MyoKardia Announces Positive Results from Low-Dose Cohort of Phase 2 PIONEER-HCM Study of Mavacamten in Symptomatic, Obstructive Hypertrophic Cardiomyopathy Patients

Met Primary Endpoint and Key Secondary Endpoints with Statistical Significance

Study Results Inform Phase 3 EXPLORER-HCM Dosing;
First Patient Planned for Q2 2018

Conference Call Today at 4:30 p.m. ET (1:30 p.m. PT); Data Presentation at American College of Cardiology on Sunday, March 11, 2018

SOUTH SAN FRANCISCO, Calif., March 08, 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 positive results from the Phase 2 PIONEER-HCM clinical study of the investigational agent mavacamten in symptomatic, obstructive hypertrophic cardiomyopathy (oHCM) patients, including results from a low-dose patient cohort ("Cohort B"), which studied once-daily 2mg and 5mg oral doses of mavacamten.

The first cohort ("Cohort A") of the PIONEER-HCM clinical trial studied 10mg, 15mg and 20mg doses and demonstrated a reduction in patients' left ventricular outflow tract (LVOT) gradient before steady-state mavacamten concentrations were reached. Cohort B's primary goal was to evaluate lower doses (2 mg and 5mg) of mavacamten in patients with oHCM. Both cohorts of the PIONEER-HCM clinical trial met the primary endpoint of reduction in post-exercise LVOT gradient from baseline to Week 12 with statistical significance (Cohort A p=0.002; Cohort B p=0.020). Several key secondary endpoints, including improvements in New York Heart Association (NYHA) classification and dyspnea score, also achieved statistical significance within each cohort. For the secondary endpoint of change in exercise capacity (peak VO_2), statistical significance was met in Cohort A, with a positive trend toward improvements in Cohort B. Taken together, data from the PIONEER-HCM study indicate that optimal daily dosing for most patients may be between 5 and 15mg. Baseline patient characteristics, including disease severity, were similar across Cohorts A and B. The use of background beta blockers, permitted only in Cohort B, did not appear to impact mavacamten's safety or pharmacodynamic profile.

The PIONEER-HCM study has informed a target concentration range at which mavacamten is expected to achieve clinically meaningful improvements in oHCM symptoms, functional classification (e.g., NYHA class), and exercise capacity (peak VO_2) while maintaining left ventricular ejection fraction (LVEF) in a normal range of greater than or equal to 50 percent. These data will inform the starting dose and guide dose-adjustment for MyoKardia's planned Phase 3 pivotal EXPLORER-HCM clinical trial of mavacamten in symptomatic oHCM patients. EXPLORER-HCM is expected to commence patient dosing in the second quarter of 2018.

“The lives of symptomatic obstructive HCM patients are limited by the debilitating progression of their condition. Unfortunately, current therapeutic options are either procedurally invasive or have limited effectiveness,” said Daniel Jacoby, M.D., Director, Cardiomyopathy Program and Comprehensive Heart Failure Program at the Yale School of Medicine, and principal investigator in the PIONEER-HCM study. “In the Phase 2 PIONEER-HCM study, we are seeing patients on mavacamten feeling better across both quantitative and qualitative measures, including the elimination of their LVOT obstruction, increased functional and exercise capacity and alleviation of shortness of breath. These results are very encouraging and I look forward to mavacamten’s advancement into the Phase 3 EXPLORER study.”

“Data from the two cohorts of the PIONEER-HCM study provide us with a greater understanding of the relationship between dosing and the pharmacodynamic effects of mavacamten in treating oHCM patients,” said Marc Semigran, M.D., MyoKardia’s Chief Medical Officer. “As we advance into the pivotal Phase 3 EXPLORER-HCM trial, we feel confident that we can appropriately treat patients with the aim of optimizing the therapeutic effects of mavacamten to improve patients’ symptoms and functional capacity while preserving left ventricular ejection fraction.”

On behalf of the PIONEER-HCM investigators, Dr. Jacoby will present results from the Phase 2 clinical trial, including results from Cohort B, in a talk titled “*Reduction in Left Ventricular Outflow Tract Gradient With Mavacamten (MYK-461) in Symptomatic Obstructive Hypertrophic Cardiomyopathy Patients (PIONEER-HCM)*” at the American College of Cardiology’s (ACC) 67th Annual Scientific Session during the Highlighted Original Research: Heart Failure and Cardiomyopathies and the Year in Review session on Sunday, March 11, 2018 at 8:00 am ET.

PIONEER-HCM Cohort B Results

Ten patients with symptomatic oHCM were enrolled in Cohort B, all of whom completed the study. Nine of ten patients remained on background beta blockers. Patients received daily 2mg doses of mavacamten during Weeks 1-4 before increasing to daily 5mg doses of mavacamten during Weeks 5-12 per protocol. Patients continued to be monitored for an additional four-week washout period during which time LVOT gradient, NYHA class and LVEF values reverted towards values at baseline.

Mavacamten was generally well-tolerated. Adverse events (AEs) were mild to moderate, and a majority of the AEs were deemed to be unrelated to study drug.

	Cohort A	
Number of patients	n=11*	
Mavacamten doses studied	10mg, 15mg, 20mg QD	
Change, from baseline to W12	**Mean ± SD**	***p*-va**
Post-exercise LVOT gradient (mmHg)	-112 ± 63.8	0.00
Resting LVOT gradient (mmHg)	-55 ± 41.8	0.00
Resting LVEF (%)	-16 ± 14.1	0.00
NYHA class	-0.9 ± 0.7	0.01
Peak VO_2 (mL/kg/min)	+3.5 ± 3.25	0.00
Dyspnea numerical rating scale	-3.1 ± 1.4	0.00

* In this first patient cohort of PIONEER-HCM, 11 patients enrolled and 10 completed the study.

Mavacamten reduced LVOT gradient while maintaining ejection fraction in Cohort B.

- Reductions in post-exercise LVOT gradient were observed from a baseline mean of 86 mmHg to a mean of 64 mmHg at Week 12 (p=0.020).
- Resting LVOT gradient was reduced from 86 mmHg at baseline to 38 mmHg at Week 12 (p=0.004).
- Changes in resting LVEF from baseline were relatively minimal and patients in Cohort B maintained ejection fractions above 50 percent.

Mavacamten also demonstrated improvements in secondary endpoints intended to measure symptoms and functional capacity in Cohort B.

- Nine of ten patients saw improvements in NYHA class from baseline, including one patient who experienced a two class improvement (p=0.004).
- Peak VO_2 scores improved by a mean value of 1.7 ml/kg/min, which corresponded to a greater than 10 percent increase from baseline (p=0.121) and 50 percent of Cohort B patients had a greater than 2.9 ml/kg/min improvement in peak VO_2. Four of nine patients on beta blocker showed an improvement in peak VO_2 of greater than or equal to 2.9 ml/kg/min.
- A rapid and statistically significant improvement in shortness of breath, as measured by a standard numerical rating scale for dyspnea, was also observed across all patients (p=0.008).

Conference Call and Webcast

MyoKardia management will host a conference call and live audio webcast today, March 8, at 4:30 p.m. ET / 1:30 p.m. PT to review data from the Phase 2 PIONEER-HCM clinical trial, as well as fourth quarter and year end 2017 financial results. 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 8496928. 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.

PIONEER-HCM Study Design

PIONEER-HCM is a Phase 2 open-label study to assess the efficacy, safety, pharmacokinetics, pharmacodynamics, and tolerability of mavacamten in patients with symptomatic oHCM. Twenty-one oHCM patients with LVEF ≥ 55 percent, clinically significant LVOT obstruction (resting gradient ≥ 30 mmHg, post-exercise peak LVOT gradient ≥ 50 mmHg) and New York Heart Association (NYHA) Class ≥ II, all as determined by the investigator, were treated with mavacamten for 12 weeks, followed by a four-week washout phase. The primary endpoint of PIONEER-HCM is the change in post-exercise peak LVOT gradient from baseline to Week 12. Additional endpoints include change from baseline to Week 12 in peak VO_2, VE/VCO_2, NYHA Class, NT-proBNP, rest and exercise LVEF, and dyspnea score. Safety endpoints include treatment-emergent AEs and serious AEs, and changes from baseline in laboratory test results, vital signs, and electrocardiograms. PIONEER-HCM consists of two dosing

cohorts: in the first cohort, subjects received a once-daily 10mg, 15mg or 20mg dose of mavacamten and were required to discontinue background therapy including beta blockers prior to study entry; and Cohort B, in which subjects received a once-daily 2mg or 5mg oral dose of mavacamten and nine out ten patients remained on beta blocker therapy. Baseline patient characteristics were similar across both patient cohorts.

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 EXPLORER-HCM study, in patients with symptomatic, obstructive HCM and a Phase 2 clinical trial, the MAVERICK-HCM study, in patients with 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 New York Heart Association (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 MyoKardiaand 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 and a Phase 2 trial, the MAVERICK-HCM study, in patients with non-obstructive HCM. 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 (formerly MYK-461), the Company's expectations with respect to its ability to continue to advance mavacamten in the PIONEER-HCM study and its ability to use data from the PIONEER-HCM study to guide the starting dose and inform dose-adjustment for its planned Phase 3 pivotal EXPLORER-HCM trial, as well as its ability to initiate its EXPLORER-HCM trial in symptomatic oHCM and the timing of such initiation, 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 year ended December 31, 2017, 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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