

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT  
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):

February 9, 2015

**Mast Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

Delaware

001-32157

84-1318182

(State or other jurisdiction  
of incorporation)

(Commission  
File Number)

(IRS Employer  
Identification No.)

3611 Valley Centre Drive, Suite 500, San Diego, California

92130

(Address of principal executive offices)

(Zip Code)

Registrant's telephone number, including area code:

(858) 552-0866

Not Applicable

Former name or former address, if changed since last report

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 8.01. Other Events.**

The information attached as Exhibit 99.1 to this report relating to Mast Therapeutics, Inc. (the “Company”) and its development programs may be presented from time to time by the Company at various investor and analyst meetings, including on February 9, 2015 at the 17<sup>th</sup> Annual BIO CEO & Investor Conference.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

The list of exhibits called for by this Item is incorporated by reference to the Exhibit Index immediately following the signature page of this report.

By filing this report, including the information contained in Exhibit 99.1 attached hereto, the Company makes no admission as to the materiality of any information in this report. The information contained in Exhibit 99.1 hereto is summary information that is intended to be considered in the context of the Company’s filings with the U.S. Securities and Exchange Commission (the “SEC”), including its Annual Report on Form 10-K filed on March 26, 2014, Quarterly Report on Form 10-Q filed on October 31, 2014, and other public announcements that the Company makes, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report, although it may do so from time to time as it believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, or through other public disclosure.

**Forward-Looking Statements**

Mast Therapeutics cautions you that statements included in this report, including in Exhibit 99.1 attached hereto, 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 include, but are not limited to, statements regarding the Company’s development, regulatory and commercialization strategies and plans for its product candidates, including vepoloxamer (MST-188) in sickle cell disease, occlusive arterial disease, heart failure, and AIR001 in heart failure with preserved ejection fraction, as well as the timing of activities related to those plans, including commencement and completion of clinical and nonclinical studies. 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 uncertainty of outcomes in ongoing and future studies of its product candidates and the risk that its product candidates may not demonstrate adequate safety, efficacy or tolerability in one or more such studies, including vepoloxamer in the ongoing EPIC study and Phase 2 study in acute lower limb ischemia; delays in the commencement or completion of clinical studies, including the EPIC study, the Phase 2 study of vepoloxamer in acute limb ischemia, the planned Phase 2 study of vepoloxamer in heart failure and the Phase 2a studies of AIR001, 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, completing manufacturing process development activities, 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 potential for institutional review boards or the FDA or other regulatory agencies to require additional nonclinical or clinical studies prior to initiation of planned clinical study of a product candidate; the risk that, even if clinical studies are successful, the FDA or another regulatory agency 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 reliance on contract research organizations (CROs), contract manufacturing organizations (CMOs), and other third parties to assist in the conduct of important aspects of development of its product candidates, including clinical studies, manufacturing, and regulatory activities for its product candidates and that such third parties may

fail to perform as expected; the Company's ability to obtain, as needed, additional funding on a timely basis or on acceptable terms, or at all; the potential for the Company to delay, reduce or discontinue current and/or planned development activities, including clinical studies, partner its product candidates at inopportune times or pursue less expensive but higher-risk and/or lower return development paths if it is unable to raise sufficient additional capital as needed; the risk that the FDA and regulatory agencies outside of the U.S. do not grant marketing approval of a product candidate, on a timely basis, or at all; the risk that, even if the Company successfully develops a product candidate in one or more indications, it may not realize commercial success with its products and may never generate revenue sufficient to achieve profitability; the risk that the Company is not able to adequately protect its intellectual property rights and prevent competitors from duplicating or developing equivalent versions of its product candidates; and other risks and uncertainties more fully described in the Company's periodic filings with the SEC and press releases.

You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date they are made. Mast Therapeutics does not intend to revise or update any forward-looking statement set forth in this report to reflect events or circumstances arising after the date hereof, except as may be required by law. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Mast Therapeutics, Inc.

February 9, 2015

By: /s/ Brandi L. Roberts

Name: Brandi L. Roberts

Title: Chief Financial Officer and  
Senior Vice President

**Exhibit Index**

**Exhibit No.**

**Description**

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99.1

Mast Therapeutics, Inc. corporate presentation, February 9, 2015



# 17<sup>th</sup> Annual BIO CEO & Investor Conference

**Brian M. Culley, CEO**

February 9, 2015

# Forward-Looking Statements

This presentation includes forward-looking statements about our business prospects, financial position, and development of MST-188 and AIR001 for therapeutic use in humans. Any statement that is not a statement of historical fact should be considered a forward-looking statement. Because forward-looking statements relate to the future, they are subject to inherent risks, uncertainties and changes in circumstances that are difficult to predict. Actual events or performance may differ materially from our expectations indicated by these forward-looking statements due to a number of factors, including, but not limited to, results of our pending and future clinical studies, the timeline for clinical and manufacturing activities and regulatory approval; our dependency on third parties to conduct our clinical studies and manufacture our clinical trial material; our ability to raise additional capital, as needed; our ability to establish and protect proprietary rights related to our product candidates; and other risks and uncertainties more fully described in our press releases and our filings with the SEC, including our annual report on Form 10-K filed with the SEC on March 26, 2014.

We caution you not to place undue reliance on any of these forward-looking statements, which speak only as of the date of this presentation. We do not intend to update any forward-looking statement included in this presentation to reflect events or circumstances arising after the date of the presentation, except as may be required by law.

# Corporate Overview

- **Developing vepoloxamer to improve blood flow and cell membrane integrity**
  - **Sickle Cell Disease (SCD) – Phase 3 enrolling (data expected Q1'16)**
  - **Acute Limb Ischemia (ALI) – Phase 2 enrolling**
  - **Acute Heart Failure (ADHF) – Phase 2 initiation Q2'15**
  
- **Developing AIR001 to improve cardiovascular hemodynamics and exercise tolerance**
  - **Heart Failure with Preserved Ejection Fraction (HFpEF) – Phase 2a**



# Vepoloxamer

*(Purified Poloxamer 188)*

# Vepoloxamer Overview

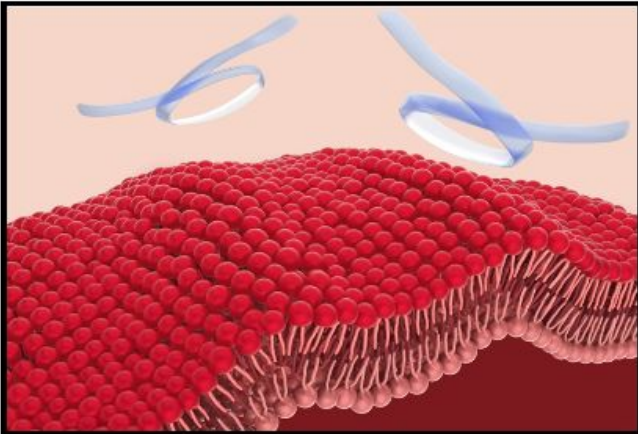


API Structure:	$\text{HO} - (\text{CH}_2\text{CH}_2\text{O})_{79} - (\text{CH}_2\text{CHO})_{30} - (\text{CH}_2\text{CH}_2\text{O})_{79} - \text{H}$ $\quad \quad \quad  $ $\quad \quad \quad \text{CH}_3$
CMC:	<ul style="list-style-type: none"><li>• Large, synthesized polymer with extraction process to remove undesirable (toxic) components.</li><li>• Composition of matter claims pending.</li></ul>
Administration:	<ul style="list-style-type: none"><li>• IV infusion</li></ul>
ADME:	<ul style="list-style-type: none"><li>• Rapidly and predominantly cleared by kidneys (4-8h)</li><li>• Ether linkages cannot be cleaved; no drug metabolites</li></ul>

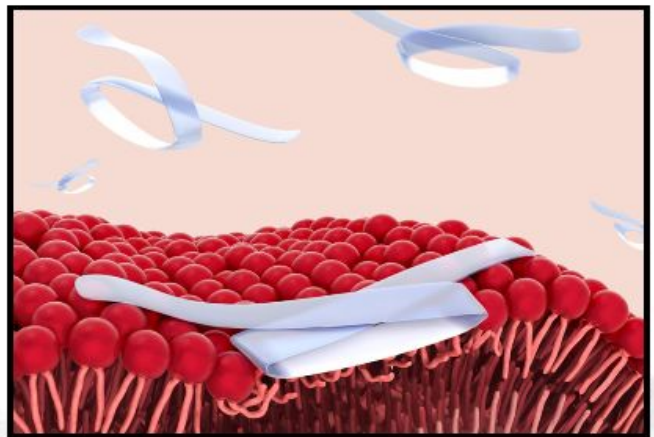
# Vepoloxamer Mechanism of Action

Core of molecule adheres to hydrophobic domains on cell surface, such as damaged membranes and adhesive proteins.

*No Affinity for Healthy Cell Membranes...*

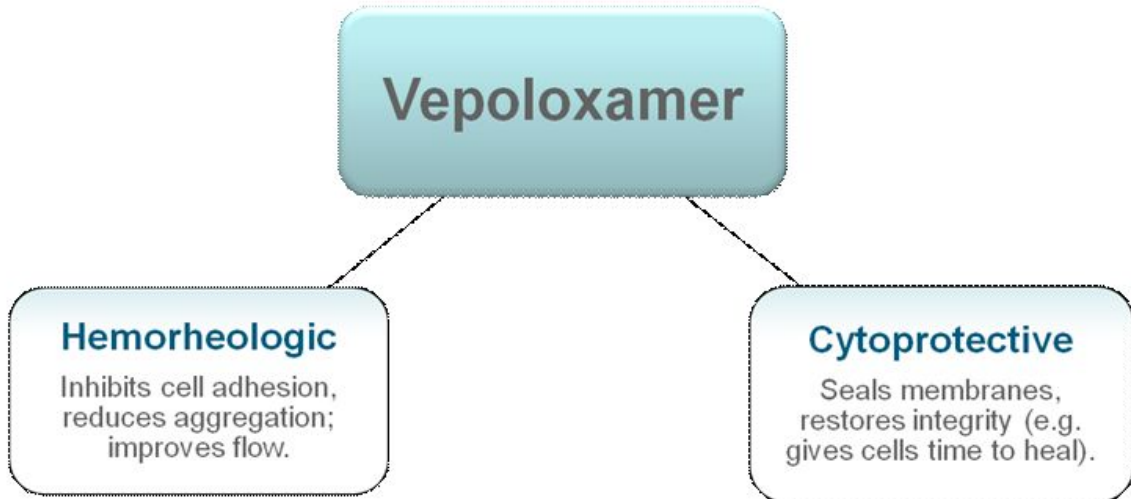


*But Adheres to Damaged Cell Membranes*

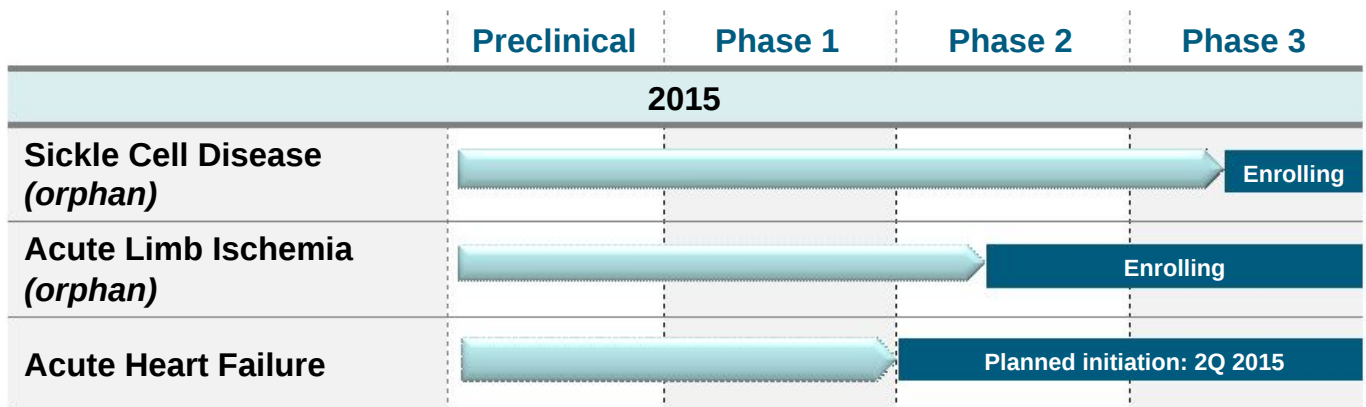


# Vepoloxamer Pharmacodynamics

Simple *biophysical* mechanism improves flow and membrane integrity.



# Vepoloxamer Clinical Development



# Sickle Cell Disease

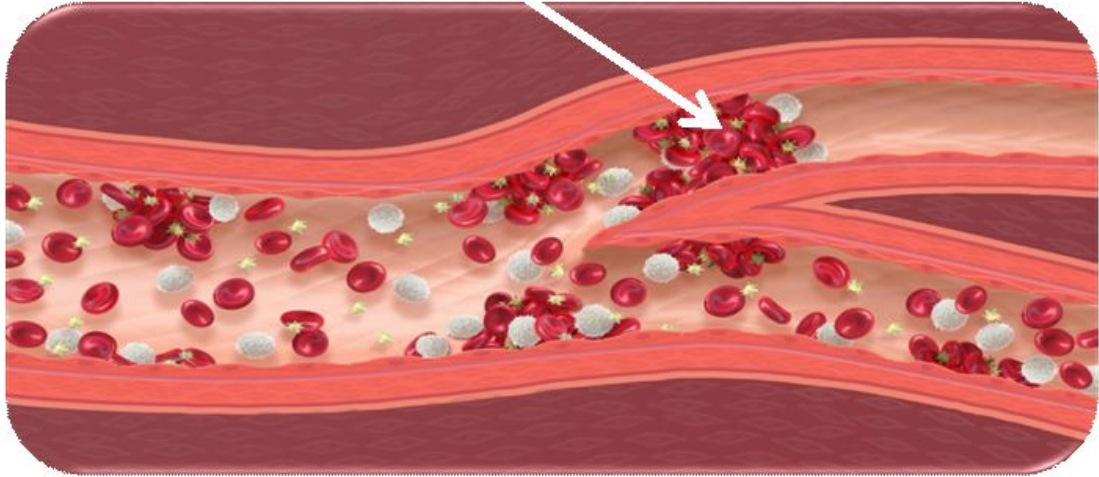
# Overview of Sickle Cell Disease

- **A chronic, genetic disorder and rare (orphan) disease**
  - Affects 90,000 to 100,000 people in the U.S.
  - Characterized by severe deformation (i.e., “sickling”) of red blood cells
- **Hallmark of disease is a “vaso-occlusive crisis”**
  - Indescribably painful condition
  - Leading cause of hospitalization
- **Significant unmet need**
  - No approved agents to shorten duration or severity of crisis
  - Standard of care (hydration and analgesics) unchanged for >10 years
- **Vaso-occlusion is associated with early death**
  - Obstructed blood flow -> hypoxia -> tissue death -> organ failure
  - Average age at death; 42 years (males), 48 years (females)

# Role of Vepoloxamer in Sickle Cell Disease

## Vaso-Occlusion:

- Adhesion of poorly-deformable, “sticky” cells to endothelium
- Entrapment of rigid, sickled cells and vessel obstruction results in ischemia and infarction



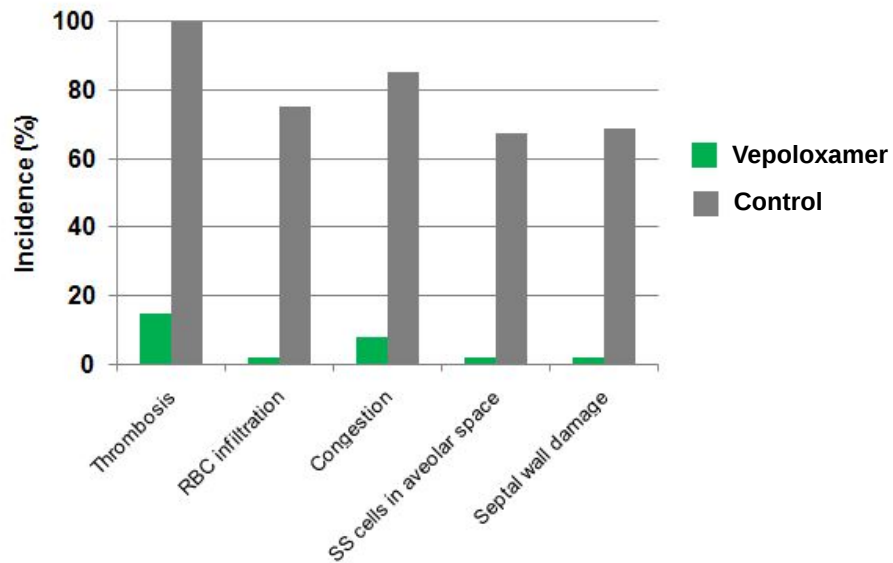
## Vepoloxamer:

- Reduces aggregation and adhesion of cells to endothelium (anti-inflammatory)
- Improves RBC deformability, lowers viscosity, restores flow (rheology), and reduces reperfusion injury (cytoprotection)



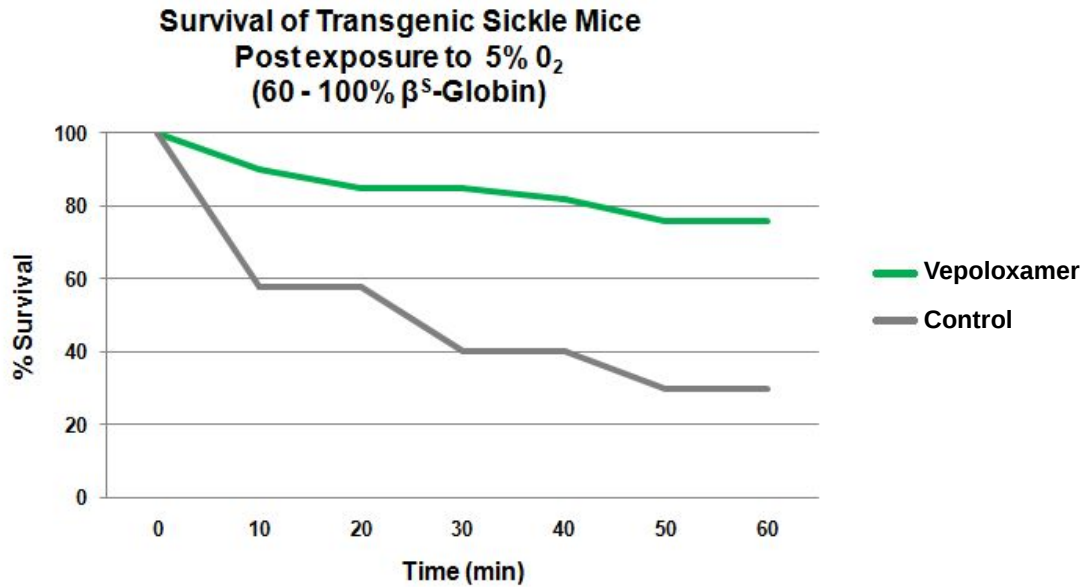
# Vepoloxamer Reduced Organ Pathology in Transgenic Sickle Mice

## Lung Pathology



Lung pathology was compared in transgenic mice pretreated with either vepoloxamer (400 mg/kg) or saline and subject to hypoxia (5% O<sub>2</sub>). (Asakura, et al.)

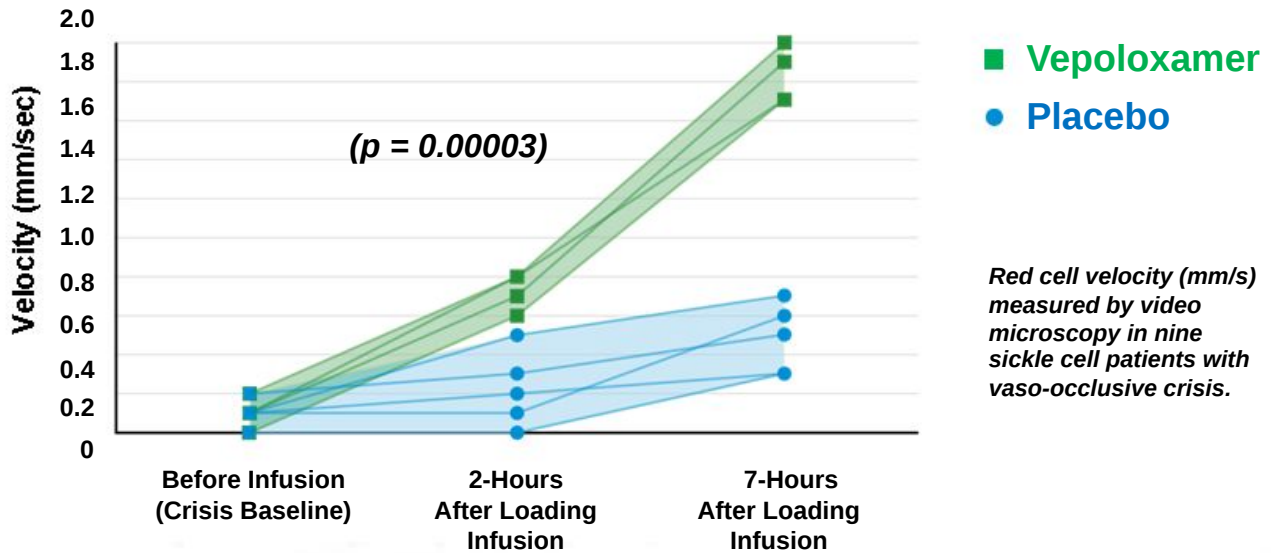
# Vepoloxamer Increased Survival in Transgenic Sickle Mice



Transgenic mice pretreated with either vepoloxamer (400 mg/kg) or saline, subject to hypoxia (5% O<sub>2</sub>), and monitored for survival. (Asakura, et al.)

# Vepoloxamer Improves Blood Flow

Vepoloxamer improved microvascular blood flow in SCD patients in crisis



# Phase 2 Study

- Randomized, double-blind, placebo-controlled, multi-center study in SCD patients hospitalized for crisis
- Significantly improved important efficacy parameters

	Subjects Who Received Full Dose <sup>±</sup>		
	Poloxamer 188* (n=18)	Placebo (n=13)	<i>p</i> value <sup>±±</sup>
Duration of Crisis	44 hours	80 hours	0.025
Duration of Hospitalization	5 days	7 days	0.111
Total Analgesic Use	34mg	145mg	0.045
Parenteral Analgesic Use	27mg	133mg	0.022

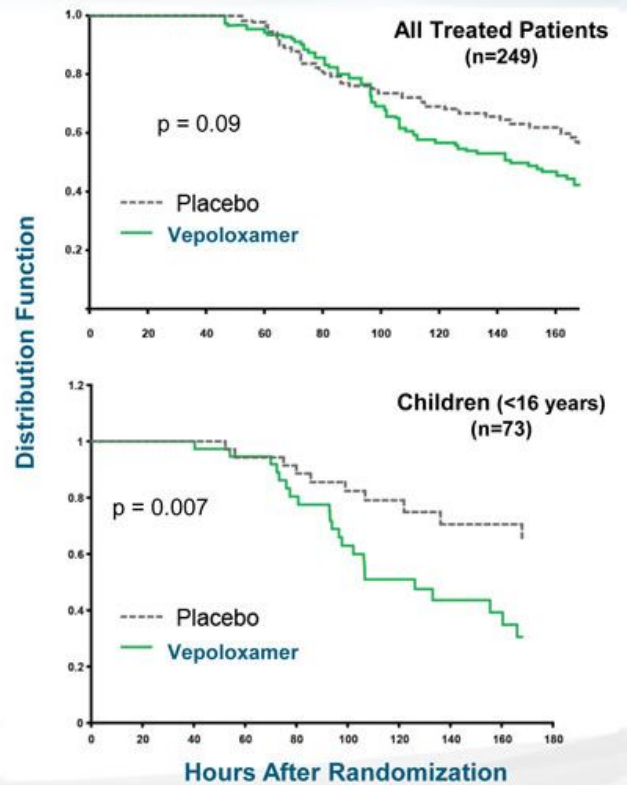
<sup>±</sup> Excludes patients who had drug administration errors or incomplete pain assessments (16), who withdrew consent (2) and who withdrew because of injection site pain after 15 minutes of infusion. Subjects were excluded equally (n=9) between poloxamer 188 and placebo.

<sup>±±</sup> Proportional hazards model adjusted for baseline pain.

Source: Blood, September 1, 1997 – Vol 90, No. 5  
\* Vepoloxamer is purified poloxamer 188

# Phase 3 Study

- Randomized, double-blind, placebo-controlled, multi-center study of vepoloxamer in 350 patients with SCD.
- Time-to-event analysis showed consistent trend in support of earlier crisis resolution.
- However, prior sponsor **ended enrollment at only 255 patients** due to capital constraints, lowering statistical power, and,
- The observation period **was specified to be only 168 hours**, eliminating observation of any late-treatment differences (e.g. “right censoring”).



# EPIC: Pivotal Phase 3 Study Design

- **Randomized, Double-Blind, Placebo-Controlled, Multicenter**
  - 388 patients
  - Standard of care +/- vepoloxamer
- **Primary Efficacy Assessment**
  - Duration of crisis (transition off IV analgesia)
  - No assessment of subjective pain scores
- **Secondary Efficacy Assessments**
  - Re-hospitalization for crisis within 14 days
  - Occurrence of acute chest syndrome
- **Power**
  - 85% power to detect a 24-hour difference ( $p=0.01$ )
  - 90% power to detect a 16-hour difference ( $p=0.05$ )
- **Open-label extension**
  - Expands safety database with repeat exposures to vepoloxamer
  - Will enroll patients who have completed treatment on EPIC

# EPIC Success Factors

- **Enrollment on-track. Top-line data expected Q1 2016**
  - ~70 sites opened, >50 within the U.S.
  - >33% enrolled as of Jan 6.
  
- **Most Advanced New Drug in SCD**
  - Potential to be first approved drug to treat an ongoing vaso-occlusive crisis
  - Substantial head start versus other new drugs in development for SCD
  
- **Positive Factors for Regulatory Decision-Making**
  - Significant unmet need
  - Fast Track designation
  - Orphan Drug designation
  - Healthcare disparity
  - FDA Div of Hematology Products: “development of new SCD treatments a top priority”

# Acute Limb Ischemia

(Vepoloxamer In Combination with Thrombolytics)



# Overview of Occlusive Arterial Disease

- A progressive circulatory problem in which obstructed arteries reduce blood flow to tissues
  - Thrombolytic agents (tPA) are used to treat acute complications
  - Significant morbidity and mortality

Acute Ischemic Cerebrovascular Infarction  
(stroke)

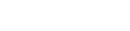
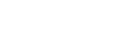
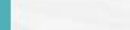
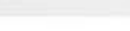
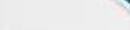


Acute Myocardial Infarction  
(heart attack)



Peripheral Arterial Disease

- Intermittent Claudication
- Critical Limb Ischemia
- Acute Limb Ischemia

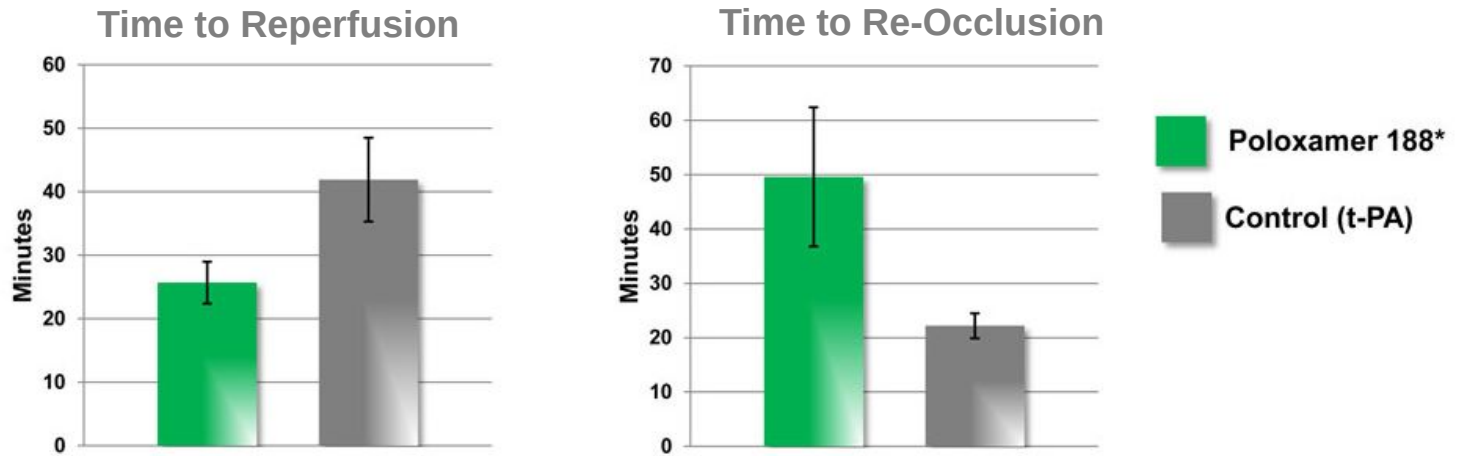


Development Strategy:

- Develop initially in ALI
- Expand into other AD markets

# Improved t-PA Effectiveness

Animals randomized to t-PA (n = 10) or t-PA + poloxamer 188\* (n = 10)



# Synergy with Thrombolytics in Heart Attack

Parameter	Poloxamer 188*	Control	Difference	p Value N=114
Myocardial Infarct Size (median)	16%	26%	38% reduction	0.031
Myocardial Salvage (median)	13%	4%	125% increase	0.033
Ejection Fraction (median)	52%	46%	13% improvement	0.020
Incidence of Reinfarction	1%	13%	92% reduction	0.016

Source: Circulation 1996; 94: 298-307  
\*Vepoloxamer is purified poloxamer 188

# Phase 2 Study in ALI

- **Clinical Proof-of-Concept Study**
  - **Biomarkers**
  - **Clinical outcomes**
- **Study Design**
  - **Randomized, double-blind, and active-controlled (t-PA)**
  - **t-PA +/- low or high dose vepoloxamer**
  - **60 subjects (20 per arm)**
- **Timing**
  - **Completion of enrollment anticipated 2H 2016**
- **ALI data can be supportive of clinical development in stroke**
  - **Embolic stroke preclinical studies initiated**

# Heart Failure

# Overview of Heart Failure

- **Chronic condition characterized by decreasing heart function**
  - Heart cannot pump enough blood to meet the body's needs
- **Significant Unmet Medical Need**
  - Leading healthcare cost in U.S. and Europe
- **Substantial and Growing Market Opportunity**
  - > 5 million individuals with heart failure in the U.S.
- **Acute Decompensation**
  - Each decompensation event contributes to worsening heart failure and damage to vital organs, decreasing survival probability following the next event
- **Vepoloxamer**
  - Membrane-sealant activity may restore weakened cardiac cell membranes, minimizing calcium overload injury
  - Durable effect may indicate a direct improvement in cardiac function

# Heart Failure Development Rationale

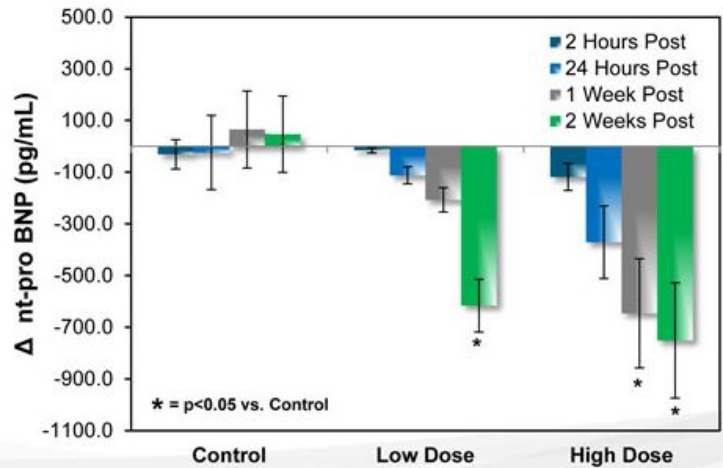
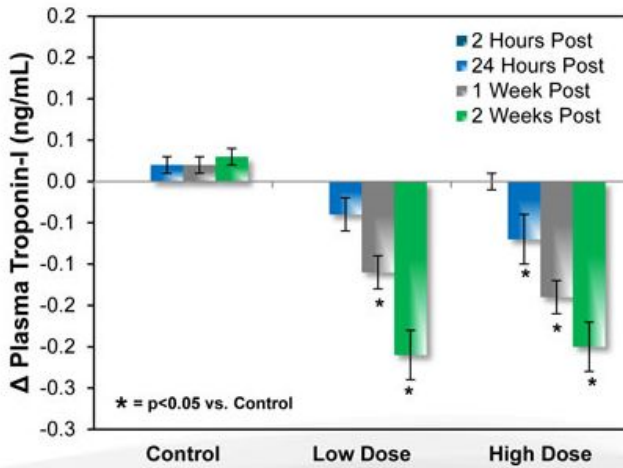
**In heart failure, elevated wall tension impairs lipid flow and membrane repair. This results in calcium influx and cardiac troponin leak.**



**Vepoloxamer re-seals membranes and reduces membrane tensions, enabling lipid flow and facilitating membrane repair, thus reducing cardiac troponin and calcium overload damage.**

# Non-clinical Model of Heart Failure

- A single, 2h infusion improved hemodynamic parameters (LVEF, CO) and biomarkers correlated with clinical outcomes (troponin, NT-proBNP)
- A potentially novel mechanism, compatible with existing treatments
- Conducting repeat dose non-clinical model; data anticipated Q1 2015
- Planning to initiate Phase 2 in acute decompensated HF in Q2 2015





# AIR001

**(sodium nitrite) inhalation solution**

# AIR001

- **AIR001 is nitrite for intermittent inhalation (via nebulizer)**
  - **Beneficial effects include dilation of blood vessels and reduced inflammation**
  - **Positive hemodynamic effects; reductions observed in:**
    - pulmonary vascular resistance
    - pulmonary capillary wedge pressure
    - right atrial pressure
  
- **AIR001 is being developed for Heart Failure with Preserved Ejection Fraction (HFpEF)**
  - **Responsible for ~50% of heart failure hospitalizations**
  - **80% develop Pulmonary Hypertension**
  - **Leads to shortness of breath, dizziness, fainting, leg swelling, etc.**
  - **No approved medications**

# AIR001 Clinical Data

## ➤ Three Phase 1 studies:

- Established MTD and safe dose level
- Confirmed conversion of nitrite to nitric oxide (NO)
- Acute improvements in hypoxia-induced pulmonary hypertension
- No drug-drug interaction with sildenafil

## ➤ One Phase 2 study:

- Well-tolerated, with no treatment-related serious adverse events
- All doses showed improvement in median pulmonary vascular resistance (PVR) & median distances obtained in the 6-minute walk test
- Methemoglobin levels remained normal (< 1.5%)

## ➤ Safety data in 124 healthy volunteers and patients with various forms of pulmonary hypertension (well-tolerated)

# AIR001 Clinical Development Plan

- **Two institution-sponsored Phase 2a studies underway at Mayo Clinic & University of Pittsburgh**
  - Evaluating the hemodynamic effects of AIR001 in both acute and exercise conditions and change in submaximal oxygen consumption before and after AIR001 versus placebo
- **Third institution sponsored Phase 2a study to begin later this year**
  - Designed to compare hemodynamic benefits versus the formation of methemoglobin comparing intravenous nitrite to AIR001
- **Preliminary data anticipated 2H 2015**
- **If positive, conduct Phase 2b proof-of-concept**

# Upcoming News & Events

Report data from nonclinical study of vepoloxamer in embolic stroke	Q1 '15
Report data from nonclinical study of vepoloxamer in heart failure	Q1 '15
Initiate enrollment in EPIC extension study (repeat exposure) (EPIC-E)	1H '15
Initiate enrollment in Phase 2 study of vepoloxamer in heart failure	Q2 '15
Complete enrollment in EPIC study	Q4 '15
Report data from Phase 2a study of AIR001 in HFpEF	2H '15
Report interim safety from Phase 2 study of vepoloxamer in heart failure	2H '15
Report EPIC study top-line data	Q1 '16
Complete enrollment in Phase 2 study of vepoloxamer in ALI	2H '16

# MSTX Financial Overview

- **Cash/investments at 12/31/14: \$57 million**
- **Market capitalization: ~\$76 million\***
- **Shares outstanding: ~159 million\***
- **Average daily volume (3 mo): ~1,000,000\***
- **No debt**

# Mast Investment Summary

- **A Leader in Areas of Significant Unmet Need (Vepoloxamer)**
  - **Sickle Cell Disease: Most advanced new drug in development**
  - **Arterial Disease: Ongoing Phase 2 in ALI with opportunity in stroke**
  - **Heart Failure: Phase 2 study to begin Q2 2015**
  
- **AIR001**
  - **Phase 2 program in heart failure with preserved ejection fraction**
  - **Two institution-sponsored phase 2a studies ongoing; third planned for later this year**
  
- **Multiple clinical readouts anticipated within 15 months**
  - **Sickle cell: Phase 3 top-line**
  - **Heart failure: Phase 2 (interim safety data)**
  - **HFpEF: Phase 2a studies**