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Trevena to Present First-in-Man Study Results for Mu-Opioid Biased Ligand TRV130

Poster at the 2013 AAN meeting describes the human safety and pharmacology of intravenous analgesic TRV130 in healthy volunteers

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc., the leader in the discovery and development of G-protein coupled receptor (GPCR) biased ligands, announced today that Michael Lark, Ph.D., Chief Scientific Officer, will present the results of a Phase 1 first-in-man study on the safety, tolerability, and pharmacology of TRV130 in healthy volunteers, as a poster at the American Academy of Neurology meeting, to be held in San Diego on March 16th through 23rd, 2013. The poster will be presented on Tuesday, March 19th.

In this study, which was completed in 2012, TRV130 was safe and generally well-tolerated, and showed pharmacodynamic effects that were consistent with its exciting preclinical profile. TRV130's pharmacokinetic profile was also shown to be suitable for an intermittent-use intravenous drug. Trevena is developing TRV130 for the intravenous treatment of acute moderate-to-severe post-operative pain. The data supports TRV130 progression to its next clinical study, in which analgesic efficacy and tolerability will be compared directly with intravenous morphine, a gold-standard post-operative analgesic.

This Phase 1 study was a multi-part, randomized, single-blind, placebo-controlled, single ascending dose study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of TRV130 in healthy adult males. Single doses of TRV130 or placebo were delivered by infusion to 74 individuals. In addition to safety, tolerability and pharmacokinetic endpoints, pupillometry, a validated pharmacodynamic measure, confirmed that TRV130 rapidly entered the CNS and engaged the mu-opioid receptor.

"TRV130 is the second Trevena molecule to enter clinical trials, and a great example of how a biased ligand can improve tolerability at a precedented target," commented Maxine Gowen Ph.D., Trevena President and CEO. "Phase 1 studies of pain drugs allow exploratory assessment of efficacy markers. We are very excited that this study suggested a beneficial dose window for TRV130 humans, in which strong analgesia and good tolerability may both occur."

TRV130 is a first-in-class biased ligand that targets the mu-opioid receptor and optimizes analgesia while minimizing receptor-mediated side effects such as nausea, vomiting, ileus and respiratory suppression. As a biased ligand, TRV130 activates the G-protein signaling pathway mediated by the mu-opioid receptor to produce analgesia, while simultaneously antagonizing the β-arrestin pathway, thereby minimizing certain typical opioid side effects. 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.

About Post-Operative Pain

Intravenous opioids are used to manage the severe acute pain which results from an estimated 30 million surgical procedures in the US per year. Currently available drugs such as *i.v.* morphine, fentanyl and hydromorphone present physicians and patients with significant dose-limiting safety and tolerability problems, leaving 80% of patients with some degree of post-operative pain. These side effects, including respiratory depression, nausea, vomiting, exacerbation of post-operative ileus, and excessive sedation, can result in delayed post-operative recuperation and longer hospital stay. There is a long-standing need for better post-operative pain drugs that have opioid-like analgesia, but which are safer to use and better tolerated by patients.

About Trevena and Biased Ligands

Trevena, Inc. is a clinical stage pharmaceutical company focused on discovering and developing the next generation of G-protein coupled receptor (GPCR) targeted medicines. GPCRs are the targets for at least one-third of modern medicinal products, and remain the predominant class of targets under clinical evaluation. Trevena's expertise lies in engineering "biased ligands" that activate only the beneficial signaling pathways downstream of a GPCR, to unlock new biology and avoid drug adverse effects. In addition to TRV130, Trevena's pipeline currently includes a Phase 2 clinical stage Angiotensin receptor biased ligand for acute heart failure, and discovery-stage programs for chronic pain and Parkinson's disease. Trevena is based in King of Prussia, Pennsylvania and is backed by leading investors including Alta Partners, Healthcare Ventures, NEA, Polaris and Yasuda Enterprise Development Company. For more information about the company, please visit www.trevenainc.com.

Trevena, Inc.
Alastair Southwell, 610-354-8840
asouthwell@trevenainc.com

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