

ARumenamide, Sodium Channel Potentiators, have the Potential to Cure Epilepsy and Related Neurological Disorders

ARumenamide, the first to ameliorate loss-of-function in voltage-gated sodium channels underlying epilepsy and other related disorders

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Reference: 2017- 014

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IP Status

Patent application submitted, Patented

Seeking

Development partner, Commercial partner, Seeking investment, University spin out

Background

The World Health Organization (WHO) reports that epilepsy, which affects about 50 million people globally and raises the risk of early death, is one of the most prevalent neurological conditions. However, when properly identified and treated, about 70% of epilepsy sufferers are seizure-free. Seizures produced by epilepsy emerge from numerous parts of the brain and are characterized by aberrant electrical signals brought on by damaged proteins. A mutation in one of the genes that codes for these proteins is present in roughly 30 to 40 percent of epilepsy sufferers. These mutations can cause early-onset cerebellar ataxia, intellectual disability, developmental delay, and mobility abnormalities in addition to epilepsy.

The main protein responsible for the electrical signal in the brain and nervous system is voltage-gated sodium channels (VGSCs). Epilepsy is caused by mutations in five different varieties of neuronal VGSCs. Mutations in VGSCs make up 5% of recognized epileptic encephalopathies. These genetic alterations give rise to gain-of-function and loss-of-function in VGSCs. Current anti-epileptic medications target gain-of-function mutations, leaving many epilepsy patients with unmet needs. Additionally, VGSC mutations frequently switch between gain-of-function and loss-of-function, necessitating the discovery of drugs to treat the latter.

Tech Overview

SFU researchers have invented a class of drugs known as *ARumenamide* that target loss-of-function in VGSCs. Initially, these compounds were screened against the VGSCs expressed in the heart. A successful pre-clinical candidate was validated and screened using a dog heart model of heart disease caused by VGSC loss-of-function and voltage-gated potassium channel gain-of-function (VGPCs). The medication effectively improves VGSCs and inhibits the nearby VGPCs, which treats the electrical heart rhythm disorder.

The preliminary findings are very promising, and *ARumenamide* may be extremely effective in treating neurological conditions like epilepsy that share a pathophysiology with heart rhythm problems. Furthermore, different epilepsies result from the loss of function of VGSCs and gain of function of VGPCs. VGSCs expressed in the heart share a high degree of homology with ones expressed in the nervous system. As a result, we believe that *ARumenamide* compounds will be extremely effective in the treatment of epilepsy and other neurological disorders.

Stage of Development

Pre-Clinical and animal studies 2021-2022 (i.e., *ex-vivo* canine wedge heart model).

Clinical trial preparation ready, pending funding.

Benefits

- Enhancing sodium current, which ameliorates loss-of-function in VGSCs.
- Unique effect in suppressing gain-of-function in VGPCs, which is a peculiar trait found in several forms of epilepsy.
- Has no other toxic or harmful side-effects when screened against other channels.

Patents

- PCT/IB2020/050853

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