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Novel GABAAR-α6 Subtype Selective Ligands for Pain and CNS Disorders

Through a joint collaboration the inventors have synthesized and tested novel non-benzodiazepine GABA A receptor ligands functionally selective to the alpha 6 subtype (GABAAR-α6). Recent studies have implicated the α6 receptors as the valid target in **trigeminal orofacial pain, neuropsychiatric disorders** with sensori-motor gating deficits, depression, and migraine. The group has observed promising results in animal models for several of these indications, and the lead compounds show a lack of cytotoxicity, improved metabolic stability, an excellent bioavailability after oral administration, and appropriate brain concentrations, rendering them potential candidates for treatment of CNS disorders.

Many GABAergic drugs on the market today offer little subtype selectivity and thus exhibit undesired side effects (sedation, ataxia, amnesia, tolerance, and addiction).

There has been a lack of new drugs developed for CNS disorders, while the social, clinical, and economic need remains. We believe our team has **discovered the first α6 selective ligands**. The team continues to explore indications including epilepsy, tic disorders, schizophrenia, obsessive compulsive disorders, attention deficit disorders, depression, migraine, and pain.

MARKETS

At some point 45% of people will be affected by some type of neuro-psychiatric disorder, and unmet needs are increasing. Global migraine sales are expected to grow to $8.7 billion by 2026, however current treatments leave a large number of patients undertreated; many of the drugs, for both acute and preventative treatment, have poor efficacy profiles which are ineffective in a large number of patients. Epidemiologists forecast the diagnosed prevalent cases of ADHD to grow by 2.86% per year over the next 10 years, to 34M cases in 2024.
People with Tourette's disorder or chronic tic disorder are over four times more likely to die by suicide than the general population, according to a new study in Biological Psychiatry. The results highlight an under-recognized need in patients with chronic tic disorders.

Joint invention: University of Wisconsin, Medical University of Vienna, TU Vienna, University of Belgrade, National Taiwan University

REFERENCE:
517.14

IPR:
US2018134698
EP3325479

COOPERATION OPTIONS:
Available for developmental research support/licensing under either exclusive or nonexclusive

FEATURES/BENEFITS:

- **Functionally selective** – The novel compounds are functionally selective for the α6 GABAA subtypes.
- **Non-Sedating** – Avoidance of the α1-subtype aids in preventing sedative and other psychomotor-impairing effects.
- **Metabolically stable** – Deuteration of the methoxy group of arylpyrazoloquino-linones improves metabolic stability and optimizes bioavailability.
- **Safer/Less addictive** – Compounds which are silent or nearly silent at the α1-and α5-subtype should demonstrate no tolerance and less addictive effects.

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