January 9, 2023

Trevena Enrolls First Subject in TRV045 Proof-of-Concept Trial Evaluating S1PR Mechanism of Action and Target Engagement

New Phase 1 clinical study designed to build on nonclinical evidence of anti-inflammatory signaling and potential disease-modifying effect of TRV045 in the treatment of epilepsy and other CNS disorders

TRV045, a novel S1P receptor modulator, is highly specific for S1PR subtype 1 and reported no lymphopenia *in a prior Phase 1 clinical study*

CHESTERBROOK, Pa., Jan. 09, 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 enrollment of the first subject in a Phase 1 proof-of-concept study of TRV045, a novel sphingosine-1-phosphate receptor modulator selective for the S1P receptor subtype 1.

The Phase 1 clinical study is a randomized, double-blind, placebo-controlled, four-way cross-over study designed to test the mechanism of action and measure evidence of target engagement for TRV045. The study will use a validated set of analgesic tests to evaluate potential central and peripheral nervous system effects and to provide insight into the potential anti-inflammatory actions of TRV045. Twenty-four healthy volunteers will be enrolled and each subject will receive three different single doses of TRV045 (50mg, 150mg and 300mg) and placebo on four separate visits across the study duration. Doses for this study were selected based on the PK exposure determined in the recently completed Phase 1 single and multiple dose ranging study, and bracket the expected targeted efficacy exposure range. Subjects will be enrolled at sites outside of the United States and the study is not being conducted under the Investigational New Drug Application (IND) for TRV045.

The first subject in the trial was dosed in December 2022 and the study is expected to complete enrollment by mid-2023.

“We believe TRV045 represents an innovative, non-opioid based approach to the treatment of pain, and has also shown promising anti-inflammatory data in nonclinical models, suggesting a potential disease-modifying role in other CNS disorders,” said Carrie Bourdow, President and CEO of Trevena. “We look forward to reporting topline data from this target engagement study, which will help inform our future development path for TRV045.”

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, 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, neuroinflammatory processes, 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 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.

For more information, please contact:

Investor Contact:

Dan Ferry

Managing Director

LifeSci Advisors, LLC

daniel@lifesciadvisors.com

(617) 430-7576

Company Contact:

Bob Yoder

SVP and Chief Business Officer

Trevena, Inc.

(610) 354-8840

Source: Trevena, Inc.