NEWS RELEASE

Results Of Vepoloxamer Nonclinical Studies In Advanced Heart Failure Presented At American College Of Cardiology 65th Annual Scientific Sessions & Expo

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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

- Results further support ongoing clinical trial of vepoloxamer for the treatment of advanced heart failure

SAN DIEGO, April 4, 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 American College of Cardiology (ACC) 65th Annual Scientific Sessions & Expo. The results were presented by Dr. Hani N. Sabbah, Professor of Medicine and Director of Cardiovascular Research at Henry Ford Health System, at 9:45 a.m. ET on April 3, 2016 and 9:45 a.m. on April 4, 2016. The ACC conference is being held at the McCormick Place Convention Center in Chicago, IL, April 2 through April 4, 2016.

The studies evaluated the effects 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, 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 as previously reported. 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, improves LV systolic function, lowers NT-proBNP and reduces Tn-I, a measure of ongoing cardiomyocyte death.

Dr. Sabbah said: "These additional findings related to the normalization of key calcium cycling proteins are consistent with the observed improvements in ventricular function. While additional studies are needed to verify these observations, the results are very promising 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 completely different from existing therapies and may offer a new approach to treating heart failure by directly improving heart function. In addition, because of its unique mechanism, vepoloxamer could be additive to existing therapies. We look forward to further demonstrating vepoloxamer's potential in our Phase 2 clinical trial in chronic heart failure patients, which is currently underway."

Poster Information:

- The poster entitled "Vepoloxamer (Purified Poloxamer-188) Restores Integrity of Cardiomyocyte Calcium Cycling Proteins in Left Ventricular Myocardium of Dogs With Advanced Heart Failure" was presented by Dr. Sabbah at 9:45 a.m. ET on April 3, 2016, at the McCormick Place Convention Center in Chicago, Illinois.
- The poster entitled "Multiple Intravenous Infusions of Vepoloxamer (Purified Poloxamer -188) Elicit Progressive Improvements in Plasma Biomarkers in Dogs with Advanced Heart Failure" will be presented by Dr. Sabbah at 9:45 a.m. ET today, April 4, 2016, at the McCormick Place Convention Center in Chicago, Illinois.
- Copies of the posters will be available after 9:45 a.m. ET 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**)

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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