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Trevena Announces Advancement of TRV045 Into Clinical Development for Diabetic Neuropathic Pain

3-part randomized, double-blind, placebo-controlled Phase 1 study will evaluate TRV045 safety, tolerability, and PK in healthy volunteers

Enrollment expected to start in early Q1 2022

CHESTERBROOK, Pa., Dec. 13, 2021 (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 it is advancing TRV045 into clinical development, following receipt of a notification from the U.S. Food and Drug Administration (FDA) that the study may proceed. TRV045 is the Company's novel $S1P_1$ receptor modulator being developed as a potential treatment for diabetic neuropathic pain (DNP). In addition, through a collaboration with the National Institutes of Health, the Company is also exploring TRV045 as a potential treatment for epilepsy.

"I am very pleased to have crossed this important milestone for the TRV045 development program and look forward to beginning our evaluation of this exciting molecule in the clinic," said Carrie Bourdow, President and CEO of Trevena. "DNP is a painful condition that affects over 5 million people in the U.S., and currently available therapies are associated with both efficacy and tolerability concerns. TRV045 represents a potentially new approach to treating this burdensome condition, with an innovative mechanism of action at the S1P receptor."

The Company will initiate a three-part Phase 1 single ascending dose (SAD), food effect, and multiple ascending dose (MAD) trial. The primary objective of the study is to evaluate the safety and tolerability of TRV045 in healthy adult subjects. The study will also assess the pharmacokinetics (PK) of TRV045 and determine whether TRV045 is associated with changes in lymphocyte counts, hemodynamic function, and QTcF interval.

In nonclinical studies, TRV045 was not associated with lymphopenia and produced no changes in blood pressure, heart rate, or respiratory function at or above pharmacologically active doses, unlike existing S1P receptor modulators, which are currently only approved by the FDA to treat multiple sclerosis and in one instance to treat moderately to severely active ulcerative colitis in adults. To date, there have been no head-to-head clinical studies of TRV045 compared to existing S1P receptor modulators.

Overview of the TRV045 Phase 1 Clinical Program

This will be a three-part randomized, double-blinded, placebo-controlled study in healthy volunteers. Part 1 of the study will investigate single ascending doses of TRV045 or placebo

administered orally in up to 6 cohorts. Part 2 will investigate the effect of a high-fat meal on the safety, tolerability, and relative bioavailability of TRV045 in a single cohort. Part 3 will investigate multiple doses of TRV045 or placebo in up to 3 cohorts in order to obtain safety, tolerability, and PK (including dose proportionality) data under multiple-dosing conditions.

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 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 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.

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 four differentiated investigational drug candidates: TRV250 for the acute treatment of migraine, TRV734 for maintenance treatment of opioid use disorder, TRV045 for diabetic neuropathic pain and epilepsy, and TRV027 for acute respiratory distress syndrome and abnormal blood clotting in COVID-19 patients.

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, commercialization of approved drug products and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "objective," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," "ongoing," or the negative of these terms or 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 commercialization of any approved drug product, 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 the discussions with the FDA or other regulatory agencies about any and all of its programs; uncertainties related to the commercialization of OLINVYK; 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 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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