NEWS RELEASE

Positive Interim Results From Phase 2 Study Of AIR001 In Patients With Pulmonary Hypertension Associated With Heart Failure With Preserved Ejection Fraction (PH-HFpEF) Published In Journal Of Clinical Investigation

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AIR001 Significantly Lowered Pulmonary Artery Pressures and Substantially Increased Pulmonary Arterial Compliance

SAN DIEGO, Nov. 3, 2016 /PRNewswire/ -- **Mast Therapeutics, Inc.** (NYSE MKT: MSTX), today announced that the Journal of Clinical Investigation (JCI) published positive interim results from an ongoing 50-patient Phase 2 study of AIR001 in patients with pulmonary hypertension (PH), including a cohort with PH associated with heart failure with preserved ejection fraction (PH-HFpEF). In the Phase 2 study, AIR001 significantly lowered pulmonary, right atrial, and pulmonary capillary wedge pressures, with a substantial increase in pulmonary artery compliance, which was most pronounced in patients with PH-HFpEF.

In the 36 patients studied to date, administration of nebulized inhaled nitrite (AIR001) significantly decreased pulmonary, right atrial, and pulmonary capillary wedge pressures, and was most pronounced in patients with PH-HFpEF. AIR001 administration also led to a substantial increase in pulmonary artery compliance, which was most pronounced in patients with PH-HFpEF. AIR001 was generally well-tolerated and no significant safety concerns were identified, satisfying the primary safety outcome of the study. In addition, there were no significant decreases in peripheral oxygen saturation nor increases in methemoglobin levels above the stopping criteria of 5%.

"The 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," stated Edwin L. Parsley, D.O, Chief Medical Officer of Mast Therapeutics, Inc. "In the study, AIR001 administration appears to be safe in Groups 1-3 PH and may be efficacious in Groups 2 and 3 PH with further study in non-Group 1 PH warranted."

"These data are consistent with results we saw in a separate investigator-sponsored Phase 2 study of AIR001 in HFpEF earlier this year and serve as a further step in validating AIR001 and establishing its potential clinical utility 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. In addition to full results from this 50-patient study, the 100-patient 'INDIE-HFpEF' study of AIR001 also is expected to complete enrollment and announce top-line results next year. We believe these are important value-creating studies which convincingly demonstrate the potential for clinical utility of AIR001 in HFpEF and potentially other settings."

Of the 36 patients enrolled, 10 were diagnosed with PH-HFpEF, 20 were diagnosed with World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH) on background PAH specific therapy, and 6 were diagnosed with WHO Group 3 PH. In the 10 patients enrolled with PH-HFpEF, AIR001 administration resulted in significant overall decreases in right atrial pressure, pulmonary capillary wedge pressure, right ventricular systolic and diastolic, and pulmonary artery systolic, diastolic and mean pressures. Of note, pulmonary capillary wedge pressure and mean pulmonary artery pressure markedly decreased by 7.5 mm Hg (95%CI: -9.0, -6.0) and 7.9 mm Hg (95%CI: -9.4, -6.3), respectively (baseline median values 18 and 34 mm Hg, respectively). With significant lowering of all pressures, there was no significant change in transpulmonary gradient and a modest but significant increase in PVR. Pulmonary artery compliance increased by 35% (+0.97 mL/mm Hg, 95%CI: +0.25, +1.68; P = 0.008).

Further analysis of the dose effect of AIR001 found that most hemodynamics were affected in a dose dependent manner with the exception of pulmonary artery compliance. There was a significant dose effect on right atrial pressure, mean pulmonary artery pressure, and pulmonary capillary wedge pressure. Cardiac index decreased in a dose-dependent manner. The increase in pulmonary artery compliance was not dose related.

About the Phase 2 Study

This is an institution-sponsored, single-center, open label Phase 2 study to evaluate the effect of AIR001 delivered in a dose escalation manner on the change in cardiovascular hemodynamics in subjects with PH who undergo standard right heart catheterization. The study will enroll a total of approximately 50 subjects with PH. Approximately 20 of the subjects will have a diagnosis of PH associated with HFpEF (WHO Group 2 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 utilizing standard formulas.

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 randomized, double-blind, placebo-controlled Phase 2a study of AIR001 in patients with HFpEF (n=26), the AIR001 treatment group showed a statistically significant decrease in pulmonary capillary wedge pressure during exercise compared to the control group and AIR001 was generally well-tolerated.

About Mast Therapeutics

Mast Therapeutics, Inc. is a publicly traded biopharmaceutical company headquartered in San Diego, California. The Company has two clinical-stage investigational new drugs, AIR001 and vepoloxamer. AIR001, a sodium nitrite solution for intermittent inhalation via nebulization, is in Phase 2 clinical development for the treatment of heart failure with preserved ejection fraction (HFpEF). More information can be found on the Company's web site at **www.masttherapeutics.com**. Mast Therapeutics™ and the corporate logo are trademarks of Mast Therapeutics, Inc.

Forward Looking Statements

Mast Therapeutics cautions you that statements in this press release that are not a description of historical fact are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by the use of words referencing future events or circumstances such as "expect," "intend," "plan," "anticipate," "believe," and "will," among others. Examples of forward-looking statements in this press release include statements relating to AIR001's potential utility to treat HFpEF, the timing of completion and results of ongoing clincial studies of AIR001, and the Company's development plans for AIR001. Forward-looking statements should not be read as guarantees of future performance or results because they involve the Company's beliefs and assumptions based on currently available information and are subject to significant known and unknown risks and uncertainties that may cause actual performance and results to differ materially from

expectations indicated by the forward-looking statements. Some of the factors that could cause actual performance or results to differ include, without limitation: the Company's need for additional funding and the risk that it may not be able to obtain sufficient additional funding as needed; risks associated with the Company's ability to manage operating expenses; uncertainty related to the Company's ability to continue to operate as a going concern; risk that the Company may not be able to continue to comply with the terms and conditions under its debt facility, which could result in the Company being required to repay its remaining outstanding debt obligation on an accelerated basis and/or at a time that could be detrimental to the Company's financial condition, operations and/or business strategy; the impact of significant reductions in the Company's operations on its ability to develop its product candidates or maintain compliance with laws and regulations relating to public companies; the Company's ability to maintain compliance with NYSE MKT continued listing standards and policies and to maintain the listing and trading of its common stock on a national securities exchange; uncertainties inherent in the conduct of clinical studies and the risk that the Company's product candidates may not demonstrate adequate safety, efficacy or tolerability in one or more clinical studies for approval by regulatory authorities; the Company's lack of control over the ongoing, investigator-sponsored Phase 2 clinical studies of AIR001, including whether any of the studies will be completed on anticipated timelines, or at all; the potential for the Company to sell or license part or all of its assets; the potential for significant delays, reductions, or discontinuation of current and/or planned development activities if the Company is unable to raise sufficient additional capital as needed; the Company's dependence on third parties to assist with important aspects of development of the Company's product candidates, including the conduct of its clinical studies, the manufacture and supply of its clinical trial material, including drug delivery devices, and the conduct of regulatory activities, and the risk that such third parties may fail to perform as expected leading to delays in product candidate development and additional costs; the risk that the Company is not able to obtain or maintain effective patent coverage or other market exclusivity protections for its products, if approved, or that the use or manufacture of the Company's products may infringe the proprietary rights of others; and other risks and uncertainties more fully described in the Company's press releases and its reports filed 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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