NEWS RELEASE

Mast Therapeutics Announces Agreement For Phase 2 Study Of AIR001 To Be Conducted By The Heart Failure Clinical Research Network

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Study to be conducted with support from a grant awarded by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH)

SAN DIEGO, April 13, 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 its wholly-owned subsidiary, Aires Pharmaceuticals, Inc., has entered into an agreement with Duke University to provide support for a multicenter, randomized, double-blind, placebo-controlled Phase 2 clinical study of the Company's product candidate AIR001 in patients with heart failure with preserved ejection fraction (HFpEF). This 100-patient study, known as the Inorganic Nitrite Delivery to Improve Exercise Capacity in HFpEF (INDIE-HFpEF) study, will be sponsored by Duke Clinical Research Institute (DCRI) as the Coordinating Center for the Heart Failure Clinical Research Network (HFN) and conducted at premier clinical centers in the United States that are part of the HFN.

HFpEF is a common form of heart failure that has not responded as well to previously tested treatments as heart failure with reduced ejection fraction. AIR001, a sodium nitrite solution that is administered by way of intermittent inhalation via nebulization, was obtained by Mast Therapeutics in 2014 through the acquisition of then privately-held Aires Pharmaceuticals. The Company recently reported positive top-line results from a blinded and randomized Phase 2a clinical study of AIR001 in HFpEF patients conducted at Mayo Clinic.

The HFN was established by the 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 National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH). Under the agreement with

the HFN Coordinating Center, as previously anticipated, the Company will provide test materials, nebulizers, and regulatory, technical and additional financial support.

The Chair of the HFN Executive Committee is Dr. Eugene Braunwald, Distinguished Hersey Professor of Medicine at Harvard Medical School. The collaborative scientific leadership for the study will include Dr. Barry Borlaug, the Principal Investigator, and other investigators from the HFN Regional Coordinating Centers. The HFN Coordinating Center will be led by Dr. Adrian Hernandez and Dr. Kevin Anstrom of the DCRI.

"We appreciate the NIH's, NHLBI's, and HFN's recognition of the study of AIR001 in heart failure as an appropriate area of investigation," stated Brian M. Culley, Chief Executive Officer of Mast Therapeutics, Inc. "This study will accelerate efforts to define the potential efficacy of AIR001 for patients who have heart failure with preserved ejection fraction. This is an area of significant unmet need. There are more than 1 million heart failure hospitalizations each year in the U.S., about half are patients with HFpEF, and, currently, there are no proven effective therapeutic agents available for this large patient population."

"The investigator initiated Investigational New Drug Application (IND) has been submitted and DCRI anticipates that the study will begin recruiting patients in the third quarter of this year," continued Mr. Culley. "We look forward to supporting DCRI and the HFN on this study."

About the INDIE-HFpEF Study

The Inorganic Nitrite Delivery to Improve Exercise Capacity in HFpEF (INDIE-HFpEF) study is a randomized, double-blind, placebo-controlled crossover study to assess 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 evaluation of whether AIR001 improves (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 conducted at Mayo Clinic, 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 in February 2016. 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 a Phase 2a study of AIR001 in patients with HFpEF is ongoing and AIR001 was recently selected by the Heart Failure Clinical Research Network for evaluation in a 100-patient, multicenter, randomized, double-blind, placebo-controlled, Phase 2 study in patients with HFpEF. 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 that are based on the Company's current expectations and

assumptions. Such forward-looking statements may include, but are not limited to, statements relating to prospects for successful development and commercialization of the Company's investigational drugs, including AIR001, and anticipated timing of achievement of development milestones, such as commencement of clinical studies or progress with regulatory activities. Among the factors that could cause or contribute to material differences between the Company's actual results and the expectations indicated by the forward-looking statements are risks and uncertainties that include, but are not limited to: that the Company is not the sponsor of the INDIE-HFpEF study and has no control over the protocol for or conduct of the study, including whether the study will commence or 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, or may incur significant unanticipated expenses in connection with procuring sufficient quantities; the uncertainty of outcomes in ongoing and future studies of the Company's product candidates and that its product candidates, including AIR001, may not demonstrate adequate safety, efficacy, or tolerability in one or more such studies, including INDIE-HFpEF; the Company's ability to obtain and maintain effective patent coverage and other market exclusivity protections for its products without infringing on the proprietary rights of others; that the Company may be required to repay its outstanding debt obligations on an accelerated basis and/or at a time that could be detrimental to its financial condition, operations, and/or business strategy; the Company's ability to obtain additional funding on a timely basis or on acceptable terms, or at all; the Company's ability to complete development of and successfully commercialize its product candidates and 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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Mast Therapeutics, Ioana C. Hone (ir@mastthera.com), 858-552-0866 Ext. 303