



NEWS RELEASE

# Mast Therapeutics Announces Positive Top-Line Results From Phase 2a Study Of AIR001 In Patients With Heart Failure With Preserved Ejection Fraction (HFpEF) Conducted At Mayo Clinic

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Study met its primary endpoint; AIR001 was generally well-tolerated, with no treatment-related serious adverse events

SAN DIEGO, Feb. 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 positive top-line results from a blinded Phase 2a study of AIR001 for the treatment of heart failure with preserved ejection fraction (HFpEF) conducted at Mayo Clinic by lead investigator Barry A. Borlaug, M.D., Associate Professor of Medicine and Director, Circulatory Failure Research, Division of Cardiovascular Diseases, Department of Internal Medicine. In the Phase 2a study, AIR001 showed statistically significant improvement for the pre-specified primary endpoint: change in pulmonary capillary wedge pressure (PCWP) at 20 Watts exercise after drug treatment relative to PCWP at 20 Watts exercise in the initial assessment prior to drug treatment, compared to placebo-treated patients. Study data show that nebulized AIR001 attenuates the hemodynamic derangements of cardiac failure that occur during exercise in HFpEF patients. AIR001 was generally well-tolerated. Detailed study results are expected to be submitted for presentation at a scientific conference later this year.

"Heart failure with preserved ejection fraction is a major public health problem that has no proven effective treatment, yet currently afflicts 2 to 3 million Americans," stated Dr. Borlaug. "One factor that complicates treatment is that the hemodynamic perturbations causing morbidity such as high filling pressures and low cardiac output are typically present only intermittently—being absent at rest but observed during stress such as exercise. As such, an ideal therapy would become more effective during stress, without untoward effects on resting cardiovascular function. The results observed with AIR001 in this study support our hypothesis that acute



administration of nebulized inhaled sodium nitrite unloads the heart during exercise without excessive reduction in resting pressures or arterial blood pressure."

"These results are an important 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. "Mayo Clinic is a well-known leader in the characterization and treatment of heart failure and we thank Dr. Borlaug for working with us and leading this study," continued Mr. Culley. "We look forward to advancing AIR001 in this area of high unmet medical need for which there is no FDA-approved therapy available. We also anticipate reporting interim data from a second investigator-sponsored Phase 2a study of AIR001 in HFpEF patients around the middle of this year."

## About the Phase 2a Study Design

The Phase 2a study was a randomized, double-blind, placebo-controlled clinical trial of AIR001 in 30 patients with HFpEF referred to the catheterization laboratory for invasive exercise stress testing. Standard right heart catheterization using high fidelity micromanometers was performed at rest and during supine exercise with simultaneous expired gas analysis. Hemodynamic, arterial and mixed venous blood gas, as well as expired gas data were acquired at rest, during each exercise stage and at peak exercise. Venous blood samples were obtained at rest and at 20 Watt exercise. Perceived symptoms of dyspnea and fatigue will be quantified using the Borg dyspnea and effort scores at each stage of exercise.

The primary endpoint of the study measured PCWP at 20 Watts exercise after administration of study drug relative to PCWP at 20 Watts exercise in the initial assessment prior to administration of study drug. Secondary endpoints measured changes in resting PCWP after administration of study drug, as well as rest and exercise-related changes in right atrial pressure, PCWP, pulmonary artery pressure, pulmonary vascular resistance, systemic BP, heart rate, cardiac output,  $VO_2$ ,  $Ve/VCO_2$  slope and Borg dyspnea/effort scores. Sodium nitrite levels were evaluated at rest and 20 Watt exercise stages before and after study drug administration. Regression analysis was performed to explore how changes in  $NO_2$  levels relate to observed hemodynamic effects.

## About AIR001

AIR001 is a sodium nitrite solution for intermittent inhalation via nebulization. Nitrite is a physiological signaling molecule with roles in intravascular endocrine nitric oxide (NO) production, hypoxic vasodilation signaling, and cytoprotection after ischemia-reperfusion. Nitrite serves as the largest physiologic reservoir of NO and can be converted to NO independent of nitric oxide synthase (NOS) activity. In experimental models, nitrite use has demonstrated improved remodeling both in the pulmonary vasculature and right ventricle. Hemodynamic effects include venodilation with reductions in right atrial pressures, pulmonary and systemic vasodilation with reductions in pulmonary vascular resistance and left atrial pressures, and improved cardiac relaxation. Mast Therapeutics obtained the AIR001 program through its acquisition of privately-held Aires Pharmaceuticals, Inc. in 2014.

## About Mast Therapeutics

Mast Therapeutics, Inc. is a publicly traded biopharmaceutical company headquartered in San Diego, California. The Company is leveraging its **MAST platform**, derived from over two decades of clinical, nonclinical and manufacturing experience with purified and non-purified poloxamers, to develop vepoloxamer (also known as MST-188), its lead product candidate, for serious or life-threatening diseases and conditions typically characterized by impaired microvascular blood flow and damaged cell membranes. The Company is also developing AIR001, a sodium nitrite solution for inhalation via nebulization.

Vepoloxamer is an investigational new drug being tested in a pivotal Phase 3 study called **EPIC** for the treatment of vaso-occlusive crisis in patients with sickle cell disease and in a Phase 2 study for the treatment of patients with chronic heart failure. AIR001 is an investigational new drug in Phase 2a clinical development for treatment of patients with heart failure with preserved ejection fraction (HFpEF). More information can be found on the Company's web site at [www.masttherapeutics.com](http://www.masttherapeutics.com). (Twitter: [@MastThera](https://twitter.com/MastThera))

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## 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, development plans, including decisions regarding advancement and the timing thereof, and anticipated timing of achievement of development milestones, such as completion of clinical studies and announcement of study data. 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: the potential that unfavorable findings may arise from additional analyses of existing clinical data or new clinical data; the risk that results from a clinical study are not predictive of future clinical study results; the uncertainty of outcomes in ongoing and future studies of the Company's product candidates and the risk that its product candidates, including AIR001, may not demonstrate adequate safety, efficacy or tolerability in one or more such studies; delays in the commencement or completion of clinical studies, including as a result of difficulties in obtaining regulatory agency agreement on clinical development plans or study design, opening trial sites, enrolling study subjects, supplying sufficient quantities of clinical trial material, being subject to a "clinical hold," and/or suspension or termination of a clinical study, including due to patient safety concerns or lack of funding; 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 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; 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](http://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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