Umecrine Cognition presents nonclinical data at AD/PD™ 2025 showing that golexanolone reverses dopamine loss and sustains improvements of Parkinsonian symptoms

STOCKHOLM – April 1, 2025. Umecrine Cognition today announces that the company will attend the 19th International Conference on Alzheimer's and Parkinson's Diseases 2025 in Vienna, Austria, April 1–5th. At the meeting, the company will present recent preclinical data from a study conducted in a well-established laboratory model of Parkinson's disease. The data show that golexanolone improves mechanisms in the midbrain important for brain functions such as motor and cognitive behaviors (substantia nigra) that cause striatal dopamine loss and Parkinsonian deficits. The increased understanding of golexanolone's mechanism of action supports the further development of the drug candidate as a potential treatment for Parkinson's disease.

At AD/PD™ 2025, Umecrine Cognition and its collaborating research partner will present new data based on an investigation of how golexanolone affects brain function and behavior. The study aimed to deepen the understanding of how golexanolone interacts with brain cells involved in dopamine production and downstream signalling. The results show that in untreated Parkinson's animals, brain immune cells (microglia) become overactive and increase the levels of the neurotransmitter glutamate, which disrupts normal brain function. This, in turn, leads to an increase in GABAergic neurotransmission in the substantia nigra with subsequent lowering of neural dopamine levels in the striatum, ultimately causing movement disruptions, fatigue, and memory difficulties.

Golexanolone completely reversed excessive glutamate activity, restoring balance in the brain. Further, the drug candidate significantly reduced GABAergic signalling and improved dopamine levels and the down stream BDNF-TrkB system, key factors in controlling movement and motivation. Motor function, fatigue, and memory all showed sustained improvement. Further analyses of movement behaviors (gait analysis, i.e., gate hesitation/"freezing" and postural instability) revealed positive effects, suggesting potential benefits for mobility in Parkinson's patients.

"This data supports the hypothesis that the main effect of golexanolone is the reduction of activation of microglia, which allows to prevent the enhancement of the dopamine pathway. Thus, this is likely the main mechanism by which golexanolone induces sustained improvement on fatigue, anxiety, depression, some aspects of motor coordination and locomotor gait, and short-term memory. The results suggest that golexanolone may be a very useful drug for the treatment of PD, acting on different steps of the process leading to motor and non-motor impairment. An

additional advantage is that golexanolone does not induce secondary effects induced by current treatments such as dopamine-induced dyskinesia," comments Dr. Vicente Felipo, Principal Investigator of the study and Head of the Laboratory of Neurobiology, Centro de Investigación Principe Felipe in Valencia, Spain.

"It is promising that the positive effect on motor and non-motor symptoms, which has previously been reported for golexanolone in a pre-clinical model of Parkinson's disease, now also become understandable. These findings suggest that golexanolone may help restore normal brain function in Parkinson's disease by targeting key underlying mechanisms responsible for dopamine loss and downstream signalling. While further clinical studies are needed to confirm these benefits in humans, the results provide a promising step toward developing new treatments for the disease. If successful, this drug candidate could offer a new therapeutic approach for managing both motor and non-motor symptoms of the condition," says Magnus Doverskog, SVP and Chief Scientific Officer, Umecrine Cognition.

The company's abstract has been accepted for presentation at the on-site paper poster session "Alpha-Synucleinopathies, Therapeutic Targets, Mechanisms for Treatment" on Friday, April 4th, as well as at the oral ePoster presentation, a virtual format for digital meeting attendees. A representative from Umecrine Cognition's scientific collaborator, Dr Maria A. Pedrosa, will present the abstract titled: Golexanolone improves the mechanisms in substantia nigra leading to striatal dopamine loss and motor and non-motor alterations in 6-OHDA rats (abstract #427).

For further information, please contact:

Magnus Doverskog, SVP & CSO, Umecrine Cognition AB
Phone: +46 73 039 20 52, email: magnus.doverskog@umecrine.se

About Parkinson's disease and golexanolone

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the world and affects over 10 million people globally, and 1.2 million in Europe. Beyond motor symptoms like tremors and bradykinesia, PD is characterized by debilitating non-motor symptoms such as cognitive impairment, fatigue, and excessive daytime sleepiness, which significantly diminish the quality of life of patients and their relatives. Current treatments, largely rely on levodopa (L-DOPA), a synthetic form of the neurotransmitter dopamine that is depleted in PD. Focused primarily on motor symptoms, L-DOPA fails to address several important aspects of motor function such as gait and non-motor issues, leaving a critical gap in care. In addition, L-DOPA does not possess any disease-modifying attributes and is known to induce debilitating side effects over the course of the treatment duration.

Previous research on golexanolone's effect in a Parkinson's disease model (6-OHDA rats) indicates that it partially impedes the decrease of the enzyme tyrosine hydroxylase (TH), which when reduced causes a drop in dopamine levels and worsened motor symptoms. Furthermore, previous study analyses shows normal levels of a-synuclein and a decreased activation of brain immune cells indicating lowered levels of neuroinflammation, a central mechanism in Parkinson's disease progression.

About Umecrine Cognition AB

Umecrine Cognition AB develops a completely new class of pharmaceuticals against neurological disturbances in the brain that may arise as a consequence of several underlying diseases, leading to strongly reduced cognitive functions and wakefulness. Results from an internationally recognized clinical Phase 2 study indicates that the company's most advanced drug candidate, golexanolone, normalizes the brain's signaling and improves cognition as well as wakefulness in patients diagnosed with hepatic encephalopathy. The continued drug development will initially focus on patient groups whose symptoms arise from chronic liver diseases. The mode of action is however relevant in a number of other indications. For more information, visit www.umecrinecognition.com.

Attachments

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