Umecrine Cognition presents data showing reversal of fatigue in a model of PBC following treatment with golexanolone

Stockholm, September 28, 2022 – Umecrine Cognition AB today announced results showing that the company's clinical drug candidate golexanolone largely eliminated fatigue in a preclinical disease model of cholestasis. These results further increase the understanding of golexanolone's potential in treating symptoms related to the rare autoimmune disorder Primary Biliary Cholangitis (PBC). The study was carried out in collaboration with Dr. Vicente Felipo, at the Laboratory of Neurobiology, Centro de Investigación Principe Felipe in Valencia, Spain.

The preclinical disease model of cholestatic liver disease (bile duct ligation; BDL) used in the present study induces steatosis, fibrosis, lobular inflammation, and cholangitis comparable to what is observed in patients with PBC. Fatigue was measured using a widely approved test method [1]. Two weeks after surgery, subjects in the BDL group showed significantly more fatigue than a control-operated group. A one-week-treatment with golexanolone significantly decreased fatigue, normalizing the test results ($p<0.05$). Further analyses showed that impairments in other CNS symptoms such as locomotor performance and motor coordination, as well as short-term memory, were reversed following treatment with golexanolone. Together, the results indicate that by targeting the GABAA receptor with golexanolone, fatigue and other disease-associated symptoms could be alleviated.

"Altered central neurotransmission has been a leading explanation to the development of fatigue in PBC patients which may account for the lack of effect on fatigue by the present liver-associated treatments. Evidence points towards an inflammatory connection between the liver and the brain in the pathogenesis of cholestatic fatigue. Our study results link beneficial effects of golexanolone on fatigue to previous results, showing beneficial effects on neuroinflammation and improved neurological function," comments Dr. Vicente Felipo, Centro de Investigación Principe Felipe, Valencia.

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 disturbed neural signaling.

"The new data from the preclinical study of cholangitis is yet another important piece of information for the development of golexanolone in PBC-associated fatigue and cognitive impairment. The results further de-risk our planned Phase 2 clinical study in PBC, as they demonstrate for the first time that fatigue can be reversed through pharmaceutical treatment with a selective inhibitor of neurosteroids on the GABAA receptor," said Anders Karlsson, CEO of Umecrine Cognition.

For further information, please contact:

Anders Karlsson, CEO, Umecrine Cognition AB
Phone: 46 70 - 918 00 10, e-mail: anders.karlsson@umecrine.se

About Primary Biliary Cholangitis, PBC

Primary biliary cholangitis (PBC) is characterized by cholestasis due to immune-mediated destruction of the intrahepatic bile ducts. Up to 80% of PBC patients are affected by chronic fatigue, frequently accompanied by cognitive impairment – which results in extreme tiredness and inability to function due to a lack of mental energy. Both first- and second-line treatments have proven ineffective in improving PBC-related symptoms, and there is thus a major unmet need for novel treatments that specifically limit these disabling symptoms. Recent data showing increased levels of allopregnanolone in PBC patients with fatigue and cognitive impairment support the hypothesis that these symptoms result from neurosteroid-mediated alterations in GABAergic signaling [2,3]. Moreover, there is growing evidence that the cognitive dysfunction associated with advanced liver diseases of all types may be attributable to neurosteroid-mediated allosteric activation of GABAergic signaling and neuroinflammation [4]. Umecrine Cognition is developing golexanolone, a novel GABAA receptor modulating steroid antagonist, which in non-clinical models has been shown to normalize GABAergic signaling and to reduce inflammation both in the brain and peripherally [5].

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 indicates 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. For more information, visit www.umecrinecognition.com.

References

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Attachments

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