Preclinical Studies with MyoKardia's Mavacamten Demonstrate Evidence of Reduced Contractility and Improved Left Ventricular Compliance

SOUTH SAN FRANCISCO, Calif., Nov. 15, 2017 (GLOBE NEWSWIRE) -- MyoKardia, Inc. (Nasdaq:MYOK), a clinical-stage biopharmaceutical company pioneering a precision medicine approach for the treatment of heritable cardiovascular diseases, presented data that further elucidates the mechanism of action of the company's lead drug candidate, mavacamten (formerly MYK-461) at this week's American Heart Association (AHA) Scientific Sessions. Data from MyoKardia's *in vivo* study demonstrated that treatment with mavacamten improved myocardial compliance while preserving systemic pressures. Mavacamten is an investigational agent that has been shown in clinical studies to modulate cardiac myosin to reduce the excess contractility characteristic of hypertrophic cardiomyopathy (HCM). HCM is a severe and progressive genetic condition in which the walls of the heart thicken and can obstruct blood flow from the left ventricle. The thickened heart muscle is less compliant than normal and therefore fills with less blood, reducing cardiac output.

"The observation that mavacamten may improve distensibility while reducing contractility increases our understanding of mavacamten's mechanism of action and hemodynamic effects," said Robert McDowell, Ph.D., Chief Scientific Officer of MyoKardia. "We look forward to potentially verifying the clinical implications of this early evidence of improved myocardial relaxation and of a rightward shift in the diastolic pressure-volume relationship, as it could greatly inform MyoKardia's ongoing research to address diseases of impaired diastolic function."

In healthy animals, the pharmacodynamic effect of mavacamten was compared to that of metoprolol, a beta blocker commonly prescribed in the management of HCM, in an acute setting. Mavacamten reduced systolic performance and increased end diastolic volume (EDV) while preserving end diastolic pressures (EDP) and systemic blood pressure. By contrast, metoprolol, at matched levels of negative systolic performance, caused increased EDP with significantly less increase in EDV. Chronic treatment with mavacamten over a nine-month period showed a comparable profile, characterized by preserved echocardiographic indices of diastole and filling pressure. Taken together, these data indicate a distinct and unique mode of action for mavacamten, providing evidence of improved left ventricular compliance that accompanies reduced myocardial contractility.

The presentation detailing these results, *In Vivo Cardiac Effects of Mavacamten (MYK-461): Evidence for Negative Inotropy and Improved Compliance* (#405), was part of the Drug Discovery for Heart Failure session.

About Mavacamten (MYK-461)
Mavacamten is a novel, oral, allosteric modulator of cardiac myosin that reduced hypercontractility in a Phase 1 clinical study of hypertrophic cardiomyopathy (HCM) patients. MyoKardia has evaluated mavacamten in multiple Phase 1 clinical studies, primarily designed to evaluate safety and tolerability of oral doses of mavacamten, and

provide pharmacokinetic and pharmacodynamic data. In April 2016, the U.S. FDA granted Orphan Drug Designation for mavacamten for the treatment of symptomatic oHCM, a subset of HCM. MyoKardia is currently studying mavacamten in the Phase 2 PIONEER-HCM study.

About MyoKardia

MyoKardia is a clinical-stage biopharmaceutical company pioneering a precision medicine approach to discover, develop and commercialize targeted therapies for the treatment of serious and rare cardiovascular diseases. MyoKardia's initial focus is on the treatment of heritable cardiomyopathies, a group of rare, genetically-driven forms of heart failure that result from biomechanical defects in cardiac muscle contraction. MyoKardia has used its precision medicine platform to generate a pipeline of therapeutic programs for the chronic treatment of the two most prevalent forms of heritable cardiomyopathy—hypertrophic cardiomyopathy (HCM), and dilated cardiomyopathy (DCM). MyoKardia's most advanced product candidate is mavacamten (formerly MYK-461), a novel, oral, allosteric modulator of cardiac myosin that has been shown to reduce hypercontractility in early clinical studies and is currently being studied in the Phase 2 PIONEER-HCM clinical trial. MYK-491, MyoKardia's second product candidate, is designed to increase the overall extent of the heart's contraction in DCM patients by increasing cardiac contractility. MyoKardia is currently evaluating MYK-491 in a Phase 1 study in healthy volunteers. A cornerstone of the MyoKardia platform is the Sarcomeric Human Cardiomyopathy Registry (SHaRe), a multi-center, international repository of clinical and laboratory data on individuals and families with genetic heart disease, which MyoKardia helped form in 2014. MyoKardia's mission is to change the world for patients with serious cardiovascular disease through bold and innovative science.

Contacts

Beth DelGiacco (Investors)
Stern Investor Relations, Inc.
212-362-1200
beth@sternir.com

Steven Cooper (Media)
Edelman
415-486-3264
steven.cooper@edelman.com

MyoKardia, Inc.