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Trevena Acute Heart Failure Drug TRV027 Unloads the Heart and Maintains Renal Function When Co-administered with Furosemide in Dog Heart Failure Model

A Mayo Clinic animal pharmacology study of TRV027, a β-arrestin biased ligand at the Angiotensin II Type I Receptor, is published in Circulation Heart Failure

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc., the leader in the discovery of G-protein coupled receptor (GPCR) biased ligands, announced that results have been published from a new preclinical pharmacology study of its phase 2 clinical acute heart failure molecule, TRV027. The study was the second to be published as part of a multi-year collaboration between Trevena and Drs. John C. Burnett, Jr, and Guido Boerritger, of the Mayo Clinic.

On August 13th, 2012 in *Circulation: Heart Failure*, an article entitled "TRV120027, a Novel Beta-Arrestin Biased Ligand at the Angiotensin II Type I Receptor (AT1R), Unloads the Heart and Maintains Renal Function When Added to Furosemide in Experimental Heart Failure" was published online before print.

Building on previous publications showing that TRV027 has beneficial hemodynamic and renal effects in a canine model of heart failure, this new publication shows that when TRV027 is co-administered with furosemide, it reduces cardiac preload and afterload, while preserving the natriuretic and diuretic effects of furosemide, and protecting renal function. These findings indicate that TRV027 may work additively or synergistically with loop diuretics like furosemide, which are current standard of care for treating acute heart failure.

"These data in experimental heart failure strongly support the concept that TRV027, in combination with Lasix to treat acute heart failure, is a solid strategy which both preserves and enhances cardiorenal function. Now is the time to test this therapeutic strategy in seminal clinical studies so as to reduce the burden of acute heart failure," commented Dr. Burnett, consultant to Trevena.

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. For more information about the company, please visit **www.trevenainc.com**.

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Source: Trevena, Inc.