

Umechrine Cognition presents preclinical results showing significant decreases in PBC-like symptomology and neuroinflammation

Stockholm, November 28, 2023 – Umechrine Cognition AB today announced positive preclinical results that indicate normalizing effects of the clinical drug candidate golexanolone on PBC-like symptomology including cognitive symptoms, such as fatigue, motor impairments, neuroinflammation, and neural signaling. The results are published in the November issue of the internationally renowned journal *Liver International*.

Patients with the chronic cholestatic liver disease primary biliary cholangitis (PBC) exhibit, among other symptoms, debilitating fatigue and cognitive impairments that substantially reduce their quality of life. Current PBC treatments do not improve the symptomology, and new, more effective, treatments are therefore required. Results from the current preclinical study in a validated and well-known disease model of cholestasis (BDL) show that golexanolone improves PBC-like symptoms. In the study, the researchers observed a clear reduction in central fatigue, marked improvements in short term memory, and normalized motoric functions following a 4-5 week treatment regimen with golexanolone.

Furthermore, a growing body of molecular and clinical research suggests there is a connection between inflammation of different origins, i.e., both peripherally and in the brain, and the onset of the cognitive and motoric symptoms observed e.g., in PBC. In the current study, the research team set out to investigate the effect of golexanolone on inflammatory biomarkers. The results show a dampening effect on pro-inflammatory biomarkers both systemically and in the brain. Notably, golexanolone had an important effect on the activity of immune cells in the central nervous system. Tissue analyses show that golexanolone clearly reduces the activity of a subset of immunological cells (microglia and astrocytes) in the brain, which reportedly has a deteriorating effect on brain neurons, partly by inducing an excessive release of GABA. Indicatively, by normalizing this immune activity in the brain, golexanolone prevents central inflammation.

Collectively, these results point toward golexanolone's potential in treating symptoms in patients suffering from PBC, as well as early signals that the drug candidate could disrupt neuroinflammatory signaling and, in effect, normalize GABA signaling to prevent cognitive symptoms observed in PBC.

"Primary biliary cholangitis patients suffer severely from symptoms such as extreme fatigue, which hinder everyday activities. Due to the complexity of the symptomology, no therapies are available to treat these symptoms, creating a notable unmet need. The results from the current study provide strong mechanistic and clinical phenotype data that underpins the potential of golexanolone as a first-ever specific therapy for the commonest symptoms in PBC," comments David Jones, Professor of Liver Immunology at the Translational and Clinical Research Institute, Newcastle University, and Honorary Hepatologist at Newcastle's Freeman Hospital, United Kingdom.

Umecrine Cognition has previously shown, in two separate preclinical studies, evidence supporting the normalizing effect of golexanolone on PBC-like symptoms in hyperammonemic disease models, as well as evidence confirming the proposed mechanism of action. The results from the current study further elucidate the drug candidate's mechanism of action, strengthen previous findings concerning its effect on symptoms, and provide important insights that will guide the future clinical development of golexanolone.

"These results add to our understanding of the connection between chronic liver disease and neuroinflammation, i.e., inflammation in the brain, and what possible steps can be taken to mitigate cognitive symptoms such as central fatigue in PBC patients. At this stage, our collected evidence points toward golexanolone's potency in inhibiting neuroinflammation and breaking the signaling chain that leads up to severe symptomology. This attribute is valuable not only in treating PBC, and similar chronic liver diseases, but could very well open the door toward other conditions where neuroinflammation plays a pivotal role, e.g., neurodegenerative diseases," said Magnus Doverskog, CSO of Umecrine Cognition.

Publication details: Arenas, Y.M., et al. Golexanolone improves fatigue, motor incoordination and gait and memory in rats with bile duct ligation. *Liver Int.* 2023;00:1-13. doi:10.1111/liv.15782.

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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.

Attachments

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