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6/23/14

## Trevena Announces Positive Phase 1 Results for TRV734 for Acute and Chronic Pain

*Results demonstrate oral availability, CNS activity, and promising tolerability*

**KING OF PRUSSIA, PA, June 23, 2014** – Trevena, Inc. (NASDAQ: TRVN) today announced positive results from its Phase 1 trial of TRV734, which Trevena is developing with the goal of providing improved analgesia while avoiding gastrointestinal and respiratory side effects typically associated with opioids. The study tested single ascending doses and the relative bioavailability of oral TRV734 in healthy subjects, and demonstrated that TRV734 is pharmacologically active at a range of safe and well-tolerated doses. The data suggest that TRV734 provides dose-related exposure, speed of onset, and duration of action suitable for treating moderate-to-severe acute pain.

“This trial showed that TRV734 is orally bioavailable and produces central nervous system activity consistent with analgesia, at doses that are safe and generally well-tolerated,” said David Soergel, M.D., senior vice president, clinical development. “We identified an active dose range that was very well tolerated, supporting our belief that TRV734 could present a superior therapeutic profile compared to currently prescribed opioids.”

Highlights of the two-part trial involving a total of 76 healthy subjects include:

- Dose-related increases in plasma concentrations, with peak plasma concentrations reached approximately one hour after dosing and a terminal half life consistent with use for treating acute pain
- Pupil constriction indicative of analgesia observed at doses of 80 mg and higher, and mild-to-moderate adverse effects reported at the maximum explored dose of 250 mg. This suggests that the analgesic efficacy of TRV734 may be separable from opioid-related adverse effects
- No clinically significant changes in vital signs, laboratory values or ECG parameters, and no severe or serious adverse events reported

“These results are highly encouraging and provide a path towards Phase 2 clinical studies of this molecule,” said Maxine Gowen, Ph.D., president and chief executive officer. “In addition, the data further validate the shared mechanism of action of TRV734 and TRV130, and underscore the potential for these agents to provide prescribers and patients with new and differentiated treatment options in both hospital and outpatient settings.”

### Phase 1 trial of TRV734

This study was a two-part first-in-human trial and was designed to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of TRV734. Part A assessed single ascending doses of TRV734 in 64 healthy male subjects. The potentially efficacious dose range of TRV734 was evaluated using pupillometry, a validated biomarker for mu-opioid receptor engagement in the central nervous system that correlates with analgesic efficacy. Cohorts of eight subjects were randomized to receive a single dose of up to 250 mg of TRV734 or placebo. Part B of the study was a randomized, open-label, three-period crossover study of single 125 mg doses of TRV734 in 12 healthy male subjects, designed to compare the PK and PD of an oral capsule and oral solution, each administered after a fast, and an oral capsule when administered after a high-fat meal.

### About TRV734

The mu-opioid 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 vs. 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 and advanced three differentiated biased ligand product candidates into the clinic – TRV027 to treat acute heart failure, TRV130 to treat moderate-to-severe acute pain intravenously, and TRV734 to treat moderate-to-severe acute and chronic pain orally. Trevena also is advancing additional product candidates in its portfolio, including a preclinical program focused on central nervous system indications.

#### 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 the interpretation of the Phase 1 study of TRV734, the potential of TRV734 to have a superior profile to currently prescribed opioids and plans for future clinical development of this molecule; 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 will be indicative of the results of 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, the Company specifically disclaims any obligation to do so, except as may be required by law.

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