

Scientific review of golaxanolone's therapeutic potential on symptoms arising from neuroinflammation published in *Frontiers in Pharmacology*

STOCKHOLM – March 15, 2024. Umecrine Cognition today announces that the company has contributed to a review article outlining the scientific support of its lead candidate drug **golexanolone** and its potential to treat cognitive symptoms arising from neuroinflammation in chronic liver diseases (CLD). Golexanolone represents a new class of drug candidates that effectively normalize GABA signaling and decrease neuroinflammation. The candidate drug is currently being evaluated in a clinical Phase 2 trial, in patients with primary biliary cholangitis (PBC) exhibiting central fatigue, awaiting final results in 2025. The article is published in the March issue of *Frontiers in Pharmacology*.

In the review article, co-written by the company and its scientific partners, the authors draw on the current body of literature to scrutinize the molecular interplay between neuroinflammatory activities and GABA signaling, as well as highlight amelioratory effects produced by golexanolone. Neuroinflammation is known to play a detrimental role in numerous diseases. This occurs when the brain's immune cells are activated erroneously, or too extensively, resulting in harmful effects on surrounding neurons. When this occurs in proximity to GABA-signaling neurons, a plethora of cognitive and motor symptoms arise, including fatigue and incoordination. The article describes the dynamics of these phenomena as they occur in hyperammonemia and hepatic encephalopathy. Further, the authors discuss the implication of these insights on future treatment strategies.

Golexanolone has been proven in several nonclinical studies to reduce neuroinflammation and normalize GABA signaling in animal models of hyperammonemia, hepatic encephalopathy and cholestasis, thus improving fatigue, cognitive performance, and normalizing motor incoordination. Similar responses have been reported in a clinical Phase 2 study and could be expected in patients with PBC or cirrhosis.

"Despite an outspoken need, debilitating cognitive symptoms such as fatigue, brain fog and other disturbances remain largely unaddressed in the development of new therapeutics targeting chronic liver diseases. Through its novel mechanism of action, golexanolone has shown normalizing effects on GABA signaling, without causing adverse effects, resulting in symptom relief as well as decreased inflammatory status in the brain. Therefore, we see great potential in golexanolone to treat CNS symptoms and complement current treatment regimens that primarily address molecular targets outside the brain", says Magnus Doverskog, SVP and Chief Scientific Officer, Umecrine Cognition.

Read the full article here: www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2024.1358323/full

Article Citation

Llansola M, Arenas YM, Sancho-Alonso M, Mincheva G, Palomares-Rodriguez A,

Doverskog M, Izquierdo-Altarejos P and Felipo V (2024), Neuroinflammation alters GABAergic neurotransmission in hyperammonemia and hepatic encephalopathy, leading to motor incoordination. Mechanisms and therapeutic implications. *Front. Pharmacol.* 15:1358323.

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About Umecrine Cognition AB

Umecrine Cognition AB is developing a completely new class of drugs for the treatment of chronic neuroinflammation – a devastating brain distortion that can lead to severely impaired cognition and fatigue. Chronic neuroinflammation can occur as a result of a number of underlying conditions, including a range of liver diseases as well as neurodegenerative diseases, such as Parkinson's disease. Results from an internationally acclaimed Phase 2 clinical trial indicate that the company's most advanced drug candidate, the GABAA receptor-modulating steroid antagonist golexanolone, normalizes brain signaling and improves cognition and alertness in patients with hepatic encephalopathy. A Phase 2 trial is currently ongoing in patients with primary biliary cirrhosis. Further, based on intriguing preclinical data, the company is planning to pursue the development of golexanolone in patients with Parkinson's disease. For more information, visit www.umecrinecognition.com.

Attachments

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