March 7, 2023

Trevena Initiates Targeted Proof-of-Concept Study to Evaluate TRV045 as a Potential Treatment for Epilepsy and Other CNS Disorders

New study complements the ongoing proof-of-concept study, and will provide further insight into TRV045 target engagement and mechanism of action for the potential treatment of epilepsy and other CNS disorders

CHESTERBROOK, Pa., March 07, 2023 (GLOBE NEWSWIRE) -- **Trevena, Inc. (Nasdaq: TRVN)**, a biopharmaceutical company focused on the development and commercialization of novel medicines for patients with central nervous system (CNS) disorders, today announced the initiation of a Phase 1 proof-of-concept study of TRV045, a novel sphingosine-1-phosphate receptor modulator selective for the S1P receptor subtype 1.

The study will use Transcranial Magnetic Stimulation (TMS) to evaluate how TRV045 affects the ability of brain cells to conduct electrical stimulation. The effects of TMS will be explored using both electromyography (EMG) and electroencephalography (EEG) to measure the potential effect of TRV045 on brain function.

“This is the second proof-of-concept study that we have initiated to explore TRV045 as a potential treatment of epilepsy and other CNS disorders,” said Carrie Bourdow, President and CEO of Trevena. “These studies are designed to build upon non-clinical data, which indicate the potential anti-inflammatory signaling and disease modifying effect of TRV045. We look forward to reporting topline data from both of our Phase 1 proof-of-concept studies later this year to help inform our future development path for TRV045.”

The study is a randomized, double-blind, placebo-controlled, two-way cross-over, multiple dose study designed to evaluate the pharmacodynamic effects of TRV045 on cortical excitability in healthy male adults, using both EMG and EEG to measure brain function. Twenty-four healthy male volunteers will be enrolled and each subject will receive one of two treatment sequences in random order: TRV045 250 mg followed by placebo; or placebo followed by TRV045 250 mg, each treatment sequence given once daily for four consecutive days. Both EMG and EEG outcomes in response to TMS will be explored after the first and last doses in each treatment sequence. Doses for this study were selected based on the PK exposure determined in the recently completed Phase 1 single and multiple dose study, and are designed to reach the expected target efficacy exposure range. Subjects will be enrolled at a study site outside of the United States and the study is not being conducted under the Investigational New Drug Application (IND) for TRV045. The study is expected to complete

enrollment by mid-2023.

About TRV045

TRV045 is a novel, selective sphingosine-1-phosphate subtype 1 ($S1P_1$) receptor modulator being developed as a potential treatment for acute and chronic neuropathic pain secondary to diabetic peripheral neuropathy. Through a collaboration with the National Institutes of Health, and this proof-of-concept study, Trevena is also exploring TRV045 as a potential treatment for epilepsy.

S1P receptors are located throughout the body, including the central nervous system, where they are believed to play a role in modulating neurotransmission and membrane excitability.

Trevena's discovery efforts have identified a family of compounds that are highly selective for the $S1P_1$ receptor. TRV045 reversed thermal hyperalgesia, a measure of neuropathic pain, in nonclinical models of diabetic peripheral neuropathy and chemotherapy-induced peripheral neuropathy. TRV045 was not associated with lymphopenia and produced no changes in blood pressure, heart rate, or respiratory function at or above pharmacologically active doses in nonclinical studies. TRV045 is an investigational drug and has not been approved by the FDA.

About Epilepsy

Epilepsy, one of the most common neurological diseases in the world, is a chronic disorder characterized by recurrent seizures. Epilepsy is defined as having two or more unprovoked seizures separated by at least 24 hours or after one seizure with a high risk of more.

A seizure is a sudden surge of electrical activity in the brain caused by complex chemical changes that occur in nerve cells. Usually, there is a balance of cells that either encourage or stop other brain cells from sending messages. A seizure occurs when there may be too much or too little electrical activity in the brain causing an imbalance. Seizures are a symptom of many different disorders that can affect the brain. Nearly 50 million people suffer from epilepsy worldwide, including 3 million adults and 470,000 children in the U.S. 150,000 new cases of epilepsy are reported in the United States each year. According to the CDC, 56% of adults living with diagnosed epilepsy continue to have seizures.

About Diabetic Neuropathic Pain

Diabetic neuropathy is a common complication of both type 1 and type 2 diabetes, with pain in the extremities being one of the main symptoms. Other symptoms may include numbness, tingling, allodynia and hyperalgesia. Diabetic neuropathic pain is usually characterized as moderate to severe in nature and can substantially affect patients' quality of life as well as their social and psychological well-being.

Approximately 25% of people with diabetes are affected by DNP, equaling over 5 million people in the U.S. During their lifetime, approximately 50% to 70% of diabetic patients may experience symptoms of DNP.

About Trevena

Trevena, Inc. is a biopharmaceutical company focused on the development and commercialization of innovative medicines for patients with CNS disorders. The Company has one approved product in the United States, OLINVYK® (oliceridine) injection, indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate. The Company's novel pipeline is based on Nobel Prize winning research and includes three differentiated investigational drug candidates: TRV045 for diabetic neuropathic pain and epilepsy, TRV250 for the acute treatment of migraine and TRV734 for maintenance treatment of opioid use disorder.

For more information, please visit www.Trevena.com

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development and trials of its therapeutic candidates, plans for potential future product candidates and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the status, timing, costs, results and interpretation of the Company's clinical trials or any future trials of any of the Company's investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including the Company's assessment of discussions with FDA; available funding; uncertainties related to the Company's intellectual property; uncertainties related to the ongoing COVID-19 pandemic, other matters that could affect the availability or commercial potential of the Company's therapeutic candidates and approved product; and other factors discussed in the Risk Factors set forth in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings the Company makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so, except as may be required by law.

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Source: Trevena, Inc.