NEWS RELEASE

Positive Interim Results From Second Phase 2a Study Of AIR001 In Patients With Heart Failure With Preserved Ejection Fraction (HFpEF) Presented At American Thoracic Society International Conference

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- AIR001 significantly lowered pulmonary artery pressures
- Administration was generally well-tolerated
- Enrollment is ongoing

SAN DIEGO, May 16, 2016 /PRNewswire/ -- **Mast Therapeutics, Inc.** (NYSE MKT: MSTX), a biopharmaceutical company developing novel clinical-stage therapies for sickle cell disease and heart failure today announced positive interim results from an ongoing Phase 2a study of AIR001 in patients with pulmonary hypertension (PH) associated with heart failure with preserved ejection fraction (HFpEF). The interim results were presented at the American Thoracic Society (ATS) International Conference by lead investigator Marc A. Simon, M.D., M.S., F.A.C.C. The ATS International Conference is being held May 13 – 18, 2016 at the Moscone Center in San Francisco, California.

In the 10 patients who had been studied to date, nebulized inhaled nitrite (AIR001) administration significantly lowered central pressures, specifically, right atrial, right ventricular systolic and diastolic, pulmonary artery (PA) systolic/diastolic/mean, and pulmonary artery occlusion (PAOP) pressures. Of note, pulmonary artery occlusion and mean pulmonary artery pressures were markedly decreased from baseline median values. In addition, there was an observed increase in pulmonary artery compliance. There was no significant decrease is systemic blood pressures or change in heart rate. Methemoglobin levels increased modestly, but remained less than 1.9% and did not meet stopping criteria of the study, which was 5%. AIR001 was generally well-tolerated.

"This is the first report of the acute hemodynamic effects of multiple inhaled nitrite doses in patients with pulmonary hypertension due to heart failure with preserved ejection fraction," stated Dr. Simon. "The interim

results observed to date are important as they demonstrate that AIR001 can significantly lower right atrial pressures, pulmonary artery pressures, and pulmonary artery occlusion pressures, as well as improve pulmonary artery compliance."

"These data are consistent with results we saw in a separate Phase 2a study of AIR001 in HFpEF earlier this year and are a further step in validating our second asset and establishing the potential clinical utility of AIR001 in HFpEF," stated Brian M. Culley, Chief Executive Officer of Mast Therapeutics. "We look forward to advancing AIR001 in this area of high unmet medical need for which there is no FDA-approved therapy available."

Poster Information:

- The poster entitled "Efficacy and safety of inhaled sodium nitrite in pulmonary hypertension associated with heart failure with preserved ejection fraction" will be presented by Dr. Simon at 11:00 a.m. PT on May 16, 2016, at the Moscone Center in San Francisco, California.
- A copy of the poster will be available after 11:00 a.m. PT on the Company's website at: **http://www.masttherapeutics.com/technology/publications/**.

About the Phase 2a Study

This is an institution-sponsored, single-center, open label Phase 2a study to evaluate the effect of AIR001 delivered in a dose escalation manner on the change in cardiovascular hemodynamics in subjects with pulmonary hypertension who undergo standard right heart catheterization. The study will enroll a total of approximately 50 subjects with pulmonary hypertension. Approximately 20 of the subjects will have a diagnosis of PH associated with HFpEF (WHO Group II PH). Subjects receive a first dose of 45 mg of AIR001 via nebulizer, with one subsequent escalation dosage to 90 mg approximately 60 minutes after the first dose, based on safety and tolerability. During the study, right heart/pulmonary artery hemodynamics are measured continuously, and cardiac output is measured at 15 minute intervals, as well as noninvasive systemic blood pressure and pulse oximetry monitoring. Changes in hemodynamics and calculated pulmonary systemic vascular resistances, as well as pulmonary artery compliance will be performed.

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 **http://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 for patients with HFpEF. 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 interim clinical study results may not be indicative of final study results and complete study results may not be positive with regard to efficacy or safety of AIR001 for patients with HFpEF; that the Company is not the sponsor of the ongoing Phase 2a study of AIR001 in patients with PH associated with HFpEF and has no control over the protocol for or conduct of the study, including whether the study will be completed on anticipated timelines, or at all; 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; the Company's potential inability

to continue as a going concern if it does not raise additional capital as needed, and its potential inability to obtain additional funding on a timely basis or on acceptable terms, or at all; the risk 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, including the prepayment of $10 million of the principal balance of its debt facility if results from the Company's Phase 3 study of vepoloxamer in sickle cell disease are not positive; the potential for the Company to significantly delay, reduce or discontinue current and/or planned development activities or sell or license its assets at inopportune times if it is unable to raise sufficient additional capital as needed; 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; 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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To view the original version on PR Newswire, visit:**http://www.prnewswire.com/news-releases/positive-interim-results-from-second-phase-2a-study-of-air001-in-patients-with-heart-failure-with-preserved-ejection-fraction-hfpef-presented-at-american-thoracic-society-international-conference-300268818.html**

SOURCE Mast Therapeutics, Inc.

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