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Trevena Initiates Clinical Development of TRV130, a Biased Mu-Opioid Ligand for Severe Post-Operative Pain

Biased ligand offers powerful analgesia with reduced opioid side effects

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc., the leader in discovery and development of G-protein coupled receptor (GPCR) biased ligands, announced today the initiation of a Phase I clinical trial of TRV130, a novel candidate designed for the intravenous treatment of moderate-to-severe post-operative pain. TRV130 is a biased ligand that targets the mu-opioid receptor to optimize analgesia while minimizing mu opioid receptor-mediated side effects such as respiratory suppression and constipation. As a biased ligand, TRV130 activates the G-protein signaling pathway mediated by the mu-opioid receptor while antagonizing the β-arrestin pathway. In preclinical studies, TRV130 was powerfully analgesic with an improved safety and tolerability profile when compared directly to classical opioids such as morphine.

The Phase 1 study of TRV130 is a placebo-controlled, single ascending dose study in healthy subjects to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics. In addition to traditional first-in-man study information, an experimental pain methodology will be used to provide early insight into how TRV130's preclinical profile translates to humans. The results of this study will inform dose selection for subsequent studies of TRV130.

David Soergel, M.D., Head of Clinical Development at Trevena, commented, "We are delighted to have a second biased ligand from our portfolio in the clinic. TRV130 is a great example of how ligand bias can dial out problems with safety and tolerability, while maintaining or improving opioid efficacy. If successful, TRV130 will be a better analgesic in the post-operative setting where current therapies have not met patients' needs."

There are 15 million hospital inpatient stays and a similar number of outpatient procedures in the US per year during which *i.v.* opioids are used to manage severe pain. Currently used drugs such as *i.v.* versions of morphine, fentanyl and hydromorphone present physicians and patients with significant safety and tolerability problems. These include potentially dangerous respiratory depression, slowing of gastro-intestinal motility, and excessive sedation. There is a long-standing need for new post-operative pain drugs that have opioid-like analgesia, but which are safer to use and easier for patients to tolerate.

About Biased Ligands

Traditional GPCR ligands either turn on or turn off all of the cellular signaling pathways engaged by a particular receptor, which can result in efficacy limitations or undesirable adverse effects. Trevena's novel drug discovery approach is focused on designing GPCR ligands that are "biased" toward activating one key receptor signaling pathway while blocking

another. These biased ligands provide an enhanced level of drug specificity which allows enhanced efficacy or decreased side effects to be designed into the drug candidate.

About Trevena

Trevena, Inc. is the leader in the discovery and development of GPCR biased ligand drugs. The lead drug in Trevena's portfolio is TRV027, a biased AT1R ligand currently in Phase 2 studies for the treatment of acute decompensated heart failure. Trevena is a privately held company 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, please visit **www.trevenainc.com** .

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