

Results of Vepoloxamer Nonclinical Studies in Advanced Heart Failure Presented at European Society of Cardiology 3rd World Congress on Acute Heart Failure

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- Ex vivo study results indicate that by limiting unregulated calcium entry, vepoloxamer improves calcium cycling and left ventricle (LV) function in dogs with severe heart failure

SAN DIEGO, May 23, 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 that data from nonclinical studies of vepoloxamer, its lead product candidate, were presented at the European Society of Cardiology 3rd World Congress on Acute Heart Failure by Dr. Hani N. Sabbah, Professor of Medicine and Director of Cardiovascular Research at Henry Ford Health System, at 9:30 a.m. CEST on May 21, 2016. The conference is being held in Florence, Italy May 21 through May 24, 2016.

The studies evaluated the effects of vepoloxamer on ventricular function and calcium cycling proteins in dogs with severe heart failure. Animals were randomized to receive vepoloxamer or placebo (saline) and each received two infusions of vepoloxamer or saline control administered three weeks apart. Tissue samples obtained three weeks after the second infusion were assessed for Ca^{2+} -ATPase activity, phosphorylated (p) phospholamban at serine-16 (p-PLB-s16), p-ryanodine receptors at serine-2808 (p-RYR-s2808) and p-sodium-calcium-exchanger 1 (p-NCX-1) measured using specific antibodies and Western blotting. LV tissue from seven normal animals was utilized for comparison. LV function was assessed by full hemodynamics, plasma n-terminal-pro brain natriuretic peptide (NT-proBNP) and plasma-troponin-I (Tn-I) at baseline and at 1, 2 and 3 weeks following each infusion.

With regard to calcium cycling proteins, saline infusions had no effect on any of the examined functional measures. However, as previously reported, treatment with vepoloxamer partially normalized activity and protein levels. The

results suggest that by limiting unregulated calcium entry into the cell, vepoloxamer decreased calcium overload in failing cardiomyocytes and improved calcium cycling proteins, leading to improved LV function. With regard to ventricular function, vepoloxamer increased LV ejection fraction and progressively reduced NT-proBNP and Tn-I. These benefits were sustained for up to 3 weeks after the second infusion of vepoloxamer. The results suggest that therapy with repeat intravenous 2-hour infusions of vepoloxamer, pulsed at 3-week intervals, limits calcium overload, normalizes sarcoplasmic reticulum (SR) calcium cycling, improves LV systolic function, lowers NT-proBNP and reduces Tn-I, a measure of ongoing cardiomyocyte death.

Dr. Sabbah said: "Reducing calcium overload and normalization of key calcium cycling proteins along with improvements in LV systolic function are very promising findings and suggest significant potential to improve treatment for both acute and chronic heart failure patients."

Dr. R. Martin Emanuele, the Company's Senior Vice President, Development, said: "We believe the activity of vepoloxamer is very different from existing therapies and may offer a new approach to treating heart failure by directly improving heart function. Also, because of its unique mechanism, vepoloxamer should be additive to existing therapies. We look forward to further demonstrating vepoloxamer's potential in our ongoing Phase 2 clinical trial in chronic heart failure patients."

Presentation Information:

- Dr. Sabbah's presentation, entitled "Vepoloxamer (purified poloxamer-188) improves LV function, limits cardiomyocyte calcium overload and restores integrity of calcium cycling proteins in myocardium of dogs with advanced heart failure," was given during a rapid fire session at 9:30 a.m. CEST on May 21, 2016, in Florence, Italy.
- A copy of the presentation is now available on the Company's website at:
<http://www.masttherapeutics.com/technology/publications/>

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)

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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 within the meaning of the Private Securities Litigation Reform Act of 1995 that are based on the Company's current expectations and assumptions. Such forward-looking statements may be identified by the use of forward-looking words such as "intend," "plan," "anticipate," "believe," "expect," among others, and include, but are not limited to, statements relating to prospects for successful development of vepoloxamer as a treatment for heart failure patients. There are a number of factors that could cause or contribute to material differences between actual events or results and the expectations indicated by the forward-looking statements. These factors include, but are not limited to: the inherent uncertainty of outcomes in ongoing and future studies of the Company's product candidates and the risk that its product candidates may not demonstrate adequate safety, efficacy or tolerability in one or more such studies, including in the ongoing Phase 2 study of vepoloxamer in patients with chronic heart failure; 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 clinical study design, opening trial sites, enrolling study subjects, manufacturing 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; delays in clinical study closeouts, including blinded data review and quality control and assurance procedures; the risk that, even if current and planned clinical studies are successful, the FDA or other regulatory agencies may determine they are not sufficient to support a new drug application; the potential that, even if clinical studies of a product candidate in one indication are successful, clinical studies in another indication may not be successful; the Company's dependence on third parties to assist with important aspects of development of its product candidates, including conduct of its clinical studies and supply and manufacture of clinical trial material, and, if approved, commercial product, and the risk that such third parties may fail to perform as expected, leading to delays in product candidate development or approval or inability to meet market demand for approved products, if any; 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 if results from the EPIC study are not positive; risks associated with the Company's ability to manage operating expenses and/or obtain additional funding to support its operations on a timely basis or on acceptable terms, or at all; the potential for the Company to significantly delay, reduce or discontinue current and/or planned development and commercial-readiness activities or sell or license its assets at inopportune times if it is unable to raise sufficient

additional capital as needed; the risk that, even if the Company successfully develops a product candidate in one or more indications, it may not realize commercial success and may never achieve profitability; the risk that the Company is not able to obtain and maintain effective patent coverage or other market exclusivity protections for its products, if approved, without infringing the proprietary rights of others; 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/results-of-vepoloxamer-nonclinical-studies-in-advanced-heart-failure-presented-at-european-society-of-cardiology-3rd-world-congress-on-acute-heart-failure-300272845.html>

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