MyoKardia Announces 48-week Data from PIONEER-OLE Study of Mavacamten

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Mavacamten's Safety and Efficacy Profile in the PIONEER Study Maintained Through One Year in Open-Label Extension Study of 12 Patients with Symptomatic, Obstructive HCM

Evidence Suggests Mavacamten's Favorable Impact on Cardiac Structure

Conference Call Today at 8:30 a.m. ET (5:30 a.m. PT);
Data Presentation at American Heart Association Scientific Sessions on Monday, November 18, 2019

SOUTH SAN FRANCISCO, Calif., Nov. 11, 2019 (GLOBE NEWSWIRE) -- MyoKardia, Inc. (Nasdaq: MYOK) today announced new data from the company's PIONEER open-label extension (OLE) study of mavacamten for the treatment of symptomatic, obstructive hypertrophic cardiomyopathy (HCM).

Data for twelve patients at 48 weeks of treatment with mavacamten were consistent with prior safety and efficacy observations at the 12, 24, and 36-week readouts. Highlights of the data include continued safety and tolerability and sustained clinical benefits, including reductions in left ventricular outflow tract (LVOT) gradient, improvements in NYHA functional class and improvement of multiple biomarkers toward normal ranges. A reduction in septal wall thickness, a defining characteristic of HCM, as well as an improvement in patient reported quality of life, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ), were also reported.

"Mavacamten's continued favorable safety profile and the apparent consistency and durability across so many parameters through one year of treatment are incredibly encouraging and enhance our confidence that mavacamten has the potential to make a lasting impact on the lives of people with HCM. We look forward to building on these data with the results from our pivotal EXPLORER-HCM Phase 3 study in the first half of next year," said Jay Edelberg, M.D., Ph.D., Senior Vice President of Clinical Development at MyoKardia.

"The hearts of people with HCM beat as if they are in fight-or-flight mode all the time, and as disease progresses, that excessive contraction can result in a cascade of damaging, and ultimately fatal, consequences for HCM patients. Mavacamten acts at a molecular level on specific heart muscle proteins to reduce the excessive contractility driving disease," said Daniel Jacoby, M.D. Director, Comprehensive Heart Failure Program at the Yale School of Medicine and an investigator in the PIONEER-OLE clinical trial. "Over time, and across multiple measures, we are seeing evidence that mavacamten treatment is bringing the HCM heart toward a more normal state. The new data being reported during the AHA sessions, including the improvement of patient-reported outcomes and heart structure, add further weight to the sustained safety and efficacy observed to date in this study population."

PIONEER-OLE 48-week Results

Twelve patients with symptomatic (NYHA Class II-III), obstructive HCM are currently enrolled in the PIONEER-OLE study and receive individualized doses of mavacamten aimed at reducing or eliminating their LVOT obstruction. All twelve patients were evaluable at 48 weeks.

- Mavacamten was well tolerated throughout the one-year treatment period. Consistent with data reported at Week 36, there were no cardiac-related adverse events (AEs) attributed to study drug throughout the 48-week period. To date, all AEs attributed to treatment have been mild or moderate and transient.
- LVOT gradient, a measure of obstruction of the left ventricle, was decreased from baseline with statistical significance among the twelve patients under multiple conditions of testing: i.e. at rest, post-exercise and upon provocation with a Valsalva maneuver. At week 48, resting LVOT gradient for all patients was below 50mmHg, the guideline-based threshold for an invasive intervention, and 11 of 12 patients were below the 30mmHg threshold at which obstructive HCM is diagnosed. Provoked gradient measurements, taken using a Valsalva maneuver and post-exercise, were also below 50mmHg in all but two patients at Week 48.
- Left ventricular ejection fraction (LVEF) remained above normal (50%) for all 12 patients at all times of assessment.

PIONEER-OLE: Observed Mean Values (SD)
LVOT Gradient and LVEF

	Baseline (N=13)	Week 12 (N=13)	Week 24 (N=13)	Week 36 (N=12)	Week 48 (N=12)
Resting LVOT gradient (mmHg)	67.3 (42.80)	11.8 (5.20)	11.6 (6.01)	21.1 (20.89)	14.0 (9.70)
Valsalva LVOT gradient (mmHg)	89.9 (30.72)	22.5 (19.60)	20.5 (10.59)	31.5 (23.25)	22.4 (18.96)
Post-exercise gradient (mmHg)	127.5 (33.38)	-	-	-	39.8 (31.13)†

Resting LVEF (%)	72.0 (4.90)	67.5 (6.93)	69.0 (6.11)	69.4 (6.04)	70.6 (9.10)

† n=11

Note: Post-exercise gradient was collected at Baseline and Week 48.

- NT-proBNP, an established circulating blood marker of cardiac wall stress, significantly decreased to ranges closer to normal (considered less than 125 pg/mL). NT-proBNP levels in HCM patients of <310 pg/mL have been associated with a 75 percent reduction in the rate of heart failure-related death or hospitalization, progression to end-stage disease, and stroke, as compared with patients with levels ≥310 pg/mL.(1)
- E/e', an echocardiographic measure of left ventricular filling pressure, decreased from a mean baseline measure of 12.8 to 9.1.
- Left atrial volume index decreased to normal levels from a baseline mean of 41 mL/m^2 to a mean of 32 mL/m^2. Left atrial volumes are a measure of the filling pressure of the left ventricle, and increased volumes are potentially associated with an increased risk of atrial fibrillation in HCM patients.(2)
- Reductions in interventricular septal (IVS) thickness as measured by echocardiography were observed in PIONEER-OLE patients. Overall, PIONEER-OLE patients began the study with a mean IVS of 17mm at baseline, and progressively decreased to 15mm after 48 weeks of mavacamten treatment. Studies of HCM patients following septal reduction interventions have shown that IVS reductions in HCM patients are associated with improvements in LVOT gradient, functional capacity and symptoms. The risk of sudden cardiac death in HCM patients has been observed to increase progressively as wall thickness increases above 15mm.(3)

PIONEER-OLE: Biomarker Measurements, Mean (SD)
Cardiac Wall Stress, Diastolic Filling Pressure and Structural Changes

	Normal ranges	Baseline (N=13)	Week 12 (N=13)	Week 24 (N=13)	Week 36 (N=12)	Week 48 (N=12)	Change from Baseline to Week 48
NT-proBNP (pg/mL), median (IQR)	<125	594	99	93	168	137	-472(-2467, -157)**
E/e' lateral	<13	12.8 (2.9)	9.8 (2.5)	10.2 (2.7)	8.5 (2.3)	9.1 (2.0)†	-3.4 (3.0)**
LA volume index (mL/m^2)	16-34	40.9 (16.4)	31.8 (8.4)	30.8 (8.0)	30.4 (8.7)	31.5 (6.9)	-9.8 (13.5)*
IVS (mm)	6-10mm	16.7 (2.8)	16.0 (2.7)	15.8 (2.7)	15.4 (2.7)	15.3 (2.2)	-1.5 (2.6)

† n=11
***p<0.01*
**p<0.05*

Improvements in both symptom burden and quality of life has been observed among the PIONEER-OLE patients.

- At baseline, patients enrolled in PIONEER-OLE were symptomatic with a NYHA classification of Class II or III. NYHA classifications were measured at Week 24 and Week 48 and have consistently demonstrated improvements, with nine out of twelve patients achieving asymptomatic (Class I) status.
- Positive results from the KCCQ, designed to measure patients' perception of their heart failure health status and its impact on the activities of daily living, were also reported. In PIONEER-OLE, KCCQ mean scores went from 74.1 at baseline to 87.3 at Week 48 (scores range from 0-100, and higher scores reflect better status). A clinically significant change in KCCQ is defined as greater than or equal to 6.

These data will be presented at the 2019 American Heart Association's Annual Scientific Sessions by Stephen Heitner, M.D., Director of the Hypertrophic Cardiomyopathy Clinic at Oregon Health and Science University, on Monday, November 18, 2019 at 2:05 p.m. during the session titled: *Pharmacological Therapy in HF/Cardiomyopathy: The Next Important Indication or Agent?*

Conference Call and Webcast
MyoKardia management will host a conference call and live audio webcast this morning at 8:30 a.m. ET / 5:30 a.m. PT to review new data from the PIONEER-OLE study and the topline data reported today from the MAVERICK Phase 2 clinical trial. Investors and analysts are invited to participate in the call by dialing 844-494-0913 (U.S.) or 508-637-5584 using the conference ID 3177984. The webcast may be accessed live on the investor section of the MyoKardia website. A replay of the webcast will be available on MyoKardia's website for 90 days following the call.

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)
Mavacamten is a novel, oral, allosteric modulator of cardiac myosin being developed for the treatment of hypertrophic cardiomyopathy (HCM). Mavacamten is intended to reduce cardiac muscle contractility by inhibiting the excessive myosin-actin cross-bridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance characteristic of HCM. MyoKardia is currently evaluating mavacamten in multiple clinical trials for the treatment of obstructive and non-obstructive HCM. The pivotal Phase 3 clinical trial, known as EXPLORER-HCM, is being conducted in patients with symptomatic, obstructive HCM and MyoKardia anticipates data from this program in Q2'2020. Two long-term follow-up studies are also ongoing, the PIONEER open-label extension study of obstructive HCM patients from MyoKardia's Phase 2 PIONEER trial and the MAVA-LTE, an extension study for patients who have completed either EXPLORER-HCM or MAVERICK-HCM, the company's Phase 2 clinical trial of symptomatic non-obstructive HCM patients. In April 2016, the U.S. FDA granted Orphan Drug Designation for mavacamten for the treatment of symptomatic obstructive HCM.

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 advancement. MyoKardia's initial focus is on small molecule therapeutics aimed at the muscle 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) in Phase 3 and Phase 2 clinical trials for hypertrophic cardiomyopathies (HCM); MYK-491 in Phase 2 for patients with stable heart failure; and MYK-224 in Phase 1 development for HCM.

MyoKardia's mission is to change the world for people with serious cardiovascular disease through bold and innovative science.

(1) Amato, et al, *American Journal of Cardiology*, 2013
(2) Debonnaire, et al, *Circulation: Arrhythmia and Electrophysiology*, 2017
(3) Spirito P, et al, *New England Journal of Medicine*, 2000

Forward-looking Statement

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 the availability of data from EXPLORER-HCM, the Company's expectation with respect to release of data from EXPLORER-HCM, as well as the Company's expectations for the potential for success of EXPLORER-HCM, 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 September 30, 2019, 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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