

# First patient included in Umecrine Cognition's clinical Phase 2 study of golexanolone in primary biliary cholangitis

**STOCKHOLM – April 17, 2023. Umecrine Cognition today announces the inclusion of the first patient in a clinical Phase 2 study with its lead compound golexanolone in patients with primary biliary cholangitis. The study is designed to investigate the safety profile, pharmacokinetics, and preliminary efficacy of the drug candidate in the targeted patient population and expects to be finalized by the end of 2024.**

The study's main objectives are to assess the safety and tolerability, pharmacokinetic profile, and preliminary efficacy of golexanolone in patients diagnosed with primary biliary cholangitis (PBC), fatigue, and cognitive dysfunction. The first patient was recruited at a clinical trial site in Hungary. For this initial part of the study, two additional sites in the UK have recently been approved by the British Medicines and Healthcare Products Regulatory Agency, MHRA. In the next phase of the study, a total of 35 sites in eight countries will contribute to the patient enrollment.

"Fatigue is often the most debilitating symptom of primary biliary cholangitis, frequently accompanied by cognitive impairment, and there are currently no approved treatments available that improve these symptoms in this patient population. We are excited to advance the clinical development of golexanolone by initiating the clinical Phase 2 study and also to have increased the ability to recruit patients through the addition of two new trial sites in the UK," said Anders Karlsson, CEO of Umecrine Cognition.

Golexanolone is in clinical development for the treatment of the spectrum of cognitive dysfunction associated with chronic liver disease, including hepatic encephalopathy in patients with cirrhosis and clinical decompensation as well as the fatigue and cognitive dysfunction experienced by many patients with PBC, even prior to developing cirrhosis. The drug candidate is a GABAA receptor modulating steroid antagonist (GAMSA) designed to antagonize GABAA receptor activation and neuroinhibition by endogenous neuroactive steroids. The chemical properties of golexanolone allow it to enter the central nervous system, where it may reduce neuroinflammation and reverse the inhibitory effects that the neurosteroid allopregnanolone exerts on brain function. Golexanolone has previously been shown to restore several forms of neurological impairments in preclinical models, including fatigue, cognition, sleep, and motor functions. Collectively, these findings strongly support the drug candidate's potential as a promising novel treatment targeting a wide range of cognitive-, motor-, and sleep disorders.

## Contact

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### **About primary biliary cholangitis**

Primary biliary cholangitis (PBC) is a chronic cholestatic orphan disease characterized by progressive destruction of the intra-hepatic bile ducts. This leads to impairment of bile flow and progressive cholestasis leading, ultimately, to biliary cirrhosis. Patients at all disease stages may experience significant cognitive symptoms. These symptoms are distinct from hepatic encephalopathy (HE), as most patients do not develop cirrhosis, and conventional HE is uncommon in PBC. Central fatigue is the most common symptom and affects about 60% of patients, of which approximately half experience a markedly reduced quality of life. Standardized testing indicates that cognitive dysfunction, characterized by patients as "brain fog", including difficulty in concentrating and processing information and impaired short-term memory, is the next most common symptom. Fatigue and cognitive dysfunction also overlap in a significant subset of patients. The mechanism of non-cirrhotic cognitive dysfunction in PBC remains unknown. However, the elevation of neurosteroid levels has been reported by the company and is related to fatigue severity [1]. Effective treatment for central nervous system (CNS) symptoms in PBC is a key area of unmet clinical need in PBC [2]. Recently the company presented data showing reversal of fatigue in a model of PBC following treatment with golexanolone [3].

### **About the Phase 2 study with golexanolone in PBC**

The phase 2 study of golexanolone in patients with primary biliary cholangitis (PBC) is a randomized, double-blind, placebo-controlled, two-part study to evaluate the pharmacokinetics, safety and tolerability, and preliminary efficacy of two dose levels of golexanolone in subjects with primary biliary cholangitis, fatigue, and cognitive dysfunction. The study consists of two separate parts: Part A, 5 days twice daily (BID) oral administration with golexanolone 40 mg /placebo for assessment of safety and PK; and Part B, 28 days BID oral administration with two dose levels of golexanolone/placebo for safety and preliminary efficacy. Part A will enroll eight patients. Part B will enroll 84 patients as a base case which may after an interim analysis for sample-size re-assessment increase to a maximum of 126 evaluable patients.

### **About Umecrine Cognition AB**

Umecrine Cognition's golexanolone (aka GR3027) represents a first-in-class orally active product designed to normalize GABA-ergic transmission, of which allosteric activation by neurosteroids is implicated in several major CNS-related disorders, including HE, a potentially life-threatening disorder with high and growing unmet medical need, and cognitive dysfunction associated with PBC. Golexanolone was shown to inhibit allosteric activation by neurosteroids and normalize GABA-ergic transmission in humans. For more information, please visit [www.umecrinecognition.com](http://www.umecrinecognition.com) and see the references below.

[1] Company Press Release on November 3, 2021 (<https://www.umechrinecognition.com/en/umechrine-cognition-presents-data-supporting-a-new-predictive-biomarker-in-patients-with-primary-biliary-cholangitis-at-the-aasld-international-liver-meeting-2021/>)

[2] Phaw NA., Dyson JK., Mells G., Jones. D. Understanding fatigue in primary biliary cholangitis. Dig Dis Sci. 2021. PMID: 32851498

[3] Company Press Release on September 28, 2022 (<https://www.umechrinecognition.com/en/umechrine-cognition-presents-data-showing-reversal-of-fatigue-in-a-model-of-pbc-following-treatment-with-golexanolone/>)

## Attachments

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[First patient included in Umechrine Cognition's clinical Phase 2 study of golexanolone in primary biliary cholangitis](#)