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): June 25, 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, CA	**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 (see General Instructions A.2. below):

☐ 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 Exhibits 99.1 and 99.2 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.

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 Exhibits 99.1 and 99.2 attached hereto, the Company makes no admission as to the materiality of any information in this report. The information contained in Exhibits 99.1 and 99.2 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 24, 2015, Quarterly Report on Form 10-Q filed on May 11, 2015, 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 Exhibits 99.1 and 99.2 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, arterial disease, and heart failure, and AIR001 in heart failure with preserved ejection fraction, as well as the timing of activities and events 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 clinical or nonclinical studies prior to initiation of a planned clinical study; 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 and may never 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 or that the use or manufacture of its products or product candidates infringe the proprietary rights of others; 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.

Date: June 25, 2015

By: */s/ Brandi L. Roberts*
Brandi L. Roberts
Chief Financial Officer and Senior Vice President

Exhibit Index

Exhibit Number	Description
99.1	Mast Therapeutics, Inc. corporate presentation, June 25, 2015
99.2	Summary of the development history of vepoloxamer, June 2015

MAST THERAPEUTICS, INC.

NYSE MKT: MSTX

Corporate Overview

June 25, 2015

Forward-Looking Statements

This presentation includes forward-looking statements about our business prospects, financial position, and development of vepoloxamer 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 24, 2015.

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

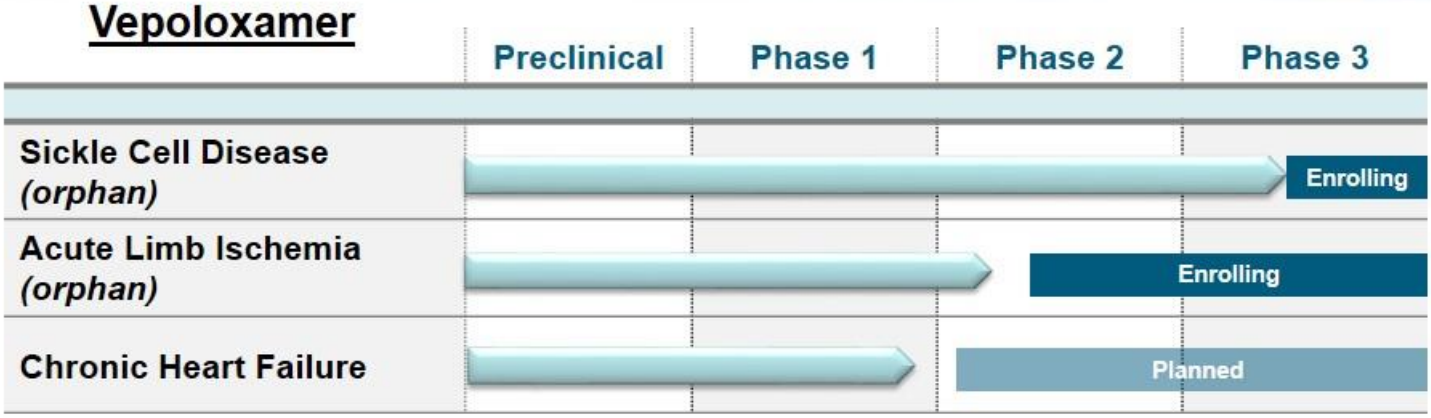
- **Publicly-traded biopharmaceutical company based in San Diego**

- **Developing vepoloxamer (MST-188) for:**
  - **Rare ("orphan") diseases:**
    - **Sickle Cell Disease**
    - **Acute Limb Ischemia**
  - **Large market opportunities:**
    - **Heart Failure**
    - **Stroke**

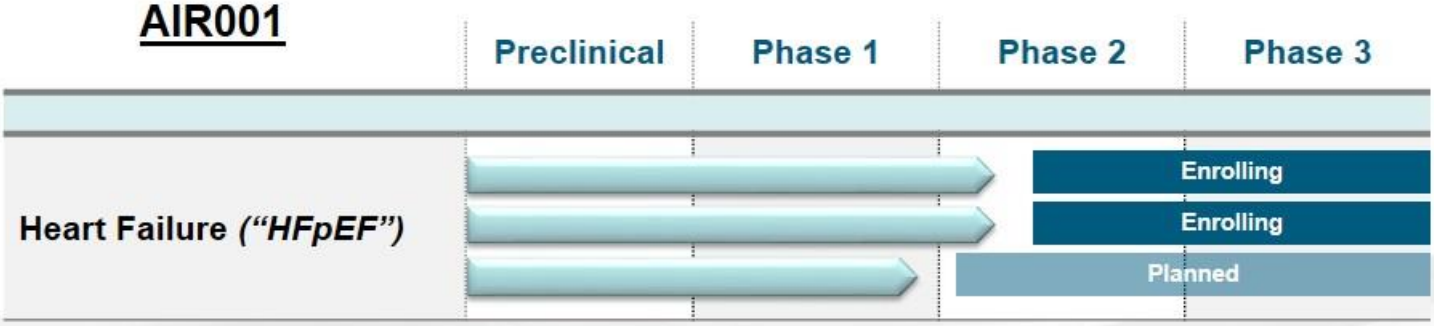
- **Developing AIR001 for:**
  - **Heart failure with preserved ejection fraction**
  - **Commercially complementary to vepoloxamer**

Product Candidate Pipeline

Vepoloxamer



AIR001



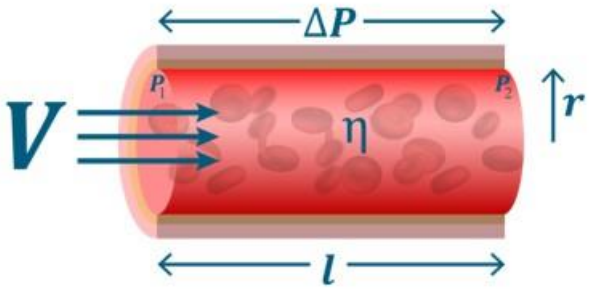
Lead Program

Vepoloxamer

Vepoloxamer: A Biophysical Agent

Poiseuille's Law describes Newtonian flow

$$V = \frac{\pi}{8} \times \frac{1}{l} \times \frac{1}{\eta} \times \Delta P \times r^4$$



with V = flow (volume/time)

l = length of the capillary

η = viscosity of the media

ΔP = pressure drop over the length

r = radius of the capillary

- **Want lower viscosity?**
  - **Reduce friction by lowering adhesion and improving the deformability of cells**
- **How?**
  - **Reduce surface tension with *vepoloxamer***

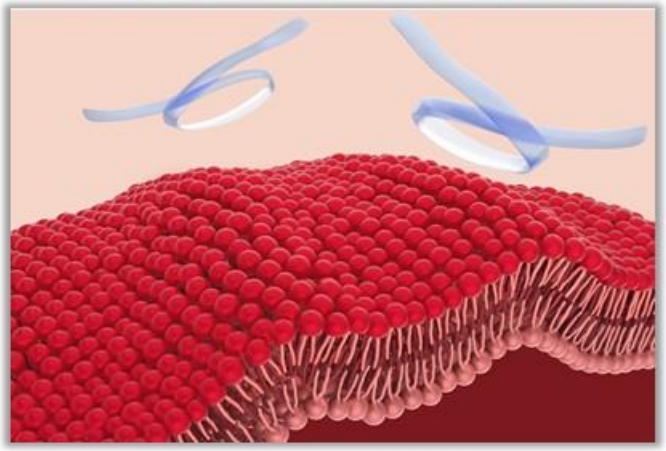
Vepoloxamer Overview

API Structure:	$HO-(CH_2CH_2O)_{79}-(CH_2CHO)_{30}-(CH_2CH_2O)_{79}-H$ $\vert$ CH_3
CMC:	• Large, synthesized polymer with extraction process to remove undesirable (toxic) components • Composition of matter claims pending
Administration:	• IV infusion
ADME:	• Rapidly and predominantly cleared by kidneys (4-8h) • Ether linkages cannot be cleaved; no drug metabolites

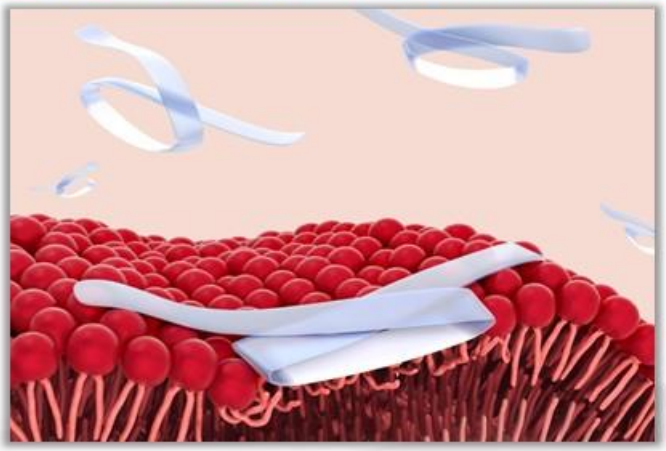
Vepoloxamer Mechanism of Action

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

No Affinity for Healthy Cell Membranes…



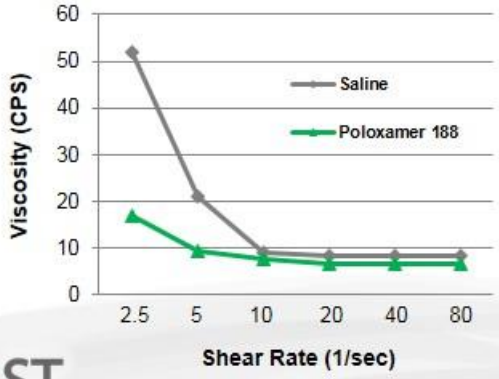
But Adheres to Damaged Cell Membranes



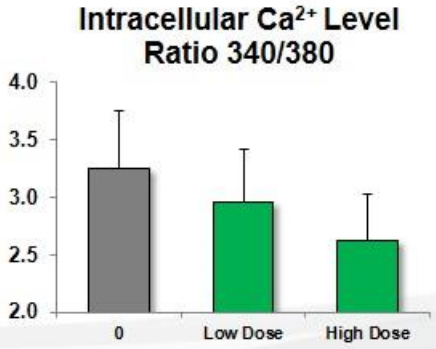
Vepoloxamer Pharmacodynamics

Vepoloxamer adheres to hydrophobic domains on cells and lowers surface tensions

Viscosity is reduced
Lowers adhesion
Improves flow



Membranes are sealed
Cell integrity maintained
Ca2+ influx reduced



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Vepoloxamer Pharmacodynamics

Vepoloxamer adheres to hydrophobic domains on cells and lowers surface tensions

Viscosity is reduced
Lowers adhesion
Improves flow

Membranes are sealed
Cell integrity maintained
Ca2+ influx reduced

Sickle Cell Disease:	**Less cell adhesion, reduced hemolysis**
Acute Limb Ischemia:	**Faster thrombolysis, less reperfusion injury**
Heart Failure:	**Lower viscosity, more membrane repair**

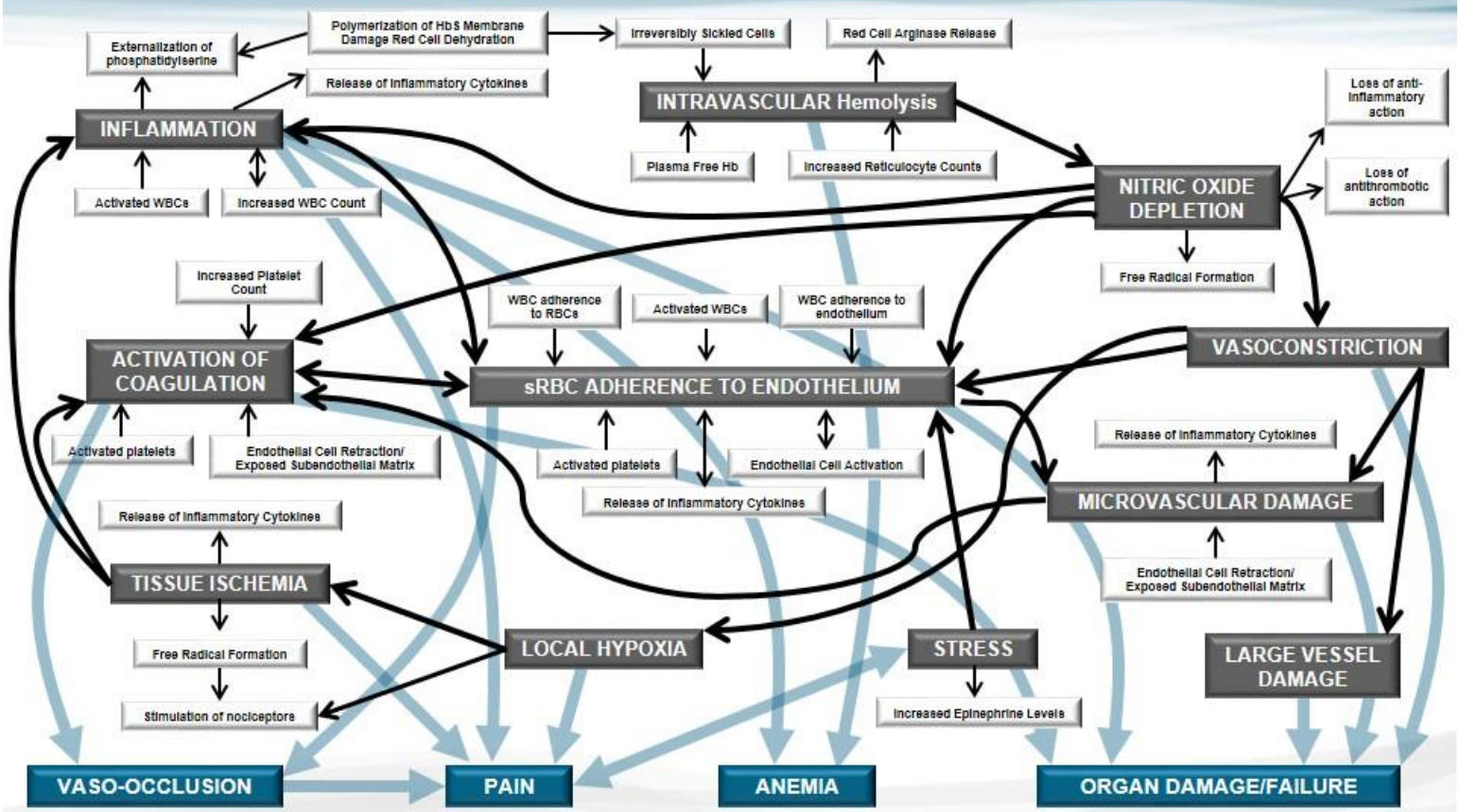
Sickle Cell Disease

Objective ***Improve blood flow and shorten the duration of crisis***

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"**
  - Exceedingly 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)

A More Realistic Representation of SCD (many points of intervention)



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Source: Curr Probl Pediatr Adolesc Health Care 2006; 36: 346-376 (1538-5442)

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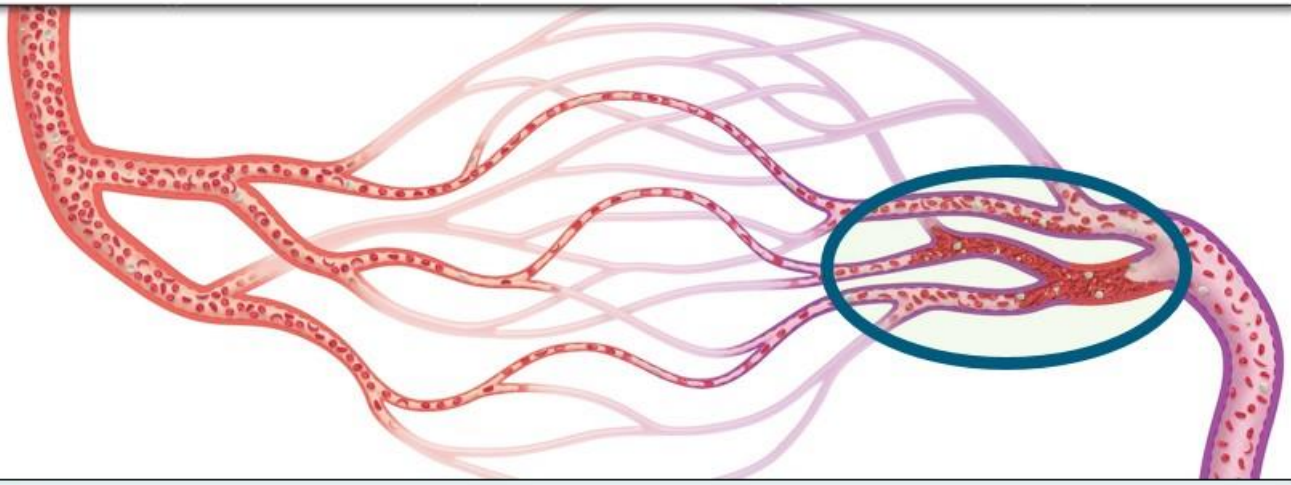
Role of Vepoloxamer in Sickle Cell Disease

Vaso-Occlusive Crisis:

- Adhesion of poorly-deformable, "sticky" cells to endothelium and to each other leads to vessel obstruction
- Occluded RBC's cannot deliver oxygen, leading to ischemia, pain, organ damage

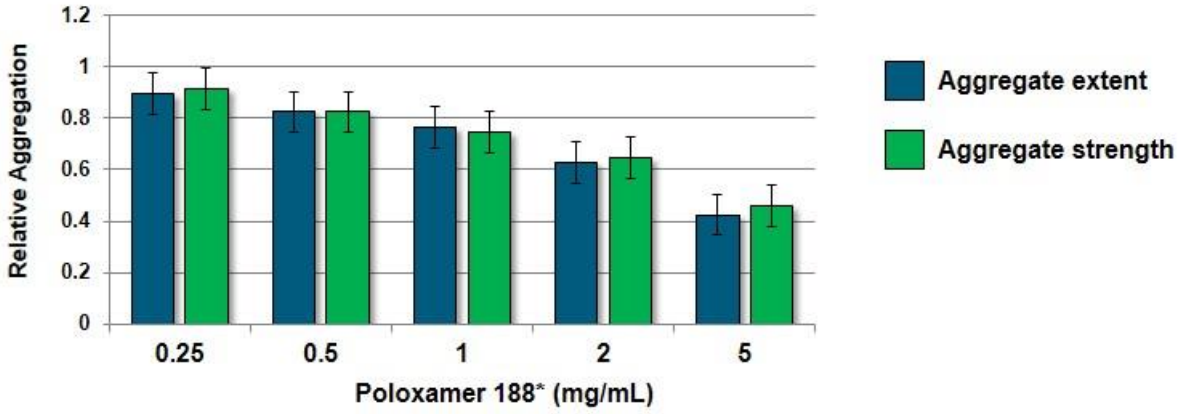


Vepoloxamer:

- Lowers viscosity, reduces adhesion of cells to endothelium, lowers RBC aggregation, improves RBC deformability and restores blood flow

Vepoloxamer Reduces RBC Aggregation (normal volunteers)

Dose-dependent effect on red blood cell aggregation

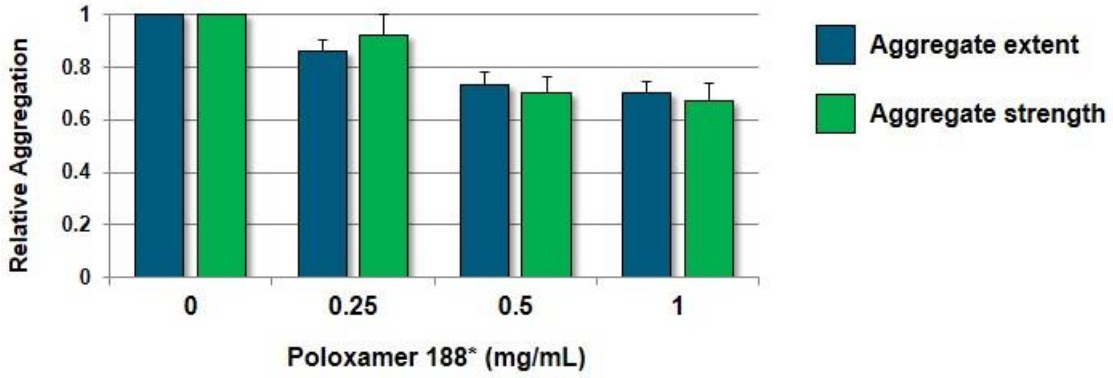


- The effect of five concentrations of poloxamer 188* on RBC aggregation was determined using a Myrenne aggregometer.
- Results represent the mean of samples from 20 healthy volunteers relative to PBS controls. (Meiselman, et. al.)

*Vepoloxamer is purified poloxamer 188

Vepoloxamer Reduces RBC Aggregation (sickle cell patients)

Dose-dependent effect on sickle cell red blood cell aggregation

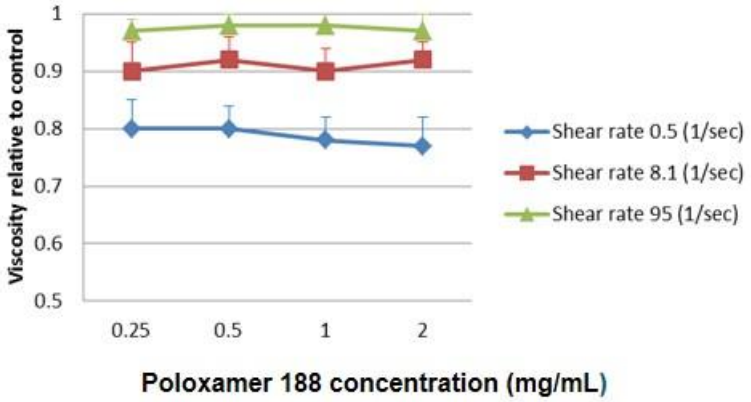


- The effect of poloxamer 188 on sickle cell RBC aggregation determined by a Myrenne aggregometer
- Results represent the mean from 11 patients relative to PBS controls (Meiselman, et al.)

*Vepoloxamer is purified poloxamer 188

Vepoloxamer Decreases Blood Viscosity Under Low Shear Rates

Poloxamer 188* decreased viscosity of sickle cell whole blood



Poloxamer 188 concentration (mg/mL)

- Poloxamer 188 added to whole blood (40% hematocrit) and viscosity measured using a Contraves viscometer at 3 shear rates.
- Results represent the mean of samples from 11 SCD patients relative to PBS controls. (Meiselman, et al.)

*Vepoloxamer is purified poloxamer 188

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Vepoloxamer Effect on Sickle Cells

Lower surface tension improves flow and deformability (video)

Before vepoloxamer **After vepoloxamer**

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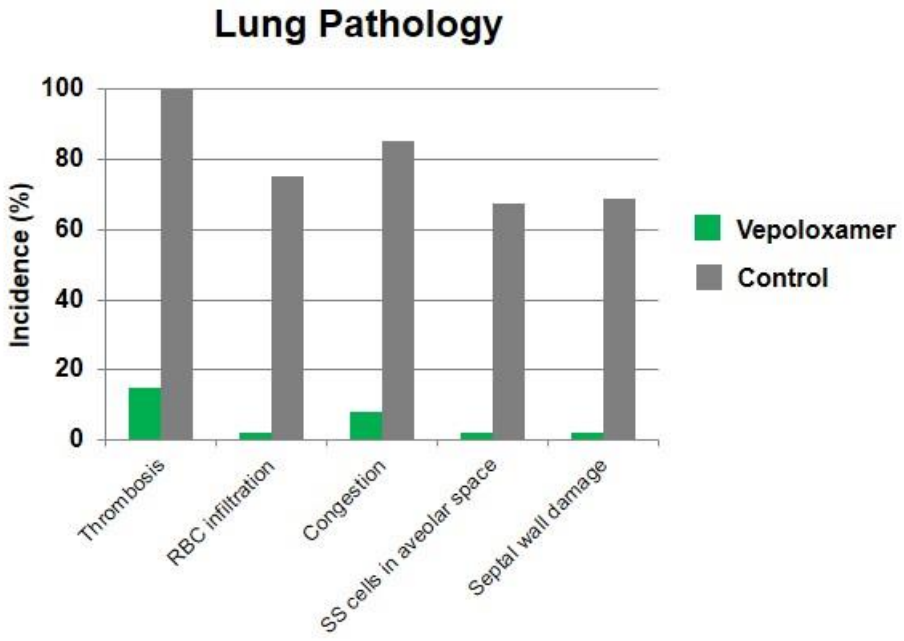
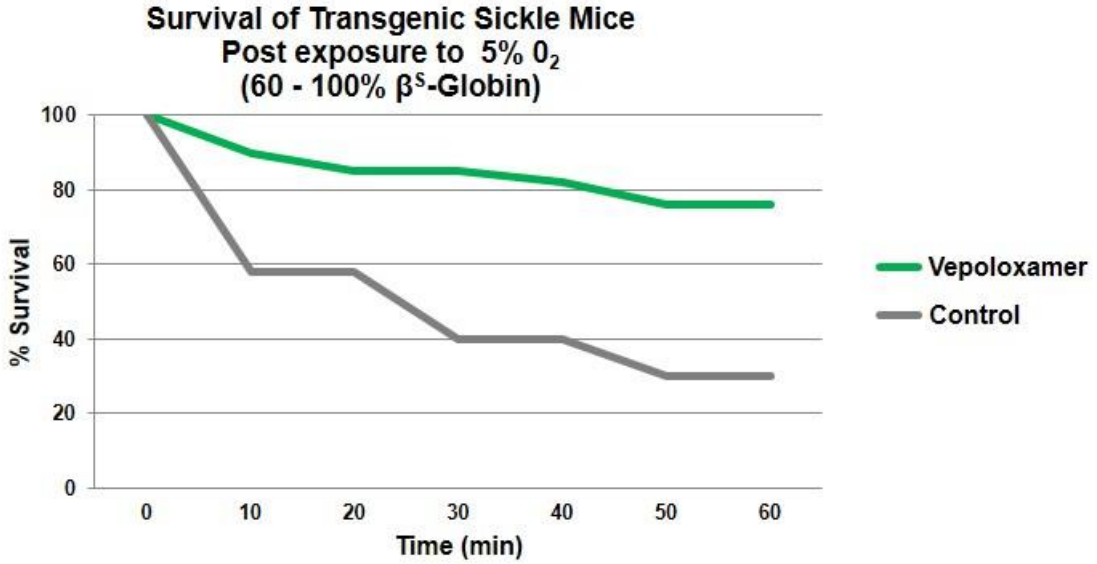
Vepoloxamer Reduced Organ Pathology in Transgenic Sickle Mice



Lung pathology was compared in transgenic mice pretreated with either vepoloxamer (400 mg/kg) or saline and subject to hypoxia (5% O_2). (Asakura, et al.)

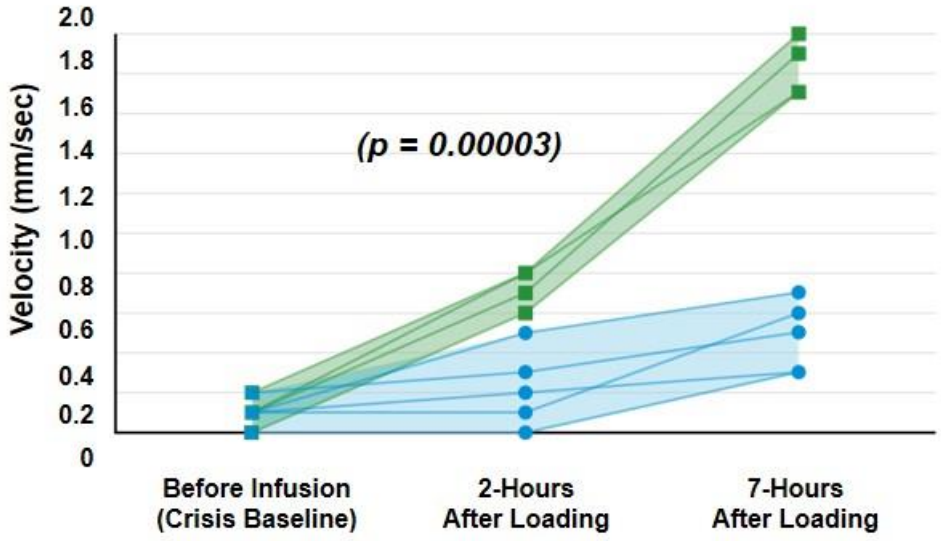
Vepoloxamer Increased Survival in Transgenic Sickle Mice



Transgenic mice pretreated with either vepoloxamer (400 mg/kg) or saline, subject to hypoxia (5% O_2), and monitored for survival. (Asakura, et al.)

Vepoloxamer Improves Blood Flow

Vepoloxamer improved microvascular blood flow in SCD patients during vaso-occlusive crisis



Red cell velocity (mm/s) measured by video microscopy in nine sickle cell patients with vaso-occlusive crisis.

Source: J. Investig. Med. 2004;52(6):402-6

Phase 2 Study

Randomized, double-blind, placebo-controlled, multi-center study in SCD patients hospitalized for vaso-occlusive crisis

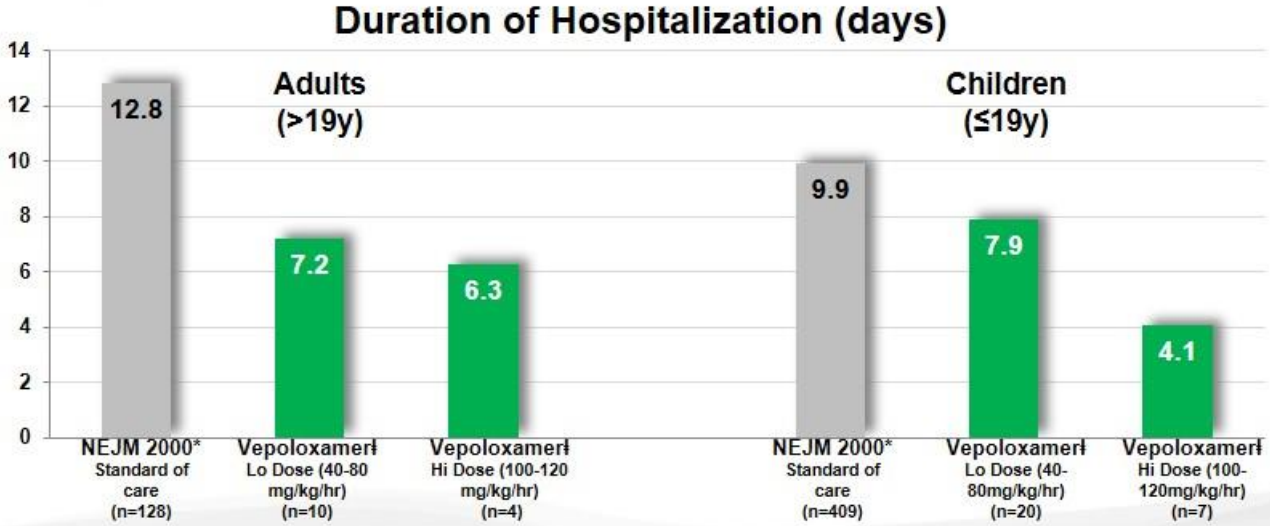
	Subjects Who Received Full Dose±		
	Poloxamer 188* (n=18)	Placebo (n=13)	*p* value±±
Duration of Crisis	44 hours	80 hours	0.025
Duration of Hospitalization	5 days	7 days	0.111
Total Analgesic Use	34mg	145mg	0.045
Parenteral Analgesic Use	27mg	133mg	0.022

± 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.
±± Proportional hazards model adjusted for baseline pain.
* Vepoloxamer is purified poloxamer 188

Source: Blood, September 1, 1997 – Vol 90, No. 5

Acute Chest Syndrome Clinical Study

- **Acute Chest Syndrome (ACS)**
  - **Serious complication of SCD that results in prolonged hospitalizations**
  - **A leading cause of death in SCD patients**
- **Vepoloxamer reduced duration of hospitalization in SCD patients with ACS compared to standard of care**



*Source: NEJM, June 22, 2000, Vol 342, No 25
‡ Data on file

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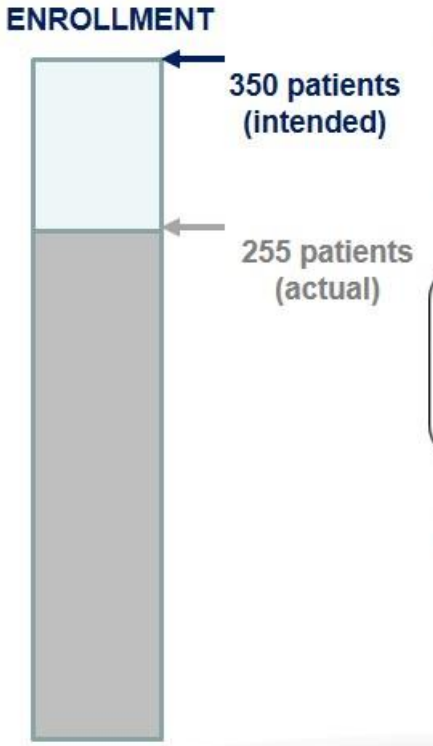
Prior Sponsor's Phase 3 Study



- First large trial in sickle cell crisis ever conducted
- Flawed endpoint selection and premature termination led to loss of power
- Responder's analysis highly informative:
  - All ages: 52% vs. 37% (n=249, p=0.02)
  - Under 16y*: 60% vs. 28% (n=73, p=0.009)
- <u>Lessons learned</u> for Mast Phase 3 study:
  - Vepoloxamer has activity in SCD
  - Incorporate FDA, expert, and patient input
  - Use a clinically-relevant, objective endpoint
  - Anticipate and address data loss

Average age of patients in Mast's Phase 3 trial (EPIC) as of April 2015: 14 years

Source: JAMA, November 17, 2001 – Vol 286, No. 17

Current Phase 3 Study "EPIC" (Mast study)

- **Double-Blind, Placebo-Controlled, Multicenter**
  - 388 patients, randomized 1:1 (standard of care +/- vepoloxamer)
- **Primary Endpoint:**
  - Duration of crisis from randomization to last dose of parenteral opioid
    - Clinically relevant (no IV meds = readiness for discharge)
    - Sensitive data collection (patient-controlled analgesia device)
    - Reduction in data loss (PCA device)
- **Secondary Endpoints and Other Assessments:**
  - Re-hospitalization for crisis within 14 days
  - Occurrence of acute chest syndrome
  - Duration of hospitalization
  - Biomarkers
- **Power Calculations**
  - 90% power to detect a 16-hour difference (p=0.05), CV >50%
  - 85% power to detect a 24-hour difference (p=0.01), CV >50%

EPIC Success Factors

- **Enrollment on-track**
  - Enrollment surpassed halfway mark in April 2015
  - Top-line data anticipated Q1 2016
- **Most Advanced New Drug in SCD**
  - Potential to be 1st drug ever approved to treat on-going vaso-occlusive crisis
  - Substantial head start versus other drugs in development
- **Considerations for Regulatory Decision-Making**
  - Significant unmet need – standard of care unchanged for years
  - Increased reliance on disease experts in rare diseases
  - Support among medical / advocacy communities
  - Fast Track designation
  - Orphan Drug designation
  - Healthcare disparity concerns
  - Supportive clinical studies: QT and repeat-administration

SCD Market Opportunity

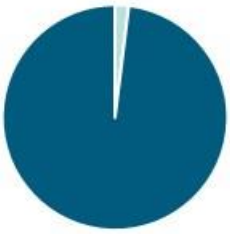
United States
- Approximately 100,000 hospitalizations annually
- ~50% of events occur in just 16 metropolitan areas
- Effective coverage with small, targeted field force

Europe
- Approximately 40,000 patients
- ~50% of patients reside in 2 cities:
  - Paris and London

Vepoloxamer Market Opportunity

Approximately 100,000 Hospitalizations Annually for Crisis (U.S.)

Bone Marrow Transplant (1%)



Gene Therapy (<25%*)

Crisis Intervention (100%)

- **Addressable market for vepoloxamer is substantially larger than for current curative approaches (e.g. not limited to just "severe" patients)**

** Estimated research analyst consensus (range 5-25%)*

Vepoloxamer Positioned for Success in SCD

- **Novel Therapy for Rare Disease with High Unmet Need**
  - Unique mechanism
  - Orphan Drug Designation (U.S. and EU)
  - New composition of matter provisional patent application
  - No approved therapies available for crisis intervention
- **First-To-Market Advantage**
  - Clinical development >2 years ahead of nearest competitor
- **Concentrated, In-Patient Setting**
  - 50% of U.S. patients live in just 16 metropolitan areas
  - 80% public payer (NTAP, DRG, DSH strategies)
- **Pharmacy Director Support**
  - Based on qualitative market research, perceived as a 4.4 out of 5; a "breakthrough medical innovation"

Arterial Disease

Vepoloxamer in Combination with Thrombolytics

- ***Acute Limb Ischemia***
- ***Stroke***

Objective ***Accelerate time to thrombolysis and restore tissue perfusion***

Overview of Arterial Disease

- **A progressive circulatory problem in which obstructed arteries <u>reduce blood flow</u> 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:
- Evaluate initially in ALI
- Expand into other markets

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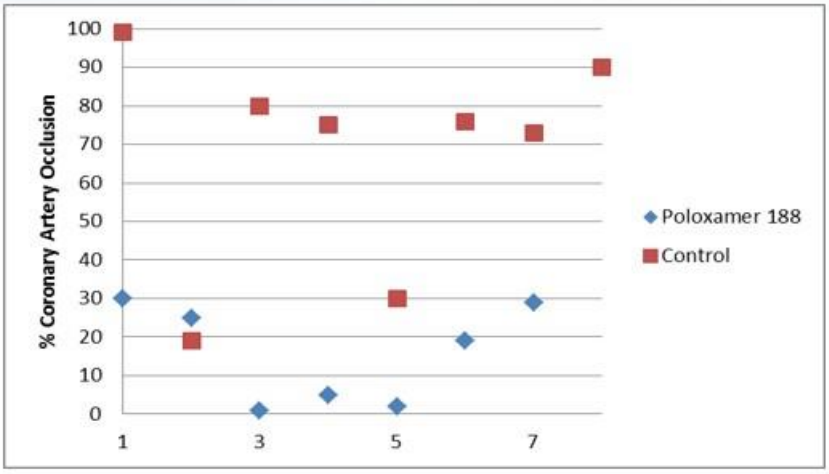
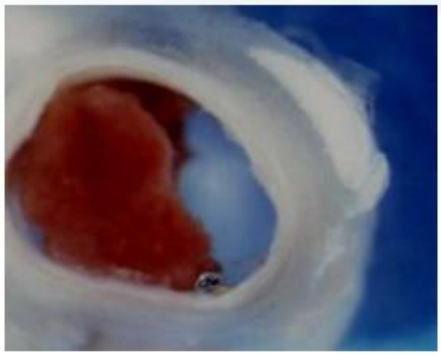
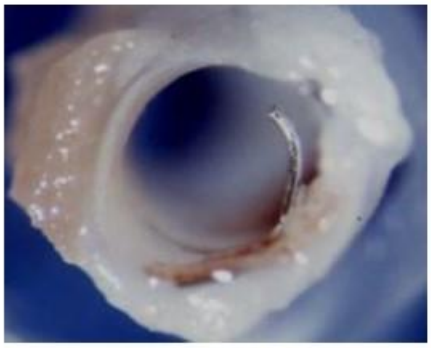
Vepoloxamer is Antithrombotic







- Juvenile pigs were subjected to balloon angioplasty using excessive pressure and placement of a wire stent
- Animals were randomized to either heparin plus P188* (50 mg/kg as a bolus followed by a constant infusion of 25 mg/kg/hr) or a comparable volume of Heparin in normal saline ($p < 0.01$ Control vs P188).

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Vepoloxamer is purified poloxamer 188 (P188)

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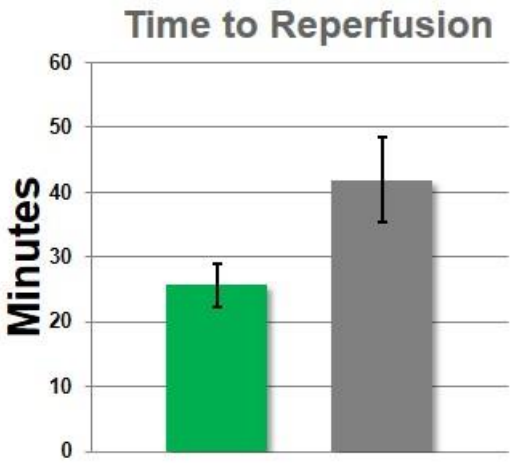
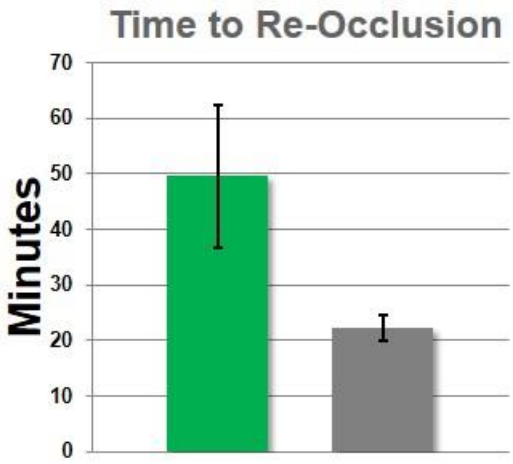
Accelerated tPA Activity

Animals subjected to femoral thrombotic occlusion randomized to tPA or tPA + poloxamer 188* (n=10), then monitored for blood flow





Poloxamer 188

Control (tPA)

*Vepoloxamer is purified poloxamer 188

Source: Data on file

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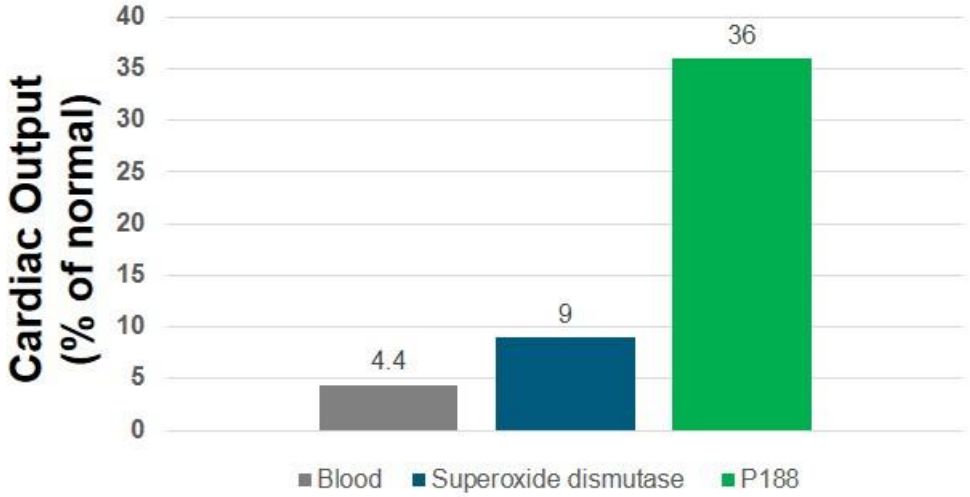
Effect on Reperfusion Injury

Poloxamer 188* protected against no-reflow and reperfusion injury



- Rat hearts perfused with human packed red cells and heparin subjected to 90% ischemia followed by 10 min reperfusion.

*Vepoloxamer is purified poloxamer 188

Synergy with Thrombolytics in Heart Attack Clinical Trial

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

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

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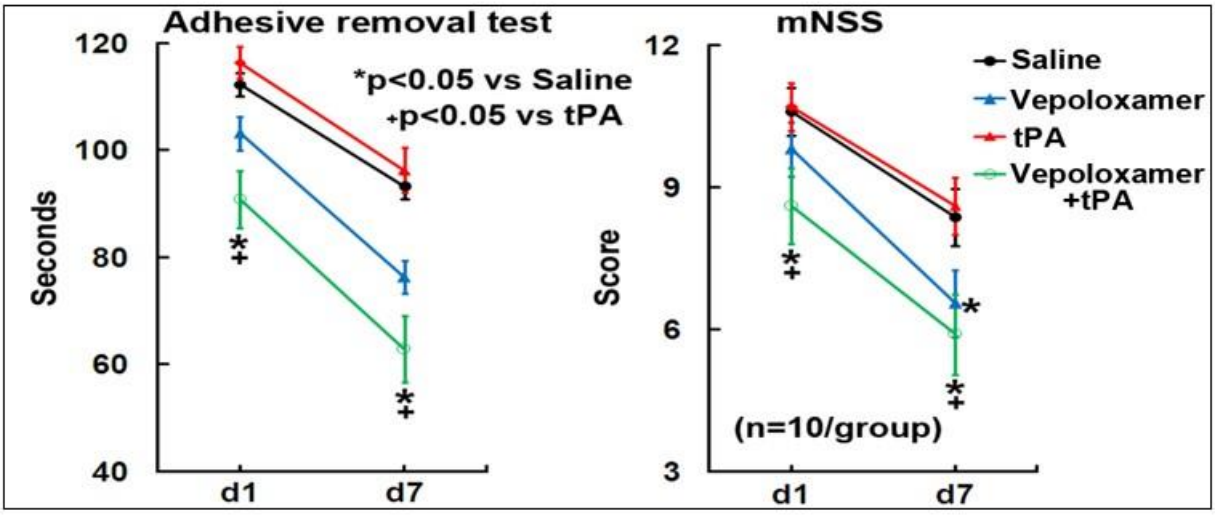
Phase 2 Study in Acute Limb Ischemia

- **Clinical Proof-of-Concept Study**
  - Biomarkers
  - Clinical outcomes
- **Study Design**
  - Dose-finding, randomized, double-blind, and active-controlled
  - tPA +/- low or high dose vepoloxamer
  - 60 subjects (20 per arm)
- **Timing**
  - Completion of enrollment anticipated 2H 2016
- **Data can be supportive of *clinical development in stroke***

Vepoloxamer in Stroke Model

Vepoloxamer alone or in combination with tPA improved neurological outcomes



- Vepoloxamer alone or in combination with tPA reduced neurological functional deficits following middle cerebral artery occlusion (MCAO) compared with animals treated with saline or tPA alone
- Note: tPA administration occurred 4 hours following MCAO

Conducted by Michael Chopp, Ph.D.
Henry Ford Health System

Data presented at 2015 International Stroke Conference

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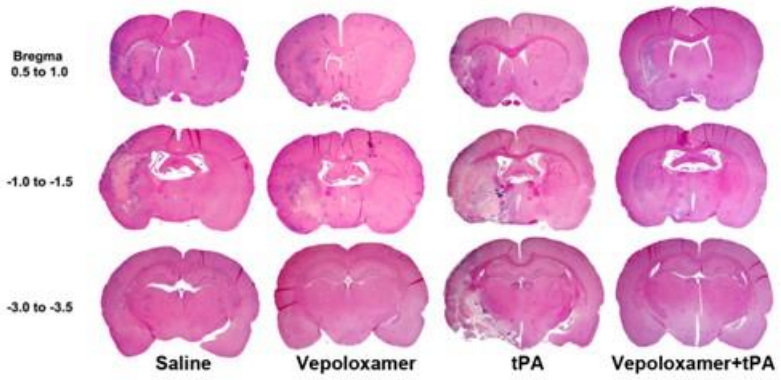
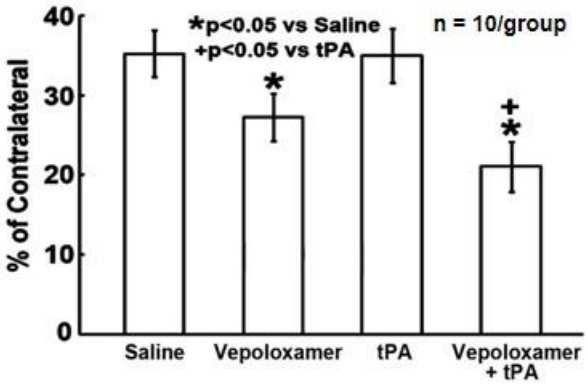
Vepoloxamer in Stroke Model

Vepoloxamer alone or in combination with tPA reduced lesion volume





- Panels are H&E stained coronal sections obtained from representative rats treated with saline, vepoloxamer alone, tPA alone, and the combination of vepoloxamer and tPA following MCAO.
- Bar graph shows that treatments with vepoloxamer alone and in combination with tPA significantly reduced lesion volume compared to ischemic rats treated with saline and tPA monotherapy.

Conducted by Michael Chopp, Ph.D.
Henry Ford Health System

Data presented at 2015 International Stroke Conference

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Heart Failure

(Chronic and Acute)

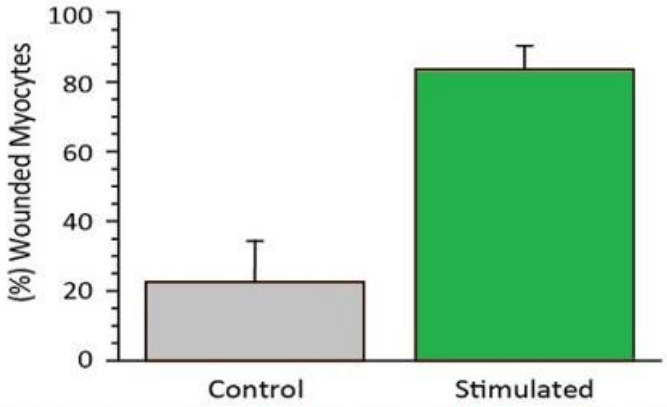
Objective ***Preserve heart cells and improve cardiac function***

Overview of Heart Failure

- **Chronic condition characterized by decreasing heart function**
  - Heart cannot pump enough blood to meet the body's needs
  - Primary clinical symptom is difficulty breathing (fluid in lungs – "congestive")
- **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.
  - $21 billion of direct costs for heart failure in the U.S. in 2012
- **Vepoloxamer**
  - Membrane-sealing activity may restore weakened cardiac cell membranes, minimizing calcium overload injury
  - Durable effect may indicate a direct improvement in cardiac function

Background: Membrane Injury and Repair in Cardiomyocytes

- **Membrane injury and repair is a constitutive event in healthy cells, especially those subjected to increased wall tensions from mechanical stress, such as cardiomyocytes.**
- **In healthy rat hearts, adrenergic stimulation increases myocyte wounding 3-fold.**

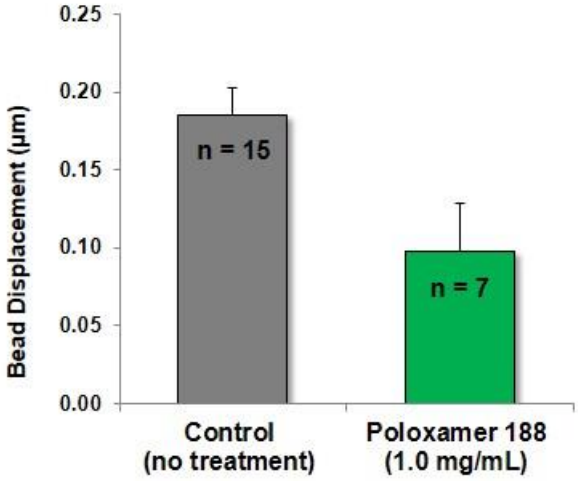


- Frozen sections of normal rat heart were immunostained to reveal the distribution of serum albumin (wound marker).
- Quantitative image analysis indicated that an average of 25% of myocytes contained cytosolic serum albumin (i.e., had suffered a plasma membrane wound). Frequency increased approximately 3-fold after β-adrenergic stimulation (0.5ug/kg isoproterenol). *p<0.001

(Circ Res 1995;76:927-934)

Development Rationale in Heart Failure

- **Elevated wall tension in a stressed heart impairs membrane repair, leading to calcium influx and cardiac troponin leak.**
- **Vepoloxamer seals membranes and reduces surface tension, reducing calcium damage and preserving cells.**
- **Vepoloxamer led to statistically significant improvements in hemodynamic parameters (LVEF, CO) and biomarkers (troponin, NT-proBNP) in model of heart failure.**



Effect of poloxamer 188* on cell surface tension (bead displacement) using membrane tethered beads. Cells treated with 1.0 mg/mL poloxamer 188, had significantly reduced membrane tension.

*Vepoloxamer is purified poloxamer 188

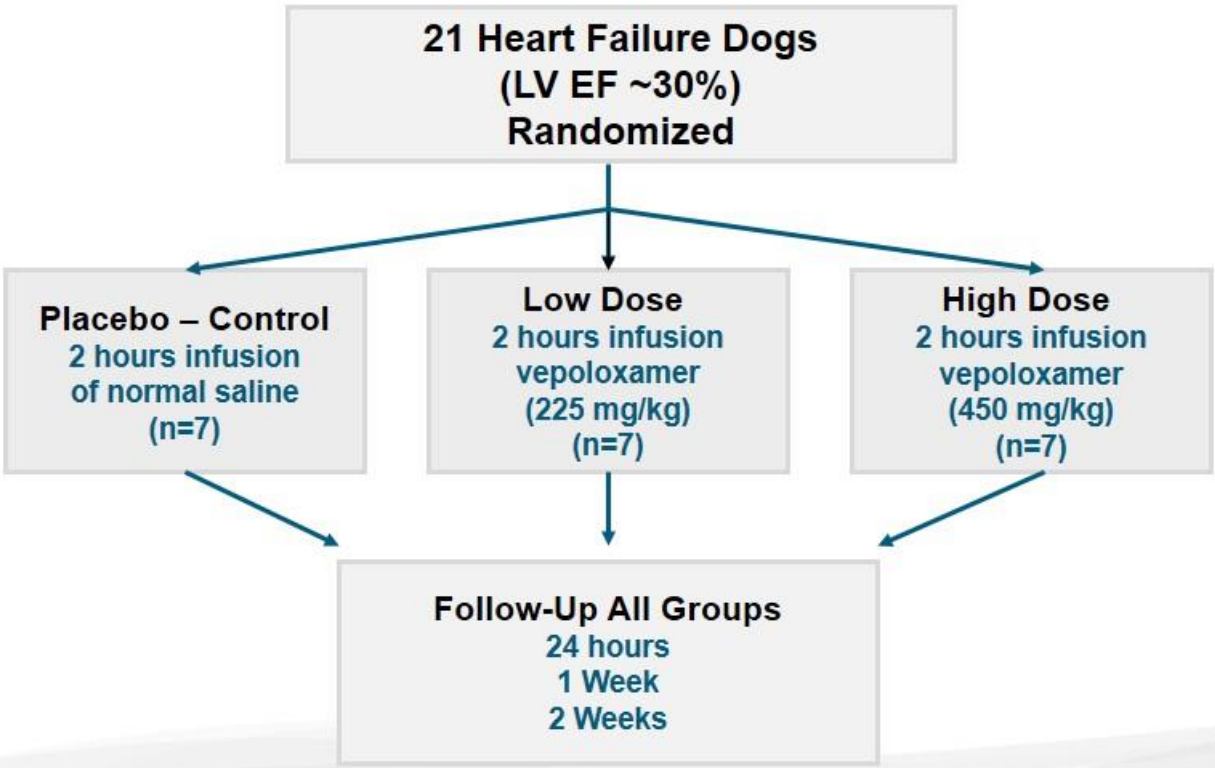
Chronic Heart Failure Model

Study 1: Single-administration

- The primary objective of this study was to examine the effects of acute intravenous administration of vepoloxamer on left ventricular (LV) systolic and diastolic function in dogs with advanced heart failure produced by intracoronary microembolizations

Conducted by Hani N. Sabbah, Ph.D., Henry Ford Health System
Data presented at American Heart Society Scientific Sessions, November 2014

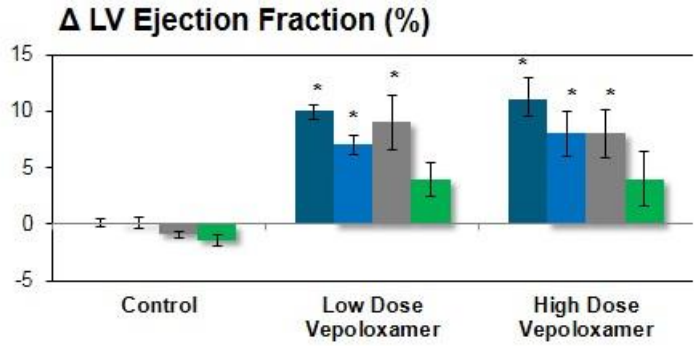
Study 1 – Single Administration Protocol

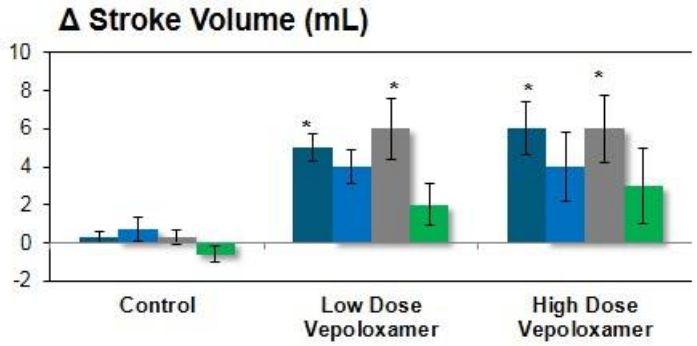


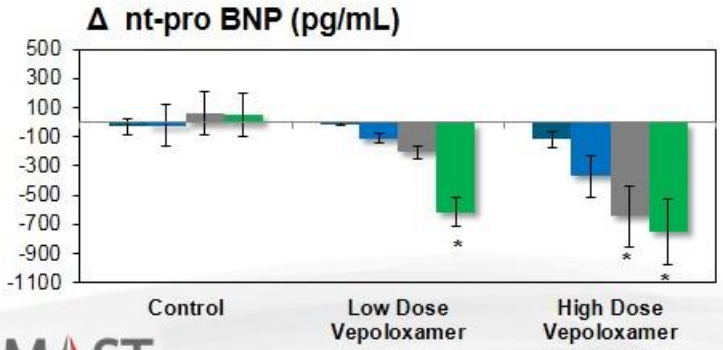
Study 1 – Single Administration Results

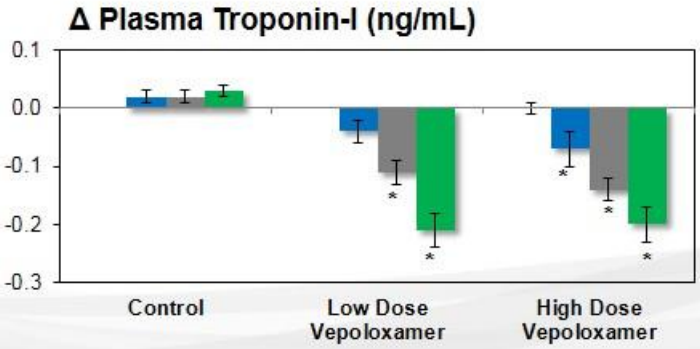
2 Hours Post | 24 Hours Post | 1 Week Post | 2 Weeks Post

* p < 0.05 vs. Control









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Study 1: Single Administration Conclusions

- **Intravenous vepoloxamer elicits improvements in LV systolic and diastolic function that last for at least one week after end of drug infusion**
  - **The functional improvement is supported by significant reductions of NT-proBNP for up to 2 weeks**

- **The decline in plasma troponin-I level suggest that vepoloxamer may act to limit ongoing cardiomyocyte loss by limiting unregulated calcium entry into the cell and thus limiting calcium overload**

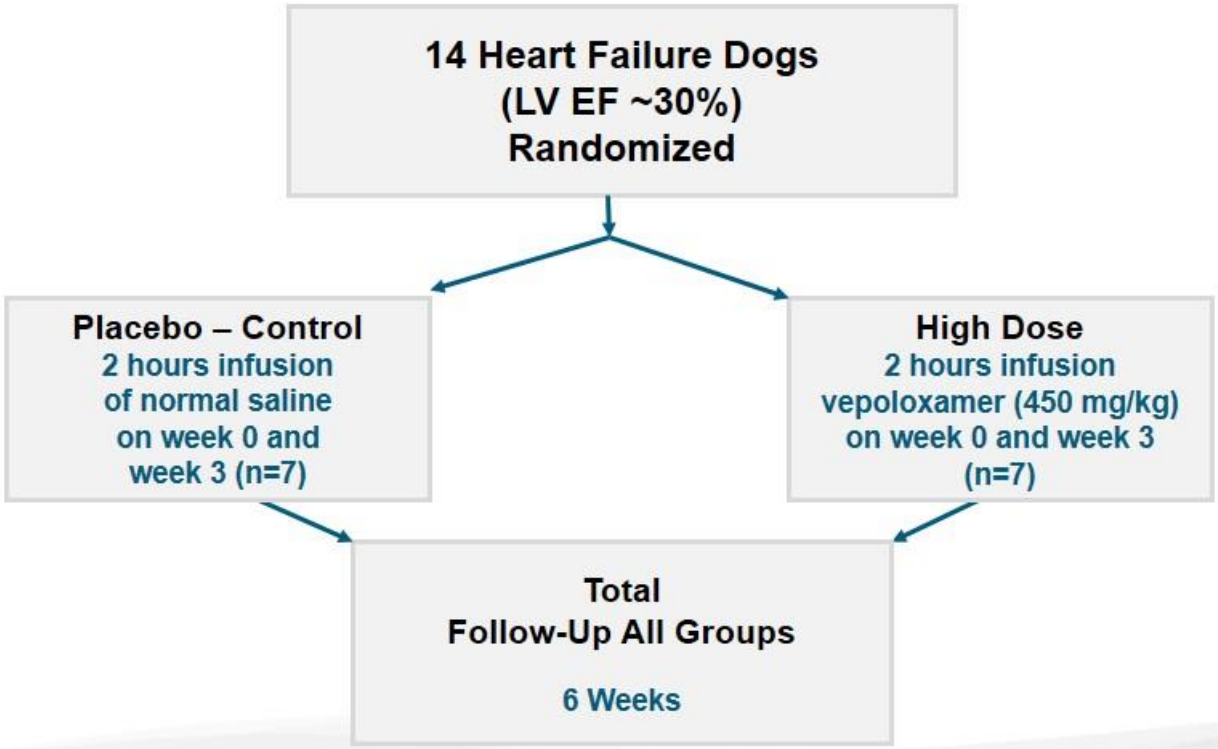
Chronic Heart Failure Model

Study 2: Repeat-administration

- **The primary objective of this study was to examine the effects of acute intravenous administration of multiple doses of vepoloxamer on left ventricular (LV) systolic and diastolic function in dogs with advanced heart failure produced by intracoronary microembolizations**

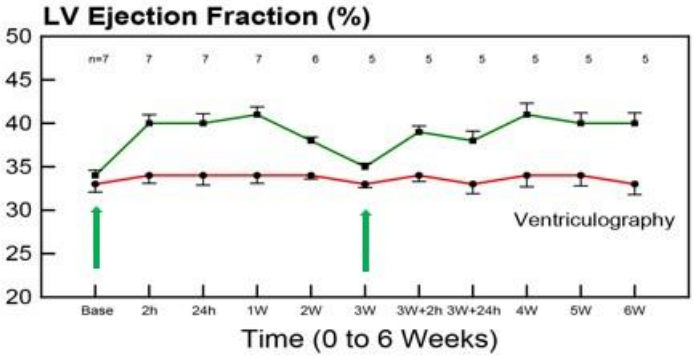
Conducted by Hani N. Sabbah, Ph.D.
Henry Ford Health System

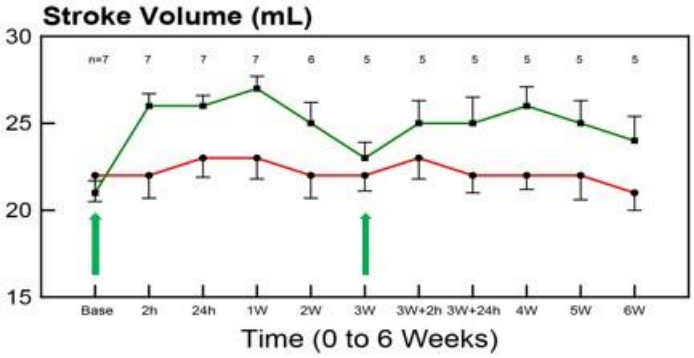
Study 2 – Repeat Administration Protocol

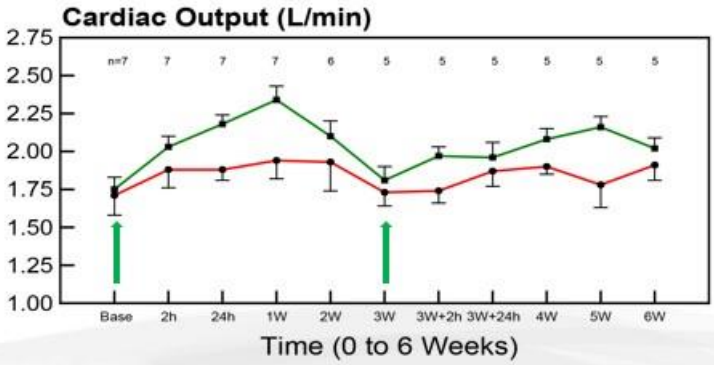


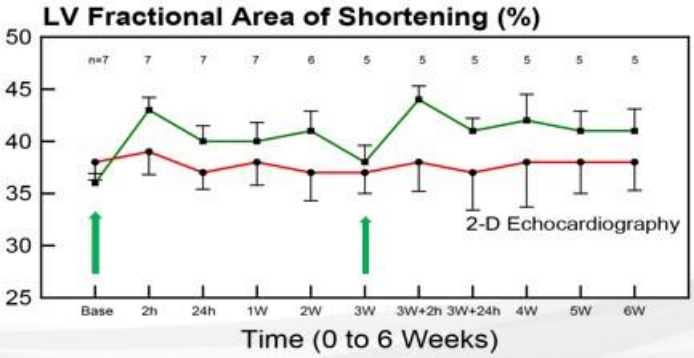
Study 2 – Repeat Administration Results

Placebo Control — Vepoloxamer









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*Preliminary data. Arrows indicate dose events.

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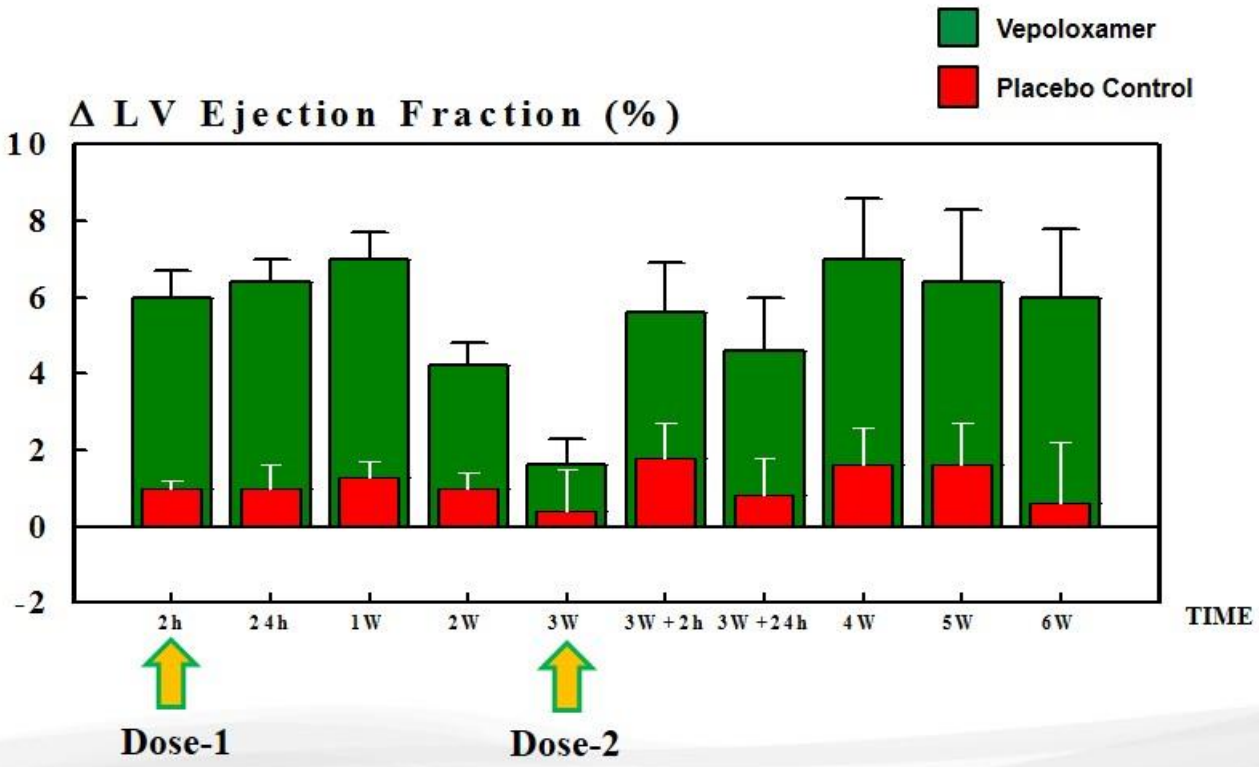
Study 2 – Repeat Administration
Focus On Left Ventricle Ejection Fraction



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Study 2 – Repeat Administration Conclusions

- Reproduced Study 1 findings
- In addition, intravenous vepoloxamer pulsed once every 3 weeks elicits improvements in LV systolic and diastolic function that can be sustained for at least 6 weeks.

Study 2 – Repeat Administration Supplemental Findings

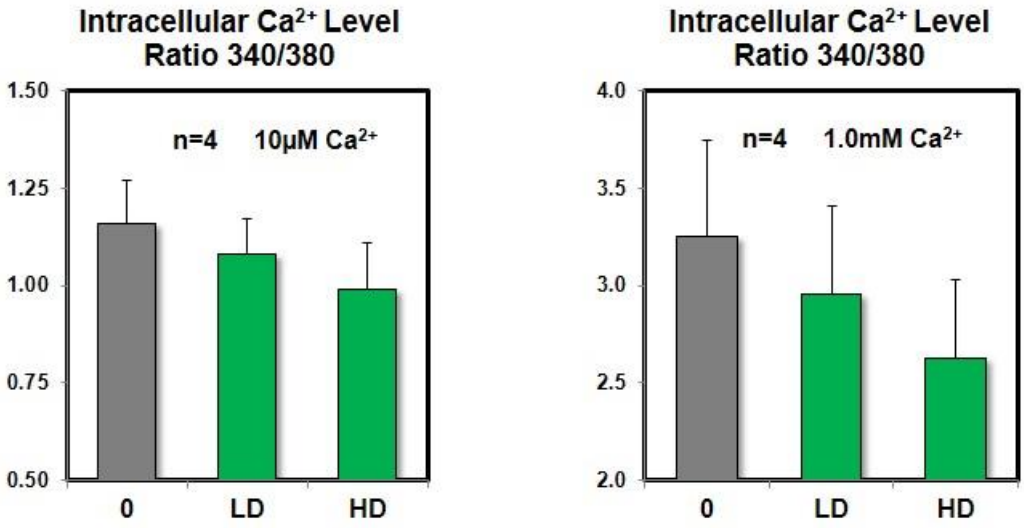
Sealing membranes with vepoloxamer

- Protocol: Isolated cardiomyocytes were treated with vepoloxamer at room temperature for 2 hours
- Cells were then washed and treated with 10 uM Fura-2 AM dye for 1 hour
- Excess dye was then washed out and cells were resuspended in EDTA (calcium chelator) or 0.5 mM calcium chloride and flourescence intensity readings were obtained after 2 hours at 340/510 and 380/510
- Calcium level (based on florescence levels) within the cell was calculated as the ratio of 340/380

Conducted by Hani N. Sabbah, Ph.D.
Henry Ford Health System

Vepoloxamer Seals Cardiomyocyte Membranes

Cardiomyocytes Isolated from Animals with Advanced Heart Failure Exhibit Reduced Intracellular Calcium



LD = 1.5 mg/mL vepoloxamer
HD = 4.5 mg/mL vepoloxamer

Vepoloxamer Repairs Disrupted Membranes

- **Seals skeletal muscle cells against carboxyfluorescein dye loss following electroporation** (Lee et. al., 1992, PNAS 89 4524 – 4528)
- **Restores action potentials and prevents Ca^{++} mediated axonal degeneration following crush injury in neurons** (Borgens et. al., J Neurosci Res 2004, 76 (1) 141-54)
- **Prevents Ca overload in Lysophospatidylcholine induced sarcolemmal injury in isolated perfused hearts** (Watanabe & Okada, Mol. & Cell Biochem. 2003, 248: 209-215)
- **Prevents contraction induced membrane injury and heart failure in MDX mice** (Yasuda et. al., Nature, 2005, 436:1025 – 1029)
- **Prevents contraction induced membrane injury and heart failure in golden retriever dogs** (Townsend et. al., JCI 2010, 120 (4) 1140 – 1150)

AIR001

(sodium nitrite) inhalation solution

Objective *Improve hemodynamics and exercise tolerance of patients with heart failure*

AIR001 Overview

- **Nitrite for intermittent inhalation (via nebulizer)**
  - **Different molecule and activity than organonitrates or nitric oxide**
  - **Beneficial effects include dilation of blood vessels and reduced inflammation**
  - **Hemodynamic benefits include reductions in**
    - pulmonary vascular resistance
    - pulmonary capillary wedge pressure
    - right atrial pressure
  - **Safety data available in 124 subjects (well-tolerated) including exposures beyond 52 weeks**

AIR001 Clinical Data

- **Three Phase 1 studies:**
  - Established MTD and safe dose level
  - Acute improvements in hypoxia-induced pulmonary hypertension
  - No drug-drug interaction with sildenafil

- **One Phase 2 study:**
  - Well-tolerated; no treatment-related serious adverse events
  - Showed improvement in median pulmonary vascular resistance (PVR) & median distances in 6-minute walk test
  - Methemoglobin levels remained normal (< 1.5%)

AIR001 Clinical Development Plan

- **AIR001 for Heart Failure with Preserved Ejection Fraction (HFpEF)**
  - Responsible for ~50% of heart failure hospitalizations
  - 80% develop pulmonary hypertension
  - No approved medications
- **Supporting three institutional-sponsored Phase 2a studies to:**
  - Evaluate the acute hemodynamic effects
  - Evaluate the acute effects versus placebo on submaximal oxygen consumption and exercise hemodynamics
  - Evaluate inhaled versus intravenous administration of nitrite and safety of multiple doses
- **Preliminary data announcements 2H 2015**

MSTX Financial Overview

- **Cash/investments at 3/31/15: $49.9 million**
- **Market capitalization: ~$83 million***
- **Shares outstanding: ~163 million***
- **Average daily volume (3 mo): ~1.1 million***
- **No debt**

MAST THERAPEUTICS, INC.

* As of June 19, 2015

NYSE MKT: MSTX

Mast Therapeutics Summary

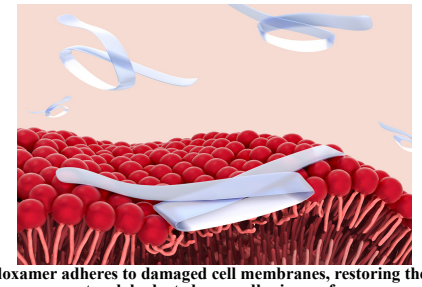
- **A Leader in Areas of Significant Unmet Need**
  - **Sickle Cell Disease: Most advanced new drug in development**
  - **Acute Limb Ischemia: Phase 2 ongoing; gateway to stroke**
  - **Heart Failure: two distinct programs with new mechanisms**
- **Mast Therapeutics is committed to showing the clinical benefit of improving blood flow and sealing cell membranes in dysfunctional circulatory diseases**

A Brief History of Vepoloxamer

Definitions

Poloxamer 188 *– Refers to unpurified, excipient-grade poloxamer 188 material, which was the active ingredient in drug product tested in early clinical studies conducted by CytRx and Burroughs Wellcome. Associated with elevated serum creatinine.*

Vepoloxamer (also known as MST-188) *– Refers to purified poloxamer 188, which is the active ingredient in drug product previously tested in CytRx's Phase 3 study in sickle cell disease and currently being developed by Mast Therapeutics. Certain low molecular weight substances present in poloxamer 188 that are associated with elevated serum creatinine are not present in vepoloxamer. No clinically significant elevations in creatinine have been observed in completed clinical studies conducted with vepoloxamer (>300 administrations).*



Vepoloxamer adheres to damaged cell membranes, restoring the cell's natural, hydrated, non-adhesive surface.

The CytRx Corporation/Burroughs Wellcome Alliance

Poloxamer 188 is an extensively-studied compound. It was originally used as an emulsifying agent in topical wound cleansers and parenteral nutrition products. The potential *therapeutic* use of poloxamer 188 was largely conceived by Dr. Robert Hunter, MD, PhD (Distinguished Professor and Chairman, Department of Pathology and Laboratory Medicine, University of Texas Medical School at Houston). While at Emory University, Dr. Hunter identified the compound's rheologic, cytoprotective, and antithrombotic activities through an extensive series of laboratory studies. His work led to the formation of CytRx Corporation, a start-up company led by Jack Luchese which licensed Dr. Hunter's inventions from Emory. CytRx conducted a wide range of pre-clinical and clinical studies with poloxamer 188 (the drug product was then known as RheothRx). These studies led to a major alliance with Burroughs Wellcome. Burroughs Wellcome also performed an extensive series of nonclinical studies and eight clinical trials, primarily focused on acute myocardial infarction (AMI). Early studies investigating poloxamer 188 were promising. The largest AMI trial planned to enroll approximately 20,000 patients. However, during the 3,000-patient lead-in phase of that study, elevations in serum creatinine were observed, particularly in those patients aged 65 years and older and in subjects with elevated creatinine at baseline. This phenomenon was referred to as "acute renal dysfunction" and eventually resulted in the discontinuation of the program by Glaxo Wellcome, which had recently been formed by the merger of Glaxo and Burroughs Wellcome.

Addressing Renal Toxicity and Pursuing Sickle Cell Disease

Glaxo returned the poloxamer 188 program to CytRx, which then investigated the source of the renal dysfunction and determined the elevation in serum creatinine was attributable to preferential absorption of certain low molecular weight substances by the proximal tubule epithelial cells in the kidney, causing an osmotic nephrosis. Nonclinical studies demonstrated the osmotic nephrosis was reversible and deemed to be an exaggeration of the normal vacuolar reabsorption pathway. CytRx developed a proprietary manufacturing method based on supercritical fluid chromatography that reduced the level of low molecular weight substances present in poloxamer 188, creating a *purified* poloxamer 188 compound, which has been assigned the unique generic name "vepoloxamer" by the United States Adopted Names (USAN) Council.

Nonclinical testing of vepoloxamer demonstrated less accumulation in kidney tissue, less pronounced vacuolization of proximal tubular epithelium, more rapid recovery from vacuolar lesions, and less effect on serum creatinine. A full report of the differential effects of vepoloxamer and poloxamer 188 on renal function has been published by Mast Therapeutics.[1]

[1] Emanuele, M. and Balasubramaniam, B. Differential Effects of Commercial-Grade and Purified Poloxamer 188 on Renal Function. *Drugs in R&D* April 2014. Available at http://link.springer.com/article/10.1007/s40268-014-0041-0.

Satisfied that it had identified the source of renal dysfunction, CytRx sought to re-introduce vepoloxamer into clinical development. The company lacked the resources to conduct a large heart attack study and, instead, focused the development of vepoloxamer in sickle cell disease, a genetic condition with a significant unmet need and which is a rare (orphan) disease in the United States. Under Burroughs Wellcome, poloxamer 188 had demonstrated positive results in a pilot Phase 2 study. In that study (n=50), vepoloxamer markedly and significantly reduced the duration of vaso-occlusive crisis, pain intensity, and total analgesic use and showed trends to shorter days of hospitalization in the subgroup of patients who received the full dose of study drug (n=31). These data were reported more fully by Adams-Graves et al.[2] Notably, CytRx conducted safety studies in both adult and pediatric sickle cell patients and even at significantly higher levels of exposure than the anticipated therapeutic doses, there were no clinically significant changes in serum creatinine observed and no acute kidney failure reported. Based on these promising Phase 1 and 2 results, CytRx launched a randomized, double-blind, placebo-controlled Phase 3 study of vepoloxamer in 350 patients with sickle cell disease. The primary endpoint of this initial Phase 3 study was a reduction in the duration of a crisis. However, CytRx concluded the study at 255 patients, in part due to capital constraints. Despite its early conclusion and certain design flaws, the study demonstrated treatment benefits in favor of vepoloxamer. However, it did not achieve statistical significance in the primary study endpoint (p=0.07). Mast believes that enrolling fewer than the originally-planned number of patients and certain features of the study's endpoint and observation period adversely affected the outcome of the study. In particular, the study assumed that most patients would resolve their crisis within one week (168 hours). However, a substantial number of patients did not achieve crisis resolution within 168 hours and were assigned a "default" value of 168 hours, which had a potentially significant effect on the primary endpoint. Notably, in a post hoc "responder's analysis" of the intent-to-treat population (n=249), which analyzed the proportion of patients who achieved crisis resolution within 168 hours (e.g. excluding those who had been assigned the default of 168 hours), over 50% of subjects receiving vepoloxamer achieved crisis resolution within 168 hours, compared to 37% in the control group (p=0.02). Data from the Phase 3 study are reported more fully by Orringer et al.[3] Following conclusion of the Phase 3 study, CytRx merged with a private company and modified its business strategy by discontinuing development of all of its existing programs (including vepoloxamer) to focus on assets held by the private company with which it merged.

SynthRx

After the corporate reorganization at CytRx, a group of individuals, including Dr. Hunter, formed a private entity, which they named SynthRx, Inc., to acquire rights to the data, know-how, and extensive clinical, pre-clinical, and manufacturing information necessary to continue development of vepoloxamer. SynthRx developed new intellectual property and conducted additional analyses of the existing data. However, they were unable to raise capital to fund additional clinical development of vepoloxamer, particularly during a period of economic recession in the U.S.

Mast Therapeutics

In 2010, Mast met with Dr. Hunter and his colleagues to negotiate the acquisition of SynthRx and thereby continue the development of vepoloxamer. The merger was finalized in April 2011.

Beginning in April 2011, Mast re-established the unique manufacturing process through a partnership with Pierre Fabre (FRA) and met with the FDA multiple times to discuss a pivotal study protocol for vepoloxamer in sickle cell disease. In early 2013, Mast initiated the "EPIC" study, a 388-patient pivotal Phase 3 trial of vepoloxamer in sickle cell disease that is being conducted in approximately 70 sites around the world. In 2014, building upon promising nonclinical data of vepoloxamer in combination with thrombolytics, Mast initiated its second clinical program featuring vepoloxamer, a Phase 2, proof-of-concept study of vepoloxamer in combination with recombinant tPA in patients with acute limb ischemia. In early 2015, based on recent nonclinical animal studies showing improvements in cardiac ejection fraction and key biomarkers and prior studies showing vepoloxamer improved cardiac function without increasing cardiac energy requirements, Mast announced its intent to initiate a Phase 2 clinical study of vepoloxamer in chronic heart failure.

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[2] Adams-Graves P, Kedar A, Koshy M, et al. RheothRx (Poloxamer 188) Injection for the Acute Painful Episode of Sickle Cell Disease: A Pilot Study. *Blood* 1997;90:2041-6

[3] Orringer EP, Casella JF, Ataga KI, et al. Purified poloxamer 188 for treatment of acute vaso-occlusive crisis of sickle cell disease: A randomized controlled trial. *JAMA* 2001;286(17):2099-106