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Trevena Initiates Phase 2 Study of TRV130 in Acute Postoperative Pain

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 the initiation of a Phase 2a/b clinical trial with TRV130, a small molecule G protein biased ligand at the mu opioid receptor, which Trevena is developing as a first-line intravenous treatment for patients experiencing moderate to severe acute pain where intravenous administration is preferred.

In this multicenter, randomized, double-blind, placebo- and active-controlled, multiple dose, adaptive study (NCT02100748), the effects of TRV130 will be assessed in patients following bunionectomy surgery. The aim of this clinical trial is to evaluate TRV130's efficacy and tolerability in the management of postoperative pain using the gold-standard morphine as a benchmark. Top line data are expected in the first quarter of 2015.

This study will enroll a total of approximately 400 patients who undergo first metatarsal bunionectomy and are then randomized to receive TRV130, morphine or placebo to manage their pain postoperatively. Pain intensity and pain relief will be measured using validated rating scales at multiple time points up to 48 hours during the study period. The study will be conducted in 2 parts: in Part 1 (pilot phase, 150 patients), 25 patients per group will be randomized to 4 doses of TRV130 (1, 2, 3, 4 mg every 4 hours), morphine, or placebo. In Part 2, approximately 10 cohorts each of 25 patients will be randomized successively to 2 adaptive doses of TRV130, morphine and placebo, allowing the trial to focus on-going recruitment on the optimal doses of TRV130 versus morphine. This study is designed to facilitate the ensuing Phase 3 development by providing information on dose- and interval-ranging and furthering the differentiation of TRV130 versus morphine.

"This study has been designed to explore dose-regimens of TRV130 in a robust postoperative pain setting in order to support subsequent Phase 3 development," said Maxine Gowen, Ph.D., chief executive officer of Trevena. "This trial reflects our confidence in the profile of TRV130 by directly comparing its therapeutic window to that of morphine."

Results from the bunionectomy trial will build upon data from the phase 1 clinical studies of TRV130. The company recently completed a Phase 1b pharmacokinetic/pharmacodynamic trial comparing TRV130 with morphine in healthy subjects, using an evoked pain model. The full results of that trial will be presented at the American Pain Society meeting in May 2014. In October 2013, Trevena announced the publication of data from a Phase 1 clinical trial of TRV130 in the Journal of Clinical Pharmacology. At several pharmacologically active doses, as measured by pupil constriction, subjects did not report nausea or vomiting. Trevena believes this suggests that TRV130 may be better tolerated than unbiased opioids like morphine, which frequently produce nausea and vomiting at active doses.

About TRV130 and acute pain

Trevena anticipates that the initial market opportunity for TRV130 will be in the acute care hospital setting, with a focus on postoperative pain. Mu opioid agonists are the most effective class of analgesics currently available and are the standard of care; however, their benefit is limited by severe side effects such as respiratory depression, nausea and vomiting, constipation and postoperative ileus. In published national surveys, a significant proportion of surgical patients have reported inadequate pain relief despite use of opioid analgesics. Trevena believes that TRV130 may have an improved profile compared to these agents and could offer enhanced pain relief with a reduced burden of opioid-related adverse events.

The mu opioid receptor is a well-established target for analgesics such as fentanyl and morphine, which are unbiased mu opioid agonists. TRV130 is a biased ligand – it activates the mu opioid G protein pathway, associated with analgesia, while inhibiting the β-arrestin pathway, which, in preclinical studies, was associated with reduced analgesia, respiratory depression, and constipation. The preclinical pharmacology of this novel molecule has been previously published in the Journal of Pharmacology and Experimental Therapeutics, suggesting that TRV130 is powerfully analgesic with an improved safety and tolerability profile when compared directly to classical opioids such as 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 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 the availability and timing of data from ongoing clinical trials, 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" 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.

Investor Contacts:
Trevena, Inc.
Jonathan Violin
Director, Investor Relations
610-354-8840 x231
jviolin@trevenainc.com
or
Argot Partners
Andrea Rabney
President and chief executive officer
212-600-1902
andrea@argotpartners.com
or
Media Contact:
Argot Partners
Eliza Schleifstein
917-763-8106
eliza@argotpartners.com

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