

Umecrine Cognition presents new preclinical data that elucidates the mechanism-of-action of golexanolone in cholestatic liver disease

Stockholm, June 7, 2023 – Umecrine Cognition AB today announced new results from a preclinical model of cholestasis that elucidate the mechanism-of-action of the company's clinical drug candidate golexanolone in reversing fatigue. This important finding is based on additional data from a preclinical study carried out in collaboration with Dr. Vicente Felipo at the Laboratory of Neurobiology, Centro de Investigación Príncipe Felipe in Valencia, Spain. This new supplementary data was generated to inform on potential intervention studies in PBC patients. The results show that golexanolone may have beneficial effects to treat fatigue, and motor and cognitive impairment in patients with chronic cholestatic liver disease PBC. The data will be presented as a poster during the International Liver Congress EASL in Vienna, June 21-24.

Cholestasis may appear in patients with primary sclerosing cholangitis, primary biliary cholangitis, or drug-induced liver injury. Patients with these chronic cholestatic liver diseases may show fatigue and other symptomatic alterations that severely reduce their quality of life. There are no effective treatments for these alterations. The aim of the study was to assess if golexanolone treatment reduces peripheral inflammation and improves fatigue and cognitive and motor functions in a preclinical bile-duct ligation (BDL) model of cholestatic liver disease and also to identify the mechanisms involved.

The results from the preclinical study showed that golexanolone reversed the increase of several pro-inflammatory interleukins and reversed specific alterations in GABAergic neurotransmission in the cerebellum. Golexanolone also reduced the content of pro-inflammatory factors in the cerebellum. These findings are following previously reported mechanisms of golexanolone and further elucidate the mechanism-of-action of golexanolone in reversing fatigue and improving short-term memory in cholestatic liver diseases.

"Currently available treatments of PBC are exclusively used to slow or prevent disease progression and have no impact on symptomatic relief. Fatigue is recognized as the most burdensome symptom of the disease and we are strengthened by every study result that supports golexanolone as a symptom-relieving treatment, in this case by showing a reduction of peripheral inflammation which is associated with improvement in fatigue, locomotor gait, and coordination, and short-term memory," said Anders Karlsson, CEO of Umecrine Cognition.

Umecrine Cognition's drug candidate golexanolone is currently in clinical development for primary biliary cholangitis and hepatic encephalopathy, two indications involving pathogenic accumulation of toxic metabolites, proposedly resulting in neuroinflammation and disturbed neural signaling.

"The present results underpin that golexanolone may have beneficial effects to treat fatigue, and motor and cognitive impairment in patients with chronic cholestatic liver disease PBC and provide mechanistic support to our ongoing phase 2 study in PBC patients with fatigue and cognitive dysfunction," said Magnus Doverskog, SVP, and Chief Scientific Officer at Umecrine Cognition.

Abstract title: *Golexanolone, a GABA receptor-modulating steroid antagonist, improves peripheral inflammation, fatigue, locomotor gait, motor incoordination, and short-term memory in rats with cholestasis and hepatic encephalopathy due to bile duct ligation.*

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About Umecrine Cognition AB

Umecrine Cognition AB develops a completely new class of pharmaceuticals against neurological disturbances in the brain that may arise as a consequence of several underlying diseases, leading to strongly reduced cognitive functions and wakefulness. Results from an internationally recognized clinical Phase 2 study indicate that the company's most advanced drug candidate, golexanolone, normalizes the brain's signaling and improves cognition as well as wakefulness in patients diagnosed with hepatic encephalopathy. The continued drug development will initially focus on patient groups whose symptoms arise from chronic liver diseases. The mode of action is however relevant in a number of other indications some of which are now being investigated. For more information, visit www.umecrinecognition.com.

References:

1. Mincheva, G., et al., Golexanolone, a GABAA receptor modulating steroid antagonist, restores motor coordination and cognitive function in hyperammonemic rats by dual effects on peripheral inflammation and neuroinflammation. *CNS Neurosci Ther.* 2022 Nov;28(11):1861-1874 (Open access: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9532914/>).
2. <https://www.umecrinecognition.com/en/first-patient-included-in-umecrine-cognitions-clinical-phase-2-study-of-golexanolone-in-primary-biliary-cholangitis/>

Attachments

[Umecrine Cognition presents new preclinical data that elucidates the mechanism-of-action of golexanolone in cholestatic liver disease](#)