**Gate Neurosciences Doses First Subject in a Translational EEG Biomarker Study of Apimostinel, a Rapid-Acting Treatment for Acute Depressive Disorders**

- *Apimostinel previously demonstrated rapid and robust 24-hour antidepressant effects in a Phase 2a MDD study (p=0.0034)*
- *The ongoing translational biomarker study uses EEG to confirm NMDA receptor target engagement and further define dosing dynamics for a next Phase 2b study*
- *Topline readout from the study is expected 1H 2023*

INDIANAPOLIS, November 29, 2022 — Gate Neurosciences, a clinical-stage biotechnology company using precision medicine approaches to develop next-generation neuroscience therapies, today announced that the first cohort of subjects has been dosed in its Phase 1 biomarker and multiple ascending dose study of apimostinel, the company's 2nd generation rapid-acting injectable NMDAR modulator program.

Gate Neurosciences is developing apimostinel to address urgent patient and evolving practice needs for a safe, rapid-acting, in-office treatment of acute depressive disorders such as postpartum and episodic depression, and depression with suicidality. The NIMH has identified these patients as a critical area of need for innovation: suicidal ideation accounts for millions of ED visits every year and current demand for mental health services are at unprecedented levels.

Apimostinel previously demonstrated proof-of-concept in a Phase 2a MDD study and the ongoing biomarker study aims to further enhance the understanding of dose dynamics using various electroencephalogram (EEG) measures after single and multiple ascending doses in 40 healthy subjects. The study also aims to confirm NMDA receptor target engagement and evaluate measures of cognitive processing and synaptic function using event-related potentials (ERP) such as mismatch negativity and P300 latency. Topline readout from the study is expected in 1H 2023.

"The ongoing apimostinel biomarker study enables us to further define optimal dose levels and intervals and de-risk a next apimostinel Phase 2b confirmatory efficacy study." Said Dr. Anantha Shekhar, Chief Scientific Officer at Gate Neurosciences and Dean of the University of Pittsburgh School of Medicine. "Understanding dose dynamics is central to this emerging treatment paradigm in neuropsychiatry where rapid and durable changes in synaptic function are achieved with single doses of our NMDAR modulators."

In a previously completed Phase 2a study, a single dose of apimostinel showed rapid and robust statistically significant antidepressant effects at 24 hours (p=0.0034) and a safe, well-tolerated profile with no ketamine-like dissociative or psychotomimetic side effects. The program is intended as a fast (less than 1 minute) and safe injectable procedure, administered in-office by physicians, that would be commercially complementary to Gate's lead oral program in development for MDD – zelquistinel, a 3rd generation NMDAR modulator.

“We are in a unique position at Gate with two different product candidates that cover patient needs for both acute and longer term treatment of depression. Apimostinel is an acute injectable procedure that is complementary to our lead oral candidate, zelquistinel, and this paradigm could completely transform how depressive disorders are managed” said Mike McCully, President and CEO of Gate Neurosciences. “Apimostinel offers an opportunity for physicians to administer a safe rapid-acting antidepressant to patients on-site, providing advantages for both patients and physician practices alike.”

Gate Neurosciences plans to use results from the EEG biomarker study to further de-risk dose selection in a confirmatory Phase 2b efficacy study of apimostinel planned for initiation in mid-2023.

For additional detail about the study, please visit:
https://clinicaltrials.gov/ct2/show/NCT05597241

**About Gate Neurosciences**

Gate Neurosciences is a precision medicine biotechnology company focused on advancing next-generation CNS treatments that address growing needs in mental health. The company is developing a portfolio of novel mechanisms of action that enhance synaptic function to address neuropsychiatric and neurocognitive diseases, including major depressive disorder (MDD). Using learnings from extensive clinical, preclinical, and translational data and a better understanding of CNS development challenges, the company is advancing its clinical pipeline using evidence-driven, precision psychiatry approaches.

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