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Study demonstrates MYK-461 prevents and reverses disease in HCM mice

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MyoKardia, Inc., a clinical stage biopharmaceutical company pioneering a precision medicine approach for the treatment of heritable cardiovascular diseases, today announced the publication of an article in the leading medical journal *Science*. The article demonstrates the ability of MYK-461, the company's lead drug candidate, to prevent and reverse development of disease in multiple genetic mouse models of hypertrophic cardiomyopathy (HCM). The published research represents the product of collaboration among scientists from MyoKardia, Harvard Medical School, the University of Colorado and Stanford University. These data add to a growing body of laboratory and clinical research demonstrating the potential of MYK-461 as an important and novel approach to treating HCM.

The study, titled "A Small-Molecule Inhibitor of Sarcomere Contractility Suppresses Hypertrophic Cardiomyopathy in Mice," will be published in the February 5 issue of the journal *Science*.

"I am encouraged by these data that illustrate MYK-461's ability to effectively reduce the consequences of HCM mutations at the biochemical, cellular and whole animal levels," said Jonathan Fox, M.D., Ph.D., chief medical officer of MyoKardia. "Translation of these findings from mouse to human could offer great potential to improve the lives of patients living with this devastating disease."

To study the role of sarcomere mutations in the development of HCM, MyoKardia used previously generated mouse models of HCM, which

recapitulate key morphologic and functional features of human HCM. To quantify the level of left ventricular hypertrophy, the cardinal manifestation of HCM, the researchers noninvasively measured left ventricular wall thickness (LVWT).

MyoKardia researchers and their collaborators demonstrated that early and chronic administration of MYK-461 could prevent the development of disease. Compared to the characteristic increase in LVWT observed in untreated mutant mice, no increase in LVWT was observed in mutant mice treated with MYK-461. The research also showed that MYK-461 promoted partial reversal of disease, as shown by a measurable decline, upon administration of MYK-461, of LVWT in HCM mice that had already developed hypertrophy. Furthermore, the research showed that MYK-461 could prevent the development of left ventricular fibrosis, which is an important histopathological feature of HCM and causally implicated in other potentially dangerous heart conditions.

"We are encouraged by these findings, which support our therapeutic hypothesis that reduction in contractility can prevent or reverse the abnormalities in structure and function leading to symptoms that afflict patients living with HCM," said Tassos Gianakakos, chief executive officer of MyoKardia. "We believe that MYK-461 is the first drug in clinical development to achieve either of these effects. This approach could represent a more general paradigm for the treatment of heritable cardiomyopathies and may bring us closer to our ultimate goal, to improve the lives of patients and their families with this debilitating disease."

MyoKardia is currently evaluating MYK-461 in three Phase 1 clinical trials, which are primarily designed to evaluate the safety and tolerability of MYK-461 and are expected to provide data on its pharmacokinetic and pharmacodynamic profile.

More information: "A small-molecule inhibitor of sarcomere contractility suppresses hypertrophic cardiomyopathy in mice" DOI: 10.1126/science.aad3456

Provided by MyoKardia