MyoKardia Announces Dosing of First Patient in Phase 2 PIONEER-HCM Study of MYK-461 in Symptomatic, Obstructive Hypertrophic Cardiomyopathy

Pilot Study Designed to Enable Progression to Larger Phase 2 Trial to Finalize Dosing and Endpoints Prior to Single Pivotal Study

Trial Will Assess 12-week Safety and Tolerability in Outpatient Setting; Topline Data Expected in Second Half of 2017

SOUTH SAN FRANCISCO, Calif., Nov. 02, 2016 (GLOBE NEWSWIRE) -- MyoKardia, Inc. (Nasdaq:MYOK), a clinical stage biopharmaceutical company pioneering a precision medicine approach for the treatment of heritable cardiovascular diseases, today announced dosing of the first patient in its Phase 2 PIONEER-HCM study of MYK-461. PIONEER-HCM is assessing safety, tolerability and efficacy of MYK-461 in patients with symptomatic, obstructive hypertrophic cardiomyopathy (oHCM). The U.S. Food and Drug Administration (FDA) has granted the company Orphan Drug Designation for MYK-461 for the treatment of symptomatic oHCM.

Relationships among important disease biomarkers such as contractility, left ventricular outflow tract (LVOT) gradient and anticipated registrable endpoints of functional capacity and clinical symptoms are to be studied in the 12-week trial. Topline data from PIONEER-HCM is expected in the second half of 2017.

"The initiation of PIONEER-HCM is an important milestone for MyoKardia and for patients with oHCM," said Tassos Gianakakos, chief executive officer. "PIONEER-HCM was designed to provide important outpatient safety support and operational insights that we believe will allow for more efficient subsequent clinical studies. PIONEER will generate data relating to a wide range of clinically meaningful measurements, including those we believe appropriate to support a new drug application for MYK-461 in oHCM. Furthermore, we expect PIONEER to help enable future studies evaluating MYK-461 in both non-obstructive and pediatric HCM patients. This is an important and exciting step toward potentially providing the first targeted therapy designed to correct the underlying biomechanical cause of this debilitating disease."

PIONEER-HCM is planned to assess the effect of multiple doses of MYK-461 in symptomatic oHCM patients. The primary endpoint of PIONEER-HCM is the level of reduction in post-exercise LVOT gradient over 12 weeks of drug exposure. PIONEER-HCM will also explore the relationship between reduction in contractility and LVOT gradient, endpoints measuring functional capacity (i.e., exercise) and clinical symptoms in addition to gathering safety and tolerability data on MYK-461 in an outpatient setting.

Per current treatment guidelines, the degree of LVOT gradient is a key metric for diagnosing oHCM and is the primary criterion used by clinicians to determine clinical course of action, including invasive surgery. Reduction of the LVOT gradient has been shown in published studies to improve symptoms, increase functional capacity and reduce the incidence of heart failure and stroke related death in oHCM patients.

The Clinical Path to Registration for MYK-461

Interactions between MyoKardia and the FDA earlier this year support a precision clinical development pathway for MYK-461 in oHCM, with the following key conclusions: 1) mortality-based efficacy endpoints will not be required for registration; 2) improvement in functional capacity and/or clinical symptoms are suitable endpoints for registration; and 3) a single Phase 3 pivotal study demonstrating significant improvement in functional capacity or symptoms may be adequate for approval.

As a result, and informed by data collected in PIONEER-HCM, MyoKardia intends to initiate a subsequent, 12-week Phase 2 study of MYK-461 in oHCM, which would further characterize gradient reduction, as well as symptoms and function, at multiple dose levels, with the ultimate goal of finalizing the design of a single, potential Phase 3 pivotal study, including endpoints and dosing. The proposed Phase 3 pivotal study of MYK-461 in oHCM is currently expected to have a treatment duration of 12-24 weeks, and study safety and clinical benefit sufficiently to support registration of MYK-461 in this patient population.

About MYK-461 and PIONEER-HCM

MYK-461 is an orally administered small molecule designed to reduce left ventricular contractility by allosterically modulating the function of cardiac myosin, the motor protein that drives heart muscle contraction. MyoKardia has evaluated MYK-461 in three Phase 1 clinical trials, which have been primarily designed to evaluate safety and tolerability of oral doses of MYK-461 and have provided data on its pharmacokinetic and pharmacodynamic profile. In April 2016, the U.S. FDA granted the company Orphan Drug Designation for MYK-461 for the treatment of symptomatic oHCM, a subset of HCM. MyoKardia is currently studying MYK-461 in PIONEER-HCM, a Phase 2 open-label single-arm pilot study to evaluate safety, tolerability and efficacy of MYK-461 in patients with symptomatic oHCM.

About HCM and oHCM

It is estimated that one in every 500 people in the United States has HCM, the most prevalent form of heritable cardiomyopathy. HCM is defined as an otherwise unexplained thickening of the walls of the heart, known as hypertrophy. The consequences include reduced left ventricular volumes and cardiac output, reduced ability of the left ventricle to expand, and elevated filling pressures. These can all contribute to reduced effort tolerance and symptoms that include shortness of breath and chest pain. HCM is a chronic disease and for the majority of patients, the disease

progresses slowly and can be extremely disabling. HCM substantially increases the risk of developing atrial fibrillation that can lead to stroke or malignant ventricular arrhythmias that can cause sudden cardiac death. There are currently no approved drug products indicated for the treatment of HCM. Patients are typically prescribed one or more drugs (including beta blockers, non-dihydropyridine calcium channel blockers and disopyramide) indicated for the treatment of hypertension, heart failure or other cardiovascular disorders more generally.

Approximately two thirds of all HCM patients have obstruction, either at rest or with provocation like exercise. oHCM is a physiological complication of HCM in which the thickened heart muscle obstructs the left ventricular outflow tract (LVOT). Measured most commonly by non-invasive imaging (echocardiography), oHCM is defined as ≥30 mm Hg pressure gradient across the LVOT. Symptoms of oHCM can include shortness of breath, chest pain, dizziness, fainting, and palpitations. The presence of obstruction in an HCM patient further increases risk of progression to severe symptoms, and risk of death from heart failure or stroke.

The degree of LVOT obstruction in oHCM patients is a primary criterion for surgical and other invasive interventions (recommended for symptomatic patients with LVOT gradients measured at ≥50 mmHg). Relief of obstruction has been associated with improved symptoms, function and clinical outcomes. Surgical or other invasive interventions, including septal myectomy, an open heart procedure, may be appropriate. There are no approved drug products indicated for this condition. The primary endpoint of the Phase 2 PIONEER-HCM study is to assess level of reduction in LVOT gradient over 12 weeks of drug exposure. The trial is also exploring relationships among reductions in contractility, LVOT gradient and endpoints that include functional capacity and clinical symptoms.

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, or HCM, and dilated cardiomyopathy, or DCM. MyoKardia's most advanced product candidate, MYK-461, is an orally-administered small molecule designed to reduce excessive cardiac muscle contractility leading to HCM and has been evaluated in three Phase 1 clinical trials. MyoKardia is now studying MYK-461 in a Phase 2 PIONEER-HCM pilot study in symptomatic oHCM, for which the FDA has granted MYK-461 Orphan Drug Designation. A cornerstone of the MyoKardia platform is the Sarcomeric Human Cardiomyopathy Registry, or 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 believes that SHaRe, currently consisting of data from approximately 10,000 individuals, is the world's largest registry of patients with heritable cardiomyopathies. MyoKardia's mission is to change the world for patients with serious cardiovascular disease through bold and innovative science. For more information, please visit www.myokardia.com.

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 MYK-461, the Company's ability to generate topline data from its Phase 2 PIONEER-HCM study, the potential for data from the Company's ongoing and planned Phase 2 trials to support advancement into Phase 3 clinical development and a new drug application, the timing of these events, and the anticipated clinical endpoints and pathway to approval for MYK-461, 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2015, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, our Registration Statement on Form S-1 (File No. 333-213680) filed with the Securities and Exchange Commission (SEC) on September 16, 2016, as amended, 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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