# 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): September 12, 2016**

# 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 7.01 Regulation FD Disclosure.**

The information furnished in Exhibit 99.1 to this report, which relates 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.

In accordance with General Instruction B.2. of Form 8-K, the information in Item 7.01 of this report and Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any incorporation language in such a filing, except as expressly set forth by specific reference in such a filing.

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 14, 2016, Quarterly Report on Form 10-Q filed on August 9, 2016, 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 in this report, including in Exhibit 99.1 attached hereto, that are not a description of historical facts are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by the use of words referencing future events or circumstances such as "expect," "intend," "plan," "anticipate," "believe," and "will," among others. Examples of forward-looking statements include, but are not limited to, statements regarding the Company's development, regulatory and commercialization strategies and plans for its investigational new drugs, vepoloxamer (also known as MST-188) and AIR001, as well as the timing of activities and events related to those plans, including commencement and completion of clinical studies, announcements of study results, submission of applications to regulatory authorities for marketing approval, and product launch, and prospects for clinical, regulatory and commercial success. Forward-looking statements should not be read as guarantees of future performance or results because they involve the Company's beliefs and assumptions based on currently available information and are subject to significant known and unknown risks and uncertainties that may cause actual performance and results to differ materially from expectations indicated by the forward-looking statements. Some of the factors that could cause actual performance or results to differ include, without limitation: the potential for additional delays in EPIC study closeout procedures, including blinded data validation and quality assurance/quality control procedures; the inherent uncertainty of outcomes in clinical studies and the risk that the Company's product candidates may not demonstrate adequate safety, efficacy or tolerability in one or more such studies, including vepoloxamer in the EPIC study; the risk that, even if EPIC results are positive, the FDA or other regulatory agencies may determine they are not sufficient to support a new drug application; uncertainties related to future feedback from the FDA regarding the development of vepoloxamer, including the risks that the FDA may determine another Phase 3 study or other clinical or nonclinical studies are necessary to demonstrate vepoloxamer's development and/or safety for the treatment of patients with sickle cell disease or may require changes to manufacturing controls or processes, any of which could delay filing of a new drug application, significantly increase the cost of vepoloxamer's development and/or ultimately lead to denial of regulatory approval of vepoloxamer; the Company's need for additional funding to continue to operate as a going concern; risks associated with the Company's ability to manage operating expenses and obtain additional capital as needed; uncertainty related to the Company's ability to comply with the terms and conditions under its debt facility and risk that it may be required to repay its outstanding debt obligations on an accelerated basis and/or at a time that could be detrimental to the Company's financial condition, operations and/or business strategy, including prepayment of $10 million of the principal balance of its debt facility if results from EPIC are not positive and/or are not available on or before October 14, 2016; delays in the commencement or completion of clinical studies, including the EPIC study, the Phase 2 study of vepoloxamer in heart failure, and the Phase 2 studies of AIR001 in HFpEF, 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 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 the risk that such third parties may fail to perform as expected, leading to delays in product candidate development, regulatory approval, commercial launch and/or inability to meet future market demand for any approved products; the potential for the Company to significantly delay, reduce or discontinue current and/or planned development, regulatory 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 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 obtain and maintain effective patent coverage or other market exclusivity protections for its products, if approved, or that the use or manufacture of the Company's products may infringe the proprietary rights of others; and other risks and uncertainties more fully described in the Company's press releases and periodic filings with the SEC.

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 Exchange Act 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: September 12, 2016

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, September 12, 2016 |

Exhibit 99.1

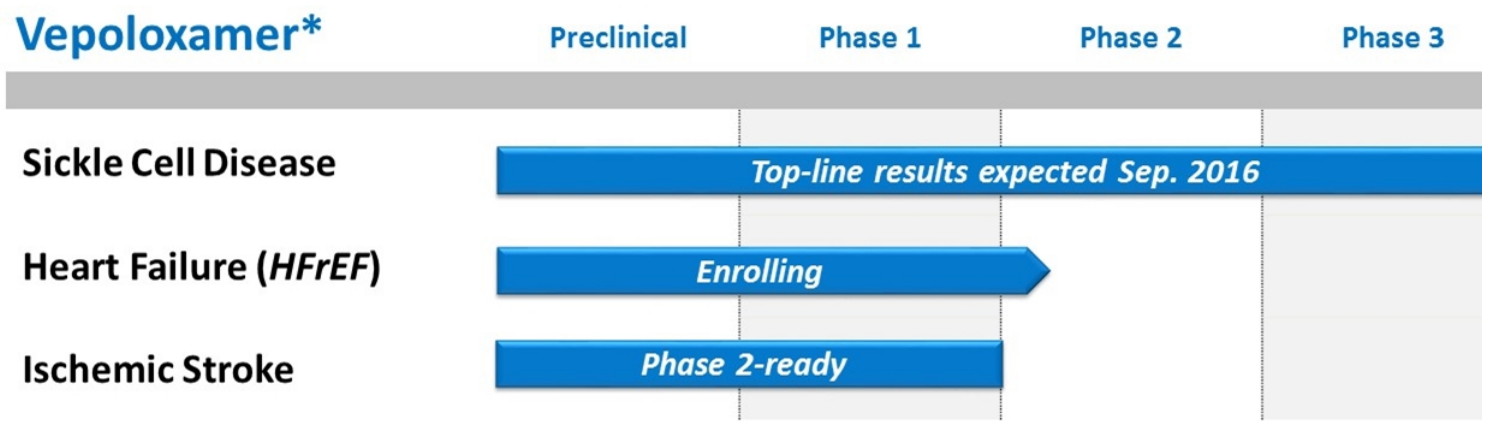

# Corporate Overview
# September 12, 2016

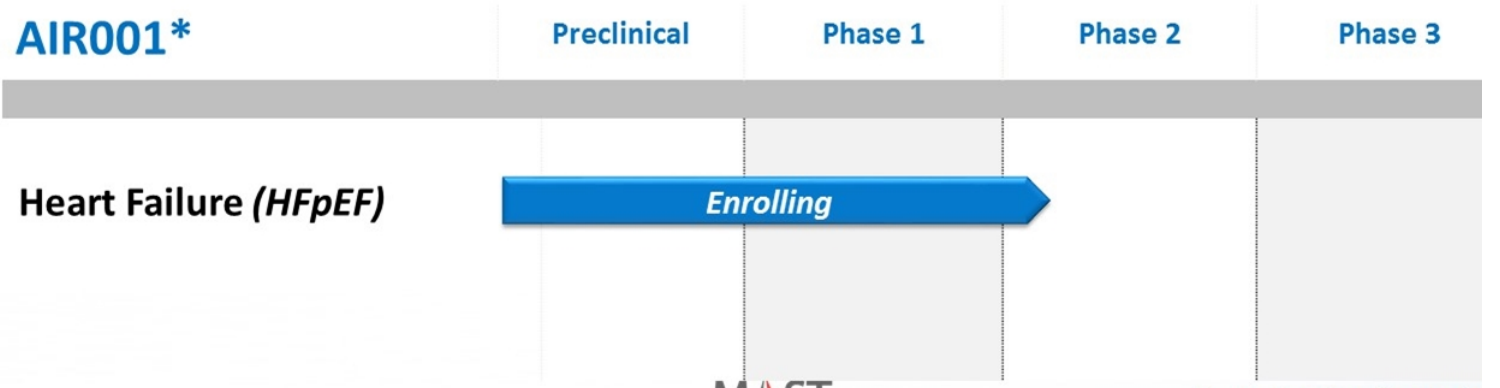
# Safe Harbor Statement

This presentation includes forward-looking statements about our business prospects, financial position, ar development of vepoloxamer and AIR001 for therapeutic use in humans. Any statement that is not a statement historical fact should be considered a forward-looking statement. Because forward-looking statements relate the future, they are subject to inherent risks, uncertainties and changes in circumstances that are difficult predict. Actual events or performance may differ materially from our expectations indicated by these forwar looking statements due to a number of factors, including, but not limited to, results of our pending and futu clinical studies, the timeline for clinical, manufacturing and regulatory activities; failure to obtain regulato approval of our product candidates; our dependency on third parties to conduct clinical studies and supply manufacture clinical trial material and/or product for commercial sale, if approved; our ability to raise addition capital as needed; our ability to repay outstanding debt as payments come due; our ability to establish ar protect proprietary rights related to our product candidates; and other risks and uncertainties more ful described in our press releases and our filings with the SEC, including our quarterly report on Form 10-Q filed wit the SEC on August 9, 2016.

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

# Product Candidate Pipeline




*Investigational new dru



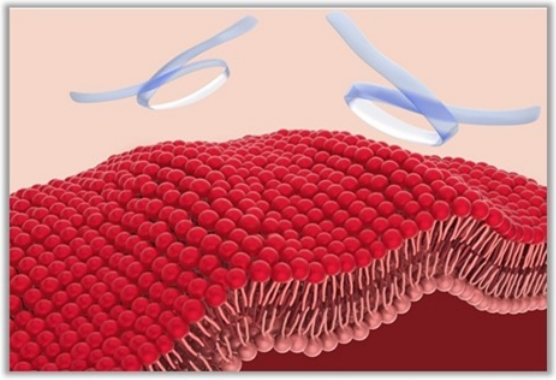
MAST THERAPEUTICS, INC.
NYSE MKT: MSTX

# Vepoloxamer: A Novel Biophysical Agent

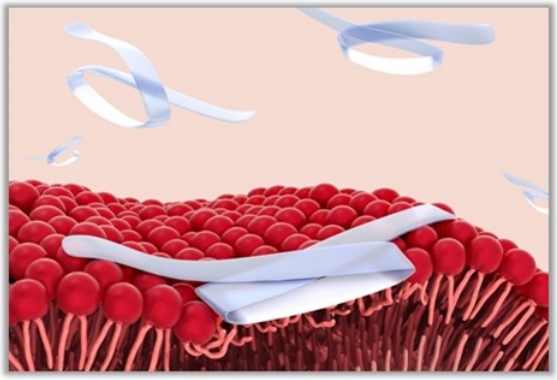
- **Mechanism hypothesis: Vepoloxamer adheres to damaged cell membranes, correcting defects in membrane surface tension, an underlying feature of multiple diseases**

- **Potential benefits of "biophysical" mechanism of action:**
  - Targets damaged tissue; little or no activity in healthy tissue
  - Not metabolized; no active metabolites to track, no difference in fast vs slow metabolizers, less susceptible to drug-drug interactions
  - Less susceptible to genetic variation; independent of receptors, etc.

***Normal Cell Membrane? Vepoloxamer Inactive***



***Damaged Cell Membrane? Vepoloxamer Adheres***



# Pathologies and Conditions Related to Defects in Membrane Surface Tension

| Surface Tension Pathologies | Examples |
| --- | --- |
| Elevated blood viscosity | Sickle Cell Disease |
| Cellular aggregation | Chronic & Acute Heart Failure |
| Cellular adhesion | Ischemic Stroke |
| Loss of membrane barrier function / repair capacity | |
| Dysfunctional coagulation | |

# Vepoloxamer in Sickle Cell Disease

## Objective: Improve blood flow to prevent ischemic injury and shorten duration of crisis

## Phase 3 Study – Enrollment Complete

# Overview of Sickle Cell Disease

- **A chronic genetic disorder and rare (orphan) disease**
  - Affects ~100,000 people in the U.S. and is characterized by severe deformation of red blood cells
- **Hallmark of disease is a "vaso-occlusive crisis" (VOC)**
  - Reduces blood flow and causes ischemic injury to tissues and organs
  - Exceedingly painful condition and a leading cause of hospitalization
  - 80-100k hospitalizations annually in the U.S. with average hospital stay of 4-5 days
- **Current treatment is palliative**
  - Consisting of hydration and IV opioids
  - Does not treat underlying pathophysiology of the disease
  - No VOC interventional therapy available
- **Significant unmet need**
  - No approved agents to shorten duration or severity of crisis
  - Shorter life expectancy due to ischemic injury (~45y)

Sources: Life-expectancy: Hassell, K. Am J Prev Med 2010; 38(4S): S512-521; Utilization data calculated from data in Brousseau, D., et al., Acute Care Utilization and Rehospitalizations for Sickle Cell Disease. Apr 7 2010 and HCUP 2010-2012; SCD prevalent pop: Brousseau DC, Panepinto JA, Nimmer M, Hoffmann RG. The number of people with sickle-cell disease in the United States: national and state estimates Hematol 2010;85:77-8; Steinberg, M.H., Management of Sickle Cell Disease, New Eng J Med; 1999; Vol 340, No 13; Platt, et al., Mortality in Sickle Cell Disease (N Engl J Med 1994;330:1639-44)

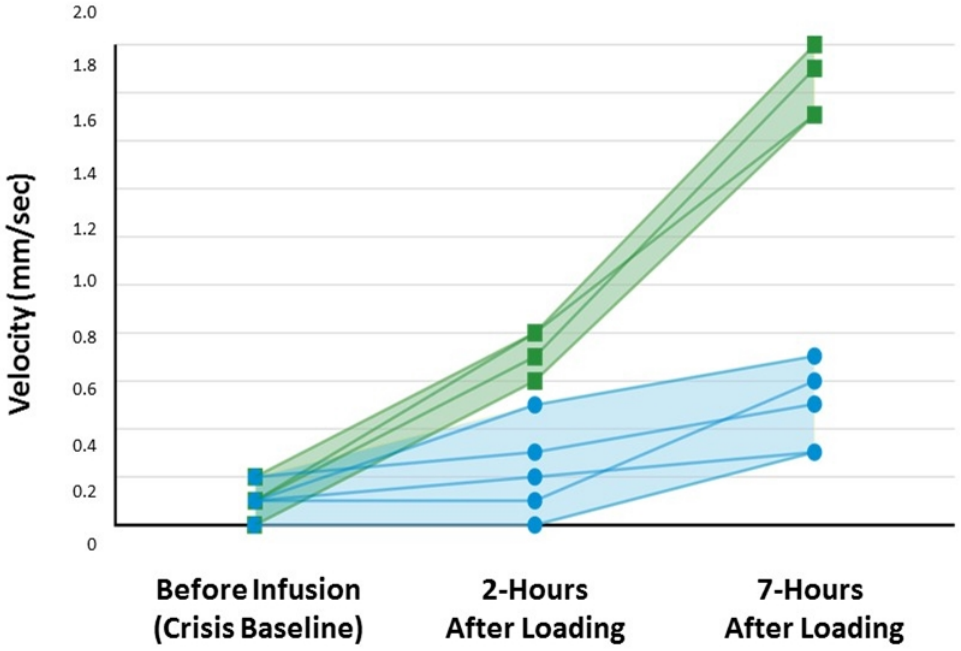
# Vepoloxamer in Sickle Cell Disease (SCD)

- **The underlying pathology of vaso-occlusive crisis is reduced blood flow**
- **Studies suggest vepoloxamer improves blood flow by addressing multiple pathological mechanisms:**
  - Adhesion
  - Hemolysis
  - Aggregation
  - Viscosity

**Objective of treatment with vepoloxamer: Improve blood flow to prevent ischemic injury and shorten the duration of crisis**

# Vepoloxamer Improved Blood Flow in Sickle Cell Patients

**Vepoloxamer significantly improved microvascular blood flow in sickle cell patients experiencing crisis (randomized sub-study)**




- Vepoloxamer
- Placebo

**Double-blind assessment of red cell velocity in nine sickle cell patients experiencing vaso-occlusive crisis (p = .00003)**



MAST THERAPEUTICS, INC.
NYSE MKT: MSTX

*Source: J. Investig. Med. 2004;52(6):40*

# Vepoloxamer Development History

- **Over 100 nonclinical studies completed**
- **Phase 2 SCD – statistically significant shorter crisis and less opioid use**
- **Phase 2 ACS* – ~50% shorter hospitalization stay vs. historical control**
- **Phase 3 SCD – shorter duration of crisis (p-value = 0.07)**

**Lessons learned from prior sponsors and applied to Mast's Phase 3 study:**

1. Vepoloxamer has activity in SCD
2. Study design is key to success (prior endpoint poorly designed)
3. Key FDA feedback:
   - Utilize a clinically meaningful endpoint
   - Use as objective an endpoint as possible
   - Avoid use of pain scores due to variability
   - Provide a plan to minimize data loss

**(*Acute chest syndrome, a serious complication of sickle cell cris**

# The Phase 3 "EPIC" Study

## Evaluation of Purified Poloxamer 188 In Vaso-Occlusive Crisis

- **Largest placebo-controlled study in sickle cell disease ever concluded**
- **Double-Blind, Placebo-Controlled, International (~75 sites)**
  - 388 patients, randomized 1:1 to standard of care +/- vepoloxamer
  - 1hr loading dose followed by 48h continuous infusion
- **Primary Endpoint**
  - Duration of crisis (time of randomization to last dose of parenteral opioid)
- **Secondary Endpoints**
  - Re-hospitalization for VOC within 14 days
  - Occurrence of acute chest syndrome within 120 hours of randomization
- **Other Assessments**
  - Safety
  - Duration of hospitalization
  - Biomarkers
  - Opioid utilization
  - Sub-study outcomes

# EPIC Study: Primary Endpoint

- **Assessment: Duration of vaso-occlusive crisis**

- **Definition: Time from randomization to last dose of parenteral opioid (LPC**

- **Advantages:**
  - Aligns with FDA recommendations
    - Sensitive and specific data collection
    - Objective
    - Minimal data loss
  - Medical expert support
  - Clinically meaningful to experts in the field

- **Powering:**
  - 90% power to detect a 17% difference in treatment arms with a statistical significan level of p=0.05

# EPIC Study: Safety

- **DSMB Evaluations**
  - Independent, unblinded DSMB (4 clinicians and 1 statistician)
  - Meetings at 25, 58, 145 and 250 patients

- **DSMB meeting held at 250 patients**
  - No unexpected safety signals identified
  - DSMB members deemed no additional meetings were necessary

# EPIC Study: Key Characteristics

- **U.S. patients = ~60%**
- **Average patient age = 15 years (range 4-46, ~30% adults)**
- **Hydroxyurea use = >60%**
- **Blinded analysis at 250 patients:**
  - Average duration of crisis (pooled) & coefficient of variation consistent with statistical assumptions in study design (79h and ~50%)
  - Minimal regional variability (U.S. vs ex-U.S.)

✓ **Top-line data anticipated September 2016**

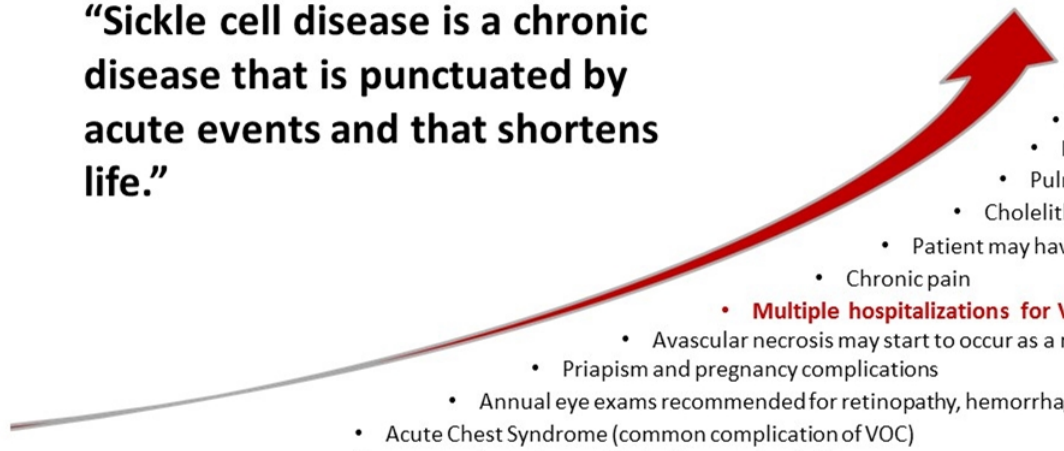
# Vepoloxamer in SCD: Regulatory Consideration

- **Significant unmet need – no disease-modifying therapies for an ongoing cri**
- **Support among medical / advocacy / patient communities**
- **Orphan Drug Designation**
- **Fast Track Designation**
- **SCD is part of FDA "Patient-Focused Drug Development Initiative"**
- **Healthcare disparity concerns**
- **NDA-supportive clinical studies:**
  - Thorough QT study - *complete*
  - Special population study - *enrolling*
  - Repeat-administration study – *enrolling*
    - ✓ One patient who completed the EPIC Study has subsequently received three dos of vepoloxamer in the elective repeat-dose study

# Vepoloxamer: Commercial Opportunity in Sickle Cell Disease

# SCD: A Lifetime of Complications

**"Sickle cell disease is a chronic disease that is punctuated by acute events and that shortens life."**



- Premature death
- Multiple organ damage and failure
- Acute papillary necrosis of the kidneys
- Leg ulcers
- Pulmonary hypertension
- Cholelithiasis (gallstones)
- Patient may have early signs of renal disease
- Chronic pain
- **Multiple hospitalizations for VOC per year**
- Avascular necrosis may start to occur as a result of ischemia
- Priapism and pregnancy complications
- Annual eye exams recommended for retinopathy, hemorrhages, and retinal detachments
- Acute Chest Syndrome (common complication of VOC)
- Transfusions may begin for cerebral infarction (stroke)
- Splenectomy (usually before age 8)
- Daily penicillin prophylaxis (through age 5)
- Diagnosis (at birth)

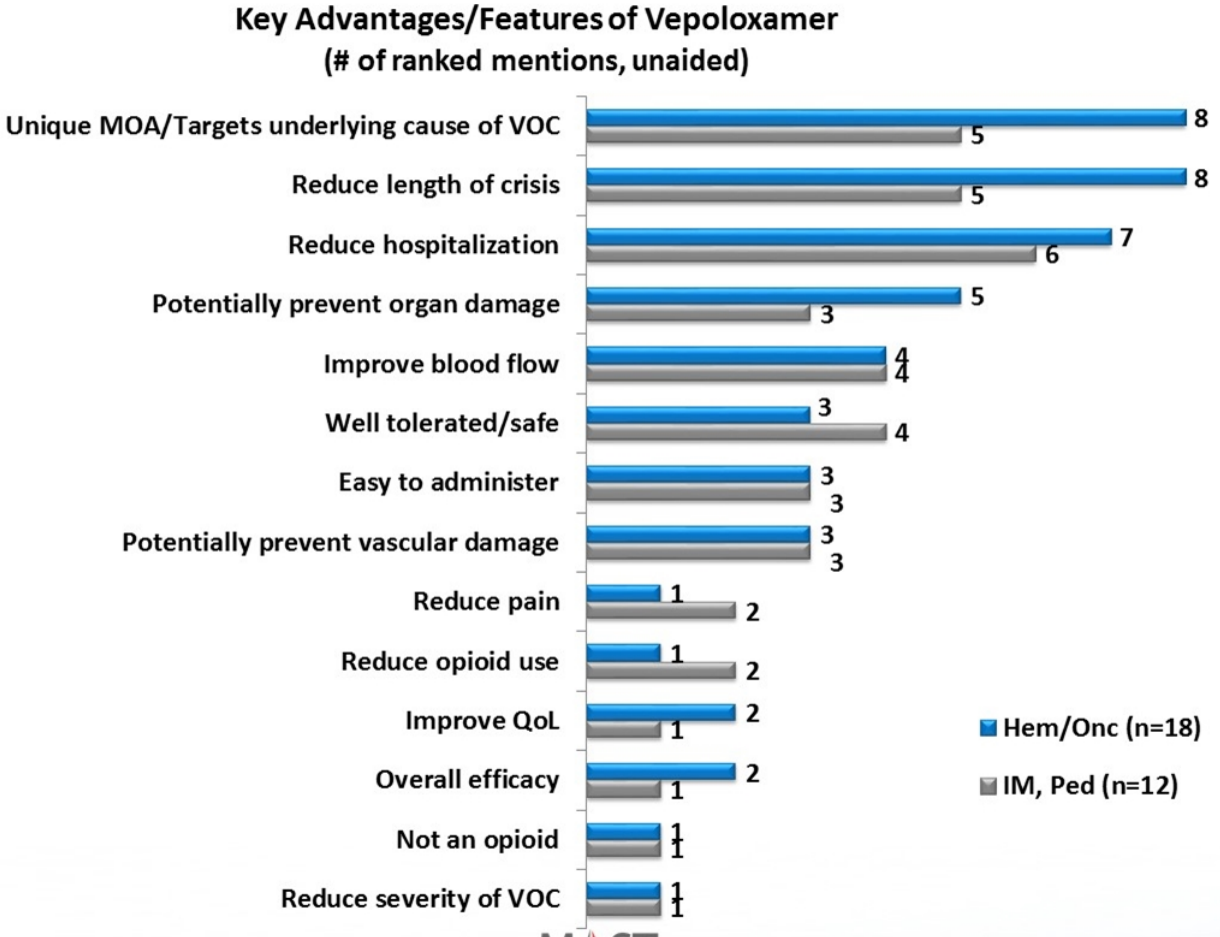

Source: Martin H. Steinberg, M.D., Management of Sickle Cell Disease, New Eng J Med; 1999; Vol 340, No 13

# Vaso-Occlusive Crisis is the Hallmark of SCD

- 80-100k hospitalizations annually in the U.S.
- Current treatment is palliative
  - Consisting of hydration and IV opioids
  - Does not treat underlying pathophysiology of the disease
  - No VOC interventional therapy available
- Hospitalized on average for approximately 4-5 days
- 40% of patients will have acute chest syndrome complication
- 12-41% are re-hospitalized within 30 days of hospital discharge
- Shorter life expectancy due to ischemic injury to organs (~45y)
- Organ failure is leading cause of death

Sources: Life-expectancy: Hassell, K. Am J Prev Med 2010; 38(4S): S512-521; Utilization data calculated from data in Brousseau, D., et al., Acute Care Utilization and Rehospitalizations for Sickle Cell Disease JAMA Apr 7 2010 and HCUP 2010-2012; SCD prevalent pop: Brousseau DC, Panepinto JA, Nimmer M, Hoffmann RG. The number of people with sickle-cell disease in the United States: national and state estimates. Am J Hematol 2010;85:77-8; Steinberg, M.H., Management of Sickle Cell Disease, New Eng J Med; 1999; Vol 340, No 13; Platt, et al., Mortality in Sickle Cell Disease (N Engl J Med 1994;330:1639-44)

# Market Research: Expected Features and Potential Benefit Align with Unmet Needs for VOC Treatment

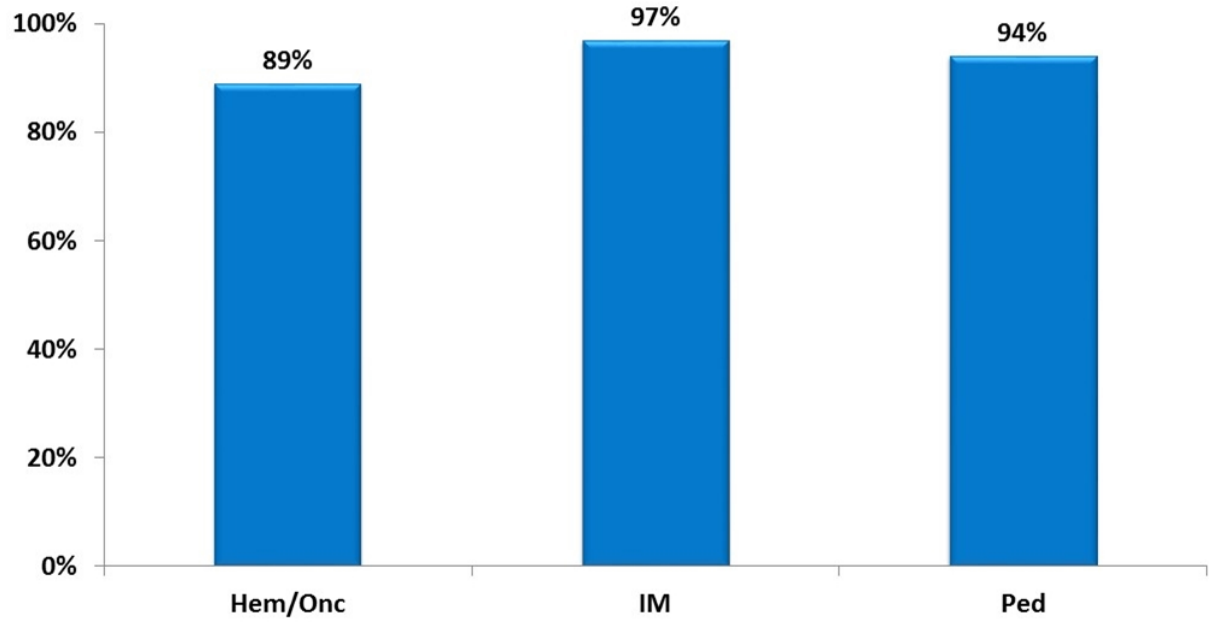



Source: RDS Consulting Group Research Report, 2015

# Market Research: Physicians Report a High Percent of Patients to be Treated with Vepoloxamer at Peak

**Average % of Patients Treated with Vepoloxamer at Peak**

**n=30**




**Survey-reported time to peak adoption: approx. 6 months)**



Source: RDS Consulting Group Research Report, 2015, n=30

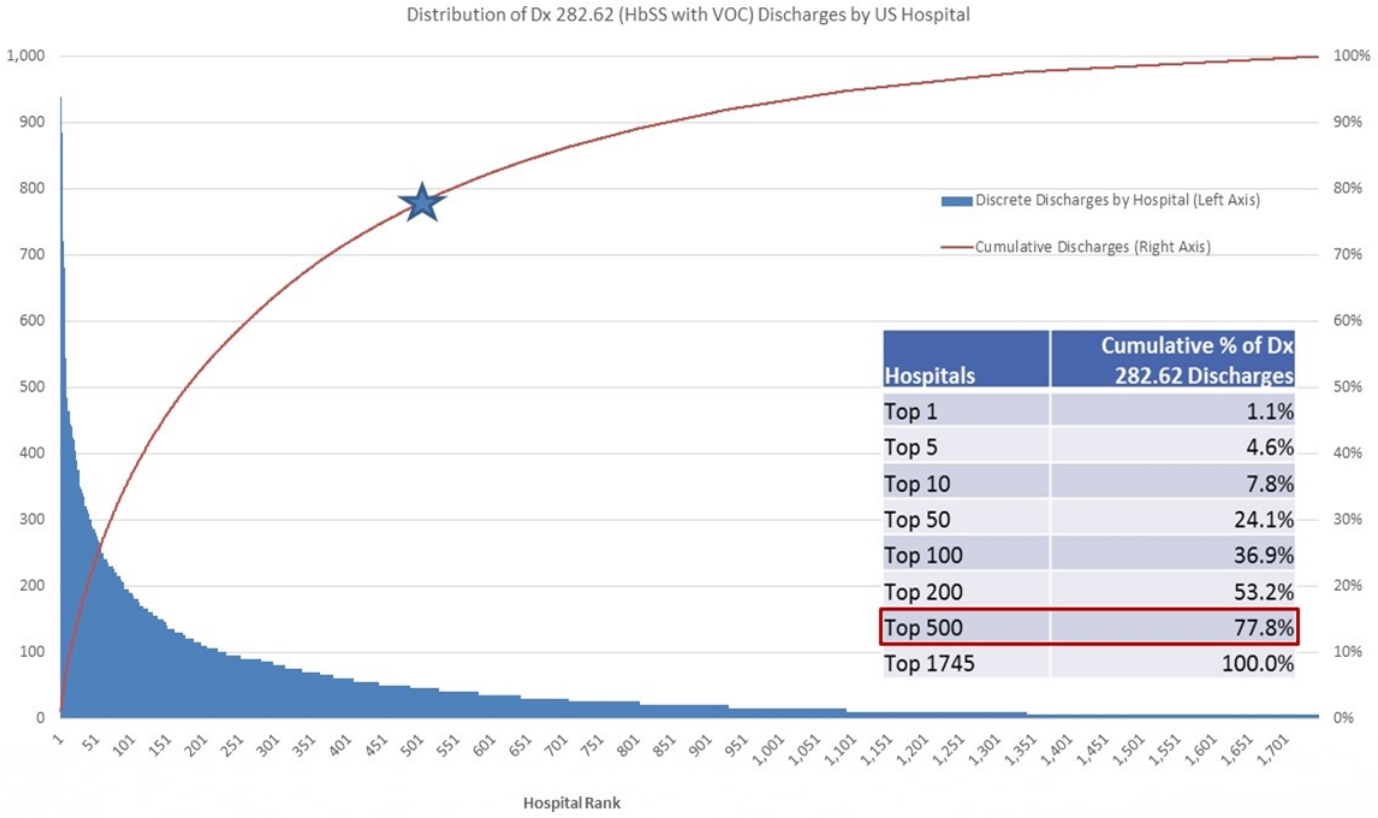
# Development Landscape in SCD

**Vepoloxamer has the potential to be the <u>first and only</u> interventional treatment to reduce the duration and severity of an ongoing VOC**

| Stage | VOC Intervention | VOC Reduction | SCD Corrective Treatment |
|---|---|---|---|
| **Marketed** | | hydroxyurea | Bone Marrow Transplant |
| **Phase 3** | vepoloxamer<br>rivipansel | L-glutamine | |
| **Phase 2** | | SC-411<br>Sanguinate<br>Sevuparin<br>SelG1<br>GBT440 | |
| **Phase 1** | | CXA-10<br>NiCord/CordLn<br>NKTT120<br>PF-04447943<br>SCD-101 | Gene therapy |

# Concentration of SCD Treatment in the U.S. Offers an Attractive Commercial Opportunity

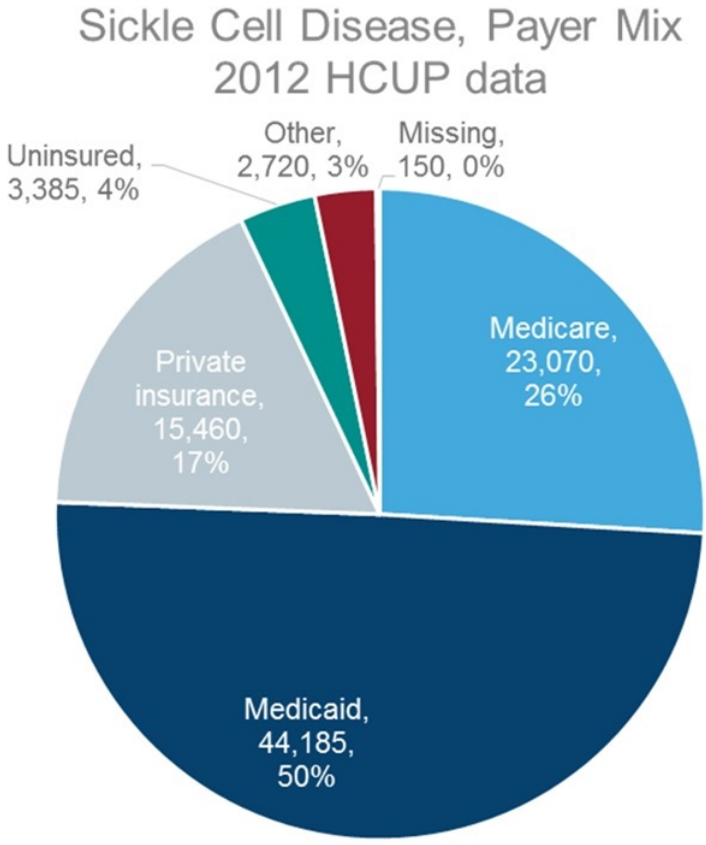
- **Top 500 U.S. hospitals treat nearly 80% of SCD patients in crisis**
- **Effective field promotion with small hospital sales force (~30)**




| Hospitals | Cumulative % of Dx 282.62 Discharges |
|---|---|
| Top 1 | 1.1% |
| Top 5 | 4.6% |
| Top 10 | 7.8% |
| Top 50 | 24.1% |
| Top 100 | 36.9% |
| Top 200 | 53.2% |
| Top 500 | 77.8% |
| Top 1745 | 100.0% |

Source: Analysis of HCUP NIS 2013 data; Dx 282.62 is 89.7% of all VOCs.

# U.S. Sickle Cell Disease Hospital Payer Mix




- **Inpatient prospective payment system (IPPS)**
- **Patients with public insurance have minimal share of costs**
- **Medicaid plans may seek additional funding via CHIP, per diem rates, or modified FFS rates**
- **Vepoloxamer expected to meet criteria for additional Medicare payment (NTAP)**

Source: ADVI analysis, 2015

# Commercial Potential Outside the U.S.

- **Over 10 million patients worldwide**

- **Europe**
  - Approximately 40,000 patients
  - >50% reside in two countries: UK and France
  - Most patients concentrated in large metro areas: Paris and London

- **MENA**
  - Over 850,000 with SCD
  - Many treatment centers provide care on par with standard of the U.S. and E.U.

Sources: Hassell KL. Population estimates of sickle cell disease in the U.S. *Am J Prev Med* 2010;38(4 Suppl):S512-21; Data on file, Mast Therapeutics 2015; VOI Consulting analysis, 2015

# Vepoloxamer Positioned for Success in SCD

- **Novel therapy for a genetic disease with high unmet needs**
  - Unique and relevant mechanism of action
  - No approved disease-modifying therapies available for VOC intervention
- **Significant first-to-market advantage in multiple territories**
  - Clinical development >2 years ahead of other SCD programs
  - Orphan Drug Designation in U.S. and E.U.
- **Concentrated market**
  - Top 500 U.S. hospitals treat nearly 80% of SCD patients in crisis
  - 96% of SCD patients in the U.S. have insurance coverage
- **Research supports rapid adoption & significant market penetration**
  - Ranked 4.4 out of 5 as a "breakthrough medical innovation" by pharmacy directors at key SCD institutions
  - KOLs and community physicians express high intent to use

# Development of Vepoloxamer in Heart Failure

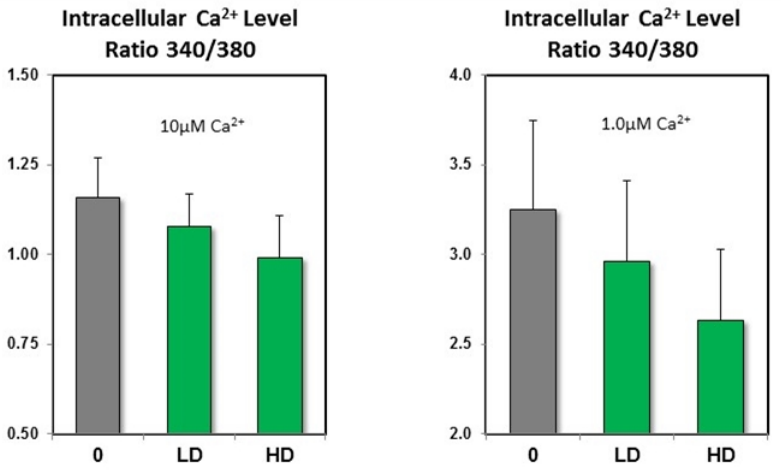
## Objective: Restore Membrane Integrity To Improve Cardiac Performance

## Phase 2 Study - Enrolling

# Development Rationale in Heart Failure

- **Elevated wall tension in a dilated (e.g. failing) heart impairs normal membrane repair activity**
- **Permeabilized membranes allow *unregulated calcium influx* and cardiac troponin leak**

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



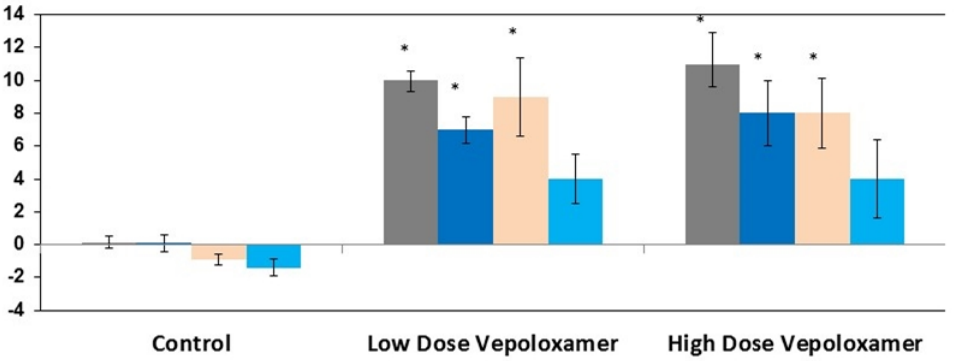

LD = 1.5 mg/mL vepoloxamer
HD = 4.5 mg/mL vepoloxamer

# Heart Failure Model Results

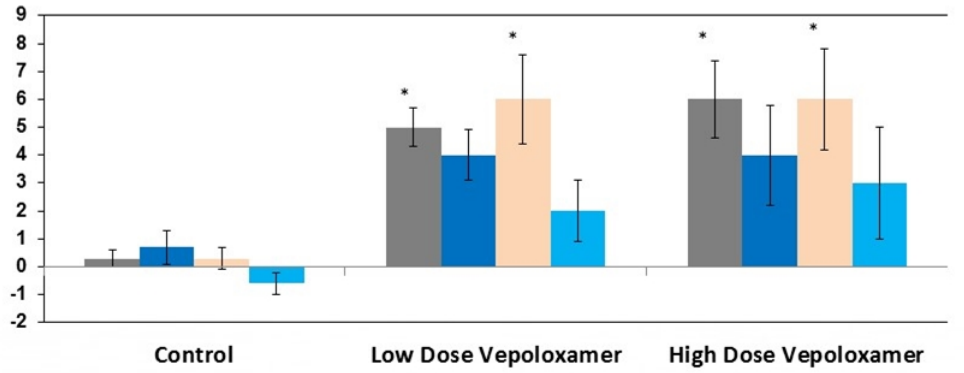
- **Functional improvement (single administration)**
  - Vepoloxamer elicited improvements in Left Ventricle (LV) systolic and diastolic function that persisted for up to 2 weeks
  - Ejection fraction (EF) and stroke volume (SV) increased
- **Biomarkers (single administration)**
  - Functional improvements supported by significant reductions of NT-pro BNP fo up to 2 weeks
  - Membrane sealing supported by significant reductions in plasma troponin for up to 2 weeks
  - Data suggests vepoloxamer can preserve cardiomyocytes by limiting calcium entry into the cell
- **Results support clinical development of vepoloxamer for the treatment of acute and chronic heart failure**

# Heart Failure Model – Functional Improvement (sing administration)

**Δ LV Ejection Fraction (%)**




**Δ Stroke Volume (mL)**




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

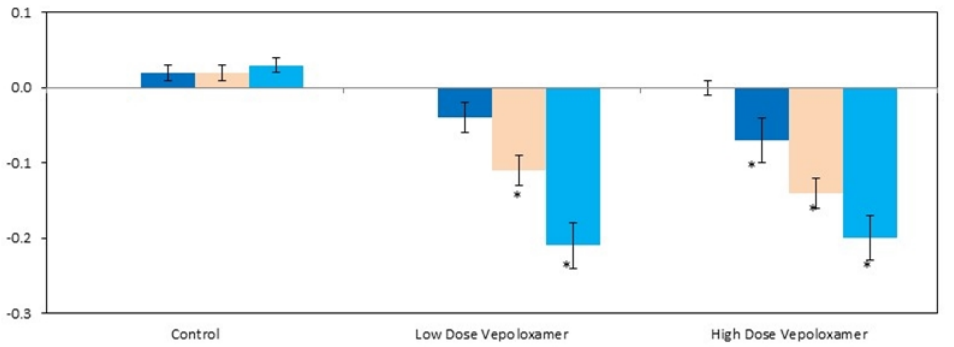
* $p < 0.05$ vs. Control

- Vepoloxamer elicited improvements in LV systolic and diastolic function that lasted for up to 2 weeks

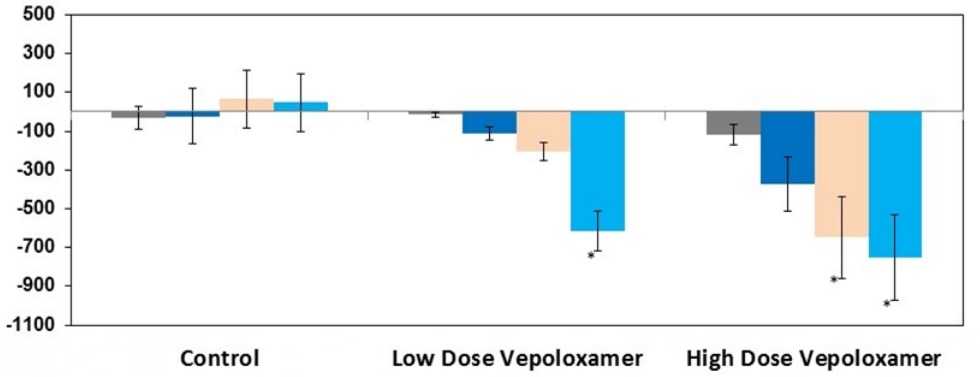
Study conducted by: Hani N. Sabba
Henry Ford Health System

# Heart Failure Model – Biomarkers (single administration)

**Δ Plasma Troponin-I (ng/mL)**




**Δ nt-pro BNP (pg/mL)**




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

* p < 0.05 vs. Control

- Troponin data suggests vepoloxamer can preserve cardiomyocyte by limiting calcium entr into the cell.
- Functional improvemer supported by significan reductions of NT-proBN for up to 2 weeks.

Study conducted by: Hani N. Sabba
Henry Ford Health System



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# Heart Failure Phase 2 Study

- **Randomized, double-blind, placebo-controlled, multi-center Phase 2 study in chronic heart failure**

- **N=150 patients, single 3-hour administration of vepoloxamer**

- **Efficacy assessments:**
  - Cardiac function
  - Biomarkers
  - Exercise tolerance

- **Patient enrollment ongoing**
  - First patient dosed January 2016

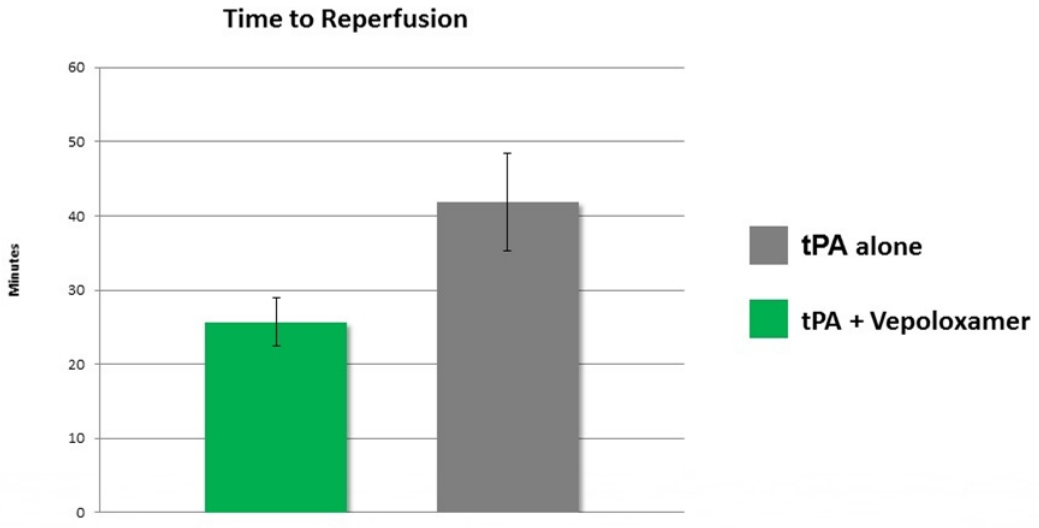
# Development of Vepoloxamer in Ischemic Strok

## Objective: Accelerate reperfusion and reduce reperfusion injury

## Phase 2-Ready

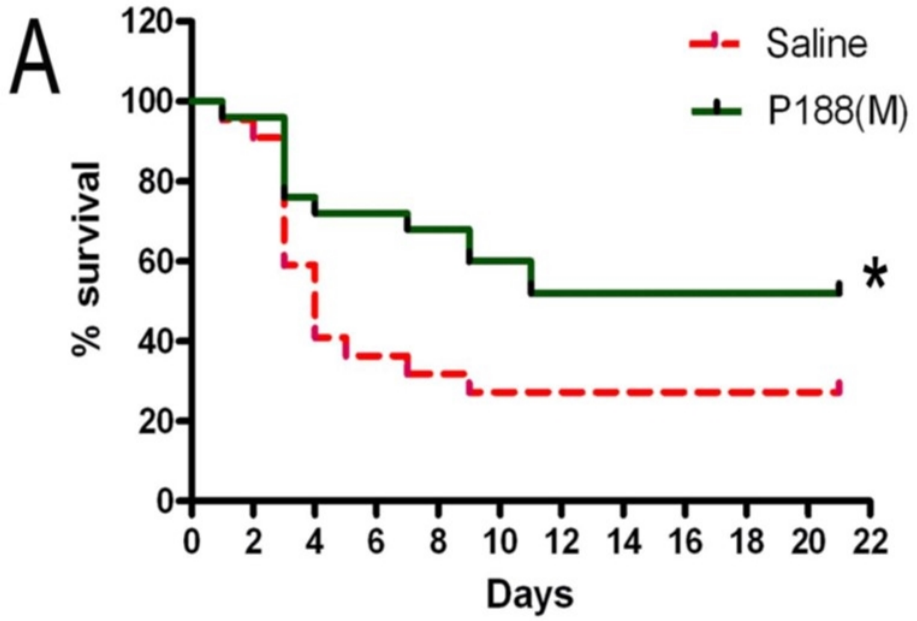
# Vepoloxamer in Ischemic Stroke

- **In stroke, restoring blood flow is critical ("time is tissue")**
  - Vepoloxamer has improved blood flow as a stand-alone agent
  - In combination with a thrombolytic, vepoloxamer has shortened time to thrombolysis by up to 40%
  - Seals and protects ischemia-injured tissue
    - Neuronal tissue
    - Blood brain barrier integrity



# Vepoloxamer Alone or with tPA Improved Outcomes in Experimental Stroke Models

- **Two hour occlusion of MCA with silicon coated nylon suture**
- **Only 27% of control mice survived vs. 52% of mice treated with poloxamer 188* (n=51)**



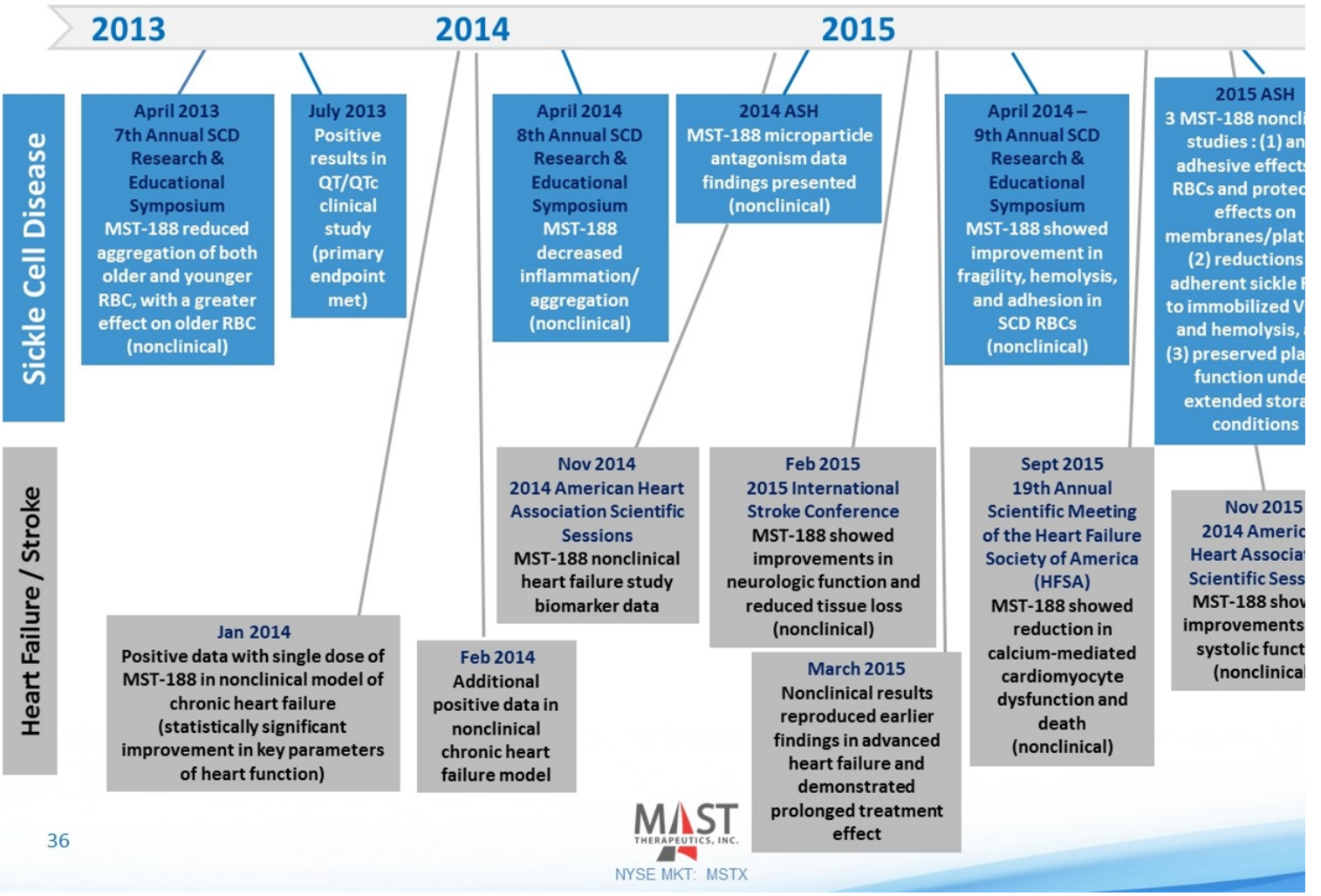

PLOS ONE 2013 (8) 4: e61641
* Vepoloxamer is purified poloxamer 188

# SBIR Grant-Funded Research

- **SBIR grant awarded by NIH in August 2016**

- **Phase 1 nonclinical study**
  - Evaluate the effect of a combination treatment with vepoloxamer and tissue plasminogen activator (tPA) on infarct volume and functional outcome in a nonclinical model of embolic stroke

# Key Data Generated by Mast Following Acquisition o Vepoloxamer



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# Vepoloxamer Market Exclusivity

| Form of Protection | Indication | Status |
|---|---|---|
| Orphan Drug Designation (Market Exclusivity) | SCD | Granted (US/EU) |
| Patents – Composition of matter | SCD, HF, IS | US 9,403,941 (to 2035), also pending w/w |
| Patents – New formulation | HF | Filed, pending w/w |
| Patents – Methods of use | SCD, HF, IS | Filed, pending w/w |
| Data Exclusivity | SCD, HF, IS | Eligible (US/EU) |
| Trade Secret & Know-How | SCD, HF, IS | Varies |

SCD = sickle cell disease
HF = heart failure
IS = ischemic stroke

# Development of AIR001 in Heart Failure

## Objective: Improve exercise tolerance and hemodynamics in HFpEF patients

## Multiple Phase 2 Studies

# AIR001 Overview

- **AIR001 is nitrite* for intermittent inhalation**
  - Delivered via proprietary handheld nebulizer
  - Activity includes dilation of blood vessels and reduced inflammation
    - Not limited to role as nitric oxide donor as nitrite has direct mitochondrial oxygen-sparing activity
  - Hemodynamic benefits include reductions in:
    - Pulmonary capillary wedge pressure
    - Right atrial pressure
    - Mean pulmonary arterial pressure
  - Safety data available in approximately 140 subjects (well-tolerated)

* Note: Nitrite is a different molecule and has separate activity compared to organonitrates or nitric oxide.

# AIR001 Clinical Data

- **Three Phase 1 studies**
  - Established Maximum Tolerated Dose (MTD)
  - Acute improvements in hypoxia-induced pulmonary hypertension
  - No drug-drug interaction with sildenafil
- **Phase 2a study in PAH (n=29)**
  - Well-tolerated; no treatment-related serious adverse events
  - Improvements seen in median pulmonary vascular resistance (PVR) and median distances in 6-minute walk test
  - Methemoglobin levels remained normal (<1.5%)
- **Phase 2a study in HFpEF (n=30)**
  - Met primary endpoint; statistically significant decrease in pulmonary capillary wedge pressure during exercise compared to placebo
  - Well-tolerated; no treatment-related serious adverse events

# AIR001 Clinical Development Plan

- **Heart Failure with Preserved Ejection Fraction (HFpEF)**
  - Responsible for ~50% of heart failure hospitalizations
  - No approved medications

- **Supporting ongoing institutional-sponsored Phase 2a study**
  - Evaluating hemodynamic effects
  - Reported positive interim data in May 2016

- **AIR001 recently selected by the Heart Failure Clinical Research Network fo Phase 2 study in HFpEF**
  - n=100
  - Multicenter, randomized, double-blind, placebo-controlled
  - First patient enrolled July 2016

# MSTX Financial Overview

- **Cash/investments at 6/30/2016: $35.1 million**
- **Principal debt balance: $13.7 million***
  - $10 million prepayment on 10/14/16 if EPIC data not positive or not announced
- **Market capitalization: ~$120 million***
- **Average daily volume (3 mo.): ~ 3.4 million***



* As of September 2, 2

# Management Team and Board of Directors

## Management Team

| | |
|---|---|
| Brian Culley, CEO | Neurocrine, UC San Diego, The Scripps Research Inst. |
| Ed Parsley, CMO | Aires, Pfizer, CSL, Encysive, U. Texas Medical |
| Brandi Roberts, CFO | Alphatec, Artes, Stratagene, Pfizer, PwC |
| Martin Emanuele, SVP Development | DaVita, SynthRx, Kemia, Avanir, DuPont |
| Greg Gorgas, SVP Commercial | Theragence, Biogen Idec, Chiron, Cetus, Upjohn Co. |
| Mark Longer, VP Regulatory | AstraZeneca, Amylin, Pfizer |

## Board of Directors

| | |
|---|---|
| Matthew Pauls, CEO | StrongBridge Biopharma |
| Peter Greenleaf, CEO | Sucampo Pharmaceuticals |
| Brian Culley, CEO | Mast Therapeutics |
| Howard Dittrich, EIR, CMO | Frazier Healthcare Partners |
| David Ramsay, CFO (ret.) | Halozyme |

# Key Takeaways and Investment Highlights

1. **Mast is the leader in sickle cell disease**
   - Potential first-in-class therapy for an orphan disease with high unmet need
   - Enrollment completed in pivotal Phase 3; top-line data expected September
   - More than 2 years ahead of nearest competitor
   - Extensive patient-focused activity:
     - Created the leading SCD app, VOICE Crisis Alert (>3000 downloads)
     - Created the (5th Annual) SCD Drug Development Conference
     - Sponsor and volunteer at charity events, SCD radio show, etc.

2. **Vepoloxamer has potential in other serious vascular diseases, including heart failure and stroke**

3. **Encouraging clinical data generated from AIR001 for heart failure**
   - Met primary endpoint in 30-patient randomized blinded trial
   - Selected by HFN as subject of 100-patient Phase 2 study in HFpEF


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