Umecrine Cognition announces Orphan Drug Designation granted by FDA for golexanolone

STOCKHOLM – January 17, 2023. Umecrine Cognition AB today announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) for the company's proprietary compound golexanolone, a novel neurosteroid-based drug candidate for the treatment of Primary Biliary Cholangitis (PBC). The ODD will play an important role in the planned clinical development of golexanolone in patients with PBC.

There is a significant unmet need for the treatment of PBC patients with cognitive impairment and no medical treatment has been shown effective in alleviating these symptoms. PBC is a chronic autoimmune liver disease leading to the progressive destruction of the bile ducts in the liver which may lead to liver cirrhosis and subsequently to hepatic encephalopathy (HE). PBC primarily affects women with a prevalence of up to 1 in 1,000 women over 40 years of age. There is no cure for PBC except liver transplantation and treatment is focused on slowing the progression. Furthermore, approximately one-third of PBC patients experience cognitive symptoms (often described as 'brain fog') and 50% of patients experience significant fatigue that can have a significant impact on quality of life (QOL) and therefore, improved symptomatic relief of fatigue and cognitive impairment plays a major role in patient's management. However, symptoms of cognitive dysfunction and fatigue do not improve with the currently approved therapies and fatigue is identified as a priority for research for patients with PBC.

The mechanisms leading to fatigue and cognitive impairment in PBC are not fully understood but include periphery (liver)-to-brain inflammatory communication. A key component of the signaling process, leading to this neuroinflammation, is the activation of the immune cells resident in the brain which leads to the release of molecules such as neurosteroids (allopregnanolone) that activates GABAA receptors and affects neurons leading to altered neurotransmission.

Umecrine Cognition is developing golexanolone, a novel small molecule GABAA receptor-modulating steroid antagonist that inhibits the action of allopregnanolone on GABAA receptors. Golexanolone is currently under development for the treatment of patients with PBC and HE and other CNS diseases that share similar underlying mechanisms are being investigated [1]. Nonclinical and clinical studies performed by the company have shown promise for reducing neuro-inflammation [2] and the potential treatment of cognitive dysfunction and fatigue related to PBC [3]. Over-production of allopregnanolone has been linked to cognitive dysfunction and fatigue in PBC patients [4], which through clinical and nonclinical studies has shown the potential to be improved by golexanolone [5].

FDA's Orphan Drug Designation is granted to investigational therapies addressing rare medical diseases or conditions that affect fewer than 200,000 people in the United States. Orphan drug status provides benefits to drug developers, including assistance in the drug development process, tax credits for clinical costs, exemptions from certain FDA fees, and seven years of post-approval marketing exclusivity.

"The Orphan Drug Designation is an important milestone in the development of golexanolone and highlights the need for potential new treatment options for patients with PBC. This is a valuable and significant regulatory feedback from the FDA and a validation of our development program in PBC which we are enthusiastic about advancing for the benefit of patients and families of those suffering from this severe disease," said Anders Karlsson, CEO of Umecrine Cognition.

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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. For more information, please visit www.umecrinecognition.com and see the references below.

[1] Company Press Release on January 3, 2023 (https://www.umecrinecognition.com/en/umecrine-cognition-presents-data-showing-improved-symptoms-in-a-model-of-parkinsons-disease-following-treatment-with-golexanolone/)

[2]Mincheva, G. et al., Golexanolone, a GABAA receptor modulating steroid antagonist, restores motor coordination and cognitive function in hyperammonemic rats by dual effects on peripheral inflammation and neuroinflammation. CNS Neurosci Ther. 2022 Nov;28(11):1861-1874.

[3] Company Press Release on February 21, 2022 (https://www.umecrinecognition.com/en/umecrine-cognition-presents-data-showing-reversal-of-fatigue-in-a-model-of-pbc-following-treatment-with-golexanolone/)

[4] Wetten, A., et al., Neurosteroid Activation of GABA-A Receptors: A Potential Treatment Target for Symptoms in Primary Biliary Cholangitis? Can J Gastroenterol Hepatol. 2022 Dec 6;2022: 3618090.

[5] Johansson et al., 2018. GR3027 reversal of neurosteroid-induced, GABA-A receptor-mediated inhibition of human brain function: an allopregnanolone challenge study Psychopharmacology (Berl). 235(5):1533-1543.

Attachments

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