# GRIN Therapeutics Announces Positive Topline Data from Honeycomb Trial of Radiprodil in GRIN-Related Neurodevelopmental Disorder

- Radiprodil appeared to be generally well-tolerated in patients with gain-of-function (GoF) variants in GRIN genes, both with and without countable motor seizures (CMS) at baseline
- Patients with CMS saw a median reduction of 86% in seizure frequency from baseline, over and above background anti-seizure medications, with 71% experiencing a greater than 50% reduction
- Results are expected to support planned discussions with regulators to potentially advance radiprodil to a Phase 3 pivotal trial
- GRIN Therapeutics is backed by a $200 million capital commitment from Blackstone Life Sciences

**NEW YORK, NY,** September 9, 2024 – GRIN Therapeutics, Inc., a leader in the development of therapies to treat serious neurodevelopmental disorders, reported topline results from the Company's ongoing two-part 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 the treatment of GRIN-related neurodevelopmental disorder. The results were presented in a podium presentation yesterday at the International League Against Epilepsy (ILAE) 15th European Epilepsy Conference in Rome, Italy.

"The results of this trial are very encouraging as they suggest that radiprodil has the potential to substantially reduce the occurrence of seizures and possibly improve behaviors in children with gain-of-function mutations who are not responding well to current treatments," said Prof. Renzo Guerrini, MD, FRCP, FAES, Director, Neuroscience and Human Genetics Department, Phase 1 Clinical Trial Centre, Children's Hospital A. Meyer IRCCS, University of Florence, Italy. "Given these initial efficacy data and promising safety profile, we look forward to continuing to advance this important research program into the next phase of development."

The Honeycomb study enrolled 15 pediatric patients with confirmed GoF mutations in the GRIN1, GRIN2A, or GRIN2B genes. The primary objectives of the study were to assess the safety and pharmacokinetics of radiprodil, while key secondary objectives focused on evaluating efficacy on both seizures and non-seizure outcomes. At study enrollment, patients were divided into two cohorts based on the frequency of countable motor seizures (CMS) they experienced during a 28-day screening period (Cohort 1) and baseline severity of non-seizure behavioral symptoms (Cohort 2).

Following screening and observation periods, patients were escalated from a starting dose level of 0.05 mg/kg based on tolerability, pharmacokinetics, and predicted GluN2B receptor occupancy to a dose level to be maintained through an eight-week maintenance period. Part B of the Honeycomb

study, an open-label extended treatment period for patients who completed Part A and were eligible for continued study treatment, remains ongoing.

As of the July 15 data cut, 15 patients were available for analysis. Demographics and baseline disease characteristics were representative of the targeted GRIN population and generally balanced between the seizure (Cohort 1) and non-seizure behavior (Cohort 2) cohorts. There was a high level of seizure activity at baseline in Cohort 1 with a mean of 37.0 and a median of 25.5 CMS per patient (range of 4.8 to 85.9). There were zero CMS at baseline in Cohort 2.

Radiprodil appeared generally well tolerated throughout Part A and B of the study to date. The treatment-emergent adverse events (TEAEs) most commonly observed (i.e., in three or more patients) were those associated with infections or underlying disease symptoms including pyrexia, diarrhea, respiratory tract infection, abnormal behavior, agitation, cough, dystonia, fatigue, and gastroenteritis. There were no deaths in the study. Three patients experienced a serious adverse event (one patient each with obstructive bronchitis, viral pneumonia, or adenovirus infection). None were considered related to treatment with radiprodil and none met study stopping rule criteria.

During Part A of the study, patients treated with radiprodil showed a median reduction of 86% in seizure frequency versus baseline, which was a key secondary endpoint in the trial. During this same period, 71% of patients had a greater than 50% reduction in CMS, with 43% seeing a greater than 90% reduction and one patient being seizure free. Clinicians and caregivers also generally assessed patients as improved clinically over the course of the study.

“We believe the findings from the Honeycomb study in gain-of-function patients with treatment resistant symptoms provide strong rationale to progress this promising program into Phase 3 development as quickly as possible,” said Bruce Leuchter, MD, President and Chief Executive Officer at Neurvati Neurosciences and GRIN Therapeutics. “I am proud of the progress we have made to address the profound unmet need in GRIN-related neurodevelopmental disorder since we launched the company three years ago with an investment from Blackstone Life Sciences. These compelling data represent the first major milestone in our development plans for radiprodil and will help us build new levels of momentum toward achieving our goal of bringing the first approved treatment to patients living with GRIN-related neurodevelopmental disorder.”

**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 receptor subtype 2B (NR2B or GluN2B). In nonclinical studies, radiprodil has been shown to potently and selectively modulate the N-methyl-D-aspartate (NMDA) receptor subtype 2B (NR2B or 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 disorder.

**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 the investigational product radiprodil as a novel therapy 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.

**Corporate Contact**:
Elliott Ruiz
+1 201.674.5417
elliott.ruiz@neurvati.com