May 2, 2016

Trevena Announces Successful End-of-Phase 2 Meeting with FDA and Outlines Phase 3 Program for Oliceridine

– Pivotal efficacy studies to start in 2Q 2016, with topline data expected in 1Q 2017, and NDA filing expected in 2H 2017 –

– Phase 3 program includes comparisons to both placebo and morphine –

– Webcast and call scheduled for today at 5:30 pm EDT –

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc. (NASDAQ: TRVN), a clinical stage biopharmaceutical company focused on the discovery and development of biased ligands targeting G protein coupled receptors, today announced the successful completion of the End-of-Phase 2 Meeting process with the United States Food and Drug Administration (FDA). The company has reached general agreement with the FDA on key elements of the Phase 3 program to support a New Drug Application (NDA) for oliceridine (TRV130), to which the FDA has granted Breakthrough Therapy designation.

“We are very pleased with the outcome of our End-of-Phase 2 discussion with the FDA,” said Maxine Gowen, Ph.D., chief executive officer. “We appreciate the valuable guidance the FDA has provided, and look forward to continuing a constructive relationship as we advance our Phase 3 registration program. We remain focused on bringing oliceridine to market as a new and potentially differentiated analgesic for patients and caregivers seeking alternatives to conventional opioids.”

End-of-Phase 2 meeting

The FDA agreed that pivotal efficacy trials in bunionectomy and abdominoplasty patients include appropriate patient populations to support an indication for moderate to severe acute pain. The agency also confirmed the need for at least 1,100 patients exposed to oliceridine across the development program for the purposes of evaluating safety and tolerability. This database should include a sufficient number of patients with higher exposures and longer durations of oliceridine therapy. In addition, general agreement was reached on the company’s planned clinical, nonclinical, clinical pharmacology, and chemistry, manufacturing and control (CMC) activities to support the planned NDA.

Overview of the Oliceridine Phase 3 program

- The oliceridine Phase 3 program includes two pivotal efficacy trials evaluating moderate-to-severe acute pain: the APOLLO-1 study will evaluate pain for 48 hours following bunionectomy, and the APOLLO-2 study will evaluate pain for 24 hours following abdominoplasty. In each trial, patients will be randomized to receive placebo, morphine, or one of three regimens of oliceridine by patient-controlled analgesia (PCA)

for the management of their post-operative pain. Each study will enroll approximately 375 patients, allocated equally across study arms.

- The primary endpoint for both APOLLO studies will be a responder analysis proposed by the company comparing active treatment arms to placebo. A responder is defined as a patient experiencing a sum of pain intensity difference (SPID) at the end of the treatment period that corresponds to at least a 30% improvement from baseline without early discontinuation and without rescue pain medication.
- Secondary endpoints in both APOLLO studies will include comparisons of oliceridine efficacy, safety, and tolerability to morphine. A respiratory safety endpoint will measure prevalence and duration of hypoventilation, which will be a clinical assessment as in the company's Phase 2b abdominoplasty study.
- The APOLLO study designs were informed in part by the company's Phase 2b abdominoplasty study, which also used PCA dosing. Powering assumptions included similar performance of PCA-administered oliceridine in both APOLLO studies as was observed in the Phase 2b study. In a post-hoc evaluation using the Phase 3 responder analysis, both doses in the company's Phase 2b study in abdominoplasty yielded analgesic efficacy similar to morphine, and significantly higher than placebo ($p \leq 0.0005$ for both oliceridine treatment arms). In addition, using the Phase 3 respiratory safety endpoint, both doses in the company's Phase 2b study showed significantly less respiratory safety burden for oliceridine than morphine ($p \leq 0.0003$ for both oliceridine treatment arms).
- The development program will include at least 1,100 patients exposed to oliceridine. The on-going open-label ATHENA-1 safety study is enrolling patients experiencing pain as a result of either a medical diagnosis or surgery. In this study, patients may receive oliceridine as-needed either as an intermittent bolus or via PCA device, with doses and durations appropriate to manage their pain.

Both APOLLO-1 and APOLLO-2 are expected to start in the second quarter of this year, and the company expects to report top-line data in the first quarter of 2017. The company continues to expect to file an NDA for oliceridine in the second half of 2017. The company also continues to expect that its available cash and investments will be sufficient to fund operations into 2018.

Conference Call and Webcast

The company will host a conference call and webcast to discuss its Phase 3 plans. The webcast will be available for replay for 30 days.

Date:	Monday, May 2nd
Time:	5:30pm (EDT)
Telephone Access:	(855) 465-0180 (U.S. and Canada)
International:	(484) 756-4313 (International)
Conference ID:	5089524
Online Access:	http://edge.media-server.com/m/p/6cgu4kpv

About oliceridine

Oliceridine (TRV130) is a new chemical entity (NCE) designed to optimize mu opioid receptor pharmacology to deliver an improved analgesic profile, and has been granted Breakthrough Therapy designation by the U.S. Food & Drug Administration. Oliceridine is the first mu receptor G protein pathway selective modulator (muGPS) – a biased mu opioid receptor ligand that in preclinical studies activated pathways associated with analgesia while avoiding pathways that can promote respiratory depression and gastrointestinal dysfunction and limit analgesia. In Phase 2, intravenous oliceridine demonstrated rapid and powerful analgesic efficacy with reduced frequency of opioid-related adverse events including nausea, vomiting, and hypoventilation compared to intravenous morphine. Trevena believes that oliceridine may offer an improved safety and tolerability profile compared to conventional opioid analgesics while providing powerful pain relief to patients. Trevena anticipates that the initial market opportunity for oliceridine will be in the acute care settings, with a focus on moderate to severe acute pain in the hospital.

About Trevena

Trevena, Inc. is a clinical stage biopharmaceutical company that discovers, develops and intends to commercialize therapeutics that use a novel approach to target G protein coupled receptors, or GPCRs. Using its proprietary product platform, Trevena has identified four biased ligand product candidates – oliceridine (TRV130) to treat moderate to severe acute pain intravenously (Phase 3), TRV027 to treat acute heart failure (Phase 2b), TRV734 to treat moderate to severe acute and chronic pain orally (Phase 1), and TRV250 for acute episodic migraine and other CNS disorders (preclinical).

Cautionary Note on 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 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: uncertainties related to the Company's intellectual property; the status, timing, costs, results and interpretation of the Company's clinical trials, including whether oliceridine will prove to be a differentiated analgesic for patients and caregivers seeking alternatives to conventional opioids; the uncertainties inherent in conducting clinical trials, including the timing around the initiation of the pivotal efficacy studies in the Phase 3 program and the potential filing of an NDA; whether interim results from a clinical trial will be predictive of the final results of the trial or results of early clinical trials, including the Phase 2 oliceridine studies and any post-hoc analysis of such trial results, will be indicative of the results of future trials; expectations for regulatory approvals, including the Company's assessment of the results of the End-of-Phase 2 meeting with FDA and whether the Company ultimately will achieve regulatory approval for oliceridine; availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; 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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