News Release

MyoKardia Begins Patient Dosing in Phase 1b Clinical Study of MYK-491 in Dilated Cardiomyopathy Patients

Topline Results from First-in-Human Phase 1 Study of MYK-491 in Healthy Volunteers Demonstrated Tolerability and Increased Contractility

SOUTH SAN FRANCISCO, Calif., Feb. 14, 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 that dosing has commenced in a Phase 1b single-ascending dose patient study of its investigational drug candidate MYK-491.

MYK-491 is being developed in an ongoing collaboration between MyoKardia and Sanofi for the treatment of patients with dilated cardiomyopathy (DCM). DCM is a form of heart failure in which the left ventricle is enlarged and weakened and the heart's contractility is reduced, resulting in symptoms ranging from shortness of breath and fatigue to stroke and death. MYK-491 is intended to increase contractility of the heart (systolic function) with minimal adverse effects on myocardial relaxation (diastolic function). The Phase 1b randomized, double-blind, placebo-controlled, cross-over single-ascending dose trial is enrolling DCM patients with stable heart failure. The trial will evaluate the safety, tolerability and preliminary pharmacokinetics and pharmacodynamics of oral doses of MYK-491. Pharmacodynamic measures will include changes in established echocardiographic measures of cardiac contractility. Topline results from the Phase 1b study are anticipated in the second half of 2018.

"Patients with DCM suffer from debilitating symptoms due to inadequate cardiac contraction and the consequent insufficient blood flow characteristic of their disease. There are currently no approved therapies that directly target the depressed contractility present in dilated cardiomyopathy," said Marc Semigran, M.D., Chief Medical Officer of MyoKardia. "MYK-491 was designed to address the underlying biomechanical cause of DCM. As we advance into further clinical testing, we look forward to gaining insights into MYK-491's potential to increase cardiac contractility and we are hopeful this drug candidate may restore the heart's contractility towards normal function in patients."

MyoKardia also announced topline results from the company's Phase 1 trial of MYK-491 in healthy volunteers. Sixty-four healthy adults (48 active, 16 placebo) were enrolled and randomized to receive either single-ascending doses of MYK-491 or a placebo. MYK-491 was generally well tolerated across the range of oral doses tested. Adverse events (AE) observed were benign and transient. The most common AE was headache. Extra heartbeats were reported in three subjects, possibly related to cardiac irritability. Evidence of clinical proof-of-mechanism was observed at higher

dose levels in the form of increased contractility, as measured by echocardiographic biomarkers. MyoKardia plans to present detailed results from the healthy volunteer dosing study at a future medical meeting.

“This Phase 1 first-in-human study of MYK-491 in healthy volunteers has met the core objective of helping us to determine a starting dose for our Phase 1b trial in dilated cardiomyopathy patients,” said Lisa Alaimo, MyoKardia’s Vice President, Project Management and Project Team Leader. “MYK-491 was generally well tolerated and we are encouraged by the confirmation of expected cardiac pharmacodynamic effects. Results from our Phase 1b patient study, plus the results shared today from our single-ascending dose trial of MYK-491 in healthy volunteers, will provide us with valuable data to inform future clinical plans.”

“Sanofi remains committed to driving forward our collaboration with MyoKardia to develop new treatment options for patients with heritable cardiomyopathies,” said Anthony Muslin, M.D., Head of Cardiovascular Research at Sanofi. “We’re excited about the prospects for MYK-491.”

About MYK-491

MYK-491 is an oral, small molecule, allosteric activator of myosin designed to restore the inadequate output characteristic of a DCM heart by targeting the biomechanical defects underlying disease and improving cardiac contractility. Based on preclinical research across multiple animal models, MYK-491 may hold potential for controlled increases in the heart’s contractility with minimal impact on relaxation (diastole). MYK-491 is currently being studied in a Phase 1a single-ascending dose trial in healthy volunteers and a Phase 1b single-ascending dose trial in DCM patients. MYK-491 is being developed in an ongoing collaboration between MyoKardia and Sanofi.

About Dilated Cardiomyopathy (DCM)

DCM is a form of heart failure that affects about one million people in the United States. In DCM, the walls of the left ventricle are thin and over-expanded, leading to diminished contraction and insufficient blood being pumped by the heart. Diastolic function, or the heart’s ability to relax and fill with blood, is also impaired. Typical symptoms include shortness of breath, fatigue, swelling in the extremities, or an irregular heartbeat. As the disease progresses, patients become increasingly debilitated, and may develop heart failure symptoms and severe complications such as stroke, arrhythmias and death. There is currently no approved medical therapy that targets the underlying depressed contractility characteristic of DCM.

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 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 that has been shown to reduce hypercontractility in early clinical studies and is currently being studied in the Phase 2 PIONEER-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 MYK-491, the availability of topline results from the Company's Phase 1b trial of MYK-491 in DCM patients, the availability of additional data from the Company's Phase 1 single-ascending dose trial of MYK-491 in healthy volunteers, 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 September 30, 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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