NEWS RELEASE

Gate Neurosciences Announces Positive Topline Human EEG Biomarker Results Demonstrating Dose-Dependent Target Activation in Phase 1 Study of Apimostinel

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- Demonstrated changes in qEEG biomarkers of target activation from baseline versus placebo, in response to single and multiple doses
- Dose-dependent qEEG effects were consistent with antidepressant efficacy observed in a prior Phase 2a depression study
- Well-tolerated with no psychotomimetic effects
- Results support upcoming Phase 2 study of zelquistinel, the company's lead oral NMDA receptor modulator for major depressive disorder

INDIANAPOLIS--(BUSINESS WIRE)-- **Gate Neurosciences**, a clinical-stage biotechnology company using precision medicine approaches to develop next-generation neuroscience therapies, today announced positive topline qEEG biomarker and safety results from its Phase 1 multiple ascending dose study of apimostinel in healthy volunteers.

Results demonstrated a dose-dependent increase in qEEG pharmacodynamic biomarkers of NMDA receptor target activation from baseline, compared with subjects who received placebo. Maximal qEEG effects were observed at dose levels consistent with antidepressant efficacy observed in a prior Phase 2a proof of concept (POC) study of apimostinel, validating the biomarker for informing dose selection in future clinical efficacy studies across the class of molecules. Apimostinel was also generally well-tolerated with no ketamine-like dissociative side effects, highlighting its novel mechanistic approach of enhancing synaptic function.

The positive human qEEG biomarker results with apimostinel are consistent with prior biomarker observations with zelquistinel, Gate's lead program, which is currently being developed as a rapid-acting, once weekly, oral treatment for major depressive disorder (MDD).

"We are very excited to see a consistent, objective biomarker of receptor activation across two independent clinical programs in both apimostinel and zelquistinel. These new positive qEEG results further advance our confidence in dose selection and our understanding of how this novel class of molecules achieves rapid and durable effects through event-driven pharmacology," said Mike McCully, CEO of Gate Neurosciences. "We now have even more conviction in our upcoming Phase 2 depression study of zelquistinel, our lead rapid-acting oral program."

Summary of Apimostinel Phase 1 Safety and qEEG Topline Results:

Safety & Tolerability

- Apimostinel was generally safe and well-tolerated across three ascending dose cohorts (1, 5, and 10 mg) receiving multiple doses and one single dose cohort (25 mg), in a total of 40 healthy volunteers.
- No observation of ketamine-like psychotomimetic or dissociative effects, consistent with safety from two prior clinical trials and reflective of apimostinel's novel and differentiated NMDA receptor mechanism.

qEEG Biomarker of Target Activation

- qEEG analysis showed a dose-dependent increase in pharmacodynamic biomarkers of NMDA receptor activation compared to placebo after IV administration, adjusted from baseline, at all evaluated timepoints.
- Maximal enhancement of qEEG signature was observed with apimostinel 10mg:
    - qEEG dose response was consistent with drug CSF concentrations that maximally enhance the NMDA receptor in nonclinical studies.
    - qEEG dose response was consistent with antidepressant efficacy observed in a prior POC clinical study, where a single 10mg IV dose of apimostinel demonstrated rapid, statistically significant antidepressant effects at 24 hours.
- Results validate similar qEEG biomarker observations with zelquistinel in prior clinical studies, confirming a class effect of these compounds, and inform dose selection in the next efficacy studies.

Apimostinel is a rapid-acting injectable program behind the company's lead oral small molecule zelquistinel, both of which are novel positive modulators of the NMDA receptor designed to enhance synaptic function in patients with mood and cognitive disorders. Gate plans to initiate a Phase 2 study of zelquistinel to confirm efficacy in MDD in Q1 2024.

About Gate Neurosciences

Gate Neurosciences, headquartered in Indianapolis, is a precision medicine biotechnology company focused on advancing next-generation central nervous system (CNS) treatments that address the 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. Using learnings from extensive clinical, preclinical and translational data, along with a better understanding of CNS development challenges, the company is advancing its clinical pipeline using evidence-driven, precision psychiatry approaches.

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