

Trevena Completes First-in-Human Study of TRV130, an Injectable Mu-Opioid Biased Ligand for Acute Pain

TRV130 is generally well-tolerated and rapidly enters the CNS in healthy adult males

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc., the leader in discovery and development of G-protein coupled receptor (GPCR) biased ligands, today announced the successful completion of a Phase I first-in-human clinical trial of TRV130. Trevena is developing TRV130 for the intravenous treatment of acute moderate-to-severe post-operative pain. The drug was safe and generally well-tolerated in this study, with pharmacodynamic effects recapitulating its exciting preclinical profile. The next clinical study of TRV130 will investigate analgesic efficacy and tolerability, and will include intravenous morphine, a gold-standard post-operative analgesic, as a comparator.

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. In this study, single doses of TRV130 or placebo were delivered by infusion to 74 subjects. In addition to safety, tolerability and pharmacokinetic endpoints, pharmacodynamic measurements including pupillometry confirmed that TRV130 rapidly entered the CNS and engaged the mu-opioid receptor. Data from the study will be presented at an upcoming scientific conference.

David Soergel, M.D., Head of Clinical Development at Trevena commented, "We are delighted to have shown that TRV130 is safe and well-tolerated in humans and that, in this first study, its preclinical pharmacology has translated well into the clinic. With its expected therapeutic index advantage over morphine, TRV130 has the potential to make it easier for physicians to more effectively manage post-operative pain and to reduce hospital length of stay following a surgical procedure."

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 antagonizing the β -arrestin pathway, thereby minimizing typical opioid side effects. In preclinical studies, TRV130 was 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.* versions of morphine, fentanyl and hydromorphone present physicians and patients

with significant safety and tolerability problems, which often limit dose levels, and consequently leave up to 80% of patients enduring some degree of post-operative pain. Side effects include potentially dangerous respiratory depression, nausea, vomiting, exacerbation of post-operative ileus, and excessive sedation. There is a long-standing need for better post-operative pain drugs that have opioid-like analgesia, but which are safer to use and easier for patients to tolerate.

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.

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