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First Clinical Experience of Trevena's lead CNS Biased Ligand, TRV130, Published in Journal of Clinical Pharmacology

KING OF PRUSSIA, Pa., Oct. 15, 2013 /PRNewswire/ -- Trevena, Inc. (Trevena), a clinical stage pharmaceutical company and the leader in the discovery of G protein coupled receptor (GPCR) biased ligands, today announced the electronic publication of the first clinical manuscript of its lead CNS asset, TRV130. The manuscript entitled, "First clinical experience with TRV130: pharmacokinetics and pharmacodynamics in healthy volunteers." can be viewed online at the Journal of Clinical Pharmacology's website (**http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1552-4604/accepted**).

TRV130 is a small molecule G protein biased ligand at the mu-opioid receptor, which Trevena is developing as a first-line treatment for patients experiencing moderate to severe acute pain where intravenous administration is preferred. Trevena expects to initiate a Phase 2 trial in the first half of 2014. The manuscript summarizes results from the first-in-human clinical study in which the compound was administered to healthy human subjects. In this study, the tolerability, pharmacokinetics and pharmacodynamics of ascending doses of TRV130 were explored. As demonstrated in preclinical studies, TRV130 showed dose-dependent increases in exposure in this clinical study. At these low pharmacologically active doses, as measured by pupil constriction, study subjects experienced no nausea and vomiting. This suggests that TRV130 may be better tolerated than unbiased opioids like morphine, which frequently produce nausea and vomiting at active doses, and that the beneficial therapeutic index seen preclinically may translate in the clinic.

"We are very excited to be advancing our CNS portfolio into clinical development. These findings support our hypothesis that biased GPCR ligands may provide beneficial benefit/risk profiles in the clinic. We are looking forward to our next clinical studies which will evaluate the safety and effectiveness in patients suffering from pain," commented Trevena's CEO, Maxine Gowen.

The printed manuscript will appear in a future print issue of the journal. David G. Soergel, M.D., Trevena's senior vice president of clinical development, Jonathan D. Violin, PhD, director of biology and co-founder of Trevena, and Michael W. Lark, PhD, Trevena's chief scientific officer and senior vice president of research were among the publication's authors.

About TRV130 and acute pain

The mu-opioid receptor is a well-established target for analgesics such as fentanyl and morphine, which are unbiased mu-opioid agonists. TRV130 activates the mu-opioid G protein pathway, associated with analgesia, and inhibits the beta-arrestin pathway, which, in preclinical studies, was associated with respiratory depression and constipation. The preclinical pharmacology of this novel molecule has been previously published in the Journal of Pharmacology and Experimental Therapeutics, showing that TRV130 is powerfully

analgesic with an improved safety and tolerability profile when compared directly to classical opioids such as morphine. Trevena presented the preliminary results from this first clinical study of TRV130 in March 2013, at the American Academy of Neurology meeting.

There were approximately 30 million reimbursement claims made for intravenous opioids by hospitals in the United States in 2010. Trevena anticipates that the initial market opportunity for TRV130 will be in this acute care hospital setting, with a focus on postoperative pain. The dosing of the most effective class of analgesics currently available, mu-opioid agonists, is limited by severe side effects such as respiratory depression, nausea and vomiting, constipation and postoperative ileus, which is a condition that most commonly occurs after surgery involving interruption of movement of the intestines in which the bowel enters spasm and stops passing food and waste. Trevena believes that TRV130 may have an improved profile compared to unbiased mu-opioid agonists, which are the current standard of care in terms of efficacy, safety and tolerability.

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 two differentiated product candidates into the clinic -- TRV027 to treat acute heart failure and TRV130 to treat moderate to severe acute pain intravenously. Trevena also plans to advance additional product candidates, including two preclinical programs focused on central nervous system indications.

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