February 9, 2015

Trevena Announces Positive Results from Phase 1 Multiple Ascending Dose Study of TRV734 for Moderate to Severe Acute and Chronic Pain

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc. (NASDAQ: TRVN), a clinical-stage biopharmaceutical company and leader in the discovery and development of G protein coupled receptor (GPCR) biased ligands, today announced positive data from a Phase 1 multiple ascending dose study of TRV734, a novel drug candidate in development as an orally administered treatment for moderate-to-severe acute and chronic pain. TRV734 showed pharmacokinetics, safety, tolerability, and CNS activity consistent with a previous Phase 1 study, and showed effectiveness similar to immediate-release oxycodone in an experimental pain model.

“This trial showed that, after repeated dosing, the performance of TRV734 is consistent with results of our previous single ascending dose Phase 1 study,” said David Soergel, M.D., chief medical officer. “In addition, TRV734 at the tested doses performed similarly to a high 10 mg dose of oxycodone in the cold pain test. Promising trends in safety and tolerability were observed, including in the Bowel Function Index, supporting further development of TRV734 to test its differentiation from currently prescribed unbiased opioids like oxycodone.”

“These results, together with our previous clinical data for TRV734, are very encouraging and informative for planning Phase 2 clinical studies,” said Maxine Gowen, Ph.D., president and chief executive officer. “The pupil constriction and cold pain test signals correlate well with opioid analgesia, increasing our confidence in the potential efficacy of TRV734 for moderate-to-severe pain. We believe that TRV734 may offer an improved therapeutic profile compared to opioids like oxycodone.”

About the trial

This two-part trial evaluated the safety, tolerability, pharmacokinetics, and pharmacodynamics of oral TRV734 in healthy males and females. In part A of the study, 125 mg TRV734 was given to 13 males following a high fat meal, a standard meal, and in three split portions following a fast via randomized cross-over design. Results showed that dosing paradigm did not affect TRV734 bioavailability. TRV734 in each dosing paradigm was associated with pupil constriction, a marker of CNS opioid activity, lasting approximately 4-6 hours, consistent with previous data. This suggests that TRV734 should have an appropriate duration of action for the treatment of acute pain when taken with or without food. The pharmacokinetics of different formulations of TRV734 will be evaluated further prior to commencing Phase 2 studies.

In part B of the study, 62 male and female subjects fed standard meals were given placebo,

10 mg immediate-release oxycodone, or 60, 80, 125, or 175 mg of TRV734 every 6 hours for 24 hours. Pharmacokinetics after the first and last dose were similar. Trends in pupil constriction and increased tolerability of cold-induced pain after the first and last dose were noted for all doses of TRV734, with duration of approximately 4-6 hours. These effects were similar to that seen with 10 mg oxycodone.

TRV734 was generally safe and well tolerated, and there were no serious or severe adverse events in either part of the study. Adverse events were generally opioid-related; the most common were somnolence, nausea, headache, dizziness, and vomiting, and were observed for both TRV734 and oxycodone. The Bowel Function Index (BFI), a validated tool to evaluate clinical constipation, was used to explore the potential for TRV734 to cause opioid-induced constipation and in this study showed encouraging trends compared to oxycodone. These data are consistent with preclinical data in which TRV734 produced less constipation than oxycodone at equianalgesic doses.

About TRV734

TRV734 is being developed to optimize analgesia while minimizing on-target gastrointestinal and central nervous system adverse effects through its novel mode of action at the mu-opioid receptor. This receptor is a well-established target for effective analgesics such as fentanyl and morphine, which are unbiased mu-opioid agonists. TRV734 is a biased ligand at the mu-opioid receptor, activating the G protein pathway, associated with analgesia, without activating the mu-opioid beta-arrestin pathway, associated with respiratory depression and constipation in preclinical studies. TRV734 takes advantage of the same novel biased ligand mechanism at the mu-opioid receptor as TRV130, the company's Phase 2 intravenous clinical candidate which has shown promising differentiation versus morphine.

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 with potential to treat serious unmet medical needs - TRV027 to treat acute heart failure (Phase 2b), TRV130 to treat moderate to severe acute pain intravenously (Phase 2b), TRV734 to treat moderate to severe acute and chronic pain orally (Phase 1), and TRV250 for treatment-refractory 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: the status, timing, costs, results and interpretation of the company's clinical trials, including whether the results seen and the trends observed in this

Phase 1 multiple ascending dose study of TRV734 will support future development of this molecule and whether TRV734 could ultimately offering an improved therapeutic profile over oxycodone; the uncertainties inherent in conducting clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or results of early clinical trials such as this Phase 1 study of TRV734 will be indicative of the results of any future trials; expectations for regulatory approvals; 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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Source: Trevena, Inc.