Umecrine Cognition publishes review highlighting the therapeutic potential of golexanolone in treating neuroinflammatory disorders

STOCKHOLM – November 19, 2025. Umecrine Cognition today announced that a review article on golexanolone, a first-in-class drug candidate targeting overactive inhibitory brain signaling, has been published in *Pharmaceuticals* on November 18, 2025. The article highlights robust preclinical and early clinical data showing that golexanolone reduces neuroinflammation and restores normal brain function through a unique dual mechanism. These findings support golexanolone's potential as a novel treatment for brain disorders driven by disordered GABA signaling or neuroinflammation manifested by motor and cognitive symptoms involving memory, mood and consciousness.

Golexanolone is a novel class of drugs (GAMSA; GABAA receptor-modulating steroid antagonist) that act by rebalancing brain activity in conditions marked by overactive inhibitory GABA signaling (GABAergic), which can impair consciousness, thinking and behavior. By blocking the excessive influence of endogenous steroids in the brain (neurosteroids), such as allopregnanolone, which increase during inflammation, golexanolone helps restore balanced brain signaling. Its dual mechanism acts both in the brain and the rest of the body, reducing inflammation and improving nerve cell communication. This profile suggests that golexanolone could have disease-modifying effects in disorders involving both inflammation and disrupted neural signaling associated with diseases of the liver, e.g., minimal hepatic encephalopathy (MHE), primary biliary cholangitis (PBC) and in the central nervous system, e.g., Parkinson's disease (PD).

In preclinical studies, golexanolone broke the cycle of inflammation, thus improving cognition, behavior, and motor control. In disease models of elevated blood ammonia (hyperammonemia) and MHE, treatment reduced activation of brain immune cells (microglia and astrocytes) and restored normal brain function. Similar improvements were seen in disease models of PBC, where golexanolone mitigated fatigue, memory loss, and impaired coordination. In PD models, golexanolone reduced glial activation in key brain regions controlling movement, preserved dopamine-producing neurons, and reduced buildup of toxic proteins such as alpha-synuclein – leading to improvements in fatigue, motivation, and gait. A Phase II study in patients with cirrhosis and MHE supports these findings, showing that golexanolone is well-tolerated and improves measures of cognitive function.

"Collectively, the findings presented in the recently published review highlight the broad therapeutic potential of golexanolone across multiple disease areas and indications that share abnormal GABA-ergic signaling and neuroinflammation as a common underlying mechanism. Its applicability to treat debilitating tiredness and brain fog in chronic autoimmune liver diseases is

currently being evaluated in a clinical Phase 1b/2a study in primary biliary cholangitis. While the study is primarily intended to evaluate safety and tolerability, exploratory measures of efficacy will guide the continued clinical development of golexanolone both in this disease and other broader disease areas," said Dr. Viktor Drvota, CEO of Umecrine Cognition.

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The article

The article "Golexanolone Attenuates Neuroinflammation, Fatigue, and Cognitive and Motor Impairment in Diverse Neuroinflammatory Disorders" was published in *Pharmaceuticals* as part of the Special Issue "Innovative Approaches to GABAergic Drug Discovery: From Molecular Mechanisms to Advanced Therapeutics" and is available online at the following link: https://www.mdpi.com/1424-8247/18/11/1757

About the Phase 1b/2a study UCAB-CT-05
UCAB-CT-05 is a randomized, double-blind, placebo-controlled, two-part Phase 1b/2a study designed to evaluate the safety, pharmacokinetics, and preliminary efficacy of golexanolone in patients with primary biliary cholangitis (PBC) who experience clinically significant fatigue and cognitive symptoms. Part A (5 days, 40 mg twice daily) assessed safety and pharmacokinetics, while Part B (28 days, 40 mg or 80 mg twice daily) is evaluating efficacy using validated patient-reported and clinical measures. Key efficacy assessments include changes from baseline in the PBC-40 domains (cognition, fatigue, itch, social, emotional, and general symptoms), EQ-5D-3L, Epworth Sleepiness Scale, a cognitive test battery (PHES, RAVLT, D-KEFS), and the Clinical Global Impression of Change specific for PBC (CGI-C-PBCÔ). A pre-specified interim analysis supports adaptive sample-size re-estimation based on conditional power. The study, conducted across more than 30 European sites, continues to recruit participants following positive interim data from the first part of the study, presented at The Liver Meeting® 2024 (AASLD).

About Umecrine Cognition
Umecrine Cognition AB is developing a completely new class of drugs for the treatment of symptoms in the central nervous system related to 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 and possibly several other diseases. Results from an internationally acclaimed Phase 2 clinical study 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 study is currently ongoing in patients with primary biliary cholangitis. Recurrent preclinical findings suggest that golexanolone may also have a modifying effect on the underlying cause of the disease. Further, based on intriguing preclinical data, the company is considering pursuing the development of golexanolone in patients with Parkinson's disease. For more information, visit www.umecrinecognition.com.

Attachments

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