



## MyoKardia Announces Positive Topline Data from its Phase 2 MAVERICK-HCM Clinical Trial of Mavacamten

November 11, 2019

*Achieved Primary Study Objective of Safety and Tolerability in Patients with Non-obstructive HCM*

*Significant Reductions in Biomarkers of Cardiac Stress Observed in Patients on Treatment vs. Placebo*

*Data Support Advancement of Mavacamten in Non-obstructive HCM; Regulatory Update Anticipated in the First Half of 2020*

*Phase 2 Study of Mavacamten Targeting Subgroup of Patients with Diastolic Heart Failure (HFpEF) Anticipated to Begin in the Second Quarter of 2020*

*Conference Call Today at 8:30 a.m. ET (5:30 a.m. PT)*

SOUTH SAN FRANCISCO, Calif., Nov. 11, 2019 (GLOBE NEWSWIRE) -- MyoKardia, Inc. (Nasdaq: MYOK), today announced topline data from MAVERICK-HCM, the company's Phase 2 clinical trial of mavacamten in patients with non-obstructive hypertrophic cardiomyopathy (HCM). The study achieved its primary objective of establishing safety and tolerability of mavacamten in non-obstructive HCM over a treatment period of 16 weeks. Meaningful reductions in biomarkers of cardiac stress were observed across both mavacamten drug concentration cohorts and clear signals of clinical benefit were noted in a subgroup with elevated cardiac filling pressures and in a pre-specified group of patients at higher risk for morbidity and mortality.

"We are encouraged by the evidence from MAVERICK of improved diastolic function in non-obstructive HCM patients with guideline-based measures of diastolic impairment, and by mavacamten's robust effect in reducing cardiac wall stress in patients across all our HCM studies," said Jay Edelberg, Senior Vice President of Clinical Development at MyoKardia. "Consistent with our precision medicine approach, the results of MAVERICK have provided us with important insights, including how to identify groups of patients with diseases of diastolic dysfunction and how to best measure clinical benefit. These data will inform enrollment criteria, dosing, duration and potential endpoints for our planned future clinical trials of mavacamten in non-obstructive HCM and targeted HFpEF patients."

Based on the safety and pharmacologic benefits observed in MAVERICK, MyoKardia plans to advance mavacamten into additional studies in defined groups of patients with non-obstructive HCM and heart failure with preserved ejection fraction (HFpEF). For the non-obstructive indication, the company will seek to consult with the U.S. Food and Drug Administration (FDA) on potential pathways to registration and expects to provide a regulatory update in the first half of 2020. For the targeted HFpEF population, MyoKardia plans to initiate a Phase 2 study in the second quarter of 2020 in a subgroup of patients sharing many characteristics with the subgroups identified in MAVERICK. Further analysis of the findings from MAVERICK is ongoing, and these data will be submitted for presentation at an upcoming scientific conference.

"Of all our prior attempts to address the needs of our patients with non-obstructive HCM, for whom there are no effective medical therapies, the MAVERICK-HCM trial provides us with the most encouraging data to date," said Stephen Heitner, M.D., Director of the Hypertrophic Cardiomyopathy Clinic at Oregon Health & Science University and a principal investigator for the MAVERICK-HCM trial. "The data reported today are especially promising in that they provide a glimpse into how we may better phenotype this group of patients, and may begin to understand the unpredictability of symptoms. I am hopeful that this study will prove to be the springboard for the thoughtful development of the next phase of studies aimed at bringing mavacamten, a unique and precise therapy, to our non-obstructive HCM patients and potentially other similar individuals suffering from HFpEF."

Heart failure with preserved ejection fraction is a heterogeneous clinical syndrome, which in many patients is characterized by impairment of the left ventricle's ability to relax and fill during diastole, resulting in insufficient blood flow to meet the body's needs. HFpEF is estimated to affect approximately three million people in the U.S. and is associated with significant morbidity and mortality. There are currently no approved therapies for HFpEF. The subgroup identified for future evaluation of mavacamten is estimated to include approximately 10-20 percent of the broader HFpEF population.

### Phase 2 MAVERICK-HCM Trial – Topline Results

Mavacamten was well tolerated and the observed safety data were consistent with prior studies. The rate of adverse events (AEs) was greater in the mavacamten groups than the placebo group. The majority of AEs reported were mild or moderate in severity and reversible or self-resolving. Serious adverse events (SAEs) occurred twice as frequently in the placebo arm as compared to patients receiving mavacamten. Transient ejection fraction reductions below the protocol-defined threshold of 45% occurred in five participants in the active drug arms.

For the intent-to-treat population, there were no statistically significant differences at 16 weeks between active and placebo groups in exploratory endpoints, with the exception of levels of the biomarker NT-proBNP, which were markedly reduced in patients receiving mavacamten ( $p=0.004$ ) across both treatment cohorts, as compared to the placebo group. NT-proBNP is a well-established biomarker of cardiac wall stress, and elevated NT-proBNP levels are associated with heart failure-related death or hospitalization, progression to end-stage disease and stroke.

In a pre-specified subgroup representing patients believed to be at higher risk of morbidity and mortality, meaningful trends suggesting clinical benefit were observed for patients on treatment versus placebo across multiple endpoints of symptoms, function, biomarkers of cardiac stress and diastolic compliance.

Additionally, similar trends were observed in a subgroup of patients with elevated cardiac filling pressures (measured by  $E/e'$ ), suggesting improvement driven by reduced left ventricular pressure, consistent with mavacamten's targeted mechanism.

"The topline data reported today are important in the advancement of mavacamten across multiple indications. The safety and tolerability data, evidence of mavacamten's beneficial impact on parameters of diastolic function, and placebo response observations confirm our assumptions and increase our confidence in the EXPLORER-HCM Phase 3 clinical study of mavacamten in obstructive HCM," said Tassos Gianakakos, Chief Executive Officer of MyoKardia.

#### **About MAVERICK-HCM**

The Phase 2 MAVERICK-HCM trial was designed to assess the safety and tolerability of a range of exposures over 16 weeks of treatment in patients with symptomatic, non-obstructive HCM. All study participants were required to be diagnosed with non-obstructive HCM, with left ventricular wall thickness either  $\geq 15$ mm or  $\geq 13$ mm with a family history of HCM, New York Heart Association (NYHA) classifications of Class II or III, and NT-proBNP levels of greater than 300 pg/mL at rest. Baseline characteristics, such as age, weight, gender, pathogenic mutation status, background beta blocker use, NYHA classification and exercise capacity were evenly distributed between active and placebo arms.

A total of 59 participants were enrolled in the study and randomized into one of three groups to receive once-daily doses of mavacamten or placebo. The active mavacamten treatment arms were designed to assess a range of drug concentrations around target levels of 200ng/mL and 500ng/mL. All participants in the active treatment arms began the study receiving 5mg doses of mavacamten. At Week 4, pharmacokinetic (PK) assessments were conducted and doses were adjusted in a blinded fashion per the protocol based on the participant's assigned cohort. Following the 16-week treatment period, participants were monitored for an additional eight weeks and became eligible to participate in MyoKardia's MAVA Long-Term Extension (LTE) study.

#### **Conference Call and Webcast**

MyoKardia management will host a conference call and live audio webcast this morning at 8:30 a.m. ET / 5:30 a.m. PT to review the topline data reported today from the MAVERICK Phase 2 clinical trial and new data from the PIONEER-OLE study. Investors and analysts are invited to participate in the call by dialing 844-494-0913 (U.S.) or 508-637-5584 using the conference ID 3177984. The webcast may be accessed live on the Investor Relations section of the MyoKardia website. A replay of the webcast will be available on MyoKardia's website for 90 days following the call.

#### **About Non-obstructive HCM**

Hypertrophic cardiomyopathy is the most common genetic form of heart disease, affecting an estimated one in every 500 people worldwide. There are two main forms of HCM, obstructive HCM and non-obstructive HCM, which often share the same underlying genetic defects in the sarcomere that results in hypercontractility. In non-obstructive HCM, the heart contracts excessively and the left ventricle becomes abnormally thick, restricting the ability of the heart to relax and fill or pump to meet the body's needs, but no physical obstruction is present in the outflow tract of the left ventricle. Non-obstructive HCM affects an estimated one-third of all HCM patients and presents unique treatment challenges. Patients may progress to a more advanced state of disease than those with obstructive disease before being diagnosed, and there are no approved treatment options available. As non-obstructive HCM progresses, symptoms begin to resemble those of a congestive heart failure patient and heart transplantation may become the only viable treatment option.

#### **About Mavacamten (MYK-461)**

Mavacamten is a novel, oral, allosteric inhibitor of cardiac myosin being developed for the treatment of hypertrophic cardiomyopathy (HCM). Mavacamten is intended to reduce cardiac muscle contractility by inhibiting the excessive myosin-actin cross-bridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance characteristic of HCM. MyoKardia is currently evaluating mavacamten in multiple clinical trials for the treatment of obstructive and non-obstructive HCM. The pivotal Phase 3 clinical trial, known as EXPLORER-HCM, is being conducted in patients with symptomatic, obstructive HCM and MyoKardia anticipates data from this program in Q2'2020. Two long-term follow-up studies are also ongoing, the PIONEER open-label extension study of obstructive HCM patients from MyoKardia's Phase 2 PIONEER trial and the MAVA-LTE, an extension study for patients who have completed either EXPLORER-HCM or MAVERICK-HCM, the company's Phase 2 clinical trial of symptomatic non-obstructive HCM patients. In April 2016, the U.S. FDA granted Orphan Drug Designation for mavacamten for the treatment of symptomatic obstructive HCM.

#### **About MyoKardia**

MyoKardia is a clinical-stage biopharmaceutical company discovering and developing targeted therapies for the treatment of serious cardiovascular diseases. The company is pioneering a precision medicine approach to its discovery and development efforts by 1) understanding the biomechanical underpinnings of disease, 2) targeting the proteins that modulate a given condition, 3) identifying patient populations with shared disease characteristics and 4) applying learnings from research and clinical studies to inform and guide pipeline growth and advancement. MyoKardia's initial focus is on small molecule therapeutics aimed at the muscle proteins of the heart that modulate cardiac muscle contraction to address diseases driven by excessive contraction, impaired relaxation, or insufficient contraction. Among its discoveries are three clinical-stage therapeutics: mavacamten (formerly MYK-461) in Phase 3 and Phase 2 clinical trials for hypertrophic cardiomyopathy (HCM); MYK-491 in Phase 2 for patients with stable heart failure; and MYK-224 in Phase 1 development for HCM.

MyoKardia's mission is to change the world for people with serious cardiovascular disease through bold and innovative science.

#### **Forward-Looking Statements**

Statements we make in this press release may include statements which are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are usually identified by the use of words such as "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "seeks," "should," "will," and variations of such words or similar expressions. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements, including statements regarding the clinical and therapeutic potential of mavacamten, our plans to consult with the FDA on potential pathways to registration and to provide a regulatory update, the initiation, progress and availability of data from our ongoing and planned clinical trials, and the timing of these events, reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, risks associated with the development and regulation of our product candidates, as well as those set forth in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, and our other filings with the SEC. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or

otherwise.

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