Umecrine Cognition to present at the EASL International Liver Congress 2017

STOCKHOLM – April 21, 2017. Umecrine Cognition AB, a Karolinska Development (Nasdaq Stockholm: KDEV) portfolio company whose novel orally-active $GABA_A$ receptor modulating steroid, GR3027, is in clinical development for hepatic encephalopathy (HE), will present clinical results from its Phase 1 study at The International Liver Congress™ 2017, the annual meeting of the European Association for the Study of the Liver, being held April 19-23, 2017, in Amsterdam, The Netherlands.

The poster, entitled "*GR3027 reverses neurosteroid-induced $GABA_A$ receptor-mediated inhibition of brain function: A human challenge study*", presents results of the human challenge part of the Phase 1a study designed to evaluate single-dose safety, tolerability and CNS target engagement of GR3027 in healthy adults. The challenge component involved a three-part cross-over design, in which healthy male subjects were randomized to receive placebo or two different doses of GR3027 prior to challenge. Its principle objective was to evaluate the ability of GR3027 to antagonize allopregnanolone-induced activation of $GABA_A$ as determined by its pharmacodynamic effects on two $GABA_A$-modulated CNS functions, Saccadic Eye Velocity (SEV) and self-rated sedation using a Visual Analogue Scale (VAS).

Key findings presented in the poster include the following:

- In predefined statistical analyses, GR3027 significantly inhibited the allopregnanolone-induced decrease in SEV (p=0.03; Wilcoxon Signed Rank Test); the results also provided evidence that GR3027 mitigates the impaired self-rated sedation produced by allopregnanolone.

- In post-hoc statistical analyses that included only subjects who exhibited allopregnanolone-induced changes when pretreated with placebo, GR3027 significantly inhibited both the allopregnanolone-induced decrease in SEV (p=0.04; Wilcoxon Signed Rank Test) and allopregnanolone-induced sedation (p=0.01 and p=0.05 for low and high dose, respectively; Wilcoxon Signed Rank Test).

Enhanced GABAergic tone via neurosteroid-induced allosteric activation of $GABA_A$ receptors is emerging as critical to the pathogenesis of HE, prompting efforts to develop agents that antagonize $GABA_A$ receptor-potentiating neurosteroids [1]. GR3027, a novel orally active small molecule designed to reduce $GABA_A$ receptor mediated inhibition of brain function by antagonizing endogenous inhibitory neurosteroids such as allopregnanolone, has been shown to be effective in animal models of HE [2], and the present findings demonstrate its ability to modulate the function of CNS $GABA_A$ receptors in humans. A Phase 1b/2a clinical study designed to assess safety, tolerability and PK of multiple ascending doses in healthy adults and patients with cirrhosis as well as preliminary exploration of the effect of GR3027 on cognitive function in cirrhotics is underway.

The poster will be presented on Friday, April 21, 2017, in Hall 1 session Cirrhosis and its complications: Clinical aspects, RAI Amsterdam Convention Center.

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] Butterworth RF. 2016. Neurosteroids in hepatic encephalopathy: novel insights and new therapeutic opportunities. *J Steroid Biochem Mol Biol*., 160: 94-97. [2] Johansson M, Agusti A, Llansola M, Montoliu C, Strömberg J, Malinina E, Ragagnin G, Doverskog M, Bäckström T, Felipo V. GR3027 antagonizes GABAA receptor-potentiating neurosteroids and restores spatial learning and motor coordination in rats with chronic hyperammonemia and hepatic encephalopathy. Am J Physiol Gastrointest Liver Physiol. 2015; 309:G400-9

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