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Trevena Reports Favorable TRV045 Topline Safety and Tolerability Data from Proof-of-Concept Studies

TRV045 was well tolerated with results generally consistent with prior first-in-human study

No drug-related adverse events and no serious adverse events reported

No drug-related lymphopenia, bradycardia, or change in blood pressure reported

CHESTERBROOK, Pa., Oct. 16, 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 reported topline safety and tolerability data for the two Phase 1 proof-of-concept (POC) studies of TRV045, a novel sphingosine-1 phosphate receptor modulator selective for the S1P receptor subtype 1.

TRV045 POC Studies

The Target Engagement POC study was a randomized, double-blind, placebo-controlled, single dose four-way cross-over study (n=25 subjects). Each subject received three different single doses of TRV045 (50mg, 150mg and 300mg) and placebo on four separate visits across the study duration.

The TMS POC study was a randomized, double-blind, placebo-controlled, multiple dose, two-way cross-over study (n=25 subjects). Each subject received one of two treatment sequences in random order: TRV045 at a dose of 250mg, followed by placebo; or placebo followed by 250mg of TRV045, each treatment sequence given once daily for four consecutive days.

Subjects in both studies were enrolled outside of the United States, and the studies were not conducted under the Investigational New Drug Application for TRV045.

TRV045 Safety and Tolerability Data

There were no drug-related adverse events reported in either POC study, and no serious adverse events were reported in either POC study. Of the adverse events, 98% (102 of 104) were reported as mild in the Target Engagement POC study, and 99% (79 of 80) were reported as mild in the TMS POC study. The most common adverse events reported were headaches, somnolence, dizziness and fatigue.

In screening and follow-up physical exams (including ophthalmologic exams) there were no clinically significant observations. Laboratory results also showed no clinically significant reduction in total lymphocyte count, no clinically significant changes in heart rate or blood

pressure, and no clinically significant changes in ECG interval measures (including no prolongation of PR or QTcF intervals).

This new safety and tolerability data in 50 subjects is generally consistent with, and further builds upon, the 89-subject data from the first-in-human study of TRV045 reported in November 2022. The data supports the Company's belief that TRV045 has the potential to effectively target indications, such as neuropathic pain and epilepsy, without adverse events such as lymphopenia, bradycardia, pulmonary adverse events and ophthalmologic adverse events, which have been reported with other S1P receptor modulators.

As previously announced, TRV045 demonstrated a statistically significant, dose-dependent analgesic effect in capsaicin-induced model of neuropathic pain in the Target Engagement POC study. In the TMS POC study, TRV045 provided statistically significant evidence of CNS activity on day 4 as measured by EEG power spectral analysis. Data from both studies demonstrated CNS penetration and target engagement, as well as plasma exposures in the anticipated active dose range, supporting the therapeutic potential of TRV045.

"We are pleased to report additional safety and tolerability data which is consistent with what we have observed in prior datasets," said Carrie Bourdow, President and CEO of Trevena. "The two proof-of-concept studies builds upon our confidence to advance development of TRV045. Discussions with potential strategic partners are ongoing, and we look forward to advancing TRV045, on our own or with a partner, for potential treatment of neuropathic pain and other CNS disorders."

About TRV045

TRV045 is a novel, highly 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. TRV045 is an investigational product and is not yet 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; 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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