NEWS RELEASE

Mast Therapeutics Announces Initiation Of Phase 2 Study Of AIR001 Conducted By The Heart Failure Clinical Research Network

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Study conducted with support from a grant awarded by the National Heart, Lung, and Blood Institute, part of the National Institutes of Health

SAN DIEGO, Aug. 1, 2016 /PRNewswire/ -- **Mast Therapeutics, Inc.** (NYSE MKT: MSTX), a biopharmaceutical company developing novel, clinical-stage therapies for sickle cell disease and heart failure, today reported that the first patient has been enrolled in a multicenter, randomized, double-blind, placebo-controlled Phase 2 clinical study of AIR001 in patients with heart failure with preserved ejection fraction (HFpEF). The 100-patient study, known as the Inorganic Nitrite Delivery to Improve Exercise Capacity in HFpEF (INDIE-HFpEF) study, is sponsored by Duke Clinical Research Institute (DCRI) as the Coordinating Center for the Heart Failure Clinical Research Network (HFN) and is being conducted at premier clinical centers that are part of the HFN.

HFpEF is a common form of heart failure. Earlier this year, the Company reported positive top-line results from a blinded and randomized Phase 2a clinical study of AIR001 in HFpEF patients as well as positive interim results from an ongoing Phase 2a clinical study of AIR001 in patients with pulmonary hypertension associated with HFpEF.

"AIR001, a sodium nitrite solution administered via inhalation, has potential as an effective treatment for heart failure, and we are pleased that patient enrollment is underway," stated Brian M. Culley, Mast Therapeutics' CEO. "This study will advance our efforts to characterize the efficacy of AIR001 for patients who have heart failure with preserved ejection fraction. There are more than 1 million heart failure hospitalizations each year in the U.S., about half of which involve patients with HFpEF. Currently, no proven effective therapeutic agents are available for this large patient population. We look forward to continuing to support DCRI and the HFN on this study."

The HFN was established by the National Heart, Lung, and Blood Institute (NHLBI) to expedite clinical research on treatments and strategies to improve the management of acute and chronic heart failure. The HFN's work is supported by a grant awarded by the NHLBI, part of the National Institutes of Health (NIH). The Company's wholly-owned subsidiary, Aires Pharmaceuticals, Inc., is providing test materials, nebulizers, and regulatory, technical and additional financial support for the INDIE-HFpEF study. The Chair of the HFN Executive Committee is Dr. Eugene Braunwald, Distinguished Hersey Professor of Medicine at Harvard Medical School.

About the INDIE-HFpEF Study

The INDIE-HFpEF study is a randomized, double-blind, placebo-controlled crossover study to evaluate the effect of AIR001 on peak exercise capacity as assessed by cardiopulmonary exercise testing (CPET). Approximately 100 patients with a diagnosis of HFpEF will be enrolled across approximately 20 clinical centers in the United States. The primary endpoint will be the peak oxygen consumption (VO_2) after four weeks of treatment with nebulized inhaled AIR001 or placebo as assessed by CPET performed at peak drug levels. Secondary objectives include (i) submaximal activity tolerance chronically, (ii) quality of life, (iii) chronic filling pressures as assessed by echocardiography and natriuretic peptide levels, and/or (iv) ventilator efficiency or submaximal exercise capacity at peak drug levels, and evaluation of the safety and tolerability of AIR001.

About the Heart Failure Clinical Research Network (HFN)

The HFN is an NHLBI clinical research network. The primary goal of the HFN is to conduct multiple clinical trials to evaluate treatments and strategies to improve management of acute and chronic heart failure. The HFN provides a unique platform for collaborative research by bringing together many premier centers across North America. HFN is composed of nine Regional Coordinating Centers and their affiliated sites, whose investigators provide scientific leadership in the collaborative development of the HFN's scientific agenda. The HFN is recognized for robust enrollment in heart failure clinical trials and high scientific productivity. The goal of partnering with HFN is to accelerate research and medical innovation, and provide early results that may improve public health. More information can be found on the HFN's website, **https://www.hfnetwork.org/**.

About AIR001

AIR001 is a sodium nitrite solution for intermittent inhalation via nebulization. Nitrite is a direct vasodilator and can be recycled in vivo to form nitric oxide (NO) independent of the classical NO synthase (NOS) pathway. Nitrite mediated NO formation has several beneficial effects, including dilation of blood vessels and reduction of inflammation and undesirable cell growth. Generation of NO from sodium nitrite is not dependent upon endothelial function and is enhanced in the setting of tissue hypoxia and acidosis, conditions in which NOS activity typically is depressed. In early clinical studies, AIR001 demonstrated positive hemodynamic effects with reductions observed in right atrial pressure and pulmonary capillary wedge pressure, as well as improvements in mean pulmonary artery pressures, cardiac output, and exercise tolerance as measured by six-minute walk distance. In a

recently completed randomized, double-blind, placebo-controlled Phase 2a study of AIR001 in 30 patients with HFpEF, the AIR001 treatment group showed a statistically significant decrease in pulmonary capillary wedge pressure during exercise compared to the control group and was generally well-tolerated.

About Mast Therapeutics

Mast Therapeutics, Inc. is a publicly traded biopharmaceutical company headquartered in San Diego, California. The Company is developing two clinical-stage investigational new drugs for serious or life-threatening diseases and conditions. Vepoloxamer, the Company's lead product candidate, is in Phase 3 clinical development for the treatment of vaso-occlusive crisis in patients with sickle cell disease and in Phase 2 clinical development for the treatment of patients with heart failure. Enrollment in the Company's 388-patient Phase 3 study of vepoloxamer in patients with sickle cell disease, known as the EPIC study, was completed earlier this year. Enrollment in the Company's Phase 2 study of vepoloxamer in patients with chronic heart failure is ongoing. AIR001, the Company's second product candidate, is in Phase 2 clinical development for the treatment of patients with heart failure with preserved ejection fraction (HFpEF). Enrollment in Phase 2 studies of AIR001 in patients with HFpEF are ongoing, including a 100-patient, multicenter, randomized, double-blind, placebo-controlled, Phase 2 study in patients with HFpEF being conducted by the Heart Failure Clinical Research Network. More information can be found on the Company's web site at **www.masttherapeutics.com**. (Twitter: **@MastThera**)

Forward Looking Statements

Mast Therapeutics cautions you that statements included in this press release that are not a description of historical facts are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are based on the Company's current expectations and assumptions. Such forward-looking statements may be identified by the use of forward-looking words such as "intend," "plan," "anticipate," "believe," "expect," among others, and include, but are not limited to, statements relating to prospects for successful development of AIR001 as a treatment for heart failure patients. There are a number of factors that could cause or contribute to material differences between actual events or results and the expectations indicated by the forward-looking statements. These factors include, but are not limited to: that the Company is not the sponsor of the INDIE-HFpEF study and has no control over the conduct of the study, including whether the study will be completed on anticipated timelines, or at all; the Company's reliance on third parties for the manufacture and supply of test material and nebulizer devices for use in the INDIE-HFpEF study and that the Company may not be able to supply such material or devices for the study on a timely basis, or at all; the inherent uncertainty of outcomes in clinical studies of new investigational drugs, such as AIR001 and vepoloxamer and the risk that these product candidates may not demonstrate adequate safety, efficacy or tolerability in ongoing or future clinical studies; the risk that, even if current and planned clinical studies are successful, the FDA or other regulatory agencies may determine they are

not sufficient to support a new drug application; the risk that the Company is not able to obtain and maintain effective patent coverage or other market exclusivity protections for its products, if approved, without infringing the proprietary rights of others; risks associated with the Company's ability to manage operating expenses and obtain additional capital as needed; the Company's potential inability to continue as a going concern if it does not raise additional capital as needed; uncertainty related to the Company's ability to remain in compliance with the terms and restrictions under its debt facility and the potential that it may be required to repay outstanding debt obligations on an accelerated basis and/or at a time that could be detrimental to the Company's financial condition, operations and/or business strategy, including the prepayment of $10 million of the principal balance if results from the EPIC study are not positive and/or not available on or before October 14, 2016; the potential for the Company to significantly delay, reduce or discontinue current and/or planned development and commercial-readiness activities or sell or license its assets at inopportune times if it is unable to raise sufficient additional capital as needed; the Company's dependence on third parties to assist with important aspects of development of its product candidates, including conduct of its clinical studies and supply and manufacture of clinical trial material, and, if approved, commercial product, and the risk that such third parties may fail to perform as expected, leading to delays in product candidate development or approval or inability to meet market demand for approved products, if any; the risk that, even if the Company successfully develops a product candidate in one or more indications, it may not realize commercial success and may never achieve profitability; and other risks and uncertainties more fully described in the Company's press releases and periodic filings with the Securities and Exchange Commission. The Company's public filings with the Securities and Exchange Commission are available at **www.sec.gov**.

You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date when made. Mast Therapeutics does not intend to revise or update any forward-looking statement set forth in this press release to reflect events or circumstances arising after the date hereof, except as may be required by law.

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