Umecrine Cognition to present at two scientific conferences on the importance of neurosteroids in cognitive dysfunction associated with liver disease

STOCKHOLM – October 6, 2021. Umecrine Cognition AB, whose novel orally-active GABAA receptor modulating steroid antagonist, golexanolone, is in clinical development for hepatic encephalopathy (HE) and other CNS-related disorders, will present at two upcoming meetings pertaining to the potential benefit of golexanolone for cognitive abnormalities in patients with liver disease.

At the meeting of the International Society for Hepatic Encephalopathy and Nitrogen Metabolism (ISHEN) http://www.ishen.org/ to be held October 6-8, 2021, Dr. Torbjörn Bäckström, Umecrine Cognition founder, Professor of Clinical Sciences at Umeå University in Sweden and a pioneer in the field of neurosciences, will deliver an invited lecture entitled "*Neurosteroids in HE – Potential Treatment Targets*" as part of the session "The future in hepatic encephalopathy" (lecture S9C1).

At *"The Liver Meeting®";* i.e., the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) https://www.aasld.org/, a major international forum for liver diseases and research to be held November 12-15, 2021, Umecrine Cognition will present a poster entitled " *Neurosteroid activation of GABAA receptors: a potential treatment target for cognitive symptoms in primary biliary cholangitis*" [1]. The poster presents results from a study of circulating levels of the neurosteroid allopregnanolone in 160 subjects with primary biliary cholangitis (PBC) conducted in collaboration with the University of Newcastle and the UK-PBC organization, UK.

About Umecrine Cognition AB
Umecrine Cognition's golexanolone (aka GR3027) represents a first-in-class orally active product designed to normalize GABA-ergic transmission, of which allosteric activation by neurosteroids is implicated in several major CNS-related disorders, including HE, a potentially life-threatening disorder with high and growing unmet medical need, and cognitive dysfunction associated with PBC. Golexanolone was shown to inhibit allosteric activation by neurosteroids and normalize GABA-ergic transmission in humans [2]. For more information, please visit www.umecrinecognition.com and see the references below.

About Hepatic Encephalopathy (HE)
Hepatic encephalopathy (HE) is defined as brain dysfunction due to acute and chronic liver disease. Its pathophysiology is multifactorial and, while lowering of plasma ammonia levels reduces the risk and frequency of overt HE events, recent studies suggest that the effects on the brain of hyperammonaemia and other injurious insults such as neuroinflammation are mediated by

neurosteroid-induced allosteric activation of inhibitory GABAA receptors [3]. In a pilot phase 2a study, golexanolone was well tolerated and associated with improvement in cognitive performance [4]. These results implicate GABAA receptor-modulating neurosteroids in the pathogenesis of HE and support the therapeutic potential of golexanolone.

About Primary Biliary Cholangitis (PBC)
PBC is an orphan and autoimmune liver disease characterized by destruction of the intra-hepatic bile ducts. Almost a third of patients with primary biliary cholangitis (PBC) experience cognitive symptoms unrelated to cirrhosis (often described as 'brain fog') that can have a significant impact on quality of life (QoL) and there is no effective medical treatment [5]. The mechanistic basis remains poorly understood although elevated levels of neurosteroids has been reported and related to fatigue severity [6]. The neurosteroid allopregnanolone is a potent positive allosteric modulator of GABAA receptors. It is linked to disorders with adverse effects on cognition and memory. Novel compounds targeting allopregnanolone such as golexanolone could potentially offer a new therapy for those with severe symptomatic PBC, satisfying a significant unmet need.

[1] Wetten A et al., Neurosteroid activation of GABAA receptors: a potential treatment target for cognitive symptoms in primary biliary cholangitis?
[2] Johansson M et al., GR3027 reversal of neurosteroid-induced, GABA-A receptor-mediated inhibition of human brain function: an allopregnanolone challenge study. Psychopharmacology 2018; 235:1533-1543.
[3] Johansson M et al., GR3027 antagonizes GABAA receptor potentiating neurosteroids and restores spatial learning and motor coordination in rats with hepatic encephalopathy, Am J Physiol Gastrointest Liver Physiol. 2015;309:G400-9.
[4] Montagnese S et al., A pilot study of golexanolone, a new GABA-A receptor-modulating steroid antagonist, in patients with covert hepatic encephalopathy. J. Hepatology 2021; 75:98-107.
[5] Phaw, NA. et al., Understanding Fatigue in Primary Biliary Cholangitis. Dig. Dis. Sci., 2020, PMID 32851498.
[6] Ahboucha S. et al., Neuroactive steroids and fatigue severity in patients with primary biliary cirrhosis and hepatitis C. Neurogastroenterol Motil. 2008; 20: 671-679.

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Attachments

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