

# Trevena Angiotensin Receptor Biased Ligand Promotes Cell Survival During Acute Cardiac Injury

*A pharmacology study of TRV120023, a  $\beta$ -arrestin biased AT1R ligand from Trevena, conducted by Duke scientists in an animal cardiac ischemia model is published in the American Journal of Physiology: Heart and Circulation Physiology*

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc., the leader in the discovery of G-protein coupled receptor (GPCR) biased ligands, announced that results from a study into the cardioprotective actions of its Angiotensin II Type 1 Receptor (AT1R) biased ligands has been published. The publication describes the results of experiments conducted at Duke University in the laboratory of Dr. Howard Rockman, in collaboration with Trevena, showing that  $\beta$ -arrestin biased AT1R ligands can protect cardiac tissue from injury. The molecule tested, TRV120023, is closely related to TRV027, Trevena's experimental acute heart failure molecule currently in mid-stage clinical trials.

The article, entitled " $\beta$ -Arrestin-biased AT1R stimulation promotes cell survival during acute cardiac injury" was published online ahead of print on August 10<sup>th</sup> 2012 in the American Journal of Physiology: Heart and Circulation Physiology. In mice subject to transient cardiac ischemia, compared to an unbiased angiotensin receptor blocker, TRV120023 stimulated the activation of the pro-survival kinase Akt and significantly reduced cardiac apoptosis. Like TRV027 in rats, TRV120023 also increased cardiac contractility in mice in a  $\beta$ -arrestin-dependent manner. This work suggests that TRV027 may support cardiac function during acute heart failure by increasing contractility and reducing the cardiac deterioration which can result from excessive myocardial metabolic demand.

"These data further support the benefits of targeting the AT1R with a  $\beta$ -arrestin biased ligand. The combination of  $\beta$ -arrestin mediated cardioprotection, with increased  $\beta$ -arrestin-mediated contractility, should translate into both short and longer-term benefits in the setting of acute heart failure," stated Dr. Rockman.

## About Acute Heart Failure

AHF represents a serious challenge for patients, physicians and healthcare systems. The American Heart Association estimated that heart failure hospitalization costs the U.S. healthcare system more than \$20 billion each year. AHF is already the leading reason for hospitalization of individuals over 65 years old in the United States, with an estimated 1.5 million admissions last year, and is the most costly diagnosis for Medicare. 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. For all of these reasons, there is an urgent need for better treatments, and a clear incentive for regulators

and payers to approve and reimburse them.

### **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 they remain the predominant class of targets under clinical evaluation. Trevena's expertise lies in understanding which signaling pathways downstream of a GPCR are associated with beneficial versus adverse biological effects, and in engineering "[biased ligands](#)" that activate only the beneficial pathways to unlock new biology and avoid drug adverse effects. Trevena's platform can be broadly applied across therapeutic areas and its pipeline currently includes programs in cardiovascular and CNS diseases. Founded in 2008, Trevena is based in King of Prussia, Pennsylvania and is a privately held company backed by leading investors including Alta Partners, Healthcare Ventures, NEA, Polaris and Yasuda Enterprise Development Company. Drs. Howard A. Rockman and Robert J. Lefkowitz of Duke University are scientific co-founders of Trevena. For more information about the company, please visit [www.trevenainc.com](http://www.trevenainc.com).

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Source: Trevena, Inc.