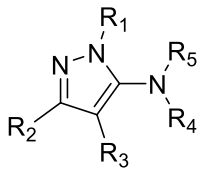
CLAIMS

What is claimed is:

1. A compound represented by Formula 1:



Formula 1

wherein:

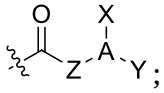
R_1 is optionally substituted C_{1-4} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{5-10} aryl, optionally substituted C_{2-8} heteroaryl, optionally substituted C_{2-8} heterocyclyl, or optionally substituted -C(O)NHC_{1-4} alkyl, wherein each optional substituent is independently selected from the group consisting of halogen, OH, CN, -C(O)NH_2, -N(C_{1-4} alkyl)$_2$, C_{1-4} alkyl, C_{5-10} aryl, and C_{5-10} haloaryl;

R_2 is H, halogen, optionally substituted C_{1-8} alkyl, optionally substituted C_{1-8} haloalkyl, optionally substituted -OC_{1-8} alkyl, optionally substituted C_{2-8} alkanoyl, optionally substituted C_{3-10} cycloalkyl, optionally substituted benzo(C_{3-8} cycloalkyl), optionally substituted C_{5-10} aryl, optionally substituted benzoyl, optionally substituted -OC_{5-10} aryl, optionally substituted C_{2-8} heteroaryl, or optionally substituted -OC_{2-8} heteroaryl, wherein each optional substituent is independently selected from the group consisting of halogen, OH, CN, CO_2H, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, -OC_{1-4} alkyl, -OC_{1-4} haloalkyl, C_{3-8} cycloalkyl, C_{3-8} halocycloalkyl, -CO_2H, -SO_2C_{1-4} alkyl, -SO_2C_{1-4} haloalkyl, C_{5-10} aryl, and C_{5-10} haloaryl, -N(C_{1-4} alkyl)$_2$, -NC_{1-4} alkyl, or optionally substituted C_{2-8} heterocyclyl;

R_3 is H, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted C_{2-8} heterocyclyl, or optionally substituted C_{5-10}

aryl, wherein each optional substituent is independently selected from the group consisting of halogen, OH, $N(R_7)(R_8)$ wherein R_7 and R_8 are independently H or C_{1-4} alkyl and wherein R_7 and R_8 are optionally connected to form a ring, CN, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, and C_{1-4} haloalkyl;

R_4 is H, C_{1-3} alkyl, C_{3-8} cycloalkyl, or C_{1-4} hydroxyalkyl;

R_5 is 

;

A is C_{1-8} alkyl, C_{2-8} alkenyl, C_{3-8} cycloalkyl, C_{5-10} bicycloalkyl, C_{2-5} heterocyclyl, C_{5-10} aryl, or C_{2-8} heteroaryl;

X is H, F, Cl, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted -OC_{1-6} alkyl, optionally substituted C_{2-5} heterocyclyl, or optionally substituted C_{5-10} aryl, wherein each optional substituent is independently selected from the group consisting of halogen, OH, C_{1-3} alkyl, C_{1-3} haloalkyl, -OC_{1-3} alkyl, C_{3-8} cycloalkyl, C_{3-8} halocycloalkyl, and CN.

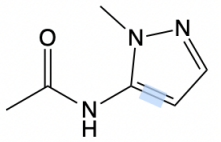
Y is H, halogen, OH, optionally substituted C_{1-3} alkyl, optionally substituted C_{3-6} cycloalkyl, optionally substituted -OC_{1-3} alkyl, optionally substituted C_{1-3} haloalkyl, or optionally substituted -OC_{1-3} haloalkyl, wherein each optional substituent is independently selected from the group consisting of halogen, OH, C_{1-3} alkyl, C_{1-3} haloalkyl, -OC_{1-3} alkyl, C_{3-8} cycloalkyl, C_{3-8} halocycloalkyl, and CN;

Z is a bond, $C(R_6)_2$, NR_6, O, $C(R_6)_2NR_6$, $C(R_6)_2O$, $NR_6C(R_6)_2$, or $OC(R_6)_2$; and

R_6 is H, C_{1-3} alkyl, or C_{1-4} hydroxyalkyl;

or a pharmaceutically acceptable salt thereof,

provided that the following compound is excluded:



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2. The compound of Claim 1, wherein R_1 is optionally substituted C_{1-4} alkyl or optionally substituted C_{3-8} cycloalkyl.

3. The compound of Claim 1, wherein R_2 is optionally substituted C_{3-10} cycloalkyl.

4. The compound of Claim 1, wherein R_3 is optionally substituted C_{1-6} alkyl or optionally substituted C_{3-8} cycloalkyl.

5. The compound of Claim 1, wherein R_4 is H.

6. The compound of Claim 1, wherein A is C_{1-8} alkyl or C_{3-8} cycloalkyl.

7. The compound of Claim 1,

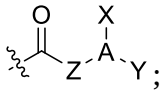
wherein

R_1 is optionally substituted C_{1-4} alkyl or optionally substituted C_{3-8} cycloalkyl;

R_2 is optionally substituted C_{3-6} cycloalkyl;

R_3 is optionally substituted C_{1-4} alkyl or optionally substituted C_{3-6} cycloalkyl;

R_4 is H; and

R_5 is 

;

A is C_{1-4} alkyl or C_{3-6} cycloalkyl;

X is H, F, optionally substituted C_{1-6} alkyl or optionally substituted C_{3-8} cycloalkyl,

Y is H or halogen; and

Z is a bond, $C(R_6)_2$, NR_6, and O.

8. The compound of Claim 7, wherein R_1 is optionally substituted C_{1-4} alkyl.

9. The compound of Claim 7, wherein R_1 is optionally substituted C_{3-8} cycloalkyl.

10. The compound of Claim 7, wherein R_2 is C_{3-6} cycloalkyl substituted with at least one F.

11. The compound of Claim 7, wherein R_3 is C_{1-4} alkyl or C_{3-6} cycloalkyl.

12. The compound of Claim 1, wherein the compound is selected from Compounds 1 to 574 in Table 1, or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a compound of any one of Claims 1-12, or a pharmaceutically acceptable salt thereof.

14. Use of a therapeutically effective amount of a compound of Claim 1, or pharmaceutically acceptable salt thereof in the manufacture of a medicament to treat a disease or disorder, wherein the compound or pharmaceutically acceptable salt thereof is to be administered to a subject in need thereof, wherein the disease or disorder is selected from a Kv7 associated disorder, a disorder associated with a KCNQ subunit, a disorder associated with a mutation in a KCNQ subunit, a neurodegenerative disease, a disease or disorder that would benefit from the activation of a Kv7.2 homomer, a neurodevelopmental disease or disorder, or a disease or disorder of Group CA.

15. The use of Claim 14, wherein the disease or disorder is a Kv7 associated disorder.

16. The use of Claim 15, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus, frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

17. The use of Claim 14, wherein the disease or disorder is a disorder associated with a mutation in a KCNQ subunit.

18. The use of Claim 17, wherein the disorder associated with a mutation in a KCNQ subunit is a disorder associated with a KCNQ2 mutation.

19. The use of Claim 18, wherein the disorder associated with a KCNQ2 mutation is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypsarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and combinations thereof.

20. The use of Claim 14, wherein the disease or disorder is a neurodevelopmental disease or disorder.

21. The use of Claim 20, wherein the subject is a fetus, an infant from about birth to about 12 months, or a child of about 1 year to about 12 years old.

22. The use of Claim 20, wherein the neurodevelopmental disease or disorder is selected from the group consisting of Angelman syndrome, neonatal abstinence syndrome, early myoclonic encephalopathy, Landau Kleffner syndrome, electrical status epilepticus during sleep, Ohtahara syndrome, autism spectrum disorders, Dravet syndrome, Lennox-Gastaut syndrome, Rett syndrome, Hirschsprung's disease (HSCR), West syndrome, SCN8A-related epilepsy with encephalopathy (EIEE13), Epilepsy of infancy with migrating focal seizures (EIMFS), Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE), Doose syndrome, and combinations thereof.

23. The use of Claim 14, wherein the compound modulates Kv7.2/7.3 and does not modulate $GABA_A$.

24. The use of Claim 14, wherein the therapeutically effective amount does not result in unwanted side effects.

25. The use of Claim 24, wherein the unwanted side effects are selected from the group consisting of dizziness, fatigue, drowsiness, confusion, vertigo, tremor, ataxia, double or blurred vision, attention deficit, memory impairment, muscle weakness, skin discoloration, withdrawal seizures, QT interval changes, suicidal behavior, urinary retention, sleepiness, hallucination, confusion, and combinations thereof.

26. The use of Claim 14, wherein the compound is more potent than ezogabine.

27. The use of Claim 14, wherein the therapeutically effective amount has greater tolerability than ezogabine.

28. The use of Claim 14, wherein the disease or disorder is a disease or disorder of Group CA.

29. The use of Claim 28, wherein the disease or disorder of Group CA is selected from the group consisting of alcohol use disorders, Dravet syndrome, traumatic brain injury, cerebral vasospasm following subarachnoid hemorrhage, stroke, gout pain, temporomandibular joint (TMJ) pain, chronic cough, asthma or chronic obstructive pulmonary disease, trigeminal neuralgia (TN), atypical facial pain, cluster headache, neuropathic pain induced by chemotherapy drugs, orofacial cold hyperalgesia, depression, major depressive disorder, peripheral nerve hyperexcitability (PNH) syndromes, neuromyotonia, cramp-fasciculation syndrome (CFS), Morvan's syndrome, diseases involving hypoxic pulmonary vasoconstriction (HPV), hypoxia-induced pulmonary hypertension and high altitude pulmonary edema, pre-eclampsia, paroxysmal dystonia, psychostimulant addiction, bipolar disorder, posttraumatic stress disorder (PTSD), noise induced tinnitus, salicylate induced hearing loss and tinnitus, and combinations thereof.