MyoKardia Announces Primary and All Secondary Endpoints Met in Phase 3 EXPLORER Clinical Trial of Mavacamten for the Treatment of Obstructive Hypertrophic Cardiomyopathy

Highly Statistically Significant Improvements in NYHA Classification, Peak VO₂, and LVOT Gradient Observed vs. Placebo

Mavacamten Well Tolerated; Safety Results Comparable to Placebo

U.S. Regulatory Submission Planned for Early 2021

MyoKardia to Host Conference Call at 8:00 a.m. ET

Brisbane, Calif., May 11, 2020 -- MyoKardia, Inc. (Nasdaq: MYOK) today announced positive topline data from the company’s Phase 3 pivotal EXPLORER-HCM clinical trial of mavacamten for the treatment of patients with symptomatic, obstructive hypertrophic cardiomyopathy (HCM) (clinicaltrials.gov NCT03470545). Mavacamten demonstrated a robust treatment effect: the primary and all secondary endpoints of the EXPLORER trial were met with statistical significance (p≤0.0006 for all endpoints). Mavacamten was well tolerated, and meaningful improvements in symptoms, functional status and quality of life, as well as reduction or elimination in obstruction of the left ventricle, were observed among patients on treatment versus placebo.

“The extraordinary data from the EXPLORER pivotal trial confirm mavacamten’s ability to relieve dynamic outflow obstruction, control symptoms and improve quality of life in patients with hypertrophic cardiomyopathy,” said Iacopo Olivotto, M.D., Careggi University Hospital and lead clinical investigator for the EXPLORER-HCM clinical trial. “HCM is the most common inherited cardiovascular disease, and patients face an uncertain journey that all too frequently includes debilitating symptoms, as well as serious complications, such as heart failure, stroke and cardiac arrest. Mavacamten is the first drug developed to target the specific molecular defect of the disease. EXPLORER represents a major achievement toward a precision-medicine approach in cardiomyopathies and should provide great hope to a community painfully aware of the lack of disease-specific treatment options.”

The 30-week treatment with mavacamten resulted in a highly statistically significant outcome relative to placebo (p=0.0005) for the primary endpoint in the EXPLORER-HCM trial, a composite functional analysis designed to capture the treatment effect of mavacamten relative to placebo on both symptoms and cardiac function.

All secondary endpoints also demonstrated statistically significant and clinically meaningful improvements for mavacamten as compared to placebo. Secondary endpoints in the EXPLORER-HCM trial evaluated improvements in post-exercise left ventricular outflow tract (LVOT) peak gradient (p<0.0001), New York Heart Association (NYHA) functional classification (p<0.0001), peak VO₂ (p=0.0006), the Kansas City Cardiomyopathy Clinical Summary Score (KCCQ-CSS) (p<0.0001), and the HCM Symptom Questionnaire Shortness of Breath Domain Score (p<0.0001).

Mavacamten was well tolerated and demonstrated safety results comparable to placebo, with no new findings observed. Ninety-eight percent of patients enrolled completed the study. Of the two percent who dropped out, none were due to reduced ejection fraction or symptoms of heart failure. Overall rates of adverse events, serious adverse events, and cardiac adverse events, including atrial fibrillation, were comparable for patients treated with mavacamten and placebo.

“The resoundingly positive data from EXPLORER bring us a significant step closer to improving the lives of people with serious cardiovascular conditions, starting with HCM, a debilitating disease estimated to affect one in every 500 people,” said Tassos Gianakakos, Chief Executive Officer of MyoKardia. “The activity and tolerability profile observed for mavacamten in this pivotal study underscores the profound
impact and potential for therapeutics that target the underlying biology of disease. We look forward to the submission of MyoKardia’s first New Drug Application and, importantly, to serving the many patients that stand to benefit from mavacamten.”

The EXPLORER-HCM clinical trial is part of MyoKardia’s pivotal program studying mavacamten as a treatment for symptomatic, obstructive hypertrophic cardiomyopathy. MyoKardia plans to submit a New Drug Application to the U.S. Food and Drug Administration (FDA) in the first quarter of 2021. Results from the Phase 3 EXPLORER-HCM clinical trial will be submitted to a future professional meeting in 2020.

Investor and Analyst Conference Call and Live Webcast
MyoKardia management will host a conference call and webcast today beginning at 8:00 am. ET/5:00 AM PT to discuss the EXPLORER results. Investors and analysts may access the call by dialing +1 (844) 494-0193 (domestic) or (508) 637-5584 (international) and referencing the conference ID 6270668. A live webcast of the conference call will be available on Investor section of MyoKardia’s website at http://investors.myokardia.com. A replay of the webcast, and accompanying slides, will be available on the MyoKardia website for 90 days following the call.

About EXPLORER-HCM
The EXPLORER-HCM Phase 3 trial enrolled a total of 251 patients with symptomatic (NYHA Class II or III), obstructive hypertrophic cardiomyopathy. All participants had measurable LVOT gradient (resting and/or provoked) ≥50 mmHg at baseline. Patients were randomized on a 1:1 basis to receive individualized once-daily dosing of mavacamten or placebo. Patients started on a dose of 5mg, with up to two opportunities for dose adjustments (2.5mg – 15mg) based on a combination of residual LVOT gradient, drug plasma concentration and left ventricular ejection fraction (LVEF) levels.

The primary endpoint for EXPLORER-HCM was a composite functional analysis designed to capture mavacamten’s effect on both symptoms and function. The composite functional endpoint is defined by either (1) the achievement of a ≥1.5 mL/kg/min improvement in peak VO2 accompanied by an improvement of ≥1 NYHA functional class, or (2) the achievement of a ≥3.0 mL/kg/min improvement of peak VO2 with no worsening in NYHA functional class. In addition to the endpoints reported today, the EXPLORER-HCM study also assessed mavacamten’s effect on patient-reported outcomes, health-related quality of life and symptom severity assessments, changes from baseline to Week 30 in echocardiographic indices, circulating biomarkers, cardiac rhythm patterns and accelerometry.

About HCM
Hypertrophic cardiomyopathy (HCM) is a chronic, progressive disease in which excessive contraction of the heart muscle and reduced ability of the left ventricle to fill can lead to the development of debilitating symptoms and cardiac dysfunction. HCM is estimated to affect one in every 500 people. The most frequent cause of HCM is mutations in the heart muscle proteins of the sarcomere. In approximately two-thirds of HCM patients, 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 (obstructive HCM). In other patients, the thickened heart muscle does not block the LVOT, and their disease is driven by diastolic impairment due to the enlarged and stiffened heart muscle (non-obstructive HCM). In either obstructive or non-obstructive HCM patients, exertion can result in fatigue or shortness of breath, interfering with a patient’s ability to participate in activities of daily living. HCM has also been associated with increased risks of atrial fibrillation, stroke, heart failure and sudden cardiac death.

About Mavacamten (MYK-461)
An investigational, novel, oral, allosteric modulator of cardiac myosin, mavacamten reduces cardiac muscle contractility by inhibiting excessive myosin-actin cross-bridge formation that results in hypercontractility, left ventricular hypertrophy and reduced compliance. In clinical and preclinical studies, mavacamten has consistently reduced biomarkers of cardiac wall stress, lessened excessive cardiac contractility and increased diastolic compliance. MyoKardia is developing mavacamten for the treatment of conditions in which excessive cardiac contractility and impaired diastolic filling of the heart are the underlying cause. Mavacamten is initially being developed for the treatment of symptomatic, obstructive hypertrophic
cardiomyopathy (HCM). Based on its mechanism of action and evidence of therapeutic activity, mavacamten is also being studied in the clinic for the treatment of symptomatic non-obstructive HCM and among a targeted population of patients with heart failure with preserved ejection fraction (HFpEF).

**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 product advancement. MyoKardia’s initial focus is on small molecule therapeutics aimed at the 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); danicamtiv (formerly MYK-491) and MYK-224.

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, danicamtiv and MYK-224, our expectations regarding our continuation of discussions with the FDA and our plan to submit a New Drug Application for mavacamten, our presentation of results from the Phase 3 EXPLORER-HCM clinical trial at a future professional meeting, 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 and any ongoing effects of the COVID-19 pandemic, as well as those set forth in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, 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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