MyoKardia Outlines Path to Registration for MYK-461 in Symptomatic, Obstructive Hypertrophic Cardiomyopathy Patients and Provides Pipeline and Research Updates at Inaugural R&D Day

Phase 2 PIONEER-HCM Pilot Study of MYK-461 Under Way with Topline Data Expected in Second Half of 2017

Mortality-Based Efficacy Endpoints Not Required for Registration of MYK-461 Obstructive Hypertrophic Cardiomyopathy (oHCM) Program

Phase 1 Program for MYK-491 for Dilated Cardiomyopathy (DCM) Expected to Initiate in First Half of 2017

SOUTH SAN FRANCISCO, Calif., Sept. 21, 2016 (GLOBE NEWSWIRE) -- MyoKardia, Inc. (Nasdaq:MYOK), a clinical stage biopharmaceutical company pioneering a precision medicine approach for the treatment of heritable cardiovascular diseases, will highlight today the expected path to registration for its lead product candidate MYK-461 in the initial indication of symptomatic oHCM and its plans to progress MYK-491 into the clinic for DCM. The Company's scientific leadership will also provide further insights into MyoKardia's precision medicine and pipeline strategy enabled by its product engine. The updates will be presented at MyoKardia's inaugural R&D Day today in New York.

"We believe our precision medicine strategy and strong scientific foundation will continue to drive novel therapies aimed at addressing important treatment needs for patients with serious cardiovascular diseases," said Tassos Gianakakos, chief executive officer. "The encouraging early results from our two most advanced programs have supported our enthusiastic advancement of both into the next stage of development."

"Our recent discussions with the U.S. Food and Drug Administration (FDA), including confirmation that mortality-based efficacy endpoints will not be required for registration, represent an important milestone for MyoKardia, allowing us to confirm MyoKardia's plans for registration of MYK-461 in oHCM."

Mr. Gianakakos continued, "We are also excited to share more detail around our MYK-491 clinical program for the treatment of DCM. MYK-491 is the second clinical candidate generated by MyoKardia's product engine and has shown promising preclinical data that supplies us with a compelling rationale to support advancement into Phase 1 in the first half of next year in a disease area desperate for more therapeutic options."

MYK-461 in oHCM

Conclusions from Recent Regulatory Interactions

Additionally, MyoKardia will report key conclusions from recent regulatory interactions, which clarify the potential clinical development pathway in oHCM:

- Mortality-based efficacy endpoints will not be required for registration.
- Improvement in functional capacity and/or clinical symptoms are suitable endpoints for registration.
- A single Phase 3 pivotal study demonstrating significant improvement in functional capacity or symptoms may be adequate for approval.

Further Detail on PIONEER-HCM

MyoKardia has initiated a Phase 2 study, PIONEER-HCM, which is an open-label, single-arm pilot study of MYK-461 in patients with symptomatic oHCM, an indication for which the FDA granted MYK-461 Orphan Drug Designation in 2016. Other details include:

- First outpatient study with MYK-461 in target indicated population for anticipated treatment duration.
- Primary endpoint is to assess level of reduction in left ventricular outflow tract (LVOT) gradient over 12 weeks of drug exposure.
    - Based on published studies and MyoKardia research, LVOT gradient reduction is expected to improve symptoms and functional capacity.
    - PIONEER-HCM will begin to characterize relationships among reductions in contractility, LVOT gradient and endpoints including functional capacity and clinical symptoms.
- Topline data is expected to be released in the second half of 2017.
- Study is designed to enable progression to larger Phase 2 study to finalize dosing and endpoints before subsequent single pivotal study.

Phase 1 Data

Duke University School of Medicine Professor Andrew Wang, M.D., a participant in the MYK-461 investigational program, will review Phase 1 data in detail, including additional information around the two patients with LVOT obstruction dosed in the Company's Phase 1 single ascending dose (SAD) study in HCM patients and additional pharmacokinetic, or PK, and pharmacodynamic, or PD, data from the SAD and multiple ascending dose (MAD) studies of MYK-461.

MYK-491 in DCM

MYK-491 is the Company's candidate for several well-defined sub-groups of DCM, including genetic DCM, designed to return the diseased DCM heart to normal contractility by increasing the overall force of the heart's contraction. Similar to MYK-461, MYK-491 targets the underlying biomechanical defect caused by sarcomere mutations and has been designed to be potentially disease modifying.

Other updates on the MYK-491 program include:

- Preclinical research demonstrates across multiple animal model systems that MYK-491 is able to achieve significant, dose-dependent increases in stroke volume with minimal effect on diastolic function.
- MyoKardia intends to initiate a Phase 1 SAD study in the first half of 2017, with topline results expected in the third quarter of 2017.

Precision Medicine Platform and Vision 2020

During the R&D Day presentations, MyoKardia leadership will also discuss key elements of the Company's strategy, including its precision medicine approach and product engine and future objectives for its research activities.

“We are working hard at MyoKardia to build a company that represents much more than two product candidates. The efficiency with which these drugs have moved into and through clinical trials and their promising early results are a testament to our team and to our precision approach. Through the dedication of our employees, the commitment of our founders and the cardiomyopathy community’s support, in just four years we have built a durable competitive advantage in our field, which forms the basis for our Vision 2020 strategy,” said Mr. Gianakakos.

“We look forward to sharing more details on how we hope to fulfill our mission to change the world for patients with serious cardiovascular disease through bold and innovative science.”

In addition to Mr. Gianakakos and Dr. Wang, R&D Day presenters include:

- Jonathan Fox, M.D., Ph.D., chief medical officer; Michael Graziano, Ph.D., vice president, research biology; Robert McDowell, Ph.D., senior vice president, drug discovery
- Christine Seidman, M.D., a MyoKardia co-founder and professor of genetics and the Thomas W. Smith professor of medicine at Harvard Medical School and Brigham and Women's Hospital
- Srihari Naidu, M.D., director, Cardiac Catheterization Laboratory, Interventional Cardiology Fellowship Program and HCM Treatment Center at Winthrop University Hospital
- Daniel Judge, M.D., associate professor of medicine, Johns Hopkins University School of Medicine; Medical Director, Center for Inherited Heart Disease

R&D Day Webcast

To access the live webcast of MyoKardia’s R&D Day presentation, please visit the “Events & Presentations” page within the Investors & Media section of the MyoKardia website at http://investors.myokardia.com. A replay of the webcast will be available on the MyoKardia website for 30 days following the event.

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 driving 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 are providing data on its pharmacokinetic and pharmacodynamic profile. These studies assess MYK-461’s engagement of cardiac myosin by measuring reduction in cardiac muscle contractility via several independent echocardiographic measurements. In April 2016, the U.S. FDA granted the company Orphan Drug Designation for MYK-461 for treatment of symptomatic oHCM, a subset of HCM. MyoKardia is currently enrolling patients for PIONEER-HCM, a Phase 2 open-label pilot study to evaluate safety and efficacy of MYK-461 in subjects 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. MyoKardia plans to explore obstruction relief as measured by LVOT gradient reduction as a primary endpoint in the Phase 2 PIONEER-HCM pilot 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, 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 purpose is to improve the lives of patients and families suffering from cardiovascular disease by creating targeted therapies that can change the course of their condition. 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 and MYK-491, the Company’s ability to generate topline data from its Phase 2 PIONEER-HCM study, the Company’s ability to advance MYK-491 into a Phase 1 clinical trial for DCM and generate topline data from this trial, 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 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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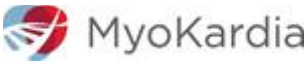

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