Umecrine Cognition announces first patient included in clinical Phase 1b/2a study with GR3027, a novel drug candidate for Hepatic Encephalopathy

STOCKHOLM – March 17, 2017. Umecrine Cognition AB, a Karolinska Development (Nasdaq Stockholm: KDEV) portfolio company in clinical development, today announces the inclusion of the first patient in a clinical Phase 1b/2a study of GR3027, which is in development as a potential new treatment for Hepatic Encephalopathy.

The objectives of the study (protocol UCAB-CT-02) are to evaluate the safety and pharmacokinetics of steady-state dosing in healthy adults and patients with cirrhosis, assess the potential efficacy of the GR3027 on cognitive function in patients with cirrhosis and covert HE, and determine the Phase 2b dose.

Liver disease accounts for a growing and substantial disease burden worldwide. Hepatic encephalopathy (HE) is a syndrome of impaired brain function that frequently occurs in patients with liver cirrhosis. Symptoms of HE range from subtly impaired cognition (covert HE) to confusion, decreased levels of consciousness to coma (overt HE). There are today no treatments available that directly target the brain abnormalities responsible for HE.

GR3027 is a $GABA_A$ receptor modulating steroid antagonist (GAMSA) designed to antagonize $GABA_A$ receptor activation by endogenous neuroactive steroids. GR3027 has been shown to improve or normalize cognitive function and learning in two models of hepatic encephalopathy [1]. In a single ascending dose study in healthy volunteers, GR3027 exhibited satisfactory safety and linear PK, and a human challenge study further indicated that GR3027 enters the CNS and can reverse the inhibitory effects of the endogenous neurosteroid allopregnanolone on brain function. Collectively, the findings strongly implicate neurosteroid activation of $GABA_A$ receptors in the pathogenesis of HE and indicate that GR3027 shows promise as novel treatment for this disorder.

Magnus Doverskog, CEO of Umecrine Cognition, said: “Based on the encouraging results from the completed Phase 1a study in healthy volunteers, we are excited to start exploring GR3027 in patients with cirrhosis, a population in need of new treatments to improve the impaired neurological functions that severely affect their lives.”

About the GR3027 Phase 1b/2a study

The Phase 1b part of protocol UCAB-CT-02 is a randomized, double-blinded, placebo-controlled multiple ascending dose study designed to assess the safety, tolerability and pharmacokinetics (PK) of steady-state oral dose administration of GR3027 in healthy male volunteers, as well as the safety and PK of a single oral dose of GR3027 in cirrhotic patients. It will enroll up to 18 healthy male subjects and up to eight cirrhotic patients, who will be enrolled and randomized to receive placebo or GR3027. The Phase 1b part of the protocol is also designed to define dosing for the Phase 2a portion of the protocol, which, following approval by the Swedish Medical Products Agency, will involve a randomized, double-blind, placebo-controlled assessment of the safety, tolerability and PK of ascending steady-state oral GR3027 dosing in 18 patients with cirrhosis. Part 2a of the protocol will also involve extended dosing of patients with cirrhosis and evidence of covert HE to assess preliminary efficacy of GR3027 on cognitive function.

About Umecrine Cognition AB

Umecrine Cognition’s GR3027 represents a first-in-class product against a target that is implicated in several major CNS-related disorders, including HE, a potentially life-threatening disorder with high and growing unmet medical need. For more information, please visit www.umecrinecognition.com

[1] Johansson M et al., GR3027 antagonizes $GABA_A$ receptor potentiating neurosteroids and restores spatial learning and motor coordination in rats with hepatic encephalopathy, Am J Physiol Gastrointest Liver Physiol. 2015 Sep 1;309(5):G400-9

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