GRIN Therapeutics Presents Data from Honeycomb Trial of Radiprodil at the American Epilepsy Society Annual Meeting

- Previously reported Honeycomb topline results showed radiprodil was generally well-tolerated
- A key secondary analysis demonstrated a median reduction of 86% in countable motor seizure frequency consistent across GRIN genotypes with gain-of-function variants
- Company also outlined proposed plans for a Phase 3 pivotal trial expected to begin early 2025

NEW YORK, NY, December 9, 2024 – GRIN Therapeutics, Inc., a leader in the development of therapies to treat serious neurodevelopmental disorders, presented additional topline data this weekend from the Company's Honeycomb trial, an ongoing global Phase 1b open-label trial evaluating the safety, tolerability, pharmacokinetics and efficacy of radiprodil, an investigational, selective and potent negative allosteric modulator of the N-methyl-D-aspartate receptor subtype 2B (NR2B or GluN2B), in development for the treatment of GRIN-related neurodevelopmental disorder with gain-of-function (GoF) variants. The results, together with an overview of the proposed design of the Company's planned Phase 3 pivotal trial for radiprodil, were presented as a late-breaking poster at the American Epilepsy Society (AES) Annual Meeting in Los Angeles, California.

"We are excited to share updated data from the Honeycomb trial, which highlights the significant progress we've made in our effort to bring a new treatment to people living with GRIN-related neurodevelopmental disorder," said Bruce Leuchter, MD, president and chief executive officer of GRIN Therapeutics. "As we plan for the launch of our pivotal Phase 3 trial for radiprodil, we are deeply grateful to the patients and families whose dedication and participation have been instrumental in driving this development program forward. Our team remains fully committed to collaborating closely with regulators, advocates, investigators, clinicians, and the broader community to advance this important research effort as rapidly as possible."

As the next phase in the development program for radiprodil, GRIN Therapeutics plans to initiate a randomized, double-blind, placebo-controlled Phase 3 pivotal trial in early 2025, which will include two cohorts of patients with confirmed GoF mutations in the GRIN1, GRIN2A, GRIN2B, or GRIN2D genes, one cohort enrolling patients who have experienced qualifying countable motor seizures (CMS) and a second cohort enrolling patients without qualifying CMS.

The proposed Phase 3 pivotal trial was designed based on analysis of positive topline data from the Phase 1b Honeycomb trial in which radiprodil appeared generally well-tolerated, with the most commonly observed adverse events associated with infections or underlying disease symptoms. Patients in the qualifying seizure cohort saw a median reduction of 86% in CMS frequency versus baseline which was consistent across GRIN genotypes. During the trial period, 71% of patients had a greater than 50% reduction in CMS and six of seven were seizure-free during at least 80% of days in the eight-week maintenance period. There were signs of favorable effect on clinical outcomes regardless of the occurrence of seizures as measured by Clinician and Caregiver Global

Impressions of Change (CGI-C and CaGI-C) and the Aberrant Behavior Checklist – Community (ABC-C).

“GRIN-related neurodevelopmental disorder was first characterized in 2010 and only formally named in 2014. Since then, research and advocacy communities have worked tirelessly to identify approaches to treatment that are both targeted and able to alter the natural course of the disease,” said Michael A. Panzara, MD, MPH, chief medical officer of GRIN Therapeutics. “The readout from the Honeycomb trial is an important milestone towards the goal of providing treatment options to patients with and without seizures who suffer from GRIN-related neurodevelopmental disorder with GoF variants. Our plans for a rapid transition to a pivotal Phase 3 study reflect our sense of urgency and commitment to these patients.”

About GRIN-related neurodevelopmental disorder

GRIN-related neurodevelopmental disorder is a family of rare, genetically defined pediatric neurodevelopmental disorders caused by mutations in GRIN genes. While symptoms of GRIN-related neurodevelopmental disorder can present as early as infancy, a diagnosis is often not confirmed until age two or later when a child fails to reach developmental milestones. Individuals may experience developmental delay, intellectual disabilities, epilepsy, muscular hypotonia, movement disorders, spasticity, feeding difficulties and behavioral problems. There are currently no approved therapies for GRIN-related neurodevelopmental disorder.

About Radiprodil

Radiprodil is an investigational, selective and potent negative allosteric modulator of the N-methyl-D-aspartate (NMDA) receptor subtype 2B (NR2B or GluN2B). In nonclinical studies, radiprodil has been shown to potently and selectively modulate GluN2B. Radiprodil has also demonstrated an antiseizure effect in a number of in vitro and in vivo preclinical seizure and epilepsy models and specifically in models characterized by an enhanced GluN2B NMDA transmission, which can occur with gain-of-function (GoF) mutations in GRIN-related neurodevelopmental disorder. In vitro analysis of brain tissues extracted from both tuberous sclerosis complex (TSC) and focal cortical dysplasia (FCD) lesions has shown enhanced GluN2B NMDA expression supporting the potential ability of radiprodil to control seizures in these conditions.

About GRIN Therapeutics

GRIN Therapeutics is dedicated to the research and development of precision therapeutics for pediatric neurodevelopmental disorders with the goal of bringing hope to patients and caregivers. Working to develop novel therapies for patients with neurodevelopmental disorders, the company has two ongoing clinical trials to evaluate radiprodil for the potential treatment of GRIN-related neurodevelopmental disorder and other neurological conditions including tuberous sclerosis complex (TSC) and focal cortical dysplasia (FCD) type II. GRIN Therapeutics is an affiliate of Neurvati Neurosciences, a portfolio company of Blackstone Life Sciences (BXLS). For more information, please visit www.grintherapeutics.com

About Neurvati Neurosciences

Neurvati Neurosciences, a portfolio company of Blackstone Life Sciences, identifies and advances the development of high-potential drug candidates across the neuroscience landscape. Neurvati employs a collaborative model that establishes fit-for-purpose affiliate companies, aligning dedicated resources with long-term strategic capital to catalyze innovative treatment options in areas of unmet need. Neurvati's team of experienced operators and drug developers seeks opportunities to challenge current treatment paradigms and make a difference for patients suffering from a wide range of neurological and psychiatric disorders. For more information, please visit www.neurvati.com

About Blackstone Life Sciences

Blackstone Life Sciences is an industry-leading private investment platform with capabilities to invest across the life cycle of companies and products within key life science sectors. By combining scale investments and hands-on operational leadership, Blackstone Life Sciences helps bring to market promising new medicines and medical technologies that improve patients' lives and currently has more than $9 billion in assets under management.

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