News Release

MyoKardia Announces Design of Phase 3 EXPLORER-HCM Study Evaluating Mavacamten in Symptomatic, Obstructive Hypertrophic Cardiomyopathy

Single Pivotal to Support Registration; Target Enrollment of 220 Patients; Primary Endpoint of Clinical Response Using Peak VO_2 and NYHA Classification Improvements

Expected to Initiate in Second Quarter 2018; Topline Data Anticipated in Second Half 2020

Management to Host Conference Call Today at 8:30 a.m. ET/5:30 a.m. PT

SOUTH SAN FRANCISCO, Calif., May 21, 2018 (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 the design of its pivotal Phase 3 EXPLORER-HCM clinical trial to evaluate the use of mavacamten for the potential treatment of patients with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). The company has incorporated input on the study design from the Division of Cardiovascular and Renal Products of the U.S. Food and Drug Administration (FDA), and plans to conduct this single pivotal study along with a long-term extension study to support registration. MyoKardia expects to dose the first patient in the EXPLORER-HCM trial in the second quarter of 2018 and expects that data from the Phase 3 trial will be available in the second half of 2020.

EXPLORER-HCM is a multi-national randomized double-blind study designed to assess the effects of a 30-week treatment of mavacamten versus placebo with a primary endpoint of clinical response. The clinical response endpoint is intended to broadly capture the potential benefits of treatment with mavacamten on how patients feel and function by utilizing both peak oxygen consumption (peak VO_2) and New York Heart Association (NYHA) functional classification. Clinical response can be achieved by meeting either of two definitions: 1) an improvement of at least 1.5 mL/kg/min in peak VO_2 accompanied by a reduction from baseline of at least one NYHA functional class or 2) an improvement from baseline of 3.0 mL/kg/min or greater in peak VO_2 without worsening in NYHA functional class.

“The extensive analysis by our team in designing the EXPLORER-HCM Phase 3 trial, incorporating thoughtful input from the FDA, has resulted in a study designed to provide a robust readout of mavacamten’s safety and efficacy, while minimizing the impact of a

placebo effect. Importantly, we believe the innovative design of EXPLORER will allow us to capture the potential benefits of mavacamten across metrics that are of significant importance to patients and clinicians," said June Lee, M.D., MyoKardia's Chief Developmentand Operating Officer. "Should the data from the EXPLORER trial meet our expectations, we believe they will be sufficient to support a marketing application when combined with the safety information we will be gaining in parallel from our long-term extension studies."

Approximately 220 patients will be enrolled and randomized on a 1:1 basis to receive either mavacamten or placebo. The EXPLORER-HCM trial design includes two opportunities for individualized dose adjustment throughout the 30-week treatment period. Patients in the active treatment arm will start on a once-daily 5mg dose of mavacamten. At Weeks 8 and 14, daily doses may be increased to 10mg or 15mg, or remain unchanged, based on measurements of provoked left ventricular outflow tract (LVOT) gradient conducted at Weeks 6 and 12. A reduction in provoked LVOT gradient under 50 mmHg has been shown in PIONEER to correlate to improvements in several clinical measurements, including NYHA class and peak VO_2. All assessments and dose adjustments will be conducted in a blinded fashion. Patients will be allowed to maintain their HCM-related background medications for the duration of the EXPLORER-HCM Phase 3 trial, including beta blockers or calcium channel blockers.

Secondary endpoints in the Phase 3 EXPLORER-HCM trial will include the average change from baseline in post-exercise peak LVOT gradient, NYHA functional class, peak VO_2,the proportion of patients achieving post-exercise peak LVOT gradient below 50 mmHg or 30 mmHg at Week 30 and patient-reported outcome measures. Exploratory endpoints will include changes in echocardiographic indices of cardiac structure and function, N-terminal pro b-type natriuretic peptide (NT-proBNP) concentrations, quality of life questionnaire scores and daily physical activity assessed using a wearable accelerometer.

"Symptomatic oHCM patients cope with significant functional limitations and debilitating symptoms that negatively impact their daily lives. The design of our EXPLORER-HCM Phase 3 trial prioritizes the patient's experience by evaluating mavacamten's activity in ways that correlate to their daily lives living with oHCM. Measuring peak VO_2 tells us how well the heart is working, while the NYHA classification provides information on how patients are functioning during daily activities," said Marc Semigran, MyoKardia's Chief Medical Officer. "I'm proud of our team and appreciative of the collaboration from the patient and clinical community as we get ready to embark on this important study."

Throughout the EXPLORER-HCM study, patients will be monitored for adverse events and certain assessments will be performed. If at any time during the trial, a patient's plasma concentration is above an upper target range or LVEF falls below the normal range, doses of mavacamten may be decreased. Following the 30-week treatment period and eight-week post-treatment wash-out period, patients will be able to participate in a long-term extension study of mavacamten.

Conference Call and Webcast
MyoKardia will host a conference call and live audio webcast today, May 21, 2018, at 8:30 a.m. ET / 5:30 a.m. PT to review the Phase 3 EXPLORER-HCM trial design. The call may be accessed by phone by calling (844) 494-0193 from the U.S. and Canada or (508) 637-5584 internationally and using the conference ID 6896475. The webcast may be accessed live on the Investor Relations section of the Company's website at http://investors.myokardia.com. A replay of the webcast will be available on the MyoKardia website for 90 days following the call.

About Obstructive HCM
Hypertrophic cardiomyopathy is the most common genetic cause of heart disease in which the walls of the heart thicken and prevent the left ventricle from expanding, resulting in a reduced pumping capacity. HCM is a chronic disease and for the majority of patients, the disease progresses slowly and can be extremely disabling. In approximately two-thirds of HCM patients, or an estimated 410,000 people in the U.S., the path followed by blood exiting the heart, known as the left ventricular outflow tract (LVOT), becomes obstructed by the enlarged and diseased muscle, restricting the flow of blood from the heart to the rest of the body. Mild exertion can quickly result in fatigue or shortness of breath, and a patient's ability to participate in normal work, family or recreational activities can be substantially curtailed. Patients with oHCM are at an increased risk of severe heart failure and death. HCM can also cause stroke or sudden cardiac death.

About Mavacamten (MYK-461)
Mavacamten is a novel, oral, allosteric modulator of cardiac myosin being developed for the treatment of hypertrophic cardiomyopathy (HCM). MyoKardia is currently advancing mavacamten into a pivotal Phase 3 clinical trial, known as the EXPLORER-HCM study, in patients with symptomatic, obstructive HCM and is currently dosing patients in a Phase 2 clinical trial, the MAVERICK-HCM study, in patients with symptomatic non-obstructive HCM. Mavacamten is intended to reduce cardiac muscle contractility by inhibiting the excessive myosin-actin crossbridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance characteristic of HCM.

In MyoKardia's Phase 2 PIONEER-HCM clinical trial of patients with symptomatic oHCM, primary and secondary endpoints were achieved across key signs and symptoms of disease, such as elimination of LVOT gradient post-exercise and at rest, increased exercise capacity as measured by peak VO_2, improved NYHA classification and reduced dyspnea over time. Mavacamten has been generally well tolerated in multiple clinical trials. In April 2016, the U.S. FDA granted Orphan Drug Designation for mavacamten for the treatment of symptomatic oHCM, a subset of HCM. Mavacamten is being developed in an ongoing collaboration between MyoKardia and Sanofi.

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 two of the 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 intended to reduce hypercontractility. Mavacamten is advancing into a pivotal Phase 3 clinical trial, known as EXPLORER-HCM in patients with symptomatic, obstructive HCM. MyoKardia is also developing mavacamten in a second indication, non-obstructive HCM, in the Phase 2 MAVERICK-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 1b study in DCM patients. 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.

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 and MYK-491, the initiation of patient dosing in the Phase 3 EXPLORER-HCM trial, mavacamten's ability to achieve applicable endpoints in the Phase 3 EXPLORER-HCM trial, the ability for patients who participate in the Phase 3 EXPLORER-HCM trial to participate in a long-term extension study, the availability of data from the Phase 3 EXPLORER-HCM trial, the potential for data from the Company's clinical trials of mavacamten to support a marketing application, as well as 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 March 31, 2018, 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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