NEWS RELEASE

Mast Therapeutics Announces Initiation Of Patient Enrollment In Additional Phase 2 Study Of AIR001 For The Treatment Of Heart Failure With Preserved Ejection Fraction

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SAN DIEGO, Dec. 6, 2016 /PRNewswire/ -- **Mast Therapeutics, Inc.** (NYSE MKT: MSTX) today reported that the first patient has been enrolled in an investigator-sponsored Phase 2 study of the Company's lead product candidate, AIR001, for the treatment of heart failure with preserved ejection fraction (HFpEF). The Inorganic Nitrite to Amplify the Benefits and Tolerability of Exercise Training (INABLE-TRAINING) in HFpEF study will evaluate AIR001's potential to improve the clinical responses to exercise training in individuals with HFpEF. The INABLE-TRAINING study is expected to enroll approximately 68 patients who will undergo 12 weeks of cardiac rehabilitation, including exercise training, and will be randomized to receive either AIR001 or placebo inhalation solution through the training period. The primary endpoint of the study will be the change in exercise capacity as measured by peak oxygen consumption.

"We are pleased to report that patient enrollment is underway in this Phase 2 study of AIR001 for the treatment of HFpEF," stated Brian M. Culley, Chief Executive Officer of Mast Therapeutics, Inc. "There are now three Phase 2 studies actively enrolling patients to evaluate AIR001 for the treatment of HFpEF and we remain excited about its potential in this indication. Data from this and other studies will help guide our clinical and regulatory strategy in this area of significant unmet need. Currently, HFpEF affects approximately half of the more than 5 million people in the U.S. diagnosed with heart failure and has no proven effective treatment. Heart failure is a leading cause of morbidity and mortality among the elderly worldwide and is the primary diagnosis in more than 1 million hospitalizations each year, with medical costs projected to rise to more than $50 billion in the U.S. alone by 2030."

About the INABLE-TRAINING Study

This is a Phase 2 randomized, double-blind, parallel-group placebo-controlled clinical trial testing whether inhaled AIR001 (sodium nitrite solution), as compared to inhaled placebo, can enhance the benefits from chronic exercise training (ET) in subjects with HFpEF. All subjects will undergo 12 weeks of ET. Participants will be randomized to receive inhaled AIR001 three times daily or inhaled sodium chloride (placebo) three times daily during the study period. Study subjects will wear accelerometry devices to track daily activity levels at home. After 12 weeks of ET as part of standard cardiac rehab, subjects will repeat the assessment of cardiovascular function and exercise capacity as performed at study entry to assess efficacy at a final visit.

The Phase 2 study has 2 aims. First, determine whether treatment with inhaled AIR001 in addition to ET for 12 weeks improves exercise capacity and hemodynamic reserve in HFpEF. Expired gas analysis, inert gas (C_2H_2) rebreathe, and echocardiography will be performed during rest and exercise to measure oxygen consumption (VO_2), CO, and hemodynamics before and after completion of 12 weeks of ET with inhaled NO_2^- vs ET with inhaled placebo. Second, determine whether treatment with inhaled AIR001 in addition to ET for 12 weeks increases daily activity levels and quality of life (QOL), and reduces symptoms of effort intolerance during ET. Subjects will use externally worn accelerometer devices to track daily physical activity. Tolerability of ET will be assessed by Borg perceived effort and dyspnea scores. Large and small vessel endothelial function (brachial and digital arteries) and QOL will also be assessed. Secondary endpoints include cardiac output reserve, peak exercise workload, rest and exercise hemodynamics assessed by echocardiography, Borg dyspnea and fatigue scores recorded during ET, endothelial function assessed by tonometry and brachial artery flow mediated dilation, QOL assessed by the Kansas City Cardiomyopathy Questionnaire. (ClinicalTrials.gov Identifier: NCT02713126)

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 heart failure with preserved ejection fraction (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 to treat HFpEF, the timing of completion of any clinical studies, 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 of an event of default under the Company's debt facility that could result in the Company being required to repay its outstanding debt obligation and related fees 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 investigator-sponsored clinical studies of AIR001, including whether any of the studies will commence or 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 clinical and nonclinical studies, the manufacture and supply of 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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To view the original version on PR Newswire, visit:**http://www.prnewswire.com/news-releases/mast-therapeutics-announces-initiation-of-patient-enrollment-in-additional-phase-2-study-of-air001-for-the-treatment-of-heart-failure-with-preserved-ejection-fraction-300373270.html**

SOURCE Mast Therapeutics, Inc.

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