GRIN Therapeutics Receives Positive Opinion for EU Orphan Designation for Radiprodil for Treatment of GRIN-Related Neurodevelopmental Disorder

- Positive opinion follows recent EMA Priority Medicines (PRIME) designation and FDA Breakthrough Therapy and Orphan Drug designations for radiprodil

NEW YORK, NY, May 6, 2025 – GRIN Therapeutics, Inc., a leader in the development of therapies to treat serious neurodevelopmental disorders, today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive orphan designation for radiprodil, an investigational drug for the treatment of GRIN-related neurodevelopmental disorder (GRIN-NDD).

Radiprodil is a targeted, selective, and potent negative allosteric modulator of the GluN2B subunit of the N-methyl-D-aspartate (NMDA) receptor. Variants of this receptor cause GRIN-NDD, a rare, genetically defined developmental and epileptic encephalopathy (DEE). Radiprodil was recently granted EMA PRIME designation, U.S. Food and Drug Administration (FDA) Orphan Drug designation for the treatment of GRIN-NDD, and FDA Breakthrough Therapy designation for the treatment of seizures associated with GRIN-NDD with gain-of-function (GoF) variants. The company remains on track to initiate a global, pivotal Phase 3 clinical trial for radiprodil for the treatment of GRIN-NDD in mid-2025.

"This milestone further reinforces the significant potential of radiprodil to be a first-in-class treatment for patients who are in desperate need of disease-modifying therapies that can address the physical, cognitive and behavioral symptoms of this devastating disorder," said Anne-Marie Li-Kwai-Cheung, Senior Vice President, Development, Regulatory, and Quality at Neurvati Neurosciences and GRIN Therapeutics. "We are very pleased to have support from both the EMA and FDA, reflecting their understanding of the urgent need for treatments for people and families affected by GRIN-NDD. We look forward to our continued close engagement with both agencies as we work to advance radiprodil as rapidly as possible, including preparing to launch our global pivotal Phase 3 trial in GRIN-NDD in the coming months."

Orphan designation is granted by the EMA to clinical-stage medications that are intended to treat, prevent or diagnose diseases that are life-threatening or chronically debilitating and have a prevalence of no more than five in 10,000 people in the European Union. Candidates for orphan designation must also offer significant benefit to those affected by conditions that have no satisfactory current methods of treatment. This designation comes with several incentives, including protocol assistance, fee reductions, and market exclusivity once the medicine is brought to market.

About GRIN-related neurodevelopmental disorder

GRIN-related neurodevelopmental disorder (GRIN-NDD) is a family of rare, genetically defined pediatric neurodevelopmental disorders caused by mutations in GRIN genes. These genes encode subunits of the NMDA receptor, an important contributor to the maintenance of excitatory/inhibitory balance in neural circuitry. While symptoms of GRIN-NDD 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 and requires further evaluation. Individuals may experience

developmental delay, intellectual disabilities, seizures, muscular hypotonia, movement disorders, spasticity, feeding difficulties and behavioral problems. There are currently no approved therapies specifically for GRIN-NDD.

About Radiprodil

Radiprodil is an investigational, selective and potent negative allosteric modulator of the N-methyl-D-aspartate (NMDA) receptor subtype 2B (GluN2B). It has received Breakthrough Therapy designation and Orphan Drug designation from the U.S. Food and Drug Administration (FDA) as well as Priority Medicines (PRIME) designation and Orphan designation from the European Medicines Agency (EMA). In both in vitro and in vivo preclinical models, radiprodil has been shown to potently and selectively modulate GluN2B. In 2024, data from the Phase 1b/2a Honeycomb trial of radiprodil in pediatric patients with GRIN-related neurodevelopmental disorder and confirmed gain-of-function (GoF) mutations showed that patients in the qualifying seizure cohort experienced a median reduction of 86% in countable motor seizure (CMS) frequency compared to baseline, with 5 of 7 patients seeing greater than 50% reduction. Clinicians and caregivers generally assessed patients as improved clinically over the course of the trial as measured by Clinician and Caregiver Global Impressions of Change (CGI-C and CaGI-C) with a trend towards improved irritability scores as shown by the Aberrant Behavior Checklist – Community (ABC-C) scales. In addition, the drug appeared to be generally well-tolerated. Adverse events most commonly observed were those associated with infections or underlying disease symptoms. Three patients experienced a serious adverse event associated with infection; all were assessed as unrelated to radiprodil.

Radiprodil is also being developed for the treatment of tuberous sclerosis complex (TSC) and focal cortical dysplasia (FCD). In vitro analysis of brain tissues extracted from both TSC and FCD lesions has shown enhanced GluN2B NMDA expression, supporting the potential ability of radiprodil to address disease sequelae stemming from these conditions, including seizures and behavioral symptoms. RAD-GRIN-201, also known as the Astroscape trial, is an ongoing, open-label Phase 1b/2a trial assessing the safety, tolerability, pharmacokinetics (PK), and potential efficacy of radiprodil in participants with TSC or FCD type II.

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. Late last year, GRIN Therapeutics reported promising topline data from a Phase 1b/2a clinical trial (the Honeycomb trial) evaluating radiprodil in GRIN-related neurodevelopmental disorder in patients with GoF variants, leading to the decision to advance to a Phase 3 trial. The company has an additional ongoing clinical trial to evaluate radiprodil for the potential treatment of tuberous sclerosis complex (TSC) and focal cortical dysplasia (FCD) type II. GRIN Therapeutics, Inc. is an affiliate of Neurvati Neurosciences, a portfolio company of Blackstone Life Sciences. 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 $12 billion in assets under management.

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