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Neurosteroids in Epilepsy

https://www.iocbtech.cz/project/neurosteroids-2-2/

NOVEL NEUROSTEROIDS FOR THE TREATMENT OF EPILEPSY AND SEIZURE DISEASES

Scientists

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CHALLENGE

With ca. 50 million people affected worldwide, epilepsy is one of the most common diseases of the central nervous system. Despite the wide therapeutic arsenal currently available, up to 30 % of adult patients and 25 % of children have poorly controlled seizures. Therefore, there remains a significant unmet need for novel, more efficacious therapies.

TECHNOLOGY

Endogenous steroidal compounds called neurosteroids and their synthetic derivatives (neuroactive steroids) can modulate neuronal activity through interaction with various ligand-gated ion channels, voltage-gated ion channels, or G-protein coupled receptors. Most of the research prioritizes allosteric modulation of □-aminobutyric acid receptors type A (GABAARs) and N-methyl-D-aspartate receptors (NMDARs). Indeed, both receptors play a pivotal role in the regulation of neuronal excitability. Their dysfunction underlies many neuropsychiatric diseases, including seizure conditions and epilepsy syndromes.
We have synthesized novel neuroactive steroids, which act as allosteric modulators of GABA- and NMDA-induced currents. Moreover, our neuroactive steroids showed potent anticonvulsant efficacy in multiple animal models of seizures, including models of

pharmacoresistance (Figure 1).

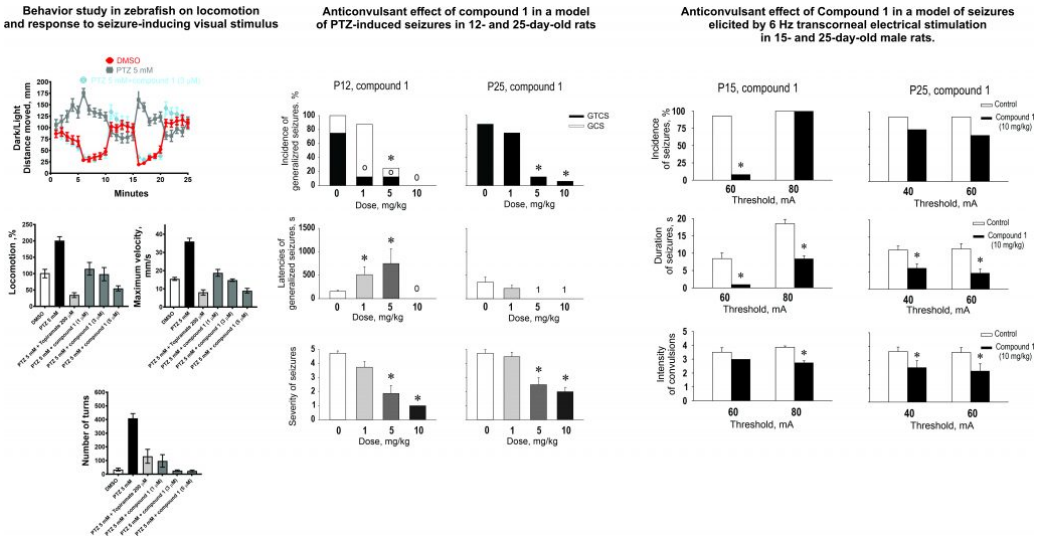

Figure 1. Overview of animal models used for evaluation of anticonvulsant potential our novel neuroactive steroids

At the moment, our lead compound is in a late-stage of studies performer by the Epilepsy Therapy Screening Program (ETSP) of the National Institute of Neurological Disorders and Stroke (NIH). ETSP is a program that arranges screening of the accepted compound in a battery of rodent seizure models (Figure 2). These tests are performed at a contract facility based at the University of Utah on a blinded and confidential basis and at no cost to the ETSP participants. As for early 2021, testing in Post-Kainic Acid Spontaneously Recurrent Seizures model is ongoing. For details, please do see the following link https://www.ninds.nih.gov/Current-Research/Focus-Research/Focus-Epilepsy/ETSP

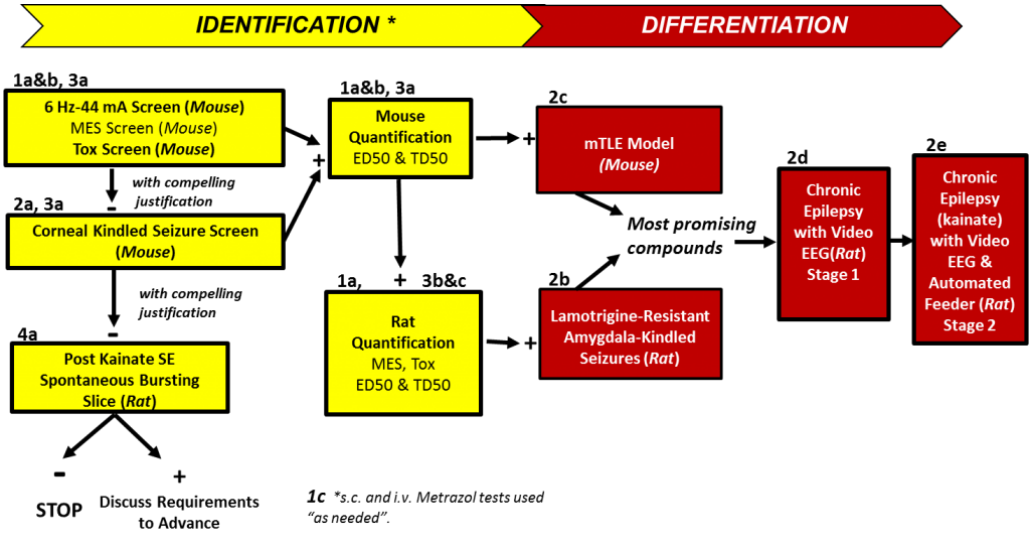

Figure 2. Workflow for Pharmacoresistant Epilepsy (https://panache.ninds.nih.gov/CurrentModels.aspx)

COMMERCIAL OPPORTUNITY

This project is ready for collaboration/co-development.

DEVELOPMENT STATUS

The project is in the preclinical/lead optimization phase.

PATENT SITUATION

PCT/CZ2020/050017 „3 5 -Neuroactive steroids for treating epilepsy and seizure diseases" filled on 2nd April 2020.

FURTHER READING

Recent review:
Miziak et al.: Neurosteroids and Seizure Activity, Front. Endocrinol., 2020, 11, 766. https://doi.org/10.3389/fendo.2020.541802