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Mechanism for Cardiac Effects of Trevena Angiotensin Receptor Biased Ligands Examined in Published Study

KING OF PRUSSIA, Pa., July 30, 2013 /PRNewswire/ -- Trevena, Inc., the leader in the discovery of G-protein coupled receptor (GPCR) biased ligands, announced today the publication of new findings related to the mechanism of action of its Angiotensin II Type 1 Receptor (AT1R) biased ligands. The publication describes work led by R. John Solaro PhD, Distinguished University Professor and Head of the Department of Physiology and Biophysics at the University of Illinois at Chicago, performed in collaboration with Trevena scientists. The studies evaluated the molecular mechanisms of action for TRV120023, a molecule closely related to Trevena's clinical stage asset, TRV027, which is in Phase 2 testing for the treatment of acute heart failure. TRV027 is being developed by Trevena under a recently announced collaborative licensing option agreement with Forest Laboratories Inc. (NYSE: FRX).

The article, entitled "The Beta-arrestin-Biased Ligand TRV120023 Inhibits Angiotensin II-Induced Cardiac Hypertrophy While Preserving Enhanced Myofilament Response to Calcium", was published online, ahead of print, July 19, 2013, in the American Journal of Physiology - Heart and Circulatory Physiology.

Work in Dr. Solaro's laboratory showed that TRV120023 blocked cardiac hypertrophy in rats, while stimulating biochemical pathways linked to increased cardiac contractility. TRV120023 increased the sensitivity of cardiac myofilaments to calcium, suggesting that TRV120023 and molecules like it, such as TRV027, can increase cardiac contractile force ("inotropy") through a mechanism distinct from classic inotropes, which are associated with cardiac arrhythmia and increased mortality. Dr Solaro said of the published work, "these experiments suggest that Trevena's biased ligands regulate the heart's contractile machinery through a novel mechanism which may simultaneously block cardiac dysfunction while promoting cardiac contractility"

Michael Lark Ph.D., Trevena's Chief Scientific Officer, commented that "these findings further support the hypothesis that beta-arrestin biased ligands like TRV120023 and TRV027 may offer unique benefits in treating cardiovascular disease."

About Acute Heart Failure

The American Heart Association estimated that acute heart failure (AHF) hospitalization costs the U.S. healthcare system more than $20 billion each year in direct spending. AHF is already the leading reason for hospitalization of individuals over 65 years old in the United States, with over 1 million hospital admissions per year. AHF is also the most costly diagnosis for Medicare in the nation. Despite the significance of this problem, current therapies are not producing meaningful improvements in patient outcomes. AHF incidence is

increasing globally, and both heart failure mortality and hospital re-admission following an AHF event remain extremely high.

About Trevena

Trevena, Inc. is dedicated to discovering and developing the next generation of 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 TRV027, Trevena's pipeline currently includes a clinical stage mu-opioid biased ligand, TRV130, for post-operative pain, and discovery-stage programs for chronic pain and Parkinson's disease.

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