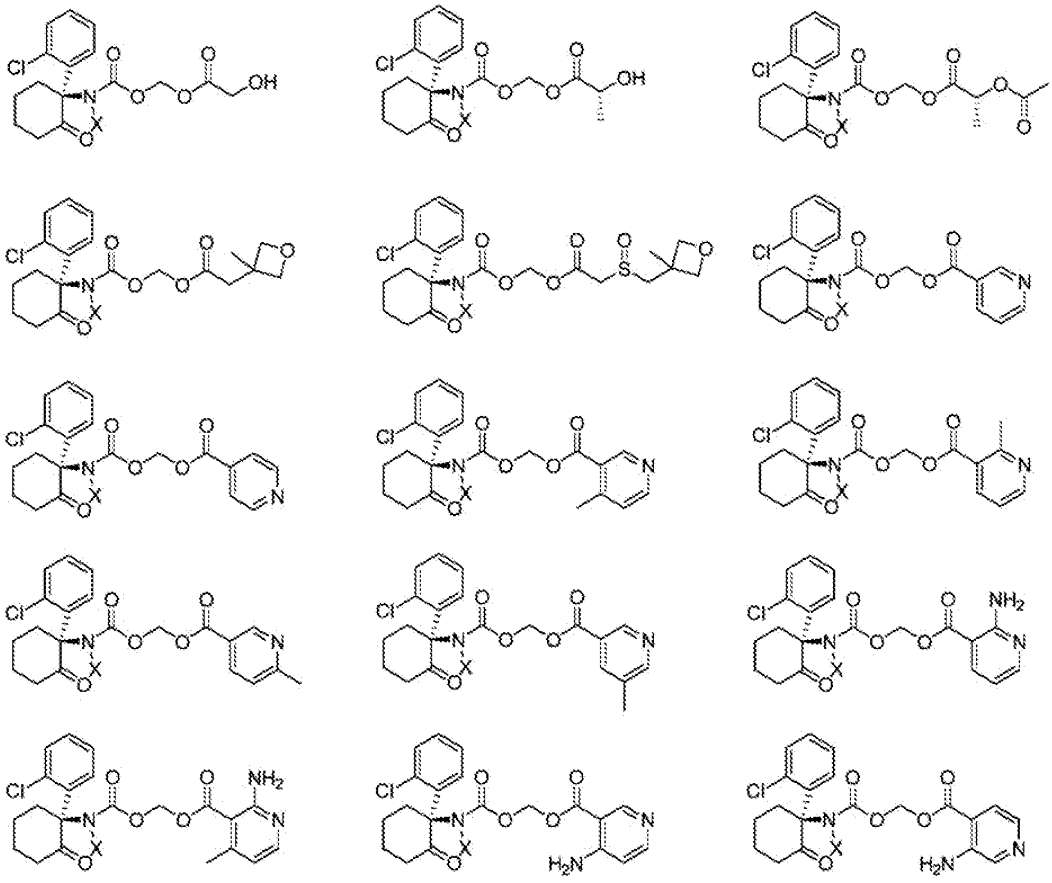
[0941] In further embodiments, the NMDA receptor antagonist is selected from:

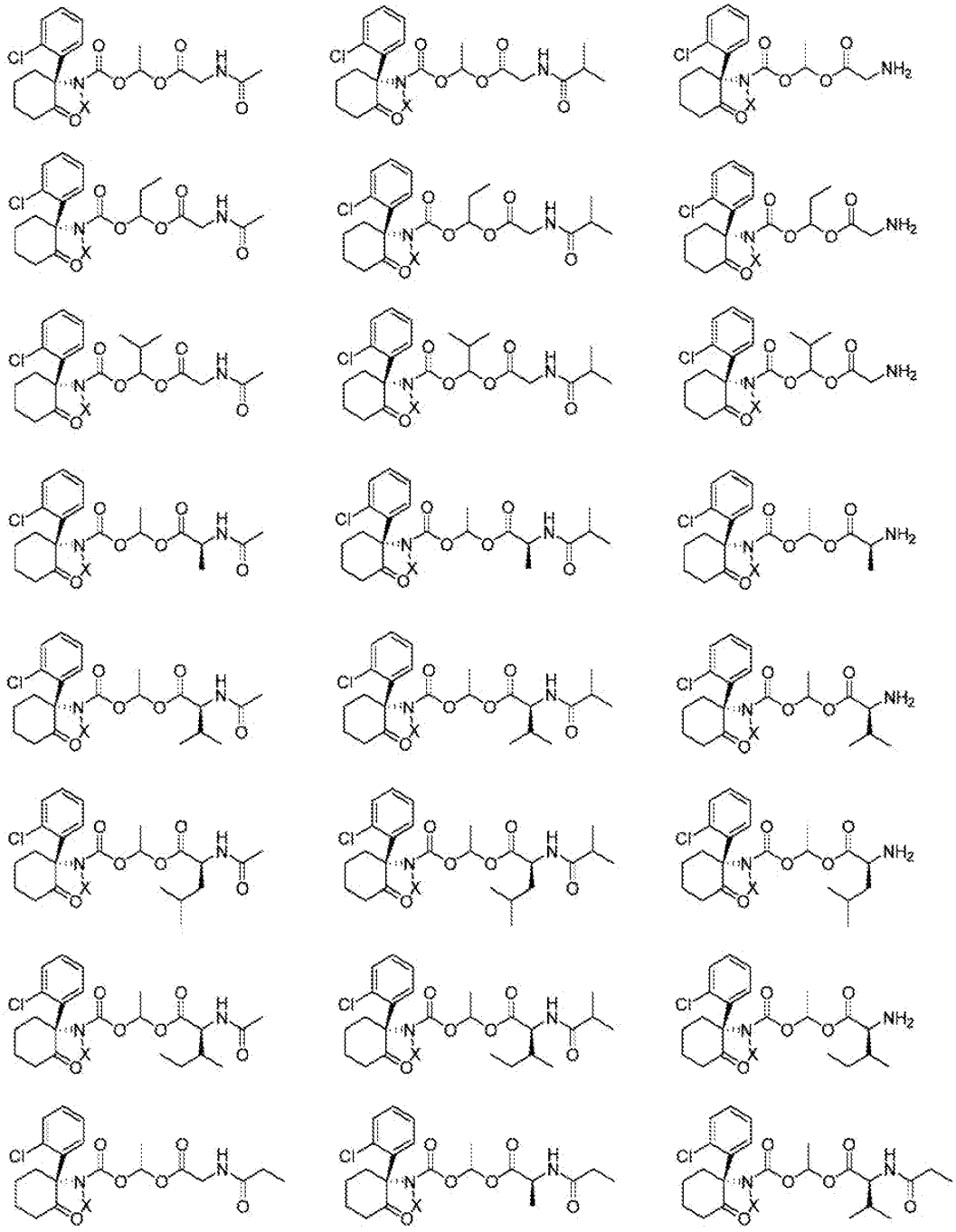


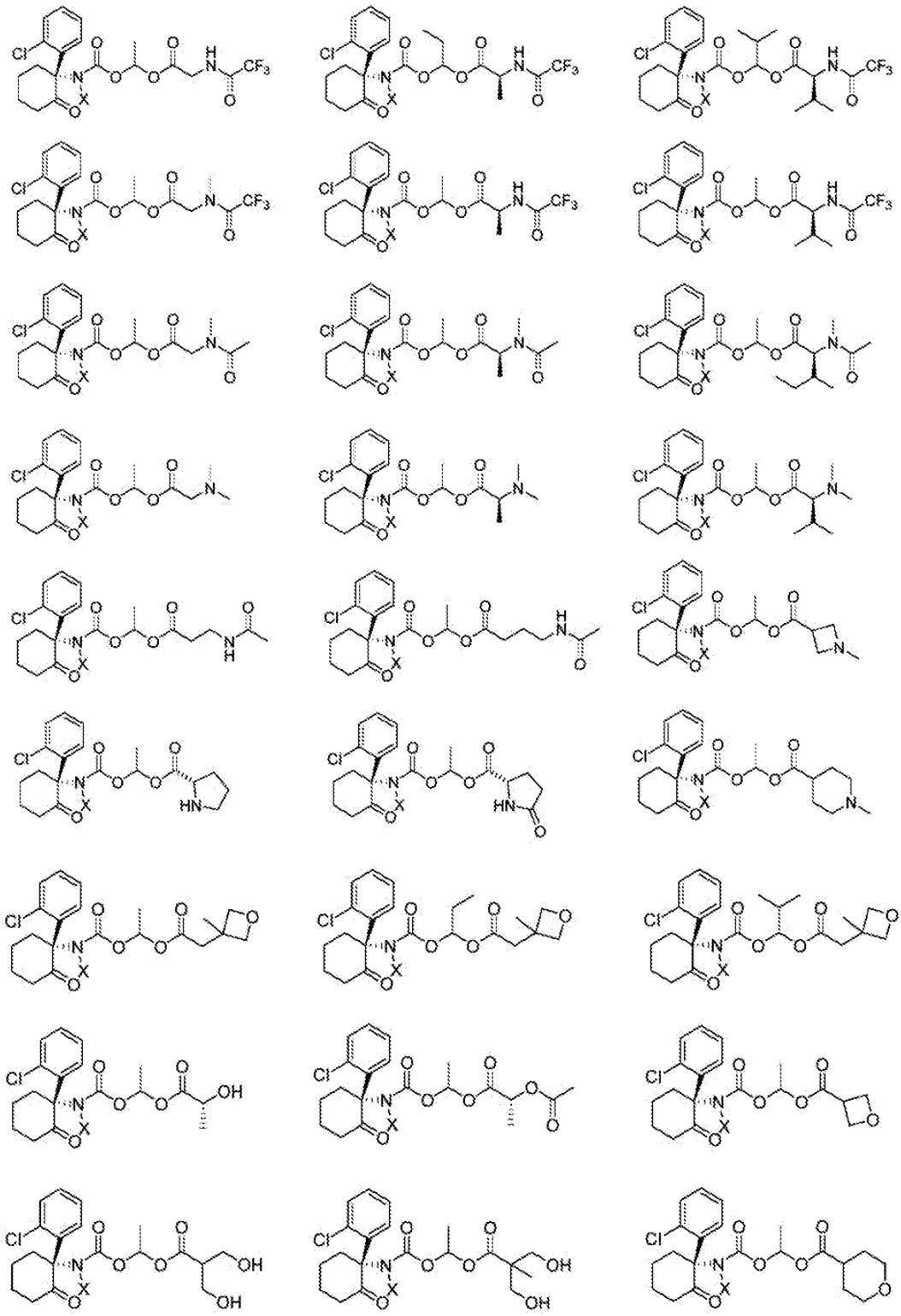


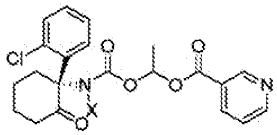
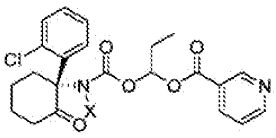
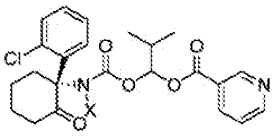
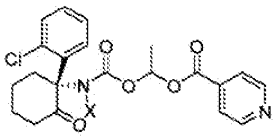
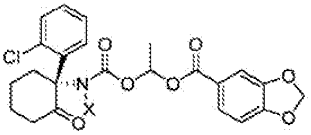
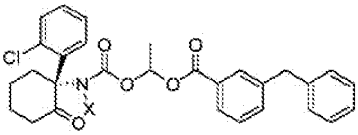
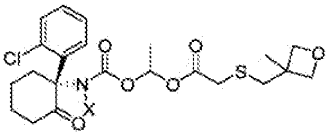
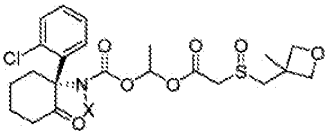
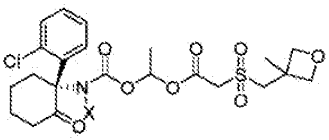


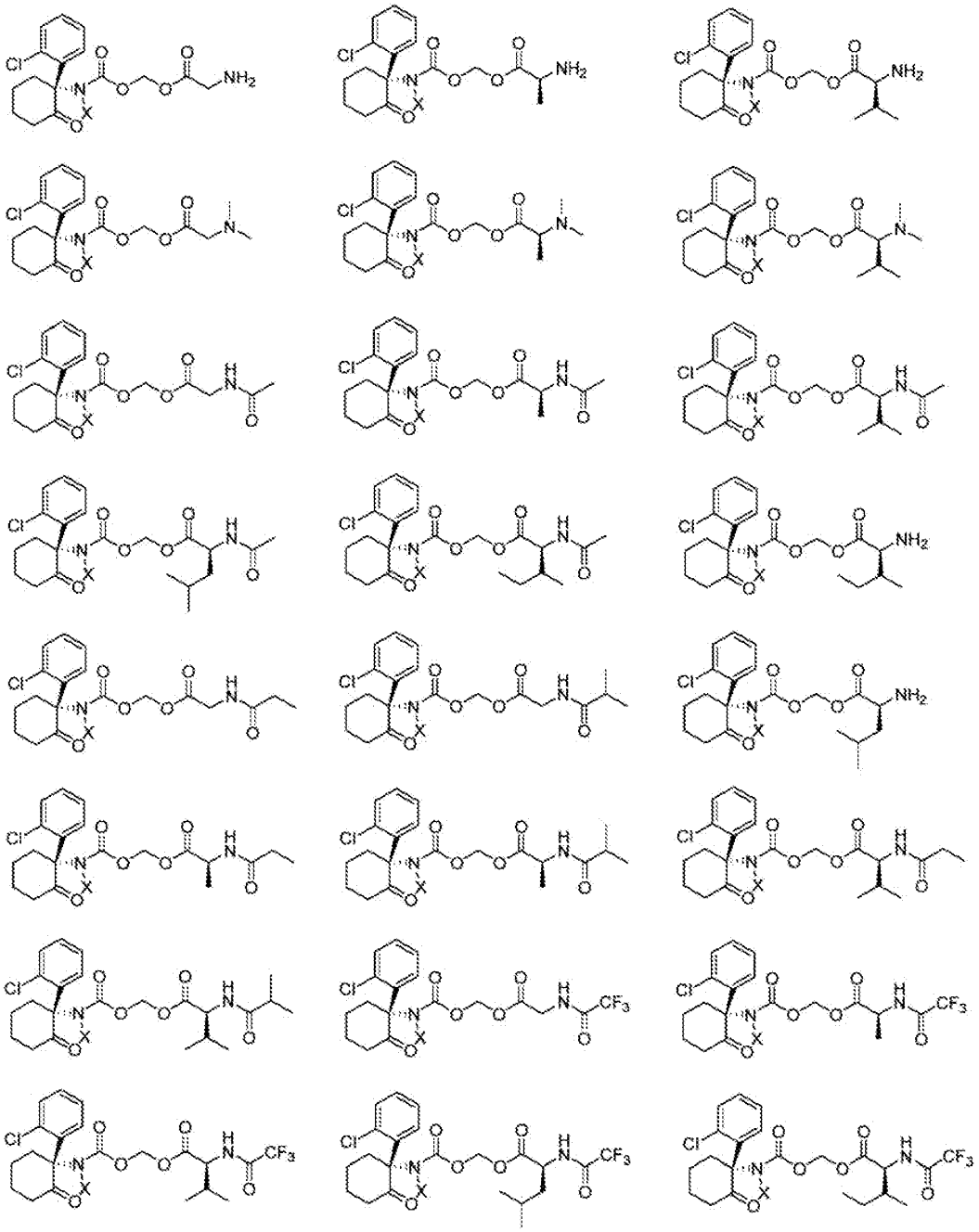


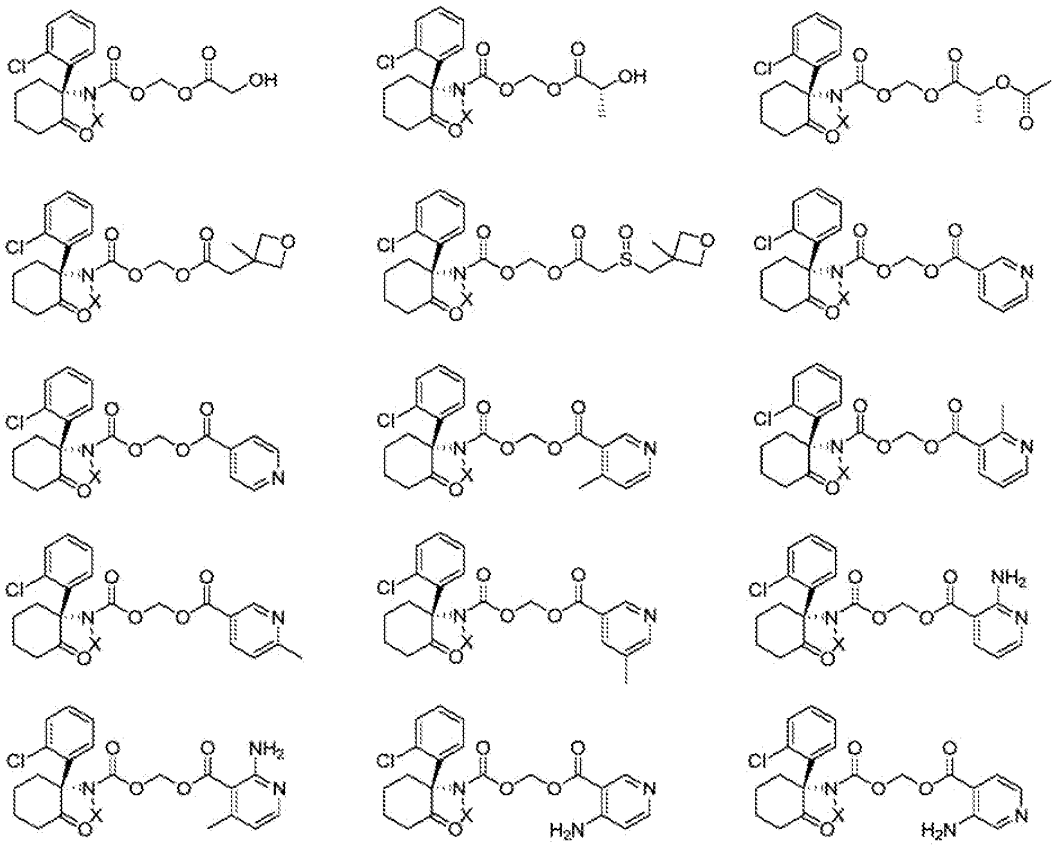






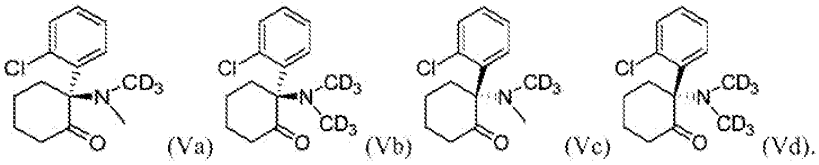














, wherein X is -CH3 or -CD3, including pharmaceutically acceptable salts thereof.

[0942] In further embodiments, the NMDA receptor antagonist is selected from:


(Va) (Vb) (Vc) (Vd), including pharmaceutically acceptable salts thereof.

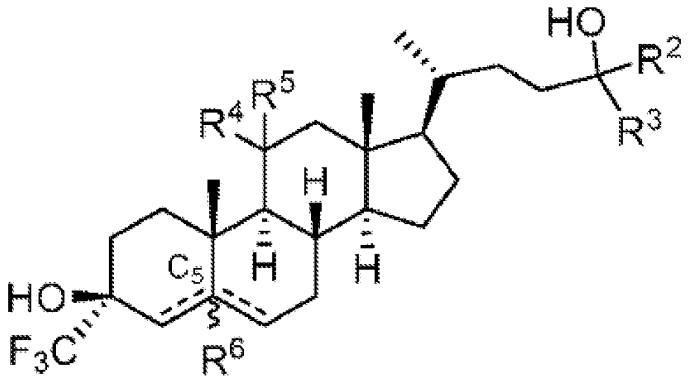
Formula 207

[0943] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 207. Such compounds are described in WO2018/075699, published April 26, 2018 and corresponding to PCT/US2017/057277, filed October 18, 2017, and US 11,149,054, issued October 19, 2021, which are each incorporated

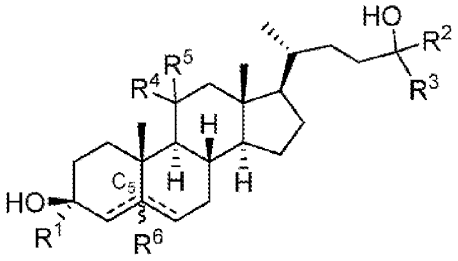
by reference in their entirety herein. In the case of any conflict of terminology of Formula 207, these references incorporated by reference herein control.

[0944] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 207:

Formula 207

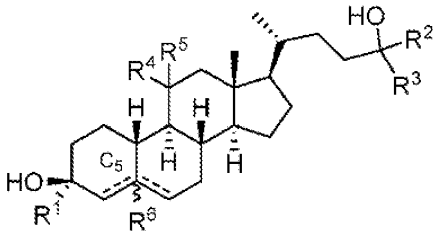


, or a pharmaceutically acceptable salt thereof, wherein: each of R2 and R3 is independently hydrogen, substituted or unsubstituted C1-C6 alkyl, substituted or unsubstituted carbocyclyl, or substituted or unsubstituted heterocyclyl, or R2 and R3, together with the carbon atom to which they are attached form a substituted or unsubstituted 3-8 membered ring; each of R4 and R5 is independently hydrogen, halo, or -ORc, wherein Rc is hydrogen or substituted or unsubstituted C1-C6 alkyl, or R4 and R5, together with the carbon atom to which they are attached form an oxo group; R6 is absent or hydrogen; and represents a single or double bond, wherein when one of is a double bond, the other is a single bond; when both of are single bonds, then R is hydrogen; and when one of is a double bond, R is absent, or

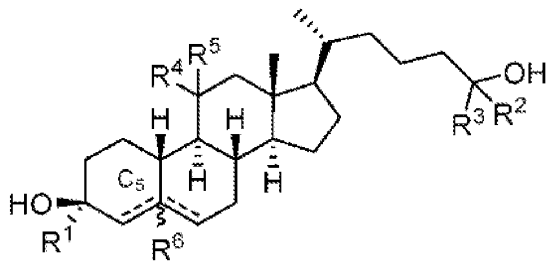


, or a pharmaceutically acceptable salt thereof, wherein: R1 is substituted or unsubstituted C1-C6 alkyl; R2 is substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R3 is hydrogen, substituted or unsubstituted C1-C6

alkyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, aryl, or substituted or unsubstituted heteroaryl; each of R4 and R5 is independently hydrogen, halo, or -ORc, wherein Rc is hydrogen or unsubstituted or substituted C1-C3 alkyl, or R4 and R5, together with the carbon atom to which they are attached form an oxo group; R6 is absent or hydrogen; and represents a single or double bond, wherein when one of is a double bond, the other is a single bond; when both of are single bonds, then R6 is hydrogen; and when one of is a double bond, R6 is absent, or



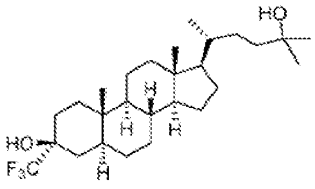
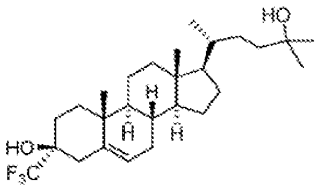
or a pharmaceutically acceptable salt thereof, wherein: R1 is hydrogen or substituted or unsubstituted C1-C6 alkyl; each of R2 and R3 is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted carbocyclyl, or substituted or unsubstituted heterocyclyl or R2 and R3, together with the carbon atom to which they are attached for a 3-8 substituted or unsubstituted membered ring; each of R4 and R5 is independently hydrogen, halo, or -ORc, wherein Rc is hydrogen or substituted or unsubstituted C1-C6 alkyl, or R4 and R5, together with the carbon atom to which they are attached form an oxo group; R6 is absent or hydrogen; and represents a single or double bond, wherein when one of is a double bond, the other is a single bond; when both of are single bonds, then R6 is hydrogen; and when one of is a double bond, R6 is absent, or



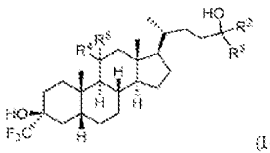
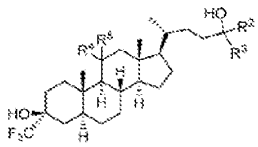
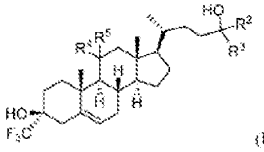
or a pharmaceutically acceptable salt thereof, wherein, R1 is hydrogen or substituted or unsubstituted C1-C6 alkyl; each of R2 and R3 is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted carbocyclyl, or substituted or unsubstituted heterocyclyl or R2 and R3, together with the carbon atom to which they are attached, form a 3-8 substituted or unsubstituted membered

ring; each of R4 and R5 is independently hydrogen, halo, or -ORc, wherein Rc is hydrogen or substituted or unsubstituted C1-C6 alkyl, or R4 and R5, together with the carbon atom to which they are attached form an oxo group; R6 is absent or hydrogen; and represents a single or double bond, wherein when one of is a double bond, the other is a single bond; when both of are single bonds, then R6 is hydrogen; and when one of is a double bond, R6 is absent.

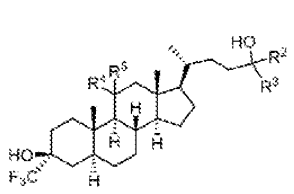
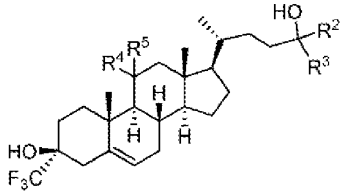
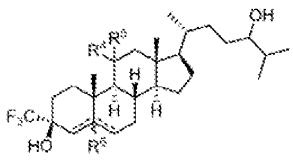
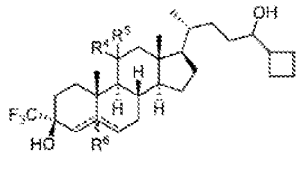
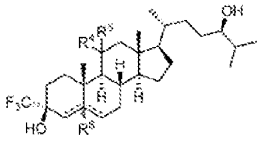
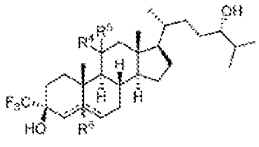
[0945] In further embodiments, the NMDA receptor antagonist is a compound selected from:

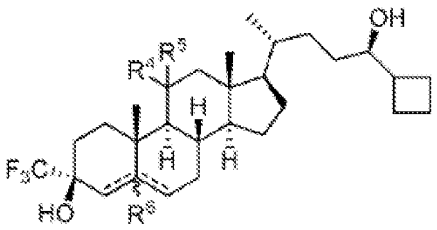



[0946] In further embodiments, the NMDA receptor antagonist is a compound selected from:

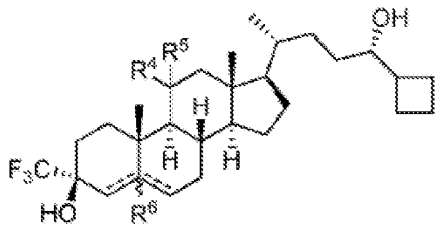

(I-A59),

(I-B59),

(I-C59).

[0947] In further embodiments, the NMDA receptor antagonist is a compound selected from:

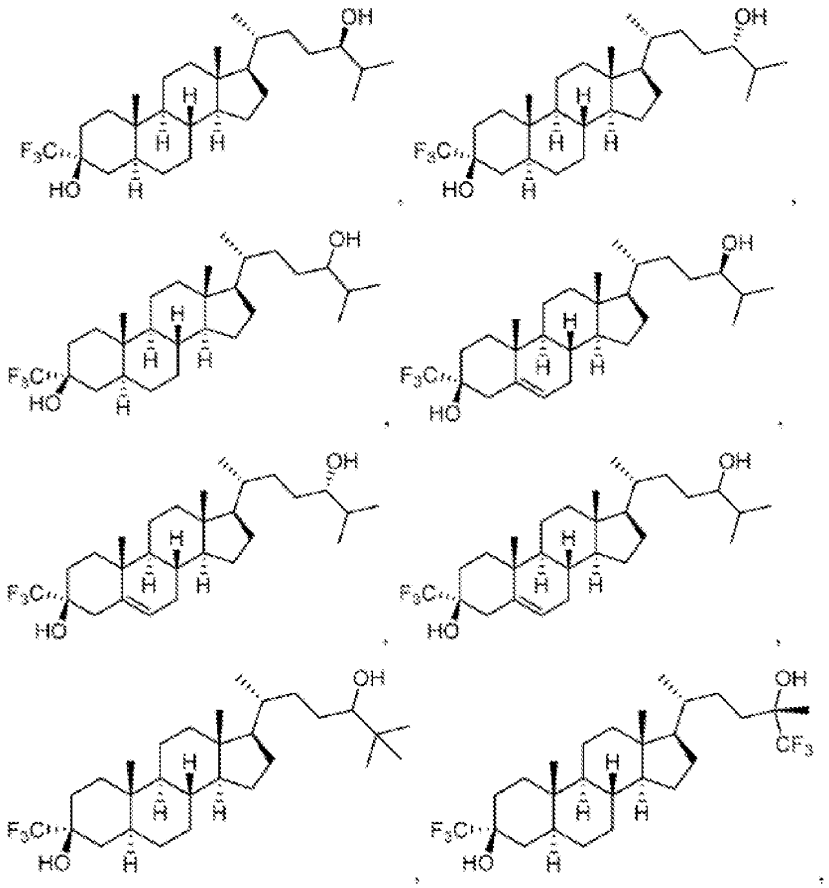

,

,

,

,

(I-D-59) or

, and

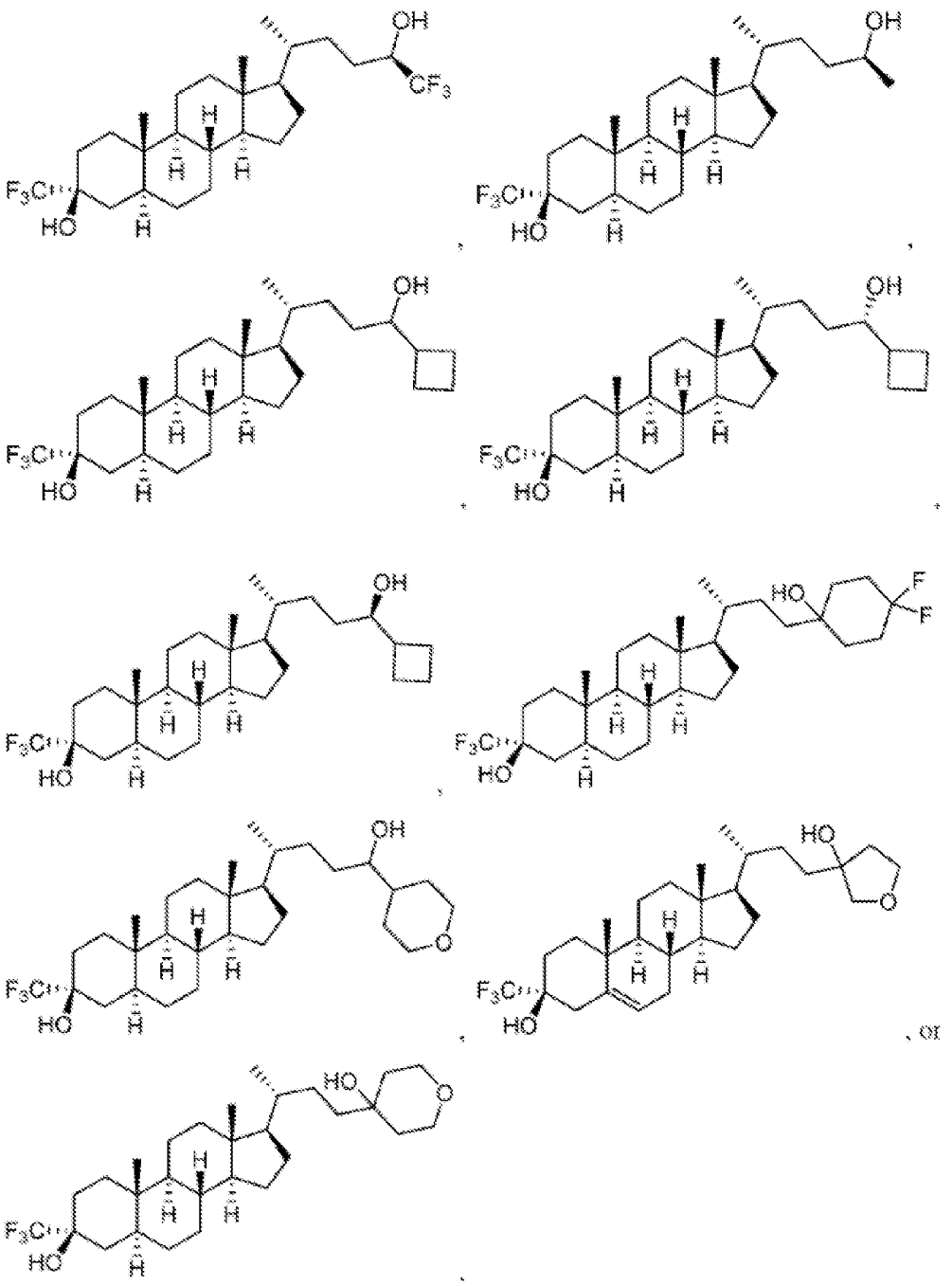


(I-P-150) or

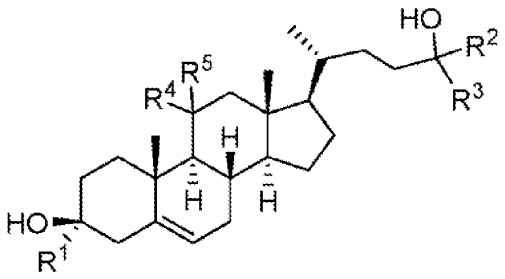


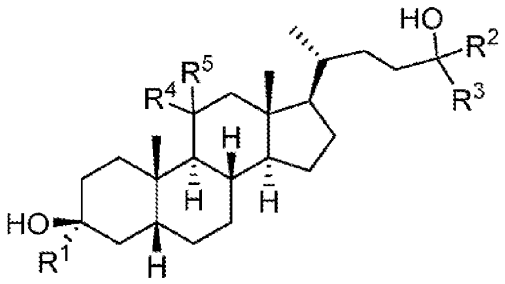
[0948] In further embodiments, the NMDA receptor antagonist is a compound selected from:

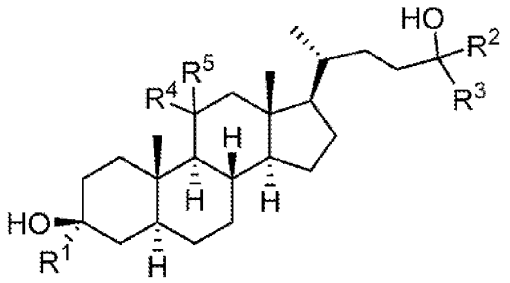


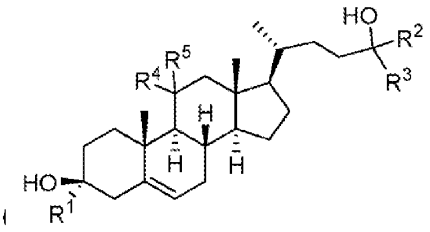


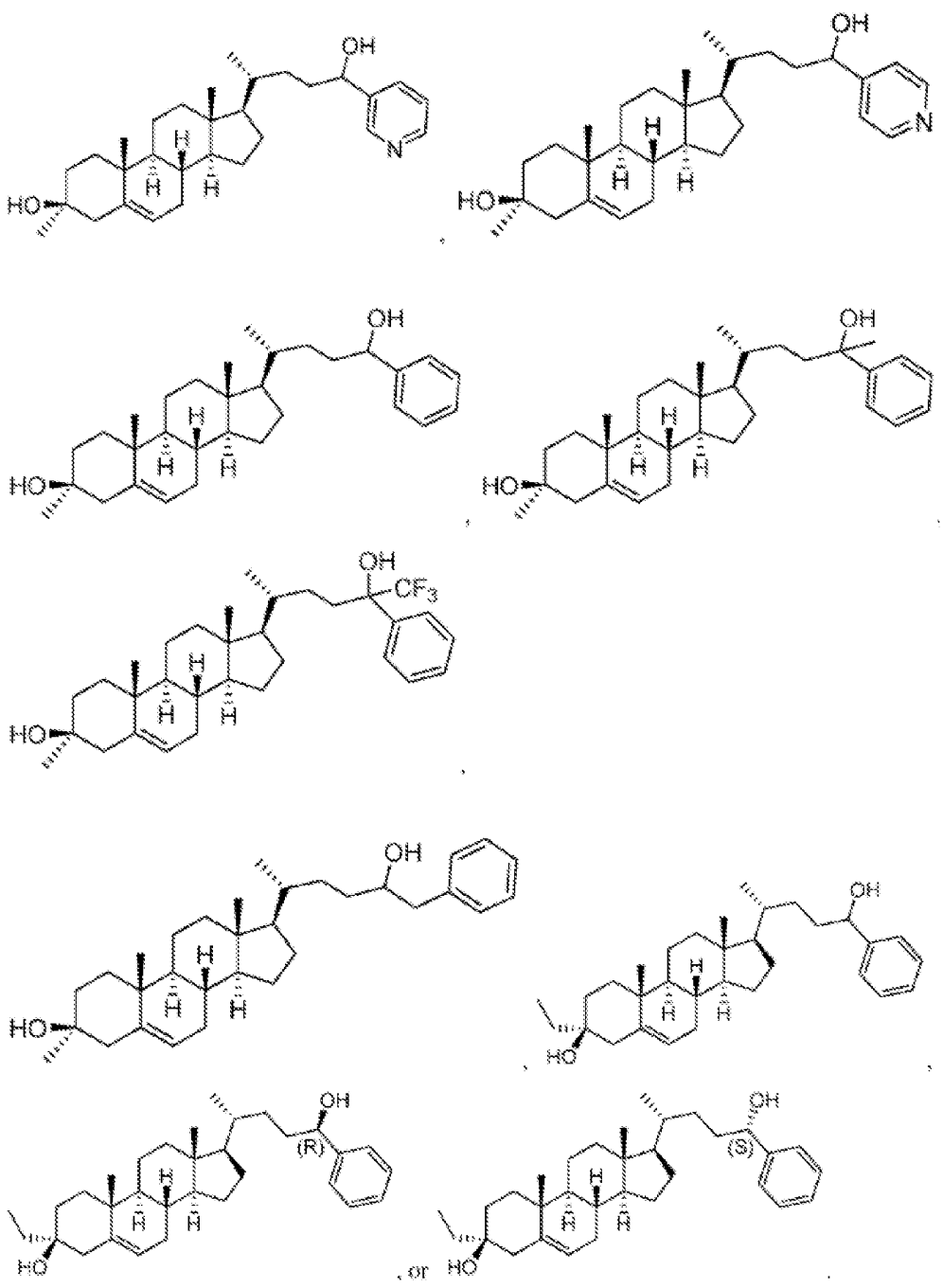
[0949] In further embodiments, the NMDA receptor antagonist is a compound selected from:


HO
R2
R3
R5
R4
H
H
H
HO
R1

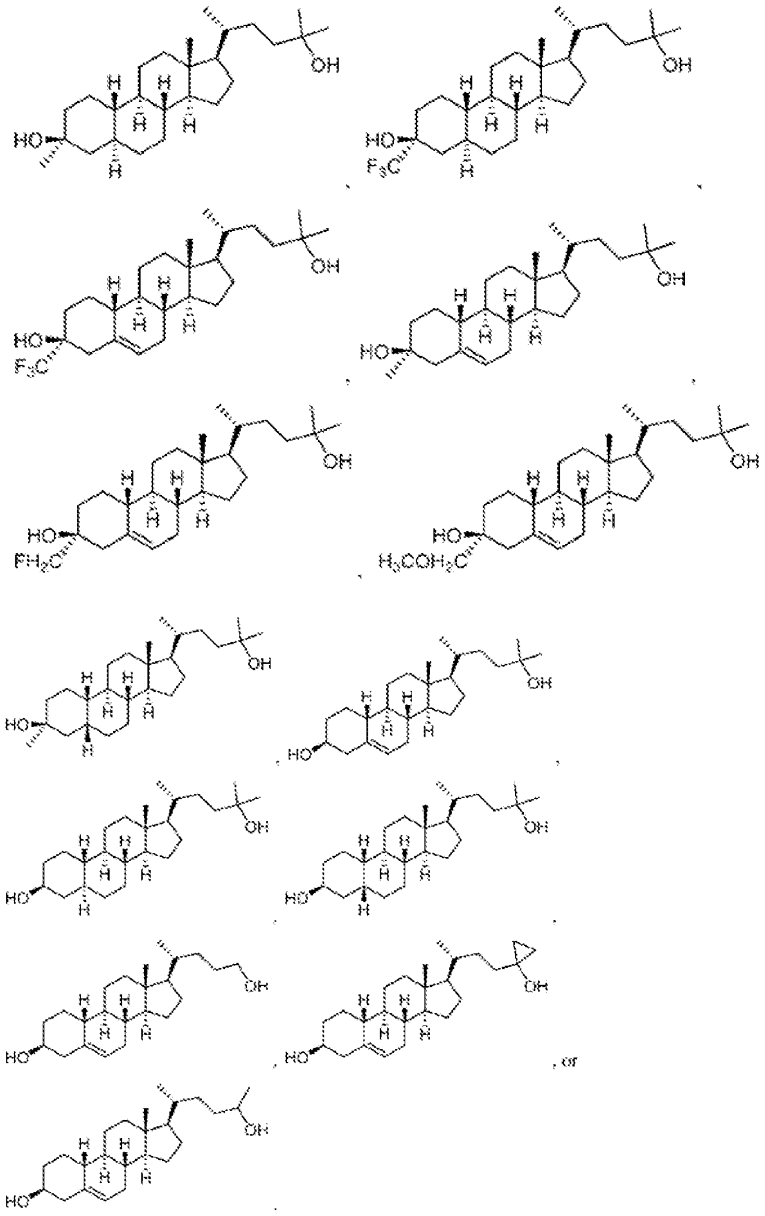

HO
R2
R3
R5
R4
H
H
H
HO
R1
H


HO
R2
R3
R5
R4
H
H
H
HO
R1
H

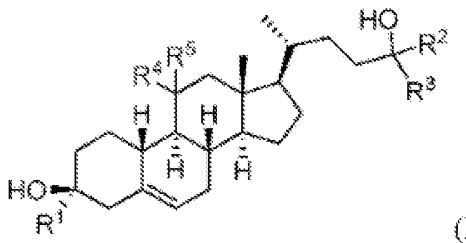

HO
R2
R3
R5
R4
H
H
H
HO
R1



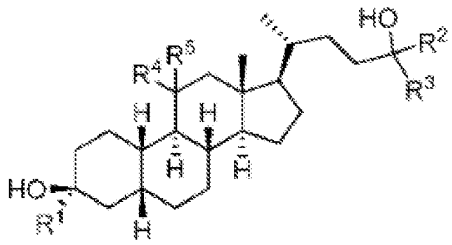
[0950] In further embodiments, the NMDA receptor antagonist is a compound selected from:



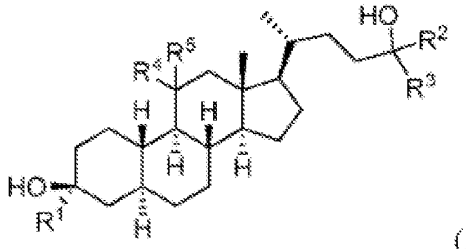
[0951] In further embodiments, the NMDA receptor antagonist is a compound selected from:



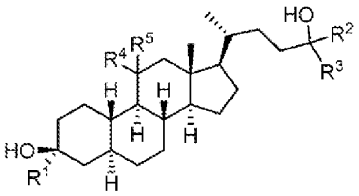
(I-A61)



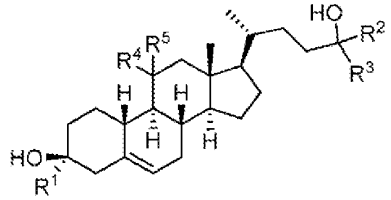
(



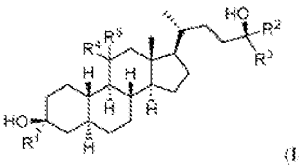
(I-C61).



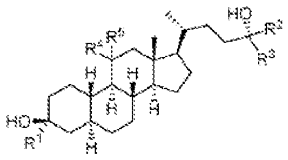
,



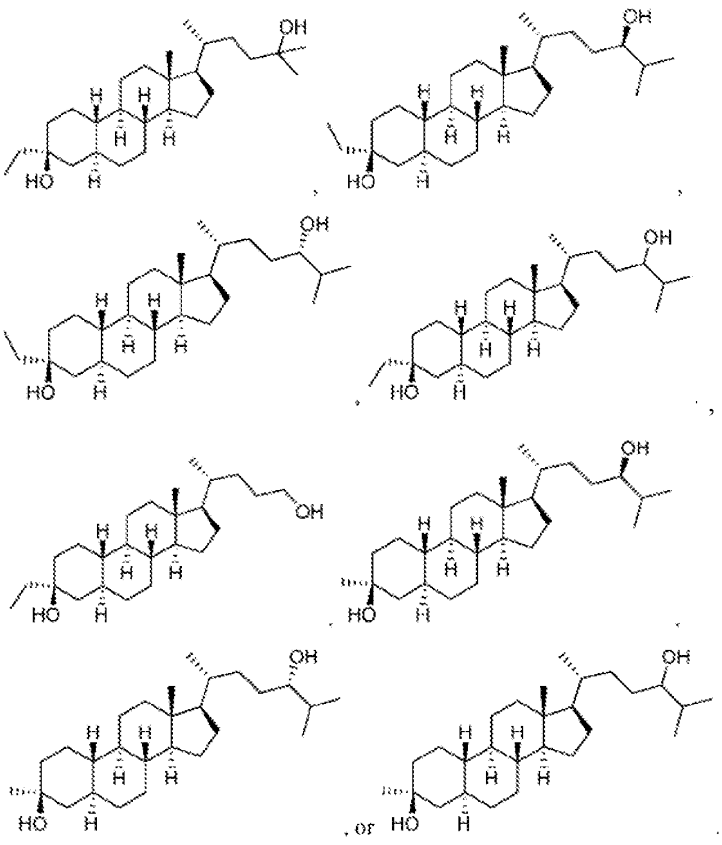
,



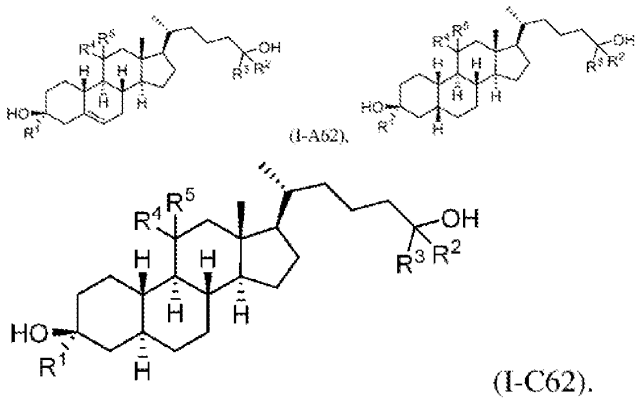
(I-C-i61)



,

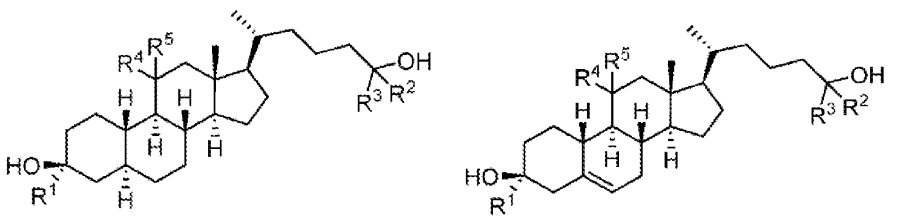


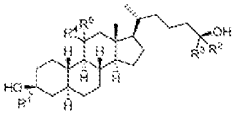
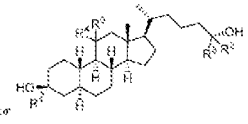
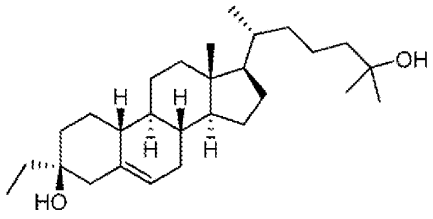
[0952] In further embodiments, the NMDA receptor antagonist is a compound selected from:



(I-A62),

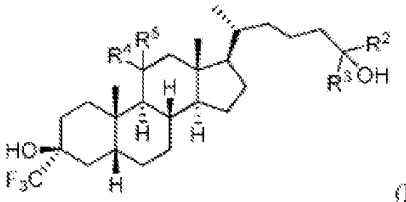
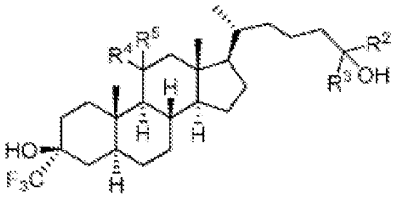
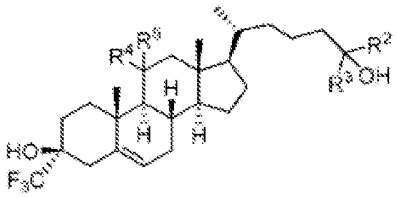
(I-C62).

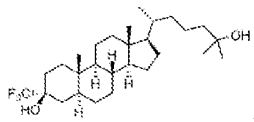
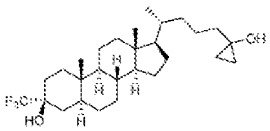
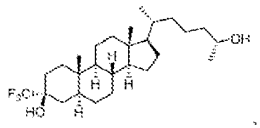
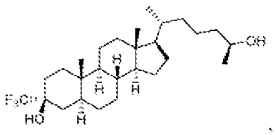
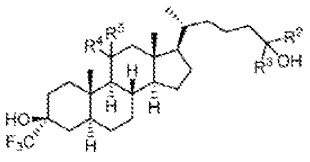
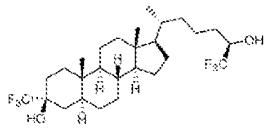


,

compound of Formula (I-A60), (I-B60), or (I-C60):


(I-A60),

(I-B60), or

(I-C60).

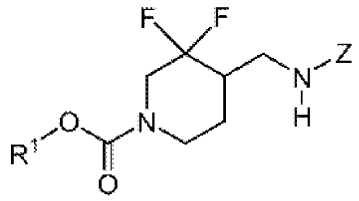




, or


, or .

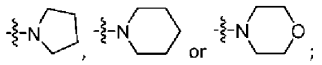
Formula 208

[0953] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 208. Such compounds are described in WO 2016/196513, published December 8, 2016, corresponding to PCT/US2016/035098, filed May 31, 2016, and US 10,584,127 issued March 10, 2020, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 208, these references incorporated by reference herein control.

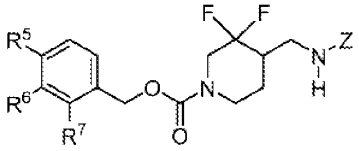
[0954] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 208:

Formula 208

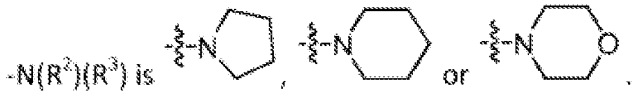


, wherein R1 is alkyl, cycloalkyi, (cycloalkyl)alkyl, heterocyclyl, (heterocyclyl)alkyl, aryl, (aryl)alkyl, heteroaryl or (heteroaryl)alkyl, wherein each of cycloalkyi, (cycloalkyl)alkyl, heterocyclyl, (heterocyclyl)alkyl, aryl, (aryl)alkyl, heteroaryl and (heteroaryl)alkyl is independently optionally substituted with 1 to 3 groups independently selected from -F, -CI, C1-C4 alkyl, cyclopropyl, -C≡CH, -CFH2, -CF2H, -CF3, -CF2CH3, -CH2CF3, C1-C4 alkoxy, -OCFH2, -OCF2H, -OCF3, -CN, -N(R2)(R3), -N02, C1-C4 alkylthio, C1-C4 alkylsulfonyl and -S(0)2CF3; wherein each instance of R2 and R3 independently is -H or C1-C4 alkyl, or $-N(R^2)(R^3)$ is  ; Z is 5- or 6-membered monocyclic or 9- or 10-membered bicyclic heteroaryl having ring carbon atoms, 1 nitrogen ring atom and 0-3 additional ring heteroatoms independently selected from N, O and S, which is optionally substituted with 1 or 2 Rx groups and optionally substituted with 1 Ra group, wherein each Rx is attached to a ring carbon atom and Ra is attached to a ring nitrogen atom; wherein: each instance of Rx independently is -F, -CI, -CH3, -CFH2, -CF2H, -CF3, -OH, -OCH3, -OCF3 or -CN; and Ra is C1-C4 alkyl, C3 – C4 cycloalkyl or -S())2-C1-C4 alkyl, including pharmaceutically acceptable salts thereof.

[0955] In further embodiments, the NMDA receptor antagonist is a compound selected from:

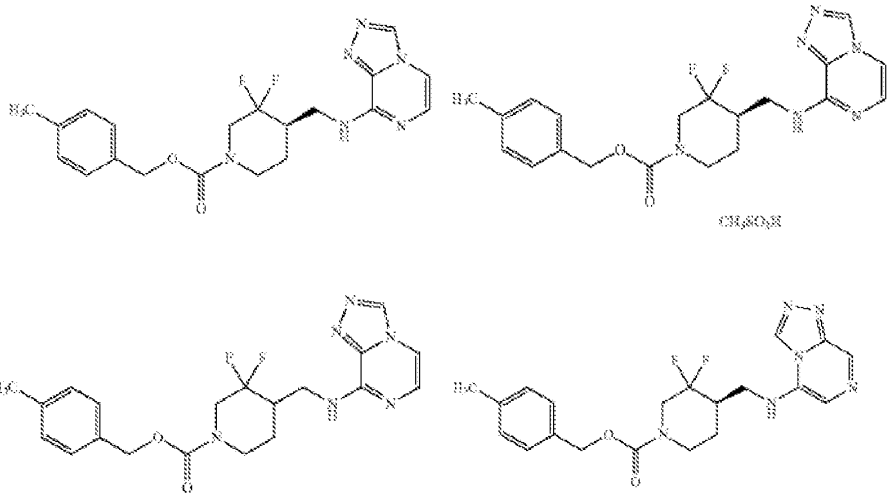


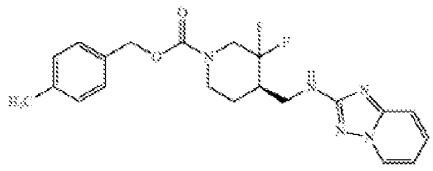
, wherein R5, R6 and R7 independently are -H, -F, -CI, C C alkyl, cyclopropyl, -C≡CH, -CFH2, -CF2H, -CF3, -CF2CH3, -CH2CF3, C1-C4 alkoxy, -OCFH2, -OCF2H, -OCF3, -CN, -N(R2)(R3), -NO2, C C4 alkylthio, C1-C4 alkylsulfonyl or -S(O)2CF3; wherein each instance of R2 and R3 independently is -H or C1-C4 alkyl, or C1-

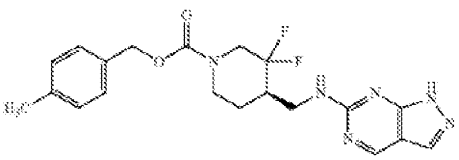


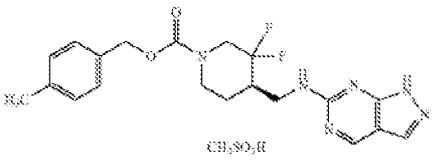
C4 alkyl, or , including pharmaceutically acceptable salts thereof.

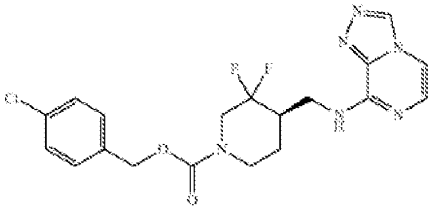
[0956] In further embodiments, the NMDA receptor antagonist is a compound selected from:

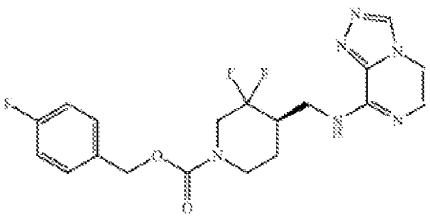


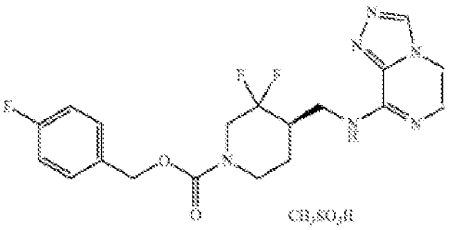


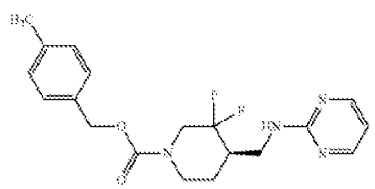


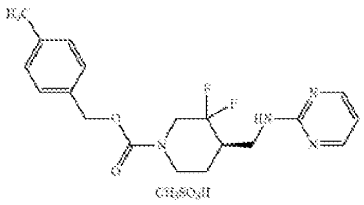


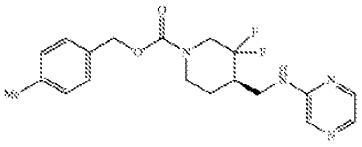


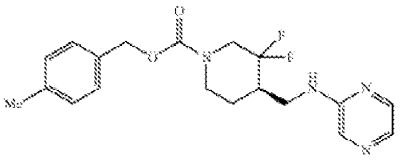


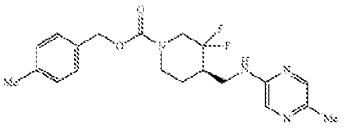


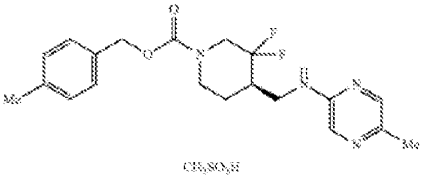


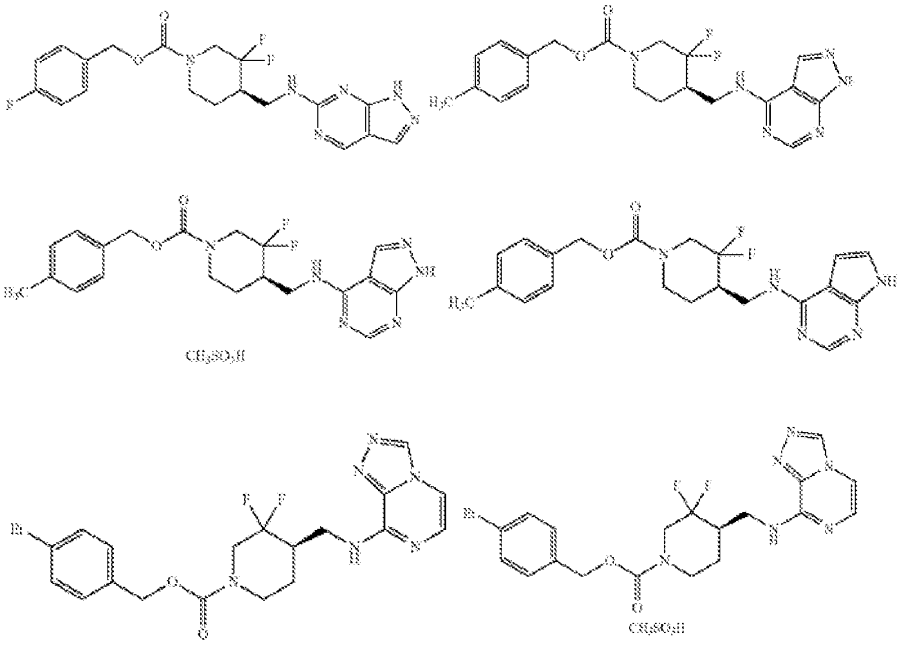




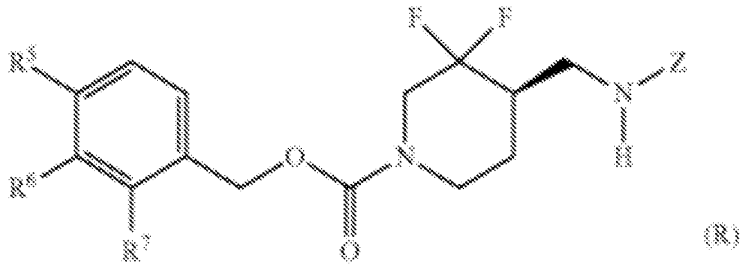








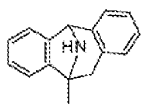
[0957] In further embodiments, the NMDA receptor antagonist is selected from:



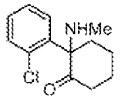
(R)

compound	Z	R^5	R^6	R^7
E1-22.1	Z22	H	H	H
E1-22.2	Z22	CH_3	H	H
E1-22.3	Z22	Cl	H	H
E1-22.4	Z22	F	H	H
E1-22.5	Z22	CH_2CH_3	H	H
E1-22.6	Z22	CF_2H	H	H
E1-22.7	Z22	CH_2F	H	H
E1-22.8	Z22	CF_3	H	H
E1-22.9	Z22	CF_2CH_3	H	H
E1-22.10	Z22	CH_2CF_3	H	H
E1-22.11	Z22	cyclopropyl	H	H
E1-22.12	Z22	OCF_3	H	H
E1-22.13	Z22	OCF_2H	H	H
E1-22.14	Z22	Cl	H	F
E1-22.15	Z22	CH_3	H	F
E1-22.16	Z22	CH_3	F	H
E1-22.17	Z22	Cl	F	H
E1-22.18	Z22	F	F	H
E1-22.19	Z22	F	H	F
E1-22.20	Z22	F	H	Cl
E1-22.21	Z22	F	H	CH_3
E1-22.22	Z22	Cl	H	CH_3
E1-22.23	Z22	SCH_3	H	H
E1-22.24	Z22	SO_2CH_3	H	H
E1-22.25	Z22	ethynyl	H	H

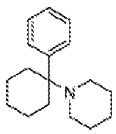
[0958] In further embodiments, the NMDA receptor antagonist is selected from:



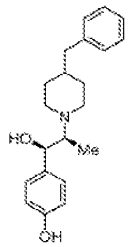
MK801 (dizocilpine)



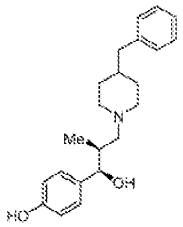
Ketamine



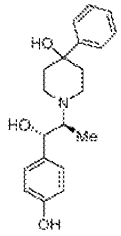
Phencyclidine (PCP)



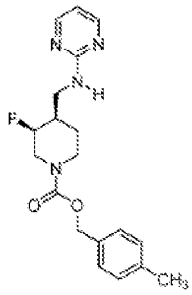
ifenprodil



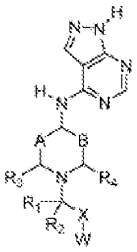
Ro-25,6981



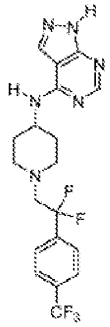
CP-101,606



MK0657



LX



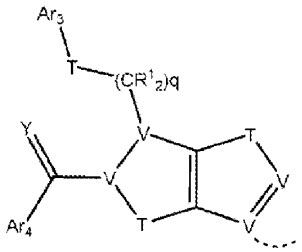
LX-1

Formula 209

[0959] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 209. Such compounds are described in International application publication no. WO2010/088414, published August 5, 2010, corresponding to PCT/US2010/022439, filed January 28, 2010, International application publication no. WO 2010/088408, published August 5, 2010, corresponding to PCT/US2010/022432, filed January 28, 2010, and US 8,822,462, issued September 2, 2014, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 209, these references incorporated by reference herein control.

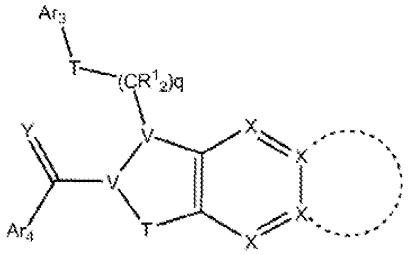
[0960] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 209a – 209b:

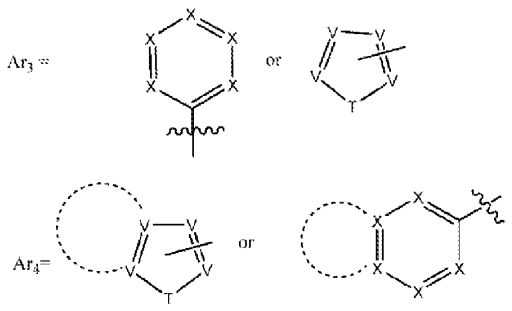
Formula 209a



,

Formula 209b



wherein:  ;

X is, independently, N or C bonded to H or a substituent, J, with the proviso that no more than three of X are N;

Y is independently selected from O, S, NR1, CH2, and CR2;

R1 and R2 are, independently, selected from H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and hydroxy, and, when R1 is attached to a carbon atom, it can be halo or cyano,

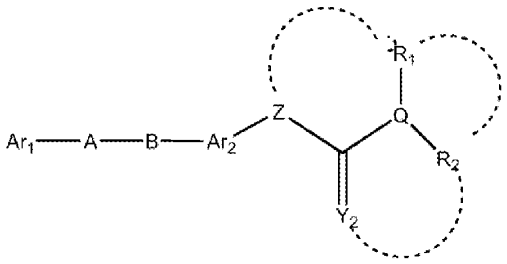
T is, independently, CHR1, CR2, O, S, or NR1,

V is, independently, N, or C bonded to H or a substituent J,

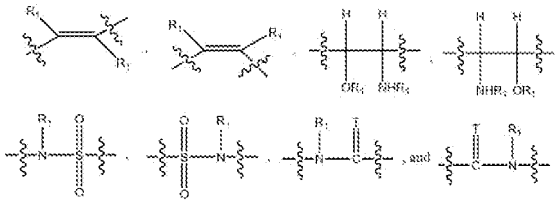
J is a non-hydrogen substituent selected from the group consisting of halo (-F, -Cl, -Br, -I,), nitro, amino (NR1R2), OR1, SR1, -R1, -CF3, -CN, -C2R1, -SO2CH3, -CC=O)NR1R2 - NR1CC=O)R1, - CC=O)R1, -CC=O)OR1, -(CHz)9OR1, -OCC=O)R1, -OCC=O)NR1R2, - NR1CC=Y)-NR1R2, -NR1CC=Y)- OH, -NR1CC=Y)-SH, sulfonyl, sulfinyl, phosphoryl, and

azo, and q is 0-5, wherein the aryl ring moiety Ar4 can optionally be replaced with a saturated ring, and pharmaceutically acceptable salt, esters, prodrugs, or derivatives thereof.

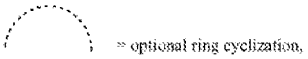
[0961] In further embodiments, the NMDA receptor antagonist is a compound according to Formula 209c:



wherein A-B i s a linker moiety selected from:

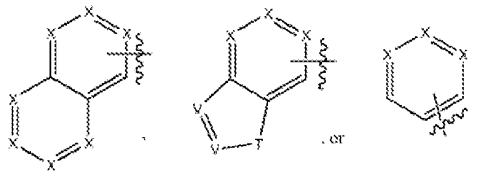


or an acetylenic moiety, ——≡——,



= optional ring cyclization,

Ar1 =



, or

Ar2 =



X is, independently, N, or C bonded to H or a substituent, J, with the proviso that no more than three of X are N;

Y1 and Y2 are, independently, selected from O, S, NR1, CH2, and CRX^1_2;

R1 and R2 are independently selected from H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and hydroxy,

R1 and R2 can optionally join to form a C3-10 heterocyclic moiety, which heterocyclic moiety can optionally include a second heteroatom selected from O, S, and N,

R2 is absent when Q is O or S,

Z is, independently, $(CH2)_n$, CHR, CR2, O, S, or NR1,

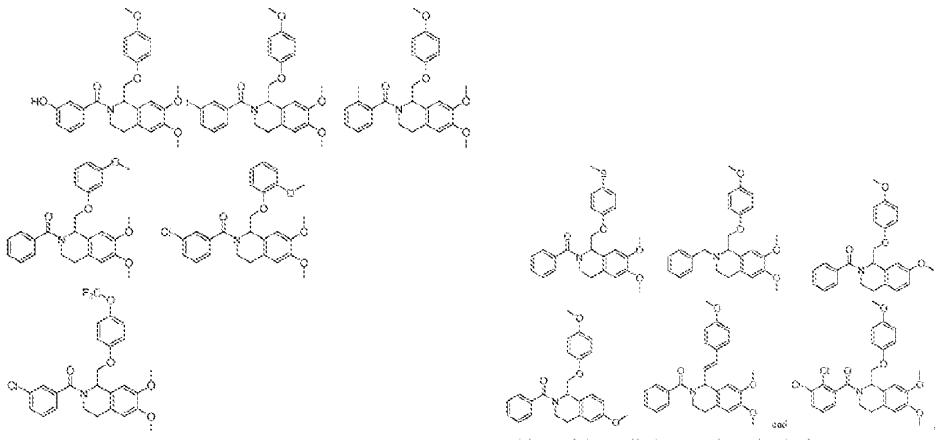
T is, independently, CHR, C(R1)2, O, S, or NR1,

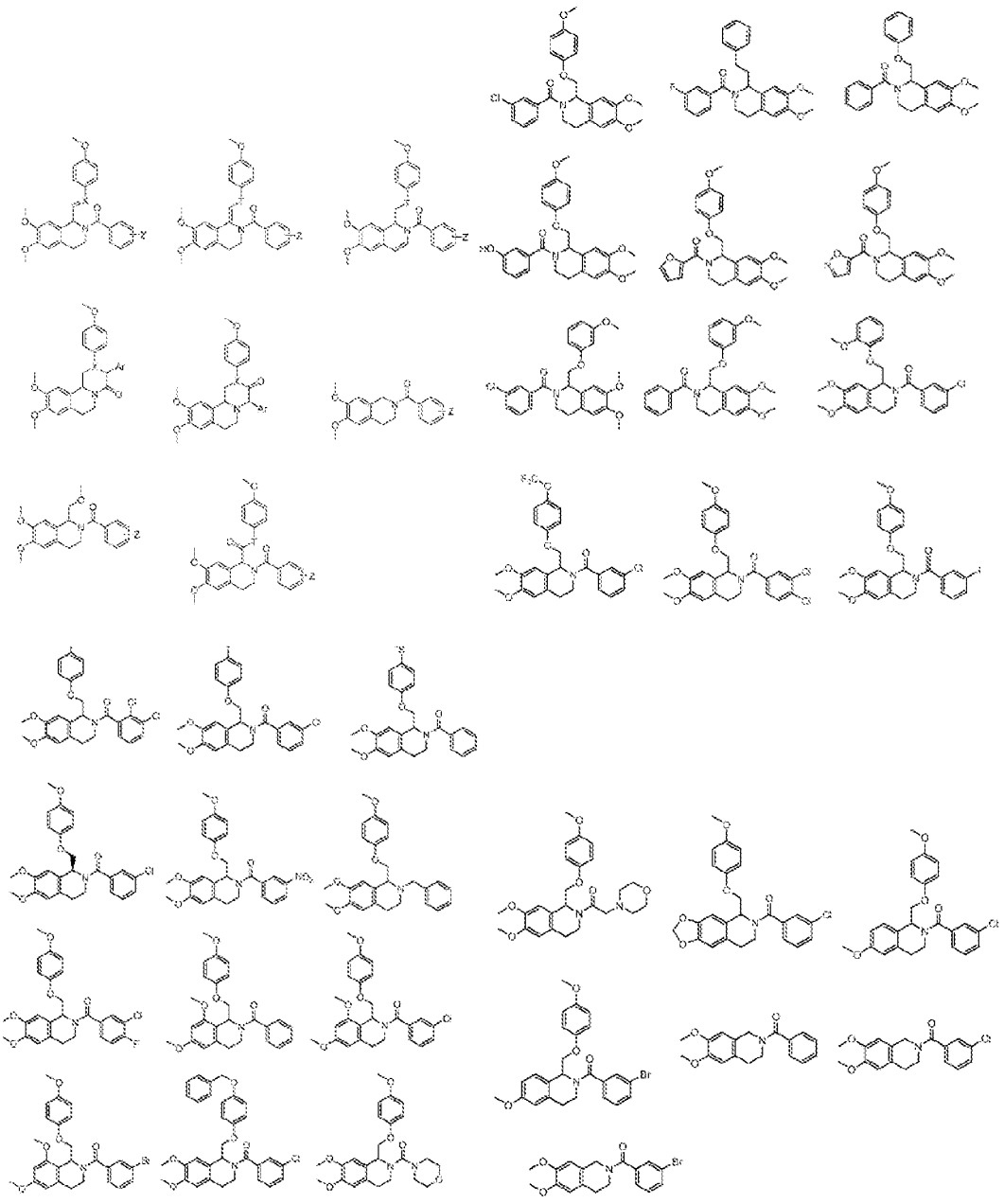
Q is independently selected from CH, C-halo, or N, or O or S if R2 is absent,

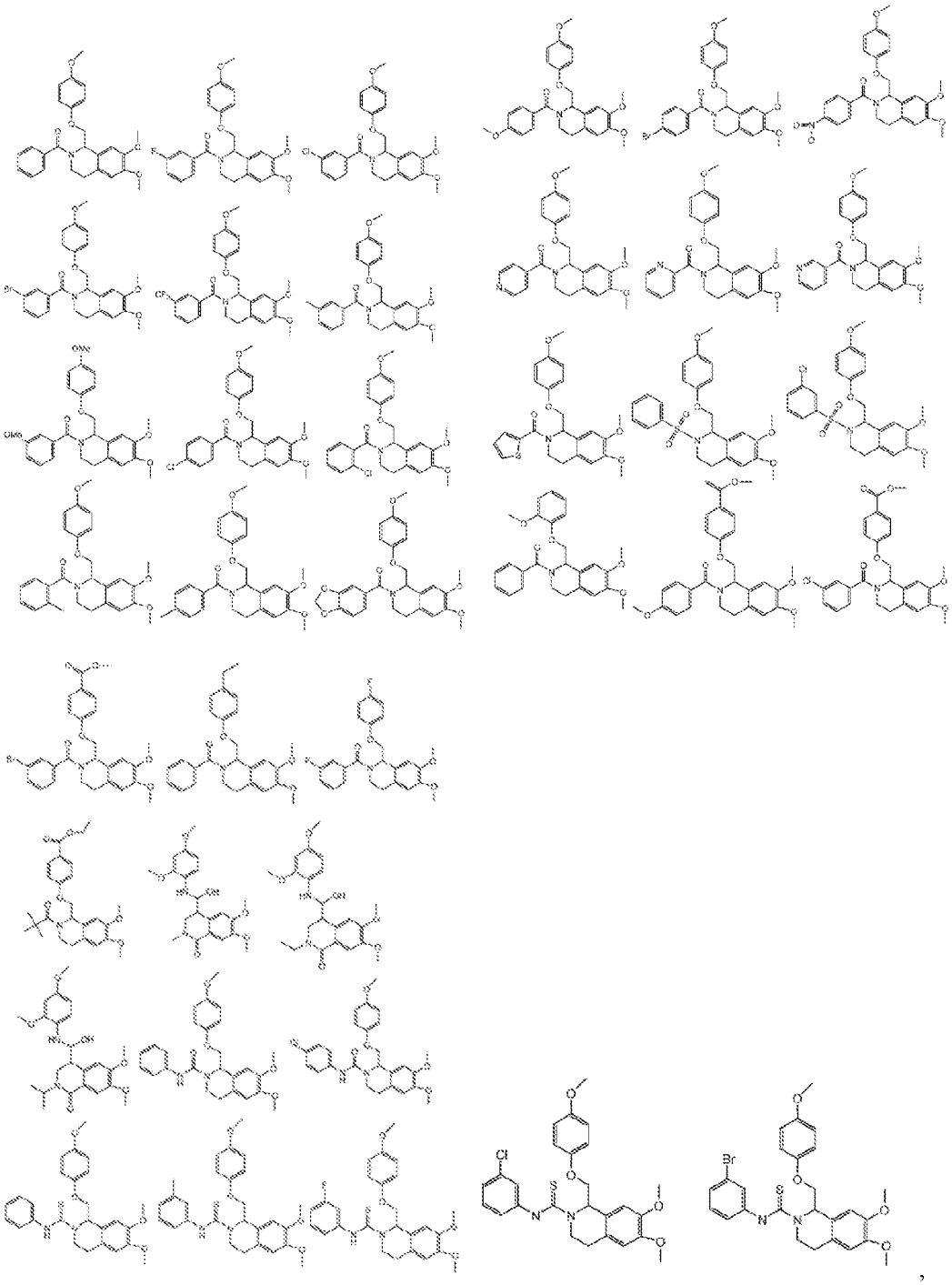
V is, independently, N or C bonded to H or a substituent J,

J is a non-hydrogen substituent selected from the group consisting of halo (-F, -Cl, -Br, - I,), nitro, amino (NR1R2), OR1, SR1, -R1, -CF3, -CN, -C2R1, -SO2CH3, -Q=O)NR1R2 - NR1CX=O)R1, -O=O)R1, -CC=O)OR1, -(CH2) ,OR1, -OC(=O)R1, -OQ=O)NR1R2, - NR1CC=Y)- NR1R2, -NR1CC=Y)-OH, -NR1CC=Y)-SH, sulfonyl, sulfinyl, -SO2NHR1, - NHSO2R , phosphoryl, and azo, and pharmaceutically-acceptable salts, prodrugs, and esters thereof.

[0962] In further embodiments, the NMDA receptor antagonist is a compound selected from:



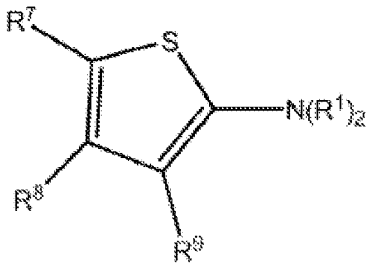




and pharmaceutically acceptable salts, esters, prodrugs, or derivatives thereof.

[0963] D

[0964] In additional embodiments, the NMDA receptor antagonist has a structure according to Formula I or J:

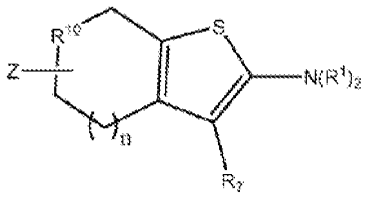


Formula I

wherein R1 is as defined above in Claim 1 ,

R7 is selected from the group consisting of H, -Ci_6 alkyl, -Ci_6 substituted alkyl, -C6-io aryl, - Ce io substituted aryl, -Ce io heteroaryl, -Ce io substituted heteroaryl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-arylalkyl, C(O)-substituted arylalkyl, -C(O)-alkylaryl, -C(O)-substituted alkylaryl-CN, N3, NO2, -OH, -NH2, -SH, -OR1, -NHR1, -N(R1K -SR1, -OC(O)R1, NHC(O)R1, -SC(O)R1, -OC(O)OR1, -NHC(O)R1, -CH2OH, -CH2CN, -CH2N3, -CO2R1, -CON(R1),, - C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-heteroaryl, and -C(O)- substituted heteroaryl,

R8& R9 are, individually, H, OH, -NH2, -SH, -OR1, -NHR1, -N(R1K -SR1, -OC(O)R1, NHC(O)R1, -C1-6 alkyl, -C1-6substituted alkyl, -C1-6 aryl, -C1-6 substituted aryl, -C6-10 heteroaryl, -C6-10 substituted heteroaryl,



Formula I

wherein R1 is as defined above,

R1 is as defined above,

R7 is selected from the group consisting of H, -C1-6 alkyl, -C1-6 substituted alkyl, -C6-10 aryl, C6 - 10 substituted aryl, -C6-10 heteroaryl, -C6-10 substituted heteroaryl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-arylalkyl, C(O)-substituted arylalkyl, -C(O)-alkylaryl, -C(O)-substituted alkylaryl-CN, N3, NO2, -OH, -NH2, -SH, -OR1, -NHR1, -N(R1)2 -SR1, -OC(O)R1,

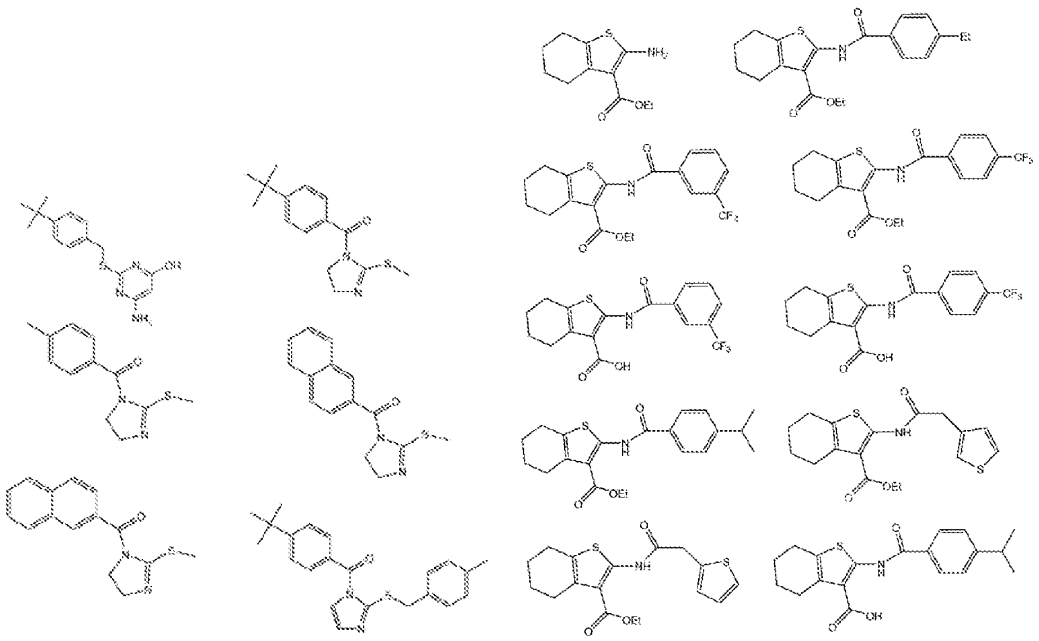
NHC(O)R1, -SC(O)R1, -OC(O)OR1, -NHC(O)R1, -CH2OH, -CH2CN, -CH2N3, -CO2R1, -CONtR1)^ - C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-heteroaryl, and -C(O)- substituted heteroaryl,

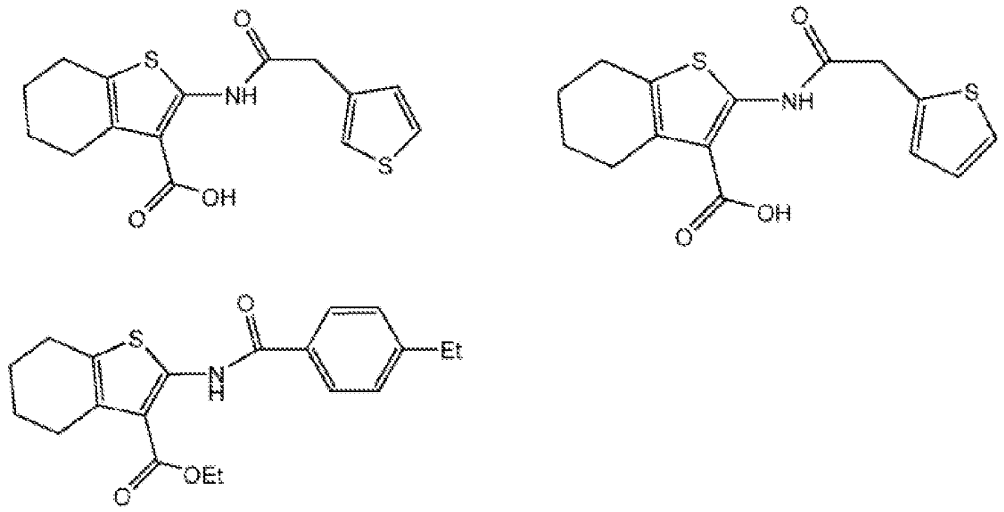
R10 is -CH2-, -S-, -0-, -NHR1-, -N(R:)2-, -C(O)-, -C(S)-, -C(NR1V,

N is 0-4, and

Z is a substituent as defined in Claim 1 , and pharmaceutically acceptable salts, esters, prodrugs, or derivatives thereof.

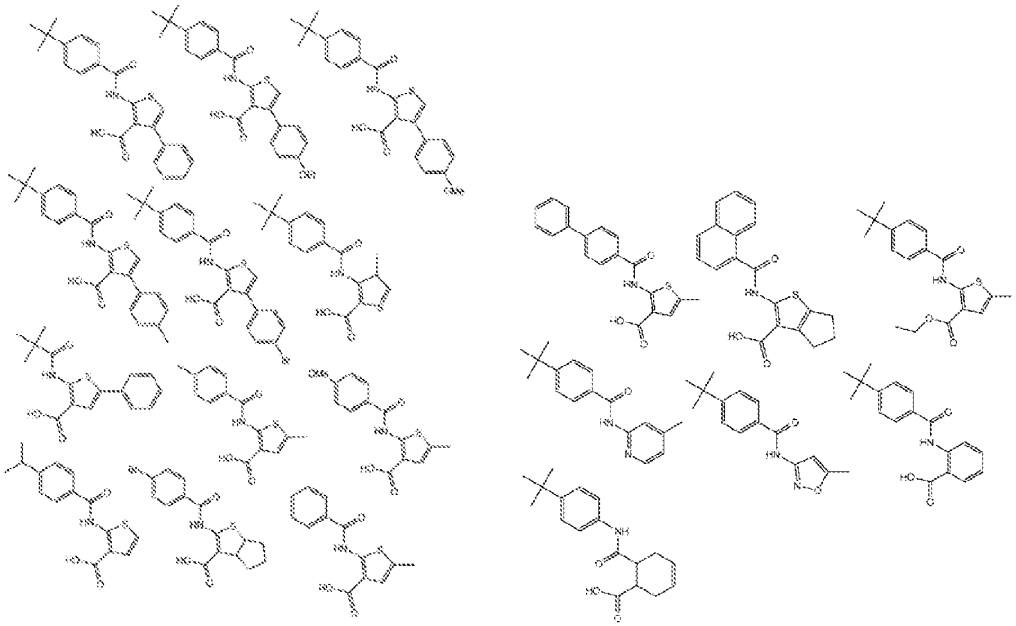
[0965] In further embodiments, the NMDA receptor antagonist is a compound according to:





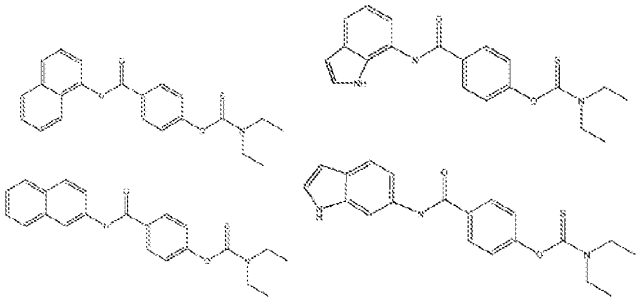
, including pharmaceutically acceptable salts, esters, prodrugs, and derivatives thereof.

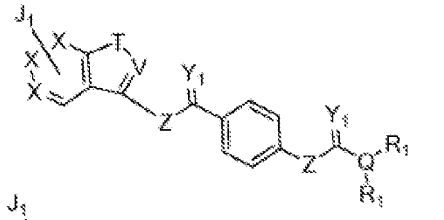
[0966] In further embodiments, the NMDA receptor antagonist is a compound according to:

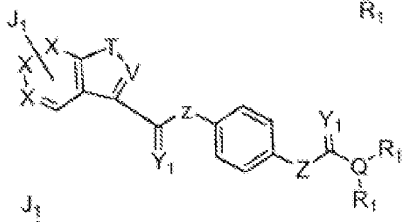


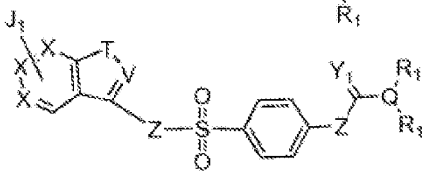
, and pharmaceutically acceptable salts, esters, prodrugs, or derivatives therof.

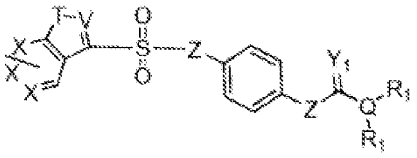
[0967] In further embodiments, the NMDA receptor antagonist is a compound according to:

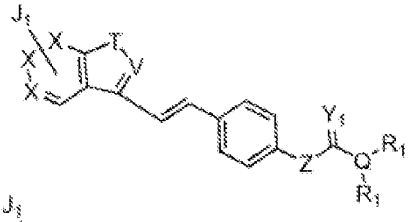


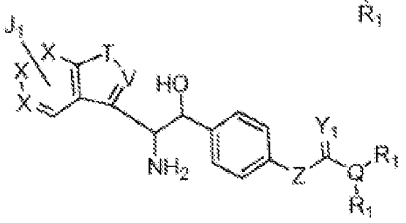


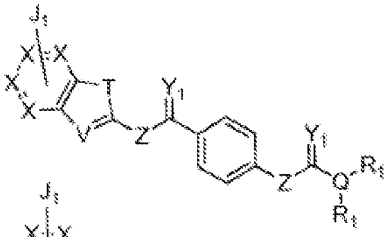


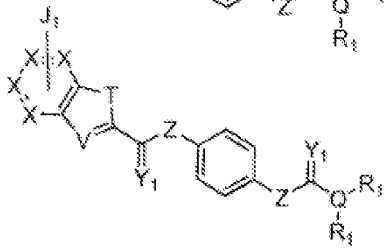


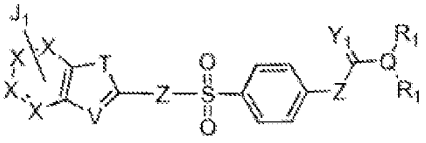


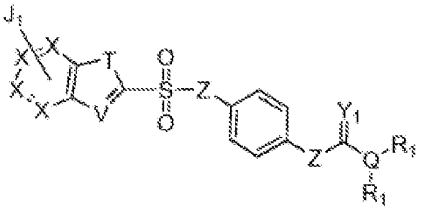


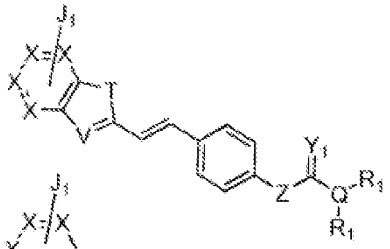


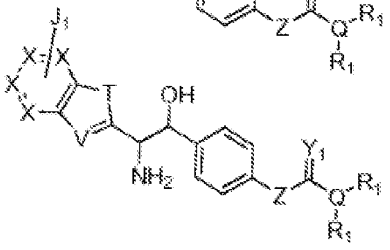


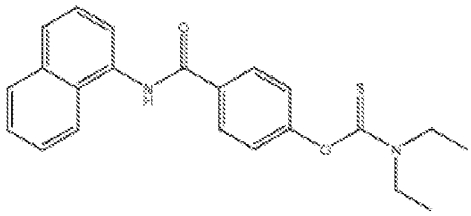


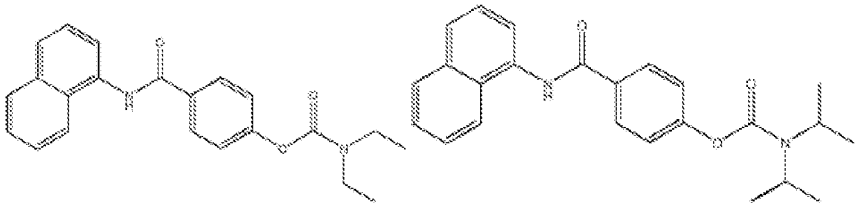


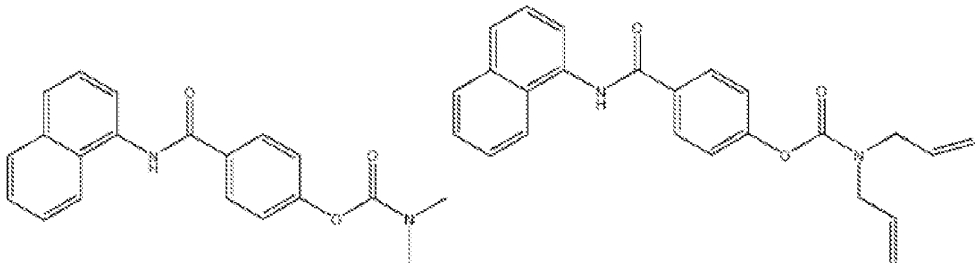


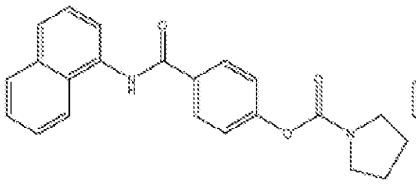


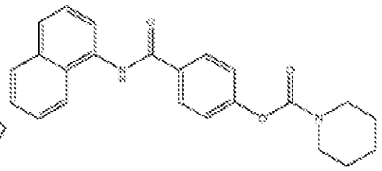


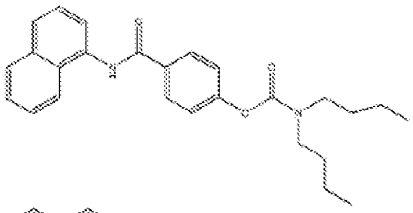


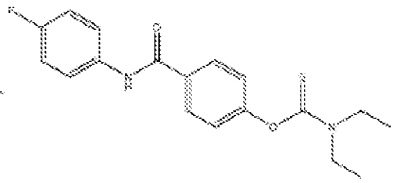


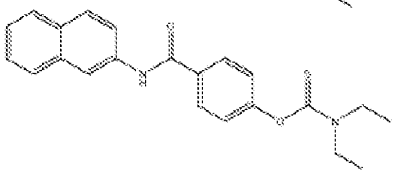


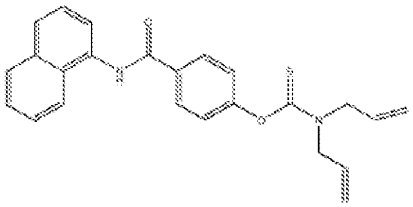


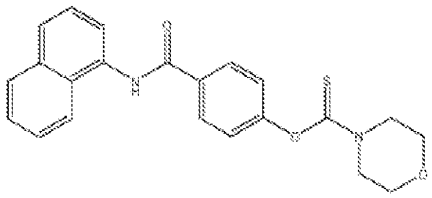


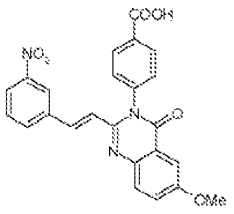




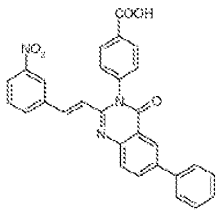




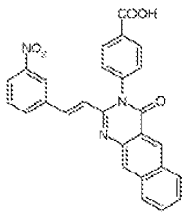




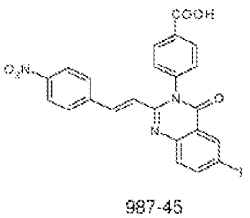
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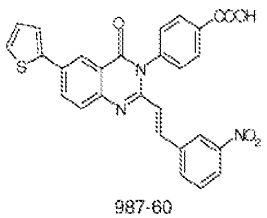
987-35



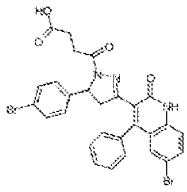
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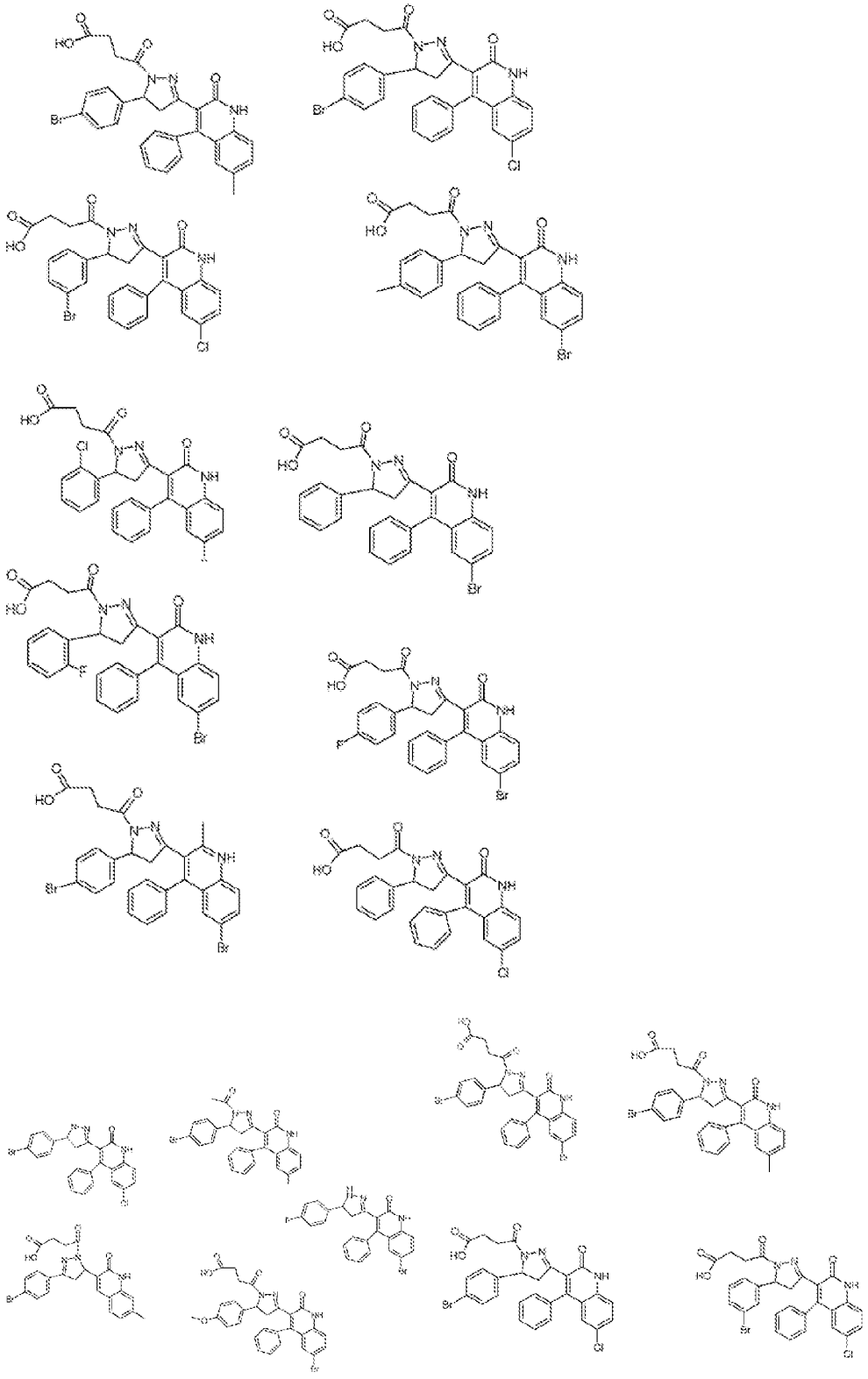


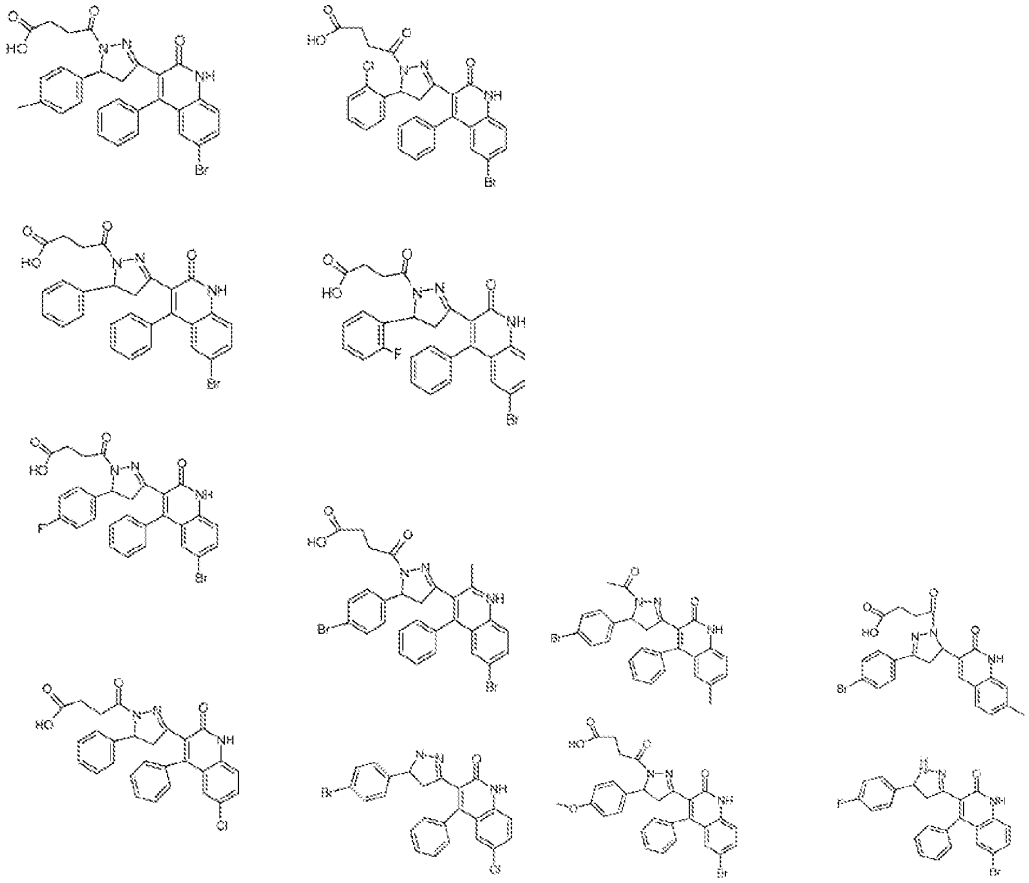
987-45



987-60

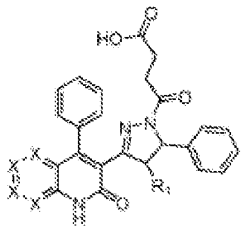


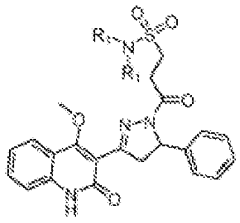


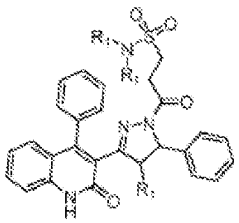


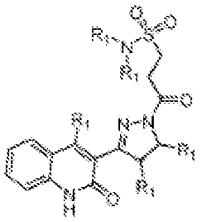
, including pharmaceuitcally acceptable salts, prodrugs, and esters thereof.

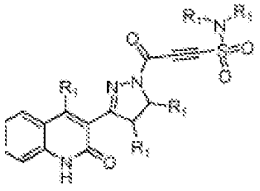
[0968] In further embodiments, the NMDA receptor antagonist is a compound according to:

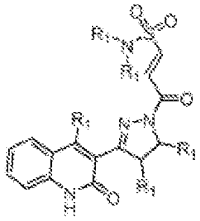




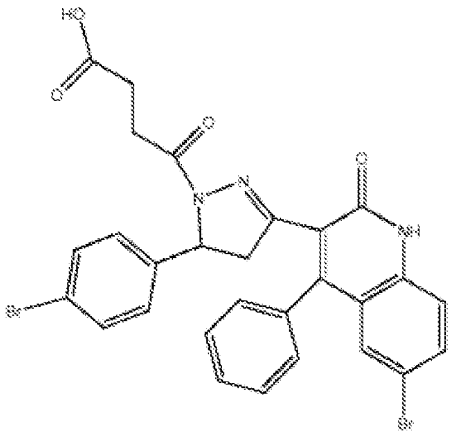


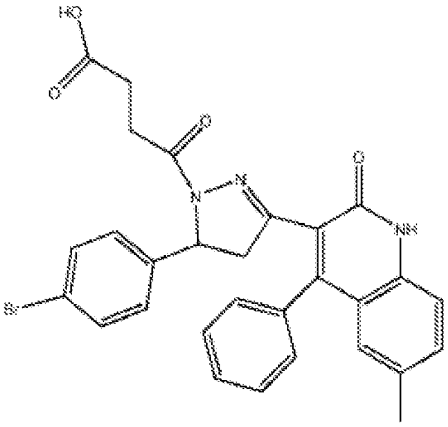


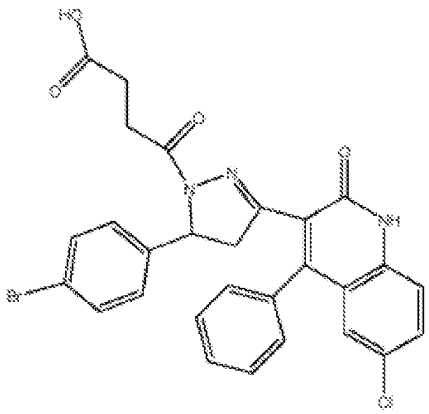


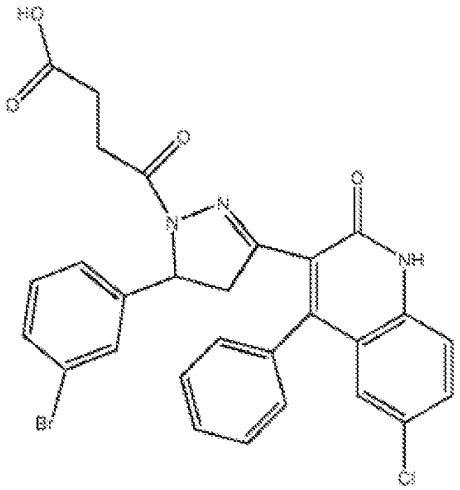


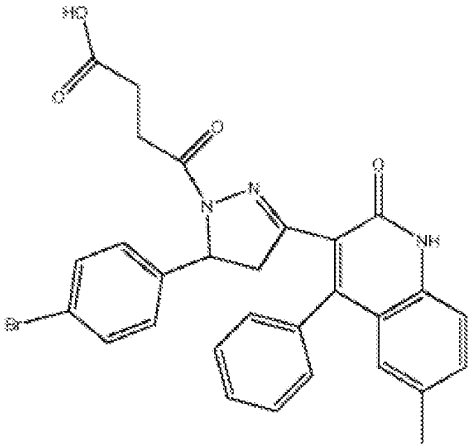
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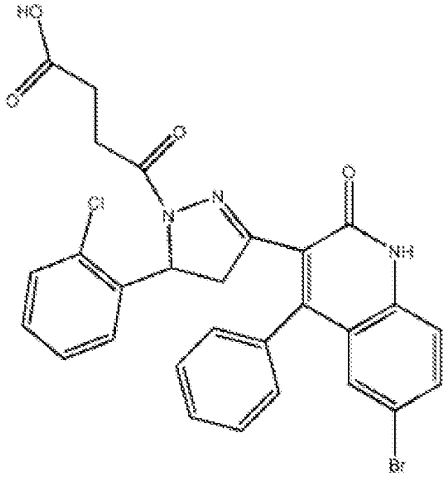


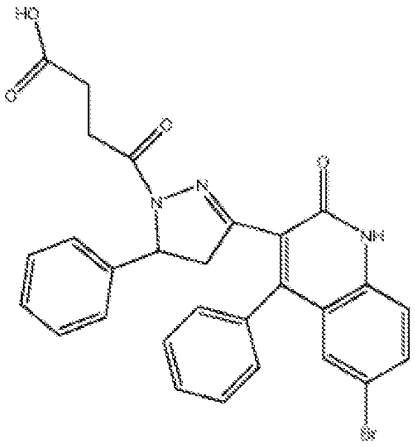


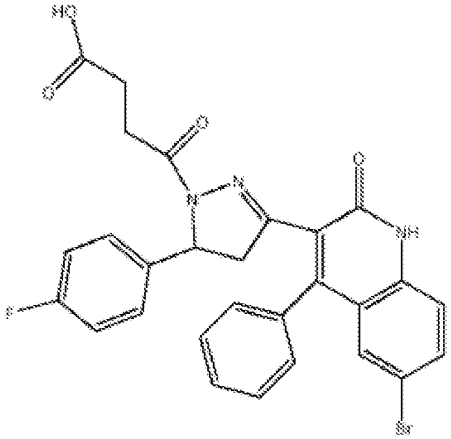


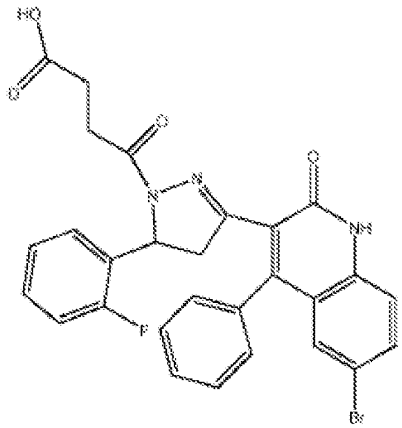


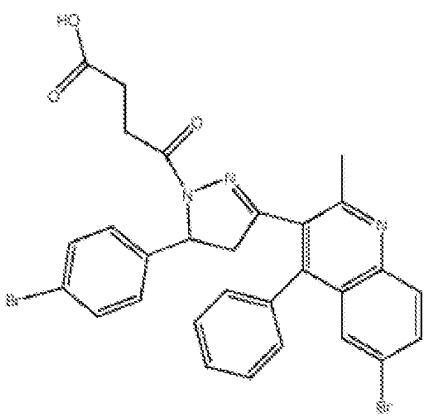


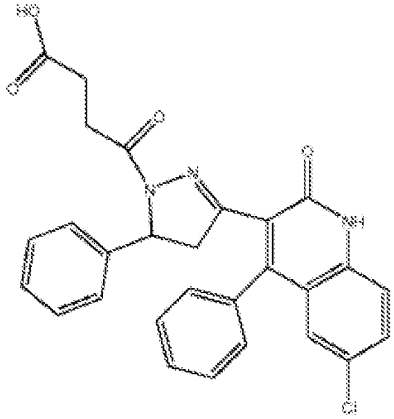


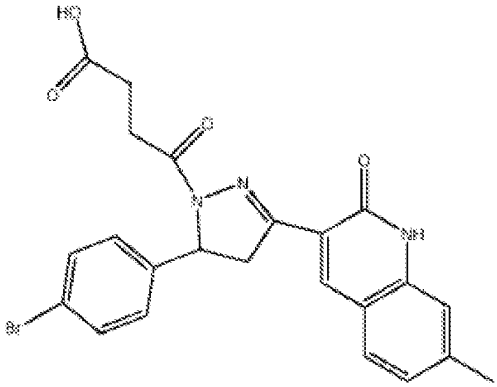


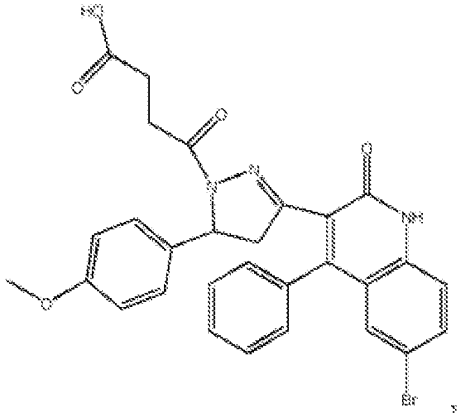


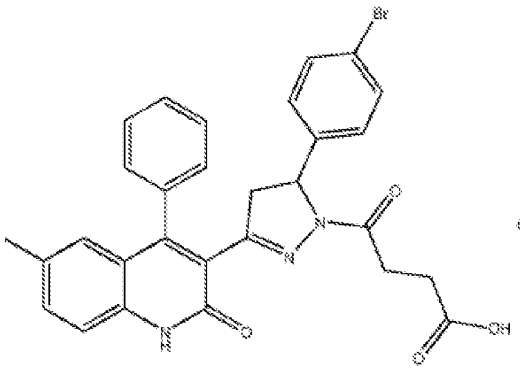


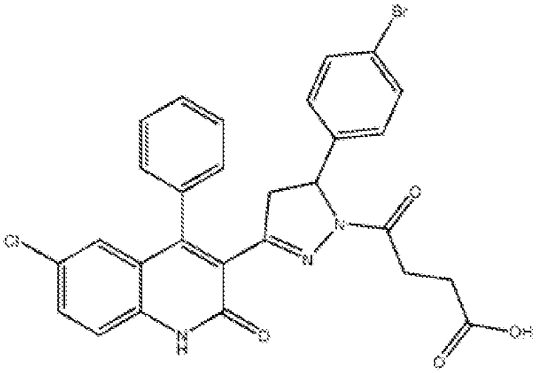


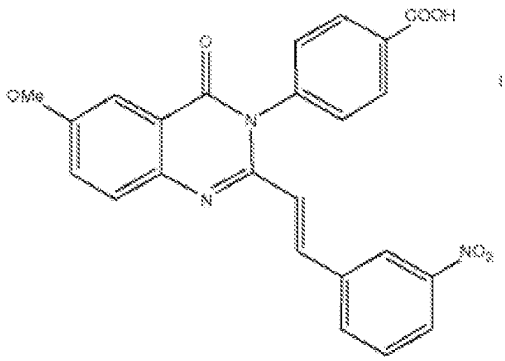
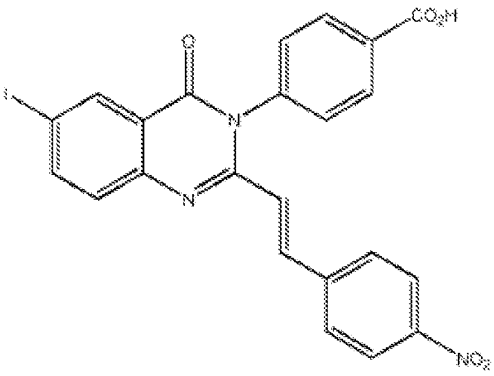
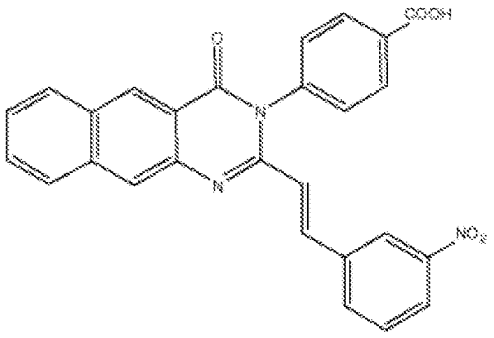








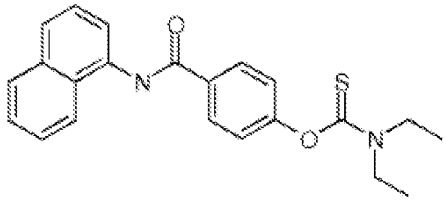
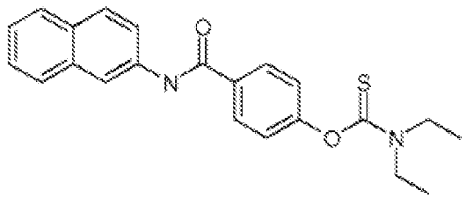


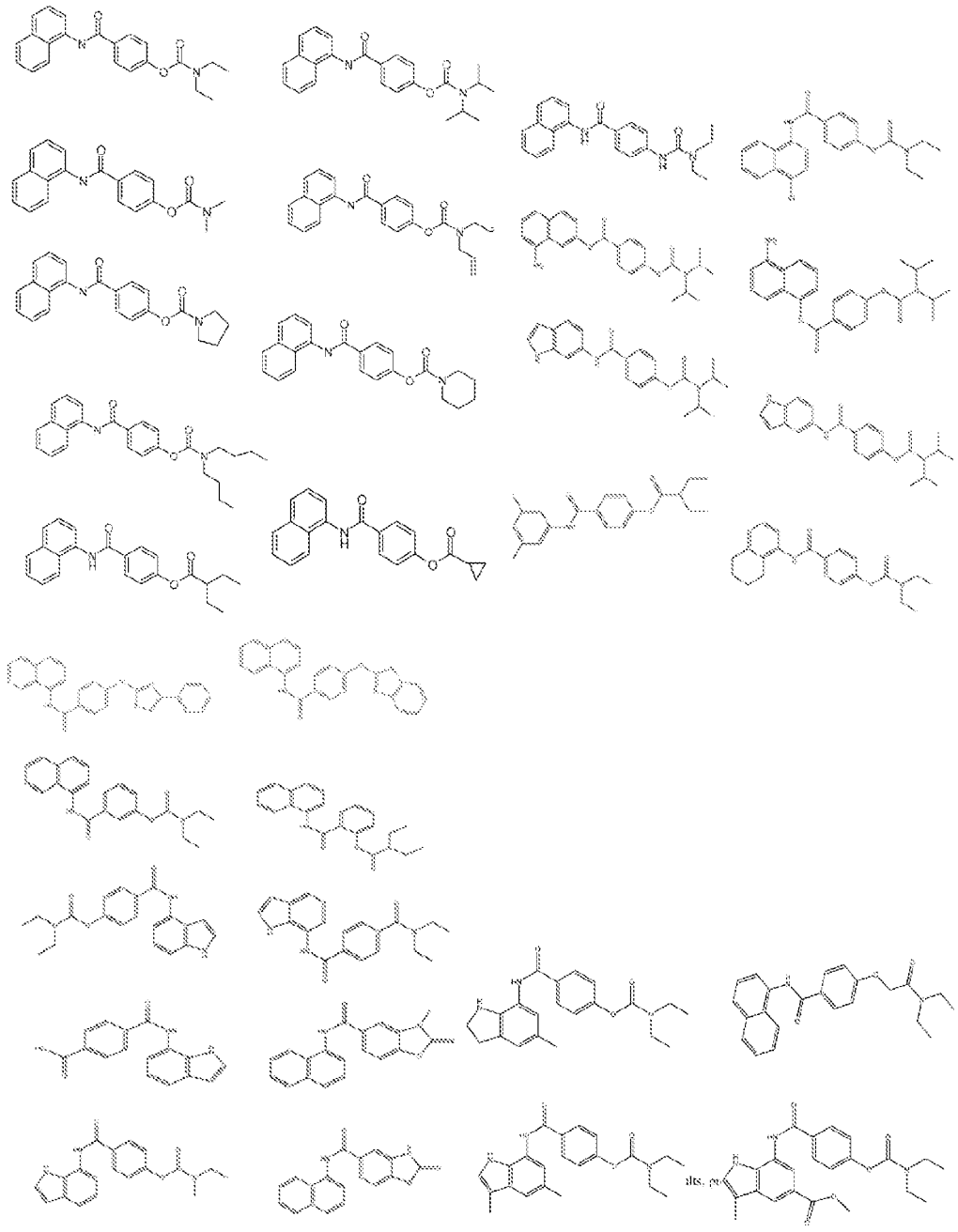




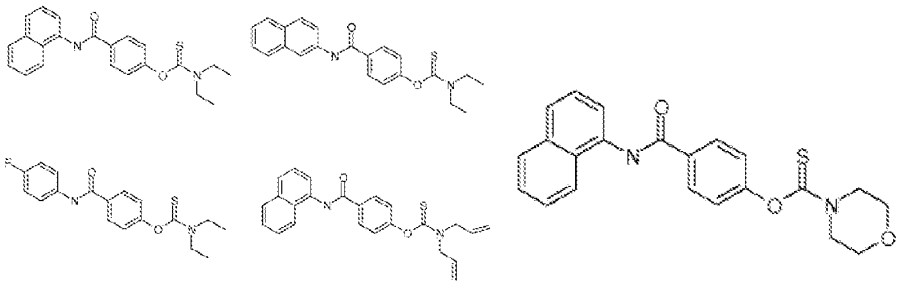
,

including pharmaceutically acceptable salts, esters, prodrugs and derivatives thereof.

[0969] In further embodiments, the NMDA receptor antagonist is a compound according to:



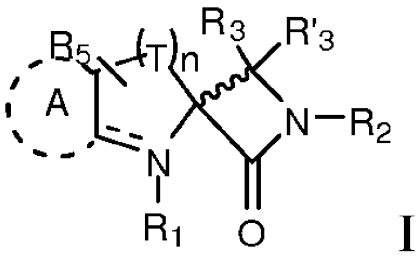


Formula 210

[0970] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 210. Such compounds are described in WO 2011/100585, published August 18, 2011, corresponding to PCT/US2011/024583, filed February 11, 2011, and US 9,101,612, issued August 11, 2015, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 210, these references incorporated by reference herein control.

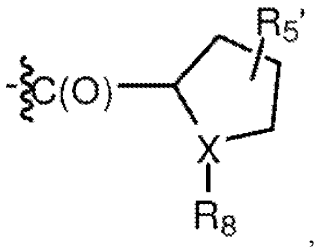
[0971] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 210:

Formula 210



I

and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof; wherein T is, independently for each occurrence, CR4R4 , and n is 0, 1, 2 or 3;
A is optionally present and is selected from phenyl or pyridine, wherein A is optionally substituted by one or more substituents selected from Ra;
Ri is selected from the group consisting of H, hydroxyl, -S(O)2-C1-4alkyl; -SO2, C1- 4alkyl, C2-C4alkenyl, phenyl, R7, or



, wherein C1-4 alkyl, C2-4alkenyl, or phenyl is optionally substituted by one or more substituents selected from Ra;

X is CH or N;

R3 and R3 are independently selected from the group consisting of H, halogen, hydroxyl, phenyl, C1-4alkyl, amido, amine, C2-4alkenyl, wherein C1-4alkyl, C2-4alkenyl, and phenyl are optionally substituted by one or more substituents selected from Ra;

R4 and R4 are independently selected from the group consisting of H, halogen, hydroxyl, phenyl, C1-4alkyl, amido, amine, C1-4alkoxy or C2-4alkenyl, wherein C1-4alkyl, C2-4alkenyl, C1-4alkoxy, and phenyl are optionally substituted by one or more substituents selected from Ra;

R2 is selected from the group consisting of H, R7, $-S(O)_2$, $S(O)_2$-C1-C4alkyl, C1-4alkyl, hydroxyl, or phenyl wherein C1-4alkyl, C2-4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra;

R5 and R5' are each independently selected from group consisting of H, halogen, C1-4alkyl, C1-4alkoxy, C2-4alkenyl, cyano, amino, phenyl, and hydroxyl, wherein C1-4alkyl, C2-4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra;

R7 is selected from group consisting of -C(O)-R9, -C(O)-O-R9, or $-C(O)-NR_d$-R9, R9 is selected from the group consisting of H, C1-4alkyl, phenyl, or heterocyclic, wherein C1-4alkyl, phenyl or heterocyclic is optionally substituted by 1, 2 or 3 substituents selected from Rb;

R8 is selected from group consisting of H, -C(O)- C1-4alkyl or C(O)-O- C1-4 alkyl, wherein C1-4alkyl is optionally substituted by 1, 2 or 3 substituents selected from Ra;

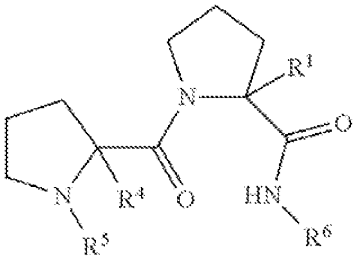
Ra is selected, independently for each occurrence, from carboxy, hydroxyl, halogen, amino, phenyl, C1-4alkyl, and C1-4alkoxy;

Rb is selected, independently for each occurrence, from the group consisting of carboxy, hydroxyl, halogen, amino, phenyl, C-14alkyl, C1-4alkoxy, and -NH-RC;

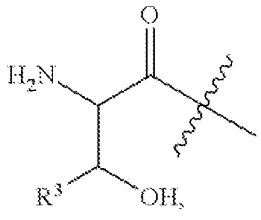
Rc is selected, independently for each occurrence from the group consisting of: -C(O)- O-C1-4alkyl; and -C(O)-C1-4alkyl; and

Rd is selected, independently for each occurrence, H and C1-4alkyl.

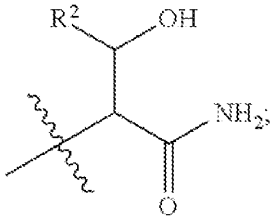
[0972] In further embodiments, the NMDA receptor antagonist is a compound according to:



, wherein R4 is H, R1 is benzyl, R5 is

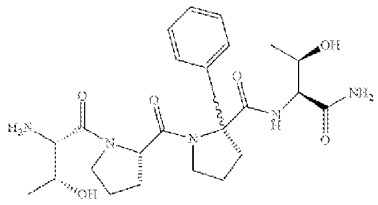


, R6 is

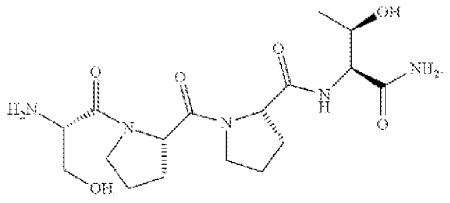


, R2 is H or CH3, R3 is H or CH3, and stereoisomers, N-oxides or pharmaceutically acceptable salts thereof.

[0973] In further embodiments, the NMDA receptor antagonist is a compound according to:

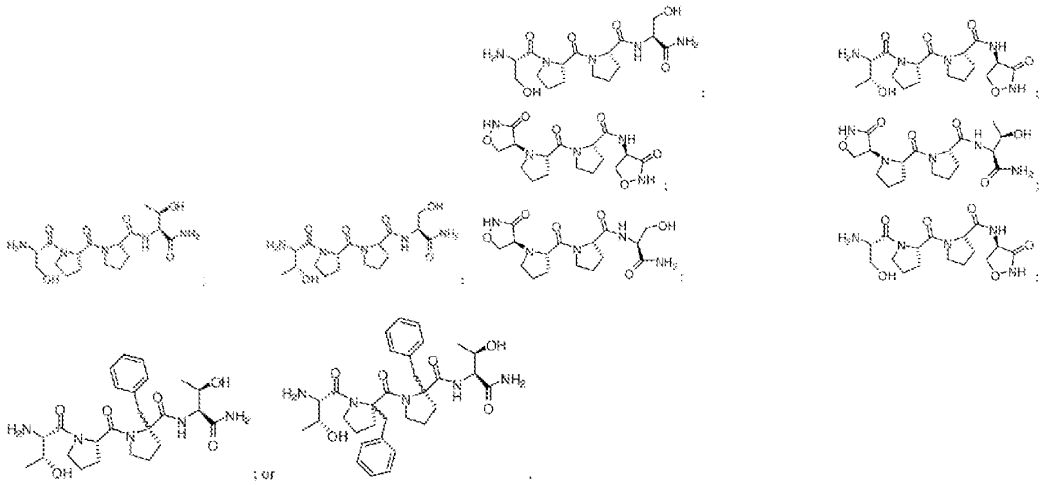


or

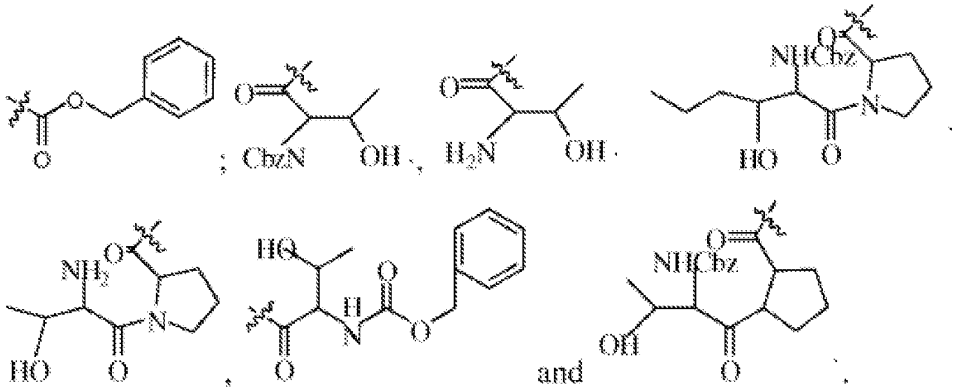


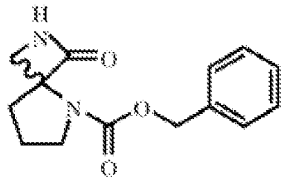
.

[0974] In further embodiments, the NMDA receptor antagonist is a compound according to:

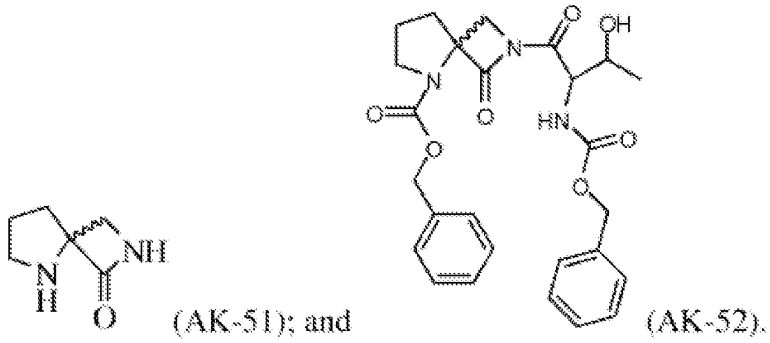


[0975] In an embodiment, the NMDA receptor antagonist is a compound according to:



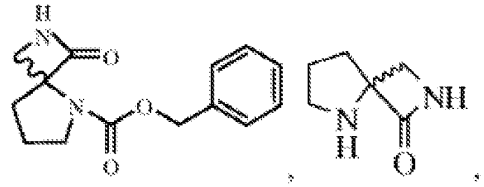


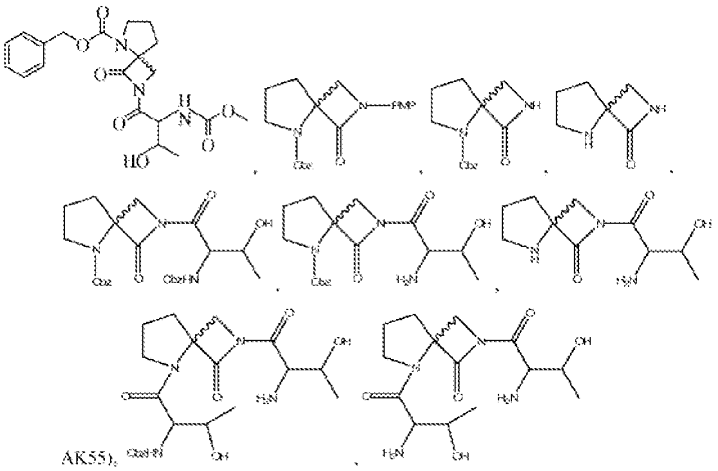
(compound B),



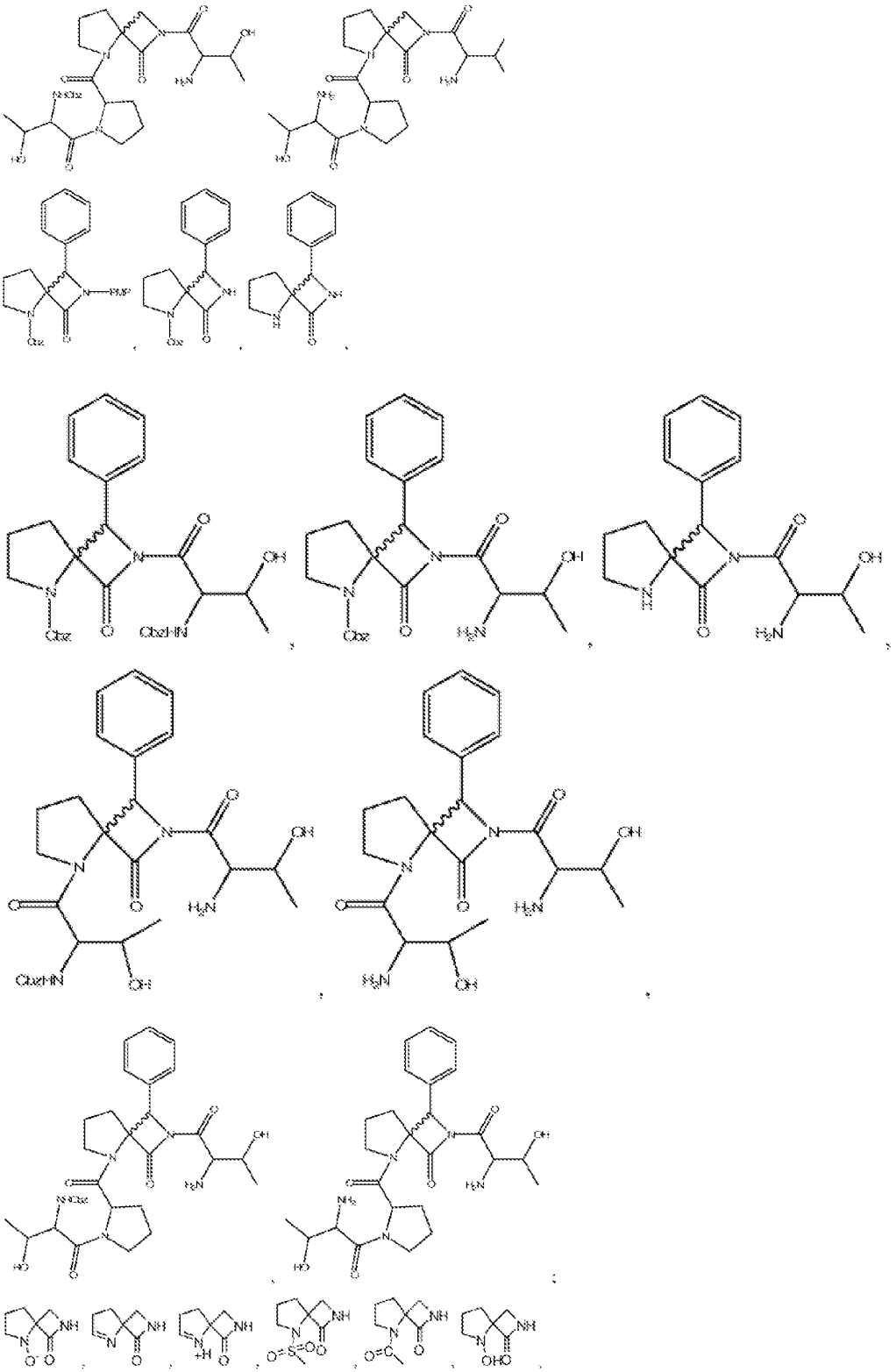
(AK-51); and

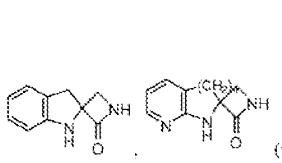
(AK-52).

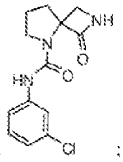




AK55),





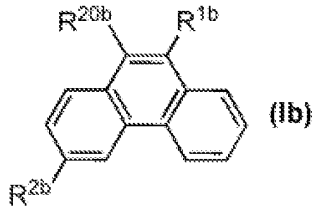
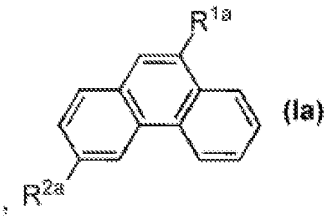
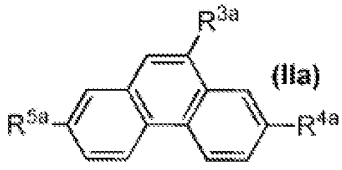
(where n is 0, 1, 2 or 3), and

; or pharmaceutically acceptable salts thereof.

Formula 211

[0976] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 211. Such compounds are described in WO 2012/019106, published February 9, 2012, correcponding to PCT/US2011/046756, filed August 5, 2011, which is incorporated by reference in its entirety herein. In the case of any conflict of terminology of Formula 211, this references incorporated by reference herein controls.

[0977] In an embodiment, the NMDA receptor antagonist is a compound according to formulas 211 a – c:

Formula 211a - c

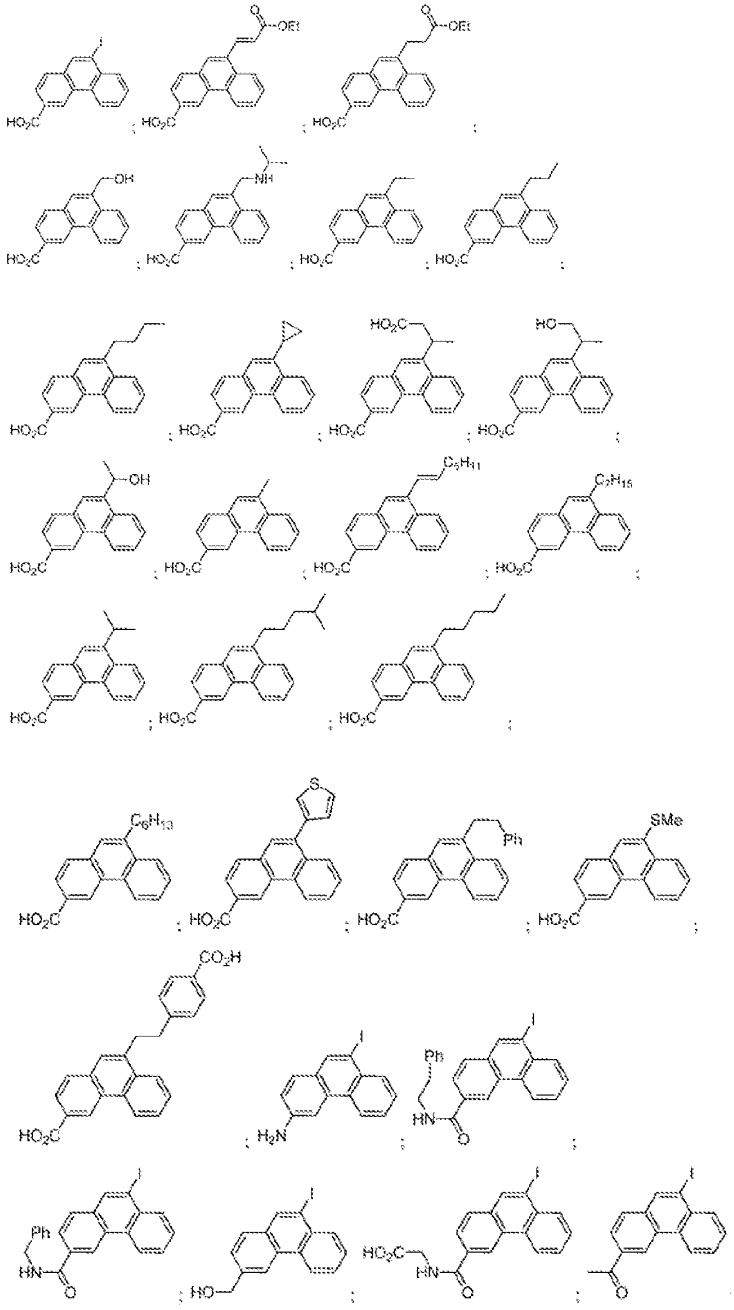

(Ib)

(Ia)

(IIa)
, or

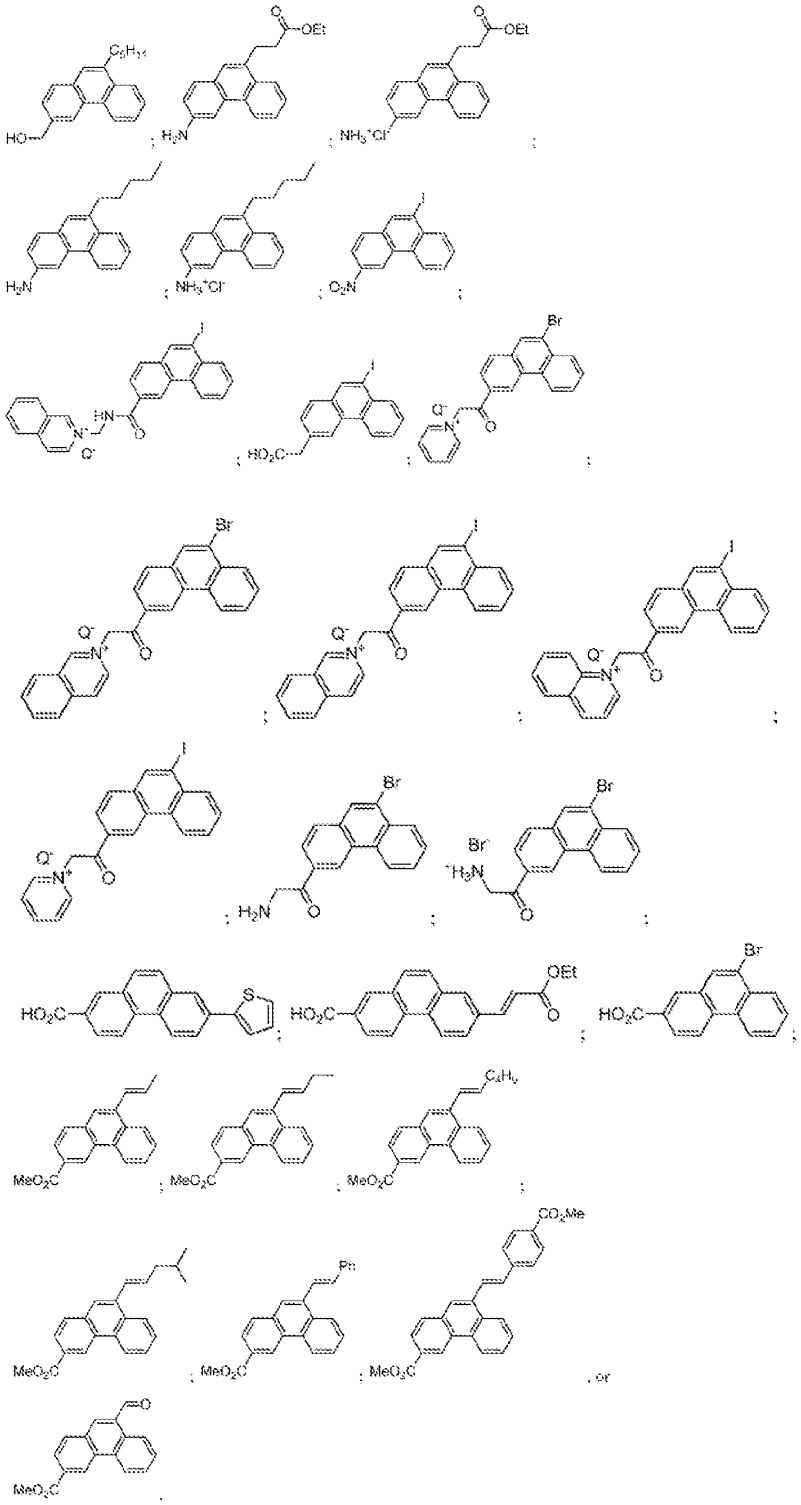
, wherein R1b is iodo, alkyl, alkenyl, alkynyl, alkoxy, amino, cycloalkyl, aryl, heteroaryl, alkyleneamino, alkylene-CO2H, alkenylene-CO2alkyl, alkylene-OH, alkylene-cycloalkyl, alkylenearyl, alkenylenearyl, CHO, or thioalkyl;
R2b and R5a are each independently R^A, alkylene-R^A, NH_2, C(O)NH-alkylenearyl, C(O)NH-alkyleneheteroaryl, C(O)NH-alkylene-R^A, alkylene-OH, C(O)alkyl, or NO2;
Rla is halo;
R2a is C(O)alkylene-NH2 or C(O)alkylene-heteroaryl;
R3a is H or halo;
R4a is H, heteroaryl, alkenylene-CO2H, or alkenylene-CO2-alkyl;
R20b is alkyl, alkenyl, alkynyl, NO2, amino, aryl or heteroaryl; and
RA is CO2H, CO2alkyl, P(O)(OH)(OH), P(O)(OH)(Oalkyl), P(O)(Oalkyl)(Oalkyl), P(O)(alkyl)(OH), SO2H, SO3H, C(O)NHOH, SO2NH2, or tetrazole,

optionally with the proviso that R3a and R4a cannot each be H,

or a salt, ester, solvate, tautomer, enantiomer, or hydrate thereof.

[0978] In further embodiments, the NMDA receptor antagonist is a compound selected from:

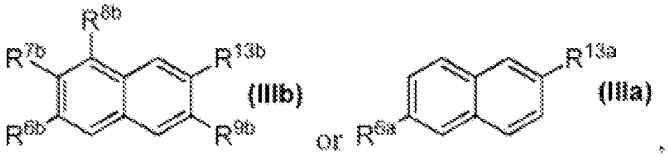




wherein Q is a pharmaceutically acceptable anion.

[0979] In yet further embodiments, the NMDA receptor antagonist is a compound according to Formula 212d-e:

Formula 212d and 212e



, wherein

R6b is RA or alkylene-RA;

R7b is OH, alkoxy, or CO2H;

R8b is H, halo, or C4-C20alkyl;

R9b is halo, alkenyl, aryl, or alkyl;

R13b is H, C4-C2oalkyl, alkenyl, aryl, heteroaryl, alkeylenearyl, or alkenylenearyl;

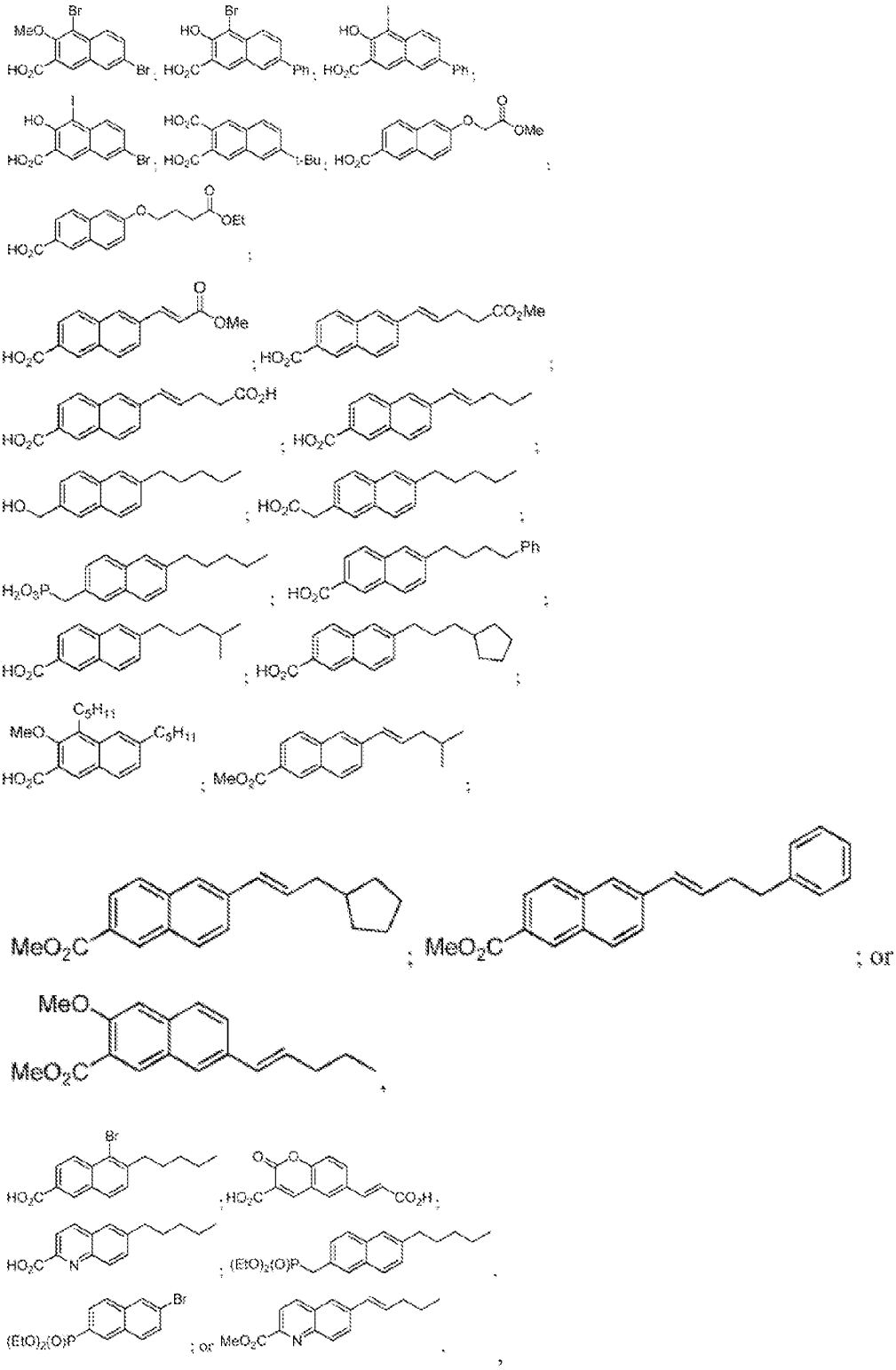
R13a is C4-C20alkyl, alkenyl, alkenylene-CO2H, alkenylene-CO2alkyl, O-alkylene-CO2alkyl, or alkylenearyl;

R6a is RA, alkylene-RA, or alkylene-OH;

RA is CO2H, P(O)(OH)(OH), P(O)(OH)(Oalkyl), P(O)(Oalkyl)(Oalkyl), P(0O(alkyl)(OH), SO2H, SO3H, C(O)NHOH, SO2NH2, or tetrazole;

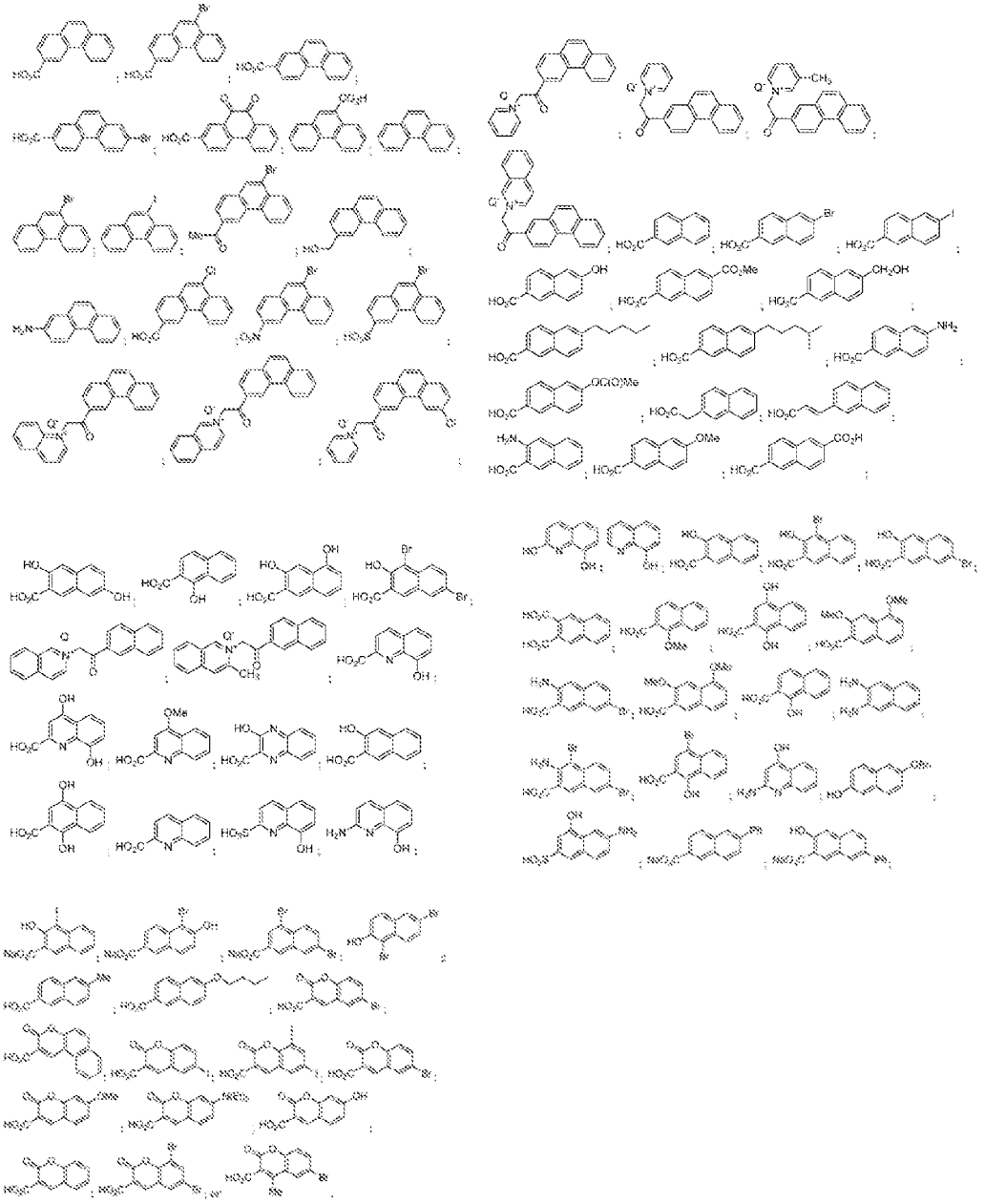
or a salt, ester, solvate, tautomer, enantiomer, or hydrate thereof.

[0980] In further embodiments, the NMDA receptor antagonist is a compound selected from:



Or a salt, ester, solvate, tautomer, enantiomer, or hydrate thereof.

[0981] In further embodiments, the NMDA receptor antagonist is a compound according to:

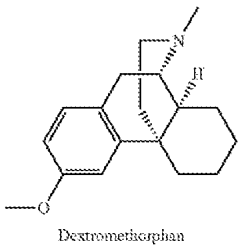


Formula 212

[0982] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 212. Such compounds are described in US 2011/0206780 published August 25, 2011 corresponding to US 12/984,989 filed January 5,

2011 which is incorporated by reference in its entirety herein. In the case of any conflict of terminology of Formula 212, this reference incorporated by reference herein controls.

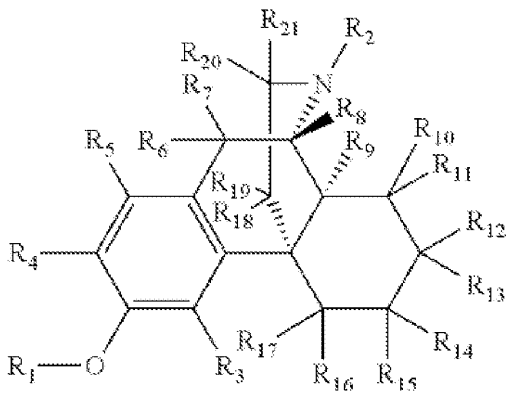
[0983] In an embodiment, the NMDA receptor antagonist is dextromethorphan:



Dextromethorphan

[0984] In further embodiments, the NMDA receptor antagonist is dextromethorphan or a dextromethorphan analogue having one or more H replaced with deuterium (D).

[0985] In further embodiments, the NMDA receptor antagonist is a compound according to Formula 212:



or a salt thereof, wherein:

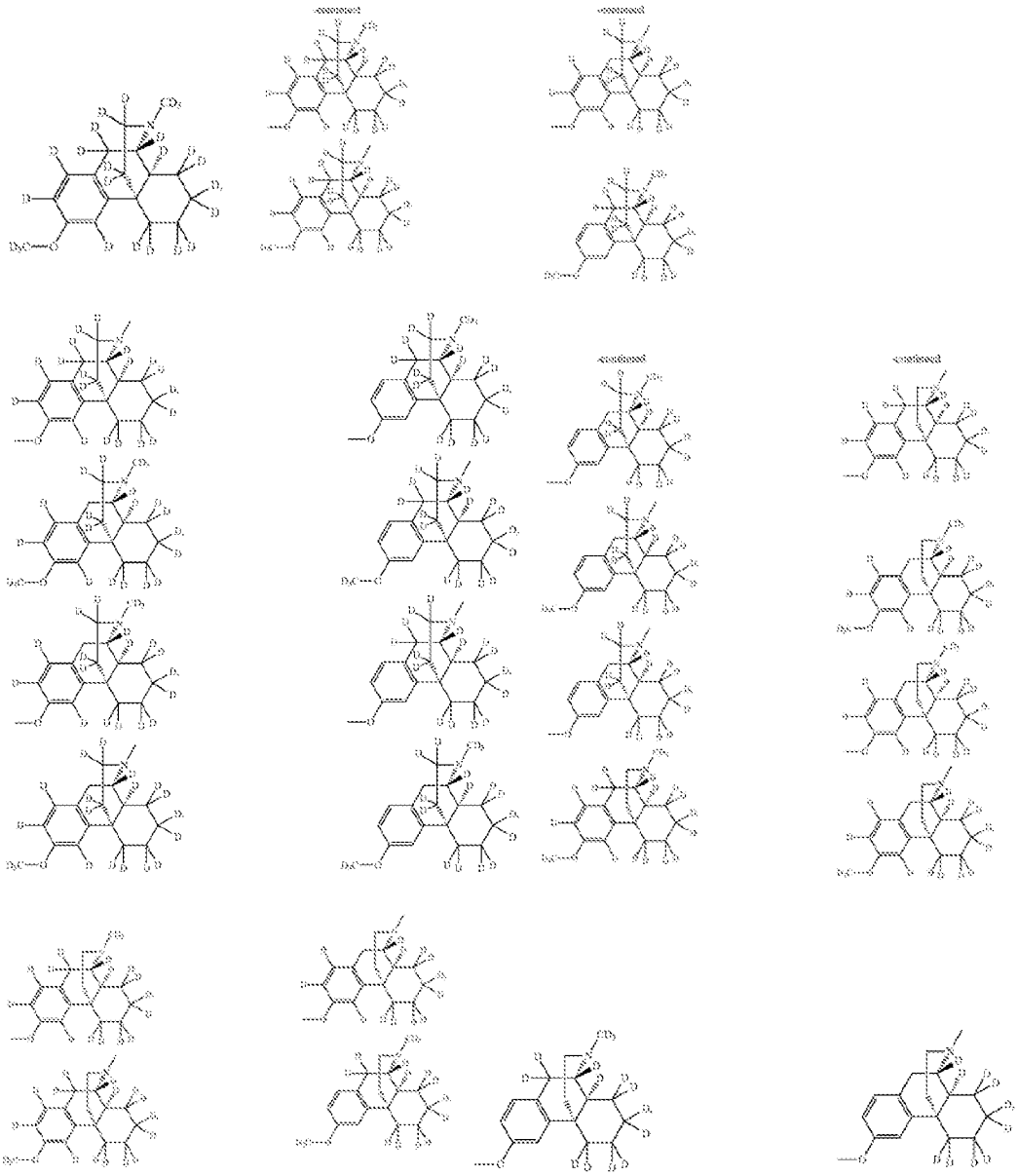
R1 and R2 are independently selected from the group consisting of —CH3, —CH2D, —CD2H, and —CD3;

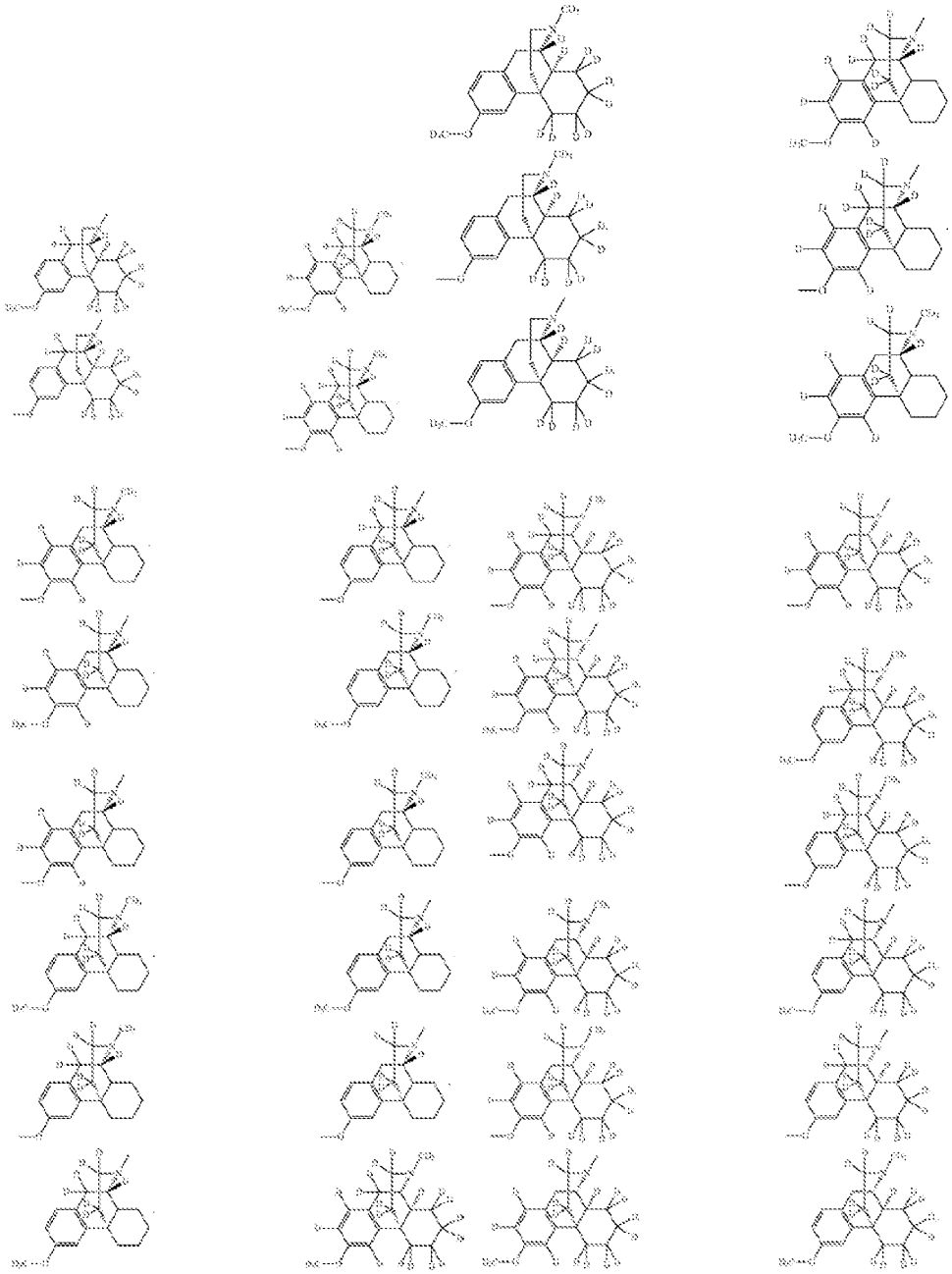
R3-R25 are independently selected from the group consisting of hydrogen and deuterium;

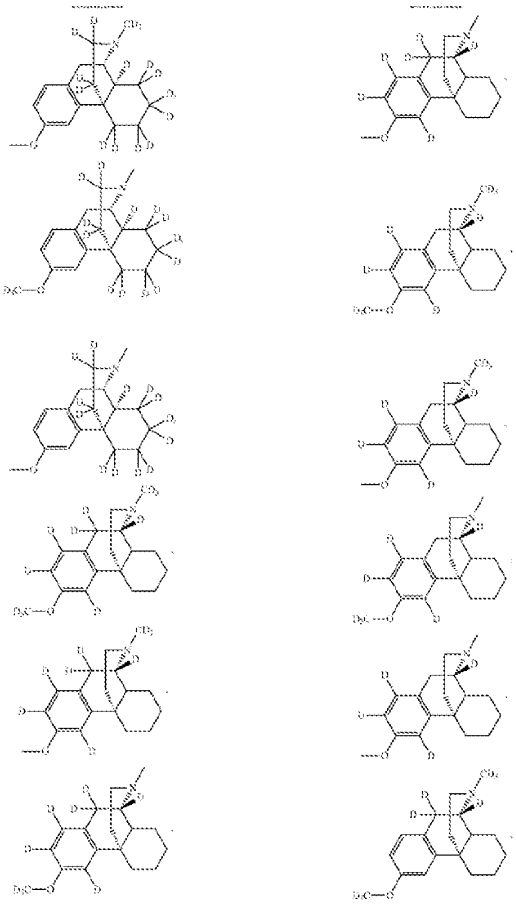
at least one of R3-R25 is deuterium; and

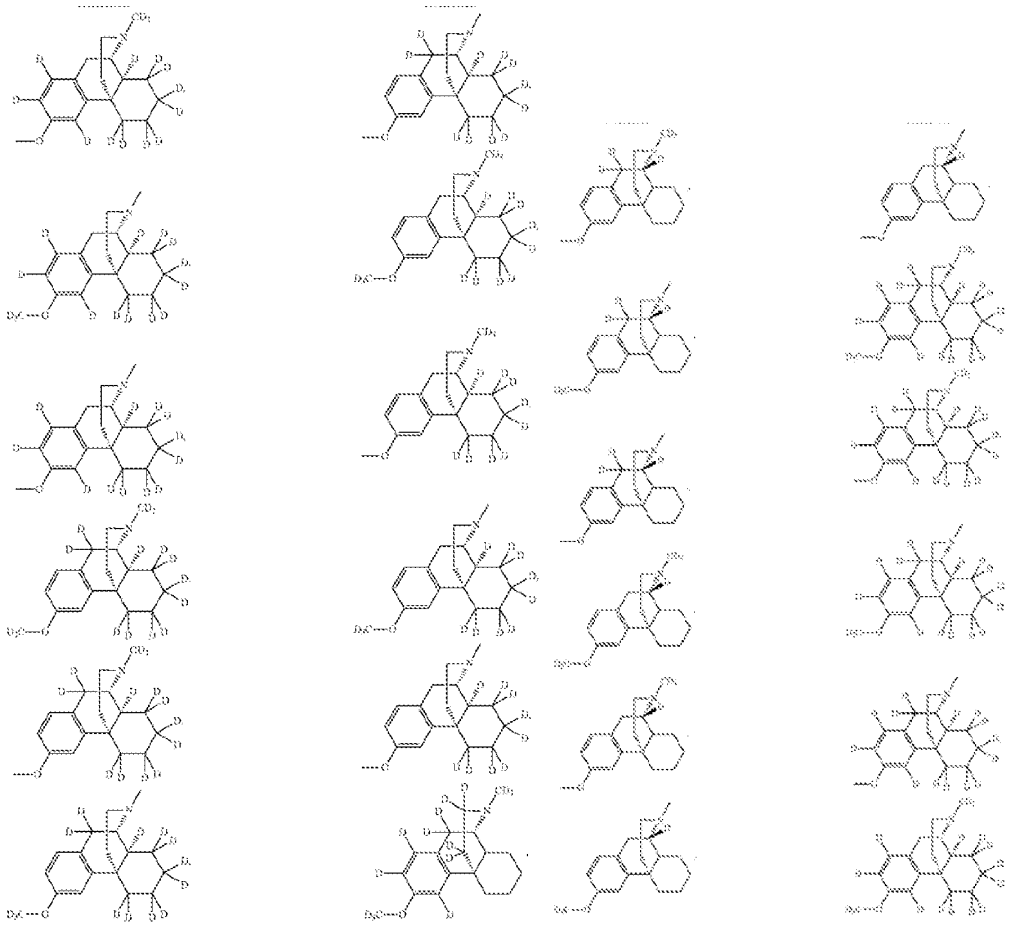
if R6-R8 and R20-R21 are deuterium and R2 is —CD3, then at least one of R1-R5, R9-R19, and R22-R25 is deuterium or contains deuterium.

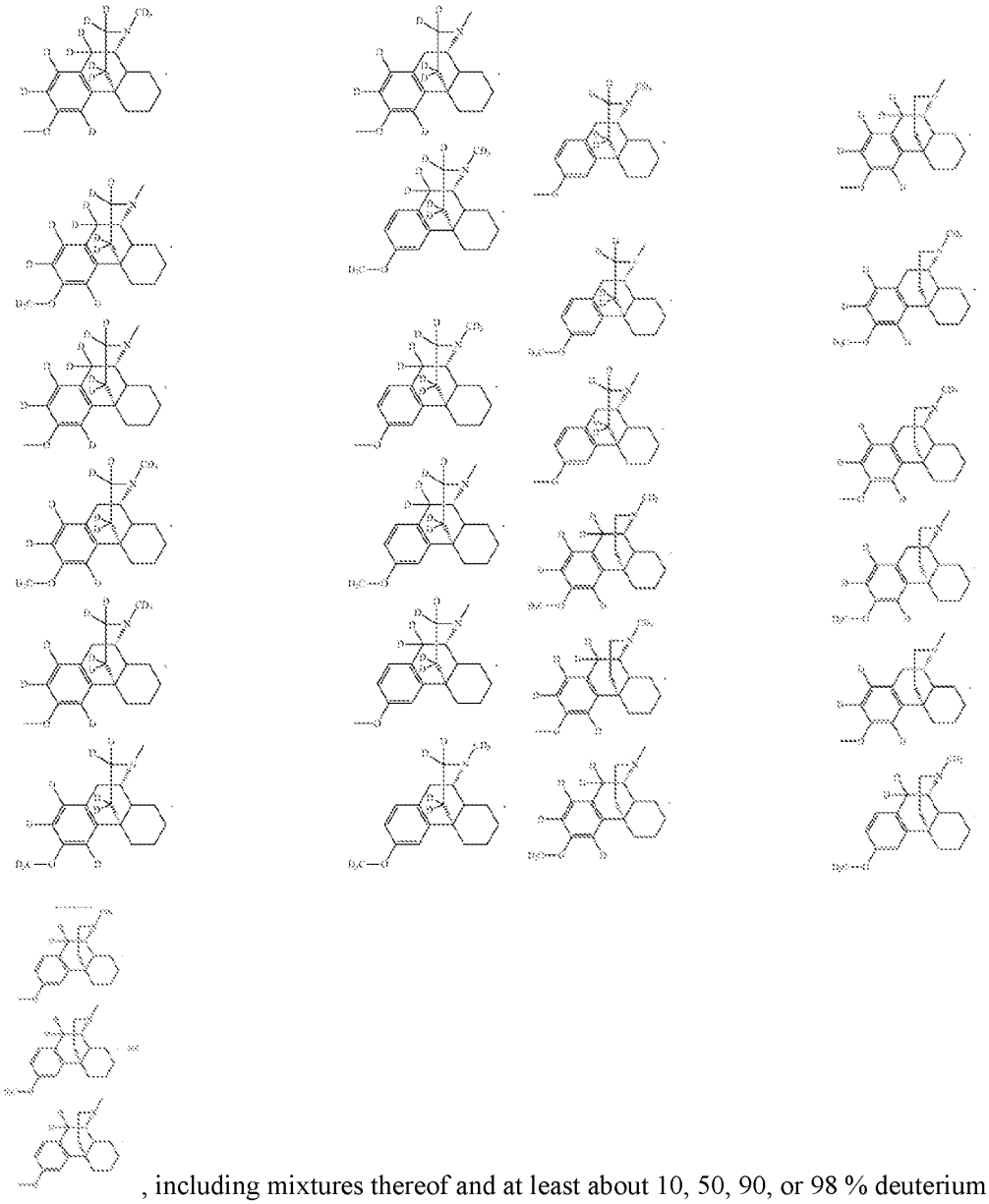
[0986] In further embodiments, the NMDA receptor antagonist is a compound selected from:









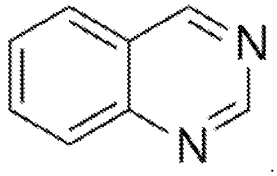


, including mixtures thereof and at least about 10, 50, 90, or 98 % deuterium enrichment.

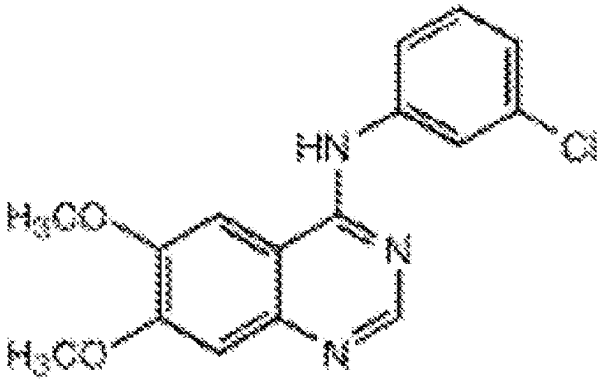
Formula 213

[0987] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 213. Such compounds are described in, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 213, these references incorporated by reference herein control.

[0988] In an embodiment, the NMDA receptor antagonist is a derivative of quinazoline, i.e. the following molecule portion, substituted in any manner:

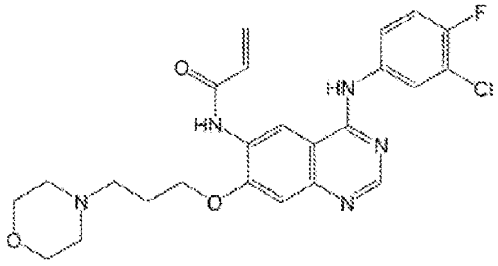


[0989] In an embodiment the NMDA receptor antagonist is:



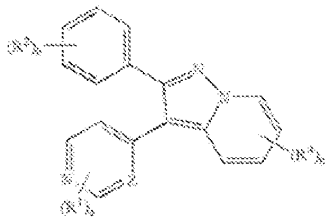
, or a pharmaceutically acceptable salt or derivative thereof.

[0990] In an embodiment, the NMDA receptor antagonist is a compound according to:



, or a pharmaceutically acceptable salt or derivative thereof.

[0991] In further embodiments, the NMDA receptor antagonist is a compound according to:



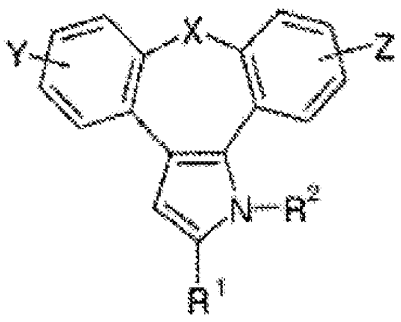
, wherein Z is N; a is 1 or 2; b is 1, 2or 3; c is 1, 2 or 3; each R1 is independently selected from groups of the formula ~(X)d~(CH2)e~R5 wherein d is 0 or 1; e is 0 to 6; X is O, NR or S(O)f where f is 0, 1 or 2; R is hydrogen, halogen, Ci_6 alkyl, C2-6 alkyl, C2-6 alkenyl, C3-12 cycloalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, cyano, nitro, trihalomethyl, NR7R8, C5H4NR7R8, C5H4(CH2)NR7R8, C(O)R7, C(O)NR7R8, OC(O)R7, OC(O)NR7R8, CO2R7, OCO2R7, SO2R7, SO2NR7R8, C(=NR7)NR7R8, NR7(C=NR7)NR7R8, NHC(O)R7 or N(1-3alkyl)C(O)R7; each R2 is independently selected from hydrogen, cyano, halogen, trihalomethyl, OC2-5alkyl, C2-5alkyl, C2-5alkenyl, C2-5alkynyl, S(O)gC1-5 alkyl where g is 0, 1 or 2, NC1-5 alkyl(C1-5 alkyl), hydroxyl or nitro; each R4 is independently selected from groups of the formula

$$--(Y)_d--(CH_2)_e--R^3$$

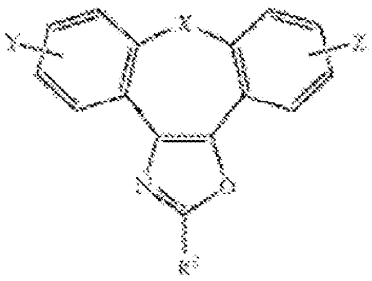
wherein d is 0 or 1; e is 0 to 6; Y is O or S(O)f where f is 0, 1 or 2; R3 is hydrogen, halogen, C1-6 alkyl, C2-5 alkyl, C2-5 alkenyl, C3-12 cycloalkyl, heterocyclyl, aryl, heteroaryl, hydroxyl, cyano, nitro, trihalomethyl, phthalamido, C5H4NR7R8, C5H4(CH2)NR7R8, C(O)R7, C(O)NR7R8, OC(O)R7, OC(O)NR7R8, CO2R7, OCO2R7, SO2R7, SO2NR7R8 or C(=NR7)NR7R8; R6 is H, C1-5 alkyl, C2-5 alkyl, C2-5 alkenyl, C3-12 cycloalkyl, or heterocyclyl; R7and R8 are each independently H, C1-8 alkyl, C2-5 alkenyl, SO2C1-5 alkyl, (CH2)m-C3-12 cycloalkyl, (CH2)m -aryl, (CH2)m -heterocyclyl, (CH2)m -heteroaryl, wherein m=0, 1 or 2, or may, together with the nitrogen atom to which they are bound, form a heterocyclyl group; and wherein any of said alkyl, alkenyl and alkynyl groups may be optionally substituted with up to three members selected from halogen, hydroxyl, oxo, cyano, NR7R8, C1-6 alkyl, OC1-6 alkyl, S(O)C1-5 alkyl, S(O)2C1-5 alkyl and SO2NNR7R8; and wherein any of said cycloalkyl, heterocyclyl, aryl, and heteroaryl groups may be optionally substituted with substituents selected from a group consisting of C1-6alkyl, C1-6 alkoxy, C1-6 alkylsulfenyl, C1-6 alkylsulfinyl, C1-6 alkylsulfonyl, hydroxy, oxo, mercapto, nitro, cyano, halogen, C1-6 perfluoroalkyl, amino optionally substituted by C1-6 alkyl, carbamoyl optionally

substituted by C1-6 alkyl, NR R , carboxy and aminosulfonyl optionally substituted by C1-6 alkyl.

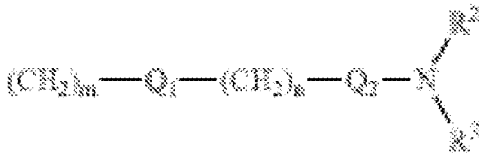
[0992] In another embodiment, the NMDA receptor antagonist is a compound according to:



or



[0993] wherein X is O, S, S(=O), S(=O)2, or NRa, wherein Ra is hydrogen or a substituent selected from C1-C3-alkyl, C1-C3-alkanoyl, C1-C7-alkoxycarbonyl, C7-C10- arylalkyloxycarbonyl, C7-C10-aroyl, C7-C10-arylalkyl, C3-C7-alkylsilyl or C5-C10- alkylsilylalkyloxyalkyl ; Y and Z independently from each other mean one or more identical or different substituents linked to any available carbon atom selected from the group consisting of hydrogen; halogen, C1-C4-alkyl, C2-C4-alkenyl, C2-C4-alkinyl, halo-C1-C4 alkyl, hydroxy, C1- C4-alkoxy, trifluoromethoxy, C1-C4-alkanoyl, amino, amino-C1-C4-alkyl, N-(C1-C4-alkyl) amino, N,N-di(Ci-C4-alkyl)amino, thiol, C1-C4 alkylthio, sulfonyl, C1-C4 alkylsulfonyl, sulfinyl, C1-C4 alkylsulfinyl, carboxy, Ci-C4 alkoxycarbonyl, cyano and nitro; R1 is hydrogen, CHO, (CH2)2COOH, (CH2)2CO2CH2CH3, $(CH2)_mL$ wherein m is an integer from 1 to 3, n is an integer between 0-3 and L is OH or Br, or a substituent set forth by formula VII:



[0994]

[0995] R2 and R3 are either or both hydrogen, C1-C4-alkyl, aryl such as an aromatic ring or fused aromatic rings containing one ring of at least 6 carbon atoms or two rings with a total of 10 carbon atoms and conjugated double bonds; or together with N are heterocyclic having 5, or 6-member rings or heteroaryl fully saturated or partly unsaturated heterocycle group containing at least one hetero atom such as O, S or N

and where said heterocycle is optionally substituted with one or two substituents such as halogen, C1-C4-alkyl, cyano, nitro, hydroxy, C1-C4-alkoxy, thiol, C1-C4-alkylthio, amino, N-(C1-C4) alkylamino, N,N-di(C1-C4- alkyl)amino, sulfonyl, C1-C4 alkylsulfonyl, sulfinyl, C1-C4 alkylsulfinyl; and wherein heteroaryl relates to aromatic and partially aromatic groups of a monocyclic or bicyclic ring with 4 to 12 carbon atoms and at least one of O, S or N and where said heteroaryl is optionally substituted with one or two substituents which are selected from halogen, C1-C4-alkyl, cyano, nitro, hydroxy, C1-C4-alkoxy, thiol, C1-C4-alkylthio, amino, N-- (C1-C4) alkylamino, N,N-di(C1-C4-alkyl)amino, sulfonyl, C1-C4 alkylsulfonyl, sulfinyl, C1-C4 alkylsulfinyl;

[0996] In one embodiment, N is substituted with a heterocycle or heteroaryl that is morpholine-4-yl, piperidine-1-yl, pyrrolidine- 1-yl, imidazole- 1-yl or piperazine-1-yl

[0997] Qi and Q2 are either or both oxygen, CH2, sulfur or a group set forth by:



[0998] wherein yi and y2 are either or both; hydrogen, halogen (F, Cl or Br); C1-C4-alkyl, aryl wherein aryl has the meaning as defined above, -OH, C1-C4-alkyloxy, C1-C4 alkanoyl, thiol, C1-C4-alkylthio, sulfonyl, C1-C4 alkylsulfonyl, sulfinyl, C1-C4 alkylsulfinyl, cyano, nitro or together form carbonyl or imino group, and of their pharmaceutically acceptable salts and solvates for the manufacture of pharmaceutical formulations for the treatment and prevention of diseases, damages and disorders of the central nervous system caused by disorders of neurochemical equilibrium of biogenic amines or other neurotransmitters.

[0999] In another embodiment, the compound is l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; l,8-dioxa-3-aza-dibenzo[e,h]azulene; 3-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-yl)- propionic acid ethyl ester; 3-(l,8-dioxa-3-aza-dibenzo[e,h]azulen-2-yl)-propionic acid ethyl ester; 2-methyl-l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; 2-methyl-l,8-dioxa-3-aza- dibenzo[e,h]azulene; 1 l-chloro-2-methyl-l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; 5-chloro- 2-methyl-l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; l l-chloro-2-methyl-l,8-dioxa-3-aza- dibenzo[e,h]azulene; 5-chloro-2-methyl-l,8-dioxa-3-aza-dibenzo[e,h]azulene; l-oxa-8-thia- 3-aza-dibenzo[e,h]azulene-2-carbaldehyde; 3-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-yl)-propionic acid; 3-(l,8-dioxa-3-aza-dibenzo[e,h]azulen-2-yl)-propionic acid; (l-oxa-8-

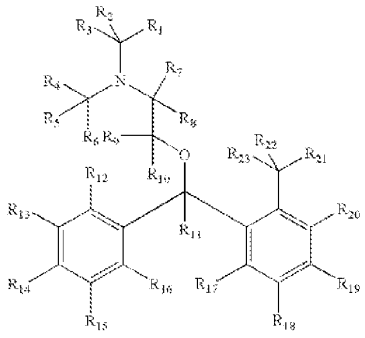
thia- 3-aza-dibenzo[e,h]azulen-2-yl)-methanol; 3-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-yl)- propane-1-ol; 3-(l,8-dioxa-3-aza-dibenzo[e,h]azulen-2-yl)-propane-l-ol; 2-bromomethyl- 1- oxa-8 -thia- 3 - aza-dibenzo [e,h] azulene ; 2-bromomethyl- 1 , 8 -dioxa- 3 - aza-dibenzo [e,h] azulene ; 2-bromomethyl-5-chloro-l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; 2-bromomethyl- 11- chloro-l-oxa-8-thia-3-aza-dibenzo[e,h]azulene; 2-bromomethyl-5-chloro-l,8-dioxa-3-aza- dibenzo [e,h] azulene ; 2-bromomethyl- 11 -chloro- 1 , 8 -dioxa- 3 - aza-dibenzo [e,h] azulene ; dimethyl-[2-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-am- ine; dimethyl- [3-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-ylmethoxy)-propyl]-a- mine; dimethyl- {2- [3-(l-oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-yl)-propoxy]-ethy- 1} -amine; dimethyl-{3-[3-(l- oxa-8-thia-3-aza-dibenzo[e,h]azulen-2-yl)-propoxy]-prop- yl}-amine; {2-[3-(l,8-dioxa-3- aza-dibenzo [e,h] azulen-2-yl) -propoxy] -ethyl } -dimethyla- mine ; { 3 - [3 -(1 , 8 -dioxa- 3 - aza- dibenzo[e,h]azulen-2-yl)-propoxy]-propyl}-dimethyl-amine; [2-(l,8-dioxa-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-dimethylamine; [3-(l,8-dioxa-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-propyl]-dimet- hylamine; 2-(5-chloro-l-oxa-8-thia-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-dim- ethylamine; [3-(5-chloro-l-oxa-8-thia-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-propyl]-d-imethylamine; [2-(l l-chloro-l-oxa-8-thia-3- aza-dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-d- imethylamine; [3-(ll-chloro-l-oxa-8-thia-3- aza-dibenzo[e,h]azulen-2-ylmethoxy)-propyl]— dimethylamine; [2-(5-chloro-l,8-dioxa-3- aza-dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-dimet- hylamine; [3-(5-chloro-l,8-dioxa-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-propyl]-dime- thylamine; [2-(l l-chloro-l,8-dioxa-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-ethyl]-dime- thylamine; or [3-(l l-chloro-l,8-dioxa-3-aza- dibenzo[e,h]azulen-2-ylmethoxy)-propyl]-dim- ethylamine, including pharmaceutically-acceptable salts and derivatives thereof.

Formula 214

[1000] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 214. Such compounds are described in US 2010/0130617, published May 27, 2010 and corresponding to US application No. 12/623,948, filed November 23, 2009, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 214, these references incorporated by reference herein control.

[1001] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 214:

Formula 214



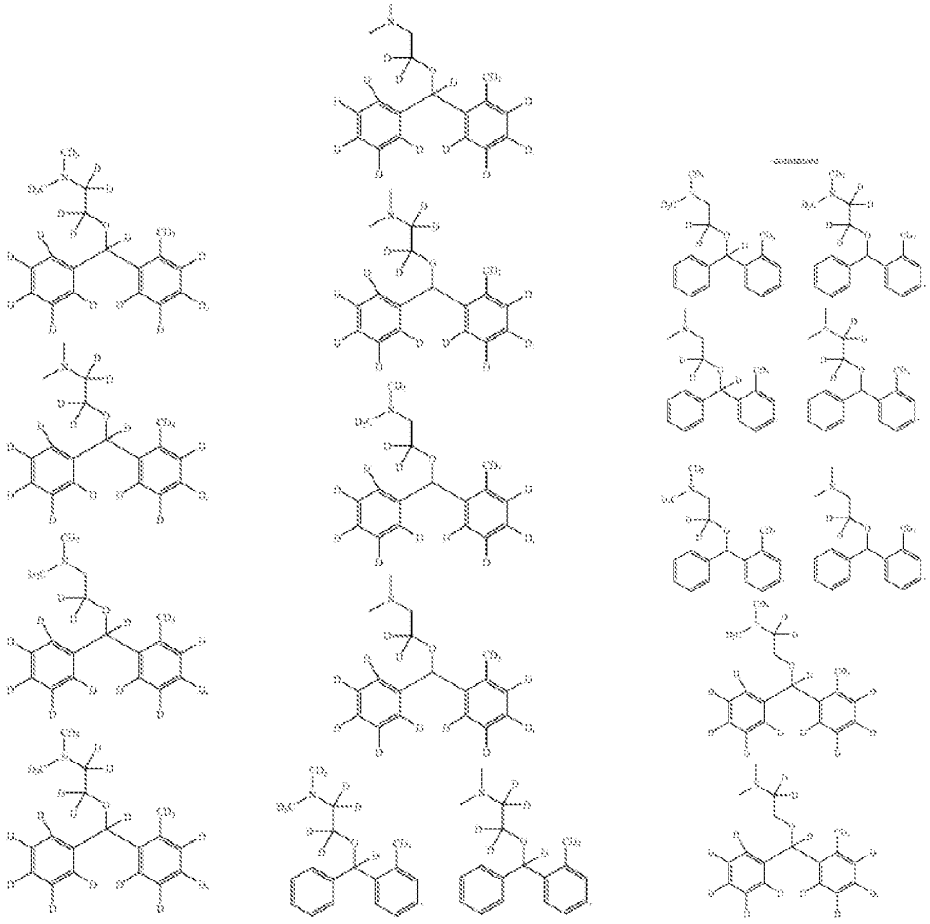
, or a salt thereof, wherein:

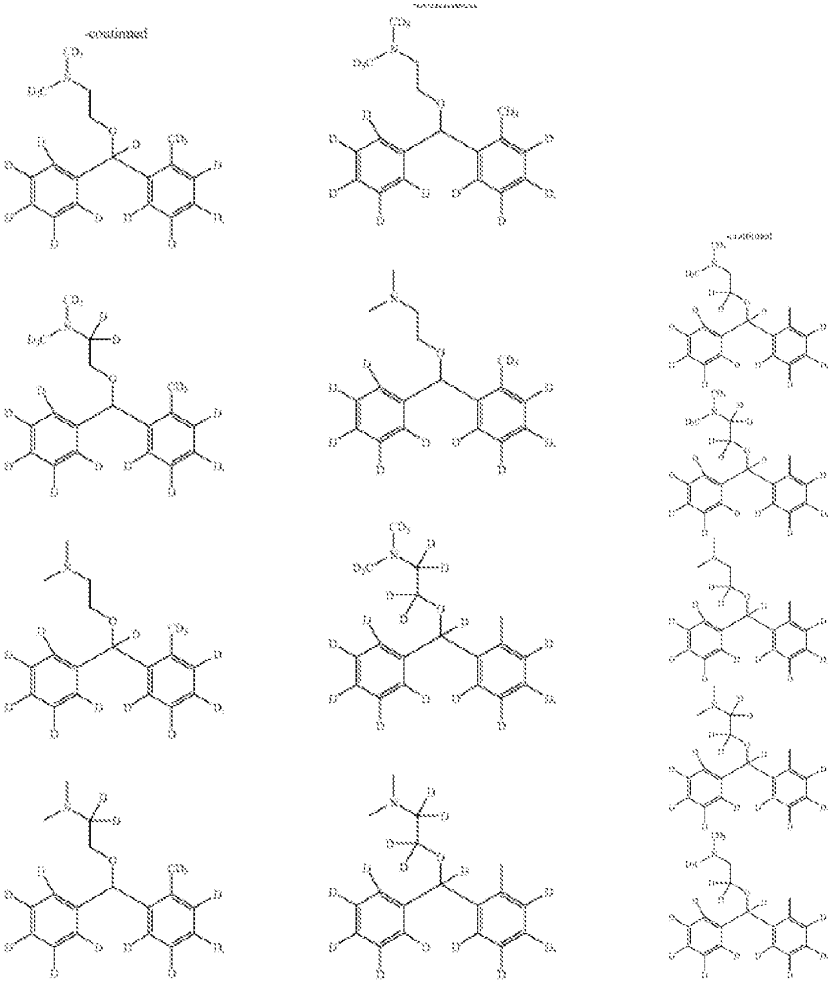
R1-R23 are independently selected from the group consisting of hydrogen and deuterium;

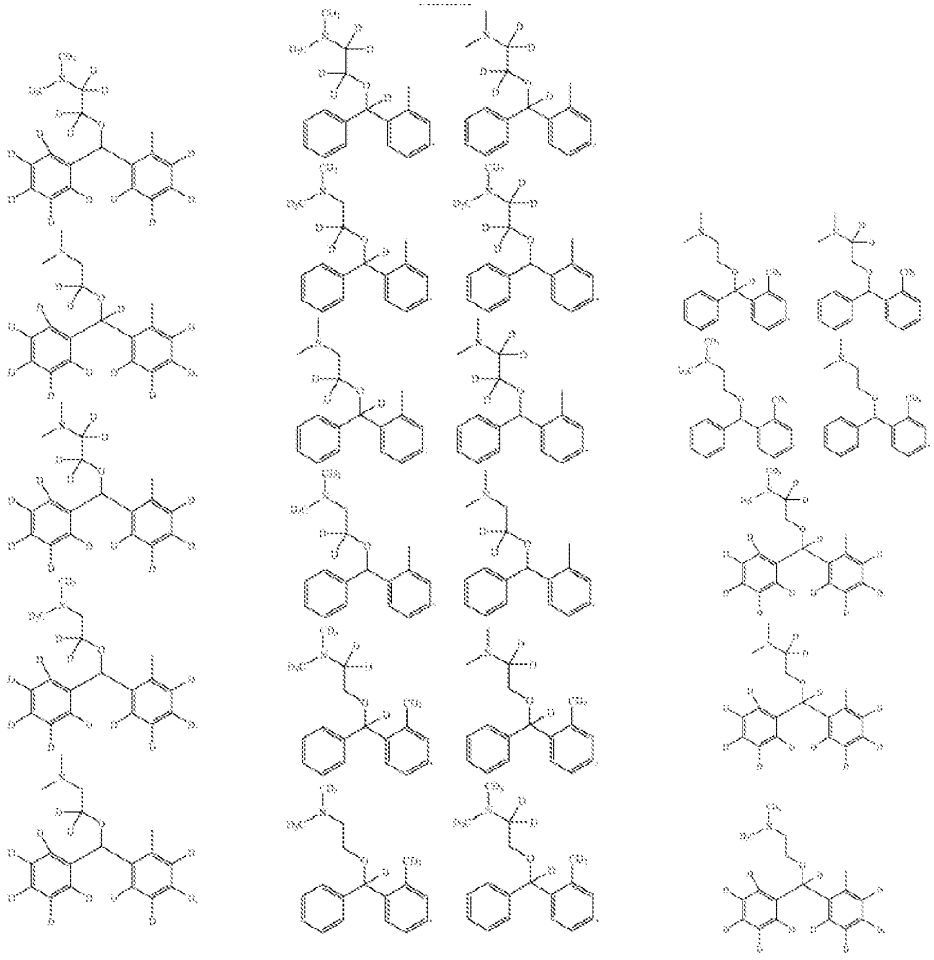
at least one of R1-R23 is deuterium; and

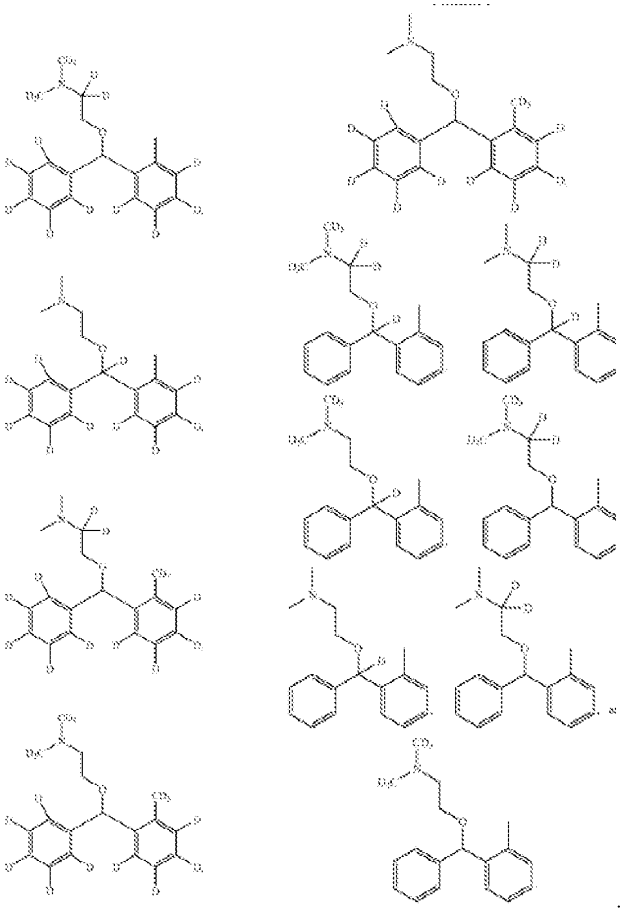
if each of R1-R3 are deuterium, then at least one of R4-R23 is deuterium.

[1002] In further embodiments, the NMDA receptor antagonist is a compound according to:





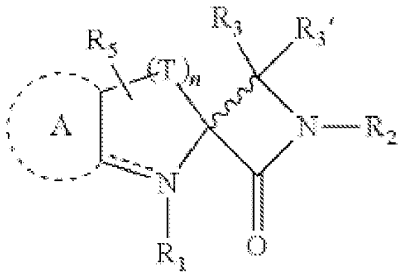




[1003] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 215. Such compounds are described in WO 2010/0033757, published March 25, 2010 and corresponding to PCT/US2009/057401, filed September 18, 2009, US 9,512,133, issued December 6, 2016, US 9,802,946, issued October 31, 2017, and US 10,906,913, issued February 2, 2021, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 215, these references incorporated by reference herein control.

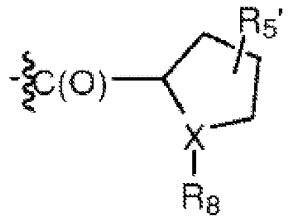
[1004] In an embodiment, the NMDA receptor antagonist is a compound according to:

Formula 215



, and pharmaceutically acceptable salts, stereoisomers, and N-oxides thereof; wherein

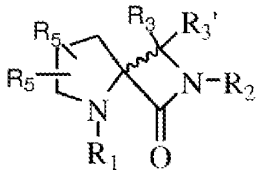
T is, independently for each occurrence, CR4R4 , and n is 0, 1, 2 or 3; A is optionally present and is selected from phenyl or pyridine, wherein A is optionally substituted by one or more substituents selected from Ra; R1 is selected from the group consisting of H, hydroxyl, -S(O)2-C1-C4alkyl; -SO2, C1- C4alkyl, C2-C4alkenyl, phenyl, R7, or



, wherein C1-C4alkyl, C2-C4alkenyl, or phenyl is optionally substituted by one or more substituents selected from Ra; X is CH or N; R3 and R3 are independently selected from the group consisting of H, halogen, hydroxyl, phenyl, C1-C4alkyl, amido, amine, or C2-C4alkenyl, wherein C1-C4alkyl, C2- C4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; R4 and R4 are independently selected from the group consisting of H, halogen, hydroxyl, phenyl, C1-C4alkyl, amido, amine, CrC4alkoxy or C2-C4alkenyl, wherein C1-C4alkyl, C2-C4alkenyl, C1-C4alkoxy, and phenyl are optionally substituted by one or more substituents selected from Ra; R2 is selected from the group consisting of H, R7, -S(O)2, S(O)2-C1-C4alkyl, Q-Qalkyl, hydroxyl, or phenyl wherein C1-C4lkyl, C2-C4 alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; R5 and R5' are each independently selected from group consisting of H, halogen, C1- C4alkyl, C1-C4alkoxy, C2-C4alkenyl, cyano, amino, phenyl, and hydroxyl, wherein C1-C4alkyl, C2-C4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; R7 is selected from group consisting of -C(O)-C1-C4alkyl or C(O)-O-C1-C4alkyl, wherein C1-C4 alkyl is optionally substituted by 1, 2 or 3 substituents selected from Rb; R8 is selected from group

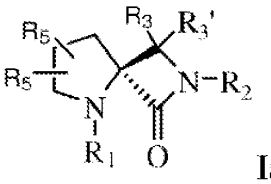
consisting of H, -C(O)- C1-C4 alkyl or C(O)-O- C1-C4 alkyl, wherein C1-C4alkyl is optionally substituted by 1, 2 or 3 substituents selected from Ra; Ra is selected, independently for each occurrence, from carboxy, hydroxyl, halogen, amino, phenyl, C1-C4 alkyl, and C1-C4 alkoxy; Rb is selected, independently for each occurrence, from the group consisting of carboxy, hydroxyl, halogen, amino, phenyl, C1-C4 alkyl, C1-C4 alkoxy, and -NH-RC; and Rc is selected, independently for each occurrence, -C(O)-O-C1-C4alkyl; and -C(O)-C1- C4alkyl.

[1005] In further embodiments, the NMDA receptor antagonist is a compound according to:

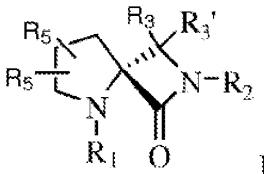


, wherein R1 is C(O)-C2-C4alkyl, wherein C2-C4alkyl is substituted at one carbon with NH2 or -N- carbobenzyloxy and at a different carbon by hydroxyl.

[1006] In further embodiments, the NMDA receptor antagonist is represented by:

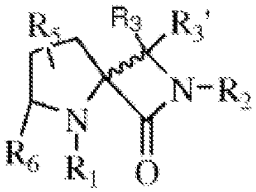


Ia or

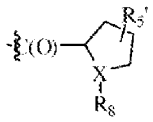


Ib.

[1007] In further embodiments, the NMDA receptor antagonist is a compound according to:

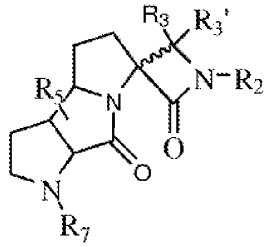


II and pharmaceutically acceptable salts, stereoisomers and N-oxides thereof; wherein R1 is selected from the group consisting of H, hydroxyl, -S(O)2-C1-C4alkyl; -SO2, C1-



C 4alkyl; R7, or

X is CH or N; R3 and R3' are each independently selected from the group consisting of H, halogen, hydroxyl, phenyl, C1-C4alkyl, amido, amine, or C2-C4alkenyl, wherein C1-C4alkyl, C2- C4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; R2 is selected from the group consisting of H, R7, -S(O)2, S(O)2-C1-C4alkyl, C1-C4 alkyl, hydroxyl, or phenyl wherein C1-C4alkyl, C2-C4 alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; R5 is selected from group consisting of H, halogen, C1-C4 alkyl, C1-C4 alkoxy, C2-C4 alkenyl, cyano, amino, phenyl, and hydroxyl, wherein C1-C4alkyl, C2-C4alkenyl and phenyl are optionally substituted by one or more substituents selected from Ra; Re is selected from group consisting of H, halogen, C1-C4 alkyl, C1-C4 alkoxy, C2- C4alkenyl, cyano, amino, phenyl, and hydroxyl wherein C1-C4 alkyl, C2-C4alkenyl and phenyl are optionally substituted by 1, 2 or 3 substituents selected from Ra; R7 is selected from group consisting of -C(O)-C1-C4alkyl or -C(O)-O-C1-C4alkyl, wherein C1-C4 alkyl is optionally substituted by 1, 2 or 3 substituents selected from Rb; or or R1 and R6, taken together with formula II form:

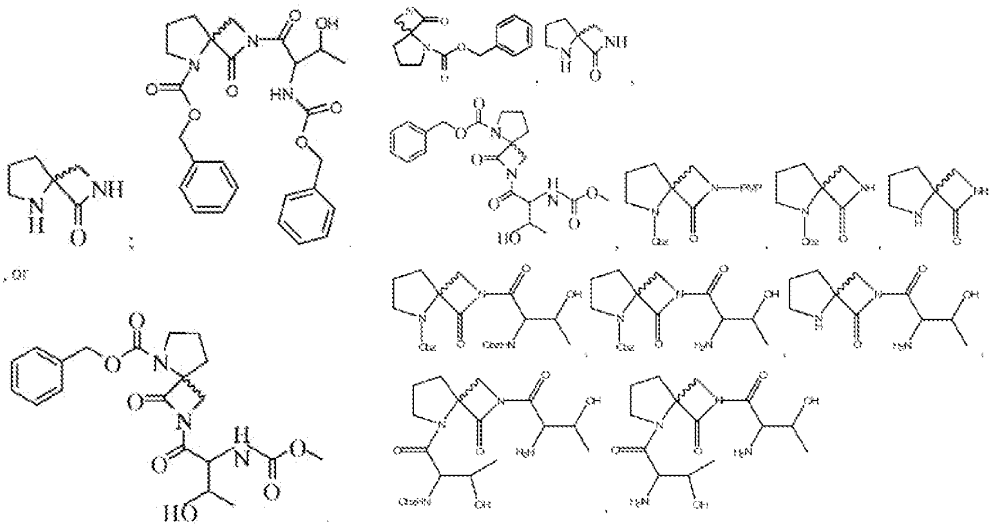


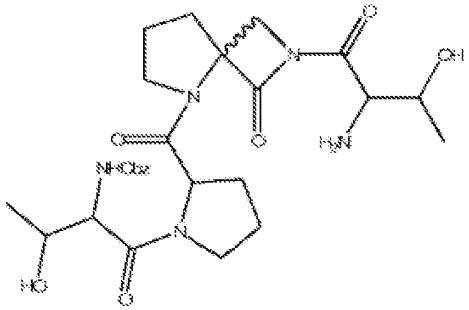
; R8 is selected from group consisting of H, -C(O)- C1-C4alkyl or C(O)-O-C1-C4 alkyl, wherein C1-C4alkyl is optionally substituted by 1, 2 or 3 substituents selected from Ra; Ra is selected, independently for each occurrence, from carboxy, hydroxyl, halogen, amino, phenyl, C1-C4alkyl, and C1-C4alkoxy;

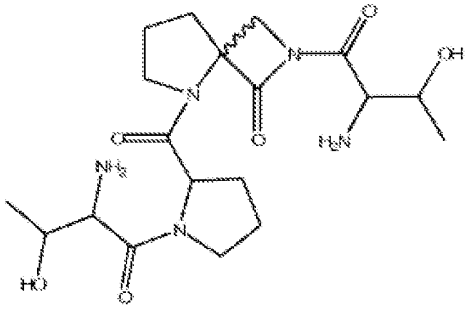
Rb is selected, independently for each occurrence, from the group consisting of carboxy, hydroxyl, halogen, amino, phenyl, C1-C4alkyl, C1-C4alkoxy, and -NH-RC; and

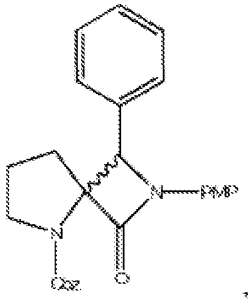
Rc is selected, independently for each occurrence, -C(O)-O-C1-C4alkyl; and -C(O)-C1-C4alkyl.

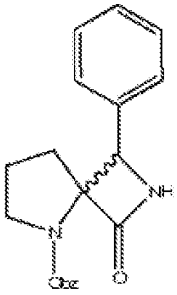
[1008] In further embodiments, the NMDA receptor antagonist is a compound selected from:

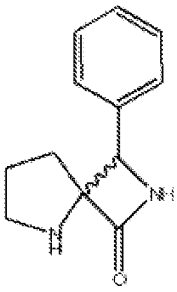


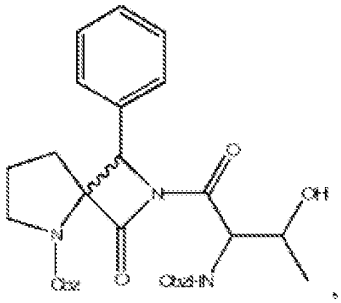


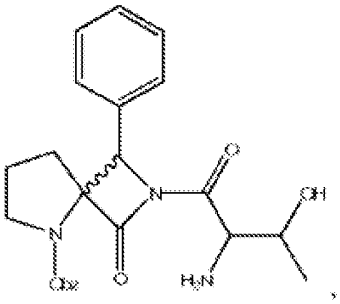


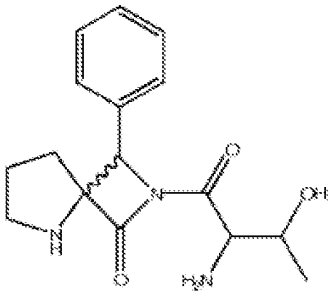


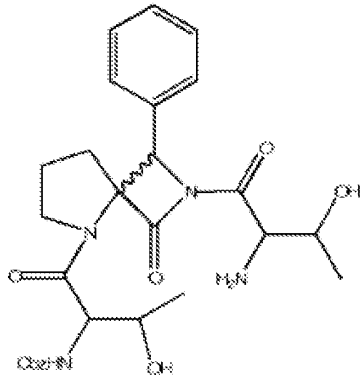


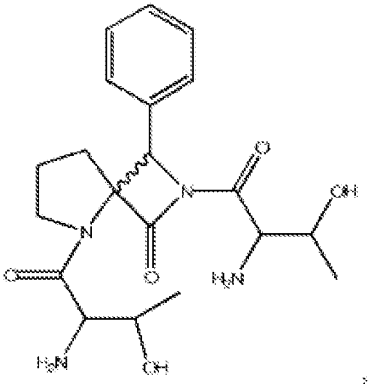


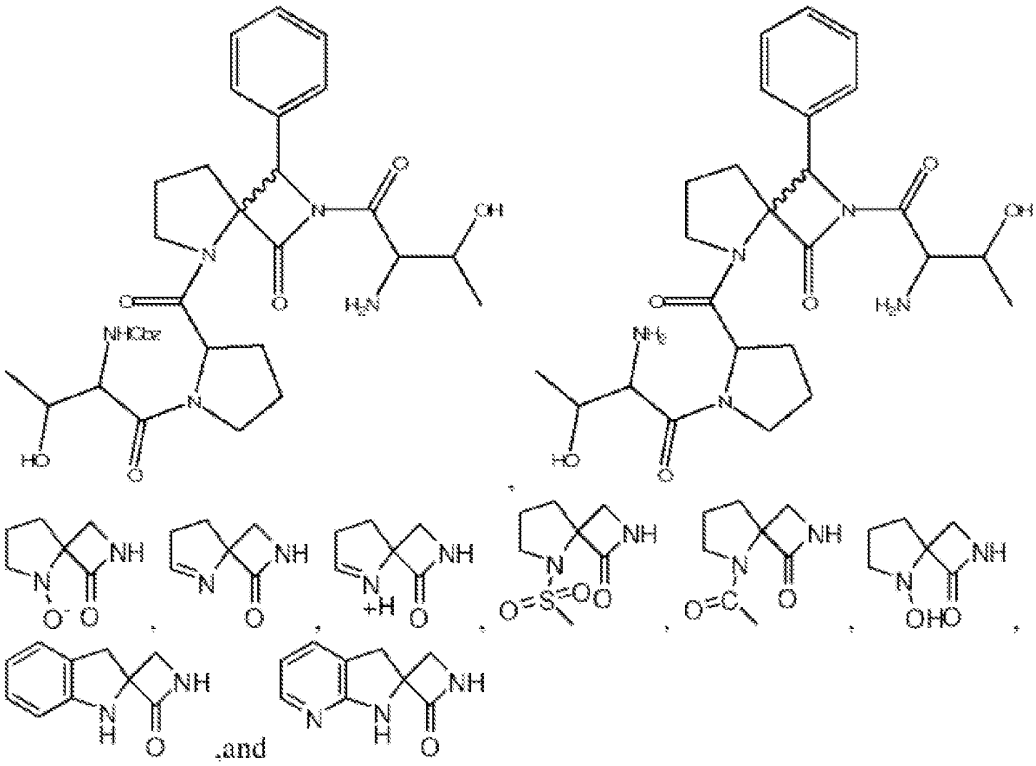






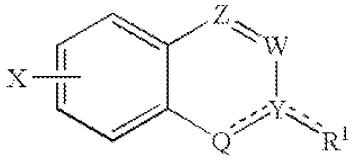






[1009] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 216. Such compounds are described in US 2009/0004112, published January 1, 2009 and corresponding to application no 12/049,782, filed March 17, 2008, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 216, these references incorporated by reference herein control.

[1010] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 216:



or a pharmaceutically acceptable base or acid addition salt, hydrate, stereoisomer, or mixture thereof, wherein

X is one or more halogen radicals;

Q is NH or N;

W is CR2, CHR2, NR3, or CH=COH;

Y is C or CH;

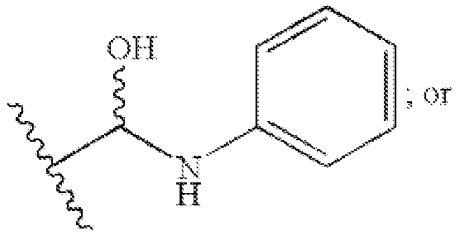
Z is C=O, SO2, COH, CHOH, or NHR4;

R1 is CO2H or oxo (=O);

R2 is H, C(=O)—C1-C6 alkyl, C(=O)O—C1-C6 alkyl, or C(=O)—C3-C8 cycloalkyl;

R3 is optionally substituted C3-C10 aryl; and

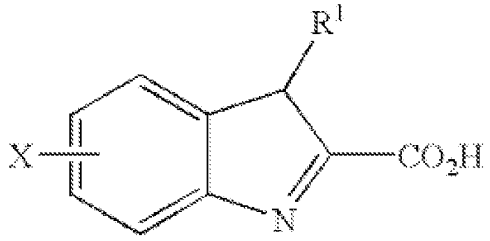
R4 is



; or

R2 and R1 combine with the carbons to which they are attached to form a 6 membered heterocycle that is optionally substituted at one or more of the heteroatoms with C3-C10 aryl, wherein the aryl may be substituted with one or more of C1-C6 alkyl or —O—C1-C6 alkyl, and the heteroatoms in the heterocyclic ring are one or more nitrogen atoms.

[1011] In further embodiments, the NMDA receptor antagonist is a compound according to:



or a pharmaceutically acceptable base or acid addition salt, hydrate, stereoisomer, or mixture thereof, wherein

X is one or more halogen radicals;

R1 is (CH2)n—CO2H, or CH=CHC(=O)NHR2; and

R2 is C3-C10 aryl optionally substituted with one or more of C1-C6 alkyl, —O—C1-C6 alkyl, or halogen; and

n is 0, 1, 2, 3, 4, 5, or 6.

[1012] In an embodiment, the NMDA receptor antagonist is an NMDA receptor glycine site antagonist.

[1013] In an embodiment of the present invention, the NMDA receptor antagonist is ACEA 1021 (liconstinel), GV150526 (Gavestinal), GV196771, MDL 105,519, L-701324, L-687414, RPR 104632, ACPC (SYM2030), ZD9379, AR-R15896AR, or RPR118723.

[1014] In an embodiment, the NMDA receptor antagonist is selected from:

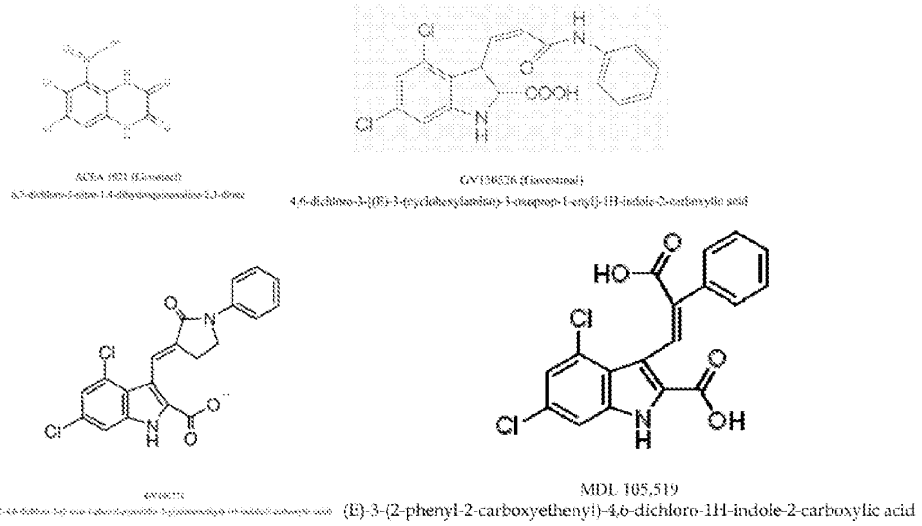
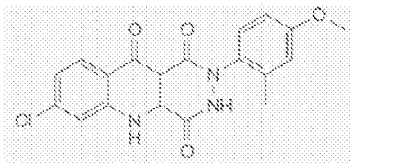
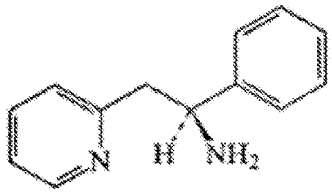


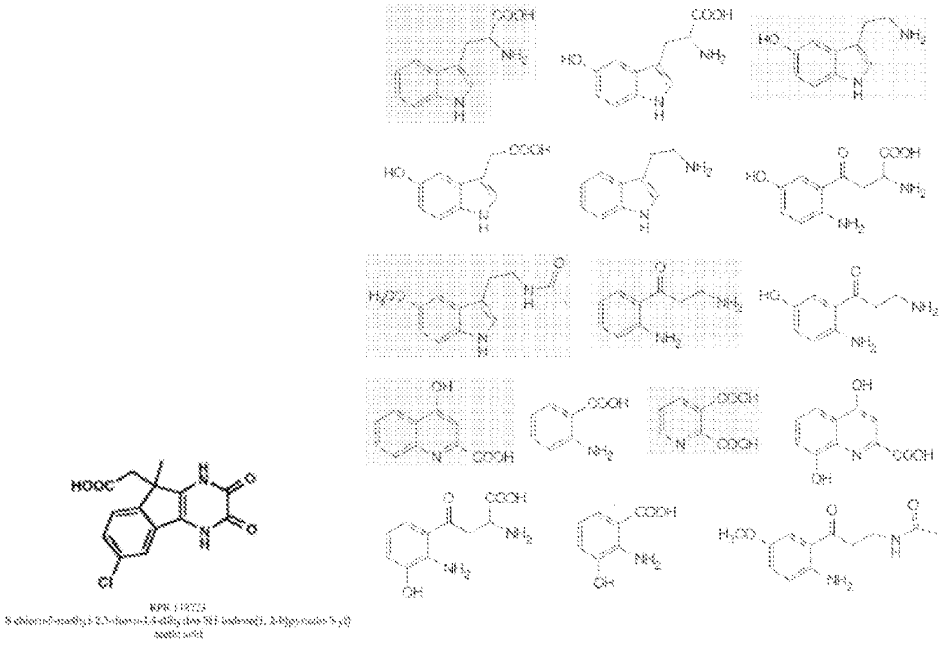
Figure 15



ZD9379



AR-R15896AR
[*RS*]-alpha-phenyl-2-pyridine-ethanamine



, or a pharmaceutically acceptable salt thereof.

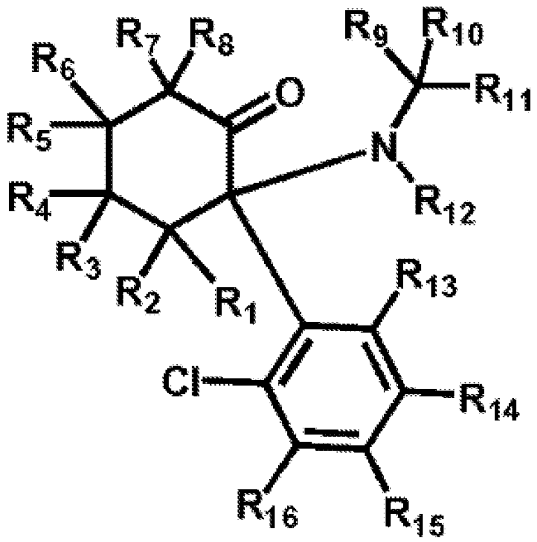
Formula 217

[1015] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 217. Such compounds are described in WO2008/134525, published November 6, 2008 and corresponding to PCT/US2008/061598, filed April 25, 2008, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 217, these references incorporated by reference herein control.

[1016] In an embodiment, the NMDA receptor antagonist is a deuterium-labeled ketamine analogue.

[1017] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 217:

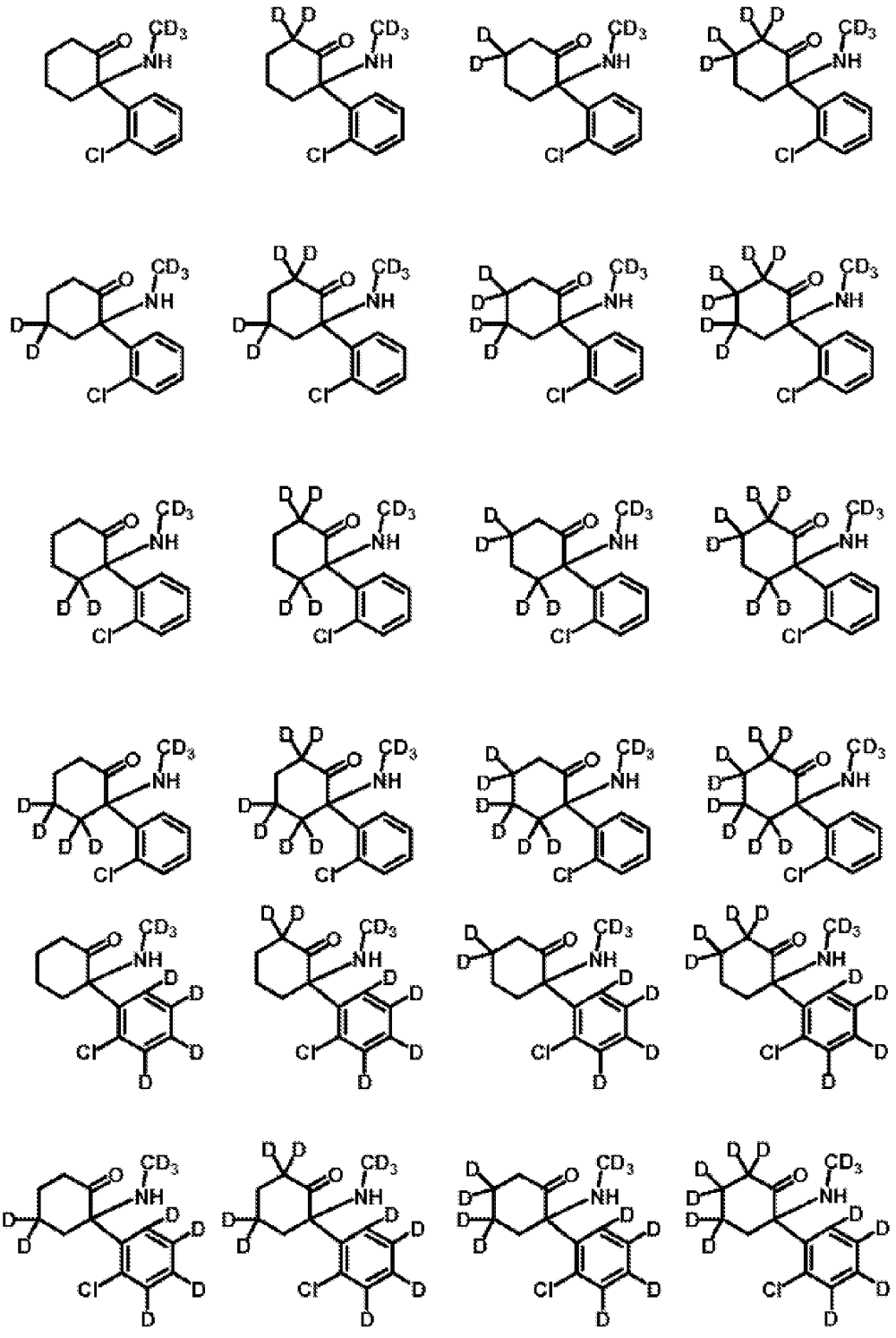
Formula 217

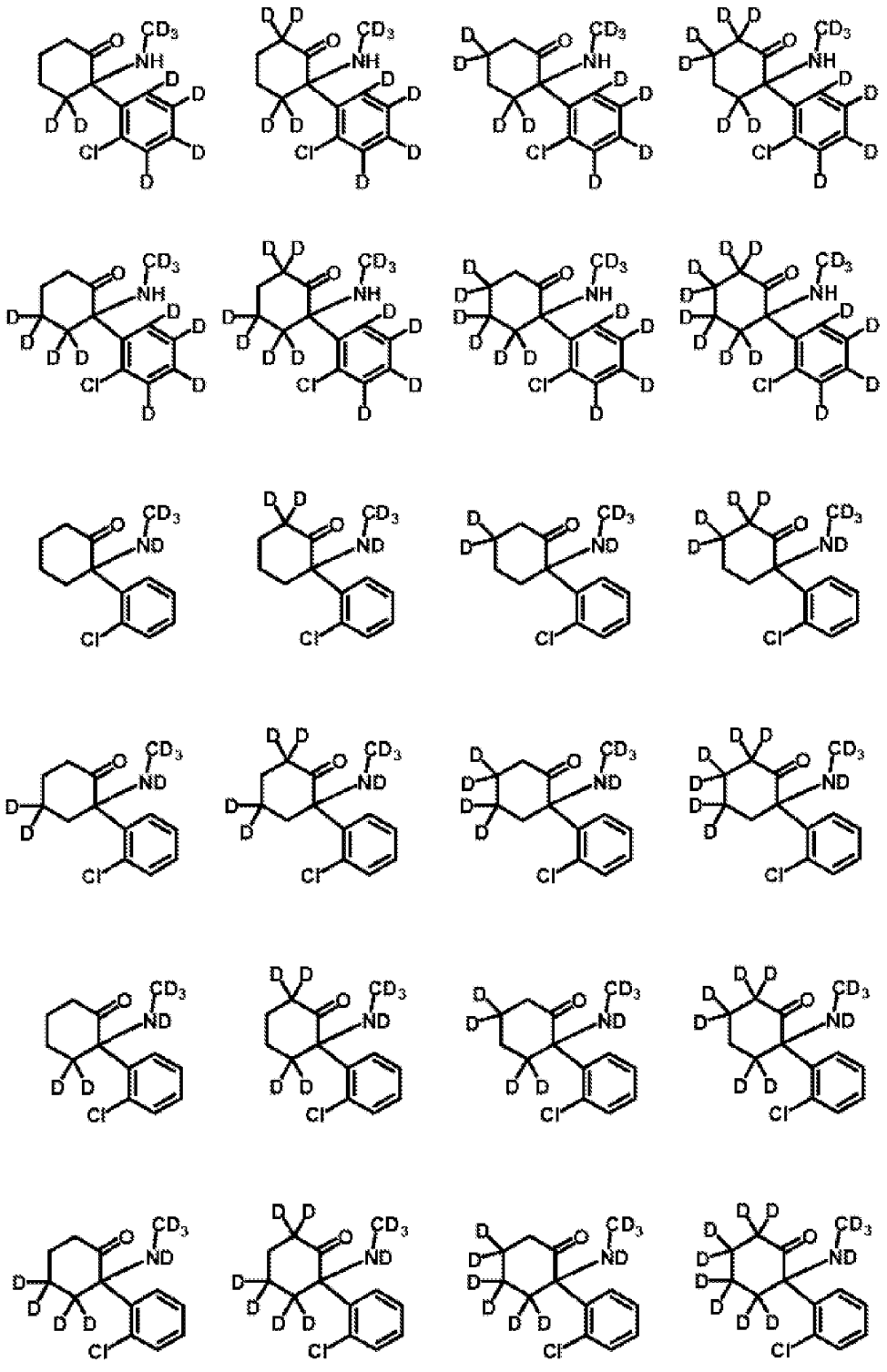


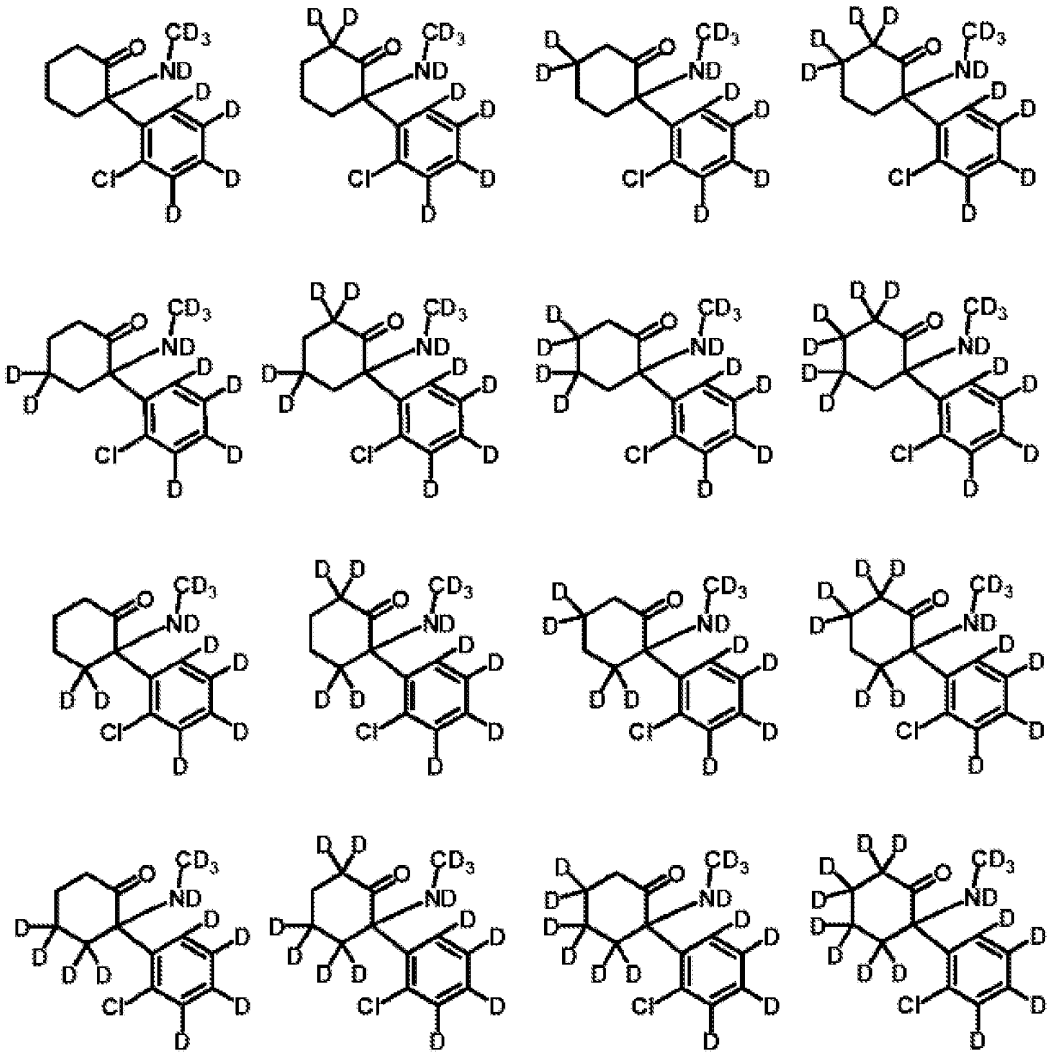
, or a pharmaceutically acceptable salt, solvate, or prodrug thereof; wherein:

R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, and R16 are independently selected from the group consisting of hydrogen and deuterium; and at least one of R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, and R16 is deuterium.

[1018] In further embodiments, the NMDA receptor antagonist is a compound selected from:





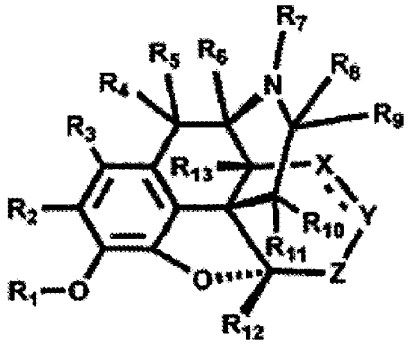


, or a pharmaceutically acceptable salt, solvate or prodrug thereof.

[1019] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 218. Such compounds are described in WO 2008/022285, published February 2008, corresponding to PCT/US2007/076146, filed August 16, 2007 which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 218, these references incorporated by reference herein control.

[1020] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 218:

Formula 218



a single enantiomer, a mixture of a (+)-enantiomer and a (-)-enantiomer, a mixture of about 90% or more by weight of the (-)-enantiomer and about 10% or less by weight of the (+)-enantiomer, a mixture of about 90% or more by weight of the (+)-enantiomer and about 10% or less by weight of the (-)-enantiomer, an individual diastereomer, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

any bond represented by a dashed line and a solid line represents a bond selected from the group consisting of a single bond and a double bond, and any carbon-carbon double bond has a configuration selected from the group consisting of cis and trans;

R2, R3, R4, R5, R6, R8, R9, R10, R11 and R12 are independently selected from the group consisting of hydrogen, and deuterium;

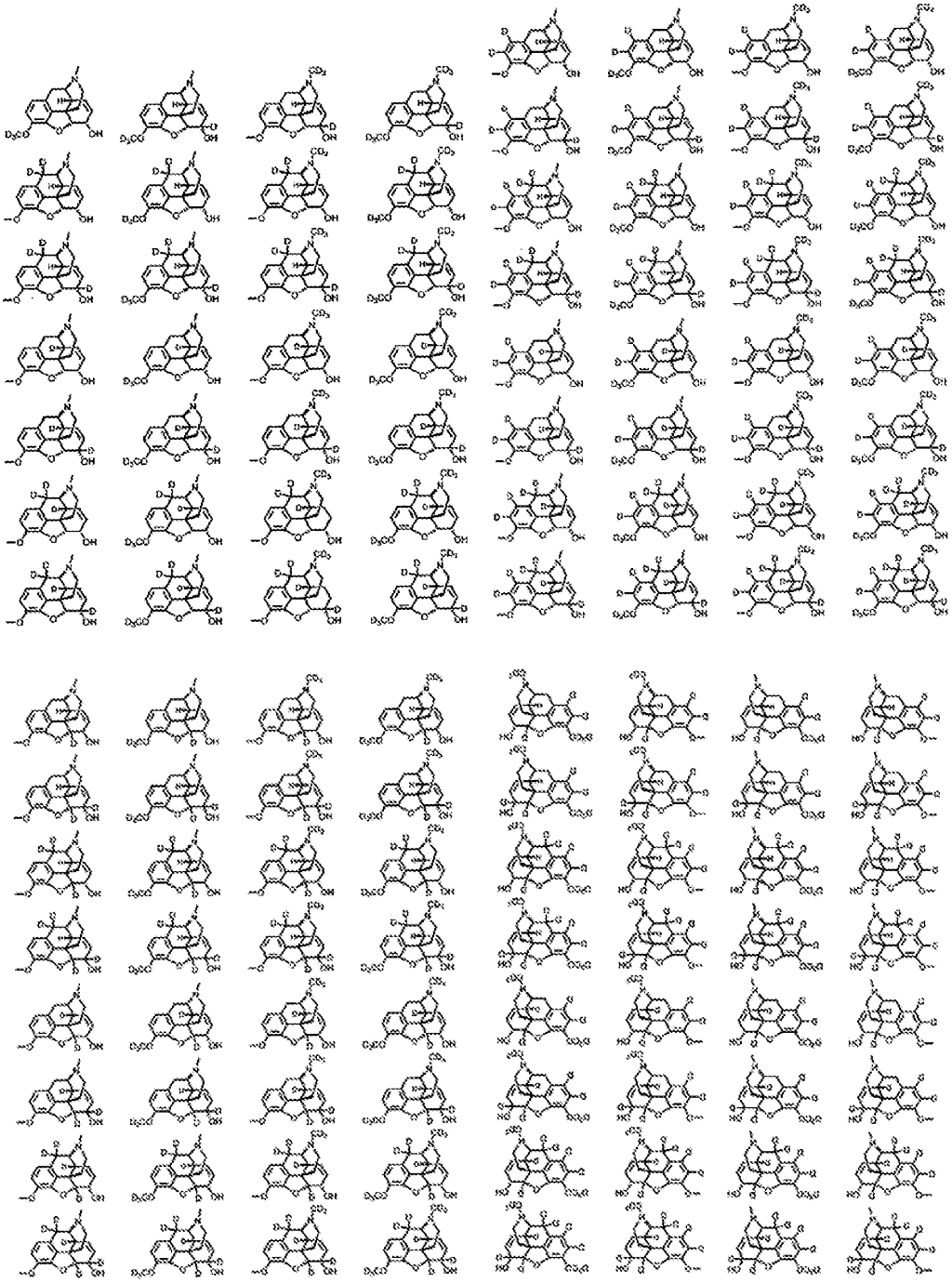
R1 and R7 are independently selected from the group consisting of hydrogen, deuterium, -CH3, -CDH2, -CD2H, and -CD3;

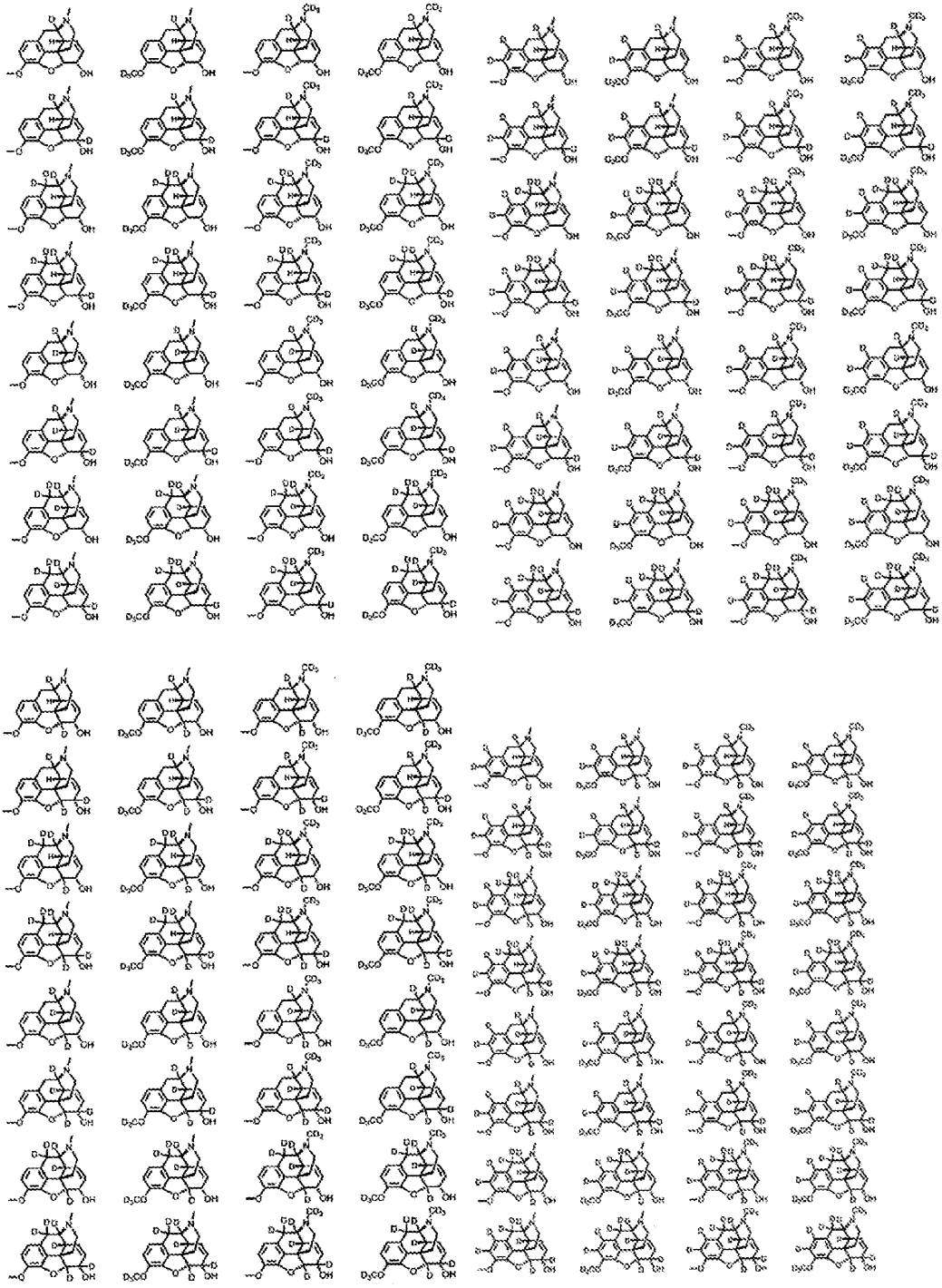
R13 is selected from the group consisting of hydrogen, deuterium, -OH, and -OD;

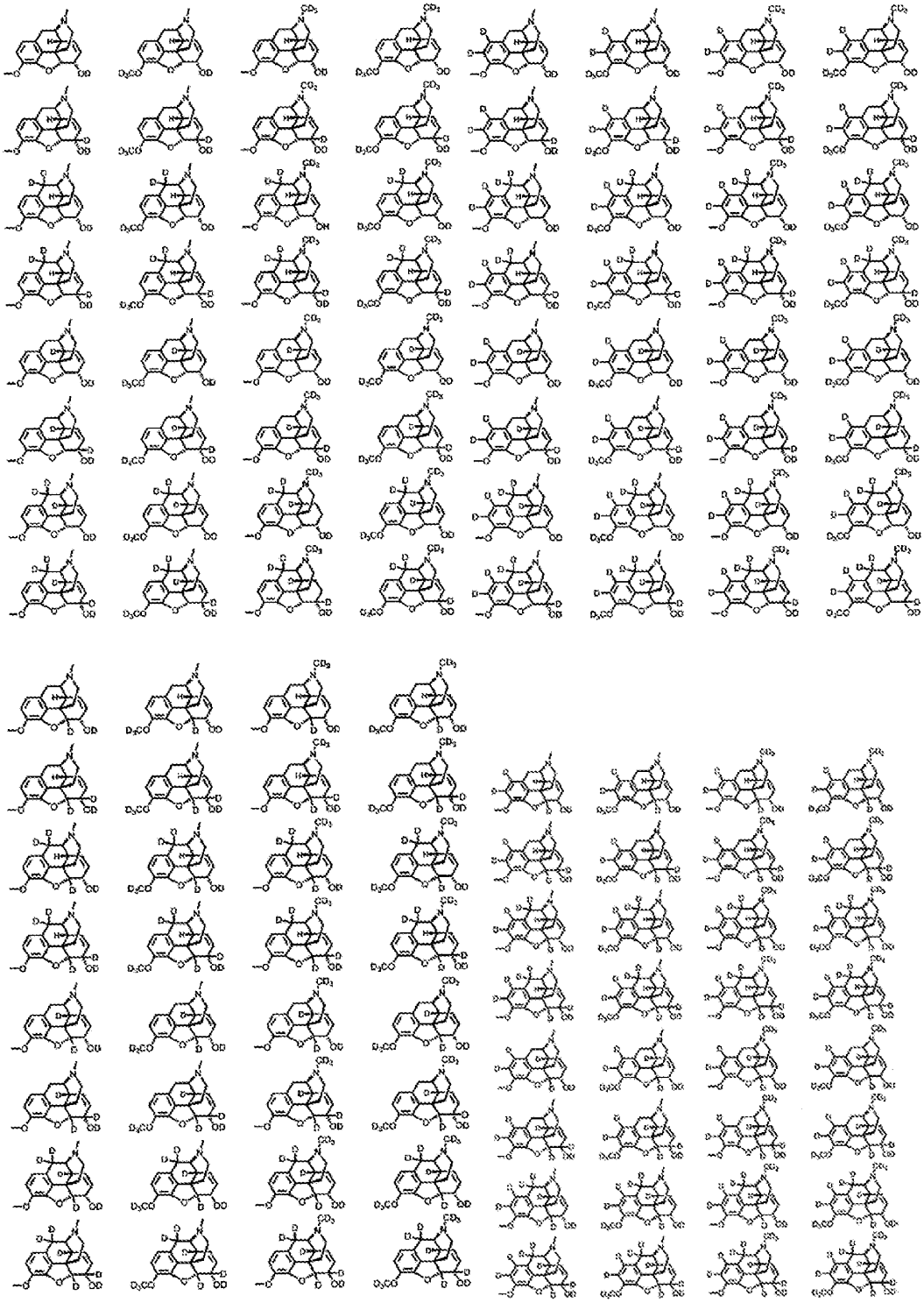
when the bond represented by a dashed line and a solid line represents a double bond, X and Y are independently selected from the group consisting of C-H, and C-D; when the bond represented by a dashed line and a solid line represents a single bond, X and Y are independently selected from the group consisting of CH2, CHD, and CD2;

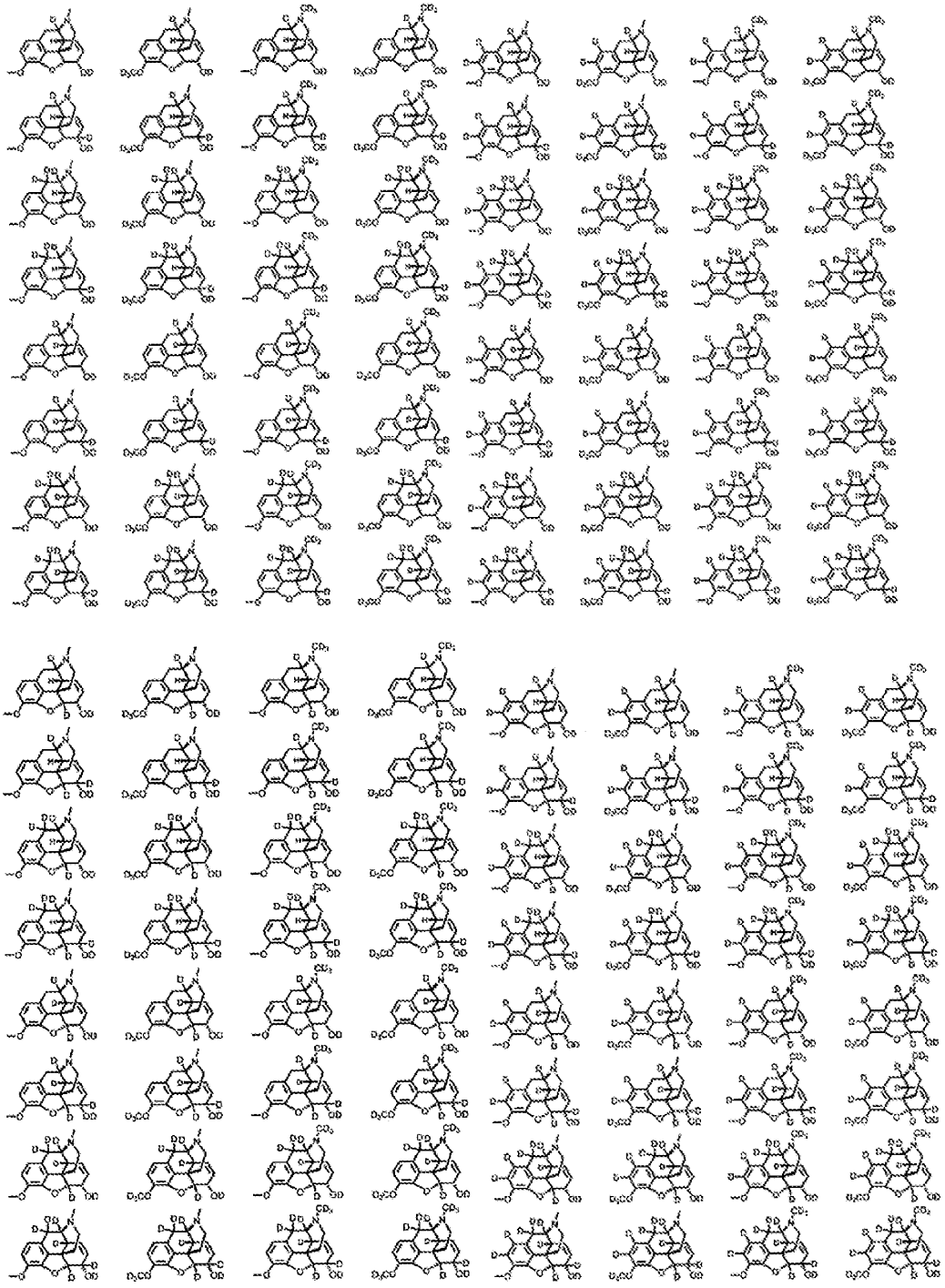
Z is selected from the group consisting of C(H)OH, C(H)OD, C(D)OH, C(D)OD, and carbonyl (C=O); provided that the compound contains at least one deuterium atom and that deuterium enrichment in the compound is at least about 1%.

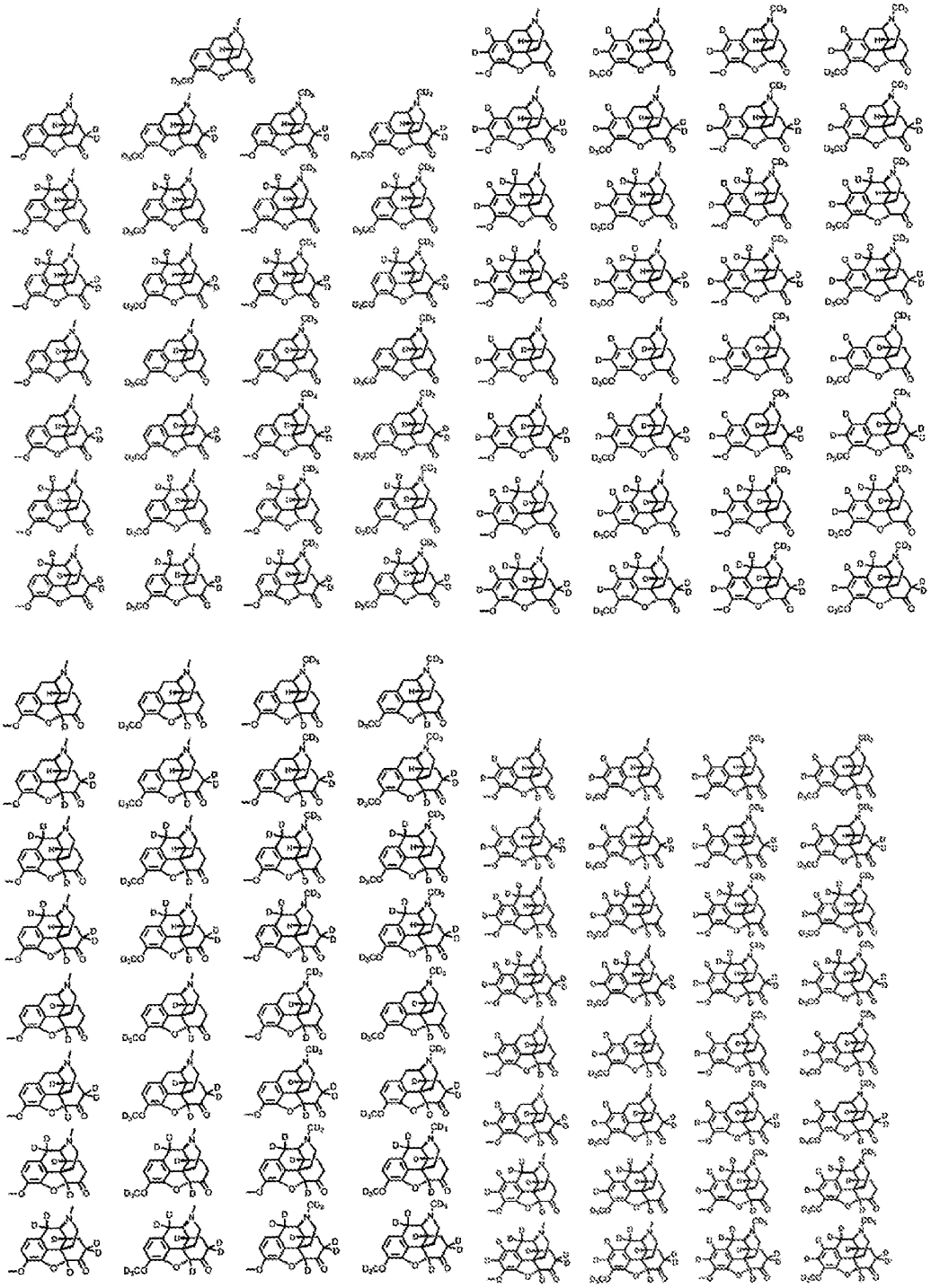
[1021] In an embodiment, the NMDA receptor antagonist is a compound according to:

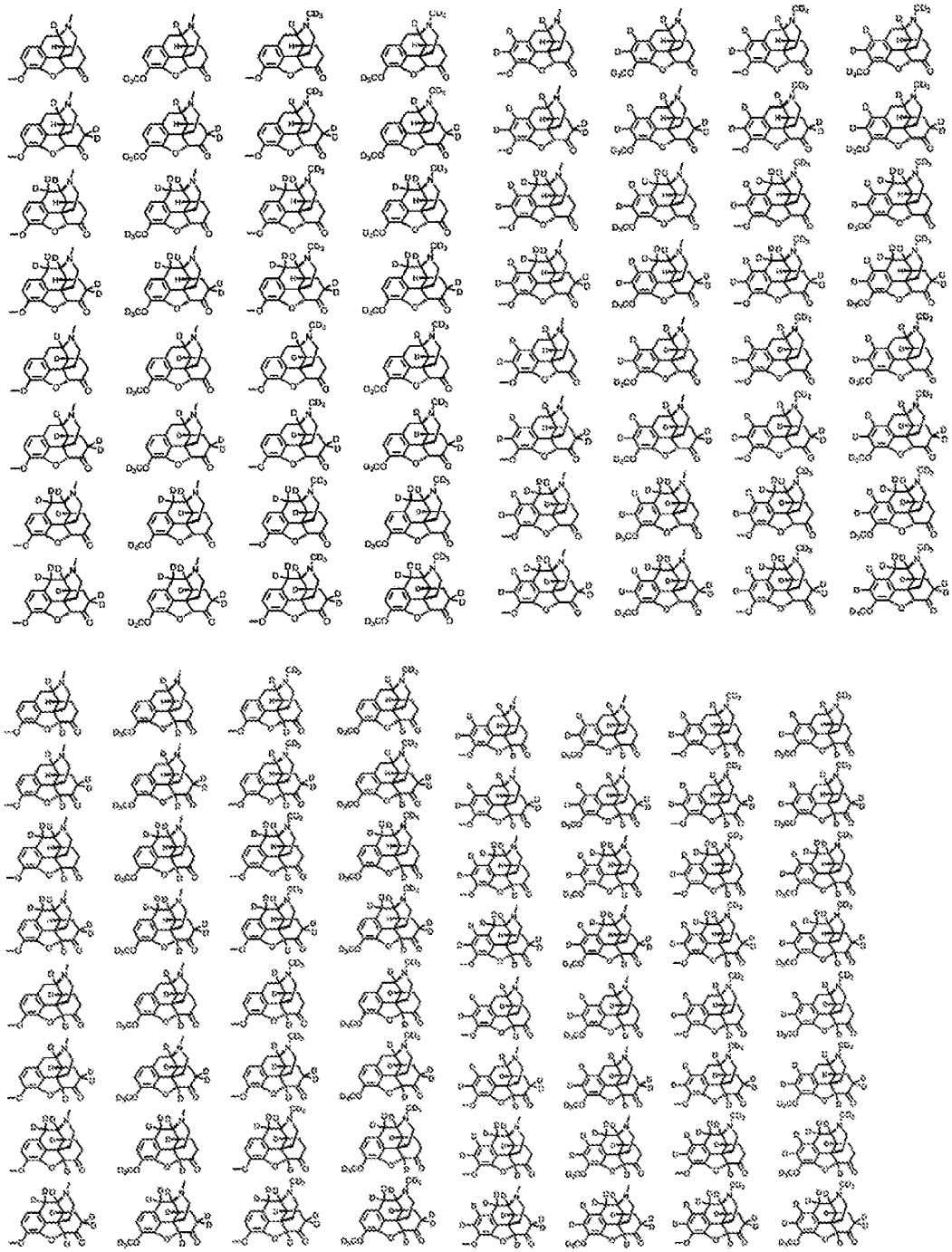


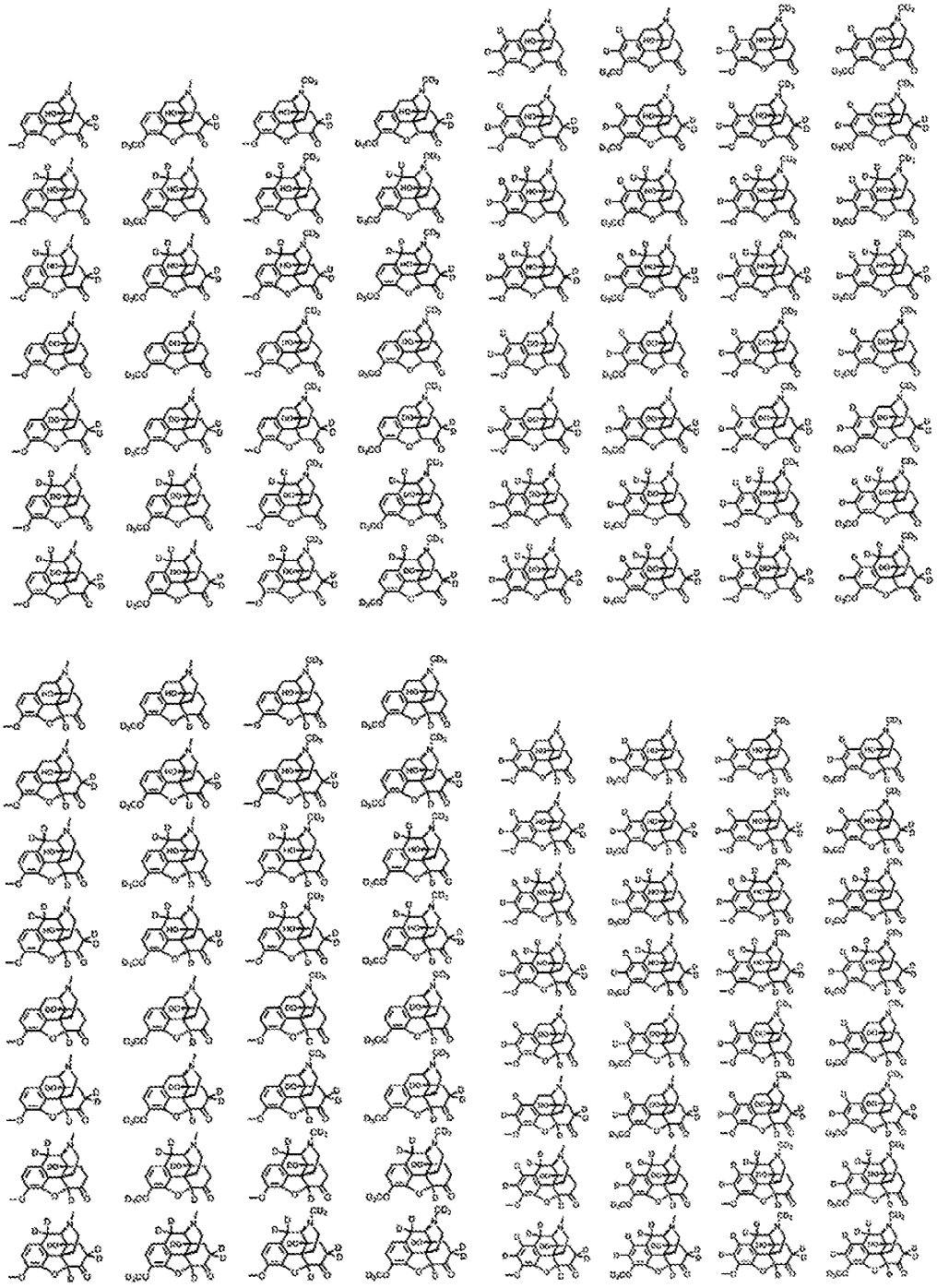


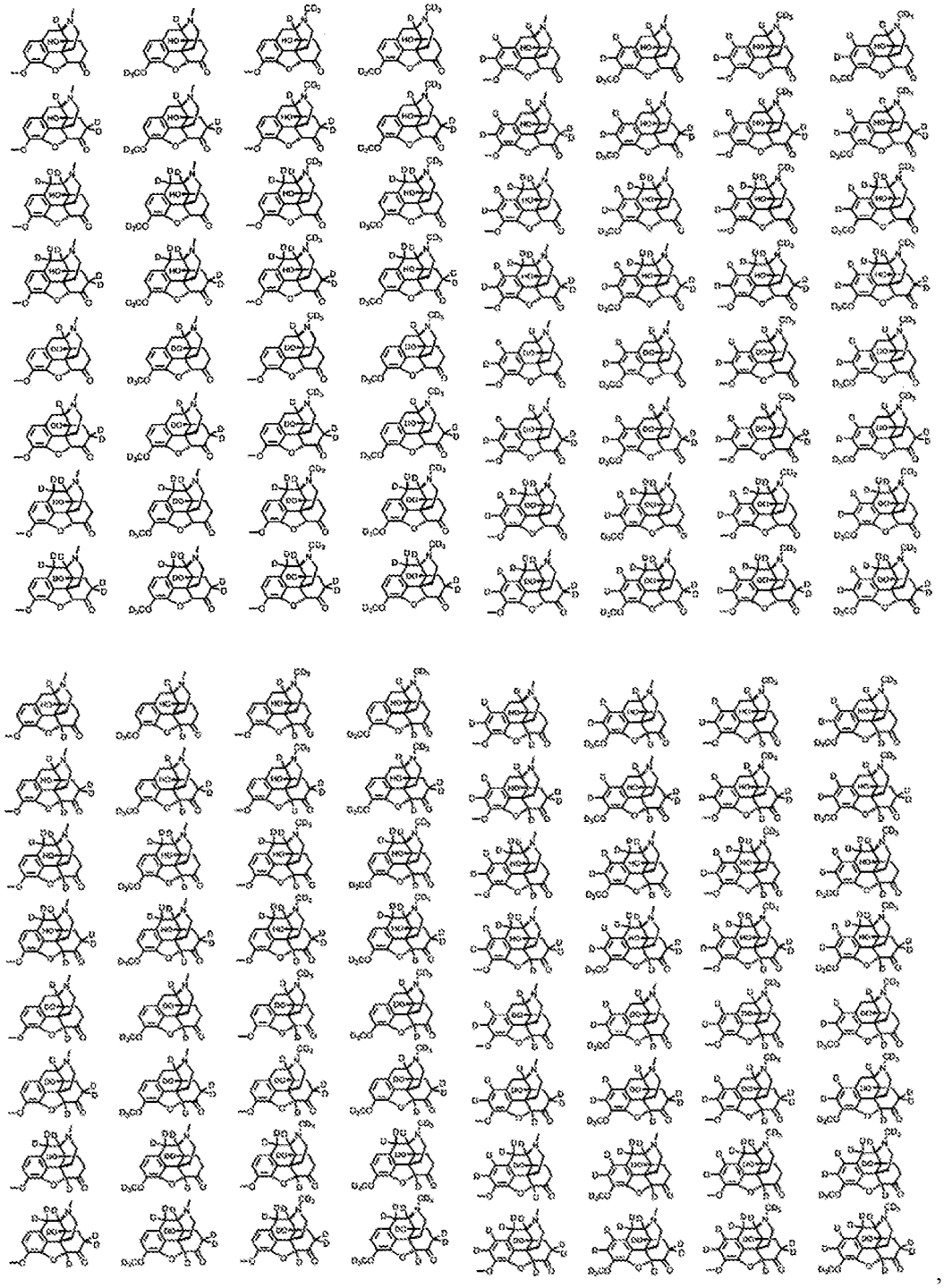












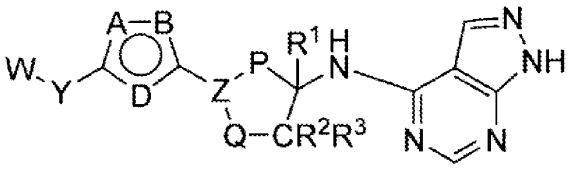
including enantiomers, pharmaceutically acceptable salts, solvates, or prodrugs thereof.

[1022] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 219. Such compounds are described in WO

2006/017409, published February 16, 2006 and corresponding to PCT/US2005/027160, filed July 29, 2005, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 219, these references incorporated by reference herein control.

[1023] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 219:

Formula 219



, wherein W is aryl or heteroaryl, unsubstituted or substituted with 1-5 substituents independently selected from halogen and C1-6 alkyl optionally substituted with one or more substituents selected from halogen, hydroxy, and C1-4 alkoxy, C1 -4 alkoxy, C3-6 cycloalkyl, cyano and N(R4)2;

Y is absent or is selected from C 1-3 alkyl optionally substituted with one or more substituents selected from halogen, hydroxyl and C 1-4 alkoxy, cyclopropyl and C(O);

Z is N and P and Q are C(R4)2, or Z is CR5 and P and Q are C(R5)2;

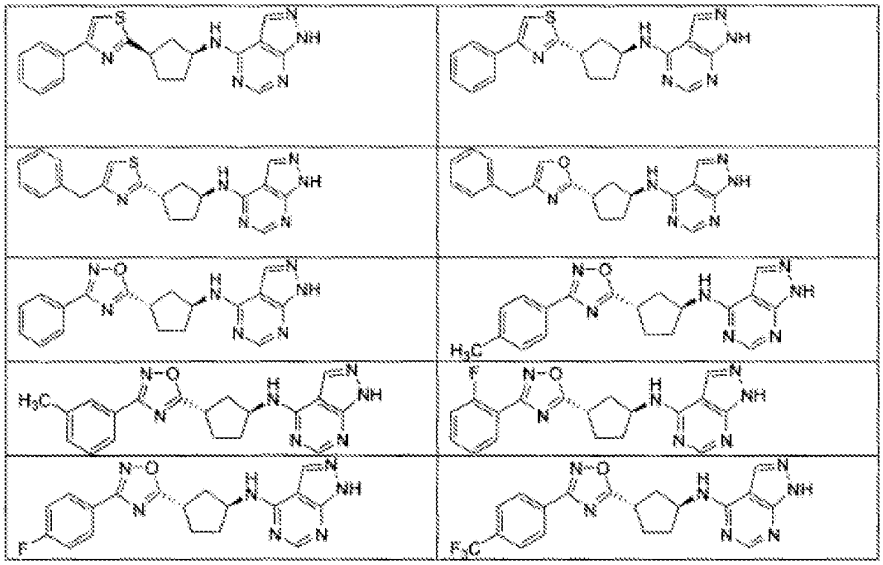
A, B and D are each independently selected from O, CR6, S and NR6;

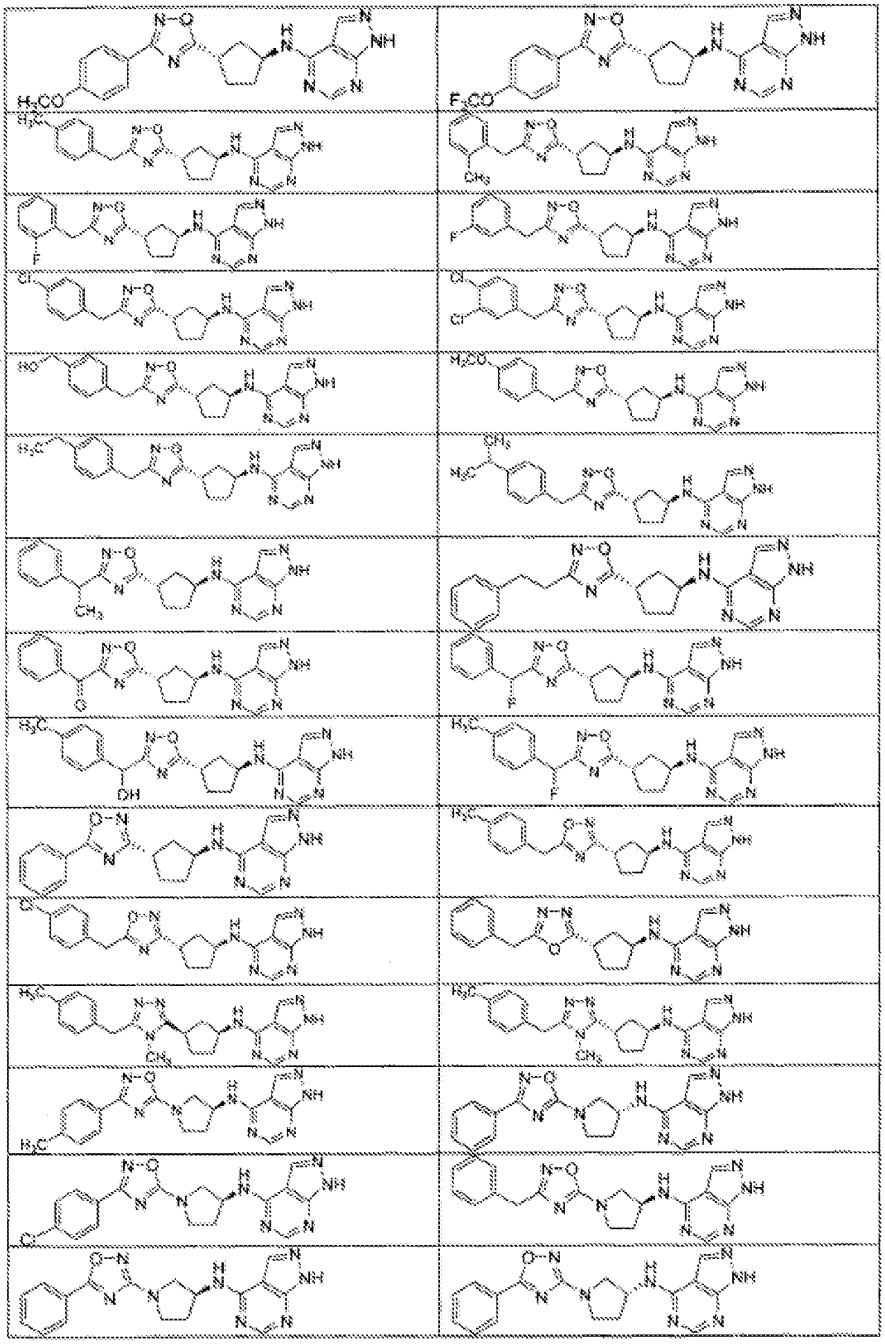
Rl , R4 and R6 are each independently selected from hydrogen or C 1-4 alkyl optionally substituted with one or more of halogen and hydroxyl; and

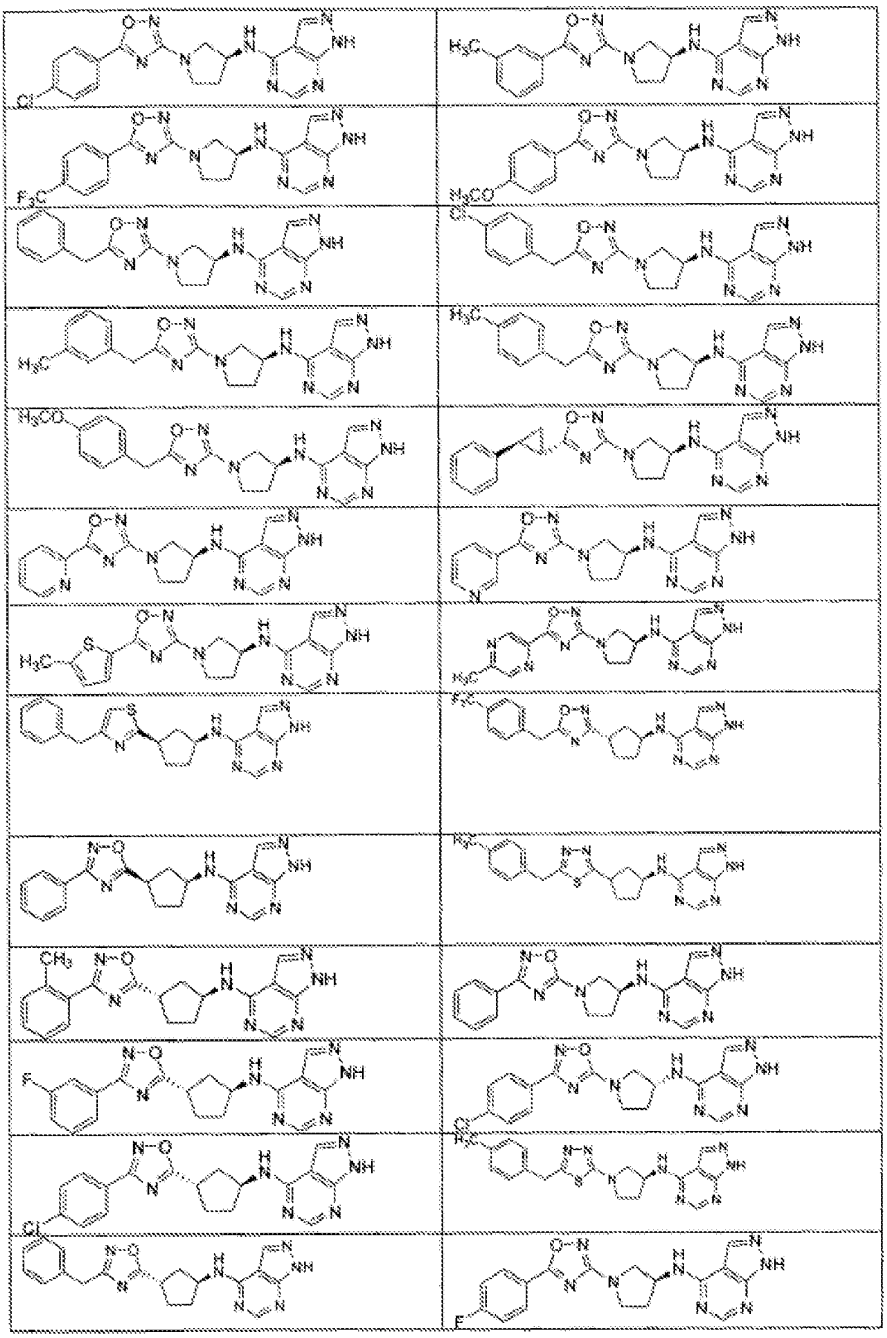
R2, R3; and R5 are each independently selected from hydrogen, halogen, hydroxyl, C 1-4 alkyl optionally substituted with one or more substituents selected from halogen and hydroxyl, C 1-4 alkoxy, cyano and N(R4)2;

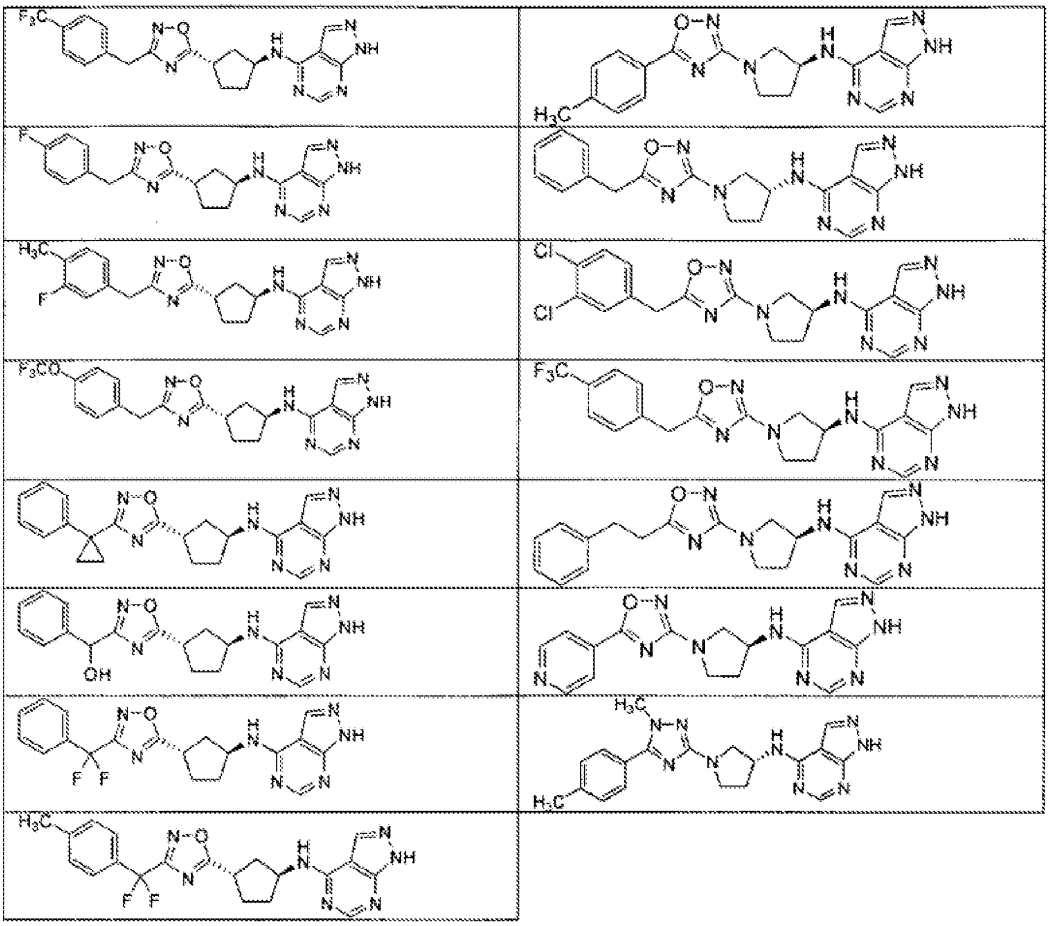
and pharmaceutically acceptable salts and individual enantiomers and stereoisomers thereof.

[1024] In an embodiment, the NMDA receptor antagonist is a compound selected from:







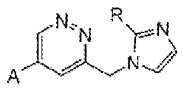
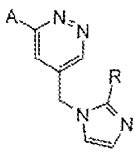


, and pharmaceutically acceptable salts and individual enantiomers and stereoisomers thereof.

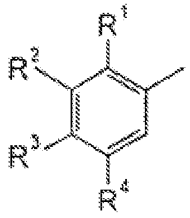
Formula 220

[1025] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 220. Such compounds are described in WO 2003/097637, published November 27, 2003 and corresponding to PCT/EP2003/005151, filed May 16, 2003, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 220, these references incorporated by reference herein control.

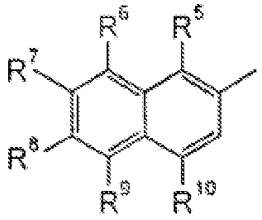
[1026] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 220a or 220b:


IA or

IB

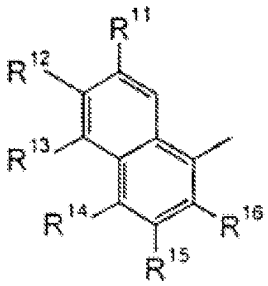
, wherein A is an unsubstituted or substituted cyclic group; and R is a hydrogen or lower alkyl; and pharmaceutically acceptable salts thereof.



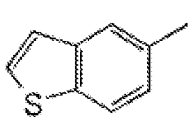
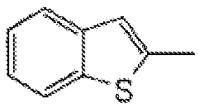
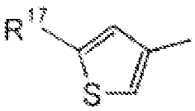
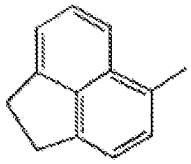
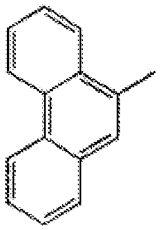
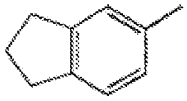
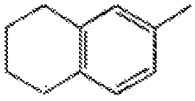
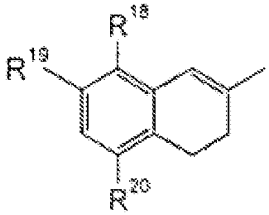
[1027] In an embodiment, A is the group: , and wherein R1, R2, R3, and R4 are independently hydrogen, halogen, CF3, CHF2, C(CH3)F2, C3-C6 cycloalkyl, lower



alkoxy, lower alkyl, OCF3, or phenyl; or A is , and R5, R6, R7, R8, R9, R10 are independently hydrogen, halogen, lower alkyl, lower alkoxy, or CHF2; or A



is , and R11, R12, R13, R14, R15, and R16 are independently hydrogen, halogen, lower alkoxy, or lower alkyl.

[1028] In further embodiments, A is  , or  , or  , wherein R17 is hydrogen or CHF2; or A is  , or  , or  , or  , or  , wherein R18, R19, and R20 are independently hydrogen, lower alkyl or lower alkoxy.

[1029] In further embodiments, the compound is:

5-(3-chloro-4-fluoro-phenyl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
3-(2-methyl-imidazol-1-yl-methyl)-5-(3-trifluoromethyl-phenyl)-pyridazine,
5-(3-difluoromethyl-4-fluoro-phenyl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-[3-(1,1-difluoro-ethyl)-phenyl]-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-[3-(1,1-difluoro-ethyl)-4-fluoro-phenyl]-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-(4-fluoro-3-methyl-phenyl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-(4-chloro-3-methyl-phenyl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-[3-(1,1-difluoro-ethyl)-5-fluoro-phenyl]-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine,
5-(3-difluoromethyl-4-fluoro-phenyl)-3-(2-ethyl-imidazol-1-ylethyl)-pyridazine or
5-(3-cyclopropyl-4-fluoro-phenyl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine.

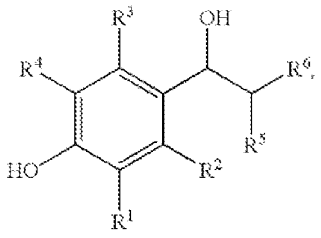
, or 5-benzo[b]thiophen-5-yl-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine. , or
5-(3,4-dihydro-naphthalen-2-yl)-3-(2-methyl-imidazol-1-yl-methyl)-pyridazine hydrochloride.

Formula 221

[1030] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 221. Such compounds are described in US 2002/0072485, published June 13, 2002, corresponding to Application No. 09/969,354, filed October 2, 2001, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 221, these references incorporated by reference herein control.

[1031] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 221:

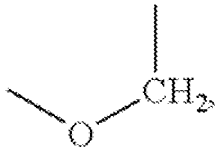
Formula 221



, or a pharmaceutically acceptable acid addition salt thereof, wherein:

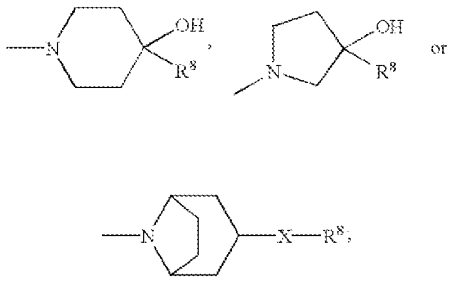
(a) R2 and R5 are taken separately and R1, R2, R3 and R4 are each independently hydrogen, (C1-C6) alkyl, halo, CF3, OH or OR7 and R5 is methyl or ethyl; or

(b) R2 and R5 are, taken together,



thereby forming a chroman-4-ol ring, and R1, R3 and R4 are each independently hydrogen, (C1-C6) alkyl, halo, CF3, OH or OR7;

R6 is



R7 is methyl, ethyl, isopropyl or n-propyl;

R8 is phenyl optionally substituted with up to three substituents independently selected from the group consisting of (C1-C6) alkyl, halo and CF3;

X is O, S or (CH2)n; and

n is 0, 1, 2, or 3.

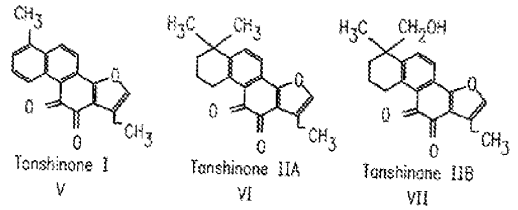
[1032] In an embodiment, the NMDA receptor antagonis is selected from:

(+)-(1S, 2S)-1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;
a pharmaceutically acceptable acid addition salt thereof;
(1S, 2S)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-4-phenylpiperidino)-1-propanol;
a pharmaceutically acceptable acid addition salt thereof;
(3R,4S)-3-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-chroman4,7-diol;
a pharmaceutically acceptable acid addition salt thereof; and
(1R*, 2R*)-1-(4-hydroxy-3-methylphenyl)-2-(4-(4-fluorophenyl)-4-hydroxypiperidin-1-yl)-propan-1 -ol-mesylate.

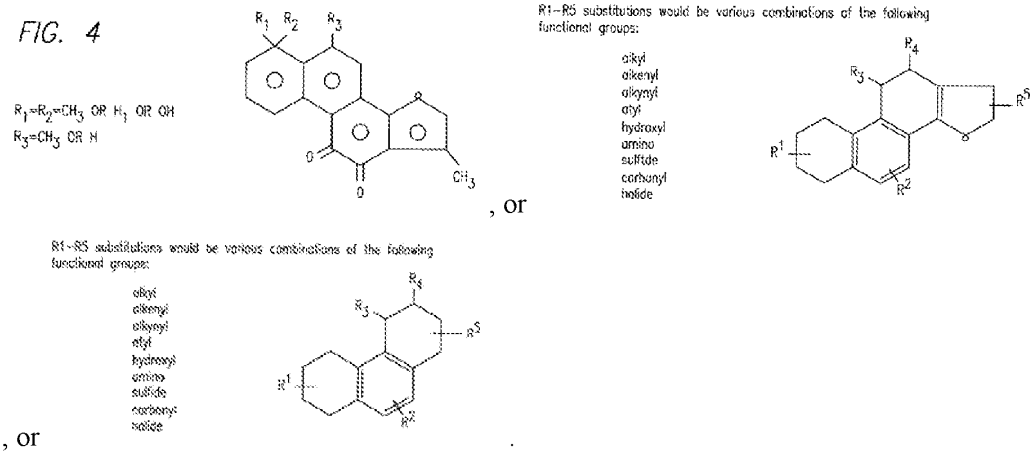
Formula 222

[1033] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 222. Such compounds are described in US 2002/0077352, published June 20, 2002, corresponding to US application No. 09/922,535, filed August 3, 2001, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 222, these references incorporated by reference herein control.

[1034] In an embodiment, the NMDA receptor antagonist is selected from:



[1035] In further embodiments, the NMDA receptor antagonist is:



Formula 223

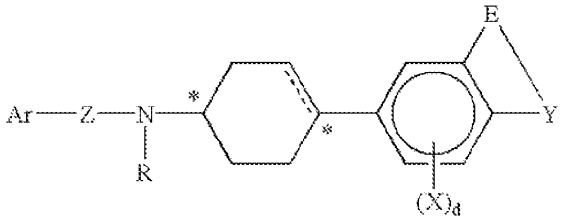
[1036] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 223. Such compounds are described in US 6,794,402, issued September 21, 2004, and PCT/US2001/014763, filed May 8, 2001 and

corresponding to WO/2001/092239, published December 6, 2001, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 223, these references incorporated by reference herein control.

[1037] In an embodiment, the NMDA receptor antagonist is a bicycle-substituted cyclohexylamine.

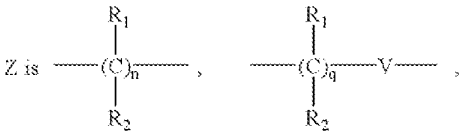
[1038] In an embodiment, the NMDA receptor antagonist is a compound of Formula 223:

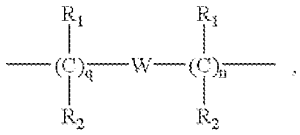
Formula 223

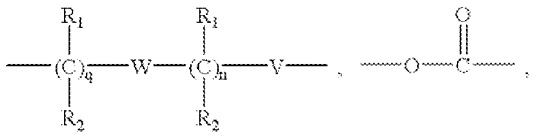


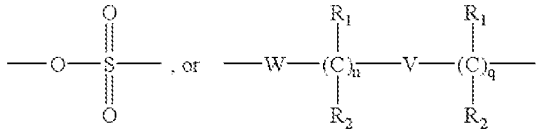
wherein:

Ar is substituted 1 to 3 times or unsubstituted aryl or substituted 1 to 3 times or unsubstituted heteroaryl, which heteroaryl is from 5 to 14 atoms having from 1 to 2 heteroatoms selected from N, O, and S wherein the substituents are selected from the groups F, Cl, Br, I, OH, NH2, SH, CN, NO2, OCH3, OC(O)CH3, CF3, OCH2CH2OH, NHC(O)CH3, NHCH3, or N(CH3)2;

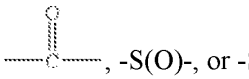
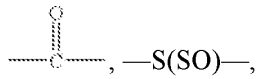
Z is 







, wherein V is $-(CH_2)_n-$,

 , -S(O)-, or $-S(O)_2-$; W is $-(CH_2)_n-$,  , —S(SO)—, —S(O)2—, —O—, —S—, —C≡C—, or entgegen or zusammen —CH(R1)═CH(R2)—, d is an integer from 0 to 2;

n is an integer from 1 to 6;

q is an integer from 0 to 6;

R1 and R2 are independently selected from the group consisting of hydrogen, alkyl, OH, hydroxyalkyl, aminoalkyl, aralkyl, or N(R4)(R5) wherein R4 and R5 are independently selected from hydrogen, alkyl, aralkyl, heteroaryl, heteroaralkyl, aminoalkyl, hydroxyalkyl, and thioalkyl;

R is hydrogen, alkyl, C(O)R6, C(O)OR6, C(O)NHR6, -alkyl-C(O)NH2, aralkyl, (C3-C7 cycloalkyl)-alkyl, hydroxyalkyl, aminoalkyl, amino(hydroxy)alkyl, carboxyalkyl, heteroaralkyl, alkenylalkyl, or OH wherein R6 is alkyl or aralkyl;

X is independently selected from hydrogen or an electron withdrawing group;

—E—Y— is —CH═CH—N(H)—;

—(CH2)2—N(H)—,

—CH═N—N(H)—,

—C(O)—CH2—N(H)—,

—CH2—C(O)—N(H)—,

—CH2—S(O)—N(H)—,
—CH2—S(O)2—N(H)—,
—CH=CH—CH(OH)—,
—(CH2)2—CH(OH)—,
—C(O)—CH2—C(O)—,
—C(O)—NH—C(O)—,
—N=CH—N(H)—,
—N(H)—C(O)—N(H)—,
—O—C(O)—NH—,
—S—C(O)—NH—,
—O—N=CH(OH)—,
—S—N=CH(OH)—,
—N=N—N(H)—,
—CH=CH—CH=C(OH)—,
—(CH2)3—CH(OH)—,
—(CH2)2—S(O)—N(H)—,
—(CH2)2—S(O)2—N(H)—,
—CH=CH—C(O)—N(H)—,
—C(O)—NH—N=C(OH)—,
—CH=N—NH—C(O),
—CH=N(O)—N=C(OH)—,
—N(H)—C(O)—N(H)—C(O)—,
—N=CH—C(O)—NH—,
—O—CH2—C(O)—NH—,
—S—CH2—C(O)—NH—, or
—N(H)—C(O)—C(O)—N(H)—,

- - - denotes a single or double bond; and

* denotes cis or trans or a mixture thereof.

[1039] In further embodiments, the NMDA receptor antagonist is a compound selected from:

6-[trans-4-(3-Phenylpropylamino)cyclohexyl]-3H-benzoxazol-2-one;

6-{trans-4-[2-(4-Fluorophenoxy)ethylamino]cyclohexyl}-3H-benzoxazol-2-one;

6-[trans-4-(2-Phenoxyethylamino)cyclohexyl]-3H-benzoxazol-2-one;

6-{trans-4-[3-(4-Fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;

6-{cis-4-[3-(4-Fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-[trans-4-(2-Phenylsulfanylethylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[cis-4-(2-Phenylsulfanylethylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[4-(3-Phenylpropylamino)cyclohex-1-enyl]-3H-benzoxazol-2-one;
6-{trans-4-[2-(4-Fluorophenylsulfanyl)ethylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[(R)-1-Methyl-3-phenylpropylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[(S)-1-Methyl-3-phenylpropylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[(1S,2S)-2-Hydroxy-2-(4-methoxyphenyl)-1-methylethylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{cis-4-[(1S,2S)-2-Hydroxy-2-(4-methoxyphenyl)-1-methylethylamino]-cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[(1S,2R)-2-Hydroxy-1-methyl-2-phenylethylamino]-cyclohexyl}-3H-benzoxazol-2-one;
6-[cis-4-(3-p-Tolylpropylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[trans-4-(3-p-Tolylpropylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[trans-4-(2-Benzenesulfinylethylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[trans-4-(2-Benzenesulfonylethylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-{trans-4-[Methyl(3-phenylpropyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Fluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(cis-4-{[3-(4-Fluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-[4-(2-Methyl-3-phenylpropylamino)cyclohexyl]}-3H-benzoxazol-2-one
6-{trans-4-[Methyl(2-methyl-3-phenylpropyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-[4-(3-Phenyl-prop-2-ynylamino)cyclohexyl]}-3H-benzoxazol-2-one;
6-{trans-4-[Methyl(3-phenylprop-2-ynyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[2-(4-Fluorophenylsulfanylethyl)methylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[3-(4-Trifluoromethylphenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[Methyl-3-(p-tolylpropyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[Methyl(2-phenoxyethyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[Methyl-3-(4-tifluoromethylphenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[3-(2,4-Difluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(2,4-Difluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Isopropylphenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Isobutylphenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;

6-(trans-4-{[Ethyl-[3-(4-fluorophenyl)propyl]amino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{Ethyl-[3-(4-trifluoromethylphenyl)propyl]amino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{Ethyl-[(R)-1-methyl-3-phenylpropyl]-amino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{Ethyl-[(S)-1-methyl-3-phenylpropyl]-amino}cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[[3-(4-Fluorophenyl)propyl]-(2-hydroxyethyl)amino]-yclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{Cyclopropylmethyl-[3-(4-fluorophenyl)propyl]amino}-cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Fluorophenyl)propyl]furan-3-cylmethylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{Allyl-[3-(4-Fluorophenyl)propyl]amino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Fluorophenyl)propyl]isobutylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{(2-Aminoethyl)-[3-(4-fluorophenyl)propyl]amino}-cyclohexyl)-3H-benzoxazol-2-one;
2-{[3-(4-Fluorophenyl)propyl]-[4-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-cyclohexyl]amino}acetamide;
(S)-6-{trans-4-[1-(4-Fluorophenylsulfanyl)pentan-2-ylamino]cyclohexyl)}3H-benzoxazol-2-one;
(S)-6-{trans-4-[Ethyl(1-(4-fluorophenylsulfanyl)pentan-2-yl)amino]-cyclohexyl}-3H-benzoxazol-2-one;
6-[trans-4-(3-Phenylbutylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-[trans-4-(Methyl-3-phenylbutylamino)cyclohexyl]-3H-benzoxazol-2-one;
6-{trans-4-[3-(4-Chlorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Chlorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(2,4-Dichlorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-[3-(3,5-Difluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(3,5-Difluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-[3-(3,4-Difluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(3,4-Difluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-{[3-(2,3,4-Trifluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(4-{[3-(trans-4-Dimethylaminophenyl)propyl]methylamino}-cyclohexyl)-3H-benzoxazol-2-one;

6-(trans-4-{[3-(2,4,6-Trifluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-[3-(2,4-Dimethylphenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-{4-[Methyl(2,4-dimethylphenylpropyl)amino]cyclohexyl})-3H-benzoxazol-2-one;
6-{trans-4-[3-(2-Chloro-4-fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(2-Chloro-4-fluorophenyl)propyl]methylamino}-cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[3-(4-Chloro-2-fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(4-Chloro-2-fluorophenyl)propyl]methylamino}-cyclohexyl)-3H-benzoxazol-2-one;
6-(trans-4-[3-(4-Fluoro-2-methylphenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-{4-[Methyl(4-fluoro-2-methylphenylpropyl)amino]cyclohexyl})-3H-benzoxazol-2-one;
6-{trans-4-[3-(3-Fluoro-2-methylphenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(3-Fluoro-2-methylphenyl)propyl]methylamino}-cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[3-(2-Fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(2-Fluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[3-(3-Fluorophenyl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{[3-(3-Fluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[(3-Cyclohexylpropyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[(3-Cyclohexylpropyl)methylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-{trans-4-[4-(3-Thiophen-3-yl)propylamino]cyclohexyl}-3H-benzoxazol-2-one;
6-[trans-4-{[3-(3-Thiophen-3-yl)propyl]methylamino}cyclohexyl)-3H-benzoxazol-2-one;
6-{trans-4-[Methyl(3-thiazol-2-ylpropyl)amino]cyclohexyl}-3H-benzoxazol-2-one;
6-(trans-4-{Methyl-[2-(methylphenylamino)ethyl]amino}cyclohexyl)-3H-benzoxazol-2-one;
N-(2-{Methyl-[4-(2-oxo-2,3-dihydrobenzoxazol-6-yl)cyclohexyl]amino}-ethyl)benzamide;
N-{2-[4-(2-Oxo-2,3-dihydrobenzoxazol-6-yl)cyclohexylamino]ethyl}-benzamide;
6-{trans-4-[3-(4-Fluorophenyl)propylamino]cyclohexyl}-3H-benzthiazol-2-one;
3-(4-Fluorophenyl)-N-methyl-N-[trans-4-(2-oxo-2,3-dihydrobenzoxazol-6-yl)cyclohexyl]propionamide;
6-(trans-4-{[3-(4-Fluorophenyl)propyl]methylamino}cyclohexyl)-3H-benzthiazol-2-one;
5-{trans-4-[3-(4-Fluorophenyl)propylamino]cyclohexyl}-1,3-dihydrobenzoimidazol-2-one;

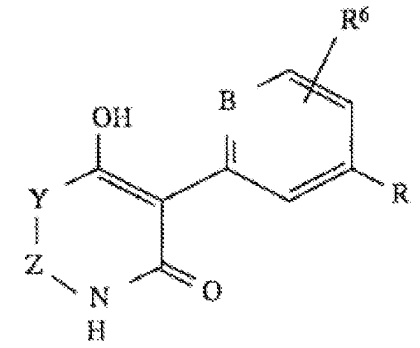
5-(trans-4-{[3-(4-Fluorophenyl)propyl]methylamino}cyclohexyl)-1,3-dihydrobenzoimidazol-2-one;
6-(4-{[3-(4-Fluorophenyl)propyl]methyl-amino}cyclohexyl)-5-methyl-3H-benzoxazol-2-one; and
6-(trans-4-{[3-(4-Fluorophenyl)propyl]methylamino}cyclohexyl)-5-methoxy-3H-benzoxazol-2-one.

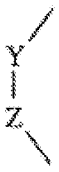
Formula 224

[1040] In an embodiment, the NMDA receptor antagonist may be selected from one of the following compounds according to Formula 224. Such compounds are described in, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 224, these references incorporated by reference herein control.

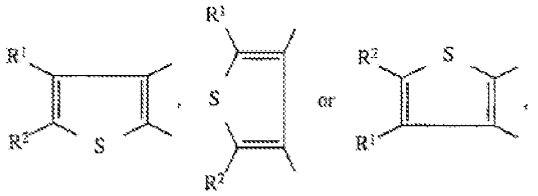
[1041] In an embodiment, the NMDA receptor antagonist is a compound according to Formula 224:

Formula 224:

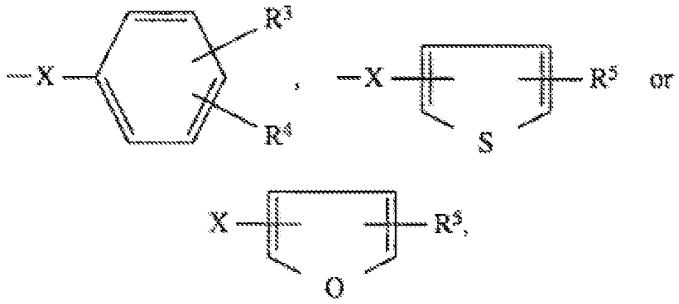




, wherein B is CH or N, is



, R is H,



,

R1, R2, and R5 are independently H, A, or halogen,

R3 and R4 are independently H, A, OH, OA, halogen, CF3, NO2, NH2, NHA, N(A)2 or NHAc, R6 is H or halogen, X is -CH2-, -CO-, -O-, -NH-, -NA- or -S-, A is alkyl having 1-4 carbon atoms, Ac is an alkanoyl having 1-6 carbon atoms, or benzoyl and halogen is F, Cl, Br, or I, and pharmaceutically acceptable salts thereof.

[1042] In an embodiment, the NMDA receptor antagonist is 2-Chloro-3-methyl-4-hydroxy-5-phenyl-6,7-dihydrothieno-2,3-bipyridin-6-one

Peptide NMDA Receptor Antagonists

[1043] In an embodiment, the NMDA receptor antagonist is a peptide agent. For ease of reference, the peptide NMDA receptor antagonists are classified under Formula numbers, each of which may refer to one or more different peptide sequences. Where a sequence

homology percentage is recited, e.g. at least 80% sequence homology, it is contemplated that higher percentages are also contemplated. Specifically, where the term "at least 80% sequence homology" or, for short, "at least 80% homology" is recited, it should be understood that other percentages including at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, and at least 99% sequence homology are expressly contemplated and included.

[1044] In various embodiments, the peptides may be useful as therapeutic agents. In further various embodiments, the peptides may be produced *in vivo* from a therapeutic agent containing a polynucleotide sequence encoding the peptide. In an embodiment, a polynucleotide sequence may be a DNA sequence or an RNA sequence. In an embodiment, the sequence may be delivered or introduced to the patient by a plasmid or vector. It should be appreciated that any known delivery technique or construct is contemplated.

Formula 250

[1045] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 250. Such peptides are described in US 10,689,418, issued June 23, 2020 and corresponding to Application No. 16/065,078, filed June 21, 2018, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 250, these references incorporated by reference herein control.

[1046] In an embodiment, the NMDA receptor antagonist is a peptide comprising the amino acid sequence GEDDLQDNQDLIRDKSN, or a sequence having at least 80% sequence homology thereto.

[1047] In an embodiment, the NMDA receptor antagonist is a peptide comprising the amino acid sequence GEDDYQDAQDLIRDKSN, or a sequence having at least 80% sequence homology thereto.

[1048] In an embodiment, the NMDA receptor antagonist is a peptide comprising the amino acid sequence KLGMRSELQIDNDQDAD, or a sequence having at least 80% sequence homology thereto.

Formula 251

[1049] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 251. Such peptides are described in WO

2021/137245, published July 8, 2021 corresponding to PCT/IL2021/050013, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 251, these references incorporated by reference herein control.

[1050] In an embodiment, the NMDA receptor antagonist is a natural or modified conantokin-P peptide.

[1051] In an embodiment, the NDMA receptor antagonist is a peptide comprises one or more amino acid sequences according to:

WT Con-P (Conus purpurascens)	GEγγHSKYQγCLRγIRVNKVQQγC
WT Con-G (Conus geographus)	GEγγLQγNQγLIRγKSN
WT Con-Pr3 (Conus parius)	GEPγVAKWAγGLRγKAASN

, or one or more amino acid sequences having at least 80% sequence homology thereto.

[1052] In an embodiment, the NMDA receptor antagonist comprises one or more amino acid sequences according to:

Naked Con-P	GEEEHSKYQECLREIRVNKVQQEC
Ala-sub Con-P	GAAAHSKYQACLRAIRVNKVQQAC
Asp-Sub Con-P	GDDDHSKYQDCLRDIRVNKVQQDC
Gly-Sub Con-P	GGGGHSKYQGCLRGIRVNKVQQGC
Naked Con-G	GEEELQENQELIREKSN
Naked Con-G E7A	GEEELQANQELIREKSN
S. (short) Naked Con-G 1-13	GEEELQENQELIR
S. Naked Con-G E7A 1-13	GEEELQANQELIR
Alanine-substituted Con-G	GAAALQANQALIRAKSN
Naked Con-Pr3	GEPEVAKWAEGLREKAASN
Con-G-like APP (cAPP)	ADTDYADGSEDKVVE
Scrambled naked Con-G	NELQQESILEPKENEGE

. or one or more amino acid sequences having at least 80% sequence homology thereto.

Formula 252

[1053] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 252. Such peptides are described in WO 2019/074858, published April 18, 2019, corresponding to PCT/US2018/054889, filed October 8, 2018, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 252, these references incorporated by reference herein control.

[1054] In an embodiment, the NMDA receptor antagonist is a peptide comprising one or more amino acid sequences according to:

GSMCMPCFTTDHQMARRCDDCCGGRGRGRCYGPQCLCR
GSEVIRCSGSKQCYGPCKQQTGCTNSKCMNKVCKCYGCG
GSSEKDCIKHLQRCRENKDCCSKKCSRRGTNPEKRCR
GSSCAKPRENCNRMNILCCRGECVCPTFGDCFCYGD
GSGVPINVKCRGSRDCLDPCKKAGMRFGKCINSKCHCTP
GSVRIPVSCKHSGQCLKPCKDAGMRFGKCMNGKCDCTPK
GSDCVRFWGKCSQTSDCCPHLACKSKWPRNICVWDGSVG
GSMCMPCFTTRPDMAQQCRACCKGRGKCFGPQCLCGYD
GSGCFGYKCDYYKGCCSGYVCSPTWKWCVRPGPGR

GSQVQTNVKCQGGSCASVCRREIGVAAGKCINGKCVCYRN
GSGDCLPHLKRCKENNDCCSKKCKRRGANPEKRCR
GSNFKVEGACSKPCRKYCIDKGARNGKCINGRCHCYY
GSQKILSNRCNNSSECIPHCIRIFGTRAAKCINRKCYCYP
GSDRDSCIDKSRCSKYGYYQECQDCCKKAGHNGGTCMFFKCKCA
GSAVCNLKRCQLSCRSLGLLGKCIGDKCECVKHG
GSQFCGTNGKPCVNGQCCGALRCVVTYHYADGVCLKMNP
GSRPTDIKCSASYQCFPVCKSRFGKTNGRCVNGLCDCF
GSNCAGYMRECKEKLCCSGYVCSSRWKWCVLPAPWRR
GSQFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS
GSQIDTNVKCSGSSKCVKICIDRYNTRGAKCINGRCTCYP
GSAEIIRCSGTRECYAPCQKLTGCLNAKCMNKACKCYGCV
GSSDYCSNDFCFFSCRRDRCARGDCENGKCVCKNCHLN
GSCIGEGVPCDENDPRCCFGLVCLKPTLHGIWYKSYYCYKK
GSSCAKPGEMCMRIKCCDGQCGCNRGTGRCFCK
GSACLAEYQKCEGSTVPCCPGLSCSAGRFRKTKLCTK
GSVVIGQRCYRSPDCYSACKKLVGKATGKCTNGRCDC
GSACQFWSCNSSCISRGYRQGYCWGIQYKYCQCQ
GSRCPPCFTTNPNMEADCRKCCGGRGYCASYQCICPGG
GSVFINVKCRGSPECLPKCKEAIGKSAGKCMNGKCKCYP
GSQVSTNKKCSNTSQCYKTCEKVVGVAAGKCMNGKCICYP
GSECLEIFKACNPSNDQCCKSSKLVCSRKTRWCKYQIG
GSQDKCKKVYENYPVSKCQLANQCNYDCKLDKHARSGECFYDEKRNL QCICDYCEY
GSGVPINVRCRGSRDCLDPCRRAGMRFGRCINSRCHCTP
GGYSRCQLQGFNCVVRSYGLPTIPCCRGLTCRSYFPGSTYGRCQRY
GSMCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLCR
GSAQEPVKGPVSTKPGSCPIILIRCAMLNPPNRCLKDTDCPGIKKCCEGSC GMACFVPQ
GSMCMPCFTTDPNMAKKCRDCCGGNGKCFGPQCLCNR
GSGIGDPVTCLKSGAICHPVFCPRRYKQIGTCGLPGTKCCKKP
GSGVPTDVKCRGSPQCIQPCKDAGMRFGKCMNGKCHCTPK
GSRCPPCFTTNPNMEADCRKCCGGRGYCASYQCICPGG
MCMPCFTTDHQMARRCDDCCGGRGRGRCYGPQCLCR
EVIRCSGSKQCYGPCKQQTGCTNSKCMNKVCKCYGCG
SEKDCIKHLQRCRENKDCCSKKCSRRGTNPEKRCR

SCAKPRENCNRMNILCCRGECVCPTFGDCFCYGD
GVPINVKCRGSRDCLDPCKKAGMRFGKCINSKCHCTP
VRIPVSCKHSGQCLKPCKDAGMRFGKCMNGKCDCTPK
DCVRFWGKCSQTSDCCPHLACKSKWPRNICVWDGSVG
MCMPCFTTRPDMAQQCRACCKGRGKCFGPQCLCGYD
GCFGYKCDYYKGCCSGYVCSPTWKWCVRPGPGR
QVQTNVKCQGGSCASVCRREIGVAAGKCINGKCVCYRN
GDCLPHLKRCKENNDCCSKKCKRRGANPEKRCR
NFKVEGACSKPCRKYCIDKGARNGKCINGRCHCYY
QKILSNRCNNSSECIPHCIRIFGTRAAKCINRKCYCYP
DRDSCIDKSRCSKYGYYQECQDCCKKAGHNGGTCMFFKCKCA
AVCNLKRCQLSCRSLGLLGKCIGDKCECVKHG
QFCGTNGKPCVNGQCCGALRCVVTYHYADGVCLKMNP
RPTDIKCSASYQCFPVCKSRFGKTNGRCVNGLCDCF
NCAGYMRECKEKLCCSGYVCSSRWKWCVLPAPWRR
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS
QIDTNVKCSGSSKCVKICIDRYNTRGAKCINGRCTCYP
AEIIRCSGTRECYAPCQKLTGCLNAKCMNKACKCYGCV
SDYCSNDFCFFSCRRDRCARGDCENGKCVCKNCHLN
CIGEGVPCDENDPRCCFGLVCLKPTLHGIWYKSYYCYKK
SCAKPGEMCMRIKCCDGQCGCNRGTGRCFCK
ACLAEYQKCEGSTVPCCPGLSCSAGRFRKTKLCTK
VVIGQRCYRSPDCYSACKKLVGKATGKCTNGRCDC
ACQFWSCNSSCISRGYRQGYCWGIQYKYCQCQ
RCPPCFTTNPNMEADCRKCCGGRGYCASYQCICPGG
VFINVKCRGSPECLPKCKEAIGKSAGKCMNGKCKCYP
QVSTNKKCSNTSQCYKTCEKVVGVAAGKCMNGKCICYP
ECLEIFKACNPSNDQCCKSSKLVCSRKTRWCKYQIG
QDKCKKVYENYPVSKCQLANQCNYDCKLDKHARSGECFYDEKRNLQCI CDYCEY
GVPINVRCRGSRDCLDPCRRAGMRFGRCINSRCHCTP
YSRCQLQGFNCVVRSYGLPTIPCCRGLTCRSYFPGSTYGRCQRY
MCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLCR
AQEPVKGPVSTKPGSCPIILIRCAMLNPPNRCLKDTDCPGIKKCCEGSCG MACFVPQ
MCMPCFTTDPNMAKKCRDCCGGNGKCFGPQCLCNR

GIGDPVTCLKSGAICHPVFCPRRYKQIGTCGLPGTKCCKKP
GVPTDVKCRGSPQCIQPCKDAGMRFGKCMNGKCHCTPK
RCPPCFTTNPNMEADCRKCCGGRGYCASYQCICPGG

, or one or more amino acid sequences having at least 80% homology thereto.

Formula 253

[1055] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 253. Such peptides are described in CN 109553685, filed September 25, 2017 which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 253, these references incorporated by reference herein control.

[1056] In an embodiment, the NMDA receptor antagonist is a polypeptide comprising one or more of an NR2B (NMDA receptor subunit NR2B) sequence, a CTM (chaperone-mediated autophagy targeting motif) sequence, and a cell-penetrating peptide (such as a TAT cell-penetrating peptide or others).

[1057] In an embodiment, the NMDA receptor antagonist comprises one or more of an TAT cell-penetrating peptide sequence having a polypeptide sequence having at least 80% homology to YGRKKRRQRRR; an NR2B peptide sequence having a polypeptide sequence having at least 80% homology to RRPPRSPDHKRYFRDKE; and a CTM sequence having at least 80% homology to KFERQKILDQRFFE.

[1058] In further embodiments, the NMDA receptor antagonist comprises the sequence YGRKKRRQRRRRRPPRSPDHKRYFRDKEKFERQKILDQRFFE, or a sequence having at least 80% homology thereto.

Formula 254

[1059] In an embodiment, the NMDA expression may be selectively reduced by administration or dosing with a peptide according to Formula 254. Such peptides are described in WO2019/036511, published February 21, 2019 and corresponding to PCT/US2018/046770, filed August 14, 2018, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 254, these references incorporated by reference herein control.

[1060] In an embodiment, the peptide comprises the polypeptide sequence VSGLNPSLWSIFGLQFILLWLVSGSRHYLW or

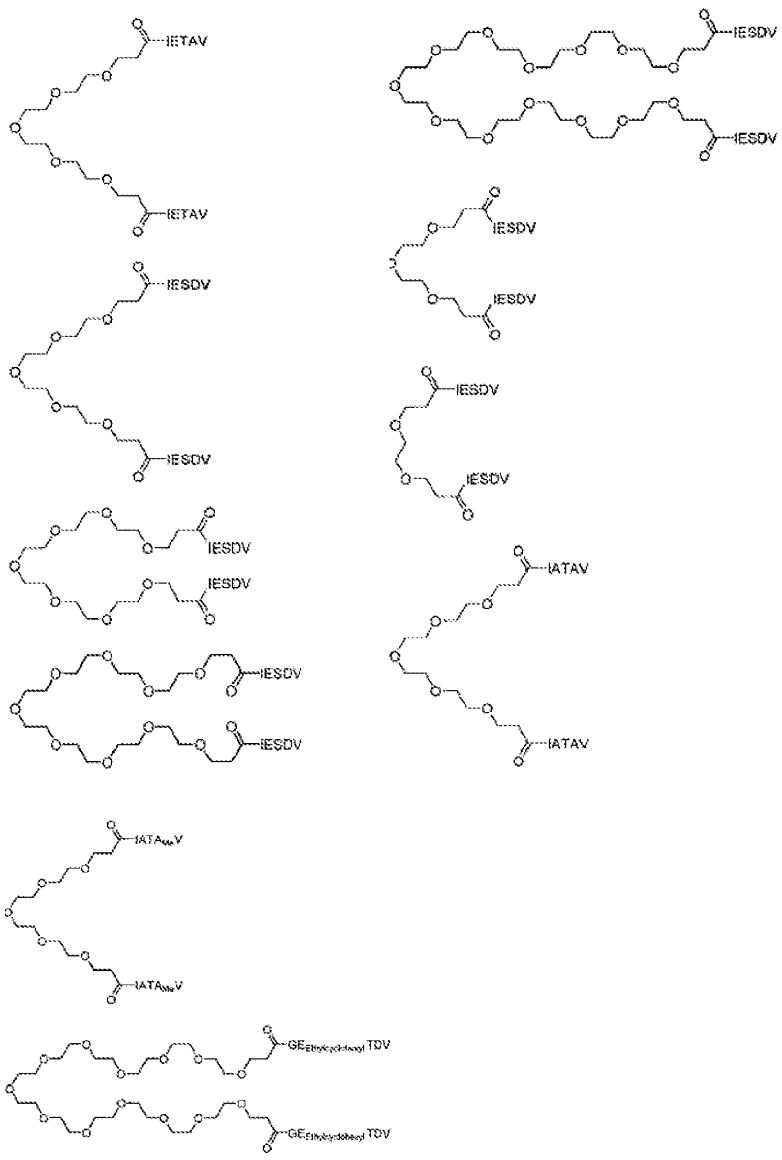
YGRKKRRQRRRVSGLNPSLWSIFGLQFILLWLVSGSRHYLW, or a sequence having at least 80% sequence homology with either of these sequences. In further embodiments, the peptide may be a polypeptide having portions (for example, three or more consecutive amino acids) of either of these sequences and having an overall length of 10 – 50 residues.

Formula 255

[1061] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 255. Such peptides are described in WO 2010/004003, published January 14, 2010, corresponding to PCT/EP2009/058752, filed July 9, 2009, and US 9,241,967, issued January 26, 2016, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 255, these references incorporated by reference herein control.

[1062] A compound comprising a first peptide or peptide analogue linked to a second peptide or peptide analogue by a linker, optionally a PEG linker, wherein said linker is associated with a N-terminus of said first and second peptide or peptide analogue, and wherein said first and said second peptide or peptide analogue comprise at least four amide-bonded residues having a sequence Xaa1-Thr-Xaa3-Val or Xaa1-Ser-Xaa3-Val, wherein: a. Xaa1 is selected from among E, Q, and A, or an analogue thereof, and b. Xaa3 is selected from among A, Q, D, N, N-Me-A, N-Me-Q, N-Me-D, and N-Me-N or an analogue thereof.

[1063] In further embodiments, the compound is selected from:



Formula 256

[1064] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 256. Such peptides are described in WO 2014/096402, published June 26, 2014 corresponding to PCT/EP2013/077780, filed December 20, 2013 and US 2015/0337276, published November 26, 2015, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 256, these references incorporated by reference herein control.

[1065] In an embodiment, the NMDA receptor antagonist is an enzyme, optionally a metalloenzyme comprising at least one divalent cation. In an embodiment, the divalent cation is Zn2+, Mg2+, Ni2+, Cd2+, Mn2+, Co2+, Fe2+, and Ag2+, preferably is Zn2+.

[1066] In further embodiments, the enzyme is a phosphotriesterase or phosphotriesterase derivative.

[1067] In further embodiments, the enzyme comprises a sequence, or functional portion thereof, having a sequence according to:

MQTRRVVLKSAAAAGTLLGGLAGCASVAGSIGTGDRINTVRGPITISEAGFTL THEHICGSSAGFLRAWPEFFGSRKALAEKAVRGLRRARAAGVRTIVDVSTFDI GRDVSLLAEVSRAADVHIVAATGLWFDPPLSMRLRSVEELTQFFLREIQYGIE DTGIRAGIIKVATTGKATPFQELVLKAAARASLATGVPVTTHTAASQRDGEQ QAAIFESEGLSPSRVCIGHSDDTDDLSYLTALAARGYLIGLDHIPHSAIGLEDN ASASALLGIRSWQTRALLIKALIDQGYMKQILVSNDWLFGFSSYVTNIMDVM DRVNPDGMAFIPLRVIPFLREKGVPQETLAGITVTNPARFLSPTLRAS; or

SIGTGDRINTVRGPITISEAGFTLTHEHICGSSAGFLRAWPEFFGSRKALAEKAV RGLRRARAAGVRTIVDVSTFDIGRDVSLLAEVSRAADVHIVAATGLWFDPPL SMRLRSVEELTQFFLREIQYGIEDTGIRAGIIKVATTGKATPFQELVLKAAARA SLATGVPVTTHTAASQRDGEQQAAIFESEGLSPSRVCIGHSDDTDDLSYLTAL AARGYLIGLDHIPHSAIGLEDNASASALLGIRSWQTRALLIKALIDQGYMKQIL VSNDWLFGFSSYVTNIMDVMDRVNPDGMAFIPLRVIPFLREKGVPQETLAGIT VTNPARFLSPTLRAS; or

MSIGTGDRINTVRGPITISEAGFTLTHEHICGSSAGFLRAWPEFFGSRKALAEK AVRGLRRARAAGVRTIVDVSTFDIGRDVSLLAEVSRAADVHIVAATGLWFDP PLSMRLRSVEELTQFFLREIQYGIEDTGIRAGIIKVATTGKATPFQELVLKAAA RASLATGVPVTTHTAASQRDGEQQAAIFESEGLSPSRVCIGHSDDTDDLSYLT ALAARGYLIGLDHIPHSAIGLEDNASASALLGIRSWQTRALLIKALIDQGYMK QILVSNDWLFGFSSYVTNIMDVMDRVNPDGMAFIPLRVIPFLREKGVPQETLA GITVTNPARFLSPTLRAS;

or a sequence comprising a portion having at least 80% sequence homology to any of these sequences.

Formula 257

[1068] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 257. Such peptides are described in WO 2013/185572, published December 19, 2013 and corresponding to PCT/CN2013/076967, filed June 8, 2013, and US 9,718,864, issued August 1, 2017. which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 257, these references incorporated by reference herein control.

[1069] In an embodiment, the NMDA receptor antagonist is a polypeptide comprising one or more sequences according to:

MKLTCVLIITVLFLTACQLTTAVTYSRGEHKHRALMSTGTNYRLPKTCRSSGR YCRSPYDCRRRYCRRITDACV; or
MKLTCVVIITVLFLTACQLTTAVTYSRGEHKHRALMSTGTNYRLPKTCRSSG RYCRSPYDCRRRYCRRITDACV; or
TCRSSGRYCRSPYDCRRRYCRRITDACV; or
MKLTCVLIITVLFLTACQLTTAVTYSRGEHKHRALMSTGTNYRLPKTCRSSGR YCRSPYDRRRRYCRRITDACV; or
MKLTCVVIITVLFLTACQLTTAVTYSRGEHKHRALMSTGTNYRLPKTCRSSG RYCRSPYDRRRRYCRRITDACV; or
TCRSSGRYCRSPYDRRRRYCRRITDACV,
or a sequence comprising a portion having at least 80% homology with any one or more of these sequences.

Formula 258

[1070] In an embodiment, the NMDA receptor antagonist (blocker) may be selected from one of the following peptides according to Formula 258. Such peptides are described in WO2008/014917, published February 7, 2008, corresponding to PCT/EP2007/006619, filed July 25, 2007, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 258, these references incorporated by reference herein control.

[1071] In an embodiment, the NMDA receptor antagonist is a polypeptide comprising entirely D-enantiomeric amino acids.

[1072] In an embodiment, the NMDA receptor antagonist is a fusion peptide comprising at least a component (I), wherein component (I) comprises a transporter peptide, and a component (II), selected from a peptide inhibiting interaction of

neuronal N-methyl-D-aspartate receptor (NMDAR) with NMDAR interacting proteins, wherein component (II) entirely consists of D- enantiomeric amino acids.

[1073] In an embodiment, component (I) is selected from cell penetrating peptides including: (a) protein transduction domains (PTD) and protein derived CPPs, including sequences derived from Antennapedia, pAntp (43-58), comprising the sequences RQI KIVVFQN RRMKWKK or RQIKIWFQNRRMKWKK-amide, including sequences derived from human immunodeficiency virus 1 (HIV-1), TAT, region 37 to 72, region 37 to 60, region 48 to 60 or region 49 to 57 from TAT, sequences GRKKRRQRRR, YGRKKRRQRRR, CGRKKRRQRRRPPQC or CGRKKRRQRRRPPQCC, including hCT(9-32) having the sequence LGTYTQDFNKFHTFPQTAIGVGAP-NH2, pVEC comprising the sequence LLIILRRRIRKQAHAHSK-NH2, plSL comprising the sequence RVIRVWFQNKRCKDKK-NH2, mouse PRP (1 - 28) comprising the sequence MANGLYWLLALFVTMWTDVGLCKKRPKP- NH2 and homologs thereto including human homologs, Ems (194-220) comprising the sequence RQGAARVTSWLGLQLRIAGKRLEGRSK-NH2, Restricocin L3 (60-73) comprising the sequence KLIKGRTPIKFGK-NH2, or

(b) model peptides including VT5 comprising the sequence DPKGDPKGVTVTVTVTVTGKGDPKPD-NH2, MAP comprising the sequence KLALKLALKALKAALKLA-NH2, arginine stretches including RRRRRRR, i.e. (Arg)7, or RRRRRRR-NH2, i.e. (Arg)7-NH2, or RRRRRRR-C, i.e. (Arg)7- C, or RRRRRRRR, i.e. (Arg)8, or RRRRRRRR-NH2, i.e. (Arg)8-NH2, RRRRRRRRR, i.e. (Arg)9, or RRRRRRRRR-NH2, i.e. (Arg)9-NH2, or

(c) designed CPPs including MPG comprising the sequence GALFLGFLGAAGSTMGAWSQPKSKRKV or GALFLGFLGAAGSTMGAWSQPKSKRKV-cysteamide;

Transportan comprising the sequence GWTLNSAGYLLGKINLKALAALAKKIL-NH2 (SEQ , Transportan 10 comprising the sequence AGYLLGKINLKALAALAKKIL-NH2, Pep-1 comprising the sequence KETWWETWWTEWSQPKKKRKV or KETWWETWWTEWSQPKKKRKV-cysteamide, or may be selected from the KALA peptide comprising the sequence

WEAKLAKALAKALAKHLAKALAKALKACEA or from Bulforin 2 comprising the sequence TRSSRAGLQFPVGRVHRLLRK, or an retro-inverso isomer of any of these sequences composed of D amino acids, or any sequences having at least 80% homology with any of these sequences.

[1074] In an embodiment, component (II) comprises the polypeptide sequence vdseisslk, or a sequence having at least 80% homology thereto. In an embodiment, the component (II) sequence comprises a length of 5 to 40 amino acids.

Formula 259

[1075] In an embodiment, the NMDA receptor antagonist may be selected from one of the following peptides according to Formula 259 Such peptides are described in US 5,854,217, issued December 29, 1998, and US 6,284,731, issued September 4, 2001, which are each incorporated by reference in their entirety herein. In the case of any conflict of terminology of Formula 259, these references incorporated by reference herein control.

[1076] In an embodiment, the NMDA receptor antagonist comprises one or more sequences according to:

Asn Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Phe Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
t-BuTyr Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Ser Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Ser Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2, wherein the serine at position 3 is phosphorylated;
Gly Glu Ala Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Tyr Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Ala Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Ser Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Ser Asn Gln Gla Leu Ile Arg Gla Lys Ser Asn-NH2 wherein the first serine is phosphorylated;
Gly Glu Gla Gla Leu Gln Gla Asn Gln Ala Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Gla Asn Gln Ser Leu Ile Arg Gla Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Gla Asn Gln Ser Leu Ile Arg Gla Lys Ser Asn-NH2, wherein the first serine is phosphorylated;

Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Ala Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Ser Lys Ser Asn-NH2;
Gly Glu Gla Gla Leu Gln Gla Asn Gln Gla Leu Ile Arg Ser Lys Ser Asn-NH2, wherein the first serine is phosphorylated; Gly Glu Gla Gla Leu Gln Ala Asn Gln Ala Leu Ile Arg Ala Lys Ser Asn-NH2; and Gla Lys Ser Asn-NH2; Tyr Gly Glu Glu Glu Leu Gln Glu Asn Gln Glu Leu Ile Arg Glu Lys Ser Asn-NH2; and
Glu Glu Glu Leu Gln Glu Asn Gln Glu Leu Ile Arg Glu Lys Ser Asn-NH2.

[1077] In further embodiments, the NMDA receptor antagonist has the structure:

A1-A2-A3-A4-A5-A6-(A7)x c-[A8-(A9-A10)x d—NH2]n
wherein
A1 is glycine, alanine, valine, leucine or isoleucine;
A2 is glutamic acid, aspartic acid, γ-carboxyglutamate (Gla), 3-carboxyaspartic acid, D-glutamic acid, phosphoserine or phosphothreonine;
A3 is glutamic acid, aspartic acid, γ-carboxyglutamate (Gla), 3-carboxyaspartic acid, D-glutamic acid, phosphoserine or phosphothreonine;
A4 is Gla;
A5 is glycine, alanine, valinc, leucine or isoleucine;
A6 is a peptide of 7-9 amino acids;
A7 is an amino acid selected from the group consisting of natural, modified or non-natural amino acids;
A8 is lysine or arginine;
A9 is an amino acid selected from the group consisting of natural, modified or non-natural amino acids;
A10 is an amino acid selected from the group consisting of natural, modified or non-natural amino acids;
xc and xd are independently 0 or 1; and
n is 0 or 1.

Formula 260

[1078] In yet further embodiments, the NMDA receptor antagonist is a histogranin or analog thereof, as described in CA 2097533, published December 4, 1993.

PHARMACEUTICAL COMPOSITIONS

[1079] In an embodiment, provided is a pharmaceutical composition comprising a metal channel activator and a NMDA receptor antagonist.

[1080] In another embodiment, the metal channel activator in said pharmaceutical composition is a potassium channel activator.

[1081] In another embodiment, the potassium channel activator in said pharmaceutical composition is a Kv7 channel activator.

[1082] In another embodiment, the Kv7 channel activator in said pharmaceutical composition is selected from the group consisting of a Kv7.1 channel activator, a Kv7.2 channel activator, a Kv7.3 channel activator, a Kv7.4 channel activator, a Kv7.5 channel activator, or any combination thereof.

[1083] In another embodiment, the Kv7 channel activator in said pharmaceutical composition is a Kv7.2/7.3 channel activator.

[1084] In another embodiment, the metal channel activator in said pharmaceutical composition is selected from one or more of the disclosed compounds according to any one or more of formulas 1 to 171 and the compounds disclosed in the "further embodiments" under the "METAL CHANNEL ACTIVATORS" subheading.

[1085] In another embodiment, the NMDA receptor antagonist in said pharmaceutical composition is selected from one or more of the disclosed compounds according to any one or more of formulas 200 to 260.

[1086] In another embodiment, the NMDA receptor antagonist in said pharmaceutical composition is selected from one or more of the disclosed compounds according to any one or more of formulas 200 to 260, and the metal channel activator in said pharmaceutical composition is selected from one or more of the disclosed compounds according to any one or more of formulas 1 to 171 and the compounds disclosed in the "further embodiments" under the "METAL CHANNEL ACTIVATORS" subheading.

[1087] In another embodiment, the NMDA receptor antagonist or a pharmaceutically acceptable salt thereof in said pharmaceutical composition is in a form of a prodrug.

METHODS OF TREATING DISEASES

[1088] The combination therapies (comprising at least one of any metal channel activator described herein and at least one NMDA receptor antagonist described herein) disclosed herein are useful for treating various depressive disorders. The depressive disorder include

major depressive disorder (MDD), disruptive mood dysregulation disorder, persistent depressive disorder, bipolar spectrum disorder, postpartum depression, premenstrual dysphoric disorder (PMDD), seasonal affective disorder (SAD), atypical depression, treatment-resistant depression (TRD), depression associated with agitation or anxiety, adjustment disorder with depressed mood, prolonged depressive reaction, or a combination thereof.

[1089] The combination therapies disclosed herein are useful for treating various neurological and neurodegenerative disorders. These disorders include amyotrophic lateral sclerosis, bipolar disorder, treatment resistant and major depression, general anxiety disorder, panic disorder, social anxiety, mood disorders, cognitive disorders, dementia, agitation, apathy, psychoses, post-traumatic stress disorders, irritability, disinhibition, learning disorders, memory loss, personality disorders, bipolar disorders, Rett syndrome, eating disorders, conduct disorder, neurodegenerative disorders, pain disorders, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, delirium, Alzheimer's disease, mild cognitive impairment, mild cognitive impairment due to Alzheimer’s disease, drug addiction, tinnitus, mental retardation, obsessive-compulsive disorder, spinal muscular atrophy, radiation therapy, multiple sclerosis, chronic cerebellar ataxia, cervical spondylotic myelopathy, spinal cord injury, hereditary cerebellar ataxia, Tourette syndrome, autism spectrum disorder, schizophrenia, fragile X syndrome, Parkinson's Disease, Huntington’s disease, or any combination thereof.

[1090] The combination therapies disclosed herein are useful for treating various pain disorders. The pain disorders include acute pain, chronic pain, neuropathic pain, nociceptive pain, radicular pain. The pain disorders may also include migraine, inflammatory pain, persistent pain, cancer pain, and postoperative pain.

[1091] The metal channel activator and the NMDA receptor antagonist may be given orally, sublingually, subcutaneously or in any other means of delivery. The agents may be delivered simultaneously or sequentially. If the agents are delivered sequentially, either agent may be dosed first, and the separation of time may include finishing the dosing of one agent completely before commencing the dosage of the other or they may be intermingled in time.

[1092] In an embodiment, provided is a kit for treating a patient afflicted with at least one of the aforementioned disorders, said kit including:

(a) a metal channel activator; and

(b) instructions for administering said metal channel activator in combination with an NMDA receptor antagonist by one of the aforementioned methods.

[1093] In another embodiment, provided is a kit for treating a patient afflicted with at least one of the aforementioned disorders, said kit including:

(a) an NMDA receptor antagonist; and

(b) instructions for administering said NMDA receptor antagonist with a metal channel activator by one of the aforementioned methods.

[1094] As used herein, the term "metal channel activator" is construed to include both metal channel activator and pharmaceutically acceptable salt thereof.

[1095] As used herein, the term "NMDA receptor antagonist" is construed to include both NMDA receptor antagonist and pharmaceutically acceptable salt thereof.

[1096] Throughout this application, various publications are referenced by author name and date, or by patent number or patent publication number. The disclosures of these publications are hereby incorporated in their entireties by reference into this application in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described and claimed herein. However, the citation of a reference herein should not be construed as an acknowledgement that such reference is prior art to the present invention.

[1097] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific procedures described herein. Such equivalents are considered to be within the scope of this invention and are covered by the following claims. For example, pharmaceutically acceptable salts other than those specifically disclosed in the description and Examples herein can be employed. Furthermore, it is intended that specific items within lists of items, or subset groups of items within larger groups of items, can be combined with other specific items, subset groups of items or larger groups of items whether or not there is a specific disclosure herein identifying such a combination.

PHARMACEUTICAL COMPOSITIONS AND METHODS OF TREATMENT

[1098] Compounds are generally given as pharmaceutical compositions comprised of a therapeutically effective amount of one or more of a compound of any one of Formulas 1 –

180, Formulas 200 – 260, those listed in "Further Embodiments" under the "METAL CHANNEL ACTIVATORS" subsection, or pharmaceutically acceptable salt(s) thereof, and a pharmaceutically acceptable carrier, further optionally containing conventional excipients. A therapeutically effective amount is the amount needed to provide a meaningful patient benefit as determined by practitioners in that art. Pharmaceutically acceptable carriers are those having acceptable safety profiles which are conventionally known. Compositions encompass common solid and liquid forms including but not limited to capsules, tablets, lozenges, liquid suspensions, syrups, elixirs, and solutions. Solid compositions may by formulated to timed or sustained release. Compositions are made using common formulation techniques, such as the aforementioned solid and liquid forms, conventional excipients, such as binding and wetting agents, and vehicles, such as water and alcohols.

[1099] The NMDA receptor antagonists of the present invention may be given orally, sublingually, intranasally, buccally, subcutaneously or in any other suitable means of delivery in table 1. The NMDA receptor antagonists may be in the form of a prodrug, which releases the agent in the body, a sustained release vehicle, a delayed release vehicle, or any other suitable delivery form. The NMDA receptor antagonists and the metal channel activator may be delivered simultaneously or sequentially. If the agents are delivered sequentially, either agent may be dosed first, and the separation of time may include finishing the dosing of one agent completely before commencing the dosage of the other or they may be intermingled in time. Typically, the NMDA receptor antagonist is administered at a time proximate to the administration of the metal channel activator, e.g., within 1 week, 1 day, 1 hour, 1 minute before or after the metal channel activator or simultaneously with the metal channel activator.

[1100] The metal channel activators of the present invention may be given orally, sublingually, intranasally, buccally, subcutaneously or in any other suitable means of delivery in table 1. Metal channel activators may be given in the form of a prodrug, which will release the active compound in the body, a delayed release formulation, which will release the active compound after a time delay, a sustained release formulation, which will release the active compound slowly over time, or any other suitable formulation to deliver the active ingredient. The metal channel activator may be delivered simultaneously or sequentially with the NMDA receptor antagonist. If the agents are delivered sequentially, either agent may be dosed first, and the separation of time may include finishing the dosing of one agent completely before commencing the dosage of the other or they may be intermingled in time. Typically, the metal channel activator will be administered at a time nearing the administration of the

NMDA receptor antagonist e.g., within 1 week, 1 day, 1 hour, 1 minute before or after the NMDA receptor antagonist or simultaneously with the metal channel activator.

[1101] The dose of the NMDA receptor antagonist and metal channel activator for use together may depend on the subject to be treated inclusive of the age, sex, weight, and general health condition thereof. In this regard, precise amounts of the agent(s) for administration will depend on the judgment of the practitioner. In determining the effective amount of the NMDA receptor antagonist and metal channel activator to be administered in the treatment or reducing of the conditions associated with the symptoms and disorders, the physician may evaluate clinical factors including symptoms severity or progression of the disorder. In some conditions, a rapid absorption of the NMDA receptor antagonist or metal channel activator may be desirable. The effective amount of the treatment will vary depending on the subject and disease state being treated, the severity of the affliction and the manner of administration, and may be determined routinely by one of ordinary skill in the art.

[1102] Some of the NMDA receptor antagonists and metal channel activators can be administered sublingually. The sublingual formulation may be administered in an effective amount to a subject in need thereof. The subject may be an animal or human. When the NMDA receptor antagonist or metal channel activator is prepared as a sublingual formulation, the sublingually administered chemical agent or the drug can diffuse into capillaries through mucous membrane under the tongue, and then enter venous circulation of the subject. As such, sublingual administration may have advantages over oral administration as allowing for direct or faster entry to venous circulation, without risks of degradation in gastrointestinal tract, alteration by drug metabolism in liver and the like.

[1103] A sublingual formulation useful in the present invention comprises an effective amount of an NMDA receptor antagonist, metal channel activator, or pharmaceutically acceptable salts, solvates, anomers, enantiomers, hydrates, or prodrugs thereof. The formulation provides sufficient solubility for a NMDA receptor antagonist and/or metal channel activator to be incorporated into the sublingual formulation at relatively large doses and sublingually delivered. The formulation is preferably a modified oral disintegrating formulation of a NMDA receptor antagonist and/or metal channel activator. The excipients, including mannitol and gelatin, are blended, solubilized with water and deaerated before being mixed with the active pharmaceutical ingredient (or "API"), a NMDA receptor antagonist and/or a metal channel activator, which have been milled separately. Particle size of the API (D50) may be less than about 2 microns. The mixture is lyophilized by flash freezing and then freeze-dried. The formulation has good oral palatability. The effective

amount of a NMDA receptor antagonist and/or metal channel activator for the sublingual formulation useful in the present invention to achieve a lower therapeutic dose may be less than that of orally administered agent. Moreover, effective dose of the sublingual formulation of the NMDA receptor antagonist and/or metal channel activator may be about 1 to 95 % of that of the orally administered agent. Sublingual formulations of the metal channel activator and/or NMDA receptor antagonist may also have improved properties.

[1104] In one aspect of the invention, the NMDA receptor antagonist and/or metal channel activator is provided in a sublingual formulation in a form of an orally dissolving or disintegrating tablet (ODT). The ODT as used herein may be prepared by mixing the NMDA receptor antagonist and/or the metal channel activator with water-soluble diluents and compressed in a tablet. A suspension comprising the active product may be prepared with appropriate excipients and the suspension may be dispensed into blister packs and freeze-dried. An exemplary freeze-dried preparation platform that could be used for the ODT is the ZYDIS® (Catalent, Somerset, NJ, USA) formulation. In particular, the excipients, including water, are blended and the NMDA receptor antagonist and/or metal channel activator are separately milled to size and mixed with the excipients. The suspension then undergoes lyophilization by flash freezing and freeze drying. Other methods of preparing ODTs may be used without limitation, and detailed description of general methods thereof have been disclosed, for example, in US Patent Nos 5,631,023; 5,837,287; 6,149,938; 6,212,791; 6,284,270; 6,316,029; 6,465,010; 6,471,992; 6,471,992; 6,509,040; 6,814,978; 6,908,626; 6,908,626; 6,982,25l; 7,282,217; 7,425,341; 7,939,105; 7,993,674; 8,048,449; 8,127,516; 8,158,152; 8,221,480; 8,256,233; and 8,313,768, each of which is incorporated herein by reference in its entirety.

[1105] The clinical or therapeutic effect of the sublingually formulated NMDA receptor antagonist may have an improved pharmacokinetic profile for the pharmaceutical agent as measured by standard testing parameters. When the NMDA receptor antagonist is administered sublingually, the T_{max}, C_{max} and AUC of the drug may be improved compared to the same dose of the orally administered version of the same compound. For example, the sublingual formulation of the NMDA receptor antagonist may have a greater C_{max} than the orally administered NMDA receptor antagonist to provide a therapeutically beneficial effect. The sublingual formulation of the NMDA receptor antagonist may have an earlier or lesser T_{max} than the orally administered NMDA receptor antagonist to provide a therapeutically beneficial effect and in some instances, a more rapid therapeutic effect. Alternatively, the sublingual formulation of the NMDA receptor antagonist may have a greater AUC per

milligram of the agent than the orally administered NMDA receptor antagonist. In addition, as the NMDA receptor antagonist may make the metal channel activator more effective, lesser amounts of the metal channel activator may be needed to achieve the same results, lessening the inherent side effects.

[1106] The clinical or therapeutic effect of the sublingually formulated metal channel activator may have an improved pharmacokinetic profile for the pharmaceutical agent as measured by standard testing parameters. When the metal channel activator is administered sublingually, the T_{max}, C_{max} and AUC of the drug may be improved compared to the same dose of the orally administered version of the same compound. For example, the sublingual formulation of the metal channel activator may have a greater C_{max} than the orally administered metal channel activator to provide a therapeutically beneficial effect. The sublingual formulation of the metal modulator may have an earlier or lesser T_{max} than the orally administered metal channel activator to provide a therapeutically beneficial effect and in some instances, a more rapid therapeutic effect. Alternatively, the sublingual formulation of the metal channel activator may have a greater AUC per milligram of the agent than the orally administered metal channel activator. In addition, as the metal channel activator may make the NMDA receptor antagonist more effective, lesser amounts of the NMDA receptor antagonist may be needed to achieve the same results, lessening the inherent side effects.

[1107] The disclosure and methods encompass all conventional modes of administration including oral, parenteral, intranasal, sublingual, topical, and transdermal methods. Among other routes of administration, the standard routes of administration described by the FDA are contemplated herein as shown in Table 1 below (FDA Routes of Administration; retrieved from www.fda.gov; content current as of 11/1/2022).

Table 1: FDA Routes of Administration

NAME	DEFINITION	SHORT NAME	FDA CODE	NCI CONCEPT ID
AURICULAR (OTIC)	Administration to or by way of the ear.	OTIC	013	C38192
BUCCAL	Administration directed toward the cheek, generally from within the mouth.	BUCCAL	030	C38193

CONJUNCTIVAL	Administration to the conjunctiva, the delicate membrane that lines the eyelids and covers the exposed surface of the eyeball.	CONJUNC	068	C38194
CUTANEOUS	Administration to the skin.	CUTAN	130	C38675
DENTAL	Administration to a tooth or teeth.	DENTAL	038	C38197
ELECTRO-OSMOSIS	Administration of through the diffusion of substance through a membrane in an electric field.	EL-OSMOS	357	C38633
ENDOCERVICAL	Administration within the canal of the cervix uteri. Synonymous with the term intracervical.	E-CERVIC	131	C38205
ENDOSINUSIAL	Administration within the nasal sinuses of the head.	E-SINUS	133	C38206
ENDOTRACHEAL	Administration directly into the trachea.	E-TRACHE	401	C38208
ENTERAL	Administration directly into the intestines.	ENTER	313	C38209
EPIDURAL	Administration upon or over the dura mater.	EPIDUR	009	C38210
EXTRA-AMNIOTIC	Administration to the outside of the membrane enveloping the fetus	X-AMNI	402	C38211
EXTRACORPOREAL	Administration outside of the body.	X-CORPOR	057	C38212
HEMODIALYSIS	Administration through hemodialysate fluid.	HEMO	140	C38200

INFILTRATION	Administration that results in substances passing into tissue spaces or into cells.	INFIL	361	C38215
INTERSTITIAL	Administration to or in the interstices of a tissue.	INTERSTIT	088	C38219
INTRA-ABDOMINAL	Administration within the abdomen.	I-ABDOM	056	C38220
INTRA-AMNIOTIC	Administration within the amnion.	I-AMNI	060	C38221
INTRA-ARTERIAL	Administration within an artery or arteries.	I-ARTER	037	C38222
INTRA-ARTICULAR	Administration within a joint.	I-ARTIC	007	C38223
INTRABILIARY	Administration within the bile, bile ducts or gallbladder.	I-BILI	362	C38224
INTRABRONCHIAL	Administration within a bronchus.	I-BRONCHI	067	C38225
INTRABURSAL	Administration within a bursa.	I-BURSAL	025	C38226
INTRACARDIAC	Administration with the heart.	I-CARDI	027	C38227
INTRACARTILAGINOUS	Administration within a cartilage; endochondral.	I-CARTIL	363	C38228
INTRACAUDAL	Administration within the cauda equina.	I-CAUDAL	413	C38229
INTRACAVERNOUS	Administration within a pathologic cavity, such as occurs in the lung in tuberculosis.	I-CAVERN	132	C38230
INTRACAVITARY	Administration within a non-pathologic cavity, such as that of the cervix, uterus, or penis, or such as that which is formed as the result of a wound.	I-CAVIT	023	C38231

INTRACEREBRAL	Administration within the cerebrum.	I-CERE	404	C38232
INTRACISTERNAL	Administration within the cisterna magna cerebellomedularis.	I-CISTERN	405	C38233
INTRACORNEAL	Administration within the cornea (the transparent structure forming the anterior part of the fibrous tunic of the eye).	I-CORNE	406	C38234
INTRACORONAL, DENTAL	Administration of a drug within a portion of a tooth which is covered by enamel and which is separated from the roots by a slightly constricted region known as the neck.	I-CORONAL	117	C38217
INTRACORONARY	Administration within the coronary arteries.	I-CORONARY	119	C38218
INTRACORPORUS CAVERNOSUM	Administration within the dilatable spaces of the corpora cavernosa of the penis.	I-CORPOR	403	C38235
INTRADERMAL	Administration within the dermis.	I-DERMAL	008	C38238
INTRADISCAL	Administration within a disc.	I-DISCAL	121	C38239
INTRADUCTAL	Administration within the duct of a gland.	I-DUCTAL	123	C38240
INTRADUODENAL	Administration within the duodenum.	I-DUOD	047	C38241
INTRADURAL	Administration within or beneath the dura.	I-DURAL	052	C38242
INTRAEPIDERMAL	Administration within the epidermis.	I-EPIDERM	127	C38243

INTRAESOPHAGEAL	Administration within the esophagus.	I-ESO	072	C38245
INTRAGASTRIC	Administration within the stomach.	I-GASTRIC	046	C38246
INTRAGINGIVAL	Administration within the gingivae.	I-GINGIV	307	C38247
INTRAILEAL	Administration within the distal portion of the small intestine, from the jejunum to the cecum.	I-ILE	365	C38249
INTRALESIONAL	Administration within or introduced directly into a localized lesion.	I-LESION	042	C38250
INTRALUMINAL	Administration within the lumen of a tube.	I-LUMIN	310	C38251
INTRALYMPHATIC	Administration within the lymph.	I-LYMPHAT	352	C38252
INTRAMEDULLARY	Administration within the marrow cavity of a bone.	I-MEDUL	408	C38253
INTRAMENINGEAL	Administration within the meninges (the three membranes that envelope the brain and spinal cord).	I-MENIN	409	C38254
INTRAMUSCULAR	Administration within a muscle.	IM	005	C28161
INTRAOCULAR	Administration within the eye.	I-OCUL	036	C38255
INTRAOVARIAN	Administration within the ovary.	I-OVAR	354	C38256
INTRAPERICARDIAL	Administration within the pericardium.	I-PERICARD	314	C38257
INTRAPERITONEAL	Administration within the peritoneal cavity.	I-PERITON	004	C38258

INTRAPLEURAL	Administration within the pleura.	I-PLEURAL	043	C38259
INTRAPROSTATIC	Administration within the prostate gland.	I-PROSTAT	061	C38260
INTRAPULMONARY	Administration within the lungs or its bronchi.	I-PULMON	414	C38261
INTRASINAL	Administration within the nasal or periorbital sinuses.	I-SINAL	010	C38262
INTRASPINAL	Administration within the vertebral column.	I-SPINAL	022	C38263
INTRASYNOVIAL	Administration within the synovial cavity of a joint.	I-SYNOV	019	C38264
INTRATENDINOUS	Administration within a tendon.	I-TENDIN	049	C38265
INTRATESTICULAR	Administration within the testicle.	I-TESTIC	110	C38266
INTRATHECAL	Administration within the cerebrospinal fluid at any level of the cerebrospinal axis, including injection into the cerebral ventricles.	IT	103	C38267
INTRATHORACIC	Administration within the thorax (internal to the ribs); synonymous with the term endothoracic.	I-THORAC	006	C38207
INTRATUBULAR	Administration within the tubules of an organ.	I-TUBUL	353	C38268
INTRATUMOR	Administration within a tumor.	I-TUMOR	020	C38269
INTRATYMPANIC	Administration within the Auris media.	I-TYMPAN	366	C38270
INTRAUTERINE	Administration within the uterus.	I-UTER	028	C38272

INTRAVASCULAR	Administration within a vessel or vessels.	I-VASC	021	C38273
INTRAVENOUS	Administration within or into a vein or veins.	IV	002	C38276
INTRAVENOUS BOLUS	Administration within or into a vein or veins all at once.	IV BOLUS	138	C38274
INTRAVENOUS DRIP	Administration within or into a vein or veins over a sustained period of time.	IV DRIP	137	C38279
INTRAVENTRICULAR	Administration within a ventricle.	I-VENTRIC	048	C38277
INTRAVESICAL	Administration within the bladder.	I-VESIC	128	C38278
INTRAVITREAL	Administration within the vitreous body of the eye.	I-VITRE	311	C38280
IONTOPHORESIS	Administration by means of an electric current where ions of soluble salts migrate into the tissues of the body.	ION	055	C38203
IRRIGATION	Administration to bathe or flush open wounds or body cavities.	IRRIG	032	C38281
LARYNGEAL	Administration directly upon the larynx.	LARYN	364	C38282
NASAL	Administration to the nose; administered by way of the nose.	NASAL	014	C38284
NASOGASTRIC	Administration through the nose and into the stomach, usually by means of a tube.	NG	071	C38285
NOT APPLICABLE	Routes of administration are not applicable.	NA	312	C48623

OCCLUSIVE DRESSING TECHNIQUE	Administration by the topical route which is then covered by a dressing which occludes the area.	OCCLUS	134	C38286
OPHTHALMIC	Administration to the external eye.	OPHTHALM	012	C38287
ORAL	Administration to or by way of the mouth.	ORAL	001	C38288
OROPHARYNGEAL	Administration directly to the mouth and pharynx.	ORO	410	C38289
OTHER	Administration is different from others on this list.	OTHER	135	C38290
PARENTERAL	Administration by injection, infusion, or implantation.	PAREN	411	C38291
PERCUTANEOUS	Administration through the skin.	PERCUT	113	C38676
PERIARTICULAR	Administration around a joint.	P-ARTIC	045	C38292
PERIDURAL	Administration to the outside of the dura mater of the spinal cord.	P-DURAL	050	C38677
PERINEURAL	Administration surrounding a nerve or nerves.	P-NEURAL	412	C38293
PERIODONTAL	Administration around a tooth.	P-ODONT	040	C38294
RECTAL	Administration to the rectum.	RECTAL	016	C38295
RESPIRATORY (INHALATION)	Administration within the respiratory tract by inhaling orally or nasally for local or systemic effect.	RESPIR	136	C38216
RETROBULBAR	Administration behind the pons or behind the eyeball.	RETRO	034	C38296
SOFT TISSUE	Administration into any soft tissue.	SOFT TIS	109	C38198

SUBARACHNOID	Administration beneath the arachnoid.	S-ARACH	066	C38297
SUBCONJUNCTIVAL	Administration beneath the conjunctiva.	S-CONJUNC	096	C38298
SUBCUTANEOUS	Administration beneath the skin; hypodermic. Synonymous with the term SUBDERMAL.	SC	003	C38299
SUBLINGUAL	Administration beneath the tongue.	SL	024	C38300
SUBMUCOSAL	Administration beneath the mucous membrane.	S-MUCOS	053	C38301
TOPICAL	Administration to a particular spot on the outer surface of the body. The E2B term TRANSMAMMARY is a subset of the term TOPICAL.	TOPIC	011	C38304
TRANSDERMAL	Administration through the dermal layer of the skin to the systemic circulation by diffusion.	T-DERMAL	358	C38305
TRANSMUCOSAL	Administration across the mucosa.	T-MUCOS	122	C38283
TRANSPLACENTAL	Administration through or across the placenta.	T-PLACENT	415	C38307
TRANSTRACHEAL	Administration through the wall of the trachea.	T-TRACHE	355	C38308
TRANSTYMPANIC	Administration across or through the tympanic cavity.	T-TYMPAN	124	C38309
UNASSIGNED	Route of administration has not yet been assigned.	UNAS	400	C38310
UNKNOWN	Route of administration is unknown.	UNKNOWN	139	C38311

URETERAL	Administration into the ureter.	URETER	112	C38312
URETHRAL	Administration into the urethra.	URETH	017	C38271
VAGINAL	Administration into the vagina.	VAGIN	015	C38313

[1108] In some embodiments, the route of administration may be oral, intranasal, inhalation, intravenous, sublingual, topical, injectable and/or transdermal.

[1109] The pharmaceutical compositions of the present invention comprising the NMDA receptor antagonist and/or metal channel activator may also include other pharmaceutically acceptable carriers and/or excipients such as binders, lubricants, diluents, coatings, disintegrants, barrier layer components, glidants, coloring agents, solubility enhancers, gelling agents, fillers, proteins, co-factors, emulsifiers, solubilizing agents, suspending agents and mixtures thereof. A skilled artisan in the art would know what other pharmaceutically acceptable carriers and/or excipients could be included in the formulations according to the invention. The choice of excipients would depend on the characteristics of the compositions and on the nature of other pharmacologically active compounds in the formulation.

[1110] The formulator will understand that excipients are used primarily to serve in delivering a safe, stable, and functional pharmaceutical. Excipients may also serve as part of the overall vehicle for delivery. Excipients may also be used to achieve effective absorption by the recipient of the active ingredient. An excipient may fill a role as simple and direct as being an inert filler, or an excipient as used herein may be part of a pH stabilizing system or coating. Excipients herein may also serve an antimicrobial function or improve pharmaceutical composition characteristics such as lubricity, flowability, disintegration and taste.

[1111] Pharmaceutical compositions may comprise one or more pharmaceutically acceptable carriers, excipients, or diluents. Examples of such carriers are well known to those skilled in the art and can be prepared in accordance with acceptable pharmaceutical procedures, such as, for example, those described in Remington's Pharmaceutical Sciences, 17th edition, ed. Alfonoso R. Gennaro, Mack Publishing Company, Easton, Pa. (1985), the entire disclosure of which is incorporated by reference herein for all purposes. As used herein, “pharmaceutically acceptable” refers to a substance that is acceptable for use in pharmaceutical applications from a toxicological perspective and does not adversely interact with the active ingredient. Pharmaceutically acceptable carriers are biologically acceptable and compatible with the

other ingredients in the formulation. Appropriate excipients are known to those skilled in the art (see Handbook of Pharmaceutical Excipients, fifth edition, 2005 edited by Rowe et al., McGraw Hill) and have been utilized to yield a novel sublingual formulation with unexpected properties. Pharmaceutical compositions herein are not limited to a single active ingredient, and supplementary active ingredients can also be incorporated.

[1112] Examples of pharmaceutically acceptable carriers that may be used in preparing the pharmaceutical compositions of the present invention may include, but are not limited to, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropyl methyl-cellulose, sodium carboxymethylcellulose; other carriers such as, polyvinylpyrrolidone (PVP), talc, calcium sulphate, vegetable oils, synthetic oils, polyols, alginic acid, phosphate buffered solutions, emulsifiers, isotonic saline, pyrogen-free water and combinations thereof. If desired, disintegrating agents may be combined as well, and exemplary disintegrating agents may be, but not limited to, cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. The compositions may be prepared by any of the methods of pharmacy but all methods include the step of bringing into association one or more chemical agents as described above with the carrier which constitutes one or more necessary ingredients. In general, the pharmaceutical compositions of the present invention may be manufactured in conventional methods known in the art, for example, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, lyophilizing processes, and the like. NMDA receptor antagonists, metal channel activator, and/or the pharmaceutically acceptable salts thereof can be formulated using pharmaceutically acceptable carriers well known in the art into dosages suitable for sublingual, intranasal or buccal administration. Such carriers enable the NMDA receptor antagonists and/or metal channel activator to be formulated in dosage forms such as tablets, powders, pills, capsules, liquids, gels, films, syrups, slurries, suspensions, and the like.

[1113] The NMDA receptor antagonist and/or metal channel activator compounds disclosed can be administered orally or parenterally, neat or in combination with conventional pharmaceutical carriers. Applicable solid carriers can include one or more substances which can also act as flavoring agents, lubricants, solubilizers, suspending agents, fillers, glidants, compression aids, binders or tablet-disintegrating agents, or encapsulating materials. Oral formulations containing a compound disclosed can be any conventionally used oral form, including but not limited to tablets, capsules, buccal forms, troches, lozenges and oral liquids,

suspensions, or solutions. In powders, the carrier can be a finely divided solid, which is an admixture with a finely divided compound. In tablets, a compound disclosed herein can be mixed with a carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired. The powders and tablets can contain up to 99% of the compound.

[1114] Capsules can contain mixtures of one or more compound(s) disclosed herein with inert filler(s) and/or diluent(s) such as pharmaceutically acceptable starches (e.g., corn, potato, or tapioca starch), sugars, artificial sweetening agents, powdered celluloses (e.g., crystalline and microcrystalline celluloses), flours, gelatins, gums, and the like.

[1115] Useful tablet formulations can be made by conventional compression, wet granulation or dry granulation methods and utilize pharmaceutically acceptable diluents, binding agents, lubricants, disintegrants, surface modifying agents (including surfactants), suspending or stabilizing agents, including, but not limited to, magnesium stearate, stearic acid, sodium lauryl sulfate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, microcrystalline cellulose, sodium carboxymethyl cellulose, carboxymethylcellulose calcium, polyvinylpyrrolidone, alginic acid, acacia gum, xanthan gum, sodium citrate, complex silicates, calcium carbonate, glycine, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, low melting waxes, ion exchange resins, benzyl alcohol, eucalyptol, gelatin, limonene, mannitol, menthol, menthone, methyl acetate, sucralose, and vanillin. Surface modifying agents include nonionic and anionic surface modifying agents. Representative examples of surface modifying agents include, but are not limited to, poloxamer 188, benzalkonium chloride, calcium stearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, colloidal silicon dioxide, phosphates, sodium dodecyl sulfate, magnesium aluminum silicate, and triethanolamine. Oral formulations herein can utilize standard delay or time-release formulations to alter the absorption of the compound(s). The oral formulation can also consist of administering a compound disclosed herein in water or fruit juice, containing appropriate solubilizers or emulsifiers as needed.

[1116] Liquid carriers can be used in preparing solutions for oral, parenteral (such as intravenous, intramuscular, or other injections), or inhalation administration including but not limited to suspensions, emulsions, syrups, and elixirs. An NMDA receptor antagonist and/or metal channel activator compound of the present teachings can be dissolved or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, or a mixture of both, or pharmaceutically acceptable oils or fats. The liquid carrier can contain other suitable pharmaceutical additives such as solubilizers, emulsifiers, buffers, preservatives, sweeteners,

flavoring agents, suspending agents, thickening agents, colors, viscosity regulators, stabilizers, and osmo-regulators. Examples of liquid carriers for oral and parenteral administration include, but are not limited to, water (particularly containing additives as described herein, e.g., cellulose derivatives such as a sodium carboxymethyl cellulose solution), alcohols (including monohydric alcohols and polyhydric alcohols, e.g., glycols) and their derivatives, and oils (e.g., fractionated coconut oil and arachis oil). For parenteral administration, the carrier can be an oily ester such as ethyl oleate and isopropyl myristate. Sterile liquid carriers are used in sterile liquid form compositions for parenteral administration. The liquid carrier for pressurized compositions can be halogenated hydrocarbon or other pharmaceutically acceptable propellants.

[1117] Liquid pharmaceutical compositions, which are sterile solutions or suspensions, can be utilized by, for example, intramuscular, intraperitoneal, or subcutaneous injection. Sterile injectable solutions can also be administered intravenously. Compositions for oral administration can be in either liquid or solid form.

[1118] Preferably the pharmaceutical composition is in unit dosage form, for example, as tablets, capsules, powders, solutions, suspensions, emulsions, granules, or suppositories. In such form, the pharmaceutical composition can be further sub-divided to contain appropriate quantities of the compound. The unit dosage forms can be packaged compositions, for example, packeted powders, vials, ampoules, prefilled syringes, or sachets containing liquids. Alternatively, the unit dosage form can be a capsule or tablet itself, or it can be the appropriate number of any such compositions in package form. Such doses can be administered in any manner useful in directing the compound(s) to the recipient's bloodstream, including orally, via implants, parenterally (including intravenous, intraperitoneal, and subcutaneous injections), rectally, vaginally, and transdermally.

[1119] When administered for the treatment or inhibition of a particular disease state or disorder, it is understood that an effective dosage can vary depending upon the particular compound utilized, the pharmaceutical composition formulated, the mode of administration, physical factors related to the individual being treated, and severity of the condition being treated. In therapeutic applications, a compound of the present teachings can be provided to a patient already suffering from a disease in an amount sufficient to cure or at least partially ameliorate the symptoms of the disease and its complications. The dosage to be used in the treatment of a specific individual typically must be subjectively determined by the attending physician. The variables involved include the specific condition, stage of said condition, and

the characteristics of the patient including their size, age and response pattern to the compound utilized.

[1120] In some cases, it may be desirable to administer a compound directly to the airways of the patient, using devices such as, but not limited to, metered dose inhalers, breath-operated inhalers, multidose dry-powder inhalers, pumps, squeeze-actuated nebulized spray dispensers, aerosol dispensers, and aerosol nebulizers. For administration by intranasal or intrabronchial inhalation, the compounds of the present teachings can be formulated into a liquid composition, a solid composition, or an aerosol composition. The liquid composition can include, by way of illustration, one or more compounds of the present teachings dissolved, partially dissolved, or suspended in one or more pharmaceutically acceptable solvents and can be administered by, for example, a pump or a squeeze-actuated nebulized spray dispenser. The solvents can be, for example, isotonic saline or bacteriostatic water. The solid composition can be, by way of illustration, a powder preparation including one or more compounds of the present teachings intermixed with lactose or other inert powders that are acceptable for intrabronchial use, and can be administered by, for example, an aerosol dispenser or a device that breaks or punctures a capsule encasing the solid composition and delivers the solid composition for inhalation. The aerosol composition can include, by way of illustration, one or more compounds of the present teachings, propellants, surfactants, and co-solvents, and can be administered by, for example, a metered device. The propellants can be a chlorofluorocarbon (CFC), a hydrofluoroalkane (HFA), or other propellants that are physiologically and environmentally acceptable.

[1121] Compounds described herein can be administered parenterally or intraperitoneally. Solutions or suspensions of these compounds or a pharmaceutically acceptable salts, hydrates, or esters thereof can be prepared in water suitably mixed with a surfactant such as hydroxyl-propylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof in oils. Under ordinary conditions of storage and use, these preparations typically contain a preservative to inhibit the growth of microorganisms.

[1122] The pharmaceutical forms suitable for injection can include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In some embodiments, the form can be sterile and its viscosity permits it to flow through a syringe. The form preferably is stable under the conditions of manufacture and storage and can be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol and liquid polyethylene glycol), suitable mixtures thereof, and vegetable oils.

[1123] Compounds described herein can be administered transdermally, i.e., administered across the surface of the body and the inner linings of bodily passages including epithelial and mucosal tissues. Such administration can be carried out using the compounds of the present teachings including pharmaceutically acceptable salts, hydrates, or esters thereof, in lotions, creams, foams, patches, suspensions, solutions, and suppositories (rectal and vaginal).

[1124] Transdermal administration can be accomplished through the use of a transdermal patch containing a compound, such as a compound disclosed herein, and a carrier that can be inert to the compound, can be non-toxic to the skin, and can allow delivery of the compound for systemic absorption into the blood stream via the skin. The carrier can take any number of forms such as creams and ointments, pastes, gels, and occlusive devices. The creams and ointments can be viscous liquid or semisolid emulsions of either the oil-in-water or water-in-oil type. Pastes comprised of absorptive powders dispersed in petroleum or hydrophilic petroleum containing the compound can also be suitable. A variety of occlusive devices can be used to release the compound into the blood stream, such as a semi-permeable membrane covering a reservoir containing the compound with or without a carrier, or a matrix containing the compound. Other occlusive devices are known in the literature.

[1125] Compounds described herein can be administered rectally or vaginally in the form of a conventional suppository. Suppository formulations can be made from traditional materials, including cocoa butter, with or without the addition of waxes to alter the suppository's melting point, and glycerin. Water-soluble suppository bases, such as polyethylene glycols of various molecular weights, can also be used.

[1126] Lipid formulations or nanocapsules can be used to introduce compounds of the present teachings into host cells either in vitro or in vivo. Lipid formulations and nanocapsules can be prepared by methods known in the art.

Pharmacokinetics and Dosing

[1127] In some embodiments, a method of treating a neurological disease may be characterized by one or more pharmacokinetic parameters such as AUC, C_{max}, T_{max}, and others known and understood to persons of skill in the art. The term “pharmacokinetic” (PK) as used herein is used in its ordinary sense to mean the pharmacokinetic aspects of drug delivery. By definition pharmacokinetics (PK) is the study of how an organism affect a drug, e.g., how, and how fast it metabolizes the drug. The pharmacokinetics typically vary based upon the dosage amount of one or more of the disclosed NMDA receptor antagonists and/or metal channel activators. The

pharmacokinetics may or may not vary as a function of administration route, and, if any, the binders, excipients, and dilutants in the pharmaceutical composition.

[1128] In some embodiments, a method of treating a neurological disease may be characterized by an AUC for a NMDA receptor antagonist and/or metal channel activator compound according to Formulas 1 – 180, Formulas 200 – 260, compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof. In some embodiments, the $AUC_{0\text{-}t}$ and/or $AUC_{0\text{-}inf}$ (collectively referred to in the alternative as, simply, AUC) may be from about 80 – 125% of a given AUC value. In some embodiments, the AUC may be within 80 – 125 % of about 25, 50, 100, 150, 200, 250, 300, 400, 500, 600, 700, 800, 900, 1000, 1300, 1600, 1900, 2500, 3500, 5000, 7500, 10,000, 15,000, 20,000, 30,000, 50,000, and/or 100,000 hr*ng/mL. In some embodiments, a systemic treatment may have a larger AUC than a localized (such as topical or subdermal) treatment.

[1129] In some embodiments, a method of treating a neurological disease may be characterized by a C_{max} for a NMDA receptor antagonist and/or metal channel activator compound according to Formulas 1 – 180, Formulas 200 – 260, compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof. In some embodiments, the C_{max} may be from about 80 – 125% of a given C_{max} value. In some embodiments, the C_{max} may be within 80 – 125 % of about 1, 2, 3, 4, 5, 8, 10, 20, 35, 50, 80,100, 150, 200, 250, 300, 400, 500, 600, 700, 800, 900, 1000, 1300, 1600, 1900, 2500, 3500, 5000, 7500, 10,000, 15,000, 20,000, 30,000, 50,000, and/or 100,000 ng/mL. In some embodiments, a systemic treatment may have a larger C_{max} than a localized (such as topical or subdermal) treatment.

[1130] In some embodiments, a ratio C_{max}/AUC may be used to characterize a method of treating a neurological disease wherein one or more of a NMDA receptor antagonist and/or metal channel activator compound according to Formulas 1 – 180, Formulas 200 – 260, compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof are administered to a subject. In some embodiments, the C_{max}/AUC ratio may be from about 80 – 125 % of a given C_{max}/AUC ratio. In some embodiments, the C_{max}/AUC ratio may be from about 80 – 125 % of about 0.01, 0.03, 0.05, 0.08, 0.1, 0.13, 0.17, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.6, 0.7, 0.8, and 0.9.

[1131] In some embodiments, the T_{max} may range from about 0.1 – 16 hours, or from about 0.3 – 8 hours, or from about 0.5 – 4 hours, or from 0.5 – 2 hours, or from about 1 – 2 hours. In

some embodiments, the route of administration, which may be any route described herein or known to a person of skill in the art, may affect the T_{max} of a compound according to Formulas 1 – 180, Formulas 200 – 260, compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof. Excipients or other pharmaceutically acceptable carriers in pharmaceutical compositions of one or more compounds according to Formulas 1 – 180, Formulas 200 – 238, compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof may alter the T_{max} value by making it larger or smaller than a pharmaceutical composition having the excipient or carrier excluded.

[1132] Solid compositions are normally formulated in dosage units providing from about 0.1 to about 1000 mg of the active ingredient per dose. Some examples of solid dosage units are 0.1 mg, 1 mg, 10 mg, 100 mg, 500 mg, and 1000 mg. Liquid compositions are generally in a unit dosage range of 0.1-100 mg/mL. Some examples of liquid dosage units are 0.1 mg/mL, 1 mg/mL, 10 mg/mL, 25 mg/mL, 50 mg/mL, and 100 mg/mL.

[1133] In some embodiments, a dose is daily. In some embodiments, a dose is twice daily. In some embodiments, a does is one, two, three, four, or five times daily. In some embodiments, a dose is once every other day, once every second day, once every third day, once every fourth day, once every fifth day, once every sixth day, weekly, bi-weekly, or monthly. Typically, a dose may be from 0.01-100 mg/kg body weight, or from .05 – 50 mg/kg body weight, or from 0.1 – 10 mg/kg body weight, or from 0.15 – 5 mg/kg body weight, or from 0.2 – 2 mg/kg body weight, or from 0.5 – 1.5 mg/kg body weight, or from 1 – 1.5 mg/kg body weight. In some embodiments, the dosing regimen may comprise one or more optional loading doses and a subsequent maintenance dose regimen. A loading dose may be larger than the doses given in a subsequent maintenance dose regimen.

[1134] In some embodiments, the dosage is adjusted based upon neurological disease symptoms observed in the patient. A symptom-dependent regimen may have a larger treatment dose while symptoms are present and a smaller preventative dose while symptoms are lessened, in remission, controlled, etc. In some embodiments, a treatment dose may comprise a unit dosage of about 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 75 mg, 80 mg, 100 mg, 120 mg, 140 mg, 160 mg, 180 mg, or 200 mg of an NMDA receptor antagonist according to any one of Formulas 1 – 180, and/or a metal channel activator according to any one of Formulas 200 – 260, or a compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof . In

some embodiments, a preventative dose may comprise a unit dosage of about 1 mg, 2 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 75 mg, 80 mg, 100 mg, 120 mg, or 140 mg of a NMDA receptor antagonist according to any one of Formulas 200 – 260, and/or a metal channel activator according to any one of Formulas 1 – 180, or a compounds disclosed in the "further embodiments section" under the "METAL CHANNEL ACTIVATOR" subheading, and/or pharmaceutically acceptable salts thereof . In some embodiments, the preventative dose is an amount that is about 7/8, 3/4, 5/8, 1/2, 3/8, 1/4, or about 1/8 of the amount of the treatment dose. In some embodiments, if a patient receiving a preventative dosing regimen experiences recurrence or onset of symptoms, a treatment dosing regimen may replace the preventative dosing regimen until symptoms have lessened or subsided. Each of the treatment and/or preventative doses may be adjusted during the regimen based upon the severity of neurological disorder symptoms.

CLAIMS

1. A pharmaceutical composition comprising a metal channel activator and an NMDA receptor antagonist.

2. The pharmaceutical composition of Claim 1, wherein the metal channel activator is a potassium channel activator.

3. The pharmaceutical composition of Claim 2, wherein the potassium channel activator is a Kv7 channel activator.

4. The pharmaceutical composition of Claim 3, wherein the Kv7 channel activator is a Kv7.1 channel activator, a Kv7.2 channel activator, a Kv7.3 channel activator, a Kv7.4 channel activator, a Kv7.5 channel activator, or any combination thereof.

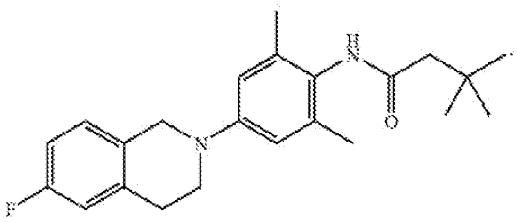
5. The pharmaceutical composition of Claim 3 or 4, wherein the Kv7 channel activator is a Kv7.2/7.3 channel activator.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the metal channel activator is selected from one or more compounds according to any one or more of formulas 1 to 171.

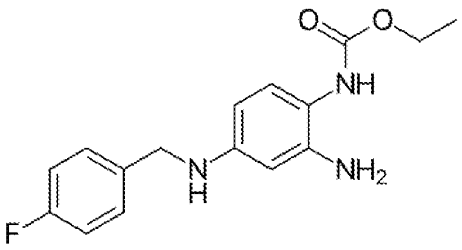
7. The pharmaceutical composition of any one of claims 1 to 6, wherein the NMDA receptor antagonist is selected from one or more compounds according to any one or more of formulas 200 to 260.

8. The pharmaceutical composition of any one of claims 1 to 5, wherein the NMDA receptor antagonist is selected from one or more compounds according to any one or more of formulas 200 to 260, and wherein the metal channel activator is selected from one or more of the disclosed compounds according to any one or more of formulas 1 to 171.

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the metal channel activator is



10. The pharmaceutical composition of any one of claims 1 to 8, wherein the metal channel activator is



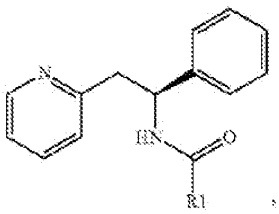
11. The pharmaceutical composition of any one of claims 1 to 10, wherein the NMDA receptor antagonist is ketamine, lanicemine, dextromethorphan (DXM), phencyclidine (PCP), methoxetamine (MXE), or a pharmaceutically acceptable salt thereof.

12. The pharmaceutical composition of any one of claims 1 to 11, wherein the NMDA receptor antagonist or a pharmaceutically acceptable salt thereof is in a form of a prodrug.

13. The pharmaceutical composition of any one of claims 1 to 12, wherein the NMDA receptor antagonist is lanicemine or a pharmaceutically acceptable salt thereof.

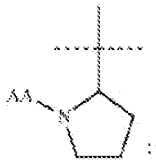
14. The pharmaceutical composition of Claim 13, wherein the lanicemine or a pharmaceutically acceptable salt thereof is in a form of a prodrug.

15. The pharmaceutical composition of Claim 14, wherein the prodrug of lanicemine has the following structure:



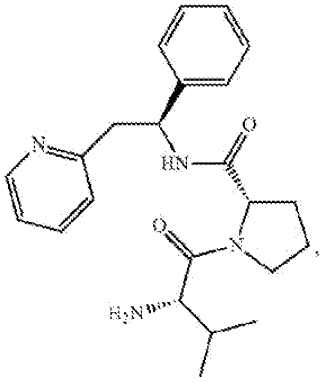
(I)

wherein R1 is C_{1-6} alkylC(O)O(C_{1-6}alkoxy), or



AA is a peptide bond-linked natural amino acid;
or a pharmaceutically acceptable salt thereof.

16. The pharmaceutical composition of Claim 14 or 15, wherein the prodrug of lanicemine has the following structure:



or a pharmaceutically acceptable salt thereof.

17. A method of treating a depressive disorder, comprising administering the pharmaceutical composition of any one of Claims 1-17.

18. The method of Claim 17, wherein the depressive disorder is major depressive disorder (MDD), disruptive mood dysregulation disorder, persistent depressive disorder, bipolar spectrum disorder, postpartum depression, premenstrual dysphoric disorder (PMDD), seasonal affective disorder (SAD), atypical depression, treatment-resistant depression (TRD), depression associated with agitation or anxiety, adjustment disorder with depressed mood, prolonged depressive reaction, or a combination thereof.

19. A method of treating a neurological or neurodegenerative disorder, comprising administering the pharmaceutical composition of any one of Claims 1-16.

20. The method of Claim 19, wherein neurological or neurodegenerative disorder is amyotrophic lateral sclerosis, bipolar disorder, treatment resistant and major depression, general anxiety disorder, panic disorder, social anxiety, mood disorders, cognitive disorders, dementia, agitation, apathy, psychoses, post-traumatic stress disorders, irritability, disinhibition, learning disorders, memory loss, personality disorders, bipolar disorders, Rett syndrome, eating disorders, conduct disorder, neurodegenerative disorders, pain disorders, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, delirium, Alzheimer's disease, mild cognitive impairment, mild cognitive impairment due to Alzheimer's disease, drug addiction, tinnitus, mental retardation, obsessive-compulsive disorder, spinal muscular atrophy, radiation therapy, multiple sclerosis, chronic cerebellar ataxia, cervical spondylotic myelopathy, spinal cord injury, hereditary cerebellar ataxia, Tourette syndrome, autism spectrum disorder, schizophrenia, fragile X syndrome, Parkinson's Disease, Huntington's disease, or any combination thereof.

21. A method of treating a pain disorder, comprising administering the pharmaceutical composition of any one of Claims 1-16.

22. The method of Claim 21, wherein the pain disorder is acute pain, chronic pain, neuropathic pain, nociceptive pain, and/or radicular pain.

23. The method of Claim 21, wherein the pain disorder is migraine, inflammatory pain, persistent pain, cancer pain, and/or postoperative pain.

24. A kit for treating a patient afflicted with a disorders in which a metal channel activator is clinically relevant, said kit including:

(a) the metal channel activator; and

(b) instructions for administering said metal channel activator in combination with an NMDA receptor antagonist by one of the methods of Claims 17-23.

25. A kit for treating a patient afflicted with a disorder in which an NMDA receptor antagonist is clinically relevant, said kit including:

(a) the NMDA receptor antagonist; and

(b) instructions for administering said NMDA receptor antagonist with a metal channel activator by one of the methods of Claims 17-23.