GRIN Therapeutics Announces Initiation of Astroscape Clinical Trial of Radiprodil for Treatment of Tuberous Sclerosis Complex and Focal Cortical Dysplasia Type II

Dosing of patients in the second clinical research program for radiprodil follows recent announcement of positive topline data from the Honeycomb trial in GRIN-related neurodevelopmental disorder; radiprodil appeared generally well-tolerated and demonstrated a median reduction of 86% in seizure frequency.

New York, NY (October 8, 2024) – GRIN Therapeutics Inc., a leader in the development of therapies to treat serious neurodevelopmental disorders, today announced initiation of the Astroscape study, the Company's global open-label clinical trial of radiprodil, an investigational, selective and potent negative allosteric modulator of the N-methyl-D-aspartate receptor subtype 2B (NR2B or GluN2B), for the treatment of tuberous sclerosis complex (TSC) and focal cortical dysplasia (FCD) type II.

"Following the announcement of encouraging data from our global Phase 1b open-label Honeycomb study evaluating radiprodil in children with GRIN-related neurodevelopmental disorder, our team is very pleased to continue our momentum with dosing of patients in the Astroscape study," said Michael A. Panzara, M.D., MPH, chief medical officer of GRIN Therapeutics. "Like people living with GRIN-related neurodevelopmental disorder, people living with TSC or FCD type II are in urgent need of treatment options. We look forward to working with families impacted by these disorders and our investigators to advance this promising development program as rapidly as possible."

In vitro analysis of brain tissues extracted from both TSC and FCD lesions has shown enhanced GluN2B-NMDA expression which supports investigation of GluN2B modulation with radiprodil as a potential therapeutic approach in these conditions. The open-label Astroscape study will evaluate different doses of radiprodil in children and adolescents between the ages of six months and 18 years with TSC or FCD type II who experience treatment-resistant seizures. Target enrollment will include approximately 20 participants with TSC and 10 participants with FCD type II. The study will evaluate safety and tolerability of radiprodil as well as pharmacokinetic measures and the effect of radiprodil on the frequency and severity of epileptic seizures and other symptoms related to

behavior, sleep and quality of life. Upon completion of treatment, participants may have the option to enroll in a long-term extension study.

“The initiation of treatment in the first patients enrolled in this landmark study is an important milestone for the TSC and FCD communities,” said Dr. Manuel Toledo, MD, PhD, Head of the Epilepsy Unit at Vall d’Hebron University Hospital, Barcelona, Spain, who enrolled the first patient in the study. “We appreciate GRIN Therapeutics’ commitment to making a positive difference for patients and families impacted by these serious conditions and we look forward to completing this clinical trial and reporting results as quickly as possible.”

In September 2024 GRIN Therapeutics announced topline results from the company’s Phase 1b open-label trial evaluating the safety, tolerability, pharmacokinetics, and efficacy of radiprodil in the treatment of GRIN-related neurodevelopmental disorder. Throughout the study to date, radiprodil appeared generally well-tolerated. 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, and there were no deaths in the study. Three patients experienced a serious adverse event, but 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 countable motor seizures (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. For additional information, click here.

About Tuberous Sclerosis Complex (TSC) and Focal Cortical Dysplasia (FCD) Type II:
TSC is a multi-system genetic disorder caused by a mutation in the TSC1 or TSC2 genes that causes non-cancerous tumors to form in many different organs including the brain, eyes, heart, kidneys, skin and lungs. The disease impacts the central nervous system and can cause cognitive impairment, developmental delays, seizures, behavioral problems and autism spectrum disorder. TSC is the leading genetic cause of epilepsy and autism. While some patients are treated with antiseizure drugs, only about one third become seizure-free and many require surgery in an attempt to control seizure activity.

FCD type II is a rare disorder characterized by malformations of cortical development caused by abnormal brain formation in utero. Genetic factors may play a role in causing the condition in some cases. The abnormal morphology and function of brain cells disrupts normal cell layers resulting in a high risk of seizures and disruption of brain function. While antiseizure medications represent the standard of care to control seizures in people living with FCD type II, many individuals experience drug-resistant seizures and only about one in five achieve sufficient seizure control with these medications alone. Similar to TSC, many patients require surgery to obtain seizure control.

About Radiprodil:
Radiprodil is an investigational, selective and potent negative allosteric modulator of the N-methylD-aspartate (NMDA) receptor subtype 2B (NR2B or GluN2B). In nonclinical studies, radiprodil has been shown to potently and selectively modulate NMDA 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 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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