Umecrine Cognition announces results from a Phase 2a study of GR3027 in patients with idiopathic hypersomnia

STOCKHOLM/UMEÅ. Umecrine Cognition today reports results from a phase 2a study of GR3027 – a first-in-class drug candidate being developed as a potential new treatment for a range of CNS-related disorders. The primary study objectives were met in regard to safety and pharmacokinetics. The study also showed preliminary evidence of clinical efficacy in a subset of patients, but the data needs to be further analyzed before a decision to potentially move forward with the development of GR3027 in idiopathic hypersomnia or other sleep disorders. In parallel, Umecrine Cognition will continue the clinical development in hepatic encephalopathy.

Idiopathic hypersomnia (IH) is an orphan disease characterized by chronic excessive daytime sleepiness (EDS) without other known causes. No approved treatments are currently available for this lifelong, often severely debilitating condition which has a profound effect on patients and their families. Umecrine Cognition's drug candidate GR3027 is a GABAA receptor modulating steroid antagonist (GAMSA) that has previously been shown to improve neurological impairments – including cognitive and sleep alterations – in animal models and mitigate the brain-inhibitory effects of intravenously administered neurosteroid, allopregnanolone, in humans1,2. GR3027 is currently in clinical development for hepatic encephalopathy and sleep disorders.

The exploratory phase 2a study of GR3027 in patients with idiopathic hypersomnia enrolled 10 patients, including 5 females and 5 males, at Sleep Centers in Finland, Denmark and Sweden. The study consisted of two parts; part one was an open-label trial to assess safety, tolerability and pharmacokinetics (PK) of a single oral 50 mg dose of GR3027 in female patients. Part two was a randomized, double-blind, placebo-controlled crossover study to assess safety, tolerability, and exploratory efficacy of twice daily 80 mg oral doses of GR3027 during two weeks in adult male and female IH patients. Patients were randomized to one of two-treatment sequences, starting with a 2-week treatment with either placebo or GR3027, followed by no treatment for 1 week and finally the alternate 2-week treatment with either GR3027 or placebo. Each patient therefore received either GR3027 or placebo during one of the two treatment periods.

The Maintenance of Wakefulness Test (MWT) and the Epworth sleepiness scale (ESS) were designated as the main exploratory efficacy measures. MWT objectively measures the patients' ability to stay awake in a controlled setting while ESS is based on patients' subjective assessment of sleepiness. Additionally, a number of other exploratory measures of efficacy were followed including the actigraphy that objectively record sleep/wake patterns, and some subjective measurements like the Clinician Global Impression of Change (CGIC), Patient Global Impression of Change (PGIC), Karolinska Sleepiness Scale (KSS), Sleep-wake diary and Chalder Fatigue Scale (CFS).

The results showed that the PK characteristics of GR3027 in females are similar to those previously observed in men2. The safety profile, which has previously been studied for up to 5 days of multiple ascending doses in adult males, continues to be favorable with no dose-limiting toxicities or serious adverse events (SAEs) in either males or females.

The results of the ability to stay awake, as determined by the objective measurement MWT, showed a favorable trend (p = 0.098). The drug candidate GR3027 had little effect on the subjective measurement ESS (p = 0.92). As expected in a small exploratory study, none of the results were statistically significant. A subgroup of 5 out of 10 subjects exhibited directionally favorable changes in 3 or more efficacy measures. Altogether, Umecrine Cognition deems that the favorable pharmacokinetic and safety results, together with these early indications of clinical effect in a subset of patients, suggest that GR3027 merit further evaluation in hypersomnia and other sleep disorders.

"We are pleased by the excellent safety profile of GR3027 in patients with idiopathic hypersomnia. It is also encouraging that we, already in this comparatively short and small Phase 2a study, were able to see indications of clinical benefit. Idiopathic hypersomnia is a complex disease with a heterogenic patient population, as demonstrated by the lack of approved treatments. We will therefore further analyze the results and evaluate the need for complementary studies to properly identify the right patient population before potentially proceeding with a larger trial. In parallel, the clinical development of GR3027 in hepatic encephalopathy continues, with Phase 2-data expected early 2020," comments Magnus Doverskog, CEO, Umecrine Cognition.

When a complete analysis of the Phase 2a data has been completed, Umecrine Cognition intends to submit the full results to upcoming medical meetings and for peer-reviewed publication.

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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.

About Idiopathic hypersomnia

Idiopathic hypersomnia (IH) is a potentially debilitating orphan disease characterized by chronic excessive daytime sleepiness (EDS) despite normal sleep in patients in whom other causes of EDS have been excluded. The disease has a profound effect on the quality of life for affected patients, as well as their families, and there are no approved treatments. Several wake-promoting treatments are used off-label, but are inadequate to alleviate symptoms in most patients and many patients are treatment refractory.

References

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