Reunion Neuroscience Announces Publication of Results from Early Preclinical Studies Demonstrating the Potential of RE104 for Development in Depressive Disorders

- *Reunion's lead asset, RE104, is a potential best-in-class, clinical-stage serotonergic psychedelic drug candidate designed as a safe, fast-acting, short duration therapy to provide lasting benefits to patients with underserved mental health disorders*

- *RE104 has shown it is an efficient prodrug for the delivery of 4-HO-DiPT, a unique short-duration psychedelic with potential in depressive disorders*

- *Company expects to start enrolling patients this quarter in the RECONNECT Phase 2 clinical trial of RE104 for postpartum depression (PPD)*

MORRISTOWN, New Jersey, May 20, 2024 – Reunion Neuroscience Inc., a clinical-stage biopharmaceutical company committed to pushing the boundaries of neuroscience, today announced the publication of the results of preclinical studies in *ACS Chemical Neuroscience* that validate the decisions to pursue RE104, a proprietary, patented prodrug of 4-OH-DiPT as a potential therapeutic in depressive disorders. The paper, titled "RE104: Synthesis and Activity of a Novel Serotonergic Psychedelic Prodrug of 4-Hydroxy-N,N-diisopropyltryptamine," was co-authored by Robert Alexander, Ph.D., Reunion's Chief Medical Officer, Dr. Aviva Asnis-Alibozek, DMSc, PA-C, DFAAPA, President and Founder of Viva Bio Pharma Services LLC, and Michael D. Ehlers, M.D., Ph.D., Chief Scientific Officer and Venture Partner at Apple Tree Partners, with Nathan Bryson, Ph.D., Reunion's Chief Scientific Officer, as senior author.

"Serotonergic psychedelic compounds have demonstrated significant potential to treat a variety of mental health disorders," said Nathan Bryson, Ph.D., Chief Scientific Officer of Reunion. "The preclinical data published in *ACS Chemical Neuroscience* was the impetus for selecting 4-OH-DiPT as the psychedelic substrate at the core of our development program, as well as the choice of the RE104 prodrug strategy for its delivery. The findings present evidence supporting our target profile of an antidepressant drug product with reproducible pharmacokinetics, a short duration of psychoactivity, as well as fast-onset and durable action in depression."

“The data observed in these preclinical studies suggest that RE104 could potentially provide life-changing benefits to the large population of patients with underserved mental health disorders, including in postpartum depression, Reunion’s lead indication,” said Dr. Robert Alexander, Ph.D., Chief Medical Officer of Reunion. “The preclinical models were affirmed in a Phase 1 Study in healthy volunteers and we now look forward to evaluating RE104 in patients with postpartum depression in our RECONNECT Phase 2 clinical trial, which is expected to begin enrolling patients this quarter.”

Study Results

RE104 is a 4-OH-DiPT prodrug comprising a glutarate pro-moiety that cleaves rapidly in situ, providing excellent bioavailability of the active drug shortly after administration. The newly published study describes the synthesis, as well as the chemical, preclinical, and translational characterization of RE104, including conversion to 4-OH-DiPT and subsequent metabolism in vivo. In a forced swim model of behavior to assess antidepressive activity, RE104 demonstrated efficacy similar to a psilocybin analog at Day 7, 14 and 28. This study used RE109, a psilocin prodrug of similar structure to RE104, which is also described in the paper. The article is open-source and can be found at the following link: https://doi.org/10.1021/acschemneuro.4c00058.

RE104 and Clinical Programs

The Company’s lead asset, RE104, is a proprietary, potential best-in-class, patented prodrug of 4-OH-DiPT. RE104 targets the serotonin 2A receptor (5HT2AR), which is the recognized target for the antidepressant effects of psychedelic compounds. As psychedelic drugs require monitoring by trained healthcare providers, per recent FDA Guidance (June 2023), Reunion designed RE104 to deliver a short duration psychedelic experience and it requires only about half a day in-clinic, a significantly shorter time commitment than required for longer duration psychedelics, like psilocybin and MDMA.

In a Phase 1 study, RE104 produced a psychedelic, psychoactive state similar in intensity and quality to psilocybin, but lasting only about half the time (3-4 hours) while demonstrating a similar, favorable safety profile.

A Phase 2, Multicenter, Randomized, Double-Blind, Parallel-Group, Active Dose-Controlled study evaluating RE104 in moderate and severe PPD patients (The RECONNECT Trial) is expected to start enrolling patients this quarter (NCT06342310). Results from the RECONNECT Trial are expected in Q2 2025.

Reunion is actively investigating the use of RE104 in additional neuropsychiatric indications, including adjustment disorder in cancer patients, where there remains a significant unmet need that is not addressed by the current standard of care.

About Reunion Neuroscience Inc.

Reunion Neuroscience is committed to pushing the boundaries of neuroscience to develop innovative therapeutic solutions for postpartum depression (PPD) and other underserved mental health disorders. In August of 2023, Reunion Neuroscience was acquired by MPM BioImpact, a world-leading biotechnology investment firm with three decades of experience creating and investing in innovative biotechnology companies seeking to deliver transformative therapies to patients. As part of the MPM BioImpact portfolio, the Company is evaluating its lead asset, RE104, a proprietary, potential best-in-class, serotonergic psychedelic compound and the only 4-OH-DiPT prodrug in clinical development, as a potential treatment for postpartum depression, (NCT06342310), that could provide rapid symptom relief and durable efficacy. Reunion is actively investigating the use of RE104 in additional neuropsychiatric indications where there remains a significant unmet need that is not addressed by the current standard of care.

For more information about the company, visit https://reunionneuro.com.

For further information:

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