Umecrine Cognition announces completion of enrollment in clinical Phase 2a study with golexanolone in patients with liver cirrhosis and hepatic encephalopathy

STOCKHOLM. Umecrine Cognition AB, a Karolinska Development (Nasdaq Stockholm: KDEV) portfolio company, today announced that enrollment has been completed in its Phase 2a study designed to assess the safety, pharmacokinetics and potential benefit of golexanolone, a novel GABAA receptor modulating steroid antagonists, in development for treatment of Hepatic Encephalopathy (HE) in patients with liver cirrhosis.

The study (UCAB-CT-02 parts A-D) is a prospective, double-blind, randomized, placebo-controlled multi-center phase 1b/2a protocol designed to evaluate the safety and pharmacokinetics of multiple ascending doses of golexanolone (aka GR3027) in healthy adults and patients with cirrhosis, as well as its potential effect on cognitive function in patients with cirrhosis and impaired cognition (covert HE).

"We are very pleased to reach this important milestone in the development of golexanolone. Umecrine Cognition is, to the best of our knowledge, the only company with a CNS-acting drug candidate in clinical development designed to improve cognitive function in patients with liver disease," said Magnus Doverskog, CEO of Umecrine Cognition. "We are grateful to the Investigators and patients who have collaborated with us in this study and look forward to sharing results by mid H1 2020."

In part A of the trial, 24 healthy adult male subjects were randomized to receive golexanolone or placebo (6:2) at doses ranging from 50 mg QD (once daily) to 100 mg BID (twice daily) for five consecutive days. All subjects completed the study. Adverse events were mild and transient and golexanolone was well tolerated at doses exceeding those shown to mitigate the brain inhibitory effects in humans of intravenously administered allopregnanolone, a potent neurosteroid [1].

In part B of the trial, 8 adult male patients with Child-Pugh B cirrhosis were randomized (6:2) to receive a single dose of 10 mg of golexanolone or placebo. Golexanolone was well tolerated, adverse events were mild and mainly judged as unrelated to study treatment.

In part C of the trial, which was designed to assess the safety and PK of multiple ascending doses in adults with cirrhosis, dosing was recently completed. 24 adult male and female patients with Child-Pugh A or B cirrhosis were randomized to receive golexanolone or placebo (6:2) at doses ranging from 10 mg BID (twice daily) to 80 mg BID for five consecutive days. As with healthy adults, safety continued to be excellent for all dose levels in patients with cirrhosis with no serious adverse events and generally mild adverse events. Golexanolone also exhibited linear PK characteristics in cirrhotic patients, as in healthy adults.

Part D of protocol UCAB-CT-02, for which the company today announced completion of enrollment, is designed to further assess safety during 3-weeks of dosing as well as the potential benefit of golexanolone on cognitive function in cirrhotic patients with impaired brain function at the time of enrollment. 45 adult male and female patients with Child-Pugh A or B cirrhosis without manifest HE and with an abnormal cognitive status were randomized to receive golexanolone or placebo (10:4) at doses ranging from 10 mg BID to 80 mg BID for 21 consecutive days.

Liver disease and its complications account for a growing and substantial disease burden worldwide. HE is a syndrome of episodically impaired brain function which remains the most common reason for readmission of patients hospitalized with decompensated cirrhosis. Symptoms of HE range from impaired cognitive function (covert HE) to clinically evident impairment (overt HE) manifested by a spectrum of abnormalities ranging from confusion to depressed consciousness and coma. Impaired cognitive function is associated with an increased risk of overt HE and there are today no treatments available that directly target the brain abnormalities believed to responsible for HE. Golexanolone has been shown to improve or normalize cognitive function and learning abilities in two animal models of HE [2] and to mitigate the inhibitory effects on brain function in humans of intravenously administered allopregnanolone, a potent neurosteroid and molecular target for golexanolone on GABAA receptors in the brain [1].

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TO THE EDITORS

About Umecrine Cognition AB

Umecrine Cognition, a Karolinska Development (Nasdaq Stockholm: KDEV) portfolio company, is developing a potential therapy that represents a new target class relevant for several major CNS-related disorders. The primary focus is to develop a treatment for life-threatening overt hepatic encephalopathy and long-term treatment in minimal hepatic encephalopathy in patients with liver disease, a growing area with high unmet medical need. The current lack of therapeutics that directly addresses the neurocognitive signs and symptoms of hepatic encephalopathy makes a novel treatment likely to become a major contribution for the treatment of this disorder. For more information, please visit www.umecrinecognition.com.

References

1. Johansson et al., Psychopharmacology 2018; 235:1533-1543.
2. Johansson et al., Am. J. Physiol Gastrointest. Liver Physiol. 2015; 309: G400–G409.