November 17, 2014

Trevena Announces Positive Top-Line Results from Phase 2a/b Study of TRV130 in Acute Postoperative Pain

– Study successfully achieved primary endpoint –

– Demonstrated differentiation versus morphine –

– Company to host conference call at 5:00 PM Eastern time –

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc. (NASDAQ: TRVN), a clinical stage pharmaceutical company focused on the discovery and development of G protein coupled receptor (GPCR) biased ligands, today announced positive top-line data from its randomized, double-blind, placebo- and active-controlled Phase 2a/b trial of TRV130 in moderate-to-severe postoperative acute pain. At doses of 2 mg and 3 mg TRV130 administered every 3 hours, the study achieved its primary endpoint of statistically greater pain reduction than placebo over 48 hours, successfully demonstrating proof of concept for TRV130.

The trial was designed with key secondary endpoints to evaluate the differentiation of TRV130 from gold-standard morphine at a standard reference dose of 4 mg every 4 hours. Over the 48 hour study period, TRV130 3 mg every 3 hours showed statistically superior analgesic efficacy compared to morphine. Additionally, the 2 mg and 3 mg doses of TRV130 demonstrated statistically superior analgesic efficacy compared to 4 mg morphine in the first 3 hours of dosing, when study pain was most severe. For these doses, patients also reported maximum pain relief during the first dosing period that was statistically superior compared to morphine. Notably, in this study TRV130 at 2 mg and 3 mg demonstrated similar tolerability to morphine 4 mg over 48 hours. TRV130 and morphine were both associated with opioid-related adverse events, including dizziness, headache, somnolence, nausea, vomiting, flushing, and itching.

“The data from this trial are impressive, suggesting that TRV130 may offer a superior product profile versus morphine, which frequently causes dose-limiting adverse events and often fails to fully manage post-surgical pain,” said Lynn Webster, M.D., past president of the American Academy of Pain Medicine. “Importantly, the study data demonstrate that treatment with TRV130 significantly improved analgesia versus a standard dose of morphine particularly in the early hours after surgery, when pain levels are at their highest. This increased efficacy was achieved with tolerability similar to morphine over the study period. TRV130 may therefore represent an important advance in pain management.”

Study Results

- Success on primary endpoint: Doses of 2 mg and 3 mg of TRV130 at 3 hour intervals

achieved a statistically significant reduction in pain intensity difference from placebo over 48 hours, measured as the time-weighted average change in pain score (TWA0-48). At 2 mg, TRV130 reduced average pain score (LS mean change in TWA0-48) by 1.4 points ($p=0.0024$ vs. placebo; all p-values 1-sided). At 3 mg, TRV130 reduced LS mean TWA0-48 by 2.4 points ($p<0.0001$ vs. placebo). Baseline pain rating was approximately 7 out of 10, a pain level considered severe. TRV130 achieved a reduction in mean pain intensity of up to approximately 6 points, with notable efficacy at 5 minutes, the first pain intensity assessment after dosing.

- Over 48 hours, 3 mg of TRV130 at 3 hour intervals achieved a statistically significant reduction in pain intensity difference from 4 mg morphine at 4 hour intervals, reducing average pain score (LS mean change in TWA0-48) by 1.0 point vs. morphine ($p=0.014$). Morphine reduced LS mean change in TWA0-48 by 1.3 points vs. placebo ($p = 0.0023$).
- When study pain was most severe, during the first 3 hours after the initial dose, TRV130 at 1 mg, 2 mg and 3 mg showed a statistically significant reduction in pain (TWA0-3) vs. placebo (LS mean change -1.0, -2.4, and -3.0 respectively; $p = 0.021$, $p < 0.0001$, and $p < 0.0001$, respectively). In addition, TRV130 at 2 mg and 3 mg showed a statistically significant reduction in pain vs. 4 mg morphine during this time (LS mean change: TRV130 2 mg -1.2 vs. morphine, $p = 0.0029$; TRV130 3 mg -1.8 vs. morphine, $p < 0.0001$).
- Consistent with these findings, more patients reported statistically greater peak pain relief during the first dosing period for 2 mg and 3 mg TRV130 compared to 4 mg morphine ($p = 0.005$ and $p < 0.0001$ for TRV130 2 mg and 3 mg vs. morphine, respectively). Complete pain relief during this period was reported in 13%, 31%, and 52% of patients receiving 1 mg, 2 mg, and 3 mg TRV130, respectively, compared to 0% and 8% for patients receiving placebo and 4 mg morphine, respectively.
- Adverse events associated with TRV130 were largely opioid-related; the most frequent reported events were dizziness, headache, somnolence, nausea, vomiting, flushing, and itching. Adverse effects were generally dose-related. No serious adverse events were reported in any study group.
- Tolerability for 2 mg and 3 mg TRV130 over the full 48 hours of dosing was similar to morphine.
- Rescue medication (acetaminophen or ketorolac) was used in all groups.

Full results will be presented at a future scientific conference or in a journal publication.

“The results from this trial support the potential of TRV130 to provide more rapid, reliable, and powerful pain relief than may be achievable with currently used opioids,” said David Soergel, M.D., senior vice president of clinical development at Trevena. “In this study, the magnitude of efficacy associated with TRV130 suggests it may be able to relieve the most severe types of pain, for which effective therapies are lacking. We look forward to building on these results with an upcoming Phase 2 trial in soft-tissue surgery patients and preparing for Phase 3 development.”

“The positive data from this study represent a significant achievement for both the TRV130 program and our biased ligand platform,” said Maxine Gowen, Ph.D., chief executive officer

of Trevena. “The trial results, including the striking level of analgesic efficacy achieved using an FDA-recommended endpoint for registration, provide us with a wealth of information that will enable a robust and efficient Phase 3 development program for TRV130. The data also provide further evidence that Trevena’s novel, proprietary platform can deliver differentiated drug candidates with impressive clinical performance that may improve the current standard of care.”

Study Design

The Phase 2a/b study was a multicenter, randomized, double-blind, placebo- and active-controlled, multiple dose, adaptive study in 333 women and men undergoing a primary unilateral first-metatarsal bunionectomy surgery at four centers in the United States. Patients were randomized after surgery to receive TRV130, morphine or placebo to manage their pain. Pain intensity was measured using validated numeric rating scales at multiple time points up to 48 hours; based on these scales, analgesic efficacy was assessed as a time-weighted average change over 48 hours, an FDA-recommended endpoint.

The study was conducted in two parts, with the goal of providing information on dose- and interval-ranging and furthering the differentiation of TRV130 versus morphine. In Part A, a pilot phase, patients were randomized to receive one of 4 doses of TRV130 (1 mg, 2 mg, 3 mg, 4 mg), morphine, or placebo, all given at four hour intervals. In Part B, the trial’s adaptive phase, 8 cohorts were randomized successively to one of two adaptive doses of TRV130 given every 3 hours, morphine, given every 4 hours, and placebo in a double-blind, double-dummy fashion. In Part B, doses of 0.5 mg, 1 mg, 2 mg, and 3 mg TRV130 were evaluated. 141 patients were treated in Part A, and 192 patients were treated in Part B.

Conference Call and Webcast

The company will host a conference call and webcast to discuss the top-line results of the study. Slides will be available on the Investors section of the Trevena website at www.trevenainc.com. The webcast will be available for replay for 7 days.

Date:	Monday, November 17, 2014
Time:	5:00 p.m. (EST)
Telephone Access:	(855) 465-0180 (U.S. and Canada)
International:	(484) 756-4313 (International)
Conference ID:	36872822
Online Access:	http://www.media-server.com/m/p/nmvzazsq

About moderate-to-severe acute pain

Mu opioid receptor agonists such as morphine and fentanyl are the most effective class of analgesics currently available and are the standard of care in postoperative pain; however, in published national surveys, a significant proportion of surgical patients have reported inadequate pain relief despite use of opioid analgesics. Opioid-related adverse effects such as respiratory depression, nausea and vomiting, and constipation and postoperative ileus are frequently dose-limiting, complicating pain management and increasing the burden of care.

About TRV130

TRV130 was designed to optimize opioid receptor pharmacology to deliver an improved analgesic profile. TRV130 is a biased mu opioid receptor ligand, a novel opioid receptor modulator which in preclinical studies activated analgesic signals while avoiding signals that can interfere with analgesia and promote respiratory depression and gastrointestinal dysfunction. A previous study in healthy volunteers showed that TRV130, in a series of experimental models, elicited analgesia superior to morphine with less respiratory depression and vomiting and less severe nausea. Trevena believes that TRV130 may have an improved profile compared to currently used opioid analgesics and could offer enhanced pain relief with a reduced burden of opioid-related adverse events. Trevena anticipates that the initial market opportunity for TRV130 will be in the acute care settings, with a focus on postoperative 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 and advanced three 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 plans to advance 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, its future operations, clinical development of its therapeutic candidates, its plans for potential future product candidates and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "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 whether the Company’s interpretation of the results of clinical trials will be indicative of the results of any future trials, including the magnitude of the efficacy and safety results of the TRV130 Phase 2a/b study versus placebo and morphine, whether TRV130 will offer more rapid, reliable and powerful pain relief versus other opioids and be suitable for use in the most severe types of pain, whether the Phase 2a/b study results will provide sufficient information to enable a robust and efficient Phase 3 development program and whether these study results provide evidence to support the Company’s proprietary platform; the availability and timing of data from ongoing clinical trials, the uncertainties inherent in conducting clinical 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" section of the Company’s Annual Report on Form 10-K for the year ended December 31, 2013 filed with the Securities and Exchange Commission on March 20, 2014 and other filings the Company makes with the Securities

and Exchange Commission from time to time. In addition, the forward-looking statements included in this press release represent the Company's views 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. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

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